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Original article

Targeting Human Immunodeficiency Virus Pre-Exposure Prophylaxis to Adolescent Sexual Minority Males in Higher Prevalence Areas of the United States: A Modeling Study

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A B S T R A C T

Purpose: Pre-exposure prophylaxis (PrEP) is an effective and safe intervention to prevent human immunodeficiency virus (HIV) transmission in men who have sex with men; current Centers for Disease Control and Prevention guidelines indicate its use among high-risk adults. Adolescent sexual minority males (ASMM) also have significant HIV risk, but implementation strategies are likely to differ for this population. We aimed to estimate impact and efficiency of PrEP for ASMM in higher prevalence US settings, using a variety of implementation strategies and assumptions about coverage, adherence, and background prevalence.

Methods: We develop a stochastic, dynamic, network-based model, parametrized using numerous ASMM behavioral and clinical data sources. We simulate 10 years with and without PrEP, comparing percent of incident infections averted (impact) and number of person-years on PrEP per infection averted (efficiency).

Results: Our main scenario (PrEP for 16- to 18-year-old ASMM, initiating PrEP 6 months after first anal intercourse, 40% coverage, adherence profiles from the ATN 113 trial; 2.9% background HIV prevalence among ASMM) prevents 27.8% of infections, with 38 person-years on PrEP per infection averted. Expanding implementation to cover younger ages or earlier initiation has small effects on impact and efficiency. Targeting highest risk ASMM increases efficiency, but requires querying sexual histories. Across levels examined, coverage and adherence do not have major impacts on efficiency, whereas background prevalence does.

IMPLICATIONS AND CONTRIBUTION

This study uses modeling and recent trial data to estimate impact and efficiency for HIV pre-exposure prophylaxis (PrEP) among adolescent sexual minority males in higher prevalence US settings under different targeting strategies. Results show that PrEP can have a large impact on HIV incidence in this population, with reasonable efficiency.

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Conclusions: PrEP can have a large impact on HIV incidence among ASMM in the United States, especially in settings with high prevalence. However, willingness of, and support for, providers will be central to achieving the coverage needed to make this a success.

Pre-exposure prophylaxis (PrEP) with daily oral combined tenofovir or emtricitabine is an effective and safe intervention to prevent human immunodeficiency virus (HIV) infection in adult men who have sex with men (MSM) [1,2]. Current Centers for Disease Control and Prevention (CDC) guidelines indicate use for sexually active adult MSM at substantial risk of HIV acquisition, based on recent patterns of anal sex, monogamy, condom use, partner HIV status, and sexually transmitted infection (STI) diagnosis, or who have injected drugs and shared needles [3]. PrEP initiation requires a prescription; current CDC guidelines for ongoing PrEP users promote quarterly HIV tests, STI tests every 6 months, and screening for various side effects at both intervals.

Adolescent sexual minority males (ASMM), that is, males under 18 who identify as gay or bisexual, or are sexually active with other males, have significant HIV risk. For instance, sexually debuted high school ASMM report higher frequencies of multiple risk behaviors than do sexually debuted high school adolescent males with only female partners, including prevalence of four or more lifetime partners (33.4% vs. 25.4%), condomless last sex (48.6% vs. 37.9%), and use of drugs or alcohol at last sex (32.2% vs. 24.1%) [4]. Although surveillance-based HIV incidence measures are not available for ASMM [5], measures of new diagnoses illuminate the high HIV risk that ASMM experience nationally. The CDC estimated that in 2015, 13- to 24-year-old adolescents and young adults comprised 22% of all new US HIV diagnoses, and 81% of the adolescent or young adult diagnoses were in ASMM, for a total of 7,159 of 39,920 diagnoses [6]. Nineteen percent of ASMM diagnoses occurred by age 19 and it remains unknown what proportion of all ASMM diagnoses reflect infections that occurred before 18. Per total population-based rates for 13- to 24-year-old MSM illustrate this group to have consistently the second highest diagnosis rates among MSM, but stable diagnosis rates since 2010. In the absence of surveillance-based incidence estimates and ASMM-specific denominators for estimating most relevant rates [7], research studies have provided critical insights into the HIV burden among ASMM. HIV incidence among 16- to 17-year-old Chicago ASMM has been estimated at 5.2 per 100 person-years, and prevalence among 16- to 20-year-olds at 7.6% [8]. Studies of adult MSM find HIV in the youngest participants, implying substantial risk in adolescents; for example, HIV prevalence estimates among 18- to 22 year-old MSM from three rounds of the National HIV Behavioral Surveillance system were 11%–14% [9]. The InvolveMENt cohort (Atlanta) estimated 7.0% HIV prevalence among 18- to 19-year-olds [10], and the P18 cohort (New York City) reported HIV incidence of 2.9 per 100 person-years in MSM of the same ages [11]. These population-specific estimates of HIV incidence are more than 200-fold those seen in the general US population [5].

Initial PrEP trials and demonstration projects for MSM included only adults aged 18+ [1,2,12]. Given the lack of adolescent-specific efficacy and safety data, current Food and Drug Administration indications include only adults, and CDC's clinical practice guidelines currently recommend that the risks and benefits of PrEP for adolescents be weighed carefully "in the context of local laws and regulations about autonomy in health care decision-making by minors" [3]. One safety and feasibility study of PrEP in ASMM in the United States aged 15–17 (ATN 113) was recently completed. Averaged across measured time points, high adherence (four or more doses/week) in ATN 113 (41.6%) was lower than in a recent demonstration project with adult MSM (61.9%) [12–14]. ATN 113 showed a high incidence rate (6.41 infections per 100 person-years), higher than the 3.29 infections per 100 person-years observed in its 18- to 22-year-old MSM counterpart ATN 110 [15], although all infections in ATN 113 were among those whose drug levels indicated poor to no adherence. These results highlight the need for targeted research in adolescents to understand the impact PrEP may have on HIV incidence, and the unique challenges for ASMM in uptake, adherence, and defining and accessing target populations. Because risk behaviors evolve rapidly during adolescence, this could be a uniquely valuable time to get ASMM on PrEP surrounding specific high-risk behaviors, establishing early a norm of sexual health protection.

A broad definition of ASMM includes adolescents who identify as either gay or bisexual or have a history of sex with males; one key decision for future PrEP guidelines among ASMM, then, is whether to target adolescent populations based on sexual identity or reported risk behaviors. Overall impact (i.e., cases averted) and efficiency (i.e., number needed to treat) may depend on targeting strategy and the existing distribution of sexual risk. However, methods for identifying ASMM must recognize that they may be in early stages of sexual identity formation and may not self-identify as ASMM, nor disclose identity or risk behaviors to clinicians or counselors; moreover, not all providers for adolescents are prepared to elucidate this information.

In this study, we developed an agent-based network model of HIV transmission among ASMM to inform future guidelines and studies of PrEP interventions in adolescents. We modeled an open cohort of 13- to 18-year-old ASMM, and considered different targeting strategies, adherence and coverage levels, and baseline prevalence levels. We estimated the impact and efficiency of each strategy, and we interpret these results in the context of each strategy's feasibility within different settings.

Methods

We developed a stochastic, dynamic model built in the EpiModel software platform (www.epimodel.org) based on separable-temporal exponential-family random graph models [16]. This general statistical model class specifies the probability each pair forms or breaks a relationship at each time step in ways that allow users to preserve arbitrarily complex data-derived features of network structure. As with our previous adult MSM model [13], we modeled relationship formation and dissolution; sexual behavior within relationships (anal sex acts, condom use, role selection); HIV testing; HIV treatment initiation, adherence and cessation; PrEP initiation and adherence; transmission; intra-host viral dynamics; and agent demographic change. We restructured