A Review of the Pre-Exposure Prophylaxis (PrEP) Research and Evidence Landscape in Kenya and Uganda for adolescent girls and young women

ATHENA Initiative, July 2017

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Determined Resilient Empowered AIDS-Free Mentored Safe

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Executive Summary

The review aims to take a comprehensive approach to assessing the landscape of HIV pre-exposure prophylaxis (PrEP) research and programming in Kenya and Uganda, including examining strategies and national level implementation. Furthermore, the aim is to create a knowledge base for the project, so that we know about HIV and adolescent girls and young women (AGYW) in the two countries, what we know about PrEP and how to make it work for AGYW.

A supplementary stakeholder mapping was done by our partners, PIPE and ICWEA, to give on-the-ground context. Each provided in-country background and information on:

- The current PrEP situation
- Clinical and implementation research
- Related organizational work on PrEP
- Civil society engagement
- AGYW
- PrEP stakeholders

The results of this stakeholder mapping is summarized below by country.

Uganda:

- PrEP is available through research sites, programs with funding and demonstration projects.
- PrEP is mentioned in the National Strategic Plan but no specific policies or guidance are in place at this time.
- There are many stakeholders involved in working on PrEP advocacy and research (see stakeholder mapping for detailed list).
- ICWEA is a member of a CSO Coalition on PrEP in Uganda and has been involved in the drafting process of PrEP guidelines and advocacy activities including a CSO campaign to the government to take responsibility in PrEP implementation and advocacy for guideline dissemination
- There are concerns over funding for PrEP implementation by the National Program. There has been a clear statement by the National HIV Program to leave PrEP implementation to partners who may have the resources to do so.

Kenya:

- PrEP is available through government facilities targeting sero-discordant couples and is offered as coverage before the partner living with HIV achieves viral

suppression after ARV initiation; for pregnancy among sero-discordant couples; or when there is non-adherence to ARVs among the partner living with HIV.

- PrEP is also available in specific districts receiving Global Fund and PEPFAR funds.
- PrEP is included in the National Strategic Plan however it is not focused on as a single intervention but as a combined intervention for HIV prevention. The HIV prevention revolution focuses on both biomedical and structural interventions but there has been less funding for behaviour change interventions that address other underlying issues such as gender based violence and gender inequality
- Advocacy from civil society and researchers has been aimed at advancing PrEP access in country through dialogues and advocacy strategies among key populations. However, very little is known on PrEP and adolescent girls and young women therefore advocates have been working on guidelines development and PrEP roll-out.

List of abbreviations

AGYW	Adolescent girls and young women
ARV	Antiretroviral
DHS	Demographic and health survey
DREAMS	Determined, Resilient, Empowered, AIDS-free, Mentored, and Safe
FSW	Female sex worker
PEPFAR	U.S President's Emergency Plan for AIDS Relief
PrEP	Pre-exposure prophylaxis
UNAIDS	Joint United Nations Programme on HIV/AIDS
VMMC	Voluntary medical male circumcision
WHO	World Health Organization

Pre-exposure prophylaxis (PrEP) medication

TDF	tenofovir disoproxil fumarate
TDF-FTC (Truvada®)	emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg (manufactured by Gilead)

Methodology

The content of this document is based on information collected through a systematically approached review of available documents relevant to PrEP research, roll-out and implementation among adolescent girls and young women. This includes web research and consultation with experts in the field.

Literature review by analyzing secondary data: during the desk review, HIV and PrEP related materials were reviewed, including policies, strategies, reports and other relevant documents. The literature review covered global publications, such as WHO and UNAIDS documents and publications related to the target countries themselves.

Introduction

Adolescent girls and young women (AGYW) have been identified as a group at disproportionate risk of acquiring HIV. Addressing this uneven burden is increasingly prioritized in the global HIV response. Global estimates indicate that AGYW account for 60% of the new HIV acquisitions among young people (UNAIDS, 2016). Sub-Saharan Africa faces a particularly high proportion of young women – 80% of the world's AGYW living with HIV reside here (UNAIDS, 2014).

High levels of HIV acquisition among AGYW and the unequal distribution have prompted a focus on adolescents as a target for HIV prevention, including the target to reduce new HIV acquisition to fewer than 100,000 among AGYW by 2020 as set forth by the 2016 UN Political Declaration on Ending AIDS (UNAIDS, 2016). The DREAMS Partnership, led by PEPFAR, along with the Bill and Melinda Gates Foundation, and Girl Effect, seeks to achieve a reduction in HIV acquisition among AGYW through the scale up of interventions targeting causes of young women's vulnerability including biological, behavioural and structural sources. Among a package of recommended interventions is pre-exposure prophylaxis, known as PrEP.

PrEP is the daily use of anti-retroviral HIV medicines (ARVs) by a HIV negative individual to prevent the acquisition of HIV. When taken consistently, data show that PrEP has reduced HIV acquisition by up to 92% in people who are at high risk (CDC, 2017). Currently, the ARV used for this purpose is tenofovir disoproxil fumarate and emtricitabine known as TDF-FTC or Truvada under the brand name. Regular HIV testing – at the time of PrEP initiation and then on an on-going basis, is required for the intervention. According the World Health Organization (WHO) PrEP should be offered in addition to a comprehensive prevention package that includes HIV testing, counselling, male and female condoms, lubricants, ARV treatment for partners living with HIV, voluntary medical male circumcision (VMMC), and harm reduction interventions for people who use drugs (WHO, 2012).

The Young Women Lead, Evidence, Advocate, Research, Network (LEARN) project is a two-year project funded by PEPFAR through the DREAMS Innovation Challenge (DREAMS-IC) led by the ATHENA Initiative and their community partners PIPE and ICWEA. The objective of LEARN is to enhance the rollout of PrEP by, with, and for adolescent girls and young women. The overarching goal is to achieve an HIV prevention agenda that is responsive to the needs, rights, priorities, and preferences of AGYW through the meaningful participation of AGYW in research.

Through past and present work, the ATHENA Initiative has identified clear deficits in reaching and engaging adolescent girls and young women in funding decisions to policy making or technology development, as well as in providing the education, services, and tools they need to help them protect themselves against HIV. We have created new

models of consultation, engagement, coalition building, and inquiry for entities such as the WHO, UNAIDS, the Global Fund to Fight AIDS, Tuberculosis and Malaria, and UN Women among others. We've also established new ways of supporting meaningful participation of young women through virtual movement building and online dialogues. For example, #WhatWomenWant is a global movement, led by the ATHENA Initiative that seeks to promote this very simple principle: that the most affected are the most informed, and real solutions come from lived realities. Through it, ATHENA seeks to amplify women's voices, highlight our realities, and power our solutions by creating a platform for women, including young women, to influence global policy discourse that doesn't require an invitation, or a visa and with a social media reach in the millions. Our recent consultation and participatory accountability process engaged AGYW across East and Southern Africa to review UNAIDs HIV prevention guidance. 185 AGYW from more than nine different countries engaged through WhatsApp with each other and with key decision-makers, providing rich, insightful feedback on what was needed to ensure strategies are implemented effectively for AGYW.

Young Women LEARN is an exciting opportunity to continue this work of **meaningful engagement, participation, and leadership with adolescent girls and young women**. LEARN will enable a cadre of HIV prevention ambassadors among AGYW most impacted by HIV to:

- define their priorities
- set agendas and lead research
- gather meaningful data in safe learning environments
- contribute to the formal evidence base around HIV prevention science, and
- advocate for prevention programming reflecting AGYW's lived realities, values and preferences.

LEARN is a tremendously vital and timely project given the HIV epidemiological and PrEP context in Kenya and Uganda as it will **develop a robust, relevant knowledge base to inform PrEP roll-out and implementation while also partnering with AGYW as effective change agents.**

Global PrEP Picture

In 2014, the WHO's guidance recommended PrEP for persons at substantial risk of HIV infection including offering PrEP to men who have sex with men (MSM) and the negative partner in serodiscordant couples (WHO, 2012). As a result, high and middle income countries are starting to prioritize its use in the MSM population (Baggaley, et al., 2016).

In 2015, the WHO amended their original briefing on PrEP to expand upon the recommendations from serodiscordant couples and MSM to an all-encompassing

"people at substantial risk". This risk is defined as places where incidence of HIV is high (>3 per 100 person-years) in the absence of PrEP. In these settings classified as having "high" HIV incidence among young women aged 15 to 24 years, PrEP should be offered voluntarily (WHO, 2016).

Context of HIV Epidemic

Epidemiology data

HIV prevalence – the proportion of the population living with HIV - is consistently and substantially higher among adolescent girls and young women than their male peers (UNAIDS, 2016). According to the UNAIDS Gap Report 2014, a worrisome pattern of rapidly increasing prevalence between the ages of 15 and 24 among AGYW is found in almost every country in Eastern and Southern Africa. AGYW are disproportionately vulnerable and at high risk for new HIV acquisition (incidence). Globally, almost 380 000 (95% Confidence Interval 340 000 – 440 000) HIV acquisitions occur among this vulnerable population.

Strategies aimed at reducing HIV acquisition require an understanding of the epidemiologic context of the HIV epidemic. Estimates by geographic location differ greatly with uneven distribution of HIV due to complexities surrounding social, structural, and economic environments. Certain locations and populations are more vulnerable than others (Global Fund, 2017). While the figures summarized in the table below are an important starting point, it is crucial to understand that national level data often mask local variations and substantial heterogeneity exists in countries in terms of where and in whom HIV acquisitions take place. For example, in Kenya, the geographic regions of Homa Bay and Kisumu experience >15% HIV prevalence (hyper-endemic) compared to Mandera where the HIV prevalence among the general population is 1-4.9% (UNAIDS, 2014).

Available sex and age disaggregated HIV incidence and prevalence data on adolescents are limited (Idele, et al., 2014) however the available Kenya and Uganda country level HIV epidemic indicators clearly show that young women and adolescent girls are disproportionately affected. In Kenya, infection rates among 15-24 years old females are approximately two times higher than in males of the same age group. Uganda experiences a similar HIV epidemic picture where AGYW experienced new HIV acquisition rates significantly higher compared to their male peers. (29,000 and 17,000 respectively).

The HIV prevalence among AGYW in the central Uganda district, which covers Mubende, Mukono, and Mityana, is 5.1% (Uganda AIDS Indicator Survey, 2011). Distinct district level HIV estimates for AGYW are unavailable.

Table 1: Country Level HIV Epidemic Indicators		
Indicators	Uganda (2013)	Kenya (2013)
People living with HIV	1 600 000 [1 500 000 – 1 700 000]	1 600 000 [1 500 000-1 700 000]
AIDS-related deaths	63 000 [56 000 71 000]	58 000 [49 000-72 000]
HIV prevalence (adults aged 15-49)	7.4% [7.0-8.0%]	6.0% [5.6-6.6%]
HIV incidence (adults aged 15-49)	0.80% [0.70-0.92%]	0.44% [0.34-0.56%]
HIV prevalence among young women (15-24 years)	4.2% [3.7-5.0%]	2.8% [2.4-3.4%]
HIV prevalence among young men (15-24 years)	2.4% [1.7-3.3%]	1.7% [1.3-2.3%]
New infections among young women (15-24 years)	29 000 [35 000-35 000]	19 000 [15 000 – 25 000]
New infections among young men (15-24 years)	17 000 [12 000-21 000]	10 000 [7 500-14 000]
Sources: UNAIDS 2013 HIV estimates; Uganda Global AIDS Response Progress Report, 2013; Kenya AIDS Indicator Survey (2007 & 2012).		

Table 2: District Level Estimates				
Kenya	HIV Prevalence of general population	New HIV Acquisition (0-14 years)	New HIV Acquisition (15+ years)	Population of Girls 15-24
Homa Bay	25.7%	2,724	12,279	238,746
Nairobi	8.0%	316	3,098	219,152
Kenya HIV Estimates 2014; Kenya Population Census 2015 Projections				

Knowledge and Behavior Data

Although not sufficient to change behavior and reduce risk on its own, a basic understanding of HIV and how it spreads is a necessary component of prevention. Comprehensive knowledge is an indicator that measures how much young people know about transmission and prevention of HIV. Comprehensive knowledge includes knowing that condoms and monogamy prevent HIV transmission, that a healthy person can have HIV, and rejects the two most common local misconceptions about HIV transmission (National AIDS Control Council, 2015)

Demographic and Health Surveys (DHS) are nationally-representative household surveys that provide data for a wide range of indicators including HIV/AIDS knowledge, attitudes, and behavior. Participants are asked if it is possible to reduce the risk of HIV acquisition through the following prevention methods: consistent condom use during sexual intercourse, limiting the number of sexual partners or staying faithful to one

partner, and sexual abstinence. The last DHS in Kenya was in 2014 and in 2011 in Uganda.

The table below summarizes the most recent Kenya and Uganda DHS and shows that knowledge about condom use and limiting sexual partners as methods of avoiding HIV transmission is generally high and widespread. Seventy-seven percent of young women and 86 percent of young men aged 15-24 years know that the risk of HIV acquisition can be reduced by using condoms. In both countries, knowledge of HIV prevention methods is consistently higher among men compared to women in each knowledge area. This pattern is consistent in most affected regions globally. These disparities are linked to gender, education, household health, and place of residence (Idele, et al., 2014).

Knowledge of HIV Prevention Methods: condom use and limiting sexual partners								
	Women (15-24 years)				Men (15-24 years)			
	Using condoms	Limiting sexual intercourse to one uninfected partner	Using condoms and limiting sexual intercourse to one uninfected partner	Number of women	Using condoms	Limiting sexual intercourse to one uninfected partner	Using condoms and limiting sexual intercourse to one	Number of men
Kenya	77.4%	89.3%	72.8	11,555	86.1%	92.0%	82.0%	4,666
Uganda	79.0%	87.3%	73.6	3,677	83.9%	90.9%	79.1%	872
Kenya DHS 2014; Uganda DHS 2011								

Comprehensive knowledge about HIV prevention is defined in the DHS as knowing that consistent use of condoms during sexual intercourse and having just one HIV negative faithful partner can reduce the chance of HIV acquisition, knowing that a healthy-looking person can have HIV, knowing that HIV cannot be transmitted by mosquito bites, and knowing that HIV cannot be acquired by sharing food with a person who has AIDS.

Data from the Kenya DHS survey of 2014 found that comprehensive knowledge about HIV prevention among young people aged 15-24 years was 64 percent.

In 2014 in Uganda, the percentage of young men and women aged 15-24 years who correctly identify ways of preventing transmission of HIV and who reject major misconceptions about HIV transmission was 38.5 percent. Disaggregating the data by sex revealed that young women's comprehensive knowledge was significantly less: 42.3 percent of young men and 35.7 percent of young women had comprehensive knowledge of HIV prevention (LQAS, 2014).

Evidence

A growing body of high-quality evidence supports that PrEP is an effective intervention for HIV prevention. The research landscape currently includes implementation research on delivering daily oral PrEP and clinical trials of new delivery mechanisms, including vaginal ARV-containing rings. Globally, there are numerous ongoing and planned PrEP demonstration and implementation studies. Of these, around twelve include adolescent girls and young women. Results for these have yet to be published (AVAC, 2016).

Key evidence show that PrEP is: effective when taken consistently, has an exceptional safety profile, the risk of drug resistance is low, can be used with hormonal contraception and during pregnancy, and is acceptable among the populations studied (WHO, 2015).

A systematic review of eighteen studies demonstrated that PrEP was effective at preventing HIV transmission across sexes, types of sexual exposure, regimes and dosing schemes (Fonner, et al., 2016). Worldwide, PrEP has demonstrated efficacy for HIV protection in multiple geographies and at-risk populations including MSM, serodiscordant couples, heterosexual men, women, people who inject drugs, and transgender women (Baeten, et al., 2012; Thigpen, et al., 2012; Grant, et al., 2010).

The first study showing evidence of PrEP efficacy was presented at the 2010 International AIDS Conference in Vienna. The trial assessed the effectiveness and safety of TDF gel for the prevention of HIV acquisition in women in KwaZulu-Natal, South Africa. Overall, women with high adherence experienced 54 percent reduced HIV acquisition. Following this formative study, a series of other studies were released with various populations – men having sex with men, serodiscordant couples and sex workers. A picture emerges when examining all of the studies together – effectiveness of PrEP in men is clear across the board (Fonner, et al., 2016). Unfortunately, the situation among women is not as clear cut. Studies show varying levels of effectiveness and have complex and disparate results (Cohen, et al., 2012 & Baeten, et al., 2012).

PrEP Facts

Efficacy

When taken as prescribed, PrEP is highly effective for preventing HIV acquisition
PrEP does not prevent pregnancy or other sexually transmitted infections (GC/CT/syphilis/genital warts/HCV)

Side-effects

1 in 10 PrEP users may have side-effects such as nausea, abdominal cramps, headache; these are usually mild and resolve over the first month of taking PrEP. 1 in 200 may have creatinine elevation (typically reversible if stop PrEP). 1% average loss of bone mineral density; recovers after stopping PrEP.

Special situations:

- Pregnancy and breastfeeding: PrEP can be offered and continued.
- HBsAg+: Assess HBV treatment indications, consider risk of flare if PrEP stopped. Exposure to HIV in the past 72 hours: Use PEP for 28 days, then start PrEP.
- Acute viral syndrome: Check HIV RNA or Ag; consider a 3-drug PEP or ART.

(WHO Clinical PrEP Essentials: http://www.who.int/hiv/topics/prep/en/)

PrEP Evidence for AGYW

This evidence summary focuses on five randomized trials as they provide the best available evidence for use of PrEP for AGYW in a Kenya/Uganda setting. The following trials explored the efficacy of daily oral TDF or TDF-FTC to prevent HIV acquisition in several high risk populations of sexually active women:

- FEM-PrEP (Van Damme, et al., 2012)
- VOICE trial (Marrazzo, et al., 2015)
- Partners PrEP (Baeten, et al., 2012)
- TDF2 Study (Thigpen, et al., 2012)
- ADAPT (Bekker, et al. 2015)

The FEM-PrEP study and the VOICE trials, two trials of daily oral PrEP, were unable to accurately assess the effect of TDF-FTC on HIV acquisition or safety. The FEM-PrEP study (Pre-exposure Prophylaxis Trial for HIV Prevention among African Women) was a

double-blind, placebo-controlled trial in Kenya, South Africa, and Tanzania examining the effectiveness of daily oral TDF-FTC. Among all participants, including women younger than 25 years old, adherence was too low and lost to follow up was too high (13%) to make any clear conclusions regarding PrEP effectiveness and safety in the study population (Van Damme, et al. 2012).

The VOICE trial (Vaginal and Oral Interventions to Control the Epidemic) tested the effectiveness of daily dose of ARVs in oral form, either TDF or TDF-FTC, or as a vaginal gel. It took place between 2009 and 2012 in 15 clinic sites in South Africa, Uganda, and Zimbabwe and enrolled 5,029 HIV negative women. Participants reported perceiving themselves to be at risk for HIV, however many experienced a lack of support for study participation from partners and/or community, while some felt suspicious and confused by taking medication when healthy. The trial was stopped early due to a lack of effectiveness due to low adherence, a finding similar to the FEM-PrEP study. Results from this trial demonstrated low adherence (measured by drug levels in blood) to oral or vaginal ARV tenofovir products among women in South Africa, Uganda, and Zimbabwe however no conclusions can be drawn about PrEP effectives in these populations.

The data from these trials were further analyzed and revealed that adherence was low to the PrEP regime and ultimately, the researchers were unable to determine whether the intervention provided any protection. Furthermore, the results clearly highlight the need to better understand indicators of adherence to ensure effectiveness of daily oral PrEP roll out and implementation.

The Partners PrEP study (Baeten et al. 2012 and Baeten et al. 2014) was a double-blind randomized controlled trial evaluating TDF-FTC or TDF or placebo in 4,747 HIV-negative individuals in serodiscordant relationships in Kenya and Uganda. This study, in contrast to the FEM-PrEP and VOICE studies, found that PrEP was efficacious overall and among young women under the age of 30. It found that when participants adhered closely to the daily drug regimen, TDF-FTC reduced HIV acquisition by 73 percent among heterosexual partners.

The Centers for Disease Control Botswana TDF-2 Study found TDF-FTC to be effective at preventing HIV acquisition among sexually active heterosexual adults. The overall protective efficacy of TDF-FTC as compared with placebo was 62.2 to 77.9 percent. However, the study was concluded early due to low retention and logistic limitations and found a significant decrease in bone mineral density among participants receiving PrEP. The authors conclude that the long-term safety of daily oral TDF-FTC remains unknown (Thigpen, et al. 2012).

The ADAPT Study (HPTN 067) was designed to investigate whether a non-daily versus daily PrEP dosing, resulted in equivalent prophylactic pre and post sex coverage. Participants were randomly assigned to one of three dosing regimens after 6 weeks of once a week directly observed dosing. 24 weeks of self-administration of PrEP were

either: daily, twice weekly with a post-sex dose, or event driven before and after sex dosing. The study was conducted across geographies and groups – women in Cape Town, South Africa, and MSM and transgender women in Bangkok, Thailand and Harlem, N.Y. The findings support that daily dosing of PrEP results in better coverage of sex acts and adherence, and higher drug levels and supports recommendations of daily oral PrEP in women (Bekker, et al, 2015).

A behavioral sub-study of ADAPT was also conducted to evaluate the feasibility of nondaily PrEP regimens among the participants from Cape Town. Themes characterizing discourse suggested that the participants place high value on contributing to the well-being of the community, experienced a degree of skepticism towards PrEP and the study more generally, and reported a wide range of approaches towards PrEP. In the context of the ADAPT trial, the use of PrEP was highly influenced by underlying beliefs about safety, reciprocity of contributions to the community and trust in transparency and integrity of the research (Amico, et al., 2017).

Summary of research

- The evidence base for oral PrEP for women is somewhat mixed as estimates of effectiveness vary in each trial.
- There is enough evidence to show that PrEP does work for women – if we can support effective adherence.
- Understanding indicators of adherence is necessary to ensure effectives of PrEP roll out and implementation
- As with any prevention tool, it won't be right for everyone and adherence is a major consideration for this population.

The following table, borrowed and adapted from PrEPwatch, summarizes completed, ongoing, and planned daily oral PrEP clinical trials involving adolescent girls and young women as participants.

Daily oral PrEP clinical trials with AGYW				
Trial/Project	**Type/Category**	**Population**	**Design**	**Status**
KENYA				
Partners PrEP trial	Demonstration project	Serodiscordant couples	Evaluates HIV prevention preferences among serodiscordant couples, adherence to PrEP and ART and interface of	Completed

			reproductive health priorities and ART-based interventions	
Partners PrEP OLE	Open Label Extension	Serodiscordant couples	After recommendation, placebo arm discontinued and active arms continued and placebo arm was re-randomized to PrEP collect additional comparative data.	Complete
FEM-PrEP	Phase III trial RCT	Women aged 18-35 years	Evaluated the safety and effectiveness of once-daily Truvada for HIV prevention in women.	Complete
POWER: Prevention Options for Women Evaluation Research	Demonstration project	AGYW aged 16-24 years	Assessing women's preference for using microbicides and PrEP	Ongoing
LVCT Health and SWOP Kenya (IPCP-Kenya)	Demonstration project	FSW (+18 years) and young women at high HIV risk (aged 15-29 years)	Assessing consumer perceptions, cost, delivery option, potential barriers, and opportunities and acceptability among participants;	Ongoing
Gender-specific Combination HIV Prevention for Youth in High Burden Settings (MP3-Youth)	Demonstration project	Adolescent men and women aged 15-24 years	To evaluate the acceptability of a gender-specific combination HIV prevention package for youth in high burden settings	Ongoing
MTN-034/IPM 045	Phase IIa, Open Label	AGYW aged 16-17	Purpose of trial is to collect safety and adherence data and acceptability of study products, including oral TDF	Planned
UGANDA				

Partners PrEP trial	Demonstration project	Serodiscordant couples	Evaluates HIV prevention preferences among serodiscordant couples, adherence to PrEP and ART and interface of reproductive health priorities and ART-based interventions	Completed
IMPAACT 2009 (DAIDS ID 30020): Feasibility, Acceptability, and Safety of Oral Pre-Exposure Prophylaxis for Primary HIV Prevention during Pregnancy and Breast Feeding in Adolescents and Young Women	Observational study	AGYW aged 16-24 years	Parallel, observational cohort study of HIV-uninfected pregnant AGYW; designed to characterize adherence among women who initiate once daily oral PrEP during pregnancy and continue into the first 6 months following delivery.	Planned (expected completion 2019/2020)
Partners PrEP OLE	Open Label Extension	Serodiscordant couples	After recommendation, placebo arm discontinued and active arms continued and placebo arm was re-randomized to PrEP collect additional comparative data.	Complete
OTHER COUNTRIES				
Choices for Adolescent Methods of Prevention in South Africa (CHAMPS)	Demonstration project	Heterosexual adolescent men and women aged 15-19 years	Designed to combine different HIV prevention strategies into an optimized prevention 'menu'	Ongoing
CAPRISA 082: Prospective	Observational study	AGYW aged 18-24 years	Examines: HIV risk perception and	Ongoing

Study of HIV Risk Factors and Prevention Choices in Young Women in KZN, South Africa			behavior; data on PrEP uptake	
3Ps for Prevention Study; South Africa	Demonstration project	AGYW aged 16-25 years	Assesses oral PrEP uptake and incentives for adherence	Planned
UNICEF PrEP Demonstration Program; South Africa, Brazil, Thailand	Demonstration project	Adolescents	Addresses the regulatory, structural, and capacity challenges in PrEP roll out	Planned
Church of Scotland Hospital PrEP Project; South Africa	Demonstration project	Adolescent girls	Aims to recruit pregnant adolescents at their first ANC visit. Focus will be on assisting young mothers to return to school, preventing acquisition of HIV and postpone further pregnancies.	Planned
HPTN 082: Evaluation of daily oral PrEP as a primary prevention strategy for young African women: A Vanguard Study; South Africa, Zimbabwe	Demonstration project	AGYW aged 16-25 years	Evaluation of effectiveness of PrEP as an HIV prevention tool	Planned
Right to Care (DREAMS); South Africa	Demonstration project	AGYW	Aim is to reduce HIV infections among AGYW; PrEP is among the package of interventions for DREAMS	Planned
EMPOWER (Enhancing	Demonstration project	AGYW aged 16-24 years	Integration of violence prevention	Planned

Methods of Prevention and Options for Women Exposed to Risk) Consortium; South Africa, Tanzania			and combination efforts, including PrEP. Aims to assess feasibility, safety, and acceptability of PrEP.	
[adapted from PrEP watch website] http://www.avac.org/resource/ongoing-and-planned-prep-demonstration-and-implementation-studies				

PrEP picture in Kenya and Uganda

The following table summarizes TDF-FTC registration, policy and regulatory documents, and the organizations implementing, researching, delivering, providing technical assistance, funding, and advocating for PrEP roll-out among adolescent girls and young women in Kenya and Uganda. The table is an adaptation of information provided on AVAC's PrEPwatch website and includes relevant information through the review process undertaken for this desk review.

	Kenya	Uganda
Truvada (TDF/FTC) Registration	May 2005	January 2005 (for treatment but not prevention)
Policy/Regulatory	**Kenya Ministry of Health –** creates national plans and oversees HIV specific divisions: • NACC – implementation strategic plans, coordinates stakeholders, leverages resources • NASCOP – oversees policy and guidelines, coordinates technical HIV programming, manages supply chains and capacity building, performs M&E • National technical working groups – provides leadership and strategic guidance for implementation **Kenya Prevention Revolution Roadmap** – led by ministry of health through NACC and NASCOP	**National Strategic Plan** – PrEP is mentioned but there are no specific guidance documents available. Currently, decision makers and politicians are discussing the cost and demand for PrEP against demands for treatment for those HIV positive. **PEPFAR's Country Operational Plan (COP) 2017 – "**PrEP implementation guidelines allow for expansion of services among key and priority populations".

	Kenya Strategic Framework **Kenya's Fast-track Plan to end HIV and AIDS among Adolescents and Young People (2015) –** identifies adolescents and young people as a priority population for the HIV response. PrEP is mentioned as a strategic intervention for high incidence counties including Homa Bay **Framework for the Implementation of Pre-Exposure Prophylaxis of HIV in Kenya –** published by the National AIDS & STI Control Program (NASCOP) Kenya will offer PrEP as part of HIV combination prevention for people at substantial ongoing risk of HIV infection.	PrEP will be delivered as an integrated package within accredited health facilities with the COP17 scale up being informed by results from pilot interventions in COP16. As part of COP15, PrEP will be given to 1000 AGYW as part of a DREAMS demonstration project.
Implementation	Began with planning and formulation of a national TWG enabling Kenya to prepare for pilot and eventual scale-up with evaluation phases.	
Advocacy Organizations*	Civil society groups and researchers have worked together to advance PrEP nationally. Efforts include dialogues and advocacy among key populations and at the national stakeholder level. ➢ ICW Global ➢ Kenya Legal and Ethical Issues Network on HIV/AIDS ➢ Nyanza Initiative for Girl's Education and Empowerment ➢ Orga Foundation ➢ UNAIDS ➢ WACI-Health	Civil society groups have been working to articulate the need for PrEP.
Service Delivery Organizations *	➢ NASCOP (AGYW) ➢ PEPFAR ➢ LVCT Health	
Implementing Organizations *	➢ ICRHK – International Center for Reproductive Health Kenya ➢ Jhpiego	
Research Organizations *	➢ CONRAD ➢ MTN	

	➢ New York University ➢ RTI International ➢ University of Pittsburgh ➢ University of Washington	
Evaluation Organizations *	➢ Population Council (AGYW) – (community based assessment; program impact; feasibility/ acceptability; program evaluation) ➢ African Population & Health Research Center (impact evaluation) ➢ LSHTM (impact evaluation) ➢ Avenir (M&E)	
Demand Creation *	➢ PS Kenya	
Funding Organizations *	➢ PEPFAR ➢ USAID	
Guidelines *	➢ NACC (government) ➢ WHO (technical assistance)	
Marketing/media Organizations *	➢ McCann ➢ African Gender and Media Initiative (GEM) ➢ Community Media Trust Kenya ➢ The African Centre for Women, Information & Communications Technology	
Technical Assistance	➢ AVAC ➢ CHAI ➢ FSG	
Introduction Activities	➢ **LVCT Health demonstration project** – focused on entry points for FSW and AGYW ➢ **MP3 Youth Project** – mobile service delivery of PrEP ➢ **Partners Demonstration Project** – PrEP is provided to the HIV-negative partners in serodiscordant couples ➢ **PEPFAR's DREAMS initiative** – adolescent and youth friendly services and an impact evaluation (the London School of Hygiene and Tropical Medicine) and qualitative research around implementation of DREAMS (the	**USAID Microbicide Product Introduction Initiative (MPii):** ➢ **CHARISMA –** support women's agency to safely used ARV-based prevention products and reduce vulnerability to IPV.

	Population Council). Of the ten countries where DREAMS operates, five have included PrEP for adolescent girls and young women in their country plans to address HIV. **USAID Microbicide Product Introduction Initiative (MPii) -** USAID's office of HIV/AIDS is supporting 5 interconnected projects on ARV-based prevention. Agreements/projects run from 2015-2020. They include: ➢ **OPTIONS –** support to provide access to ARV-based HIV prevention products ➢ POWER – develop cost-effective and scalable models for implementation of ARV-based prevention for women. ➢ **GEMS –** Kenya – inform policies and define programmatic considerations related to use ARV-based HIV prevention products and risk of resistance. ➢ **EMOTION –** Kenya – increase uptake and correct and consistent use of ARV-based HIV prevention products by women at high risk of HIV infection	
*HIV Prevention Market Manager – AVAC (excel sheet) http://www.prepwatch.org/scaling-up/kenya-close-up/ All organizations listed are working with AGYW OPTIONS – Country Situation Analysis Interim Findings: Kenya		

Other PrEP resources and guidance

Population Council Guidance

The Population Council have developed a guidance document to provide DREAMS country teams with practical guidance on building evidence to guide PrEP introduction for adolescent girls and young women. Its aim is to complement emerging global guidance documents and to examine the factors that influence informed choice, demand, and use of PrEP by young women. The document has five sections outlining: a framework for PrEP introduction to AGYW, key actors (e.g. AGYW themselves, service providers, male partners, etc.) that influence AGYW's choices, additional data

collection techniques, practical advice for conducting analysis, and an overview of practices to foster research utilization (Pilgrim, et al. 2016).

FHI360 Guidance for providing informed-choice counseling on sexual health for women interested in PrEP

The purpose of the guidance is to promote informed decision-making for women who have expressed interest in using PrEP. It is written for service providers who provide HIV risk-reduction counseling at facilities that offer PrEP.

OPTIONS consortium

The Optimizing Prevention Technology Introduction on Schedule (OPTIONS) consortium is a project funded by USAID in partnership with PEPAR to expedite and sustain access to ART-based prevention tools. It brings together a combination of ARV research experts across global, regional and country fields. OPTIONS is led by FHI 360 and comprises of two additional partners: Wits Reproductive Health and HIV Institute (Wits RHI) and AVAC. It operates in Kenya, South Africa, and Zimbabwe.

Questions/Challenges

Ethical and equitable introduction of PrEP has to take into consideration the particular challenges and barriers that adolescent girls and young women may have. These include, but are not limited to, the following: legal and policy constraints affecting access to SRH services, stigma and social acceptability, gendered power dynamics, risk perception and risk compensation, and service delivery strategies and models (Mathur, et al., 2016).

Challenges to PrEP roll-out and implementation can be categorized in the following areas: adherence/behavior, biology, delivery, sustainability, awareness, and research gaps.

Adherence

Available PrEP evidence shows that if taken consistently, it is an effective HIV prevention tool however behavioral factors undermine the effectiveness of PrEP. Studies show the level of adherence correlates well with the level of protection (CAPRISA, Partners PrEP, VOICE, FACTS 001) and this points to the importance of strategies to maximize adherence (AVAC, 2016). Several studies included in a systematic review of 18 studies indicated that younger participants had poorer adherence to PrEP when compared with older participants (Fonner, et al., 2016).

PrEP for adolescent girls and young women must be considered in the wider context of the under-representation of women in HIV research, and the challenging experiences

PrEP trials have demonstrated in supporting and enabling effective levels of adherence. This problem is evident in the results of the VOICE trial where the trial was discontinued early due to the findings that none of the products tested were effective in preventing HIV acquisition. The lack of success was attributed to insufficient adherence, although study participants reported good adherence.

Reports that emerged after the trial attributed blame to the young women for the trial's failure. Following the closure of the study, Stadler, et al. (2015) conducted interviews and qualitative studies with the participants that showed a number of reasons participants had low adherence and concealed it. The following themes emerged:

- The medical monitoring and pregnancy and HIV testing offered through the trial motivated participants to join
- Participants were aware it was a placebo-controlled trial and stock-piled the product until there was proof it worked, or gave it to others
- They believed rumors of PrEP being unsafe, that it made you infertile or actually gave you HIV

It is important to consider the environment of trials and the nature of participation under which adherence to PrEP has been studied. Stadler, et al. (2015) state:

> "While some critics saw the adherence lie as a deliberate act of 'elaborate deception', this interpretation is ultimately too simplistic. A focus on individual motives of self-interest or 'altruism' fails to recognize the inherently political nature of trial participation and the multi-layered and competing subjectivities that it may engender"

The remarkable variability of findings from the studies relevant to PrEP use among AGYW highlights the importance of additional research to allow further understanding of other factors that might influence efficacy as the reason for differing results remains unclear (Cohen, et al., 2012 & Baeden, et al. 2012). Further, adherence in real world settings – where people know they are receiving a real, effective drug -is likely to be motivated by different factors and drivers than in a placebo-controlled blind trial.

We can learn from the experience of supporting adherence among AGYW in other contexts. For example, adherence to ARVs amongst AGYW living with HIV, or to other preventative drugs like the contraceptive pill. Evidence from cohort studies suggests that adolescents find it more difficult to adhere to ART compared to adults. AGYW may require increased adherence support, tailored to their age and lifestyle (Nachega, et al., 2009). The HPTN 067/ADAPT Cape Town trial demonstrated that AGYW in this population were able to adhere to daily dosing of PrEP when supported to do so (Bekker, et al. 2016).

Further questions on adherence remain to be answered – is there evidence on adherence to PrEP in real life or is that still to be seen?

HIV Drug Resistance

Addressing concerns around HIV drug resistance (HIVDR) will be an important consideration for PrEP roll-out and implementation. Pre-treatment HIVDR (PDR) is described in the *WHO's Global Action Plan on HIV Drug Resistance 2017 - 2021* as Resistance detected in individuals starting ART and is acquired due to previous ARV drug exposure. The action plan states that resistance can hamper the effectiveness of PrEP. In order to combat this, the WHO among other PrEP recommendations, recommends delivering drugs in ways that minimize treatment interruptions and maximize adherence. At a country level, it is recommended that PrEP services and programs are monitored to ensure quality. For researchers, evidence is needed on public health interventions that have the greatest impact in preventing and responding to HIVDR for that to be used for national and global-decision making, including in the area of PrEP implementation. As stated above, good quality programs that support adherence among adolescent girls and young women are necessary.

Increased risk of STIs

A study on Australian PrEP users found a significant reduction in condom use with a concomitant significant increase in STIs over the first year of PrEP use (Lal, et al., 2017). This study, among other research on MSM and PrEP, highlight the concerns that PrEP may be associated with risk compensation and an increase in STIs. Research is needed to investigate the relationship between PrEP use among AGYW and STIs.

Behavior

Providing acceptable and effective HIV prevention services is complex and involves choices that take into consideration behavioral, social and structural barriers. Successful adoption of prevention interventions is often compounded by behavioral factors.

Risk perception – as evidenced by the VOICE trial, perception of risk alone is not always the barrier – although study participants reported perceiving themselves to be at risk for HIV, many experienced a lack of support for study participation from partners and/or community members, while some felt suspicious and confused by taking medication when healthy.

HIV testing - testing for HIV negative at risk persons is crucial to the delivery of PrEP and is the first step for initiation. PrEP also requires on-going HIV testing to reduce the

risk of ART resistance. HIV self-testing was found to be highly acceptable among Kenyan couples – recommended adjunct to PrEP delivery – what about among AGYW? (Ngure, et al., 2017).

Consent

There are challenges related to who provides consent to those under age 18, as with any medication prescribed or offered to minors.

Biology

Vaginal microbiome and PrEP effectiveness may be related. Research has begun to shed light on women's biological vulnerability to HIV including the relationship between the female reproductive tract, the immune system's inflammatory response, and the vaginal microbiome (Adimora, et al. 2013). Data suggest vaginal tenofovir gel may not effectively prevent HIV among women with bacterial vaginosis raising concern whether daily oral tenofovir could be less effective for these women.

Now, some researchers are beginning to examine the relationship between the vaginal bacteria and PrEP efficacy in women. In the CAPRISA 004 trail, which tested a 1% tenofovir vaginal gel for HIV prevention, researcher compared bacterial genetic material from women who acquired HIV and those who remained HIV negative. They found that women who carried the bacteria Prevotella bivia were 13 times more likely to contract HIV. The findings from related studies examining the results of the trial indicate that the disparity in PrEP efficacy between men and women is not entirely due to lower adherence and raise the possibility that eliminating harmful bacteria could lower women's risk to HIV infection (Burgener, 2016, Passmore, 2016, and Abdool Karim 2016)

Researchers from the UNC Chapel Hill have published a novel translational pharmacology investigation that shows vaginal, cervical, and rectal tissue all respond differently to PrEP. Colorectal mucosal tissue concentrations of tenofovir, emtricitabine, and their active metabolites was 10 times higher than that in the lower female genital tract. Adherence to 6 of 7 doses/week was required to protect lower female genital tract tissue from HIV, while 2 of 7 doses/week was needed to protect colorectal tissue (Cottrell, et al, 2016).

Delivery

PrEP must fit within the broader HIV response and therefore PrEP implementation should enhance HIV programs, including testing and scaling up treatment, and its delivery must be a part of a combination prevention package approach (UNAIDS, 2015).

Sustainability

Funding for PrEP in the long-term is an important consideration.

Awareness

Awareness of PrEP among adolescent girls and young women is unknown. Given the limited data on AGYW's awareness and perceived barriers regarding PrEP, there is a clear need for advocacy strategies to increase knowledge and awareness of HIV prevention tools including PrEP.

In order to inform and enhance the implementation of PrEP programs for AGYW, it must be responsive to the needs, preference, priorities, and rights of the young women who will be accessing the drugs as a prevention tool.

In support of PrEP roll-out and implementation, OPTIONS Consortium plan to develop and conduct knowledge, attitude, and practice (KAP) surveys for providers around PrEP. These will assist in development of training tools and other guidance documents that will facilitate implementation of PrEP for AGYW.

Special Considerations

Effective PrEP implementation will need to include understanding the different needs and perceptions of all AGYW. Attention is needed to account for the unique needs of transgender youth in the context of PrEP research and implementation; identifying their needs is critical to meeting the goal of reducing health disparities among transgender youth, including the disproportionate HIV burden they face. The results of an American study that examined facilitators and barriers to participation of transgender youth in a PrEP adherence study suggest lack of concern about HIV, potential medication side effects, remembering to take PrEP daily and reluctance to discuss gender identify with study staff were all barriers faced by transgender youth (Fisher, et al., 2017).

Findings from this study may be helpful in the context of PrEP roll out and implementation in Kenya and Uganda. For example, building trust to address histories of gender and sexual orientation discrimination and medical training tailored to the sexual health care needs of AGYW, including transgender youth are important considerations in this context.

Research gaps

There is an overall lack of social and qualitative evidence base on PrEP for women and in particular, adolescent girls and young women. Recognizing this gap and the diversity of views about PrEP, ATHENA convened a virtual roundtable process with women thought leaders. The process included women living with HIV, researchers, activists,

medical doctors, human rights specialists and gender experts. Each contributor prepared their own submission and then a collective roundtable was developed.

Other research gaps:

- Risk perception of adolescent girls and young women.
- Qualitative data on community perception towards those using PrEP may have usefulness to access and up-take of this HIV prevention tool.
- There is currently no data on long term use of PrEP specifically and the effect it may have on the reproductive system and bone and kidney health among others. However, data from the experience of Truvada as treatment can be a source of learning.
- There is also limited data on PrEP providers working with AGYW however provider stigma is well-documented and remains a barrier to PrEP accessibility for a range of populations (OPTIONS, 2016).
- Operational/implementation research is needed.

Human rights-based framework

- The right to the highest attainable standard of health
- The right to be free from discrimination
- The right to benefit from scientific progress
- The right to education and information

Historically, the HIV response has demonstrated the necessity of a human rights-based and gender responsive approach. Many of the concerns that women have voiced around PrEP can be understood through this lens.

Recognizing the diversity of views about PrEP and the overall lack of social and qualitative evidence base on PrEP for women – ATHENA convened a roundtable process with women thought leaders. The process included women living with HIV, researchers, activists, medical doctors, human rights specialists and gender experts. Each contributor prepared their own submission and then we collectively developed a roundtable article. In the roundtable process, a human rights-based framework for implementation of PrEP was developed by Susana T. Fried, calling for an approach which balances four key human rights principles: the right to the highest attainable standard of health, the right to be free from discrimination, the right to benefit from scientific progress, and the right to education and information.

There are three key ways in which these intersect:

1) The rights to the *highest attainable standard of health* and to *benefit from scientific progress*: demand an approach that ensures the rights of women and girls are prioritised – a lack of adequate consideration of gender in PrEP research not only inhibits women's ability to benefit from PrEP but also compromises their right to benefit from scientific progress. To uphold this right, trials must be designed around the needs and realities of women.

2) The right to be *free from discrimination* calls for explicit attention to marginalized groups and carries an obligation for governments to respect, protect and fulfil rights.

3) A sustainable solution to HIV must promote greater knowledge and information. The principle of *informed consent* means governments must develop and implement laws, policies and practices that promote and protect the human rights and fundamental freedoms of all people including with education and information about sexual and reproductive health and rights.

Other challenges

ATHENA, Salamander Trust and AVAC with UN Women support, led a global review of women's access to HIV treatment, which highlighted many key barriers, which must also be considered in relation to PrEP implementation.

- GBV, including stigma and discrimination at various levels/in various settings
- Side effects of treatment
- Inability to meet basic needs such as nutrition and housing
- Gender roles and responsibilities
- Violation of rights to privacy, confidentiality and bodily integrity in healthcare settings
- Mental health
- Care-giving responsibilities
- Punitive laws, including criminalization

Conclusion

Whilst the efficacy of PrEP is established, the global evidence base around AGYW's knowledge and preferences regarding PrEP is slim, at best. Adherence challenges, and failure to adequately account for AGYW's priorities and needs during trials – indeed at all stages of the research continuum – suggests holes in the data. Many questions

remain unanswered in regards to legal and policy constraints affecting access to SRH services, adherence and behavioral factors, sustainability and delivery mechanisms.

There is great opportunity, as well as challenges, as Kenya and Uganda continue to devise and implement PrEP roll-out strategies. Adherence and behavioral barriers among AGYW must be understood and guideline developers and program implementers need to know precisely what AGYW want and need in terms of prevention and adherence literacy.

In light of its potential to help reduce HIV acquisitions among AGYW, it is vital to acknowledge outstanding questions regarding PrEP before wide scale introduction.

References

Abdool Karim S. (2016). *Understanding high rates of HIV in young women in Africa: Implications of new epidemiological, phylogenetic, genomic and proteomic evidence*. 21st International AIDS Conference, Durban, presentation TUSS0606.

Adimora, A., Ramirez, C., Auerbach, J., Aral, S., Hodder, S., & Wingood, G. et al. (2013). Preventing HIV Infection in Women. *Journal Of Acquired Immune Deficiency Syndrome*, *2*, S168-S173. http://dx.doi.org/10.1097/QAI.0b013e318298a166

Amico, K. Rivet et al. (2016) *Experiences with HPTN 067/ADAPT Study-Provided Open-Label Prep Among Women In Cape Town: Facilitators And Barriers Within A Mutuality Framework*. AIDS and Behavior 21.5. 1361-1375.

AVAC. (2017). *PrEP Watch.* http://www.prepwatch.org/

Baeten JM, Donnell D, Mugo NR, Ndase P, Thomas KK, Campbell JD, et al. Single-agent tenofovir versus combination emtricitabine plus tenofovir for pre-exposure prophylaxis for HIV-1 acquisition: an update of data from a randomised, double-blind, phase 3 trial. Lancet Infectious Diseases 2014; 14:1055–1064

Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. New England J Med. 2012 Aug 2;367(5):399–410.

Baggaley, Rachel et al. "Beyond The 90-90-90: Refocusing HIV Prevention as Part of the Global HIV Response". *Journal of the International AIDS Society* 19.1 (2016).

Bekker LG, Hughes JP, Amico KR, Roux S, Hendrix C, Anderson PL, et al. (2015). HPTN 067/ADAPT Cape Town: a comparison of daily and nondaily PrEP dosing in African women.

Burgener A and Klatt N. *Uncovering the role of the vaginal microbiome in undermining PrEP efficacy in women*. 21st International AIDS Conference, Durban, presentation TUSS0605, 2016.

Cohen, M.S., and Lindsey R. Baden. "Preexposure Prophylaxis For HIV — Where Do We Go From Here?". *New England Journal of Medicine* 367.5 (2012): 459-461. Web.

Cottrell, Mackenzie L. et al. "A Translational Pharmacology Approach To Predicting Outcomes Of Preexposure Prophylaxis Against HIV In Men And Women Using Tenofovir Disoproxil Fumarate With Or Without Emtricitabine". *Journal of Infectious Diseases* 214.1 (2016): 55-64. Web.

DHS Survey 2008/09 as cited in the Kenya AIDS Response Progress Report 2014 Progress towards Zero.

FHI 360, Impact Research and Development Organization, Setshaba Research Centre. Guidance for Providing Informed-Choice Counseling on Sexual Health for Women Interested in Pre- Exposure Prophylaxis (PrEP). Durham, NC: FHI 360; 2015

Fisher, C., Fried, A., Desmond, M., Macapagal, K., & Mustanski, B. (2017). Facilitators and Barriers to Participation in PrEP HIV Prevention Trials Involving Transgender Male and Female Adolescents and Emerging Adults. *AIDS Education And Prevention*, *29*(3), 205-217. http://dx.doi.org/10.1521/aeap.2017.29.3.205.

Fonner, Virginia A. et al. "Effectiveness and Safety of Oral HIV Pre-exposure Prophylaxis for all Populations". AIDS 30.12 (2016): 1973-1983.

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. New England J Med. 2010 Dec 30;363(27):2587–99.

HIV Prevention Market Manager – AVAC http://www.prepwatch.org/scaling-up/kenya-close-up/

http://www.cdc.gov/hiv/risk/prep/

http://www.dreamspartnership.org/innovation-challenge/#innovation

Idele, Priscilla et al. "Epidemiology of HIV and AIDS Among Adolescents". *JAIDS Journal of Acquired Immune Deficiency Syndromes* 66 (2014): S144-S153.

Kenya AIDS Indicator Survey (2007 & 2012). http://www.prb.org/pdf09/kaiskenyadatasheet.pdf . http://www.unaids.org/sites/default/files/country/documents/KEN_narrative_report_2014.pdf

Kenya Demographic and Health Survey 2014. https://dhsprogram.com/pubs/pdf/fr308/fr308.pdf

Lal, L., Audsley, J., Murphy, D., Fairley, C., Stoove, M., & Roth, N. et al. (2017). Medication adherence, condom use and sexually transmitted infections in Australian preexposure prophylaxis users. *AIDS*, *31*(12), 1709-1714. http://dx.doi.org/10.1097/qad.0000000000001519

Mathur, Sanyukta, Nanlesta Pilgrim, and Julie Pulerwitz. "Prep Introduction for Adolescent Girls and Young Women". *The Lancet.* 3.Comment (2017): e406.

Nachega J, Hislop M, Nguyen M, Dowdy D, Chaisson RE, Regensburg L, et al. Antiretroviral treatment adherence, virologic and immunologic outcomes in adolescents compared with adults in Southern Africa. J Acquir Immune Defic Syndr. 2009;51(1):65–71. doi:http://dx.doi.org/10.1097/QAI.0b013e318199072e.

National AIDS Control Council. (2015). *Kenya's Fast-track Plan To End HIV and AIDS Among Adolescents and Young People*. Retrieved from http://www.lvcthealth.org/online-library?format=raw&task=download&fid=55

OPTIONS consortium https://www.fhi360.org/projects/optimizing-prevention-technology-introduction-schedule-options-consortium

OPTIONS consortium https://www.fhi360.org/projects/optimizing-prevention-technology-introduction-schedule-options-consortium

Passmore J-A and Williams B. *Role of vaginal microbiota in genital inflammation and enhancing HIV acquisition in women*. 21st International AIDS Conference, Durban, presentation TUSS0604, 2016.

PEPFAR, USAID: LQAS in 60 districts under USAID, 2014. http://www.unaids.org/sites/default/files/country/documents/UGA_narrative_report_2015.pdf

Pilgrim, N, Mathur, S., Gottert, A., Rutenberg, N., Pulerwitz, J. (2016). *Building Evidence to Guide PrEP Introduction for Adolescent Girls and Young Women*. Population Council. http://www.popcouncil.org/uploads/pdfs/2016HIV_PrEPGuidanceForAGYW.pdf

Political Declaration on HIV and AIDS: On the Fast Track to Accelerating the Fight against HIV and to Ending the AIDS Epidemic by 2030. http://www.unaids.org/en/resources/documents/2016/2016-political-declaration-HIV-AIDS

Stadler, Jonathan et al. "Adherence and the lie in a HIV Prevention Clinical Trial". *Medical Anthropology* 35.6 (2015): 503-516.

The Global Fund. Technical brief: adolescent girls and young women in high-HIV burden settings. 2017. https://www.theglobalfund.org/media/4576/core_adolescentgirlsandyoungwomen_technicalbrief_en.pdf

Thigpen MC, Kebaabetswe PM, Paxton LA, Smith DK, Rose CE, Segolodi TM, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. New England J Med. 2012 Aug 2;367(5):423–34.

Uganda AIDS Indicator Survey (2011). https://dhsprogram.com/pubs/pdf/AIS10/AIS10.pdf

Uganda Demographic and Health Survey 2011. https://dhsprogram.com/pubs/pdf/FR264/FR264.pdf

Uganda Global AIDS Response Progress Report 2013. http://www.unaids.org/sites/default/files/country/documents/UGA_narrative_report_2015.pdf

UNAIDS 2013 HIV estimates. http://www.unaids.org/sites/default/files/media_asset/UNAIDS_Global_Report_2013_en_1.pdf

UNAIDS 2014. Kenya HIV epidemic profile. http://www.unaids.org/en/regionscountries/countries/kenya

UNAIDS 2016 guidance: HIV prevention among adolescent girls and young women, putting HIV prevention among adolescent girls and young women on the fast-track and

engaging men and boys. http://www.unaids.org/sites/default/files/media_asset/UNAIDS_HIV_prevention_among_adolescent_girls_and_young_women.pdf

UNAIDS Global Aids Update 2016. http://www.unaids.org/sites/default/files/media_asset/global-AIDS-update-2016_en.pdf

UNAIDS: The Gap Report 2014. http://files.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2014/UNAIDS_Gap_report_en.pdf

Van Damme, L., Corneli, A., Ahmed, K., Agot, K., Lombaard, J., & Kapiga, S., et al. (2012). Preexposure Prophylaxis for HIV Infection among African Women. *The New England Journal Of Medicine*, (367), 411-422. http://dx.doi.org/10.1056/NEJMoa1202614

WHO Global action plan on HIV drug resistance 2017-2021. http://apps.who.int/iris/bitstream/10665/255883/1/9789241512848-eng.pdf?ua=1

WHO expands recommendation on oral pre-exposure prophylaxis of HIV infection (PrEP) Policy brief. 2014. http://www.who.int/hiv/pub/prep/policy-brief-prep-2015/en/

WHO Policy brief 2015 on oral pre-exposure prophylaxis of HIV infection. http://www.who.int/hiv/pub/prep/policy-brief-prep-2015/en/

WHO: Guidance on oral pre-exposure prophylaxis (PrEP) for serodiscordant couples, men and transgender women who have sex with men at high risk of HIV. 2012. http://www.who.int/hiv/pub/guidance_prep/en/