# *Preventing HIV Infection in High-Risk Adolescents Using Preexposure Prophylaxis (PrEP)*



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***Key words:*** *adolescent men who have sex with men (AMSM), bisexual, HIV, homosexual, PrEP*

Preexposure prophylaxis (PrEP) has emerged as a major tool in the prevention of HIV infection. Appropriate use of once-daily emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg (Truvada®; Gilead, Foster City, CA) in combination with safer sex activities significantly reduces the risk of HIV infection. Trials initially supported efficacy of PrEP in adults, prompting its approval for adult use by the U.S. Food and Drug Administration (FDA) in July 2012 (Gilead, 2018). Due to growing data suggesting PrEP as beneficial in preventing HIV in high-risk adolescents, the FDA approved it for prevention of HIV in this patient population in May 2018 (Gilead, 2018; Smart + Strong, 2018). The purpose of this article is to discuss the use of PrEP to prevent HIV infection in high-risk adolescents.

Topics covered include a review of the data supporting PrEP as effective in adults and adolescents, reaching the decision to initiate PrEP in adolescents, sexual history-taking considerations, and initiating and monitoring PrEP in this group of vulnerable individuals.

## Support for PrEP in Adults in Clinical Trials

The FDA approved the once-daily use of Truvada® to prevent HIV in high-risk adults in July 2012 (U.S. Department of Health and Human Services, 2012). Known as preexposure prophylaxis (PrEP), efficacy of the regimen was supported by several clinical trials that suggested appropriate use of PrEP in combination with risk-reduction behaviors could reduce HIV infection significantly (Baeten et al., 2012; Blackwell, 2014; Grant et al., 2010). Data from the Preexposure Prophylaxis Initiative and the tenofovir disoproxil fumarate and emtricitabine studies showed that HIV infection was reduced by 90% when patients appropriately adhered to PrEP and were also provided with a prevention program including providing condoms, screening for HIV each month, and educating about reducing risk (Centers for Disease Control and Prevention [CDC], 2012; 2013).

Other studies have also supported PrEP as an effective tool in the prevention of HIV in special high-risk populations. For example, while the tenofovir disoproxil fumarate and emtricitabine; Partners PrEP; Preexposure Prophylaxis Trial for HIV Prevention among African Woman; Phase 2 Trial of Preexposure Prophylaxis with Tenofovir Among Women in Ghana, Cameroon, and Nigeria; and Vaginal and Oral Interventions to Control the Epidemic trials all supported the efficacy of the regimen among heterosexual men and women, the Preexposure Prophylaxis Initiative and U.S. Men Who Have Sex with Men Safety Trials focused on the effectiveness of PrEP in men who have sex with men (MSM; U.S. Public Health Service, 2014). In addition, the Bangkok

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JOURNAL OF THE ASSOCIATION OF NURSES IN AIDS CARE, Vol. 29, No. 5, September/October 2018, 770-774
https://doi.org/10.1016/j.jana.2018.06.001

Tenofovir Study emphasized PrEP as an effective tool to prevent HIV infection in injecting drug users (U.S. Public Health Service, 2014).

## Support for PrEP in Adolescents in Clinical Trials

Very few inquiries have been devoted to evaluating the efficacy of PrEP in the adolescent patient population. A review by Hosek and colleagues (2016) of the small number of studies being conducted across the United States and South Africa indicated likelihood that PrEP would make a positive impact on population HIV incidence in adolescents. Goodreau and colleagues (2018) echoed similar assumptions. In their modeled study, these scholars found "PrEP can have a large impact on HIV incidence among adolescent sexual minority males in the United States, especially in settings with high prevalence" (Goodreau et al., 2018, p. 312). A major component of the study used in the modeling procedure by Goodreau and colleagues (2018) was the Adolescent Medicine Trials Network (ATN) 113 trial. The results of this trial prompted the May 2018 FDA expansion of approval for PrEP to include adolescents (Gilead, 2018; Rosenberg, 2018).

ATN 113 focused on 78 uninfected individuals with an average age of 16.5 years. Thirty-three percent of participants were mixed race, 29% were Black, 21% were Latino, 14% were White, and 3% were Asian or Pacific Islander (Smart + Strong, 2016). Participants consisted of adolescent MSM (AMSM) who were at higher risk for sexually transmitted diseases (STDs). Most participants disclosed they had engaged in unprotected anal intercourse during the study; and 15.4% were diagnosed and treated for STDs during the 48-week trial (Smart + Strong, 2016). At the study's conclusion, three had contracted HIV, yielding a 6.41% HIV infection rate per year (Smart + Strong, 2016).

## Reaching the Decision to Initiate PrEP in Adolescents

In 2016, individuals between the ages of 13 and 24 years made up 21% of all new HIV diagnoses in the United States (CDC, 2018). Because 81% of these diagnoses occurred in AMSM, these adolescents were identified as being especially affected (CDC, 2018). AMSM have a number of factors that place them at higher risk for HIV infection, including high numbers of sexual partners, condomless sex, and use of alcohol/drugs during sex (Goodreau et al., 2018). Just 4% of infections resulted from heterosexual contact, and even fewer (3%) were from male-to-male sexual contact in combination with intravenous drug use or intravenous drug use alone (1%; CDC, 2018). Among infected AMSM, 54% were African American; Hispanic/Latino AMSM made up 25% of these diagnoses, while White AMSM accounted for 16% (CDC, 2018). Between 2011 and 2015, rates of infection remained stable in African American and White AMSM, but rose by 19% among young Hispanic/Latino AMSM while dropping 25% in young women (CDC, 2018).

The May 2018 expanded indication for PrEP by the FDA to include adolescents was largely devoid of specific guidelines about which adolescents the clinicians should consider as appropriate for PrEP therapy, with Gilead (2018) distinctly indicating PrEP for at-risk adolescents in their press release regarding the new expanded indication. Modeling research by Goodreau and colleagues (2018) predicted the efficacy of PrEP, specifically in AMSM, which was appropriate given the most recent incidence data on HIV infections provided by the CDC (2018). The researchers recommended targeting 16- to 18-year-old AMSM (Goodreau et al., 2018), which would include the FDA-approved ages of 15 to 17 years for PrEP. Other risk factors identified as appropriate for initiation of PrEP in adults (Blackwell, 2014) that might be applicable to adolescents include being the uninfected partner of a person living with HIV, having multiple sex partners regardless of sexual orientation, participation in sex work, use of illicit substances, and failure to use condoms consistently during sex.

State regulations related to consent for preventative services and treatment in these persons is an important factor to consider when choosing to initiate PrEP in non-adult populations (Culp & Caucci, 2013). Clinicians should research their state regulations that stipulate how minors are defined and what consents they are able to legally provide. Culp and Caucci (2013) specifically focused on issues

related to consent when initiating PrEP in adolescents in their study. Unfortunately, their work yielded little direction for clinicians and suggested more research is needed to determine the legality of providing PrEP to minors without parental consent throughout the country.

## Sexual History Taking: Implications in Adolescents

Obtaining a sexual health history from an adolescent is vital. Data have demonstrated improved screening and clinical outcomes in adolescents who were asked about sexual history by their providers (Goyal, McCutcheon, Hayes, & Mollen, 2011; Ouelette, Wingelear, Peterson, Emery, & Jones, 2018). In addition, surveys have indicated that 45% of 15- to 19-year-olds have had vaginal sex with an opposite sex partner, while 2.5% of males in this age category have had anal or oral sex with other males and 11% of females in this age range have had sexual activities with other females (Marcell & Burstein, 2017). Unfortunately, research has shown a great amount of inconsistency by clinicians in obtaining a sexual history during adolescent health care encounters (Goyal et al., 2011; Riese, Tarr, Baird, & Alverson, 2018; Sargant, Smallwood, & Finlay, 2014).

All 50 states allow minors to consent for screening of STDs (Marcell & Burstein, 2017), and the American Academy of Pediatrics recommends that clinicians provide "confidential time during health maintenance visits to discuss sexuality, sexual health promotion, and risk reduction" (Marcell & Burstein, 2017, p. 2). Clinicians should make no assumptions about any adolescent's sexual history. Adolescents should be asked directly about sexual activities with men, women, or both; frequency of condom use during oral, vaginal, and anal sexual activities; use of alcohol or drugs during sex; and history of sex work (Blackwell, 2014; Goyal et al., 2011).

## Initiating and Monitoring PrEP

Before initiating PrEP therapy, clinicians need to document a negative HIV antibody screening test, confirm a creatinine clearance of at least 60 mL/min using the Cockgroft-Gault formula, assess status of care in partners with HIV (providing necessary referral as needed), screen for hepatitis B virus (HBV) and initiate appropriate treatment (as needed), document a patient weight of at least 35 kg, and screen for and treat any STDs. In addition, females must have a documented negative urine pregnancy test and acknowledge understanding that there are few data assessing the risk of using PrEP during pregnancy. Females who are breastfeeding should not be prescribed PrEP (Blackwell, 2014; Gilead, 2018).

The PrEP regimen consists of one daily emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg (Truvada®) tablet taken with or without food. In addition to this prescription, clinicians need to ensure proper education about consistent use of condoms during every sexual encounter. Providing condoms directly to patients has also been found to be beneficial (CDC 2012; 2013). It is paramount that adolescents understand that PrEP does not exclude the importance of consistent condom use and provides no protection against other STDs (Gilead, 2018).

An important distinction between follow-up in adults compared to adolescents relates to frequency. While it is recommended that adults follow up with their providers every 3 months while on PrEP (Blackwell, 2014), adolescents may need more frequent follow-up (Gilead, 2018; Rosenberg, 2018; Smart + Strong, 2016; 2018). This is because a major finding from the ATN 113 study was poor adherence by adolescents, particularly as the time between follow-up visits increased. As reported by Smart + Strong (2016):

> Overall, adherence dropped considerably once the study switched from monthly to quarterly clinic visits. At weeks 4, 8, 12, 24, 36, and 48, the proportion of the participants who took at least four tablets of Truvada per week according to dried blood spot testing was a respective 60%, 52.4%, 55%, 31.5%, 22.7%, and 28.21%. Previous research has found that taking Truvada four or more times per week confers maximum protection against HIV. (¶ 9)

Thus, monthly visits by adolescents on PrEP may be indicated (Smart + Strong, 2016). The safety

profile of Truvada® for adolescents is similar to that of adults, with headache, abdominal pain, and weight loss being the most frequently reported adverse events (Gilead, 2018). Bone mineral density loss, a far less frequently reported adverse event, occurred in four patients enrolled in the ATN 113 study (Gilead, 2018).

Patients should be screened for HIV every 3 months and PrEP should be immediately discontinued if a patient tests positive for HIV (Gilead, 2018). Finally, exacerbations of HBV infections have been found in patients infected with HBV after discontinuation of PrEP. Thus, patients with HBV will need close monitoring of liver function assays for several months after discontinuing therapy (Gilead, 2018). Other information about prescribing Truvada®, including boxed warnings, other warnings and precautions and adverse events, information on pregnancy and lactation, and dosage and administration have been noted (Gilead, 2018).

## Summary and Conclusion

The expanded indication for the use of PrEP in adolescents is very recent. Therefore, there are no longitudinal studies that address the long-term impacts of the use of PrEP in this patient population. Nonetheless, advanced practice nurses, physicians, and physician assistants who have the opportunity to prescribe PrEP for adolescents in their clinical practices should be intimately familiar with the regimen. Data suggest that PrEP is effective and probably cost-effective (Goodreau et al., 2018) in adolescents.

But clinicians must consider other issues, as discussed in this article, that are unique to the use of PrEP in this patient population. These practice points include the appropriate taking of sexual histories in adolescents, evaluating the risk for HIV infection, providing appropriate preevaluation and monitoring services, and optimizing frequency of follow-up appointments to best promote adherence.

Finally, health care providers must emphasize with adolescent patients that PrEP is not a substitute for consistent condom use during sexual activities and that PrEP provides no protection against any other STD. With patient safety as the paramount consideration, PrEP use in adolescents may have a significant influence on the overall national incidence of HIV infection in the near future.

## Disclosures

The author reports no real or perceived vested interests that relate to this article that could be construed as a conflict of interest.

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