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Care continuum entry interventions: Seek and test strategies to engage persons most impacted by HIV within the United States

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Abstract

The current review re-conceptualizes seek and test strategies, particularly given the changing importance of HIV testing as care continuum entry for persons irrespective of their HIV status. Care continuum entry advances previous seek and test strategies for client engagement with two next-generation functions: 1) use of testing to engage (or re-engage) HIV negative clients in pre-exposure prophylaxis (PrEP) care; and 2) testing individuals who may already be known positives for care continuum re-entry. We review existing seek and test strategies for most impacted community members with a goal of optimizing care continuum entry as we move towards HIV transmission elimination. These strategies are context, sub-group, community and epidemic specific. This review is timely given the initiation of routine PrEP care, which shifts and broadens our conceptualization of care continuum entry triggered by the HIV testing event. In addition, as the epidemic becomes more concentrated, focusing on re-engagement of HIV infected persons becomes increasingly important given that transmission events involve both those acutely and newly infected as well as the large numbers who may not be virally suppressed. We start with examination of routine testing in healthcare settings, emphasizing its potential role in re-engagement for persons out of care. Subsequently, we describe risk-based testing to identify key populations. We then review network-based approaches and their impact on the epidemic. We close with future directions of individual and combination care continuum entry strategies most relevant for elimination of HIV transmission in the United States.

Keywords

HIV; key populations; seek and test strategies; HIV care continuum; implementation science; social network

Introduction

HIV remains a significant public health concern in the United States and internationally. Elimination of new sexual and injection transmission events requires optimization of

effective intervention strategies, including finding marginalized populations most likely to acquire and transmit HIV and providing access to care and treatment. HIV currently has no cure; yet we do have effective antiretrovirals (ARV) that when used appropriately dramatically limit acquisition and transmission and also have the benefit of creating a manageable chronic disease [1, 2]. Transmission risk is thus directly related to engagement in care continuums. In turn, HIV prevention efforts require that persons living with HIV (PLWH) are not only identified via testing, but also have access to quality healthcare and ARV, and achieve and maintain viral suppression.

HIV prevention has rapidly evolved over the past 7 years with development of high-impact interventions such as treatment as prevention (TasP), or treating PLWH with ARV in order to decrease transmission events to uninfected partners [2]; HIV pre-exposure prophylaxis (PrEP) [1]; and test and treat strategies for rapid initiation of ARV to quickly lower viral load in acute and new HIV infections [3, 4]. Early identification and treatment clearly results in decreased mortality and ongoing transmission [2, 5]. While HIV incidence has declined in the general U.S. population, it has remained stable and even increased in certain vulnerable populations [6]; furthermore, a significant proportion of PLWH are unaware of their status, and even more are aware but not in care or virally suppressed [7]. The National HIV/AIDS Strategy (NHAS) goals of increasing linkage to care within one month of HIV diagnosis to 85%, increasing retention in care to 90%, and attaining 80% viral suppression still remain to be realized [8].

Social determinants of health are recognized for the crucial role they play in HIV prevention – stable housing, education, access to water and food, and criminal justice involvement all impact viral suppression and ongoing ARV-based prevention. Racial/ethnic inequity exists, exhibited by the burden of the epidemic, and in particular subpar healthcare access in certain US populations [9–12]. Furthermore, economic and social hardships influence HIV risk and highlight the role of structural factors in HIV prevention [13]. All of these contribute to the stigma that continues to persist 35 years into the epidemic that limits testing and engagement in care, as well as the extent to which HIV has become a priority on a national level [8, 14–16]. Despite these barriers, a mandate to halt HIV transmission remains.

“Seek, test, treat, and retain” describes a model of care introduced by the National Institutes on Drug Abuse (NIDA) in 2010, referring to approaches to reach at-risk groups for HIV testing that have not been diagnosed or recently tested for HIV, counsel and engage them in HIV testing, link those who test positive to medical care, treat with ARV, and retain in care [17–19]. While the model in its entirety is important for prevention and transmission, in this review we focus on seek and test aspects to engage and re-engage at-risk persons as *care continuum entry* strategies. Initially developed for drug misuse, this model has been expanded to apply to other vulnerable populations [20]; in this paper we re-conceptualize seek and test not only as the traditional approach to identification of newly infected persons, but importantly as a purposeful strategy to engage existing HIV infected persons who may not be retained as well as persons at risk for HIV acquisition.

Eliminating HIV transmission in well-resourced countries such as the United States will require that marginalized populations be more readily engaged. Accessible and widespread

HIV testing is one component of HIV transmission elimination strategies and serves as the entry into the care continuum [21]. Interventions targeted towards this entry point are discussed here. Advancing HIV testing technology has assisted HIV prevention strategies in many cases and we acknowledge these technologies' contributions; however in-depth discussion of these approaches is beyond our scope and has been reviewed elsewhere [22, 23]. Similarly, sampling methods in marginalized populations has also been described and will only be discussed here when relevant to seek and test strategies [24]. Many of these seek and test strategies have been applied to the HIV epidemic worldwide yet we choose to focus on concentrated epidemics and in particular the United States where many of the approaches were first described and developed.

Towards integrated care continuums

Engagement in HIV care is now recognized as a continuum, with points resembling a cascade including HIV diagnosis, linkage to care, initiation of ARV, retention in care, and viral suppression [7, 25–27]. Through simulations, Gardner et al. determined that significant improvement in engagement along the entire continuum of care is necessary to curb the HIV epidemic, finding that achievement of 90% engagement in care, treatment of 90% of engaged individuals, and 90% viral suppression would result in improvement in viral suppression and subsequent transmission [27]. The HIV care continuum provides a motivating visual for how care delivery needs to improve to achieve these goals and is widely used by public health departments in describing the state of the HIV epidemic on worldwide, national, and local levels [7].

PrEP offers an opportunity for primary prevention of HIV and subsequently there has been a paradigm shift in that both HIV positive and HIV at-risk individuals can be incorporated into the care continuum [28]. Several care continuums for HIV negative persons exist [29–31]. For example, Horn et al. present a comprehensive, integrated care continuum to illustrate both primary HIV prevention for negative individuals through HIV testing, identification of risk behaviors and needs assessment, counseling for risk reduction, linkage to care, retention and adherence, and re-testing at-risk individuals [28]. For both HIV positive and negative but at-risk individuals, the HIV testing event is a crucial entry into the healthcare system and serves as an important point in time where individuals can be evaluated for appropriate engagement interventions, which has the potential to impact downstream care continuum engagement. Care continuum entry interventions encompass a range of healthcare-based testing (HbT), community-based testing (CbT), and network interventions to engage and re-engage persons in care (Figure 1). These interventions overlap in their efforts to reach key populations. We will review HIV testing interventions as strategies to engage and re-engage in care continuums.

Care continuum entry interventions

Healthcare-based testing

With the development of the first HIV test in 1985, screening within healthcare settings was applied to blood donations [32]. This program was extremely successful in decreasing HIV infections transmitted via blood transfusion, virtually eliminating hemophiliacs as a group at

risk of HIV infection and transmission in the US, and continues today in the form of donor screening and blood testing [33, 34]. More widespread HbT was not recommended until further knowledge about methods of transmission and risk factors was elucidated. In 1987 the Centers for Disease Control and Prevention (CDC) recommended that all individuals considered to be at high risk based on behavior or seeking treatment for STIs be tested for HIV, and over the years that followed broadened this recommendation in a step-wise approach to also include acute-care hospital settings in high prevalence areas (>1%), and then pregnant women for the prevention of perinatal transmission [32, 35, 36]. During this process, the CDC expanded its recommendation to make HIV testing a routine part of medical care, similar to other screening tests [32]. With advancement in the treatment of HIV, in 2006 the CDC endorsed conducting universal opt-out HIV screening during routine medical care in all healthcare settings for persons aged 13–64 years and all pregnant women on the basis that there is a clear benefit in morbidity, mortality, and transmission that is obtained by identifying early infections and initiating ARV [32]. Repeat screening was recommended for at-risk persons (people who inject drugs (PWID), persons who exchange sex for money or other goods, sex partners of HIV-infected individuals, men who have sex with men (MSM), and heterosexuals with multiple sexual partners) [32]. The USPSTF followed in 2012, aligning with CDC and NHAS goals [8, 32, 37, 38].

Universal opt-out screening has been very effective in nearly eliminating perinatal transmission risk but uptake has been inconsistent across other settings due to societal, legal, organizational and individual-level barriers [21, 39]. Mandated separate written consent and pre-test counseling requirements made it difficult to perform screening in busy clinical environments, therefore many laws have been successfully amended in recent years to promote acceptance through less burdensome procedures [40–42]. Continuing stigma associated with HIV contributes to suboptimal uptake of routine HbT [16, 43]. Providers' concern for follow up on abnormal tests further inhibits the willingness to offer screening, particularly in settings such as the emergency department (ED) where they are more likely to encounter patients who do not otherwise access the healthcare system [39, 44–46]. Establishing institutional policies that support providers in these areas have been successful in overcoming these barriers, including personnel trained in notification and linkage procedures [47–50].

Best practices for implementation of universal opt-out screening processes in healthcare settings are still being explored, but the ability to leverage existing infrastructure and staff for HIV testing is propelled by the national move towards electronic health records (EHR) [51]. Bioinformatics tools using predictive analytics to incorporate EHR-based algorithms into workflow have enhanced testing rates and improved acceptability of universal screening programs [52, 53]. Algorithms that use sociodemographic characteristics and risk behaviors can be implemented to determine who needs more frequent testing and can help identify at-risk individuals who may qualify for further HIV prevention interventions, including PrEP [54–56].

PLWH who are aware of their HIV infection but not retained in care are now understood to contribute to a significant number of new transmission events, and efforts for re-engagement can begin with the testing event [57]. Universal screening programs implemented in places

such as the ED have found that up to 50% of positive HIV tests occur in those already aware of their diagnosis, many of whom are out of care [47]. This group has been difficult to link back to care and novel strategies are being identified to address this problem such as the CDC's Data to Care program funded through local health departments, as well as using surveillance data to identify and reach these individuals [58–60]. Shifting guidance around the CD4 level appropriate for treatment initiation can send mixed messages to clients not in care who are then re-tested; however, this offers an opportunity for discussions around treatment initiation or re-initiation.

Outreach

HIV testing in non-healthcare, or community-based, settings has become essential for identifying individuals within key populations who do not have frequent contact with the healthcare system [61, 62]. These groups who do not utilize mainstream services, yet are still at risk, are often considered “hidden” populations and are typically at increased risk of health inequity based on identity or socioeconomic status: sexual minorities including gay, bisexual and other MSM; racial minorities, particularly African Americans; gender minorities such as transgender individuals; recently incarcerated individuals; PWID; sex workers; and the unstably housed [63–65]. Frequently the most at-risk groups are dual or even triple minorities (e.g. gender, racial and/or sexual minority); at current rates, 1:2 black MSM will be diagnosed with HIV in their lifetime, the highest of any group [66, 67]. Localization of the epidemic within these vulnerable groups has given rise to tailored CbT strategies, which in addition to case-finding can deliver behavioral interventions to key populations [68–70].

Venue-based interventions have been particularly effective for MSM and PWID, who often display homophily in their choice of sexual and drug-sharing partners, allowing for seek and test efforts to be focused at certain sites such as specific bars and street corners where groups or individuals with risk behaviors are known to congregate [71]. Fujimoto et al. has used social and sexual network dynamics to delineate the relationship between HIV-susceptible individuals and venues; findings indicate centralized venues that have clustering of individuals by sexual behavior and HIV status, with overlap in individuals frequenting these sites [72]. This provides important opportunities for focused interventions and also avoiding duplication of efforts [72]. Furthermore, online venues such as mobile geo-social networking apps (Jack'd, Grindr, Scruff) have become popular for MSM seeking sexual partners [73]. These apps may provide a conduit for locating venues for care continuum entry interventions and distributing information on HIV prevention methods [74].

Additional CbT and outreach efforts have focused on a number of sites seeking susceptible populations such as the unstably housed, youth, the incarcerated, and PWID. Mobile testing has been employed to reach individuals in a wide range of high-risk settings, providing flexibility in testing sites and populations targeted [61]. HIV testing in jails and prisons is high yield for new diagnoses and frequently offers an opportunity for re-engagement [75, 76]. While universal screening in jails and prisons would be ideal, it is not always feasible; thus studies evaluating the relationship between arrest charge and HIV risk are promising to efficiently target testing [77]. Care continuum entry interventions targeting PWID,

specifically HIV testing in needle exchange programs and opioid treatment programs, have been crucial to early identification of HIV [78].

Home-based testing has been explored through several different approaches. The first includes door-to-door CbT focusing on micro-epidemics within high prevalence neighborhoods [79]. Home-based self-testing has proven to be acceptable to groups of vulnerable individuals and can provide additional privacy, but has additional challenges to face in engagement in the care continuum after the testing event [80]. In addition, online interventions can tap into widespread groups of people who may be at risk for HIV but not otherwise be identified through other methods, particularly youth who frequently have a strong online presence [81, 82]. The expansion of home-based self-testing and online interventions may remove some barriers such as privacy and healthcare access, but must also be affordable and coupled with a plan for timely care continuum entry and engagement.

These targeted outreach strategies depend on fostering public health partnerships for surveillance and the flexibility to expand services to areas and populations as surveillance information evolves. Tools such as AIDSVu can help direct efforts to specific geographic areas, providing key information on where to deploy mobile units and which communities need allocation of resources. Using the geographic surveillance data to expand HIV testing services, including offering routine testing in non-traditional healthcare settings such as pharmacies and retail clinics in high-prevalence areas is a promising method of expanding access [83]. In addition, real-time surveillance allows for rapid response to emerging epidemics, such as that within PWID in southern Indiana, which prompted statewide mobilization of resources to curb ongoing transmission through a multi-pronged approach [84]. More granular information on community viral load may also further inform seek and test strategies, as well as innovative approaches such as network viral load [85, 86].

Non-targeted outreach programs include general educational efforts as well as public service and media campaigns. In the US, HIV prevention education provided in schools has potential to make an impact, but has been limited by political policies and quality of sexual education [87]. Public service and media campaigns focused on reaching the general public include CDC's Act Against AIDS Campaign and Chicago's PrEP4Love. These campaigns have the benefit of reaching a wide audience and can be effective if done in a culturally sensitive manner with a clear, sustained message [88, 89]. They also act to increase awareness among the general population of the ongoing public health implications of HIV. Although media campaigns appear to be less successful in developed countries as compared to developing countries, there is still a role for their use in key populations and specific geographic areas in need of health communication around HIV [89].

Network-based Approaches

The use of contact tracing for venereal disease control has been widespread since 1936, when the Public Health Service first recommended that sex contacts of those infected with syphilis be found, notified, and interviewed for their own protection [90]. Since that time, contact tracing has become the standard of care and primary method of control efforts employed by local Public Health Departments for syphilis and HIV across the United States [91, 92]. Contact tracing has been utilized effectively to eradicate other infectious diseases

such as smallpox and is a key strategic element in ongoing polio eradication efforts. Typically, the process of contact tracing in the context of HIV involves Disease Interventionist Specialists querying newly infected clients about their sex or drug contacts and then locating those contacts in the field to inform them that they have been exposed. Models suggest that this approach could be effective in reducing transmission and it may be cost-effective compared to other Public Health Department control efforts [93–96]. For these reasons the approach has been adopted in several other international settings [97, 98].

In the standard-of-care network tracing strategy that has not changed much since 1937, staff interview infected people (called index cases) to elicit names of their sexual or needle-sharing partners (risk partners); notify risk partners of potential risk of infection; and provide prevention services, including HIV testing and linkage/referrals to medical care for partners who have been notified [90]. Partner notification (PN) is an efficacious method of diagnosing HIV-positive individuals, especially when facilitated by a health provider or trained professional [92, 99–104]; in a systematic review of nine studies, 8% of all sex partners listed by index clients were successfully diagnosed with HIV through PN [102]. Another systematic review demonstrated that one new HIV diagnosis was made for every 8–10 partners interviewed through PN [101]. PN reduces HIV burden through diagnosis and subsequent decreases in risky behavior [105–111], HIV/STI transmission [2, 109, 112–114], and improved health outcomes through earlier linkage to treatment [2, 113, 115–118]. The CDC therefore recommends that PN and comprehensive partner services be offered to all recently HIV-diagnosed individuals [92].

Other strategies include network services, referred to as the Social Network Strategy (SNS) by the CDC, where staff conduct similar activities to partner services but elicit names of HIV infected people's *social* network rather than limiting it to recent risk partners [119]. Variations on how long the chains are continued from an index client such as 2-steps from an infected client or even 3-step partners services (or network services) where partner engagement occurs 3-steps from an infected client until terminal chains are 3-steps away [120]. Strategies beyond three steps include network mobilization approaches such as snowball or respondent driven sampling and are considered network interventions [121]. We do not include these larger network engagement strategies as they are less targeted and are analytically difficult in observational studies due to contamination and cross-over across clusters as more individuals are engaged.

Policies criminalizing transmission of HIV make contact tracing and partner services for HIV testing and prevention difficult to implement effectively; these laws remain in place in many states [42]. This stigmatizes HIV and prevents effective infection control measures. IDSA and HIVMA have released a statement against policies that criminalize HIV [122]. While it is promising that ongoing de-stigmatization efforts may create safe spaces to discuss sex partners; social network strategies are increasingly utilized given less stigma and may provide benefit in yielding clients infected and at risk for HIV infection. As we enter final HIV elimination efforts, the social network strategy may need to revert back to sexual network care continuum entry approaches.

Molecular care continuum entry approaches

Molecular HIV surveillance is increasingly recognized as a promising approach to both improve care continuum entry and target limited public health resources. Sexually transmitted infections diffuse through contact networks, and the number of onward transmissions varies widely [123, 124]. With limited public health resources, it is important to target care continuum entry efforts towards those most likely to transmit and their sexual partners. Simulations also demonstrate that targeting HIV-seropositive individuals already highly connected in molecular clusters disproportionately decreases onward transmissions [125]. In a recent first effort at intervening in phylogenetically derived networks, members of a rapidly expanding drug resistant HIV cluster in Canada were targeted with enhanced public health follow up to ensure linkage to care - and transmission of drug resistant HIV from this cluster was reduced [126]. In the United States in 2017, 27 jurisdictions participate in molecular HIV surveillance (MHS), an integrated component of CDC's National HIV Surveillance System to which commercial laboratories report HIV *pol* nucleotide sequences from clinical drug resistance screening [127]. The HIV-1 *pol* region has limited length variation (insertions or deletions); this permits robust pairwise alignment, which in turn allows molecular cluster determination from aligned sequences, as well as drug resistance surveillance.

Secure HIV TRACE was launched in March 2017 by Joel Wertheim and others as a feasible approach to guide local health department HIV care continuum entry efforts. HIV-TRACE creates molecular clusters of HIV sequences by calculating all pairwise genetic distances between aligned sequences [128, 129]. Genetic distance is a proxy for epidemiological relatedness, because it increases as a function of time since transmission (recipient's virus diverging from source's virus, with each changing). The molecular clock underlying this sequence divergence between source-recipient pairs of HIVs, however, is highly imprecise due to immune/drug selection pressure, viral latency, and other factors. Furthermore, the virus can evolve at different rates in the donor and recipient, so the genetic distance between source and recipient strains is not simply translatable to a standardized time since they diverged. Clusters include sequences that diverge less than a pre-specified threshold (usually 0.5-2%). This threshold is chosen because it is an average estimate of within patient evolution [130], segregates well between the two distributions of distances seen in large sets of sequences [127], and agrees with the genetic distance seen between named HIV risk partners [131]. Clustered sequences can help target intervention based on concern for their size, associated epidemiological or clinical features, or growth.

Next generation care continuum entry strategies

Next generation care continuum entry strategies should include combination approaches that leverage strengths of each testing method to maximize case finding and engagement. Routine healthcare-based testing should trigger social and sexual network testing, particularly in individuals from vulnerable groups such as MSM or PWID. Linking care continuum entry interventions may be difficult to implement in practice, but has the potential to widen the scope of those receiving highly effective social and sexual network testing that identify vulnerable persons, as well as additional wraparound services available in clinical settings.

A second approach to combination care continuum entry includes combining multiple network approaches to best identify individuals who are transmitting as well those who are most at risk for HIV infection. A combined network approach includes social, sexual (both online and offline) and molecular. Such an approach ensures that individuals at greatest risk of acquisition and those who are least likely to be engaged in care or with acute/recent infection (both with high viremia) are getting engaged in HIV care continuum. Inclusion of the online and offline social and sexual networks allow public health practitioners to move beyond a network of positive individuals that is generated from molecular network, but also to include important ties of HIV negative individuals connected to clusters or other HIV infected persons. An example of such an approach (Figure 2), was developed from a population-based cohort of young Black MSM in Chicago from 2013–2016 [132, 133].

What can be seen from this network visualization is that there is limited overlap between social and molecular networks and that various network typologies fill in ties and clusters of individuals ideal for care continuum-entry. While Facebook has the most numbers of ties in this network; other online (i.e. Jack'd) and offline (i.e. gay family) networks could fill in important ties that would further risk stratify individuals most in need of care continuum entry.

Targeting interventions for an evolving epidemic

Comprehensive national policies and procedures that integrate healthcare-based HIV testing into routine care and establish performance metrics for health systems around HIV screening will help continue to decrease numbers of PLWH who are unaware of their infection currently, but will have less of an impact as the epidemic becomes increasingly concentrated. Routine HbT has not supplanted the need for ongoing targeted and non-targeted outreach. Sub-populations affected by the HIV epidemic that do not regularly access healthcare may be better served by CbT and outreach, the social network strategy, or partner services, which identify some of the most susceptible individuals. Studies have reported testing strategies' ability to detect new HIV diagnoses in populations that may be harder to reach due to infrequent or unequal access to healthcare and suggest that these populations may benefit from employing a combination of strategies [134–137]. To be successful in eliminating HIV, systems will need to pivot towards using a combination of evidence-based approaches to reach vulnerable individuals both within and outside of the healthcare system, and closely integrate these approaches for biomedical prevention and care. More research is needed to understand how testing strategy can best be matched to epidemic phase.

Here we focus on strategies to identify and test key populations for HIV in an effort to engage these populations in continuums of care, keeping in mind the dynamic nature of the entire continuum as a cyclical process [28]. Together, those who are HIV infected but undiagnosed and those who are diagnosed but not retained in care account for a significant proportion of new transmission events [57]. Improving care at each point in the continuum, particularly increasing the use of ARVs for prevention, the proportion of PLWH who are virally suppressed, and engagement in biomedical prevention, is the key to HIV elimination. As we develop and hone these strategies for care continuum entry, in turn decreasing the number of PLWH who are unaware of their infection, we must do the same for each step in

the continuum. Care continuum entry is only effective in stemming the HIV epidemic if it ultimately leads to decreasing transmission of HIV.

As we move to HIV elimination in the United States, cost-efficient strategies that combine, modify or enhance existing care continuum entry strategies are critical to engage the most vulnerable populations, in which the epidemic is concentrating. The number of new HIV diagnoses in the US is still high and while decreasing overall, it is rising in some groups such as young Black MSM. Real time surveillance by the public health department is promising and incorporating phylogenetic information about transmission patterns may lead to the ability to quickly adapt services and create an early warning system to mobilize resources to areas of the community with high viral loads and active transmission networks. Developing models utilizing this real-time information about where new clusters of diagnoses are occurring and then mobilizing the system to allocate available resources such as mobile testing, partner services, condom distribution, and education may get us closer to identifying the newest cases, and most importantly, those connected to them in order for early intervention. Providing these resource-intensive services will be limited by the stage of the epidemic and only feasible if numbers of new transmissions continue to decline.

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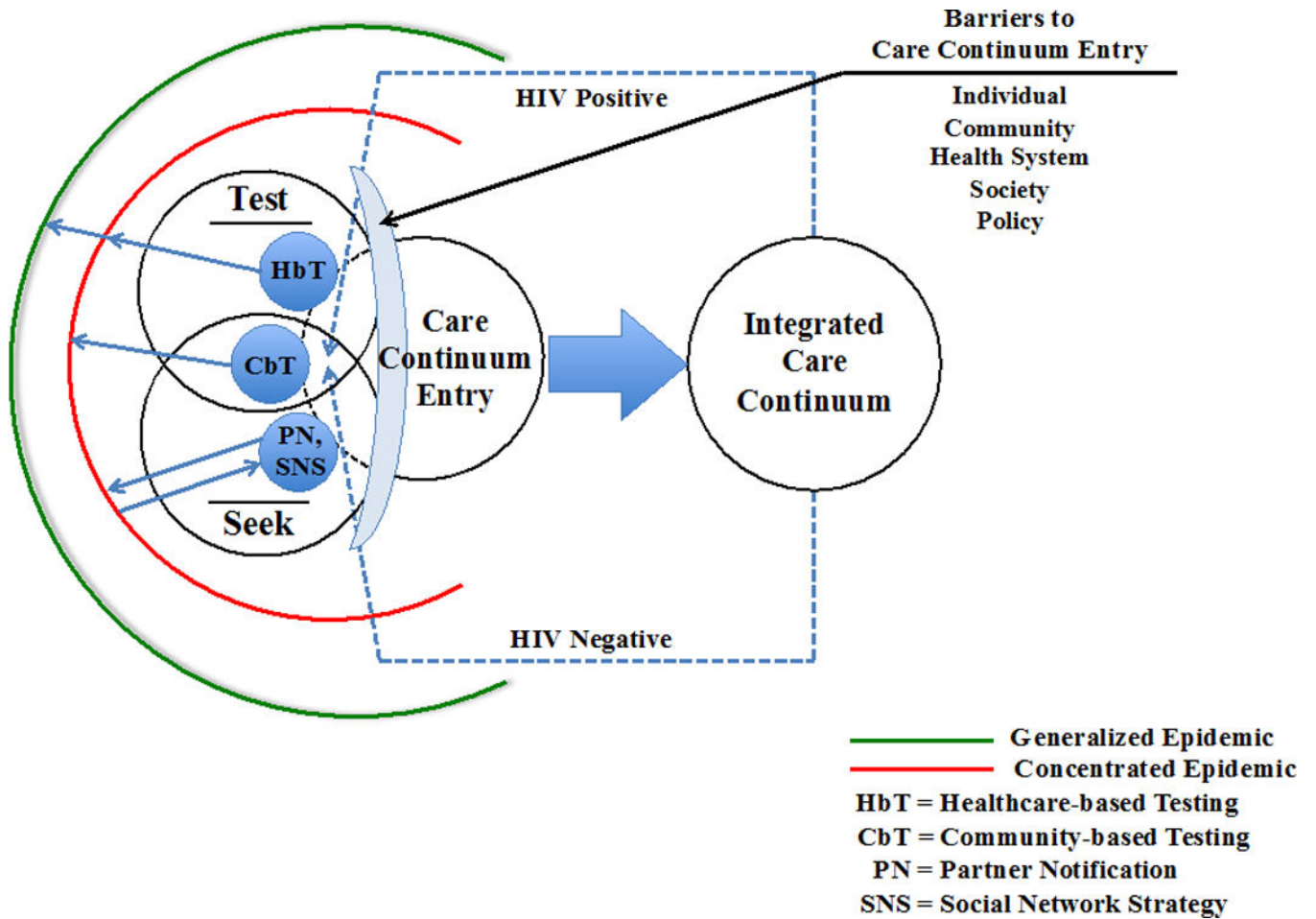


Figure 1. Conceptual model of care continuum entry strategies in the context of epidemic phase. The model depicts the intersection between seek and test strategies and care continuum entry. Seek and test strategies include healthcare-based testing (HbT), community-based testing (CbT), and network approaches of partner notification (PN) and social network strategy (SNS). Strategies are related to epidemic phase, as depicted by the blue arrows [138]. HIV testing is an entry point into the integrated care continuum for both HIV positive and at-risk individuals, who, if not retained, will require re-engagement via care continuum entry interventions [28]. The lens depicts barriers to care continuum entry, which occur on multiple levels: individual, community, health system, society, and policy [26].

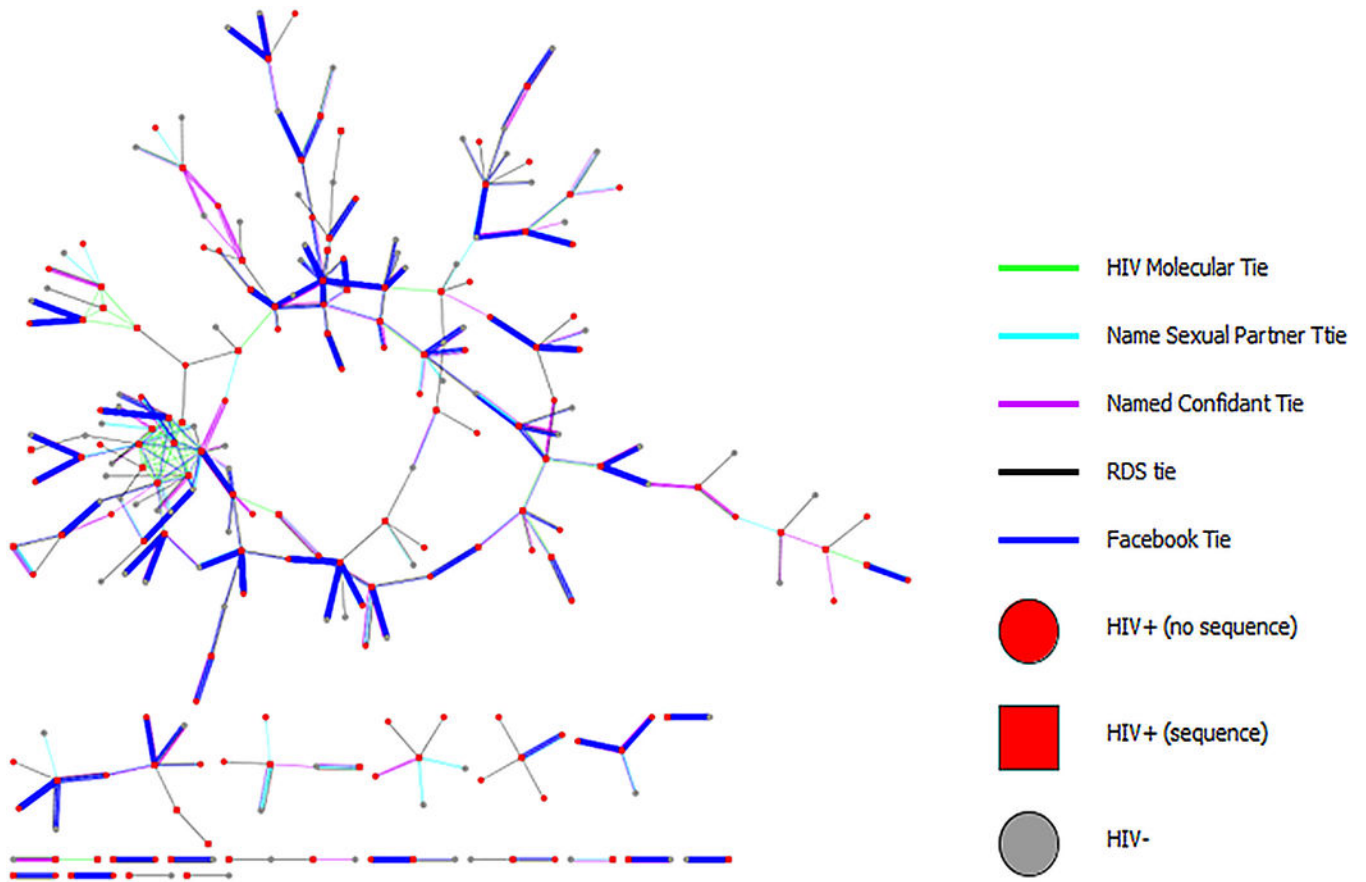


Figure 2. Combined social, sexual, digital and molecular networks among a population-based cohort of young Black MSM (n=618), Chicago IL 2013-2016. Visualization created by Ethan Morgan, PhD.