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Trajectories to HIV Viral Suppression and Nonsuppression: Case Studies From Rural East African Adolescents and Young Adults in the SEARCH-Youth Trial

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Abstract

Background: While research has identified many associations between socioeconomic factors and human immunodeficiency virus (HIV) nonsuppression, few qualitative studies have defined the mechanisms by which these factors interrelate and lead to HIV nonsuppression. The development of interventions to achieve universal virologic suppression and eliminate transmission will require a deeper understanding of the individual and social processes that drive antiretroviral therapy (ART) nonadherence and consequent viral nonsuppression.

Methods: We used a semistructured interview-based case-study approach to characterize changes across 3 time points in the lived contexts of 11 adolescents and young adults (aged 15-24 years) from intervention and control arms of a longitudinal HIV intervention trial in rural Kenyan and Ugandan communities. We sought to determine commonalities among those who never virally suppressed, those who became nonsuppressed, and those who moved from nonsuppression to viral suppression, exploring social and behavioral micro-processes or causal chains observed among individuals who share these trajectories.

Results: We found that supportive family environments, high-quality service provision, and residential and partnership stability free of violence, or that permitted freedom to move and maintain extensive social ties both inside and outside one's immediate community, enabled ART adherence. We also found that several factors combine to have effects beyond each individual factor taken singly, for example, medication side effects were influenced by food insecurity;

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disclosure was most effective with individuals around whom one may potentially take medication, such as co-resident partners; and mobility compromised adherence when patients did not know how or where to access care in new places.

Recommendations: Our findings suggest that to improve virologic suppression, clinical care and interventions should include assessment and strategies to address food insecurity, ART disclosure, and home-based violence from intimate partners or other family members. When such factors are present, we suggest referral for services, including violence prevention and protection services, and food provision for those patients who do not adhere because of medication side effects amplified by lack of food. We further recommend that clinics coordinate regionally to anticipate mobility, facilitate transfer of care to other areas, and ensure clients have access to information about care clinics elsewhere in the region.

Plain Language Summary

Longitudinal Case Studies Tracking HIV Viral Suppression or Nonsuppression From Rural East African Adolescents and Young Adults With HIV

Research has identified many associations between socioeconomic factors and human immunodeficiency viruses (HIV) nonsuppression, but few qualitative studies have defined how these factors interrelate and lead to HIV nonsuppression. We used a case-study approach drawn from semi-structured interviews to identify changes in the lives of 11 adolescents and young adults (aged 15-24 years) in an HIV intervention trial in rural communities in Kenya and Uganda. We found that supportive family environments, high-quality service provision, and residential and partnership stability free of violence, or one that permitted freedom to move and maintain extensive social ties both inside and outside one's immediate community, enabled antiretroviral therapy (ART) adherence. Our findings suggest that to improve virologic suppression, clinical care, and interventions should include assessment and strategies to address food insecurity, ART disclosure, and home-based violence from intimate partners or other family members.

Keywords

adolescent, young adult, HIV, viral load, transition to adult care, Uganda, Kenya, marriage, rural population, domestic violence, food insecurity, economic factors, viral suppression, viral nonsuppression

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Background

Achieving the aim of zero human immunodeficiency virus (HIV) new infections and zero HIV deaths means identifying the pathways by which people with HIV can achieve and maintain viral suppression. For the purposes of this article, viral suppression is determined to be 400 copies of HIV per milliliter of blood or lower; "undetectable" refers to 40 c/mL or lower.[1] Viral suppression, which helps prevent the onward transmission of HIV, is particularly important among populations vulnerable to disruptions in care and treatment, such as people displaced by conflict and economic deterioration[2]; people engaged in mobile occupations like fishing, transportation, and sex work[3–6]; and young people transitioning from pediatric to adult care.[7–10]

Adolescents and young adults with HIV (AYAH) face unique life stage-related obstacles as they navigate HIV care in the context of school, marriage, and childbirth turning points, including the initiation of HIV care following a new diagnosis, or transition from pediatric to adult HIV care during adolescence.[11] Challenges encompass individual, familial, and community-wide barriers, and include cross-cutting factors like stigma, interpersonal violence, and food insecurity.[12]

Within eastern and southern Africa, multiple studies have documented associations between HIV nonsuppression and factors including male sex, rural residence, food insecurity, older age at initiation of antiretroviral therapy (ART), side effects, and dissatisfaction with service delivery.[13–15] Studies have reported mixed associations relating to the length of time on ART,[16] age at diagnosis (or disclosure), and being an adolescent or young adult.[17] Despite *quantitative* studies examining barriers to ART adherence,[18] few have *qualitatively* examined the case histories of people who either failed to achieve viral suppression or to maintain it, in order to tie these variables together as social or structural processes. Moreover, few studies have qualitatively explored factors that may facilitate viral suppression beyond HIV status self-disclosure.[19,20] Such qualitative studies are necessary to elucidate the mixed associations found in the qualitative data and design interventions that match the background social or cultural contexts more closely to replicate desired results in new settings.

To inform the development of interventions that will increase engagement with care and viral suppression, qualitative researchers can answer several key questions raised from the quantitative data about risk factors by

attending to the specifics of cultural contexts and socially informed networks. For those who never suppress during such interventions, what socio-structural processes interfere with achieving viral suppression? For those who begin such studies virally suppressed and become virally non-suppressed, what events and contexts influence behavioral changes that then appear to lead to nonsuppression? For those who remain virally suppressed but whose viral loads slowly begin to increase, what contextual warning signs—signs that can also be elicited during clinical interviews—match the situations observed in participants from the previous two groups? Finally, for those whose viral loads markedly decrease, what socially replicable factors appear to facilitate movement towards viral suppression, and in what ways are these the inverse or independent of the processes leading to nonsuppression in the previous groups?

This article attempts to answer such questions using a case study approach of 11 participants in a longitudinal intervention study among youth with HIV in rural Kenya and Uganda. The region in which these participants live is characterized by economies based on fishing, farming, and trading; school-going youth may attend boarding schools or day schools, though not all adolescents complete their primary education. The Luo and Nkole are the primary ethnic groups in the respective countries, though participants or their families may often have connections to Luhya, Kisi, Maasai, and Buganda majority areas, as well as further afield in the capitals and coastal cities where pastoralism and other industries are more common. HIV care in both regions is decentralized and provided at both government (Ministry of Health) and privately run clinics. NGOs historically filled gaps as the countries worked to build up their healthcare infrastructure.

Methods

Study Context

The SEARCH-Youth study (Strategic Antiretroviral Therapy and HIV testing for Youth in Rural Africa, NCT03848728; KEMRI: SERU 3834; and UNCST: HS 2542) sought to evaluate whether a combination intervention would improve viral suppression among AYAH aged 15 to 24 years during a community cluster-randomized controlled trial in 28 rural communities in western Kenya and southwestern Uganda. During the trial, both intervention and control arm participants received local standard of care for clients of their age. For intervention arm participants, a life-stage approach addressing psychosocial needs and structural barriers such as timing of care and location of services, whose aim was to improve viral load suppression and overall health outcomes, additionally informed their care.[1] The study intervention did not address employment services, health literacy campaigns, or family counseling (ie, we provided no structural interventions in those economic or social relations). The main (quantitative) results of the study have been reported elsewhere; briefly, the overall trial enrolled 1988 participants; 88% of those in the intervention arm achieved viral suppression, compared to 80% in the control arm.[1]

Participants

A longitudinal qualitative component embedded within the SEARCH-Youth study followed a cohort of adolescents and young adults aged between 15 and 24 (n = 111) for 3 years, to identify the barriers, facilitators, and mechanisms that helped these participants engage, maintain, or reengage in HIV care, as described in a prior paper.[1] These youth were purposively selected from eight communities to attain adequate heterogeneity across the groupings of sex, life stage (15-17 years vs 18-24 years), and HIV care status at trial enrolment. The HIV care status categories included new to care (started treatment within the past 6 months); out of care (previously started care more than 6 months previous, but with no clinic visit during the prior 6 months); and engaged in care (having begun care more than 6 months prior and with a clinic visit within the antecedent 6 months).[1]

Data Collection and Analysis

Native speakers of the local languages DhuLuo, Runyankole, Swahili, and English comprised the gender-balanced team of trained qualitative researchers (2 female: 3 male: CA, AO; LO, FA, and TOA) who conducted audio-recorded in-depth, semi-structured interviews following guides designed by the senior author [CSC] with contributions from the interviewers and other research team members [MG and JL]. Questions explored participant experiences with HIV diagnosis and care history, ARV adherence, social support systems, HIV status disclosure, and other contextual life elements.

We attempted to interview youth three times: at baseline (BL: June-December 2019), n = 83 were interviewed; at year 1 (F1: September 2020-February 2021), n = 76 were interviewed, among whom n = 27 were new participants, replacing baseline participants who could no longer be contacted (eg, because they moved out of the community). Finally, among intervention arm participants only, at year 2 (F2: October-December 2021), n = 46 were interviewed, all of whom had either baseline or follow-up year 1 interview. Interviews were conducted in locations comfortable for the participants to ensure confidentiality, such as clinic rooms, outside at a distance from others, or in private homes. All youth provided written informed consent. After transcription and translation of the audio recordings into English, the team applied codes based on a coding framework that reflected both a priori and emergent codes. The a priori codes formed the basis for parent codes derived from theory and prior empirical research.

Table 1. Characteristics of Case Study Participants.

Participant	BL; F1; F2 VLs	VL status changes	Sex	Age	Community	Country
"Odhiambo"	288 000; 151 000; 151 000	Nonsuppressed → nonsuppressed	Male	18	H - Control	Kenya
"Natukunda"	40; 40; 1 million	Suppressed → nonsuppressed	Female	21	C - Intervention	Uganda
"Auma"	40; 106 000; 106 000	Suppressed → nonsuppressed	Female	21	H - Control	Kenya
"Anyango"	40; 967; 3440	Suppressed → nonsuppressed	Female	23	G - Intervention	Kenya
"Ochieng"	40; 40; 361	Suppressed → low-level viremia	Male	24	G - Intervention	Kenya
"Otieno"	10 300; 191; 376	Nonsuppressed → low-level viremia	Male	15	D - Intervention	Kenya
"Awuor"	257 000; 64; 40	Nonsuppressed → suppressed	Female	22	D - Intervention	Kenya
Female A	202,000; 40; 40	Nonsuppressed → suppressed	Female	23	B - Control	Kenya
Female B	24 100; 121; 65	Nonsuppressed → suppressed	Female	20	D - Intervention	Kenya
Female C	859; 40; 40	Nonsuppressed → suppressed	Female	21	D - Intervention	Kenya
Female D	62 600; 40; 40	Nonsuppressed → suppressed	Female	22	C - Intervention	Uganda

BL = Baseline; F1 = Follow-up Year 1; F2 = Follow-up Year 2; VL = Viral Load Pseudonyms reference participants who are quoted in this article; those not quoted are assigned letters. We selected participants who completed at least BL and F1, or F1 and F2 interviews, and whose VL changes met inclusion criteria for this article. All other participants began virally suppressed and remained suppressed throughout the study.

The emergent codes resulted from a full group review and discussion of an early set of transcripts; these codes reflected phenomena and concepts derived from the inductive analysis of the data, refining the parent codes by adding child codes. A six-person team [LO, AO, CA, FA, IM, and JL] then coded data using Dedoose software.[21]

Within the cohort of n = 46, one individual started and ended *without* achieving viral suppression (n = 1), several moved from viral nonsuppression to viral suppression (n = 6), and a few moved from viral suppression to becoming virally *non*suppressed (n = 3). The remaining 36 participants began and ended the study virally suppressed. The first author [JJP] created longitudinal memos based on reading the full transcripts of all participants who completed BL-F1-F2 interviews (n = 20); those who completed BL or F1 and F2 (n = 23); and, to include control participants, those who had done BL and F1 interviews and whose HIV RNA viral load (VL) was available at F2 (n = 29). We then matched viral load data to the closest interview dates, which we filtered to achieve the categories mentioned in the introduction (in the case of the three control participants from whom we have only BL and F1 interviews and an F2 VL, the VL changes in these participants coincidentally occurred between BL and F1 interviews).

Eleven cases met the criteria to be included for analysis in this article (movement towards or away from viral suppression). We selected seven for the focused presentation, as we summarized accounts of three of the four participants who moved from nonsuppression to suppression. We provide details for one of those four cases as exemplary for this group to keep the focus of our analysis on factors leading to viral nonsuppression. For this purpose, we decided to also include two participants whose viral loads were beginning to creep up but who had not technically become virally nonsuppressed. Our examination of those two cases was guided by whether we could potentially foresee "warning signs" informed by the experiences of those three participants who did become unsuppressed. All presented cases use pseudonyms (see Table 1).

Results

Nine participants who completed at least two interviews (baseline, F1, or F2) had changed viral load status. Only one participant, who happened to be in the control arm, began and ended with a nonsuppressed VL (ie, no VL status change), while another participant had begun with a suppressed VL and, while not yet nonsuppressed, had a final VL which was climbing towards nonsuppression (ie, low-level viremia). Overall, three participants were from the control arm, falling into each of the three categories of virologic control: never suppressed, suppressed to nonsuppressed, and nonsuppressed to suppressed. The remaining participants were in the intervention arm and began the study either already in care or were reengaging in care; none were new to care. Among the intervention arm participants, in addition to the categories of suppressed to nonsuppressed and nonsuppressed to suppressed, we also included two people who ended with low-level viremia, one of whom began with a nonsuppressed VL, and the previously mentioned adolescent who began with a suppressed VL.

Below, we examine the social and case histories of those participants who either never suppressed or who moved towards nonsuppression. All cases use pseudonyms. We then summarize the commonalities between the five participants whose VL status moved from nonsuppressed to suppressed. Table 2 provides a comparison of the identified factors that influenced viral load changes among our participants.

Never Virally Suppressed

Odhiambo was a perinatally infected 18 y.o. Kenyan male already in care at the start of the study who never virally

Table 2. Comparison of Social and Behavioral Factors Influencing Changes in Viral Load Status Among Case Study Participants.

	Participant viral load trajectories		
Comparisons by trajectory and contextual factors	Becoming unsuppressed	Nearing nonsuppresson	Suppression
Geographic considerations	Rural farmstead, isolation	Uncertainty about where to begin care after moving	Stable living environment; wider social network
Influence of food security	Side effects due to food insecurity	Food insecurity leads to missing doses	Food security
Provider influence and adherence	Poor service delivery	Missing pill time means entirely skipping dose for the day (unclear advice on adherence)	Supportive providers
Home situations	Interpersonal violence	Bad living situations at home	Wide social network permitting escape from violence in home
Support system characteristics	Losing immediate support system	Income precarity causing loss of support system	Wide social network and disclosure
Economic influences	Job interferences with pill time	Need for income leads to longer work hours and missing doses	Financial security; disclosure to employers or co-workers
Attitude towards diagnosis	Difficulty believing diagnosis	Coming to terms with diagnosis	Self-acceptance

Note that in the sample, only women became unsuppressed, only men neared nonsuppression, and only women became suppressed.

suppressed. As a control arm participant, he completed both BL and F1 interviews. Odhiambo never knew his parents, who both died when he was quite young. He was diagnosed as a child of around 11 years. He seems to have initially been brought to the hospital by his sister-in-law when he got sick; she left him there because the queue was too long for her to stay and wait. A doctor disclosed his HIV status to him and initiated him into care. However, his eldest sister later discouraged him from taking ART, "saying that I should not use those drugs, but later she toned down and bothered less." Being still quite young and not understanding what ART was for, he stopped taking them for "a long time." He dropped out of school in form seven (roughly equivalent to seventh grade in the United States) since he had to juggle earning money to purchase food and clothing and didn't have time for school. Overall, he was a person with few social ties.

At baseline, he was staying with his sister-in-law, working small jobs of unskilled labor to support himself. His relatives sometimes refused to support him — his sister-in-law would deny him food when his brother was not around — and would make derogatory statements towards him. He relied on the nurse in his home village to remind him of his clinic dates and ART refills, but his brothers discouraged him from visiting her home, even for refills. The situation was very unstable in terms of his ability to take ART.

> My brother has a small house which he moved from and that is where I keep the drugs. I used to [keep them at my brother's house] but removed them because my sister-in-law could sometimes leave without notice and even fail to come back, which was compromising my adherence [since I couldn't get into the house], and that is why I changed the storage. … She could even spend four days out [and] I could miss drugs. (*Odhiambo Baseline: VL: 288000*)

A year later, he had left his relatives' home and became a cowherder among the Maasai. Despite the improved living and work situation, he admitted he felt "*No one can help me.*" He was afraid to disclose to others since they might stigmatize him in various ways and he was afraid to take his ART in front of other people. Since he was staying with other people and his current employers did not know his HIV status, he would miss taking his dose. Further, reliance on the nurse in his home village to remind him of his clinic dates and ART refills, meant he did not remember these dates himself. He did not recognize how not remembering the date of a clinic appointment could be a barrier to attending appointments. As a control arm participant, we did not conduct a final-year interview with him. Nevertheless, the viral load of 151 000 that we have from this time indicates persistent issues with adherence, perhaps even complicated by the development of ARV resistance.

Beginning With Undetectable VL, Ending Nonsuppressed

Three participants, two in the intervention arm and one in the control arm, began the study virally suppressed but ended nonsuppressed. In two cases, the change was rather sudden, while one intervention arm case showed gradual progression to nonsuppression. Changes in work routines, and spending time in multiple locations, were common

factors leading to interrupted ART adherence among all three.

Natukunda, a 21 y.o. Ugandan female in the intervention arm reengaging in care was undetectable around the time of her first two interviews, but by the third year, her viral load had increased to one million. She completed all three interviews. Before enrolling, Natukunda had worked as a house help, where she had stopped taking ART despite having a newborn baby since she had not disclosed her status to the boss. She claimed that she never had time to go to health facilities in that area, and even if she had the time, she didn't know which facilities to go to. As a result, she became very ill and was sent back home, where she reenrolled in care:

> There's a woman who also gets her HIV medication from Nsiika clinic, I think we had met there on one clinic day, so she went and told my grandmother how I pick drugs up from the same clinic. So, my grandmother still insisted and asked me, "N. we are two people talking, please tell me the truth, how do you feel? I met with some woman from our community who told me about what you are suffering from, so why do you have to hide a sickness that can even kill you?!" She called a certain man related to us, and who used to work at the health facility, who helped me talk to the health workers and made an appointment with them. (*Natukunda Baseline: VL: 40*)

Having reenrolled in care, Natukunda's strength returned. She remained very mobile, cycling through various work locations—restaurants, bars, tea plantations—and supplementing her income with sex work. She typically spent about 3 months away from home looking for work, as her only support was what she brought in herself. At baseline, she was working in tea gardens and staying at her father's home with her siblings and child. She was raising the child alone because the father's family did not accept the child as theirs, and had forced her out of her marital home. The mother-in-law had also discovered her status by going through Natukunda's personal property and finding her bottle of ARTs.

A year later, Natukunda was still working in tea gardens and staying at the same place, but now she had a new boyfriend. She preferred to keep her status a secret to avoid HIV stigma. It was at this interview that she opened up about her diagnosis experience in more detail:

> I had a boyfriend who wanted to marry me, so before we could marry, he suggested that we first go for an HIV test, but my heart refused. I first went alone and got tested, I never believed from there that I was HIV positive. After some time, I went somewhere else and tested again to confirm, I was also told that I had HIV, that's when I accepted that I was indeed HIV positive. … I hated myself and started becoming careless. … It took me around 6 months [to accept things]. [What helped was that] there are girls that I was working with then, one of them tested positive, she's the one who comforted me and advised me to accept my status because I was not the only one. (*Natukunda Year 1: VL: 40*)

Despite coming to terms with her status, between the second interview and the final interview her viral load increased to one million. During that time, she started working as a barmaid and moved in with three other women from work, all in the same room. Two of the three had also been diagnosed with HIV. Importantly, Natukunda was also no longer living with her child, whom she left with her mother—yet she started ART for the child's health:

> After testing with the health providers that used to pass around the village, two female providers sat me down encouraging me to start taking the HIV medicine, though I was reluctant at the start. I even kept quiet and refused, but after delivering, the nurses told me that I would infect my child if I didn't take the medicine. Then they explained to me what to do, gave me the medicine, and I went home with it. (*Natukunda Year 2: VL: 1 million*)

In the final interview, Natukunda never directly claimed adherence but instead referenced periods when she was adherent. She knew what a viral load was, and "hated herself" when it was high. Thus, her reason for no longer taking ART remains unstated.

Auma, a 21 y.o. Kenyan female in the control arm was new to care and completed both BL and F1 IDIs. She started the study undetectable but between the first and second interviews, her viral load became nonsuppressed, continuing through the second year.

At baseline, Auma was staying at her father-in-law's place, where her brother-in-law also resided. She worked as a farmer, growing kale. Her mother-in-law helped with weeding and gardening. Her economic situation was challenging as she lacked enough customers to purchase the produce, so she planned to return to school. She learned her HIV status at an antenatal care appointment. Because her spouse was unwilling to come for couples testing, she felt she had no opportunity to disclose her own status to him safely:

> I have not disclosed to him yet because he does not want to come for couple's testing. … I do not want to disclose to him until we come to the clinic together where he is able to learn my status from the providers as I also learn his, because it might cause conflict. I would like us to know each other's status at the same time. (*Auma Baseline: VL: 40*)

Despite her low viral load, she mentioned she sometimes missed her pill time—though not the actual taking of pills. At the end of the interview, she inquired about what the effect of taking pills 30 min before or after pill

time might be. She had not asked the providers about this because she was not open with them, though she felt they treated her well.

A year later, when she had become virally nonsuppressed, the participant indicated she had disclosed to the husband through the couple's counseling, but had not disclosed to others. During this time, she had also changed her means of livelihood: she and her husband now owned a hotel with a friend, and she worked there every day. While they still lived on the father-in-law's homestead with his wife, her brothers-in-law had moved out. She also mentioned that her co-wife, someone she used to be able to confide in, did not live with them, but in another town closer to her own parents and siblings. She specifically said she did not want her parents and parents-in-law to know about her status, because "I just want it to be a secret. You may be walking around yet other people are gossiping about you." *(Auma Year 1: VL: 106000)*

Even though she claimed to still be using ARVs, her viral load indicated otherwise, and she admitted that she did not take her ART when her husband was immediately present. A lack of disclosure to parents and parents-in-law (where she was living) suggests that she also would not take medication if her in-laws were around, or when she was at work. She continued nonsuppressed into the final year of the study (VL: 106000).

Anyango, a 23 y.o. Kenyan female in the intervention arm who was already in care saw her viral load creep up during the course of the study. She completed all three interviews. At baseline, she lived with her mother and her son. She had trained as a seamstress but didn't have consistent work, so she sometimes worked at a hotel. Her sister helped provide for them. She was diagnosed when she had a boyfriend who got sick. They both tested together; he had HIV, and she was negative. Two months later, she seroconverted. She was initially resistant to starting treatment until a provider came to her home to encourage her.

> I feared taking ARVs at first but, at the same time, had no option. It was hard taking them during the first days, but I got used to it in the long run. Time was another issue here; I first started taking them before 9 pm, but this was marked by lots of forgetfulness, and I had to change to 10 pm, after which things went well. (*Anyango Baseline: VL: 40*)

After her diagnosis, she and some classmates formed a support group at school for those on HIV treatment. She claimed to be motivated by friendly providers and by having seen people die of HIV or having lived poorly after dropping out of treatment. She disclosed to a female cousin, who was also HIV-positive, and she used the phone to remind her to take her ART.

A year later, when her viral load had risen to nonsuppression, Anyango claimed this was because she was taking medication a bit later than usual, though she claimed she wasn't skipping them. However, she also gave evidence to the contrary:

> We had some visitors at home; hence, I worked until past time. When I checked my watch, it was already around 10:30 pm. Then I decided that there was no need to take the drugs at 10 pm. Therefore, I skipped it. (*Anyango Year 1: VL: 967*)

Additionally, she divided her time between three places: her maternal home, her rural matrimonial home, and the home with her husband in a trading center. She was living with her musician husband (the boyfriend from baseline), but her child still lived with her mother. She noted they sometimes lacked fare to come to the clinic.

By the final year, when her viral load was even higher than year one, Anyango had split with her husband because when he was away on music tours, he cared little for his family. Despite this fact, she was still in the hotel business with her sister-in-law. She admitted to having a new boyfriend, to whom she had disclosed, but she indicated he may not believe her, and he hadn't yet tested with her. She also disclosed this to her mother, who "just took it as normal." She was living with her two sons and sometimes confided in a half-sister. Nevertheless, she still occasionally missed doses for consecutive days, as in this instance of travel for a funeral:

> The first time, I went to some funeral at Kirindo, thinking that we would come back the same day but that did not happen. The ferry was too full to carry any more passengers. We had to board other means through land, and I reached home at around ten or eleven o'clock in the night. It was late and I then resolved not to take that day's dose. The second day was the burial day and there was a lot of movement and so I didn't get time to take the drugs. (*Anyango Year 2: VL: 3440*)

During this time, a provider began to counsel her about the relationship between viral load and medication adherence, and she saw how taking ART lowered her viral load. Thus, the elements that allowed her viral load to increase seemed to be due either to ignorance (feeling that skipping doses is better than taking a dose late), an increasingly unstable home life (three locations, absent husband) despite having support through disclosure, or both.

Ending With Low-Level Viremia

Two examples of intervention-arm participants who had low-level viremia, suggested partial adherence, viral resistance to ARVs, or both. They shared common features with the foregoing participants but also several unique elements, making them useful comparison cases.

Ochieng, was a 24 y.o. Kenyan fisherman in the intervention arm, already in care at baseline. He completed all three interviews, at the third of which his viral load had begun to approach nonsuppression. At baseline, Ochieng was living with his second wife, who was HIV negative, and his child; he had separated from his first wife, though they remained married. He said it had taken him 2 years to accept his diagnosis:

> We were tested in a group and we were to share results among us, but it seems like the provider noticed different results and decided to share out to individuals. I faced hard times that day. What disturbed me at that time was that I was going to live a miserable life without even a wife because in my mind, even approaching a lady for a relationship is something I did not see coming true. I feared that she could even propose a couple's HIV test, which could definitely be an embarrassment to me. (*Ochieng Baseline: VL: 40*)

With the support of his parents and a friend who disclosed to him, though, he came to accept his status and began treatment. He disclosed this to his second wife after one year of marriage when she found his clinic book. Through treatment, he recognized he could continue to make positive contributions to society. Around this time, Ochieng's HIV providers told him not to take ARTs if he was going to miss the usual time taking them (eg, if 3 hours late, don't bother taking the pills that day). Additionally, his wife had a PrEP provider who wanted to have a relationship with her. This caused problems between her and Ochieng, and she stopped accessing PrEP.

A year later, while still virally suppressed, he began missing his daily dose when at someone's house, if he had visitors, or when he put the pill in his pocket and the pocket got wet while fishing, melting the pill. Additionally, since it had been a bad year for fishing, he might spend all night on the lake and again miss taking his pill. Overall, though, he had changed his regimen and found it easier to remain adherent with one pill per day. The hospital to which he had transferred, however, only gave him ART; they did not take his viral load. He continued to stay with his wife and child, and had been joined by a young sister-in-law. His wife, in fact, seemed to be the primary support reminding him to take his medication:

> Now, if I have friends in the house, my wife tries very hard to ensure that I take my pills when the time reaches because she even calls me out to take my drugs. I can also take it dry while outside then I come and take water from inside. Yes, so my wife is really helping me on that—unless she is not around; that is when I can find it hard a bit, but mostly we are together. … The only thing she can talk to me about if time is passing and I have not taken my drugs is when she can quarrel with me asking, 'Are you okay? Why don't you take your drugs?' but she did not talk to me badly. (*Ochieng Year 1: VL: 40*)

By follow-up year two, when his viral load began to increase, fishing was bringing in such a reduced catch that his wife had moved back to her maternal home. The wife was still supportive, but she was no longer physically present to remind him to take his medication. In the final interview, he also mentioned the effect rude pharmacists had on his willingness to take ARTs, plus some stories he'd heard about medication:

> I have heard it severally from people that if you are on care, or rather when you are using ARVs, then you can die abruptly. The other thing is that if you are using ARVs then you can turn mad or suffer from mental health problems. Those are my major concerns. (*Ochieng Year 2: VL: 361*)

Despite these rumors, he seemed to place more trust in his providers, so that he could share information like viral load with his wife, so the extent to which these rumors affected his adherence seemed slim. Thus, his increasing viral load might be attributable to the combination of many late nights on the lake searching for fish and his wife being away and unable to remind him of his pill time.

The second participant who was approaching viral unsuppression, Otieno, was a 15 y.o. Kenyan male in the intervention arm already in care. During the study, he moved from nonsuppression to suppression and then appeared to be moving (back) to nonsuppression**.** He completed all three interviews, which provided insight into this U-curved viral load progression. During the final interview, he opened up about what had been going on before he enrolled:

> It was worse during those days. I could come for refills and then throw the whole content into the toilet and then keep the packaging bottle and would return them during my next refill. … The previous healthcare providers were so cruel. I remember I was caned because of the drug issue [ie for not taking the ARVs]. They were forcing us to take the drugs. I was around nine years old. … [chuckles] … They were using the file spring to cane us. *[Interviewer: Were you taking the drugs after being caned?]* Not at all. … I was only caught off-guard when the healthcare provider came to visit me home. My grandmother went for my bottle of drugs, and they were surprised to find them empty. Since then, they started counselling me, talking to me politely until I started taking the drugs. Then I later came to realize that it was my new habit and I had to embrace it for me to be safe and healthy. I realized that I was digging my own grave by throwing the drugs away and not taking them. (*Otieno F2 interview reflecting on situation prior to BL*)

By the time he interviewed at baseline, Otieno was living with his paternal grandmother and his father who didn't speak ("grandfather made him be like that") and was seriously ill. Additionally, he was food insecure:

with porridge not always available for taking ART, he would take them with water but then vomit them up. Additionally, he complained that the ART denied him the ability to concentrate at school. He took medicine twice a day.

A year later, in class seven, he was still living with his grandmother, but his father had passed away. He was working odd jobs (MPESA seller, technology work), which brought in enough income that his neighbors thought he'd joined the Illuminati because he suddenly had money to pay for his needs. He admitted to having four girlfriends with whom he was sexually active; he claimed to be using condoms with them. His viral load had dropped to suppressed; he knew it was below 300, and aimed to get it even lower:

> Last time when I went, I was told that it was 283 copies/ml but the latest result I have not received yet—I am going to ask him after this. But I would like to take it down within these three months because I am sure within this period if I just adhere well to my medication, and I eat very well, then it can go down. (*Otieno Year 1: VL: 191*)

By the final year, when his viral load began to rise again, he once again found himself food insecure, without money for transport, had dropped out of school, and was even arrested under unclear circumstances. The result was that his grandmother wanted to keep him home unless he was away for school or work. He mentioned that his mother was now ailing because she had stopped taking her ART and didn't seem to be adhering to her TB medication either. His provider had conceded to a two-month ART interruption, and by the interview date it seems he had resumed taking them, changing his medication routine to the mornings:

> It was around March when I failed to honour my appointment after two successive appointments in January and February. The situation wasn't favourable for me back at home. There was no food to eat. I even asked the healthcare provider, "We used to be given some flour from the facility, are they still given out?" He told me that it was no longer provided. Back at home, there was no maize to grind for flour. When I used to take the drugs without food, it was affecting me and so used to skip taking the drugs. When the healthcare provider found out, he told me just find a way of taking the drugs. (*Otieno Year 2: VL: 376*)

In this case, Otieno's viral load seems to have risen because of the ART interruption, but factors present at baseline and absent at F1 had also returned. Of those factors, food insecurity and a bad living situation were the most prominent. With his father gone and his (step-) mother ailing, he also lost support for remembering to take medication. At the midpoint of the study, he had gained experience in supporting himself, which might help mitigate the return of these earlier factors.

Beginning Nonsuppressed, Ending Virally Suppressed

Five participants moved from nonsuppression to suppression. The majority had recently experienced food or financial insecurity at baseline. Many had felt alone at their diagnosis, and a few hadn't disclosed their HIV status to their spouses. One also had bad experiences with providers sharing their information, leading them to withdraw from care for a time. Most of these participants were re-engaging in care; only one was new to care.

Shared reasons for achieving suppression included repeated, close counseling by providers, who focused first on helping participants accept their status and initiate medication, and then to giving appointment reminders and encouragement to adhere. Some participants were motivated to remain in care because of their children, and all had achieved some form of steady income or stability. Several had also set their medication time not by the clock but by taking ART after a daily meal. One participant had internalized this to such an extent that at two successive interviews, she simply said her body knew it was time and would wake her if she had fallen asleep without taking her medication. Wider disclosure to others was not a consistent finding, but contextual factors helping them adhere may have played a role: people in their communities generally knew that ART increases health and prolongs life, though self-stigma remained present in the same communities. As one participant remarked: "You hear people say, 'If I find myself HIV positive, I can't fail to start care', and then another one says, 'if I find myself HIV positive, I would kill myself'."

Awuor is a typical example of this group. Awuor was a 22 y.o. female in the Kenyan intervention arm, new to care at baseline. Her story is not entirely encouraging; by the final interview, cracks in her hard-won stability began to show. Awuor was one of at least two in this group whose viral load measures improved after changing residences to a more stable and supportive environment. At baseline, she had left her marital home on the coast; her ex-husband, who was having numerous affairs, had assaulted her with a gas cylinder and caused her baby to die in the womb. The assault and miscarriage required an operation, which an uncle paid for. Thereafter, she returned to western Kenya, where she lived with an aunt who sold alcohol. Awuor became ill at that time, with diarrhea and rashes that prevented her from working as a house help. Her aunt suggested she go to the hospital and test for HIV. Awuor was initially shocked to receive a positive diagnosis but began treatment anyway. She then disclosed this to multiple people.

A year later, her viral load had dropped to near undetectable levels. After several fights with the aunt she was staying with, Awuor had moved to another town to stay with a different aunt, where she could maintain good ART adherence; the previous aunt expected her to take alcohol while conducting business, leading to missed pill times. In the new location, Awuor worked in a hotel.

> Yes, I used to stay with my aunt at X. before I moved to Y. [Now,] I stay with another aunt of mine. … My aunt [in X] sells alcohol and I used to help her. I was also involved in that business to the extent that I could not adhere well to my medication since my pill time could pass. That is why I shared with the other aunt of mine, and then I went to her place, and currently, I am doing well. Even my viral load has been suppressed. (*Awuor Year 1: VL: 64*)

By the final interview, however, she had returned to live with the previous aunt who sold alcohol. They again had a falling out. The aunt thought that Awuor had stolen money from their alcohol business, and she did not like that the providers had come to their home for a follow-up with Awuor. She had otherwise been supportive of Awuor engaging in HIV care, apart from making Awuor work until she missed her pill time.

> She can reprimand me in front of people; she says that she does not want the providers to come to her home. This is why I feel the need to have my own business. … There were times when she would reprimand me and I would stop taking my medication for up to 2 weeks. Just a week ago, she reprimanded me in front of people and beat me up, and I decided to leave … I did not even carry my medication. (*Awuor Year 2: VL: 40*)

Awuor had a potential job opportunity through a friend to work as a house help, where she would be able to take medication in peace.

> Personally, I have to disclose my status because I cannot hide in their home while taking my medication. I have to tell them that it is my pill time because it is not something that one should keep secret. If you do not disclose to them, they might still check your bag and find them when you go to the market. You have to tell them about it. (*Awuor Year 2: VL: 40*)

Awuor also had a backup plan to start her own business so that she would not have to rely on this aunt anymore. Additionally, she had a boyfriend who was also in care. They had mutually disclosed their status, and he was supportive of where she received treatment. By the end of the second year, the participant had a wider network which formed a sort of 'safety net' for her to maintain ART adherence.

However, she admitted that if she got a position in a different place, it could challenge her to maintain care. Not only was she where she first initiated care, but she also had a negative interaction with a previous provider when she asked for a transfer letter. Because of his harshness, she thought of no longer coming to her appointments. Thus, although the participant had achieved not only viral suppression but also an undetectable VL level, fissures were beginning to appear which might compromise that status. Nevertheless, Awuor had strengthened her network of social connections and resources by disclosing to potential employers and improving her appearance enough via adherence to become a house help. Having found a boyfriend who was both on treatment himself and supportive of her further increased her social capital and support network.

Discussion

In these seven case studies illustrating social and behavioral factors influencing measured viral load changes among adolescents and young adults in rural East African communities, the stability of home life appeared to be of fundamental importance. While mobility could interrupt medication adherence, mobility in specific circumstances could also be protective: having extensive social ties permitted one participant to move away from two homes where she experienced violence. Conversely, lack of permission to leave home led others, both dependent adolescent males as well as young adult women, to miss clinic appointments or medication refills. Mobility thus had positive and negative pathways of influence on ART adherence. Key characteristics of a stable home environment—freedom from physical and psychological violence, food security, and established routines—strengthened the ability of adolescents and young adults to adhere to ART. Supportive home environments with food security enabled adolescents and young adults to mitigate the side effects of ARTs when taken on an empty stomach, showing one chain of support for medication adherence. Food security further allowed participants to set their pill time with mealtime, rather than a particular hour and minute, fostering adherence through inculcating a routine not dependent on phone or radio access. These findings confirm and extend prior research reporting that side effects hinder ART adherence.[15] Freedom from violence at home permitted participants to maintain such routines, suggesting that food security on its own is not enough (see Table 2).

Food security is intimately tied to economic stability. Work environments, like situations at home, can also influence behaviors that lead to viral suppression.[2,15] Similar to studies in Rwanda that found economic conditions affect ART adherence,[16] we found that lack of disclosure to employers or co-workers might affect both male and

female participants' ability to take ART while working, whether as cowherds or house help. Both these occupations also require living closely with employers. In this respect, we nuance other findings which indicate disclosure as such promotes care engagement; rather, it is the disclosure of treatment status that is key.[7] Expectations around job performance, like the expectation to take alcohol, also negatively affected ART adherence, particularly among our female participants. This aligns with other studies which indicate the already vulnerable position of women engaged in house help, which leaves them open to everyday violence, sexual exploitation, and close surveillance by their employers.[22–24] Job mobility, like instability at home, interfered with care continuity (including beginning care elsewhere). An overlooked factor in some studies is also unexpectedly lengthened job hours, particularly for men, that can interrupt medication habits.

Social capital was key to our participants' ability to extricate themselves from unstable or potentially violent living and work situations. Having a wider network through whom they could obtain job opportunities or find peaceful places to stay was essential to addressing some of the underlying factors which compromised medication adherence. An important concomitant factor was self-acceptance of one's status, which included starting medication. In this respect, our cohort differs from others in Kenya, who reported that self-acceptance did not impact adherence.[15] Importantly, support could be found not only by moving away from a bad situation, but also by finding partners who were also open about their status and engaged in care.

Providers played a role either by encouraging participants to engage in care, by inciting resistance to their own advice, or even by repelling participants from the clinic (pharmacy). Lack of confidentiality, a finding from other studies conducted in Rwanda, also kept at least one of our participants away from care for some time.[14] Our cohort, however, recognized that providers are individuals and several mentioned providers who continued to counsel and encourage them. In fact, a notable finding is that repeated counseling, especially when reengaging in care, is foundational to developing the habit of taking medication and adhering to appointments. Conversations to elicit misinformation from clients, as well as stories of trauma around HIV care and ART adherence, seem especially useful for providers to better support clients.

Our findings also point to the importance of providers knowing the proper guidance to give clients around not missing ART doses even if pill time has elapsed by several hours, but provider knowledge should also extend to the poor outcomes that result from permitted ART interruptions and low-level viremia.[25] Education of providers includes all allied providers, including pharmacists, as our cohort mentioned several instances of poor treatment not at the hands of immediate providers, but at the hands of associated health staff.

Our case study approach followed a small selection of our participants, which is a potential limitation even as it allowed deeper engagement with each case. We had a mostly female cohort, although we included some men. Despite this, we were unable to posit a mechanism for how gender influences viral load outcomes. Similarly, because we included three control group participants, we did not have F2 interviews for everyone. In those instances, however, viral load changes happened between baseline and F1 interview dates, so we had data suggesting potential causes of nonsuppression. Some studies have found late initiation into ART care is associated with nonretention in care.[7,18] While we had participants who initiated ART care late, we were unable to ascertain how late initiation fits into other processes already mentioned.

We were further limited to rural areas around Lake Victoria and southwest Uganda, so our findings may not be widely applicable to other settings, with perhaps less usefulness for pastoralist communities but some utility in fishing and farming communities. Finally, this was not an ethnographic study allowing us to pinpoint the mechanisms behind increasing social capital or expanding one's social network in these contexts, nor did we focus on the role of disclosure. Nevertheless, we were able to glean enough information from our interviewees to highlight contextual factors in participants' lives that hindered or facilitated ART adherence and consequent viral suppression or nonsuppression.

Our case studies linked quantitatively described variables together into an interconnected whole, uncovering distinct root causes that catalyze a chain of associated factors whose result is viral nonsuppression (or suppression). Because complaints about ART side effects are clearly linked to food insecurity, we recommend that clinics provide food-insecure youth with porridge flour to enable them to develop the habit of taking medication with a small meal. We also recommend that providers encourage participants to focus on a daily pill time associated with a meal for those who eat regularly, rather than on a specific hour-and-minute regimen, which in our cohort led participants to skip ART doses entirely. Finally, the findings suggest that national health system-level care coordination be improved, to enhance the ability of people on the move to maintain HIV care continuity whether in transit or in new destinations because of work, family life, or any other reason, and to enable providers to share information with patients about where they can access care in other locations and ease transfer of care. Beyond health system improvements, programs and policies to strengthen the stability and social capital of families and households and their economic opportunities would have positive downstream effects, improving the health of adolescents and young people with HIV.

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Author Contributions

JJP conceived and wrote the paper. CSC, TR, DVH, FM, MK, and LB edited and commented on various sections of the manuscript. CA, FA, TOA, AO, and LO gathered data, transcribed, and translated the interviews. CA, FA, TOA, AO, LO, and JJP coded the transcripts. CA, FA, TOA, AO, LO, JJP, and CSC participated in and contributed to overall data analysis and theme identification. All authors approved the final product.

Data Availability

Source data are transcribed and translated interview data, which require redaction to protect confidentiality, but are otherwise available upon request.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

The SEARCH-Youth study was approved by the Kenya Medical Research Institute (KEMRI, 3834), the Makerere University School of Medicine Research and Ethics Committee (REC REF 2019-014), the Uganda National Council of Science and Technology (UNCST, HS 2542), and the University of California San Francisco (UCSF) Committee on Human Research (18-25703). All study participants provided written informed consent to be interviewed. For our youth participants, national guidelines in Kenya and Uganda do not require parental consent for youth over the age of 12 and 14 respectively, to participate in research if they have a sexually transmitted disease, including HIV.

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