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Early HIV viral suppression associated with subsequent 12-month treatment success among people living with HIV in South Africa

Lauren R Violette[1,2], **Katherine K Thomas**[3], **Jienchi Dorward**[4,5], **Justice Quame-Amaglo**[6], **Nigel Garrett**[4,7], **Paul K Drain**[1,2,3]

[1.] Department of Epidemiology, University of Washington, Seattle, WA, USA

[2.] Department of Medicine, University of Washington, Seattle, WA, USA

[3.] Department of Global Health, University of Washington, Seattle, WA, USA

[4.] Centre for the AIDS Program of Research in South Africa (CAPRISA), University of KwaZulu-Natal, Durban, KwaZulu-Natal, South Africa

[5.] Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, Oxfordshire, UK

[6.] Department of Psychology, University of Washington, Seattle, WA, USA

[7.] Discipline of Public Health Medicine, School of Nursing and Public Health, University of KwaZulu-Natal, Durban, KwaZulu-Natal, South Africa

Abstract

Background: We analyzed the Simplifying HIV TREAtment and Monitoring (STREAM) study to determine risk factors associated with HIV viremia and poor retention 18 months post-ART initiation.

Methods: The STREAM study was an open-label randomized controlled trial in Durban, South Africa that enrolled 390 people living with HIV presenting for their first HIV viral load approximately 6-months post-ART initiation. We used modified Poisson regression with robust standard errors to describe associations between baseline characteristics and three HIV outcomes 18-months post-ART initiation: HIV viremia (>50 copies/mL); poor retention in HIV care; and a composite outcome of poor retention in care and/or HIV viremia.

Results: Approximately 18-months post-ART initiation, 45 (11.5%) participants were no longer retained in care and 43 (11.8%) had viremia. Those with CD4 counts<200 and those with viremia 6-months post-ART initiation were significantly more likely to have viremia at 18-months post-ART initiation (aRR: 4.0, 95% CI: 2.1–7.5 and aRR: 5.5, 95% CI: 3.3–9.0, respectively). Those who did not disclose their HIV status and had viremia post-ART initiation were more likely to not be retained in care 12 months later (aRR 2.6, 95% CI: 1.1–6.1 and aRR 2.2, 95% CI 1.0–4.8). A CD4 count <200 and those with viremia were more likely to not achieve the composite outcome 18-months post-ART initiation.

Corresponding Author: Lauren R Violette, lvio@uw.edu.

Conclusions: Viremia after ART initiation was the strongest predictor of subsequent viremia and poor care retention. Understanding early indicators can help target our interventions to better engage those who may be more likely to experience persistent viremia or disengage from HIV care.

Keywords

HIV; viral load monitoring; viral failure; point-of-care; retention in care

INTRODUCTION:

The World Health Organization recommends routine viral load testing to monitor responses to antiretroviral therapy (ART) among people living with HIV (PLHIV).[1] Viral load monitoring can be critical to achieving viral suppression, which is associated with less morbidity and mortality among PLHIV, and decreased risk of onward transmission of HIV.[2,3]

In South Africa, approximately one-third, or roughly 2.4 of 7.5 million, PLHIV have not achieved viral suppression.[4] Utilizing point-of-care (POC) technologies may improve viral suppression by providing real-time feedback to providers and patients, allowing for more individually-tailored care and ART adherence counseling.[5] Moreover, POC monitoring can address barriers related to cost, receipt of viral load results, and linkage to and retention in care.[5–10] Even in the context of POC viral load monitoring, some patients still face challenges achieving viral suppression and staying retained in HIV care.

We conducted the Simplifying HIV TREAtment and Monitoring (STREAM) trial in South Africa to determine whether POC HIV viral load testing could impact HIV viremia and retention in care. In this secondary analysis, we sought to determine which risk factors were associated with HIV viremia and poor retention during the trial.

METHODS:

The STREAM study was an open-label randomized controlled trial in Durban, South Africa from February 2017 to October 2018. The research protocol and primary trial findings have been described previously.[5,11] Briefly, individuals who were 18 years or older, non-pregnant, living with HIV and on ART, and attending for their first HIV viral load test approximately six months after ART initiation were enrolled. Participants (N=390) were randomized 1:1 to receive either POC viral load monitoring with task-shifted care provided by enrolled or professional nurses or standard of care laboratory-based viral load monitoring with care provided by professional nurses. Participants were followed for 12 months, or to approximately 18 months post-ART initiation.

Sociodemographic data were collected at study enrollment and included information about participant age, sex, highest level of education, monthly income in South African Rand (ZAR), report of a stable or regular partner, and number of living children. We collected data on travel to the study clinic, including time, distance, and primary method of transportation. Health and behavioral factors collected included current smoking status, recreational drug

use in the previous six months, binary level of alcohol use (high/low) measured by the WHO Alcohol Use Disorder Identification Tool (AUDIT-C), and a binary depression screen (negative/positive) measured by the Patient Health Questionnaire-2 (PHQ-2). Finally, baseline HIV monitoring data included time since HIV diagnosis, whether the participant had disclosed their HIV status to others, self-reported four-day ART adherence, CD4 count, and HIV viral load.

We estimated adjusted relative risks (aRRs) and 95% confidence intervals using modified Poisson regression with robust standard errors to describe associations between baseline characteristics and each of three HIV outcomes 18 months post-ART initiation, adjusted for study arm. The outcomes were: HIV viremia, defined as a detectable and quantifiable viral load of >50 copies/mL measured by a laboratory-based nucleic acid test; poor retention in HIV care, defined as failure to receive ART within the 12-month visit window; and a composite outcome of having poor retention in care and/or HIV viremia. Statistical analysis was performed using SAS software, version 9.4 (SAS Institute, Cary, NC).

RESULTS:

Among the 390 people enrolled, more participants were female (60.3%, 235/390), reported a regular or stable partner (79.7%), 311/390) and had been diagnosed with HIV within one year of study enrollment (67.2%, 262/390, Table 1). Most participants were virally suppressed (<50 copies/mL) at enrollment (86.7%, 338/390), which was 6 months post-ART initiation, and median CD4 count was 468 (interquartile range [IQR]: 309–666) cells/mm^3.

Approximately 18 months post-ART initiation (12 months after enrollment), 11.5% (45/390) of participants were no longer retained in care (Table 2). Those who had not disclosed their HIV status to others and those with an HIV viral load >200 copies/mL six months post-ART initiation were more likely to not be retained-in-care (26.7%, adjusted relative risk (aRR): 2.6, 95% CI: 1.1–6.1 and 22.2%, aRR: 2.2, 95% CI: 1.0–4.8, respectively).

Of the 367 participants with a viral load result 18 months post-ART initiation, only 11.8% (43/367) participants had viremia. Those with CD4 count <200 cells/mm^3 6 months post-ART initiation were significantly more likely to have viremia 12 months later compared to those with a CD4 count >350 cells/mm^3 (30.6%, aRR: 4.0, 95% CI: 2.1–7.5). Moreover, those with viremia (>50 copies/mL) 6 months post-ART initiation were five times more likely to have viremia one year later (38.3%, aRR: 5.3, 95% CI: 3.2–8.8); this finding was consistent when the threshold for viremia at 6 months post-ART initiation was increased to 200 copies/mL (50.0%, aRR: 5.5, 95% CI: 3.3–9.0).

We found no significant associations between age, sex, education, having a primary partner, travel time to the study clinic, time since HIV diagnosis, or self-reported ART adherence and either viremia or poor retention in care.

Combining these outcomes, 21.5% (84/390) of participants were either not retained or retained but had viral load>200 copies/mL. Those with CD4 count<200 and those with viremia 6 months post-ART initiation were more likely to be either not retained or be retained but with viremia 18 months post-ART initiation.

DISCUSSION:

In this cohort of PLHIV in South Africa, those who had viremia (HIV viral load >50 copies/mL) approximately six months after ART initiation were five times more likely to have a viremia 18 months after ART initiation. Among the variables measures, achieving early viral suppression at 6 months was the strongest predictor of sustained viral suppression at 18 months. Moreover, those with a CD4 count of <200 cells/mm^3 at six months post-ART initiation compared to those with a CD4 count >350 cells/mm^3 were four times more likely to be viremic one year later. Similarly, having an HIV viral load >200 copies/mL at six months, along with not having disclosed one's HIV status was significantly associated with later disengagement in HIV care.

Our findings largely support what has been described to date in the literature. Several studies among PLHIV in sub-Saharan Africa, including one among men living in the same area as our study population, found that disclosure of HIV status to others was linked to improvements in both ART adherence and retention in care, likely through increased access to social support.[12–14] Similarly, modeling and cohort studies among PLHIV across sub-Saharan Africa indicate that higher baseline HIV viral loads and CD4 counts below 350 cells per mm^3 have been associated with the inability to achieve viral suppression over time.[15,16] Longitudinal studies among post-partum women in Malawi found that those with undetectable viral loads were both more likely to remain engaged in HIV care and be virally suppressed up to two years later.[17]

We did not observe significant differences in retention or viral suppression for the majority of demographic or behavioral characteristics. In multiple studies across Africa, male sex, younger age, and self-reported missed ART doses were associated with disengagement from HIV care and/or HIV viremia.[16,18–20] It is possible that we did not observe these differences due to a small sample size, or because the STREAM trial enrolled individuals who had already remained in care for 6 months post-initiation, which is the time period when most attrition occurs.

Our analysis has some limitations. First, participants were already clinically stable on ART for approximately six months when enrolled in the study, so findings may not be generalizable to everyone first initiating ART and are more likely specific to the time of the first viral load check at six months post ART initiation. Questionnaires at baseline were verbally administered and may have resulted in underreporting of stigmatized behaviors like drug and alcohol use, ART non-adherence, and depression, which could explain our null findings for those factors. Finally, our modest sample size and relatively low rate of participants being disengaged from care or having viremia 18 months post-ART initiation limited our statistical power to look for associations.

In conclusion, early viral suppression after ART initiation was the strongest predictor of retention in care and sustained viral suppression, which ensures positive health outcomes for PLHIV. Understanding risk factors and early indicators can help target our interventions to better engage those who may be more likely to experience persistent viremia or disengage from HIV care. Our results support the current policy focus on viral suppression to guide

progress with HIV care. Future research should further investigate how POC viral load monitoring can be used to target patients with persistent viremia for adherence counseling, especially in the period immediately following ART initiation.

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Table 1.

Baseline characteristics of participants enrolled in the STREAM trial

Baseline characteristics	**n (%)**
Median age (IQR) – years	32 [27–38]
Sex	
Female	235 (60.3%)
Male	155 (39.7%)
Highest level of education	
Less than secondary school	193 (49.5%)
Passed secondary school or more	197 (50.5%)
Regular or stable partner	
No	79 (20.3%)
Yes	311 (79.7%)
Travel time to clinic	
≤60 minutes	359 (92.1%)
>60 minutes	31 (8.0%)
Time since HIV diagnosis	
≤12 months	262 (67.2%)
>12 months	128 (32.8%)
Disclosed HIV status to others	
No	15 (3.9%)
Yes	375 (96.2%)
Self-reported ART adherence over previous 4 days	
No doses missed	316 (81.0%)
Missed 1 or more doses	74 (19.0%)
CD4 count	
<200 cells/mm^3	39 (10.0%)

Baseline characteristics	n (%)
200–350 cells/mm^3	92 (23.6%)
>350 cells/mm^3	259 (66.4%)
HIV viral load	
Undetectable (<50 copies/mL)	338 (86.7%)
Detectable (≥50 copies/mL)	52 (13.3%)
HIV viral load	
<200 copies/mL	363 (93.1%)
≥200 copies/mL	27 (6.9%)

Table 2.

Univariate analyses for viremia, not being retained in HIV care, and failure to achieve the composite outcome 18 months post-ART initiation

Baseline characteristics	Viral suppression among those with a viral load result N=367			Retention in HIV care N=390			Composite outcome: retention in care and viral suppression N=390		
	Viremia (>50 copies/mL) n (%) N=43	aRR[1] (95% CI)	p-value	Not retained n (%) N=45	aRR[1] (95% CI)	p-value	Did not achieve outcome n (%) N=84	aRR[1] (95% CI)	p-value
Median age (IQR) – years	32 (27–37)	0.99 (0.96–1.03)	0.623	30 (26–35)	0.97 (0.94–1.01)	0.131	32 (26.5–36)	0.99 (0.96–1.01)	0.268
Study arm									
POC viral load monitoring	17/189 (9.0%)	0.62 (0.35–1.10)	0.099	**15/195 (7.7%)**	**0.50 (0.28–0.90)**	**0.021**	**28/195 (14.4%)**	**0.50 (0.33–0.75)**	**<0.001**
Standard of care	26/178 (14.6%)	1.0	-	**30/195 (15.4%)**	**1.0**	-	**56/195 (28.7%)**	**1.0**	-
Sex									
Female	24/222 (10.8%)	0.83 (0.47–1.45)	0.511	29/235 (12.3%)	1.21 (0.69–2.13)	0.513	50/235 (21.3%)	0.98 (0.67–1.43)	0.918
Male	19/145 (13.1%)	1.0	-	16/155 (10.3%)	1.0	-	34/155 (21.9%)	1.0	-
Highest level of education									
Less than secondary school	18/179 (10.1%)	0.77 (0.43–1.36)	0.363	24/193 (12.4%)	1.20 (0.69–2.06)	0.521	41/193 (21.2%)	1.00 (0.69–1.45)	0.987
Passed secondary school or more	25/188 (13.3%)	1.0	-	21/197 (10.7%)	1.0	-	43/197 (21.8%)	1.0	-
Regular or stable partner									
No	8/74 (10.8%)	0.91 (0.44–1.88)	0.801	13/79 (16.5%)	1.61 (0.90–2.89)	0.112	19/79 (24.1%)	1.15 (0.75–1.79)	0.511
Yes	35/293 (12.0%)	1.0	-	32/311 (10.3%)	1.0	-	65/311 (20.9%)	1.0	-
Travel time to clinic									
≤60 minutes	39/339 (11.5%)	1.0	-	40/359 (11.1%)	1.0	-	76/359 (21.2%)	1.0	-
>60 minutes	4/28 (14.3%)	1.26 (0.48–3.31)	0.646	5/31 (16.1%)	1.46 (0.63–3.43)	0.379	8/31 (25.8%)	1.23 (0.65–2.33)	0.518
Time since HIV diagnosis									

Baseline characteristics	Viral suppression among those with a viral load result N=367			Retention in HIV care N=390			Composite outcome: retention in care and viral suppression N=390		
	Viremia (>50 copies/mL) n (%) N=43	aRR[1] (95% CI)	p-value	Not retained n (%) N=45	aRR[1] (95% CI)	p-value	Did not achieve outcome n (%) N=84	aRR[1] (95% CI)	p-value
≤12 months	28/246 (11.4%)	1.0	-	30/262 (11.5%)	1.0	-	56/262 (21.4%)	1.0	-
>12 months	15/121 (12.4%)	1.07 (0.60–1.92)	0.825	15/128 (11.7%)	1.01 (0.56–1.81)	0.979	28/128 (21.9%)	1.01 (0.68–1.50)	0.970
Disclosed HIV status to others									
No	1/13 (7.7%)	0.71 (0.10–4.86)	0.727	**4/15 (26.7%)**	**2.63 (1.14–6.05)**	**0.023**	4/15 (26.7%)	1.34 (0.60–3.01)	0.472
Yes	42/354 (11.9%)	1.0	-	**41/375 (10.9%)**	**1.0**	-	80/375 (21.3%)	1.0	-
Self-reported ART adherence over previous 4 days									
No doses missed	33/299 (11.0%)	1.0	-	34/316 (10.8%)	1.0	-	65/316 (20.6%)	1.0	-
Missed 1 or more doses	10/68 (14.7%)	1.39 (0.72–2.68)	0.320	11/74 (14.9%)	1.48 (0.79–2.77)	0.218	19/74 (25.7%)	1.34 (0.86–2.08)	0.193
CD4 count									
<200 cells/mm^3	**11/36 (30.6%)**	**4.01 (2.14–7.52)**	**<0.001**	4/39 (10.3%)	0.88 (0.33–2.32)	0.791	**15/39 (38.5%)**	**2.10 (1.36–3.26)**	**<0.001**
200–350 cells/mm^3	12/89 (13.5%)	1.74 (0.89–3.40)	0.105	8/92 (8.7%)	0.74 (0.35–1.54)	0.415	17/92 (18.5%)	1.00 (0.61–1.63)	0.998
>350 cells/mm^3	20/242 (8.3%)	1.0	-	33/259 (12.7%)	1.0	-	52/259 (20.1%)	1.0	-
HIV viral load									
Undetectable (<50 copies/mL)	**25/320 (7.8%)**	**1.0**	-	36/338 (10.7%)	1.0	-	**59/338 (17.5%)**	**1.0**	-
Detectable (≥50 copies/mL)	**18/47 (38.3%)**	**5.28 (3.17–8.80)**	**<0.001**	9/52 (17.3%)	1.82 (0.94–3.55)	0.077	**25/52 (48.1%)**	**3.12 (2.21–4.40)**	**<0.001**
HIV viral load									
<200 copies/mL	**32/345 (9.3%)**	**1.0**	-	**39/363 (10.7%)**	**1.0**	-	**67/363 (18.5%)**	**1.0**	-
≥200 copies/mL	**11/22 (50.0%)**	**5.48 (3.34–9.00)**	**<0.001**	**6/27 (22.2%)**	**2.22 (1.02–4.84)**	**0.045**	**17/27 (63.0%)**	**3.67 (2.64–5.10)**	**<0.001**

1. Adjusted for study arm