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Understanding HIV disparities by examining trends and partnership characteristics in racial/ethnic and sexual minorities in the United States

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Doctor of Philosophy
Epidemiology

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By

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MPH, Emory University, 2013
BA, Johns Hopkins University, 2008

Advisor: Eli S. Rosenberg, PhD

An abstract of
a dissertation submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
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By Johanna Chapin Bardales

Racial/ethnic and sexual minorities are disproportionately affected by HIV and AIDS in the United States. National HIV/AIDS strategies seek to reduce HIV disparities, yet limited research has evaluated HIV disparity measures over time. Among men who have sex with men (MSM), sexual networks of partnerships likely facilitate HIV transmission and may contribute to age and race disparities. In this dissertation, we evaluate historical trends in HIV-related racial/ethnic disparities and examine how partner-related factors may be driving age and race disparities for MSM.

In **Aim 1**, we evaluated trends in US racial/ethnic disparities of new AIDS diagnoses over a 30-year period. Black-White disparity increased at varying magnitudes from 1984 through 2001, narrowed from 2002-2005, then rose again from 2006-2013. Hispanic-White disparity increased from 1984-1997, then declined. For MSM, Black-White and Hispanic-White disparities increased from 2008-2013.

Aim 2 examined trends in partner counts and composition among MSM to assess how partner type may be changing in the context of increasing acceptance of same-sex partnerships. Overall, the total number of male sex partners in the past year increased, while the number of main partners remained stable. We observed a shift from MSM having ≥1 main partners and 0 casual partners to having ≥1 main partners and ≥2 casual partners.

In **Aim 3**, we simulated the effects of age and partner type on HIV transmission in a dynamic sexual network model of MSM. Approximately 60% of all HIV transmissions arose from casual and one-time partners combined, though main partners still accounted for 40%. This distribution by partner type did not differ by age.

In this dissertation, we found that HIV-related racial/ethnic disparities increased in recent years, particularly for MSM. Among MSM, the increases in casual partnerships and shift towards having both main and casual partnerships suggest that sexual partnering patterns conducive to HIV transmission, such as concurrency, may be increasing for MSM and possibly contributing to increases in HIV incidence or disparity trends. As casual partnerships accounted for most HIV transmissions across ages of MSM and casual partnering may be recently increasing, MSM with casual partnerships remain a high-leverage target for HIV prevention interventions.

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CHAPTER 1: Background and Significance

1.1 HIV Prevalence and Incidence in the United States

Approximately 1.1 million persons were living with HIV in the United States and about 40,000 were newly diagnosed with HIV in 2016.[1] Over the past decade, the annual incidence of HIV has remained stable or slightly declined for some subgroups of the population, while HIV prevalence continues to increase given longer life expectancy in the era of effective combination antiretroviral therapy (ART).[2-5] AIDS diagnoses have decreased steadily over the past two decades since the introduction of ART. In 1995, there were over 70,000 annual AIDS diagnoses; in 2016, this figure had declined to 18,000 AIDS diagnoses.[1,6] Despite decreasing AIDS rates and stable or declining HIV rates in recent years, large disparities in HIV and AIDS remain for racial/ethnic and sexual minorities.

1.2 HIV in Racial/Ethnic Minorities

HIV and AIDS disproportionately affect racial/ethnic minority groups including Blacks/African Americans (Blacks) and Hispanics/Latinos (Hispanics).[2] Blacks and Hispanics represent 12% and 16% of the total US population, but accounted for 43% and 20% of people living with a diagnosed HIV infection and 42% and 22% of people living with a diagnosed HIV infection ever classified as AIDS, respectively, in 2013.[2,7] Additionally, the annual rate of new HIV diagnoses in 2014 was 49.2 per 100,000 among Blacks, 17.3 per 100,000 among Hispanics, and 5.9 among Whites, indicating that Blacks experience 8 times, and Hispanics 3 times, the rate of HIV diagnoses compared to Whites.[7] These estimates of disparity are similar for annual new AIDS diagnoses, with rates of 25.4 per 100,000 among Blacks, 7.7 per 100,000 among Hispanics, and 2.7 per 100,000 among Whites in 2014, resulting in a 9-fold and a 3-fold higher disparity for Blacks and Hispanics, respectively, compared to Whites.[7] Because of the inequalities in HIV that racial minorities face, the US National HIV/AIDS Strategy (NHAS) established goals to reduce HIV disparities in racial/ethnic and sexual minorities. Yet, research to improve methods examining racial/ethnic disparities in HIV over time and their possible causes will be critical to identifying and intervening on factors driving these disparities.

Trends in Racial/Ethnic Disparities in HIV and Limitations of Trend Analyses

Several studies have considered trends in the racial/ethnic disparities in HIV, AIDS, and HIV-related mortality over time. [8-12] HIV surveillance reports have shown that annual rates of HIV diagnoses from 2001-2004 were decreasing for Blacks and Hispanics while remaining stable for Whites.[8] Yet, from 2005-2008, HIV diagnosis rates for Black men appeared to be slightly increasing.[9] Although surveillance reports provide timely data that inform racial/ethnic disparities, limited research has assessed how disparities have evolved using consistently-defined disparity measures as the primary outcomes of interest. Most surveillance reports present trends only in the individual race-specific rates of HIV/AIDS diagnoses separately, and although these are important for context in understanding trends, they do not directly quantify changes in measures of relative or absolute disparity. As NHAS objectives seek to reduce disparities, defining consistent disparity measures and assessing changes in these outcomes over time will be vital to monitoring progress in achieving NHAS goals.

Three studies have recognized limitations in reporting only race-specific trends individually and have addressed this by modeling trends in measures of racial/ethnic disparity as the outcomes of interest. One of these analyses studied racial disparities in AIDS diagnoses and considered a period from 2000 to 2009.[10] The An et al. study found a significant decline in racial/ethnic disparities in AIDS diagnoses for most demographic groups except for young men ages 13-24.[10] This finding suggested that racial disparities in AIDS are generally declining overall in recent years, but that trends are increasing for young men, likely representing growing racial disparities among young MSM.[10] Although the An et. al study provided important evidence on recent racial/ethnic disparities in the past decade, conclusions about increasing and decreasing trends depend substantially on the length of time and years included in the analysis. Potential increases or decreases in disparity trends may be missed when limiting data to a shorter time period (one particular 5-year or 10-year interval) and assuming one uniform, linear trend in the data over this period.

Two other studies considered outcomes in the Black-White relative disparity (rate ratio) in HIV mortality over a period from 1987-2011 and 1990-2009.[11,12] One study demonstrated increasing trends in the Black-White relative disparity from 1987-1995 followed by a stabilized trend from 1995-2011.[11] The other study found a higher Black-White disparity in 2005-2009 compared to 1990-1994.[12] These studies have explored trends in racial/ethnic disparities in mortality, yet both studies relied on the arbitrary selection of 5-year intervals or the visual inspection of inflection points to define the trend periods of analysis, which may miss or hide important changes in trends.

Methodologies for empirically determining years when changes in trends occur have been employed frequently in chronic disease epidemiology and surveillance, but have not yet been applied to HIV epidemiology.[13,14] For example, Joinpoint Regression software uses Bayesian statistical methods including Monte Carlo permutation tests to identify statistically significantly different slopes in the trend and the inflection points at which these changes in trends occur.[13,14] Therefore, studying a longer period of time over the course of the HIV epidemic, allowing for changes in trends of the disparity outcomes, and empirically deriving the year(s) in which changes in disparity trends occur could provide a more accurate and precise detection and interpretation of patterns of change in racial/ethnic disparities of HIV/AIDS outcomes.[15] Stratifying racial disparity trends by age, sex, and transmission category could further help to provide accurate interpretation of trends by identifying subgroups that may be driving overall disparities. This dissertation work focuses on racial/ethnic disparity trends in new AIDS diagnoses, as AIDS diagnoses data have been the most routinely and systematically collected indicator by national HIV surveillance systems over the course of the US HIV epidemic.[16]

1.3 HIV in Men Who Have Sex With Men (MSM) in the United States

HIV has predominantly affected men who have sex with men (MSM) in the United States. MSM represent approximately 2% of the US population yet experience 70% of all new HIV diagnosess.[17] From 2008 to 2010, the number of new HIV infections among MSM increased by 12% and HIV prevalence among MSM is currently estimated at 22%.[18-20] Approximately 17% of HIV-positive MSM were not aware of their HIV infection.[21] As one of the most affected risk groups, much research and many HIV prevention efforts have targeted MSM, yet high HIV incidence rates persist.[21,22] CDC has estimated that if current incidence rates continue, up to 1 in 6 MSM could be diagnosed with HIV in their lifetime.[23] Thus, NHAS and Healthy People 2020 guidelines have emphasized urgent efforts to implement effective public health interventions and policies to reduce HIV risk among MSM.[24-26]

Age and Race Disparities in HIV among MSM

The disparate rates of HIV infection that MSM face are compounded by race and age disparities among MSM. In 2014, HIV prevalence among Black MSM was 36% compared to 17% for Hispanic MSM and 15% for White MSM.[19] From 2008-2010, HIV incidence was estimated to have increased by 10% for Black MSM, by 19% for Hispanic MSM, and 15% for

White MSM nationally.[20] In a cohort study of MSM in Atlanta, GA, Black MSM were found to have an estimated 6.5 new HIV infections per person-year (PY) compared to an incidence rate of 1.7 per PY among White MSM.[27] At current incidence and prevalence rates, CDC has estimated that as high as 1 in 2 Black MSM and 1 in 4 Hispanic MSM could experience an HIV diagnosis in their lifetime, suggesting substantial need to understand and address HIV disparities for minority MSM in the United States.[23] Black and Hispanic MSM are also less likely to be aware of their HIV infection.[21] HIV-positive Black MSM, compared to HIV-positive White MSM, are less likely to be diagnosed (75% vs. 84%), retained in care (24% vs. 43%), on ART (20% vs. 39%), and virally suppressed (16% vs. 34%).[28] Researchers estimated that if these percentages for HIV care continuum indicators in Black MSM were equivalent to those in White MSM, the relative Black-White disparity could be reduced by 27%; if both diagnosis and retention in care were increased to 95% in Black MSM, the relative Black-White disparity could be reduced by 59%.[28] A recent CDC surveillance report using 2015 data showed that among HIV-positive Black, Hispanic, and White MSM, 80%, 84%, and 89% were linked to care within 3 months of an HIV diagnosis, 54%, 58%, and 59% were retained in care, , and 52%, 61%, and 67% were virally suppressed, respectively.[29] These statistics demonstrate that Black MSM tend to have the lowest levels of engagement across the care continuum and that although Hispanic MSM are less likely to be recently tested and aware of their HIV infection[19], once they are diagnosed, they have similar levels of retention in care as their White counterparts.[29]

Young MSM (YMSM) ages 13-24 years have particularly been affected by the HIV epidemic. From 2010 to 2015, about 1 in 5 (19%) of all HIV diagnoses were in males aged 13-24 years.[30] Of all diagnoses in young men, 91% were in young MSM.[30] Racial disparities also persist among YMSM, with Black and Hispanic YMSM sharing a disproportionate burden of the current HIV epidemic in the United States. In 2016, 54% and 24% of new HIV diagnoses in YMSM were among Black and Hispanic YMSM, respectively.[30] Estimated HIV incidence from 2007-2010 was highest among young Black MSM, accounting for 45% of new HIV infections among Black MSM and 55% of new HIV infections among all YMSM.[20] In the Atlanta cohort study, HIV incidence was highest in young Black MSM ages 18-24 with an incidence rate of 10.9 per PY, nearly 12 times the incidence rate in White YMSM of the same age, demonstrating marked racial disparities for MSM overall and for YMSM.[27] YMSM are also less likely to be aware of their HIV infection. In 2014, 52% of HIV-positive MSM ages 13-24 were unaware of their HIV infection, the largest percentage of unawareness in all age groups.[21] Of HIV-positive YMSM ages 13-24, 82% are linked to care within 3 months of their diagnosis, 55% are retained in care, and 50.9% are virally suppressed, and these percentages are consistently lower compared to other age groups across each step of the care continuum.[29]

Trends in HIV among MSM Overall, By Race, and By Age

Globally, HIV diagnoses among MSM increased from 1996 through 2005, though more recent data show stabilization or slight declines in MSM HIV diagnoses from 2005 to 2014.[31,32] In the United States, HIV diagnoses in MSM overall are relatively stable, with a slight increase of 6% from 2005-2014.[33,34] However, this overall trend does not capture the heterogeneity of trends by race and age. From 2005-2014, HIV diagnoses among Black MSM increased by 22%, with most of this increase occurring from 2005-2008 and then stabilizing through 2014.[33] Among Hispanic MSM, diagnoses increased by 24% and this trend was a steady increase over the entire time period.[33] Diagnoses among White MSM declined overall by 18%, with a stable trend from 2005-2007, followed by a gradual decline through 2014.[33] These results demonstrate significant diversity in HIV trends within racial/ethnic groups of MSM. Although a stabilized trend after years of rising diagnoses for Black MSM is encouraging, Black MSM still account for the largest number of HIV diagnoses among MSM per year. A steadily increasing trend for Hispanic MSM over the past decade, including a 13% increase in the past five years (2010-2014) when trends for other racial/ethnic MSM subgroups had stabilized, is a concerning finding and suggests an increasing need for HIV prevention strategies for Hispanic MSM.[33]

In YMSM, HIV incidence increased by an estimated 22% overall from 2008-2010.[20] Other surveillance data demonstrated that from 2005-2014, HIV diagnoses in Black YMSM ages 13-24 increased by 87%, however a small 2% decline was observed in the past 5 years.[33,34] Hispanic YMSM also experienced an 87% increase in diagnoses over the past decade, and this was characterized by a steady increase across the entire time period, including a slower, but consistent increase of 16% from 2010-2014.[33] For White YMSM, diagnoses increased by 56%, though the trend stabilized for this group from 2010-2014.[33] A recent study by Wejnert et al. considered trends in HIV prevalence among MSM by age and race using data from the National HIV Behavioral Surveillance (NHBS) system at the Centers for Disease Control and Prevention (CDC).[35] In this study, HIV prevalence in Black MSM ages 18-24 years was 5 times that in White MSM of the same age in 2014.[35] When the prevalence ratio capturing Black-White disparity among MSM from 2008-2014 was compared over continuous years of age, the authors found over a 25% increase in Black-White disparity in the youngest MSM (18 years).[35] This was the largest increase in disparity from 2008-2014 and remained at a similar magnitude through age 26.[35]

Collectively, these data indicate that though trends in HIV may be stabilizing for MSM overall, racial/ethnic and age disparities in HIV for MSM continue to persist in the United States. Black MSM and Black YMSM continue to account for large proportions of HIV incidence and prevalence among all MSM, and increasing disparity trends comparing Black and White MSM appear to be highest at younger ages.[35] Furthermore, Hispanic MSM and YMSM have been experiencing increasing rates of HIV diagnoses over the past decade and in recent years, warranting further consideration of factors that may be perpetuating these disparities.

Multi-level Factors Associated with HIV Disparities in MSM Overall

Multiple factors contribute to HIV disparities for MSM in general and specifically for age and race subgroups of MSM. At the individual biological level, the per-act probability of HIV transmission for anal sex is 1.4%, approximately 18 times higher than that of vaginal sex.[36,37] In addition to increased risk from condomless anal sex (CAS), other individual risk factors include having condomless receptive anal sex and using injection and non-injection drugs.[38,39] Having a high frequency of male partners and having a high number of lifetime male sex partners have also been considered key individual risk factors for HIV.[38,39]

Although individual-level factors are important criteria for biological and behavioral intervention, researchers have long acknowledged that risk factors at the dyad-, network-, and structural-level shape individual risk for HIV. Structural-level factors such as access to healthcare have significant implications for understanding and intervening on disparities in the care continuum for MSM and particularly minority MSM.[28,40,41] For example, Black MSM were less likely to have visited a healthcare provider within 3 months of an HIV diagnosis compared to White MSM, which serves as the first step towards engagement in care.[41] Stigma and place-based social environments may also act as structural-level factors that limit utilization of health and prevention services, worsening disparities for MSM and young, minority MSM.[40]

Dyad- and network-level factors are also key to understanding HIV risk among MSM. At the dyad (or partner)-level, MSM are more likely to engage in CAS with partners they consider "main" or "steady" compared to "casual" partners, indicating that partner type is important for describing the context in which HIV transmission may be occurring in MSM.[19].[42,43] Men may also seek sex partners of the same HIV status as a form of risk reduction (serosorting), though this requires accurate disclosure of HIV status.[44-46] In addition, it is important to acknowledge that individual factors with respect to partner number (e.g., high frequency of male partners) are not only risk factors for the individual (the ego), but also for the ego's partner(s) if the ego is engaging in CAS with multiple, concurrent partners. Concurrency can be defined as "overlapping sexual partnerships where sexual intercourse with one partner occurs between two acts of intercourse with another partner."[47] Concurrency can contribute to the spread of infection in a sexual network via partners' indirect exposure to one another.[48-50] Although a high number of partners is a risk factor for the ego as he is exposed to more men that may have HIV or STIs, it is the ego's concurrency patterns that can be considered a risk factor for the ego's partners at the dyadic and network level. Estimates of concurrency in the past year among US MSM are higher than those in heterosexual men and have ranged from 18-78%; concurrent CAS in the past 6 months has been estimated at 16% in MSM.[51-54] Because of the high prevalence of concurrency in MSM, understanding and accounting for concurrency is important when studying the role of dyadic partnerships in HIV transmission and identifying drivers of HIV disparities in MSM overall and in age- and race-specific groups of MSM.

Heightened HIV disparities for Black, Hispanic, and young MSM are also attributed to factors beyond individual risk behaviors. In 2006, Millet et al. outlined 12 hypotheses to explain the striking HIV disparities for Black MSM and found that individual-level factors such as rates of CAS, disclosure of sexual identity, and drug use were not large contributors to the observed disparities, but that differences in sexually transmitted infections (STIs) and unaware infection could be key factors.[55] A subsequent meta-analysis confirmed these latter hypotheses.[56] Black MSM reported lower rates of CAS and fewer partners compared to White MSM.[56] Black MSM were also more likely to have STIs and less likely to be on antiretroviral therapy (ART), attributing disparities to differences in healthcare access and uptake as opposed to individual behavioral factors.[56,57] Existing high HIV prevalence in Black MSM and assortative racial mixing at the partner and network levels could also explain greater HIV transmission in Black MSM.[41] For example, having an HIV-positive partner with high viral load and having a partner of Black/African-American race have been associated with increased risk of HIV infection.[27,38,58] Men with high viral loads have a higher probability of transmitting HIV due to greater infectiousness.[59-61] Associations between having a Black/African American partner and HIV incidence suggest that disparities may be explained, at least in part, by differences in partner characteristics and sexual networks that are defined by assortative racial mixing patterns.[40,41,58,42,62-65] An updated literature review reiterated many of these findings, but described conflicting conclusions about the impact of partner and network factors on race and age disparities in MSM nationally.[66] Specifically in Atlanta, evidence has suggested that sexual networks and racial composition of networks contribute to HIV disparities for Black MSM and young Black MSM.[27,67,68] In one Atlanta study, the mean network HIV prevalence was 36% in sexual networks of Black MSM seed participants and 4% in sexual networks of White MSM seeds.[68] Black MSM in Atlanta were three times more likely to have HIV transmission risk (ie. viral load >400 copies/ml) and researchers estimated that Black MSM would only need to encounter three CAS partners before having a >50% chance that one of these CAS partners had

HIV transmission risk, compared to an estimate of 7 partners for White MSM.[67] These findings suggest that although risk behaviors may be similar across races, the higher HIV prevalence and racial assortativity found in the sexual networks of Black MSM are important contextual factors for racial disparities in HIV transmission. Less is known about the sexual networks of Hispanic MSM or of YMSM, yet similar partner and network characteristics could contribute to disparities for these groups. In the Atlanta study, HIV-negative Black MSM seeds ages 18-24 had a network prevalence of 9% compared to 2% among those 30 years or older.[68] In addition to assortative racial mixing, Maulsby et. al. proposed that dissortative age mixing, in which young MSM are more likely to pair with older MSM, could contribute to race and age disparities for Black YMSM, though conclusions also have varied by study.[66,69] One study found that differences in disassortative age mixing did not explain racial disparities in YMSM and advised that other partner and network characteristics, perhaps both race and age assortativity, could explain disparities.[69] Another related hypothesis is that Black MSM are more likely to have partners of unknown HIV status. A national study of MSM found that HIV-negative Black MSM were more likely to have a partner of unknown HIV status than HIV-negative White MSM and HIV-positive Black MSM were less likely to be on ART, suggesting that lack of awareness of partner's serostatus and low viral suppression could also contribute to racial disparities for Black MSM.[41]

Overall, the literature has repeatedly demonstrated how partner-, network-, and structural-level determinants shape individual HIV risk for MSM and likely contribute to race and age disparities. Factors such as partner type, concurrency, race and age assortativity, and knowledge of partner's serostatus highlight that partner-level characteristics in particular can modify HIV risk and sexual behaviors. Therefore, studying the role of partnership characteristics in HIV transmission could have important implications for understanding HIV risk among MSM and in leveraging these characteristics as mechanisms for HIV prevention.

1.4 Role of Partnerships in Understanding HIV Transmission in MSM: Theories and Conceptual Framework

Sexual partnerships shape the social context in which individuals make decisions about HIV risk and prevention behaviors, as described through interdependence theory and communal coping strategies.[70-72] Interdependence theory has served as a framework for studying emotional and behavioral dynamics in partnerships of both heterosexual and MSM populations. Interdependence theory suggests that “partners engage in patterns of mutual influence, which lead to products such as motives, emotions, or behaviors” and has been used to assess relationship outcomes such as longevity, divorce, infidelity, attachment, and autonomy.[73] The theory has also been applied to understanding health behaviors through the construct of communal coping, in which two partners shift from individually-focused perceptions of their health and well-being to relationship-focused perceptions in which both partners can work together to achieve positive health outcomes.[73] In the context of HIV prevention, interdependence theory and communal coping have been used to describe how two partners could choose to lower the number of partners outside the relationship, agree to use condoms inside the relationship and/or with partners outside of the relationship, or other actions that could reduce the risk HIV transmission within the partnership.[73] These theoretical frameworks have often been utilized in the design and development of partner-based HIV interventions such as couples’ HIV testing and counseling.[74-77]

Interdependence theory and communal coping have been applied to MSM as public health practitioners and researchers sought to adapt couples-based interventions found effective among African heterosexual couples to the context of MSM couples in the United States.[74,77] In studies of US MSM couples, theoretical constructs such as relationship quality and satisfaction, HIV-related social support, and condom attitudes were largely influenced by main or casual partnership type.[77] One study found that trust, commitment, and relationship quality were associated with less CAS with outside partners among MSM couples.[78] These results indicate that several constructs of interdependence theory and communal coping apply well to the US MSM population and that characteristics such as partner type likely impact decisions about risky sex and HIV prevention for MSM couples.[72,77]

At a micro level, HIV and STI transmission within a sexual partnership depends on use of a barrier method, such as condoms, and concurrency patterns as described in Gorbach and Holmes' conceptual framework for HIV/STI transmission at the partnership level.[79] Gorbach and Holmes demonstrate how individual characteristics of the two partners are embedded within dyadic partnership dynamics (physical, emotional, communicative, etc.) that can shape communication and decision-making about condom use and concurrent outside partners; condom use and concurrency then, in turn, have implications for biological transmission of HIV/STIs from one partner to the other. Though their conceptual framework does not take into consideration the complexities of insertive/receptive roles, partner-level sexual act frequency, PrEP use, and other factors that contribute to the probability of transmission, it does depict how partnership characteristics and dynamics serve as critical components to HIV risk and prevention in MSM couples.

The components of partnership dynamics as presented by Gorbach and Holmes are most often operationalized in research studies by characterizing partnership types as “main” or “casual” based on the level of commitment expressed by the participant. “Main” partners refer to men with whom the participant has had sex and feels committed to above anyone else and “casual” partners refer to men with whom the participant has had sex yet does not feel committed to or does not know very well.[19] Some studies may include a separate category for “one-off” partners, who are men with whom the participant has only engaged in sex on only one occasion, or may include these types of partners as “casual.” In a latent class analysis of partnering typologies among MSM in Atlanta, researchers found some variation by race in the use of “main” vs. “casual” types to describe relationships.[80] For example, Black MSM described “high involvement” (e.g., lived together, met families, likely to discuss concerns with) with only 35% of partners who they labeled as “main,” compared to 59% among White MSM.[80] Hence, a 3-level classification of “high,” “medium,” and “low” involvement was recommended when studying partner types of Black and White MSM.[80] It is not known to date how these typologies may differ by age, by age and race, or how they may differ for Hispanic MSM. Though the “main” vs. “casual” typologies neglect the diverse physical and emotional qualities of partnerships that are described in interdependence theory and may not apply uniformly across races, these are the most commonly used descriptors of partnership type in studies of MSM. Therefore, in the completion of this dissertation work, wherein possible we will consider partnerships at three-levels: main, casual, and one-off. In previous literature or existing datasets that are limited to main and casual terminology, we will use these typologies as such, though we acknowledge their limitations.

CAS and Concurrency by Partnership Type among MSM

HIV surveillance studies that operationalize partnership dynamics into “main” and “casual” partnership types have shown that MSM have high rates of CAS with both main and casual partners, but have higher rates of CAS and higher sex frequency with main partners compared to casual partners.[19,81,82] Overall, 44% of MSM reported having CAS with a main partner in the past year; 38% reported having CAS with a casual partner in the past year.[19] Estimates of annual sex acts are 50% or higher for main partners compared to casual partners and MSM are 16-31% more likely to not use a condom during sex in main partnerships.[81,82] Other studies have found similar results with MSM being less likely to use condoms during sex with main partners.[83-85] Men were also 14% more likely to engage in receptive anal sex with main partners (vs. casual) and receptive anal sex has a higher per-act risk of HIV transmission.[81]

These results are consistent with constructs of interdependence theory that posit that higher levels of intimacy, trust, and commitment in primary partnerships can lead to decreased condom use.[73,86-88] For serodiscordant couples, decreased condom use within the partnership can lead to increased risk for HIV transmission, as there is direct risk between the two individuals, though this may be offset with other risk-reducing behaviors such as having the HIV-positive partner engage in receptive anal intercourse with his partner. For true seroconcordant HIV-negative couples, decreased condom use may not lead to an increased risk of HIV transmission if neither partner engages in CAS with an outside serodiscordant partner. This underlines how HIV risk is dependent not only on condom use within the partnership but also patterns of concurrency in which one or both partners engage in CAS with an outside partner of positive or unknown HIV status. Concurrency is more likely to occur in casual partnerships compared to main partnerships, with casual partners being four times more likely than main partners to be exposed to any concurrent CAS.[50] These findings suggest that although commitment and other positive relationship dynamics may lead to potentially riskier behaviors such as CAS in main partnerships, these qualities may simultaneously reduce risk by decreasing the likelihood of a partner engaging in CAS outside of the relationship.[78]

CAS and Concurrency by Partner Type, Age, and Race among MSM

Existing HIV disparities for age and racial subgroups of MSM warrant an assessment of condom use and concurrency by race and age and how these mechanisms for HIV transmission could vary by main and casual partnership types. With respect to condom use, HIV behavioral surveillance data have shown that Black and Hispanic MSM are less likely to engage in CAS with either main or casual partners compared to White MSM. In 2014, 65% of Black MSM, 78% of Hispanic MSM, and 83% of White MSM who had a main anal sex partner in the past year engaged in CAS with a main partner; 52% of Black MSM, 57% of Hispanic MSM, and 62% of White MSM who had a casual anal sex partner in the past year engaged in CAS with a casual partner.[19] Stratified by age, 73% of YMSM ages 18-24 and 76% of MSM 25 years or older who had a main anal sex partner in the past year engaged in CAS with a main partner; 49% of YMSM ages 18-24 and 60% of MSM 25 years or older who had a casual anal sex partner in the past year engaged in CAS with a casual partner.[19] Because Black MSM and young MSM engage in CAS less frequently than their counterparts, differences in condom usage overall likely do not contribute to observed HIV disparities for Black MSM and YMSM. Yet, for both Black MSM and YMSM, a larger percentage engaged in CAS with main partners compared to casual partners, as has been found in other studies[89], indicating that HIV transmission via main partners may be commonly occurring due to increased risky sexual behavior in these relationships.

As previously discussed, the series of literature reviews and meta-analysis from Millett et. al. are consistent with the conclusion that individual sexual risk behaviors such as CAS do not explain disparities in demographic subgroups of MSM, and suggest additional research on the role of partner- and network-level factors.[55-57,66] Based on our conceptual framework, other important partner-level factors include concurrency patterns that describe sexual network structures for diverse MSM. Although concurrency is high among MSM, studies on racial differences in concurrency have reported conflicting findings.[50,51,54] One study did observe unadjusted differences in concurrency when analyzing partners' indirect exposure to concurrency at the dyad-level based on egocentric data and found that Black CAS partners were more likely to have any concurrent CAS exposure compared to White CAS partners, however this finding became null after adjustment for other covariates.[50] As described earlier, sexual networks likely contribute to disparities due to the high HIV prevalence observed in Black MSM and assortative racial mixing.[27,66,67] In a study of MSM in New York, researchers found no difference in participant-reported concurrency across racial groups; however, Black and Hispanic MSM had more HIV-positive persons in their sexual networks, similar to studies of MSM in Atlanta.[67,68,90] Research on partner- and network-level HIV transmission factors are often limited by sample size and thus have not often presented results stratified on partner type, race, age, and HIV status categories. Data that can allow for these stratifications could identify important differences in HIV-related outcomes to guide current understanding of HIV transmission risk.

Although this discussion has focused mainly on CAS and concurrency based on the presented conceptual framework, HIV transmission in MSM depends on many more complex factors including accurate knowledge and disclosure of HIV status, sex frequency, role versatility, serosorting, circumcision, PrEP use for HIV-negative partners, ART use and viral suppression for HIV-positive partners, and others. These factors can affect HIV transmission at the dyad level and the particular magnitude of risk attributed to these factors may vary by main and casual partnership type as well as by age and race. Considering multiple factors along with CAS and concurrency would be most appropriate when attempting to estimate HIV transmission in main and casual partnerships.

Estimating HIV Transmissions by Partnership Type among MSM

Because condomless sex is a biological mechanism for HIV transmission and a higher frequency of condomless sex takes place within main partnerships, the role of partnership type has been an important factor in estimating HIV transmission among MSM populations.[81,91] Yet, the proportion of HIV transmissions by partner type has been widely debated in the literature. Three key mathematical models to date have estimated that between 39% and 78% of transmissions among MSM in the United States occur in main partnerships.[81,92] In 2009, Sullivan et. al. were the first investigators to develop an HIV transmission model for US MSM that allowed for the estimation of transmissions by partner type.[81] The Sullivan model was a static, deterministic model that used data from the National HIV Behavioral Surveillance system and the Vaccine Preparedness Study to estimate parameters for the number of sex acts, number of partners, proportion of sex acts without condoms, and prevalence of HIV among partners, by main and casual partner types. The model also included parameters for the number of MSM and the per-act probability of HIV transmission. Stratified models were conducted by age, race, and education. The overall model estimated that 68% of HIV transmissions occur from main partners, mainly driven by the higher sex frequency, greater likelihood of having receptive anal sex, and lower condom use with main (vs. casual) partners.[81] MSM in the 18-24 and 25-29 age groups had the highest proportions of transmission arising from main partners.[81] This analysis was the first to examine how HIV transmission is modified by partnership type in MSM, propose key parameters and data sources for further study, and make an evidence-based recommendation for developing and implementing couples-based HIV interventions for MSM in the United States.

In 2011, Goodreau et. al. conducted a second study on this topic aimed at quantifying the number of transmissions by partner type using a dynamic, stochastic sexual network model to simulate HIV transmission in a population of US MSM. The Goodreau model included age, race, circumcision status, sexual role behavior, and propensity for CAS and accounted for transitions from HIV infection to diagnosis, treatment, AIDS diagnosis, and death. The network model allowed for the additional consideration of dynamic concurrency patterns and sexual network structure. Goodreau et. al. used several different datasets to parameterize the model including HPTN-036, HPTN-039, and EXPLORE studies, though the investigators also used NHBS data as in the Sullivan model. Overall, the Goodreau model estimated that up to 39% of transmissions occur in main partnerships of MSM, about one-third less than that estimated by the Sullivan model.[92]

Recent work by Rosenberg et al. presented at the 2015 Conference on Retroviruses and Opportunistic Infections used a unique model framework and estimated that 78% of HIV transmissions in 2009 were to main partners, a greater estimate than previously reported.[93] This model applied a similar static, deterministic modeling approach and accounted for the same parameters as the Sullivan model, but incorporated stratification of HIV transmissions by steps of the care continuum. This third model differed in that it used data on HIV-positive individuals who had the potential for transmitting HIV to partners, whereas the Sullivan model was parameterized using data on HIV-negative individuals who had the potential for acquiring HIV infection.

Researchers have questioned whether these conflicting results are due to different modeling approaches, different parameters under consideration, and/or different datasets used to parameterize the models. Nevertheless, these studies have served as the three principal studies of HIV transmission by partner type for US MSM and their findings have resulted in significant debate in public health about whether most infections are occurring in main or casual partnerships, and thus, where resources and policies for prevention should be allocated for MSM.

Partner-Based Interventions for Preventing HIV Transmissions in MSM

Partner-based HIV interventions were initially developed as a prevention strategy for reducing HIV risk among heterosexual couples in Africa.[94] Most notably, these included couples' HIV testing and counseling (CHTC) in which two partners could get tested and find out each other's' test results, talk about sexual agreements within and outside of the relationship, negotiate condom use, and create a plan for preventing HIV infection within the partnership.[94] CHCT has been shown to be effective method for recruiting individuals to get HIV tested and for reducing risky sex behaviors within the context of African heterosexual couples.[76,95] Over the past five years, couples-based HIV prevention strategies have been adapted for MSM in the United States, but these are not often included as part of routine, comprehensive HIV prevention services.[74,96] For example, CHTC has proven safe and acceptable among US MSM in main partnerships, and is considered an effective, high-impact prevention intervention by the CDC; yet, not all clinics that provide individual testing and counseling have the funding or trained programmatic staff to incorporate couples into standard services.[97-99] CHTC tailored for MSM would provide an opportunity to test two individuals at one point in time and facilitate access to partners who would benefit from re-engagement into HIV care or initiation onto pre-exposure prophylaxis (PrEP). This intervention could be particularly useful for reducing transmissions among MSM who account for most diagnoses in the United States.[22] Yet, support for funding and training for CHCT directed towards MSM partners will rely on a better understanding of whether main vs. casual partnerships are contributing most to HIV transmissions and the literature to date on this topic demonstrates conflicting results. Furthermore, identifying whether trends in main partnerships are currently increasing would also provide evidence to support the incorporation of CHCT and other partner-based HIV interventions into standard HIV prevention services, particularly in locations where HIV testing is already offered. This dissertation will examine how partnerships may be changing over historical time and how HIV transmission differs by partnership type and age for MSM to help determine the relative priority of partner-based interventions in prevention strategies for MSM.

1.5 Current Gaps in Knowledge and Objectives for Dissertation Studies

Trends in Racial/Ethnic Disparities in the US

Current evidence on trends in racial/ethnic disparities in the US relies on three main articles that specifically described and tested race-specific trends in new AIDS or HIV and AIDS diagnoses. The first study only considered years 2001-2004 and found decreasing trends in the new HIV diagnoses rates for Blacks and Hispanics.[8] A second study documented slightly increasing trends for Black males from 2005-2008.[9] Yet, neither of these two studies tested disparity measures as main outcomes and they only considered four years of data to determine trends. A third study evaluated measures of racial/ethnic disparity in new AIDS diagnoses rates directly from 2000-2009 and demonstrated a significant decrease in Black-White and Hispanic-

White disparities overall and for most age and sex subgroups.[10] Still, this study only assessed trends over a 10-year time frame and assumed one linear trend period, which may mask important changes over time. Trends in racial/ethnic disparities of AIDS diagnoses since the mid-1980s have yet to be demonstrated. These earlier studies assessed only short sections of AIDS trends; however, a long-term context for how disparities have emerged, declined, or been sustained since the beginning of the epidemic is lacking. This dissertation will fill this gap by describing and evaluating the trends in the relative racial/ethnic disparities of new AIDS diagnoses rates over a period of 30 years, allowing for changes in trends over time, and determining when those changes occur through an objective empirical approach.

Trends in the Number and Composition of Partners among US MSM

Recent findings from Rosenberg et. al. estimated that 78% of HIV transmissions in 2009 were to main partners, about a 10% increase from previous estimates in 2005 from the Sullivan model.[81,93] There are several potential reasons for this higher estimate of transmissions in main partnerships. A first hypothesis is that increasing cultural and legal acceptance of same-sex partnerships in the past decade may have resulted in growing numbers of main partnerships for MSM overall. If other factors related to transmission have remained the same (e.g., concurrency patterns, condom use), then more main partnerships might have led to an increased number of HIV transmissions arising from main partners. Although this hypothesis may be true for MSM of all ages, a second hypothesis is that there may be an age cohort effect such that young MSM who transitioned into the majority age distribution in recent years may have more main partners than previous cohorts of MSM. Thus, an increased number of main partnerships in the majority age group may be leading to an increased number of transmissions within main partnerships. Previous models stratifying by age found that younger MSM ages 18-24 and 25-29 had the highest proportions of transmissions from a main sex partner[81]; yet these models focused on estimated transmissions and did not specifically analyze trends in the relative counts of main partnerships during these periods. Examining trends in main MSM partnerships overall during the past decade will allow for testing the first hypothesis. Further evaluating trends in main partnerships by age will generate knowledge about how transmissions by partnership type may differ for age-specific groups and may also allow us to detect a potential age cohort effect as described in the second hypothesis. Assessing trends stratified by race and HIV status will highlight possible heterogeneity of trends for additional MSM subgroups.

In addition, Paz-Bailey et. al. recently studied trends in condomless anal sex among MSM from 2005-2014 and found significant increases in CAS with HIV-positive concordant, HIV-negative concordant, and HIV-discordant MSM partners.[100] One hypothesis for recent increases in CAS is that the number of main partners may be increasing, as men in main partnerships are more likely to engage in CAS.[19] Trends in CAS have not yet been stratified by partner type or partner composition, thus analyzing trends specific to the partner type would highlight important information about the context in which increasing CAS is taking place in MSM partnerships.

Beyond the context of HIV transmission, little is known in general about how MSM partnering has changed over time during recent social and legal acceptance of long-term same-sex partnerships. From 1991-2010, the General Social Survey has documented increases in public acceptance of homosexual behavior by 27% (percentage points) and of same-sex marriage by 35%.[101] Continued activism for same-sex marriage by lesbian, bisexual, gay, and transgender (LGBT) groups and this growing public support in recent years has culminated in the legal acceptance of same-sex marriage nationally by the US Supreme Court in June 2015.[101] These changes over the past two decades could have important implications for partnering among MSM. For example, it may be possible that MSM have been more likely to form, or less likely to dissolve, long-term main partnerships during this time period. It may also be possible that MSM have been less likely to form casual partnerships in general or once in a main partnership; alternatively, outside casual partnering may have remained stable. Similar trends may be observed for CAS within main and casual partnerships. How these dynamics have evolved at a national level for MSM has been understudied and may be meaningful for disparity research on MSM in main and casual partnerships. Evaluating these trends overall, and by race, age, and HIV status, could provide critical information about how partnering has changed in general for MSM and for specific subgroups of MSM. This information would then serve to demonstrate the potential public health impact of targeting men in main partnerships with partner-based HIV interventions compared to men engaging in casual relationships.

Estimation of HIV Transmission by Partner Type and Age among US MSM

Few studies have examined how partnership types shift over the life course as MSM age and how this shift may influence transmission of HIV within main partnerships.[89,102] Furthermore, existing data to assess transmission effects by partnership type as MSM age, while accounting for other partner and sexual network transmission factors over time, are limited. For example, longitudinal studies of MSM couples often oversample men who are already in committed relationships and can typically only follow partnerships over a short period of time, limiting our knowledge of how partnership types can shape HIV risk over time. Therefore, the application of network modeling methods to simulate the effect of age and partnership type on HIV transmission in MSM is a unique resource to answer these complex questions. An innovative dynamic, stochastic sexual network model for black and white MSM in Atlanta has been created by collaborators at Emory University and the University of Washington, referred to as the Modeling Approaches for Racial/Ethnic Disparities in HIV among Atlanta MSM (MARDHAM) model.[103] This model was subsequently extended and generalized, and placed within a modeling software package, EpiModel [http://github.com/statnet/EpiModel]. EpiModel is an agent-based model that accounts for network structure, formation and dissolution of partner types, patterns of concurrency, and care continuum markers that are race-specific. EpiModel can serve as a laboratory for simulating the HIV epidemic among MSM in Atlanta given a set of demographic and behavioral parameters. The model does not currently specify sexual transmission parameters by partner type and age and by adding this information into this model we could observe how transmission within main partnerships may change as men's propensity for forming and dissolving main and casual partnerships, using condoms, and frequency of sex varies with age. Studying these processes and estimating their effects will provide a better understanding of partnering patterns over the life course and how these are related to HIV transmission. These results will help establish the potential impact of current and future prevention strategies for MSM at certain ages. These findings could have important implications for the tailoring and recommendations of partner-based interventions for MSM including PrEP[104] and couples' HIV testing and counseling[74] with respect to men's age and partner types.

Implications of Addressing Knowledge Gaps

A lack of available data on MSM partnerships and behaviors over time has precluded researchers from studying these topics in depth. Yet, existing HIV surveillance systems on MSM could serve as an important resource in investigating how partnering has changed from the mid 2000's to present time in the context of an evolving cultural and political environment for MSM couples. Furthermore, mathematical modeling of HIV transmission in a simulated population of

MSM and accounting for important transmission factors can allow for estimation of transmissions by partner type across age groups of MSM. In summary, measuring disparities over historical time and examining the role of partnerships in HIV transmission overall and in age- and race-specific groups will be important to informing public health practice and developing effective intervention policies, particularly surrounding HIV testing recommendations[105] and the PrEP guidelines for MSM.[106] We aim to answer these research questions using appropriate and innovative epidemiologic methods in an effort to advance the science on these topics.

1.6 Specific Aims and Data Sources for Dissertation Studies

Aim 1

Primary Objective: Identify and evaluate historical trends in racial/ethnic disparities of AIDS diagnoses among adults and adolescents over the course of the HIV epidemic in the United States and Puerto Rico from 1984 to 2013.

Study Design: Aim 1 used national HIV/AIDS case surveillance data that were collected using ongoing case reporting systems. Data were aggregated and reported annually and were analyzed as time-series data (multiple cross-sectional data points).

Data Sources: Aim 1 utilized publicly available annual HIV surveillance data on AIDS diagnoses in the United States and Puerto Rico as well as US census data to obtain annual age-, race-, and sex-specific population denominators. HIV/AIDS case surveillance reports were available electronically through the CDC website. US Census data were obtained electronically through archived files on the Census Bureau website and the American Fact Finder website.

Aim 2

Primary Objective: Examine trends in the number and composition of sexual partners and in sexual behaviors by partnering type among MSM in 20 US cities in the context of increasing social and legal acceptance of same-sex partnerships, 2008-2014.

Study Design: Aim 2 used three rounds of National HIV Behavioral Surveillance (NHBS) data on MSM that were collected during cross-sectional studies using venue-based sampling, conducted every three years. Data were analyzed as time-series data with 3-year intervals.

Data Sources: NHBS data on MSM were collected in three rounds: 2008, 2011, and 2014. The study sample consisted of 28,061 MSM (9,247 MSM from the 2008 round, 9,229 MSM from the 2011 round, and 9,585 MSM from the 2014 round).

Aim 3

Primary Objective: Model and estimate the age-specific proportions of HIV transmissions among main, casual, and one-off partnerships of MSM in Atlanta.

Study Design: Data for Aim 3 were generated from a dynamic sexual network-based model using EpiModel software with parameters modified to include heterogeneity by partner type and age. An initial sample population of 10,000 MSM was used for each simulation.

Data Sources: Simulated data were analyzed for Aim 3. Model parameters were estimated from data on 998 MSM in the Involve[men]t and MAN Project studies that took place from 2010-2014. Involve**[**men**]**t collected longitudinal data on black and white MSM in Atlanta for a period of 2 years; MAN Project was a cross-sectional egocentric sexual network study on MSM in Atlanta. These studies included HIV/STI testing and an extensive questionnaire that detailed information on previous sexual partnerships in the past year.

1.7 Structure of this Dissertation

Chapter 2 consists of an original research manuscript that examines the historical trends in racial/ethnic disparities of AIDS diagnoses in the United States (Aim 1). Next, Chapter 3 evaluates trends in the number and composition of sexual partners and in sexual behaviors by partnering type among MSM in the United States (Aim 2). Chapter 4 then addresses the objectives of Aim 3 to estimate the proportion of HIV transmissions among MSM by age and partner type. Finally, in Chapter 5, we extend our discussion of the public health contributions of this dissertation research and propose how our findings inform on future directions in HIV research and prevention.

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CHAPTER 2: Trends in racial/ethnic disparities in new AIDS diagnoses in the United States, 1984-2013

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Abstract

Purpose: In the United States, HIV/AIDS disproportionately impacts racial/ethnic minorities. We describe and evaluate trends in the Black-White and Hispanic-White disparities of new AIDS diagnoses from 1984 to 2013 in the US.

Methods: AIDS diagnosis rates by race/ethnicity for people ≥13 years were calculated using national HIV surveillance and Census data. Black-White and Hispanic-White disparities were measured as rate ratios. Joinpoint Regression was used to identify time periods across which to estimate rate-ratio trends. We calculated the estimated annual percent change (EAPC) in disparities for each time period using log-normal linear regression modeling.

Results: Black-White disparity increased from 1984-1990, followed by a large increase from 1991-1996, and a smaller increase from 1997-2001. Black-White disparity moderated from 2002-2005 and rose again from 2006-2013. Hispanic-White disparity increased from 1984-1997, but declined after 1998. Black-White and Hispanic-White disparities increased for MSM during 2008-2013.

Conclusions: Recent increases in racial/ethnic disparities of AIDS diagnoses were observed and may be due in part to care continuum inequalities. We suggest assessing disparities in AIDS diagnoses as a high-level measure to capture changes at multiple stages of the care continuum collectively. Future research should examine determinants of racial/ethnic differences at each step of the continuum to better identify characteristics driving disparities.

Introduction

In 2012, approximately 1.2 million individuals were living with the human immunodeficiency virus (HIV) in the United States.[1] Over 500,000 people living with HIV have ever received an acquired immune deficiency syndrome (AIDS) diagnosis and about 27,000 individuals are newly diagnosed with AIDS each year in the US and dependent areas.[2] Since the introduction of effective combination antiretroviral therapy (ART), the annual rate of new AIDS diagnoses has decreased by more than half; however, important racial/ethnic disparities still remain.[2,3]

HIV and AIDS disproportionately affect racial/ethnic minority groups including Blacks/African Americans (Blacks) and Hispanics/Latinos (Hispanics). Blacks and Hispanics represent 12% and 16% of the total US population, respectively, but accounted for 46% and 21% of new HIV diagnoses and 49% and 20% of new AIDS diagnoses, respectively, in 2013.[1,2,4] Racial/ethnic disparities have received increased attention as the US National HIV/AIDS Strategy (NHAS) and Healthy People 2020 have established objectives to decrease HIV-related inequalities.[5,6] These aims include increasing the proportion of Blacks and Hispanics with undetectable viral loads by 20%.[5,6] The outlined objectives rely heavily on improvements to the HIV care continuum, particularly for Blacks and Hispanics who may experience greater barriers to prevention and care due to socioeconomic factors such as poverty, access to healthcare, stigma, and language constraints.[7] Determining if and how we may achieve these goals will further depend on researchers' ability to quantify and monitor trends in disparities over time.

According to surveillance data, Blacks and Hispanics have generally had higher rates of HIV and AIDS diagnoses compared to Whites.[2,8] Yet, limited research has evaluated the magnitude of these disparities and how they have evolved over time. One study found a significant decline in racial/ethnic disparities of AIDS diagnoses from 2000-2009 overall and for most age and sex subgroups, with the exception of young people aged 13-24 who experienced a significant increase in the Black-White disparity.[9] The authors reported that 90% of this increase among young people was due to rising AIDS diagnoses among men, suggesting increasing disparities for young Black men.[9] Although this study provides insight on racial/ethnic disparities during a period of time in the past decade, trends in racial disparities since the beginning of the HIV epidemic to present time have yet to be demonstrated.

Quantifying trends depends heavily on the years selected for analysis; thus, measuring trends in disparity over a longer time period may allow for better description and detection of changes in trends. Assessing disparity trends since the 1980s provides a historical context for how disparities emerged, were sustained, or possibly declined over the course of the HIV epidemic. For example, the number of AIDS diagnoses in the United States has declined for all racial/ethnic groups since the introduction of ART in 1996; however if and how racial/ethnic disparities in AIDS diagnoses have changed in the presence of effective treatment has not been shown to date.[10-12] Understanding how racial disparities have evolved over decades could also support hypothesis generation about which factors have contributed to changes in disparities.

This paper describes and evaluates trends in the Black-White and Hispanic-White disparities of new AIDS diagnoses from 1984 to 2013. We first sought to empirically identify chronological time periods representing distinct eras of trends in racial/ethnic disparities. We then sought to test for the significance of disparity trends for each identified time period. Overall, our objective was to determine if, when, and how racial/ethnic disparities in AIDS diagnoses have changed over 30 years of the HIV epidemic in the United States and Puerto Rico.

Material and methods

Data on cases and rates of AIDS diagnoses by race for adults and adolescents aged 13 years and older were extracted from publicly available annual HIV surveillance reports from the Centers of Disease Control and Prevention (CDC) for years 1984 to 2013.[13] US Census Bureau data were used to estimate annual population denominators for the general population by age and race (non-Hispanic Black; Hispanic; non-Hispanic White). For years when data on rates of AIDS diagnoses by age and race were reported directly in surveillance reports (1989-2007), these rates were used for analysis. For years when rates of AIDS diagnoses by age and race were not reported directly in surveillance reports (1984-1988 and 2008-2013), rates were calculated using age- and race-specific AIDS case counts as the numerator and intercensal (1984-1988, 2008-2009) or postcensal (2010-2013) annual population estimates as the denominator. The race-specific rate was calculated as the annual case counts divided by the annual population estimate for the race of interest multiplied by 100,000.

For Hispanics, rates of AIDS diagnoses by age and race for the United States and Puerto Rico were reported directly in surveillance reports from 1989-2002. For years when rates of AIDS diagnoses for US Hispanics and Puerto Rico by age were not directly reported (1984-1988 and 2002-2013), rates were calculated using age- and race-specific AIDS case counts for both US Hispanics and Puerto Rico as the numerator and either intercensal (1984-1988, 2002-2009) or postcensal (2010-2013) annual population estimates for US Hispanics and Puerto Rico as the denominator. Population estimates for Puerto Rico were obtained from electronic archives from the Puerto Rico National Institute of Statistics or the US Census Bureau and all were considered of Hispanic ethnicity. Further details on the data sources and estimation of annual age- and race-specific AIDS diagnoses rates are outlined in Table 2.A of the Supplementary Material.

Our outcome of interest was the AIDS diagnoses rate ratio, a relative measure of disparity comparing racial/ethnic groups. The rate ratios were calculated as the rate among the index racial/ethnic group (Non-Hispanic Blacks or Hispanics) divided by the rate among the reference group (Non-Hispanic Whites). After obtaining or calculating annual rate-ratio estimates, we then sought to quantify changes in these disparity measures over time. First, we empirically identified cut-point years for when trends in the disparities changed in order to determine the statistically significant trend periods. We used Joinpoint Regression software to test for significant "joinpoints," or cut-point years, that would identify time periods with unique linear trends in the rate-ratio disparity measure. Joinpoint Regression is a statistical software frequently used in cancer surveillance to measure trends in cancer rates.[14,15] The program utilizes Monte Carlo permutation tests and grid search methods to determine the joinpoints at which statistically different trends occur in time.[14,15] We allowed the default settings of the Joinpoint software (maximum number of joinpoints for 30 datapoints=5, minimum number years per trend period=4, Bonferroni-adjusted alpha for permutation tests, alpha=0.05 for significance of slope). For Joinpoint analyses, we imported annual log-transformed rate ratios and their standard errors and we performed analyses separately for each racial/ethnic comparison. Second, we quantified each disparity trend using estimated annual percent change (EAPC) measures. We applied log-normal linear modeling (PROC GLM) to determine the average annual change in the Black-

White and Hispanic-White log-transformed rate ratios for each trend period. Beta estimates were transformed to obtain EAPCs for the rate-ratio disparity measures. We also modeled rate-ratio trends using an underlying Poisson distribution and the direction, strength, and significance of the terms were similar; however, model fit was poor. We conducted two additional subanalyses of the disparities stratified on (1) sex and (2) male-to-male sexual contact. Details on methods and available data for subanalyses are described in the Table 2.2 footnotes. Analyses were conducted in SAS version 9.4.

Results

For the Black-White disparity, the Joinpoint Regression program identified four significant joinpoints (years 1991, 1997, 2002, and 2006) which corresponded to five different trend periods: 1984-1990, 1991-1996, 1997-2001, 2002-2005, and 2006-2013. For the Hispanic-White disparity, the method found only one significant joinpoint (1998), which corresponded to two different time periods: 1984-1997 and 1998-2013.

Table 2.1 shows EAPCs of the Black-White and Hispanic-White relative disparities in new AIDS diagnoses for each of the respective time periods. Black-White disparity increased from 1984 to 1990, followed by the largest increase from 1991-1996, and a continued but more gradual increase from 1997-2001. After 2002, Black-White disparity began to decrease until 2005. From 2006-2013, Black-White disparity significantly rose again, and in 2012 reached the same magnitude as had occurred at the peak of the disparity in 2002. Hispanic-White disparity also significantly increased from 1984 through 1997, though the increase was less compared to the Black-White disparity. After 1998, Hispanic-White disparity decreased slightly through

2013. Additionally, rates of AIDS diagnoses increased from 1984 to approximately year 2000 and then decreased through 2013 for all race/ethnicities. Black-White and Hispanic-White disparity trends are presented in Figures 2.1 and 2.2. Rate ratios are depicted for ease of interpretation of the disparity measure (Figure 2.1). Joinpoint Regression analysis and modeling of EAPCs relied on log-transformed rate ratios (Figure 2.2). We present trends in both measures for completeness. Black-White and Hispanic-White rate ratios calculated for this analysis are presented in the Supplementary Material (Table 2.A).

EAPCs for the disparities stratified by sex and male-male sexual contact are provided in Table 2.2. When allowing each subgroup to vary independently in their trend periods, we found that Black-White disparity among males generally followed the trends we observed in Black-White disparity overall. However, Black-White disparity among females increased until 2002, and then remained stable between 2002-2013. Hispanic-White disparity for females declined from 2002-2013 as observed overall, while that for males declined slightly from 2002-2005 and then increased from 2006-2013. During 2008-2013, Black-White and Hispanic-White disparities significantly increased for MSM and remained stable for men not reporting male-male sex. Figure 2.3 depicts disparity trends by male-male sexual contact.

Discussion

Trends in the Black-White disparity of new AIDS diagnoses were more heterogeneous, with four different inflection points, compared to Hispanic-White disparity trends which changed only once during the epidemic. Racial disparities rose sharply from 1984 to the early 2000s for Blacks and to a lesser extent for Hispanics. Since 1998, Hispanic-White disparity has declined.

Black-White disparity declined following 2002, but concerningly, we documented a significant increase from 2006-2013. Racial disparities for MSM have increased significantly in recent years. Annual rates of AIDS diagnoses for all racial/ethnic groups increased through year 2000 and have decreased or stabilized from 2000-2013. Changes in annual rates of AIDS diagnoses are related ecologically to the introduction of effective ART: the rate of AIDS cases grew in the absence of ART and subsequently declined after ART became more widely available.

Our findings about the overall trends in racial/ethnic disparities of AIDS diagnoses over the past 30 years lead us to hypothesize about factors that may have contributed to the generation, sustainment, and/or decline of these trends. Using AIDS diagnoses as an endpoint is complex because it is impacted by both historical trends in HIV incidence and gaps in one or more HIV care continuum steps. AIDS diagnoses also include people with heterogenous disease progression profiles. For both Blacks and Hispanics, increases in disparities of AIDS diagnoses in the 1980s and 1990s could reflect increasing HIV historical incidence. Yet, because AIDS diagnoses are ultimately an indicator of both HIV infection and failure of effective medical care, increasing disparity trends could also represent rising inequalities in steps of the HIV care continuum during these periods. For example, if Blacks and Hispanics were less likely to test for HIV or had poorer access to healthcare and HIV services, they may have waited longer to seek care, perhaps until after the onset of AIDS symptoms. From 2002-2005, improved access to and uptake of ART and advances in HIV testing (e.g., HIV rapid tests) may have mitigated some barriers to prevention and care that racial/ethnic minority groups had previously experienced.

The increasing trend we observed in the Black-White disparity from 2006 to 2013 likely stemmed from a combination of high HIV incidence among young Black MSM and persistent disparities in the HIV care continuum in recent years.[16-18] Other data have shown that most new HIV diagnoses are occurring among Black MSM, particularly young Black MSM.[2,19] An increase in HIV prevalence from 2008 to 2014 among Black MSM overall and young Black MSM has also been documented.[20] Some of the recent increasing trend we observed may be attributable to increases in HIV diagnoses among young Black MSM if these men are presenting with an AIDS diagnosis at the time of HIV diagnosis or are quickly transitioning to AIDS. This may be true given a high prevalence of late HIV diagnoses within this group.[21] This hypothesis is further supported by our subanalyses demonstrating that Black-White disparities for MSM significantly increased from 2008 to 2013. Among HIV-positive Black MSM, only 75% were estimated to have been diagnosed, 24% retained in care, 20% on antiretroviral therapy, and 16% virally suppressed.[16] Efforts to improve steps of the treatment and prevention cascades including testing and treatment adherence are needed among Blacks overall for whom we have not observed improvements in disparities recently, and with particular emphasis on reaching Black MSM,[16] for whom we observed this recent upward disparity trend.

Overall, trends in the Hispanic-White disparity followed similar patterns as the Black-White disparity, but the trend has slowly decreased since 1998. Though Hispanic-White disparities were never as large in magnitude as Black-White disparities, they still represented a substantial 4-fold increase, suggesting care continuum inequalities for Hispanics as well. Hispanics tend to be diagnosed later in the course of their HIV infection compared to Non-Hispanic Whites.[22] Recent studies have also found that Hispanics have higher percentages of linkage to and retention in care, but lower percentages of viral suppression.[23] CDC has reported that 80% of Hispanics living with HIV have been diagnosed, 67% linked to care, 37% retained in care, and 26% virally suppressed—all of which were lower for Hispanics compared to Non-Hispanic Whites.[24] Our subanalyses revealed that Hispanic-White disparity has steadily decreased for females, but increased for males from 2006-2013. We found significant recent increases in Hispanic-White disparity for MSM from 2008-2013, while the trend has remained stable for males not reporting male-male sex. This finding indicates that recent Hispanic-White disparity increases in MSM likely drive the increasing trends in males overall, similar to the Black-White disparity. Identifying specific steps of the care continuum such as testing uptake and late HIV diagnosis that uniquely characterize disparities for Hispanics overall and for Hispanic MSM will be important in meeting national goals.

Our study is subject to several limitations. First, we used overall population data and did not analyze trends separately by age, sex, and transmission category over the entire time period of interest. We only considered the disparities stratified by sex and male-male sexual contact over select years, limiting conclusions about changes in trends among subgroups. Unfortunately, we were not able to evaluate these risk groups over the entire study period due to limits in publicly available data and/or lack of annual population denominators. Second, data reported over the 30-year time period varied in many respects and obtaining annual race- and age-specific rates of new AIDS diagnoses required estimating population denominators for several years. Consequently these estimates were dependent on available US and Puerto Rico census data and additional assumptions presented in the Supplementary Material (Table 2.A). The definition of an AIDS diagnosis changed during the study time period; however, we did not expect these changes to be differential with respect to race/ethnicity. Lastly, the reporting of race/ethnicity in AIDS case reports also likely changed during the time period of interest; this would only affect disparity measures if improvements in reporting over time were differential by race. This may have resulted in misclassification of Hispanic ethnicity during earlier years (pre-1997) before the standard two-question format of (1) Hispanic ethnicity and (2) race was widely implemented.[25,26] Options for multiple races are now possible in case reporting and census systems; we included Hispanics of any race and single-race/ethnicity for Non-Hispanic Blacks and Non-Hispanic Whites to avoid potential misclassification of race/ethnicity from this change.

Despite these limitations, our study is the first to demonstrate the contours of racial/ethnic disparities in AIDS diagnoses over the course of the HIV epidemic in the United States and Puerto Rico. Using disparities in AIDS diagnoses as our outcome allowed us to study trends over this 30-year period because AIDS is the only HIV-related outcome that has been consistently reported by surveillance programs since the 1980s. We were able to empirically derive and describe significant trend periods using Joinpoint Regression software, allowing for a more objective view compared to analyses that select intervals based on the most recent decade or similar arbitrary timeframes. Finally, by analyzing AIDS diagnoses, we were able to obtain a high-level understanding of disparities that may be a combined result of multiple gaps in the care continuum and growing racial/ethnic inequalities for high-risk groups such as MSM.

Conclusion

From the beginning of the HIV epidemic, racial/ethnic disparities have been a hallmark of the US epidemic and grew unceasingly from the mid-1980s through the early 2000s. After more than 30 years, we still identify racial/ethnic disparities in HIV-related outcomes, but with different underlying concerns: although AIDS diagnosis rates overall have declined, our data suggest that Blacks and Hispanics in the US have not benefitted from improved antiretroviral therapies as much as Whites have. Our national strategy reflects the need to address these disparities, but our analysis reveals complexity in how to monitor disparities over time and interpret observed trends. We believe that using AIDS diagnoses as a downstream measure will help to capture changes in racial/ethnic disparities that are collectively a result of the successes or failures of both policies and programs at multiple levels of the care continuum. This should be supplemented with other metrics to assess disparity trends at each step of the HIV care continuum and better understand how certain components may be driving racial/ethnic disparities both overall and specifically for MSM. Incorporating the historical context for racial/ethnic disparities in AIDS diagnoses that we have provided here and pairing this with other indicators specific to care continuum steps will serve as important measures for monitoring NHAS goals to reduce racial/ethnic disparities in HIV/AIDS.

Contributors

PSS and JCB conceived the idea for the study. JCB led the data extraction, analysis, and manuscript writing. PSS and ESR contributed to the concept development, analysis, and writing. All authors have seen and approved the final version of the manuscript for publication.

Role of the funding source

The funding source had no role in data analysis or interpretation, manuscript writing, or the decision to submit the manuscript. The corresponding author had full access to the publicly available study data and final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

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Table 2.1 Estimated annual percent change (EAPC) of the rate ratios for the Black-White and Hispanic-White racial/ethnic disparities in AIDS diagnoses, United States and Puerto Rico, 1984-2013

Disparity	Joinpoint Period	Years	EAPC	EAPC (LL)	EAPC(UL)	P-value
Black-White Rate Ratio	1	1984-1990	5.6	3.8	7.5	<0.01
	2	1991-1996	11.6	9.1	14.1	<0.01
	3	1997-2001	3.2	0.2	6.3	0.04
	4	2002-2005	-3.0	-7.0	1.2	0.15
	5	2006-2013	1.9	0.4	3.4	0.01
Hispanic-White Rate Ratio	1	1984-1997	4.5	3.4	5.6	<0.01
	2	1998-2013	-1.2	-2.0	-0.3	<0.01

Abbreviations: AIDS=acquired immunodeficiency syndrome

Table 2.2 Estimated annual percent change (EAPC) of the rate ratios for the Black-White and Hispanic-White racial/ethnic disparities in AIDS diagnoses by sex and male-male sexual contact, United States, 1991-2013 (BW males and females), 2002-2013 (HW males and females), and 2008-2013 (BW and HW MSM)

Disparity	Joinpoint Period	Years	EAPC	EAPC (LL)	EAPC(UL)	P-value
BLACK-WHITE RATE RATIO						
Females	1	1991-2001	4.4	3.3	5.4	<0.01
	2	2002-2013	-0.3	-1.1	0.6	0.55
Males	1	1991-1996	11.4	9.5	13.4	<0.01
	2	1997-2001	2.7	0.4	5.2	0.03
	3	2002-2005	-3.4	-6.5	-0.2	0.04
	4	2006-2013	2.6	1.4	3.8	0.01
MSM[1]	1	2008-2013	6.0	3.8	8.2	<0.01
Non-MSM Males[1,2]	1	2008-2013	-1.0	-4.9	3.1	0.53
HISPANIC-WHITE RATE RATIO[3]						
Females	1	2002-2013	-3.4	-4.6	-2.1	<0.01
Males	1	2002-2005	-2.6	-4.9	-0.3	0.03
	2	2006-2013	1.5	0.7	2.4	<0.01
MSM[1]	1	2008-2013	3.3	2.0	4.6	<0.01
Non-MSM Males[1,2]	1	2008-2013	-1.5	-6.2	3.4	0.43

Abbreviations: AIDS=acquired immunodeficiency syndrome; MSM=men who have sex with men

Notes: For the analysis stratified on sex, data for the Black-White disparity were limited to years 1991 through 2013 and data for the Hispanic-White disparity were limited to years 2002 through 2013 to remain consistent with surveillance reporting by sex during previously identified trend periods. For analyses stratified on male-male sex, data were limited to years 2008-2013 when estimated diagnoses for US Black, Hispanic, and White MSM were reported.

[1]MSM include both men who reported male-male sex and men who reported male-male sex and injection drug use. Rate denominators for MSM are an estimated proportion of 3.9% of the total male population ages 13 and older by race. Rate denominators for non-MSM males were therefore an estimated 96.1% of the total male population (*Purcell et.al., 2012*). These percentages were applied to all races.

[2]Non-MSM males represent males who did not report male-male sexual contact.
[3]Hispanics in these subanalyses represent mainland US Hispanics only (do not include Puerto Rico) due to lack of data in surveillance reports on case counts in Puerto Rico by age, sex, and transmission category from 2002-2013.

Figure 2.1 Racial/Ethnic Disparities in New AIDS Diagnoses among Adults and Adolescents, US and Puerto Rico, 1984−2013

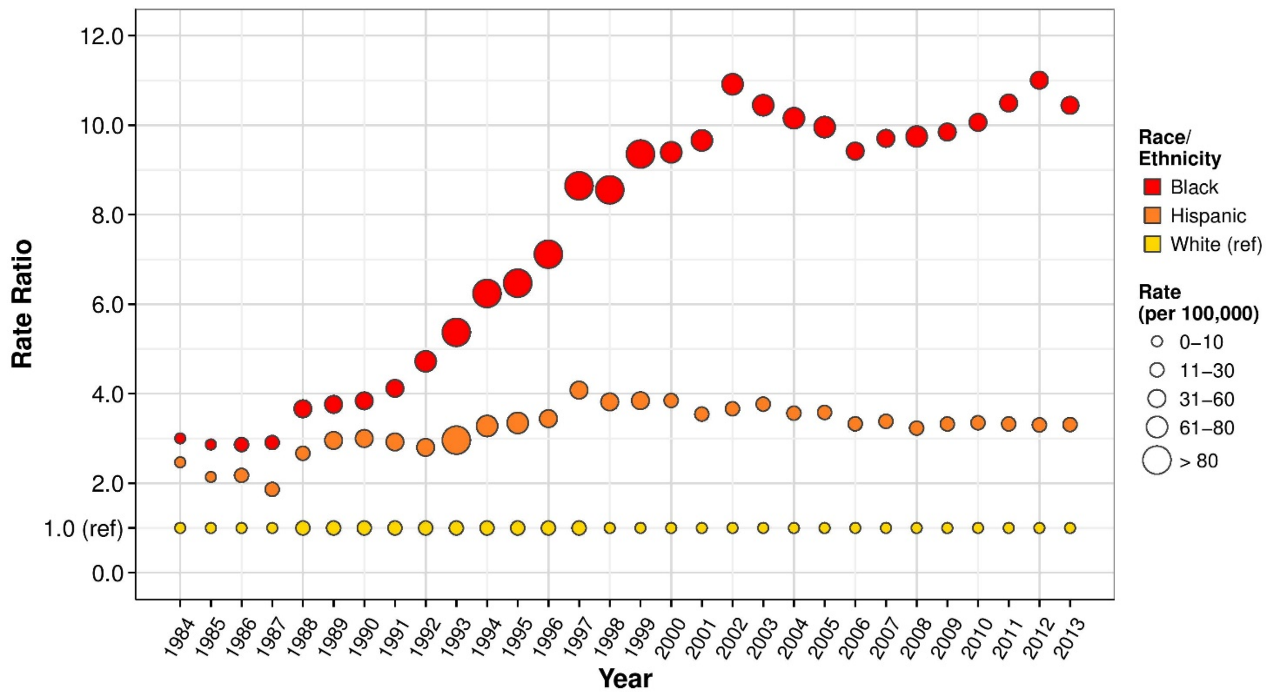


Figure 2.2 Trends in Racial/Ethnic Disparities of New AIDS Diagnoses among Adults and Adolescents, US and Puerto Rico, 1984−2013

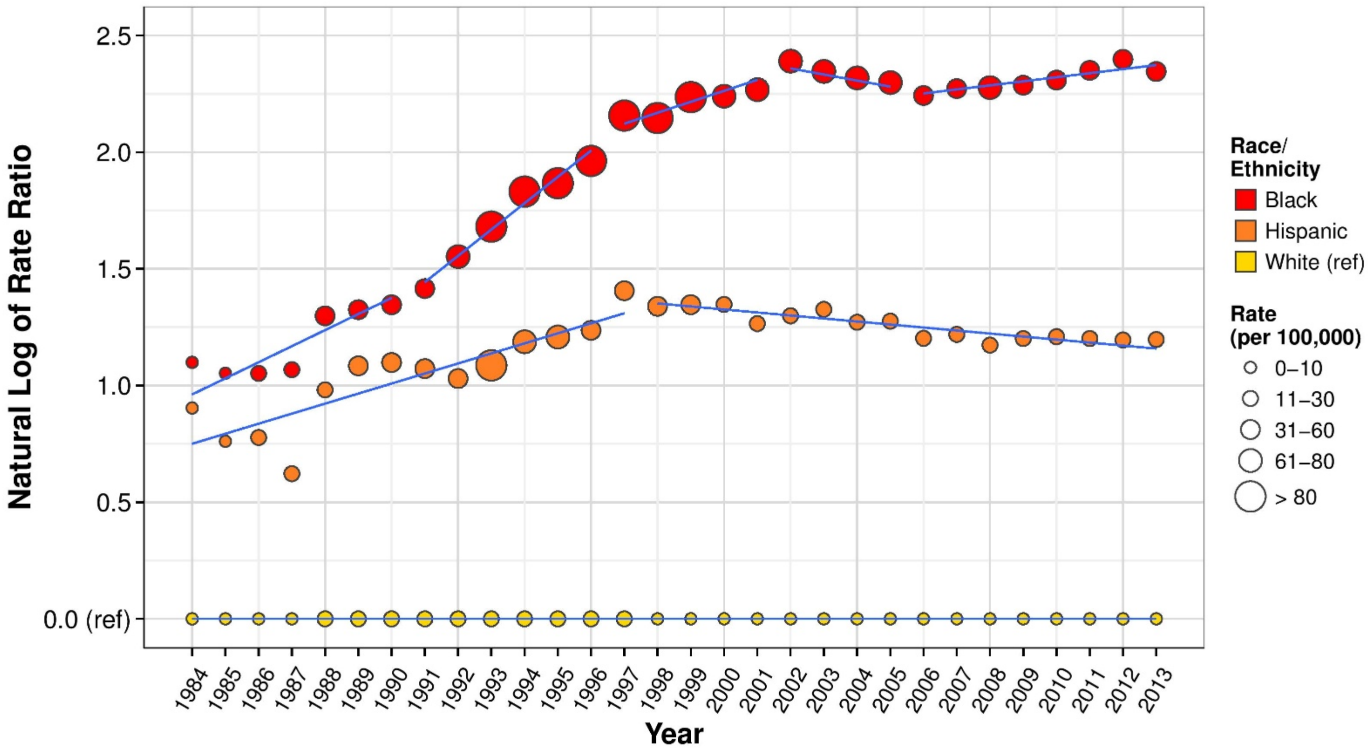
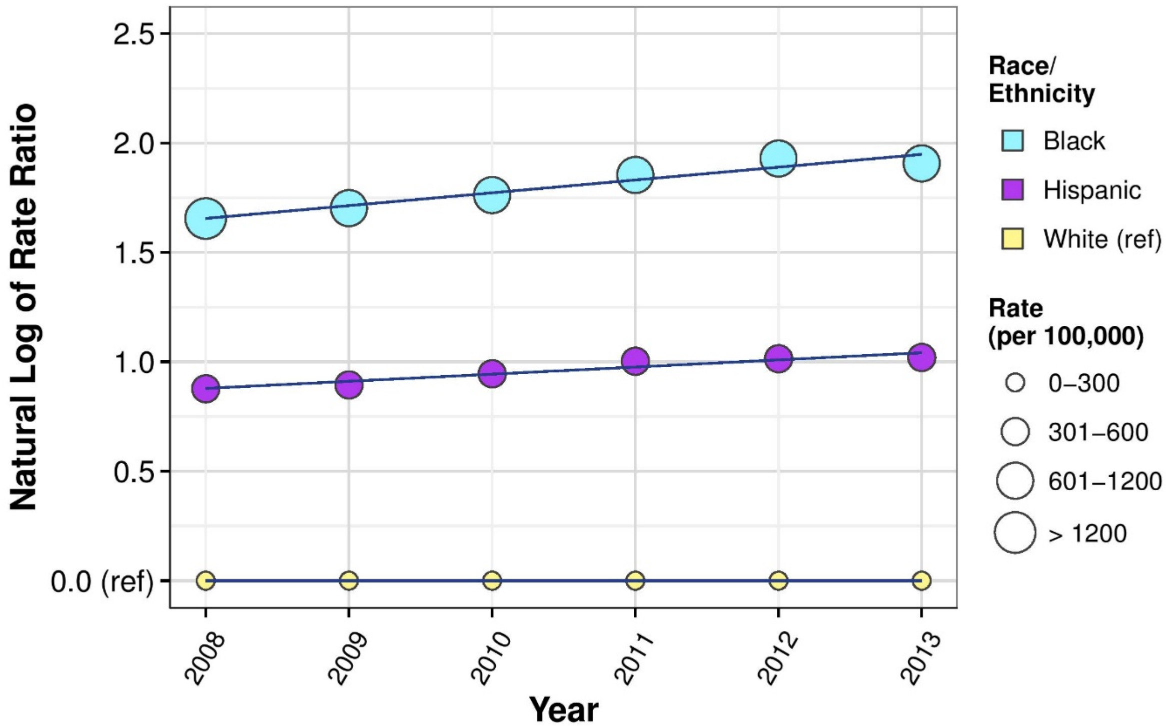


Figure 2.3 Trends in Racial/Ethnic Disparities of New AIDS Diagnoses among Men Who Have Sex with Men (MSM), United States, 2008−2013



Abbreviations: MSM=men who have sex with men

1. Rate denominators for MSM are an estimated proportion of 3.9% of the total male population ages 13 and older by race. Rate denominators for non–MSM males were therefore an estimated 96.1% of the total male population (Purcell et al. 2012).
2. Hispanics in this subanalysis represent U.S. Hispanics only (do not include Puerto Rico).
3. EAPC(Black–White Rate Ratio)=6.0, p<0.01; EAPC(Hispanic–White Rate Ratio)=3.3, p<0.01

Supplementary Material

Table 2.A Data characteristics and sources for measuring racial/ethnic disparities[1] in new AIDS Diagnoses, United States and Puerto Rico, 1984-2013

Years	Race/ethnicity	Numerator(s)	Denominator(s)	Source(s)
1984-1988	Black, NH White, NH Hispanic	Case counts by race[2]		CDC annual HIV surveillance reports
			United States (US): Intercensal state-level population estimates (aggregated) by race and 5-year age groups; intercensal state-level population estimates (aggregated) by single-year age [3] *Puerto Rico (PR):* Intercensal population estimates by 5-year age groups[4]	US Census Bureau Puerto Rico National Institute of Statistics
1989-2007	Black, NH White, NH	Reported (1989-2001) or estimated (2002-2007) rates by race for adults and adolescents (13+ years)[5]		CDC annual HIV surveillance reports
	Hispanic 1989-2001:	Reported rates by race for adults and adolescents (13+ years)[5]		CDC annual HIV surveillance reports
	2002-2007:	Estimated case counts[6]	*US:* Intercensal population estimates by race and single-year age[7] *PR:* Intercensal population estimates by single-year age[7]	CDC annual HIV surveillance reports US Census Bureau
2008-2013	Black, NH White, NH Hispanic	Estimated case counts by race		CDC annual HIV surveillance reports
			US (2008-2009): Intercensal population estimates by race and single-year age[7] *PR (2008-2009):* Intercensal population estimates by single-year age[7] *US (2010-2013):* Postcensal population estimates by race and single-year age[8] *PR (2010-2013):* Postcensal population estimates by single-year age[8]	US Census Bureau (American Fact Finder)

Abbreviations: NH=Non-Hispanic, US=United States, PR=Puerto Rico

[1] Example calculation for annual Black-White disparity from 1984-1988 and 2008-2013:

$$\text{Black-White rate ratio} = \frac{\text{(Case counts among Blacks / Population estimates for Blacks)*100,000}}{\text{(Case counts among Whites / Population estimates for Whites)*100,000}}$$

Example calculation for annual Black-White disparity from 1989-2007:

Black-White rate ratio = Reported rate per 100,000 for Blacks / Reported rate per 100,000 for Whites

[2] Only cumulative case counts by race for adults and adolescents were available for these years. Therefore, a given year's case count was calculated by subtracting the previous year's cumulative case count, and this was done for each racial/ethnic group.

[3] For 1984-1998, US intercensal aggregated state-level population estimates stratified by both race and 5-year age groups were publicly available. The same census data was available by single-year age, but not additionally stratified by race. Therefore, we applied the racial distribution for the 10-14 year old age group to the single-year population estimates for 13 and 14 year olds. We then added these to the population estimates by race for adults 15 years of age or older in order to include adults and adolescents 13 years of age and older in the estimate of our rate denominators for these years.

[4] For 1984-1988 Puerto Rico estimates, only 5-year age groups were reported, therefore the 10-14 year old group was multiplied by 2/5 to estimate the number of 13-14 year-olds and include in our population denominator. All population estimates and case counts for Puerto Rico were considered of Hispanic ethnicity.

[5] CDC annual surveillance reports used postcensal data for the calculation of denominators for reporting rates by race.

[6] For years 2002-2007, to calculate rates for Hispanics, case counts reported in the HIV surveillance report for US Hispanics were summed with case counts for Puerto Rico. The only case counts reported for Puerto Rico for these years included both adults and children, therefore we needed to subtract out new AIDS diagnoses among children each year. We used a given year's cumulative case count data for children and subtracted the previous year's cumulative case count for children to calculate the number of cases among children each year. We then subtracted this number from the total new AIDS diagnoses reported for Puerto Rico in that year to obtain the Puerto Rico case count among adults and adolescents for that given year.

[7] For 2002-2009, US and Puerto Rico population estimates for these years were available by race and single-year age to include race-specific population estimates for adults and adolescents 13 years of age and older. Intercensal estimates were used due to availability and to remain consistent with previous years when population denominators required estimation (1984-1988).

[8] For years 2010-2013, only postcensal data were available for mid-year population estimates.

Table 2.B Calculated rate ratios for the black-white and Hispanic-white racial/ethnic disparities in AIDS diagnoses, United States and Puerto Rico, 1984-2013

Disparity	Years, Rates, and Rate Ratios[1]									
	1984	**1985**	**1986**	**1987**	**1988**	**1989**	**1990**	**1991**	**1992**	**1993**
Black Rate	5.3	9.3	14.5	23.5	41.5	44.4	53.8	58.5	66.6	162.2
Hispanic Rate	4.3	6.9	11.0	15.1	30.2	34.9	42.0	41.5	39.5	89.5
White Rate	1.8	3.2	5.1	8.1	11.3	11.8	14.0	14.2	14.1	30.2
Black-White Rate Ratio	3.0	2.9	2.9	2.9	3.7	3.8	3.8	4.1	4.7	5.4
Hispanic-White Rate Ratio	2.5	2.1	2.2	1.9	2.7	3.0	3.0	2.9	2.8	3.0
	1994	**1995**	**1996**	**1997**	**1998**	**1999**	**2000**	**2001**	**2002**	**2003**
Black Rate	129.8	119.7	115.3	107.2	84.7	84.2	74.2	76.3	76.4	75.2
Hispanic Rate	68.2	61.9	55.8	50.6	37.8	34.6	30.4	28.0	25.7	27.1
White Rate	20.8	18.5	16.2	12.4	9.9	9.0	7.9	7.9	7.0	7.2
Black-White Rate Ratio	6.2	6.5	7.1	8.6	8.6	9.4	9.4	9.7	10.9	10.4
Hispanic-White Rate Ratio	3.3	3.3	3.4	4.1	3.8	3.8	3.8	3.5	3.7	3.8
	2004	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**
Black Rate	72.1	68.7	60.3	59.2	61.0	55.1	52.7	51.3	44.8	41.3
Hispanic Rate	25.3	24.7	21.3	20.6	20.2	18.6	17.5	16.3	13.4	13.1
White Rate	7.1	6.9	6.4	6.1	6.3	5.6	5.2	4.9	4.1	4.0
Black-White Rate Ratio	10.2	10.0	9.4	9.7	9.7	9.8	10.1	10.5	11.0	10.4
Hispanic-White Rate Ratio	3.6	3.6	3.3	3.4	3.2	3.3	3.4	3.3	3.3	3.3

[1] Rate ratios were calculated with unrounded race-specific rate values; rounded rates and rate ratios are presented.

CHAPTER 3: Trends in number and composition of sex partners among men who have sex with men in the United States, National HIV Behavioral Surveillance, 2008–2014

Abstract

Background: Social and legal acceptance of long-term same-sex partnerships in the United States has increased over the past decade which may impact sexual partnering among men who have sex with men (MSM). Identifying if and how partnering trends have evolved nationally could improve understanding of HIV transmission and prevention among MSM.

Methods: We used CDC's National HIV Behavioral Surveillance data from three cross-sectional surveys (2008, 2011, and 2014) to study trends in the number and composition of sex partners among US MSM. Participants were recruited through venue-based sampling and were offered a behavioral questionnaire and HIV testing. Past-12-month outcomes included the number of total partners, number of main partners, proportion of men with only 1 main partner, proportion of men with both main and casual partners, and condomless anal sex (CAS) among men with (a) only 1 main partner or (b) both main and casual partners. To measure changes over time, we used identity-linked Poisson regression for count outcomes and log-linked Poisson regression with robust standard errors for binary outcomes.

Results: Our analytic sample included 28,061 participants. Overall, the mean total number of male sex partners in the past year increased, while the mean number of main partners remained stable. The proportion of MSM engaged in only 1 main partnership in the past year had a relative 3-year decrease of 14% and the proportion of MSM with both main and casual partners had a relative 3-year increase by 9%. We observed a shift from MSM having ≥1 main partners and 0 casual partners to having ≥1 main partners and ≥2 casual partners. Condomless anal sex in the past year increased significantly regardless of partner composition.

Conclusions: Although we expected that growing social and legal acceptance of long-term same-sex partnerships could lead MSM to pair more with main partners, we did not observe this trend. MSM reported sex with a greater number of partners per year; this increase was characterized by more casual partners in addition to 1+ main partners in the past year. Because men are increasingly having both main and casual partners, partner-based and individual prevention programs remain critical to reaching MSM.

Introduction

Gay, bisexual, and other men who have sex with men (collectively referred to as MSM) are disproportionately affected by HIV and accounted for 70% of new HIV diagnoses in 2015.[1] Over the past decade, numerous prevention interventions have been introduced to reduce HIV infections among MSM, including partner-based interventions such as couples' HIV testing and counseling (CHTC).[2,3] CHTC predominantly targets main partnerships with testing and prevention services, allowing for greater reach in offering services to two individuals at one point in time.[4,5] CHTC also provides tailored counseling messages by better understanding an individual's risk through identifying the behaviors and clinical HIV status of the sexual partner. Deterministic models have previously estimated that 68-78% of HIV transmissions in MSM arise from main partnerships and researchers posit that this higher risk of acquiring HIV from a main partner is likely driven by greater condomless anal sex and higher sex frequency in main partnerships compared to casual partnerships.[6,7] Yet, sexual network models typically attribute most HIV transmissions to casual partners, perhaps because these models are able to capture increased concurrency with casual partners.[8,9] Nevertheless, network models still estimate that about 45% of HIV transmissions in MSM arise from main partners, indicating that almost one in two infections occur in main partnerships for whom we have existing partner interventions.[8]

Though the underlying drivers of HIV transmission among MSM may vary based on main and casual partner types, little is known about how the composition of sex partner types has changed nationally in recent history, and thus, which relationship contexts should be prioritized for HIV prevention. Over the last 20 years, significant progress has been made in the acceptance of long-term same-sex partnerships in the United States, culminating in the Supreme Court decision to legalize same-sex marriage in 2015. According to the General Social Survey, from 1991-2010, public acceptance of “homosexual behavior” has increased by 27% and “same-sex marriage” by 35%.[10] These recent social and legal changes over the past two decades could be leading to changes in sexual partnering among MSM, with possible implications for HIV transmission and prevention. For example, one hypothesis is that, on average, MSM may be more likely to form main partnerships during this period and reduce their number of total partners. A second hypothesis is that MSM on average may maintain the same total number of partners, but shift the composition of these partnerships towards having more main partners. Similar trends in condomless anal sex may be occurring within main and casual MSM partnerships. Previous research has shown that condomless anal sex among MSM in the US has been increasing since 2005, but it is unknown whether this could be result of an increasing number of main partnerships, within which MSM are more likely to engage in condomless anal sex.[11,12]

We sought to evaluate recent changes in the number and composition of sex partners among MSM to identify if and how sexual partnering has changed in an era of increasing social and legal acceptance of long-term same-sex partnerships in the United States. Identifying and describing these changes could provide critical information for understanding HIV transmission among MSM and for determining the relationship contexts in which HIV prevention efforts should be focused, such as the relative importance and priority for partner-based interventions targeting main partnerships.

Methods

The Centers for Disease Control and Prevention (CDC)'s National HIV Behavioral Surveillance (NHBS) collects data on HIV risk and prevention behaviors among three populations: MSM, persons who inject drugs, and heterosexuals at increased risk for HIV infection.[13] Cross-sectional data reported in this analysis were collected among MSM in three survey "rounds" (2008, 2011, 2014). NHBS sampling procedures have been previously published and are summarized briefly here.[14] MSM were recruited through venue-based, time-space sampling and, if eligible, were offered a behavioral survey and HIV testing. Eligible men included those who were male sex at birth, had ever had sex with another man, were age 18 years or older, currently resided in a participating metropolitan statistical area (MSA), had not previously participated in NHBS during that year's survey, were able to complete the survey in English or Spanish, were male sex at birth, and self-identified as male. For this analysis, eligible men also had to have at least one male sex partner in the past 12 months. NHBS activities were approved by local institutional review boards in each of the 21 participating MSAs (listed in Table 1).

Partner count outcomes included the number of total male sex partners in the past 12 months and the number of main male sex partners in the past 12 months. We estimated the adjusted mean partner counts overall and by key demographic characteristics. Total partner counts above 50 (2.1%) were set to 50 and main partner counts above 10 (0.3%) were set to 10 to avoid the influence of outliers on trends in mean counts. We used identity-linked Poisson regression to evaluate trends in the count outcomes and measured the mean change in partner count per 3-year increase in time. Descriptive statistics are reported for the binary outcomes of having only one main partner in the past year, having both main and casual partners in the past year, and having condomless anal sex in the past year among (a) men with only one main partner and (b) men with both main and casual partners. Main partners referred to “men with whom the participant has had sex and feels committed to above anyone else” and casual partners referred to “men with whom the participant has had sex yet does not feel committed to or does not know very well.”[15] Because the odds ratio can overestimate the prevalence ratio for common binary outcomes in cross-sectional studies, we used log-linked Poisson regression with robust standard errors to obtain estimated “round” percent changes (ERPCs), which represent the mean relative percent change in the outcome per 3-year increase in time.[16]

All models included year as the main, continuous term of interest; age, race, and HIV status as covariates of interest; and all two-way interaction terms between year and age, race, and HIV status in order to evaluate changes overall and by key characteristics. Because each model contained multiple interaction terms with year, when estimating the effect of year by one covariate of interest, we specified the distribution of the other two variables from the combined sample across all three survey years. This allowed for standardizing the year effects to the sample distribution of the other two variables in the model. City was also included in models to account for potential confounding and all models accounted for clustering by venue recruitment event. An alpha level of 0.05 was used to determine statistical significance. All analyses were conducted in SAS 9.4 and figures were created using R’s ggplot2 package.

Results

For this analysis, we included 28,061 men across the three NHBS-MSM rounds who consented to participate, provided complete, valid survey responses, reported having at least one male sex partner in the past year, and provided information on the key covariates of interest (age, race/ethnicity, and self-reported HIV status). Key characteristics of the sample by NHBS round are described in Table 3.1.

Partner Count Outcomes

Overall, the adjusted mean total number of male sex partners in the past year increased among MSM from 7.1 in 2008 to 7.7 in 2014 (Table 3.2; Supplementary Material—Figure 3.A). We found significant differences by age and race. On average, MSM younger than 40 experienced an increase of between 0.43 and 0.60 total partners per 3-year increase in time, while MSM ages 40 and older experienced stable total partner numbers. Black and Hispanic MSM, and MSM of other race/ethnicities apart from White, had stable trends in total partner counts; yet, White MSM had a significant increase of 0.67 total partners per 3-year increase. Total number of partners increased significantly among both HIV-negative and HIV-positive MSM.

Partner type was missing for eight observations; hence, 28,053 participants were included in analyses of the main partner count outcome (Table 3.2; Supplementary Material—Figure 3.A). The mean number of main male sex partners among MSM overall was stable from 2008 to 2014 at about 1 main partner per year. There were significant differences by age and HIV status. MSM ages 18-24 and 40 years and older both experienced a significant decrease in the number of main partners, but MSM ages 25-39 had stable trends. Although main partner counts slightly decreased for HIV-negative MSM, main partner counts increased for HIV-positive MSM. The number of main partners significantly decreased in Hispanics, but remained stable for all other race/ethnicities.

Partner Type Composition and CAS Outcomes

The proportion of MSM having only one main partner in the past 12 months significantly declined from 19.9% in 2008 to 15.1% in 2014 overall. This represented a relative percent decline of 13.5% per 3 years during this period (ERPC= -13.5%, $p<0.01$; Table 3.3 and Supplementary Material—Figure 3.B). Significant interactions were found by age and race. Although the decline in the proportion having only one main partner occurred across all age groups and all race groups, the greatest decreases were in younger MSM ages 18-24 and 25-29 years, and in White and Black MSM. The proportion having only one main partner in the past year remained stable in HIV-positive MSM and MSM with an unknown HIV status, despite declining in HIV-negative MSM.

The proportion of MSM having both main and casual partners in the past 12 months significantly increased overall from 36.9% in 2008 to 44.1% in 2014. This represented a relative percent increase of 9.1% per 3 years (ERPC=9.1%; $p<0.01$; Table 3.3 and Supplementary Material—Figure 3.B). We found no significant interactions for this outcome. When comparing the number and composition of partner types over time, the proportion of men who reported having one or more main partners and zero casual partners decreased by 7.6% (percentage points) from 2008 to 2014 while the proportion of men who reported having one or more main partners and two or more casual partners increased by 6.3% (percentage points), and all other composition types remained stable (Figure 3.1).

Of those who had only one main partner in the past year, two did not report on condom use (n=4,897); of those who had both main and casual partners in the past year, 13 did not report on condom use (n=11,566). Condomless anal sex among men with only one main partner in the past 12 months increased significantly from 53.0% in 2008 to 64.0% in 2014 (Figure 3.2 and Supplementary Material—Table 3.A). Condomless anal sex among men with both main and casual partners in the past 12 months was higher and also significantly increased from 69.0% in 2008 to 77.8% in 2014. We found no significant interactions for either outcome.

Discussion

From 2008 to 2014, the mean number of total partners in the past year among MSM significantly increased overall, driven mostly by White MSM and MSM under the age of 40, while the mean number of main partners has remained stable. During the same period, the proportion of MSM engaged in only one main partnership in the past year decreased and the proportion with both main and casual partners increased. Partnering changes were characterized by decreases in MSM reporting one or more main partners and zero casual partners and increases in MSM reporting one or more main partners and two or more casual partners. Condomless anal sex in the past year increased significantly regardless of partner type composition.

Although we expected that growing social acceptance of long-term same-sex partnerships could contribute to MSM being more likely to pair with main partners and/or have only one main partner in the past year, we did not observe this trend. Our overall findings suggest that MSM are increasingly engaging in sex with additional casual partners. These results could serve to generate new hypotheses for future research. For example, one explanation for our results may be that increasing social acceptance of same-sex relationships in general has led MSM to experience less stigma about same-sex behaviors and be more open to meet new casual sex partners in recent years. Another hypothesis is that the internet boom and accessibility to smartphones, dating apps, social media, and other online tools during the past decade has profoundly changed how men seek partners, greatly reducing the time and physical space needed to meet potential sex partners.[17] Therefore, it is possible that increasing use of the internet may be contributing to an increasing number of sex partners and/or a shift towards casual partners who may be easier to find online. A recent analysis of MSM found that Internet use to meet men has increased since 2008 and that frequent Internet use was associated with greater partner counts in 2014.[18] We conducted a limited post-hoc analysis on our 2011 and 2014 data, and found that when controlling for Internet use, the increasing trend in total partner counts slightly attenuated and the trend in the proportion with both main and casual partners became stable. We further stratified our sample by Internet use frequency and found that, among MSM who frequently (e.g., weekly or more often) used the Internet to meet or socialize with men, the mean total partner counts increased by 1.1 partners per 3 years ($p<0.01$) and the proportion of MSM with both main and casual partners increased by 5.7% per 3 years ($p=0.02$), whereas MSM with infrequent use or no use in the past 12 months had stable partner outcomes. This sub-analysis supports that partnering trends may differ by Internet use and these associations should be further examined. Future studies that consider trends in Internet use to meet partners and associated risk behaviors should focus on understanding these trends by partner type and should compare behaviors between online and offline partners by partner type. Although occurring during a period of stable overall HIV incidence for MSM, these hypotheses and proposed behavioral patterns would be consistent with our results as well as the recent increases that have been observed in condomless anal sex and sexually transmitted infections (STI) among MSM in the United States and parts of Europe.[11,19-21]

The increases in total partners and the proportion of MSM with both main and casual partners in the past year raise an important concern that these may be concurrent main and casual partnerships and that concurrency may be increasing among MSM. Concurrency is defined as the “overlapping of sexual partnerships where sexual intercourse with one partner occurs between two acts of intercourse with another partner,” and concurrency can contribute to the spread of infection via partners’ indirect exposure to one another.[22-25] Concurrency can be more common within casual partnerships, as these tend to be shorter and MSM may have multiple casual partners allowing for frequent partner turnover and potential overlap in sexual acts.[26,27] Yet, main partnerships tend to be longer in duration and have a higher frequency of sex acts and condomless anal sex than casual partnerships.[6,27] If the main and casual partnerships MSM report are not serially monogamous, it is possible that men may be having sex with additional casual partners while in a longer-duration main partnership, resulting in concurrency and increasing a main partner’s risk of acquiring HIV. This may warrant increased attention to prevent transmissions to main partners who are exposed to condomless anal sex more frequently. Unfortunately, we were not able to examine timing of these partnerships and therefore whether concurrency may be increasing among MSM, yet this should be considered in future studies. Lastly, we thought that previous findings of increasing condomless anal sex among MSM could be explained by an increasing number of main partnerships which are more likely to practice condomless anal sex; however our results do not support this and further analyses to explain current increasing condomless anal sex trends are needed.

We observed heterogeneity in partner outcomes by age, race, and HIV status. Black and Hispanic MSM had stable total partner counts and either stable or slightly declining main partner counts, yet both groups still experienced a significant increase in the proportion of MSM with both main and casual partners. These results indicate that although total partner counts were constant on average, there was still a shift in partner composition towards having both main and casual partners. This could suggest that there may only be a certain number of sex partners that Black and Hispanic MSM continue to have over a year's time, but that a similar change towards casual partners is occurring among Black and Hispanic MSM as observed for other races. Young MSM ages 18-24 had the largest increase in total partners and the greatest declines in main partner counts and the proportion with only one main partner. One explanation for these results could be that population-level exposure to technology and online dating apps is unequally distributed or unequally increasing by age, such that young MSM are more likely to use these media to seek sex partners than their older counterparts, exposing them to more casual partners.[28] MSM with a known HIV-positive status had increasing total partner counts and increasing main partner counts; however, the magnitude of the increase in main partners was not enough to account for the total increase. Therefore, additional casual partners are still largely contributing to the total partner increase in HIV-positive MSM. The proportion with both main and casual partners is also increasing in this subgroup and could indicate increasing concurrency. Though HIV transmission risk from known, non-recently-infected HIV-positive MSM to concurrent HIV-negative partners confers no additional risk over having the same number of serially monogamous HIV-negative partners, increased concurrency would still be relevant to these partners' risk of acquiring other STIs.

Our findings regarding increasing casual partners and a shift towards casual partnering suggest that individual interventions for HIV prevention should continue to receive high priority for funding resources. Men with multiple casual partners may need individual interventions where they can be regularly tested and identified as candidates for treatment or PrEP. These individual interventions should emphasize multiple options for reducing risk, including partner reduction and condom use. Yet, because the increase in casual partners did not occur alone, but in addition to having main partners, partner-based interventions that target main partnerships are still warranted for MSM. Existing partner-based interventions such as couples' HIV testing and counseling are not commonly offered as part of routine HIV testing, but these interventions can facilitate testing together and encourage discussion about HIV status and sexual agreements.[4,5,29] Utilizing main partnerships to identify positive partners and start them on treatment, and/or identify candidates for PrEP, could be important to reducing potential transmission not only within the partnership but with outside casual partners. Increasing financial support and capacity building for CHCT in facilities that already provide HIV testing could maximize the impact of testing services and prevent transmissions among men in both main and casual partnerships.

This study is subject to several limitations. First, it is possible that insufficient time has accrued since social and legal acceptance of long-term same-sex partnerships has increased to be able to observe and interpret the impact of social trends on sexual partnering norms; analyses should be revised once more data is available in future years. Second, these data were collected using venue-based sampling and therefore are not generalizable to non-venue-attending MSM.

Furthermore, it is important to note that our sample was comprised of men who visit venues such as gay-oriented bars and restaurants, and it may be that men in committed, main partnerships are less likely to attend these venues. This may result in an underestimation of men with main partners and/or only one main partner in the past year. However, we did not expect this proportion of men in committed main partnerships who do not visit venues to change substantially over time and therefore we did not anticipate this to affect our estimates. Because we focus on self-reported sexual behavior outcomes, it is possible that social desirability may bias our estimates, underestimating partner counts and condomless anal sex. Though difficult to assess how social desirability bias may have changed over time without more objective measures of behavior, MSM may be more open to sharing information and less likely to misreport sex behaviors in recent years. In future NHBS rounds with MSM, additional biological measures such as STI infections are planned and may be able to capture the magnitude of potential biases in self-reported sexual behavior data. Another limitation is that we cannot account for possible changes in men's perceptions of partner type over time. For example, there is some evidence that Black MSM are more likely to categorize a partner as "main" even if the relationship takes on qualitative characteristics objectively considered as only "low or medium involvement," compared to White MSM.[30] We do not know if perceptions of partner types may have changed over time for MSM subgroups, but the objective definitions of partner types used during NHBS interviews did not change. Despite these limitations, NHBS is the only national data source that has captured trends in partner and behavioral outcomes among a large sample of MSM during the period of interest, providing critical data to examine the proposed research questions and generate hypotheses for future research.

Conclusion

We found that total partner counts are increasing or stable across MSM subgroups, while main partner counts remain stable across most all groups. Partner type composition is changing, with an increasing proportion of MSM having both main and casual partnerships in the past year, characterized by having more casual partners in addition to one or more main partners. Condomless anal sex is increasing regardless of partner composition. Current trends do not support the original hypothesis of partner reduction or shifts towards main partnerships in an era of increasing acceptance of long-term same-sex relationships, though this should be re-examined once more years of data are available. In light of these behavioral trends, prevention efforts that utilize knowledge about partners are needed. Main partnerships can provide opportunities for routine couples' HIV testing, condom negotiation, and identification of partners who need to enter or re-enter HIV care or initiate PrEP. Individual interventions for men with multiple casual partners or both main and casual partners should continue to target MSM with at least annual HIV testing and encourage condom use and partner reduction. Future research should study potential increases in concurrency by partner type and examine post-hoc hypotheses that could explain current partnering trends, including the increasing use of Internet and dating apps where MSM may be meeting additional casual sex partners in recent years.

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Table 3.1 Sample Characteristics of MSM participating in NHBS, 21 cities, United States, 2008-2014

	2008		2011		2014		Total Combined	
	n	%	n	%	n	%	n	%
Age (yrs)								
18-24	2069	22.4	2347	25.4	1952	20.4	6368	22.7
25-29	1710	18.5	1746	18.9	2094	21.9	5550	19.8
30-39	2561	27.7	2182	23.6	2470	25.8	7213	25.7
≥40	2907	31.4	2954	32.0	3069	32.0	8930	31.8
Race/Ethnicity								
Black/African American	2188	23.7	2485	26.9	2652	27.7	7325	26.1
Hispanic/Latino	2232	24.1	2407	26.1	2523	26.3	7162	25.5
White	4024	43.5	3665	39.7	3668	38.3	11357	40.5
Other	803	8.7	672	7.3	742	7.7	2217	7.9
Education								
High school graduate or less	2712	29.3	2714	29.4	2489	26.0	2489	26.0
Some college or technical college	3021	32.7	3128	33.9	3072	32.1	3072	32.1
College or higher education	3513	38.0	3386	36.7	4023	42.0	4023	42.0
Sexual identity								
Homosexual	7499	81.2	7555	82.11	7794	81.57	22848	81.6
Bisexual/Heterosexual	1735	18.8	1646	17.9	1761	18.4	5142	18.4
Self-reported HIV status								
HIV-negative	7044	76.2	7114	77.1	7381	77.0	21539	76.8
HIV-positive	1101	11.9	1239	13.4	1581	16.5	3921	14.0
Unknown	1102	11.9	876	9.5	623	6.5	2601	9.3
City[1]								
Atlanta, Georgia	347	3.8	556	6.0	505	5.3	1408	5.0
Baltimore, Maryland	501	5.4	451	4.9	496	5.2	1448	5.2
Boston, Massachusetts	281	3.0	415	4.5	301	3.1	1123	3.6
Chicago, Illinois	566	6.1	500	5.4	517	5.4	1583	5.6
Dallas, Texas	509	5.5	471	5.1	500	5.2	1480	5.3
Denver, Colorado	544	5.9	546	5.9	513	5.4	1603	5.7
Detroit, Michigan	388	4.2	460	5.0	508	5.3	1356	4.8
Houston, Texas	448	4.8	509	5.5	508	5.3	1465	5.2
Los Angeles, California	537	5.8	519	5.6	522	5.5	1578	5.6
Miami, Florida	529	5.7	503	5.5	530	5.5	1562	5.6
Nassau-Suffolk, New York	281	3.0	337	3.7	337	3.5	955	3.4
New Orleans, Louisiana	478	5.2	484	5.2	515	5.4	1477	5.3
New York, New York	554	6.0	519	5.6	497	5.2	1570	5.6
Newark, New Jersey	98	1.1	248	2.7	245	2.6	591	2.1
Philadelphia, Pennsylvania	562	6.1	545	5.9	649	6.8	1756	6.3
St. Louis, Missouri	372	4.0	—	—	—	—	372	1.3
San Diego, California	549	5.9	470	5.1	536	5.6	1555	5.5
San Francisco, California	486	5.3	464	5.0	386	4.0	1336	4.8
San Juan, Puerto Rico	355	3.8	363	3.9	515	5.4	1233	4.4
Seattle, Washington	361	3.9	369	4.0	498	5.2	1228	4.4
Washington DC	501	5.4	500	5.4	507	5.3	1508	5.4
Total	9247	33.0	9229	32.9	9585	34.2	28061	100.0

[1]All cities were included in the 2008 survey. All cities except St. Louis, Missouri were included in the 2011 and 2014 surveys.

Table 3.2 Trends in Number of Total and Main Partners among MSM, 21 cities, United States, 2008-2014

	NUMBER OF TOTAL PARTNERS												
	2008			2011			2014			Overall (N=28061)			
	n	Adj. Mean	95% CI	n	Adj. Mean	95% CI	n	Adj. Mean	95% CI	Estimated Round Mean Change[1,2]	95% CI	P-value	Inter.[3] P-value
Age (yrs)													0.02
18-24	2069	6.4	6.1, 6.7	2347	6.7	6.4, 7.0	1952	7.3	7.0, 7.7	0.60	0.31, 0.88	<0.01	
25-29	1710	7.2	6.8, 7.5	1746	7.1	6.8, 7.5	2094	8.1	7.7, 8.4	0.52	0.18, 0.86	<0.01	
30-39	2561	7.4	7.1, 7.7	2182	7.6	7.3, 8.0	2470	8.2	7.9, 8.5	0.43	0.14, 0.73	<0.01	
≥40	2907	7.2	6.9, 7.5	2954	7.2	6.9, 7.5	3069	7.3	7.0, 7.6	0.01	-0.29, 0.31	0.95	
Race/Ethnicity													0.01
Black/African American	2188	6.0	5.7, 6.3	2485	6.0	5.7, 6.3	2652	6.1	5.8, 6.4	0.02	-0.24, 0.27	0.90	
Hispanic/Latino	2232	6.9	6.6, 7.3	2407	7.0	6.7, 7.4	2523	7.4	7.1, 7.7	0.17	-0.14, 0.49	0.29	
White	4024	7.8	7.6, 8.1	3665	8.0	7.7, 8.3	3668	9.1	8.8, 9.4	0.67	0.38, 0.96	<0.01	
Other	803	6.7	6.2, 7.3	672	7.0	6.4, 7.7	742	7.7	7.1, 8.3	0.42	-0.10, 0.94	0.11	
Self-reported HIV status													0.22
HIV-negative	7044	6.8	6.6, 7.0	7114	7.1	6.9, 7.3	7381	7.5	7.3, 7.7	0.36	0.18, 0.54	<0.01	
HIV-positive	1101	8.7	8.2, 9.2	1239	8.5	8.1, 9.0	1581	9.6	9.1, 10.0	0.54	0.03, 1.04	0.04	
Unknown	1102	6.5	6.1, 7.0	876	6.1	5.7, 6.5	623	6.5	6.0, 7.1	0.03	-0.42, 0.47	0.90	
Total	9247	7.1	6.9, 7.2	9229	7.2	7.0, 7.4	9585	7.7	7.5, 7.9	0.35	0.18, 0.52	<0.01	

	NUMBER OF MAIN[4] PARTNERS												
	2008			2011			2014			Overall (N=28053)			
	n	Adj. Mean	95% CI	n	Adj. Mean	95% CI	n	Adj. Mean	95% CI	Estimated Round Mean Change[1,2]	95% CI	P-value	Inter.[3] P-value
Age (yrs)													0.03
18-24	2069	1.3	1.3, 1.4	2347	1.3	1.3, 1.4	1950	1.2	1.2, 1.3	-0.05	-0.09, -0.01	0.02	
25-29	1709	1.1	1.0, 1.2	1746	1.1	1.0, 1.1	2093	1.1	1.1, 1.2	0.02	-0.02, 0.06	0.45	
30-39	2561	0.9	0.9, 1.0	2181	1.0	0.9, 1.0	2470	0.9	0.9, 1.0	0.01	-0.02, 0.04	0.57	
≥40	2907	0.8	0.7, 0.8	2951	0.8	0.7, 0.8	3069	0.7	0.7, 0.8	-0.04	-0.07, -0.01	0.02	
Race/Ethnicity													0.20
Black/African American	2187	1.0	1.0, 1.1	2484	1.1	1.0, 1.1	2651	1.0	0.9, 1.0	-0.03	-0.07, 0.01	0.14	
Hispanic/Latino	2232	1.0	1.0, 1.1	2406	1.0	1.0, 1.1	2523	0.9	0.9, 1.0	-0.04	-0.08, -0.01	0.01	
White	4024	1.0	1.0, 1.0	3663	1.0	0.9, 1.0	3667	1.0	0.9, 1.0	0.00	-0.03, 0.03	0.95	
Other	803	1.0	0.9, 1.0	672	1.0	0.9, 1.1	741	1.0	0.9, 1.1	0.01	-0.05, 0.07	0.69	

– Table 3.2 continued –

– Table 3.2 continued –

Self-reported HIV status												<0.01
HIV-negative	7043	1.0	1.0, 1.1	7112	1.0	1.0, 1.0	7379	1.0	0.9, 1.0	-0.03	-0.05, -0.01	<0.01	
HIV-positive	1101	1.0	0.9, 1.0	1239	1.1	1.0, 1.1	1581	1.1	1.1, 1.2	0.07	0.02, 0.11	<0.01	
Unknown	1102	0.9	0.8, 1.0	874	0.8	0.8, 0.9	622	0.8	0.8, 0.9	-0.02	-0.09, 0.04	0.47	
Total	9246	1.0	1.0, 1.0	9225	1.0	1.0, 1.0	9582	1.0	1.0, 1.0	-0.02	-0.04, 0.00	0.05	

[1]Estimated Round Mean Change (ERMC) = estimated 3-year mean change in number of partners.
[2]ERMC is adjusted for age, race, HIV status, and city and accounts for clustering by recruitment event.
[3]Interaction p-value.
[4]Main partners refer to “men with whom the participant has had sex and feels committed to above anyone else.”

Table 3.3 Trends in Partner Type Composition among MSM, 21 cities, United States, 2008-2014

	ONLY 1 MAIN[4] PARTNER IN PAST 12 MONTHS									
	2008 (N=9246)		2011 (N=9225)		2014 (N=9582)		Overall (N=28053)			
	n	%	n	%	n	%	Estimated Round Percent Change[1,2]	95% CI	P-value	Inter.[3] P-value
Age (yrs)										0.045
18-24	378	18.3	328	14.0	253	13.0	-18.8	-24.9, -12.3	<0.01	
25-29	331	19.4	280	16.0	289	13.8	-16.2	-22.0, -9.9	<0.01	
30-39	523	20.4	401	18.4	371	15.0	-13.3	-18.5, -7.8	<0.01	
≥40	610	21.0	600	20.3	535	17.4	-7.8	-12.9, -2.4	<0.01	
Race/Ethnicity										0.01
Black/African American	448	20.5	501	20.2	393	14.8	-15.0	-20.1, -9.6	<0.01	
Hispanic/Latino	396	17.7	409	17.0	421	16.7	-5.1	-11.2, 1.4	0.12	
White	849	21.1	597	16.3	519	14.2	-18.1	-22.4, -13.5	<0.01	
Other	149	18.6	102	15.2	115	15.5	-9.4	-19.5, 1.9	0.10	
Self-reported HIV status										0.09
HIV-negative	1415	20.1	1228	17.3	1086	14.7	-15.1	-18.4, -11.7	<0.01	
HIV-positive	203	18.4	222	17.9	259	16.4	-7.9	-15.4, 0.3	0.06	
Unknown	224	20.3	159	18.2	103	16.6	-7.7	-16.9, 2.4	0.13	
Total	1842	19.9	1609	17.4	1448	15.1	-13.5	-16.5, -10.4	<0.01	
	BOTH MAIN[4] AND CASUAL[5] PARTNERS IN PAST 12 MONTHS									
	2008		**2011**		**2014**		**Overall**			
	n	**%**	**n**	**%**	**n**	**%**	**Estimated Round Percent Change[1,2]**	**95% CI**	**P-value**	**Inter.[3] P-value**
Age (yrs)										0.95
18-24	899	43.5	1206	51.4	1015	52.1	9.7	6.2, 13.4	<0.01	
25-29	750	43.9	834	47.8	1074	51.3	8.2	4.5, 12.1	<0.01	
30-39	954	37.3	935	42.9	1112	45.0	9.2	5.6, 12.9	<0.01	
≥40	805	27.7	971	32.9	1024	33.4	9.2	4.9, 13.7	<0.01	
Race/Ethnicity										0.09
Black/African American	739	33.8	1004	40.4	1110	41.9	10.4	6.2, 14.8	<0.01	
Hispanic/Latino	889	39.8	1071	44.5	1113	44.1	5.0	1.5, 8.7	<0.01	
White	1472	36.6	1568	42.8	1656	45.2	10.5	7.5, 13.7	<0.01	
Other	308	38.4	303	45.1	346	46.7	11.0	4.8, 17.6	<0.01	

– Table 3.3 continued –

– Table 3.3 continued –

Self-reported HIV status										0.67
HIV-negative	2657	37.7	3112	43.8	3300	44.7	9.6	7.2, 12.0	<0.01	
HIV-positive	423	38.4	535	43.2	704	44.5	7.1	2.3, 12.2	<0.01	
Unknown	328	29.8	299	34.2	221	35.5	8.4	1.0, 16.3	0.02	
Total	3408	36.9	3946	42.8	4225	44.1	9.1	7.0, 11.3	<0.01	

[1]Estimated Round Percent Change = estimated 3-year percent change in number of partners.
[2]ERPC is adjusted for age, race, HIV status, and city and accounts for clustering by recruitment event.
[3]Interaction p-value.
[4]Main partners refer to “men with whom the participant has had sex and feels committed to above anyone else.”
[5]Casual partners refer to “men with whom the participant has had sex yet does not feel committed to or does not know very well.”

Figure 3.1 Trends in Partner Type Number and Composition in the Past 12 Months among MSM, 21 cities, United States, 2008−2014

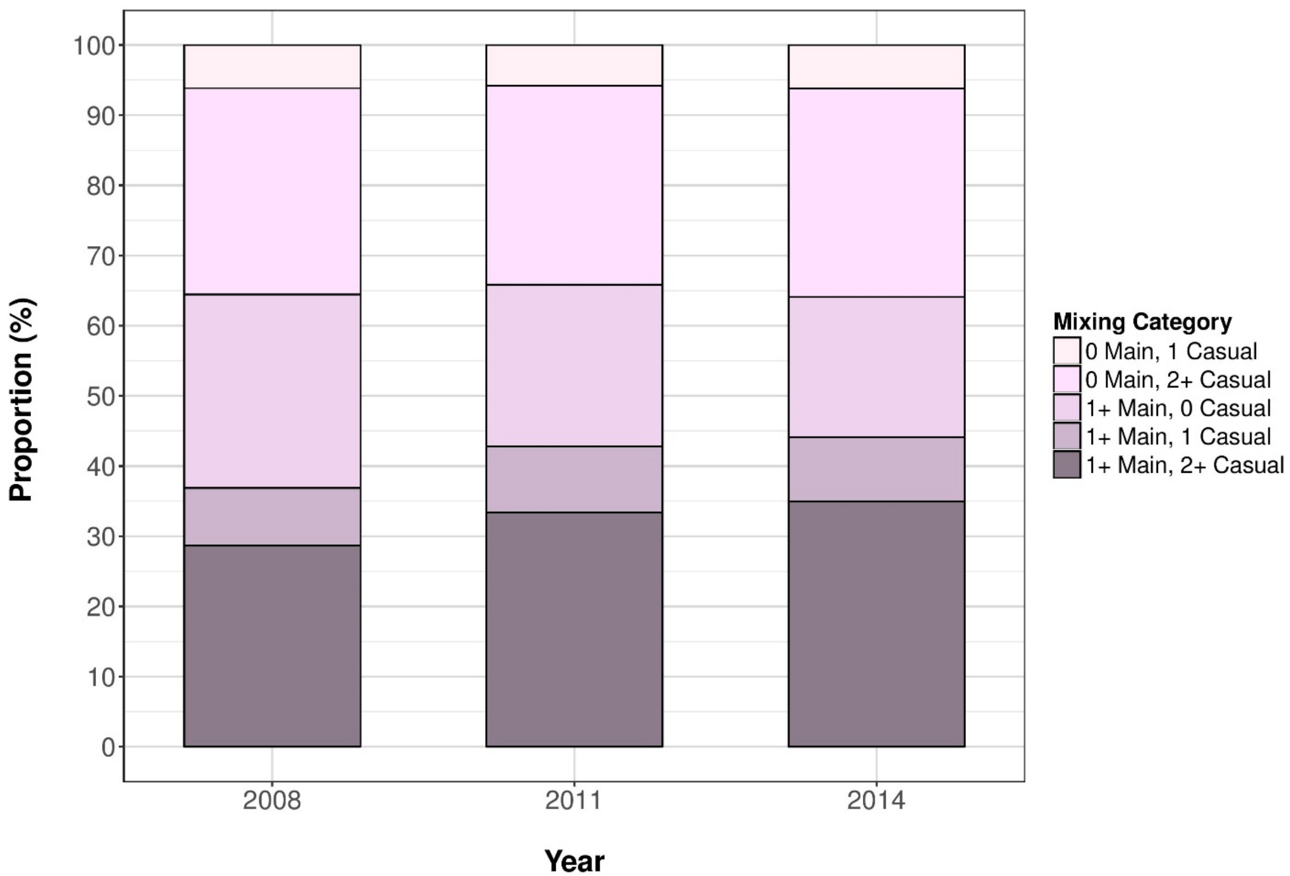
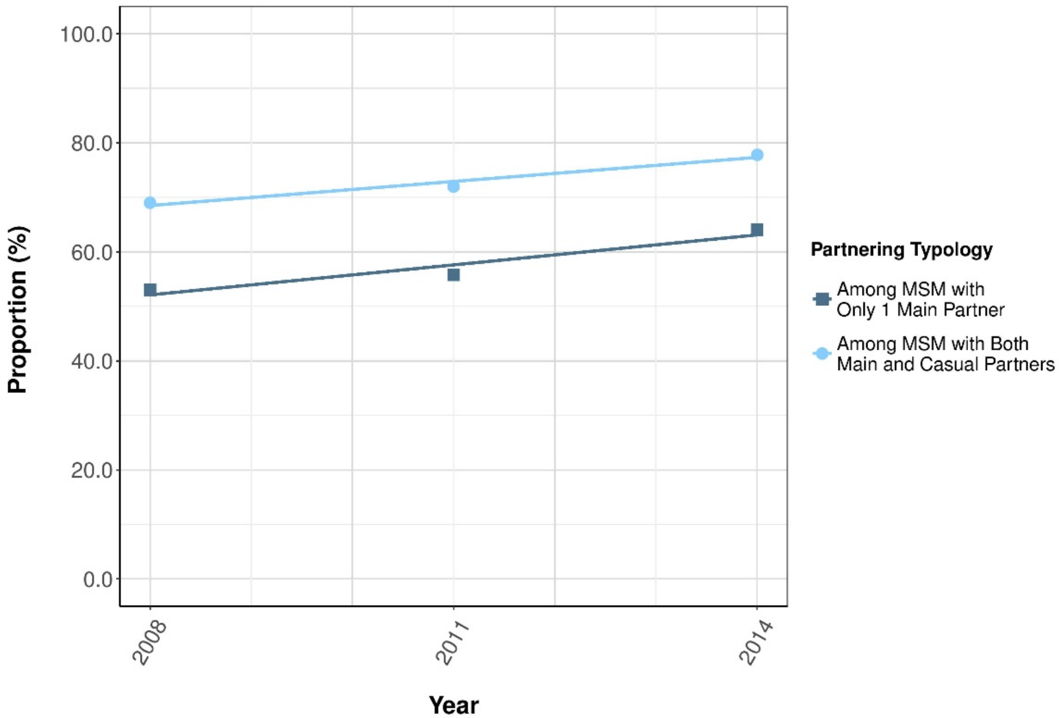


Figure 3.2 Trends in Condomless Anal Sex in the Past 12 Months among MSM by Partner Type Composition, 21 cities, United States, 2008−2014



Supplementary Material

Figure 3.A Trends in the Number of Total and Main Partners in the Past 12 Months among Men Who Have Sex With Men, 21 cities, United States, 2008−2014

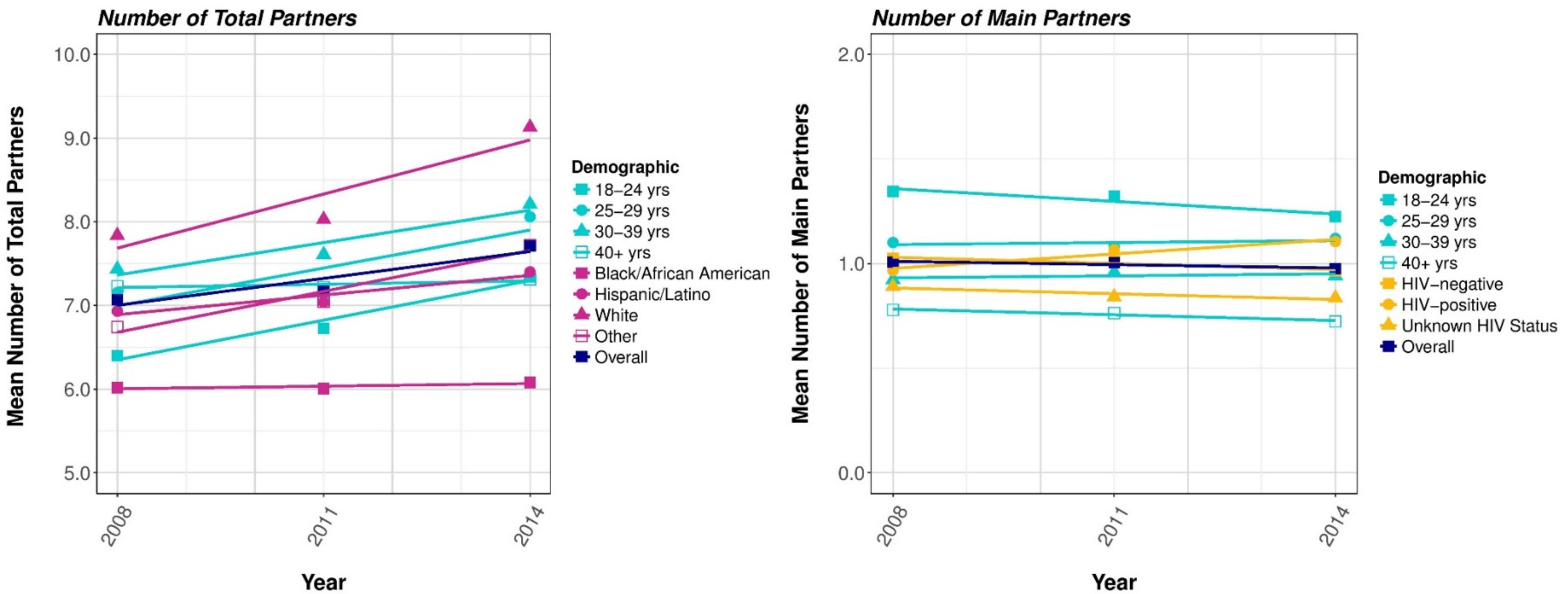


Figure 3.B Trends in the Proportion of MSM with Only One Main Partner or with Both Main and Casual Partners in the Past 12 Months, 21 cities, United States, 2008−2014

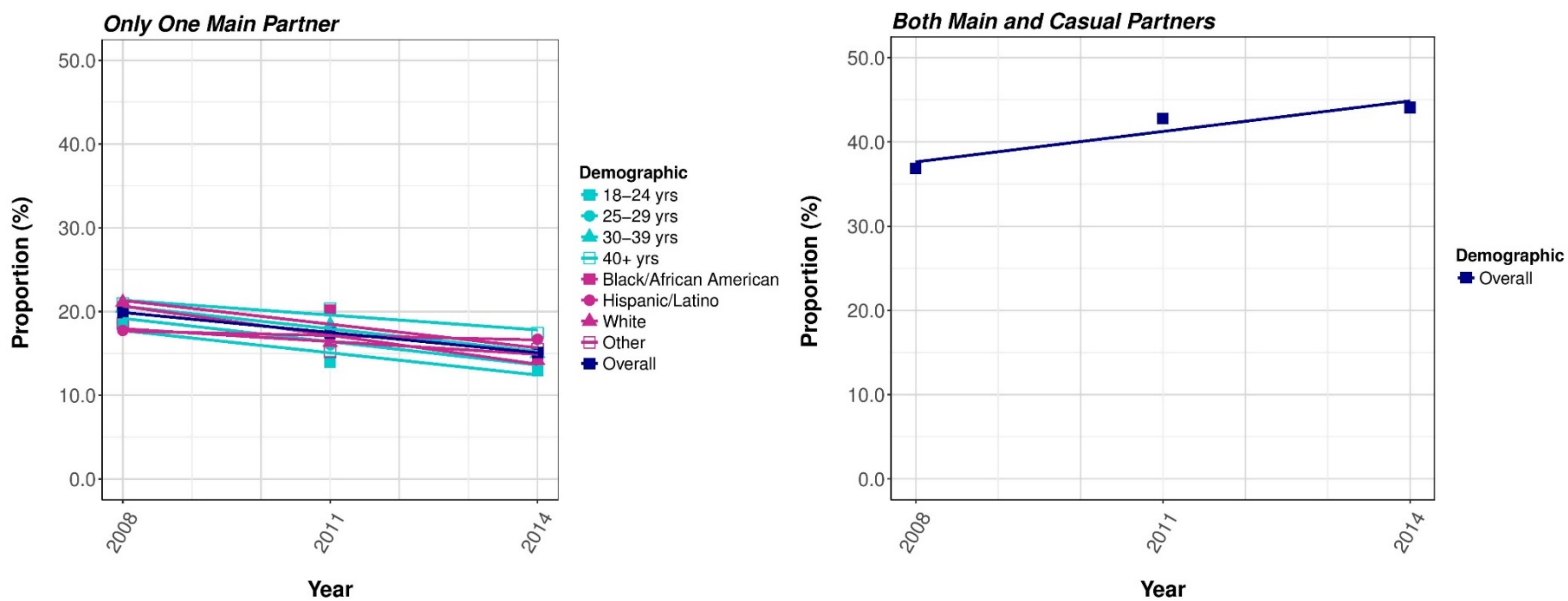


Table 3.A Trends in Condomless Anal Sex by Partner Typology among MSM, 21 cities, United States, 2008-2014

	CONDOMLESS ANAL SEX AMONG MEN WITH ONLY 1 MAIN[4] PARTNER IN PAST 12 MONTHS									
	2008 (N=1841)		2011 (N=1608)		2014 (N=1448)		Overall (N=4897)			
	n	%	n	%	n	%	Estimated Round Percent Change[1,2]	95% CI	P-value	Inter.[3] P-value
Age (yrs)										0.35
18-24	199	52.8	168	51.2	173	68.4	13.7	6.4, 21.5	<0.01	
25-29	201	60.7	161	57.5	209	72.3	9.7	3.2, 16.5	<0.01	
30-39	286	54.7	250	62.3	259	69.8	12.9	7.0, 19.2	<0.01	
≥40	290	47.5	318	53.1	286	53.5	6.4	0.5, 12.7	0.03	
Race/Ethnicity										0.95
Black/African American	193	43.1	217	43.3	200	50.9	9.2	1.4, 17.5	0.02	
Hispanic/Latino	219	55.4	258	63.1	297	70.6	11.5	5.6, 17.7	<0.01	
White	492	58.0	362	60.7	362	69.8	10.0	5.2, 15.1	<0.01	
Other	72	48.3	60	58.8	68	59.1	12.3	1.0, 24.9	0.03	
Self-reported HIV status										0.95
HIV-negative	782	55.3	719	58.6	739	68.1	10.5	6.8, 14.4	<0.01	
HIV-positive	91	44.8	90	40.5	126	48.7	8.8	-1.7, 20.4	0.10	
Unknown	103	46.2	88	55.7	62	60.2	11.4	0.2, 23.7	0.04	
Total	976	53.0	897	55.8	927	64.0	10.4	6.9, 13.9	<0.01	

	CONDOMLESS ANAL SEX AMONG MEN WITH BOTH MAIN[4] AND CASUAL[5] PARTNERS IN PAST 12 MONTHS									
	2008 (N=3406)		2011 (N=3941)		2014 (N=4219)		Overall (N=11566)			
	n	%	n	%	n	%	Estimated Round Percent Change[1,2]	95% CI	P-value	Inter.[3] P-value
Age (yrs)										0.75
18-24	625	69.5	861	71.5	784	77.4	5.7	2.8, 8.6	<0.01	
25-29	552	73.7	629	75.4	866	80.8	5.2	2.5, 8.0	<0.01	
30-39	658	69.0	688	73.7	884	79.6	7.1	4.3, 10.0	<0.01	
≥40	514	63.9	657	67.7	749	73.1	6.9	3.4, 10.5	<0.01	
Race/Ethnicity										0.74
Black/African American	479	64.9	652	64.9	790	71.3	5.0	1.5, 8.6	<0.01	
Hispanic/Latino	624	70.3	802	75.1	886	79.8	6.2	3.4, 9.0	<0.01	
White	1035	70.3	1168	74.5	1336	80.7	7.0	4.8, 9.3	<0.01	
Other	211	68.5	213	70.5	271	78.6	7.6	2.8, 12.7	<0.01	

– Table 3.A continued –

– Table 3.A continued –

Self-reported HIV status										0.30
HIV-negative	1823	68.7	2223	71.5	2548	77.3	6.4	4.6, 8.3	<0.01	
HIV-positive	292	69.0	408	76.4	570	81.0	8.1	4.3, 12.1	<0.01	
Unknown	234	71.3	204	68.2	165	75.0	2.6	-2.8, 8.4	0.35	
Total	2349	69.0	2835	71.9	3283	77.8	6.3	4.7, 8.0	<0.01	

[1]Estimated Round Percent Change = estimated 3-year percent change in number of partners.
[2]ERPC is adjusted for age, race, HIV status, and city and accounts for clustering by recruitment event.
[3]Interaction p-value.

CHAPTER 4: Distribution of HIV transmissions by age, partner type, and clinical factors among men who have sex with men in the United States

Abstract

Background: Whether most HIV transmissions occur in the context of main or casual partnerships among MSM is currently debated and may differ by partner age, HIV stage, and clinical factors.

Methods: We extended a dynamic, stochastic network model that simulated HIV transmission among MSM over time. Behavioral model parameters were stratified by partner type (main, casual, one-time) and age group (18-24 vs. 25-39 years old). We estimated the proportion of HIV transmission events by partner type and age, stage of HIV infection, and HIV clinical care status.

Results: Over half (60%) of transmissions occurred within casual and one-time partnerships, with main partners accounting for 40%. Most transmissions occurred in age-concordant older casual (22%), age-concordant older main (20%), and age-discordant casual (20%) partnerships. Most transmissions occurred while the HIV-positive partner was in the chronic stage (58%) and had not been retained on ART care (63%). For age-concordant younger partnerships, more transmissions occurred while the HIV-positive partner was undiagnosed (18% overall; 58% of younger-younger transmissions).

Conclusions: Because casual and one-time partners accounted for most HIV transmissions, MSM in casual partnerships remain an important target for prevention. Age-concordant older main partnerships may benefit from interventions that focus on retention on antiretroviral therapy for

HIV-positive partners. Younger MSM with younger partners may be indicated for regular testing, risk reduction strategies, and PrEP to prevent new transmissions that more commonly occur when an HIV-positive younger partner is undiagnosed.

Introduction

Men who have sex with men (MSM) experience a disproportionate burden of HIV infections in the United States. Seventy percent (70%) of all HIV diagnoses in 2016 occurred among MSM, who represent only 2% of the US population.[1,2] Young MSM are particularly affected, with those ages 13-24 and ages 25-34 accounting for 27% and 36% of annual HIV diagnoses in MSM respectively. Understanding partner- and network-level factors that contribute to HIV transmission in MSM at certain ages across the life course is critical to identifying targets for HIV prevention.

Determining precisely when and with whom HIV transmissions events occur remains a challenge to quantifying individual and partner characteristics that drive transmission among MSM. Capturing these events would require long-term cohort studies of MSM partnerships and sexual networks; these studies would further have to document changes in partnerships, risk behaviors, and care-related outcomes in order to identify critical age periods and partner attributes that contribute to HIV transmission. Because traditional epidemiologic studies would be logistically and financially difficult to conduct in this context, mathematical models offer a unique opportunity to examine complex HIV transmission patterns and identify dynamic individual and partner factors that increase HIV risk for MSM.

The role of partnership type has been an important factor for HIV transmission among MSM. Three key mathematical models have estimated the proportion of HIV transmissions among MSM in the United States by partner type.[3-5] Sullivan et. al. estimated that 68% of HIV transmissions arise from main partners, mainly driven by the higher sex frequency, greater likelihood of having receptive anal sex, and lower condom use with main partners.[4] Rosenberg et. al. estimated that 78% of HIV transmissions were to main partners.[5] This model differed in that it used more recent data on HIV-positive individuals who had the potential for transmitting HIV to partners. A third model by Goodreau et. al. was a dynamic, stochastic network model and estimated that 39% of transmissions occur in main partnerships.[3] This model represented sexual network structures not captured in earlier deterministic models and was parameterized with data from several different studies conducted between 1999 and 2008. The conflicting results obtained in these studies have led to significant debate about whether most HIV transmissions among MSM arise from main or casual partnerships. Discrepancies may be due to different modeling approaches, different parameters, or different data sources used. Clarifying these disagreements in findings is needed to support HIV prevention policies and interventions for MSM, including partner-based interventions.

Few studies have assessed HIV transmission by partner type and age among MSM; yet further study might help to explain high HIV incidence among young MSM and how they should be best targeted with prevention resources. Sullivan et. al. was the only previous study to estimate the proportion of transmissions by partner type and other demographic characteristics including age.[4] Here, MSM in the 18-24 and 25-29 age groups had the highest proportions of transmissions arising from main partners.[4] However, transmissions by age and partner type have not been estimated using a dynamic, sexual network modeling approach. Therefore, we simulated a dynamic model to assess the role of age and partner type on HIV transmission in MSM, while accounting for sexual network and disease transmission factors. Estimating the proportion of transmissions by partner type and age, overall and across stages of HIV infection and clinical care, will provide a deeper understanding of HIV transmission among MSM.

Methods

Study Design

We extended a network-based mathematical model of HIV transmission dynamics in an open population of MSM in the United States. This work built upon previous modeling studies in this population.[6-8] We programmed our model using R's EpiModel software package (version 1.5.1; http://epimodel.org).[9] The overarching methodological framework has been described previously.[7] We summarize this framework below and provide further information in a Supplementary Technical Appendix.

Data from two empirical studies of MSM in Atlanta, Georgia from 2010-2014 were analyzed to provide estimates for key sexual behavior and HIV prevalence parameters. Involve[men]t was a cohort study of 803 black and white MSM ages 18-39 years that used venue-based sampling for participant recruitment.[10] The Men's Atlanta Networks (MAN) Project was a cross-sectional sexual network study of 314 MSM and used venue-based sampling to recruit initial black and white participant seeds.[11] Both studies consisted of HIV/STI testing and an extensive behavioral questionnaire on previous sexual partners. In the Involve[men]t study, significantly higher HIV incidence rates were found for younger MSM ages 18-24 years compared to older MSM ages 25-39 years.[10] In addition, other research has identified important differences in cognitive and sexual development and HIV risk among MSM in "emerging adulthood" (ages 18-24) compared to adolescence (ages 13-18) or young adulthood (~25-40).[12-14] Therefore, to examine transmissions by age, we stratified by these two age groups ("younger", 18-24 years; "older", 25-39 years) and provided empirical inputs for age-specific partnering and sexual behaviors. Simulated men sexually debuted into the model at age 18 and assumed "younger" values for age-stratified parameters; as they aged continuously over time, they switched to "older" parameter values upon reaching age 25.

HIV Transmission and Progression

We modeled HIV transmission in sexual networks of MSM using the statistical framework of temporal exponential random graph models (TERGMs) which allows for simulation of the formation and dissolution of sexual partnerships over time. Three partnership networks were modeled among men in the synthetic population: main partners, casual partners with repeated contacts, and one-time partners. Factors that contributed to the formation of partnerships differed by partnership type. Predictors of formation of main partnerships included model terms for: the number of current ongoing partnerships (network degree), preferential selection of partners of the same age category (categorical age homophily) and closer in age on the continuous scale (continuous age homophily), and sorting by sexual role position (e.g., two exclusively receptive men cannot pair, nor can two exclusively insertive men). Predictors of partnership formation for casual partnerships included all of the above as well as a term for concurrency (having two or more ongoing partners). Main and casual partnerships dissolved based on a constant hazard that reflected the median duration of each type. These hazards were specific to the dyadic age combination of the partnership (younger-younger, younger-older/older-younger, older-older). Within partnerships, the model simulated sex act frequency, condom use, and role positioning (receptive vs. insertive). We stratified each of these parameters by age group. Per-act transmission probabilities were determined from a base transmission rate in receptive/insertive anal sex and were modified by factors including condom use, role positioning, viral load, circumcision for an insertive negative partner, and the presence of the CCR5-Δ32 genetic allele.[3,15-19]

HIV progression was based on the natural history of untreated infection and antiretroviral therapy (ART) status. HIV-positive persons not on ART in the model progressed through their HIV infection with changing HIV viral loads and viral loads modified the rate of HIV transmission in serodiscordant partnerships. For this analysis, acute, chronic, and AIDS stages of HIV infection were categorized based on time since infection and current HIV viral load, and depended on ART status. Acute infections occurred when the HIV-positive partner was in the first 90 days of infection. HIV-infected persons were distributed into four clinical care trajectories at the time of infection; trajectories determined the rates of HIV diagnosis, ART initiation and retention, and HIV viral suppression as consistent with existing prevalence estimates for these care stages. Time of ART initiation after an HIV diagnosis was based on current medical guidelines of early treatment; this was modeled as an average rate of initiation per week and corresponded to an average time between testing and ART initiation of 9.13 weeks.[20,21] Being on ART resulted in lower viral load and mortality.[22-24] HIV-infected persons could transition on and off ART and their viral loads would vary accordingly. For this analysis, transmissions were categorized by HIV clinical care status; these included when the HIV-positive partner was either undiagnosed, diagnosed but not yet initiated on ART, diagnosed and initiated on ART but not retained on ART, diagnosed and on ART and partially virally suppressed, or diagnosed and on ART and fully virally suppressed.

Simulation and Analysis

We began simulations with a starting population of 10,000 MSM, comprised of 3,607 younger MSM ages 18-24 and 6,303 older MSM ages 25-29, consistent with the age distribution of MSM in the empiric studies. Men entered the network at age 18 and exited at death or when they reached age 40 years; this represented the age range for individuals in the empiric data. Upon entering the network, men were assigned an HIV status based on an estimated HIV prevalence of 7% by age 18.[25-27] We performed simulations over a 50-year period and allowed a burn-in period during simulations to establish equilibrium in epidemiologic and demographic outcomes. The model was calibrated using approximate Bayesian computation methods and manually to fit stable age-specific HIV prevalences of 35% for older MSM and 22% for younger MSM; these estimates were consistent with the empiric studies.[28] Population attributable fractions (PAFs) were obtained for HIV transmissions by age, partner type, stage of HIV infection, and HIV clinical care status using results from the last 2 years of simulated data. PAFs represent the proportion of HIV transmissions in the population that are attributable to a given set of characteristics. We conducted 1,000 simulations and present median PAFs and their 95% credible intervals (middle 95% of simulated results) for each outcome.

Results

Age and Partner Type Overall

Of all HIV transmissions among MSM, repeat casual partnerships accounted for 48%, main partnerships accounted for 40%, and one-time partnerships for 11% (Table 4.1). Three of four transmissions (76%) arose from a partner ages 25-39. Forty-six percent (46%) of all transmissions were within age-concordant older partnerships, 39% were within age-discordant partnerships, and 14% were in age-concordant younger partnerships. Of age-discordant transmissions, three-quarters (76%) were directionally from older partners to younger MSM (data not shown). Age-concordant older casual partnerships (22%), age-concordant older main partnerships (20%), and age-discordant casual partnerships (20%) accounted for most transmissions. The far majority of transmissions overall occurred when the acquiring partner was engaging in receptive anal intercourse (80%).

Of transmissions that occurred to younger MSM ages 18-24, nearly the same percentages of transmissions by partner type were found (48% casual; 39% main; and 13% one-time). Two-thirds (68%) were from older partners; most arose from an older casual partner, followed by an older main partner (36% casual vs. 24% main, of all transmissions to younger MSM; 52% casual vs. 35% main, of older-to-younger transmissions). Yet, for transmissions from younger partners to younger MSM, most arose from younger main partners, followed by younger casual partners (15% main vs. 12% casual, of all transmissions to younger MSM; 47% main vs. 39% casual, of younger-younger transmissions).

By Stage of HIV Infection

Over half of all transmissions (58%) occurred while the HIV-positive partner was in chronic stage HIV infection; 18% occurred during acute stage and 23% occurred during AIDS stage (Table 4.2). Transmissions from older partners were largely concentrated in chronic (44% overall, 58% of older-partner transmissions) and AIDS (23% overall, 30% of older-partner transmissions) stages, while transmissions from younger partners were balanced between acute (10% overall, 41% of younger-partner transmissions) and chronic (14% overall, 57% of younger-partner transmissions) stages. Main and casual partnerships in chronic stage infection contributed equally to transmissions overall (both at 26%). Casual partners contributed more than main partnerships in acute stage infection (10% vs. 5% of overall transmissions, respectively).

Focusing among younger MSM who acquired HIV, a slightly higher percentage of transmissions were during the positive partner's acute infection (22%). Transmissions to younger MSM were mostly from older partners during chronic stage infection (41%), specifically older casual partners (20%), followed by older main partners (16%). Younger partners were still more likely to transmit HIV to younger MSM during chronic stage (18% chronic vs. 14% acute overall; 57% chronic vs. 43% acute of younger-younger transmissions). Yet, acute-phase transmissions were more common from younger partners (14% younger vs. 8% older overall; 64% younger vs. 36% older, of acute-phase transmissions).

By Stage of HIV Care

Of all transmissions, 63% occurred when the HIV-positive partner not retained on ART and 29% when the HIV-positive partner was undiagnosed (Table 4.3). Less than 8% of transmissions occurred while the HIV-positive partner was partially or fully virally suppressed or between the time he had been diagnosed but not yet initiated onto ART. Transmissions from older partners predominantly occurred when not retained on ART (56% overall, 74% of older-partner transmissions) compared to when undiagnosed (16% overall, 21% of older-partner transmissions). Transmissions from younger partners predominantly occurred when undiagnosed (13% overall, 56% of younger-partner transmissions) compared to not being retained on ART (7% overall, 33% of younger-partner transmissions). Transmissions while not retained on ART and while undiagnosed occurred similarly in both main and casual partnerships.

Of transmissions to younger MSM, a slightly lower percentage of transmissions occurred when the HIV-positive partner was not retained on ART (59%) which was offset by a small increase in transmissions while undiagnosed (33%). Most transmissions came from older partners who were not on ART (50%), mainly from older casual partners (25%) followed by older main partners (18%). Yet, transmissions from younger partners to younger MSM mainly occurred when the partner was undiagnosed (18% overall, 57% of younger-younger transmissions) compared to when he was not retained on ART (10% overall, 31% of younger-younger transmissions); this distribution was consistent for both main and casual younger-younger transmissions.

Discussion

This study found that over half (60%) of HIV transmissions among MSM arose from repeat casual and one-time partners combined, and this distribution did not differ by age. Age-discordant partnerships largely contributed to transmissions to younger MSM. For age-concordant older partnerships and age-discordant partnerships, most transmissions occurred while the HIV-positive partner was in chronic stage infection and had not been retained on ART. Yet, for age-concordant younger partnerships, a greater proportion of transmissions occurred while the HIV-positive partner was undiagnosed. Transmissions when not retained on ART and when undiagnosed occurred similarly across both main and casual partnerships.

Our findings on transmissions by partnership type were similar to previous findings from network modeling research, and in contrast to the results from static deterministic models.[4,5] We used more recent data on MSM from two Atlanta studies to parameterize sexual behavior inputs for our model, and still observed nearly identical results as the Goodreau et. al. network model, suggesting robustness of the network modeling method for estimating transmissions by partner type in this MSM population.[3] Nevertheless, it is still possible that the 20-30% discrepancy in the proportion of transmissions from main partners between our model and the static deterministic models is due to differences in the data sources used to parameterize the models and/or to differences in modeling approach.[4,5] For example, sexual network models allow for concurrency—when sexual acts with two or more partners overlap in time.[29] Concurrency can contribute largely to HIV and STI transmission when an individual acquires the infection from one partner and transmits to a different partner during the period of overlap, possibly when the individual is most infectious and unaware of their infection.[29,30] Because casual partnerships tend to be shorter in duration and MSM may have multiple casual partners, this could allow for more frequent overlap between acts with two or more partners.[31,32] Therefore, allowing for concurrency could have contributed to the greater proportion of transmissions from casual partners in our model compared to other non-network-based approaches.

Research and surveillance experts often rely on national HIV diagnosis data along with key assumptions to make inference about HIV transmission across stages of HIV infection or HIV clinical care. Our model provided an opportunity to simulate transmission patterns directly and estimate the distribution of transmissions not only by partner type and age, but also by stage of HIV infection and HIV clinical care. The role of acute infections has been purported as a major contributor to HIV transmission in MSM globally, particularly in an era of effective therapy and in regions with universal access to therapy. Estimates of the proportion of transmissions attributed to acute infection have ranged from 11 to 49%, demonstrating unclear direction as to whether acute infections account for only few or up to half of transmissions and whether prevention efforts should support innovative biological methods for immediate detection of HIV after infection and behavioral interventions during the short time frame of acute infection.[33-35] In our model of US MSM, we observed 18% of transmissions occurring during acute infection, compared to 58% during chronic stage and 23% during AIDS stage, and acute infections only increased to 22% for transmissions to younger MSM. These results suggest that acute infections do contribute to HIV transmission among MSM, but not at the same magnitude as chronic infections, both overall and for younger MSM. We also identified that 63% of HIV transmissions arise from HIV-positive partners who are not retained on ART and 29% from partners who are undiagnosed. One recent model (Gopalappa et. al.) has suggested that HIV-positive persons unaware of their infection and persons aware but not on ART contribute equally to new transmissions (40% and 44% respectively) and CDC has recently placed increasing emphasis on the role of delayed HIV diagnoses in preventing new infections.[36,37] While undiagnosed infections represented 3 in 10 new transmissions in our model, indicating that these do contribute meaningfully to HIV transmission in MSM, more than 6 in 10 were attributed to not being retained on ART. Our results are more similar to a previous CDC model (Skarbinski et. al.) based on extensive surveillance data that demonstrated most transmissions in MSM arising from individuals not retained in care (54%), followed by those undiagnosed (35%).[38] The Skarbinki et. al. model and our model relied on similar data sources to parameterize HIV clinical care which could explain some of the similarity in findings. Our model greatly differed, however, in that we used a dynamic network modeling approach, modeled the care continuum based on early ART initiation, allowed HIV-positive persons to transition on and off ART, and defined retention as being on or off ART rather than as a function of medical visits, and we still obtained similar results suggesting lack of ART retention as a predominant contributor to new HIV transmissions in MSM.[38]

By using dynamic network modeling to estimate transmissions, we were able to quantify the role of age and partner type on HIV transmission among MSM, both overall and across stages of HIV infection and care. In total, three of four transmissions were from older partners ages 25-39, which likely reflects higher HIV prevalence as men age, increasing their propensity for transmission to others.[39] Age-concordant older casual partnerships, age-concordant older main partnerships, and age-discordant casual partnerships accounted for nearly two-thirds of HIV transmissions in our model. These results indicate that both casual and main age-concordant older partnerships play an important role in transmissions among MSM. In addition, age discordancy remains a key contributor to new infections among younger MSM, as has been documented in other studies[40-42], and these occurred mainly in the context of casual partnerships. Transmissions that came from older partners were predominantly during chronic infection and when the partner was not retained on ART. Therefore, interventions to improve ART retention in older MSM ages 25-39, and particularly those who engage in casual sex, will be critical to preventing new transmissions to same-age and younger partners.

The 60% casual/one-time and 40% main partner distribution of HIV transmissions overall did not differ for transmissions to younger MSM. This result was in contrast to the Sullivan et. al. model that saw a higher proportion of transmissions coming from main partnerships for young MSM specifically (79% in young MSM vs. 68% overall).[4] This discrepancy could be because our analysis specifically modeled transmission in networks by partner type and age, and most transmissions to younger MSM were from casual, older partners with higher HIV prevalence. The Sullivan et. al. model did not consider age of the partner when assessing transmissions to younger MSM, however differences by partner type and by stage of HIV infection and care emerged based on the age of the transmitting partner in our model. When older partners infected younger MSM, this largely came in the context of casual partnerships followed by main partnerships, during chronic infection, and when not retained on ART. Conversely, when younger partners infected younger MSM, this came slightly more from younger main partners followed by younger casual partners, and while undiagnosed. One potential reason that younger main partners contributed slightly more than younger casual partners towards infections to younger MSM in our model could be that age-concordant younger main and casual partnership durations were found to be nearly the same in the empiric data (127 vs. 146 days). For comparison, main partnership durations for age-concordant older partnerships were much longer (548 vs. 175 days). This could indicate that partner turnover was greater for younger MSM in main partnerships, allowing a younger individual to transition to another partner as quickly as if in a casual partnership. This could lead to similar levels of concurrency for both main and casual partners of younger MSM. Future research on partnership durations and concurrency by partner type and age could help to better identify if and how these factors may influence transmission dynamics for young MSM. Furthermore, these findings suggest that while age-concordant younger partnerships accounted for only a small proportion of transmissions at the population level (14%), they still exhibit important differences relevant to prevention strategies for this group.

In an effort to inform public health practice, our results can aim to provide insight on the relative impact of targeting MSM with partner-based vs. individual HIV prevention interventions and how this may differ by age, stage of HIV infection, and clinical care status. Partner-based HIV interventions, such as couples' HIV testing and counseling (CHTC), have been adapted for MSM and are considered an effective, high-impact prevention intervention by the CDC.[43-45] CHTC and other partner-based prevention strategies can provide an opportunity for testing two individuals at one time and can facilitate increased access to partners who would benefit from re-engagement into HIV care or initiation onto pre-exposure prophylaxis (PrEP) based on HIV status and risk behaviors. Yet, partner-based interventions are not often included as part of routine, comprehensive HIV prevention services for MSM.[46-48]

Our finding that casual and one-time partnerships collectively accounted for most HIV transmissions suggests that individual-based interventions should continue to have high priority for HIV prevention among MSM. In particular, older MSM and younger MSM with older partners who engage in casual sex would be important targets for individual prevention interventions and these should incorporate regular testing as well as messaging on condom use, partner reduction, and PrEP. Transmissions in age-concordant older casual and age-discordant casual partnerships occurred mainly during chronic infection and when the partner was not retained on ART; hence, individually-targeted interventions to improve ART retention in older MSM ages 25-39 could also result in large reductions of transmissions to their same-age and younger casual partners.

Yet, because main partnerships still accounted for 40% of HIV transmissions, partner-based interventions targeting main partners could also contribute significantly to preventing HIV transmissions among MSM. Partner-based interventions would provide most impact if targeted towards age-concordant older main couples who accounted for one-fifth of new infections. Because these primarily took place during chronic infection and when not retained on ART, partner-based interventions for these older, main couples should offer new opportunities for re-engaging HIV-positive partners onto ART, an important step to reducing the risk of transmission and improving quality of life. Discussions of care re-engagement should also be supplemented with other prevention options, such as pre-exposure prophylaxis (PrEP) for the HIV-negative partner, especially if significant barriers to care re-engagement or to consistent condom use are identified.

Though age-concordant younger partnerships did not represent a large proportion of HIV transmissions among MSM at the population-level, younger MSM with younger partners did have slightly more transmissions from main partnerships. However, because of the short duration of main partnerships between two younger MSM, intervening with partner-based interventions may prove more challenging in these partnerships than in age-concordant older main partnerships. Nevertheless, younger MSM with younger partners would benefit from early interventions, either individual- or partner-based, that emphasize early and regular testing, condom use, the risks of receptive sex, and PrEP in order to prevent new infections that are more likely to occur while a younger partner is undiagnosed.

This study has several strengths and limitations. First, this study utilizes a comprehensive approach to HIV epidemiologic modeling by incorporating sexual network structure and allowing dynamic changes in that structure, sexual behaviors, and disease progression over time. We expanded upon previous models by adding age and partner type parameters to better emulate age-specific sexual network structure, sexual behaviors, and HIV prevalence. We were able to simulate transmissions directly, providing a better understanding of the context and contributing factors to incident infections that cannot easily be determined through HIV diagnoses data or incidence estimations that inherently rely on retrospective, self-reported behaviors that do not necessarily occur at the time of infection. Nevertheless, our model still exhibits similar limitations as other models due to the use of self-reported, venue-based data to parameterize the model. Any biases, such as social desirability bias or selection bias, may impact our conclusions. For example, the Involve[men]t study specifically did not recruit MSM in monogamous partnerships from venues, therefore we may be underestimating the number of men in the population with main, monogamous partners. If these are truly monogamous partnerships and the majority are seroconcordant negative or positive, then this may further shift the proportion of transmissions towards casual and one-time partners above what we observed. Furthermore, using behavioral and prevalence data from the two Atlanta studies to parameterize the model may limit the generalizability of model results to the larger US MSM population.

Conclusion

In sum, we found that casual and one-time partnerships combined account for most HIV transmissions among MSM. Both younger and older MSM in casual partnerships remain a clear, high-leverage target for HIV prevention. Individual interventions that promote regular HIV testing, condom use, partner reduction, and opportunities for PrEP are highly warranted for older and younger HIV-negative MSM in casual and one-time relationships. Interventions focused on ART retention for HIV-positive older MSM could also substantially contribute to reductions in

HIV transmission among MSM. Because main partnerships still contributed to nearly half of transmissions, partner-based interventions may remain important for prevention and these should target age-concordant older MSM partnerships with a focus on re-engagement onto ART for HIV-positive partners. Younger MSM with younger partners would benefit from early interventions that emphasize early and regular testing, behavioral risk reduction, and PrEP to prevent new infections from undiagnosed younger partners.

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Table 4.1 Estimated population attributable fractions and 95% credible intervals[1] of age and partner type characteristics for HIV transmissions among men who have sex with men in the United States

	All MSM Transmissions		Transmissions to Younger MSM	
Characteristic	**PAF (%)**	**95% credible interval[1]**	**PAF (%)**	**95% credible interval[1]**
Age of Transmitting Partner				
Younger (18-24 years)	23.0	18.4, 28.2	31.8	25.2, 38.2
Older (25-40 years)	75.9	70.8, 80.6	68.2	61.8, 74.8
Age Concordancy				
Younger – Younger	13.8	10.1, 17.6	—	—
Younger – Older[2]	39.3	34.5, 44.6	—	—
Older – Older	45.9	39.9, 51.5	—	—
Partner Type				
Main	39.9	34.7, 45.2	38.8	32.0, 45.6
Casual	47.9	42.7, 53.2	47.9	40.8, 54.6
One-off	11.1	7.9, 14.7	13.2	8.9, 17.8
Age of Transmitting Partner & Partner Type				
Younger, Main	9.7	6.8, 12.8	14.7	9.8, 19.4
Younger, Casual	10.1	7.2, 13.8	12.4	7.8, 17.6
Younger, One-off	3.1	1.4, 5.3	4.4	1.6, 7.6
Older, Main	30.1	25.5, 35.1	24.1	18.0, 30.3
Older, Casual	37.7	32.5, 42.6	35.5	28.5, 42.3
Older, One-off	7.9	5.3, 10.9	8.7	5.3, 12.7
Age Concordancy & Partner Type				
Younger – Younger, Main	6.5	4.1, 8.8	—	—
Younger – Younger, Casual	5.4	3.1, 8.3	—	—
Younger – Young, One-off	1.9	0.7, 3.5	—	—
Younger – Older, Main[2]	13.7	10.5, 17.7	—	—
Younger – Older, Casual[2]	20.2	16.5, 24.6	—	—
Younger – Older, One-off[2]	5.1	3.0, 7.6	—	—
Older – Older, Main	19.5	15.4, 23.6	—	—
Older – Older, Casual	22.1	17.8, 26.6	—	—
Older – Older, One-off	4.1	2.2, 6.4	—	—
Positioning of Acquiring Partner				
Receptive	79.7	75.3, 83.6	84.0	78.8, 88.8
Insertive	19.3	15.8, 23.2	16.0	11.2, 21.2
Total	100		100	

[1] Credible interval over 1000 simulations.
[2] Includes partnerships in which the transmitting partner was younger and the acquiring partner was older and in which the transmitting partner was older and the acquiring partner was younger.

Table 4.2 Estimated population attributable fractions and 95% credible intervals[1] of age and partner type characteristics for HIV transmissions among men who have sex with men in the United States, by stage of HIV infection

	All MSM Transmissions			Transmissions to Younger MSM		
	Stage of HIV Infection of Transmitting Partner			Stage of HIV Infection of Transmitting Partner		
Characteristic	Acute	Chronic	AIDS	Acute	Chronic	AIDS
Age of Transmitting Partner						
Younger (18-24 years)	9.5 (6.2, 13.0)	13.5 (10.1, 17.4)	0.0 (0.0, 0.0)	13.5 (8.6, 18.7)	18.2 (13.1, 24.1)	0.0 (0.0, 0.0)
Older (25-40 years)	8.6 (5.7, 12.4)	44.3 (38.7, 49.7)	22.9 (18.4, 27.8)	7.9 (4.3, 12.1)	41.2 (34.5, 48.2)	18.9 (14.0, 24.9)
Age Concordancy						
Younger – Younger	5.7 (3.4, 8.5)	8.0 (5.5, 11.1)	0.0 (0.0, 0.0)	—	—	—
Younger – Older[2]	7.1 (4.6, 10.2)	23.6 (19.7, 27.9)	8.4 (5.7, 11.5)	—	—	—
Older – Older	5.2 (3.0, 8.0)	26.0 (21.1, 31.0)	14.4 (10.7, 18.6)	—	—	—
Partner Type						
Main	5.4 (3.4, 7.9)	25.7 (20.9, 30.9)	8.6 (5.7, 11.6)	7.0 (3.4, 10.9)	26.0 (20.4, 32.1)	5.6 (2.8, 8.9)
Casual	10.0 (6.9, 13.5)	26.3 (22.0, 31.1)	11.7 (8.5, 15.2)	10.5 (6.2, 15.5)	26.6 (21.2, 32.9)	10.4 (6.8, 15.2)
One-off	2.8 (1.3, 4.8)	5.6 (3.5, 8.0)	2.5 (1.1, 4.4)	3.8 (1.1, 7.1)	6.7 (3.4, 10.1)	2.6 (0.5, 5.1)
Age of Transmitting Partner & Partner Type						
Younger, Main	3.0 (1.4, 4.8)	6.6 (4.3, 9.5)	0.0 (0.0, 0.0)	5.0 (2.2, 8.3)	9.7 (5.9, 14.0)	0.0 (0.0, 0.0)
Younger, Casual	4.7 (2.7, 7.2)	5.3 (3.2, 8.1)	0.0 (0.0, 0.0)	5.8 (2.7, 9.5)	6.5 (3.5, 10.0)	0.0 (0.0, 0.0)
Younger, One-off	1.6 (0.4, 3.3)	1.4 (0.4, 2.7)	0.0 (0.0, 0.0)	2.4 (0.5, 5.1)	1.9 (0.4, 4.0)	0.0 (0.0, 0.0)
Older, Main	2.3 (1.0, 4.2)	19.0 (15.1, 23.7)	8.6 (5.7, 11.6)	1.8 (0.4, 4.2)	16.3 (11.6, 21.4)	5.6 (2.8, 8.9)
Older, Casual	5.0 (2.9, 7.7)	21.0 (16.9, 25.3)	11.7 (8.5, 15.2)	4.5 (1.9, 7.9)	20.1 (15.0, 25.9)	10.4 (6.8, 15.2)
Older, One-off	1.1 (0.2, 2.5)	4.1 (2.3, 6.5)	2.5 (1.1, 4.4)	1.3 (0.0, 3.2)	4.7 (2.1, 7.7)	2.6 (0.5, 5.1)
Total	18.3 (13.9,22.9)	57.6 (52.2, 63.4)	22.9 (18.4, 27.8)	21.6 (15.3, 27.7)	59.5 (52.6, 66.3)	18.9 (14.0, 24.9)

[1] Credible interval over 1000 simulations.

[2] Includes partnerships in which the transmitting partner was younger and the acquiring partner was older and in which the transmitting partner was older and the acquiring partner was younger.

Table 4.3 Estimated population attributable fractions (%) and 95% credible intervals[1] of age and partner type characteristics for HIV transmissions among men who have sex with men in the United States, by stage of HIV care

	Stage of HIV Care of Transmitting Partner				
	Undiagnosed Infection	Diagnosed, Not Prescribed ART	Prescribed ART, Not Retained	On ART, Partial Viral Suppression	On ART, Full Viral Suppression
Characteristic	**All MSM Transmissions**				
Age of Transmitting Partner					
Younger (18-24 years)	12.8 (9.1, 16.9)	0.9 (0.1, 2.2)	7.4 (4.8, 10.6)	1.4 (0.4, 2.9)	0.2 (0.0, 1.0)
Older (25-40 years)	15.7 (11.8, 20.1)	0.8 (0.1, 2.0)	55.6 (50.3, 60.7)	2.9 (1.4, 4.9)	0.6 (0.0, 1.7)
Age Concordancy					
Younger – Younger	7.8 (5.0, 10.9)	0.5 (0.0, 1.6)	4.3 (2.3, 6.6)	0.8 (0.1, 2.0)	0.1 (0.0, 0.7)
Younger – Older[2]	11.3 (8.1, 14.8)	0.7 (0.0, 1.8)	25.1 (20.6, 29.9)	1.7 (0.7, 3.4)	0.3 (0.0, 1.3)
Older – Older	9.6 (6.3, 13.0)	0.4 (0.0, 1.3)	33.6 (28.6, 39.0)	1.6 (0.6, 3.3)	0.3 (0.0, 1.2)
Partner Type					
Main	10.0 (7.3, 13.0)	0.5 (0.0, 1.6)	26.7 (22.1, 31.3)	1.9 (0.7, 3.6)	0.4 (0.0, 1.4)
Casual	14.7 (11.0, 18.5)	0.9 (0.1, 2.2)	29.8 (25.1, 34.4)	1.9 (0.7, 3.6)	0.4 (0.0, 1.3)
One-off	3.9 (0.2, 6.2)	0.2 (0.0, 1.0)	6.3 (4.2, 9.0)	0.4 (0.0,1.2)	0.0 (0.0, 0.5)
Age of Transmitting Partner & Partner Type					
Younger, Main	4.6 (2.8, 7.1)	0.3 (0.0, 1.1)	3.7 (1.9, 5.9)	0.6 (0.0, 1.7)	0.1 (0.0, 0.6)
Younger, Casual	6.0 (3.6, 9.0)	0.4 (0.0, 1.4)	2.8 (1.3, 5.0)	0.5 (0.0, 1.6)	0.0 (0.0, 0.6)
Younger, One-off	2.0 (0.6, 3.8)	0.1 (0.0, 0.7)	0.7 (0.1, 1.9)	0.1 (0.0, 0.7)	0.0 (0.0, 0.2)
Older, Main	5.3 (3.2, 7.6)	0.2 (0.0, 1.0)	23.1 (18.6, 27.5)	1.2 (0.3, 2.7)	0.2 (0.0, 0.1)
Older, Casual	8.5 (5.8, 11.8)	0.4 (0.0, 1.4)	26.9 (22.2, 31.3)	1.3 (0.3, 2.8)	0.2 (0.0, 1.1)
Older, One-off	1.8 (0.6, 3.5)	0.0 (0.0, 0.6)	5.5 (3.5, 8.0)	0.2 (0.0, 0.9)	0.0 (0.0, 0.5)
Total	28.6 (24.0, 34.1)	1.8 (0.6, 3.6)	63.1 (57.8, 67.7)	4.3 (2.4, 6.7)	0.9 (0.1, 2.3)

– Table 4.3 continued –

– Table 4.3 continued –

	Transmissions to Younger MSM				
Age of Transmitting Partner					
Younger (18-24 years)	18.1 (12.7, 23.9)	1.3 (0.0, 3.3)	9.8 (5.7, 14.0)	1.9 (0.4, 4.3)	0.4 (0.0, 1.4)
Older (25-40 years)	14.5 (9.6, 20.2)	0.8 (0.0, 2.3)	49.5 (42.3, 56.4)	2.8 (0.6, 5.1)	0.5 (0.0, 1.9)
Partner Type					
Main	12.2 (7.9, 16.7)	0.5 (0.0, 2.3)	23.2 (17.2, 29.2)	2.1 (0.5, 4.5)	0.5 (0.0, 1.5)
Casual	15.5 (10.5, 20.5)	0.9 (0.0, 2.7)	28.7 (22.9, 35.0)	2.0 (0.5, 4.3)	0.5 (0.0, 1.5)
One-off	5.0 (2.1, 8.3)	0.4 (0.0, 1.5)	7.2 (3.6, 10.5)	0.5 (0.0, 1.7)	0.0 (0.0, 0.5)
Age of Transmitting Partner & Partner Type					
Younger, Main	7.8 (4.3, 11.7)	0.5 (0.0, 1.9)	5.2 (2.3, 8.5)	0.9 (0.0, 2.7)	0.0 (0.0, 0.1)
Younger, Casual	7.3 (4.0, 11.4)	0.5 (0.0, 1.9)	3.4 (1.3, 6.3)	0.5 (0.0, 2.1)	0.0 (0.0, 0.9)
Younger, One-off	2.8 (0.9, 5.5)	0.0 (0.0, 1.2)	0.1 (0.0, 2.6)	0.0 (0.0, 0.1)	0.0 (0.0, 0.5)
Older, Main	4.3 (1.7, 7.4)	0.0 (0.0, 0.1)	18.0 (13.0, 23.7)	1.0 (0.0, 2.8)	0.0 (0.0, 0.1)
Older, Casual	7.9 (4.5, 12.0)	0.5 (0.0, 1.5)	25.2 (19.5, 31.1)	1.3 (0.0, 0.3)	0.0 (0.0, 1.3)
Older, One-off	2.1 (0.4, 4.6)	(0.0, 0.0, 0.9)	6.1 (3.1, 9.2)	0.0 (0.0, 1.3)	0.0 (0.0, 0.5)
Total	32.8 (25.7, 39.4)	2.1 (0.5, 4.5)	59.2 (52.0, 66.4)	4.7 (1.9, 8.1)	0.9 (0.0, 2.7)

[1] Credible interval over 1000 simulations.

[2] Includes partnerships in which the transmitting partner was younger and the acquiring partner was older and in which the transmitting partner was older and the acquiring partner was younger.

CHAPTER 5: Conclusions and future directions

In this chapter, we review key findings from the three dissertation aims, identify their contributions to the field, and discuss future directions for research and public health practice. This dissertation focused on three topics to examine HIV disparities among racial/ethnic and sexual minorities in the United States. Collectively, the dissertation aims addressed several debated areas in the literature, including the evolution of disparities, the role of partnering changes as a potential factor in HIV risk behavior and STI increases, as well as the balance between main vs. casual, acute vs. non-acute, and undiagnosed vs. out-of-care HIV transmissions among MSM. Each aim incorporated some component of time–either taking a historical view at how disparities and behaviors associated with disparities have changed over time, or simulating how individual and partner characteristics contribute to HIV transmission dynamically over the life course. These methodological approaches extended our understanding of these debated topics with improved concepts of time and age. Assessing racial/ethnic and age disparities in this context has provided important contributions at the intersection of surveillance and prevention by demonstrating how disparities may have evolved and shaped our current epidemic and identifying future research and practices that will be needed to address existing disparities and prevent new HIV transmissions.

Trends in racial/ethnic disparities in AIDS diagnoses over the course of the HIV epidemic in the United States

Primary findings

Annual rates of AIDS diagnoses for all racial/ethnic groups increased through year 2000 and have decreased or stabilized from 2000-2013. Black-White disparity trends in new AIDS diagnoses changed four times during the course of the HIV epidemic in the United States, corresponding to five unique trend periods: 1984-1990, 1991-1996, 1997-2001, 2002-2005, and 2006-2013. This was more heterogenous than Hispanic-White disparity trends, which only had one significant change corresponding to two different trend periods: 1984-1997 and 1998-2013. Overall, the Black-White disparity increased greatly from 1984 to the early 2000s. The Black-White disparity declined following 2002, but increased significantly again from 2006-2013. The Hispanic-White disparity also increased from 1984 to the late 1990s, but at a lesser magnitude than the Black-White disparity. The Hispanic-White disparity has slowly declined since the late 1990s. Yet, both the Black-White and the Hispanic-White disparities for MSM specifically have increased in recent years from 2008-2013.

Contributions to the field and future directions

Prior to our study, HIV-related racial/ethnic disparities had only been documented over short time periods, which did not allow for understanding how trends had changed over the span of the epidemic. Furthermore, one analysis had looked at trends over a 10-year period, but did not allow for changes in trends over time and assumed one uniform linear trend. Our analysis was the first to utilize HIV outcome data from back to the mid-1980s and empirically measure changes in disparity trends over 30 years of the HIV epidemic. We employed Joinpoint Regression software to derive and identify significant trend periods.[1] Joinpoint Regression has commonly been used to determine trends in cancer and other chronic outcomes, but had not yet been applied to HIV trends to date.[1,2] Our methods allowed for a more objective approach to defining trend periods compared to previous analyses that selected limited time intervals based on the most recent few years or other arbitrary timeframes and did not permit changes in trends. This type of methodological approach using Joinpoint Regression can be applied to other types of HIV data and other disparities beyond racial/ethnic comparisons to empirically define critical trend periods. As HIV surveillance improves to provide long-term, time series data on additional indicators, this method can be employed for determining significant changes in trends over time, as opposed to simply relying on the most recent 5-year period or other definitions that are not empirically-driven and do not include all available data to inform trend analyses. In this dissertation aim, we provided a key example to HIV surveillance analysts on how to incorporate this methodological approach for future analyses of HIV disparities over time.

Most importantly, our approach contributed to a better epidemiological understanding of how racial/ethnic disparities evolved and allowed for developing hypotheses for why trends changed and what may be driving recent increases in disparities. For example, the Black-White disparity grew significantly through the 1990s and continued even after effective treatment was available, indicating that Blacks may not have been able to access treatment as a new intervention due to socioeconomic, stigma, and healthcare barriers.[3] Similarly, barriers to testing and care may be responsible for recent increases in Black-White disparity overall and Black-White and Hispanic-White disparities among MSM specifically. These differences in care may be particularly acute for subgroups of MSM, such as young Black MSM, who experience high HIV incidence yet have lower linkage to care and lower viral suppression that can contribute to an AIDS diagnosis.[4,5] Our findings suggest that care continuum inequalities likely persist for

Black and Hispanic MSM and drivers of these disparities at each step of the care continuum need to be examined to better tailor interventions to reduce disparities.

Because we considered disparities over a 30-year period, we needed to use an HIV-related indicator that had consistent reporting since early in the epidemic. AIDS diagnoses is the only consistently reported HIV indicator across all states in the 1980s and 1990s. Therefore we used AIDS diagnoses data to assess racial/ethnic disparities over the course of the epidemic. As HIV testing methods have advanced and HIV diagnosis reporting has improved, monitoring of AIDS diagnoses has received less attention in place of HIV diagnoses. However, consistent data on HIV diagnoses was not available until 2008 when participation in mandatory name-based reporting to CDC was complete for all US states. Therefore, if we seek to understand changes in HIV over time, monitoring AIDS diagnoses should remain a priority as it allows for multiple decades of time-series data that can be used to inform national progress. Furthermore, AIDS diagnoses serves as a downstream measure of all steps of the HIV care continuum—from testing to viral suppression. Although understanding trends in disparities at each step of the care continuum would provide valuable information to identify exact targets for reducing disparities, capturing the overall, downstream disparity that accounts for gaps at all steps provides important evidence for the joint magnitude of these gaps. Monitoring this measure in the future would also allow for tracking how disparities may or may not be improved with interventions targeting multiple stages of the care continuum. Lastly, our analysis using AIDS diagnoses to monitor disparities can serve as an example to other regions of the world that do not have consistent reporting of HIV diagnoses, and still rely on AIDS diagnoses as a key indicator for monitoring progress towards HIV goals. Disparities in AIDS diagnoses over time in these global contexts may be related to race/ethnicity or could also be applied to other comparisons including by age, sex, or sexual orientation.

Overall, our Aim 1 analysis provides a historical context to understand how HIV-related racial/ethnic disparities changed over decades of the HIV epidemic and has identified that racial/ethnic disparities are increasing for Blacks overall and Black and Hispanic MSM in recent years. Our work also provides a novel application of a method for measuring and monitoring disparity patterns that can inform our progress towards national HIV goals to reduce disparities.

Trends in partner counts and composition among men who have sex with men in the United States

Primary findings

In this study, we considered trends in total and main partner counts, composition of partner types, and condomless anal sex by partner composition. We found that from 2008 to 2014, mean total partner counts in the past year significantly increased overall and this was mainly among White MSM and MSM under the age of 40. Main partner counts remained stable, indicating that the increase in total counts was driven by increases in casual partners. Conclusions from the count data were supported by data on partner composition. The proportion of MSM who had only one main partner in the past year decreased, while the proportion of MSM who had both main and casual partners increased. In addition, the proportion of MSM with one or more main partners and zero casual partners decreased, offset by an increase in MSM with one or more main partners and two or more casual partners. Condomless anal sex increased regardless of partner composition.

Contributions to the field and future directions

We initially hypothesized that trends in either main partner counts or the proportion of MSM with only one main partner was increasing while total partners had remained stable or declined as a result of increasing social and legal acceptance of long-term same-sex relationships in the past decade. However, our findings did not support this hypothesis, and instead, suggested increasing trends in casual partnering. In capturing these unanticipated findings, we have been able to communicate a more accurate picture of current sexual partnering among MSM, generate new hypotheses for why casual sexual partnering is changing, and provide suggestions for how prevention strategies can address these changes.

First, our findings have the potential to contribute to the understanding of trends in sexually transmitted infections (STIs) more generally beyond HIV. Although the increasing trends in casual partnering have occurred during a time of stable HIV trends among MSM, this time has also been a period of increasing condomless anal sex and STIs.[6,7] In the US, trends in STIs including gonorrhea, chlamydia, and syphilis have increased in recent years and specifically for males and/or MSM.[7] Researchers have posited that, at least for MSM, sexual behaviors including increases in condomless anal sex, frequency of sex, and number of sex partners may be contributing to observed increases in STIs.[7] For example it is possible that we observe increases in STI and not in HIV as the per-act transmission rates for STI are likely higher than for HIV, and thus may be more sensitive to increases in risky sexual behaviors.[8] Our work did not specifically consider associations between partnering and STI prevalence, however it is plausible that the increases we observed in partner counts could lead to increased exposure to STIs and possibly contribute to the increasing trends in STIs that have been observed over the past decade.

Our work supports future research to investigate these associations between simultaneous increases in STIs and in partner counts, and in drivers of the increasing trends we see in condomless anal sex and partner counts among MSM. Furthermore, expanding our understanding of concurrency trends in the context of increasing casual partnering could help explain possible mechanisms for increasing STIs during this period as well.

Our results led us to develop other hypotheses that could be leading to increases in casual sexual partnering. One of these was the role Internet, smartphones, and dating apps have potentially played in shaping current sexual partnering trends. It is possible that increasing use of the Internet and location-based dating apps over the past decade have reduced social and physical barriers to finding sexual partners, particular casual sex partners.[9] Although we could not assess the causal association between changes in technological advances and changes in partnering, we did find that controlling for Internet use frequency attenuated some of the increase in total partner counts and stabilized the trend in men with both main and casual partners. This could indicate that Internet use is explaining at least some of the increase in casual partnering. Findings from our study and the generation of this new hypothesis warrant future research to determine the associations between Internet use and sexual partnering and whether this may be most relevant to certain subgroups of MSM. Furthermore, although the Internet may be a medium for engaging in sex with more casual partners, the Internet can equally serve as an important place for intervention. As we better understand how changes in Internet use have shaped changes in partnering patterns, the need for interventions targeting casual partners meeting online with information about HIV/AIDS, testing locations, and other prevention messaging may be further supported by our and others' work.[9-11] Analyses that address our post-hoc hypotheses including the role of Internet use could help to explain current partnering and STI trends and should be considered in future studies.

One intention of this analysis was to provide some commentary on whether individual or partner-based HIV interventions should be prioritized based on current partnering trends. Because we observed a shift towards increasing casual partners overall, we would suggest that individual-based interventions remain an integral part to preventing HIV among MSM. These individual interventions should provide at least annual HIV testing while encouraging risk reduction strategies including condoms, partner reduction, and PrEP. Yet, one finding of note in our analysis showed that the increase in casual partnering was not among men who engaged in sex only with casual partners during the past year, but rather among men who reported having one or more main partners during this time as well. Although we did not have data on whether main and casual partners overlapped in time, this result indicates that potential increases in concurrency could increase risk to main partners if sex with multiple casual partners outside of the relationship are taking place between two main-partner sexual acts. In this case, partner-based interventions would also be important to preventing transmissions within main relationships that could be exposed to greater concurrency in recent years. These partner-based interventions, including couples' HIV testing and counseling should offer routine testing, discussion of sexual agreements including condom use within and outside of the relationship, and counseling and care navigation for partners who need to enter or re-enter HIV care or initiate PrEP. Future research should consider trends in concurrency and consider concurrency by partner type to understand which types of partners, and therefore which types of interventions, may be most useful for preventing new transmissions.

Estimating HIV transmissions by age and partner type among MSM through dynamic network modeling

Primary findings

In this aim, we used dynamic network modeling methods to model the proportion of HIV transmissions among US MSM by partner type and age. We found that most HIV transmissions (60%) among MSM arose from repeat casual partners and one-time partners collectively, and main partners accounted for the remaining 40%. This overall distribution of transmissions by partner type did not vary by age, defined as younger (ages 18-24) and older (ages 25-39). Age-concordant older casual, age-concordant older main, and age-discordant casual partnerships accounted for most transmissions overall (22%, 20%, and 20%, respectively). For both age-concordant older and age-discordant relationships, transmissions mainly occurred when the HIV-positive partner was in chronic stage infection and had not been retained on ART. Age-concordant younger partnerships, on the other hand, a higher percentage of transmissions occurred when the HIV-positive partner was undiagnosed, for both main and casual partner types.

Contributions to the field and future directions

Results from Aim 2 suggested that casual partnering may be increasing in recent years, at least in White MSM and MSM under 40. Yet, there has been much debate in the literature about whether the majority of HIV transmissions occur in the context of main vs. casual partnerships, which could help to inform whether increases in casual partnering could lead to possible increases in HIV transmission via casual partners.

One of the key contributions to the field for Aim 3 was to provide further consensus on the proportion of transmissions among MSM that arise from main vs. casual partners. This proportion has previously been estimated at 68-78% in two deterministic models and at 39% in one network-based model.[12-14] Prior to our work, deterministic models have been criticized for overestimating transmissions within main partnerships due to incorporating sex act frequency and condomless sex, which are higher in main partnerships, but not accounting for sexual network structure or concurrency—key factors to HIV transmission that may affect casual partnerships more acutely due to shorter partnership durations and more frequent partner turnover.[15,16] Results from previous network-based models have been questioned, however, for using data sources from early HIV studies in the late 1990s and early 2000s which may not accurately depict current partner and behavioral outcomes in today's epidemic. Therefore, our model has provided some further consensus on this debate by utilizing network modeling methods that take into account all of these parameters, including sex act frequency, condom use, network structure, and concurrency by partner type and age. In addition, we parameterized these inputs based on more recent behavioral data from 2011-2014. Our model showed that even with updated data sources, most transmissions continue to arise from repeat casual or one-time partners collectively when using a more complex network modeling approach. Because most transmissions in Aim 3 occurred in the context of casual partnerships, the increase in casual partnering observed in Aim 2 could suggest that a greater proportion of HIV transmissions could be arising from casual partners in recent years.

A second major contribution of this aim was to build upon the previous research question about transmissions by partner type and examine how this may differ by age. Only the Sullivan et. al. model had considered transmissions by age and found that young MSM ages 18-24 had an even higher proportion of transmissions from main partners (79%).[12] We did not find this to be true in our data for transmissions to young MSM from all partners. Instead, we observed nearly the same proportion of transmissions from main partners to young MSM specifically (39%) as to MSM overall (40%). Yet, we did find some heterogeneity in this estimate when looking at the age combination of the partnership. When transmissions to younger MSM came from older partners, these more often came in casual partnerships (52% casual vs. 35% main, of older-to-younger transmissions). However, when transmissions to younger MSM came from younger partners, slightly more came from main partners (47% main vs. 39% casual, of younger-to-younger transmissions). The fact that the distribution of transmissions to younger MSM by main vs. casual partner type differed by age of the partner is informative; this finding provides insight into how interventions may be best tailored not only to the age of the individual, but the age combination of the individual and his partner(s). For example, partner-based interventions may be more appropriate for younger MSM with younger partners, within which transmissions more commonly came from main partners. Nevertheless, it is important to recognize that at the macro-scale, younger-younger main partnerships did not contribute largely to HIV transmissions among all MSM. Furthermore, we found that younger-younger main and casual partnerships had similar partnership durations of about 3 to 4 months. This short partnership duration may allow for condomless sex within a relationship, but intervening on these relationships with partner-based interventions at just the right time prior to condomless sex may prove challenging in public health practice.

The work from this aim also contributed to ongoing scientific debate about which stage of HIV infection and HIV care accounts for most HIV transmissions from HIV-positive partners. By using a dynamic network modeling approach, we were able to directly quantify transmission patterns within partnerships and offer new estimates in the literature for the population attributable fractions associated with acute and chronic infections as well as when undiagnosed and not retained on ART. Researchers have increasingly proposed acute infections as an important contributor to ongoing HIV transmission among MSM globally, particularly as universal access to effective therapy has scaled up in many countries yet HIV diagnoses rates in MSM remain stable or increasing in some countries.[17] Previous estimates of the population attributable fractions for acute infection have ranged from 11 to 49%.[18-20] In our model of US MSM, we observed acute infections contributing to 18% of transmissions compared to chronic infections at 58% and AIDS stage at 23%. Our findings indicate that although acute infections do contribute in an important way to HIV transmission among MSM, they may not contribute at the large magnitude as found in other studies. Instead, our data suggest that chronic infections play the largest role in ongoing transmissions among MSM.

Similarly, most transmissions overall occurred when the HIV-positive partner was not retained on ART and about one-fourth of infections occurred while undiagnosed. One exception was for transmissions in younger-younger partnerships, within which most occurred when the HIV-positive partner was undiagnosed. A recent agent-based model from Gopalappa et. al. estimated that 40% of HIV infections come from people who are undiagnosed and a 2017 CDC Vital Signs report has highlighted delayed diagnoses and their potential role in transmission, estimating that the average time between infection and diagnosis is approximately 3 years.[21-23]

The Gopalappa et. al. estimate is higher than what we observed for undiagnosed transmissions at 29%, perhaps because the Gopalappa et. al. estimate includes heterosexuals who are less likely to test annually for HIV than MSM and missed opportunities for testing in clinical settings are considered to be a main contributor to delays in HIV diagnoses.[21,22] Though we modeled the care continuum based on early ART initiation, allowed HIV-positive persons to dynamically fluctuate on and off ART, and defined retention as being on or off ART rather than as a function of medical visits, we still obtained similar results as an earlier CDC modeling study (Skarbinski et. al.) that demonstrated most transmissions arising from individuals not retained in care (54%).[24] Our findings and those of Skarbinski et. al. suggest that retention of HIV-positive MSM on ART plays a predominant role in HIV transmission among MSM and intervening at this stage of HIV clinical care will be critical to reducing transmission among MSM at the population-level. Because we also considered age in our model, however, we further identified that undiagnosed infections may be more important for younger-younger partnerships and therefore early detection of HIV infection will also be key to preventing transmissions, particularly for younger-younger partnerships.

Similar to Aim 2, Aim 3 also intended to provide insight on the relative priority of individual vs. partner-based HIV interventions for MSM. In translating our work in Aim 3 to public health practice, our model demonstrated that individual-based interventions will continue to be a critical point of intervention of MSM, as most transmissions occurred in the context of casual and one-time partnerships. Nevertheless, partner-based interventions remain relevant as just below half of transmissions occurred to main partners. Unfortunately, the 60%/40% split between casual and main partnerships does not allow for a clear recommendation of only one type of intervention over another. Rather, both appear to be relevant forms of intervention depending on the individual and his willingness to involve partners in his HIV prevention strategy. Furthermore, because we found that the distribution of transmissions by partner type differed by age of the partner for younger MSM, it could be that individual-based interventions may best suit younger MSM with older partners who become infected mostly through casual partnerships. Our data do suggest that couples-based interventions could be more tailored to the characteristics of the partnership. For example, if a younger MSM identifies a main, older MSM partner to participate in a partner-based intervention, this should focus on testing, engagement or re-engagement of an HIV-positive partner onto ART, and discussion of PrEP if applicable, as transmissions in age-discordant partnerships occurred mainly while a partner was not retained on ART. Though at the population-level there was a low proportion of transmissions that came from younger-younger partnerships, partner-based interventions may still be relevant for this subgroup, as a slightly higher proportion of transmissions were from main partners. Regardless of whether individual or partner-based interventions target younger MSM with younger partners, intervening early to provide testing and counseling, negotiate condom use and sexual agreements, reduce partners, and discuss opportunities for PrEP will be essential to preventing new HIV infections from younger, undiagnosed partners.

Our results from Aim 3 were significant in examining questions about transmissions by partner type and age. Nevertheless, there are two areas in which our model can be expanded in the future. First, our model only considered two categorical levels of age. This was due to the complexities of stratifying the network structure and behavioral parameters by three or more age groups and calibrating a model to the unique HIV prevalences of the three or more distinct groups that are dependent on each other (e.g., HIV prevalence at younger ages affects HIV prevalence at older ages). We chose to proceed with two levels because previous research has demonstrated higher HIV incidence rates among young MSM ages 18-24 compared to older MSM and we were most interested in looking at how the distribution of transmissions by partner type differed between these two groups. Yet, recent surveillance data has shown that HIV incidence may be increasing for MSM ages 25-29, while remaining stable or decreasing for young MSM ages 13-24 and older MSM ages 30 and above.[25] Therefore, future work could modify our analysis by more than two age groups and determine if there is further heterogeneity by age. Second, age disparities in HIV are compounded by race disparities. In the Involve[men]t study, young Black MSM had the highest HIV incidence rates at 10.9 per 100 person-years compared to older Black MSM (3.6 per 100 person-years) or to young White MSM (0.9 per 100 person-years).[4] In addition, previous work has identified that Black MSM differ from White MSM in how they perceive and define main partnerships, such that Black MSM may label partnerships with lesser forms of objective partnership involvement (knows last name, shared a meal, met each other's families) as "main" partners.[26] Though not yet researched, there may be similar differences in perceived and objective partnership involvement among young MSM in main partnerships. Because a greater amount of condomless sex takes place in main partnerships, it could therefore be possible that younger MSM, including younger Black MSM, may be engaging in condomless sex in partnerships perceived as main but that exhibit less objective involvement, and perhaps less commitment, with respect to outside partners. This may influence how the distribution of transmissions varies by race, age, and partner type. Therefore, an important next step for the research presented in this dissertation will be to modify the network structure and behavioral parameters in the Aim 3 model by partner type, age, and race. This future work will further help to determine differences in the distribution of transmissions by partner type within age and race groups and inform on whether individual vs. partner-based interventions should be prioritized for certain age and race subgroups of MSM.

Finally, it is important to recognize how our network-based model and resulting findings relate to other conclusions of this dissertation and future HIV surveillance work. In Aim 1, we found increases in racial/ethnic disparities of AIDS diagnoses in the absence of effective therapy, followed by stabilization in disparities after the introduction of ART; in recent years, we observed slight increases in disparities and hypothesized that these increases may be driven, at least in part, by differences in the care continuum. In Aim 3 we demonstrate that HIV transmissions that lead to HIV and AIDS diagnoses are attributed mainly to chronic infection and not being retained onto ART. Therefore, future surveillance efforts that seek to quantify racial/ethnic disparities should focus on disparities at these stages of infection and care and should aim to identify the socioeconomic and care-related factors that could drive disparities among those with chronic infection and not retained on ART. As surveillance data collection methods improve and remain standardized to obtain consistent measures of the care continuum over time, empirical methodologies like Joinpoint Regression could be used for monitoring future trends in these measures and disparity outcomes.

Our Aim 3 methods and results also provide insight on the partnering trends observed in Aim 2. As discussed previously, we observed increases in casual partnering among MSM and identified casual partners to contribute to 60% of HIV transmissions. In future surveillance and research, it will be important to measure trends in concurrency to inform on mechanisms for potential increases in HIV transmission if casual partnering continues to increase and HIV incidence increases or remains stable for MSM. Future work should also consider concurrency not just within casual partner contexts, but between those with casual and main partners as Aim 2 surveillance data suggested increases in casual partnering among those with at least one main partner in the past year. In addition, these findings from the behavioral surveillance data could also be used to improve network modeling methods. For example, dynamic modeling methods could replicate temporal trends to identify the possible impact of shifts in casual partnering over time, as observed in population data, on individuals' sexual risk over the life course and on population-level HIV incidence outcomes. These are a few examples of how case surveillance, behavioral surveillance, and complex network modeling methods could complement each other and build upon findings from this dissertation to inform future surveillance and research efforts.

Final Comments

The three research aims covered in this dissertation have demonstrated how racial/ethnic disparities have changed over the course of the HIV epidemic, how sexual partnering among MSM who are predominantly affected by HIV has changed in recent years, and how HIV transmissions can vary by age and partnership type for MSM over the life course. HIV-related disparities among racial and sexual minorities remain elevated and addressing care continuum inequalities will be a critical component to achieving national HIV goals to decrease HIV infections and reduce disparities. This dissertation has also contributed to understanding the relative priority of utilizing individual vs. partner-based interventions to prevent HIV infections in age-specific groups of MSM. Future research should aim to identify current trends in additional partner-related transmission factors, such as concurrency, as well as incorporate race and age into partner type models of HIV transmission in order to hone understanding about who should be targeted with individual vs. partner-based interventions. Finally, HIV disparities are often intersectional in nature, compounded by sexual networks and behaviors that are influenced by age, race, sexual orientation, and other factors combined. Our work has provided insight on racial/ethnic disparities and on partnering characteristics that can lead to age and race disparities among MSM, while highlighting the need for future studies to consider additional drivers of disparities at multiple intersections—particularly those defined by age, race, and sexual orientation in the United States.

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APPENDIX

Supplementary Technical Appendix for Chapter 4

Table of Contents

1 INTRODUCTION

This supplementary technical appendix describes the mathematical model structure, parameterization, and statistical analysis of the accompanying paper in further detail.

1.1 Model Framework

The mathematical models for HIV transmission dynamics presented in this study are agent-based microsimulation models in which uniquely identifiable sexual partnership dyads were simulated and tracked over time. This partnership structure is represented through the use of separable temporal exponential-family random graph models (STERGMs), described in Section 2. On top of this dynamic network simulation, the larger epidemic model represents demography (entries, exits, and aging), interhost epidemiology (disease transmission), intrahost epidemiology (disease progression), and clinical epidemiology (disease diagnosis and treatment). Individual attributes related to these processes are stored and updated in discrete time over the course of each epidemic simulation.

The modeling methods presented here depend upon and extend the *EpiModel* software to incorporate HIV-specific epidemiology. The HIV extensions for men who have sex with men (MSM) were originally developed by Goodreau et al. for use in prior modeling studies of MSM in the United States and South America,[1-3] and subsequently used for models of HIV preexposure prophylaxis (PrEP) among US MSM.[4,5]

The model algorithms and methods presented here build upon these prior MSM HIV transmission models and seek to investigate the role of age and partner type on HIV transmission among MSM in the United States. We added age-specific parameters to the network structure, partnership formation and dissolution formulas, and to behaviors within sexual partnerships. Two age categories were used based on previously identified differences in HIV incidence rates: younger (18-24 years) and older (25-39 years).[6] This allowed us to consider how HIV transmission varied by age and partner type overall and across different stages of HIV infection and care.

1.2 Model Software

The models in this study were programmed in the R and C++ software languages using the *EpiModel* [http://epimodel.org/] software platform for epidemic modeling. *EpiModel* was developed by the authors for simulating complex network-based mathematical models of infectious diseases, with a primary focus on HIV and other sexually transmitted infections (STIs). *EpiModel* depends on *Statnet* [http://statnet.org/], a suite of software in R for the representation, visualization, and statistical analysis of complex network data.[7]

EpiModel allows for a modular expansion of its built-in modeling tools to address novel research questions. For this current research study, we have developed extension modules into an add-on software package to *EpiModel* called *EpiModelHIV*. This open-source software is available for download, along with the scripts used in the execution of these models. The tools and scripts to run these models are contained in two GitHub software repositories:

- [http://github.com/statnet/EpiModelHIV] contains the general extension software package. Installing this using the instructions listed at the repository homepage will also load in *EpiModel* and the other dependencies. We use a branching software architecture such that the version of the software associated with this research project is *AgePT*.
- [http://github.com/statnet/agept] contains the scripts to execute the mathematical models and to run the statistical analyses provided in the manuscript.

2 DYNAMIC NETWORKS OF SEXUAL PARTNERSHIPS

We modeled networks of three interacting types of sexual relations: main partnerships, casual (but persistent) partnerships, and one-time anal intercourse (AI) contacts. We first describe the methods conceptually, including the parameters used to guide the model and their derivation (Section 2.1), and then present the formal statistical modeling methods (Section 2.2). Consistent with our parameter derivations, all relationships are defined as those in which AI is expected to occur at least once.

2.1 Conceptual Representation of Sexual Networks

Our modeling methods aim to preserve certain features of the cross-sectional and dynamic network structure as reported in behavioral studies, while also allowing for mean relational durations to be targeted to those reported for different groups and relational types. These methods do so all within the context of changing population size (due to births, deaths, arrivals, and departures from the population) and changing composition by attributes such as age and disease status.

The network features that we aim to preserve are as follows, with the parameters for each described in turn:

- The proportion of men in any given combination of main and casual partnerships (for example, in 1 main and 0 casual partnerships) at any time point, weighted by categorical age.
- The expected number of one-time contacts per time step had by men in each main-casual combination, weighted by categorical age.
- Variation across men in the numbers of one-time contacts.
- Categorical and continuous age mixing within each of the different relational types.
- Prohibitions against partnering for two men who are both exclusively insertive or both exclusively receptive.

2.1.1 Number of Ongoing Main and Casual Partnerships

Ongoing partnerships (whether main or casual) were defined from the combined dyadic dataset as those in which sex had already occurred more than once, and in which the respondent anticipated having sex again. Within this set, partnerships were defined as main if the respondent indicated that it was someone they "felt committed to above all others" or that they considered the person their "primary sex partner"; if neither of these conditions held, the partner was defined as casual. This yielded the proportions of men with a given number of main and casual relationships at a point in time (i.e. the expected *momentary degree distribution*). Momentary degree distributions were calculated by age category and weighted by the proportion of the population in each age category to obtain the following overall expected momentary degree distribution:

	0 Casual	*1 Casual*	*2 Casual*
0 Main	47.5%	16.6%	7.1%
1 Main	21.8%	4.9%	2.1%

2.1.2 Expected Number of One-Time AI Contacts, by Main/Casual Degree

Respondents in the combined dyadic dataset were asked whether they had had sex with each partner once or more than once; the former response led to the contact being defined as one-time. These contacts cannot be analyzed in terms of momentary degree distributions, since none are ongoing at the point of interview, by definition. Instead, we turned the observed frequencies into expected rates of one-time contacts per time step for men under different conditions. One of the sources of heterogeneity in men's propensity for one-time AI contacts is their current relationship status. Expected rates were calculated by age category and weighted by the proportion of the population in each age category to obtain the following overall expected numbers:

	0 Casual	*1 Casual*	*2 Casual*
0 Main	0.067	0.088	0.086
1 Main	0.058	0.059	0.059

2.1.3 Heterogeneity in the One-Time Contact Rate

In addition to differences by relational status, men also have underlying fixed heterogeneities in their propensity to engage in one-time AI. The distribution of one-time contacts was divided into quintiles, within which the expected values of one-time AI per time step are:

Quintile	**Value**
Lowest quintile	0.000
Second quintile	0.007
Third quintile	0.038
Fourth quintile	0.071
Highest quintile	0.221

Men are assigned a quintile upon entry into the population, which remains fixed. Any individual man's propensity for AI is determined as a combination of their quintile and their current main/casual partnership counts. Our statistical methods (described below) translate both propensities into conditional log-odds, allowing for their combination. Note that the means of the columns in the quintile table equal the means of the values in Section 2.1.2 weighted by the proportions in Section 2.1.1. These reflect the overall expected value across all men for one-time AI acts per time step.

2.1.4 Age Mixing

Respondents also reported on the estimated age of each partner. We modeled age mixing in two ways. First, ongoing partnerships from the combined dyadic dataset were categorized by the categorical age combination of the two partners ((1) younger-younger, (2) older-younger or younger-older, and (3) older-older). The total number of ongoing partnerships by categorical age combination was then enumerated for main and casual partnerships separately. Younger was defined as ages 18-24 and older was defined as 25-39 based on age differences in HIV incidence previously documented.[6] This yielded the following proportions of age combinations within main and casual relationships at a point in time. For one-time contacts, age mixing was not directly modeled but the stratified expected contact rate for younger and older individuals was incorporated.

Main partnerships:

Age combination of two partners	Value
Younger-younger	19.8%
Younger-older or Older-younger	29.1%
Older-older	51.1%

Casual partnerships:

Age combination of two partners	Value
Younger-younger	15.6%
Younger-older or Older-younger	36.3%
Older-older	48.1%

One-time contacts:

Age of individual	Value
Younger	0.068
Older	0.075

Second, we modeled age mixing on the continuous scale by having a single parameter for each given relational type that equals the expected mean difference in square root of the ages of men in a relationship, consistent with previous work.[1,3,8] For instance, a relationship between a 23-year-old and a 28-year-old would represent $\left|\sqrt{23} - \sqrt{28}\right|$ = 0.496.

	Value
Main partnerships	0.464
Casual partnerships	0.586
One-time contacts	0.544

2.1.5 Mixing by Sexual Role

We assigned men a fixed sexual role preference (exclusively insertive, exclusively receptive, or versatile) based on the empirical distributions of sexual role by age category of the individual. The model then included an absolute prohibition, such that two exclusively insertive men cannot partner, nor can two exclusively receptive men. Men's roles at last sex for each of the last 5 (Involve[men]t) or 10 (MAN Project) partners were aggregated; those who had engaged in one role across all of those acts in those partnerships were deemed to be exclusively receptive or insertive, and those who had engaged in at least one act of each were deemed to be versatile. Sexual role preference was assumed to be a fixed trait for the duration of each age category; upon turning 25, simulated men were assigned a new fixed sexual role consistent with the distribution for older MSM. For versatile men, the sexual role within each partnership at each simulated time step was stochastic.

Age of individual	Sexual Role	Probability
Younger (18-24 years)	Exclusively insertive	14.0%
	Versatile	32.9%
	Exclusively receptive	53.2%
Older (25-39 years)	Exclusively insertive	29.4%
	Versatile	25.9%
	Exclusively receptive	44.7%

2.1.6 Partnership Durations

We modeled relational dissolution as a memoryless process with age-specific parameters per relational type. This implies an exponential distribution for relational durations within each relationship-age combination category. As detailed in previous work,[1] for memoryless processes, the expected age of an extant relationship at any moment in time matches the expected uncensored duration of relationships, given the balancing effects of right-censoring and length bias for this distribution. To derive our values, we took the median of the observed distribution and then calculated the mean for the exponential distribution with that median. Duration was calculated as the difference between first and last sex date for each dyad the ego reported sex with more than once in the interval. The resulting expected relational durations were:

Partnership Type	Age combination of two partners	Duration (days)
Main partnerships	Younger-younger	127
	Younger-older or Older-younger	350
	Older-older	548
Casual partnerships	Younger-younger	146
	Younger-older or Older-younger	120
	Older-older	175

2.2 Statistical Representation of Sexual Networks

Exponential-family random graph models (ERGMs) and their dynamic extension separable temporal ERGMs (STERGMs) provide a foundation for statistically principled simulation of local and global network structure given a set of target statistics from empirical data. Main and casual relationships were modeled using STERGMs,[9] since they persist for multiple time steps. One-time contacts, on the other hand, were modeled using cross-sectional ERGMs.[10] Formally, our statistical models for relational dynamics can be represented as five equations for the conditional log odds (logits) of relational formation and persistence at time *t* (for main and casual relationships) or for relational existence at time *t* (for one-time contacts):

$$logit\left(P\left(Y_{ij,t}=1 \middle| Y_{ij,t-1}=0, Y_{ij,t}^{C}\right)\right) = \theta_m^{+\prime}\partial\left(g_m^{+}(y)\right)$$ Main partnership formation

$$logit\left(P\left(Y_{ij,t}=1 \middle| Y_{ij,t-1}=0, Y_{ij,t}^{C}\right)\right) = \theta_c^{+\prime}\partial\left(g_c^{+}(y)\right)$$ Casual partnership formation

$$logit\left(P\left(Y_{ij,t}=1 \middle| Y_{ij,t-1}=1, Y_{ij,t}^{C}\right)\right) = \theta_m^{-\prime}\partial\left(g_m^{-}(y)\right)$$ Main partnership persistence

$$logit\left(P\left(Y_{ij,t}=1 \middle| Y_{ij,t-1}=1, Y_{ij,t}^{C}\right)\right) = \theta_c^{-\prime}\partial\left(g_c^{-}(y)\right)$$ Casual partnership persistence

$$logit\left(P\left(Y_{ij,t}=1 \middle| Y_{ij,t}^{C}\right)\right) = \theta_o{}^{\prime}\partial\left(g_o(y)\right)$$ One-time contact existence

where:

- $Y_{ij,t}$ = the relational status of persons *i* and *j* at time *t* (1 = in relationship/contact, 0 = not)
- $Y_{ij,t}^{C}$ = the network complement of *i*,*j* at time *t*, i.e. all relations in the network other than *i*,*j*
- $g(y)$ = vector of network statistics in each model
- θ = vector of parameters in the formation model

For $g(y)$ and θ, the superscript distinguishes the formation model (+), persistence model (-) and existence models (neither). The subscript indicates the main (m), casual (c) and one-time (o) models.

The recursive dependence among the relationships renders the model impossible to evaluate using standard techniques; we use Markov chain Monte Carlo (MCMC) methods in order to obtain the maximum likelihood estimates for the $\boldsymbol{\theta}$ vectors given the $\boldsymbol{g(y)}$ vectors.

Specific model statistics are listed below. Together these sets allow us to retain all of the network features listed in Section 2.1. It is important to note that, although the statistics are expressed here in terms of number of relationships and enter into the estimation model in this form, the simulation model is then parameterized using the resulting θ coefficients. This means that, as population size and composition changes, it is not the absolute number of relationships of different kinds that will be preserved, but the relative numbers (e.g. the mean number of relationships per person). Similar conversions hold for the other statistics (e.g. the mean age difference per relationship is preserved, not the sum across all relationships).

Main partner formation model statistics: $g_m^+(y)$ vector:

- $g_{m1}^+(y)$ = number of main partnerships
- $g_{m2}^+(y)$ = number of men with 2+ main partners
- $g_{m3}^+(y)$ = number of main partnerships with age combination of younger-older/older-younger
- $g_{m4}^+(y)$ = number of main partnerships with age combination of younger-younger
- $g_{m5}^+(y)$ = number of main partnerships for men with 1 casual partner
- $g_{m6}^+(y)$ = number of main partnerships for men with 2 casual partners
- $g_{m7}^+(y)$ = sum of the absolute difference in the square root of partners' ages across main partnerships
- $g_{m8}^+(y)$ = number of main partnerships between men who were both exclusively insertive
- $g_{m9}^+(y)$ = number of main partnerships between men who were both exclusively receptive

There are structural zeroes as coefficient constraints for the terms $g_{m2}^+(y)$, $g_{m8}^+(y)$, $g_{m9}^+(y)$. This means that the logit values for their coefficients are set to negative infinity to ensure that no partnerships of these types occur.

<u>Main partner persistence model terms: $g_m^-(y)$ vector:</u>

- $g_{m1}^-(y)$ = number of main partnerships
- $g_{m2}^-(y)$ = number of main partnerships with age combination of younger-older/older-younger
- $g_{m3}^-(y)$ = number of main partnerships with age combination of younger-younger

<u>Casual partner formation model terms: $g_c^+(y)$ vector:</u>

- $g_{c1}^+(y)$ = number of casual partnerships
- $g_{c2}^+(y)$ = number of casual partnerships for men with 1 main partner
- $g_{c3}^+(y)$ = number of casual partnerships with age combination of younger-older/older-younger
- $g_{c4}^+(y)$ = number of casual partnerships with age combination of younger-younger
- $g_{c5}^+(y)$ = number of men with 2 casual partners
- $g_{c6}^+(y)$ = number of men with 3+ casual partners
- $g_{c7}^+(y)$ = sum of the absolute difference in the square root of partners' ages across casual partnerships
- $g_{c8}^+(y)$ = number of casual partnerships between men who were both exclusively insertive
- $g_{c9}^+(y)$ = number of casual partnerships between men who were both exclusively receptive

There are structural zeroes as coefficient constraints for the terms $g_{c6}^+(y)$, $g_{c8}^+(y)$, $g_{c9}^+(y)$. This means that the logit values for their coefficients are set to negative infinity to ensure that no partnerships of these types occur.

<u>Casual partner persistence model terms: $g_c^-(y)$ vector:</u>

- $g_{c1}^-(y)$ = number of casual partnerships
- $g_{c2}^-(y)$ = number of casual partnerships with age combination of younger-older/older-younger
- $g_{c3}^-(y)$ = number of casual partnerships with age combination of younger-younger

<u>One-time contact existence model terms: $g_o(y)$ vector:</u>

- $g_{o1}(y)$ = number of one-time contacts
- $g_{o2}(y)$ = total # of one-time contacts for men with 0 main and 1 casual partnership
- $g_{o3}(y)$ = total # of one-time contacts for men with 0 main and 2 casual partnerships
- $g_{o4}(y)$ = total # of one-time contacts for men with 1 main and 0 casual partnerships
- $g_{o5}(y)$ = total # of one-time contacts for men with 1 main and 1 casual partnership
- $g_{o6}(y)$ = total # of one-time contacts for men with 1 main and 2 casual partnerships
- $g_{o7}(y)$ = total # of one-time contacts for younger men
- $g_{o8}(y)$ = total # of one-time contacts for men in risk quintile 1
- $g_{o9}(y)$ = total # of one-time contacts for men in risk quintile 2
- $g_{o10}(y)$ = total # of one-time contacts for men in risk quintile 4
- $g_{o11}(y)$ = total # of one-time contacts for men in risk quintile 5
- $g_{o12}(y)$= sum of the absolute difference in the square root of partners' ages across one-time contacts
- $g_{o13}(y)$= number of one-time contacts between men who were both exclusively insertive
- $g_{o14}(y)$= number of one-time contacts between men who were both exclusively receptive

There are structural zeroes as coefficient constraints for the terms $g_{o13}(y), g_{o14}(y)$. This means that the logit values for their coefficients are set to negative infinity to ensure that no partnerships of these types occur.

Our method of converting the statistics laid out in Section 2.1 into our fully specified network models consists of the following steps:

1. Construct a cross-sectional network of 10,000 men (3,693 younger men ages 18-24 and 6,307 older men ages 25-39) with no relationships.
2. Assign men a continuous age value within the categorical age distribution (36.93% younger and 63.07% older). Assign men sexual roles based on frequencies listed in Section 2.1.5, as well as one-time risk quintiles (20% of the men per quintile).
3. Calculate the target statistics (i.e., the expected count of each statistic at any given moment in time) associated with the terms in the formation model (for the main and casual partnerships) and in the existence model (for one-time contacts).
4. Assign each node a place-holder main and casual degree (number of ongoing partnerships) that is consistent with degree matrices, and store these numbers as a nodal attribute. (Note: this does not actually require individuals to be paired up into the partnerships represented by those degrees).
5. For the main and casual networks, use the mean relational durations to calculate the parameters of the persistence model, using closed-form solutions, given that the models are dyadic-independent (each relationship's persistence probability is independent of all others).
6. For the main and casual networks, estimate the coefficients for the formation model that represent the maximum likelihood estimates for the expected cross-sectional network structure.
7. For the one-off network, estimate the coefficients for the existence model that represent the maximum likelihood estimates for the expected cross-sectional network structure.

Steps 5–7 occur within the *Statnet* software, and use the ERGM and STERGM methods therein. They are made most efficient by the use of an approximation in Step 6.[11] During the subsequent model simulation, we use the method of Krivitsky et al.[12] to adjust the coefficient for the first term in each model at each time step, in order to preserve the same expected mean degree (relationships per person) over time in the face of changing network size and nodal composition. At all stages of the project, simulated partnership networks were checked to ensure that they indeed retained the expected cross-sectional structure and relational durations throughout the simulations.

3 BEHAVIOR WITHIN SEXUAL PARTNERSHIPS

We model four phenomena consecutively within relationships at each time step: HIV+ status disclosure, number of anal sex acts, condom use per sex act, and sexual role per sex act.

3.1 Disclosure

We model the process by which someone who knows he is HIV-positive discloses this fact to partners of all types. Disclosure affects subsequent decision-making around condom use. We do not explicitly model other forms of serostatus discussion, since our source data do not include these; our behavioral estimates in the absence of HIV+ disclosure marginalize over those cases in which men disclose as concordant negative or do not discuss at all. Disclosure may occur at the point of a relationship commencing (if HIV+ status is already known) or it may occur at the point of diagnosis, in the case of ongoing relationships. In the former case, disclosure of HIV+ status was determined from the combined dyadic dataset using the HIV status of the respondent and their response to the question, “Did you and this partner share both of your HIV statuses before you first had sex?” In the latter case, we did not have data and assumed it to be universal.

Probability of Disclosure of HIV+ Status	**Probability**
to new main partner at outset of relationship	78.7%
to new casual partner at outset of relationship	67.8%
to one-time contact	56.8%
to ongoing partner if diagnosis occurs during relationship	100%

3.2 Number of AI Acts

The number of anal sex acts per week for each ongoing relationship is determined from a Poisson draw, with mean specific to the relational type and age combination. For one-time contacts, the number is set deterministically to 1 for the time step in which it occurs.

Partnership Type	Age combination of two partners	Frequency (95% CI)
Main partnerships	Younger-younger	1.10 (0.77, 1.58)
	Younger-older or Older-younger	1.15 (0.89, 1.48)
	Older-older	1.43 (1.18, 1.74)
Casual partnerships	Younger-younger	0.73 (0.51, 1.05)
	Younger-older or Older-younger	0.76 (0.60, 0.97)
	Older-older	0.95 (0.79, 1.14)

These rates were calculated based on the two Atlanta studies, derived from questions asking about the number of coital acts per partnership during the recall periods.[11,12] These were then rescaled from the length of the recall period into the weekly rates listed in the table above. During the calibration process, scalars were used to achieve stable age-specific HIV prevalences over time. These scalars corresponded to the upper limit of the empirical 95% confidence intervals for the frequency of AI acts per week for younger-younger and younger-older partnerships, and to the lower limit for older-older partnerships; these values were also used during simulation.

3.3 Condom Use

We conducted logistic regressions to identify the significant predictors of condom use within HIV-discordant relationships (whether diagnosed or not) in our data. Respondents were asked if they had had unprotected anal sex with each partner during the recall periods.[6,13] Predictors included the type of relationship, the HIV diagnosis status of the HIV+ partner (i.e. whether or not he himself knew that he was HIV+), and the disclosure status of the HIV+ partner (whether he had told his partner he was HIV+). Predictors that dropped out of the model included sexual position and perceived monogamy of the partnership. Base model coefficients for the nine partnership type-age combinations were defined as *logit*(P(condom use | anal intercourse).

Partnership Type	Age combination of two partners	Probability of condom use (95% CI)
Main partnership	Younger-younger	0.5194 (0.3466, 0.6877)
	Younger-older or Older-younger	0.3318 (0.2117, 0.4786)
	Older-older	0.3037 (0.1949, 0.4400)
Casual partnership	Younger-younger	0.2923 (0.1817, 0.4029)
	Younger-older or Older-younger	0.3286 (0.2508, 0.4064)
	Older-older	0.2363 (0.1745, 0.2980)
One-time contact	Younger-younger	0.2828 (0.1941, 0.3715)
	Younger-older or Older-younger	0.3381 (0.2595, 0.4168)
	Older-older	0.2201 (0.1639, 0.2763)

During the calibration process, scalars were used to achieve stable age-specific HIV prevalences over time. These scalars corresponded to the lower limit of the empirical 95% confidence intervals (CI) for condom use for younger-younger partnerships and younger-older/older-younger partnerships, and to the upper limit of the 95% CI for older-older partnerships; these values were also used during simulation.

Note that the reference category is the case in which the HIV+ man is undiagnosed, hence the relatively low values of condom use. Modifiers for these logit coefficients are:

Condition	Coefficient
HIV+ diagnosis	0.670
HIV+ status disclosure	0.850

Together, these values, in combination with the frequencies with which AI occurs in all of the different types of situations, imply an overall rate of condom use of approximately 50% across all acts. The rates of condom use were assumed to be stable over the course of a given partnership, but condom usage was stochastic at each time step within that partnership. Differential condom usage rates by partnership type may capture effects of lower condom use that may occur in longer-term partnerships, but subsequent models will extend this model framework to incorporate network-related data to capture temporal trends in condom usage within each type of partnership.

3.4 Sexual Role

Men are assigned an individual sexual role preference (exclusively insertive, exclusively receptive, or versatile) as described in Section 2.1.5. Relationships between two exclusively insertive or two exclusively receptive men are prohibited via the ERGM and STERGM models. Versatile men are further assigned an insertivity preference drawn from a uniform distribution between 0 and 1. When two versatile men are determined to have an AI act, their sexual positions must be determined (all other combinations have only one feasible combination). One option is for men to engage in intra-event versatility (IEV; i.e. both engage in insertive and receptive AI during the act). The probability of this is derived from the partner-specific role data described in Section 2.1.5 and varies by the age combination of the partnerships as shown in the table below. If IEV does not occur, then each man's probability of being the insertive partner equals his insertivity quotient divided by the sum of the two men's insertivity quotients.

Age combination of two versatile partners	Probability of intra-event versatility
Younger-younger	40%
Younger-older or Older-younger	48%
Older-older	40%

4 DEMOGRAPHY

In this model, there are three demographic processes: entries, exits, and aging. Entries and exits are conceptualized as flows to and from the sexually active population of interest: MSM aged 18 to 40 years old. Entry into this population represents the time at which persons become at risk of infection via male-to-male sexual intercourse, and we model these flows as starting at an age after birth (age 18) and ending at an age potentially before death (age 40).

4.1 Entry at Sexual Onset

All persons enter the network at age 18, which was the lower age boundary of our two main source studies. The number of new entries at each time step is based on a fixed rate (3 per 10,000 persons per weekly time step) that keeps the overall network size in a stable state over the time series of the simulations. The model parameter governing this rate was calibrated iteratively in order to generate simulations with a population size at equilibrium, given the inherent variability in population flows related to background mortality, sexual maturation (i.e., reaching the upper age limit of 40), and disease-induced mortality. At each time step, the exact number of men entering the population was simulated by drawing from a Poisson distribution with the rate parameter.

4.2 Initialization of Attributes

Persons entering the population were assigned attributes, some of which remained fixed by definition (e.g., race), others fixed by assumption (e.g., insertive versus receptive sexual role), and yet others allowed to vary over time (e.g., age and disease status). Here we describe three attributes in the first category:

- For **race/ethnicity**, this model was based on a population composition that was 50% black MSM and 50% white MSM. As noted, we did not explicitly model race within this study, and set all race-specific parameters to averages across stratified estimates. Subsequent models will extend this model framework to explore racial disparities among MSM. This 1:1 ratio comes close to that for the Atlanta metropolitan area and also provides analytical clarity.

- **Circumcision** status was randomly assigned to incoming men. Based on empirical data from Atlanta MSM,[6] 89.6% of men were circumcised before sexual onset. Circumcision was associated with a 60% reduction in the per-act probability of infection for HIV- males for insertive anal intercourse only (i.e., circumcision did not lower the *transmission* probability if the HIV+ partner was insertive).[2,14]

- The **CCR5-Δ32 genetic allele** was modeled by assigning a mutation for zero, one, or two chromosomes. Compared to men without a CCR5 mutation, heterozygous men (those with one mutation) were 70% less likely to become infected and homozygous men (those with two mutations) were fully immune from infection.[15,16] The population distribution of CCR5 was differential by race, with 0% of black men and 3.4% of white men expressing as homozygous, and 2.1% of black men and 17.6% of white men expressing as heterozygous.[15] But because race was not explicitly represented in these models, we averaged each set of proportions: 1.7% homozygous and 9.9% heterozygous overall.

4.3 Exits from the Network

All persons exited the network by age 40, either from mortality or reaching the upper age bound of the MSM target population of interest. This upper limit of 40 was modeled deterministically (probability = 1), but other exits due to mortality were modeled stochastically. Mortality included both natural (non-HIV) and disease-induced mortality causes before age 40. Background mortality rates were based on US all-cause mortality rates specific to age and race from the National Vital Statistics life tables.[17] The following table shows the probability of mortality per year by age and race.

Age	White	Black
18–24	0.00103	0.00159
25–34	0.00133	0.00225
35–39	0.00214	0.00348

Natural mortality was applied to persons within the population at each time step stochastically by drawing from a binomial distribution for each eligible person with a probability parameter corresponding to that person's risk of death tied to his age. Disease-related mortality, in contrast, was modeled based on clinical disease progression, as described in Section 5.

4.4 Aging

The aging process in the population was linear by time step for all active persons. The unit of time step in these simulations was one week, and therefore, persons were aged in weekly steps between the minimum and maximum ages allow (18 and 40 years old). Evolving age impacted background mortality, age-based mixing in forming new partnerships, duration of partnerships, and other behavioral features of the epidemic model. Persons transitioned from the younger age category to the older age category at the week they turned age 25 years. Persons who exited the network were no longer active and their attributes such as age were no longer updated.

5 HIV INTRAHOST EPIDEMIOLOGY

Intrahost epidemiology includes features related to the natural disease progression within HIV+ persons in the absence of clinical intervention. The main component of progression that was explicitly modeled for this study was HIV viral load. In contrast to other modeling studies that model both CD4 and viral load, our study used viral load progression to control both interhost epidemiology (HIV transmission rates) and disease progression eventually leading to mortality.

Following prior approaches,[1,2] we modeled changes in HIV viral load to account for the heighted viremia during acute-stage infection, viral set point during the long chronic stage of infection, and subsequent rise of VL at clinical AIDS towards disease-related mortality. A starting viral load of 0 is assigned to all persons upon infection. From there, the natural viral load curve is fit with the following parameters. The HIV viral load has a crucial impact on the rates of HIV transmission within serodiscordant couples in the model, and this interaction is detailed in Section 7. The parameters governing these processes are provided in the table below.

Parameter	**Value**	**Reference**
Time to peak viremia in acute stage	45 days	Little[18]
Level of peak viremia	6.886 $\log_{10}$	Little[18]
Time from peak viremia to viral set point	45 days	Little[18], Leynaert[19]
Level of viral set point	4.5 $\log_{10}$	Little[18]
Duration of chronic stage infection (no ART)	3550 days	Buchbinder[20], Katz[21]
Duration of AIDS stage	728 days	Buchbinder[20]
Peak viral load during AIDS (at death)	7 $\log_{10}$	Estimated from average duration of AIDS

After infection, it takes 45 days to reach peak viremia, at a level of 6.886 log 10. From peak viremia, it takes another 45 days to reach viral set point, which is set at a level of 4.5 log 10. The total time of acute stage infection is therefore 3 months. The duration of chronic stage infection in the absence of clinical intervention is 3550 days, or 9.7 years. The total duration of pre-AIDS disease from infection is therefore approximately 10 years. At onset of AIDS, HIV viral load rises linearly from 4.5 log 10 to 7 log 10, at which point mortality is assumed to occur. The time spent in the AIDS stage is 728 days, or 2 years. This viral load trajectory is for ART-naïve persons only, and the influence of ART on disease progression is detailed in Section 6. These transitions are deterministic for all ART-naïve persons.

6 HIV CLINICAL EPIDEMIOLOGY

Clinical epidemiological processes refer to all steps along the HIV care continuum after initial infection: diagnosis, linkage to care, treatment initiation and adherence, and HIV viral load suppression. In this model, these clinical features have critical interactions with behavioral features detailed above, as well as impacts on the rates of HIV transmission, detailed below. The features of our model's clinical processes generally follow the steps of the HIV care continuum, in which persons transition across states from infection to diagnosis to medical care linkage and ART initiation to HIV viral suppression.[22]

6.1 HIV Diagnostic Testing

Persons in our models were divided into non-testers (through age 40) and regular interval-based testers. Based on empirical data for Atlanta MSM,[6] 6.5% of MSM did not receive HIV testing before age 40. This was calculated based on a survey question about never testing prior to the study, which may overestimate the final proportion who would have never tested before age 40. A fixed individual attribute for HIV treatment trajectories that characterized progression through the care continuum was randomly assigned upon entry into the population, with this group of 6.5% of MSM not accessing HIV testing or other forms of post-diagnostic HIV medical services.

The remaining 93.5% who entered the HIV care continuum HIV tested at regular intervals, with the estimated mean time between tests for HIV-negative persons at 301 days for black MSM and 315 days for white MSM.[6,23] This was calculated based on time since last test in the survey, with the assumption that testing was a memoryless process. In this paper, we averaged over the two intervals since we did not explicitly model racial differences in the care continuum. Diagnostic testing was simulated stochastically using draws from a binomial distribution with probability parameters equal to the reciprocal of this interval. This generated a population-level geometric distribution of times since last test.

We also modeled a 21-day window period after infection during which the tests of the truly HIV+ persons would show as negative to account for the lack of antibody response immediately after infection.[24] HIV+ persons who tested after this window period would be correctly diagnosed with 100% test sensitivity. Individual-level attributes for diagnosis status and time since last HIV test were recorded for all MSM.

6.2 Antiretroviral Therapy (ART) Initiation

Consistent with previous models,[1,2] we simulated the initiation of ART and subsequent clinical outcomes of full or partial HIV viral suppression based on men being in one of three clinical states: never tested, on treatment and partially virally suppressed, and on treatment with full viral suppression. There was insufficient empirical data to represent the patterns and rates at which individual men switch among these three states over the course of their infection, since the clinical ART landscape is constantly evolving. Therefore, we modeled men as being on one of the three fixed treatment trajectories as an individual-level attribute such that our model matched the population-level data on the prevalence of durable HIV viral suppression and treatment-naïve mortality.[25,26]

Following HIV diagnosis (for the 93.5% of men who ever HIV test before age 40), MSM initiated treatment at a rate of 0.1095 per week. This translates into an average interval between testing and treatment initiation of 9.13 weeks, consistent with empirical data.[23] In the absence of quantitative data, we assumed no gap between treatment entry and ART initiation.

6.3 ART Adherence and Viral Suppression

MSM who initiated ART could cycle on and off treatment, where cycling off treatment resulted in an increase in the VL back up to the assumed set point of 4.5 $\log_{10}$. The slope of changes to VL were calculated such that it took a total of 3 months to transition between the set point and the on-treatment viral loads.[27] Men on treatment could achieve partial or full suppression. Men who with partial suppression were assumed to have a $\log_{10}$ viral load of 3.5, compared to 1.5 among those who were fully suppressed.[27] The latter corresponds to an absolute viral load below the standard levels of detection (VL = 50).[28]

The patterns of ART adherence leading to partial and full HIV viral suppression were estimated based on an analysis of HIV care patterns among MSM in the United States,[25] which was required in order to obtain parameters that were specific to young MSM by race. Parameterizing our model used three types of inputs: (1) the proportion of those diagnosed who are on ART; (2) the proportion of those diagnosed who are virally suppressed; (3) the level of durable suppression (proportion on ART who have been suppressed for a year). Our source included recent estimates for (1) by race and by age, but not the interaction of the two. We used a weighted average of their 18–29 and 30–39-year-old data, and assumed that the overall prevalence ratio by race that they observed for each outcome held within this age group as well. This suggested that 30% of young Black MSM who were diagnosed were in care, and 74% of those were on ART, for a combined value of 22% of young Black MSM who were diagnosed being on ART at any time point. Analogous figures for young White MSM were 47%, 84% and 39%. For (3), we used the same method of deriving estimates specific to young Black MSM (47% of those on ART are durably suppressed) and young White MSM (60% for the corresponding figure). For (2), we used figures by race from the same paper; however, similar figures by age were not included. Instead, we adjusted by using the relative rates of retention in care and suppression for young adults (25-44) compared to all respondents from an additional analysis of the care continuum for members of all risk groups (not just MSM-specific) in the US.[29] This yielded estimates for the percent of young MSM on ART who are virally suppressed of 62% for Blacks and 68% for Whites.

None of these three sets of values entered the model directly as inputs. Parameter (3) was converted into a per-time step probability of falling out of suppression, by using the inverse geometric function to calculate the probability consistent with observed levels of durable suppression after 1 year. Our other two input parameters were the proportion of those initiating ART who achieved full suppression, and the per-time step probability of re-achieving suppression after one had previously fallen out. We simulated our full model iteratively until we identified the unique values of these parameters by race that yielded the values estimated for parameters (1) and (2) above. The resulting set of model inputs were:

Parameter	Black	White
Proportion of those initiating ART who achieved full suppression	0.614	0.651
Per-week probability of falling out of suppression	0.0102	0.0071
Per-week probability of re-achieving suppression	0.00066	0.00291

This study averaged over the race-specific parameter estimates because race was not explicitly modeled in this study.

6.4 Disease Progression and Mortality after ART Initiation

Mortality after ART initiation was modeled based on the cumulative time on and off ART for persons who were fully or partially suppressed. The maximum time between infection and the start of AIDS was 9.7 years.[20] If a person in either the full or partial suppression categories who spent this much time off ART during the course of infection progressed to AIDS. For the partially suppressed, we assumed a maximum time on ART of 15 years, similar to previous models, to account for treatment failure.[1] For this group, the time to AIDS was an additive function of two ratios: (time on treatment / maximum time on treatment) + (time off treatment / maximum time off treatment). AIDS was simulated to occur when the sum of this score exceeded 1. Persons who had ever initiated ART progressed through AIDS at a similar rate as those who were ART-naïve.

7 HIV INTERHOST EPIDEMIOLOGY

Interhost epidemiological processes represent the HIV-1 disease transmission within the model. Disease transmission occurs between sexual partners who are active on a given time step. This section will describe how the overall rate as a function of the intrahost epidemiological profile of each member of a partnership, and behavioral features within the dyad.

7.1 Disease-Discordant Dyads

At each time step in the simulation, a list of active dyads was selected based on the current composition of the network. This was called an "edgelist." Given the three types of partnerships detailed above, the full edgelist was a concatenation of the type-specific sublists. The complete edgelist reflects the work of the STERGM- and ERGM-based network simulations, wherein partnerships formed on the basis of nodal attributes and degree distributions (see Section 2). Dyads were considered active at a specific time step if the terminus of that simulated edge was greater than or equal to the current time step (right-censored). From the full edgelist, a disease-discordant subset was created by removing those dyads in which both members were HIV- or both were HIV+. This left dyads that are discordant with respect to HIV status, which was the set of potential partnerships over which a HIV infection may be transmitted at that time step.

7.2 Per-Act HIV Transmission Probability

Within disease-discordant dyads, HIV transmission was modeled based on a sexual act-by-act basis, in which multiple acts of varying infectiousness could occur within one partnership within a weekly time step. Determination of the number of acts within each discordant dyad for the time step, as well as condom use and role for each of those acts, was described in Sections 2 and 3. Transmission by act was then modeled as a stochastic process for each discordant sex act following a binomial distribution with a probability parameter that is a multiplicative function of the following predictors of the HIV- and HIV+ partners within the dyad.

Predictor	Partner	Parameters	References
Sexual role (insertive or receptive)	HIV-	*Receptive:* 0.008938 base probability when HIV+ partner has 4.5 $\log_{10}$ viral load	Vittinghoff[30]
		Insertive: 0.003379 base probability when HIV+ partner has 4.5 $\log_{10}$ viral load	Vittinghoff[30]
HIV viral load (VL)	HIV+	Multiplier of $2.45^{(VL - 4.5)}$	Wilson[31]
Acute stage	HIV+	Multiplier of 6	Leynaert[19], Bellan[32]
CCR5 status	HIV-	Δ32 homozygote: multiplier of 0	Marmor[15]
		heterozygote: multiplier of 0.3	Marmor[15]
Condom use	Both	Multiplier of 0.25	Varghese[33], Weller[34]
Circumcision status	HIV-, insertive	Multiplier of 0.40	Gray[14]

For each act, the overall transmission probability was determined first with a base probability that was a function of whether the HIV- partner was in the receptive or insertive role, with the former at a 2.6-fold infection risk compared to the latter. The HIV+ partner's viral load modifies this base probability in a non-linear formulation, upwards if the VL was above the VL set point during chronic stage infection in the absence of ART, and downwards if it was below the set point. Following others, we modeled an excess transmission risk in the acute stage of infection above that predicted by the heightened VL during that period. Three predictors of the HIV- partner could reduce the risk of infection: the Δ32 allele on the CCR5 gene, condom use within the act, circumcision status (only if the HIV- partner was insertive in that act).

The final transmission rate per partnership per weekly time step was a function of the per-act probability of transmission in each act and the number of acts per time step. The per-act transmission probability could be heterogeneous within a partnership due to various types of acts in each interval: for example, a HIV- man who is versatile in role may have both insertive and receptive intercourse within a single partnership; some acts within a partnership may be protected by condom use while others are condomless. Transmission was simulated for each act within each serodiscordant dyad, based on draws from a binomial distribution with the probability parameter equal to the per-act transmission probabilities detailed above.

8 MODEL CALIBRATION AND PARAMETER ESTIMATION

This section describes the methods for executing the simulations and conducting the data analysis on the outcomes in further detail.

8.1 Model Calibration

Starting with a population of 10,000 MSM, HIV infection was initially seeded in 7% of the population.[35-37]. A set of burn-in simulations was then used to allow the natural dynamics of HIV and STI transmission, demography, and other population features to evolve over time. The goal of the burn-in simulation was to arrive at a network of MSM that was independent of the initial conditions resulting from the seeding. This also established a population composition with behavioral and biological features calibrated to match targets for HIV prevalence of 35% for older MSM ages 25-39 and 21% for younger MSM ages 18-24 as consistent with the network and incidence studies of Atlanta MSM.[6,38]

Many HIV and STI models of disease transmission have been parameterized using populations both in the United States and internationally. These models have differed in type, including deterministic compartmental models, stochastic models, and agent-based transmission models. They have also differed by the populations explicitly modeled, whether MSM only, heterosexual men and women only, or a combination of both populations. Given the variation in parameter values from population to population, we use and evaluate information and estimates from models of male-to-female (MTF), female-to-male (FTM), and male-to-male disease transmission to establish our parameters and prior distributions. These include calibrated estimates from published mathematical models, findings from natural history studies that have been parameters in those models, and estimates where other information is not available.

We used approximate Bayesian computation with sequential Monte Carlo sampling (ABC-SMC) methods[32,39] to calibrate behavioral parameters in which there was measurement uncertainty in order to match the simulated HIV prevalence at the end of the burn-in simulations to the targeted HIV prevalence.

The details of ABC depend on the specific algorithm used, but in this case, ABC-SMC proceeded as follows.

For each candidate parameter, θ, to be estimated, we:

1. Sampled a candidate θ^i from a prior distribution $\pi(\theta)$
2. Simulated the epidemic model with candidate value, θ^i.
3. Tested if a distance statistic, d (e.g., the difference between observed HIV prevalence and model simulated prevalence) was greater than a tolerance threshold, ϵ.
    a. If $d > \epsilon$ then discard
    b. If $d < \epsilon$ then add the candidate θ^i to the posterior distribution of θ.
4. Sample the next sequential candidate, θ^{i+1}, either independently from $\pi(\theta)$ (if 3a) or from θ^i plus a perturbation kernel with a weight based on the current posterior distribution (if 3b).

For the ABC algorithms to calibrate to the observed age-specific HIV prevalence, a total of 1,000 simulations for 50 years of calendar time each were performed. Scalars were used for condom use and sex act frequency parameters in order to calibrate to age-specific HIV prevalence targets. These scalars corresponded to the lower bound of the empirical 95% confidence intervals for condom use among younger-younger and younger-older/older-younger partnerships, and to the upper bound of the 95% CI for older-older partnerships. Similarly, these scalar values corresponded to the upper bound of the 95% empirical confidence interval of sex act frequency for younger-younger and younger-older partnerships and the lower bound for older-older partnerships. All simulations were conducted on the Hyak high-performance computing platform at the University of Washington.

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