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THINKING ETHICALLY ABOUT HIV PRE-EXPOSURE PROPHYLAXIS: RETENTION IN CARE AND SEXUALLY TRANSMITTED INFECTION TESTING IN A SOUTHEASTERN UNITED STATES LOCAL HEALTH DEPARTMENT IN THE TIME OF COVID-19

by

ELLIE PURDY

(Under the Direction of William A. Mase)

ABSTRACT

Local Health Departments (LHDs) are critical providers of Human Immunodeficiency Virus (HIV) and sexually transmitted infection (STI) prevention efforts. HIV Pre-Exposure Prophylaxis (PrEP) is an evolving public health initiative and practitioners should consider PrEP interventions in context of ethical decision-making and a broad STI prevention strategy as global incidence of bacterial STIs remains high and those at-risk for HIV are generally at-risk for other STIs. An evaluation of the Thinking Ethically framework and LHD PrEP services was performed to fill a gap in the literature and support program decision-making. A retrospective review of PrEP user medical records from a LHD in north Georgia from July 2019 to June 2020 was performed and data were assessed using descriptive statistics, negative binomial, and logistic regression. Total STI tests performed by the LHD from July 2018 to June 2020 were calculated to determine the change in STI testing services associated with the onset of the COVID-19 pandemic. The Thinking Ethically framework was valuable to PrEP-related decision-making. There were 63 PrEP users in the study period of which most were White non-Hispanic (60.3%) men who have sex with men (61.9%). Retention in care was associated with clinic site. Most bacterial STI cases diagnosed among PrEP users were asymptomatic (75%). Fifty percent of PrEP users obtained services beyond STI prevention including vaccination and referrals. District STI testing declined between the second quarter of 2020 and 2019 with a decline in HIV testing by 38%, syphilis by 48%, gonorrhea and chlamydia by over 50%. LHD decision-makers can feasibly apply the Thinking Ethically framework to public health practice. Results support the need for LHD continuous quality management as retention in

care differed by clinic site, and more resources will be needed to engage hard-to-reach populations at-risk for HIV like injection drug users. The COVID-19 pandemic impacted PrEP and STI services and more data is needed to determine the long-term effects of the COVID-19 pandemic on the STI landscape.

INDEX WORDS: Human Immunodeficiency Virus, Sexually transmitted infection, Prevention, Pre-Exposure Prophylaxis, Local health department, Southeast United States, Thinking Ethically, COVID-19

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DOCTOR OF PUBLIC HEALTH

JIANN-PING HSU COLLEGE OF PUBLIC HEALTH

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Electronic Version Approved:
May 2021

ACKNOWLEDGMENTS

I am very fortunate to have many mentors and much support. I sincerely thank Bill Mase, DrPH for his wisdom and guidance through the dissertation process. Linda Kimsey, PhD for her valuable critique and encouragement. Stacy Smallwood, PhD for his thoughtful input and advice. Mario Keko for his wonderful teaching, kindness, and patience. Zach Taylor, MD; Mark Elam, MD; Sherry Gregory, RN; Jeff Vollman, MPA; Christine Miller, RN; Aimee Dickson, RN; Pam Baker, Maria Rivera and the North Georgia Health District for their overwhelming support and encouragement. Debbie Hagins, MD; Gillian Greer, MD; and the CARE Center for their compassion and willingness to teach. Deb Dumphy, DNP, APRN and Vanessa Jones, DNP, APRN for encouraging me to pursue a doctorate in public health.

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CHAPTER 1

BACKGROUND

Statement of the Problem

Local Health Departments (LHDs) are critical providers of population-level Human Immunodeficiency Virus (HIV) and sexually transmitted infection (STI) prevention efforts and can significantly impact provision and access to HIV Pre-exposure Prophylaxis (PrEP) services.[1] PrEP is the administration of antiretroviral therapy (ART) combined with behavioral counseling for primary prevention of HIV.[1,2] Public health practitioners should consider multiple ethical principles to maximize PrEP and STI prevention resources for the greatest population-level benefit in the context of a broad STI prevention strategy.[3,4] Practitioners can elicit consideration of multiple ethical principles with use of the Thinking Ethically decision-making framework when deliberating decisions of ethical consequence[5] like whether to provide PrEP services or how best to optimize limited resources. PrEP is an evolving public health initiative and public health practitioners should weigh factors including biomedical risks, access disparities, and risk behavior with available resources when implementing PrEP interventions.[3,4] However, limited data on LHD PrEP provision, program impact, and program evaluation is available to guide decision-makers.[6] Data evaluating LHD PrEP intervention outcomes in suburban and rural LHDs in the Southeast US, an area with significant STI and HIV disease burden, is a current gap in the literature.

HIV incidence in 2018 was 11.4 per 100,000 population (about 40,000 cases per year) in the United States (US) and disparities in incidence exist.[2,7] Total HIV incidence in the US declined from 2008 to 2018, but incidence has remained steady or increased among racial minorities including Black and Latino men who have sex with men (MSM).[2,7] PrEP has demonstrated tolerability and effectiveness as HIV prevention when administered as directed with up to 99% efficacy against sexual transmission of HIV in at-risk groups.[2,8] Medications used for PrEP are generally well-tolerated and adverse events have included gastrointestinal discomfort, nausea,

decrease in bone mineral density and renal function, hepatitis B flare, and HIV viral resistance.[2] Benefits of PrEP have included reduced fear of HIV and feelings of empowerment surrounding sexual health among PrEP users.[9]

Public health practitioners should consider PrEP interventions in context of a broad STI prevention strategy as global incidence of bacterial STIs (gonorrhea, chlamydia, syphilis) remains high, and those at-risk for HIV are generally at-risk for other STIs.[10,11] STI resistance is increasing, and complications of STIs can include pain, infertility, neurological and cardiovascular disease.[10,11] STI prevention strategies should consider behavioral and pathogen-specific factors including social networks, prevention fatigue, condom use, and probability of transmission as bacterial STI infection can increase the risk of HIV acquisition.[12] Data associating PrEP use with increased risk behavior has been mixed and increased STI incidence among PrEP cohorts may be attributed to preexisting increases in STI trends, selection bias, or increased screening which can facilitate timely diagnosis and treatment.[10,11]

Public health practitioners must allocate finite resources with consideration to available resources, cost, risk, and populations most at-risk for HIV.[13,14] LHDs at the forefront of the COVID-19 pandemic response (ongoing at the time of this writing) must also allocate resources to support existing programs in addition to COVID-19 testing, syndromic surveillance, contact tracing, and vaccination campaigns. US PrEP-to-need analysis of 2017 fourth-quarter data was remarkable for disparities between those most at-risk and those receiving PrEP as those at-risk living in the South and non-Medicaid expansion states were less likely to receive PrEP relative to need.[15] PrEP can be efficient and cost-saving if those most at-risk are prioritized, but allocating resources for PrEP should be weighed against the impact of enhancing HIV treatment efforts and the burden of HIV in the target area.[13,14] HIV viral control among people living with HIV (PLWH) through use of ART is considerably effective at reducing the spread of HIV.[2] Clinical capacity can impact the feasibility of proving PrEP as providing condoms requires less clinical capacity than

oral PrEP, and oral PrEP is expected to require less clinical capacity than future injectable Long-Acting PrEP (LA PrEP).[16] Provider uptake and provision of oral PrEP has been generally slow due to multiple factors including knowledge, awareness, and stigma.[17] High attrition with PrEP use has also been appreciated.[18]

Purpose of the Study

The purpose of this study was to perform a program evaluation of LHD PrEP services in the North Georgia Health District (NGHD) between July 2019 and June 2020. Outcomes included PrEP user demographics; length of time users are enrolled in the program; diagnosis of HIV, gonorrhea, chlamydia, syphilis among PrEP users; and description of services provided to PrEP users beyond STI prevention. The study was framed through the Thinking Ethically framework to guide future LHD STI prevention efforts and PrEP-related decision-making.

This study also provided a unique opportunity to study LHD PrEP services and STI testing over the period that included the onset of the COVID-19 pandemic. The COVID-19 pandemic impacted NGHD clinical services during the study period, but this study was not planned to investigate the impact of COVID-19 on LHD PrEP and STI care. To encourage social distancing, the NGHD reduced PrEP and STI services and ceased nonessential in-person encounters for all programs in the second quarter of 2020. Quarterly total of HIV, gonorrhea, chlamydia, and syphilis tests performed in NGHD clinic sites from July 2017 to June 2020 were assessed to quantify the degree of NGHD STI service changes associated with the onset of the COVID-19 pandemic. Assessing total number of performed STI tests from July 2017 to June 2020 served to provide NGHD leadership with baseline data to determine when district STI services return to pre-pandemic quantity.

Research Questions

1. How can the Thinking Ethically framework be used to inform public health practitioners on PrEP-related decision-making?

2. Did NGHD PrEP services reach those most at-risk for HIV in the district?
3. How long did PrEP users stay in the program?
4. What additional services were provided to PrEP users beyond STI prevention?
5. How many asymptomatic bacterial STIs were diagnosed among PrEP users?
6. How much did NGHD STI testing change in the period associated with the onset of the COVID-19 pandemic?

Delimitations

The study was conducted via a retrospective chart review of NGHD PrEP users between July 2019 and June 2020, the first year NGHD district-wide PrEP services were provided. Only those receiving PrEP from the NGHD were included in the study. Those living within the NGHD but receiving PrEP from providers unaffiliated with the NGHD were excluded. Only those with STIs diagnosed by NGHD study sites were included in STI assessments. Those living within the NGHD but diagnosed with STIs by providers unaffiliated with the NGHD were excluded.

Definition of Terms

Antiretroviral Therapy (ART) – medication active against HIV used as prevention among those at-risk and treatment among those living with HIV

HIV Pre-Exposure Prophylaxis (PrEP) – prescribed antiretrovirals for primary prevention of HIV

LHD – Local Health Department

MSM – Men who have sex with men including gay, bisexual, and other men who have sex with men

North Georgia Health District (NGHD) – a local health district in north Georgia in the southeastern United States and site of data collection for this study

PLWH – People living with HIV

PWID – People who use injection drugs

Risk Compensation – increase in behavior that increases risk of STI acquisition due to perceived protection from HIV due to PrEP use

Sexually Transmitted Infection (STI) – for purpose of this study, STI generally refers to HIV, gonorrhea, chlamydia, and syphilis

Treatment as Prevention (TasP) – prescribed antiretrovirals for people living with HIV to effectively prevent HIV transmission through individual and population-level HIV viral suppression

CHAPTER 2

LITERATURE REVIEW

Thinking Ethically about HIV

Public health decision-making is complex, and practitioners must consider conflicting values and ethical considerations when making decisions at the population level.[3,19] The field of public health ethics emerged in the 1990s in response to population-level ethical concerns that could not be adequately addressed through bioethical principles during the HIV epidemic.[19,20] Bioethical principles of autonomy, beneficence, nonmaleficence, and justice are largely focused on the individual and often used in research and clinical medicine but have been inadequate to fully address community concerns of individual versus community rights, health promotion, and resource allocation.[19,20] Public health ethics must balance the values of individuals with community well-being, recognizing that what is in the best interest of the individual is not always in the best interest of the community.[19]

The HIV epidemic in the 1990s had a profound impact on public health ethics as medical providers, policymakers, and public health professionals confronted significant ethical questions regarding individual versus community rights, allocation of resources, access to care, individual privacy, and presence of social health disparities.[20] Decision-makers were forced to confront social issues like discrimination, fear and stigma, and balance individual liberty, dignity and health for those most affected.[20] Medical advances surrounding HIV and antiretroviral therapy (ART) have significantly altered the contemporary public health HIV decision-making landscape, but ethical dilemmas still exist.[3] Public health practitioners must determine how to allocate finite resources to benefit the most people while striving to reduce health disparities as HIV often impacts vulnerable and socially disenfranchised groups.[3]

In 2012, the World Health Organization (WHO) held a multidisciplinary assembly of international stakeholders including scientists, ethicists, policy-makers, human rights and HIV

community advocates to discuss the ethical considerations of ART use in HIV prevention.[3] ART use in HIV prevention can be prescribed for people living with HIV (PLWH) as Treatment as Prevention (TasP) or those of negative HIV status as Pre-Exposure Prophylaxis (PrEP); TasP and PrEP are both effective prevention strategies.[3] The assembly discussed that public health practitioners will need to use multiple, and potentially conflicting, ethical principles in ART-related decision-making, and more attention should be provided to social and policy barriers impacting HIV.[3] Decisions will widely vary based on community-level epidemiology, available resources, and sociopolitical climates as those most at-risk for HIV and sexually transmitted infections (STIs) are often disenfranchised and face barriers related to the social determinants of health.[3] Principles used in HIV-related decision-making can include utility (prioritizing interventions with the greatest net benefit), equity (prioritizing interventions that reduce health disparities), urgent need (prioritizing treatment of the sickest), rule of rescue (prioritizing treatment for those at imminent risk of death), and prioritarianism (prioritizing the least advantaged).[3]

In the context of HIV, use of ethical principles in decision-making can yield different results depending on the frame of reference.[3] An intervention chosen using the utility principle can be perceived to produce the most benefit if it prioritizes PLWH or those of HIV negative status and if it benefits the largest number of people or those most at-risk, but a strict utility focus on benefiting the greatest number of people can also result in health disparities.[3] Decisions made using the equity principle are reasonable in principle as it is generally agreed that people should have fair access to health resources although equity is difficult to achieve in practice due to real-world resource limitations.[3] Furthermore, equity priorities can conflict between prioritizing health status or health access.[3] Principles like urgent need, rule of rescue, and prioritarianism generally prioritize those of worst health status which conflict with the principle of utility because prioritizing those most affected can result in fewer resources available for the greater population.[3] It can also be difficult to determine those of worst health or highest-risk in context of HIV because HIV burden is

closely intertwined with social determinants of health.[3] Highest-risk can be interpreted as most at-risk of death from HIV, most at-risk of acquiring HIV, and most vulnerable from low socioeconomic status.[3]

HIV-related public health decision-making should generally seek to identify local priorities to guide fair distribution of resources, maximize population-level benefit, and base program decisions on data-supported evidence.[3] Optimal solutions will vary and must acknowledge social and political limitations including stigma, discrimination, and illegal nature of some HIV-associated risk factors (like injection drug use or sex work).[3] HIV prevention should also be considered in context of a comprehensive STI prevention strategy due to significant disease burden, increasing STI incidence, shared prevention strategies and shared risk factors between HIV and non-HIV STIs.[10,11,21]

Thinking Ethically is a framework created by Velasquez et al[5] at the Markkula Center for Applied Ethics as a method to identify ethical considerations and apply ethical decision-making to practice.[5] The framework was chosen for its design as an applied framework, stepwise approach to ethical decision-making, and use of multiple ethical principles which is in accordance with the WHO recommendation to assess PrEP and HIV prevention from multiple ethical perspectives.[3,5] The framework provides a series of steps to gather data and evaluate available options from multiple ethical approaches to achieve the best course of action.[5] After recognizing an ethical issue, practitioners should gather relevant data about the issue including relevant stakeholders and options for acting.[5] Practitioners should then evaluate each option through the perspective of five different ethical approaches, the utilitarian, rights, justice, common good, and virtue approach.[5]

The utilitarian approach emphasizes the action that provides the most benefit and least harm to all those affected by an action.[5] The rights approach emphasizes the moral rights of individuals which are numerous and have included autonomy, dignity, truth, privacy, and to not be injured.[5] The justice approach emphasizes fairness and equal treatment of those affected by an

action.[5] The common good approach emphasizes community welfare and prioritizes the community benefit of an action with attention to those most vulnerable and is suited to evaluate policy and public health.[5] The virtue approach emphasizes actions that align with virtuous character traits like honesty, courage, tolerance, compassion, integrity, prudence and self-control.[5] Velasquez et al[5] provided a series of questions intended to elicit the perspective of each approach:

- Which option will produce the most good and do the least harm? (The utilitarian approach)
- Which option best respects the rights of all who have a stake? (The rights approach)
- Which option treats people equally or proportionately? (The justice approach)
- Which option best serves the community as a whole, not just some members? (The common good approach)
- Which option leads me to act as the sort of person I want to be? (The virtue approach)[5]

After working through each question, practitioners should then consider all approaches, reflect on or hypothetically test the decision, implement the decision, and reflect upon the decision outcome.[5] Velasquez et al[5] discussed that ethics is a way people should act and is not a science, religion, law, cultural norm, or set of feelings.[5] There is significant room for debate in ethical decision-making, but the best action is often identified as ideal through multiple ethical approaches.[5] Thinking Ethically principles (justice, utility, rights, common good, and virtue) were used to frame the research questions of this study.

STI and HIV Disease Burden

There are over 30 different pathogens known to be sexually transmitted.[22] STIs have a substantial worldwide disease burden and STI incidence has been increasing.[11,21,23] The WHO has estimated that global STI acquisition is over one million cases per day with an annual incidence of over 350 million cases per year of one of the four common curable STIs (chlamydia, gonorrhea, syphilis or trichomoniasis).[11,22] STI public health practice considerations include newly recognized

STIs (Zika, hepatitis, Ebola virus), drug resistance (resistant gonorrhea), risk behavior (recreational drug use, risk compensation associated with antiretroviral success), commercial sex and sexual violence.[21] Generally, bacteria and parasite STIs cause acute symptoms while viral STIs cause chronic infections.[21] STI complications can include infertility, pain, neurological and cardiovascular complications (syphilis), cancer (human papillomavirus), liver disease (hepatitis A and B), and death (HIV).[11,21,23] Common curable STIs (chlamydia, gonorrhea, and syphilis) are often asymptomatic leading to delayed screening, diagnosis and treatment.[21–23] STI related tissue impairment also increases risk of HIV acquisition.[11,21–23]

Those most at-risk for STIs and HIV in the US include those living in southern states, youth, MSM, racial minorities and those of low socioeconomic status.[7,23] US STI incidence has been increasing, and youth age 15 to 24 years accounted for about half of STI diagnosis in 2018.[23] From 2017 to 2018, chlamydia, gonorrhea and syphilis incidence increased among males and females of all ethnic groups in all regions of the US.[23] In 2018, chlamydia was the most reported notifiable infectious disease with a disease burden of 539.3 cases per 100,000 population, a 2.9% increase from 2017.[23] Gonorrhea was the second most reported notifiable infectious disease with a 5% increase from 2017. Syphilis incidence was 115,045, the highest since 1991 and a 13.3% increase from 2017.[23] In 2018, primary and secondary (P&S) syphilis were predominantly identified among MSM (53.5%), PLWH (41.6%), and women (14.2%).[23] Women are an emerging risk-group for syphilis; from 2017 to 2018, a 30.4% increase in P&S syphilis incidence was appreciated among women which is concerning for maternal transmission and congenital syphilis.[23] In 2018, incidence of chlamydia and gonorrhea was highest among US states in the South, and incidence of syphilis was highest among states in the West followed by states in the South.[23]

Global HIV mortality and morbidity have made significant advances since the 1990s.[24] Global HIV mortality peaked in 2004-2005 with over two million deaths worldwide and declined to 1.1 million deaths in 2015.[24] HIV incidence peaked in 1997 with an estimated 3.5 million infections per year and declined to 2.1 million in 2015.[24] Global HIV prevalence has also declined

since 2001, and study of prevalence must take into account that PLWH are now living longer due to advances in ART efficacy, tolerability, and access.[24]

The impact of advances in ART efficacy, tolerability, and access on global HIV mortality and incidence are considered significant public health successes.[24,25] Trends in life expectancy of PLWH have increased in all parts of the globe although disparities in access to HIV testing and treatment still exist and high-income countries have appreciated the most gain.[25] In 2012, the life expectancy of PLWH in Canada was about 90% of those of negative HIV status while the life expectancy of PLWH in Rwanda was about 60% of those of negative HIV status.[24,25] In Canada, the life expectancy of a 20-year-old living with HIV compared to those of negative HIV status increased from 50.7% in 2000-2003 to 89.1% in 2008-2012.[25] PLWH who continue ART and maintain HIV viral suppression also have virtually no risk of transmitting HIV to others (Treatment as Prevention).[26] The current Joint United Nations Programme on HIV/AIDS (UNAIDS) global ending HIV epidemic campaign, 90-90-90, targets for 90% of PLWH to know their status, 90% of those to receive sustained ART, and 90% of those to achieve sustained HIV viral suppression.[24] The current US Department of Health and Human Services (HHS) ending the HIV epidemic campaign, Ending the HIV Epidemic: A Plan for America, targets a 75% reduction in new HIV infections by 2025 and 90% reduction by 2030 through sustained HIV viral suppression among 90% of PLWH in the US and prevention strategies including PrEP and syringe services programs for people who use injection drugs (PWID).[27]

In the US, PLWH are generally older while populations most at-risk for new diagnosis include youth, MSM, PWID, racial minorities, those of low socioeconomic status and in southern states.[7] In 2017, there were 1,003,782 known PLWH in the US with a prevalence rate of 308.7.[7] Those aged 50-54 (767.8) were the largest group of PLWH followed by 55-59 (660.6).[7] Rates of new HIV diagnoses have generally declined since 2013 however disparities among at-risk groups exist and incidence has increased among some sub-populations.[2,7] In 2018, the age group with the

highest HIV incidence was among those 25 to 29 years (32.5) followed by 20-24 years (27.6).[7] HIV incidence by race was highest among Black/African American (39.3) followed by Hispanic/Latino (16.2).[7] In 2018, males accounted for 81% of diagnoses and the most significant risk factors were MSM (70%) followed by PWID.[7] South US states continued to have the highest incidence (15.7) compared to the Northeast (10.0), West (9.3), and Midwest (7.2).[7]

In 2017, Georgia ranked first among US states in HIV incidence among adults and adolescents and fourth in HIV prevalence.[28] At-risk groups for HIV in Georgia mirror those of the US with Black/Non-Hispanic, youth and MSM at highest risk.[28] The North Georgia Health District (NGHD), a largely suburban and rural area, includes two counties identified among the 220 most vulnerable counties in the US for rapid transmission of HIV and hepatitis C due to injection drug use in a 2016 assessment by the Centers for Disease Control and Prevention (CDC).[29,30] In 2017, NGHD youth had the highest incidence of HIV and PLWH were generally older, which is consistent with the state and national profile, but racial and ethnic group HIV incidence and prevalence differed from the state and national data as most PLWH in the NGHD were White/Non-Hispanic.[28] In 2017, NGHD HIV incidence was largest among White/Non-Hispanic (50%) followed by Hispanic (21.4%), and Black/Non-Hispanic (17.9%) with the largest number of new diagnosis occurring among youth age 20-29 (39.3%).[28] In 2017, PLWH in the NGHD were largely White/Non-Hispanic (57.2%) followed by Black/Non-Hispanic (19.4%) and Hispanic (15.7%), and predominantly adults age 30-39 (18.9%), 40-49 (24.8%), and 50-59 (29.2%).[28]

Structural Factors Associated with STI Risk

The HIV and STI epidemic is well-established as interwoven with social determinants of health: genetic and individual factors alone cannot account for the significant discrepancy in HIV and STI risk among low income and minority populations.[31,32] Multiple studies assessing HIV and syndemic risk (accumulated risk of two or more factors that work synergistically) with intersecting negative social, behavioral, and structural factors have been performed.[33] Those most at-risk for STIs (youth, racial and ethnic minorities, people of low socioeconomic status, MSM, and PWID)

often face multiple syndemic risk factors, and global and national prevention efforts have emphasized the importance of targeting social determinants of health in HIV prevention since the 1990s.[31–34] Syndemic HIV and STI risk factors have included social instability, homelessness, unemployment, low education level, poverty, stigma, discrimination, trauma, incarceration, drug use, geographic location and limited healthcare access.[31,33,34]

A cross-sectional and longitudinal analysis comparing gonorrhea incidence to socioeconomic status by decennial census tract (1990 and 2000) in New York state (excluding New York City) between 1992-1993 and 2001-2002 found geographic associations between areas of low socioeconomic status and gonorrhea incidence, and changes in gonorrhea incidence were associated with changes in socioeconomic status.[35] Study modeling demonstrated that a 5% increase in census tract poverty rate was associated with an 8% increase in gonorrhea incidence (relative risk 1.08).[35] Multivariate modeling of census tract, gonorrhea incidence, and race were remarkable for increased gonorrhea incidence disparities among non-Hispanic Blacks in areas where non-Hispanic Blacks were less than 10% of the population.[35] In areas with less than 10% non-Hispanic Blacks, a 5% change in poverty rate was associated with a 23% increase in gonorrhea incidence among Black residents compared to areas with over 10% non-Hispanic Blacks where a significant change in gonorrhea incidence was not appreciated.[35]

Minority populations in the US, like Black and Latinos, encounter disparities in virtually all social determinants of health including poverty, racism, trauma, incarceration, and substance use compared to Whites.[33] According to the 2010 US census, Blacks had the highest rate of poverty followed by Hispanics and Whites.[33] Blacks and Latinos have been more likely to experience individual and systematic racism compared to Whites including residential segregation, environmental health stress, community violence, criminal justice discrimination, and live in a resource-poor area.[33] MSM, bisexual, and transgender individuals have faced additional stress of

homophobia and gender-related stigma or abuse which increases the risk of depression and condomless sex.[33,36]

Systematic racism and stigma limit the social and political capital of minority communities and increase the risk of psychological conditions and sexual risk behavior that subsequently increase the risk of HIV, particularly among minority youth and transgender individuals.[33,36] Research on HIV risk, childhood and adolescent sexual abuse and trauma (a known risk factor for increased risk behavior and condomless sex) since the 1990s has demonstrated higher rates of sexual and physical abuse among Black and Hispanic MSM compared to Whites.[33] In 2003, US Blacks were more likely to be incarcerated (1 in 8) compared to Latinos (1 in 27) and Whites (1 in 63).[33] Racial and ethnic minorities have also been more likely to experience substance abuse disorders, initiate injection drug use in adolescence, experience addiction, relapse after substance use treatment, and receive less substance use treatment compared to Whites.[33]

Illicit Drug Use and STI Risk

Illicit drug use has been increasing in the US and is strongly associated with high-risk sexual behavior including multiple partners and condomless sex.[37] Opioids include drugs like prescription opioids, heroin, synthetic and illicitly manufactured opioids (like illicitly manufactured fentanyl).[37,38] In 2017, 67.8% of the 70,237 drug overdose deaths in the US were opioid-related and the number of synthetic opioid-related deaths in the US increased by 45.2% from 2016 to 2017.[38] A recent cross-sectional community-based survey study investigating the intersection between lifetime STI diagnosis, illicit drug and opioid use in Alachua County, Florida (a county with STI rates higher than the state and national average) found that 204 (9.3%) of 2,194 survey respondents age 18 to 50 years self-reported ever having an STI, of which, 74.2% reported any illicit drug use, 69.6% reported marijuana use, and 52.5% reported opioid use.[37] Those self-reporting an STI were also more likely to be female, food-insecure within the last 12 months, unmarried and with less education.[37]

STI prevention programs that include content on alcohol and illicit drug use have demonstrated greater efficacy compared to those without alcohol and illicit drug content.[39] A cluster randomized clinical trial comparing the impact of STI prevention programs with content on sexual risk reduction only; sexual risk reduction and alcohol; and sexual risk reduction, alcohol, and marijuana on STI incidence at 12-months after completion of the STI prevention program found the lowest STI incidence among those in the sexual risk reduction, alcohol and marijuana group.[39] The study included 460 adolescents at an adolescent detention center from 2010 to 2014, of which 361 presented for a 12-month follow-up.[39] At 12 month follow-up, 3.9% of the sexual risk reduction, alcohol and marijuana group; 10.2% of the sexual risk reduction and alcohol group; and 12.4% of the sexual risk reduction group were diagnosed with an STI of which chlamydia (79.6%) and gonorrhea (13.6%) were the most common.[39]

STI prevention efforts among drug users should be tailored to the population as differences in HIV risk behavior by gender and drug use have been appreciated although data on gender-based differences in number of partners, condomless sex, and sex exchange among drug users has been mixed.[40] A survey assessing gender-based HIV risk among 1,429 drug users in multisite drug treatment programs across the US in 2007 was remarkable for overall increased sexual behavior risk among women drug users compared to men.[40] Women were more likely to have multiple partners (20% versus 13%) and no gender difference in unprotected sex or sex exchange was appreciated.[40] Men were more likely to use injection drugs (32% versus 24%) and no gender difference in needle sharing was appreciated.[40] Women who used alcohol were 1.11 times more likely to have risky sex behavior compared to men.[40] Women who had greater psychiatric comorbidities were 1.14 times more likely to engage in risky sex behavior compared to men.[40] Participants (male and female) who used stimulant illicit drugs were 1.57 times more likely to engage in risky sex behavior than those who did not use stimulants.[40] Participants (male and

female) who reported history of sexual abuse were 4.1 times more likely to engage in risky sex behavior compared to those without history of sexual abuse.[40]

Crisis and STI Risk

The 2020 COVID-19 pandemic is a significant factor impacting data collected in this study as global social distancing drastically changed global economic and social behavior during this study period. It was assumed that STI incidence during the pandemic declined due to reduced screening (the study sites postponed or limited PrEP and STI care during the COVID-19 pandemic) or due to an actual reduction in incidence related to social distancing. The long-term effects of COVID-19 on mental health, economics, and STI incidence are not yet known, and this study provided a unique assessment of LHD STI incidence surrounding a global pandemic in the Southeast US. Previous data has supported increased STI incidence and STI-associated risk behavior surrounding periods of political, environmental, and socioeconomic crisis like the September 11, 2001 attack and the 2008 Financial Crisis.[41–44]

A retrospective chart review of 3,520 PrEP users from January and April 2020 in Boston, Massachusetts to assess the impact of COVID-19 on PrEP care found the number of clients initiating PrEP fell by 72% (from 122 per month in January to 34 per month in April 2020).[45] The number of PrEP prescription refill lapses increased (140 in January to 407 in April) with youth, racial minorities, and those with public versus private insurance more likely to have a lapse in PrEP refill.[45] Screening for gonorrhea and chlamydia also declined by 85% between January and April.[45] A separate internet survey of 1,051 MSM in the United States to investigate the impact of COVID-19 on sexual health in April 2020 found that 51.3% reported fewer sex partners during the COVID-19 pandemic, 47.6% reported no change in number of sex partners, and 0.9% reported increased number of sex partners, 92.9% reported no change in condom use, and 68% reported reduced opportunities to have sex.[46] When asked about adherence to local COVID-19 social distancing stay-at-home orders, 20.1% reported 100% adherence, 71.4% reported between 50% and 100%

adherence, and 8.5% reported less than 50% adherence. When asked about life impact, 19.1% reported losing their job, 72.7% reported increased anxiety, 14.8% reported being food insecure within the last 12 months, 9.9% reported increased use of recreational drugs, and 26% reported increased use of alcohol.[46]

A 2002 internet survey of 2,915 MSM investigating sex and drug behavior three months before and after the September 11 attack found that drinking until drunk, condomless anal sex, and number of partners increased among those who reported death of a family member or friend in the attack (n=329) compared to those reporting seeing the attack in person (n=104) or living within a 10 mile radius of the World Trade Center or Pentagon (n=35).[41] Participants reported similar levels of drinking until drunk, condomless sex, and number of partners before the attack.[41] After the attack, the adjusted odds ratio of drinking until drunk, increased condomless sex, and increased number of partners among those reporting a death was 1.41, 1.44, and 1.94; witnessing the attack in person was 1.04, 1.14, and 0.74; and living within 10 miles of the attack site was 0.87, 0.73, and 1.72 respectively.[41]

A survey of Manhattan residents in New York found that cigarette, alcohol and marijuana use were increased at one (n=988) and six months (n=854) after the September 11 attack.[42] At six months, average reported consumption of cigarettes increased by 103.8 cigarettes per month (median of 30), alcohol increased by 17.7 drinks per month (median of 9), and occurrence of marijuana use increased by 7.6 incidents per month (median of 2).[42] Survey respondents who reported psychological or posttraumatic stress symptoms were more likely to report increased substance use, and a reduction of psychological stress symptoms at six months was not associated with a reduction in drug use.[42] The authors discussed that the addictiveness of drugs may prolong changes in drug use beyond the initial stress response to a traumatic event.[42]

A study assessing adherence to HIV treatment among MSM enrolled in the Protease Inhibitor Longitudinal Life Study (ongoing in the time surrounding the September 11 attack) found

a significant increase in missed or suboptimal ART doses immediately following the September 11 attack.[47] Of 300 study participants, 68 were found to have sufficient adherence data before and after the attack.[47] In a 14-day period, the cohort missed an average of 2.67 ART doses before and 5.07 ART doses after the attack and reported late ART administration (four or more hours off schedule) an average of 2.34 doses before and 4.34 doses after the attack.[47] ART adherence is essential to HIV TasP and suboptimal ART adherence can increase the risk of HIV transmission.[26]

Data has also demonstrated increased infectious disease and STI incidence during economic crisis as periods of individual stress can increase high-risk behavior and reduced spending often leads to fewer available resources for disease prevention, screening, and treatment.[43,44] Areas of Eastern Europe and the former Soviet Union experienced a severe economic crisis in the 1990s as average gross domestic product fell by about one-third, and rates of HIV and Tuberculosis increased during that time (Tuberculosis incidence almost tripled in Russia).[44] Increases in disease burden outlasted the economic crisis and some areas of eastern Europe and the former Soviet Union were unable to reverse or halt the spread of HIV and Tuberculosis over a decade later.[44] A systematic review of 37 studies on the impact of economic crisis on infectious disease found 30 studies that identified worsening disease outcomes during periods of crisis, and few studies identified positive outcomes including healthcare reform triggered by deteriorating disease control during the economic crisis.[44] A study assessing STI diagnosis during the 2008 global financial crisis via retrospective review of 1,437 medical records in an STI treatment clinic in Granada, Spain demonstrated an increase in STI diagnoses from 56.6% in the non-crisis period (2000-2007) to 75.2% in the crisis period (2008-2014).[43] STIs diagnosed in the crisis and non-crisis periods were human papillomavirus (n=103 and 69), candida (n=22 and 37), molluscum contagiosum (n=18 and 14), gardnerella (n=13 and 8), syphilis (n=13 and 10), gonorrhea (n=12 and 10), HIV (n=6 and 5), and trichomoniasis (n=1 and 3).[43]

Protective Factors Reducing STI Risk

Protective factors against HIV and STI acquisition can be social, behavioral, and structural.[33,34] Reduced HIV risk has been associated with structural factors like the availability of social welfare programs for finance, education, housing, and medical assistance; community factors like neighborhood cohesion and social capital; and individual psychological resilience like adaptive coping, empowerment, and self-efficacy.[33] National and community public health interventions in the US have generally attempted to reduce structural health disparities with policy, legal action, and funding through initiatives like social welfare programs, legal action against discrimination, and appropriation of funding to community organizations working to improve economic and educational disparities.[32,33] An ecological study of 66 metropolitan areas in the US from 2003 to 2015 found lower rates of STIs among women in states with higher minimum wage.[48] A one-dollar adjusted increase in minimum wage was associated with a 19.7% decrease in syphilis and 8.5% decrease in gonorrhea among women.[48] Minimum wage increase was not associated with a change in chlamydia rates.[48] Confounding variables and limitations in this study exist; however, data has supported that presence or absence of social welfare policies are associated with population STI risk.[48]

At the individual level, condoms remain the primary public health prevention strategy against multiple STIs with well documented clinical and cost-effectiveness.[49–51] Condom nonuse is the most significant risk factor for STI acquisition, and condoms have demonstrated low failure (breakage or slippage) rates in vaginal and anal sex.[49–51] STI acquisition risk also depends on number of exposures, disease-specific infectivity, and probability of condom failure.[49] Condoms are more likely to be effective in preventing STIs transmitted through body fluids (HIV, chlamydia, and gonorrhea) than direct skin contact (syphilis) and disease-specific condom effectiveness has been appreciated.[49] With condom use in vaginal intercourse, gonorrhea infectivity has been estimated at about 0.20 in men and 0.50 in women, syphilis infectivity has been estimated at about

0.30, and average HIV infectivity has been estimated to be about 0.001.[49] HIV infectivity is variable depending on an individual's HIV viral load and low estimated average HIV infectivity has been attributed to lower transmission risk among those adherent to ART with suppressed HIV (Treatment as Prevention).[49]

Numerous studies regarding sexual behavior and condom use were collected in the 1990s and data from this time strongly supported the use of condom subsidies to increase condom uptake after cost was determined to be a significant barrier to condom acquisition in the US.[52] A 1999 study comparing condom uptake and longitudinal survey data during a state-wide free condom distribution campaign and reduced cost (25 cents) condom distribution campaign in Louisiana found that condom distribution significantly declined when the price of condoms increased from free to 25 cents.[52] In the state-wide free condom campaign, condoms were distributed to state-funded health clinics and over 1,000 businesses in areas with high rates of STIs including convenience stores, salons, motels, and liquor stores with an average of 200,381 condoms distributed per month state-wide.[52] After condom cost increased from free to 25 cents, state-wide condom distribution reduced to 2% of the free condom volume with an average of 4,217 condoms distributed per month.[52] Consumers at 195 of the businesses receiving free condoms were surveyed on condom uptake and use when condoms were free (time 1), three months after condom price increased to 25 cents (time 2), and nine months after the first survey (time 3).[52] Survey data demonstrated a reduction in condom uptake after the price of condoms increased.[52] When condoms were free (time 1), 57% reported obtaining condoms of which 77% used condoms during their most recent sexual encounter.[52] When condoms were 25 cents (time 3), 30% reported obtaining condoms of which 64% used condoms during their most recent sexual encounter.[52]

A meta-analysis of structural condom interventions from 1998-2007 found that condom uptake was increased through interventions that improved condom accessibility and availability among multiple high-risk groups.[53] Effective interventions included free condom distribution,

social marketing to increase condom use, and improving in-store condom visibility.[53] A recent assessment of retail barriers to purchasing condoms in Atlanta, Georgia, an urban area in the Southeast US at high-risk for STIs, found that environmental and physical barriers to purchasing condoms exist.[54] Few stores sold condoms relative to population in the most populated areas of the city (one store per about 7,000 people), 80% of stores required interaction with retail associates to access condoms, and 28% of stores kept condoms out of sight below the checkout counter.[54] The authors discussed that at-risk populations may experience embarrassment requesting assistance from retail clerks when purchasing condoms, and environmental changes to increase condom uptake can include improved retail visibility, installation of condom vending machines, self-checkout, and online ordering.[54]

Sexual Risk Behavior and Behavior Change

A significant body of literature on risk behavior and HIV prevention has been developed since the 1980s, and behavior modification and condom use were the foundation of HIV prevention for the first 30 years of the HIV epidemic before significant biomedical advances like TasP and PrEP were available.[14,55] HIV and STI prevention behavior modification interventions are typically founded in social science behavior change theory like theory of reasoned action, theory of planned behavior, and social cognitive theory and generally attempt to reduce individual risk-taking behavior (reduced condomless sex, number of sex partners, drug use or needle sharing) by modifying a risk factor or determinant.[55,56] Risk determinants are numerous and have included individual and systematic factors.[56] Individual risk determinants and have included attitude, knowledge, self-efficacy, depression, childhood abuse, substance use, interpersonal and behavioral skills, perception of risk and HIV severity, and perception that behavior change is feasible, desirable and controlled by the individual.[55,56] Systematic factors associated with sexual risk behavior have included discrimination, cultural norms, and socioeconomic status.[55,56]

A meta-analysis of 194 HIV-related behavior change interventions from 1985 to 2003 found that interventions that focused on attitude, education, behavior and interpersonal skills were most effective, and interventions that encouraged active participation (like role-playing condom negotiation and client-centered counseling) were more effective than those using only passive techniques (like watching educational videos).[55] Intervention impact depended on participant characteristics including age, gender, risk group, ethnicity, and past condom use.[55] Youth were more impacted by normative social pressure, men often had more control on condom use than women, and interventions with MSM were generally more effective than those with women or PWID.[55] Interventions based on the information-motivation-behavioral skills model attempted to change social norms, perceptions of behavioral control and vulnerability to HIV, and were effective only when paired with behavior skills training (like carrying condoms and negotiating condom use with partners).[55] Fear-based interventions were less successful than interventions based on motivational and cognitive empowerment and could be counter-productive.[55]

Individual sexual behavior has also been considered complex to study due to the intimate nature of sex, involvement of another individual, and presence of multiple associated individual and systematic factors that can be difficult or unethical to control with experimental study design.[56] A systematic review assessing longitudinal and experimental studies on HIV prevention, sexual risk behavior and psychosocial variables from 1991 to 2014 found that temporal data on associations between sexual risk behavior and behavior risk determinants have been mixed.[56] Among 44 longitudinal studies, 44.3% assessed sexual risk behavior of MSM, and the most consistent factors with a longitudinal association on condomless sex were depression, substance use, childhood sexual abuse, and having a previously diagnosed STI although the direction of correlation was mixed.[56] Among nine experimental studies, experiment induced changes in self-efficacy, sex norms and expectations had mixed results on behavior change.[56] Experiment induced changes in knowledge had no significant effect.[56] The authors discussed that theoretical and

associated sexual behavior risk factors are significant despite a lack of experimental data due to the complexity of assessing sexual behavior as some factors (like sexual abuse or discrimination) cannot ethically be induced in a controlled experimental setting.[56]

Most data on sexual behavior change and STI incidence among PrEP users have been collected in clinical trial or open-label settings, like iPrEX, iPERGAY and the PROUD trial.[10,57] Data demonstrating increased STI incidence among PrEP users has been largely consistent, data on presence of behavior change has been mixed, and data collected in clinical trial or open-label settings and may not be generalizable to community-based settings.[10,57] A longitudinal cohort study assessing sexual behavior and condom use among 183 MSM PrEP users in a public health community-based STI clinic in Seattle, Washington from October 2014 to April 2017 found that the number of condomless sexual encounters increased and about half of PrEP users were diagnosed with a bacterial STI during the first year of PrEP use.[57] In this cohort, 13.8% reported condomless sex before starting PrEP, 22% reported condomless sex at nine months of PrEP use, and 16% reported condomless sex at 12 months of PrEP use.[57] The average STI diagnosed per person was 0.5 before starting PrEP and 1.1 in the first year after starting PrEP although it is not clear if this increase in STI incidence was due to behavior change or increased screening.[57] Number of partners, number of partners living with HIV, and sexual position (insertive or receptive) did not significantly change throughout the first year.[57]

A study of community-based PrEP users in the community-based Kaiser medical system in San Francisco from 2012 to 2015 assessed STI incidence among 657 PrEP users and behavior change among 143 survey respondents.[58] The study included 388 person-years of PrEP use and the average length of PrEP use was 7.2 months.[58] No new HIV diagnoses were appreciated among 657 PrEP users during the study period, 30% were diagnosed with a non-HIV STI within the first six months, and 50% were diagnosed with a non-HIV STI within the first 12 months.[58] In this cohort, 143 PrEP users completed a survey on sexual behavior with 76% reporting no change in number of

sex partners, 56% reporting no change in condom use, and 41% reporting decreased condom use.[58] The researchers were unable to identify factors associated with increased number of partners or reduced condom use and considered no new HIV diagnosis to be significant.[58] The researchers estimated that, in absence of PrEP, HIV incidence in this population would have been as high as 8.9 per 100 person-years based on data from a previously performed delayed-PrEP study arm with similar STI incidence.[58]

A study assessing bacterial STI incidence of 280 PrEP users at an outpatient center in New York by screening for bacterial STIs at 3-month intervals instead of 6-months intervals as recommended by current CDC clinical PrEP guidelines found 21% of PrEP users were diagnosed with a bacterial STI within the 6 months before starting PrEP, 11% were diagnosed on their initial PrEP visit, 13% were diagnosed at 3-month follow-up, and 15% were diagnosed at 9-month follow-up.[59] Ten percent of all bacterial STIs diagnosed in the study period were asymptomatic and identified by routine STI screening, 77% of those diagnosed at 3-month screening and 68% of those diagnosed at 9-month screening were asymptomatic.[59] The authors discussed that 24% of the cohort would have had delayed bacterial STI diagnosis and treatment if 3-month screening had not been performed, and more frequent STI screening may benefit timely bacterial STI diagnosis and treatment.[59]

Behavior Risk Optimism and Risk Compensation

Studies in the 1990s and 2000s on risk optimism, an optimistic feeling about HIV risk due to advances in HIV treatment, and increases in sexual risk behavior demonstrated consistent associations between risk perceptions and behavior.[56,60] Most data from that time attributed increased sexual risk behavior to risk optimism although one cross-sectional and longitudinal study using survey data of MSM age 18 to 27 from 1998/1999 (n=538) and 2000/2001 (n=275) found that HIV treatment optimism did not predict risk behavior but risk behavior did predict HIV treatment optimism.[60] These results were inconsistent with the mainstream assumption of

perception-behavior temporality.[60] The researchers suggested that HIV treatment optimism may be a rationalization after participation in condomless sex or risky sexual behavior and discussed the need for additional study to determine causality.[60] Furthermore, confounding variables that could increase sexual risk behavior at that time included emerging personal use of the internet and recreational drugs like amphetamines and sildenafil (brand name Viagra), released in 1998.[60] Contemporary STI-associated sexual risk behaviors are consistent with those over the last 30 years and include internet use with mobile dating apps and recreational drug use associated with addiction or mental health conditions like anxiety or depression.[21]

Risk compensation, an increase in risky sexual behavior due to perceived protection, was historically credited for increased STI incidence among women after the advent of oral contraceptives and in the 1990s among those presenting for HIV care.[61] Risk compensation in the context of PrEP is generally defined as a change in behavior that increases risk of STIs due to perceived protection from HIV including reduced condom use or increase in number of sex partners.[10,21,57] Data attributing PrEP user STI incidence increase to risk compensation has been mixed.[10] Risk compensation has been used by some providers and decision-makers to explain a global increase in non-HIV STI incidence and justify withholding PrEP.[21,62] Conversely, others have disputed the significance of risk compensation in global STI incidence trends arguing that PrEP-eligible individuals are generally considered to be at higher risk for STIs and increases in STI incidence can be attributed to selection bias, preexisting trends, or increased STI screening among PrEP users compared to non-users.[10,61,62] PrEP advocates argue that an association between PrEP and behavior change does not undermine the impact of PrEP on HIV prevention, and support PrEP as a part of a comprehensive STI prevention strategy that includes sexual behavior risk counseling.[62]

Qualitative interviews of 14 PrEP using MSM in Seattle, Washington found that commonly stated reasons for not using condoms were perceptions that condoms reduced

spontaneity, were awkward to use, reduced physical sensation, and reduced intimacy.[63] Many respondents perceived PrEP as a safety measure to offset a preference for condomless sex or self-recognized pattern of condomless sex behavior despite an intention to use condoms.[63] Qualitative interviews with 30 PrEP using MSM in San Francisco, California revealed reduced condom use among 73% of respondents, 40% continued to use condoms with new partners, 16.7% reduced condom use with partners who were also taking PrEP, and 13.3% reported condomless sex after starting PrEP and resumed condom use after being diagnosed with a non-HIV STI.[64] Participants also reported reduced condom use due to feeling protected from HIV or during periods of drug use that altered decision-making.[64] In the Seattle and San Francisco study, respondents who consistently used condoms reported fear of non-HIV STIs as reason for continued condom use.[63,64]

HIV and STI Prevention by Abstinence

Abstinence from sexual behavior is a clear way to prevent STIs, but abstinence education as a public health strategy has been ineffective at preventing STIs and teenage pregnancy despite support from the US federal government and many US states.[65] Two systematic reviews performed by the Community Preventative Service Taskforce, a nonfederal body that provides data to inform public health policy and decision-making in the US, found insufficient evidence to support abstinence education programs, and sufficient evidence to support comprehensive sexual risk-reduction education as a public health strategy to reduce sexual risk behavior and prevent pregnancy and STIs among middle and high school-age adolescents.[66] A comparison of US state school sex education policies in 2005 found that states with policies emphasizing abstinence education had worse teenage pregnancy rates compared to those providing education on abstinence, contraception, and condom use.[65] States placing more emphasis on abstinence were also more likely to have residents living in poverty and higher degree of religiosity than those with more comprehensive sex education programs.[65]

HIV Prevention by Treatment as Prevention

Treatment as Prevention (TasP) is a strategy to reduce HIV transmission through early initiation and consistent use of ART by PLWH.[26,67–69] TasP is effective to prevent HIV by suppressing HIV viral replication in sites of HIV transmission including blood, tissues and secretions of the genital tract.[26] A landmark study in 2011, HTPN052, demonstrated that early ART initiation reduced HIV transmission among serodiscordant couples (one negative partner and one partner living with HIV) by 96%.[26,67–69] This scientific breakthrough led to a change in global HIV treatment and prevention strategies to initiate ART among all PLWH regardless of CD4 and immune status.[26,69] Subsequent TasP studies (PARTNER, Opposites Attract, and PARTNER2) demonstrated even superior results.[68] The current US Health and Human Services core HIV prevention message states People Living With HIV who are undetectable or virally suppressed have effectively no risk of spreading HIV to their HIV negative sexual partners.[68] Current global HIV treatment and prevention strategies emphasize the importance of TasP along with other prevention measures including behavior modification, condom use, and PrEP.[69]

ART tolerability and availability have significantly improved since the completion of the first triple-drug therapy studies in 1996.[24] Reduced global HIV incidence has coincided with global scale-up of ART provision and access throughout the 2010s.[26] In 2010, WHO guidelines reserved ART for those with late-stage HIV (CD4 less than 350 cells/mm^3), landmark studies demonstrating improved HIV treatment outcomes and TasP with earlier ART initiation were completed shortly after (HTPN052 TasP study in 2011), and WHO guidelines changed to support universal ART (providing ART to every PLWH regardless of CD4 count) by 2016.[26,67]

PLWH must maintain consistent ART use to sustain HIV viral suppression, and ART should be initiated early in HIV infection for optimal TasP as people with acute or early HIV infection have been estimated to be over 20 times more likely to transmit HIV than those with established infection.[26] Those with acute HIV (two to four weeks after infection) are known to have

the highest HIV viral load (amount of circulating HIV) increasing risk of HIV transmission.[70] After the acute phase, HIV viral load declines and gradually increases over time in absence of ART (chronic HIV infection).[70] End-stage HIV occurs after about 10 years in absence of ART; is characterized by CD4 below 200 cells/mm^3, presence of opportunistic infection, and high HIV viral load that again increases the risk of HIV transmission.[70] Data on the long-term impact of acute HIV infection on population-level incidence has been mixed and PLWH of all stages can transmit HIV without consistent ART use.[26,70]

Supporting ART adherence is essential for optimal HIV treatment outcomes, HIV suppression (HIV viral load below 200 copies of viral RNA per mL of serum) and TasP.[26,68,71] In 2015, CDC national HIV surveillance estimated that 60% of all PLWH in the US were virally suppressed, 80% of PLWH engaged in HIV treatment were virally suppressed, and two of three PLWH sustained HIV viral suppression for one year.[68] In the US, the Health Resources and Service Administration's (HRSA) public health Ryan White HIV/AIDS Program has provided treatment and support services to over 50% of PLWH in the US and uses a variety of social support services in attempt to reduce treatment disparities.[71] In the US, disparities in ART access, adherence and TasP remain among youth, Blacks, women, transgender, and housing insecure populations.[71] From 2010 to 2016, national Ryan White HIV/AIDS Program HIV viral suppression increased from 69.5% to 84.9% among all clients.[71] Disparities in HIV viral suppression also declined from 2010 to 2016 between Black and White clients (13% to 8.1%), male and transgender clients (9% to 6%), male and female clients (5% to 1%), and those age 13 to 24 (youth) and 55 to 64 (33% to 20%).[71] Continued reduction of ART disparities is essential to ending the HIV epidemic.[71]

HIV Prevention by HIV Pre-Exposure Prophylaxis

ART use for PrEP in the US was FDA approved in July 2012 and provides an opportunity for at-risk groups to engage in clinical care, receive risk-reduction counseling and STI screening.[2,61] PrEP is recommended for sexually active individuals at-risk for HIV including those who are not in

a monogamous relationship with an HIV negative partner, those with recent STI diagnosis, and PWID.[2] Tenofovir disoproxil fumarate/emtricitabine (TDF/FTC, brand name Truvada) and tenofovir alafenamide/emtricitabine (TAF/FTC, brand name Descovy), a combination of two nucleoside reverse transcriptase inhibitors, are the predominant medications used for PrEP in the US and are up to 99% effective at preventing HIV through sexual transmission when taken daily as directed.[2,72,73] Event-driven (on-demand or 2-1-1 PrEP) is the use of PrEP on days of and immediately following sex and is not currently recommended by the CDC.[2]

Event-driven PrEP is recommended as an alternative schedule by the WHO for MSM who find less than daily dosing more convenient, have sex less than twice per week on average, and can postpone sex for two hours after initiating event-driven PrEP.[74] Event-driven PrEP is administered with a loading dose (two pills) 2 to 24 hours before sex, another dose (one pill) 24 hours after the first dose, and a final dose (one pill) 48 hours after the first dose (hence the description, "2-1-1 PrEP").[74] If event-driven PrEP users continue to have sex after the initial loading dose, they should continue to take one pill daily as long as sex continues and for two days after the last sexual encounter.[74] Event-driven PrEP is not recommended for women, transgender women on estrogen, transgender men having vaginal sex, men who have sex with women, or people with chronic hepatitis B infection.[74] There is limited data on event-driven PrEP efficacy in non-MSM populations with data suggesting tenofovir (TDF) may be less concentrated in the female genital tract and less effective when administered with estrogen.[74] A study of TDF/FTC drug levels in transgender women on feminizing hormones found that TDF/FTC did not affect hormone levels, but hormones decreased tenofovir plasma levels by 13% which does not reduce daily PrEP efficacy but may reduce efficacy of event-driven PrEP.[74]

Tenofovir/emtricitabine is generally well-tolerated.[2] Nausea is the most common side-effect, present in less than 10% of users, and is often self-limiting within the first month of use.[2] Adverse reactions to tenofovir/emtricitabine can include decreased bone mineral density, renal

insufficiency, hepatitis B flare, and HIV viral resistance.[2] Older adults and those with preexisting renal disease are more at-risk for tenofovir/emtricitabine-associated renal impairment.[58] tenofovir/emtricitabine is active against hepatitis B and irregular dosing or abrupt cessation can increases risk for hepatitis B flare and subsequent liver impairment in those with chronic hepatitis B infection.[2] Hepatitis B is a vaccine-preventable illness transmitted through sex or blood contact and has shared risk factors with HIV including injection drug use and multiple sex partners.[75]

Most cases of HIV viral resistance among PrEP users have been attributed to inappropriate initiation of PrEP in individuals living with HIV who should have initiated HIV treatment instead because tenofovir/emtricitabine alone is inadequate for HIV treatment.[2] Observed HIV mutations among PrEP users have included K65R and M184V conferring resistance to nucleoside reverse transcriptase inhibitors tenofovir and emtricitabine respectively.[2] Those who acquired HIV after PrEP initiation were less likely to develop HIV viral resistance but rare transmission of tenofovir/emtricitabine-resistant virus has been reported.[2,76] Overall risk of HIV resistance among PrEP users remains low when PrEP is used as directed.[2]

Long-Acting PrEP (LA PrEP) is an emerging PrEP delivery system currently in Phase III clinical trials administered via injection every two to three months with two drugs, cabotegravir (an integrase inhibitor) and rilpivirine (a non-nucleoside reverse transcriptase inhibitor).[16,72] In clinical trials, LA PrEP has been generally well tolerated with the most common side-effect of pain and redness at the injection site.[16] LA PrEP has the potential to improve PrEP adherence by reducing daily pill burden although individuals must still adhere to injection dose schedules.[16,72] LA PrEP has a long pharmacologic tail and will likely require oral PrEP co-administration to avoid subtherapeutic drug levels upon initiation and discontinuation.[72] LA cabotegravir has been detected one year after discontinuation in 14% of users.[77]

Subtherapeutic drug levels can increase the risk of HIV viral resistance if HIV is acquired during this time which is concerning among those with poor adherence or those with acute HIV

infection who were improperly initiated on PrEP.[16,72,77] Mutations conferring resistance to nucleoside and non-nucleoside reverse transcriptase inhibitors have been appreciated in PrEP users in the setting of subtherapeutic drug levels.[2,16] Mutations conferring significant resistance to all integrase inhibitors have been appreciated among macaque studies assessing viral resistance mutations in the setting of sub-therapeutic LA cabotegravir levels.[77] Resistance to integrase inhibitors and nucleoside reverse transcriptase inhibitors is concerning because these are currently recommended as initial HIV treatment for most people in the US.[78] Providers of LA PrEP may also need to increase clinical capacity if LA PrEP injections are to be administered in a clinical setting.[72] Additional emerging PrEP delivery systems include injections with better tolerability, implants, and new classes of medications.[72]

Psychosocial Benefits of PrEP

PrEP significantly reduces the risk of HIV acquisition, provides an opportunity to engage at-risk populations in STI screening, and can have psychological and emotional benefits for PrEP users.[9,10,21,79] In qualitative studies, PrEP users and PLWH have reported feeling empowered with reduced fear of HIV transmission and subsequent increased feelings of intimacy and pleasure surrounding sex.[9,79] PrEP user empowerment can be driven by control over their sexual health reducing the need to rely on others to use condoms, adhere to ART, or disclose their HIV status.[9,79] PrEP can also reduce HIV-related stigma as PrEP user social networks may be more inclusive of PLWH where serosorting, exclusion of PLWH from social networks due to HIV status, has occurred.[9] PrEP users have reported increased inclusion of PLWH in relationships, knowledge of HIV, and reduced anxiety, fear, or shame related to unknown HIV status.[9,63]

PrEP Uptake

In 2015, 1.2 million adults in the US were estimated to be eligible for PrEP of which the primary HIV risk factors were MSM (71.1%) and injection drug use (22.5%).[80] PrEP-eligibility has varied by location and race with Blacks in the South in highest need.[80] US PrEP uptake has

increased since 2013.[9] However, PrEP uptake in the US has been considered slow by public health practitioners with disparities in racial and geographic access due to a combination of real and perceived provider and client barriers including awareness, cost, stigma, and medical system mistrust.[17,81–85]

A PrEP-to-need ratio (PnR) analysis of a national US prescription database using fourth quarter 2017 data found variation in PrEP use with 30% of PrEP users in the South (PnR 1.0), 30% in the Northeast (PnR 3.3), 23% in the West (PnR 2.1), and 17% in the Midwest (PnR 2.4).[15] Low PnR was found in states with lower rates of health insurance coverage, higher rates of poverty, and larger population of Black residents which highlights disparities among those most at-risk for HIV and those most likely to use PrEP.[15] A county-level assessment of US PrEP providers relative to MSM PrEP-eligible populations in 2017 found PrEP-deserts (areas without PrEP providers within a 30-minute drive) were present among all US regions with worse disparities outside of urban centers and in the South (17.1% compared to 5.4% in the Northeast).[83] Rural areas of the West, Midwest, and states of Georgia and Texas were more likely to have significant PrEP-deserts with no PrEP providers within a 90-minute drive.[83]

Systematic barriers to PrEP uptake have included ineffective community engagement, lack of clinical capacity, and cost.[81] Inadequate identification and referral of PrEP-eligible clients can limit PrEP access, legal restrictions can limit access to minors, and lack of funding or insurance coverage has been the most commonly cited barrier to PrEP access by patients and providers.[81] PrEP messaging has largely targeted cisgender MSM with less advertising toward injection drug use, transgender, heterosexual, and minority populations that face unique stigma and disparities accessing healthcare services.[81] A cohort of 33 PrEP-eligible PWID in Massachusetts reported multiple barriers to PrEP. Limited awareness of PrEP was the primary individual level barrier, and additional barriers included drug use, homelessness, inconsistent engagement with the medical system, and possible incarceration.[84]

Barriers to formal PrEP access have prompted use of self-sourced PrEP through online purchases or other informal channels.[86] Informal PrEP users may forgo recommended screenings (like HIV or renal function tests) and the quality and safety of informal PrEP sources is unknown.[86] A qualitative study with 20 informal PrEP using MSM in the United Kingdom in 2017 found that most users self-sourced PrEP through online purchase and one participant sourced PrEP from the ART his partner used as HIV treatment.[86] Many users verbalized concern about the legitimacy of products purchased online but chose online purchase after seeing online PrEP advertised in a medical setting or after failing to obtain PrEP through formal sources because PrEP was only available through clinical trials in the United Kingdom at that time.[86] Informal PrEP users reported administering both daily and event-driven PrEP, and obtained information about PrEP dosing and side-effects online, from medical providers and friends.[86] The authors discussed that informal PrEP users heavily relied on social networks for information and support, and users could benefit from tailored interventions to promote adequate PrEP-related education, screening, and monitoring.[86]

Patient and Provider Barriers to PrEP Uptake

Patient barriers to PrEP uptake have included lack of knowledge of PrEP availability, low awareness of HIV risk, and concerns about cost, side-effects, adhering to a daily pill schedule, and stigma or mistrust of the medical system particularly among racial minorities, MSM, transgender women, and PWID.[9,81,82] PrEP is largely covered by insurance companies although many individuals with and without insurance require financial assistance to obtain PrEP (tenofovir/emtricitabine has been estimated to cost over $10,000 per year).[82,87,88] Financial assistance programs for copay and lab costs require knowledge of the medical system and clients often need assistance navigating these bureaucratic processes.[82] Furthermore, individuals with government insurance (Medicare, Medicaid, and TRICARE) and minors under the age of 18 with insurance coverage through a parent (but prefer not to use insurance due to confidentiality) are not eligible for private pharmaceutical payment assistance programs.[81]

Persistent stigma and racism surrounding HIV, homophobia, transphobia, perceived promiscuity associated with PrEP use can prohibit eligible clients from accessing or using PrEP.[81,82,85] A qualitative study comparing perceptions of homophobia and racism as barriers to PrEP among 35 gay, bisexual and MSM from sites in Massachusetts and Mississippi reported Black MSM had higher mistrust of the medical system and reported experiences of anti-gay or HIV-related stigma compared to non-Hispanic Whites.[85] A qualitative study of 14 MSM PrEP users in Seattle, Washington reported fear of PrEP-related stigma and concern about being labeled as promiscuous or irresponsible for using PrEP by peers and medical providers.[63] PrEP-related stigma can lead to feelings of shame, guilt, and internal conflict regarding respondents' sexual health and PrEP use.[63]

Provider barriers to prescribing PrEP have included concerns about inadequate knowledge or experience with PrEP; concerns about high cost or poor insurance reimbursement that may burden the patient or practice; risk of toxicity or side-effects; patient adherence and HIV resistance; risk compensation; prejudice and stigma toward those at-risk for HIV; and feeling that PrEP was not within their domain.[17,81] There has been a significant paradox between ideal PrEP providers and those most likely to care for PrEP-eligible clients.[81] HIV specialists (those most knowledgeable about PrEP) are less likely to see HIV negative PrEP-eligible clients while primary care providers (those most likely to see PrEP-eligible clients) are often less trained on providing PrEP.[81]

PrEP Adherence and Seasons of Risk

High attrition to PrEP has been appreciated.[18,89,90] A review of 7,148 PrEP users from a national US pharmacy database from 2015 to 2017 revealed only two of five clients persisted with PrEP for two years.[18] Fifty-six percent of the cohort continued PrEP through the first year of use, and 63% of those who continued PrEP through year one continued PrEP through year two.[18] Factors associated with increased adherence were male, over age 24, copay less than $20, and having commercial insurance.[18] Women and youth age 18 to 24 were less likely to have persistent

PrEP use after one year.[18] The Adolescent Trials Network 110/113 study compared self-adherence to PrEP with tracked pill bottle systems and drug concentrations via hair sample and dried blood spots among 243 participants age 15 to 24 years.[89] By week 48, half of the adolescent participants took fewer than two PrEP doses per week per hair or blood measures, 20% took daily PrEP as directed, and adherence self-report was generally overestimated.[89]

A retrospective review of 107 PrEP users at five outpatient clinics associated with an urban academic medical center in New York from 2011 to 2015 found that 58% of PrEP users discontinued PrEP within the first six months.[91] The primary reason for discontinuing PrEP was a change in perceived HIV risk due to ending a relationship with a partner living with HIV.[91] Factors associated with PrEP discontinuation were heterosexual orientation and initiation of PrEP due to having a sex partner living with HIV.[91] Age, gender, race, and insurance status were not associated with PrEP discontinuation.[91]

A longitudinal cohort qualitative survey of 36 former PrEP users who identified as gay or bisexual men found that primary reasons for discontinuing PrEP included cost, insurance discrepancy, side-effect, or difficulty taking a pill daily.[90] Many participants also reported fluctuations in behavior resulting in lower perceived HIV risk.[90] Behavior changes that lead to a perceived lower HIV risk included decreased number of partners, engagement in drug or alcohol treatment, condom use, and TasP among monogamous serodiscordant partnerships.[90] Former PrEP users who discontinued PrEP due to perceived lower HIV risk also reported intent to restart PrEP if risky behaviors were resumed.[90]

Periodic or cyclical fluctuation in risk behavior has been termed ‘Seasons of Risk’ and has impacted willingness to use PrEP among multiple eligible populations.[92] A qualitative study of 38 MSM and male sex workers assessing seasonal risk in Providence, Rhode Island in 2012 found increased risk and willingness to use PrEP during periods of vacation or holiday, summer social activities, and increased drug and alcohol use.[92] The majority of male sex workers reported

substance use with increased perceived risky behavior during periods of drug use or relapse, poverty, and housing insecurity.[92] Male sex workers reported increased PrEP interest but decreased PrEP access during periods of increased risk due to poverty, homelessness, lack of transportation, feelings of hopelessness or shame, and not prioritizing health.[92]

An internet survey of 7,305 MSM in the US in 2013 found that sexual risk behavior was generally seasonal with increased risk during periods of vacation and travel.[93] Daily PrEP administration was a reported barrier among 92.6% of survey respondents, most respondents preferred less than daily dosing of PrEP, and 74.3% reported willingness to use daily PrEP if they perceived it beneficial for short periods.[93] The authors discussed that administering PrEP daily for short intervals during periods of increased risk (like vacations) may be more attractive to PrEP-eligible individuals than long-term daily PrEP, and more research was needed to determine if daily, short-term daily, or event-driven (2-1-1) PrEP would be most beneficial to study participants.[93]

Data on PrEP among women in the US is lacking, and reasons for discontinuing PrEP among women may differ from men.[94] A qualitative study of 60 women in Kenya and South Africa found that 47% of survey respondents would likely stop PrEP in the future.[94] Those who expected to discontinue PrEP reported reasons of lower perceived HIV risk including no longer being sexually active or perceiving their partner to be of low risk.[94] Some women reported they would be likely to discontinue PrEP due to social pressure or stigma, in perinatal periods fearing PrEP may harm fetal development, or due to older age.[94] Four women in the study reported intent to stop PrEP during periods of life stress, and six reported intent to stop PrEP if they were traveling because they did not want to travel with medication or perceived they would not have time to administer the medication while traveling.[94] The authors discussed that PrEP providers should recognize social and cultural norms, consider providing PrEP education to women and their male partners, and educate women on safety and efficacy of PrEP surrounding pregnancy.[94]

Interventions to increase PrEP adherence should be tailored to meet individual adherence barriers.[95] Individuals can have difficulty obtaining refills from pharmacies, remembering to take a daily pill, and have attitudes or perceptions that reduce uptake and adherence to PrEP.[95] LA PrEP is expected to improve adherence among users who have difficulty adhering to daily pill schedules, and event-driven PrEP may improve adherence among eligible MSM who prefer less than daily dosing.[16,74] PrEP delivery systems can also model HRSA Ryan White HIV/AIDS Program services to reduce disparities in access to care and improve ART adherence among at-risk populations as those at-risk for HIV generally face the same barriers to care and adherence as PLWH.[96] Ryan White HIV/AIDS Program services use a multidisciplinary approach that often includes HIV specialists, social workers, and mental health professionals.[96] Ryan White HIV/AIDS Program sites that performed a comprehensive needs assessment and integrated provision of ART with primary care have generally demonstrated superior outcomes.[96] Likewise, PrEP providers that perform a comprehensive needs assessment and integrate provision of PrEP with primary care may also increase access and adherence.[96]

Cost and Resource Allocation

Assessing cost-benefit of HIV prevention is complex and largely dependent on local factors including HIV prevalence, characteristics of at-risk populations, healthcare infrastructure, cost, and availability of resources.[6,13,14,97] HIV prevention interventions are often divided into categories along a prevention cascade including behavior risk reduction (condoms), biomedical prevention (PrEP), HIV testing, linkage to care, HIV treatment and retention in care (TasP).[6] In the US, the cost of PrEP and HIV prevention is variable and dependent on factors including generic availability, insurance coverage, laboratory and provider fees, 340B drug-pricing, and eligibility for pharmaceutical payment assistance programs.[13,87,88,98] ART medications are the largest cost item to PrEP delivery as payers are charged over $1,000 for a 30-day supply of tenofovir/emtricitabine in the US.[87] ART cost is often shared by insurance payers and pharmaceutical payment assistance

programs.[88,99] Clinical care (laboratory, testing, and provider fees) are variable depending on the type of test ordered and are often funded by insurance payers or state and local funding among uninsured populations.[87,99,100]

A cost analysis of unmet need (no funding coverage or inadequate funding coverage) to fund PrEP medication, clinical visits, and laboratory costs in the US in 2015 found that the percent of individuals with health insurance coverage to fund PrEP varied by transmission category (PrEP-eligible MSM were more likely to have private insurance than women or PWID).[100] The authors estimated the national cost of covering PrEP for all eligible individuals in 2015 was about $208 million per year ($119 million to cover the cost of those in need of assistance for clinical care only, and $89 million to cover the cost of those in need of assistance for clinical care and ART).[100] The authors discussed that providing PrEP for all eligible people is less than the allocated funds available for HIV care and treatment (19.7 billion in fiscal year 2016), PrEP uptake has been generally slow, and not all eligible people have attempted to access PrEP.[100]

In the US, condom use as HIV prevention has been estimated to cost less than $4 annually per person while PrEP can cost over $10,000 annually per person but is more effective than condoms when used as directed for HIV prevention.[87,97,98] PrEP has more cost-effectiveness when delivery is targeted toward those at highest risk for HIV, like MSM, although allocating resources to PrEP may divert resources from less expensive prevention methods or HIV treatment and has not been supported as the most cost-effective HIV prevention intervention.[13,98] Conversely, interventions supporting HIV treatment, adherence, and retention in care (TasP) have been largely supported as a cost-effective strategy to maximize health benefits among varying populations, including heterosexual and PWID, in the US and globally.[6,14,97,98] A review of HIV program cost analysis in 23 countries found that increasing funds to treat HIV would reduce new HIV infections and HIV-related death and the degree of impact varied by resource availability.[14] The analysis

supported targeting populations with the highest HIV incidence and optimizing ART availability for PLWH before increasing capacity for HIV testing and counselling.[14]

Resource allocation for STI and HIV prevention in LHDs is critical for population STI prevention.[101] LHDs are a safety-net for low income, uninsured and underinsured populations, and are ideal providers of PrEP as they are engaged with populations at-risk for HIV.[101] Data has supported an inverse relationship between bacterial STI incidence and LHD STI funding with higher rates of gonorrhea and syphilis in periods of lower funding.[101,102] Despite public need, federal funding for public health STI prevention has declined since 2002 and future budget restrictions are expected.[101,102] A 2013 and 2014 survey of 148 US LHDs recruited from the National Association of County and City Health Officials' (NACCHO) 2010 National Profile of Local Health Departments survey found that 61.5% experienced STI budget cuts in the previous fiscal year; about 40% reduced STI clinic hours of operation and STI screening due to budget cuts and 6.8% closed STI clinics due to budget cuts.[101] Reduced funding for LHD STI programs can negatively impact populations most vulnerable to HIV and STIs.[101,102]

PrEP in Local Health Departments

US public health agencies are critical providers of HIV prevention services, and LHDs are in an ideal position to support PrEP delivery and leverage data.[1,6,101,103] Most available literature on PrEP delivery has been collected in clinical trial or academic settings, and little data on PrEP delivery in local health departments exist. Available data on PrEP delivery in LHDs have predominantly assessed LHD engagement or willingness to provide PrEP services. Despite the critical role of LHDs in STI and HIV prevention in the US, data regarding population outcomes of PrEP provision by LHDs is a current gap in the literature, and no literature on STI incidence among LHD PrEP users or PrEP provision by LHDs in the US state of Georgia could be identified.

A 2015 US survey of 284 LHDs on PrEP engagement found 29% of respondents were engaged in PrEP services through activities including linkage to PrEP care (74%), PrEP education

to community members (51%), or participation in state or local PrEP workgroups (32%).[1] LHDs engaged in PrEP services were most often located in the West (47%) and served large jurisdictions (68%).[1] LHDs engaged in PrEP services were also more likely to provide HIV testing (98%), HIV linkage to care (83%), or operate STI clinics (81%) than those not engaged in PrEP services.[1] Only 9% of survey respondents reported actively providing PrEP and barriers to PrEP provision at the LHD level included concerns about clinical capacity (61%), cost to clients (53%), and lack of knowledge among staff (47%).[1] A 2016 survey of 56 LHDs in North Carolina regarding PrEP provision found that two LHDs actively provided PrEP and seven referred clients to PrEP services. Primary reasons for LHDs not engaging in PrEP were concerns about cost, lack of PrEP prescribing protocol, and belief that PrEP provision was more appropriate for non-LHD clinics.[104]

The NGHD, a LHD in north Georgia, aims to optimize local population HIV and STI health outcomes in coordination with national and state prevention goals. The Georgia Integrated HIV Prevention and Care Plan for 2017-2021 goals include preventing new infections, improving access to care and health outcomes, and reducing HIV-related health disparities.[105] To achieve these goals, the NGHD started providing PrEP services in July 2019 in addition to previously existing STI and HIV prevention and treatment services. PrEP services provide the NGHD an opportunity to screen, refer, and vaccinate a population that may otherwise be unengaged in care or forgo services. PrEP users at NGHD LHD study sites are routinely screened for HIV, STIs, and hepatitis C; mental health conditions like depression; substance use including tobacco, alcohol, and illicit drug use; and vaccination status. Treatment and referrals are provided as needed.

PrEP Program Performance Evaluation

The WHO has described PrEP delivery as a cascade of services where individuals at-risk of HIV are identified and linked to PrEP care, screened for interest and eligibility, provided PrEP, retained in care with optimal adherence, and discontinue PrEP as indicated.[106] Routine program monitoring is essential to assess PrEP uptake, effectiveness, and to predict demand.[106] The WHO

has recommended that program measures assess each step in the PrEP delivery cascade to determine if the program is reaching the target population with safe, effective, and sustained PrEP care.[106] The WHO has suggested PrEP program measures include PrEP uptake, retention in PrEP care for more than three consecutive months, PrEP toxicity, and seroconversion (number of PrEP users who are diagnosed with HIV).[106] The CDC has suggested PrEP program quality measures include presence of baseline HIV screening before initiating PrEP, interval HIV screening, PrEP medication adherence, seroconversion, and seroconversion with ART-resistant HIV.[107] No national US PrEP program comparison benchmarks could be identified.

A PrEP program evaluation in New York assessing 171 PrEP users from five clinics throughout the state from 2014 to 2015 found that the primary demographics of PrEP users were male (93.6%), white (60%), age 25-34 (46%), with predominant risk factor of anal sex (55.2%), and most had private insurance (66.7%).[108] Twenty-four percent of the cohort discontinued PrEP within the 12-month study period and the majority discontinued PrEP within the first six months of PrEP use.[108] The primary reason for PrEP discontinuation was a change in perceived HIV risk.[108] One client seroconverted with HIV between PrEP initiation and one-month follow-up, 17 PrEP users were found to have a bacterial STI on PrEP intake, and 9 were found to have a bacterial STI on 6-month screening.[108] Eighty-three PrEP users responded to a survey on their experience with PrEP and generally reported being satisfied with PrEP with 94% of respondents reporting they would recommend PrEP to a friend and 82% reporting less worry of HIV.[108] Thirty-three percent reported having insurance issues related to PrEP, and a high deductible or copay for laboratory or provider fees was the primary insurance-related issue.[108] Staff reported that developing infrastructure to support PrEP delivery (PrEP-related clinical training and increased administrative support) was essential to successfully initiate a PrEP program.[108] No program evaluation of PrEP services, retention in care or STI incidence among PrEP users in a Southeast US LHD setting could be identified despite the key role of LHDs in community STI prevention. This practice-based study

served to provide NGHD leadership with data to evaluate PrEP program delivery and guide decision-making in absence of available LHD PrEP service data.

CHAPTER 3

METHODS

The goal of this study was to perform an evaluation of LHD PrEP services in the North Georgia Health District (NGHD), a local health department that includes six counties in north Georgia, between July 2019 and June 2020 (the first year PrEP services were provided), quantify the impact of COVID-19 on NGHD STI testing services, and determine how the Thinking Ethically framework can be effectively applied to PrEP-related public health practice. The study was performed through a secondary analysis of longitudinal data obtained through a retrospective review of NGHD PrEP client medical records from July 1, 2019 to June 30, 2020; aggregated NGHD STI testing from July 1, 2017 to June 30, 2020; and an analysis of literature cited in this study. The study was approved by the Georgia Southern University Institutional Review Board (Appendix A).

Data obtained from this study were intended to be applied by NGHD leadership to guide future PrEP service delivery, determine the rate of bacterial STI diagnosis among PrEP users, and determine what additional services were provided to PrEP users beyond STI prevention. Outcomes included PrEP user demographics; length of time users were enrolled in the program; diagnosis of HIV, gonorrhea, chlamydia, syphilis among PrEP users; type of additional services provided to PrEP users; sum of NGHD STI tests performed; and ethical considerations to PrEP services identified via literature review. It was assumed that PrEP services provide an opportunity to engage a population that may otherwise forgo health services and routine STI screening. Individuals with asymptomatic STIs may forgo routine STI screening with subsequent delays in STI diagnosis and treatment. Routine STI screening among PrEP users benefits timely STI treatment and prevention.

The study period included the onset of the 2020 COVID-19 pandemic, and it was assumed that the COVID-19 pandemic impacted NGHD STI and PrEP service delivery. The number of total STI tests (HIV, gonorrhea, chlamydia, and syphilis) provided by the NGHD between July 1, 2017

and June 30, 2020 were assessed in attempt to quantify the impact of the COVID-19 pandemic on NGHD STI services. Total STI tests provided during this period provided NGHD leadership with baseline data to determine when STI services return to pre-pandemic quantity. NGHD STI testing services were assessed because HIV prevention and PrEP should be considered in the context of a broad STI prevention strategy.[10,11] The study served to answer the following research questions:

1. How can the Thinking Ethically framework be used to inform public health practitioners on PrEP-related decision-making?
2. Did NGHD PrEP services reach those most at-risk for HIV in the district?
3. How long did PrEP users stay in the program?
4. What additional services were provided to PrEP users beyond STI prevention?
5. How many asymptomatic bacterial STIs were diagnosed among PrEP users?
6. How much did NGHD STI testing change in the period associated with the onset of the COVID-19 pandemic?

The research questions were developed with consideration to NGHD STI screening priorities along with CDC and WHO recommended PrEP practice quality indicators which include appropriate screening, retention in care, and the number of patients with confirmed HIV diagnosis while prescribed PrEP medication.[106,107] The questions were framed with regard to the Thinking Ethically framework which incorporates multiple ethical principles and uses a stepwise approach to ethical decision-making.[5] All Thinking Ethically principles (justice, utility, rights, common good, and virtue) were analyzed in research question 1, and the principles of justice (the fair distribution of resources) and utility (acting to produce the greatest net benefit) were used to frame research questions 2 – 6.[5] Ethical considerations surrounding NGHD PrEP services have included reaching the target population as those at-risk for HIV are often vulnerable or hard to reach and may require allocation of additional resources,[3] and the potential impact of PrEP services on the broader STI landscape as PrEP use has been associated with increased bacterial STI incidence and those at-risk

for HIV are often at-risk for other STIs.[10,11] PrEP user demographics and length of time enrolled in the PrEP program were assessed to determine if NGHD PrEP services equitably reach those at-risk for HIV in the district (justice approach). Additional non-HIV prevention services provided to PrEP users (like vaccination or referrals) and asymptomatic bacterial STI diagnosis among PrEP users were assessed to weigh the net benefits of NGHD PrEP services and potential impact of PrEP provision on the STI landscape (utility approach).

It was assumed that the medical record was an accurate reflection of the medical encounter and the Thinking Ethically framework would benefit PrEP-related public health decision-making in practice. It was expected that the NGHD had between 50 and 100 PrEP users within the study period and minority of PrEP users were prescribed PrEP with on-demand (2-1-1) administration. It was expected that the NGHD PrEP user population was largely homogenous in race (White), ethnicity (non-Hispanic), gender (male), and primary HIV risk factor (MSM), and differed in age. It was estimated that length of time in PrEP care would mirror the experience of other PrEP clinics with 20-50% of PrEP users discontinuing PrEP within the first six months. Providing PrEP services was expected to benefit NGHD ability to identify asymptomatic bacterial STIs through routine screening. Duplicate bacterial STI diagnoses were expected in some cases and were not considered an error in data collection (for example, clients diagnosed with pharyngeal and urethral gonorrhea on the same screening encounter). It was expected that PrEP users were provided with additional services including routine vaccination, referrals (primary care, mental health care, social services), and tobacco cessation counseling as indicated. It was expected that the largest disruption in NGHD STI testing services associated with the onset of the COVID-19 pandemic occurred between April and June 2020.

The NGHD provides PrEP to eligible clients using the Georgia Department of Public Health (DPH) Registered Nurse Protocol and CDC guidelines. NGHD clients are eligible for PrEP if they meet DPH and CDC criteria which include a primary HIV risk factor of MSM,

heterosexually active men and women, and PWID with additional risk factors including multiple partners, recent bacterial STI, inconsistent condom use, or partner living with HIV.[2] Clients must have documented negative HIV test and no sign of acute HIV, no medical contraindication to tenofovir/emtricitabine, and be willing to return for follow-up one month after starting PrEP and three months thereafter. Screening for syphilis, gonorrhea, and chlamydia via 3-point testing (pharynx, urethral or vaginal, and rectal) is performed on the initial PrEP encounter and every six months (more frequently as needed). The NGHD postponed in-person PrEP visits in the second quarter of 2020 due to the COVID-19 pandemic during which time PrEP users were provided with prescription refills if they were able to be contacted by phone, had no symptoms of acute HIV, verbalized adherence to PrEP and willingness to continue therapy.

Sample and Population

The cohort was selected via convenience sampling. Medical records of all PrEP users in the NGHD from July 2019 to June 2020 (the first year that PrEP services were provided) were reviewed. Sixty-three clients obtained PrEP from the NGHD during the study period and were included in the study. During the study period, the NGHD provided PrEP only to those over 18 years of age, so only data from those of 18 years or older were included in the study. NGHD PrEP users who tested positive for HIV were to be included in the cohort until date of HIV diagnosis, but no NGHD PrEP users were diagnosed with HIV during the study period. The study also examined the total number of STI tests performed by the NGHD from July 2017 through June 2020 to quantify the degree of service delivery change associated with the onset of the COVID-19 pandemic. This data included all HIV, gonorrhea, chlamydia, and syphilis tests performed at NGHD clinic sites. Tests of HIV, gonorrhea, chlamydia, and syphilis not performed at NGHD clinic sites were excluded.

Data Collection

Data to inform analysis of the Thinking Ethically framework used literature cited in this study (research question 1). Client data was obtained via a retrospective chart review of NGHD electronic medical record data from all NGHD PrEP clinic sites (research questions 2 – 6). Data obtained included PrEP user age, race/ethnicity, sex/gender, HIV risk factor, bacterial STI diagnosis, length of time on PrEP, and NGHD clinic site. Data on presence of STI symptoms at the time of bacterial STI diagnosis was obtained to determine the rate of asymptomatic STIs diagnosed through routine program STI screening. Data on additional services provided (like vaccination and referrals) were obtained to assess benefits of PrEP provision beyond STI prevention. To protect privacy, data was recorded in deidentified form, each NGHD clinic site was assigned a confidential name (Clinic A, Clinic B, Clinic C), and clinics with fewer than 10 PrEP users were reported in aggregate form instead of confidential clinic name to protect client confidentiality as some NGHD sites had low PrEP program census.

NGHD district-level HIV, gonorrhea, chlamydia, and syphilis data from July 2017 to June 2020 were assessed using an electronic medical record STI report utilized by the district to routinely assess STI incidence (research question 6). This report had no patient identifiers and was captured in Excel software. Data was captured using a secured on-site computer on an Excel file without any personal identifiers and stored on the researcher's password-protected computer and NGHD internal password-protected virtual drive.

Data Analysis

Research Question 1

Analysis and synthesis of the Thinking Ethically framework (research question 1) was performed using literature cited in this study and study outcomes of research questions 2 – 6. Outcomes included pairing each Thinking Ethically principle (utilitarian, justice, rights, common good, and virtue) with a PrEP-related ethical consideration. An analysis was performed to

determine how the Thinking Ethically framework benefits PrEP-related public health practice and decision-making.

Research Questions 2 – 5

Chart review data from July 1, 2019 to June 30, 2020 was analyzed using Excel and SPSS version 27 software to answer research questions 2-5. NGHD PrEP user demographic variables (clinic site, age, race/ethnicity, sex/gender, and HIV risk factor), presence of any additional services provided to PrEP users, months in program, and asymptomatic STI diagnosis among PrEP users were assessed. To determine how long NGHD PrEP users stay in the program, client length of time using PrEP was assessed in months (four weeks) from the initial encounter date to the end of the study period or to the date of last documented contact with the client, whichever came first. Discontinuation dates that fell between two months were rounded to the nearest month, and data of one client who discontinued and restarted PrEP within the study period reflected the sum months of program participation.

Descriptive statistics including means, standard deviation, and frequencies were used to answer research questions 2 – 5. Negative binomial and multiple logistic regression models were performed to further assess research question 3. Regression analyses included 62 of the 63 PrEP users in the study. Cohort demographic variables with low events per variable were transgender (n=1), IV drug user HIV risk (n=1), and clients prescribed on-demand (2-1-1) PrEP (n=1). The one transgender female was coded as female, the one IV drug user was excluded, and the one on-demand PrEP user was coded in the same way as daily PrEP users to reduce the risk of type 1 error due to overfit of cohort data (Table 3.1). A forced entry approach including all independent variables on the first step was used because previous literature suggested factors of age, HIV risk, and race/ethnicity have been associated with PrEP use.[18,85,89,91]

Table 3. 1. Regression modeling variables and type

Study Variable		Type
Dependent variables	Months in Program	Continuous
	Months in Program of 4 or More (yes/no)	Categorical
Independent variables (PrEP user demographic variables)	Clinic Site:	Categorical
	Clinic A	
	Clinic B	
	Clinics C/D/E	
	Sex/Gender:	Categorical
	Male	
	Female	
	Race/Ethnicity:	Categorical
	Black non-Hispanic	
	White Hispanic	
	White non-Hispanic	
	Age	Continuous
	Primary HIV Risk Factor:	Categorical
	MSM	
	Heterosexual risk	

Negative binomial regression. Negative binomial was performed to assess for association between PrEP user demographics factors on probability of number of months in the PrEP program (research question 3). The negative binomial regression model is a linear Poisson distribution with the addition of a λ parameter to consider data variance in the equation. This improves the model fit for data that is over-dispersed (variance greater than the mean) compared to a Poisson distribution that assumes variance equals the mean. The negative binomial λ parameter follows a gamma distribution (a continuous probability function that assesses the variance and mean to determine the average waiting time for skewed events with a natural minimum of 0). Test assumptions were presence of a continuous dependent variable, observations that are independent of each other, and independent variables that have a multiplicative effect on the event. The following regression function was used to predict the probability of months in program:

$$P(y_i = n|x_i) = \frac{\Gamma(m_i + y_i)}{\Gamma(m_i)\Gamma(y_i)}\left(\frac{m_i}{\lambda_i + m_i}\right)^{m_i}\left(\frac{\lambda_i}{\lambda_i + m_i}\right)^{y_i}; n \geq 0$$

where $P(y_i = n|x_i)$ is the probability of the dependent variable occurrence, Γ is the gamma distribution, y_i is the dependent variable, $n|x_i$ is the independent variable with a positive continuous n, λ_i is an exponential equation:

$$\exp(x_i\beta)$$

where x_i is the independent variable and β is the beta coefficient (a standardized measure indicating the degree change in the outcome variable for every 1-unit change in the independent variable), and m_i is an exponential equation:

$$\exp[(2 - P)x_i\beta - \ln(\delta)]$$

where P is a probability, and $\ln(\delta)$ is the natural log of delta (a difference in measures).

The dependent variable was PrEP user months in program as a continuous numerical measure. The independent variables were PrEP user demographic factors. Clinic site compared enrollment at Clinic A or Clinic B to Clinics C/D/E. Sex/gender compared females to males. HIV risk factor compared those of heterosexual risk to MSM. Race/ethnicity compared Black non-Hispanic or White Hispanic PrEP users to White non-Hispanic PrEP users. Age in years at program enrollment was a covariate. Independent variables were considered statistically significant if the corresponding p-value was less than 0.05.

Multiple logistic regression. Multiple logistic regression was performed to assess for association between PrEP user demographic factors on odds of retention in care of four or more months (research question 3). Four or more months was selected in accordance with recommended WHO program measures to assess retention in care by consecutive PrEP use greater than three months.[106] The multiple logistic regression model solves for the odds of an outcome occurring and calculates the natural log of the odds ratio so that the relationship can be plotted linearly. Test assumptions were presence of a binary dependent variable, observations that are independent of each other, little to no multicollinearity among independent variables, and independent variables

should have 10 or more events per variable. The following regression function was used to predict the odds of retention in care of four or more months:

$$\ln\left(\frac{\hat{p}}{(1-\hat{p})}\right) = b_0 + b_1X_1 + b_2X_2 + \ldots + b_pX_p$$

where $\ln\left(\frac{\hat{p}}{(1-\hat{p})}\right)$ is the expected log of the odds that the outcome is present, $\hat{p}$ is the expected probability the outcome is present, X_1 through X_p are independent variables, and b_0 through b_p are regression coefficients of the line.

The dependent variable was PrEP user months in program coded as 'yes' if the PrEP user months in the program were four or more and 'no' if PrEP user months were three or less. The independent variables were PrEP user demographic factors. Clinic site compared enrollment at Clinic A or Clinic B to Clinics C/D/E. Sex/gender compared females to males. HIV risk factor compared those of heterosexual risk to MSM. Race/ethnicity compared Black non-Hispanic or White Hispanic PrEP users to White non-Hispanic PrEP users. Age in years at program enrollment was a covariate. Independent variables were considered statistically significant if the corresponding p-value was less than 0.05.

Research Question 6

The total number of STI tests performed by the NGHD was calculated from July 2017 through June 2020 using Excel software to determine how much NGHD STI testing changed in the period associated with the onset of the COVID-19 pandemic (research question 6). STI testing totals from July 2018 through June 2020 were assessed quarterly and totals were compared using descriptive statistics. STI testing totals from July 2017 to June 2018 were excluded due to missing or inconsistent data and it was determined that two years of historic STI testing data (July 2018 to June 2020) were sufficient to assess changes associated with the onset of the COVID-19 pandemic.

CHAPTER 4

RESULTS

Thinking Ethically About PrEP

Question 1: How can the Thinking Ethically framework be used to inform public health practitioners on PrEP-related decision-making?

Providers of PrEP, HIV and STI care must make complex ethical decisions on resource distribution and clinical services that can have significant public health impact. The Thinking Ethically framework is of practical use to inform public health practitioners on PrEP, HIV and STI-related decision-making by leading the practitioner to think critically and consider multiple ethical perspectives in a step-by-step manner. Use of multiple ethical perspectives is necessary to adequately assess the multifaceted nature of PrEP as decision-makers must consider available data, available resources, and possibly conflicting stakeholder perspectives when providing PrEP services.[3] The Thinking Ethically framework facilitates practitioners to select the best plan of action by first collecting data on an ethical issue and then evaluating outcomes against each ethical principle (utilitarian, rights, justice, common good, and virtue).[5] The following section serves to demonstrate how the Thinking Ethically framework can be used to inform public health practitioners on PrEP-related decision-making. Each question posed in the Thinking Ethically framework will be addressed to exemplify the stepwise decision-making process as it applies to providing PrEP care at the Local Health Department (LHD) level.

Which option will produce the most good and do the least harm? (The utilitarian approach)[5] The best decision from the utilitarian approach is one that produces the most good and least harm for those impacted by the decision (greatest net gains).[5] LHDs are key providers of HIV and STI prevention, clinical, and data management services in the community[101,103] and are therefore ideal providers of PrEP services. Areas of high HIV incidence (like the Southeast US) can have the greatest benefit from PrEP provision.[23] PrEP services benefit timely bacterial STI diagnosis and treatment[10] and serve as an opportunity to engage a population that may otherwise

forgo medical care. In this study, 75% of the bacterial STIs identified among NGHD PrEP user were asymptomatic. Providing PrEP care offered an opportunity to identify, treat, and prevent further transmission of asymptomatic STIs as it was assumed that those with asymptomatic STIs may have delayed STI screening if they had not been engaged in PrEP services. About half of NGHD PrEP users were also provided with non-HIV-related services including vaccination, tobacco cessation counseling, and referrals as indicated; it was assumed that PrEP users may not have engaged the medical system to obtain these services in absence of PrEP care. PrEP users have also reported psychosocial benefits of PrEP including feelings of empowerment and reduced fear of HIV.[9]

Potential risks of PrEP have included adverse reactions from ART and HIV viral resistance among PrEP users if seroconversion occurs in the setting of subtherapeutic drug levels.[2] ART used in oral PrEP has been generally well tolerated, and the risk of developing HIV viral resistance among oral PrEP users has been low.[2] The rate of HIV viral resistance among Long Acting PrEP (LA PrEP) users in the community is not yet known as LA PrEP is being studied in ongoing clinical trials at the time of this study, although data has supported a risk of HIV viral resistance among macaque LA PrEP models that can have significant implications for HIV care.[77] LHD PrEP providers will need to determine if the risk of HIV resistance outweighs the right of PrEP users to access LA PrEP once approved and available for use.

Which option best respects the rights of all who have a stake? (The rights approach)[5] The best decision from the rights approach is one that honors the moral rights of those affected.[5] Moral rights include dignity, autonomy, privacy, to be told the truth and not injured.[5] Ethical rights surrounding PrEP can include the right to access PrEP, right to safe and effective therapy, and right to privacy. LHD provision of PrEP services can serve to improve an individual's right to access PrEP as LHDs often provide care to vulnerable populations at-risk for HIV.[101] Oral PrEP has been generally well tolerated and considered up to 99% effective as HIV prevention when used as

directed.[2] Long Acting PrEP (LA PrEP) has also demonstrated high effectiveness in HIV prevention in clinical trials although the risk of LA PrEP on HIV viral resistance in the community is not yet known.[72] The right to privacy surrounding PrEP can be complex; regulation requiring involvement of parents in PrEP care may be required for minors.[81] PrEP users may also be subject to disclosures from laboratories or health insurers. For example, the primary insurance holder (like a parent, guardian, or spouse) may receive an itemized statement of service charges or payments from the laboratory or insurer that could inadvertently disclose PrEP use among minors or adult PrEP users who are not the primary insurance holder.

Which option treats people equally or proportionately? (The justice approach)[5] The best decision from the justice approach is one that treats everyone equally, or unequally with a justifiable standard (for example, income that is stratified by skill).[5] When providing PrEP, LHDs must determine how to fairly appropriate resources to provide PrEP to multiple at-risk populations in addition to other public health priorities, like the ongoing COVID-19 pandemic response. PrEP-deserts have been appreciated in rural areas with worse access in rural areas of the US South,[83] and a low PrEP-to-Need (PnR) ratio has been appreciated in states in the South and non-Medicaid expansion states compared to other regions of the US.[15] This indicates that PrEP is not currently equally distributed among those at-risk in the US. LHDs often serve as a healthcare safety net and LHDs in Southeast and rural areas could improve PrEP distribution inequality by providing PrEP services.

The NDHD integrated PrEP with its preexisting STI screening and treatment program in 2019, and staff was allocated to perform administrative tasks associated with PrEP care (like assisting clients with enrollment in pharmaceutical payment assistance programs). The majority of NGHD PrEP users were MSM despite a known population of PWID[30] indicating that the NGHD did not successfully reach all groups at-risk for HIV in the service area. Additional resources would need to be allocated to reach and retain the NGHD IV drug user population in PrEP care as PWID

have reported additional barriers to PrEP uptake including poor awareness, drug use, and low socioeconomic status.[84]

Which option best serves the community as a whole, not just some members? (The common good Approach)[5] The best decision from the common good approach is one that benefits community welfare for everyone (including vulnerable populations).[5] Services including public education, police and fire response are often evaluated from the common good approach.[5] Ethical considerations to LHD PrEP assessed in the utilitarian approach are also generally applicable for analysis under the common good approach. Providing PrEP services can reduce HIV transmission risk,[2] improve timely diagnosis and treatment of non-HIV STIs,[10] and provide an opportunity to vaccinate individuals who may have otherwise forgone services. These services are beneficial to the community as reducing HIV and STI transmission among individuals reduces community level incidence, and vaccinating individuals improves community-level immunity. There has been debate on whether to allocate ART to PrEP or HIV treatment in resource limited settings where access to ART for treatment may be impacted if resources were allocated to PrEP care.[3] Literature has supported prioritizing ART for HIV treatment (Treatment as Prevention) instead of PrEP in resource limited settings.[98] The NGHD had adequate resources to initiate PrEP services without restricting HIV treatment services.

Which option leads me to act as the sort of person I want to be? (The virtue approach)[5] The best decision from the virtue approach is one that enable decision-makers to act in accordance with their highest character standard.[5] Honesty, compassion, integrity, self-control, and prudence are common virtues used to evaluate acting from one's best self.[5] PrEP-related virtues include compassion, fairness, and overcoming stigma and discrimination that surrounds HIV, STI, and PrEP services. PrEP users have reported reduced stigma, fear and discrimination against PLWH because of PrEP.[9] Conversely, PrEP-eligible individuals have reported a fear of being labeled promiscuous or irresponsible as a barrier to PrEP use.[63] Many at-risk groups (MSM, transgender

individuals, minorities, PWID) have also reported fear of stigma or discrimination when engaging the medical system.[84,85] LHDs should work to provide outreach and PrEP care in a culturally sensitive manner to overcome stigma-related barriers to PrEP, HIV and STI prevention.

North Georgia Health District PrEP Services

Question 2: Did NGHD PrEP services reach those most at-risk for HIV in the district?

There were 63 NGHD PrEP users in the study period. NGHD Clinic A served 35 clients, Clinic B served 18 clients; Clinics C, D, and E (C/D/E) served a total of 10 clients. Most NGHD PrEP users identified as male followed by female and transgender. Most PrEP users identified as White non-Hispanic followed by Black non-Hispanic and White Hispanic. The primary HIV risk factor among PrEP users was MSM followed by heterosexual contact and intravenous drug use. PrEP users were widely distributed in age with a range of 18 to 69 years (Figure 4.1). Most PrEP users were under age 35 with 39.7% between 18 to 24 years followed by 25 to 34 years, 35 to 44 years, and over 45 years (Table 4.1). The median age was 28 years and mean age was 30 years with a standard deviation of 11.5.

Figure 4. 1. Age and PrEP user primary HIV risk factor

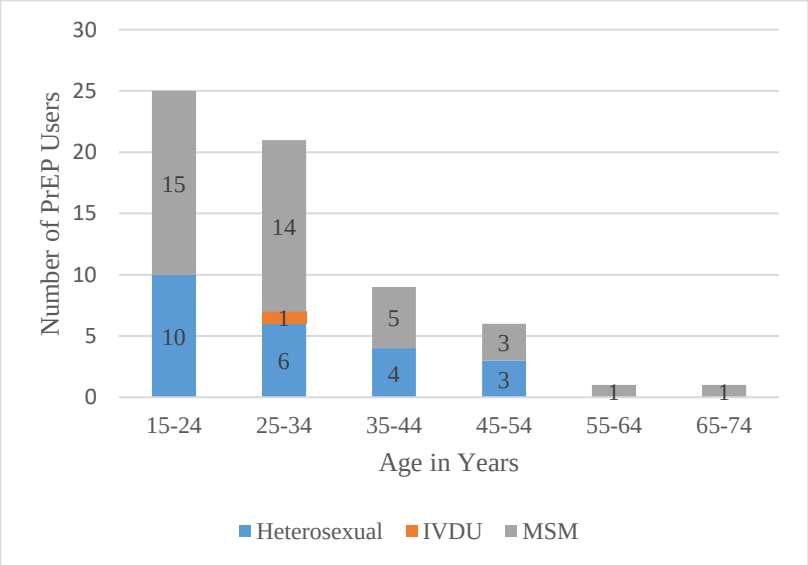


Table 4. 1. Count of cohort demographic factors

Demographic factor	n	(%)
Clinic Site:		
Clinic A	35	(55.6)
Clinic B	18	(28.6)
Clinics C/D/E	10	(15.9)
Sex/Gender:		
Male	47	(74.6)
Female	15	(23.8)
Transgender	1	(1.6)
Race/Ethnicity:		
Black non-Hispanic	16	(25.4)
White Hispanic	9	(14.3)
White non-Hispanic	38	(60.3)
Age in years		
18-24	25	(39.7)
25 to 34	21	(33.3)
35 to 44	9	(14.3)
45 or older	8	(12.7)
Primary HIV Risk Factor:		
MSM	39	(61.9)
Heterosexual risk	23	(36.5)
Injection drug use	1	(1.6)

Study sites were found to have differing client demographic factors (Table 4.2). PrEP users at Clinic A were 62.9% male followed by female, 48.6% White non-Hispanic followed by Black non-Hispanic and White Hispanic, and with primary HIV risk factor of heterosexual risk followed by MSM and injection drug use. PrEP users at Clinic B were 88.9% male followed by female and transgender, 72.2% White non-Hispanic followed by Black non-Hispanic and White Hispanic, and with primary HIV risk factor of MSM followed by heterosexual risk. PrEP users at Clinics C/D/E were 90% male followed by female, 80% White non-Hispanic followed by White Hispanic, and with primary HIV risk factor of MSM followed by heterosexual risk.

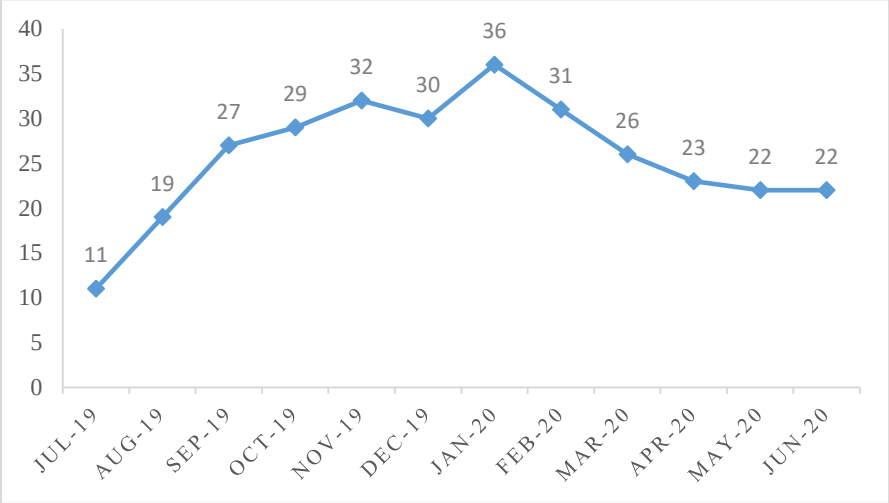
Table 4. 2. PrEP user demographics by clinic site

Demographic Factor	Clinic A		Clinic B		Clinics C/D/E	
Sex/Gender:						
Male	62.90%	n=22	88.90%	n=16	90%	n=9
Female	37.10%	n=13	5.60%	n=1	10%	n=1
Transgender Female	0%	n=0	5.60%	n=1	0%	n=0
Race/Ethnicity:						
Black non-Hispanic	40%	n=14	11.10%	n=2	0%	n=0
White non-Hispanic	48.60%	n=17	72.20%	n=13	80%	n=8
White Hispanic	11.40%	n=4	16.60%	n=3	0%	n=2
Primary HIV Risk Factor:						
MSM	42.90%	n=15	83.30%	n=15	90%	n=9
Heterosexual	54.30%	n=19	16.70%	n=3	10%	n=1
PWID	2.90%	n=1	0%	n=0	0%	n=0

Question 3: How long did PrEP users stay in the program?

The NGHD had 22 active PrEP clients at the end of the study period and 41 of 63 clients (65%) discontinued PrEP use during the study period. Of the 41 clients that discontinued PrEP, 90.2% (n=37) were lost to follow-up with unknown or undocumented reason in the medical record, 4.9% (n=2) discontinued due to a change in HIV risk, 2.4% (n=1) moved out of the service area, and 2.4% (n=1) discontinued due to medication side effect. The highest monthly NGHD PrEP census was in January 2020 (n=36), and a drop in census associated with the time of the onset of the COVID-19 pandemic was appreciated. NGHD PrEP census declined by 27.8% between January and March 2020 (36 to 26 PrEP users) but remained largely consistent between April and June 2020 with 23 PrEP users in April and 22 PrEP users in June (Figure 4.2).

Figure 4. 2. Total NGHD PrEP users per month



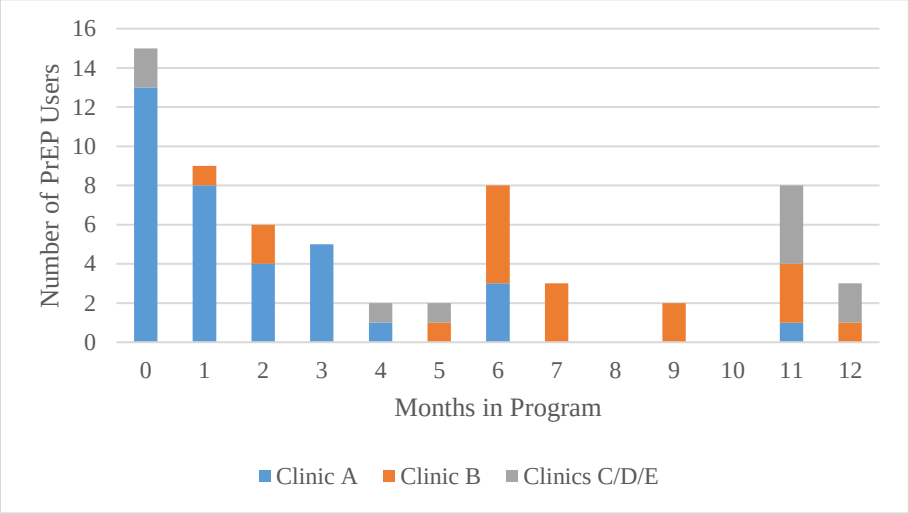
Study sites were also found to have differing census, mean, median, and mode monthly retention during the study period (Table 4.3; Figure 4.3). Clinic A had 35 PrEP users with the lowest mean monthly retention (1.8 months). Clinic B had 18 PrEP users with a mean monthly retention of 6.9 months. Clinics C/D/E had 10 PrEP users with a mean monthly retention of 7.7 months. Clients with less than one month enrolled in the program were found to have attended an intake PrEP appointment for a PrEP eligibility screen and pre-prescription laboratory testing but either fell out of care before being prescribed PrEP therapy or did not attend the one-month follow-up appointment.

Table 4. 3. PrEP user months in program by clinic site

Clinic Site	Mean	Median	Mode	Range
Clinic A	1.8	1	0	0 to 11
Clinic B	6.9	6	6	1 to 12
Clinics C/D/E	7.7	11	11	0 to 12

Note: mean, median, mode and range of PrEP user months in program

Figure 4. 3. PrEP user months in program by clinic site



A negative binomial regression was performed to assess the effect of PrEP user demographic variables on months enrolled in the PrEP program (Table 4.4). Test assumptions of presence of a continuous dependent variable, observations that are independent of each other, and independent variables that have a multiplicative effect on the event were met. The negative binomial regression model was statistically significant with Omnibus test of model coefficients X^2=24.606, p=.001 with a p-value <.05 indicating significance. Clinic A was the only PrEP user demographic factor that was significantly associated with months in program. PrEP user months in program were 76% lower in Clinic A compared to Clinics C/D/E with a 95%CI of 35.6% to 91%.

Table 4. 4. Negative binomial regression for PrEP user demographic factors on probability of months in the PrEP program

			95% Wald CI						95% CI for EXP(B)	
Demographic Factor	B	Std.Error	Lower	Upper	Wald	df	Sig.	Exp(B)	Lower	Upper
(Intercept)	2.151	.6651	.847	3.455	10.458	1	.001	8.593	2.333	31.647
Clinic Site										
Clinic A	**-1.426**	**.5031**	**-2.412**	**-.440**	**8.029**	**1**	**.005**	**.240**	**.090**	**.644**
Clinic B	-.120	.4328	-.969	.728	.078	1	.781	.886	.380	2.070
Clinics C/D/E	0[a]	.	.	.	.	.	.	1	.	.
Sex/Gender										
Female	.482	.5725	-.640	1.604	.709	1	.400	1.619	.527	4.974
Male	0[a]	.	.	.	.	.	.	1	.	.
Race/Ethnicity										
Black non-Hispanic	.517	.3959	-.259	1.293	1.703	1	.192	1.677	.772	3.643
White Hispanic	-.036	.4332	-.885	.813	.007	1	.933	.964	.413	2.254
White non-Hispanic	0[a]	.	.	.	.	.	.	1	.	.
HIV Risk Factor										
Heterosexual	-.822	.5545	-1.909	.265	2.196	1	.138	.440	.148	1.304
MSM	0[a]	.	.	.	.	.	.	1	.	.
Age in Years	-.003	.0152	-.033	.027	.031	1	.861	.997	.968	1.028

Abbreviations: CI, confidence interval

Note: X^2=24.606, p=.001 (Omnibus)

a. Category reference variable

Bold text indicates statistically significant demographic variables at p <0.05

A multiple logistic regression was performed to assess the effect of PrEP user demographic factors on odds of retention in care of four or more months (Table 4.5). Test assumptions of a binary dependent variable, observations that are independent of each other, and little to no multicollinearity among independent variables were met. Test assumption that independent variables should have 10 or more events per variable were met for all independent variables except HIV risk factor of White Hispanic (n=9). The logistic regression model was statistically significant with Omnibus test of model coefficients X^2=36.296, p=.000 with a p-value <.05 indicating significance. Hosmer and Lemeshow test X^2=4.183, p=.840 with a p-value >.05 indicating good model fit. The model explained 59.3% (Nagelkerkle R^2) of the variance in months in program of four or more months and correctly classified 83.9% of cases compared to 54.8% of cases in the null model. Clinic A was the only PrEP user demographic factor that was significantly associated with retention in care of 4 or more months. PrEP users in Clinic A were .017 times less likely to stay in the program 4 or more months than those in Clinics C/D/E with a 95%CI of .001 to .218 times.

Table 4. 5. Logistic regression for PrEP user demographic factors on odds of months in program of four or more months

							95% CI for EXP(B)	
Demographic Factor	B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Clinic Site								
Clinics C/D/E			15.500	2	.000			
Clinic A	**-4.079**	**1.304**	**9.791**	**1**	**.002**	**.017**	**.001**	**.218**
Clinic B	.057	1.078	.003	1	.958	1.058	.128	8.755
Age in Years	-.041	.034	1.464	1	.226	.960	.898	1.026
Sex/Gender								
Female	1.262	1.622	.605	1	.437	3.533	.147	84.933
HIV Risk Factor								
Heterosexual	-2.062	1.615	1.630	1	.202	.127	.005	3.014
Race/Ethnicity								
White non-Hispanic			3.123	2	.210			
Black non-Hispanic	1.416	1.024	1.911	1	.167	4.120	.554	30.667
White Hispanic	-1.071	1.144	.876	1	.349	.343	.036	3.228
Constant	3.339	1.731	3.722	1	.054	28.204		

Abbreviations: CI, confidence interval

Note: X^2=36.296, p=.000 (Omnibus); X^2=4.183, p=.840 (Hosmer & Lemeshow); .593 (Nagelkerkle R^2)

Bold text indicates statistically significant demographic variables at p <0.05

Question 4: What additional services were provided to PrEP users beyond STI prevention?

About half (50.8%, n=32) of NGHD PrEP users had documentation of additional services beyond STI prevention provided during the PrEP encounter. Of the additional services provided, 17 PrEP users were provided vaccines, 11 PrEP users were provided referrals, 5 PrEP users were provided alcohol reduction counseling, and 4 PrEP users were provided smoking cessation counseling. Vaccines provided were hepatitis A, hepatitis B, influenza, tetanus-diphtheria-pertussis, and human papillomavirus. Referrals provided were primarily to Federally Qualified Health Centers for primary care, social services for food or housing assistance, mental health providers, or other NGHD site for vaccination (Table 4.6).

Table 4. 6. Count of additional services provided

Service Provided	n	(%)
Vaccines		
Hepatitis A	9	(34.4)
Hepatitis B	2	(7.7)
Influenza	5	(19.2)
Tdap	4	(15.4)
Human papillomavirus	6	(23.1)
Referrals		
Primary care	6	(50)
Food or housing assistance	2	(16.7)
Mental health	2	(16.7)
Other NGHD site	2	(16.7)
Health Behavior Counseling		
Alcohol reduction counseling	5	(55.6)
Smoking cessation counseling	4	(44.4)

Question 5: How many asymptomatic bacterial STIs were diagnosed among PrEP users?

Most PrEP users (81%, n=51) were not diagnosed with an STI (HIV, gonorrhea, chlamydia, or syphilis) during the study period, and 19% (n=12) of PrEP users were diagnosed with an STI during the study period. There were 16 STI cases of which 50% (n=8) were chlamydia, 31.3% (n=5) were gonorrhea, 18.8% (n=3) were syphilis, and none were HIV. The majority of STI cases (75%, n=12) had no symptoms documented at time of STI screening as 62.5% (n=5) of

chlamydia cases were asymptomatic, 80% (n=4) of gonorrhea cases were asymptomatic, and 100% (n=3) of syphilis cases were asymptomatic (Figure 4.4). Sites of chlamydia diagnosis were pharyngeal, rectal, urethral, and vaginal, and four cases involved multiple sites. Sites of gonorrhea diagnosis were pharyngeal, rectal, and vaginal, and two cases involved multiple sites (Table 4.7). STI cases were primarily diagnosed on the PrEP intake encounter (62.5%, n=10), followed by as-needed screening (25%, n=4) and the 6-month encounter (12.5%, n=2).

Figure 4. 4. Presence of STI symptom at time of STI diagnosis

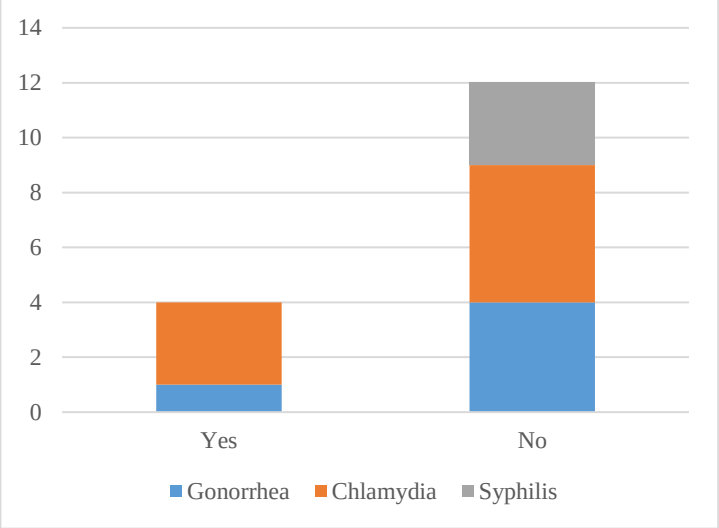


Table 4. 7. Count of chlamydia and gonorrhea diagnosis site and presence of symptom

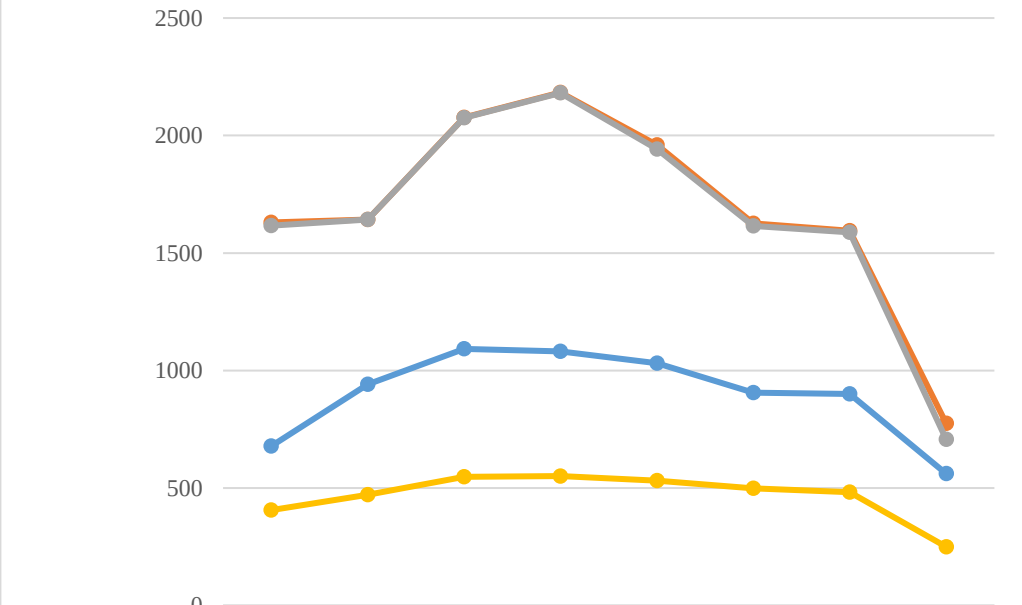
	Total		Symptomatic		Asymptomatic	
Site of Diagnosis	n	(%)	n	(%)	n	(%)
Chlamydia						
Pharyngeal	2	(16.7)	0	(0)	2	(100)
Rectal	5	(41.7)	0	(0)	5	(100)
Urethral	3	(25)	1	(33.3)	2	(66.7)
Vaginal	2	(16.7)	2	(100)	0	(0)
Gonorrhea						
Pharyngeal	3	(42.9)	0	(0)	3	(100)
Rectal	3	(42.9)	0	(0)	3	(100)
Urethral	1	(14.3)	1	(100)	0	(0)

STI Services in the time of COVID-19

Question 6: How much did NGHD STI testing change in the period associated with the onset of the COVID-19 pandemic?

STI tests performed by the NGHD declined between the first and second calendar year quarter (Q1 and Q2) of 2020 as well as between Q2 of 2019 and Q2 of 2020 (Figure 4.5). Between 2020 Q1 and Q2, tests performed for HIV declined by 38% (901 to 561), gonorrhea by 51% (1,595 to 775), chlamydia by 55% (1,588 to 707), and syphilis by 48% (482 to 250). Between 2019 Q2 and 2020 Q2, tests performed for HIV declined by 48% (1,082 to 561), gonorrhea by 64% (2,183 to 775), chlamydia by 68% (2,181 to 707), and syphilis by 55% (551 to 250).

Figure 4. 5. Total NGHD STI tests performed per quarter



	2018 Q3	2018 Q4	2019 Q1	2019 Q2	2019 Q3	2019 Q4	2020 Q1	2020 Q2
HIV	679	941	1092	1082	1031	906	901	561
Gonorrhea	1630	1643	2077	2183	1960	1626	1595	775
Chlamydia	1617	1643	2075	2181	1942	1615	1588	707
Syphilis	406	472	548	551	531	499	482	250

CHAPTER 5

DISCUSSION

Thinking Ethically About PrEP

Question 1: How can the Thinking Ethically framework be used to inform public health practitioners on PrEP-related decision-making?

The Thinking Ethically framework was designed as an applied model to aid decision-makers in choosing the best action through multiple ethical approaches. The Thinking Ethically framework was assessed to determine how it can be used to inform public health practitioners on PrEP-related decision-making and serve as a useful tool for LHDs deliberating whether to provide PrEP services. In this study, the Thinking Ethically framework was found to be feasible and appropriate to evaluate LHD services and provision of PrEP care. Framework theoretical concepts were presented in a concrete step-by-step process that translated well to public health practice and the use of multiple ethical approaches (utilitarian, rights, justice, common good, and virtue) was appropriate to assess the multifactorial impact of PrEP services. The Thinking Ethically framework can be applied to future PrEP considerations like how to best allocate LHD resources to provide PrEP services to those most at-risk or whether to provide Long Acting (LA) PrEP once available given the risks and resource-intensity of LA PrEP compared to currently available oral PrEP services.

LHD PrEP services were considered to provide a greater net benefit than risks to stakeholders (utilitarian approach) through the opportunity to prevent HIV, STIs and provide non-HIV services. Services were considered to abide by the rights of most users (rights approach) although dilemmas remain surrounding privacy and access to PrEP care among minors. Resources allocated for PrEP (justice approach) facilitated reaching at-risk populations of MSM but did not adequately reach PWID within the service area. PrEP services were considered to benefit all members of the community (common good approach) through additional non-HIV services, like STI prevention and vaccinations. Services were also considered virtuous (virtue approach) by

targeting vulnerable populations at-risk for HIV although dilemmas remain surrounding stigma of HIV and STIs in the community.

North Georgia Health District PrEP Services

Question 2: Did NGHD PrEP services reach those most at-risk for HIV in the district?

The NGHD served 63 PrEP users between July 2019 and June 2020 which could be considered modest enrollment compared to other NGHD programs or PrEP programs in larger urban centers. The lower NGHD PrEP census was anticipated given the study period assessed the first year of NGHD PrEP services and the suburban and rural geographic distribution of the NGHD (which extends from the north Atlanta suburbs into the north Georgia mountains). Suburban and rural areas can face additional challenges to PrEP awareness and stigma compared to urban centers. NGHD PrEP services primarily reached the MSM population and PWID were considered to be largely underrepresented considering two counties in the NGHD service area were previously identified by the CDC as high-risk for HIV and hepatitis C transmission due to injection drug use.[29,30] Additional resources would be needed for the NGHD to reach and retain PWID in PrEP care as drug users have faced multiple barriers to care and have been considered a hard-to-reach population. The predominance of youth in the cohort was consistent with populations identified as at-risk as youth are generally at higher risk for STIs, and the racial/ethnic distribution of PrEP users was consistent with the larger population demographics of the service area.

Question 3: How long did PrEP users stay in the program?

Low retention in PrEP care has been documented in the literature and multiple community-based studies have reported about half of PrEP users discontinued within the first year.[18,91] Program discontinuation may indicate an individual's reduced risk of HIV or the existence of barriers to care. Low PrEP program retention supports the need to reduce barriers to PrEP care and continue other HIV prevention strategies like behavioral change interventions and Treatment as Prevention (TasP). In this study, 65% of NGHD PrEP users discontinued PrEP within the one-year study

period and retention in care was found to vary by clinic site. No other demographic factors were significantly associated with retention in care via negative binomial or logistic regression modeling. Clinic A had a higher census but lower retention while the other clinic sites had lower census but higher retention. The discrepancy in retention by clinic site is significant to program management as variations between clinic sites indicate a need for further exploration for internal consistency and quality control. Site retention discrepancies could be due to variation in site PrEP user demographics as Clinic A served more females and those of heterosexual HIV risk compared to other sites (populations that have been associated with lower retention in PrEP care compared to MSM).[18,85] Discrepancies in clinic site retention could also be due to variation in clinic processes (program enrollment or follow-up), staff bedside manner, or diversion of resources toward the COVID-19 pandemic during the study period.

Short retention in PrEP care poses ethical considerations to LHD PrEP program management including staffing resource distribution and the risk of future LA PrEP provision. LHDs should consider PrEP retention when distributing staffing resources between multiple programs as LHDs in suburban and rural areas may not have the PrEP census to justify multiple dedicated PrEP staff. Conversely, dedicating case-management staff to assist PrEP users facing psychosocial or administrative barriers to care may benefit program retention. LHDs should also consider retention in care when deciding whether or not to provide LA PrEP in the future due to the risk of HIV viral resistance if PrEP is abruptly discontinued and HIV is acquired during the period of LA PrEP subtherapeutic drug tail.[16,77]

Question 4: What additional services were provided to PrEP users beyond STI prevention?

Services provided beyond STI prevention were provided to 50.8% of NGHD PrEP users. Vaccines were the primary additional service provided (45.9%) followed by referrals (29.7%), and alcohol (13.5%) and smoking cessation counseling (10.8%). LHD provision of PrEP services is considered an opportunity to engage individuals in holistic preventative care as PrEP users may

forgo routine services in absence of PrEP use. Referrals provided were primarily to local low-cost primary care followed by mental health and social services. Referral follow-up was not assessed in this study and it is unknown how many clients used referral services. The presence of additional provided services supports that NGHD PrEP users were screened for psychosocial and medical needs outside of sexual healthcare and attempt to refer individuals to community resources was made as needed. Providing preventative services to populations at-risk for HIV can benefit both individual and community wellness.

Question 5: How many asymptomatic bacterial STIs were diagnosed among PrEP users?

Routine NGHD PrEP care includes bacterial STI screening for gonorrhea, chlamydia, and syphilis to detect asymptomatic STI infection. Previous literature has demonstrated bacterial STI infection in pharyngeal and rectal sites were more often asymptomatic compared to urethral sites among MSM populations.[23] In this study, 19% of PrEP users were diagnosed with a bacterial STI during the study period and 75% of bacterial STIs diagnosed were asymptomatic. Chlamydia and gonorrhea were primarily diagnosed in extra-urethral sites (pharyngeal and rectal), and the majority (62.5%) of STI cases were diagnosed on the initial PrEP encounter. The rate of asymptomatic STI diagnosis in this study is higher than previous literature. In a study of 280 PrEP users in New York, 10% of diagnosed STIs were asymptomatic and 11% were diagnosed on the initial PrEP encounter.[59] Results of this study highlight the importance of routine global STI screening of all exposure sites among PrEP users in the LHD setting.

STI Services in the time of COVID-19

Question 6: How much did NGHD STI testing change in the period associated with the onset of the COVID-19 pandemic?

The onset of the COVID-19 pandemic impacted NGHD clinical services during the study period and was therefore considered in the interpretation of study results, but this practice-based study was not designed or intended to investigate the impact of COVID-19 on LHD PrEP and STI

care. To encourage social distancing during the pandemic, NGHD LHD sites ceased nonessential in-person encounters for all programs in the second quarter of 2020. Multiple NGHD clinical sites providing PrEP care diverted staffing resources toward the pandemic response including COVID-19 testing, syndromic surveillance, contact tracing, and vaccination campaigns. Local health departments, like the NGHD, were (and continue to be at the time of this writing) on the forefront of the COVID-19 pandemic response.

The total number of STI tests performed by the NGHD from June 2018 to July 2020 was evaluated to quantify the change in STI services associated with the COVID-19 pandemic and provide a baseline for leadership to determine when services rebound to pre-pandemic quantity. Between the first and second calendar year quarter (Q1 and Q2) of 2020, testing for HIV declined by 38%, gonorrhea by 51%, chlamydia by 55%, and syphilis by 48%. Between 2019 Q2 and 2020 Q2, testing for HIV declined by 48%, gonorrhea by 64%, chlamydia by 68%, and syphilis by 55%. Gonorrhea and chlamydia testing were correlated as they are generally tested together. The full impact of COVID-19 on the STI landscape is not yet known, although any reduction in STI incidence appreciated during the time of the pandemic could be due to a true reduction in STI incidence due to community social distancing or reduced screening and testing. NGHD STI testing services also serve as an opportunity to screen individuals for PrEP eligibility, and a reduction in NGHD STI services is assumed to have impacted enrollment in the PrEP program.

During the period of COVID-19 related clinical service disruption, NGHD PrEP providers refilled tenofovir/emtricitabine prescriptions if the PrEP user could be contacted by phone for a verbal adherence and HIV symptom screen. Many NGHD PrEP users also obtained prescription refills from a mail-order pharmacy in the Ryan White AIDS Drug Assistance Program (ADAP) pharmacy network. It is reasonable to suspect that PrEP users with reliable phone service were better able to be retained in care during this time and use of a mail order pharmacy likely

benefited PrEP users during periods of social distancing, but more research is needed to investigate retention trends during the COVID-19 pandemic.

Future Research

The COVID-19 pandemic was a significant confounding variable during the study period, and additional research on the impact of the COVID-19 pandemic on the STI landscape and PrEP care is needed as the long-term impact of the COVID-19 pandemic on STI trends, LHD fiscal resources, and resource distribution is not yet known. Follow-up NGHD PrEP program reviews should also be performed as one year is not enough time to determine long-term trends or impact of LHD PrEP services. Follow-up program reviews would also benefit from a state-wide evaluation that includes regional PrEP retention and STI incidence trends from LHD and private providers. Remaining gaps in the literature include PrEP-related stigma in rural and suburban areas and reasons for PrEP user discontinuation in suburban and rural LHD settings. Barriers to LHD PrEP services in rural and suburban areas may differ from urban centers and research on stigma in non-urban LHDs may benefit uptake and provision of rural and suburban PrEP services. Future research on LA PrEP is needed as LA PrEP is an emerging delivery system and poses additional risk of HIV viral resistance.[16,77] Consideration should also be given to PrEP retention, LA PrEP cost, and clinical capacity prior to initiating LA PrEP services in the LHD setting.

Limitations

Limitations included the review period of one year after NGHD PrEP service implementation as one year is not enough time to appreciate long-term effects of PrEP service delivery. The study did not determine presence of causal relationships between PrEP use and STI incidence as assessment of temporality or experimental control was not performed. The study only included NGHD clinic sites and is therefore not a comprehensive assessment of PrEP user population STI incidence because STIs diagnosed at private, non-NGHD clinics were not included due to data access limitations. Data obtained in this study was specific to the NGHD (a suburban

and rural LHD in the Southeast US) and is possibly not generalizable to other settings although generalizability is not essential for a practice program review to be valuable to LHD practice program management. The small sample size of the study population and wide confidence interval of statistical regression results reduces the meaningfulness of point estimates. The retrospective medical record data may also have some variability in documentation between nurse-provider staff, and care was taken to select research questions utilizing data that should be consistently present in the medical record.

Possible confounding variables included PrEP user income and insurance status as these have been associated with PrEP uptake and retention in PrEP care but were not assessed due to a lack of available data. The COVID-19 pandemic also occurred during the study period and is expected to have significantly impacted PrEP provision and STI incidence between March and June 2020 because the NGHD significantly reduced PrEP and STI service delivery during this time due to social distancing and redistribution of resources toward COVID-19 public health response. Obtaining qualitative data from NGHD PrEP provider staff and PrEP users would have been ideal but could not be performed due to NGHD staffing priorities in response to the ongoing COVID-19 pandemic and risk of COVID-19 exposure to NGHD PrEP users during the time of data collection.

Conclusion

LHDs are critical to the healthcare safety-net, provide key STI prevention services in the community, and are well-suited to provide PrEP care to those most at-risk for HIV. This practice-based study demonstrated the value of ethical decision-making and practice-based research to LHD program planning and the need for continuous quality management initiatives in public health practice. The Thinking Ethically framework adequately elicited potentially conflicting ethical PrEP considerations and was found to be well-suited to LHD PrEP-related decision-making when seeking the best course of action. The first year of NGHD PrEP services saw a modest census compared to urban PrEP programs and study results indicated possible discrepancies in service

delivery between NGHD study sites. LHD PrEP services were considered an opportunity to screen for STIs, provide additional health services, and engage vulnerable populations that may otherwise forgo medical care. The COVID-19 pandemic impacted STI and PrEP service delivery during the study period and follow-up evaluation is needed as NGHD PrEP census is expected to increase after the pandemic subsides and the full impact of COVID-19 on program delivery and STI incidence is not yet known.

REFERENCES

1. Weiss G, Smith DK, Newman S, Wiener J, Kitlas A, Hoover KW. PrEP implementation by local health departments in US cities and counties: Findings from a 2015 assessment of local health departments. *PLoS ONE*. 2018;13(7). doi:10.1371/journal.pone.0200338

2. Centers for Disease Control and Prevention. US Public Health Service: Preexpoure prophylaxis for the prevention of HIV infection in the United States -2017 Update: A clinical practice guideline. Published online March 2018. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

3. World Health Organization. WHO/UNAIDS consultation on the ethics of PrEP and early initiation of ART for prevention. How should countries reach a decision? In: World Health Organization; 2012. Accessed January 31, 2020. https://apps.who.int/iris/bitstream/handle/10665/112800/9789241507189_eng.pdf;jsessionid=49ED9A387AA61A62237AB00D65BE364C?sequence=1

4. Sugarman J, Mayer KH. Ethics and Pre-Exposure Prophylaxis for HIV-infection. *J Acquir Immune Defic Syndr 1999*. 2013;63(0 2):S135-S139. doi:10.1097/QAI.0b013e3182987787

5. Velasquez M, Moberg D, Meyer M, et al. A framework for ethical decision making. Published online 2015. Accessed May 6, 2020. https://www.scu.edu/ethics/ethics-resources/ethical-decision-making/a-framework-for-ethical-decision-making/

6. Ryan GW, Bloom EW, Lowsky DJ, et al. Innovation Profile: Data-driven decision-making tools to improve public resource allocation for care and prevention of HIV/AIDS. *Health Aff (Millwood)*. 2014;33(3):410-417. doi:doi: 10.1377/hlthaff.2013.1155

7. Centers for Disease Control and Prevention. HIV Surveillance Report 2018 (Preliminary). 30:129.

8. Fonner VA, Dalglish SL, Kennedy CE, et al. Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. *AIDS Lond Engl*. 2016;30(12):1973-1983. doi:10.1097/QAD.0000000000001145

9. Grant RM, Koester KA. What people want from sex and PrEP. *Curr Opin HIV AIDS*. 2016;11(1):3-9. doi:10.1097/COH.0000000000000216

10. Jenness SM, Weiss KM, Goodreau SM, et al. Incidence of Gonorrhea and Chlamydia following Human Immunodeficiency Virus preexposure prophylaxis among Men Who Have Sex With Men: A modeling study. *Clin Infect Dis*. 2017;65(5):712-718. doi:10.1093/cid/cix439

11. Unemo M, Bradshaw CS, Hocking JS, et al. Sexually transmitted infections: Challenges ahead. *Lancet Infect Dis*. 2017;17(8):e235-e279. doi:10.1016/S1473-3099(17)30310-9

12. Aral SO, Over M, Manhart L, Holmes KK. Sexually Transmitted Infections. In: Jamison DT, Breman JG, Measham AR, et al., eds. *Disease Control Priorities in Developing Countries*. 2nd ed. World Bank; 2006. Accessed January 31, 2020. http://www.ncbi.nlm.nih.gov/books/NBK11734/

13. Hankins C, Macklin R, Warren M. Translating PrEP effectiveness into public health impact: Key considerations for decision-makers on cost-effectiveness, price, regulatory issues, distributive justice and advocacy for access. *J Int AIDS Soc*. 2015;18(4Suppl 3). doi:10.7448/IAS.18.4.19973

14. Stuart RM, Grobicki L, Haghparast-Bidgoli H, et al. How should HIV resources be allocated? Lessons learnt from applying Optima HIV in 23 countries. *J Int AIDS Soc*. 2018;21(4). doi:10.1002/jia2.25097

15. Siegler AJ, Mouhanna F, Giler RM, et al. The prevalence of pre-exposure prophylaxis use and the pre-exposure prophylaxis–to-need ratio in the fourth quarter of 2017, United States. *Ann Epidemiol*. 2018;28(12):841-849. doi:10.1016/j.annepidem.2018.06.005

16. Landovitz RJ, Kofron R, McCauley M. The promise and pitfalls of Long Acting injectable agents for HIV prevention. *Curr Opin HIV AIDS*. 2016;11(1):122-128. doi:10.1097/COH.0000000000000219

17. Grippo J, Smallwood S, Pincura K, Wright T, Mase W. Physician attitudes toward the ethics of Pre-exposure Prophylaxis (PrEP): Cost, safety, and resource allocation. *J Ga Public Health Assoc*. 2017;7(1). doi:10.21633/jgpha.7.104

18. Coy KC, Hazen RJ, Kirkham HS, Delpino A, Siegler AJ. Persistence on HIV preexposure prophylaxis medication over a 2-year period among a national sample of 7148 PrEP users, United States, 2015 to 2017. *J Int AIDS Soc*. 2019;22(2). doi:10.1002/jia2.25252

19. Lee LM. Public health ethics theory: Review and path to convergence. *J Law Med Ethics*. 2012;40(1):85. doi:10.1111/j.1748-720X.2012.00648.x.

20. Kass NE. Public health ethics: From foundations and frameworks to justice and global public health. *J Law Med Ethics*. 2004;32(2):232-242. doi:10.1111/j.1748-720x.2004.tb00470.x

21. Soriano V, del Romero J. Rebound in Sexually Transmitted Infections following the success of antiretrovirals for HIV/AIDS. *AIDS Rev*. 2018;20(4):187-204. doi:10.24875/AIDSRev.18000034

22. World Health Organization. Sexually transmitted infections (STIs). Accessed February 21, 2020. https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis)

23. Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2018. Published online 2019:176. doi:10.15620/cdc.79370

24. Danforth K, Granich R, Wiedeman D, Baxi S, Padian N. Global Mortality and Morbidity of HIV/AIDS. In: Holmes KK, Bertozzi S, Bloom BR, Jha P, eds. *Major Infectious Diseases*. 3rd ed. The International Bank for Reconstruction and Development / The World Bank; 2017. Accessed April 25, 2020. http://www.ncbi.nlm.nih.gov/books/NBK525184/

25. Wandeler G, Johnson LF, Egger M. Trends in life expectancy of HIV-positive adults on ART across the globe: comparisons with general population. *Curr Opin HIV AIDS*. 2016;11(5):492-500. doi:10.1097/COH.0000000000000298

26. Holmes CB, Hallett TB, Walensky RP, Bärnighausen T, Pillay Y, Cohen MS. Effectiveness and Cost-Effectiveness of Treatment as Prevention for HIV. In: Holmes KK, Bertozzi S, Bloom BR, Jha P, eds. *Major Infectious Diseases*. 3rd ed. The International Bank for Reconstruction and Development / The World Bank; 2017. Accessed April 25, 2020. http://www.ncbi.nlm.nih.gov/books/NBK525180/

27. U.S. Department of Health and Human Services. Ending the HIV Epidemic: A Plan for America. Published online February 2020. https://files.hiv.gov/s3fs-public/ending-the-hiv-epidemic-flyer.pdf

28. Georgia Department of Public Health HES. *HIV Surveillance Summary, Georgia 2017*.; 2019. https://dph.georgia.gov/data-fact-sheet-summaries

29. Van Handel MM, Rose CE, Hallisey EJ, et al. County-level vulnerability assessment for rapid dissemination of HIV or HCV infections among Persons who Inject Drugs, United States - Supplemental appendix. *J Acquir Immune Defic Syndr 1999*. 2016;73(3):323-331. doi:10.1097/QAI.0000000000001098

30. Van Handel MM, Rose CE, Hallisey EJ, et al. County-level vulnerability assessment for rapid dissemination of HIV or HCV infections among Persons who Inject Drugs, United States. *J Acquir Immune Defic Syndr 1999*. 2016;73(3):323-331. doi:10.1097/QAI.0000000000001098

31. Sharpe TT, Harrison KM, Dean HD. Summary of CDC consultation to address social determinants of health for prevention of Disparities in HIV/AIDS, Viral Hepatitis, Sexually Transmitted Diseases, and Tuberculosis. *Public Health Rep*. 2010;125(4_suppl):11-15. doi:10.1177/00333549101250S404

32. Dean HD, Fenton KA. Integrating a social determinants of health approach into public health practice: A five-year perspective of actions implemented by CDC's National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. *Public Health Rep*. 2013;128(Suppl 3):5-11.

33. Wilson PA, Nanin J, Amesty S, Wallace S, Cherenack EM, Fullilove R. Using Syndemic Theory to understand vulnerability to HIV infection among Black and Latino Men in New York City. *J Urban Health*. 2014;91(5):983-998. doi:10.1007/s11524-014-9895-2

34. German D, Latkin CA. Social stability and HIV risk behavior: Evaluating the role of accumulated vulnerability. *AIDS Behav*. 2012;16(1):168-178. doi:10.1007/s10461-011-9882-5

35. Du P, McNutt L-A, O'Campo P, Coles FB. Changes in community socioeconomic status and racial distribution associated with Gonorrhea rates: An analysis at the community level. *Sex Transm Dis*. 2009;36(7):430-438. doi:10.1097/OLQ.0b013e31819b8c2f

36. Nuttbrock L, Bockting W, Rosenblum A, et al. Gender abuse, depressive symptoms, and HIV and other Sexually Transmitted Infections among Male-to-Female Transgender Persons: A three-year prospective study. *Am J Public Health*. 2013;103(2):300-307. doi:10.2105/AJPH.2011.300568

37. Acheampong AB, Striley CW, Cottler LB. Prescription opioid use, illicit drug use, and sexually transmitted infections among participants from a community engagement program in North Central Florida. *J Subst Use*. 2017;22(1):90-95. doi:10.3109/14659891.2016.1144805

38. Centers for Disease Control and Prevention. Annual Surveillance Report Of Drug-related Risks And Outcomes. Published online 2019:128.

39. Bryan AD, Magnan RE, Gillman AS, et al. Effect of including alcohol and cannabis content in a sexual risk-reduction intervention on the incidence of Sexually Transmitted Infections in adolescents. *JAMA Pediatr*. 2018;172(4). doi:10.1001/jamapediatrics.2017.5621

40. Brooks A, Meade CS, Potter JS, Lokhnygina Y, Calsyn DA, Greenfield SF. Gender differences in the rates and correlates of HIV risk behaviors among drug abusers. *Subst Use Misuse*. 2010;45(14):2444-2469. doi:10.3109/10826084.2010.490928

41. Chiasson MA, Hirshfield S, Humberstone M, Difilippi J, Koblin BA, Remien RH. Increased high risk sexual behavior after September 11 in men who have sex with men: An internet survey. *Arch Sex Behav*. 2005;34(5):527-535. doi:doi: 10.1007/s10508-005-6278-5

42. Vlahov D, Galea S, Ahern J, Resnick H, Kilpatrick D. Sustained increased consumption of cigarettes, alcohol, and marijuana among Manhattan residents after september 11, 2001. *Am J Public Health*. 2004;94(2):253-254. doi:10.2105/ajph.94.2.253

43. Angeles Perez-Morente M, Teresa Sanchez-Ocon M, Martinez-Garcia E, Martin-Salvador A, Hueso-Montoro C, Garcia-Garcia I. Differences in Sexually Transmitted Infections between the Precrisis Period (2000-2007) and the Crisis Period (2008-2014) in Granada, Spain. *J Clin Med*. 2019;8(2). doi:10.3390/jcm8020277

44. Suhrcke M, Stuckler D, Suk JE, et al. The impact of economic crises on communicable disease transmission and control: A systematic review of the evidence. *PLoS ONE*. 2011;6(6):1-12. doi:10.1371/journal.pone.0020724

45. Walker M. COVID-19 Upended HIV Prevention Efforts at Boston Clinic. Published July 6, 2020. Accessed July 7, 2020. https://www.medpagetoday.com/meetingcoverage/iac/87423

46. Sanchez TH, Zlotorzynska M, Rai M, Baral SD. Characterizing the Impact of COVID-19 on Men Who Have Sex with Men Across the United States in April, 2020. *AIDS Behav*. 2020;24(7):2024-2032. doi:10.1007/s10461-020-02894-2

47. Halkitis PN, Kutnick AH, Rosof E, Slater S, Parsons JT. Adherence to HIV medications in a cohort of Men Who Have Sex With Men: Impact of September 11th. *J Urban Health Bull N Y Acad Med*. 2003;80(1):161-166. doi:10.1093/jurban/jtg161

48. Ibragimov U, Beane S, Friedman SR, et al. States with higher minimum wages have lower STI rates among women: Results of an ecological study of 66 US metropolitan areas, 2003-2015. *PLoS ONE*. 2019;14(10). doi:10.1371/journal.pone.0223579

49. Mann JR, Stine CC, Vessey J. The role of disease-specific infectivity and number of disease exposures on long-term effectiveness of the latex condom. *Sex Transm Dis*. 2002;29(6):344-349. doi:10.1097/00007435-200206000-00006

50. Steiner MJ, Cates W, Warner L. The real problem with male condoms Is nonuse. *Sex Transm Dis*. 1999;26(8):459-462. doi:10.1097/00007435-199909000-00007

51. Siegler AJ, Rosenthal EM, Sullivan PS, et al. Levels of clinical condom failure for anal sex: A randomized cross-over trial. *EClinicalMedicine*. 2019;17. doi:10.1016/j.eclinm.2019.10.012

52. Cohen D, Scribner R, Bedimo R, Farley TA. Cost as a barrier to condom use: The evidence for condom subsidies in the United States. *Am J Public Health*. 1999;89(4):567-568. doi:10.2105/ajph.89.4.567

53. Charania MR, Crepaz N, Guenther-Gray C, et al. Efficacy of structural-level condom distribution interventions: A meta-analysis of U.S. and international studies, 1998–2007. *AIDS Behav*. 2011;15(7):1283-1297. doi:10.1007/s10461-010-9812-y

54. McCool-Myers M, Myo A, Carter JA. Barriers to purchasing condoms in a high HIV/STI-risk urban area. *J Community Health*. 2019;44(4):836-843. doi:10.1007/s10900-019-00670-5

55. Albarracín D, Gillette JC, Earl AN, Glasman LR, Durantini MR, Ho M-H. A test of major assumptions about behavior change: A comprehensive look at the effects of passive and active HIV-prevention interventions since the beginning of the epidemic. *Psychol Bull*. 2005;131(6):856-897. doi:10.1037/0033-2909.131.6.856

56. Huebner DM, Perry NS. Do behavioral scientists really understand HIV-related sexual risk behavior? A systematic review of longitudinal and experimental studies predicting sexual behavior. *Arch Sex Behav*. 2015;44(7):1915-1936. doi:10.1007/s10508-015-0482-8

57. Montaño MA, Dombrowski JC, Dasgupta S, et al. Changes in sexual behavior and STI diagnoses among MSM initiating PrEP in a clinic setting. *AIDS Behav*. 2019;23(2):548-555. doi:10.1007/s10461-018-2252-9

58. Volk JE, Marcus JL, Phengrasamy T, et al. No new HIV infections with increasing use of HIV Preexposure Prophylaxis in a clinical practice setting. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2015;61(10):1601-1603. doi:10.1093/cid/civ778

59. Golub S, Pena S, Boonrai K, Douglas N, Hunt M, Radix A. STI data from community-based PrEP implementation suggest changes to CDC guidelines. Presented at the: Conference on Retroviruses and Opportunistic Infections; February 2016; Boston, MA. Accessed July 7, 2020. https://www.croiconference.org/abstract/sti-data-community-based-prep-implementation-suggest-changes-cdc-guidelines-0/

60. Huebner DM, Rebchook GM, Kegeles SM. A longitudinal study of the association between treatment optimism and sexual risk behavior in young adult gay and bisexual men. *JAIDS J Acquir Immune Defic Syndr*. 2004;37(4):1514-1519. doi:10.1097/01.qai.0000127027.55052.22

61. Freeborn K, Portillo CJ. Does pre-exposure prophylaxis for HIV prevention in men who have sex with men change risk behaviour? A systematic review. *J Clin Nurs*. 2018;27(17-18):3254-3265. doi:10.1111/jocn.13990

62. Rojas Castro D, Delabre RM, Molina J. Give PrEP a chance: Moving on from the "risk compensation" concept. *J Int AIDS Soc*. 2019;22:N.PAG-N.PAG. doi:10.1002/jia2.25351

63. Collins S, McMahan V, Stekler J. The impact of HIV Pre-exposure Prophylaxis (PrEP) use on the sexual health of Men Who Have Sex with Men: A qualitative study in Seattle, WA. doi:10.1080/19317611.2016.1206051

64. Storholm ED, Volk JE, Marcus JL, Silverberg MJ, Satre DD. Risk perception, sexual behaviors, and PrEP adherence among substance-using men who have sex with men: A qualitative study. *Prev Sci Off J Soc Prev Res*. 2017;18(6):737-747. doi:10.1007/s11121-017-0799-8

65. Stanger-Hall KF, Hall DW. Abstinence-only education and teen pregnancy rates: Why we need comprehensive sex education in the U.S. *PLoS ONE*. 2011;6(10). doi:10.1371/journal.pone.0024658

66. Chin HB, Sipe TA, Elder R, et al. The effectiveness of group-based comprehensive risk-reduction and abstinence education interventions to prevent or reduce the risk of adolescent pregnancy, Human Immunodeficiency Virus, and Sexually Transmitted Infections. *Am J Prev Med*. 2012;42(3):272-294. doi:10.1016/j.amepre.2011.11.006

67. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 Infection with early antiretroviral therapy. *N Engl J Med*. 2011;365(6):493-505. doi:10.1056/NEJMoa1105243

68. Centers for Disease Control and Prevention. TasP Technical Fact Sheet. Published online 2018. Accessed February 24, 2020. https://www.cdc.gov/hiv/pdf/risk/art/cdc-hiv-art-viral-suppression.pdf

69. Mayer K, Gazzard B, Zuniga JM, et al. Controlling the HIV epidemic with antiretrovirals: IAPAC consensus statement on Treatment as Prevention and Preexposure Prophylaxis. *J Int Assoc Provid AIDS Care JIAPAC*. 2013;12(3):208-216. doi:10.1177/2325957413475839

70. U.S. Department of Health and Human Services. The Stages of HIV Infection Understanding HIV/AIDS. AIDSinfo. Published June 25, 2019. Accessed April 26, 2020. https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/19/46/the-stages-of-hiv-infection

71. Mandsager P, Marier A, Cohen S, Fanning M, Hauck H, Cheever LW. Reducing HIV-related health disparities in the Health Resources and Services Administration's Ryan White HIV/AIDS Program. *Am J Public Health*. 2018;108:S246-S250. doi:10.2105/AJPH.2018.304689

72. Barnhart M. Long-Acting HIV treatment and prevention: Closer to the threshold. *Glob Health Sci Pract*. 2017;5(2):182-187. doi:10.9745/GHSP-D-17-00206

73. U.S. Department of Health and Human Services. Pre-Exposure Prophylaxis. HIV.gov. Published December 3, 2019. Accessed August 23, 2020. https://www.hiv.gov/hiv-basics/hiv-prevention/using-hiv-medication-to-reduce-risk/pre-exposure-prophylaxis

74. World Health Organization. *What's the 2+1+1? Event-Driven Oral Pre-Exposure Prophylaxis to Prevent HIV for Men Who Have Sex with Men: Update to WHO's Recommendation on Oral PrEP*.; 2019. Accessed March 14, 2020. https://apps.who.int/iris/bitstream/handle/10665/325955/WHO-CDS-HIV-19.8-eng.pdf?ua=1

75. Centers for Disease Control and Prevention. *2017 Hepatitis Surveillance Report*. Accessed April 5, 2020. https://www.cdc.gov/hepatitis/statistics/2017surveillance/pdfs/2017HepSurveillanceRpt.pdf

76. Markowitz M, Grossman H, Anderson PL, et al. Newly acquired infection with multidrug-resistant HIV-1 in a patient adherent to Preexposure Prophylaxis. *JAIDS J Acquir Immune Defic Syndr*. 2017;76(4):e104. doi:10.1097/QAI.0000000000001534

77. Radzio-Basu J, Council O, Cong M, et al. Drug resistance emergence in macaques administered cabotegravir long-acting for pre-exposure prophylaxis during acute SHIV infection. *Nat Commun*. 2019;10. doi:10.1038/s41467-019-10047-w

78. U.S. Department of Health and Human Services. What to Start Adult and Adolescent ARV. AIDSinfo. Published December 18, 2019. Accessed April 5, 2020. https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/11/what-to-start

79. Underhill K. Intimacy, condom use, and Pre-Exposure Prophylaxis (PrEP) acceptability among men who have sex with men (MSM) in primary partnerships: A comment on Gamarel and Golub. *Ann Behav Med Publ Soc Behav Med*. 2015;49(2):151-153. doi:10.1007/s12160-014-9651-6

80. Smith DK, Van Handel M, Grey J. Estimates of adults with indications for HIV pre-exposure prophylaxis by jurisdiction, transmission risk group, and race/ethnicity, United States, 2015. *Ann Epidemiol*. 2018;28(12):850-857.e9. doi:10.1016/j.annepidem.2018.05.003

81. Pinto RM, Berringer KR, Melendez R, Mmeje O. Improving PrEP implementation through multilevel interventions: A synthesis of the literature. *AIDS Behav*. 2018;22(11):3681-3691. doi:10.1007/s10461-018-2184-4

82. Elion R, Coleman M. The preexposure prophylaxis revolution: From clinical trials to routine practice: Implementation view from the USA. *Curr Opin HIV AIDS*. 2016;11(1):67-73. doi:10.1097/COH.0000000000000222

83. Siegler AJ, Bratcher A, Weiss KM. Geographic access to Preexposure Prophylaxis clinics among men who have sex with men in the United States. *Am J Public Health*. 2019;109(9):1216-1223.

84. Biello KB, Bazzi AR, Mimiaga MJ, et al. Perspectives on HIV pre-exposure prophylaxis (PrEP) utilization and related intervention needs among people who inject drugs. *Harm Reduct J*. 2018;15. doi:10.1186/s12954-018-0263-5

85. Cahill S, Taylor SW, Elsesser SA, Mena L, Hickson D, Mayer KH. Stigma, medical mistrust, and perceived racism may affect PrEP awareness and uptake in black compared to white gay and bisexual men in Jackson, Mississippi and Boston, Massachusetts. *AIDS Care*. 2017;29(11):1351-1358. doi:10.1080/09540121.2017.1300633

86. Paparini S, Nutland W, Rhodes T, Nguyen V-K, Anderson J. DIY HIV prevention: Formative qualitative research with men who have sex with men who source PrEP outside of clinical trials. *PLoS ONE*. 2018;13(8). doi:10.1371/journal.pone.0202830

87. Horberg M, Raymond B. Financial policy issues for HIV Pre-Exposure Prophylaxis: Cost and access to insurance. *Am J Prev Med*. 2013;44(1, Supplement 2):S125-S128. doi:10.1016/j.amepre.2012.09.039

88. Smith DK, Van Handel M, Huggins R. Estimated Coverage to Address Financial Barriers to HIV Preexposure Prophylaxis Among Persons With Indications for Its Use, United States, 2015: *JAIDS J Acquir Immune Defic Syndr*. 2017;76(5):465-472. doi:10.1097/QAI.0000000000001532

89. Koss CA, Hosek SG, Bacchetti P, et al. Comparison of aeasures of adherence to Human Immunodeficiency Virus Preexposure Prophylaxis among adolescent and young men who have sex with men in the United States. *Clin Infect Dis*. 2018;66(2):213-219. doi:10.1093/cid/cix755

90. John SA, Whitfield THF, Rendina HJ, Parsons JT, Grov C. Why I quit Pre-Exposure Prophylaxis (PrEP)? A mixed-method study exploring reasons for PrEP discontinuation and potential re-

initiation among gay and bisexual men. *AIDS Behav*. 2018;22(11):3566-3575. doi:10.1007/s10461-018-2045-1

91. Lankowski AJ, Bien-Gund CH, Patel VV, Felsen UR, Silvera R, Blackstock OJ. PrEP in the Real World: Predictors of 6-Month Retention in a Diverse Urban Cohort. *AIDS Behav*. 2019;23(7):1797-1802. doi:10.1007/s10461-018-2296-x

92. Underhill K, Guthrie KM, Colleran C, Calabrese SK, Operario D, Mayer KH. Temporal fluctuations in behavior, perceived HIV risk, and willingness to use Pre-Exposure Prophylaxis (PrEP). *Arch Sex Behav*. 2018;47(7):2109-2121. doi:10.1007/s10508-017-1100-8

93. Elsesser SA, Oldenburg CE, Biello KB, et al. Seasons of risk: anticipated behavior on vacation and interest in episodic antiretroviral Pre-Exposure Prophylaxis (PrEP) among a large national sample of U.S. men who have sex with men (MSM). *AIDS Behav*. 2016;20(7):1400-1407. doi:10.1007/s10461-015-1238-0

94. Namey E, Agot K, Ahmed K, et al. When and why women might suspend PrEP use according to perceived seasons of risk: implications for PrEP-specific risk-reduction counselling. *Cult Health Sex*. 2016;18(9):1081-1091. doi:10.1080/13691058.2016.1164899

95. Dubov A, Altice FL, Fraenkel L. An Information–Motivation–Behavioral Skills model of PrEP uptake. *AIDS Behav*. 2018;22(11):3603-3616. doi:10.1007/s10461-018-2095-4

96. Trent-Adams S, Cheever LW. Providing HIV Pre-Exposure Prophylaxis: Lessons learned from the Ryan White HIV/AIDS Program. *Am J Prev Med*. 2013;44(1, Supplement 2):S147-S150. doi:10.1016/j.amepre.2012.09.031

97. Bernard CL, Brandeau ML, Humphreys K, et al. Cost-effectiveness of HIV Preexposure Prophylaxis for people who inject drugs in the United States. *Ann Intern Med*. Published online April 26, 2016. doi:10.7326/M15-2634

98. Juusola JL, Brandeau ML. HIV treatment and prevention: A aimple model to determine optimal investment. *Med Decis Making*. 2016;36(3):391-409. doi:10.1177/0272989X15598528

99. National Alliance of State and Territorial AIDS Directors. NASTAD PrEP financing models chart. Published online 2018. Accessed May 5, 2020. https://www.nastad.org/sites/default/files/nastad_prep_financing_models_chart_8.1.16.pdf

100. Smith DK, Van Handel M, Huggins R. Estimated coverage to address financial barriers to HIV Preexposure Prophylaxis among persons with indications for its use, United States, 2015. *JAIDS J Acquir Immune Defic Syndr*. 2017;76(5):465-472. doi:10.1097/QAI.0000000000001532

101. Leichliter JS, Heyer K, Peterman TA, et al. U.S. public STD clinical services in an era of declining public health funding: 2013–14. *Sex Transm Dis*. 2017;44(8):505-509. doi:10.1097/OLQ.0000000000000629

102. Sukhija-Cohen AC, Beymer MR, Engeran-Cordova W, Bolan RK. From control to crisis: The resurgence of Sexually Transmitted Diseases. *Sex Transm Dis*. 2019;46(2):e8-e10. doi:10.1097/OLQ.0000000000000960

103. Myers JE, Edelstein ZR, Daskalakis DC, et al. Preexposure Prophylaxis monitoring in New York City: A public health approach. *Am J Public Health*. 2018;108:S251-S257. doi:10.2105/AJPH.2018.304729

104. Zhang HL, Rhea SK, Hurt CB, et al. HIV pre-exposure prophylaxis implementation at local health departments: A statewide assessment of activities and barriers. *J Acquir Immune Defic Syndr 1999*. 2018;77(1):72-77. doi:10.1097/QAI.0000000000001546

105. Georgia Department of Public Health. *Georgia Integrated HIV Prevention and Care Plan 2017-2021*. Accessed May 6, 2020. https://dph.georgia.gov/health-topics/office-hivaids

106. *WHO Implementation Tool for Pre-Exposure Prophylaxis (PrEP) of HIV Infection*. World Health Organization; 2018. Accessed July 7, 2020. https://apps.who.int/iris/bitstream/handle/10665/279834/WHO-CDS-HIV-18.10-eng.pdf?ua=1

107. Centers for Disease Control and Prevention. *Preexposure Prophylaxis for the Prevention of HIV Infeciton in the United States - 2017 Update Clinical Provider's Supplement*. US Public Health Service; 2018. Accessed July 8, 2020. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-provider-supplement-2017.pdf

108. Parisi D, Warren B, Leung SJ, et al. A Multicomponent Approach to Evaluating a Pre-exposure Prophylaxis (PrEP) Implementation Program in Five Agencies in New York. *J Assoc Nurses AIDS Care JANAC*. 2018;29(1):10-19. doi:10.1016/j.jana.2017.06.006

APPENDIX

INSTITUTIONAL REVIEW BOARD APPROVAL FORM

GEORGIA SOUTHERN UNIVERSITY
RESEARCH INTEGRITY

Institutional Review Board (IRB)
Veazey Hall 3000
PO Box 8005 • STATESBORO, GA 30460
Phone: 912-478-5465
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IRB@GeorgiaSouthern.edu

To:	Purdy, Ellie; Mase, William; Smallwood, Stacy; Kimsey, Linda
From:	Eleanor Haynes, Director, Research Integrity
Approval Date:	10/9/2020
Subject:	Institutional Review Board Exemption Determination - Limited Review

Your proposed research project numbered **H21095,** and titled **"Thinking Ethically about HIV Pre-Exposure Prophylaxis: Retention in Care and Sexually Transmitted Infection Testing in a Southeastern United States Local Health Department in the time of COVID-19."** involves activities that do not require full approval by the Institutional Review Board (IRB) according to federal guidelines.

According to the Code of Federal Regulations Title 45 Part 46, your research protocol is determined to be exempt from full review under the following exemption category(s):

Exemption 4 Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met: The identifiable private information or identifiable biospecimens are publicly available; Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects.

Any data use agreement or agreement change required by the data owner must be supplied to the IRB prior to execution for review. This approval is contingent upon researcher compliance with the conditions of the data use agreement (where required) and current institutional data security policy.

Any alteration in the terms or conditions of your involvement may alter this approval. *Therefore, as authorized in the Federal Policy for the Protection of Human Subjects, I am pleased to notify you that your research, as submitted, is exempt from IRB Review. No further action or IRB oversight is required, as long as the project remains the same. If you alter the project, it is your responsibility to notify the IRB and acquire a new determination of exemption. Because this project was determined to be exempt from further IRB oversight, this project does not require an expiration date.*