

# Prevention of HIV in Adolescent Girls and Young Women: Key to an AIDS-Free Generation

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**Abstract:** The Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive (Global Plan) has ensured that more infants in high-HIV burden countries survive childhood HIV-free. Although equal numbers of boy and girl children have survived to age 10, a gender divergence starts to emerge as they enter adolescence. Up to 3 times as many young women aged 15–24 years in eastern and southern Africa are living with HIV compared with their male peers. Further, more adolescent girls and young women are sick and/or dying from AIDS-related or HIV-related complications during pregnancy and in the postpartum period, underscoring the importance of strengthening HIV treatment and prevention services for this group. Failure to prevent HIV in adolescent girls and young women and keep them alive will reverse the infant HIV prevention and survival gains made under the Global Plan. The promising global declines in HIV infection in young women need to be strengthened to realize the goals of an AIDS-free generation. The DREAMS initiative of the United States President's Emergency Plan for AIDS Relief (PEPFAR), which specifically addresses adolescent girls and young women at highest risk of HIV acquisition, brings new hope for meeting the prevention and care needs of this important and vulnerable population through political commitment, leadership, financial and human resource investments, advocacy efforts, and a focus on the highest priority settings. Importantly, to achieve the goal of keeping mothers alive, we have to place more emphasis on access to sexual and reproductive health services that (1) include HIV prevention and treatment services for adolescent girls and young women; (2) increase male/paternal responsibility in mother and infant health; and (3) ensure a supportive social environment that enables young women to grow up into young adults who are free to graduate from high school and plan their pregnancies, ultimately entering adulthood safe, healthy, and free from HIV.

**Key Words:** young women, adolescents, HIV, prevention, DREAMS, Global Plan

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## INTRODUCTION

The Global Plan towards eliminating HIV infections among children by 2015 and keeping their mothers alive (Global Plan) revolved around 4 prongs: (1) prevent HIV among women of reproductive age; (2) prevent unintended pregnancies among women living with HIV; (3) prevent HIV transmission through the use of antiretroviral medicines during pregnancy and breastfeeding; and (4) provide treatment, care, and support for mothers living with HIV, their children, partners, and families.<sup>1</sup> Since the launch of the Global Plan, coverage of services to prevent mother-to-child transmission of HIV increased dramatically, reaching 77% in 2015. As a result, new HIV infections among children aged 0–14 years have declined by 51% since 2010. In addition, the number of children aged 0–14 years on antiretroviral therapy globally has increased from 452,000 children in 2010 to 910,000 children by 2016, reducing AIDS-related deaths among children by 44%.<sup>2</sup> The substantial reductions in new HIV infections among children and huge declines in AIDS-related deaths among infants were because of the early initiation of antiretroviral therapy for infants infected with HIV based on compelling scientific evidence and the implementation of prong 3 and prong 4. In contrast, progress made in keeping mothers alive has been limited primarily because of challenges in preventing HIV infection in women and operational challenges in implementing prongs 1 and 2 (and facets of prong 4), most notably in relation to treatment, care, and support of mothers living with HIV, their partners, and families. These limitations have been most pronounced in the high HIV burden settings of eastern and southern Africa.

The rationale for prongs 1 and 2 is based on scientific evidence and is an effective strategy for indirectly preventing infants from acquiring HIV.<sup>1</sup> It also is an important opportunity to engage and link women to essential HIV prevention, treatment, care, and sexual and reproductive health services. However, adolescent girls and young women—particularly unmarried pregnant teenagers and/or survivors of sexual abuse—are less likely than older women to use the appropriate and available prevention or treatment services.

Given that entry into prevention of mother-to-child transmission (PMTCT) programs is usually through antenatal

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services, adolescent girls and young women who do not access antenatal care services also will not access PMTCT services. Furthermore, a study in KwaZulu-Natal among 19,093 women found that even when adolescent girls do access antenatal care during pregnancy, they do not always receive the appropriate HIV treatment and prevention services. There was also an apparent age disparity, where the HIV transmission rate at 4–8 weeks of age was significantly higher among infants of adolescent mothers than among infants of older mothers (OR: 1.7, 95% CI: 1.2 to 2.4).<sup>3</sup>

Notably, there has been insufficient progress in HIV prevention options for adolescent girls. As we move into the post-Global Plan era, particular attention needs to turn to 3 groups of adolescents: (1) children infected at birth or in infancy who are now transitioning to adolescence; (2) those who are HIV-negative but at high risk of acquiring HIV because of social circumstances (eg, AIDS orphans and children of child-headed households); and (3) other adolescents who engage in high-risk behavior.

In this study, we draw attention to the complexities associated with adolescence, describe factors impacting the risk of acquiring HIV among adolescents, and discuss the progress made both in preventing HIV in adolescent girls and young women—with specific reflections on its implications for fully realizing the goal of eliminating HIV among infants and keeping their mothers alive—and in sustaining the gains and progress made to date.

## EPIDEMIOLOGY OF HIV IN ADOLESCENT GIRLS AND YOUNG WOMEN

Although global HIV trends indicate a decline in the number of new cases of HIV infection (from 3.4 million in 2001 to 2.1 million in 2015), these trends mask the continued spread of HIV in certain regions, populations, and age groups.<sup>4</sup> Of the

10 countries that contribute two-thirds of all HIV infections globally, 7 are in eastern and southern Africa.<sup>5</sup> In these regions, women account for 59% of all people living with HIV, and adolescent girls and young women aged 15–24 years are particularly vulnerable (Table 1). Of the estimated 3.9 million young people aged 15–24 years living with HIV in 2014, 2.3 million (58%) were young women. Throughout sub-Saharan Africa, HIV prevalence among adolescent girls and young women exceeds that of their male peers, with HIV prevalence up to 6 times higher in South Africa (Box 1).<sup>18</sup> Although the cause of this vulnerability has not been fully elucidated, it is compounded by structural, social, and biological factors.

### BOX 1. Focus on KwaZulu-Natal, South Africa

South Africa accounts for 18% of the global burden of HIV infection, with about 1000 new infections each day.<sup>6</sup> The province of KwaZulu-Natal is at the epicenter of the pandemic: 4 of its 11 districts have HIV prevalence among pregnant women of greater than 40%, and the remaining 7 districts having an HIV prevalence between 35.9% and 39.9%.<sup>7</sup>

### IMPORTANCE OF AGE STRATIFICATION

HIV surveillance in pregnant women and repeated cross-sectional studies conducted over the past decade in the high burden KwaZulu-Natal subdistrict of uMgungundlovu show that, although HIV prevalence has remained stable over recent years, incidence rates remain unacceptably high in women below 30 years of age. In the uMgungundlovu subdistrict, by age 16, 1 in every 10 women coming to antenatal services are already infected with HIV. This increases to 1 in 3 by age 20 and 1 in 2 by age 24 (see table below).<sup>8</sup> A survey conducted among high school students in this subdistrict found that HIV prevalence in girls was 6-fold higher than in boys. An age-specific breakdown from this survey indicates that by age 18, 7.1% of girls are infected with HIV; by age 25, this increases to 24%.<sup>9</sup> Several other cohort and longitudinal studies in South Africa show high HIV incidence rates among young women.<sup>10–16</sup> High HIV incidence rates also have been observed in postpartum women in periurban communities in KwaZulu-Natal.<sup>17</sup>

HIV in Pregnant Women in the uMgungundlovu Subdistrict, KwaZulu-Natal, South Africa (2001–2013)

**TABLE 1.** HIV Prevalence in Adults and Young Women in Selected Countries of Southern and Eastern Africa, 2015

Country	HIV Prevalence (%)		
	Adults (>15 years) (95% Confidence Interval)	Females (15–24 years) (95% Confidence Interval)	Males (15–24 years) (95% Confidence Interval)
Kenya	5.9 (4.9 to 7.0)	4.0 (3.1 to 5.1)	2.3 (1.6 to 3.2)
Lesotho	22.7 (20.8 to 24.3)	9.1 (7.9 to 11.2)	5.1 (3.4 to 7.6)
Malawi	9.1 (8.4 to 9.9)	3.2 (2.6 to 4.0)	1.8 (1.4 to 2.4)
Mozambique	10.5 (8.3 to 13.3)	4.0 (2.9 to 5.6)	2.3 (1.3 to 3.9)
South Africa	19.2 (18.4 to 20.0)	11.6 (10.1 to 14.1)	4.0 (2.8 to 5.8)
Swaziland	28.8 (26.7 to 30.5)	16.7 (14.7 to 20.0)	7.3 (5.0 to 10.7)
Uganda	7.1 (6.6 to 7.7)	3.2 (2.7 to 4.0)	1.9 (1.3 to 2.7)
Tanzania	4.7 (4.2 to 5.3)	1.6 (1.4 to 2.0)	1.0 (0.8 to 1.5)
Zambia	12.9 (12.3 to 13.4)	5.0 (4.4 to 6.0)	3.1 (2.3 to 4.4)
Zimbabwe	14.7 (13.3 to 16.0)	5.9 (5.0 to 7.3)	3.8 (2.7 to 5.2)

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Age Group, yrs	HIV Prevalence (N = 2966), %
≤16	11.5
17–18	21.3
19–20	30.4
21–22	39.4
23–24	49.5
>25	51.9

Source: Adapted from Kharsany AB, Mlotshwa M, Frohlich JA, et al. HIV prevalence among high school learners—opportunities for schools-based HIV testing programmes and sexual reproductive health services. *BMC Public Health*. 2012;12:231. Adaptations are themselves works protected by copyright. So in order to publish this adaptation, authorization must be obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

## FACTORS CONTRIBUTING TO THE INCREASED VULNERABILITY OF YOUNG WOMEN IN ACQUIRING HIV

### Adolescence and the Complexities of the Transition to Adulthood

Adolescence is a development phase characterized by increased risk-taking, instant gratification, and greater peer influence in decision-making. During this time, new boundaries are explored, and parental and societal rules and norms that were unchallenged during childhood are reexamined, questioned, and/or defied in preparation for adulthood and autonomy.<sup>19</sup> The period of adolescence is associated with complex emotional, physical, and cognitive changes.<sup>20</sup>

Vulnerabilities in youth often are exacerbated by the interaction of the effects of social disparities and the realities of everyday life. Sexual risk-taking in settings where HIV infection is rare has a different impact and implication when compared to communities with a high prevalence of HIV, where the probability of acquiring HIV is substantially higher. In addition, where social disparities exist—for example in relation to access to health services—the outcomes from exposure to HIV or being infected also are different.<sup>21,22</sup>

Although adolescents comprise about 25% of the global population, sub-Saharan Africa is the only region in the world where more than one-third of the population is between 10 and 24 years of age, creating what is referred to as the “youth bulge” in the population pyramid.<sup>23</sup> The implications of a high burden of HIV in adolescent girls and young women, together with increased HIV-related morbidity and mortality rates, have profound social implications in this setting given the central and critical social and economic role of women in society. This situation is exacerbated by an emerging trend of convergence between communicable and noncommunicable diseases.<sup>22</sup> Concerted effort and investment are needed to ensure that equal numbers of young boys and girls in sub-Saharan Africa are able to enter adulthood healthy and realize their full potential. The age–sex disparities in HIV infection and survival being experienced, notably in eastern and southern Africa, pose a significant threat to social cohesion and economic development in the region, both immediately and in the long term, and they require urgent attention.

The “youth bulge,” in combination with the delayed rollout of treatment with antiretroviral medicines that led to the loss of several hundreds of thousands of parents from AIDS-related causes, contributed to a significant increase in child-headed households in sub-Saharan Africa.<sup>24</sup> The implications of this situation are manifold, and they include poverty, concerns about livelihood, precocious familial responsibilities, and isolation and marginalization because of social stigma and discrimination. All of these implications impact the sexual decisions of adolescent girls and young women differently compared with boys. In some instances, this can lead to sex for survival or increased exposure to gender-based violence, which in turn has consequences that include sexually

transmitted infections (STIs) and pregnancy.<sup>25</sup> Young women in child-headed and poor households are especially vulnerable to acquiring HIV.

### Sexual Coupling Patterns

In sub-Saharan Africa, adolescent girls and young women tend to acquire HIV infection at a much earlier age than their male peers.<sup>26,27</sup> This age–sex disparity in infection rates is a consequence of young girls partnering with men who are about 5–10 years older than them, and who may have recently acquired HIV or who are already living with HIV but are not on treatment with antiretroviral medicines.<sup>28–31</sup> Adolescent girls and young women engage in sexual relationships with older men for multiple reasons. Although some relationships are based on love or sexual curiosity, in some instances, particularly for those from impoverished backgrounds, young women may engage in transactional sex and form relationships with older men for financial and social security.<sup>32–34</sup> Understanding the drivers of this partnering pattern and learning more about these male partners is critical for addressing the prevention needs of adolescent girls and young women.<sup>35</sup>

In addition to unknowingly choosing a sexual partner who may be already infected with HIV, early sexual debut, teen pregnancies, early school dropout, and sexual violence also increase the vulnerability of adolescent girls and young women to acquiring HIV infection and maintain them in vicious cycles of poverty and dependency.

Young people, on average, have their first sexual encounters during their teenage years: in sub-Saharan Africa, about 60% of young women are sexually active by the time they reach the age of 18 (Table 2). In this region, although unprotected sex between adolescent peers can result in pregnancy, HIV is rare. In contrast, sex with an older man is more likely to result in HIV acquisition and pregnancy. Data from South Africa show that women who have a young age of sexual debut are more likely to have an older first sexual partner and are more likely to have experienced sexual coercion.<sup>36</sup> Early sexual debut has also been associated with subsequent sexual risk-taking, such as having multiple partners.<sup>28,37,38</sup> Young people also are less likely to be experienced in discussing safe sex. Gender-power imbalances that exist in age-disparate relationships result in challenges for younger women in negotiating safer sex practices, including consistent condom use.

Adolescent girls and young women who engage in unprotected sex can become pregnant, which has the potential to adversely impact a young woman’s opportunities for education, as it has been found that the majority of pregnant teenagers rarely return to school after childbirth.<sup>39</sup> The vulnerability of teenage girls who drop out of school is further perpetuated as they transition to adulthood because of the limited economic options available or accessible to those who do not complete high school.

In addition to the economic disadvantages, pregnant adolescent girls below the age of 15 face a particularly high risk of maternal mortality. According to the United Nations Population Fund (UNFPA), girls below the age of 15 are 5

**TABLE 2.** Most Recent Available Population-Based Data on Sexual Behavior, Contraceptive Use, Experiences of Sexual Violence, Pregnancy, Marital Status, and Education in Women From Selected Countries in Eastern and Southern Africa

Country	Year	% Current Use of Any Method of Contraception (All Women)	% Unmet Need for Family Planning, Total (All Women)	Median Age at First Sexual Intercourse in Women, yrs	% of Women Who Ever Experienced Sexual Violence		% of Teenagers Who Are Mothers	% Women First Married by Age 18	% Women With Secondary or Higher Education
					Age 15–49	Age 15–19			
Kenya	2014	42.6	12.8	18.2	14.1	6.5	14.7	27.4	42.7
Lesotho	2009	35.9	15.8	18.3	—	—	15.8	25.8	52.2
Malawi	2010	35.4	20.0	17.4	25.3	17.8	20.1	51.6	20
Mozambique	2011	12.3	20.8	16.1	12.3	9.3	29.3	43.9	17.1
South Africa	1998	50.1	12.1	17.8	—	—	13.2	12.7	68.3
Swaziland	2006–07	37.9	16.5	18.2	—	—	18.5	14.5	59.3
Tanzania	2010	28.8	17.7	17.4	20.3	13.2	17.2	39.4	16.2
Uganda	2011	23.6	24.5	17.5	30.6	19.2	18.1	48.6	27.7
Zambia	2013–14	35.1	16.7	17.7	17.4	8.2	23.3	41.8	44.8
Zimbabwe	2010–11	41.3	10.3	18.9	27.2	18.0	18.6	30.7	69.7

—, data not available.

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times as likely—and those aged 15–19 years are 2 times as likely—to die from complications of childbirth than women in their 20 seconds. A systematic analysis of population health data shows that complications in pregnancy and childbirth are one of the leading causes of death among adolescent girls in developing countries.<sup>40</sup> Young women also are more likely than older women to seek abortions, particularly if the pregnancy is unintended. The estimated unintended pregnancy rate in Africa in 2008 was 86 per 1000 women, one-third of which were terminated through abortions, often under unsafe conditions.<sup>41</sup> Globally, unsafe abortions are estimated to cause 70,000 maternal deaths each year.<sup>41</sup> About 13% of the unsafe abortions that occur annually in the developing world (2.5 million of the approximately 19 million) are among adolescents.<sup>41</sup>

Provision of family planning and the prevention of unintended pregnancies is important for all women but especially for adolescent girls, who are at greater risk for pregnancy-related complications (such as obstetric hemorrhage and hypertension). Eliminating the unmet need for family planning among all women (including women living with HIV) is one prong of the Global Plan; however, the most recent population-based surveys show that most countries in eastern and southern Africa do not meet the need for family planning among at least 25% of all sexually active unmarried women (Table 2).

There is a bidirectional relationship between gender-based violence and HIV infection. Women who have been subjected to intimate partner violence or gender-based violence face an increased risk for acquiring HIV<sup>30,31,42,43</sup> because they often adopt risky behaviors.<sup>44</sup> A study in South Africa among 1099 women found an HIV incidence rate of 9.6 per 100 women-years of follow-up among women who reported more than 1 episode of intimate partner violence; this was compared with 5.2 per 100 women-years of follow-up among those who reported

1 or no episode (IRR: 1.51, 1.04–2.21,  $P = 0.032$ ).<sup>42</sup> In Rwanda, women who were HIV-positive were more likely to report a history of violent relationships (46% versus 29%) and sexual coercion by their partners (43% versus 29%) than those who were HIV-negative.<sup>45</sup> A Tanzanian study found that women younger than 30 who were living with HIV were 10 times more likely to report at least 1 event of physical or sexual violence than HIV-negative women of similar age (OR: 9.99; 95% CI: 2.67 to 37.37).<sup>46</sup>

### Biological Risk Factors

The high HIV incidence rates observed among adolescent girls and young women in sub-Saharan Africa suggest that factors beyond behavior may be contributing to the heightened vulnerability in this group. Women are biologically more vulnerable to HIV and are, on average, twice as likely as men to become infected after a single sexual encounter.<sup>47</sup> The biological mechanisms that make women more vulnerable than men in acquiring HIV are in the process of being established, although one contributing factor could be that the large exposed mucosal surface of the vagina may facilitate HIV acquisition. Furthermore, the high levels of immune cell activation (which is the viral target for infection) in the female genital tract and the increased expression of HIV coreceptors in cervical cells (compared with foreskin cells) may explain why women have a higher per-act risk of HIV acquisition than men.<sup>48,49</sup> Genital trauma experienced as a result of forced or unwanted sexual intercourse can facilitate HIV transmission.<sup>50</sup>

Inflammation in the female genital tract also may be an important risk factor: analysis of female genital tract samples from a recent microbicide trial that assessed tenofovir gel for HIV prevention showed that genital inflammation, defined by combinations of elevated proinflammatory cytokines, was associated with a 3-fold



increase in the risk of HIV acquisition.<sup>51</sup> The cause of this inflammation is still unclear, and a better understanding of the immunological basis of correlates of HIV transmission in young women could yield useful clues to future HIV prevention technologies and strategies.

Sexual debut also marks the initial exposure to a number of sexually transmitted pathogens, including viruses such as herpes simplex type-2 virus (HSV-2) and human papilloma-virus (HPV), which have been associated with a 2-fold to 3-fold increased risk of HIV transmission.<sup>52,53</sup>

The use of injectable hormonal contraception, particularly depot-medroxyprogesterone acetate (DMPA), has recently emerged as a potential mediator of HIV risk. Although uncertainty remains about the association between DMPA use and HIV risk in young women, DMPA remains the most common choice of contraceptive in sub-Saharan Africa. A meta-analysis that included 18 studies has suggested that DMPA is associated with a moderate increase in the risk of HIV acquisition.<sup>54</sup> Although we wait for definitive evidence of the association between DMPA and HIV risk from an ongoing randomized controlled trial, women at high risk of HIV using this method should be strongly advised to also use condoms (male or female). The United States Agency for International Development (USAID) has developed a strategic communication framework to guide country-level activities to communicate the risks and benefits of hormonal contraception among women at risk of, or living with, HIV through the use of an easy-to-understand and comprehensive format.<sup>55</sup>

### Limitations of Current HIV Prevention Options for Adolescent Girls and Young Women

Although the number of HIV prevention options has expanded, the number of strategies that empower women to directly control their risk of HIV remains quite limited. Numerous social and behavioral change interventions aimed at preventing HIV—including peer education, mass media communication, school-based sex education programs, and behavioral counseling—have been assessed.<sup>56</sup> Although many of the studies result in slight improvements in behavioral outcomes (increased HIV knowledge, increased condom use, and a reduction in high-risk sexual behavior), few show a significant impact on biological outcomes (such as HIV incidence).

Campaigns promoting abstinence, mutual faithfulness, condom use, and circumcision also have had a limited impact on HIV incidence in young women. A systematic review that included 13 trials and 15,940 youths found that abstinence programs had no impact reducing unprotected vaginal sex, reducing the number of partners, increasing condom use, or delaying sexual initiation.<sup>57</sup> Data from South Africa show that rates of reported early sexual debut (ie, before the age of 15 years) have remained almost stable at 10% since 2002.<sup>27</sup>

Male and female condoms are an essential component of HIV prevention programs. They are inexpensive and, when used correctly and consistently, provide protection against acquisition and transmission of HIV and a variety of other

STIs, and against pregnancy.<sup>58</sup> However, gender inequality and the threat of intimate partner violence also limit a women's ability to successfully negotiate condom use with male partners, to insist on mutual monogamy, or to convince partners to have an HIV test. Furthermore, medical male circumcision, which is widely promoted for HIV prevention in high HIV burden countries, primarily benefits the male partner. Any protective benefits for women are likely to be realized only 5 or more years later.<sup>59</sup>

### Progress on Women-Initiated HIV Prevention Technologies

The development of HIV prevention strategies that can be directly controlled by women remains an important global goal. One promising HIV prevention option that could directly empower women to limit their HIV risk is the topical (microbicides) or oral use of antiretroviral-containing agents by HIV-uninfected persons, also referred to as preexposure prophylaxis (PrEP).

Although no topical microbicides are yet licensed or available, results from the CAPRISA 004 tenofovir gel trial provided proof-of-concept that topical antiretroviral microbicides, when used before and after sex, can reduce sexual transmission of HIV and HSV-2 in women.<sup>16</sup> However, the 2 confirmatory trials—the FACTS 001 trial of pericoital gel use and the VOICE trial of daily tenofovir gel—were unable to confirm the CAPRISA 004 trial results.<sup>60,61</sup> This may have been primarily because of suboptimal adherence: measurement of tenofovir concentrations in blood found that only 25% of women assigned to the tenofovir gel group in the VOICE trial and about half of the women in the FACTS 001 trial had detectable drug levels, meaning that most women in the trials did not take the study drug as prescribed.<sup>60,61</sup>

Given the adherence challenges, the field has shifted its focus to developing products that are long-acting and less user-dependent. Data from 2 efficacy trials evaluating the long-acting antiretroviral dapivirine intravaginal ring are encouraging and show that high levels of adherence are achievable (82% in ASPIRE and 73% in the IPM Ring study).<sup>62,63</sup> The monthly dapivirine vaginal ring reduced HIV incidence rates by 27% in the MTN ASPIRE trial and 31% in the IPM Ring study.<sup>62,63</sup> However, adherence (based on drug levels in plasma samples) was shown to be 2-fold to 4-fold lower in young women (<21 years) than older women; as a result, no protection was observed in young women.<sup>62</sup> An open-label, posttrial access study is planned to further investigate this finding. If licensed, the product could become available as an HIV prevention option for women in about 4–5 years.

New formulations and delivery devices, such as PrEP injections lasting 2–3 months and implants lasting 6–12 months, are being evaluated. Furthermore, passive immunization studies using broadly neutralizing antibodies for HIV prevention are in development. Successful outcome of these trials could expand the prevention options for women and pave the way for multipurpose technologies that are being developed to simultaneously address HIV prevention, fertility control, and STI prevention for women.<sup>64</sup>

Several randomized double-blind, placebo-controlled trials in a range of settings and populations have demonstrated that oral PrEP, when used correctly and consistently, can prevent sexual transmission of HIV.<sup>65–70</sup> Oral PrEP is an important HIV prevention option for women, and it is one of the few strategies that a woman can directly control. Oral PrEP is therefore a potentially promising strategy for reducing HIV among adolescent girls and young women. However, the evidence of efficacy in women is inconsistent.<sup>61,71</sup> Although 2 trials (Partners PrEP<sup>68</sup> and Botswana TDF2<sup>69</sup>) have demonstrated a protective effect of oral PrEP ranging from 66% to 75% in women, 2 other trials (the FEMPrEP and VOICE trials) showed no protective effect of PrEP in this group.<sup>61,71</sup> An analysis of drug concentrations revealed that less than 30% of the women in these trials were able to adhere to the prescribed intervention.<sup>71</sup> The ADAPT Study (HPTN 067), conducted among women in Cape Town, has shown that young, single black women in South Africa can take and adhere to a daily regimen of PrEP.<sup>72</sup> Nevertheless, consistent use is essential for the intervention to be effective. Notably, none of these trials included women under age 18 years. Data from the ongoing CHAMPS (“Pluspills”) study, which is the first adolescent PrEP study to be conducted in adolescent females globally, therefore will provide valuable information on the feasibility, acceptability, and use of oral PrEP in this vulnerable age group.<sup>73</sup>

Notwithstanding these challenges, the World Health Organization (WHO) released guidelines in 2015 on the use of oral PrEP containing tenofovir for HIV prevention to all populations at high risk of acquiring HIV and as part of combination prevention interventions.<sup>74</sup> Several countries—including France, Kenya, South Africa, and the United States—have approved the use of oral tenofovir in combination with emtricitabine PrEP formulations for HIV prevention. The challenges are now to determine how best to implement PrEP services in populations that would benefit most and support high levels of adherence. Several combination HIV prevention and demonstration projects of oral PrEP have been initiated throughout the world to inform scale-up of PrEP in populations such as young women.

### HIV Prevention Interventions to Address Structural Drivers of HIV

The use of microfinance, cash transfers, contingency management, and behavioral economics is a novel strategy being evaluated in several settings to incentivize safer HIV risk behaviors, particularly in settings where poverty, gender inequality, high school dropout rates, and other human rights violations are key drivers in HIV risk-taking.<sup>75</sup> The use of contingency management has been successful in smoking cessation, adherence in substitution therapy, keeping girls in school, improving reproductive health outcomes, and enhancing childhood immunization coverage.<sup>76–80</sup> The impact of cash transfers on reducing risky sexual behavior and HIV infection is mixed: some studies report reductions in risky sexual behavior among adolescents, such as delaying sexual debut, increasing condom use, and increasing retention in school.<sup>81</sup> In South Africa, an assessment of a publically

funded social grant program found that cash transfers were associated with a 51% decrease in transactional sex and a 71% reduction in age-disparate sex among girls, but that they had no impact among boys.<sup>82</sup> A cluster randomized controlled trial in Malawi of cash incentives for school attendance resulted in lower HIV prevalence at 18 months in the intervention communities.<sup>83</sup>

However, 2 randomized controlled trials that assessed the impact of cash transfers on HIV incidence showed no impact. The HPTN 068 Swa Koteka study ( $n = 2448$ ), which provided cash incentives for school attendance, found that there was no difference in HIV acquisition rates between the young women who received the cash transfer and those who did not.<sup>84</sup> The CAPRISA 007 cluster randomized controlled trial, which involved 3217 consenting male ( $n = 1517$ ) and female ( $n = 1700$ ) students in grades 9/10 in 14 schools in rural KwaZulu-Natal, showed that conditional cash incentives for meeting any combination of 4 conditionalities (annual HIV testing, school performance, participation in an HIV prevention program, and participation in a community project) was associated with a 30% reduction in HSV-2 incidence, but the trial did not have sufficient statistical power to demonstrate an impact on HIV incidence rates.<sup>85</sup>

The use of contingency management for HIV prevention would need to carefully consider the desired behaviors that need to be changed and the feasibility and desirability thereof in relation to the outcome. Regardless of age, risk factors and context, HIV prevention is challenging, with no quick fixes or one-size-fits-all solutions.

### Integrating HIV Prevention Efforts With Sexual and Reproductive Health Services

Early sexual debut, high teenage pregnancy rates, and high school dropout rates are more common among adolescent girls and young women from poorer socioeconomic settings than they are among those from wealthier settings. Not only is a woman's risk of acquiring HIV increased in high HIV burden settings, but there also is a high probability of transmission to infants, particularly if there are delays in seeking care and treatment. Information on sexual and reproductive health that includes information about HIV prevention is crucial from a young age. Schools are an important venue for information dissemination and support for young girls to complete high school and remain free from HIV, STIs, and pregnancy.

In addition, access to adolescent-friendly sexual and reproductive health services—including contraceptive choice, safe abortions, and antenatal care—is particularly important for the prevention of unintended pregnancies and maternal deaths.<sup>35</sup> Integration of these services with HIV prevention efforts is an opportunity to reduce the obstacles between adolescent girls and young women and the information, support, and services they require. The Family Planning Association in Malawi for example has successfully introduced mobile clinics offering services for sexual and reproductive health and HIV testing in rural areas. These mobile education services can vastly increase the number of

adolescent girls and young women who can obtain sexual health knowledge and services.<sup>86</sup>

Societal norms that place a high value on young women and men assuming more responsibility for their sexual behavior and that do not tolerate gender-based violence or older men having sex with teenagers are equally important to ensuring adolescent girls and young women are able to grow up in a safe environment and reach their full potential without bearing children as children or acquiring HIV and other STIs. Lessons from the PMTCT program in Malawi have shown that, when the male partner is involved in the process—from initial testing, to PMTCT, and through to the confirmation of HIV status—adherence and uptake rates are significantly higher.<sup>87</sup> Greater male involvement increases uptake of PMTCT, acceptance of HIV-positive status, use of fertility control, and adherence to antiretroviral therapy (if infected); it also results in a gradual positive attitude shift toward prevention and reduces the rate of pediatric infections.<sup>88</sup> In contrast, unsupportive male partners have been associated with poor communication between partners and higher rates of intimate partner violence, abandonment, and discrimination once a woman reveals her positive HIV status.<sup>89</sup>

### NEW HOPE IN PREVENTING HIV IN ADOLESCENT GIRLS AND YOUNG WOMEN

UNAIDS estimates that the number of new HIV infections in the overall population in sub-Saharan Africa declined by about 46% between 2000 and 2015, and by 37% in young people.<sup>6</sup> Although promising, these declines are too small and too slow to alter the vulnerability of adolescent girls and young women. After years of neglect, a global convergence is emerging around the urgency to address the multiple factors driving the HIV epidemic in adolescent girls and young women.<sup>90</sup>

PEPFAR's DREAMS (**D**etermined, **R**esilient, **E**mpowered, **A**IDS-free, **M**entored, and **S**afe) initiative, which was launched on World AIDS Day in 2014, brings new hope for meeting the prevention needs of adolescent girls and young women and for creating an environment that supports them. DREAMS is a public-private partnership that aims to reduce HIV infections among adolescent girls and young women in the 10 countries in sub-Saharan Africa that account for nearly half of all new HIV infections. This is the first time in the history of the HIV epidemic that a concerted advocacy and programmatic effort is being made with substantial funding to address the problem through a multipronged approach that includes national campaigns, access to combination prevention, the engagement of men (eg, linkage to HIV testing and counseling, treatment and voluntary medical male circumcision), integration of HIV services into sexual and reproductive services, and efforts to keep girls in school.

The goal of DREAMS is to ensure that adolescent girls and young women have access to prevention technologies and strategies, and the opportunity to complete high school and graduate HIV-negative, STI-free, and without pregnancies. This will be accomplished using a combination of available evidence and best practices (Fig. 1). It addresses gender-based violence, young women's rights, and the

## The DREAMS Innovation Challenge seeks solutions in six focus areas:

### STRENGTHENING CAPACITY FOR SERVICE DELIVERY



Strengthening leadership and capacity of community-based organizations, such as non-profits, indigenous, and/or grassroots organizations, to support the expansion of interventions included in the DREAMS Core Package

### KEEPING GIRLS IN SECONDARY SCHOOL



Ensuring girls' transition and access to enrollment in secondary school and addressing underlying retention issues

### LINKING MEN TO SERVICES



Pioneering new ways to engage young and adult men and link them to HIV testing and counseling, treatment, and voluntary medical male circumcision services

### SUPPORTING PRE-EXPOSURE PROPHYLAXIS (PrEP)



Supporting PrEP interventions by identifying adolescent girls and young women appropriate for PrEP initiation and adherence services

### PROVIDING A BRIDGE TO EMPLOYMENT



Providing a post-secondary school bridge to employment for young women (ages 19-24) to decrease their risk for transactional sex and HIV

### APPLYING DATA TO INCREASE IMPACT



Increasing the availability and use of data for DREAMS to inform policy, increase program impact, and help identify and support innovative solutions

**FIGURE 1.** DREAMS package: best practices for preventing HIV infection in adolescent girls and young women. Source: DREAMS Innovation Challenge Fact Sheet: <https://www.pepfar.gov/documents/organization/247602.pdf>. Used with permission from Office of the U.S. Global AIDS Coordinator and Health Diplomacy.

creation of supportive communities that address the structural drivers that directly and indirectly increase HIV risk among girls (including poverty, gender inequality, sexual violence, abbreviated schooling, and poor access to treatment for those already infected with HIV). The inclusion of oral PrEP in the DREAMS prevention package enhances access to a novel HIV prevention option for young women. Together, these efforts could help sustain the gains made to date and address some of the key gaps and challenges that persist after the end of the Global Plan by focusing on the most vulnerable group.



Although focusing on adolescent girls and young women is an important strategy to reduce the number of new infections, unplanned pregnancies, and premature maternal deaths; given the gender power disparities that underlie the vulnerability of adolescent girls and young women, inclusion of their male sexual partners in sexual and reproductive health information sessions and access to HIV prevention and treatment services could substantially enhance the effectiveness of these initiatives. The role of community and supportive environments to keep young girls in schools and reduce teenage pregnancies and HIV is equally important. The inclusion of both these aspects in the DREAMS initiative makes the intervention even more powerful.

## CONCLUSIONS

To date, there have been limited concerted efforts to focus on or address the health needs of adolescents and young people, as they are assumed to be healthy and not in need of preventive, promotive, or therapeutic services. The “youth bulge” in sub-Saharan Africa—and the notably disproportionate burden of HIV infection, premature loss of life, and unmet sexual and reproductive health needs among adolescent girls and young women—and the convergence of communicable and noncommunicable diseases highlight this important gap that requires urgent attention if we are to bridge and reduce gender disparities. The gender divergence in HIV acquisition and AIDS-related survival mirror where the foundations for gender disparities and outcomes have been laid. These age and sex differences in HIV infection place young women in developing countries at substantial disadvantage that widens with age and has ramifications beyond health. Preventing HIV infection in adolescent girls and young women not only benefits this vulnerable population, but it is critical to altering the current epidemic trajectories and enabling epidemic control in eastern and southern Africa, while sustaining the achievements of the Global Plan.

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