

The Importance of the Individual in PrEP Uptake: Multilevel Correlates of PrEP Uptake Among Adolescent Girls and Young Women in Tshwane, South Africa

Courtney Peasant Bonner^{1,*}, Alexandra M. Minnis², Jacqueline W. Ndirangu¹, Felicia A. Browne¹, Ilene Speizer³, Laura Nyblade², Khatija Ahmed^{4,5}, Wendee M. Wechsberg¹

¹ Substance Use, Gender, and Applied Research Program, RTI International, 3040 East Cornwallis Road, Research Triangle Park, NC 27709, USA

² Women's Global Health Imperative, RTI International, NC, USA

³ Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, USA

⁴ Setshaba Research Centre, Soshanguve, South Africa

⁵ Faculty of Health Sciences, Dept of Medical Microbiology, University of Pretoria, Pretoria, South Africa

Contributions

CPB and AMM led the analysis and writing of the manuscript. WW contributed to the writing of the background, methods, and discussion sections. FAB, KA, JWN, IS, LN, and WW reviewed and provided critical feedback.

*Correspondence to Courtney Peasant Bonner. Email: cpbonner@rti.org

Abstract

Adolescent girls and young women (AGYW) account for 25% of new HIV infections in South Africa. Pre-exposure prophylaxis (PrEP) is approved by the South African Government, but the factors that promote PrEP uptake among AGYW are not well understood. This study examines multilevel factors associated with PrEP uptake among AGYW in six clinic catchment areas in Tshwane (Pretoria), South Africa. After consent/assent, PrEP-eligible AGYW (n = 448) completed a questionnaire assessing factors at the individual, network/interpersonal, and community levels and were prescribed PrEP in study clinics, if interested. A multivariable model, adjusting for clustering, assessed factors associated with PrEP uptake over a 9-month period. At the individual level, multiple partners in the past 3 months (OR = 0.47), perceived risk of HIV (OR = 0.71), and PrEP-related shame (OR = 0.63) were correlated with lower odds of PrEP uptake ($p \leq 0.05$). The findings highlight modifiable factors that should be addressed to support PrEP uptake efforts.

Keywords: Adolescent girls and young women · Sub-Saharan Africa · Multilevel factors · PrEP initiation · PrEP

Introduction

Adolescent girls and young women (AGYW) aged 15 to 24 account for nearly one-quarter of all new HIV infections in South Africa and estimates suggest HIV prevalence increases by 10% as young women reach ages 20 to 24 [1]. This highlights the critical need to address HIV prevention during adolescence and emerging adulthood in South Africa. Oral pre-exposure prophylaxis (PrEP) for HIV prevention was approved for use among cisgender women by the South African Government in 2015 and an expanded set of PrEP delivery forms are under development and imminent that will help end the global HIV epidemic [2,3,4,5,6,7]. PrEP for HIV prevention is revolutionary for AGYW, enabling them to control their HIV risk instead of relying on a partner for condom use. However, research identifying the factors that promote PrEP uptake among AGYW in South Africa is in a nascent stage [8,9,10].

The modified social-ecological model articulates how factors at the individual, network, community, public policy, and epidemic levels influence HIV risk context and is useful for understanding predictors of PrEP uptake [11]. At the individual level, AGYW's thoughts and feelings about PrEP, including HIV risk perception and internalized stigma about PrEP, and their risk behaviors—such as engagement in concurrent or multiple sexual partnerships—may impact their likelihood to adopt PrEP [9]. At the network level, defined as interpersonal relationships, sexual communication with partners and intimate partner violence may impact PrEP adoption [10]. At the community level, perceived community-level stigma related to PrEP may influence AGYW's desire for PrEP [12]. Public policy and the epidemiology of HIV infection can be viewed as structural factors. For example, AGYW account for a large proportion of HIV prevalence and incidence (epidemiology), and South Africa has invested heavily in HIV prevention among AGYW, explicitly highlighting AGYW as a priority population for PrEP provision (public policy) [1, 13].

Building on clinical trials evaluating PrEP efficacy, research conducted in the context of PrEP implementation has explored factors associated with PrEP interest, uptake, and persistence [8,9,10, 12]; yet few quantitative studies have characterized the correlates of PrEP uptake in AGYWs in South Africa. One recent quantitative study demonstrated that HIV risk perception may mediate the association between HIV risk and interest in PrEP [14]. However, as PrEP becomes more readily available in the public sector to AGYW, more guidance is needed to understand what modifiable factors may increase PrEP uptake among AGYW in real-world settings. This article addresses this gap by examining multilevel factors associated with PrEP uptake among a community sample of AGYW in South Africa.

Methods

Study Setting and Population

The study was conducted in 12 clinic catchment areas in Tshwane (Pretoria), Gauteng province, South Africa. The clinics were selected in collaboration with the health department and all had the following: (1) community ward-based outreach teams; (2) comprehensive sexual and reproductive health (SRH) services; and (3) designated youth-friendly nurses and/or services for adolescents.

AGYW were recruited in communities in the study clinic's catchment area. Trained project staff conducted recruitment using successful outreach methods in areas and establishments where AGYW are known to frequent [15]. Recruitment also occurred through referrals from the clinic, nongovernmental organizations based in the clinics, and other community health workers who conduct HIV and/or pregnancy testing in the community.

Eligibility criteria included (1) identified as female, (2) HIV-negative status per biological testing, (3) aged 16 to 24 years, (4) condomless sex with a male partner in the past 3 months, (5) not currently pregnant nor wanting to get pregnant within the next year, (6) interested in taking daily oral PrEP for HIV prevention, (7) no previous participation in the study's formative phase, (8) no previous nor current participation in any other PrEP-related or HIV project or research study, (9) not on multidrug-resistant tuberculosis (MDR-TB) treatment, and (10) lived in one of the target communities and intended to stay for the next 12 months [16].

Study Design

A previously published protocol paper presented the design and methods of this cluster-randomized trial to assess the efficacy of a multilevel intervention to reduce stigma toward AGYW and increase uptake of PrEP, contraceptive services, and condoms [16]. Here, we present an examination of PrEP uptake that includes AGYWs from the first 6 clinics enrolled in the study prior to the onset of the COVID-19 pandemic. These clinics experienced the fewest COVID-19 – related interruptions to PrEP dispensing and uptake and to youth-friendly services.

After obtaining informed consent/assent, participants signed a medical records release permitting the release of information on PrEP and SRH services obtained. Participants then completed a sociodemographic and behavioral questionnaire administered using audio computer-assisted self-interviewing. Trained research assistants were available during the interview to address questions. Study visits were conducted in Tswana and English.

At enrollment, all participants were offered oral PrEP. Participants who were interested in PrEP received clinical screening (serum creatinine and hepatitis B testing) and initiated PrEP in their study clinic. Research staff extracted prescription data from medical records.

Measures

Exposures

The individual-, network- or interpersonal-, and community-level exposure variables were measured at baseline. All measures were adapted, translated, and cognitively tested with individuals in the local communities.

Individual

HIV risk was assessed using the composite VOICE HIV risk score [17]. We also examined several behavioral measures individually, including condom use at last sex, condomless vaginal and anal sex in the past 3 months, multiple sex partners in the past 3 months, transactional sex (lifetime), and use of alcohol or other drugs before sex in the past 3 months.

HIV risk perception was measured with one item that assessed the extent to which AGYW believed that they might acquire HIV within the next year. Response options were given on a Likert scale, with 1 = “Not a risk at all” to 4 = “Great chance” [18].

PrEP-related shame was assessed using one internalized stigma item, modified from previous research, which asked participants if they would be ashamed to use PrEP. Response options were given on a Likert scale, with 1 = “Strongly disagree” to 4 = “Strongly agree” [18].

Sociodemographic characteristics included race (black, coloured, white); age; housing status; household composition; schooling; and two social determinants of health, economic insecurity and food insecurity.

Network or Interpersonal Relationships

Condom negotiation was assessed using an item that measured the frequency that participants asked their main male partner to wear a male condom in the past 3 months. Response options were given on a Likert scale, with 1 = “Not at all” to 4 = “All the time”.

Sexual empowerment was measured using a 5-item scale that assessed the extent to which AGYW felt able to negotiate when they engaged in sexual intercourse with their main male partner—for example, “Sometimes you have sex with your main male partner even when you do not want to because you are afraid to say NO”. Response options were given on a Likert scale, with 1 = “Strongly disagree” to 4 = “Strongly agree”, and recoded such that higher numbers indicate greater empowerment ($\alpha = 0.85$).

Social support for PrEP use was measured with items adapted from HPTN 082 that assessed anticipated disclosure of PrEP use (4 items) and anticipated PrEP-related support (3 items) from household members, friends, and partner(s) [18].

Physical and sexual partner violence in the past 3 months was measured using a questionnaire modified from previous research conducted by the World Health Organization [19]. Response options were coded separately for physical and sexual violence.

Community

Community-level measures focused on anticipated PrEP stigma from others in the community. Anticipated stigma was conceptualized and assessed as the extent to which people would think that participants were “loose” if they took PrEP. Response options were given on a Likert scale, with 1 = “Strongly disagree” to 4 = “Strongly agree”.

Outcome

PrEP Uptake

PrEP uptake was defined based on medical record evidence of having filled a prescription for PrEP: pharmacy dispensing of a PrEP prescription [20]. All participants were able to initiate PrEP over a 9-month period. If participants filled a PrEP prescription at any point over the 9-month follow-up period after enrolling in the study they were coded as 1 = PrEP uptake and

0 if they had not. It is important to note that PrEP was not readily available to AGYW in South Africa outside of the study; consequently, it is unlikely that AGYW would have obtained PrEP from a pharmacy not affiliated with the study.

Analysis

We calculated descriptive statistics for sociodemographic, PrEP-related, and individual-level, network-level, and community-level factors. We examined associations between the multilevel exposures and PrEP uptake in bivariate analyses. Factors associated with PrEP uptake (p values ≤ 0.05) in the bivariate analyses were included in a multivariable model that adjusted for clinic catchment area to account for the clustered data. We assessed potential collinearity among measures that met criteria for inclusion in the multivariable model and selected among those highly correlated to minimize missing data. The results are reported as odds ratios (OR) with 95% confidence intervals (CI).

Results

Most participants (70%) filled a PrEP prescription over the 9-month follow-up period. Characteristics of the sample are shown in Table 1, with distributions presented overall and by PrEP uptake. In bivariate analyses, several factors were correlated with PrEP uptake, including condomless last sex (OR = 1.58), condomless vaginal sex (OR = 0.50), condomless anal sex (OR = 0.39), multiple sex partners (OR = 0.47), HIV risk perception (OR = 0.72), and internalized stigma, (OR = 0.67; $ps \leq 0.05$). The network-level and community-level measures we assessed were not correlated with PrEP uptake.

Table 1. Individual-, network-, and community-level correlates of PrEP uptake among adolescent girls and young women in Tshwane, South Africa

	Total (SD/%)	PrEP uptake ^a	Did not uptake PrEP	p-value
	448 (100%)	317 (70.1%)	134 (29.9%)	
Individual-level factors				
<i>Sociodemographic characteristics</i>				
Black African	448 (100%)	-	-	-
Age in years, mean (range: 19 to 24)	19.95 (2.3)	19.75 (2.4)	20.04 (2.4)	0.22
Housing				0.30
Formal housing	350 (78.1%)	245 (78.0%)	105 (78.3%)	
Informal housing (e.g., shelter)	59 (13.1%)	45 (14.3%)	14 (10.5%)	
Combination	39 (8.7%)	24 (7.6%)	15 (11.2%)	
Lives with partner	47 (10.5%)	32 (10.2%)	15 (11.2%)	0.75
Economic insecurity: Runs out of money for necessities				0.84
Never	138 (32.1%)	94 (31.2%)	44 (34.1%)	
< Monthly	206 (47.9%)	146 (48.5%)	60 (46.5%)	
≥ Monthly	86 (20.00%)	61(20.3%)	25 (19.4%)	
Food insecurity: Goes to bed hungry				0.70
Never	332 (74.1%)	299(73.2%)	103 (76.9%)	
< Monthly	65 (14.5%)	48 (15.3%)	17 (12.7%)	
≥ Monthly	65 (14.5%)	36 (11.5%)	14 (10.5%)	
In school	228 (51.2%)	162 (52.1)	66 (49.3)	0.58
<i>Individual-level behaviors and perceptions</i>				
HIV Risk Score (range: 1 to 7)	4.79 (1.6)	4.82 (1.6)	4.69 (1.7)	0.44
Condom use at last sex	137 (30.8%)	105 (33.6%)	32 (24.2%)	0.05
Condomless vaginal sex in the past 3 months	333 (74.3%)	222 (70.7%)	111 (82.8%)	0.01
Condomless anal sex in the past 3 months	176 (39.3%)	102 (32.5%)	74 (55.2%)	<0.01
Multiple partners in the past 3 months	333 (74.3%)	221 (70.4%)	112 (83.6)	<0.01
Lifetime transactional sex	83 (18.7%)	56 (18.1%)	27 (20.1%)	0.61
Alcohol or other drug use before sex in the past 3 months	81 (21.0%)	58 (21.6%)	23 (19.8%)	0.70
HIV risk perception (range: 1 to 4)	1.49 (0.80)	1.42 (0.7)	1.66 (1.0)	0.01
Level of internalized stigma: would be ashamed to take PrEP (range: 1 to 4)	1.59 (0.6)	1.54 (0.6)	1.71 (0.7)	0.01
Network-level factors				
Condom negotiation (range: 1 to 4)	2.10 (1.58)	2.064 (1.74)	2.20 (1.13)	0.42
Sexual empowerment (range: 1 to 4)	13.57 (6.3)	13.56 (6.2)	13.60 (6.4)	0.96
Anticipated PrEP disclosure (range: 4 to 20)	12.56 (2.8)	12.61 (2.9)	12.46 (2.7)	0.62
Anticipated PrEP social support (range: 3 to 15)	9.53 (2.2)	9.53 (2.1)	9.5 (2.4)	0.88
Recent physical violence	106 (23.7)	75 (23.9)	31 (23.1)	0.86
Recent sexual violence	50 (11.2)	34 (10.8)	16 (11.9)	0.73
Community-level factor				
Level of anticipated stigma: belief that people would think they were “loose” (range: 1 to 4)	2.05 (0.9)	2.00 (0.9)	2.17 (0.9)	0.08

^aPrEP uptake defined based on evidence of filling a PrEP prescription

In multivariate analyses (Table 2), having multiple sex partners in the past 3 months (OR: 0.47, 95% CI: 0.24, 0.93) and higher perceived risk of HIV (OR: 0.71, 95% CI: 0.61, 0.83) were each correlated with lower odds of PrEP uptake. Internalized stigma tied to PrEP-related shame was correlated with lower odds of PrEP uptake (OR: 0.63, 95% CI: 0.40, 0.98).

Table 2. Adjusted odds ratios estimating the association between PrEP uptake and individual-level factors (n = 426)^a

Individual-level factor	AOR ^b	95% CI	p-value
Condom use at last sex	1.59	0.94, 2.69	0.08
Multiple sex partners, past 3 months	0.47	0.24, 0.93	0.03
HIV risk perception	0.71	0.61, 0.83	<0.001
Internalized stigma: PrEP-related shame	0.63	0.40, 0.98	0.04

^a19 individuals were dropped from the analysis because of missing data on exposure variables.

^bAOR = Adjusted Odds Ratio; adjusted for clinic catchment area to account for clustered data.

Discussion

South Africa continues to have a substantial disease burden attributable to HIV among AGYW [1]. Oral PrEP for HIV prevention provides effective protection against HIV and is widely available in South Africa, yet challenges persist with daily use, particularly for AGYW. Two next-generation long-acting PrEP options have recently been approved for use in South Africa. These modalities will contribute to a prevention landscape in which users have a choice among prevention options and can select the option that best meets their needs [21,22,23]. These forthcoming prevention options notwithstanding, oral PrEP remains a core prevention option.

Understanding factors associated with oral PrEP uptake among AGYW will help to inform intervention targets to support realizing the public health benefits PrEP can offer. In this examination of multilevel influences on PrEP uptake among South African AGYW, individual-level behaviors such as HIV risk perception, having multiple sex partners, and internalized stigma were correlated with PrEP uptake, signaling opportunities for efforts to address these factors to ensure AGYWs at highest risk for HIV acquisition recognize PrEP as an attractive option and are supported in adopting it for prevention.

AGYW who reported engaging in sex with multiple partners had a lower odds of PrEP uptake over the 9-month follow-up period than AGYW not reporting this behavior. Likewise, AGYW with higher HIV risk perception had a lower odds of PrEP uptake. While all AGYW in the study met PrEP eligibility at enrollment, these findings highlight that AGYW at highest risk for HIV (based on reported behaviors) did not envision adopting a daily tablet-taking behavior. Although not statistically significant, condom use at last sex was correlated with higher odds of PrEP uptake. Consequently, it is plausible that there is increased comfort in adoption of

biomedical prevention or openness to trying a new prevention option, either as a complement to or replacement for condoms among AGYW. Other recent research with AGYW has similarly found an inverse relationship between risk perception and PrEP adoption, with mixed findings [24,25,26].

The findings indicate an opportunity to create demand for oral PrEP and/or other PrEP delivery forms among AGYW with elevated risk perception. Additionally, this research underscores the need to further understand barriers to oral PrEP use in this group with higher risk perception to determine whether they can be addressed or will require alternative prevention tools, including alternative PrEP delivery forms.

Internalized stigma, specifically PrEP-related shame, constitutes an important barrier to adoption of HIV prevention behaviors, including use of biomedical prevention. Previous research has demonstrated the relationship between PrEP-related shame and PrEP interest and uptake among other populations [27,28,29]. Recent research has started to explore how PrEP-related shame may impact PrEP uptake among AGYW in Southern Africa [30]. Our findings align with this existing work. Notably, the perception that others may think that AGYW were sexually “loose” did not correlate with participants’ decisions about PrEP uptake. This demonstrates that *internalized* PrEP-related shame, more than external perceptions of community stigma, is a potential intervention target for efforts to change attitudes related to PrEP and increase PrEP uptake among AGYW in South Africa.

Partner and relationship factors are known to influence the use of HIV prevention by AGYW. However, in this study, relationship-based measures, including condom negotiation and sexual empowerment, were not correlated with PrEP uptake. Given the high uptake of PrEP, it may be that these factors prove more important to adherence and persistence over time rather than to decisions to initiate PrEP [31].

Several other factors also were not associated with PrEP uptake in this study but warrant further study. For example, economic factors such as food insecurity, financial security, and education were not related to PrEP uptake. This is likely because PrEP was freely available in the study and this finding may hold true in South Africa where oral PrEP is currently freely available to individuals via public healthcare settings. However, if other modalities of PrEP, such as the dapivirine ring or injectable PrEP, require payment the impact of economic factors on uptake may be significant. Future research should also continue to examine how economic and other factors examined in this study may impact the uptake of different PrEP modalities in South Africa across time.

This is one of the few studies to examine multilevel factors associated with PrEP uptake among a community-based population of South African AGYW. The study participants were diverse in relation to education and economic indicators and were drawn from a geographic area comprising peri-urban and semirural communities. PrEP uptake also occurred in the context of public healthcare settings, strengthening the evidence base to inform future introduction and access and the external validity of the findings.

Some limitations of this study should be noted. First, exposure data were drawn from baseline assessments in an ongoing trial; consequently, the analysis focuses on correlates of PrEP

uptake owing to most PrEP uptake occurring shortly after study enrollment. Consequently, causality cannot be inferred from this analysis. Longitudinal assessments of the exposures and other measures of PrEP use, including persistence and adherence, are critical to understanding how to overcome the substantial declines in PrEP use over time that have been found in other demonstration projects and real-world rollout of PrEP for AGYW [32,33,34]. Second, our assessment of PrEP uptake—evidence of filling a PrEP prescription provided through the study—is limited because AGYW may not have actually initiated PrEP use. These limitations notwithstanding, this study underscores the need to address potential barriers to PrEP uptake, such as risk perceptions, and to consider stigma-reduction strategies to support PrEP use among South African AGYW who may benefit the most from biomedical HIV prevention tools.

Conclusion

Our findings highlight the need to engage AGYW in the development of demand-creation and stigma-reduction activities for AGYW who are at increased risk of acquiring HIV. Key decision-makers may support bolstering demand-creation efforts, providing alternative forms of PrEP, and leveraging existing interventions that have demonstrated efficacy to reduce sources of stigma that affect PrEP use among AGYW.

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Ethics declarations

Conflict of Interest

The authors have no conflicts of interest to disclose.

Ethics Approval

This study was approved by the ethics review committees of the South African Medical Association Research Ethics Committee, which served as the Institutional Review Board (IRB) of Record, and by the Tshwane District Health Research Committee and the Skills Development for Tshwane Municipal Clinics.

Consent to Participate

All participants provided written informed consent (or assent, if aged 16 or 17) prior to data collection.

Data Availability

Data is available upon request from Dr. Wendee Wechsberg.

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