Correlates of ART Use Among Newly Diagnosed HIV Positive Adolescent Girls and Young Women Enrolled in HPTN 068

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Abstract

Despite expanded access to HIV treatment worldwide, poor HIV care outcomes persist among adolescent girls and young women (AGYW). This study was conducted among AGYW recruited from the HPTN 068 cohort who had sero-converted to HIV during the main trial between 2011 and 2014. The aim was to examine correlates of anti-retroviral treatment (ART) use. Log binomial regression was used to estimate the crude associations between social support, stigma, and HIV status disclosure and current ART use. Adjusted analyses were also conducted controlling for age and time since diagnosis. Seventy-nine AGYW were included in this analysis. Median age of participants was 20 (range: 17 to 24) and time since diagnosis ranged from 0.5 to 4.8 years (median = 2.1). Over 75% of AGYW (n = 60) had sought HIV care at some point, with the same number reporting previous disclosure of their sero-status. However, just 43% (n = 34) of participants were on treatment at the time of the interview. Over half of participants (n = 44; 55.7%) reported social support was available to them most or all of the time, and the median stigma score was 90 (range 80–113). Adjusted analyses found higher current ART use among those who had disclosed their status (adjusted prevalence ratio (aPR): 3.19; 95% confidence interval (CI) 1.09, 9.32; p = 0.0339) and those with lower scores on the disclosure concern sub-scale of the Berger HIV Stigma Scale (aPR: 0.88; 95% CI 0.79, 0.98; p = 0.0236). ART use among AGYW living with HIV and enrolled in HPTN 068 was low despite relatively high linkage to care during the trial. Interventions aimed at minimizing individuals' concerns about disclosure and improving onward disclosure of one's status could further improve ART utilization among AGYW living with HIV in South Africa.

Keywords HIV/AIDS · Adolescents · Sub-saharan Africa · Anti-retroviral therapy · Linkage · Retention

Introduction

Adolescents continue to bear a disproportionate burden of the HIV epidemic worldwide. In South Africa specifically, over one-third of all new HIV infections occur among individuals ages 15 to 24 [1–3], with the majority of these infections occurring among young people ages 20 to 24 [4]. Evidence-based interventions aimed at improving access to HIV treatment among all people living with HIV, such as the adoption of the World Health Organization's Universal Test and Treat policy in September 2016 [5], have been implemented nation-wide. However, improvements in HIV care outcomes among adolescents and young people continue to lag behind improvements seen in adult people living with HIV [3]. The most recent country estimates suggest that while 63.1% of people ages 25–49 living with HIV are currently on anti-retroviral therapy (ART) just 39.9%

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of young people ages 15 to 24 living with HIV are taking treatment [2, 6].

Though there is a dearth of empirical data regarding factors influencing linkage to and retention in care among adolescents and young people, as compared to adults [7], research has identified a number of factors which may contribute to the disparities in HIV care outcomes described above. Adolescence is a time of physical and mental maturation, as well as identity experimentation [8]. It is a period characterized by limited social support, lack of access to age-appropriate healthcare services, and increased vulnerability to stigma, discrimination, and poor mental health outcomes [9–15]. Evidence suggests that these factors, as well as low proportions of HIV status disclosure, could contribute to poor HIV care outcomes among adolescents living with HIV (ALHIV) [9, 10, 14–21].

Given that the majority of South African ALHIV are not on treatment or virally suppressed [2, 3], there is a need to better understand factors associated with ART use in this highly vulnerable population. This study aims to characterize the association between: (1) social support, (2) HIV-related stigma, and (3) status disclosure, and current ART use among a cohort of recently infected adolescent girls and young women (AGYW) living with HIV in rural South Africa. The goal of this work is to better inform interventions to alleviate current treatment and care gaps in the area.

Methods

Study Design

This sub-study, henceforth referred to as "Engage", is a cross-sectional study nested within the individually randomized control trial HIV Prevention Trials Network (HPTN) 068. Engage was conducted between 2011 and 2017 with the primary aim of assessing the influence of key factors of interest on HIV treatment and care uptake among AGYW living with HIV.

Location

This study was conducted in the South African Medical Research Council and Wits University's Agincourt Health and Socio-Demographic Surveillance System (HDSS) site in the Bushbuckridge sub-district of Mpumalanga province, South Africa [22]. The rural study site, with a population of roughly 115,000, is approximately 500 km northeast of Johannesburg and includes nine publicly funded healthcare facilities, which service a large proportion of the population [23, 24]. The site is characterized by high levels of HIV infection, poverty, and unemployment [4, 23, 24].

Study Population

Individuals included in this sub-study were originally enrolled in the HPTN 068 study conducted in the Agincourt HDSS [22]. Details of the HPTN 068 trial are listed elsewhere [22, 25], but briefly, 2533 young women were enrolled. At baseline, participants were ages 13–20 years, enrolled in grades 8–11, were not married or pregnant, were able to complete a computer survey on their own, and could open a post office or bank account. Participants were randomized to either a cash transfer intervention conditional on school attendance, or a control group. These AGYW were followed annually and interviewed to assess factors such as socio-economic factors, sexual behaviors, mental health, intimate partner violence, and alcohol and drug use. AGYW were also tested for HIV and herpes simplex virus type 2 (HSV-2) at baseline and at each annual study visit until they were considered lost to follow-up or matriculated from secondary school and formally exited the trial a maximum of three years following enrollment into the trial [22].

Individuals testing HIV positive at the baseline HPTN 068 trial visit were invited to complete a separate follow-up visit for the Engage sub-study approximately 12 to 18 months after their initial enrollment in the HPTN 068 trial. Individuals testing newly HIV positive throughout the main HPTN 068 trial were invited to complete a separate follow-up visit for the Engage sub-study after their initial diagnosis during the trial. This analysis utilizes Engage data collected between March 2015 and July 2017 from all individuals diagnosed with incident HIV throughout the main trial. Individuals who tested HIV positive at trial baseline were excluded, as it was difficult to ascertain a reliable measure of time since HIV diagnosis, a key covariate of interest in this sub-study.

Data Collection and Measures

For all Engage study visits, locally hired and trained HPTN 068 HIV counselors administered a paper-based questionnaire in the participant's preferred language (English or Xitsonga, the predominant local language).

Self-reported current ART use was the primary outcome of interest. Current ART use was dichotomized as "currently taking any daily treatment for HIV" or no current daily treatment for HIV. Specific exposures of interest included social support, HIV-related stigma, and prior disclosure of HIV status.

Social support was captured in multiple ways. Participants were first asked to identify how many individuals in their life they felt at ease with and then completed an abbreviated 12-item version of the Medical Outcomes Study social support scale (MOS-SSS), which captures emotional and informational support, tangible support, affectionate support, and positive social interaction [26, 27]. A composite score was obtained by summing the responses to all 12 scale items. A minimum score of 12 represents rare to no support, and a maximum score of 36 represents support most or all of the time. Each of the four sub-scales are comprised of three items and have a minimum score of three and a maximum score of nine.

Perceived stigma was measured using the 40-item Berger HIV Stigma Scale [28, 29]. The minimum composite stigma score of 40 represents the lowest degree of perceived stigma. The maximum score of 160 represents the highest degree of perceived stigma. This scale is comprised of four subscales which measure personalized or enacted stigma (18 items; score range: 18 to 72), disclosure concerns (10 items; score range: 10 to 40), negative self-image (13 items; score range: 13 to 52), and concern with public attitudes about people with HIV (20 items; score range: 20 to 80).

Self-reported HIV status disclosure to at least one person was dichotomized as yes or no. Information was also collected on who participants disclosed their status to and these individuals' reactions following the disclosure.

Other variables of interest included time since HIV diagnosis (calculated as the time in years between the individual's date of diagnosis in the main HPTN 068 trial and date of Engage interview), age at Engage interview, self-reported care-seeking behaviors, and self-reported experiences with the healthcare system. Specifically, AGYW were asked if they had previously sought HIV-related medical care since their diagnosis and if they had ever taken treatment for HIV. AGYW that had previously sought HIV-related care were asked to respond to a series of questions about what motivated them to seek HIV care, how they were treated by medical staff during their last HIV-related medical visit, how they got to the clinic, how long it took to get to the clinic, and how long they waited for clinic services. Individuals who reported they had never sought HIV-related care were instead asked why they had not previously sought care for HIV.

Ethical Considerations

Written informed consent was obtained from all participants ages 18 and older, and written parental consent and assent were obtained for any participant under the age of 18. Ethical approval for this study was obtained from the University of North Carolina at Chapel Hill Institutional Review Board, the University of the Witwatersrand Human Research Ethics Committee, and the Mpumalanga Province Health Research Committee.

Analysis

In this analysis we describe general care and support seeking behaviors following HIV diagnosis. For individuals who self-reported previously seeking HIV-related care, we describe their motivations for seeking care and experiences with the local healthcare system at their last medical visit. For individuals who self-reported no prior HIV-related care-seeking, we describe self-reported barriers to care.

Internal consistency and reliability of the modified MOS-SSS and Berger HIV Stigma scale was assessed using Cronbach's alpha. Alpha values > 0.70 were considered acceptable. To determine the crude and adjusted associations between current ART use and each exposure of interest, log binomial regression was used to calculate prevalence ratios and the corresponding 95% confidence intervals. Adjusted analyses controlled for age and time since HIV diagnosis, the a priori determined covariates of interest based on a literature review of factors influencing ART use and retention in HIV care [30–33]. All analyses were conducted using SAS Studio 3.8 (SAS Institute, Cary, NC).

Results

Of the 2,533 AGYW enrolled in HPTN 068, 81 tested HIV-positive at baseline and 107 incident cases were identified throughout the trial. Of these 188 AGYW living with HIV, 143 (76.1%) consented to participate in Engage and were subsequently interviewed. Eighty AGYW who participated in Engage (55.9%) were incident cases in the main trial, and therefore eligible for inclusion in this sub-study. One individual was excluded due to missing data on current ART use, yielding a sub-study sample size of 79. Participant ages at time of Engage interview ranged from 17 to 25 (median = 20) and the median time since initial HIV diagnosis was 2.1 years (range: 0.51 to 4.78) (Table 1).

Care-Seeking

Over 75% of AGYW (n = 60) had sought HIV care at some point since diagnosis, yet just 43% (n = 34) were on treatment at the time of the Engage interview. Among those who had previously sought care (n = 60), the three most commonly reported reasons for visiting the clinic were because the AGYW was told to at a main trial study visit (75.0%), they did not want to fall ill (66.7%), and they wanted to get medicine for HIV (65.0%) (Table 2). The one factor the majority of these 60 AGYW (n = 22; 36.7%) reported was most helpful during their care-seeking experience was family support for seeking care.

Most individuals who sought care took public transportation to the clinic (n = 30; 50%), and median travel time

Table 1 Characteristics of 79 adolescent girls and young women living in the Agincourt Health and Socio-Demographic Surveillance System site in rural Mpumalanga province, South Africa and newly diagnosed with HIV in HPTN 068

	Current ART use (n = 34) N (%) or median (range)	No current ART use (n = 45) N (%) or median (range)	Total (n = 79) N (%) or median (range)
Age	20 (17 to 24)	20 (17 to 24)	20 (17 to 24)
Years since diagnosis	2.26 (0.89 to 3.16)	1.98 (0.51 to 4.78)	2.12 (0.51 to 4.78)
Ever sought HIV care			
Yes	34 (100)	26 (57.8)	60 (75.9)
No	0 (0.0)	19 (42.2)	19 (24.1)
Ever disclosed HIV status			
Yes	31 (91.2)	29 (64.4)	60 (75.9)
No	3 (8.8)	16 (35.6)	19 (24.1)
Stigma	88 (80 to 113)	92 (83 to 113)	90 (80 to 113)
Personalized or enacted stigma	37 (30 to 51)	38 (36 to 52)	37 (30 to 52)
Disclosure concerns	25 (20 to 29)	27 (22 to 31)	26 (20 to 31)
Negative self-image	29 (26 to 38)	30 (27 to 39)	30 (26 to 39)
Concern with public attitudes	43 (38 to 57)	44 (36 to 56)	44 (36 to 57)
Social support	36 (14 to 36)	35 (22 to 36)	36 (14 to 36)
Emotional/information support	9 (3 to 9)	9 (4 to 9)	9 (3 to 9)
Tangible support	9 (5 to 9)	9 (6 to 9)	9 (5 to 9)
Affectionate support	9 (3 to 9)	9 (5 to 9)	9 (3 to 9)
Positive social interaction	9 (3 to 9)	9 (5 to 9)	9 (3 to 9)
Number of people at ease with	2 (1 to 10)	2 (1 to 10)	2 (1 to 10)

Table 2 Self-reported reasons for seeking HIV care services among 60 adolescent girls and young women newly diagnosed with HIV during HPTN 068

Reason for seeking care	N (%)
Told to at a study visit in main trial	45 (75.0)
Did not want to fall ill	40 (66.7)
To get medicine for HIV	39 (65.0)
Told to by parent/guardian	20 (33.3)
Heard on the radio/TV that you should seek care if have HIV	11 (18.3)
Feeling ill	11 (18.3)
Heard at school that you should seek care if you have HIV	7 (11.7)
Friends suggested that you go	2 (3.3)

was 30 min (range: 5–90). Thirty-two individuals (53.3%) reported waiting more than one hour for services, and 26 (43.3%) felt staff members did not spend sufficient time with them. Fifty-seven AGYW (95.0%) reported feeling better after their most recent medical visit because of their experience with clinic staff. However, three participants (5.0%) would not recommend the facility they attended to someone else living with HIV, with all three individuals citing unfriendly clinic staff as their reason for this response.

Of the 19 individuals who had not previously sought care, two individuals did not report barriers to care, 10 (58.8%) stated that their belief that they did not have HIV was somewhat important in influencing their decision to postpone care, and nine individuals (52.9%) stated they did not feel sick or did not think seeking care would help (Table 3).

Disclosure

Sixty AGYW (75.9%) had disclosed their HIV status to at least one individual since they were diagnosed at a trial visit, and most (n=35; 58.3%) eported they had disclosed to more than one person. Most commonly, individuals had disclosed their status to their mother (n = 35; 58.3%) and their boyfriend (n = 35; 58.3%), with 28 (46.7%) of the 60 AGYW who disclosed reporting they disclosed to their mother first.

The primary reactions AGYW reported receiving after disclosing their status included positive reactions like comforting the AGYW (n = 49; 81.7%) and suggesting the AGYW see a doctor (n = 52; 86.7%). Negative reactions to study participants' disclosure included being sad (n = 26; 43.4%), becoming angry (n = 10; 16.7%), forcing AGYW to leave their house (n = 2; 3.3%), and leaving the room (n = 1; 1.7%). Twenty-three (38.3%) AGYW who had shared their HIV positive status with someone stated the individual they disclosed to sought testing following the disclosure. Among the 35 young women who reported disclosing to a boyfriend, 18 (51.4%) reported that the partner tested for HIV as a result of disclosure.

Table 3 Self-reported barriers to care among 17 out of 19 adolescent girls and young women who had not sought HIV care since their diagnosis during HPTN 068

Self-reported barriers to care (n = 17)[a]	Somewhat important N (%)
Do not believe you have HIV	10 (58.8)
Do not feel sick so you think it's okay to wait for a while	9 (52.9)
Do not think it will help you	9 (52.9)
Too embarrassed to go	6 (35.3)
Worried that the clinic staff will not treat you well	5 (29.4)
Worried someone might find out you have HIV if you go	5 (29.4)
Worried about the side effects of HIV treatment	4 (23.5)
Scared they will tell your family or friends that you have HIV	4 (23.5)
Do not have money to pay for transport	3 (17.6)
Do not know where to go	3 (17.6)
Parent or carer does not want you to go to the clinic	2 (11.8)
Clinic is too far away	1 (5.9)
Feel too sick to go	1 (5.9)
Clinic timings are inconvenient	1 (5.9)
Prefer to go to a traditional healer	0 (0.0)

[a] Two individuals that have not sought care are missing data on these responses

Among the individuals who had not disclosed their HIV status (n = 19), the most commonly reported reason for postponing disclosure was being concerned the individual might tell others (n = 16; 84.2%). This concern was followed by fear of the individual thinking the AGYW is a bad person (n = 15; 79.0%) and not wanting to worry the individual (n = 15; 79.0%). Fourteen (73.7%) AGYW also reported they were concerned the individual might physically hurt them if they disclosed their status.

Social Support

Overall reliability of the MOS-SSS was high (Cronbach's α = 0.86), though reliability of the subscale measures varied (Cronbach's α ranging from 0.54 to 0.69). All sub-scales were maintained in result reporting as they have been previously used throughout the country [34, 35].

The median number of individuals AGYW reported feeling at ease with was 2 (range: 1–10). This was the same regardless of current ART use. The median composite social support score was 36 (range: 14–36), the highest possible score on the scale. This indicates that over half of study participants (n = 44; 55.7%) felt emotional and informational support, tangible support, affectionate support, and positive social interaction most or all of the time when needed. There was no difference in reported social support by ART status.

Stigma

Overall reliability of the Berger HIV Stigma Scale was high (Cronbach's α = 0.90), though reliability of subscale measures varied (Cronbach's α ranging from 0.59 to 0.90). All sub-scales were maintained in result reporting for comparative purposes as subscales have been used among ALHIV in similar settings [36].

After dropping one outlier with a composite stigma score of 53, the median composite stigma score among AGYW in this study was 90 (observed range: 80 to 113; possible scale score range: 40–160). Among those currently on ART, the median stigma score was 88 (range: 80 to 113), while among those not on ART, the median score was 92 (range: 83 to 113), indicating those on ART had a lower perception of HIV-related stigma than those not on ART. Median scores on each of the four stigma subscales also differed by current treatment status, with those not on ART generally reporting higher perceived stigma on each of the four stigma subscales (Table 1).

Current ART Use

Just 43% (n = 34) of AGYW were on treatment at the time of the Engage interview, a median of 2.1 years (range: 0.5 to 4.8) after their initial diagnosis with HIV. Univariate analysis suggested a statistically significant relationship between: (1) prior HIV status disclosure (p = 0.0294), (2) composite Berger HIV stigma scale score (p = 0.0484), and (3) the disclosure concern subscale of the stigma scale (p = 0.0076), and current ART use (Table 4). After adjusting for age and time since diagnosis, these relationships were attenuated slightly, and the composite stigma score was no longer significantly associated with current ART use (p = 0.0656). Prevalence of ART use among AGYW who had previously

Table 4 Correlates of antiretroviral therapy use among 79 adolescent girls and young women newly diagnosed with HIV during HPTN 068

	uPR (95% CI)	p-value	aPR[a] (95% CI)	p-value
Prior HIV status disclosure	3.27 (1.13, 9.51)	0.0294	3.19 (1.09, 9.32)	0.0339
Berger HIV stigma score[b]	0.96 (0.92, 1.00)	0.0484	0.96 (0.92, 1.00)	0.0656
Personalized or enacted stigma	0.94 (0.87, 1.02)	0.1574	0.94 (0.87, 1.03)	0.1812
Disclosure concerns	0.86 (0.77, 0.96)	0.0076	0.88 (0.79, 0.98)	0.0236
Negative self-image	0.93 (0.84, 1.03)	0.1480	0.93 (0.84, 1.03)	0.1774
Concern with public attitudes	0.96 (0.90, 1.02)	0.1956	0.96 (0.90, 1.03)	0.2210
Social support	1.05 (0.96, 1.15)	0.3155	1.03 (0.95, 1.14)	0.4155
Emotional/information support	1.08 (0.87, 1.34)	0.4940	1.05 (0.84, 1.32)	0.6744
Tangible support	1.10 (0.76, 1.60)	0.6238	1.07 (0.74, 1.55)	0.7181
Affectionate support	1.07 (0.76, 1.50)	0.7019	1.05 (0.75, 1.47)	0.7695
Positive social interaction	1.13 (0.88, 1.47)	0.3370	1.12 (0.86, 1.45)	0.4151

[a] Adjusted for age and time since diagnosis

[b] Excluding outlier with composite stigma score of 53

disclosed their status was 3.19 (95% CI 1.09, 9.32) times that of AGYW who had not previously disclosed their status. For each one-unit increase in AGYW's score on the disclosure concern stigma sub-scale, ART use was 0.88 (95% CI 0.79, 0.98) times as likely, indicating AGYW with greater concern about disclosing their status were significantly less likely to report current ART use. While no statistically significant relationship was observed between the composite stigma scale score or the other stigma subscale scores and current ART use in adjusted analyses, trends in regression results suggest that individuals with higher perceived stigma were less likely to report current ART use. No statistically significant relationship was observed between the number of individuals AGYW feel at ease with, composite social support scale score, or the four social support sub-scales and current ART use (Table 4).

Discussion

AGYW living with HIV in South Africa face myriad complex barriers to engagement and retention in HIV care. Though HIV care initiation in this study was relatively high compared to the national estimates, with over 75% of study participants reporting they had sought care at some point since their diagnosis, treatment utilization remained low with just 43% of participants on ART a median of 2.1 years after diagnosis. In this study of AGYW living with HIV, prior disclosure of an individual's HIV status and concerns around disclosure were the only factors significantly associated with self-reported current ART use.

A large proportion of AGYW (75.9%) reported prior disclosure of their HIV status, which was significantly associated with current ART use in the sample. The primary reasons for avoiding HIV status disclosure in this analysis included fear that the individual to whom they would like to disclose their status might tell others or become physically violent. While violence can be a risk of HIV status disclosure, prior research suggests this is uncommon in relationships with no prior history of violence [37]. One study conducted among pregnant and postpartum women enrolled in a randomized control trial in Durban, South Africa, found no association between HIV diagnosis and incident intimate partner violence [37]. This same study saw an elevated risk of incident intimate partner violence among those who chose *not* to disclose their HIV status, indicating non-disclosure could serve as a marker for unhealthy relationships and suggests those fearing violence following disclosure should seek support from someone other than their intimate partner [37]. A potential intervention that could improve onward disclosure and is recommended in the South Africa Department of Health's current ART guidelines for adolescents [38], involves assisting individuals living with HIV in identifying an individual that would support them in their diagnosis and creating a safe environment for disclosure to take place, alleviating AGYW's concerns regarding reactions following disclosure [39].

A large majority of the literature on disclosure in ALHIV focuses on parental or guardian disclosure of perinatally-infected adolescents' status to the adolescent themselves. There is minimal literature focusing solely on establishing the relationship between adolescents' disclosure of their own HIV status to others and HIV care outcomes [39]. However, one study conducted in Harare City, Zimbabwe found that the odds of virological failure among ALHIV who had not previously disclosed their HIV status was 5.88 times the odds of virological failure among those who had previously disclosed [40]. While ensuring perinatally infected adolescents know their HIV status remains crucial to improved care outcomes, increasing onward disclosure among AGYW living with HIV can yield increased support for care seeking and has the potential to improve HIV treatment outcomes as seen in this study and others [39–41]. It is crucial for disclosure to be viewed as a complex process rather than a one-time event, with interventions such as multi-session support groups showing the most promise for improving onward disclosure in adolescents [42–44].

Stigma has also been repeatedly shown to impede access to and retention in care in a number of populations living with HIV, including AGYW living with HIV [11, 45–48]. A systematic review on factors influencing ART adherence among ALHIV in sub-Saharan Africa found that stigma was the main barrier to ART adherence in the region [49]. In this review, AGYW reporting higher perceived stigma were less likely to be on ART than those with lower scores. Elevated scores on the "disclosure concerns" sub-scale of the Berger HIV Stigma Scale was significantly associated with no current ART use in this population of AGYW living with HIV, corroborating our results that suggest HIV status disclosure plays a crucial role in facilitating ART use among AGYW. While no statistically significant associations were observed between individuals' composite stigma scale score or the additional stigma sub-scales and current ART use, trends in adjusted regression results suggest overall perceived stigma could be important in influencing current ART use among AGYW living with HIV. In future studies, utilization of Pantelic et al.'s ALHIV stigma scale, which was psychometrically assessed and validated among ALHIV in South Africa specifically [50], could improve reliability of population stigma measures.

AGYW in this study reported high levels of social support overall. Research conducted in similar contexts suggests an association between social support and retention in HIV care among adults [51]; however, we did not see that association here. Over half of study participants stated they had emotional and informational support, tangible support, affectionate support, and positive social interactions most or all of the time when needed, and all AGYW surveyed reported at least one individual they felt at ease with. These high levels of support likely contributed to the lack of an association observed between social support and ART use in this population.

Perceptions of individual's healthcare seeking experiences among AGYW who had previously sought HIV-related healthcare were largely positive despite reports of clinic wait times exceeding one hour and insufficient time spent with providers. Very few participants who had sought HIV-related care stated they would not recommend the clinic they attended to someone else living with HIV, while most individuals reported feeling better after meeting with a service provider at their last visit. Positive experiences of healthcare seeking may also be linked to ART being provided for free at all public health facilities in South Africa.

Among individuals who had not previously sought HIV care, holding a belief that they were not infected and not feeling ill were the most frequently cited reasons for delaying care, a common finding among ALHIV that delay care initiation [10]. Concerns about clinic quality of care and accessibility appeared to be less important in this context, unlike the results from a number of similar studies [52, 53]. Together, our data suggest that challenges to healthcare service delivery persist in the Agincourt HDSS, but that AGYW living with HIV in the area do not consider this the most influential factor impacting their care-seeking behavior. This is consistent with evidence suggesting linkage to care among ALHIV remains the greatest hurdle in improving HIV care outcomes, while retention in care over time is less problematic after young people are linked [54].

Several key differences between the study population and AGYW living with HIV more broadly should be considered when interpreting study findings. First, all newly diagnosed AGYW enrolled in HPTN 068 were offered active linkage to HIV care services through trained study staff at the time of their diagnosis. It is well known that active linkage to care programs yield higher proportions of individuals initiating ART than passive referral processes [55–57], potentially contributing to the overall high percentage of AGYW reporting they had previously sought HIV-related healthcare services. Additionally, all AGYW in the trial were enrolled in school at trial baseline. While this may limit generalizability of study findings to AGYW attending school, we believe this cohort is more representative of the general population of AGYW than a clinical cohort or cohort of individuals specifically seeking HIV counseling and testing services. Finally, individuals in this trial were repeatedly asked about their sexual behaviors and were aware of the fact that they were being followed each year by a team of HIV researchers. This has the potential to increase motivation to link to care at the time of diagnosis and increase care-seeking throughout the duration of the trial. While it is unlikely that these factors would directly influence long-term outcomes such as ART utilization at the time of Engage interview, they should be considered as upstream factors that could impact individual care-seeking behaviors more broadly.

Several study limitations should also be considered when interpreting the results of this sub-study. Notably, South African ART treatment initiation guidelines were altered during the course of data collection for this study. In September 2016, South Africa launched the nation-wide test and treat campaign in alignment with recommendations from the World Health Organization. This policy recommends immediate ART initiation for all individuals living with HIV, regardless of clinical stage or CD4 count [5, 58]. Prior to this policy change, individuals with a CD4 count above 500 were ineligible for ART initiation. This could potentially contribute to the low levels of observed current ART use in the population, as some AGYW were interviewed prior to September 2016. This study was also limited by the relatively small sample size of AGYW who were newly diagnosed with HIV during HPTN 068 (n = 107) and subsequently consented to participation in the Engage sub-study (n = 81; 75.7%). Further, current ART use may have been over-reported due to social desirability bias and lack of capacity to validate self-reported outcomes through clinical record review.

Future longitudinal studies conducted in the era of Universal Test and Treat should aim to ascertain current ART use through blood drug level testing, and recruit a larger number of participants. This will allow investigators to explore more comprehensive exposure-outcome pathways while simultaneously maintaining sufficient power to detect statistically significant associations.

Conclusions

Low levels of HIV treatment use remain a substantial barrier to improved health outcomes among AGYW living with HIV in this resource-limited setting in rural South Africa. Disclosure of one's HIV status is recommended by the South African Department of Health and can improve ART utilization. Disclosure is a process and should therefore be encouraged at the time of an individual's initial diagnosis with HIV and at routine care visits following diagnosis. Perceived stigma among ALHIV may also impede ART utilization and interventions to address HIV-related stigma must persist. It is essential to routinely monitor barriers to treatment use among highly vulnerable AGYW living with HIV in an effort to improve the long-term health outcomes of these individuals and eliminate onward transmission of the virus. While treatment outcomes among AGYW living with HIV may be improving in the era of Universal Test and Treat, as suggested by these study findings, significant progress is still needed if we are to meet UNAIDS' 90-90-90 targets.

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Compliance with Ethical Standards

Conflict of interests The authors declare that they have no competing interests.

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