MODULE 12 ADOLESCENTS AND YOUNG ADULTS

# WHO IMPLEMENTATION TOOL FOR PRE-EXPOSURE PROPHYLAXIS (PrEP) OF HIV INFECTION

JULY 2018





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# Introduction

Following the WHO recommendation in September 2015 that "oral pre-exposure prophylaxis (PrEP) should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches", partners in countries expressed the need for practical advice on how to consider the introduction of PrEP and start implementation. In response, WHO has developed this series of modules to support the implementation of PrEP among a range of populations in different settings.

Although there is growing acknowledgement of PrEP's potential as an additional HIV prevention option, and countries are beginning to consider how PrEP might be most effectively implemented, there has been limited experience with providing PrEP outside research and demonstration projects in low- and middle-income countries. Consequently, there is often uncertainty around many implementation issues. The modules in this tool provide initial suggestions for the introduction and implementation of PrEP based on currently available evidence and experience. However, it is recognized that this evidence may evolve following wider PrEP use; therefore, it is likely that this tool will require regular updating.

PrEP should not replace or compete with effective and well-established HIV prevention interventions, such as comprehensive condom programming for sex workers and men who have sex with men and harm reduction for people who inject drugs. Many people who could benefit most from PrEP belong to key population groups that may face legal and social barriers to accessing health services. This needs to be considered when developing PrEP services. Although the public health approach underpins the WHO guidance on PrEP, the decision to use PrEP should always be made by the individual concerned.

# Target audience and scope of tool

This PrEP tool contains modules for a range of stakeholders to support them in the consideration, planning, introduction and implementation of oral PrEP. The modules can be used on their own or in combination. In addition, there is a module for individuals interested in or already taking PrEP. (See summary of modules below.)

This tool is the product of collaboration between many experts, community organizations and networks, implementers, researchers and partners from all regions. The information presented is aligned with WHO's 2016 consolidated guidelines on antiretroviral medicines.

All modules make reference to the evidence-based 2015 WHO recommendation on PrEP. They do not make any new recommendations on PrEP, focusing instead on suggested implementation approaches.

# **Guiding principles**

It is important to adopt a public health, human rights and people-centred approach when offering PrEP to those at substantial risk of HIV. Similar to other HIV prevention and treatment interventions, a human rights-based approach gives priority to issues concerning universal health coverage, gender equality and health-related rights including accessibility, availability, acceptability and quality of PrEP services.

#### SUMMARY OF MODULES



Module 1: Clinical. This module is for clinicians, including physicians, nurses and clinical officers. It gives an overview of how to provide PrEP safely and effectively, including: screening for substantial risk of HIV; testing for HIV before initiating someone on PrEP and how to follow up PrEP users and offer counselling on adherence.



Module 2: Community educators and advocates. Community educators and advocates are needed to increase awareness about PrEP in their communities. This module provides information on PrEP that should be considered in community-led activities that aim to increase knowledge about PrEP and generate demand and access.



Module 3: Counsellors. This module is for staff who counsel people as they consider PrEP or start taking PrEP and support them in coping with side-effects and adherence strategies. Those who counsel PrEP users may be lay, peer or professional counsellors and healthcare workers, including nurses, clinical officers and doctors.



Module 4: Leaders. This module aims to inform and update leaders and decision-makers about PrEP. It provides information on the benefits and limitations of PrEP so that they can consider how PrEP could be effectively implemented in their own settings. It also contains a series of frequently asked questions about PrEP.



Module 5: Monitoring and evaluation. This module is for people responsible for monitoring PrEP programmes at the national and site levels. It provides information on how to monitor PrEP for safety and effectiveness, suggesting core and additional indicators for site-level, national and global reporting.



Module 6: Pharmacists. This module is for pharmacists and people working in pharmacies. It provides information on the medicines used in PrEP, including on storage conditions. It gives suggestions for how pharmacists and pharmacy staff can monitor PrEP adherence and support PrEP users to take their medication regularly.



Module 7: Regulatory officials. This module is for national authorities in charge of authorizing the manufacturing, importation, marketing and/or control of antiretroviral medicines used for HIV prevention. It provides information on the safety and efficacy of PrEP medicines.



Module 8: Site planning. This module is for people involved in organizing PrEP services at specific sites. It outlines the steps to be taken in planning a PrEP service and gives suggestions for personnel, infrastructure and commodities that could be considered when implementing PrEP.



Module 9: Strategic planning. As WHO recommends offering PrEP to people at substantial HIV risk, this module offers public health guidance for policy-makers on how to prioritize services, in order to reach those who could benefit most from PrEP, and in which settings PrEP services could be most cost-effective.



Module 10: Testing providers. This module is for people who provide testing services at PrEP sites and laboratories. It offers guidance in selecting testing services, including screening of individuals before PrEP is initiated and monitoring while they are taking PrEP. Information is provided on HIV testing, creatinine, HBV and HCV, pregnancy and STIs.



Module 11: PrEP users. This module provides information for people who are interested in taking PrEP to reduce their risk of acquiring HIV and people who are already taking PrEP – to support them in their choice and use of PrEP. This module gives ideas for countries and organizations implementing PrEP to help them develop their own tools.



Module 12: Adolescents and young adults. This module is for people who are interested in providing PrEP services to older adolescents and young adults who are at substantial risk for HIV. It provides information on: factors that influence HIV susceptibility among young people; clinical considerations for safety and continuation on PrEP; ways to improve access and service utilization; and inclusive monitoring approaches to improve the recording and reporting of data on young people.

# **ANNEXES**

Review of evidence. A wide range of evidence including the following two systematic reviews informed the 2015 WHO recommendation on PrEP for people at substantial risk of HIV infection: (i) Fonner VA et al. Oral tenofovir-based HIV pre-exposure prophylaxis (PrEP) for all populations: a systematic review and meta-analysis of effectiveness, safety, behavioural and reproductive health outcomes; (ii) Koechlin FM et al. Values and preferences on the use of oral preexposure prophylaxis (PrEP) for HIV prevention among multiple populations: a systematic review of the literature.

Annotated Internet resources. This list highlights some of the web-based resources on PrEP currently available together with the stakeholder groups they are catering to. WHO will continue to provide updates on new resources.

# The PrEP module on adolescents and young adults

This module is intended to complement the 11 other modules that are part of the WHO PrEP tool. It addresses unique aspects and considerations for delivering HIV prevention and care services to sexually mature adolescents and young adults – typically, people ages 15–24 years. The intended audience for this module is the range of stakeholders for other modules in this WHO PrEP tool who may also have interest in or provide services to at-risk populations of vulnerable young people, including those from five key populations (men who have sex with men, people in prisons and closed settings, people who use drugs, people who sell sex and transgender people).

Age group definitions Adolescent: 10–19 years Youth: 15–24 years Young adult: 18–24 years Young person: 10–24 years

# Epidemiology of HIV among adolescents and young adults

The HIV epidemic among young people has many faces around the world. Each day, 37% of the approximately 4,500 daily new HIV infections occurring beyond childhood, are among youth ages 15 to 24 years (1). Adolescent girls and young women make up approximately one in every five of these new infections, and in sub-Saharan Africa where the youth population has expanded by nearly 100 million over the past three decades, infection rates in adolescent girls and young women outpace those in their male counterparts by three to one (Fig. 1) (2).

#### Fig. 1. Twenty countries with the highest HIV incidence rate among young women ages 15–24 years



Source: UNAIDS, 2018 estimates.

Globally, the HIV epidemic has disproportionately impacted key populations and their sexual partners (*3*). In regions including Central Asia, Europe, North America, the Middle East and North Africa, new HIV infections among members of these key populations account for more than 90% of all new infections (*4*). The few data that are available on young key populations suggest that they are even more disproportionately affected by HIV in most settings (*3*, *5*). Young members of key populations often face tremendous challenges, including legal and socio-cultural issues related to societal attitudes about sexuality in youth, compounded by behaviours that are highly stigmatized (for example, same-sex relationships, transactional sex, alcohol and drug use, teenage pregnancy), leading to increased vulnerability to HIV infection and considerable barriers to care including HIV testing and treatment services. These issues can also impede an appropriate public health response for these vulnerable populations, resulting in gaps in areas such as crucially needed epidemiologic surveillance across regions (*3*) and vital research on how to address knowledge gaps concerning the care and treatment of HIV-affected young communities (*6*, *7*).

In both generalized and concentrated epidemic settings, HIV in young people often occurs within the context of a range of conditions such as poor mental health, substance use (alcohol and other drugs) and emotional and social issues including gender-based violence. These conditions can place young people at substantial risk of acquiring HIV and other sexually transmitted infections (STIs) (8–12). Although data on adolescents and young adults infected with HIV are limited in resource-constrained settings, it is clear that these comorbidities can also make health-seeking behaviours more challenging for youth (13). Further contributing to risk in this population is poor access to and uptake of effective biomedical HIV prevention interventions, such as PrEP (14, 15), due to structural challenges in the form of ethical, legal, policy and regulatory hurdles (16). Furthermore, perceived challenges in working with adolescents often leads to their exclusion from critical research studies that are conducted in adults, resulting in an absence of data that can help to inform guidance and policy on programme implementation among young people (17).

# Factors influencing HIV susceptibility among adolescents and young adults

A number of factors are associated with the risk of the transmission and acquisition of HIV by young people, including biologically mediated conditions and events, compounded by psychosocial, behavioural and structural drivers.

# **Biological factors**

Biological factors that are linked with the transmission and acquisition of HIV by young people include perturbations of the mucosal microbiome (18) and inflammatory milieu, which can be the result of early sexual debut in young women (19). STIs, including herpes simplex virus (20, 21), human papillomavirus (22), gonorrhoea, chlamydia and syphilis (23), which lead to inflammation and disruptions in the mucosal epithelium (24), increase the risk of HIV acquisition and disproportionately affect young people. The data are mixed on the role of cervical ectopy in increased HIV risk. Cervical ectopy occurs when the columnar epithelium of the endocervical canal extends outwards into the ectocervix, which is common in developing adolescent girls. Methodological limitations with many studies preclude definitive conclusions about ectopy and HIV risk (25).

# Behavioural and psychosocial factors

Behavioural and psychosocial factors experienced by adolescents and young adults may further increase their susceptibility to HIV infection. Beginning with lower levels of overall health literacy, adolescents and young adults ages 15–24 years in 79 countries that contributed data to the Joint United Nations Programme on HIV/AIDS (UNAIDS) in 2016 had very low levels of knowledge about HIV risk and prevention, with a median rate of 29% across these countries (*26*). Stigmatized behaviours among key populations, such as sex among men, injecting drugs or selling sex, also can lead to increased HIV risk (*27–29*). Furthermore, common behaviours during adolescent development (for example, poor impulse control, risk taking, inadequate planning for safe sex, and mood disorders) (*30–33*) place some individuals at risk for HIV infection and correlate with poor health-seeking behaviours and poor adherence to health care. Adolescents who have older partners, difficulty negotiating condom use, rely on transactional sex for basic material needs, experience high rates of sexual violence, or use substances with sex, can have very high rates of STIs (*34*). Adolescents and young adults attending PrEP programmes need to be routinely screened for STIs and promptly treated. Adolescents and young adults will need youth-friendly services and strategies to ensure that they adhere to daily PrEP as an HIV prevention tool (*14*, *35–37*).

# Lerato's story: Risky relationships

Lerato is 22 years old. She lives in Soweto, South Africa. She has a grade 12 certificate, and she is unemployed. Lerato lives with her mother and her young daughter, who was fathered by a previous partner. She is currently in a relationship that she describes as "on and off" and "complicated". After a series of risky relationships, Lerato started taking PrEP to protect herself from HIV. She first heard about PrEP from the clinic nurse when visiting the adolescent clinic in Hillbrow just over 6 months ago, to collect her monthly supply of contraceptive pills.

"I'm lucky to have escaped HIV this far in my life. I want to keep it that way."

She and Sizwe, her current boyfriend, have been together for about 18 months. Lately, there has been intense conflict and mutual mistrust. Sizwe is "a jealous man", who regularly checks the messages on her phone to see if she is conducting other relationships in secret. Sizwe works in a town several hours' drive from Johannesburg, which means that they cannot spend much time together. Over the course of their relationship, Sizwe has assaulted Lerato physically several times, during arguments when he accuses her of infidelity. Lerato says she loves Sizwe, despite his temper and increasingly possessive behaviour. She also trusts him and believes that he has been faithful to her even while living far away in another town, although her friends tell her that he probably has other partners because "that's just how men are". When he comes to visit on weekends, they have sex without condoms. Lerato believes it would be futile to try to insist on using them, as they have been together for too long and because to do so would simply trigger an argument.

Before Sizwe, Lerato had a relationship with Isaac, the father of her child. She describes him as "a good man" and someone whom she had hoped to marry. They had been together only six months when she fell pregnant (at the age of 18). Initially, they had used condoms "most of the time", but condom use became more erratic as the relationship became more serious. Lerato had also stopped using the injectable contraceptive because of the frequent spotting between periods that it was causing. When her pregnancy became known, Isaac deserted her and was never seen or heard from again. Lerato was deeply hurt by his abandonment and sees this break up as the start of a risky period for her.

Initially, Lerato found it challenging to fit PrEP into her lifestyle. She was also worried about possible side effects and whether she would manage to take a pill every day. The clinic nurse gave her useful tips on how to remember – such as taking the pill every evening at the same time when her daily TV soap opera started, or setting up an alarm on her phone. She has now become accustomed to the routine of daily pill-taking, although she has not yet told Sizwe that she is taking PrEP. She regards it as "none of his business" and knows she is "doing something good and taking control of [her] life."

Lerato sees PrEP as a fresh start and a chance to start planning her future – for herself and her daughter. Looking back on her relationships, Lerato says, "I'm lucky to have escaped HIV this far in my life. I want to keep it that way".

\* Name changed for confidentiality.

### **Structural factors**

Like anyone else, adolescents and young adults have basic needs for food, shelter, education, family and social support and economic security (including work opportunities). They might also desire commodities (for example, fashionable clothes, jewellery, makeup, mobile phones) that enable them to attain a certain lifestyle and an enhanced social network (*38, 39*). To meet both these basic needs and desires, adolescents and young adults sometimes engage in partner selection behaviours that can increase the risk of HIV acquisition, including engaging in transactional sex or intergenerational sex (*38–41*). These behaviours, with their inherent problems such as power imbalance and intimate partner violence, can compound the risk of HIV acquisition (*42*). However, in generalized epidemic settings, where HIV risk is high, even sexual activity that does not involve these partner selection behaviours or psychosocial problems can result in HIV acquisition.

While the multiple factors that can make adolescents and young adults susceptible to HIV can and often do seem to occur together in a way that multiplies the likelihood of infection, these factors also provide important opportunities for interventions that mitigate the risk of HIV acquisition. With appropriate planning and support, comprehensive HIV prevention programmes that include PrEP can offer substantial benefits to adolescents and young adults during periods of HIV risk.

# Identifying adolescents and young adults who may benefit from PrEP

Prioritizing young people at substantial risk of HIV infection who are willing to take PrEP, or who may, with assistance, be motivated to continue PrEP, is important for programme efficiency. Identifying these individuals can be a challenge.

In the context of PrEP, WHO defines substantial risk as an incidence of HIV infection in the absence of PrEP that is sufficiently high (>3%) to make offering PrEP potentially cost-effective. Due to the heterogeneity in new infections by age, sex and location, the best approach to identifying groups with this level of incidence is to analyse all local and national epidemiologic data available to identify specific geographic and subpopulation groups at particularly high risk.

National and regional estimates of HIV prevalence and incidence by age and sex are available for most countries globally. Where available, subnational estimates of HIV incidence show considerable heterogeneity at finer geographic levels (Fig. 2) and may be used to more precisely situate HIV prevention interventions. Where incidence estimates are not available to inform decision-making, proxy indicators such as HIV prevalence and data from cohort studies or programme data, among other sources, can be considered, although each of these has its limitations (see strategic planning module in this PrEP tool). For adolescents in particular, HIV prevalence estimates are often a good measure of age-specific cumulative HIV incidence for sexually acquired HIV, as mortality in this age group is low and infections are likely recently acquired. In addition to looking at the incidence rate, considering the total number of estimated new infections by age and sex is important; some settings or groups may have much higher expected numbers of new infections than others, even when overall HIV prevalence and incidence are similar. Focusing PrEP services where large numbers of new infections are expected will increase their potential impact. Taken together, these types of analyses will assist in assessing where phased implementation of PrEP services for young people could start.

# Fig. 2. Sub-national estimates of HIV incidence among youth in southern and eastern Africa



Source: UNAIDS, special analysis of 2016 estimates.

# Venues and platforms for providing HIV prevention services to young people

When considering where to introduce PrEP services for adolescents and young adults, a first step is assessing the current availability of services where integration of PrEP could be considered. Health services in areas with high HIV incidence and where demographic data point to the presence of large numbers of young people could be priority locations. It will then be necessary to determine how well young people are being reached currently and where more focused outreach may be necessary. Coverage assessments could be mapped by the location, availability and uptake (by sex, age and population) of related health services where PrEP could be integrated. Integrating PrEP into services that already provide HIV testing and ART will often be practical. For example, training existing staff who already provide ART to offer PrEP as well, may be more straightforward than training providers who lack familiarity with antiretroviral medications.

Other health services where PrEP may also be integrated are those that offer specific services that young people need or that specialize in youth-friendly services such as tertiary education institutions. It is particularly important for PrEP services to be integrated into platforms that are conveniently located and accessible to adolescents and young adults, demonstrate sensitivity towards women, and offer additional services such as contraception and reproductive health services. In each instance, the offer of PrEP should be part of a comprehensive package of HIV prevention and sexual and reproductive health services designed to suit the needs of various age/sex-specific groups so that adolescents and young adults can choose how to protect themselves from acquiring HIV.

Health services where integration of PrEP services could be considered may include those often used by sexually active adolescents and young adults, for example:

- HIV testing and partner notification services
- antenatal and postnatal care
- family planning services
- STI clinics
- antiretroviral therapy services for people in serodiscordant relationships
- gender-based violence services
- voluntary medical male circumcision clinics
- health services of tertiary education institutions
- specific services for young people
- mobile health clinics near educational establishments
- sites offering health services for key populations, for example: clinics serving sex workers, men who have sex with men, and transgender populations; detention facilities; and harm reduction services for people who inject drugs.

### **Risk screening**

Even in settings of high HIV incidence and prevalence, not all young people or all young members of key populations will be at substantial risk, and among those who are at high risk some may choose not to take PrEP. Furthermore, risk is not constant over time; it changes as circumstances change (43, 44). Therefore, once gaps in health service coverage at the subregional and subpopulation levels have been identified and country/programme thresholds for offering PrEP have been decided, it is important to distinguish vulnerable youth who are at risk of HIV acquisition from those who are not, based on a nuanced understanding of what constitutes "risk". This includes careful consideration of the normative adolescent developmental trajectory together with the epidemiologic, biologic, behavioural, psychosocial and structural factors influencing susceptibility to HIV.

At an individual level, identifying at-risk adolescents and young adults is challenging due to the social norms around sexual activity of young people, which can make young people reluctant to disclose their sexual behaviour. Furthermore, many adults and young people do not perceive themselves to be at risk for HIV (45–49). Perceptions can underestimate risk for a number of reasons, particularly when feelings of trust grow in sexual relationships. A literature review of qualitative studies found that people considered condoms acceptable in casual sexual relationships not characterized by expectations of commitment or fidelity. As relationships became more committed, however, continued condom use was difficult to maintain (46). For example, early data from a demonstration PrEP study in Eswatini shows sharply different risk perceptions between men and women who were screened for PrEP with a health care worker administered risk screening tool, with women viewing themselves at lower risk (Fig. 3). Moreover, approximately half of young clients determined to be at risk did not initiate PrEP (Fig 4) (50).

Risk screening tools are one means of identifying individuals at high risk for HIV and who may benefit from PrEP, especially if the client has not self-identified as being at risk. Available risk scoring tools have been validated for young women ages 18 and older and for men who have sex with men in the United States of America (51–54). The questions most often used in these tools for adolescent girls and young women include the person's age, age of sexual debut, the number and age of their sex partners, condom use, history of STIs and exposure to violence. One validated tool for men who have sex with men in the United States assessed age, number of male sex partners, unprotected anal sex, HIV status of sex partners and use of drugs such as amphetamine-type stimulants/speed (53). While risk scores can be useful, in high HIV prevalence settings a large proportion of young women may have a moderate to high risk score, which can make prioritizing PrEP challenging.

# Fig. 3. Perceived risk of HIV infection among people identified to be at risk by sex and age group in Eswatini (n=652)



Source: Hughey et al. (50)

# Fig. 4. PrEP initiation among young and adult clients identified to be at risk using a risk-screening tool administered by a health-care provider, Eswatini (n=652)







Source: Hughey et al. (50)

Since indicators of incidence/risk will differ depending on the HIV distribution among people with untreated HIV infection, antiretroviral therapy (ART) coverage, and other social and cultural contextual factors where screening is conducted, risk calculators may not apply uniformly to all subpopulations at risk. Further research is needed to determine their usefulness in different populations. In any case, some PrEP providers may not want to use risk calculators, or some potential PrEP users may not want to answer the questions. Certainly, risk calculators should not be used

Risk calculators should not be used to exclude young people from PrEP services, especially if they identify themselves as at risk and/or they are motivated to take PrEP.

to exclude young people from PrEP services, especially if they identify themselves as at risk and/or they are motivated to take PrEP. As with adults, it is likely that adolescents and young adults who seek out PrEP and are motivated to use it, whether or not they disclose their reasons for doing so, may indeed be at substantial risk. It will likely be beneficial to offer PrEP to these young clients and to make efforts to retain them in care.

An alternative or potentially complementary approach that is under evaluation is the use of decision-making tools that are patient-facing and designed to help young people consider their risk of HIV and motivation for HIV prevention in general

and to guide them in deciding which prevention methods best fit their needs. These may be paper, app-based or online tools that allow young people to assess their own risk independently without relying on health-care workers, who may not have the time to counsel them adequately or whose attitudes may influence whether or not they offer PrEP to young people. The South African She Conquers roadmaps to services are one such tool that are available in both paper format or online. It asks young people such questions as, "Are you having sex?" and "Are you using a condom each time you have sex?" before making suggestions on what to know about HIV testing, STI screening and access to contraception.

Another novel client-empowered approach that has been used for qualitative research on sexual behaviour and is being explored in the HPTN 082 PrEP trial, helps individuals understand their risk for HIV acquisition using visual narrative timelines that help to reveal the influence of emotions on sexual risk-taking and perceptions of HIV risk (55). This technique uses nonthreatening visual symbols for types of sexual experiences and enables clients to first place their experiences on a timeline rather than verbally describing them. For example, different coloured dots indicate types and frequency of sexual activity and feelings of love, and informal labels describe relationships and emotions (Fig. 5). The use of tools such as these can increase comfort when addressing sensitive topics and facilitate disclosure of intimate information that otherwise might not be shared with a health-care provider. The visual representations help clients recognize patterns in their behaviour and can form the basis of discussions between providers/counsellors and potential PrEP users about decision-making and prevention choices.



#### Fig. 5. Clients' visual representations of their own sexual history and HIV/STI risk

Key: Yellow = relationship definitions, blue = emotions experienced during relationship, hearts = experienced love, green dots = anal intercourse with a condom, purple dots = condomless anal intercourse (smaller $\rightarrow$ larger = less frequent $\rightarrow$ most frequent), pink number = HIV/STI risk ranking (5 = least risky, 1 = most risky).

Source: Goldenberg et al. © 2016 Global Public Health, 11:5-6, 699-718. Reprinted with permission from Taylor & Francis Ltd. (55)

# Marcelo's\* story, Brazil 2018

I am a cheerful young man of 22 years who discovered my gay sexual orientation at age 16. Since I came out of the closet, I have been living in fear of getting HIV. While this fear may have saved the lives of several teenagers who are discovering themselves to be gay, that same fear makes me just survive rather than truly live. I feared condoms breaking, boyfriends betraying me, and getting carried away in the moment and then getting exposed to HIV. This doubt of getting infected corroded me.

"As a gay man, PrEP lets me see my future ahead of me. Nothing replaces that peace of mind."

I first took PrEP at the age of 19. I heard about PrEP because I was always searching the Internet about the risks associated with various sexual behaviors, but PrEP had not yet arrived in Brazil. I thought it would not be free in Brazil even once it was available. When I found out that it was available here in Salvador, I decided to take PrEP as it is crucial for my physical and mental well-being. When I got to the clinic and asked for PrEP, I was directed to do a blood test, and then told to talk to a nurse. I reported unprotected anal sex several times and that is why I wanted the medication. She explained to me that condom use should continue as a habit, but I would have an extra layer of protection. Then they directed me to make an appointment with a PrEP prescriber. The conversation with the health professionals was very calm and enlightening, with many explanations, which cleared my doubts and helped me understand what to expect from taking PrEP.

I felt sick during the first cycle of 28 days, with constant nausea and headaches. In the end, it just reaffirmed to me how bad it would be to have to take pills like this forever if I got HIV. At first when I took the medicine in the morning, I had a little stomach ache, as I do not really enjoy eating breakfast (the doctor warned me that I might get sick in the first few days). As it persisted, I changed the schedule for after lunch, and always leave the medication in the backpack that I take to the university. After this change, I felt okay, no symptoms! It all boils down to remembering to take the medication. For that, I have associated taking my pills with another habit: I like to drink juice with meals, so I leave some to drink when I have the medicine nearby.

Regarding the follow-up, an inconvenience is the need to do an HIV test in all future consultations. This is because I can only go to the clinic in the afternoon due to my internship, and I have to arrive much earlier than the appointment time to take the test and wait for the result. So, I have to leave the internship early so I can fit in the time to be tested for HIV.

Four months ago, I went to the HIV reference clinic in Salvador looking for PrEP again. This time, a partner went with me and we ended up knowing that PrEP was being offered for free.

In the end, taking PrEP has been the key to not feeling any more like getting HIV is a matter of time in the life of a gay man. Rather I see my whole future ahead of me, and nothing replaces that peace of mind.

\* Name changed for confidentiality.

# **Clinical considerations**

# Maximizing continuation on PrEP and minimizing loss to follow up

PrEP efficacy trials have demonstrated that, although adherence to PrEP is crucial for protection against HIV infection, many young participants struggled to take the pill daily. Continuation on PrEP also has appeared to be a problem in open-label cohort, or "real world", studies. The iPrEx Open Label Extension (OLE) reported no significant difference of PrEP uptake on the basis of age. However, after starting PrEP, younger people found it more difficult to take PrEP regularly, as evidenced by the odds of having detectable drug in plasma; drug concentrations among those 18 to 24 years of age were significantly lower than among those 30 and older (*56*). Similar results were seen in the ATN 110 and 113 studies, Project PrEPare (*57*). In these studies of young men who have sex with men, ages 15–22, adherence, as measured by drug concentrations, declined over time, with the most precipitous drop-off occurring at week 24, when visits to the facility moved from monthly to quarterly. Early results from the PlusPills Study in Cape Town, which is evaluating PrEP acceptability in male and female adolescents, show a similar drop-off in adherence during quarterly visits (*58*). In sum, PrEP appears to be of interest to young people, but inattention to adherence or inability to continue may reduce its effectiveness, particularly among those who may be most vulnerable to HIV infection. Based on these studies, it appears

that adolescents and young adults (24 years old or less) may benefit from additional monitoring and adherence support, such as more frequent clinic visits or other approaches, to address their changing routines and multiple needs.

Since programmatic implementation of PrEP is at early stages in most countries, evidence from other prevention interventions requiring daily medication adherence such as the use of oral contraceptive pills (OCPs), antiretroviral therapy, and medications for the management of chronic diseases including asthma and diabetes, may suggest successful strategies to improve continuation on medication. A systematic literature review (Velloza et al., unpublished results) of intervention strategies that improve daily OCP medication initiation, adherence and continuation among adolescents and young adults, ages 10–24 years, found mixed results, but some encouraging indications for text messaging and dispensing larger numbers of pill packs. Most of these studies took place in the United States, and one study each was conducted in China, Iceland and Cameroon (*59–73*). There were four main categories of interventions among the OCP-focused studies included: individual level, interpersonal level, health facility level and community level (Fig. 6).

# Fig. 6. Summary of reviewed interventions to improve uptake, adherence and continuation of oral contraceptive use among adolescents and young women



Source: Velloza et al., unpublished.

One study found that participants who received daily text messages about OCP use as well as two-way communication to address their questions and concerns had 44% greater odds of still using OCPs after six months than those in the control arm who received routine care including counselling by staff and educational pamphlets on OCP use, effectiveness, benefits and risks *(61)*. In a study of increased pill pack dispensation, participants receiving seven OCP pill packs had 7.6 times the odds of OCP continuation at six months than those receiving three pill packs, but this study had considerable loss to follow-up and the outcome was only assessed among 43 participants *(73)*. No other reviewed studies assessed the influence of text messages or increased pill packs on OCP continuation for comparison of these effects. Therefore, while text messages and multiple pill packs show some promise for OCP continuation and could be adapted for improving HIV PrEP use in similar populations of young women, caution is warranted as the motivators and mediators of youth continuation in the context of preventing pregnancy and those for preventing a life-long illness like HIV may be different. Also, in the case of PrEP, since studies so far suggest that additional monitoring and support of continuation such as more frequent follow up is clearly needed for young people, a balance will need to be struck between providing a larger volumes of pills and regular follow up through phone, text or in person visits.

Work on adolescent-focused interventions for ART adherence have similarly reported better initiation, retention, and adherence with directly observed therapy and mobile phone education and reminder messages, along with enhanced in-person counselling, financial incentives, and adolescent-friendly health-care clinics (74–76). However, these studies vary in methodological quality, geographic region and sample size. Studies of asthma and diabetes medication adherence among 10–19 year olds have also employed text messaging strategies, directly observed therapy and motivational

interviewing with some success (77, 78) in supporting daily inhaler use, blood glucose testing and insulin adherence. Other interventions that also merit further exploration in settings where PrEP interventions are most needed include peer support through social media such as WhatsApp groups, two-way text messaging, in-person youth-led PrEP adherence clubs, cognitive behavioural counselling and regular follow-up through phone, text or in person visits (Table 1). They should be evaluated especially with young members of key populations that are often stigmatized, particularly since the drivers of and barriers to PrEP continuation are likely to vary within these vulnerable young populations.



Frequent contact	• To maximize PrEP engagement and continuation, adolescents may need to be seen more often.
	• Ask a young person, "When would you like to come back?" and help young people to cope with the need for frequent follow-up.
	Offer interim contact between visits if desired, including text messages or phone calls.
Counselling strategies	• The relationship between the counsellor and the patient is a critical component of success. Trust has to be earned through genuine and nonjudgmental interactions.
	<ul> <li>More directive approaches to counselling may work better for adolescents. Counsellors should be active, asking questions and suggesting topics of discussion.</li> </ul>
	<ul> <li>Skills-building activities can be included in counselling with adolescents (for example, role-playing, decisional balance activities, homework).</li> </ul>
Additional support	• Discuss supportive others in the adolescent's life: Explore who might be a PrEP ally for them.
	Consider peer-support strategies such as adherence buddies, social support groups and adherence clubs.
	• Provide information on available social media support groups such as Whatsapp, chat forums and others.
	<ul> <li>Provide adherence tools that are adolescent-friendly, such as attractive bags, pill containers that are key chains, lipstick holders and so forth.</li> </ul>
	Discuss economic barriers such as transportation costs.
	<ul> <li>Ask about gender-based violence if indicated.</li> </ul>
	<ul> <li>Refer to other services such as voluntary medical male circumcision, STI diagnosis and treatment, contraception and harm reduction alongside PrEP.</li> </ul>

# Medical follow-up for adverse outcomes

Information on clinical considerations for managing adverse outcomes can be found in the clinical module of this PrEP tool.

# Bone mineral density

Given that bone plates are still developing in adolescents, it is important to determine the effect of tenofovir/emtricitabine (TDF/FTC) – the drugs used in PrEP – on bone mineral density (BMD), particularly among young women on hormonal contraception. The data on the effect of TDF/FTC on BMD in adolescent boys and girls is limited. Furthermore, measuring and interpreting BMD in this age group can be challenging, in part due to the lack of standards for bone mineral densitometry (Dexa-scans) among younger populations and the variability introduced by pubertal growth (79, 80). Consequently, the age- and gender-adjusted BMD Z score can be a helpful measure of bone health for children and adolescents. However, detailed analyses using Z scores have not been published for postpubertal young people participating in adult PrEP studies. In a study in the United States among adolescent men who have sex with men, the median BMD Z scores for the hip and spine each declined by 0.1 while the men were taking PrEP. These are very modest changes and were negatively correlated with TDF levels. Corresponding measures of median absolute BMD (g/cm<sup>2</sup>) for the hip also declined very modestly (1%). There was a nonsignificant smaller decrease in BMD Z scores for the spine, which were negatively correlated with TDF levels (81). The only data on BMD among young Africans comes from the TDF-2 study in Botswana, which indicated a 1.7% decline in spine mean BMD and a 1.5% decline in the hip mean BMD (82). The number of participating women who were also initiating hormonal contraception was too small to be informative. In the VOICE trial, there was no decline in mean BMD overall in women randomized to oral TDF or TDF/FTC. However, there was a 1% decline in mean BMD among the subset of women with higher plasma TFV levels (83). This reversed after PrEP was stopped. Similar rebounds of declines were seen in participants over 18 years of age in the ATN trial after they discontinued PrEP (84). None of these studies showed an association between TDF/FTC, BMD reductions and fractures.

In addition to the data on TDF/FTC and BMD in adolescents not infected with HIV, there is significant clinical experience using this medication to treat children and adolescents living with HIV – with reassuring results. In one study, increases from baseline in spine and total body BMD Z scores were seen while adolescents were taking a TDF-containing combination ART regimen, suggesting that skeletal growth (height) was not impaired (85).

An ongoing study in Uganda is prospectively assessing BMD in young women initiating PrEP and hormonal contraception. Overall, the available data indicate very small and reversible decreases in BMD. Particularly given the challenges with clinical interpretation of Dexa-scans in this age group (80), there are no recommendations to perform routine BMD testing in adolescents initiating PrEP or to provide calcium supplements.

### Creatinine

Although TDF can cause a decrease in creatinine clearance and proximal tubulopathy, there was no increase compared with placebo in PrEP efficacy trials. Subsequent analyses have shown that the effect on creatinine clearance in the very small subset that experienced a decline was reversible within weeks (86). Since the vast majority of adolescents will have normal baseline kidney function, the risk of TDF renal toxicity is very small. Thus, PrEP can be initiated the same day that baseline creatinine testing is performed and samples sent to the laboratory for analysis.

#### **Reproductive health services**

Important services for adolescents who are being screened for PrEP are contraceptive counselling and provision and STI testing and treatment. A young woman should be helped to develop an effective pregnancy prevention strategy and informed of their contraceptive choices. Oral contraceptive pills and long-term methods such as contraceptive injections and implants and intrauterine devices (IUDs) are options. TDF and FTC do not interact with hormonal contraception, and there is no reduction in PrEP efficacy in women using injectable contraceptives depot medroxyprogesterone acetate (DMPA) and norethisterone enanthate (NET-EN) and PrEP (*87*). Likewise, PrEP does not diminish the contraceptive effectiveness of hormonal contraception (*88*).

### Pregnancy and breastfeeding

In many settings adolescent and other young women may first hear about PrEP in antenatal care services. In many countries with high-prevalence, generalized HIV epidemics, women continue to acquire HIV during pregnancy and breastfeeding. Women who become infected during this time also risk transmitting HIV to their infants. Based on a review of the literature (89), current WHO guidance concludes that there is no safety-related rationale for disallowing or discontinuing PrEP during pregnancy and breastfeeding for HIV-negative women who remain at risk of HIV acquisition (90). The guidelines conclude that in such situations, the benefits of preventing HIV acquisition in the mother and the accompanying reduced risk of mother-to-child HIV transmission outweigh any potential risks of PrEP, including any risks of fetal and infant exposure to the drugs in PrEP regimens.

#### Sexually transmitted infections

STIs are responsible for considerable morbidity and mortality worldwide and have profound complications in both men and women when left untreated (91). PrEP is being recognized as an opportunity to optimize STI screening and treatment for PrEP clients (92). From a programmatic standpoint, where resources permit, aligning screening for bacterial STIs in PrEP users should be considered. Syndromic management of STIs has limitations however, as many infections are asymptomatic. STI point-of-care testing in settings where HIV and STI incidence rates remain high (93) may have a role in the future if these technologies become more widely available.

A key observation in early PrEP projects among adolescent and young women in sub-Saharan Africa was the high prevalence – 30–40% – of curable STIs, such as chlamydia, gonorrhoea, trichomonas and syphilis, in this population group. Over 90% of these STI cases were asymptomatic and, thus, missed by syndromic management (94, 95). In particular, a 25–30% prevalence of chlamydia was seen in PrEP projects for adolescent girls and young women in Kenya, South Africa and Zimbabwe. Similarly, a recent study among lesbian, gay, bisexual and transgender clients in a community health centre in New York City found that one risk factor for a diagnosis of STIs diagnosis in the 12 months after starting PrEP was being under 25 years of age (96). Etiologic STI screening and treatment should become a cornerstone of PrEP delivery for young people, both to reduce the risk of HIV acquisition due to STI infection and to preserve their fertility.

#### PrEP and other drug interactions

Antiretroviral drugs used for PrEP (TDF, FTC and lamivudine) do not have any known interactions with contraceptive hormones (97), hormones used for feminization by transgender women or hormones used for masculinization by transgender men. Detailed drug–drug interactions can be evaluated in a database maintained by the University of Liverpool (http://www.hiv-druginteractions.org/checker##table-view-wrap) or the database provided by the University of California, San Francisco (http://hivinsite.ucsf.edu/interactions).

There are no known interactions between PrEP medicines and alcohol or recreational drugs. However, if a PrEP user thinks that her or his use of alcohol or other substances is interfering with taking PrEP regularly, this should be discussed with her/his PrEP provider, and/or the PrEP user could contact appropriate local services and support groups.

### Condoms

Although many people who choose PrEP will do so because they have difficulty using condoms consistently, male and female condoms and lubricants should always be available as part of PrEP services, and their benefit of preventing both STIs and unplanned pregnancies should be highlighted.

# Improving access to PrEP among adolescents and young adults: Addressing health system and regulatory barriers

### Service provision and its utilization

A variety of challenges can impede adolescents' access to and utilization of health services and PrEP services in particular. These challenges come at individual, health systems, community, and other structural levels. WHO has developed a framework called Global Accelerated Action for the Health of Adolescents (AH-HA!), with the goal of helping countries to understand the health needs of adolescents and to provide a practical resource for planning, implementing and monitoring programmes to meet these needs (98).



**Ethical, legal, policy and regulatory impediments** to the provision of sexual and reproductive health services to adolescents can be considerable. Although they vary by country, many are common. Health care providers will have to consider a range of issues.

• Age of consent for providing HIV testing and PrEP.

**HIV testing** is the entry point to PrEP services: A confirmed negative test result is required before starting PrEP, and regular testing is required thereafter for PrEP users to monitor break-through infections. Thus, to use PrEP, clients must be able to consent to testing. Some countries, such as South Africa (99), have adopted legislation that reflects an adolescent's evolving capacity to consent independently for specific health services and interventions.

Ministries of health in countries implementing PrEP are encouraged to review their HIV testing age of consent policies in light of the need to uphold adolescents' rights to make choices about their own health and well-being (with consideration for differences in levels of maturity and understanding).

• **Provision of PrEP.** Country restrictions on prescribing to younger age groups without parental consent may need review. Often, restrictions on prescription are due to concerns about safety in prescribing medications to individuals at younger ages. The United States Food and Drug Administration (FDA) has recently approved the fixed-dose combination of TDF/FTC for PrEP, in combination with safer sex practices, to reduce the risk of sexually acquired HIV in adolescents at risk of HIV acquisition who weigh at least 35 kg (100). The extended indication to include adolescents was based on data from the ATN 113 study, which demonstrated that TDF/FTC is safe and well tolerated in HIV uninfected at-risk adolescent males ages 15–17 years.

Countries should assess their current legal frameworks and see what the limitations and possibilities are for offering PrEP to adolescents without parental/guardian consent, if parents/guardians are not supportive.

• **Reporting requirements.** Legal reporting requirements may have to be considered in situations where reporting is mandatory should a young person disclose engaging in sexual activity with an adult or, in the case of key populations, criminalizes activities such same-sex behavior, sex work or substance use. Health-care providers need to feel protected in order to provide PrEP to adolescents.

# Making PrEP practical, accessible and impactful

### **Creating demand for PrEP**

Increasing awareness and uptake of PrEP among young people will require multi-pronged strategies to create demand. Reaching sexually active young people with PrEP can be challenging, as PrEP is a comparatively new intervention and may not be widely available or understood. Where it has been implemented, early data on uptake among young women has varied from low to substantial compared with that of other population groups (Figs. 7 and 8); demand creation may help (95).

Providing young adults and peers with accurate and trustworthy information from a reliable source, such as a ministry of health, is important. Adults, including parents, teachers, relatives and respected community members may be gatekeepers to young people's access to PrEP. Therefore, information should be addressed to community and opinion leaders to allay their concerns and counter myths. Peers play an important role in the decision-making and behaviour of adolescents and young adults, especially in communities where parents may be absent or unavailable because they work long hours or away from home. Identifying peer PrEP users who can be advocates for PrEP and supporting them to speak openly about their PrEP use is an important demand creation strategy.

When communicating with young people about PrEP, avoiding stigmatization and creating materials that are positive about sex and normalize HIV prevention are key. For young people a "sex-positive" approach may be even more important, especially in communities where adults hold negative attitudes towards sexual activity in young people, particularly young women.

Information, as well as attitudes, is important. Youth who are considering PrEP may have concerns about potential side-effects, such as changes in weight or body appearance. Such side-effects are not expected with PrEP but may be rumoured on the Internet or mentioned by friends who are taking ART. Young people may have a greater need than older people for this information, as they have less experience using health products generally. Thus, it is important to create communication materials that provide information specifically for youth, spelling out how PrEP works, what to expect





Note: MSM=men who have sex with men; FSW=female sex worker; AGYW=adolescent girls and young women. *Source*: Jilinde, Kenya.



#### Fig. 8. Distribution of 243 PrEP initiations by subpopulations and age group in Eswatini

Note: sub-population categories are not mutually exclusive. Source: Sihlomile PrEP study, Eswatini.

(or not) and how it should be used. Social media and videos can be a useful medium to explain PrEP efficacy, safety, the importance of adherence for high-level protection and the potential for mild side-effects in the first few weeks of taking PrEP. An example of a video designed for young women in southern Africa that provides information about PrEP in a simple and graphic way is: "Get PrEPared: What African women need to know". Young people participated in developing and filming the video, and in the video they provide the information.

Understanding where young people primarily get information, and using multiple channels to deliver content through these mediums, will increase the chances of reaching youth who would benefit from PrEP. The Internet, while clearly an important source of information, should not be assumed to be the only or biggest source for young people. Ensuring consistent messaging across multiple media platforms (television, radio, print) and social media and phone apps helps to address different audiences with variable access to technology.

#### Enabling access to PrEP

PrEP delivery sites for adolescents and young people should ensure that they can provide services that are integrated, efficient, ensure privacy and are non-judgemental. In addition, WHO recommends a set of criteria for assessing whether services are youth-friendly or youth-competent (98). At the most fundamental level, services that aspire to offer PrEP to young people should have dedicated time and space for young people. This may be as simple as having clinic opening times that are convenient for young people or a period once a week dedicated to providing care to young people. Attention should be paid to youth health literacy. Services should ensure that there are age-appropriate information materials on hand, that peer educators are trained in the health information needs of young people, that signage and information about the services is available in the community and that the service can link young people to other referral or information groups, for example, community support groups.

Ideally, PrEP should be introduced as part of the package of combination HIV prevention and sexual and reproductive health care for adolescents. While PrEP can prevent HIV infection when used consistently, it cannot prevent other sexually transmitted infections or pregnancy. Young people who are seeking or using PrEP to prevent sexual acquisition of HIV are also at risk for STIs and unplanned pregnancy. Thus, these services should ideally be delivered as part of an integrated package of sexual and reproductive health services. Thus, potential areas to locate PrEP services include family planning clinics, reproductive health clinics, youth clinics, STI clinics, school and university health clinics, clinics serving key populations and mobile outreach services. Consideration should be given to the cost of travelling to clinics; adolescents may not be able to afford to travel as far as an adult might. Mobile testing services provide an opportunity to reach remote areas where HIV risk is high. Young people who are students or working may appreciate the convenience and efficiency of mobile testing services. Radio, television, print media and social media can publicize the locations where mobile services stop.

Peer navigators may also play an important role in PrEP services for young people. They help young people link to prevention services after testing HIV-negative. In particular, peer navigators can support PrEP initiation and link young people to adherence support.

Other services to offer include asking about gender-based violence if indicated, mental health and substance use, which are common causes of health problems among adolescents and young adults and may make consistent use of PrEP difficult. For example, a PrEP project in South Africa included screening for gender-based violence as a part of HIV counselling and testing (101). Screening proved feasible and acceptable to health-care providers and adolescent clients, and it helped to generate demand for violence prevention services.

Young people should be involved in the design of services so that their perspectives as users are taken into account from the onset. Programme design structures and processes should institutionalize youth participation at local, district and national levels through, for example, youth advisory groups (98). Young people may identify issues and opportunities associated with access that may not be apparent to health-care providers, who are generally adults. They may also help with planning effective programmes, including selecting points of delivery and designing follow-up. When developing a PrEP service for adolescents, mapping stakeholders and community resources that provide services for young people is important to ensure adequate referrals for other health and social services.

### **Training service providers**

Providers are an important influence in young people's PrEP decision-making and uptake (102–104). Providers who have concerns about the use of ART in HIV-negative populations or preconceived judgments may limit their prescribing of PrEP to young people. Providers benefit from training in the provision of adolescent-friendly services generally as well as specifically in providing PrEP. Pre-service and in-service training in HIV services, as well as national HIV training materials, should cover these topics. Training may include how to talk with young people about sensitive topics such as sexual activity and disclosure to parents. Specifically relevant to offering PrEP is training that reduces providers' stigmatizing attitudes as well as improving providers' knowledge and competency in providing PrEP. Providers will also need to follow up with young people on a more frequent basis than with adults. For example training may highlight that follow-up with adolescents and young adults by phone or text message can identify which youth are having side-effects or adherence concerns and increase their PrEP continuation.

#### Counselling young people on risk reduction

PrEP trials in the United States (ATN 082 and 110) used a group-based engagement strategy with young men who have sex with men ages 18 years and over. These facilitated group sessions sought to raise awareness of HIV risk, strategies for prevention and how PrEP can be used (*105, 106*). The strategy was focused on an evidence-based behavioural intervention called "Many Men, Many Voices" (*107*). This approach was highly acceptable to young adult black and Latino men in the United States who were anticipating starting PrEP (106). In sub-Saharan Africa the FACTS 001 (*108*) and ASPIRE trials (*109*) also used group strategies, as will the HPTN 082 trial (PrEP for young women in South Africa and Zimbabwe). More information on counselling in clinical settings can be found in the counsellors module of this implementation tool.

Counselling for adolescents needs to take into account their developmental stage and needs such as establishing autonomy. Other age-related issues may include privacy about medical decisions and consent to testing and HIV services. Delaying sexual intercourse may be a viable protection strategy for some adolescents and young adults who are not yet sexually active. However, adolescents and young adults who are asking about PrEP will have often already engaged in intercourse or else are preparing to do so safely. For them, a delay or even a return to abstinence is likely to be unacceptable or not feasible. Although condoms remain central to HIV prevention and must be provided in all PrEP services, young people who request or could benefit from PrEP will often have difficulties in using condoms or negotiating their consistent use.

# Monitoring PrEP utilization among adolescents and young adults

Monitoring PrEP eligibility, offer, uptake and continuation among adolescents and young adults presents unique challenges. PrEP indicators should be integrated into national health management information systems (see monitoring and evaluation module). However, standard monitoring systems for adults may need adjustment to incorporate the enrolment and follow-up of young people taking PrEP. For example, as young PrEP users need more frequent follow-up, registers and reporting forms will need to allow for reporting different frequencies of follow-up. Other differences with PrEP programmes for youth will become known as programmes are rolled out and reach more users. Some of these differences will affect monitoring needs and procedures. Therefore, tools and recording materials will benefit from flexibility as well as annual review and adjustment as needed.

Reaching vulnerable young people who may most benefit from PrEP, including those who are not in school and who do not visit health facilities, requires focused outreach. Measuring the outcomes of community contacts and outreach should be built into reporting systems in order to measure their performance. The outcomes to be measured will depend on the priorities of programmes and stakeholders. They may include HIV test results, number of contacts/counselling sessions before uptake, changes in behaviour and the outcomes of referrals to other services. Other aspects of routine monitoring that may require special considerations and adjustments for adolescents and young adults include:

- screening assessments for PrEP eligibility, including assessments based on sexual risk behaviour
- obtaining informed consent for PrEP with/without an adult guardian
- prescribing PrEP with or without the consent of an adult guardian
- frequency of adherence counselling and of follow-up
- follow-up on referrals to other services, such as reproductive and sexual health services, STI testing, contraception, voluntary medical male circumcision, harm reduction and antenatal care
- adverse events or situations that warrant or require breaching confidentiality and reporting to law enforcement.

# Data disaggregations

Health-related data on people under the age of 18 years have been sparse regardless of their focus. There are many reasons for this, including the additional protections and requirements to conduct research among those under the age of 18 years and to obtain informed consent without a legal guardian. Routine monitoring systems have struggled to provide accurate information on adolescents. In the past broad age categories, such as <15 years and 15–49 years, grouped some adolescents with children and others with adults. However, this is changing; narrower age bands (10–14, 15–19 and 20–24 years), are now used more commonly. All PrEP programmes should use these narrower age bands for disaggregated data, including for the core PrEP indicators suggested in the monitoring and evaluation module of this tool.

Successful programme management and quality improvement requires high-quality data. Monitoring age- and sexdisaggregated data allows programmes to see whether they are reaching their intended populations with PrEP and to identify gaps that need to be filled. Additional disaggregations for key populations, in particular to distinguish men who have sex with men from transgender people, will further help to refine services. At the same time, room should be made to account for overlaps among key population groups (for example, men who have sex with men who also inject drugs). Also, people may not continue to identify with a particular group over time. For example, sex work or injection of drugs may be temporary. Therefore, how a client is classified should be revisited periodically.

In summary, PrEP is a positive and empowering HIV prevention intervention for adolescents and young adults. Their need for PrEP is demonstrated by persistent high HIV incidence rates, particularly among adolescent girls and young women in sub-Saharan Africa and young members of key populations in many settings. PrEP delivery is feasible and should be part of broader combination HIV prevention and reproductive health-care delivery that also provides contraception and STI screening and treatment. For young people, continuation on PrEP can be challenging, as risk and motivations for taking PrEP may change. Facilitating accurate self-perception of risk, providing PrEP continuation support and evaluating adverse events will need health-care providers' focused attention. In addition, addressing legal and policy barriers, creating demand and providing youth-friendly services all will serve to improve access to and enable the uptake of PrEP among adolescents and young adults.

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# References

- Core epidemiology slides. Geneva: Joint United Nations Programme on HIV/AIDS; 2017. (http://www.unaids.org/sites/default/files/media\_asset/ UNAIDS\_2017\_core-epidemiology-slides\_en.pdf, accessed 11 July 2018).
- 2. PEPFAR DREAMS Partnership Fact Sheet. Washington (DC): The United States President's Emergency Plan for AIDS Relief; 2017 (https://www.pepfar.gov/ documents/organization/252380.pdf, accessed 6 July 2018).
- 3. Key populations atlas. Geneva: Joint United Nations Programme on HIV/AIDS; 2017 (http://www.aidsinfoonline.org/kpatlas/#/home, accessed 6 July 2018).
- Global AIDS update: Geneva: Joint United Nations Programme on HIV/AIDS (UNAIDS); 2016 (http://www.unaids.org/en/resources/documents/2016/Global-AIDS-update-2016, accessed 6 July 2018).
- Baggaley R, Armstrong A, Dodd Z, Ngoksin E, Krug A. Young key populations and HIV: a special emphasis and consideration in the new WHO Consolidated Guidelines on HIV Prevention, Diagnosis, Treatment and Care for Key Populations. J Int AIDS Soc. 2015;18(2 Suppl 1):19438.
- 6. Kapogiannis BG, Legins KE, Chandan U, Lee S. Evidence-based programming for adolescent HIV prevention and care: operational research to inform best practices. J Acquir Immune Defic Syndr. 2014;66 Suppl 2:S228–35.
- 7. Mavedzenge SN, Luecke E, Ross DA. Effective approaches for programming to reduce adolescent vulnerability to HIV infection, HIV risk, and HIV-related morbidity and mortality: a systematic review of systematic reviews. J Acquir Immune Defic Syndr. 2014;66 Suppl 2:S154–69.
- 8. Vos T, Kyu HH, Pinho C, Wagner JA, Brown JC, Bertozzi-Villa A et al. Global and national burden of diseases and injuries among children and adolescents between 1990 and 2013: findings from the Global Burden of Disease 2013 Study. JAMA Pediatr. 2016;170(3):267–87.
- 9. Hail-Jares K, Choi S, Duo L, Luo Z, Huang ZJ. Occupational and demographic factors associated with drug use among female sex workers at the China-Myanmar border. Drug Alcohol Depend. 2016;161:42–9.
- 10. Margolis AD, MacGowan RJ, Grinstead O, Sosman J, Kashif I, Flanigan TP et al. Unprotected sex with multiple partners: implications for HIV prevention among young men with a history of incarceration. Sex Transm Dis. 2006;33(3):175–80.
- 11. Reisner SL, Biello KB, White Hughto JM, Kuhns L, Mayer KH, Garofalo R et al. Psychiatric diagnoses and comorbidities in a diverse, multicity cohort of young transgender women: baseline findings from Project LifeSkills. JAMA Pediatr. 2016;170(5):481–6.
- 12. Yi S, Tuot S, Chhoun P, Pal K, Choub SC, Mburu G. Mental health among men who have sex with men in Cambodia: implications for integration of mental health services within HIV programmes. Int J Equity Health. 2016;15:53.
- 13. Vreeman RC, McCoy BM, Lee S. Mental health challenges among adolescents living with HIV. J Int AIDS Soc. 2017;20(Suppl 3):21497.
- 14. Hosek SG, Landovitz RJ, Kapogiannis B, Siberry GK, Rudy B, Rutledge B et al. Safety and feasibility of antiretroviral preexposure prophylaxis for adolescent men who have sex with men aged 15 to 17 years in the United States. JAMA Pediatr. 2017;171(11):1063–71.
- 15. Mullins TLK, Zimet G, Lally M, Xu J, Thornton S, Kahn JA. HIV Care providers' intentions to prescribe and actual prescription of pre-exposure prophylaxis to at-risk adolescents and adults. AIDS Patient Care STDS. 2017;31(12):504–16.
- 16. Kapogiannis BG, Handelsman E, Ruiz MS, Lee S. Introduction: Paving the way for biomedical HIV prevention interventions in youth. J Acquir Immune Defic Syndr. 2010;54 Suppl 1:S1–4.
- 17. Preexposure prophylaxis for the prevention of HIV infection in the United States 2017 Update: a clinical practice guideline 2017. Atlanta (GA): Centers for Disease Control and Prevention; 2017. (https://www.cdc.gov/hiv/pdf/guidelines/cdc-hiv-prep-guidelines-2017.pdf, accessed 11 July 2018).
- Gosmann C, Anahtar MN, Handley SA, Farcasanu M, Abu-Ali G, Bowman BA et al. Lactobacillus-deficient cervicovaginal bacterial communities are associated with increased HIV acquisition in young South African women. Immunity. 2017;46(1):29–37.
- Jespers V, Hardy L, Buyze J, Loos J, Buve A, Crucitti T. Association of sexual debut in adolescents with microbiota and inflammatory markers. Obstet Gynecol. 2016;128(1):22–31.
- 20. Freeman EE, Weiss HA, Glynn JR, Cross PL, Whitworth JA, Hayes RJ. Herpes simplex virus 2 infection increases HIV acquisition in men and women: systematic review and meta-analysis of longitudinal studies. AIDS. 2006;20(1):73–83.
- 21. Masese L, Baeten JM, Richardson BA, Bukusi E, John-Stewart G, Graham SM et al. Changes in the contribution of genital tract infections to HIV acquisition among Kenyan high-risk women from 1993 to 2012. AIDS. 2015;29(9):1077–85.
- Houlihan CF, Larke NL, Watson-Jones D, Smith-McCune KK, Shiboski S, Gravitt PE et al. Human papillomavirus infection and increased risk of HIV acquisition. A systematic review and meta-analysis. AIDS. 2012;26(17):2211–22.
- Marcus U, Ort J, Grenz M, Eckstein K, Wirtz K, Wille A. Risk factors for HIV and STI diagnosis in a community-based HIV/STI testing and counselling site for men having sex with men (MSM) in a large German city in 2011–2012. BMC Infect Dis. 2015;15:14.
- 24. Abbai NS, Wand H, Ramjee G. Biological factors that place women at risk for HIV: evidence from a large-scale clinical trial in Durban. BMC Womens Health. 2016;16:19.
- Venkatesh KK, Cu-Uvin S. Assessing the relationship between cervical ectopy and HIV susceptibility: implications for HIV prevention in women. Am J Reprod Immunol. 2013;69 Suppl 1:68–73.
- Knowledge about HIV prevention among young people (15–24) (Data Sheet). Geneva: Joint United Nations Programme on HIV/AIDS; 2017. (http://aidsinfo. unaids.org/, accessed 11 July 2018).
- 27. Fay H, Baral SD, Trapence G, Motimedi F, Umar E, lipinge S et al. Stigma, health care access, and HIV knowledge among men who have sex with men in Malawi, Namibia, and Botswana. AIDS Behav. 2011;15(6):1088–97.
- 28. Flom PL, Friedman SR, Kottiri BJ, Neaigus A, Curtis R, Des Jarlais DC et al. Stigmatized drug use, sexual partner concurrency, and other sex risk network and behavior characteristics of 18- to 24-year-old youth in a high-risk neighborhood. Sex Transm Dis. 2001;28(10):598–607.
- 29. Lieber E, Li L, Wu Z, Rotheram-Borus MJ, Guan J, National Institute of Mental Health Collaborative HIVPTG. HIV/STD stigmatization fears as health-seeking barriers in China. AIDS Behav. 2006;10(5):463–71.

- Anand P, Springer SA, Copenhaver MM, Altice FL. Neurocognitive impairment and HIV risk factors: a reciprocal relationship. AIDS Behav. 2010;14(6):1213– 26.
- 31. Costello EJ, Egger H, Angold A. 10-year research update review: the epidemiology of child and adolescent psychiatric disorders: I. Methods and public health burden. J Am Acad Child Adolesc Psychiatry. 2005;44(10):972–86.
- 32. Hazen E, Schlozman S, Beresin E. Adolescent psychological development: a review. Pediatr Rev. 2008;29(5):161–7; quiz 8.
- 33. Romer D. Adolescent risk taking, impulsivity, and brain development: implications for prevention. Dev Psychobiol. 2010;52(3):263–76.
- 34. Barnabas SL, Dabee S, Passmore JS, Jaspan HB, Lewis DA, Jaumdally SZ et al. Converging epidemics of sexually transmitted infections and bacterial vaginosis in southern African female adolescents at risk of HIV. Int J STD AIDS. 2017:956462417740487.
- Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med. 2010;363(27):2587–99.
- Marrazzo JM, Ramjee G, Richardson BA, Gomez K, Mgodi N, Nair G et al. Tenofovir-based preexposure prophylaxis for HIV infection among African women. N Engl J Med. 2015;372(6):509–18.
- 37. Van Damme L, Corneli A, Ahmed K, Agot K, Lombaard J, Kapiga S et al. Preexposure prophylaxis for HIV infection among African women. N Engl J Med. 2012;367(5):411–22.
- Boyer CB, Greenberg L, Chutuape K, Walker B, Monte D, Kirk J et al. Exchange of sex for drugs or money in adolescents and young adults: an examination of sociodemographic factors, HIV-related risk, and community context. J Community Health. 2017;42(1):90–100.
- Hawkins K, Price N, Mussa F. Milking the cow: young women's construction of identity and risk in age-disparate transactional sexual relationships in Maputo, Mozambique. Glob Public Health. 2009;4(2):169–82.
- 40. Psaros C, Milford C, Smit JA, Greener L, Mosery N, Matthews LT et al. HIV prevention among young women in South Africa: understanding multiple layers of risk. Arch Sex Behav. 2017.
- 41. Wamoyi J, Mshana G, Mongi A, Neke N, Kapiga S, Changalucha J. A review of interventions addressing structural drivers of adolescents' sexual and reproductive health vulnerability in sub-Saharan Africa: implications for sexual health programming. Reprod Health. 2014;11:88.
- 42. Sommarin C, Kilbane T, Mercy JA, Moloney-Kitts M, Ligiero DP. Preventing sexual violence and HIV in children. J Acquir Immune Defic Syndr. 2014;66 Suppl 2:S217–23.
- 43. Elsesser SA, Oldenburg CE, Biello KB, Mimiaga MJ, Safren SA, Egan JE et al. Seasons of risk: anticipated behavior on vacation and interest in episodic antiretroviral pre-exposure prophylaxis (PrEP) among a large national sample of U.S. men who have sex with men (MSM). AIDS Behav. 2016;20(7):1400–7.
- 44. Namey E, Agot K, Ahmed K, Odhiambo J, Skhosana J, Guest G et al. When and why women might suspend PrEP use according to perceived seasons of risk: implications for PrEP-specific risk-reduction counselling. Cult Health Sex. 2016;18(9):1081–91.
- Musheke M, Ntalasha H, Gari S, McKenzie O, Bond V, Martin-Hilber A et al. A systematic review of qualitative findings on factors enabling and deterring uptake of HIV testing in Sub-Saharan Africa. BMC Public Health. 2013;13:220.
- 46. Warren EA, Paterson P, Schulz WS, Lees S, Eakle R, Stadler J et al. Risk perception and the influence on uptake and use of biomedical prevention interventions for HIV in sub-Saharan Africa: a systematic literature review. PLoS One. 2018;13(6):e0198680.
- 47. Stroeken K, Remes P, De Koker P, Michielsen K, Van Vossole A, Temmerman M. HIV among out-of-school youth in Eastern and Southern Africa: a review. AIDS Care. 2012;24(2):186–94.
- Schunter BT, Cheng WS, Kendall M, Marais H. Lessons learned from a review of interventions for adolescent and young key populations in Asia Pacific and opportunities for programming. J Acquir Immune Defic Syndr. 2014;66 Suppl 2:S186–92.
- 49. Deblonde J, De Koker P, Hamers FF, Fontaine J, Luchters S, Temmerman M. Barriers to HIV testing in Europe: a systematic review. Eur J Public Health. 2010;20(4):422–32.
- 50. Hughey AB, Hettema A, Kohler S, Oldenburg C, McMahon SA, Lejeune C et al. Is self-perceived risk associated with oral HIV pre-exposure prophylaxis interest? Findings from a longitudinal cohort study among the general population at risk for HIV in Swaziland. Presented at 12th INTEREST Conference; 2018 29 May–1 June; Kigali, Rwanda.
- 51. Balkus JE, Brown E, Palanee T, Nair G, Gafoor Z, Zhang J et al. An empiric HIV risk scoring tool to predict HIV-1 acquisition in African women. J Acquir Immune Defic Syndr. 2016;72(3):333–43.
- 52. Pintye J, Drake AL, Kinuthia J, Unger JA, Matemo D, Heffron RA et al. A risk assessment tool for identifying pregnant and postpartum women who may benefit from preexposure prophylaxis. Clin Infect Dis. 2017;64(6):751–8.
- 53. Smith DK, Pals SL, Herbst JH, Shinde S, Carey JW. Development of a clinical screening index predictive of incident HIV infection among men who have sex with men in the United States. J Acquir Immune Defic Syndr. 2012;60(4):421–7.
- 54. Kahle EM, Hughes JP, Lingappa JR, John-Stewart G, Celum C, Nakku-Joloba E et al. An empiric risk scoring tool for identifying high-risk heterosexual HIV-1serodiscordant couples for targeted HIV-1 prevention. J Acquir Immune Defic Syndr. 2013;62(3):339–47.
- 55. Goldenberg T, Finneran C, Andes KL, Stephenson R. Using participant-empowered visual relationship timelines in a qualitative study of sexual behaviour. Glob Public Health. 2016;11(5–6):699–718.
- 56. Grant RM, Anderson PL, McMahan V, Liu A, Amico KR, Mehrotra M et al. Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study. Lancet Infect Dis. 2014;14(9):820–9.
- 57. Hosek SG, Siberry G, Bell M, Lally M, Kapogiannis B, Green K et al. The acceptability and feasibility of an HIV preexposure prophylaxis (PrEP) trial with young men who have sex with men. J Acquir Immune Defic Syndr. 2013;62(4):447–56.
- 58. Gill K, Dietrich J, Gray G, Pidwell T, Kayamba F, Bennie T et al. Pluspills: an open label, safety and feasibility study of oral pre-exposure prophylaxis (PrEP) in 15–19 year old adolescents in two sites in South Africa. Presented at 9th International AIDS Society Conference on HIV Science; 2017 July 23–26; Paris, France.
- 59. Bender SS, Geirsson RT. Effectiveness of preabortion counseling on postabortion contraceptive use. Contraception. 2004;69(6):481-7.
- 60. Berenson AB, Rahman M. A randomized controlled study of two educational interventions on adherence with oral contraceptives and condoms. Contraception. 2012;86(6):716–24.

- Castano PM, Bynum JY, Andres R, Lara M, Westhoff C. Effect of daily text messages on oral contraceptive continuation: a randomized controlled trial. Obstet Gynecol. 2012;119(1):14–20.
- 62. Chewning B, Mosena P, Wilson D, Erdman H, Potthoff S, Murphy A et al. Evaluation of a computerized contraceptive decision aid for adolescent patients. Patient Educ Couns. 1999;38(3):227–39.
- 63. Edwards SM, Zieman M, Jones K, Diaz A, Robilotto C, Westhoff C. Initiation of oral contraceptives start now! J Adolesc Health. 2008;43(5):432–6.
- 64. Gilliam M, Knight S, McCarthy M, Jr. Success with oral contraceptives: a pilot study. Contraception. 2004;69(5):413-8.
- 65. Hanna KM. Effect of nurse-client transaction on female adolescents' oral contraceptive adherence. Image J Nurs Sch. 1993;25(4):285–90.
- 66. Jay MS, DuRant RH, Shoffitt T, Linder CW, Litt IF. Effect of peer counselors on adolescent compliance in use of oral contraceptives. Pediatrics. 1984;73(2):126–31.
- 67. Kirby D, Korpi M, Adivi C, Weissman J. An impact evaluation of project SNAPP: an AIDS and pregnancy prevention middle school program. AIDS Educ Prev. 1997;9(1 Suppl):44–61.
- Kirby D, Korpi M, Barth RP, Cagampang HH. The impact of the Postponing Sexual Involvement curriculum among youths in California. Fam Plann Perspect. 1997;29(3):100–8.
- 69. Minguez M, Santelli JS, Gibson E, Orr M, Samant S. Reproductive health impact of a school health center. J Adolesc Health. 2015;56(3):338-44.
- 70. Van Rossem R, Meekers D. An evaluation of the effectiveness of targeted social marketing to promote adolescent and young adult reproductive health in Cameroon. AIDS Educ Prev. 2000;12(5):383–404.
- 71. Wang B, Hertog S, Meier A, Lou C, Gao E. The potential of comprehensive sex education in China: findings from suburban Shanghai. Int Fam Plan Perspect. 2005;31(2):63–72.
- 72. Westhoff C, Heartwell S, Edwards S, Zieman M, Cushman L, Robilotto C et al. Initiation of oral contraceptives using a quick start compared with a conventional start: a randomized controlled trial. Obstet Gynecol. 2007;109(6):1270–6.
- 73. White KO, Westhoff C. The effect of pack supply on oral contraceptive pill continuation: a randomized controlled trial. Obstet Gynecol. 2011;118(3):615–22.
- 74. Shaw S, Amico KR. Antiretroviral therapy adherence enhancing interventions for adolescents and young adults 13–24 years of age: a review of the evidence base. J Acquir Immune Defic Syndr. 2016;72(4):387–99.
- MacPherson P, Munthali C, Ferguson J, Armstrong A, Kranzer K, Ferrand RA et al. Service delivery interventions to improve adolescents' linkage, retention and adherence to antiretroviral therapy and HIV care. Trop Med Int Health. 2015;20(8):1015–32.
- Ridgeway K, Dulli LS, Murray KR, Silverstein H, Dal Santo L, Olsen P et al. Interventions to improve antiretroviral therapy adherence among adolescents in low- and middle-income countries: a systematic review of the literature. PLoS One. 2018;13(1):e0189770.
- 77. Schaefer MR, Kavookjian J. The impact of motivational interviewing on adherence and symptom severity in adolescents and young adults with chronic illness: a systematic review. Patient Educ Couns. 2017;100(12):2190–9.
- Salema NE, Elliott RA, Glazebrook C. A systematic review of adherence-enhancing interventions in adolescents taking long-term medicines. J Adolesc Health. 2011;49(5):455–66.
- 79. Wren TA, Kalkwarf HJ, Zemel BS, Lappe JM, Oberfield S, Shepherd JA et al. Longitudinal tracking of dual-energy X-ray absorptiometry bone measures over 6 years in children and adolescents: persistence of low bone mass to maturity. J Pediatr. 2014;164(6):1280–5 e2.
- 80. Gordon CM. Low bone density during childhood: what does it predict? J Pediatr. 2014;164(6):1252-4.
- 81. Havens PL, Stephensen CB, Van Loan MD, Schuster GU, Woodhouse LR, Flynn PM et al. Decline in bone mass with tenofovir disoproxil fumarate/ emtricitabine is associated with hormonal changes in the absence of renal impairment when used by HIV-uninfected adolescent boys and young men for HIV preexposure prophylaxis. Clin Infect Dis. 2017;64(3):317–25.
- 82. Kasonde M, Niska RW, Rose C, Henderson FL, Segolodi TM, Turner K et al. Bone mineral density changes among HIV-uninfected young adults in a randomised trial of pre-exposure prophylaxis with tenofovir-emtricitabine or placebo in Botswana. PLoS One. 2014;9(3):e90111.
- 83. Mirembe BG, Kelly CW, Mgodi N, Greenspan S, Dai JY, Mayo A et al. Bone mineral density changes among young, healthy African women receiving oral tenofovir for HIV preexposure prophylaxis. J Acquir Immune Defic Syndr. 2016;71(3):287–94.
- 84. Mulligan K, Hosek S, Kapogiannis BG, Landovitz RJ, Liu N, Cofield SS et al. Changes in bone mass after discontinuation of PrEP with tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) in young men who have sex with men (YMSM): extension phase results of Adolescent Trials Network (ATN)110. Presented at 21st International AIDS Conference; 2016 July 22–28; Durban, South Africa.
- 85. Della Negra M, De Carvalho AP, De Aquino MZ, Pinto JA, Da Silva MT, Andreatta KN et al. Long-term efficacy and safety of tenofovir disoproxil fumarate in HIV-1-infected adolescents failing antiretroviral therapy: the final results of study GS-US-104-0321. Pediatr Infect Dis J. 2015;34(4):398–405.
- Mugwanya KK, Wyatt C, Celum C, Donnell D, Kiarie J, Ronald A et al. Reversibility of glomerular renal function decline in HIV-uninfected men and women discontinuing emtricitabine-tenofovir disoproxil fumarate pre-exposure prophylaxis. J Acquir Immune Defic Syndr. 2016;71(4):374–80.
- Heffron R, Mugo N, Were E, Kiarie J, Bukusi EA, Mujugira A et al. Preexposure prophylaxis is efficacious for HIV-1 prevention among women using depot medroxyprogesterone acetate for contraception. AIDS. 2014;28(18):2771–6.
- Murnane PM, Heffron R, Ronald A, Bukusi EA, Donnell D, Mugo NR et al. Pre-exposure prophylaxis for HIV-1 prevention does not diminish the pregnancy prevention effectiveness of hormonal contraception. AIDS. 2014;28(12):1825–30.
- Mofenson LM, Baggaley RC, Mameletzis I. Tenofovir disoproxil fumarate safety for women and their infants during pregnancy and breastfeeding. AIDS. 2017;31(2):213-32.
- 90. Preventing HIV during pregnancy and breastfeeding in the context of PrEP. Technical brief. Geneva: World Health Organization; 2017.
- 91. Global health sector strategy on sexually transmitted infections 2016–2021. Geneva: World Health Organization; 2016.
- Marrazzo JM, Dombrowski JC, Mayer KH. Sexually transmitted infections in the era of antiretroviral-based HIV prevention: priorities for discovery research, implementation science, and community involvement. PLoS Med. 2018;15(1):e1002485.

- 93. Garrett NJ, Osman F, Maharaj B, Naicker N, Gibbs A, Norman E et al. Beyond syndromic management: opportunities for diagnosis-based treatment of sexually transmitted infections in low- and middle-income countries. PLoS One. 2018;13(4):e0196209.
- Morton J, Bukusi E, Delany-Moretlwe S, Bekker L-G, Omollo V, Travill D et al. High prevalence of curable STIs among young women initiating PrEP in Kenya and South Africa. 22nd International AIDS Conference; Amsterdam (in preparation).
- 95. Celum CL, Delany-Moretlwe S, Hosek S, Dye BJ, Bekker L-G, Mgodi N et al. Risk behavior, perception, and reasons for PrEP among young African women in HPTN 082. Presented at Conference on Retroviruses and Opportunistic Infections; 2018 March 2–7; Boston (MA).
- 96. Golub SA, Peña S, Fikslin R, Goldberg M, Radix A. Partners not condom use drive STI rates among PrEP users in a community health center. Paper presented at Conference on retroviruses and opportunistic infections; 2018 March 2–7; Boston (MA).
- Nanda K, Stuart GS, Robinson J, Gray AL, Tepper NK, Gaffield ME. Drug interactions between hormonal contraceptives and antiretrovirals. AIDS. 2017;31(7):917–52.
- Global Accelerated Action for the Health of Adolescents (AA-HA!): guidance to support country implementation. Geneva: World Health Organizaton; 2017 (WHO/FWC/MCA/17.05).
- 99. Strode A, Essack Z. Facilitating access to adolescent sexual and reproductive health services through legislative reform: lessons from the South African experience. S Afr Med J. 2017;107(9):741–4.
- Truvada prescribing information. 2018. Washington (DC): United States Food and Drug Administration; 2018. (http://www.gilead.com/~/media/Files/pdfs/ medicines/hiv/truvada/truvada\_pi.pdf, accessed 1 June, 2018).
- 101. Colombini M, Ramskin L, Khoza N, Stangl A, Scorgie F, Harvey S et al. Integrating gender-based violence (GBV) screening and support into HIV counselling and testing for adolescent girls and young women accessing PrEP in South Africa and Tanzania – experiences from the EMPOWER study. 22nd International AIDS Conference; Amsterdam (in preparation).
- 102. Pilgrim N, Jani N, Mathur S, Kahabuka C, Saria V, Makyao N et al. Provider perspectives on PrEP for adolescent girls and young women in Tanzania: the role of provider biases and quality of care. PLoS One. 2018;13(4):e0196280.
- 103. Goparaju L, Praschan NC, Warren-Jeanpiere L, Experton LS, Young MA, Kassaye S. Stigma, Partners, providers and costs: potential barriers to PrEP uptake among US women. J AIDS Clin Res. 2017;8(9).
- 104. Yi S, Tuot S, Mwai GW, Ngin C, Chhim K, Pal K et al. Awareness and willingness to use HIV pre-exposure prophylaxis among men who have sex with men in low- and middle-income countries: a systematic review and meta-analysis. J Int AIDS Soc. 2017;20(1):21580.
- 105. Hosek SG, Rudy B, Landovitz R, Kapogiannis B, Siberry G, Rutledge B et al. An HIV preexposure prophylaxis demonstration project and safety study for young MSM. J Acquir Immune Defic Syndr. 2017;74(1):21–9.
- 106. Hosek SG, Green KR, Siberry G, Lally M, Balthazar C, Serrano PA et al. Integrating behavioral HIV interventions into biomedical prevention trials with AGYW: lessons from Chicago's Project PrEPare. J HIV AIDS Soc Serv. 2013;12(3–4).
- 107. Wilton L, Herbst JH, Coury-Doniger P, Painter TM, English G, Alvarez ME et al. Efficacy of an HIV/STI prevention intervention for black men who have sex with men: findings from the Many Men, Many Voices (3MV) project. AIDS Behav. 2009;13(3):532–44.
- 108. Rees H, Delany-Moretlwe SA, Lombard C, Baron D, Panchia R, Myer L et al. FACTS 001 Phase III Trial of Pericoital Tenofovir 1% Gel for HIV Prevention in Women. Presented at Conference on Retroviruses and Opportunistic Infections; 2015 23–26 Feb; Seattle (WA).
- 109. Baeten JM, Palanee-Phillips T, Brown ER, Schwartz K, Soto-Torres LE, Govender V et al. Use of a vaginal ring containing dapivirine for HIV-1 prevention in women. N Engl J Med. 2016;375(22):2121–32.

### For more information, contact:

World Health Organization Department of HIV/AIDS 20, avenue Appia 1211 Geneva 27 Switzerland

E-mail: hiv-aids@who.int

www.who.int/hiv