



Composite Risk for HIV: A New Approach Towards Integrating Biomedical and Behavioral Strategies in Couples-Based HIV Prevention Research

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Abstract

A substantial number of new HIV infections among gay, bisexual, and other men who have sex with men and transgender women occurs in the context of primary partnerships. Given the diversity of risk reduction needs and various approaches available for reducing risk within couples, condomless sex is no longer the gold standard HIV outcome. We present a novel, comprehensive, and flexible Composite Risk for HIV (CR-HIV) approach for integrating evolving biomedical and behavioral HIV prevention strategies into couples-based HIV prevention intervention and survey research. We provide illustrative examples of the utility of the CR-HIV approach based on couples' HIV status.

Keywords Couples · HIV prevention · Men who have sex with men · Transgender women

Introduction

Gay, bisexual and other men who have sex with men (GBMSM) and transgender women (i.e., individuals with a feminine and/or female gender identity who were assigned male sex at birth) are disproportionately affected by HIV in the United States [1]. Among GBMSM, between one-third and two-thirds of new HIV infections occur in the context of primary partnerships [2, 3]. Similarly, evidence suggests that HIV transmission risk among transgender women is

particularly high in the context of primary partnerships with cisgender or non-transgender male partners [4–9]. As a result, there have been a number of HIV prevention research efforts designed to study and intervene on HIV risk within GBMSM and transgender women's dyadic partnerships [10–15].

At the same time, there have been significant biomedical advances in combating HIV in the recent years. A once-daily pill has been approved by the US Food and Drug Administration (FDA) to be used as a pre-exposure prophylaxis (PrEP) for HIV. This drug regimen lowers the risk of HIV infection by over 98% when taken consistently. The strategy of treatment as prevention (TasP) involves preventing new infections by treating existing infections through early initiation of antiretroviral therapy (ART) and maintaining viral load suppression [16, 17]. Both PrEP and TasP have been shown to be highly effective in preventing HIV transmissions [18]. However, the majority of published couples-based HIV prevention interventions with GBMSM and transgender women pre-dated biomedical prevention strategies and/or focused on a single biomedical or behavioral prevention strategy [12, 14, 15, 19]. Furthermore, "HIV risk" has been most often defined as whether or not an individual engaged in condomless sex with a serodiscordant or unknown status partner within some predetermined timeframe without considering whether they or their sexual partner is using any biomedical

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strategy and is adherent to it. In these instances, the individual may be misclassified as engaging in risk behavior. Thus, there is an urgent need to develop methods that allow for integrating evolving biomedical and behavioral strategies into couples-based HIV prevention research.

Presently, the prevention of new HIV transmissions is the most promising strategy for curtailing the HIV epidemic [18, 20]. Given the diversity of an individual’s risk-reduction needs based on their HIV serostatus and relationship contexts [21], there is no longer one gold standard HIV prevention strategy (e.g., consistent condom use or ART adherence). Thus, the HIV prevention landscape is swiftly shifting towards attending to the complexity of evolving biomedical prevention strategies in combination with behavioral outcomes. For couples-based HIV-prevention, this would imply that any singular strategy may not be appropriate or desired for GBMSM and transgender women and their primary partners. Most importantly, HIV prevention strategies are no longer static due to the continuous advances in biomedical modalities, such as long-acting injectable (LAI) ART [22–24]. At the same time, the advancement of behavioral theories and the necessity of attending to the relationship, social, and structural contexts of individuals’ lives presents an additional layer for consideration in preventing new HIV infections [25, 26]. Although there have been great strides towards achieving the UNAIDS 90–90–90 targets [27], there are notable inequities in HIV testing, uptake of PrEP, engagement in care, ART and PrEP adherence, and achieving sustained viral suppression [28–32] and we have yet to achieve these goals with GBMSM and transgender women in virtually every locale in the U.S. [33–36]. Thus, there is an

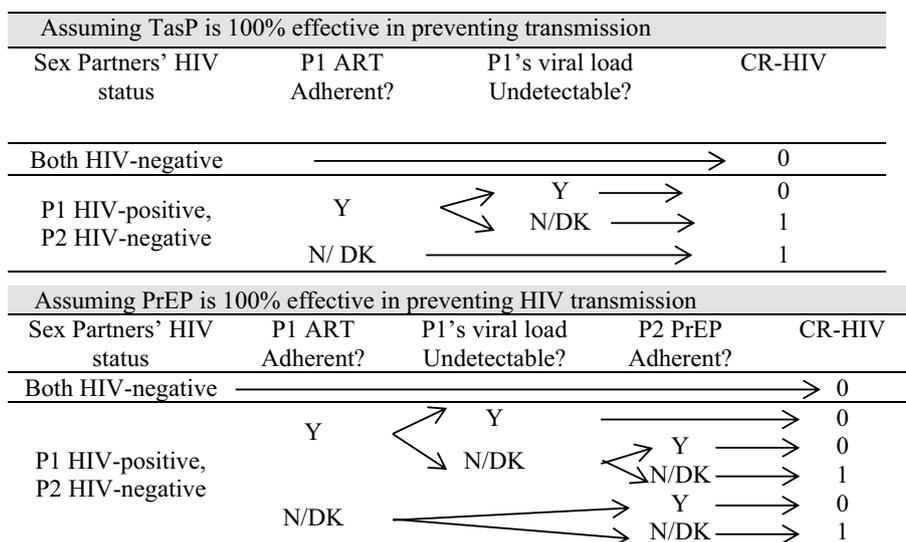
urgent need to develop an outcome measure in HIV prevention research that is flexible enough to capture the full range of biomedical and behavioral HIV prevention options available for GBMSM and transgender women in their primary relationship contexts. Our approach for integrating disparate evolving biomedical and behavioral HIV risk reduction strategies into a composite risk outcome has the potential to be a comprehensive tool for research efforts that can then be readily translated and implemented into real world settings.

Discussion

This paper presents an integrative Composite Risk for HIV (CR-HIV) approach for HIV prevention research for GBMSM and transgender women in the context of their primary relationships. The CR-HIV approach incorporates information regarding sexual behavior, utilization of one or more biomedical prevention strategy, and adherence to biomedical strategies. We believe that this approach will prove useful for survey planning, standardizing measurement across heterogeneous samples, guiding interventions and thereby ultimately reducing HIV incidence among priority populations globally. We describe the CR-HIV approach in further detail below.

The CR-HIV approach (see Fig. 1) calculates a binary indicator (0 = No, 1 = Yes) of an individual’s risk for HIV acquisition based on an algorithm that factors their own, as well as their partner’s, serostatus, sexual risk behavior, and status on the adoption of and adherence to biomedical strategies. For instance, to arrive at the CR-HIV indicator for a

Fig. 1 Calculation of CR-HIV if one or both partners report condomless sex with a serodiscordant or unknown HIV status partner



Note: P1=Partner1, P2=Partner2; Y=Yes; N=No; N/DK=No or Don't Know; PrEP=pre-exposure prophylaxis; TasP=treatment as prevention

HIV-negative man or transgender woman, the questions to consider would be:

- (1) ‘Did the participant have condomless anal or vaginal sex in the past 3 months (or similar interval deemed appropriate)?’,
- (2) If yes to (1), ‘What was the HIV serostatus of his or her sex partner(s)?’,
- (3) ‘Is the participant on PrEP?’
- (4) ‘If yes to (3) then is he or she adequately adherent for it to be effective in preventing HIV transmission?’
- (5) ‘Are his or her HIV-positive partner(s) on ART?’
- (6) ‘If yes to (5), are they virally suppressed?’

The responses to each of these questions would together determine his or her indicator value on CR-HIV. This makes CR-HIV both inclusive and flexible. In the simplest case, HIV-negative individuals are coded 0 if they do not report condomless anal or vaginal sex. It is also important to recognize and account for the fact that not all GBMSM and transgender women are engaging in HIV transmission risk behaviors. Specifically, some couples may have a monogamous sexual agreement whereby they only engage in condomless sex with one another and test regularly for HIV and other sexually transmitted infections. This CR-HIV approach allows for researchers to account for couples that have different prevention needs and preferences while also being easily updated and adapted to integrate future biomedical prevention strategies, such as LAI. Below we provide two illustrative examples to demonstrate the utility of the CR-HIV approach.

A CR-HIV Approach in the Context of HIV Serodiscordant Couples

PrEP has been shown to be highly effective in several priority populations, including HIV serodiscordant couples [37]. With the proven efficacy of TasP in preventing new infections, PrEP is now considered a “bridging strategy” for the HIV-negative partner in serodiscordant couples until the HIV-positive partner is sufficiently adherent to their ART regimen to become virally suppressed [38]. In fact, the World Health Organization recommends the use of early treatment with ART (i.e., up to 6 months after HIV infection) for the HIV-positive partner to reduce the chances of HIV transmission or in combination with PrEP [39]. As noted above, biomedical HIV prevention efficacy and demonstration-implementation trials relied on behavioral approaches to motivate individuals and resolve barriers to initiating and adhering to these strategies [25, 40, 41]. A case of calculating CR-HIV could be as follows: if the HIV-negative partner in a serodiscordant relationship reports

condomless anal sex with his or her primary partner, then his or her CR-HIV will enumerate to 1 (yes) if (i) he or she is not on or non-adherent to PrEP and/or (ii) the HIV-positive partner is not virally suppressed. Thus, the proposed CR-HIV approach allows researchers the flexibility to account for evolving biomedical prevention strategies and guidelines while simultaneously capitalizing on successful behavioral approaches to HIV prevention and care.

A CR-HIV Approach in the Context of HIV Seroconcordant Negative Relationships

While a number of biomedical HIV preventive strategies exist for GBMSM and transgender women in HIV seroconcordant negative relationships, it is worrisome that uptake of these strategies by this at-risk population remains low. Studies have demonstrated that GBMSM and transgender women in relationships test infrequently for HIV and other STIs even in the presence of risky sexual behaviors [42–47] and fewer than half of transgender women know their HIV status [48]. Since the FDA’s approval of PrEP in 2012, there has been growing awareness and adoption intentions among GBMSM and transgender women in primary partnerships [49–51]; however, uptake outside of clinical trials and demonstration projects has remained low [52–54].

In this context of HIV-negative seroconcordant relationships, a case of calculating CR-HIV could be as follows: if a partner reports condomless sexual intercourse with a sexual partner, then his or her CR-HIV will enumerate to 1 if (i) he or she is not on PrEP or is not adherent to PrEP or (ii) his or her partner is not on PrEP or is non-adherent to PrEP. Thus, a CR-HIV approach would allow researchers to assess both partners’ sexual risk behaviors individually in order to determine the most appropriate biomedical prevention and/or behavioral strategy, which may include communication skills building regarding sexual agreements, regular HIV and STI testing, and PrEP use.

Strengths and Challenges

One of the primary strengths of the CR-HIV approach is that it recognizes that one singular HIV prevention strategy may not be best for all couples and that individuals’ HIV risk profiles may vacillate. The CR-HIV approach also captures possible HIV risk with both primary and outside partners, which is important for couples-based HIV prevention research, given the common occurrence of secondary partnerships across relationship types. Given the notable social and structural barriers to accessing and using biomedical prevention strategies, such as PrEP (e.g., stigma, costs and access to financial assistance for medications)

[26], the CR-HIV approach has the potential to overcome these challenges. Specifically, the CR-HIV approach is not constrained by geography, finances, or even specific populations and can be adapted for use in different geographic locales, including mobile platforms. Additionally, the CR-HIV approach can be used as a means of developing a more uniform outcome in HIV prevention intervention research that considers a multitude of factors when calculating HIV risk. The CR-HIV approach can be assessed with self-report measures or PrEP adherence and viral suppression can be verified through blood tests, which is a substantially more robust outcome given problems with self-report adherence data [55].

There are some notable challenges in the use of biomedical prevention strategies as outcomes in HIV prevention research. For example, the measurement of PrEP drug levels in plasma (as an objective metric of adherence) has been shown to be an effective measure of PrEP adherence [56]. However, plasma measures of tenofovir (TFV) and emtricitabine (FTC) only capture short-term exposure [57]. Concentrations of TFV and/or FTC in dried blood spots (DBS) and hair samples assess longer term adherence [58], and have therefore been increasingly incorporated as adherence metrics into PrEP programs. Regardless of the collection method, the current window for detecting the appropriate blood levels of PrEP is 2 weeks; whereas, the window for detecting viral load is approximately 1 month. Thus, the challenge is that the window for detecting PrEP drug levels to measure adherence is short and risk for HIV could occur outside this short window of adherence assessment. Although the short time period is currently a challenge, there continue to be rapid developments in the measurement of blood levels of PrEP over longer windows. Ideally, the CR-HIV approach would require that both partners complete the survey together and preferably at the same time so that the windows of sexual behavior and drug adherence are the same. The timing of dyadic data collection can be a challenge but not insurmountably so, as has been demonstrated by multiple large longitudinal studies in couples; and the benefits are substantial in determining the best prevention strategies for both members of a couple. The CR-HIV approach could allow for an individual to self-report on their partners' sexual behavior as well as use of and adherence to biomedical strategies; however, caution should be taken in such cases since individuals tend to overestimate their partner's viral suppression, reporting that they believe they are suppressed when they actually are not [59]. Although sexual behavior is the central aspect of the CR-HIV approach, it can also be adapted to address other forms of HIV risk (e.g., needle sharing). The critical component of the CR-approach is inquiring about sexual risk behavior and status of adoption of and adherence to biomedical strategies within sexual partnerships. As such, this approach also has the potential to be translated into a tool for providers to more accurately assess the dyadic context of HIV risk.

Conclusions

Our proposed CR-HIV approach provides a roadmap for integrating evolving biomedical prevention strategies and behaviors into HIV prevention intervention and survey research to meet and even surpass the UNAIDS 90–90–90 targets by identifying each partners' risk and identifying points of intervention. The CR-HIV approach entails calculating HIV transmission risk by means of an algorithm that can be easily adapted to include future biomedical prevention strategies, such as LAI. Our CR-HIV approach also acknowledges that one singular HIV prevention strategy may not be the most desired or appropriate one for everyone, given that individuals and their partners may fluctuate in their HIV risk profiles and needs. The CR-HIV approach provides researchers and clinicians a means for evaluating the risk profiles of both members of the dyad and subsequently to determine the best HIV prevention strategy to reduce HIV transmission for couples, especially those in priority populations. Finally, our CR-HIV approach has the potential to be a comprehensive tool for intervention efforts that can be easily translated into the real world, such as providing an algorithm that can be programmed into user-friendly software (i.e., Internet platforms) for a quick and comprehensive risk assessment. Given that the relationship context has been shown to influence several aspects of the HIV continuum (e.g., HIV testing, ART adherence, PrEP adoption intentions), the development of an approach to incorporate the complexity inherent in dyads can potentially lead to an improvement in HIV outcomes for populations that shoulder a disproportionate burden in the epidemic.

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Compliance with Ethical Standards

Conflict of interest Each of the authors declare that they have no conflict of interest.

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