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Original article

Individualized diagnosis interventions can add significant effectiveness in reducing human immunodeficiency virus incidence among men who have sex with men: insights from Southern California

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ABSTRACT

Purpose: In this article, we examine the effectiveness of a variety of HIV diagnosis interventions in recently HIV-diagnosed men who have sex with men (MSM). These interventions use the preventive potential of postdiagnosis behavior change (PDBC), as measured by the reduction in the number of new infections. Empirical evidence for PDBC was presented in the behavioral substudy of the Southern California Acute Infection and Early Disease Research Program. In previous modeling work, we demonstrated the existing preventive effects of PDBC. However, a large proportion of new infections among MSM are either undiagnosed or diagnosed late, and the preventive potential of PDBC is not fully utilized.
Methods: We derive empirical, stochastic, network-based models to examine the effectiveness of several diagnosis interventions that account for PDBC among MSM over a 10-year period. These interventions involve tests with shorter detection windows, more frequent testing, and individualized testing regimens.
Results: We find that individualized testing interventions (i.e., testing individuals every three partners or 3 months, whichever is first, or every six partners or 6 months, whichever is first) result in significantly fewer new HIV infections than the generalized interventions we consider.
Conclusions: This work highlights the potential of individualized interventions for new public health policies in HIV prevention.

Introduction

Men who have sex with men (MSM) continue to be the population most affected by human immunodeficiency virus (HIV) in the United States [1,2]. MSM account for an estimated 63% of all new HIV infections in the United States [3]. Additionally, many infections in this population are either undiagnosed [3,4] or diagnosed late [5]. There are at least two public health benefits to early diagnosis: timely enrollment in treatment [6–8] and early adoption of behaviors to reduce risk of transmission to one's partners; examples of the latter include partner reduction [9–11], serosorting [12–15], and increased condom use [10]. Multiple interventions to increase testing frequency (TF), testing promptness after exposure, and test sensitivity, or to reduce the window period, are under consideration. The public health impacts of these interventions tend to be indirect because cases averted are not among testers themselves but among their partners and partners' partners. Empirically derived mathematical models and computational analyses can help assess the effectiveness of various interventions to reduce HIV incidence among MSM.

Early HIV diagnosis is a function of the "detection window" (DW; time between infection and development of a positive test result) of the test used. HIV tests with shorter DWs continue to be developed,

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and third- and fourth-generation enzyme immunoassays (EIAs) have DWs of 20 to 30 days and 15 to 20 days, respectively [16]. Fourth-generation EIAs are widely used in industrialized economies [17–19]. Rapid nucleic acid amplification tests (NAATs) are an alternative, as are antigen tests that can detect HIV as early as 10 to 15 days after infection [16,20]. However, NAATs are much more expensive than antibody tests [21]. Current recommendations in high-incidence populations include pooled NAAT or fourth-generation assays [22].

Early diagnosis also depends on MSM's testing patterns and their risk behavior. Currently, the Centers for Disease Control and Prevention recommends that all MSM test for HIV every year and states that sexually active MSM may benefit from testing every 3 to 6 months [3], regardless of risk behavior including number of partners. Estimates from clinical data in four metropolitan US centers suggest that MSM tend to test on average about once a year [23], but data from the Centers for Disease Control and Prevention's National HIV Behavioral Surveillance system suggest that a high proportion of HIV-infected MSM (approximately 44%) are undiagnosed [4]. As previously shown [24], these sources are difficult to reconcile; our knowledge of true testing frequencies and diagnosis levels for MSM remains imperfect.

Some health jurisdictions are exploring individually tailored testing interventions. For example, the "*Find Your Frequency*" program, recently implemented in the Seattle metropolitan area, uses a Web site to encourage MSM to evaluate their risk based on the status and number of partners, type of sex, drug use, and history of sexually transmitted diseases and uses a simple algorithm to make recommendations to test every 3 or 12 months, contingent on individual risk characteristics [25]. Similarly, other health departments are interested in exploring an approach that proposes that MSM test after a certain number of partners or period of time, for example every 3 months or three partners, whichever comes first (known as "the oil change model") [26]. Under this approach, testing recommendations are dependent on recent risk, with the hope that a tailored approach will result in more frequent testing among those at highest risk of HIV acquisition. Both these programs recognize that a single testing recommendation does not capture the diversity of risk among MSM.

The preventive potential of diagnosis-induced behavior change also depends on its timing and magnitude. Interventions to maximize this prevention potential require knowledge of the network-level effects of such behavior change; network approaches for the implementation and assessment of interventions have traditionally been relatively uncommon but have great potential [27]. Postdiagnosis behavior change (PDBC) in Southern Californian MSM was documented in the behavioral substudy of the Southern California Acute Infection and Early Disease Research Program (AIEDRP) [9,10]. These studies demonstrated a statistically significant reduction in the mean number of partners and in the likelihood of unprotected anal intercourse (UAI) with the last partner of negative or unknown HIV status soon after a positive diagnosis [10]. In prior work, we demonstrated the epidemiologic significance of PDBC; our findings indicated that without observed levels of PDBC, HIV prevalence in this population would be much higher [24].

How such behavior change can be used to better design interventions to impact incidence among MSM, however, remains largely unknown. The benefits of early diagnosis are recognized [28] and are being explored in modeling studies [29]. Much of this focus is on early initiation of treatment to prevent transmission through viral suppression ("treatment as prevention") [30–33]. Relatively little attention is given to the preventive power of diagnosis-induced behavior change through changes in testing patterns (what we might call "testing-as-prevention"). In this article, we develop network-based mathematical models, parameterized with detailed data on PDBC among US MSM, to examine the effectiveness of three types of HIV testing interventions to reduce incidence: (1) instituting tests with shorter DWs, (2) increasing frequency of testing generally, and (3) increasing testing using risk-based individually tailored algorithms.

Table 1
Sources of key parameters

Source	Parameters
AIEDRP	Mean number of main and nonmain partnerships, mixing by diagnosis status, daily probability of UAI, mixing by age, mean duration of main partnerships, mean number of partnerships for methamphetamine users and nonusers
PUMA	DW for HIV tests in baseline models, proportion of treated men who achieve partial, full, or no viral suppression, role versatility in main partnerships, all biological parameters (including evolution of viral load trajectories, adjustment parameters for acute and late-stage infection, and transmission)

AIEDRP represents the Southern California substudy of the Acute Infection and Early Disease Research Program; study details are in two prior publications [9,10]. Parameters marked PUMA are from the modeling component of the Prevention Umbrella for MSM in the Americas project [34]. Complete details for all our parameters are in the online appendix to a prior study [24].

Methods

We retain the model structure from our work on PDBC and HIV prevalence among Southern Californian MSM [24]. These models are derived from the exponential-family random graph model framework, which is increasingly used to model HIV transmission [34–36]. We incorporate numerous key processes: demographic (birth, death, and aging), epidemiologic (testing behavior, treatment, methamphetamine use, and circumcision), sexual network (partnership types, activity levels, concurrent partnerships of various types, sexual role heterogeneity, and seroadaptive behaviors) and biological (viral load trajectories, variable infectivity by stage, treatment status, and adherence). One key focus here is on the heightened risk of transmission due to acute infection during the first 40 days after seroconversion [34].

As in our previous work, the behavioral data are primarily from the Southern California (Los Angeles and San Diego counties) AIEDRP study [9,10], supplemented with published biological and demographic data (see the online appendix of our prior study [24]). Newly HIV-diagnosed men completed AIEDRP questionnaires via computer-assisted self-interviewing at baseline; follow-up computer-assisted self-interviewing interviews occurred at 3-month intervals. At baseline, respondents provided detailed information on their three most recent partners, and at follow-up, on the most recent partner, in addition to reporting total numbers of partners at baseline and follow-up [10]. The types of partnerships MSM engage in are complex [37], but for simplicity, we dichotomize these partnerships as "main" and "nonmain" [24]. We model nonmain partnerships as discrete UAI events and main partnerships using temporally evolving networks, in which UAI episodes may occur on any given day. We do not consider protected anal intercourse, seropositioning (explicit adoption of roles by serostatus), or oral intercourse. Our baseline models assume a 22-day test DW, consistent with the third- and fourth-generation EIAs, and other modeling work [34]. The key parameter sources are in Table 1.

Our model is meant to represent only those MSM whose HIV risk is more than occasional, and not reflective of the unknown percentage of MSM who never engage in UAI, or whose lifetime UAI only occurs within concordant seronegative mutually monogamous main partnerships. This risk structure is reflected in the distribution of behaviors present in our baseline model. Of specific relevance to