Who's slipping through the cracks? A comprehensive individual, clinical, and health system characterization of people with virologic failure on first-line HIV treatment in Uganda and South Africa

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Abstract

Objective: HIV virological failure remains a major threat to programme success in sub-Saharan Africa. While HIV drug resistance (HIVDR) and inadequate adherence are the main drivers of virological failure, the individual, clinical and health system characteristics that lead to poor outcomes are not well understood. The objective of this paper is to identify those characteristics among people failing first-line antiretroviral therapy (ART)

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Methods: We enrolled a cohort of adults in HIV care experiencing virologic failure on first-line antiretroviral therapy (ART) at five sites and used standard statistical methods to characterize them with a focus on three domains: individual/demographic, clinical, and health system, and compared each by country of enrollment.

Results: Of 840 participants, 51% were women, the median duration on ART was 3.2 years (IQR, 1.1, 6.4) and the median CD4 cell count prior to failure was $281/mm^3$ (IQR 121, 457). Half of participants (53%, 95% CI, 0.49-0.56) stated they had greater than 90% adherence and 75% (95% CI, 0.72-0.77) take their ART on time all or most of the time. Conversely, the vast majority (90%, 95% CI, 0.86-0.92) with a completed genotypic drug resistance test had any HIVDR. This population had high health system use, reporting a median of 3 (IQR, 2,6) healthcare visits and a median of 1 (IQR, 1,1) hospitalization in the preceding 6 months.

Conclusion: Patients failing first-line ART in sub-Saharan Africa generally report high rates of adherence to ART, have extremely high rates of HIVDR and utilize significant health-care resources. Health systems interventions to promptly detect and manage treatment failure will be a prerequisite to establishing control of the HIV epidemic.

Keywords

HIV drug resistance; treatment failure; virologic failure; Africa; first-line

Background

Great strides have been made towards achieving global targets for testing, treatment, and viral suppression for people living with HIV (PLWH) (1). The realization of the global "treat all" strategy has provided antiretroviral therapy (ART) to over 25 million of the estimated 38 million PLWH (1). The next stage of the pandemic will require long-term maintenance of virologic suppression particularly in sub-Saharan Africa where the largest proportion of the world's HIV burden can be found.

With increasing populations of individuals accessing ART and emphasis on virologic monitoring (2), there has been a concomitant increased identification of virologic failure among PLWH. In sub-Saharan Africa, virologic failure has reportedly ranged from 9% to 24% of PLWH on ART, whether recently initiated or after prolonged use (3–8). While the World Health Organization and most endemic countries have drafted guidelines for the management of virologic failure, poor management of virologic failure persists in many contexts (9–11). Moreover, those with persistent failure are known to suffer poor outcomes and higher rates of mortality (12).

To maintain the benefits of global public health investments in HIV treatment and care, a greater understanding of the patient and health-system determinants of virologic failure is needed. Although broadly-speaking, virologic failure is driven by a combination of HIV drug resistance (HIVDR) and sub-optimal adherence, the upstream determinants of these factors are complex and remain poorly understood. Existing characterizations of PLWH at the time of virologic failure are most frequently representative of populations in high-resource settings (13–15). These studies investigate the role of low-level viremia,

adherence, CD4 cell count, substance abuse, duration on ART, and HIV visit history, among others. Data from sub-Saharan Africa often focuses on incidence of failure, adherence rates, and viral load (VL) monitoring (3,16,17), with limited characterization of clinical and social characteristics of those failing ART (18). We examined enrollment data from a large, multi-center clinical trial in Uganda and South Africa to explore individual, clinical and health-system characteristics among individuals failing first-line ART. The goal of this analysis was to provide a robust description of each of these three domains for individuals with first-line virologic failure to help inform interventions to improve its prevention and management.

Methods

Study Design

The REVAMP study (Resistance testing versus adherence support for management of patients with virologic failure on first-line antiretroviral therapy in sub-Saharan Africa) was an open, randomized controlled trial designed to evaluate the impact and cost-effectiveness of resistance testing on rates of virologic re-suppression after virologic failure among people in HIV care in sub-Saharan Africa (NCT02787499). Full details of the study design have been described previously (19). The study hypothesized that immediate resistance testing after detection of first-line virologic failure would promote expedited and sustained virologic suppression compared to World Health Organization-based standard of care virologic monitoring guidelines. Results of the primary outcome of the clinical trial are expected in late 2021.

The study enrolled adults 18 years and older on first-line (non-nucleoside reverse transcriptase inhibitor-based) ART for at least five months with evidence of virologic failure, defined as a VL >1,000 copies/mL within the preceding three months. Participants who met a current indication for change to second-line therapy, such as two or more elevated VL results over a six-month period prior to enrollment, were excluded from the study. Consenting participants were randomized into one of two arms: 1) the WHO-based standard of care (SOC) for management of virologic failure arm, or 2) immediate resistance testing (RT) arm. The study was implemented in urban public, government-operated HIV care sites in both Uganda and South Africa. The primary outcome of interest was achievement of viral suppression (<200 copies/milliliter [mL]) 9 months after enrollment.

All data from this analysis were derived from the enrollment visit. Study nurses completed questionnaires to assess demographics, self-reported ART adherence using three scales, and health resource use. They also completed chart reviews to collect laboratory and ART regimen history. In the RT arm, we performed HIV-1 RNA genotypic resistance testing using Sanger sequencing on plasma specimens obtained from the enrollment visit. We interpreted results of genotypic resistance tests using the Stanford algorithm (20). We calculated genotypic susceptibility scores (GSS) for the ART regimen at the time of enrollment for each participant in the RT arm. Scores for each drug in the regimen were assigned with 0, 0.25, 0.5, 0.75, and 1 corresponding to high-level resistance, intermediate resistance, low-level resistance, potential low-level resistance, and susceptible, respectively (21). The sum of the scores for each drug represents the total GSS for the regimen with a possible

range of 0 to 3. We defined HIV drug resistance as any Stanford-defined resistance mutation (22).

Data Analysis

We divided descriptive data into three domains: 1) individual patient factors including sex, age, and self-reported adherence patterns (categorical average adherence, categorical frequency of taking ART on time, and likert scale of ability to take pills as directed) (23), 2) clinical factors including most recent CD4 cell count, VL, ART duration, presence and pattern of HIV drug resistance, and opportunistic infection history, and 3) health system factors including health care visitation, providers seen, and measurement of virologic failure over time. For each of these domains we used standard statistical techniques to summarize central tendencies and distributions. We compared characteristics between country by testing the hypothesis that the average characteristic was equal between country, using chi-squared testing for categorical variables, rank sum testing for non-normally distributed continuous variables, and studentized t-tests for normally distributed continuous variables. Finally, we graphically depicted time on ART, genotypic susceptibility scores, and historical number of VLs over and under 1,000 copies/mL in Uganda beginning in 2015 for which historical clinical data were available via electronic medical records (this data was not available for South Africa). Data was analyzed using Stata statistical software version 13 (24).

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author and will be published on a public data repository after completion and publication of the parent clinical trial.

Ethical Considerations

Study procedures were approved by Mbarara University of Science and Technology Research Ethics Committee, the Ugandan National Council of Science and Technology, the University of KwaZulu-Natal Biomedical Research Ethics committee, and the Partners Human Research Committee. All study participants gave written informed consent.

Results

Individual Factors

Participants were enrolled in both Uganda and South Africa at the time of virologic failure, with 420 participants enrolled in each country. The median age in Uganda was 37 (interquartile range [IQR] 30,45) and 38 (IQR, 31, 44) in South Africa (Table 1). Approximately half of participants were female (57% [238/420] in Uganda, 95% CI, 0.52 – 0.61, and 46% [192/420] in South Africa, 95% CI, 0.41 – 0.51.

More than half of respondents in both Uganda and South Africa reported greater than 90% adherence (52.7% [443/840], 95% CI, 0.49 – 0.56) in the preceding one month. Similarly, close to three out of four respondents in each country reported taking their antiretroviral therapy (ART) on time all or most of the time in the past month (74.6% [627/840], 95% CI, 0.71 – 0.77). However, there were notable differences between sites when asked about

ability to take all of the ART tablets as directed, with approximately 60% (251/420) of respondents in Uganda reporting they had excellent or very good adherence (95% CI, 0.54 – 0.64), while only 30% (127/420) of respondents in South Africa stated the same (*P*-value for difference by country <0.001, 95% CI, 0.26 – 0.435).

Clinical Factors

ART History—The median duration of ART at the time of virologic failure was 5.0 years (IQR, 2.5, 7.8) in Uganda and 1.7 years (IQR, 0.8, 4.1) in South Africa, with 50.2% (211/420) and 20.2% (85/420) of individuals in each country being on ART for five or more years (Table 2, Figure 1). Approximately 76% (639/840) of participants were on tenofovir, emtricitabine/lamivudine, efavirenz at time of virologic failure, although that percentage was higher in South Africa (94% [396/420]) than Uganda (58% [243/420], *P*-value <0.001). In Uganda an additional 42% of individuals were on zidovudine-based therapy. ART side effects were commonly reported – 15% (64/420) of respondents in Uganda and 12% (42/420) of respondents in South Africa reported at least one.

CD4 and Opportunistic Infection History—The median of the most recent CD4 cell count at time of virologic failure was 344 cells/uL (IQR, 163, 526) for Ugandan participants and 226 cells/uL (IQR, 103, 372) for South African participants (Table 2). Most had achieved some immune reconstitution, with nadir CD4 cell counts less than 200 cells/uL in over 50% (437/640) of all participants. More respondents in South Africa reported a prior opportunistic infection compared to the Ugandan participants (51% [215/420], 95% CI, 0.46 – 0.56, vs 20% [85/420], 95% CI, 0.16 – 0.24, respectively, *P*-value <0.001). Among those who previously had an opportunistic infection, the most-commonly reported infection in both countries was tuberculosis, reported in 44% (186/420) of respondents in South Africa and 13% (55/420) of respondents in Uganda (*P*-value <0.001). Apart from HIV treatment, 32% of respondents reported taking at least one other medication for a separate health issue (26% [109/420] in Uganda and 38% [159/420] in South Africa, *P*-value <0.001).

Viral Loads and HIV Drug Resistance—A VL over 1,000 copies/mL within the preceding three months was an eligibility requirement for inclusion in the study. The median VL was 10,987 copies/mL (IQR, 2,646, 58,386) and approximately 18% (148/420) had a VL over 100,000 copies/mL. HIV resistance testing was attempted for all participants in the RT arm. Sequencing was successful in 77% (322/416) with success rates of 70% [146/210] in Uganda vs 85% [176/207] in South Africa. For those with a successful sequence, 89% (287/322) had at least one Stanford-defined HIV resistance mutation, which was similar between groups (88% [128/146] in Uganda and 91% 160/176] in South Africa). For those with HIVDR, NNRTI resistance was nearly universal (89% [287/322] overall, 88% [128/146] in Uganda vs 91% [159/176] in South Africa, 95% CI, 0.85 – 0.92). NRTI resistance was seen in 80% (116/146) of participants in Uganda and 76% (133/176) in South Africa. The presence of specific mutations such as M184V and K65R was not significantly different between those in Uganda and South Africa (overall prevalence of M184V 67% [215/322], K65R [96/322] 30%). The median GSS score was .5 (IQR, 0.25, 1) with 49% (159/322) having a GSS score of 1 or higher, 23% (74/322) having a GSS score of 2 or higher, and 11% (35/322) with a score of 3 (Figure 2).

Health System Factors

Eighty-three percent of participants went to a physician's office or clinic for any type of healthcare visit in the past six months with a median of 3 healthcare visits (IQR, 2, 6, Table 3). Among those who visited a healthcare facility at least once in the past 6 months, all participants reported routine visits for HIV care, whereas 34% (234/679) reported non-HIV related medical visits and 6% (50/840) reported at least one visit for an opportunistic infection. Seven percent (57/840) of participants were admitted to hospital in the past six months.

Viral Load History in Uganda—Since the rollout of routine VL monitoring in Uganda in 2015, participants had a median of 0.9 VL measurements per year (median 0.9, IQR, 0.5, 1.1). Seventy-eight percent (327/420) of participants in Uganda were enrolled after their first VL result over 1000 copies/mL, whereas 16% (67/420) had at least one prior high VL and 6% (26/420) had more than one prior (Figure 3). HIV clinic charts in Uganda also show that close to half had two or more detectable VLs under 1,000 copies/mL in the past.

Discussion

In this analysis of individuals with virologic failure on first-line ART at clinics in Uganda and South Africa, we extremely high rates of HIVDR, that a majority of individuals reported high rates of adherence, and and evidence of significant use of the health system. Overall, these results paint a picture of a patient population that remains highly engaged in care, with virologically-mediated factors for treatment failure. These data, derived from a large cohort of over 800 individuals in ambulatory care in prototypical publicly-supported HIV care centers in sub-Saharan Africa reinforce the critical value of close monitoring for virologic failure and the need to ensure rapid and efficient transitioning to effective drug regimens for this high-risk patient population.

Our data reinforce that HIVDR is extremely common, and seen in a majority of individuals with virologic failure in this population. HIVDR testing was completed for one arm of the study and confirmed a hypothesis of high rates of HIVDR: 90% (95% CI 0.86-0.93) had Stanford-defined HIV drug resistance mutations. These levels of HIVDR are similar to other studies in the region (25,26). Prior studies also found similarly high rates of HIVDR despite optimal adherence (27,28). By contrast, participants reported generally high rates of adherence according to three different scales of self-reported adherence. Nine out of ten respondents said they had "good" to "excellent" ability to take their tablets as directed. Three quarters said they took their ART on time "most of the time" or "all of the time", and more than half said they took their treatment more than 90% of the time. Poorer self-reported adherence has been shown to be associated with viremia (29,30). While self-reported adherence is not without bias (31), the three measures together suggest generally high rates of perceived treatment adherence in a majority of participants. However, without retrospective and more objective adherence data, we cannot exclude sub-optimal prior adherence that may be under-reported or led to the high rates of HIVDR observed. Nonetheless, the phenomenon of high adherence and HIVDR is noted particularly with NNRTI therapies (32) supporting the need for greater focus on interventions which promptly

identify and switch individuals failing NNRTI-based first-line therapy. Importantly, although programmatic switches from NNRTI-based to integrase inhibitor (INSTI)-based first-line ART are underway in much of the region, most of these guidelines prohibit switching to INSTI-based therapy for those with detectable VLs on NNRTI-based therapy (33,34). Consequently, such interventions will be particularly valuable during this transition period.

Our data illuminate region-specific characteristics and challenges of virologic failure. Multiple indicators we reviewed appeared to suggest more advanced disease and greater psychosocial challenges to care in South Africa compared to Uganda. For example, individuals in South Africa had significantly lower CD4 counts, higher rates of opportunistic infections, were failing earlier in the course of treatment, had higher HIV-1 RNA viral loads, were more likely to have HIVDR, and were significantly more likely to report imperfect adherence. These data are consistent with prior work demonstrating lower treatment adherence and higher rates of virologic failure among individuals initiating ART in these two countries (35), and suggest the need for regional approaches to care. Indeed, our data would support a focus on early ART initiation and enhanced support in the period after ART initiation are most crucial in South Africa, whereas persistent, longer-term attention to virologic failure is likely required to detect and support patients failing therapy in Uganda.

These data also highlight the continued presence of advanced HIV disease despite a long duration of ART use for people failing therapy. For example, despite an overall median ART duration of 3.2 years (IQR, 1.1, 6.4), the most recent CD4 count prior to virologic failure in this study was less than 200 cells/uL in approximately one third of participants, and a large proportion had experienced an opportunistic infection at any point (half of participants in South Africa and one-fifth in Uganda). The presence of advanced disease translates into high health system use. The median number of 3 (IQR, 2,6) healthcare visits and a median of 1 (IQR, 1,1) hospitalization in the past 6 months among the 6% with an admission exceeds expected hospitalizations but is in line with 3-6 visits expected due to monthly or bimonthly HIV care visits. We would anticipate people with well-controlled HIV to only have HIV-related visits every six months, although it is clear that some participants seek treatment for other conditions as shown by a third of participants taking medication for a non-HIV issue. These data are in keeping with prior data demonstrating increased healthcare use and expense for PLWH with uncontrolled HIV (36), and further reinforce the benefits of VL monitoring and interventions for this population.

Unfortunately, delays in switching regimens after first-line ART failure in sub-Saharan Africa are well documented (37). Moreover, these delays result in poor outcomes, including reductions in CD4 cell counts, missed clinical visits, incidence of opportunistic infections, lower suppression on second-line regimens, and mortality (37–41). A multi-factorial approach to management of first-line ART failure is needed. The introduction of a regimen containing tenofovir disoproxil fumarate, lamivudine, and dolutegravir (TLD), with a higher barrier to resistance, as a first-line regimen in many countries (42,43) is an important advance. However, PLWH failing NNRTI-based ART are rarely transitioned to TLD due to concerns about the potency of dolutegravir with resistance to the nucleoside reverse transcriptase inhibitor backbone (44) despite growing documented safety of the switch (42). The implications for virologic failure on TLD are not well understood (44), particularly if

adherence is not an issue. In fact, recent data suggest that resistance to the NNRTI class of drugs also reduces the efficacy of TLD (45), but data have suggested that dolutegravir with two NRTIs to be an effective second-line treatment (46). The World Health Organization has recently updated treatment guidelines to recommend immediate switching regimens after a single elevated VL measurement (47). Consequently, ongoing vigilance for virologic monitoring for both those on NNRTI and INSTI-based therapy will remain critical, and novel interventions, such as differentiated models of care for high-risk patients (48), point-of-care VL testing (49), and long-acting injectable therapies for those with poor adherence (50) warrant further exploration.

Our study had multiple strengths, including enrollment of a large population of people enrolled in HIV care in prototypical clinics in the public sector in sub-Saharan Africa. Our dataset also includes a rich array of information ranging from healthcare utilization to HIV-1 genotypic resistance testing, enabling us to take a multifactorial approach to characterizing this patient population. Our study should also be interpreted with a number of limitations in its design and generalizability. The study population is one that was already engaged in care and participating in a clinical trial and are assumed to represent the patient population at their respective sites. This population may differ in substantial ways from PLWH who are not as consistently engaged in care. Additionally, questions related to healthcare-seeking behavior and HIV treatment adherence rely on self-report, which have limitations related to social desirability bias and comprehension (51). Finally, medical data in this analysis relied on clinic chart and electronic medical record systems, which are imperfect measures of laboratory and clinical history. This may be particularly true for CD4 count which is no longer checked regularly in these clinics, limiting our ability to assess advanced disease at the time of study participation.

In conclusion, PLWH with first-line virologic failure in sub-Saharan Africa are characterized by generally high rates of self-reported adherence and extremely high prevalence of significant HIVDR, tend to have advanced disease despite years of ART exposure, and consume high levels of health system resources. These data reinforce the public health crisis that HIVDR represents in the sub-Saharan African region, the urgent need for effective monitoring and response systems to HIV virologic failure in the region that go beyond adherence counseling, and the importance of a rapid transition to INSTI-based therapy as first-line therapy. Future research should explore interventions which aid in the prompt detection and support for regimen transition for people with virologic failure in the region and similarly explore the correlates and repercussions of virologic failure among individuals on INSTI-based therapy.

Acknowledgements

Conflicts of Interest

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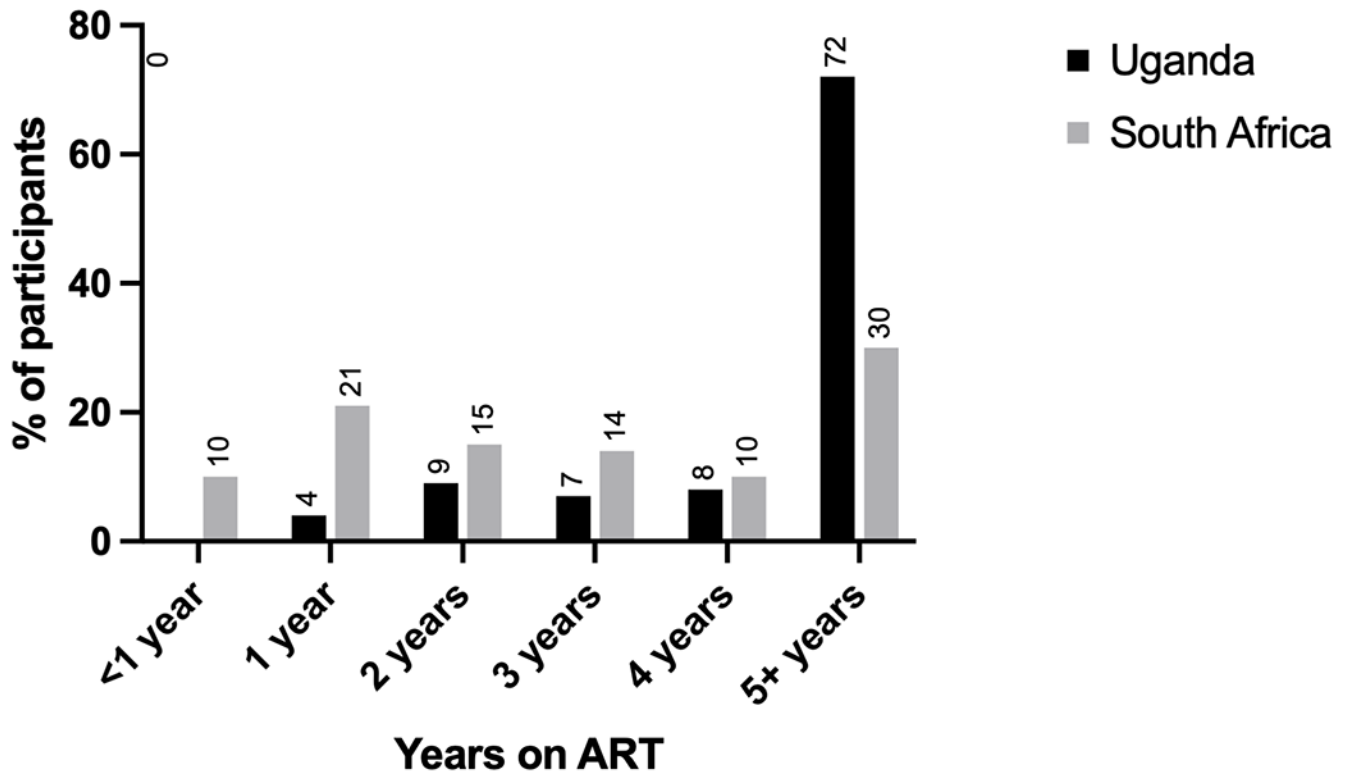
Figure 1.
Duration of antiretroviral therapy at time of detection of virologic failure in the REVAMP clinical trial

Figure 2.

Distribution of genotypic susceptibility scores (GSS), as determined by the Stanford Database, at the time of virologic failure among participants in the REVAMP clinical trial

Figure 3.
Proportion of participants with prior records of virologic failure in the medical record among participants in Uganda in the REVAMP clinical trial

Table 1.

Demographic characteristics and self-reported adherence among individuals failing first-line ART in South Africa and Uganda enrolled in the REVAMP clinical trial
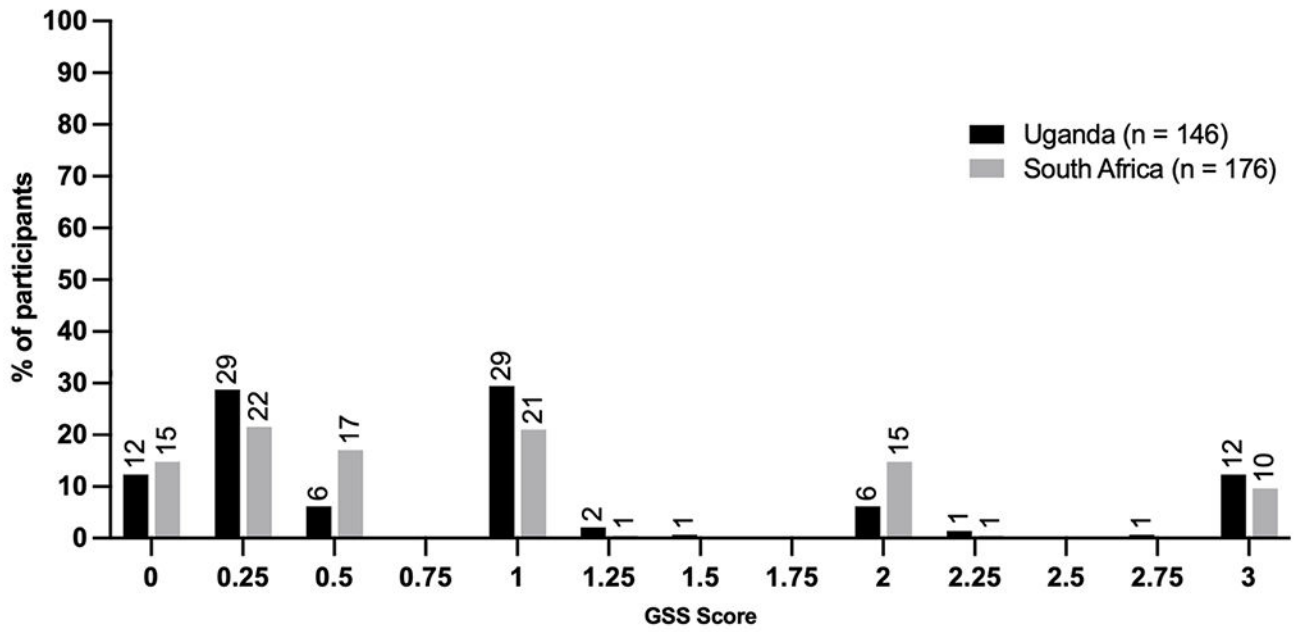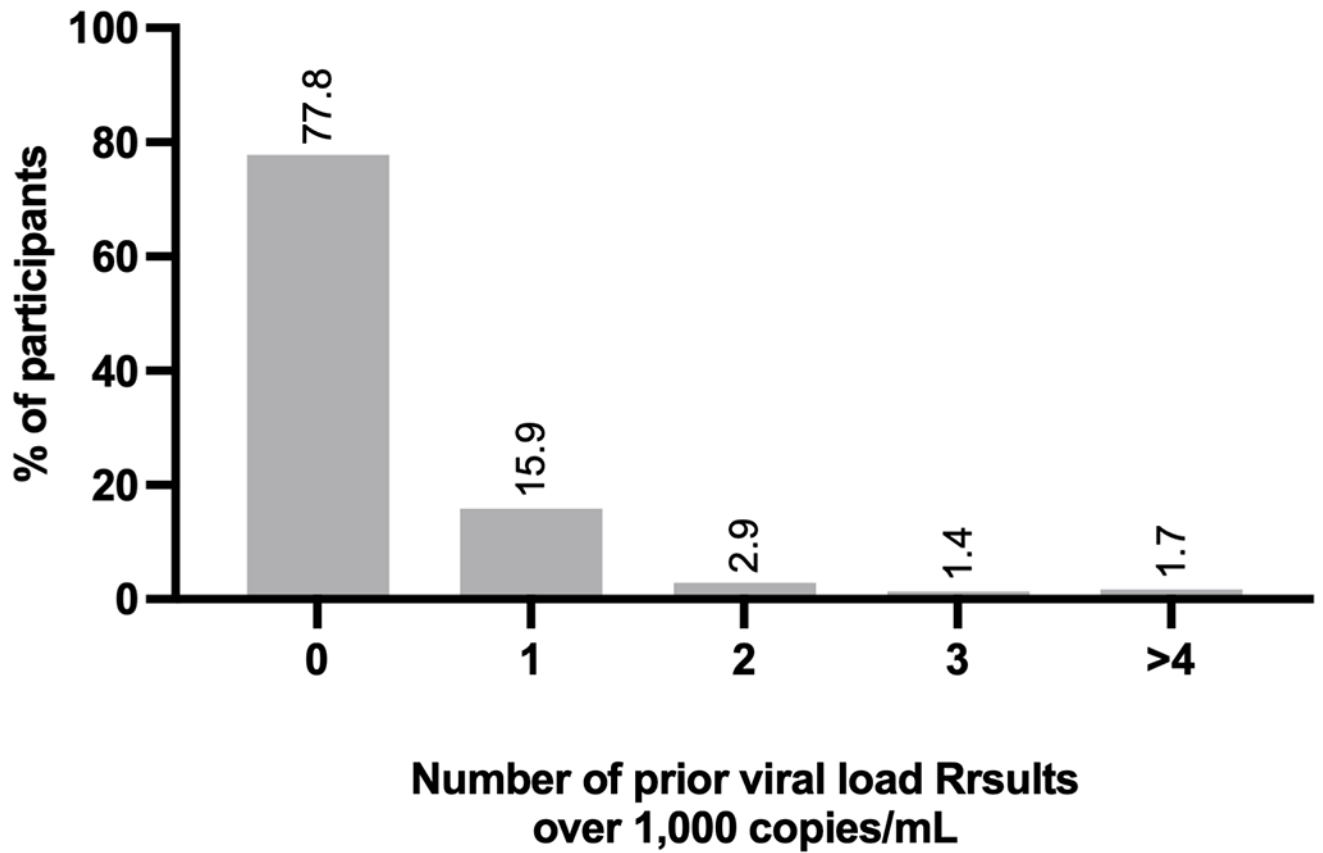
Demographic and Adherence Characteristics	Uganda (n=420)	South Africa (n=420)	*P*-value
Age			
<30 (%, n)	20.5% (86)	19.3% (81)	0.103
30-50 (%, n)	64.5% (271)	70.2% (295)	
>50 (%, n)	15.0% (63)	10.5% (44)	
Median age (IQR)	37 (30-45)	38 (31-44)	0.695
Sex			
Female (%, n)	56.7% (238)	45.7% (192)	0.001
Self-reported adherence			
Average adherence			
>90% (%, n)	50.7% (213)	54.8% (230)	0.297
50-90% (%, n)	45.0% (189)	42.9% (180)	
<50% (%, n)	4.1% (17)	2.4% (10)	
Decline to answer (%, n)	0.2% (1)	0.0% (0)	
Frequency of taking ART on time			
All or most of the time (%, n)	76.0% (319)	73.3% (308)	0.007
A good bit or some of the time (%, n)	22.1% (93)	20.5% (86)	
A little or none of the time (%, n)	1.9% (8)	6.2% (26)	
Ability to take all tablets as directed			
Excellent or very good (%, n)	59.8% (251)	30.2% (127)	<0.001
Good or fair (%, n)	35.7% (150)	64.3% (270)	
Poor or very poor (%, n)	4.1% (17)	5.5% (23)	
Decline to answer (%, n)	0.5% (2)	0.0% (0)	

Table 2.

Clinical and virologic characteristics of individuals failing first-line ART in South Africa and Uganda enrolled in the REVAMP clinical trial

Clinical and Virologic Characteristics	Uganda (n=420)	South Africa (n=420)	*P*-value
Duration on ART at baseline			
Median (IQR)	5.0 (2.5, 7.8)	1.7 (0.8, 4.1)	<0.001
5+ years (%, n)	50.2% (211)	20.2% (85)	<0.001
ART regimen at baseline			
TDF (3TC) EFV/TDF (FTC) EFV (%, n)	57.9% (243)	94.3% (396)	<0.001
AZT (3TC) EFV/AZT (3TC) NVP/AZT (FTC) NVP (%, n)	41.7% (175)	0.7% (3)	
Other (%, n)	0.5% (2)	5.0% (21)	
Any self-reported side effects to ART			
Yes (%, n)	15.2% (64)	12.4% (52)	0.306
Most recent CD4 count			
Median (IQR)	344 (163, 526)	226 (103, 372)	<0.001
<200 (%, n)	25.7% (108)	45.5% (191)	<0.001
200-500 (%, n)	35.7% (150)	40.5% (170)	
>500 (%, n)	38.6% (162)	14.1% (59)	
Lowest CD4 count on record			
<200 (%, n)	42.6% (179)	61.4% (258)	<0.001
200-500 (%, n)	32.9% (138)	32.4% (136)	
>500 (%, n)	1.7% (7)	4.8% (20)	
Missing/no prior CD4 (%, n)	22.9% (96)	1.4% (6)	
Any prior opportunistic infection			
Yes (%, n)	20.2% (85)	51.2% (215)	<0.001
Types of opportunistic infections			
Tuberculosis (%, n)	13.1% (55)	44.3% (186)	<0.001
Cryptococcal meningitis (%, n)	1.9% (8)	4.1% (17)	0.069
Pneumonia (%, n)	0.5% (2)	16.4% (69)	<0.001
Esophageal candidiasis (%, n)	1.0% (4)	4.8% (20)	0.001
Kaposi's sarcoma (%, n)	1.0% (4)	0.0% (0)	0.045
Taking medication for any other issue			
Yes (%, n)	26.0% (109)	37.9% (159)	<0.001
HIV-1 RNA viral load prior to enrollment (copies/mL)			
Median (IQR)	8,817 (2257, 48900)	13,184 (3297, 68062)	0.007
1,000-10,000 (%, n)	52.4% (220)	44.8% (188)	0.087
10,001-100,000 (%, n)	31.2% (131)	36.4% (153)	
>100,000 (%, n)	16.4% (69)	18.8% (79)	
HIV subtype			
A1 (%, n)	54.8% (80)	Presumed 0%	NA
B (%, n)	11.6% (17)	Presumed 0%	
C (%, n)	7.5% (11)	Presumed 100%	

Clinical and Virologic Characteristics	Uganda (n=420)	South Africa (n=420)	*P*-value
D (%, n)	24.7% (36)	Presumed 0%	
Other/recombinant (%, n)	1.4% (2)	Presumed 0%	
Outcome of resistance testing	N=210	N=207	
Resistance testing completed (%, n)	69.5% (146)	85.0% (176)	0.001
HIV resistance with completed test	61.2% (128)	77.3% (160)	
No HIV resistance with completed test	8.6% (18)	7.7% (16)	
VL quantity not sufficient for sequencing (%, n)	30.0% (63)	15.0% (31)	
Invalid or lost result (%, n)	0.5% (1)	0.0% (0)	
Prevalence of resistance, among those with sequencing completed			
NNRTI resistance (%, n)	87.7% (128)	90.3% (159)	0.444
NRTI resistance (%, n)	79.5% (116)	75.6% (133)	0.407
Multi-class drug resistance (n, %)	78.8% (115)	75.4% (135)	0.476
M184V (%, n)	64.4% (94)	68.8% (121)	0.408
K103N (%, n)	50.0% (73)	52.8% (93)	0.612
TAMS (%, n)	30.1% (44)	15.3% (27)	0.001
K65R (%, n)	26.7% (39)	32.4% (57)	0.268
Y181C (%, n)	19.9% (29)	17.8% (26)	0.227
K65R and M184V (%, n)	17.8% (26)	29.0% (51)	0.019

Table 3.

Healthcare utilization among individuals failing first-line ART in South Africa and Uganda enrolled in the REVAMP clinical trial

Healthcare Utilization Characteristics	Uganda (n=420)	South Africa (n=420)	*P*-value
Median number of healthcare visits in the past 6 months			
Median (IQR)	3 (2,4)	4 (0,6)	0.100
Admitted to the hospital			
Yes (%, n)	6.9% (29)	6.7% (28)	0.600
Median number of hospital admissions among those hospitalized			
Median (IQR)	1 (1,1)	1 (1,1)	0.385
Type of visit in the past 6 months			
Doctor's room (%, n)	99.3% (417)	26.9% (113)	<0.001
Clinic (%, n)	33.3% (140)	64.8% (272)	<0.001
Other including community health center and mobile health clinic (%, n)	8.6% (36)	5.5% (23)	0.082
Health care worker seen for HIV/AIDS care in past 9 months			
Nurse (%, n)	56.6% (237)	98.8% (415)	<0.001
Counselor (%, n)	25.2% (106)	93.6% (393)	<0.001
Doctor (%, n)	75.7% (318)	56.2% (236)	<0.001
Physiotherapist, lab technician, radiographer (%, n)	96.0% (403)	19.5% (82)	<0.001
Other to include community care giver, medical assistant, clinical officer, specialist physician, pharmacist (%, n)	52.4% (220)	20.0% (84)	<0.001
Reasons for visits among those who had a visit in past 6 months			
Routine HIV visit (%, n)	99.3% (414)	96.0% (265)	0.003
Non-HIV related (%, n)	35.0% (146)	31.9% (88)	0.394
HIV-related opportunistic infections (%, n)	1.9% (8)	15.2% (42)	<0.001
Median number of VL tests per year			
Median (IQR)	0.9 (0.5, 1.1)	NA	NA
Median result of VL measures over 1,000 copies/mL			
Median (IQR)	19,517 (3,510, 91,769)	NA	NA