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INFECTIOUS DISEASE EPIDEMIOLOGY (AL REINGOLD, SECTION EDITOR)

Update on the Epidemiology and Prevention of HIV/AIDS in the USA

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Abstract This update on the epidemiology and prevention of HIV in the USA is intended to provide contextual background that will help inform an understanding of recent developments in the domestic HIV epidemic. We describe the epidemiology of HIV disease in the USA and the HIV continuum of care based on data collected primarily through HIV surveillance systems led by the Centers for Disease Control and Prevention including HIV incidence, prevalence, comorbidities, and death. Populations and geographic regions disparately impacted by HIV are also highlighted. The HIV prevention armamentarium is also described including behavioral approaches to prevention, the emerging availability of biomedical prevention interventions such as pre-exposure prophylaxis, and structural and population-level interventions including treatment as prevention. Finally, gaps in our understanding of the epidemic are underscored and suggestions for future epidemiologic research are proposed.

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Introduction

During the past several years, there has been an upsurge of important policy initiatives for HIV epidemic control in the USA, epidemiologic approaches that have deepened our understanding of the dynamics of HIV prevention and treatment, and critical new research that has provided substantial additions to the HIV prevention armamentarium. On a policy level, the publication of the first ever National HIV/AIDS Strategy (NHAS) with its three primary goals of "reducing HIV incidence," "increasing access to care and optimizing health outcomes," and "reducing HIV-related health disparities" was a sentinel event that has galvanized the response to the domestic HIV epidemic [1••]. Epidemiologically, the recognition that the epidemic has become stubbornly persistent in subpopulations such as youth and black men who have sex with men (BMSM) provides a focal point to guide HIV prevention activities [2]. In addition, the conceptualization of the HIV continuum of care as a spectrum from HIV diagnosis through viral suppression [3••] served as the foundation for the measurement of these population-based parameters over time [4], establishment of national goals for these outcomes [5], and development of prevention programs specifically targeting these goals [6, 7] In addition, the visualization of geographic "hot spots" through innovative mapping programs such as AIDSVu [8], and the potential to assess transmission dynamics in these hotspots using molecular epidemiology techniques [9], can be used to target the use of limited HIV prevention resources. From a research perspective, the demonstration of the efficacy of pre-exposure prophylaxis [10••] and treatment

as prevention [11••] were landmark studies that solidified the central role of antiretroviral therapy in HIV prevention programs. This update on the epidemiology and prevention of HIV in the USA is intended to provide contextual background that will help inform an understanding of these recent developments.

Epidemiology

Thirty-four years after AIDS was first described, there are an estimated 35 million people living with HIV globally [12]. There are approximately 1.2 million people living with HIV in the USA, accounting for about 3.5 % of the global burden of disease [4]. According to UNAIDS, the USA has a concentrated epidemic as the majority of infections occur in high-risk subpopulations and less than 1 % of the general population is infected [13]. This section will describe the epidemiology of HIV disease in the USA based on data collected primarily through HIV surveillance systems led by the Centers for Disease Control and Prevention (CDC) in collaboration with state and local public health departments. It will aim to highlight our current knowledge of the epidemic, populations disparately impacted by HIV, gaps in our understanding of the epidemic, and propose areas for additional research based on our current knowledge of the epidemic.

The HIV Epidemic Measured Using Surveillance Data

In addition to cohort studies that have provided essential information on the natural history of HIV disease and the impact of treatment over the decades, surveillance data have allowed documentation of the magnitude of the epidemic. The US National HIV Surveillance system (NHSS) has characterized the epidemic in the USA since the initial cases in 1981; NHSS is CDC funded in 50 states, the District of Columbia (DC), and six US dependent areas [14]. Initially focused on counting and describing cases of AIDS, the surveillance system evolved as the epidemic and our understanding of it unfolded. AIDS surveillance case definitions expanded to include certain opportunistic infections and laboratory tests such as CD4 counts with the most recent revision in 2014 [15•]. As persons with HIV began to live longer due to earlier diagnosis and the availability of life-prolonging treatments, national surveillance programs expanded to capture a more complete spectrum of HIV infection and disease—from describing behaviors antecedent to HIV infection through HIV-related illness and death. CDC surveillance systems thus mirror this pathway and include behavioral surveillance, incidence surveillance, molecular epidemiology surveillance, and the morbidity monitoring project [16].

Incidence

HIV incidence estimates are critical as they provide an indication of the leading edge of the epidemic. Identification of locations and populations in which the majority of new infections occur allows prevention efforts to be appropriately targeted. Use of BED assays has facilitated the detection of recently infected cases versus those who have been living with HIV disease but have only recently been diagnosed [17, 18]. Through the CDC's HIV Incidence Surveillance system, recent HIV incidence estimates have shown there are 50,000 new HIV infections annually in the USA [19, 20]. Populations with the highest proportion of incident cases include adolescents ages 13–24, young adults ages 25–35, Black persons, and men who have sex with men (MSM); the highest number of new infections was among young BMSM ages 13–24 in 2010 [19]. While the incidence continues to increase in these populations, new infections among persons who inject drugs (IDU) declined in recent years [19], most likely due to the implementation of harm reduction programs and syringe exchange services. Despite this, the high number of continued transmissions has unfortunately been stable without evidence of decrease, highlighting the need for enhanced prevention efforts. Epidemiologic research to understand how to identify persons who are at risk for HIV and interrupt potential transmissions should therefore be a priority area.

Prevalence

The number of persons living with HIV has increased dramatically since the start of the epidemic. This is in part not only due to identification of new infections but also due to the increasing availability of life-prolonging antiretroviral treatments. An estimated 880,440 persons have been diagnosed and are living with HIV in the USA [14]; another 14 % remain undiagnosed [4]. Although the magnitude of the US epidemic is less severe than other regions of the world such as Sub Saharan Africa, there are pockets of high prevalence in which particular subpopulations are disproportionately affected including black persons and MSM. Highlighting a critical disparity, black individuals make up 13 % percent of the US population [21] yet account for 43 % of persons living with HIV [14]. Similarly, while the epidemic started among MSM and they represent a very small proportion of the underlying US population, they continue to be the most affected risk group with an increasing trend in prevalence in the last 5 years [14].

Morbidity and Mortality

The epidemiology of HIV-related morbidity and mortality has also shifted over the past three decades. Whereas opportunistic infections such as *Pneumocystis* carinii pneumonia were

the most common AIDS defining illnesses in the early 1980s, opportunistic illnesses and AIDS defining cancers have declined significantly since the start of the epidemic. Expected survival for someone living with HIV is now over 20 years, and 40 % of persons with HIV will die from a non-HIV-related cause [22]. With recent HHS guidelines recommending antiretroviral therapy for all HIV-infected persons regardless of CD4 count [23], these issues are likely to grow in importance as increasing numbers of patients are exposed to antiretrovirals and consequently living longer.

Given improved survival among HIV-infected persons, HIV is sometimes perceived as a chronic treatable condition, which in turn can make prevention messaging and efforts more difficult to achieve [24]. Data from the CDC's Morbidity Monitoring Project found that approximately half of HIV-infected MSM engaged in unprotected anal intercourse and 33 % of injection drug users shared syringes, serving as a barrier to secondary prevention efforts [16, 25]. The HIV chronic disease model presents an area for research including the role of treatment fatigue and secondary prevention interventions. The field of HIV and aging is also emerging. Data suggest that chronic inflammation and long-term exposure to antiretrovirals may contribute to morbidity and mortality among this population, yet many questions remain as to the underlying mechanisms [26].

Disparities

Despite progress in understanding the HIV epidemic in the USA, many disparities in prevention, care, and treatment remain both geographically and demographically. Geographically, while cities such as New York, San Francisco, and Washington, DC have traditionally had some of the highest HIV prevalence rates, recent declines in the number of new cases have been observed in these cities. New York City reported a decline in new HIV diagnoses among all populations from 2001 to 2013 [27]. San Francisco also reported a decline in new HIV cases between 2007 and 2011 [28], and recently Washington, DC released data showing a 52 % decline in the number of new cases over the past 5 years [29]. In contrast, Southern cities in the USA, including Miami, Florida, and Atlanta, Georgia have seen increases in the number of persons diagnosed with HIV [30, 31]. This geographic disparity has been highlighted by Sullivan and colleagues who have developed the AIDSVu program which allows for visualization of the epidemic in the context of other social determinants including race, poverty, and access to care (Fig. 1) [8]. The emergence of the epidemic in the Southern USA has been attributed to issues such as stigma, elevated sexually transmitted disease prevalence, and treatment access [32]. The ability to identify these geographic hot spots of continued transmission may be useful in describing sexual networks and transmission patterns through phylogenetic mapping and directing prevention interventions aimed at interrupting transmission.

Racial and ethnic disparities in HIV incidence and prevalence also continue to persist. Data from CDC show that BMSM ages 13–24 accounted for 58 % of new infections among all MSM [33]. National HIV Behavioral Surveillance data estimate that 68 to 75 % of young MSM ages 18 to 24 and 59 % of BMSM were unaware of their HIV infection [34]. Potential explanations as to why this group is at highest risk for HIV include social determinants such as structural barriers to healthcare, stigma and homophobia, poverty, and unemployment as well as sexual network factors including high background prevalence of sexually transmitted infections and small and intertwined sexual networks [35•, 36–39]. Ongoing research to address the epidemic among this population include efforts on the part of the HIV Prevention Trials Network (www.HPTN.org/) and the establishment of cohorts of both HIV negative and positive MSM [36]; however, additional research focusing on prevention interventions in this population is necessary.

HIV Continuum of Care

The HIV continuum of care is a relatively new way of describing the epidemiology of HIV infection and identifying gaps in the ability to diagnose, care for, and successfully treat persons living with HIV. The continuum of engagement in HIV care was described by Cheever et al. at HRSA in 2007 [3••], adapted as the HIV treatment cascade by others in the scientific literature [40, 41] and defined as the continuum of HIV care by the CDC in 2011 [42]. The care continuum begins with HIV infection, which is followed by HIV diagnosis, linkage to and retention in care, and ends with receipt of antiretroviral therapy and viral suppression, defined as a viral load less than 200 copies/ml [4]. Viral suppression is the ultimate goal in the treatment of HIV disease as it results both in individual benefit to an HIV-infected patient's health and in public health benefit through a reduction of the risk that an infected person will transmit the virus to others [11••, 43••].

The HIV care continuum is a model that is currently being used in the USA to assist with monitoring progressing in achieving the National HIV/AIDS Strategy [5]. National estimates of the care continuum have shown that 86 % percent of people were aware of their HIV diagnosis, 80 % were linked to care within 3 months of diagnosis, 40 % were engaged in care, and 30 % achieved viral suppression [4]. The low rates of viral suppression were attributed to the 20 % of persons thought to be infected but not yet diagnosed, the 66 % of persons out of care, the 4 % who are in care but not on antiretroviral therapy, and the 10 % who are on therapy but not suppressed [4]. These gaps highlight the need for initiatives to promote non-risk-based HIV testing, to develop innovative linkage, retention, and re-engagement strategies, and to improve current adherence strategies. While the care continuum ends with the achievement of viral suppression, the ability to sustain lifelong

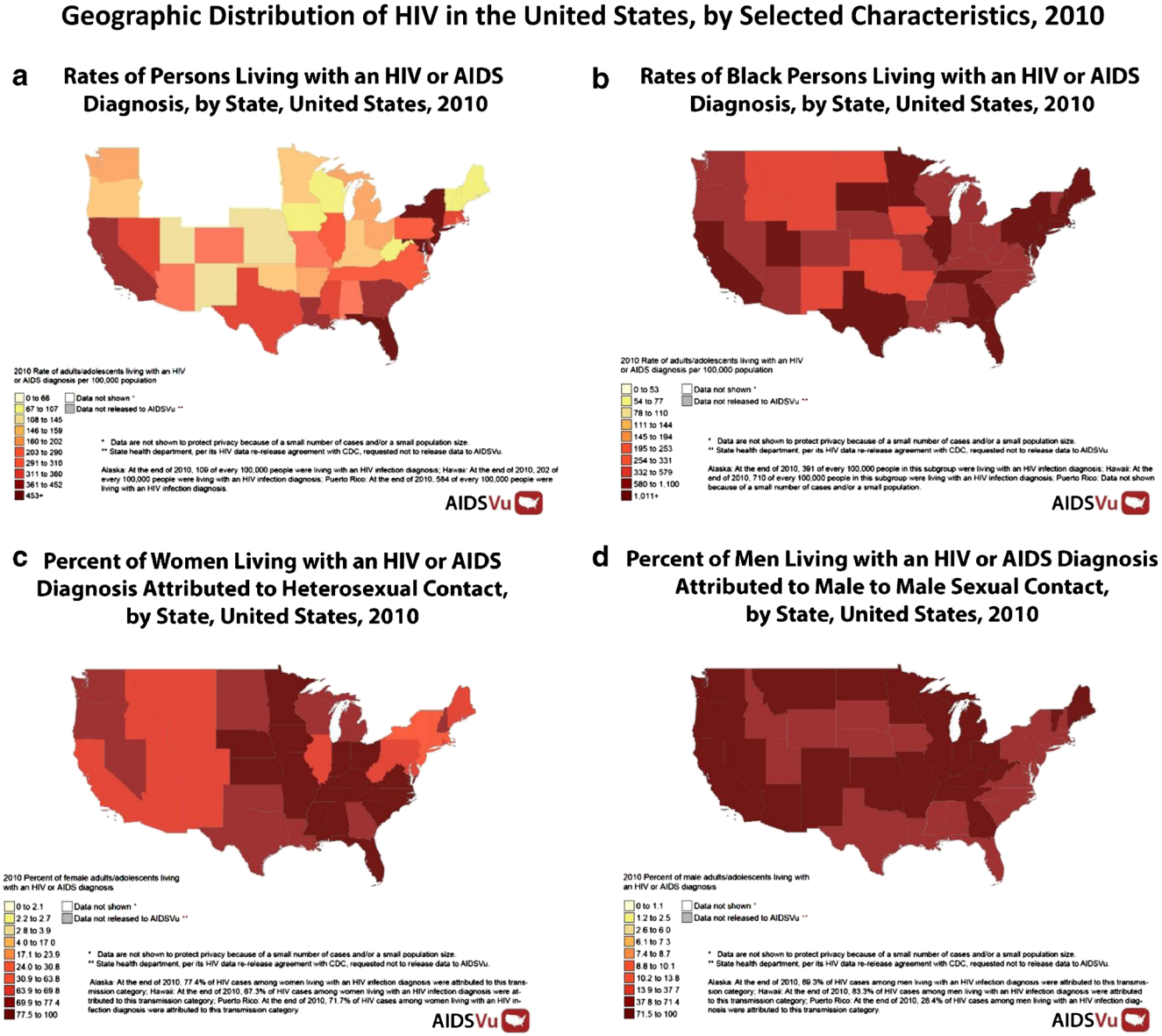

Fig. 1 Maps are from AIDSVu (www.aidsvu.org/) and highlight the disproportionate impact of HIV by geographic region (**a**), by race (**b**), and by mode of HIV transmission for males and females (**c** and **d**, respectively)

suppression is necessary among persons with this chronic illness. Thus, scientific advances are needed to facilitate the maintenance of suppression and engagement in care, whether through pharmaceutical research such as the development of long-acting antiretrovirals, or through behavioral research to assess (for example) the role of community health workers and treatment partners in supporting lifelong adherence [44].

Gaps and Future Directions

While the use of surveillance data allows for greater understanding of the HIV epidemic in the USA, it has several limitations. Persons captured through surveillance only include those who have been diagnosed and reported to a surveillance system. For example, CDC estimates that NHSS data are representative of 80 % of all HIV cases in the USA [45]. Establishing cohorts that follow high-risk groups such as young BMSM may allow researchers to better characterize risk behaviors, social and sexual networks and allow for more rapid diagnosis of incident infections and thus prevent ongoing transmission.

Many initiatives are underway to address gaps in the HIV care continuum. Routine HIV testing in medical settings has been the standard recommendation from CDC since 2006, and linkage to care rates are relatively high when coupled with testing. Many high prevalence cities, including the Bronx, New York [46], Washington, DC [47], Houston, Texas [48], and Philadelphia, Pennsylvania [49] have already implemented routine HIV testing programs in response to the revised

CDC recommendations and have all been able to test and identify thousands of infected persons. Home-based HIV testing and internet-based HIV counseling offer new opportunities to identify persons unaware of their infection. Numerous local and federal initiatives have begun to improve linkage to and retention in care [6, 7], and health information exchanges have now been shown to facilitate re-engagement in care [50].

The HIV Prevention Armamentarium

HIV prevention in the USA has in many ways evolved parallel to HIV surveillance: the addition of each new scientific breakthrough to prevent HIV has rapidly contributed to an expanding armamentarium of new tools to slow the epidemic [10••, 11••, 51, 52•, 53–55]. As with advances seen in medicine, demonstration that a given tool is effective does not immediately translate into adoption. Uptake of prevention methods in the USA and beyond remains challenging as social norms evolve, provider and patient knowledge bases expand, and healthcare infrastructure struggles to keep pace with scientific advancement. Still, with increasing approaches to HIV prevention and availability of more modalities than ever before to prevent HIV, individual-level and population-level approaches are available to suit multiple situations and subpopulation needs at nearly all points in the life course [10••, 54, 56–62]. Combination prevention efforts that enlist multiple methods to prevent HIV rather than relying on just one, and the evolving concept of a "Prevention Continuum" [4, 10••, 11••, 41, 43••, 53, 54, 56, 58, 59, 62–66], now allow healthcare providers and community agencies to identify appropriate prevention methods based on the unique needs of each individual at a given point in time in concert with testing and outreach efforts. This section will describe currently available behavioral, biomedical, population-level, and structural interventions that effectively prevent HIV along with relative strengths and challenges of each (Table 1).

Table 1 Examples of HIV prevention strategies

- Individual level
  - Behavioral
    - Abstinence
    - Serosorting, seropositioning
    - Male and female condom use
    - Individual-level counseling
    - Group counseling
    - Theoretically-based prevention programs (e.g., DEBIs, social cognitive theory, motivational interviewing)
    - Subpopulation-specific prevention programs (e.g., transgender women, at risk Latina heterosexual women, black MSM)
  - Biomedical
    - Perinatal prophylaxis (including prevention of transmission via breastmilk)
    - Post-exposure prophylaxis (occupational and non-occupational)
    - Pre-exposure prophylaxis
    - Microbicides
    - Vaginal rings
    - Combination HIV prevention/contraception interventions
    - Eventual vaccine
    - Control of sexually transmitted diseases
    - Syringe exchange programs
    - Maintenance therapies (e.g., methadone)
- Population-level and structural
  - Expanded access to health insurance
  - Treatment as prevention
  - Routine HIV screening
  - Increased access and outreach for HIV testing (traditional and nontraditional settings)
  - Increased access to contraception
  - Culturally competent care provision
  - Condom distribution programs
  - Supervised injecting facilities
  - HIV prevention education in schools

Behavioral Approaches to HIV Prevention

Early in the epidemic following identification of HIV as a sexually and parenterally transmitted disease, few prevention methods were available. Sexual transmission of HIV could be prevented largely through abstinence, fidelity, and condom use; and transmission via IDU primarily through changing addiction behaviors. In response to these challenges, behavioral interventions were developed, studied, and tested in order to characterize methods that effectively reduce risk behavior [53, 67–70]. Among other achievements, the CDC's Diffusion Effective Behavioral Interventions (DEBI) project allowed systematic development and review processes for evidence-based selection of behavioral approaches to HIV prevention [70]. The primary goal of behavioral approaches has historically been to reduce HIV-related risk behavior, and promoting harm reduction rather than elimination has become a core tenet of behavioral interventions [68, 71, 72]. Newer interventions have expanded beyond counseling to embrace testing, know-your-status campaigns, and outreach to sexual partners through peer-to-peer programs as well as mobile health application interventions [53, 55, 68, 69, 73, 74, 75••, 76].

There are many strengths to behavioral prevention methods. Behavioral strategies that focus on individual-level behaviors in order to reduce risk of acquiring HIV are in many ways the mainstay of HIV prevention activities and, as described below, integrate into combination prevention approaches and the prevention continuum. Less expensive and without side effects that often attend biomedical approaches, harm reduction can be highly effective to reduce risk of HIV acquisition or transmission.

Challenges with behavioral approaches to HIV prevention remain [53, 54, 69, 72, 77–79]. Durability of behavioral interventions is hard to measure. Such methodological concerns mean that even in the presence of studies that characterize the impact of behavioral interventions, true estimates of effect may be elusive. Further, ongoing behavioral change is difficult for most populations. Among high-risk populations, even one unprotected sexual exposure may result in a high probability of HIV transmission due to the relative prevalence of HIV in the sexual networks [80–82]. Given that risk for HIV may for some subpopulations be a continuous risk, maintenance of solely behavioral harm reduction behaviors for a lifetime can be difficult. Effective behavioral counseling, one-on-one, group-level, and marketing campaigns have been shown to have relatively low population uptake [53, 69]. So while behavioral strategies may present lower risks than biomedical ones on the surface, overall resources and resulting impact need to be incorporated into decision-making about adoption. Taking into account these challenges, biomedical interventions alone and in combination with behavioral interventions represent a promising avenue for HIV prevention.

Biomedical Approaches to HIV Prevention

In view of the challenges outlined above and the urgent need to slow the spread of HIV, attention has turned to biomedical HIV prevention approaches. Studies on biomedical modalities to interrupt mother-to-child HIV transmission by providing antiretroviral therapy to pregnant and laboring women, and their newborns had significant impact on the epidemic's course [56, 83–86]. In high-income countries, perinatal transmission has been nearly stopped; for example, the USA went from a peak of 900 perinatally acquired cases in 1992 to a historical low of 53 cases in 2011 [83, 87, 88]. Cases that do occur generally do so because of lack of antenatal diagnosis or care rather than failure of the interventions [83]. This remarkable success is mirrored in low- and middle-income countries as a result of collaborative global efforts including PEPFAR which have successfully supported scale of up antiretroviral treatment for pregnant women and their children. The concept of an *AIDS Free Generation* is now within reach [51, 52•, 89].

The concept that antiretroviral treatment can be used in preventive fashion has guided development of biomedical prevention approaches for both HIV-uninfected individuals and to HIV-infected persons to reduce risk of secondary transmission. Post-exposure prophylaxis (PEP) was first developed in response to occupational exposures to HIV, whereby antiretroviral treatment was provided to persons following HIV exposure via needlestick, surgical, or laboratory injury [59, 63]. Now, also used following high-risk sexual exposures (both consensual and non-consensual), non-occupational PEP (also known as nPEP) is a regular offering to those who may have been exposed to HIV [65]. These post-exposure biomedical treatments leverage the concept that use of antiretroviral treatment prevents HIV acquisition.

Similarly, pre-exposure prophylaxis (PrEP) offers additional promise for HIV prevention. Grant et al. demonstrated a 44 % reduction of HIV acquisition attributable to PrEP with emtricitibine-tenofovir disproxil fumurate (TDF/FTC) among men who have sex with men (MSM) and transgender women [10••], with significantly elevated efficacy among persons with detectable blood levels. PrEP using TDF/FTC was approved by the FDA in 2012 [90] and adopted by CDC with recommendations for prevention for populations at elevated risk of HIV in 2014 [62]. The efficacy of TDF/FTC when used as PrEP has also been demonstrated among heterosexuals in Botswana and among IDUs in Thailand [57, 91, 92]. In the last 2 years, new studies have evaluated uptake of PrEP focusing in particular on BMSM who are, as discussed above, the most highly affected subpopulation in the USA (www.hptn.org/).

Perhaps the most critical addition to the prevention armamentarium was the recognition in the landmark HPTN 052 study published in 2011 that effective viral suppression among HIV-infected persons can significantly reduce the risk of transmission to their sexual partners by 96 % [11••]. This study, along with observational data demonstrating population-based declines in HIV rates with increasing antiretroviral coverage [4, 41, 43••, 80, 93], has fueled the incorporation of "treatment as prevention" (TasP) as a cornerstone approach of HIV prevention programs.

The future holds still further promise for biomedical interventions. Long-acting injectable antiretroviral regimens (that could be used both for PrEP and TasP) are currently in clinical trials following considerable primate data that support their potential for efficacy [94•]. Microbicides in the form of gels (vaginal and rectal) and vaginal rings are in clinical trials currently. Future biomedical directions necessarily will include combination prevention, where behavioral, biomedical and structural interventions are integrated to provide HIV prevention approaches that suit a given person or population at a specific point in time [52•, 54].

Research on the most effective prevention strategies and on their durability will be key towards enhancing the potential of biomedical approaches. Biomedical HIV prevention strategies are hardly challenge-free; ultimately, nearly all HIV prevention success depends on behavior, whether that behavior is getting an HIV test, using a condom, taking a daily pill, or (potentially in the future) a semi-annual injection [95]. Research into determining the level of personal risk that necessitates PrEP for example is an ongoing need as is how to support adherence and how to address life course risk changes and treatment fatigue that inevitably occur. Questions surrounding cost and access to HIV testing and safety monitoring required for PrEP treatment, along with healthcare

infrastructure to support such services, remain unanswered questions in the larger rollout of this lifesaving prevention mediation.

Structural and Population-Level Approaches to HIV Prevention

Several of the aforementioned barriers to provision and uptake of behavioral and biomedical prevention interventions may ultimately only be addressed through population-level and structural approaches. Reducing stigma, training and cultural competency awareness building for healthcare providers, improved access to prevention services, improved diagnosis and treatment of sexually transmitted infections, reduced cost for services, and related counseling and monitoring are likely key components in changing the settings that offer HIV prevention services so that they are more likely to be used [38, 39, 77, 78, 96, 97]. In view of the racial, sexual, and gender disparities that exist with HIV [37, 64], reduction of healthcare disparities must be prioritized.

Routine testing in emergency departments exemplifies the strength of the structural intervention with their broad reach to those who do not chose to disclose a specific risk behavior [75••, 98]. Syringe exchange programs and supervised injection facilities decrease the spread of HIV (and Hepatitis C virus) among IDU [68, 70, 99]. There is substantial evidence that TasP is effective, and as a result, TasP has been integrated into World Health Organization guidelines [80, 100]. Structural interventions are not without challenges as they require time and considerable resources to implement. Ultimately, modifications to existing structures may be the foundation on which the prevention continuum will work in concert with behavioral and biomedical strategies.

Future Research Directions

HIV prevention research is the cornerstone on which progress in combatting the epidemic relies. Studies are critically needed to address how to best utilize combination prevention approaches for all populations, including those populations frequently excluded from research such as young BMSM [37, 39, 79, 97]. Engagement in care remains a substantial challenge; reaching persons at risk for HIV so that they may be tested and receive prevention service utilization is a further challenge. Our methods must evolve to effectively engage all populations at risk for HIV into prevention research as well as more effectively examining barriers to prevention services. Only with innovative methods that are culturally appropriate will we be able to effectively use the remarkable prevention armamentarium that has been developed.

Conclusions

Recent policy, epidemiologic and prevention advances have served to greatly inform and guide the response to the HIV epidemic in the USA and beyond. Working together, public health personnel, clinical providers and impacted communities can capitalize on these developments, thereby contributing to continued national and global reductions of HIV incidence, morbidity, and mortality.

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Compliance with Ethics Guidelines

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Human and Animal Rights and Informed Consent All studies by M Magnus and AE Greenberg involving animal and/or human subjects were performed after approval by the appropriate institutional review boards. When required, written informed consent was obtained from all participants.

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