



Interventions to increase the uptake and continuation of pre-exposure prophylaxis (PrEP) by adolescent girls and young women at high risk of HIV in low-income and middle-income countries: a scoping review

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ABSTRACT

Introduction Effective strategies to increase pre-exposure prophylaxis (PrEP) uptake and continuation among adolescent girls and young women (AGYW) who engage in sex work or transactional sex are sparsely reported. We aimed to describe the available evidence on strategies for improving the uptake and continuation of PrEP among AGYW who engage in sex work or transactional sex, or otherwise are at high risk of acquiring HIV, and report their implementation outcomes.

Method PubMed, Embase, CINAHL and Global Health were searched for studies describing strategies to increase uptake and continuation of PrEP for HIV prevention among AGYW at high risk of acquiring HIV in low-income and middle-income countries. Two independent reviewers screened citations for inclusion and performed data abstraction. Proctor's framework was used to report the implementation outcomes of the interventions.

Result We identified 1046 citations, and reviewed 69 full-text documents, of which we included 11 in the scoping review. A social marketing campaign was used in one study to create demand for PrEP. A decision support tool was used in one study to improve PrEP initiation. SMS reminders (two studies), drug-level feedback (two studies), peer group support (one study) and conditional economic incentives (one study) were used to improve PrEP continuation. Five studies reported adoption outcomes, two of which were high. Four studies reported sustainability outcomes; these were low or moderate. One study found private youth-friendly clinics a better fit for AGYW PrEP delivery compared with public hospitals, and prescription of PrEP by non-study staff in the hospital facility was low.

Conclusion Multiple promising interventions have been used to deliver PrEP to AGYW at high risk of acquiring HIV; however, more information is needed to understand how these interventions would likely perform at scale outside of a research context.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Adolescent girls and young women (AGYW) who engage in sex work and transactional sex are at high risk of HIV infection in many settings. Yet, uptake of pre-exposure prophylaxis (PrEP), an effective prevention intervention, has been reported to be suboptimal in PrEP delivery programmes.

WHAT THIS STUDY ADDS

⇒ We describe existing studies reporting PrEP-related delivery strategies and interventions tailored to AGYW who engage in transactional sex and/or sex work, or otherwise are at high risk of HIV, in low-income and middle-income countries and summarise reported implementation outcomes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This summary of existing strategies and implementation outcomes for PrEP delivery in a population at high risk of HIV infection may be useful to programme implementers who are considering deployment strategies in places of low PrEP uptake or continuation.

INTRODUCTION

Globally, adolescent girls and young women (AGYW) between 15 and 24 years who engage in transactional sex and/or sex work, are at high risk of HIV infection.^{1 2} Transactional sex is differentiated from sex work since the former is defined as 'non-commercial, non-marital sexual relationships motivated by the implicit assumption that sex will be exchanged for material support or other benefits' whereas the latter is a commercial engagement in sexual conduct in exchange for money.³ Transactional sex relationships

are more common than sex work,^{4–6} however, both behaviours increase the risk of infection.^{6–8} AGYW who engage in sex work and/or transactional sex, may be especially likely to acquire HIV⁹ due to biological, developmental and life-phase factors that increase AGYW's risk of HIV generally (eg, increased susceptibility to peer pressure, sexual violence and differential power dynamics in relationships; poverty; suboptimal knowledge of HIV transmission; inadequate sexual and reproductive health and HIV prevention services).^{10–13}

Pre-exposure prophylaxis (PrEP) is an effective intervention for protecting individual health and limiting HIV transmission, especially among groups at high risk of acquiring HIV (eg, sex workers, people who inject drugs, men who have sex with men and transgender people).^{14–16} PrEP involves the daily use of antiretroviral treatment (ART) to prevent HIV infection among people who are HIV uninfected but at high risk of contracting the virus. Trials examining tenofovir-based oral PrEP show that, with high adherence, it substantially reduces the risk of HIV acquisition.^{16 17} With proper and consistent use, PrEP is believed to be 99% efficacious.¹⁸

In many places, access to and continuation of PrEP by AGYW who are at high risk of acquiring HIV is suboptimal, and consistent PrEP use by this group after scale-up has been a major challenge for many PrEP delivery programmes.¹⁹ For example, experiences from Kenya and Uganda revealed slow uptake and frequent disengagement among AGYW receiving PrEP through national delivery programmes.^{20 21} One systematic review found that, even in the 'ideal' trial setting, females and younger participants had lower PrEP continuation levels relative to males and older participants, respectively.²²

Reasons for low uptake and continuation of PrEP by AGYW occur at the societal, health system and individual levels and likely vary by setting.¹³ Included among the structural factors are policies requiring parental consent for PrEP for AGYW who have not reached the age of consent as well as oppressive gender norms and taboos about sexuality, which may impede AGYW from protecting their health, accessing reproductive health or preventive HIV services, and making informed choices.²³ In settings where engagement in sex work is illegal, AGYW may avoid PrEP services in public health facilities to avoid stigma and/or prosecution.²⁴ HIV-related and sex-work-related stigmas also constitute important barriers: potential users may fear that PrEP will be misinterpreted as ART for HIV infection,^{25–27} or that they will be identified as members of the key populations in which PrEP use is prioritised (eg, sex workers). Health service factors (eg, long waiting times, lack of privacy at clinics, lack of comprehensive sex education and non-friendly adolescent reproductive services) have been shown to impede access to care among pregnant adolescents and youth living with HIV and could similarly pose barriers to PrEP access and continuation among AGYW at high risk of HIV acquisition.^{12 28} In addition, the challenges of maintaining an adequate supply of PrEP as demand

increases could impede access. Finally, factors related to the adolescent life phase (eg, high risk-taking propensity, susceptibility to peer pressure, an emerging sense of autonomy and assertion of independence) could influence consistent PrEP use among AGYW that engage in transactional sex even with access to the medication.^{29 30}

These factors must be considered by PrEP delivery interventions for AGYW. However, best practices for increasing PrEP uptake and continuation remain unclear. To address this knowledge gap, we conducted a scoping review of interventions and programmes designed to deliver PrEP to AGYW who engage in sex work or transactional sex or are, for other reasons, at high risk of HIV infection, in low-income and middle-income countries (LMICs). The specific aims were to (1) describe the evidence on strategies and/or interventions that may increase the uptake and continuation of PrEP medication by AGYW and (2) report the implementation outcomes of the strategies and/or interventions. This information is intended to inform programme implementers on potential models for PrEP deployment at scale in places of low uptake.

METHODS

This scoping review used the framework proposed by Arksey and O'Malley³¹ and was reported according to Preferred Reporting Items in Systematic Reviews and Meta-analyses extension to scoping reviews.³²

Selection criteria

We included studies that focused on interventions or strategies for HIV oral PrEP delivery, were published from 2010 (ie, 2 years before the approval of PrEP by the Food and Drug Administration)³³ until 15 October 2021 when the search was completed, and studies involving AGYW 15–25 years involved in sex work and/or transactional sex¹ or considered to be at high risk of HIV for other reasons. Qualitative studies were included. Sex work was defined as commercial sexual activities exchanged for money or other benefits, while transactional sex was defined as non-commercial, non-marital sexual relations exchanged for gifts or money.³ Information was sourced from any existing scholarly literature, including primary research studies, review articles, theoretical articles, editorials, letters and guidelines.

Data sources and search strategy

Studies reporting strategies to increase initiation and continuation of PrEP for HIV prevention among (1) AGYW engaged in sex work or transactional sex or (2) AGYW who, for other reasons, were considered to be at high risk of HIV, in LMICs were identified by searching Medline/PubMed (National Library of Medicine, NCBI), Embase (Elsevier, embase.com), Cumulative Index of Nursing and Allied Health Literature (CINAHL Plus, EBSCO) and Global Health (C.A.B. International, EBSCO). Controlled vocabulary terms (ie, MeSH, Emtree, CINAHL subject headings, CAB Thesaurus) were used when available and appropriate. The search

strategies were designed and executed by a librarian (CM). The publication date was limited to 2010 onward. No language limits were applied. The exact search terms used in each of the databases, and corresponding result numbers, are provided in the online supplemental file 1.

An initial limited search of Medline (via PubMed) was conducted, followed by an analysis of the text words contained in the title and abstract of retrieved papers and the index terms used to describe the articles. A second search using all identified keywords and index terms was undertaken on EMBASE, CINAHL and CABI's Global Health database. The reference list of all the identified articles was searched for additional studies. Grey literature was searched through reports retrieved from CABI's Global Health database. We substituted relevant conference proceedings with the published studies as soon as they were available and excluded those for whom no published paper was available at the time of analysis.

Data summary and synthesis

Screening of articles was performed using Covidence software. Beginning at the title and abstract level, studies were screened independently by two of the reviewers (OIE and ILE), applying the eligibility criteria. A third reviewer's opinion (VO) was requested to reach a consensus in case of disagreement about what studies to include. The same reviewers were used for the full-text screening.

Guided by Joanna Briggs Institute template,³⁴ a data extraction table was developed iteratively by two researchers (OIE and ILE), with input from a third author (VO), to record key information about the strategies and/or interventions. The key information was further refined at the review stage and the table was updated accordingly. The final charting table included

study details (title, first author, year of publication, type of publication and type of study), study aims, country of study, number, age and sex of study participants, a short description of the intervention, context of implementation, intervention outcomes and key findings. Proctor's implementation outcomes (acceptability, adoption, appropriateness, feasibility, fidelity, cost, penetration and sustainability) were used to assess key aspects of implementation (table 1).³⁵

Data analysis

Consistent with relevant guidance, study quality or a formal risk of bias was not conducted nor used as a basis for interpreting the findings.^{31 32} The reason for this was that the scoping review aimed to identify all existing evidence or studies relating to interventions to increase the uptake of PrEP in LMICs and not necessarily to examine the strength of evidence regarding a particular intervention. A narrative summary accompanied the tabulated results and described how the results relate to the review objective.

Patient and public involvement

Given the nature of the study, patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research.

RESULTS

Characteristics of included studies

A total of 1456 references were retrieved by the database searches on 15 October 2021, resulting in 1046 unique results for the title and abstract screening. Sixty-nine of the retrieved references were judged to be appropriate

Table 1 Definition of Proctor's implementation outcomes³⁵

Implementation outcome	Analysis level	Definition used in this review; other synonyms
Acceptability	Individual provider or individual consumer	Satisfaction with various aspects of PrEP delivery to AGYW; content, complexity, delivery, credibility and comfort
Adoption	Individual provider or organisation	Initiation of PrEP by AGYW; utilisation, uptake, intention to try, implementation
Appropriateness	Individual provider or individual consumer or organisation	Perceived fit of PrEP delivery; relevance, compatibility, suitability, usefulness, practicability
Feasibility	Individual provider or organisation	Actual fit of PrEP delivery; utility, suitability for everyday use; practicability
Fidelity	Individual provider	Quality of programme delivery; delivered as intended, adherence, integrity
Implementation cost	Provider or providing institution	Cost of implementing PrEP delivery; marginal cost, cost-effectiveness, cost-benefit
Penetration	Organisation or setting	Level of institutionalisation of PrEP; spread
Sustainability	Individual consumer or administrators or organisation	Continuation of PrEP by AGYW; maintenance, sustained use, durability, incorporation, integration, institutionalisation, routinisation

AGYW, adolescent girls and young women; PrEP, pre-exposure prophylaxis.

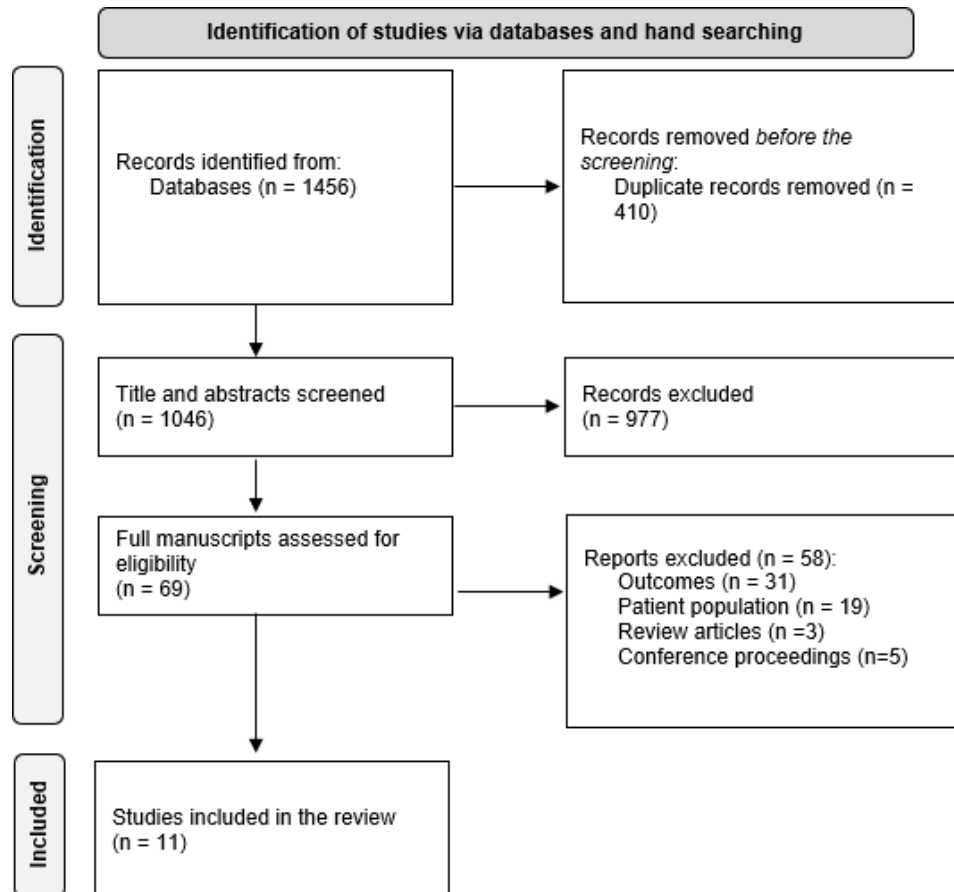


Figure 1 Flow diagram of study selection process and included studies.

after screening their title/abstract against the eligibility criteria. A total of 11 studies were included in the review after the screening of the full manuscripts against the eligibility criteria (figure 1).

As shown in table 2, 11 included studies published between 2020 and 2022 (with the newly published relevant conference proceedings) described 6 implementation studies including HPTN 082 Study,^{27 36} Power cohort study,^{37 38} Determined Resilient, Empowered, AIDS-free, Mentored and Safe (DREAMS) study in Zimbabwe,^{39 40} DREAMS study in South Africa,⁴¹ MPYA trial^{42 43} and 3Ps for Prevention study.^{44 45} The HPTN 082 and Power Cohort studies focused on how to increase PrEP uptake and continuation among high-risk AGYW. MPYA study focused mainly on improving PrEP continuation among high-risk AGYW. The DREAMS studies employed a multi-pronged approach (including PrEP) to prevent HIV among high-risk AGYW. 3Ps for Prevention study focused on generating demand for PrEP and increasing PrEP uptake among high-risk AGYW. All the studies were either conducted in southern Africa (South Africa, Zimbabwe) or eastern Africa (Kenya).

Prep delivery interventions

Details of the PrEP delivery interventions are shown in table 3. Interventions were broadly grouped into three categories: demand creation, PrEP uptake and PrEP continuation.

Demand creation

A social marketing campaign was used in 3Ps for Prevention study to increase demand for oral PrEP among high-risk AGYW.⁴⁴ Project developers identified and leveraged social networks and influencers to increase AGYW's interest in PrEP using behavior-centred design. Findings from the formative study were used to design communication materials for PrEP marketing campaigns. Messages such as 'PrEP enhances the power you have', 'PrEP protects those you love' and 'PrEP allows you to live in the sexual moment' were transmitted via a video that marketed PrEP as a desirable prevention strategy.⁴⁴

PrEP initiation

In the POWER cohort study, investigators explored the use of a decision support tool to facilitate the decision to initiate PrEP at one of their study sites in Johannesburg.³⁷ The details of this strategy were not reported in the published reports included in this review.

PrEP continuation

Strategies to increase PrEP continuation included SMS reminders, drug-level feedback, peer group supports and conditional economic incentives. In HPTN 082 study, sexually active AGYW (defined as having at least one sexual partner within the previous 3 months and interested in PrEP) on PrEP received two-way SMS and were invited to participate in optional adherence clubs

Table 2 Characteristics of the included studies (N=11)

Study name and first author	Year of publication	Type of study	Study focus	Country of study implementation
HPTN 082				
Celum ³⁶	2020	Randomised controlled trial	PrEP uptake and continuation	South Africa & Zimbabwe
Velloza ²⁷	2021	Qualitative study		
Power Cohort Study				
Celum ³⁷	2022	Pilot study	PrEP uptake and continuation	Kenya & South Africa
Roche ³⁸	2022	Qualitative study		
DREAMS				
Chabata ³⁹	2021	Non-randomised evaluation	Uptake of PrEP and other HIV prevention strategies	Zimbabwe
Hensen ⁴⁰	2021	Qualitative study		
DREAMS				
Chimbindi ⁴¹	2022	Mixed-methods study	Uptake of PrEP and other HIV prevention strategies	South Africa
MPYA				
Haberer ⁴²	2022	Cohort study	PrEP continuation	Kenya
Haberer ⁴³	2021	Randomised controlled trial		
3Ps for Prevention Study				
Celum ⁴⁴	2020	Randomised controlled trial	PrEP continuation	South Africa
Morton ⁴⁵	2020	Mixed-method study		

.DREAMS, Determined Resilient, Empowered, AIDS-free, Mentored and Safe; HPTN, HIV Prevention Trials Network; MYPYA, Monitoring Pre-Exposure Prophylaxis for Young Adult Women; POWER, The Prevention Options for Women Evaluation Research.

to support their PrEP continuation. Additionally, those in the intervention arm received enhanced adherence support with counselling based on feedback received from drug levels.³⁶ MPYA trial examined the use of SMS reminders to support PrEP continuation among high-risk AGYW defined as having a VOICE risk score ≥ 5 (signifying a risk of >5 infections/100 person-year).⁴⁶ SMS messages were sent daily to the participants in the intervention arm, although they could opt for as-needed reminders (ie, SMS sent only if they missed opening the monitored pill box).⁴³ In the 3Ps for Prevention study, incentives conditioned on tenofovir levels were used to support PrEP adherence by high-risk AGYW characterised as having had sex in the month before being screened or intending to be sexually active within the subsequent 3 months.⁴⁴ Intervention participants who demonstrated high adherence received a shopping voucher worth 200 South African Rand (about US\$13) at the following clinic visit.⁴⁴

Additionally, in the two DREAMS projects in South Africa⁴¹ and Zimbabwe,^{39,40} different strategies to increase PrEP uptake and continuation by young women who sell sex (comprising young female sex workers that sell sex and those that do but do not identify as such) were implemented in the context of other HIV prevention strategies. PrEP delivery through peer outreach approach was employed by the DREAMS project in South Africa while PrEP uptake and adherence was promoted through community empowerment and adherence support in

Zimbabwe. Other HIV preventive services offered in the DREAMS projects included HIV screening, testing and counselling, school and community-based HIV and violence prevention programmes, education subsidies, comprehensive economic strengthening, postviolence care for survivors of gender-based violence, condom promotion and provision for AGYW and their partners, improved access to youth-friendly sexual and reproductive healthcare, parenting/caregiver programmes and PrEP services.

Implementation outcomes of PrEP delivery interventions for AGYW

Adoption

The 3Ps for prevention study reported high adoption of PrEP following their demand creation strategy: 56.4% of AGYW were 'definitely interested' in taking PrEP after watching the PrEP social marketing campaign video.⁴⁴ Also, HPTN 082^{27,36} and Power Cohort Study³⁷ reported high PrEP initiation rates of 95% and 94%, respectively, among AGYW that were approached and were found eligible to participate in the studies. The DREAM project in Zimbabwe led to higher PrEP initiation in the intervention arm compared with the control arm.^{39,40} The DREAM project in South Africa reported zero uptake of PrEP although PrEP awareness increased over the years of programme implementation⁴¹ (table 4).

Table 3 Prep delivery interventions of the included studies (N= 17)

Project name	Brief description of the intervention	Study population	Intervention	Study design
HPTN 082 ^{27 36}	PrEP initiation occurred through community events, school-based clinics, primary care, family planning clinics and youth centres. Participants who accepted PrEP were randomly assigned to receive (I) drug level feedback plus standard adherence support (counselling, weekly two-way SMS in the first 3 months and monthly adherence clubs), n=215 or (C) standard adherence support only, n=212.	High-risk sexually active young women (16–25 years) defined as having at least one sexual partner within the previous 3 months and interested in PrEP.	Drug-level feedback, SMS reminders & peer group support	Impact evaluation— phase IV randomised trial
POWER Cohort study ^{37 38}	PrEP was delivered according to emerging national guidelines in family planning clinics (Kisumu, Kenya), youth-friendly clinics (Johannesburg, South Africa) and mobile youth-friendly clinics (Cape Town, South Africa). A decision support tool was used to facilitate the decision to initiate PrEP at the clinic in Johannesburg.	High-risk sexually active young women (16–25 years) defined as those that had vaginal intercourse in the last 3 months and interested in PrEP.	Decision support tool	Descriptive cross-sectional pilot study
DREAMS ^{39 40}	Implementing partners identified eligible young women through schools, clinics, HIV testing services or the community and linked them to PSI Zimbabwe which offers oral PrEP. PrEP uptake was compared between intervention (I)—DREAMS+PrEP sites, (n=538) and control (C)—non-DREAMS sites, (n=481)	Young women who sell sex (<25 years) including those that did and did not identify as such.	Social protection, economic empowerment and adherence support implemented in the context of other HIV prevention strategies	Impact evaluation – Cohort study
DREAMS ⁴¹	PrEP was introduced as part of a combination prevention package in a rural KwaZulu-natal setting with high HIV incidence. Hospitals were used as a point of delivery to offer oral PrEP and social protection, particularly to young women who sell sex.	Young women who sell sex (<25 years) including those that did and did not identify as such.	Social protection implemented in the context of other HIV prevention strategies	Descriptive cross-sectional study, qualitative study
MPYA Trial ^{42 43}	Random assignment of either (I) daily SMS reminders (with content and timing of their choosing) to enhance adherence to PrEP use (n=173) or (C) no reminder (n=175).	Young adult women (18–24 years) at high risk of HIV defined as having a VOICE risk score ≥5 (signifying a risk of >5 infections/100 person-year).	SMS reminders	Impact evaluation – Phase IV Randomised trial
3Ps for Prevention Study ^{44 45}	Young South African women were exposed to a culturally appropriate social marketing campaign on PrEP and their interest in uptake was enumerated. The enumeration was used to recruit HIV-uninfected young women who were offered daily oral PrEP and randomly assigned to (I) receive (n=101) or (C) not receive (n=99) a short-term cash incentive conditional on study drug adherence.	High-risk sexually active young women (16–25 years) characterised as having had sex in the month before being screened or intending to be sexually active within the subsequent 3 months.	PrEP social marketing campaign, drug level feedback, conditional economic incentives	Impact evaluation— phase IV Randomised trial

C, control; DREAM, Determined, Resilient, Empowered, AIDS-free, Mentored and Safe; HPTN, HIV Prevention Trials Network; I, Intervention; MPYA, Monitoring Pre-Exposure Prophylaxis for Young Adult Women; POWER, The Prevention Options for Women Evaluation Research; PrEP, pre-exposure prophylaxis.

Table 4 Implementation outcomes of the included studies

Intervention name	Implementation outcome	Findings
HPTN 082 ^{27 36}	Adoption	95% initiation rate
	Sustainability	20.9% continuity rate at 6 months (overall); I—20.1%; C—21.7%; adjusted OR 0.92, 95% CI 0.55 to 1.34, p=0.76
POWER Cohort study ^{37 38}	Adoption	94% initiation rate
	Sustainability*	20% continuity rate at 6 months. 14% restarted PrEP
	Feasibility	Private youth-friendly clinics were a better fit than family planning clinics for PrEP
	Penetration	Adoption by non-study staff was low because PrEP was perceived to be outside their work
DREAMS ^{39 40}	Adoption	PrEP initiation; I—28.1%; C—0.6%; Adjusted OR 63.82, 95% CI 19.78 to 205.90; p<0.001
DREAMS ⁴¹	Adoption	0% initiation rate. PrEP awareness increased from 2% in 2017 to 9% in 2018.
MPYA Trial ^{42 43}	Sustainability*	26.8% adherence rate at 24 months (overall); with SMS reminders—27.0%; without SMS reminders—26.7%; adjusted IR 1.16, 95% CI 0.93 to 1.45, p=0.19
3Ps for Prevention Study ^{44 45}	Adoption	56.4% were ‘definitely interested’ in taking PrEP after watching the PrEP social marketing campaign video
	Sustainability*	56% in incentive group and 41% in control group had TFV-DP levels≥700fmol/punch at month 3; RR 1.35;95% CI 0.98 to 0.067, p=0.067

*Sustainability was defined as continuation or commitment to PrEP use whether measured objectively (eg, detectable Tenofovir-Diphosphate TFV-DP levels >700fmol/punch) or via a proxy (eg, retention in care or refill after 1 month).
C, control; DREAM, Determined, Resilient, Empowered, AIDS-free, Mentored and Safe; HPTN, HIV Prevention Trials Network; I, Intervention; IR, Incidence Ratio; MPYA, Monitoring Pre-Exposure Prophylaxis for Young Adult Women (MPYA); OR, Odds Ratio; POWER, The Prevention Options for Women Evaluation Research; RR, relative risk.

Sustainability

HPTN 082 showed that enhanced adherence support including drug level feedback did not improve PrEP continuation (20.1% intervention group and 21.7% control arm; adjusted OR 0.92, 95% CI 0.55 to 1.34, p=0.76).³⁶ The Power Cohort study reported a 20% PrEP continuity rate among high-risk AGYW that initiated PrEP at 6 months and that an additional 14% of them stopped and restarted PrEP.³⁷ MPYA trial showed that SMS reminders as a strategy to improve PrEP continuation among AGYW did not have any impact as 27% of participants that received SMS adhered to PrEP compared with 26.7% of participants that did not receive SMS after 24 months (adjusted IR 1.16, 95% CI 0.93 to 1.45, p=0.19).⁴³ The 3Ps for Prevention study reported a non-significant higher proportion of PrEP adherence among AGYW that received conditional economic incentives compared with those that did not receive the incentives (56% vs 41% respectively; RR 1.35; 95% CI 0.98 to 0.067, p=0.067).⁴⁴

Feasibility

A qualitative study that evaluated the implementation of the integrated PrEP-family planning (FP) services (ie, the Power Cohort study) found that private youth-friendly clinics were a better fit (ie, more feasible) than FP clinics for PrEP delivery to AGYW.³⁸ The private youth-friendly clinic had a designated youth-friendly space (ie, a private space for serving the youths) and better clinic

flow, which meant less movement for clients, resulting in easier implementation of PrEP delivery to AGYW.

Penetration

The authors of the qualitative study that evaluated the implementation of the Power Cohort study highlighted a challenge to intervention penetration: prescription of PrEP by non-study staff in the hospital facility was low since PrEP was perceived to be outside their work.³⁸

DISCUSSION

This scoping review revealed promising interventions with the potential to improve PrEP delivery for AGYW who engage in sex work or transactional sex or are otherwise at high risk of acquiring HIV. These included interventions designed to generate demand, facilitate the initiation and encourage continuation. Most studies focused on PrEP initiation and continuation, with PrEP uptake strategies like social marketing (3Ps for Prevention Study) and social protection and economic empowerment (DREAMS Study, Zimbabwe) showing high potential for impact. On the other hand, sustained PrEP use was typically low or moderate. All interventions were evaluated in sub-Saharan Africa, raising the possibility that these interventions may generalise to the regions most affected by HIV. However, the extent to which these interventions will be effective at scale and when implemented outside the research context is unclear. Implementation

outcomes were reported by all studies. A broader use of these outcomes, in combination with an implementation framework, when evaluating PrEP delivery strategies for AGYW could help policy makers to understand how these interventions and strategies will likely perform in the ‘real world’.

The low PrEP continuation rates across studies raise the question of how to ensure that those AGYW who wish to continue PrEP can do so. Qualitative work from the Power Cohort study suggested that youth-friendly clinics were a better fit than FP clinics for PrEP delivery to AGYW.³⁸ According to the authors, it was simpler to deliver PrEP to AGYW at the private youth-friendly clinic because it had a defined youth-friendly area (ie, a private location for servicing the youths) and improved clinic flow, which meant less client mobility. Similarly, by leveraging social media, an adolescent-friendly means of communication, the 3Ps for Prevention Study was able to increase interest in PrEP. Digital innovations such as dedicated helplines or motivational text messaging have shown tremendous promise for the uptake of HIV testing and HIV and sexual health services by adolescent key populations and they could be leveraged to improve PrEP service delivery.⁴⁷ Future studies on PrEP delivery to AGYW at high-risk of HIV should seek to identify delivery mechanisms that are appealing to young people while also mitigating access barriers (ie, stigma, privacy, convenience, time, transport cost).

The need to simplify HIV care led to the concept of differentiated service delivery—a person-centred approach to HIV care that aims to simplify and adapt HIV

services in ways that serve the needs of people living with and those vulnerable to HIV while optimising resources in health systems.⁴⁸ Although the concept of differentiated service delivery was initially focused on stable HIV patients, it has increasingly been applied to prevention, testing, linkage to care, ART initiation and follow-up as well as integration of HIV care with coinfections and comorbidities. The guiding principle for differentiated care is that different groups have different needs, which should be incorporated into tailored prevention or treatment efforts. Possibilities for differentiated models of PrEP service delivery for AGYW include consideration of service location, service frequency and health worker cadre (figure 2). Community pharmacies, telemedicine clinics, youth-friendly centres, FP clinics and safe spaces for adolescent key populations could serve as alternatives to public health facilities for the initiation of PrEP and provision of HIV prevention care to AGYW. For example, pharmacies are ubiquitous, convenient to access, protect privacy, reduce stigma, and may save time and transport costs. An AGYW-specific pharmacy-based PrEP delivery model with a nurse navigator offering PrEP services to AGYW accessing contraceptive services at commercial pharmacies showed that a substantial proportion (86%) of them initiated PrEP, planned to continue its use and were also willing to pay for the services.⁴⁹ Also, another pharmacy-based PrEP delivery model is undergoing evaluation in Kenya.⁵⁰ The frequency of PrEP refill can be varied depending on how much adherence support is needed by the AGYW. Finally, non-physician prescribers such as pharmacy providers or community health workers

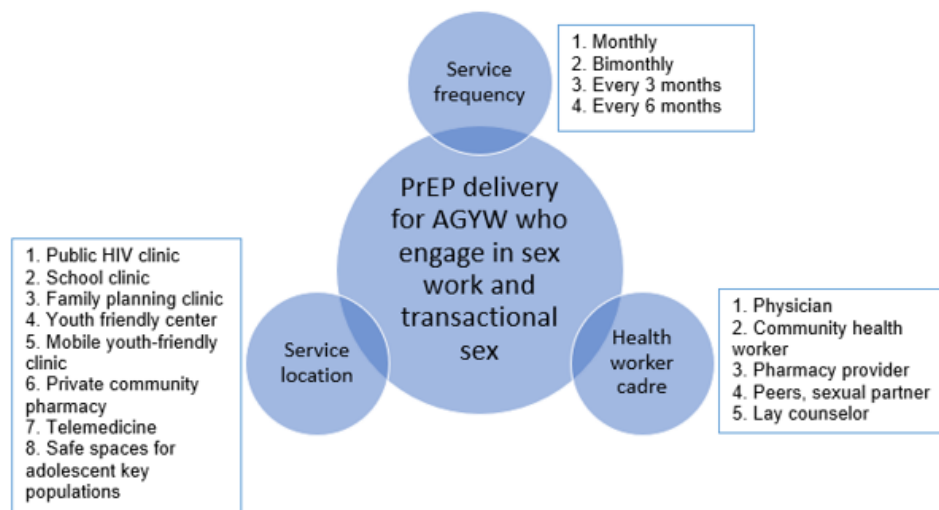


Figure 2 Differentiated models of PrEP service delivery for AGYW. AGYW, adolescent girls and young women; PrEP, pre-exposure prophylaxis.

could be considered for PrEP service delivery with physician oversight, while peers, sexual partners or lay counsellors may be effective messengers for raising awareness about HIV and prevention, including PrEP.⁵¹

The challenge of sustaining PrEP is common to other populations and will require increasing attention as PrEP delivery programmes are scaled.¹⁹ The decision to disengage from PrEP may relate to one's perception of the risk of HIV infection. One who engages in high-risk activities may opt-out of PrEP when she feels she is not at risk and resumes PrEP when she feels at risk. On the other hand, data from an implementation study in Kenya suggests that disengagement of PrEP was protracted: a sizeable proportion of AGYW did not return for their 1 month PrEP refill, and the majority withdrew within the first 6 months. Only a small fraction of these subsequently reinitiated.⁵² Therefore, it is important to distinguish between patterns of continuation of PrEP when evaluating PrEP delivery programme effectiveness. A suggestion could be to differentiate between occasional PrEP users and continuous PrEP users and assess PrEP continuation only among those in the latter category. Of note, consistent, continuous PrEP use is essential for individuals engaging in sex work or transactional sex and for those with multiple sexual partners.

Given that few implementation outcomes were reported by the studies, it was difficult to assess how successful these interventions would be in 'real-world' settings. Since these interventions are most needed in low-resourced settings, exploring mechanisms to sustain PrEP programmes through cost/cost-effectiveness analyses and willingness-to-pay/willingness-to-provide studies is important. Even if oral PrEP is donated, some resources (staff time, storage, testing) are needed for its delivery. It is necessary to determine how these extra resources will be funded (eg, through fee for service, capitation). Assessing the cost of implementation is especially important if private healthcare providers will be involved in PrEP delivery. Additionally, for overburdened health systems, implementation outcomes like appropriateness (perceived fit or compatibility) and feasibility (sustainability for everyday use) should be assessed. In addition to providing information on implementation success, these indicators also serve as key intermediate outcomes concerning clinical outcomes since interventions will be ineffective if not properly implemented.³⁵

A limitation of this scoping review is that the definitions of some of the implementation outcomes particularly uptake and continuation of PrEP varied by study and thus may not be directly comparable. And, accurate assessment of continuation is challenging as even 'objective' adherence measures (eg, pharmacy refills) may overestimate adherence. Though noteworthy, these limitations are unlikely to account for the overall conclusion that PrEP continuation was consistently low across studies.

While the findings of this scoping review present promising interventions or strategies for PrEP deployment

to high-risk AGYW, it will be important to solicit input from young people, local partners and programme managers to adapt these interventions to new settings to ensure that local peculiarities are captured.⁵³ Robust study designs such as hybrid implementation effectiveness trials and sequential assignment trials could be used to establish the real-world effectiveness of the differentiated service delivery approaches for PrEP. Measuring implementation outcomes guided by implementation outcome frameworks is necessary to gauge the success of the implementation studies in the project setting.

CONCLUSION

Although multiple interventions have been used to raise PrEP demand, uptake and continuation among AGYW at high risk of HIV, there is limited data on effectiveness and implementation outcomes. This challenges an understanding of how these programmes would do in the 'real world'. Future PrEP implementation studies for AGYW could consider incorporating an implementation outcomes framework to facilitate an understanding of how these interventions and strategies will function.

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