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ADVANCES IN PEDIATRICS

Nonoccupational Postexposure Prophylaxis and Preexposure Prophylaxis for Human Immunodeficiency Virus Prevention in Adolescents and Young Adults

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Keywords

• Human immunodeficiency virus (HIV) • Prevention • Postexposure prophylaxis
• Preexposure prophylaxis

Key points

- Nonoccupational postexposure prophylaxis decreases the risk of human immunodeficiency virus infection when initiated 72 hours or less after sexual, injection drug use, or other potential exposure to the virus.
- Preexposure prophylaxis decreases the risk of human immunodeficiency virus infection by more than 90% with high adherence and is now approved for adolescents in the United States.
- The legal rights of minors to access nonoccupational postexposure prophylaxis and preexposure prophylaxis without parental involvement vary by state; clinicians need to be familiar with their local laws.

INTRODUCTION

Of the nearly 40,000 human immunodeficiency virus (HIV) infections diagnosed in the United States in 2016, 21% were in 13- to 25-year-olds [1]. Among adolescents and young adults, 70% of newly diagnosed infections were

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attributed to men who have sex with men (MSM) or to MSM and injection drug use, and 24% of cases were attributed to heterosexual contact [1]. HIV disproportionately impacts Black/African American and Hispanic/Latino youth, with 55% of infections among 15- to 25-year-olds diagnosed in Black/African Americans and 23% in Hispanic/Latino youth [1]. Sexual risk behaviors are commonly reported among adolescents and young adults (Table 1).

The risk of acquiring HIV differs by route of exposure. Receptive anal intercourse and needle-sharing injection drug use confer the greatest risk of transmission, with a lower–but still substantial–risk associated with penile–vaginal and insertive anal intercourse [2]. Sexual partners of HIV-infected people are at significant risk of HIV: the 1-year cumulative risk of transmission is 52% for MSM practicing anal sex and 6% to 20% for heterosexuals practicing vaginal and/or anal sex [3]. Although consistent condom use reduces risk [3], condomless sex is frequently reported. HIV transmission after sexual assault has been reported [4–6]; transmission risk may be influenced by trauma, anatomic site of exposure, semen HIV viral load (male perpetrator), and cooccurring genital lesions or sexually transmitted infections (STIs) in either the perpetrator or survivor [4].

NONOCCUPATIONAL POSTEXPOSURE PROPHYLAXIS

Nonoccupational postexposure prophylaxis (nPEP) is the use of antiretroviral medication after isolated sexual, injection drug use, or other nonoccupational

Table 1
Reported HIV risk behaviors among adolescents and young adults

Patient population	Risk behavior	Percent
High school students [77]	Ever had sexual intercourse	40
	Had sexual intercourse in past 3 mo	29
	No condom use at last sex	46
	Alcohol, other substance use before last sex	19
	Never tested for HIV	91
HIV-uninfected men who have sex with men (MSM), ages 18–24 y [78]	Condomless anal sex with male partner past 12 mo	73
	Condomless sex with HIV-infected partner at last sex	17
	No HIV testing past 12 mo	21
	Transactional sex past 12 mo	10
	Any PrEP use past 12 mo	22
HIV-uninfected heterosexuals, ages 18–24 y [79]	Condomless vaginal sex past 12 mo	87–93
	No HIV testing past 12 mo	59
	Transactional sex past 12 mo	6
	Any PrEP use past 12 mo	0.1
HIV-uninfected people who inject drugs, ages 18–24 y [80]	Condomless sex with HIV-infected partner	46
	Shared injection equipment used by other(s) past 12 mo	76
	No HIV testing past 12 mo	45
	Transactional sex past 12 mo	19
	Any PrEP use past 12 mo	0.5

HIV exposure to prevent HIV infection. The US Centers for Disease Control and Prevention (CDC)/Department of Health and Human Services released its most recent nPEP recommendations in 2016 [2].

Research supporting nPEP is limited owing to the ethical and feasibility concerns of conducting a large scale, randomized, placebo-controlled clinical trial of nPEP. Thus, information from occupational PEP among health care workers, observational and case studies of nPEP efficacy in humans, nonhuman primate studies, and expert opinion form the basis for the 2016 nPEP guidelines [2]. The efficacy of occupational PEP was first described in a multinational study that demonstrated an 81% decrease in the odds of transmission in health care workers with percutaneous exposure to HIV who received zidovudine prophylaxis [7]. Intrapartum and postpartum prophylaxis prevents perinatal transmission [8,9], and most seroconversions after nPEP are due to ongoing risk behavior and not seroconversions [2]. A pooled analysis of 10 studies regarding nPEP in 8336 sexually assaulted youth revealed no new HIV infections; however, only 8% were offered nPEP and 1.5% completed treatment [2]. Another analysis of 15 studies in youth who completed nPEP revealed that only 1 of 19 seroconversions was due to failure of nPEP [2]. Studies in nonhuman primates also support the efficacy of PEP, its timing of initiation, and the use of tenofovir as part of the nPEP regimen [10]. Of note, comprehensive reviews of nPEP efficacy include older studies, which used single-dose therapy, as compared with newer studies with better tolerated multiple drug regimens, implying improved efficacy over time.

Safety

Much of the literature on adverse reactions to nPEP includes older regimens that are not currently part of the nPEP guidelines. A systematic review including 24 studies, representing 2166 victims of sexual assault using various nPEP regimens, reported that the most common side effects were nausea, vomiting, diarrhea, and fatigue; notably, only 40% of patients adhered to nPEP [11]. More serious side effects (eg, hepatic and renal toxicity) have occasionally been reported. Because of severe hepatotoxicity, nevirapine is now contraindicated for use as nPEP [12]. A study evaluating the combination of raltegravir, tenofovir disoproxil fumarate (TDF), and emtricitabine reported fewer side effects than historical controls. Side effects included mild, self-limited gastrointestinal complaints, headache, fatigue, and myalgias or arthralgias. Additionally, 57% of participants completed the regimen as prescribed, and 27% adhered to the daily medication, although some participants missed the second daily dose of raltegravir [13]. Among 100 MSM using the combination of dolutegravir, TDF, and emtricitabine as nPEP, 90% reported completion of nPEP with 98% self-reported adherence. Side effects reported included fatigue, gastrointestinal complaints, and headache, as well as mild elevation of alanine aminotransferase without hepatitis and a slight decrease in glomerular filtration rate; however, there were no discontinuations owing to toxicity [14]. Newer, more effective, and better tolerated regimens with fewer and less significant side

effects–and once daily dosing–are likely to maximize adherence to and effectiveness of nPEP.

Patient awareness of nonoccupational postexposure prophylaxis

The use of nPEP may be limited owing to potential users being unaware of its existence. In New York City, which has comparatively high HIV prevalence and a highly visible HIV prevention initiative, only 59% of high-risk individuals were aware of nPEP (80% among young MSM of color, 63% among transgender women, and 34% among cisgender women of color) [15]. Ongoing nPEP education and outreach should prioritize high-risk groups and focus on reducing stigma and barriers to access.

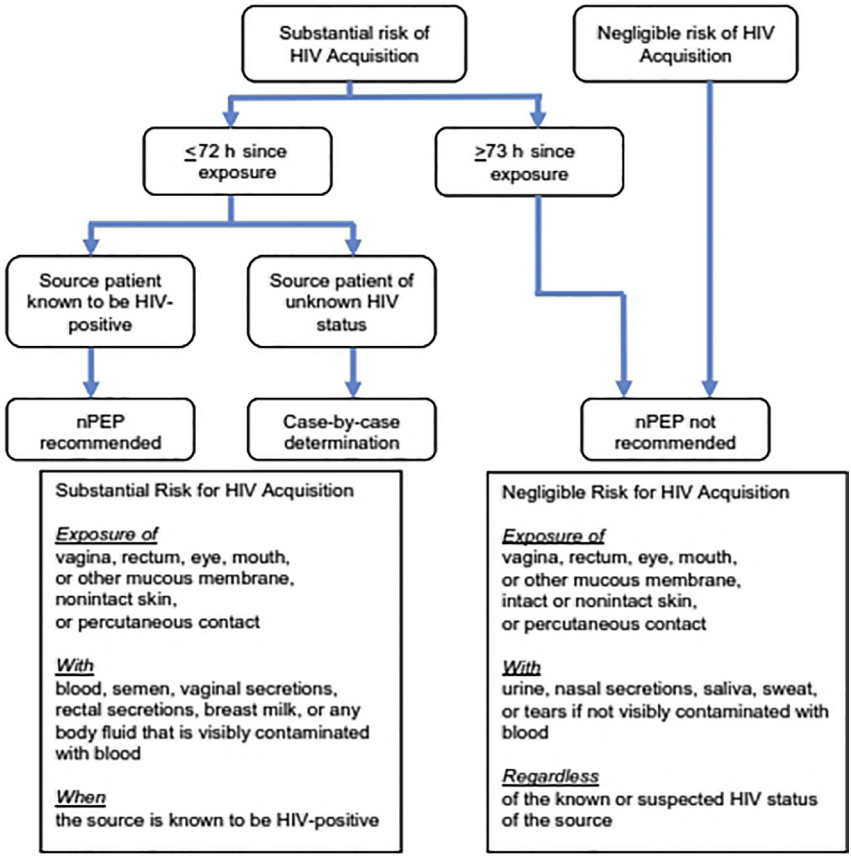

Fig. 1. Algorithm for evaluation and treatment of possible nonoccupational HIV exposure. (*From* Centers for Disease Control and Prevention. Updated guidelines for antiretroviral postexposure prophylaxis after sexual, injection drug use, or other nonoccupational exposure to HIV—United States, 2016. 2016. Available at: https://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf. Accessed December 2, 2018.)

Clinical implementation

A summary of the 2016 US CDC nPEP guidelines [2] is as follows.

- Clinicians should evaluate persons rapidly for nPEP when care is sought 72 hours or less after a potential nonoccupational exposure that presents a substantial risk for HIV acquisition. Fig. 1 displays the CDC evaluation and management algorithm, as well as definitions for ''substantial risk'' and ''negligible risk.'' If the source of the exposure is known to be HIV infected, nPEP is recommended. If the HIV status of the source of exposure is unknown, recommendation for nPEP should be determined on a case-by-case basis. nPEP should not be initiated 73 hours or more after exposure or if there is negligible risk for HIV acquisition.
- At the initial evaluation visit, the clinician should determine the HIV status of the potentially exposed person and the exposure source person (if possible), the timing and characteristics of the exposure for which care is being sought, and the frequency of possible HIV exposures, as well as assessment for other needed treatment or prophylaxis (eg, STIs, pregnancy).
- All persons considered for nPEP should be tested for HIV, preferably using rapid combined antigen/antibody, or antibody blood tests. If rapid tests are unavailable and nPEP is otherwise indicated, it should be started without delay and can be later discontinued if the patient is determined to already be infected or the exposure source is determined to not be infected.
- All persons offered nPEP should be prescribed a 28-day course of a 3-drug antiretroviral regimen.
  - The preferred regimen for otherwise healthy adults and adolescents is TDF 300 mg with emtricitabine 200 mg once daily **plus** raltegravir 400 mg twice daily or dolutegravir 50 mg/d.[a]
  - The alternative regimen for otherwise healthy adults and adolescents is TDF 300 mg with emtricitabine 200 mg once daily **plus** darunavir 800 mg and ritonavir 100 mg/d.
  - For regimens for children, persons with impaired renal function, and pregnant women, see the nPEP guidelines [2].
- All persons evaluated for possible nPEP should also be provided any indicated prevention, treatment, or supportive care for other exposure-associated health risks and conditions (eg, bacterial STIs, traumatic injuries, hepatitis B and C virus infections, or pregnancy).
- All persons who report behaviors or situations that place them at risk for frequently recurring HIV exposures (eg, injection drug use, sex without condoms) or who report receipt of 1 or more courses of nPEP in the past year should be provided risk-reduction counseling and intervention services, including consideration of preexposure prophylaxis (PrEP; discussed elsewhere in this article).
- nPEP should only be provided for infrequent exposures. Patients who have frequent, recurrent exposures should be provided with intensive risk-reduction interventions and consideration of prescription of PrEP. However, if the most recent exposure was within 72 hours of the evaluation, nPEP may be indicated with subsequent transition to PrEP.
- Laboratory testing and the recommended follow-up schedule include HIV, STI, pregnancy, and kidney and liver function testing (Table 2). Ideally, follow-up

should occur at 4 to 6 weeks, 3 months, and 6 months after exposure. Laboratory testing for the exposure source person and for individuals who seroconvert is also outlined [2].

According to the guidelines, nPEP must be initiated within 72 hours of exposure. However, exposures often occur outside of routine office hours when office staff are present to assist with the paperwork that is often required to authorize nPEP. Although manufacturers have patient-assistance programs for those without insurance and copay cards to offset high copays for medications, these programs require knowledge and familiarity on the part of the clinician and the pharmacist, as well as time to complete the necessary forms, such as a letter of medical necessity. Clinicians need to plan ahead to implement office policies to expedite the process of authorizing nPEP to ensure patients can start treatment within the required 72-hour window after exposure. Additionally, nPEP is likely to be more effective the sooner it is started after exposure, so timeliness is critical. One strategy is establishing a relationship with local pharmacies, which can dramatically improve the nPEP process. After-hours and urgent and emergent care centers should identify and develop relationships with 24-hour pharmacies, and encourage them to stock nPEP medications. A pilot program in Florida with an established nationwide retail pharmacy has proven to be an effective collaboration that has improved timely access to nPEP medications (unpublished data, D. Straub, 2018).

[a]Since the publication of the nPEP guidelines, additional data suggest safety concerns associated with use of dolutegravir in women at risk for pregnancy. In an ongoing National Institutes of Health-funded observational study in Botswana, a recent preliminary unscheduled data analysis suggested that exposure to dolutegravir-containing regimens at conception may increase the risk of neural tube defects. Four infants with neural tube defects were born to 426 women exposed to dolutegravir at conception, yielding a proportion of 0.9%, as compared with 0.1% in infants of women exposed to other antiretroviral drugs at conception. According to the manufacturer of dolutegravir, a complete package of reproductive toxicology studies showed no evidence of adverse developmental outcomes [16]. Although surveillance is ongoing, as a result of this preliminary data, the CDC recommended in May 2018 that clinicians prescribing nPEP should avoid the use of dolutegravir for nonpregnant women of childbearing potential who are sexually active or have been sexually assaulted and who are not using an effective birth control method, as well as for women early in pregnancy. The preferred regimen for nPEP for these women includes raltegravir, tenofovir, and emtricitabine (as described). Furthermore, all women of childbearing potential starting nPEP should have a pregnancy test performed. If the nPEP regimen for a nonpregnant woman of childbearing potential must include dolutegravir (eg, raltegravir is not available), she should use an effective birth control method until the nPEP regimen is completed. Additionally, dietary folic acid 400 μg is recommended daily [17].

Table 2
Recommended schedule of laboratory evaluations of source and exposed persons for providing nPEP with preferred regimens

	Source	Exposed persons			
Test	Baseline	Baseline	4–6 wk after exposure	3 mo after exposure	6 mo after exposure
		For all persons considered for or prescribed nPEP for any exposure			
HIV Ag/Ab testing[a] (or antibody testing if Ag/Ab test unavailable)	✓	✓	✓	✓	✓[b]
Hepatitis B serology, including: Hepatitis B surface antigen Hepatitis B surface antibody Hepatitis B core antibody	✓	✓	—	—	✓[c]
Hepatitis C antibody test	✓	✓	—	—	✓[d]
		For all persons considered for or prescribed nPEP for sexual exposure			
Syphilis serology[e]	✓	✓	✓	—	✓
Gonorrhea[f]	✓	✓	✓[g]	—	—
Chlamydia[f]	✓	✓	✓[g]	—	—
Pregnancy[h]	—	✓	✓	—	—
		For persons prescribed tenofovir DF + emtricitabine + raltegravir or tenofovir DF + emtricitabine + dolutegravir			
Serum creatinine (for calculating estimated creatinine clearance[i])		✓	✓	—	—
Alanine transaminase, aspartate aminotransferase		✓	✓	—	—
		For all persons with HIV infection confirmed at any visit			
HIV viral load	✓	✓[j]			
HIV genotypic resistance	✓	✓[j]			

Abbreviations: Ag/Ab, antigen/antibody combination test; tenofovir DF, tenofovir disoproxil fumarate.

[a]Any positive or indeterminate HIV antibody test should undergo confirmatory testing of HIV infection status.

[b]Only if hepatitis C infection was acquired during the original exposure; delayed HIV seroconversion has been seen in persons who simultaneously acquire HIV and hepatitis C infection.

[c]If exposed person susceptible to hepatitis B at baseline.

[d]If exposed person susceptible to hepatitis C at baseline.

[e]If determined to be infected with syphilis and treated, should undergo serologic syphilis testing 6 mo after treatment.

[f]Testing for chlamydia and gonorrhea should be performed using nucleic acid amplification tests. For patients diagnosed with a chlamydia or gonorrhea infection, retesting 3 months after treatment is recommended (1) for men reporting insertive vaginal, anal, or oral sex, a urine specimen should be tested for chlamydia and gonorrhea, (2) for women reporting receptive vaginal sex, a vaginal (preferred) or endocervical swab or urine specimen should be tested for chlamydia and gonorrhea, (3) for men and women reporting receptive anal sex, a rectal swab specimen should be tested for chlamydia and gonorrhea, and (4) for men and women reporting receptive oral sex, an oropharyngeal swab should be tested for gonorrhea (http://www.cdc.gov/std/tg2015/tg-2015-print.pdf).

[g]If not provided presumptive treatment at baseline, or if symptomatic at follow-up visit.

[h]If a woman of reproductive age, not using effective contraception, and with vaginal exposure to semen.

[i]eCrCl = estimated creatinine clearance calculated by the Cockcroft-Gault formula; eCrClCG = [(140 – age) × ideal body weight] + (serum creatinine × 72) (× 0.85 for females).

[j]At first visit where determined to have HIV infection.

From the Centers for Disease Control and Prevention. Updated guidelines for antiretroviral postexposure prophylaxis after sexual, injection drug use, or other nonoccupational exposure to HIV United States, 2016. 2016. Available at: https://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf. Accessed December 2, 2018.

PREEXPOSURE PROPHYLAXIS

PrEP is the use of antiretroviral medications before potential exposure to prevent HIV infection. In the pivotal efficacy trials, use of tenofovir-based PrEP was associated with 44% to 75% decrease in new HIV infections [18–21]. Up to a 92% reduction in infections is achieved with high levels of adherence [20–22]. However, the degree of adherence necessary to achieve high levels of protection depends on the route of exposure: no new HIV infections were documented among MSM taking 4 or more doses of PrEP per week [23], whereas protection in the female genital tract requires daily adherence [24]. In 2012, the US Food and Drug Administration (FDA) approved the first (and currently only) oral medication for PrEP (fixed-dose combination tenofovir disoproxil fumarate-emtricitabine [TDF-FTC; Truvada]) for use in adults. In May 2018, the FDA expanded the indication for TDF-FTC to include adolescents weighing 35 kg or more [25].

Preexposure prophylaxis in adolescents

To date, only 2 published studies describe the results of PrEP trials conducted with adolescents: one study included 18- to 22-year-old MSM [26] and one included 15- to 17-year-old MSM [27]. Both of these US studies were open-label demonstration projects that were not designed to assess efficacy. Among two hundred 18- to 22-year-old MSM, 70% completed the study through week 48. Although most participants reported that taking a daily oral medication was acceptable, adherence waned over time: only 34% of participants were taking 4 or more doses per week at the end of the study [26]. Among the 15- to 17-year-olds, 46 completed the 48-week study, with only 22% reporting taking 4 or more doses per week by the end of the study [27]. In both studies, adherence was 49% to 57% when study visits occurred monthly and then substantially decreased when visits occurred every 3 months [26,27], as currently recommended by the CDC PrEP guidelines [28]. These data, taken together with a metaanalysis demonstrating lower adherence to PrEP in younger users [29], suggest that more frequent follow-up of younger PrEP users may be warranted to bolster adherence.

Safety

Use of tenofovir-based PrEP is associated with dose-dependent decreases in bone density in MSM and transgender women [30,31], heterosexual adults [32], and adult women [33], which has been cited as a barrier to prescribing PrEP to youth [34]. No increase in fractures has been documented in PrEP users [30–33], and bone density recovers after the cessation of PrEP [31,33]. Among 18- to 22-year-old PrEP users, bone density also decreased [35]. Follow-up studies investigating whether bone density among younger PrEP users recovers will be critical to addressing clinician concerns about using PrEP in youth.

Tenofovir-containing PrEP is associated with decreases in renal function among adults [36,37], but these decreases quickly reversed after discontinuation of PrEP [36,37]. Among younger PrEP users, a slight increase in serum

creatinine occurred over the first 12 weeks of use, but there was no change in the estimated glomerular filtration rate [35]. Consequently, the CDC PrEP guidelines recommend that patients using PrEP have an estimated creatinine clearance of 60 mL/min or greater [28].

Although HIV viral resistance develops among PrEP users, clinical trial data suggest that it occurs less frequently among those who become HIV infected while using PrEP and more often when PrEP is started in the setting of undetected HIV infection [38–40]. Most new HIV infections that occurred in people taking PrEP were related to poor adherence [41,42], although new infections have been reported among PrEP users with excellent adherence [43]. Among those who become HIV infected while taking PrEP, detection of infection may be delayed [44], but HIV viral load and $CD4^+$ T-cell counts are similar to those of people who become infected while taking placebo [45].

Recent implementation studies suggest that some people taking PrEP participate in riskier behaviors. In 1 study, 35% of PrEP users reported less condom use, more condomless sex partners, and more condomless oral sex when compared with nonusers [46]. In another study of MSM who started PrEP, 28% had an increase in STIs from before PrEP to after PrEP [47]. Because a subset of people using PrEP may participate in riskier sexual behaviors, it is critical to routinely screen for STIs in this population as outlined in the PrEP guidelines [28].

Patient uptake and attitudes

The greatest awareness of PrEP is among adult MSM [46,48,49]; however, only 7% to 9% reported taking it [46,48]. Among young transwomen, only 31% were aware of PrEP and 5% reported having taken it [50]. Less than one-quarter of women [51] and 33% of female sex workers reported awareness of PrEP [52]. Similarly, only 18% to 37% of people who inject drugs reported awareness of PrEP [53,54], but only 0.03% to 1.80% had ever taken it [53,54]. Even HIV-infected adults have low awareness of PrEP, although most would encourage PrEP use by HIV-uninfected partners [55]. Among adolescents, 64% of transwomen [56] and 39% of black MSM reported awareness of PrEP [57].

Even though PrEP has been approved by the FDA for use in adults since 2012, few people who are eligible for PrEP have taken it. In 1 study, only 13% of MSM and transwomen who met the criteria for PrEP were taking it; the lowest rate of PrEP use was in 18- to 24-year-olds [58]. The majority of people who have received prescriptions for PrEP to date are 25 to 44 years old and have commercial insurance; 95% are men and 69% are white [59], suggesting that there may be disparities in access and uptake for other age groups (<10% of prescriptions were for 18- to 24-year-olds) [59], women, and other races/ethnicities. Even when prescribed PrEP, many people do not fill the prescription and actually start PrEP [60]. Further, rates of discontinuation are fairly high: only 47% of MSM who initiated PrEP were engaged in PrEP care 13 months later [60].

Potential PrEP users cite barriers including concerns about cost [46], side effects [46], the need for adherence to daily medication [49,61], a lack of perceived risk of HIV infection [49], uncertainty about how to access PrEP [46,61], a lack of awareness of PrEP [46], and a lack of health insurance [46]. PrEP-related stigma is also a significant barrier. Studies describe "PrEP shaming" [61], as well as patient concerns about how PrEP use would be perceived by others [51]. PrEP users report that other people may assume that they participate in risky sex or that they are HIV infected [62]. Even those who may be candidates for PrEP perceived it to be only for those who are "promiscuous". [48] Younger PrEP users, particularly those under age 18 years of age, may face additional barriers to PrEP, including a lack of trust between clinicians and youth, inexperience navigating the health care system, a lack of transportation, cost, and concerns about loss of confidentiality [63].

Clinician attitudes and behaviors

Among clinicians caring for adults, frequently cited barriers to providing PrEP include concerns about patient adherence [64,65], increases in risky behaviors among people taking PrEP [64,65], side effects [64], cost [64,65], lack of clinical time [65], development of HIV resistance [64,65], insufficient infrastructure to provide PrEP [65], failure of PrEP users to keep scheduled follow-up visits [65], and insufficient reimbursement of clinicians for PrEP services [64,65]. Few studies have examined PrEP-related attitudes of clinicians caring for adolescents. Clinicians caring for HIV-infected and -uninfected youth reported concerns including patient adherence, confidentiality, the legal ability to prescribe PrEP confidentially, increases in riskier sexual behaviors, cost/insurance coverage, a lack of organizational resources, and community stigma around HIV [34]. Among physicians from various specialties who provide primary care to adolescents, awareness of PrEP was fairly low, with 37% of physicians reporting some familiarity with PrEP. These primary care physicians identified barriers unique to PrEP use in youth, including the potential impact of PrEP on growth and development, parental opposition to PrEP use, potential breaches of confidentiality, physician concerns about prescribing PrEP to minors, a lack of legal clarity about whether PrEP could be prescribed to youth confidentially, and concerns about whether pharmacists might limit youth access to PrEP. Overall, more physicians reported the intention to recommend PrEP than prescribe it [66], which could impact youth access to PrEP. An online survey of members of the Society for Adolescent Health and Medicine found that 93% had heard of PrEP, 65% were willing to prescribe it to 13- to 17-years-olds, and 78% were willing to prescribe it to 18- to 24-years-olds [67].

Clinical implementation

The only medication currently approved by the US FDA for PrEP is a fixed-dose combination of TDF 300 mg and emtricitabine 200 mg (TDF-FTC) administered once daily. The CDC PrEP guidelines were updated in 2017

[28]. The CDC also published a clinical provider's supplement that provides resources that can be used to provide PrEP care, including counseling resources for clinicians and educational handouts for patients [68]. These documents have not been updated to reflect the recent FDA approval of PrEP for use in adolescents. Several US organizations, including the Society for Adolescent Health and Medicine [69], the American College of Obstetricians and Gynecologists [70], and the International AIDS Society-USA [71], have released statements supporting the use of PrEP among those at risk of HIV infection.

The CDC PrEP guidelines include suggested indications for PrEP (Table 3). Baseline laboratory evaluations should include HIV testing (with an antigen/antibody test [preferred], antibody test, or rapid point-of-care FDA-approved fingerstick blood test), renal function testing (including calculation of estimated

Table 3
Summary of current US PrEP guidance (2017)

	MSM	Heterosexual women and men	Injection drug users
Detecting substantial risk of acquiring HIV infection	HIV-positive sexual partner Recent bacterial STI[a] High number of sex partners History of inconsistent or no condom use Commercial sex work	HIV-positive sexual partner Recent bacterial STI[b] High number of sex partners History of inconsistent or no condom use Commercial sex work In high-prevalence area or network	HIV-positive injecting partner Sharing injection equipment
Clinically eligible	Documented negative HIV test result before prescribing PrEP No signs/symptoms of acute HIV infection Normal renal function; no contraindicated medications Documented hepatitis B virus infection and vaccination status		
Prescription	Daily, continuing, oral doses of TDF/FTC (Truvada), ≤90 d supply		
Other services	Follow-up visits at least every 3 mo to provide the following: HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment At 3 mo and every 6 mo thereafter, assess renal function Every 6 mo, test for bacterial STIs		
	Do oral/rectal STI testing	For women, assess pregnancy intent Pregnancy test every 3 mo	Access to clean needles/syringes and drug treatment services

[a]Gonorrhea, chlamydia, syphilis for MSM including those who inject drugs.
[b]Gonorrhea, syphilis for heterosexual women and men including those who inject drugs.
From Centers for Disease Control and Prevention. Preexposure prophylaxis for the prevention of HIV infection in the United States—2017 Update: a clinical practice guideline. 2018. Available at: https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf. Accessed November 6, 2018.

creatinine clearance using the Cockcroft-Gault formula), hepatitis B serology, and STI testing. An estimated creatinine clearance of less than 60 mL/min is a contraindication to TDF-FTC PrEP. Evaluating hepatitis B status is important because reactivation of hepatitis B and resultant liver toxicity can occur when PrEP is stopped [28]. Hepatitis C testing is recommended for people who have injected drugs. Patients should be counseled that the time required to achieve protective levels of PrEP ranges from 7 days for the rectal compartment to 20 days for blood and the cervicovaginal compartment [28]. The most common side effects include headache and gastrointestinal distress. The CDC recommends that PrEP be limited to a 3-month supply at a time and that patients be evaluated every 3 months for HIV testing, pregnancy testing, PrEP prescription refills, assessment of side effects and adherence, and STI testing. Creatinine clearance should be monitored every 6 months, and the continued need for PrEP should be evaluated every year [28].

Insurance coverage for PrEP and related services varies by carrier. The manufacturer of PrEP (Gilead Sciences, Inc., Foster City, CA) offers a medication assistance program [72]. The web site PleasePrEPMe.org contains links to other potential financial assistance programs [73], and the CDC published a brochure to help patients navigate paying for PrEP [74].

LEGAL ISSUES FOR MINOR-AGED ADOLESCENTS

In all 50 states and the District of Columbia, minors can consent to testing and treatment for STIs without parental consent, and 32 states include HIV as an STI [75]. However, the statutes are less clear regarding HIV prevention. The provision of nPEP could be interpreted as providing treatment, and thus within minor consent rights for those states that include HIV as an STI. For states that do not include HIV as an STI, minor consent for HIV prevention may not be legally permissible. Although the US FDA approved TDF-FTC for PrEP in youth, clinicians considering prescribing PrEP to youth should be familiar with their local legal statutes, because these vary by jurisdiction, and consider using legal expertise to help interpret the statutes where the laws are not clear. A CDC review of legal statutes demonstrated that no states explicitly prohibit minors from accessing PrEP without parental involvement, and 16 states specifically allow minors to access PrEP independently [76]. Additionally, although the age 18 years is considered the age of majority in most states, it varies among different states [76].

Finally, the legal right to consent to confidential health care does not ensure confidential health care, because insurance laws often require explanation of benefits statements be sent to the primary insurance holder. Therefore, a minor's use of insurance benefits for nPEP and PrEP services may be inadvertently communicated to their parent(s). Clinicians attempting to provide HIV prevention services to minors who are seeking confidential care should understand and explain these nuances and potential breaches of confidentiality to their patients.

SUMMARY

The nPEP and PrEP strategies reduce the risk of HIV acquisition. nPEP must be initiated within 72 hours of potential exposure to HIV and current guidelines recommend a 3-drug antiretroviral regimen taken for 28 days. PrEP should be considered for people with an ongoing high risk of HIV infection and current guidelines recommend a daily oral 2 drug antiretroviral regimen. The US CDC maintains updated published guidelines for clinicians who are prescribing nPEP and PrEP. Clinicians should be aware of local legal statutes that may impact the ability to provide confidential nPEP and PrEP services to minor-aged adolescents.

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