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Factors associated with viral load non-suppression in people living with HIV in Nigeria: cross-sectional analysis from 2001 to 2021

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Abstract

Objectives Identify demographic and clinical factors associated with a non-suppressed viral load of patients on antiretroviral therapy in Nigeria.

Design Cross-sectional study.

Setting Sixteen USAID supported states in Nigeria.

Participants 517,012 people living with HIV (PLHIV) on antiretroviral therapy (ART).

Primary outcome measures Viral load (VL) non-suppression (defined as having a VL of at least 1,000 HIV ribonucleic acid copies per mL of plasma). Chi-square testing and multivariable logistic regression were conducted on routinely collected ART program data.

Results Sixty-six percent of the study population were females. The largest age groups were 35–44 and 25–34, accounting for 32% and 31%, respectively. The greatest adjusted odds for a non-suppressed VL were associated with shorter duration MMD prescriptions of 1–2 months (adjusted odds ratio [AOR]=14.05) and 3 months (AOR=3.13). Males had 8% greater odds (AOR=1.08) of being non-suppressed. The age groups below the 45–59 age group (AOR=0.84) had higher odds of having a non-suppressed VL, with the highest odds in the 0–14 age group (AOR=1.87). Clients enrolled at tertiary and secondary level facilities had the greatest odds of having a non-suppressed VL. A shorter time on ART until the last VL (1–3 years [AOR=1.14]) was associated with a higher risk of a non-suppressed VL. Clients in the North-Central (AOR=1.83) and North-East (AOR=1.49) zones had the greatest odds of viral non-suppression.

Conclusions Enabling the provision of 3+ months of MMD to PLHIV and targeting younger age groups, tertiary and secondary health facilities, small and medium facilities, and the North-Central and North-East zones for interventions could lead to improvements in VL suppression in Nigeria. The independent factors associated with a non-suppressed VL can guide improvements in ART program development and VL suppression of PLHIV in Nigeria.

Strengths and limitations of the study

- The study uses data from over 500,000 PLHIV enrolled on ART across all geopolitical Zones in Nigeria
- The data used is routinely collected by clinics.
- Variables such as education level and marital status/cohabiting were not available.

Introduction

In 2020, 37.7 million people were living with HIV (PLHIV) globally; currently, 27.5 million (73%) have access to antiretroviral therapy (ART) [1]. In 2020, 66% of PLHIV were virally suppressed [1]. Nigeria, a country with one of the highest global HIV infection rates, was reported to have 78% of PLHIV on ART virally suppressed, against a target of 95% [1,2]. The Nigeria National Guidelines for HIV Prevention, Treatment, and Care define virologic suppression as having a viral load (VL) below 1,000 HIV ribonucleic acid copies per mL of plasma [3] (viral load non-suppression is defined as having a VL of at least 1,000 HIV ribonucleic acid copies per mL of plasma). Given that an undetectable VL makes HIV untransmissible, suppressing the VL of 95% of PLHIV on ART is key to achieving epidemic control [4,5].

Globally, including in some Nigerian states, factors that were found to be predictors of viral suppression were age, sex, duration on ART [6–9], current ART regimen [10], and adherence to medications [11]. This study explored whether similar associations alongside other factors such as geo-political zones and facility level existed in Nigeria using data over a period of 20 years from 16 States that were not necessarily under investigation before, contributing to the body of knowledge and allowing better targeted interventions to improve HIV programs, the VL of clients, and epidemic control in the country.

The objective of this study was to determine which factors were associated with a non-suppressed VL in Nigeria using a large cross-sectional database of clients who received ART. We explored several variables—sex, age group, duration on ART, multi-month dispensing (MMD) defined as dispensing of 1-2 months, 3 months, or 3+ months of ART treatment, facility level, and geopolitical zone—to identify which factors were associated with viral non-suppression. The objective of this analysis is to guide HIV programs to target population groups at the highest risk.

Methods

Study design, setting, and population

The study was a cross-sectional analysis of clients who were enrolled on ART at 580 facilities across 16 States in Nigeria that were supported by the United States Agency for International Development (USAID). The data set covered a period of 20 years, with the first ART initiation date recorded on January 1, 2001, and the most recent ART pickup date of March 26, 2021. The study was carried out to investigate the clinical and demographic factors associated with a non-suppressed VL among more than 500,000 HIV clients who had a VL test during the period.

Data Source and Management

The data were provided by the USAID-supported implementing partners (IPs) through their quarterly data submission using the retention and audit determination tool (RADET). Each IP submission was then combined into a single data set that was used for this study.

The data obtained were collected by the Federal Ministry of Health (FMOH) and IPs using standardized national HIV data collection tools that recorded demographic, clinical, and treatment information about the client at each visit in the electronic medical records (EMR) system.

The data set received contained 867,981 non-longitudinal, cross-sectional client records. Due to missing unique client identifiers for 158,898 clients, a unique identifier was created for data deduplication using the date of birth, sex, database-provided unique identifier, and client hospital number. For clarification, unique identifiers are not provided at all facilities, in such cases a client hospital number is captured instead. Data cleaning involved removing duplicate unique identifiers (n=17,267), and missing entries for MMD (n=1) and ART regimen line (n=148). In addition, data which may have contained a typo, like records with an ART start date occurring before the date of birth or after the date of last drug pickup, or a VL result date occurring earlier than the ART start date, were removed from the sample (n=3,030). Clients with a date of birth earlier than 1940 (n=961) or an ART start date earlier than 1990 (n=2) were also excluded from the analysis. An additional 2,314 clients with a VL test result date earlier than the ART start date were likewise removed. Missing values for current ART status (n=56) and sex (n=1) were excluded (Figure 1).

Of the 844,201 complete client records retained, 517,012 (61.2%) had a VL test (only the last one) on record, whereas the remaining 327,189 (38.8%) had no documented VL test (Figure 1). Clients without documented VL test results were removed from the study population before the logistic regression analysis was conducted.

Figure 1. Data cleaning process, excluded data, and study population subset analysed.

Variables explored as predictors of a non-suppressed viral load

The "age at last VL test" variable was generated by calculating the time difference (in years) between the date of received current VL and the date of birth of the client. The age at last VL test was reclassified into six age groups: 0–14, 15–24, 25–34, 35–44, 45–59, and 60+ years.

Similarly, the "duration on ART to last VL test" variable was created by calculating the time difference (in months) between the date of received current VL and the ART start date. The duration on ART was reclassified as <1 year, 2–3 years, and 3+ years, and labelled as "time to last VL."

The "facility size" variable was calculated by determining the number of clients ever receiving care at the facility, then assigning the facility size group as small [0,25) percentiles, medium [25,75) percentiles, or large [75,100] percentiles.

The "facility level" variable was created by classifying the facility name provided in the data set to the nationally recognized facility levels using the Nigeria health facility registry (HFR) [12]. The classification resulted in three levels of facilities: primary (operate at Local Government level), secondary (operate at State level), and tertiary (operate at Federal Government level) [13]. Similarly, the "facility ownership" variable was created by grouping the facilities in their respective ownership type (public or private) according to their classification in the Nigeria HFR system [12].

The "geopolitical zone" variable was created by grouping the 16 USAID-supported States into their nationally recognized geopolitical zones. This resulted in five geopolitical zone groupings: North-Central (Kwara and Niger States), North-East (Adamawa, Bauchi, Borno, and Yobe States),

North-West (Jigawa, Kano, Kebbi, Sokoto, and Zamfara States), South-South (Akwa Ibom, Bayelsa, Cross River, and Edo States), and South-West (Lagos).

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Statistical analysis

For the population with a last VL test on record, the Pearson's chi-square test was used to examine the association of each variable with a non-suppressed VL at a client's last VL test date. Unadjusted and adjusted logistic regression models were run to explore the association of variables with a non-suppressed VL. Current ART status was excluded as a factor from the regression modelling because at the time of the VL test, all clients were active, even though they may now have a different status (interruption in treatment (IIT), deceased, or stopped treatment). Similarly, the regimen line was excluded from the regression analysis because other regimen lines, aside from the first-line regimen, are prescribed in the case of a non-suppressed VL. The regimen line was therefore dependent on the VL outcome investigated and it could not be used as an independent variable associated with VL non-suppression. The variables included in the models were sex, age group, geopolitical zone, facility level, facility size, MMD of antiretrovirals (ARVs), and time to last VL test. The group accounting for the most clients in each of the independent variables analysed was set as the reference group for the respective variable. A two-tailed P value of $P<0.000001$ was used to define statistical significance [14]. Model selection was done using backward elimination where the Akaike's information criterion (AIC) was used to evaluate variable inclusion in the final model. Multicollinearity was tested using the generalized variance inflation factor (GVIF) for the set of variables used in the logistic regression model, and none of the variables exhibited multicollinearity. All data were analysed using R software for Statistical Computing v4.0. [15].

Results

Of the 517,012 clients included in the analysis, 476,218 (92%) were virologically suppressed whereas the remaining 8% were virologically non-suppressed (Table 1). Sixty-six percent of the

clients were female, with 8% of both sexes virologically non-suppressed. Clients ages 25–34 and 35–44 were the largest age groups, accounting for 31% and 32% of the total number of clients in the analysis, respectively. Clients in the 0–14 age group had the smallest proportion who were virally suppressed.

The ART status of 87% of the clients was recorded as active on treatment, with the remaining 13% being dead (2%), had transferred out to another facility (3%), or had interrupted treatment (8%) (Table 1). Most clients (95%) were on the adult first-line ART regimen, with 93% of them being virally suppressed. Both the adult second-line and paediatric first-line ART regimens had 2% of the clients, with 80% and 78% of clients on these regimens being virally suppressed, respectively. Most clients were receiving ART at a secondary health facility (54%), followed by primary health facilities (33%) (Table 1). Clients receiving treatment at a tertiary or secondary health facility were more likely to be virally non-suppressed compared with clients receiving ART at a primary health facility.

Ninety-four percent of the clients received ARVs from a publicly owned facility, with 92% of them being virally suppressed (Table 1). Only 6% of the clients were receiving treatment from a privately owned facility, with 91% of these clients virally suppressed.

Table 1. Characteristics of the 517,012 clients with a viral load test on record at Nigerian facilities between 2001 and 2021.

Factors	Non-suppressed (%)	Suppressed (%)	Total (%)	p-value
Sex				
Female	26,558 (8)	312,401 (92)	338,959 (66)	0.042873
Male	14,236 (8)	163,817 (92)	178,053 (34)	
Age group				
35–44	12,045 (7)	152,752 (93)	164,797 (32)	<0.000001
25–34	12,157 (8)	149,699 (92)	161,856 (31)	
45–59	7,006 (7)	98,026 (93)	105,032 (20)	
15–24	4,535 (9)	44,231 (91)	48,766 (9)	
60+	1,278 (7)	17,985 (93)	19,263 (4)	

0–14	3,773 (22)	13,525 (78)	17,298 (3)	
Current ART status				
Active	22,786 (5)	428,619 (95)	451,405 (87)	<0.000001
IIT	10,370 (26)	29,132 (74)	39,502 (8)	
Transferred out	3,834 (24)	12,014 (76)	15,848 (3)	
Dead	3,104 (38)	5,024 (62)	8,128 (2)	
Stopped	700 (33)	1,429 (67)	2,129 (0)	
Current regimen line				
Adult 1st line	35,558 (7)	456,863 (93)	492,421 (95)	<0.000001
Pediatric 1st line	2,706 (22)	9,695 (78)	12,401 (2)	
Adult 2nd line	2,389 (20)	9,438 (80)	11,827 (2)	
Pediatric 2nd line	123 (40)	182 (60)	305 (0)	
Adult 3rd line	10 (29)	24 (71)	34 (0)	
Salvage	8 (33)	16 (67)	24 (0)	
Facility level				
Secondary	25,233 (9)	254,063 (91)	279,296 (54)	<0.000001
Primary	8,067 (5)	163,076 (95)	171,143 (33)	
Tertiary	7,494 (11)	59,079 (89)	66,573 (13)	
Facility Ownership				
Public	38,124 (8)	448,514 (92)	486,638 (94)	<0.000001
Private	2,670 (9)	27,704 (91)	30,374 (6)	
Facility size				
Large	32,055 (7)	400,824 (93)	432,879 (84)	<0.000001
Medium	8,337 (11)	70,774 (89)	79,111 (15)	
Small	402 (8)	4,620 (92)	5,022 (1)	
MMD				
3+	10,419 (3)	308,307 (97)	318,726 (62)	<0.000001
3	15,094 (10)	135,703 (90)	150,797 (29)	
1–2	15,281 (32)	32,208 (68)	47,489 (9)	
Time to last VL				
3+ years	18,994 (9)	200,513 (91)	219,507 (42)	<0.000001

<1 year	11,031 (6)	166,782 (94)	177,813 (34)	
1–3 year	10,769 (9)	108,923 (91)	119,692 (23)	
Zone				
South-South	16,985 (6)	264,688 (94)	281,673 (54)	<0.000001
North-East	8,137 (10)	71,155 (90)	79,292 (15)	
North-West	6,065 (10)	57,112 (90)	63,177 (12)	
South-West	4,981 (9)	49,052 (91)	54,033 (10)	
North-Central	4,626 (12)	34,211 (88)	38,837 (8)	

A greater proportion of ART clients received treatment from a large volume facility (84%), with 93% of these clients being virally suppressed (Table 1). ART clients at the medium volume facilities comprised 15% of the total clients, with 89% of them being virally suppressed.

MMD of more than three months (62%) and three months (29%) of ARVs were the majority (Table 1). These two groups had the highest proportions of virally suppressed clients on treatment, at 97% and 90%, respectively.

Forty-two percent of the clients had been on ART for more than three years and 34% had been on treatment for less than one year (Table 1). Clients who were on ART for less than one year had a higher proportion of being virally suppressed (94%) than those who had been on ART for one to three years or more than three years (both 91%). The South-South zone had the largest proportion of clients (54%) in the sample and had the highest proportion of virally suppressed clients (94%) (Table 1).

A multivariable logistic regression model was run using the Sex, age group, facility level, facility size, time to last VL, MMD and Zone. All variables were significant, except for "Facility Ownership" (p-value =0.64925). The AIC for this model did not change when ownership was included (AIC= 243,815), therefore it was removed from the model. Backward elimination of variables produced the lowest AIC—243,815 with all variables combined—that is, sex, time to last VL, facility level, facility size, age group, geopolitical zone, and MMD. The logistic regression model assessing the relationship between predictor variables and a non-suppressed VL among ART clients is summarized in Table 2. All factors used in the adjusted logistic regression model

were statistically significant, with a p-value of <0.000001, except for the <1 year time to last VL, which had a p-value of 0.18893, and small facility size, with a p-value of 0.00029.

Males (adjusted odds ratio [AOR]=1.08, 95% CI: 1.05–1.10, P<0.000001) were found to have 8% higher odds of being virally non-suppressed than females (Table 2). Univariable and multivariable logistic regression indicated with statistical significance that young people ages 0–24 were associated with higher odds of viral non-suppression compared with the 35–44 age group. Younger clients ages 0–14 years had the highest adjusted odds (AOR = 1.87, 95% CI: 1.79–1.95, P<0.000001).

Table 2. Factors associated with a non-suppressed viral load presented as unadjusted odds ratio and adjusted odds ratio derived using logistic regression.

	Unadjusted OR		Adjusted OR	
Factors	OR [95% CI]	p-value	AOR [95% CI]	p-value
Sex				
Female	1 [ref]		1 [ref]	
Male	1.02 [1.00–1.04]	0.042321	1.08 [1.05–1.1]	<0.000001
Age group				
35–44	1 [ref]		1 [ref]	
0–14	3.54 [3.40–3.68]	<0.000001	1.87 [1.79–1.95]	<0.000001
15–24	1.30 [1.25–1.35]	<0.000001	1.4 [1.35–1.45]	<0.000001
25–34	1.03 [1.00–1.06]	0.027536	1.1 [1.07–1.13]	<0.000001
45–59	0.91 [0.88–0.93]	<0.000001	0.83 [0.81–0.86]	<0.000001
60+	0.90 [0.85–0.96]	0.000633	0.78 [0.73–0.83]	<0.000001
Facility level				
Secondary	1 [ref]		1 [ref]	
Primary	0.5 [0.49–0.51]	<0.000001	0.74 [0.72–0.76]	<0.000001
Tertiary	1.28 [1.24–1.31]	<0.000001	1.16 [1.12–1.19]	<0.000001
Facility size				
Large	1 [ref]		1 [ref]	
Medium	1.47 [1.44–1.51]	<0.000001	1.42 [1.38–1.46]	<0.000001

Small	1.09 [0.98–1.21]	0.106851	1.22 [1.1–1.36]	0.00029
Time to last VL				
3+ years	1 [ref]		1 [ref]	
<1 year	0.70 [0.68–0.72]	<0.000001	0.98 [0.95–1.01]	0.18893
1–3 years	1.04 [1.02–1.07]	0.000709	1.14 [1.11–1.18]	<0.000001
MMD				
3+ months	1 [ref]		1 [ref]	
1–2 months	14.04 [13.66–14.43]	<0.000001	14.05 [13.64–14.48]	<0.000001
3 months	3.29 [3.21–3.38]	<0.000001	3.13 [3.05–3.22]	<0.000001
Zone				
South-South	1 [ref]		1 [ref]	
North-Central	2.11 [2.04–2.18]	<0.000001	1.83 [1.76–1.9]	<0.000001
North-East	1.78 [1.73–1.83]	<0.000001	1.49 [1.45–1.54]	<0.000001
North-West	1.65 [1.60–1.71]	<0.000001	0.89 [0.86–0.93]	<0.000001
South-West	1.58 [1.53–1.64]	<0.000001	0.74 [0.72–0.77]	<0.000001

Compared with the South-South zone, clients in the North-Central (AOR = 1.83, 95% CI: 1.76–1.9) and North-East (AOR =1.49, 95% CI: 1.45–1.54) zones had greater odds of VL non-suppression (P<0.000001) (Table 2). Clients in the South-West zone had the lowest odds for VL non-suppression (AOR = 0.74, 95% CI: 0.72–0.77).

Clients receiving ARVs at the tertiary health facilities were 16% more likely to be virally non-suppressed (AOR=1.16, 95% CI: 1.12 –1.19) whereas primary health facilities were the most protected (AOR = 0.74, 95% CI: 0.72–0.76) (Table 2). Moreover, small (AOR=1.22, 95% CI: 1.1–1.36, P= 0.00029) and medium (AOR=1.42, 95% CI: 1.38–1.46, P<0.000001) facilities were found to have the highest odds for viral non-suppression compared with large facilities.

The MMD was significantly associated with viral non-suppression. ART clients on 1–2 MMD had the highest odds of viral non-suppression rates (AOR= 14.05, 95% CI: 13.64–14.48) in the adjusted logistic regression model.

Compared with clients who had been on ART for more than three years, those who had been on treatment between 1 and 3 years were 14% more likely to be virally non-suppressed (AOR=1.14, 95% CI: 1.11–1.18), whereas clients on ART for less than one year were found to be 2% less likely to be virally non-suppressed (AOR=0.98, 95% CI: 0.98–1.01).

Discussion

Our study found that clients in younger age groups and those on MMD of 1-2 months had the highest association with VL non-suppression. We also found that males, clients who received treatment at tertiary health facilities, at small or medium facilities, or in the North-Central or North-East zones were associated with a higher risk of VL non-suppression. Other studies have found similar results for the risk of viral non-suppression in younger age groups in Cambodia, Uganda, and South Carolina (USA) [6,8,16], and among males [17–19].

The increased odds of viral non-suppression among ART clients who received treatment at tertiary health facilities were unlike the higher odds reported for primary health facilities in Ethiopia [20]. Small and medium facilities were identified as having greater odds for viral non-suppression; this was consistent with findings that clients were more likely to miss consecutive visits at lower volume facilities [21].

ART clients who had their last VL test conducted within less than 1 year on treatment were less likely to be virally non-suppressed compared with clients who had their VL tested conducted within 1 to 3 years of being on ART. Our finding was consistent with the Center for Disease Control and Prevention's finding that PLHIV on ART could be virally suppressed within six months of initiation, provided that they adhered to their medication [22]. Moreover, a greater likelihood of viral suppression was found among PLHIV who were initiated on treatment for less than one year compared with those on ART for more than one year [23]. However, contrary to this, a shorter time on ART was identified as a factor associated with a non-suppressed VL in South Africa [24]. The contradictory findings in the literature could speak to the specific adherence patterns of the populations investigated and models that may be specific to the study settings. Also, elucidating that clients more engaged in care can have more opportunities for non-suppressed viral

load test results, though this does not necessarily mean that this population is more likely to be non-suppressed.

Short duration MMD of 1 to 3 months was identified as having the highest odds for a non-suppressed VL in both the univariable and multivariable models. This is interesting because shorter MMD is also associated with non-adherence [25]. Shorter MMD is initially prescribed to new clients and longer MMD is prescribed to virally stable clients to reduce the number of clinic visits [26]. Because of non-adherence, clients may become virally non-suppressed and be placed on shorter duration treatment, requiring more frequent check-ups and clinical support to become stable. It is apparent that MMD is dependent on the VL status of clients; however, that is not necessarily the case for new clients. The logistic regression model built here suggested that a shorter MMD was associated with a non-suppressed VL. In this case, the MMD was a confounding factor that possibly represented some degree of IIT because it was not the actual length of the prescription that can affect the VL, rather its misadministration. We found value in retaining the confounding factor in the analysis because we cannot use a factor like IIT instead, because, at the time of the VL test, the client was active on treatment. In the absence of longitudinal data that can identify IIT as a precedent to non-suppressed VL, we chose to include MMD in the analysis as a proxy indicator. In doing so, the recommendation of enrolling patients on 3+ MMD to support viral suppression is still valid, even if the improvement in VL suppression is caused by correct adherence to treatment, not by the actual length of MMD.

A possible explanation for the North-Central zone having the highest odds of viral non-suppression could be linked to health-seeking behaviour such as non-use of the service, poor adherence to treatment, and possibly religious affiliation (for example Islamic religion predominant in norther Nigeria) where in certain circumstances women require permission to leave the premises of a household which can reduce access to healthcare [27,28].

One of the limitations of our study was the inaccessibility of the longitudinal data set, leaving us unable to conduct a longitudinal study to explore the factors affecting viral non-suppression over time. We were therefore restricted to conducting a cross-sectional study. The inclusion of MMD as an independent variable is a limitation of the study because a shorter MMD can be applied based on a non-suppressed VL, in which case MMD would be a proxy for IIT.

It is likely that some of the nearly 40% of client records (eliminated from analysis) without a VL test on record are a consequence of poor adherence to treatment which could lead to viral load non-suppression that is not tested/recorded. Investigating the factors that are associated with an untested viral load could provide useful insight. At the same time, longitudinal studies into both viral load non-testing and viral load non-suppression may ultimately be of greatest use. Additional variables relating to the capacity of clinical facilities to conduct testing would reveal whether the lack of viral load testing is also affected by a low capacity.

Other unavailable variables that could be explored in future studies to identify their association with viral suppression are tuberculosis status, adherence level, ART drug regimen, marital status, and education level. The absence of VL suppression data for adolescents and recently initiated clients may have also had an impact on the study, suggesting that these findings may not necessarily apply to those sub population groups.

Conclusions

Enabling the provision of 3+ months of MMD to PLHIV and targeting younger age groups (below 35), tertiary health facility, small and medium facilities, and the North-Central and North-East geopolitical zones for interventions could lead to improvements in VL suppression in Nigeria. The independent factors associated here with a non-suppressed VL can guide the improvement of ART program development and VL suppression of PLHIV in Nigeria.

Competing interests: None declared.

Author contributions: Study Design: ST, TC, JA, FA, CC, CWK, PP; Data collection: JA, DSD, EO; Data analysis: ST, TC, JA; Funding acquisition: DSD, FA, PP; Data Interpretation: All authors; Writing – original draft: ST, TC, JA; Writing – review and editing: All authors. All authors read and approved the final manuscript.

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Data Statement: The data that support the findings of this study are owned by the Government of Nigeria and were used under license for the current study. Access to these data is subject to restrictions owing to privacy and ethics policies set by the Government of Nigeria so are not publicly available. Requests to access these data should be directed to Dauda.Sulaiman@thepalladiumgroup.com.

List of abbreviations

AIC:	Akaike information criterion
AOR:	Adjusted odds ratio
ART:	Antiretroviral therapy
ARV:	Antiretroviral
CI:	Confidence interval
Data.FI:	Data for Implementation
EMR:	Electronic medical records
FMOH:	Federal Ministry of health
HFR:	Health facility registry
HIV:	Human immunodeficiency virus
IIT:	Interruption in treatment
IP:	Implementing partner
MMD:	Multi-month dispensing

PEPFAR: United States President's Emergency Plan for AIDS Relief
PLHIV: People living with HIV
RADET: Retention audit determination tool
UNAIDS: Joint United Nations Programme on HIV/AIDS
USAID: United States Agency for International Development
VL: Viral load

Ethics approval

Ethical approvals for this study were obtained in Nigeria and the United States. Informed consent was waived from all subjects or, if subjects are under 18, from a parent and/or legal guardian by the expedited institutional review board (IRB) approvals granted by both the National Health Research Ethics Committee of Nigeria (NHREC), reference number NHREC/01/01/2007, and the HML IRB in the United States, reference number 772EQH20. Data were anonymised and handled confidentially during all phases of the research. All methods were carried out in accordance with relevant guidelines and regulations. All experimental protocols were granted approval by the institutional review board (IRB) of the National Health Research Ethics Committee of Nigeria (NHREC), reference number NHREC/01/01/2007, and the HML IRB in the United States, reference number 772EQH20.

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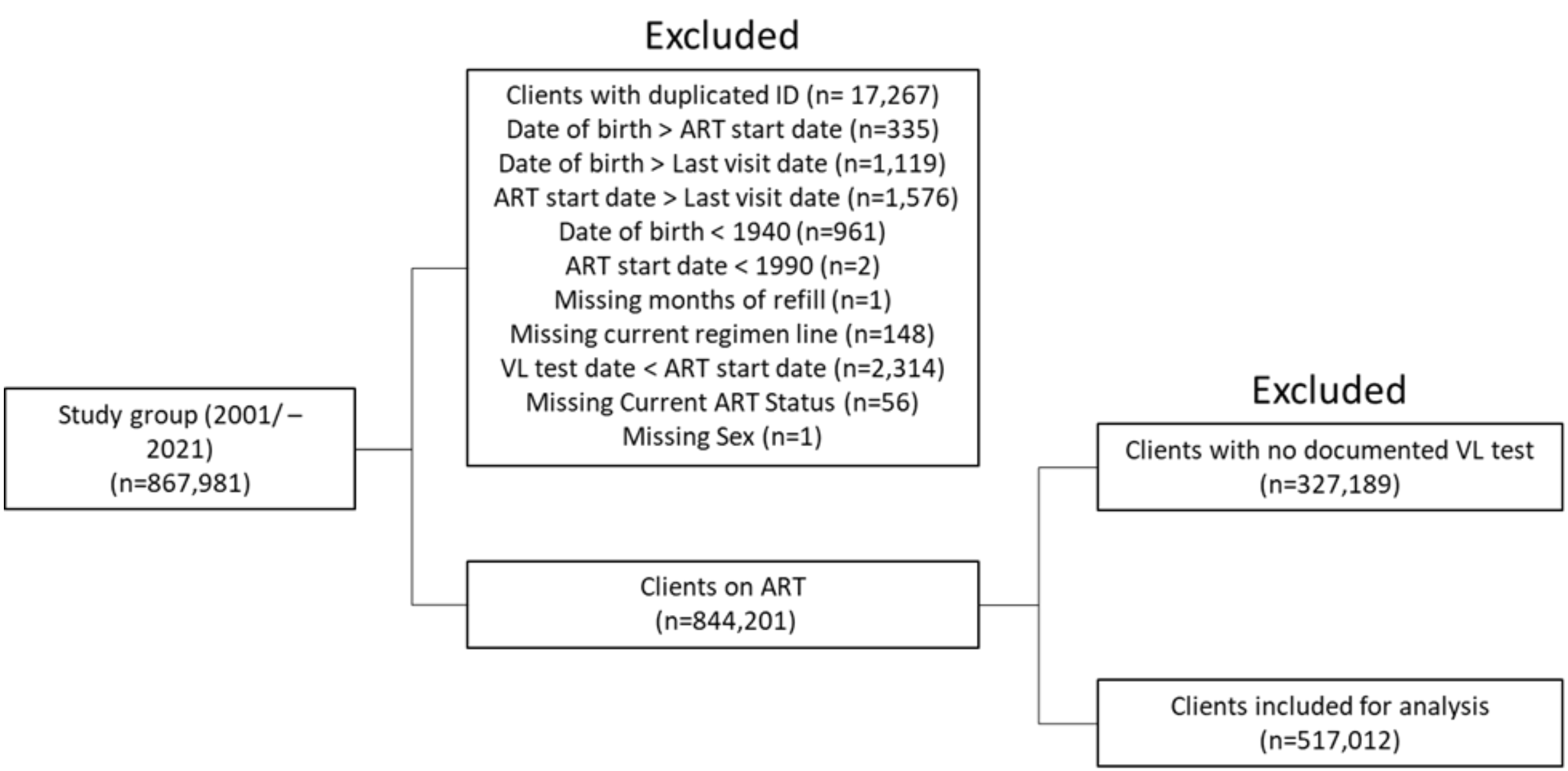
Excluded
Clients with duplicated ID (n= 17,267)
Date of birth > ART start date (n=335)
Date of birth > Last visit date (n=1,119)
ART start date > Last visit date (n=1,576)
Date of birth < 1940 (n=961)
ART start date < 1990 (n=2)
Missing months of refill (n=1)
Missing current regimen line (n=148)
VL test date < ART start date (n=2,314)
Missing Current ART Status (n=56)
Missing Sex (n=1)
Study group (2001/ – 2021) (n=867,981)
Clients on ART (n=844,201)
Excluded
Clients with no documented VL test (n=327,189)
Clients included for analysis (n=517,012)

Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

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		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	#3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	#4	Present key elements of study design early in the paper	5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of	5

		recruitment, exposure, follow-up, and data collection	
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants.	5
	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	5
Bias	#9	Describe any efforts to address potential sources of bias	7
Study size	#10	Explain how the study size was arrived at	6
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	6
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	7
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	7
Statistical methods	#12c	Explain how missing data were addressed	5
Statistical methods	#12d	If applicable, describe analytical methods taking account of sampling strategy	6
Statistical methods	#12e	Describe any sensitivity analyses	8
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	6
Participants	#13b	Give reasons for non-participation at each stage	6
Participants	#13c	Consider use of a flow diagram	6

Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	9
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	5
Outcome data	#15	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	9
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11
Main results	#16b	Report category boundaries when continuous variables were categorized	6
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	#18	Summarise key results with reference to study objectives	13
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	15
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	14
Generalisability	#21	Discuss the generalisability (external validity) of the study results	16
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

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Factors associated with viral load non-suppression in people living with HIV on ART in Nigeria: cross-sectional analysis from 2017 to 2021

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Abstract

Objectives Identify factors (demographic and clinical) associated with a non-suppressed viral load of patients on antiretroviral therapy in Nigeria.

Design Cross-sectional study.

Setting Sixteen United States Agency for International Development (USAID) supported states in Nigeria.

Participants 585,632 people living with HIV (PLHIV) on antiretroviral therapy (ART).

Primary outcome measures Viral load (VL) non-suppression (defined as having a VL of at least 1,000 HIV ribonucleic acid copies per mL of plasma). Chi-square testing and multivariable logistic regression were conducted on routinely collected ART program data.

Results Sixty-six percent of the study population were females. The largest age groups were 25-34 and 35–44, accounting for 32.1% and 31.1%, respectively. Males had 9% greater risk (ARR=1.09) of being non-suppressed. The age groups below the 60+ age group (ARR=0.65) had higher risk of having a non-suppressed VL, with the highest odds in the 0–14 age group (ARR=2.56). Clients enrolled at tertiary and secondary level facilities had the greatest risk of having a non-suppressed VL. Clients who started ART between 2010 and 2015 had the greatest risk of viral non-suppression (ARR=6.53). A shorter time on ART until the last VL (1 years [ARR=3.9]) was associated with a higher risk of a non-suppressed VL. Clients receiving care at private facilities had lower risk of viral non-suppression. Clients in the Edo (ARR=2.82) and Borno (ARR=2.62) states had the greatest risk of viral non-suppression.

Conclusions Targeting male clients within the younger age groups, receiving care for less than 3 years at tertiary and secondary health facilities, small and medium facilities, and in the Edo, Borno and Niger states for interventions could lead to improvements in VL suppression in Nigeria. The independent factors associated with a non-suppressed VL can guide improvements in ART program development and VL suppression of PLHIV in Nigeria.

Strengths and limitations of the study

- The study uses data from over 500,000 PLHIV enrolled on ART across 16 Nigeria states over four years between 2017 and 2021.
- The data used is routinely collected by clinics.
- The study included distal factors such as state, facility level, size and, ownership.
- Variables such as education level and marital status/cohabiting, adherence to treatment, opportunistic infections and side effects were not available.

Introduction

In 2020, 37.7 million people were living with HIV (PLHIV) globally; currently, 27.5 million (73%) have access to antiretroviral therapy (ART) [1]. In 2020, 66% of PLHIV were virally suppressed [1]. Nigeria, a country with one of the highest global HIV infection rates, was reported to have 78% of PLHIV on ART virally suppressed, against a target of 95% [1,2]. The Nigeria National Guidelines for HIV Prevention, Treatment, and Care define virologic suppression as having a viral load (VL) below 1,000 HIV ribonucleic acid copies per mL of plasma [3] (viral load non-suppression is defined as having a VL of at least 1,000 HIV ribonucleic acid copies per mL of plasma). Given that an undetectable VL significantly reduces the transmission risk of HIV, suppressing the VL of 95% of PLHIV on ART is key to achieving epidemic control [4,5].

Globally, including in some Nigerian states, factors that were found to be predictors of viral suppression were age, sex, duration on ART [6–9], current ART regimen [10], and adherence to medications [11]. This study explored whether similar associations alongside other factors such as geo-political zones and facility level existed in Nigeria using data over a period of four years from 16 States that were not necessarily under investigation before, contributing to the body of knowledge and allowing better targeted interventions to improve HIV programs, the VL of clients, and epidemic control in the country.

The objective of this study was to determine which factors were associated with a non-suppressed VL in Nigeria using a large cross-sectional database of clients who received ART. We explored several variables—sex, age group, duration on ART, facility level, facility ownership, State and geopolitical zone—to identify which factors were associated with viral non-suppression. The objective of this analysis is to guide HIV programs to target population groups at the highest risk.

Methods

Study design, setting, and population

The study was a cross-sectional analysis of clients who were enrolled on ART at 580 facilities across 16 States in Nigeria that were supported by the United States Agency for International Development (USAID). The data set covered a period of 4 years, with the last drug pickup dates ranging from January 1, 2017, December 31, 2021. The study was carried out to investigate the clinical and demographic factors associated with a non-suppressed VL among more than 500,000 HIV clients who had a VL test on record.

Data Source and Management

The data were routinely collected by the USAID-supported implementing partners (IPs) through their quarterly data submission using the retention and audit determination tool (RADET). Each IP submission was then combined into a single data set that was used for this study. The RADET dataset provides cross-sectional information for every client ever enrolled on ART at their last point of visit to the clinics supported of USAID and associated IPs. That is, longitudinal records for variables are not available nor ethically approved for studying, for example only the last recorded viral load test for each client is available. Depending on the purpose of the clinical visit of the clients, the data is collected to reflect the most recent clinical details of a particular client.

The data set received contained 775,013 non-longitudinal, cross-sectional client records with a last drug pickup date between January 1st, 2017, and December 31st, 2021, were retained for downstream analysis to isolate a cohort that was active during the latest VL suppression policy rolled out in Nigeria, whereby every client on treatment for 6 months is due for a VL test, and VL tests should be repeated every 12 months[12]. Due to missing unique client identifiers for 153,433 clients, a unique identifier was created for data deduplication using the date of birth, sex, database-provided unique identifier, and client hospital number. For clarification, unique identifiers are not provided for all clients, in such cases a client hospital number is captured instead. Data cleaning involved removing duplicate unique identifiers (n=5,973). Data which may have contained a typo, like records with a date of birth occurring after the ART start date (n=48) or after the date of last drug pickup (n=240) were removed. Clients with an ART start date earlier than 2002 (n=74) when the ART program started in Nigeria [13] were also excluded from the analysis. Additional 166,037

clients without a date of viral load sample collection were removed alongside a further 17,009 who did not receive their VL test results. After data cleaning, 585,632 client records were retained for analyses (Figure 1).

Figure 1. Data cleaning process, excluded data, and study population subset analysed.

Variables engineered as predictors of a non-suppressed viral load

The age variable was calculated as the time difference (in years) between the date of VL sample collection and the date of birth of the client. Then, age group was reclassified into six groups: 0–14, 15–24, 25–34, 35–44, 45–59, and 60+ years.

Similarly, the "duration on ART to last VL test" variable was created by calculating the time difference (in months) between the date of received current VL and the ART start date. The duration on ART was reclassified as <1 year, 1–3 years, and 3+ years, and labelled as "Time on ART."

The "Facility Size" variable was calculated by determining the number of clients receiving care at the facility, then group as small ([0,25) percentiles), medium ([25,75) percentiles), or large ([75,100] percentiles). The number and distribution of clients into the small, medium, and large facilities is presented in Table 1.

Table 1. Summary of the distribution of facility size by the number of clients in care.

	Number Of	Number Of Clients				
Facility Size	Facilities	Total	Min.	Max.	Mean	Median
Small	143	5,360	4	62	37	39
Medium	295	92,348	63	1,078	313	199
Large	146	487,924	1,088	13,585	3,342	2,879

The "Facility Level" variable was obtained from the Nigeria Health Facility Registry (HFR) [14]. The classification resulted in three levels of facilities: primary (operate at Local Government level), secondary (operate at State level), and tertiary (operate at Federal Government level) [15]. Similarly, the "Facility Ownership" variable was created by grouping the facilities in their respective ownership type (public or private) according to their classification in the Nigeria HFR system [14].

The "geopolitical zone" variable was created by grouping the 16 USAID-supported States into their nationally recognized geopolitical zones. This resulted in five geopolitical zone groupings: North-Central (Kwara and Niger States), North-East (Adamawa, Bauchi, Borno, and Yobe States), North-West (Jigawa, Kano, Kebbi, Sokoto, and Zamfara States), South-South (Akwa Ibom, Bayelsa, Cross River, and Edo States), and South-West (Lagos).

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Statistical analysis

For the population with a last VL test on record, the Pearson's chi-square test was used to examine the association of each variable with a non-suppressed VL at a client's last VL test date. Unadjusted and adjusted logistic regression models were run to explore the association of variables with a non-suppressed VL (a VL above 1,000 ribonucleic acid copies per mL of plasma). Current ART status was excluded as a factor from the regression modelling because at the time of the VL test, all clients were active, even though they may now have a different status (interruption in treatment (IIT) defined as missing a drug-pickup appointment for longer than 28 days, deceased, transferred out, or stopped treatment). Similarly, the regimen line was excluded from the regression analysis because other regimen lines, aside from the first-line regimen, are prescribed in the case of a non-suppressed VL or reaction or a reported side effect from the current ARVs. The regimen line was therefore dependent on the VL outcome investigated and it could not be used as an independent variable associated with VL non-suppression. The variables included in the models were sex, age group, ART start year, time on ART to last VL test, facility level, facility size, facility ownership and, State. The group accounting for the most clients in each of the independent variables analysed was set as the reference group for the respective variable. A two-tailed P value of $P<0.05$ was used to define statistical significance. Model selection was done using forward addition and backward elimination of variables where the Akaike's information criterion (AIC) was used to evaluate variable inclusion in the final model. The retained model with the lowest AIC resulted in the exclusion of the geopolitical zone variable. Multicollinearity was tested using the generalized variance inflation factor (GVIF) for the set of variables used in the logistic

regression model, and none of the variables exhibited multicollinearity (having a GVIF below 1.4). The odds ratio (OR) and confidence intervals for the logistic regression models were converted to risk ratios (RR) using Equation 1 [16] where P_0 is the prevalence of non-suppressed VL in the unexposed (reference) group of each explanatory variable. This was done to avoid over-estimation of the OR caused by the high prevalence of non-suppressed VL across some explanatory variables in the dataset which was above the 10% recommended threshold [16]. All data were analysed using R software for Statistical Computing v4.0. [17].

$$RR = \frac{OR}{(1 - P_0) + (P_0 \, x \, OR)}$$ Equation 1.

Results

Of the 585,632 clients included in the analysis, 35,539 (6.07%) were virologically non-suppressed while the remaining 93.9% were virologically suppressed (Table 2). Sixty-five percent of the clients were female, with 6.1% of both sexes virologically non-suppressed. Clients ages 25–34 and 35–44 were the largest age groups, accounting for 32.1% and 31.1% of the total number of clients in the analysis, respectively. Clients in the 0–14 age group was the smallest group (3.4%) and had the largest proportion of virally non-suppressed individuals (17.8%).

The Current ART status was recorded as active for 88.9% of the clients, with the remaining 11.1% being dead (1.7%), had stopped treatment (0.5%) had transferred out to another facility (3.1%), or had interrupted treatment (5.8%) (Table 2). Most clients (95.8%) were on the adult first-line ART regimen, with 94.5% of them being virally suppressed. Clients on the adult second-line and paediatric first-line regimens each accounted for 2% of the clients in the study, with 81.7% and 82% of clients on the two regimen lines being virally suppressed, respectively.

Most clients were receiving ART at a secondary health facility (52.2%), followed by primary health facilities (35.7%) (Table 2). Clients receiving treatment at a tertiary (9.7%) or secondary health facility (7.0%) were non-suppressed in higher proportions compared with clients receiving ART at a primary health facility.

Ninety-four percent of the clients received ARVs from a publicly owned facility, with 94% of them being virally suppressed (Table 2). Only 6% of the clients were receiving treatment from a privately owned facility, with 7.4% of these clients virally non-suppressed.

Akwa Ibom state has the highest proportion of clients in the record (36.8%) with viral suppression rate of 96.9%. While Zamfara has the smallest proportion of clients (0.9%) with a viral suppression rate of 89.6%, Kebbi state has the highest proportion of virally suppressed client with 98.4% although, a smaller proportion of the clients (1.6%) in the study. The South-south zone served the highest proportion of clients in the cohort and highest suppression rate (54.2% and 95.6%, respectively). Similarly, North-Central Zone had the smallest proportion and lowest suppression rate (7.4% and 90.6%, respectively).

Table 2. Characteristics of the 517,012 clients with a viral load test on record at Nigerian facilities between 2017 and 2021.

Factors	Viral load		Total	p-value (<0.05)
	Suppressed	Non-Suppressed		
Sex				
Female	357 783 (93.9)	23 058 (6.1)	380 841 (65.0)	0.5
Male	192 300 (93.9)	12 491 (6.1)	204 791 (35.0)	0.5
Age Group				
0-14	16 450 (82.2)	3 561 (17.8)	20 011 (3.4)	
15-24	57 434 (92.9)	4 416 (7.1)	61 850 (10.6)	
25-34	177 648 (94.4)	10 580 (5.6)	188 228 (32.1)	
35-44	172 070 (94.5)	10 097 (5.5)	182 167 (31.1)	
45-59	106 743 (94.8)	5 813 (5.2)	112 556 (19.2)	
60+	19 738 (94.8)	1 082 (5.2)	20 820 (3.6)	
Art Start Year				
<2005	542 (94.4)	32 (5.6)	574 (0.1)	
[2005-2010)	40 276 (92.8)	3 113 (7.2)	43 389 (7.4)	
[2010-2015)	82 198 (91.1)	8 012 (8.9)	90 210 (15.4)	
[2015-2020)	220 451 (92.5)	17 808 (7.5)	238 259 (40.7)	
>2020	206 616 (96.9)	6 584 (3.1)	213 200 (36.4)	
Time On Art				
<1 year	156 702 (94.5)	9 085 (5.5)	165 787 (28.3)	
1-3 years	161 118 (94.6)	9 183 (5.4)	170 301 (29.1)	
3+ years	232 263 (93.1)	17 281 (6.9)	249 544 (42.6)	
Regimen Switch				
After VL test	269 102 (94.2)	16 696 (5.8)	285 798 (48.8)	
Before VL test	22 189 (78.5)	6 084 (21.5)	28 273 (4.8)	
Not Switched	258 792 (95.3)	12 769 (4.7)	271 561 (46.4)	

Current ART Regimen			
3TC-TDF-DTG	517 510 (95.6)	24 011 (4.4)	541 521 (92.5)
3TC-TDF-EFV	8 893 (65.1)	4 759 (34.9)	13 652 (2.3)
ABC-3TC-DTG	9 356 (87.0)	1 403 (13.0)	10 759 (1.8)
Other	14 324 (72.7)	5 376 (27.3)	19 700 (3.4)
ART dispensed (months)			
1-2	26 476 (67.9)	12 515 (32.1)	38 991 (6.7)
3	99 879 (89.3)	11 911 (10.7)	111 790 (19.1)
3+	423 728 (97.4)	11 123 (2.6)	434 851 (74.3)
Current ART Status			
Active	501 083 (96.2)	19 544 (3.8)	520 627 (88.9)
Dead	6 568 (67.1)	3 217 (32.9)	9 785 (1.7)
IIT	25 849 (75.7)	8 313 (24.3)	34 162 (5.8)
Stopped	1 911 (71.9)	747 (28.1)	2 658 (0.5)
Transferred out	14 672 (79.7)	3 728 (20.3)	18 400 (3.1)
Current Regimen Line			
Adult 1st Line	529 898 (94.5)	31 006 (5.5)	560 904 (95.8)
Adult 2nd Line	9 203 (81.7)	2 066 (18.3)	11 269 (1.9)
Adult 3rd Line	21 (58.3)	15 (41.7)	36 (0.006)
Peds 1st Line	10 850 (82.0)	2 382 (18.0)	13 232 (2.3)
Peds 2nd Line	97 (57.7)	71 (42.3)	168 (0.03)
Salvage	14 (60.9)	9 (39.1)	23 (0.004)
Facility Size			
Small	4 920 (91.8)	440 (8.2)	5 360 (0.9)
Medium	84 429 (91.4)	7 919 (8.6)	92 348 (15.8)
Large	460 734 (94.4)	27 190 (5.6)	487 924 (83.3)
Facility Level			
Primary	201 847 (96.5)	7 428 (3.5)	209 275 (35.7)
Secondary	284 415 (93.0)	21 275 (7.0)	305 690 (52.2)
Tertiary	63 821 (90.3)	6 846 (9.7)	70 667 (12.1)
Facility Ownership			
Private	31 279 (92.6)	2 486 (7.4)	33 765 (5.8)
Public	518 804 (94.0)	33 063 (6.0)	551 867 (94.2)
State			
Adamawa	38 183 (92.7)	3 020 (7.3)	41 203 (7.0)
Akwa Ibom	208 852 (96.9)	6 604 (3.1)	215 456 (36.8)
Bauchi	24 565 (93.8)	1 631 (6.2)	26 196 (4.5)
Bayelsa	11 046 (91.5)	1 025 (8.5)	12 071 (2.1)
Borno	14 595 (87.3)	2 122 (12.7)	16 717 (2.9)
Cross River	59 487 (95.4)	2 893 (4.6)	62 380 (10.7)
Edo	23 832 (87.3)	3 465 (12.7)	27 297 (4.7)
Jigawa	8 580 (88.8)	1 083 (11.2)	9 663 (1.7)
Kano	37 577 (92.8)	2 897 (7.2)	40 474 (6.9)
Kebbi	9 191 (98.4)	147 (1.6)	9 338 (1.6)

Kwara	8 308 (92.2)	705 (7.8)	9 013 (1.5)
Lagos	54 689 (92.2)	4 620 (7.8)	59 309 (10.1)
Niger	30 717 (90.2)	3 333 (9.8)	34 050 (5.8)
Sokoto	8 765 (92.3)	731 (7.7)	9 496 (1.6)
Yobe	7 032 (90.6)	730 (9.4)	7 762 (1.3)
Zamfara	4 664 (89.6)	543 (10.4)	5 207 (0.9)
Zone			
North-Central	39 025 (90.6)	4 038 (9.4)	43 063 (7.4)
North-East	84 375 (91.8)	7 503 (8.2)	91 878 (15.7)
North-West	68 777 (92.7)	5 401 (7.3)	74 178 (12.7)
South-South	303 217 (95.6)	13 987 (4.4)	317 204 (54.2)
South-West	54 689 (92.2)	4 620 (7.8)	59 309 (10.1)

A greater proportion of ART clients received treatment from a large volume facility (83.3%), with 94.4% of these clients being virally suppressed (Table 2). ART clients at the medium volume facilities comprised 15.8% of the total clients, with 91.4% of them being virally suppressed.

Approximately forty-three percent of the clients had been on ART for more than three years and 28.3% had been on treatment for less than one year (Table 2). Clients who were on ART for less than three years had a higher proportion of viral suppression (94.5%) than those who had been on ART for more than three years (both 93.1%). The South-South zone had the largest proportion of clients (54.2%) in the sample and had the highest proportion of virally suppressed clients (95.6%) (Table 2).

A multivariable logistic regression model was run using the sex, age group, ART start year, time on ART, facility level, facility size, facility ownership, State and Zone. The AIC for this model did not change when Zone was included or excluded from the model by forward addition and backward elimination (AIC= 245,641.3), therefore the Zone variable was removed from the model. The odds ratios (OR) and risk ratios (RR) generated using the logistic regression model assessing the relationship between predictor variables and a non-suppressed VL among ART clients are presented in Table 3. All factors used in the adjusted logistic regression model were statistically significant, with a p-value of below 0.05.

Males (adjusted risks ratio [ARR]=1.09, 95% CI: 1.07–1.12, P<0.05) were found to have 9% higher odds of being virally non-suppressed than females, however, unadjusted logistic regression did not identify a significant difference between the odds of viral non-suppression of females and males (Table 3). Univariable and multivariable logistic regression indicated with statistical significance that young people ages 0–24 were associated with higher odds of viral non-suppression compared with the 35–44 age group. Younger clients ages 0–14 years had the highest unadjusted and adjusted risk of viral non-suppression (ARR = 1.87, 95% CI: 1.79–1.95, P<0.05).

Clients who start ART between 2010 and 2015 (ARR = 6.53, CI: 6.26-6.82) had greater risk of viral non-suppression compared to clients that started before 2010 or after 2015. Compared with clients who had been on ART for more than three years, those who had been on treatment between 1 and 3 years had greater risk to be virally non-suppressed (ARR=1.67, 95% CI: 1.62–1.72), whereas clients on ART for less than one year were found to have an even greater risk of viral non-suppression (ARR=3.9, 95% CI: 3.77–4.03).

Clients receiving ARVs at tertiary health facilities were 74% more likely to be virally non-suppressed (ARR=1.74, 95% CI: 1.67 –1.82) than primary health facilities (Table 3). Moreover, clients receiving care at small (ARR=1.66, 95% CI: 1.51–1.83) and medium (ARR=1.49, 95% CI: 1.45–1.54) facilities were found to have the higher risk of viral non-suppression compared to large facilities. Clients receiving treatment at privately owned facilities (ARR=0.86, CI: 0.82-0.9) had a lower risk of viral non-suppression than clients at publicly owned facilities.

Compared with the Akwa Ibom state, clients in the Edo (ARR = 2.82, 95% CI: 2.69–2.95) and Borno (ARR =2.62, 95% CI: 2.48–2.76) states had greater odds of VL non-suppression (P<0.05) (Table 3). Clients in the Kebbi state had the lowest risk for VL non-suppression (ARR = 0.33, 95% CI: 0.28–0.38).

Table 3. Factors associated with a non-suppressed viral load presented as unadjusted and adjusted odds ratios and risk ratios derived using logistic regression.

	Univariable			Multivariable		
Factors	uOR	uRR	p-value (<0.05)	aOR	aRR	p-value (<0.05)
Sex						
Female	1 [ref]	1 [ref]		1 [ref]	1 [ref]	
Male	1.01 [0.99 - 1.03]	1.01 [0.99 - 1.03]	0.49	1.1 [1.07 - 1.13]	1.09 [1.07 - 1.12]	
Age Group						
0-14	3.63 [3.49 - 3.79]	3.16 [3.06 - 3.28]		2.82 [2.7 - 2.94]	2.56 [2.47 - 2.65]	
15-24	1.29 [1.24 - 1.34]	1.27 [1.22 - 1.31]		1.33 [1.28 - 1.38]	1.31 [1.26 - 1.35]	
25-34	1 [ref]	1 [ref]		1 [ref]	1 [ref]	
35-44	0.99 [0.96 - 1.01]	0.99 [0.96 - 1.01]	0.3	0.85 [0.83 - 0.88]	0.86 [0.84 - 0.89]	
45-59	0.91 [0.88 - 0.94]	0.91 [0.89 - 0.94]		0.7 [0.67 - 0.72]	0.71 [0.68 - 0.73]	
60+	0.92 [0.86 - 0.98]	0.92 [0.87 - 0.98]		0.64 [0.6 - 0.69]	0.65 [0.61 - 0.7]	
ART Start Year						
<2005	1.85 [1.3 - 2.65]	1.8 [1.29 - 2.52]		5.69 [3.96 - 8.18]	4.97 [3.63 - 6.69]	
[2005-2010)	2.43 [2.32 - 2.53]	2.33 [2.23 - 2.42]		6.7 [6.29 - 7.13]	5.69 [5.4 - 5.99]	
[2010-2015)	3.06 [2.96 - 3.16]	2.88 [2.79 - 2.96]		7.94 [7.53 - 8.38]	6.53 [6.26 - 6.82]	
[2015-2020)	2.53 [2.46 - 2.61]	2.42 [2.35 - 2.49]		4.96 [4.76 - 5.16]	4.42 [4.26 - 4.57]	
>2020	1 [ref]	1 [ref]		1 [ref]	1 [ref]	
Time On ART						
<1 year	0.78 [0.76 - 0.8]	0.79 [0.77 - 0.81]		4.97 [4.75 - 5.19]	3.9 [3.77 - 4.03]	
1-3 years	0.77 [0.75 - 0.79]	0.78 [0.76 - 0.8]		1.76 [1.7 - 1.82]	1.67 [1.62 - 1.72]	
3+ years	1 [ref]	1 [ref]		1 [ref]	1 [ref]	
Facility Size						
Small	1.52 [1.37 - 1.67]	1.48 [1.34 - 1.61]		1.73 [1.56 - 1.92]	1.66 [1.51 - 1.83]	
Medium	1.59 [1.55 - 1.63]	1.54 [1.5 - 1.57]		1.54 [1.49 - 1.59]	1.49 [1.45 - 1.54]	
Large	1 [ref]	1 [ref]		1 [ref]	1 [ref]	
Facility Level						
Primary	1 [ref]	1 [ref]		1 [ref]	1 [ref]	
Secondary	2.03 [1.98 - 2.09]	1.96 [1.91 - 2.01]		1.51 [1.46 - 1.55]	1.48 [1.44 - 1.52]	

Tertiary	2.91 [2.82 - 3.02]	2.73 [2.65 - 2.82]	1.79 [1.71 - 1.88]	1.74 [1.67 - 1.82]
Facility Ownership				
Private	1.25 [1.2 - 1.3]	1.23 [1.19 - 1.28]	0.85 [0.81 - 0.89]	0.86 [0.82 - 0.9]
Public	1 [ref]	1 [ref]	1 [ref]	1 [ref]
State				
Adamawa	2.5 [2.39 - 2.61]	2.39 [2.29 - 2.49]	1.95 [1.86 - 2.04]	1.89 [1.81 - 1.98]
Akwa Ibom	1 [ref]	1 [ref]	1 [ref]	1 [ref]
Bauchi	2.1 [1.99 - 2.22]	2.03 [1.93 - 2.14]	1.6 [1.51 - 1.7]	1.57 [1.49 - 1.66]
Bayelsa	2.93 [2.74 - 3.14]	2.76 [2.6 - 2.94]	2.15 [2 - 2.31]	2.08 [1.94 - 2.22]
Borno	4.6 [4.37 - 4.84]	4.14 [3.96 - 4.33]	2.76 [2.6 - 2.92]	2.62 [2.48 - 2.76]
Cross River	1.54 [1.47 - 1.61]	1.51 [1.45 - 1.58]	1.31 [1.26 - 1.38]	1.3 [1.25 - 1.36]
Edo	4.6 [4.4 - 4.8]	4.14 [3.98 - 4.29]	2.99 [2.84 - 3.15]	2.82 [2.69 - 2.95]
Jigawa	3.99 [3.73 - 4.27]	3.65 [3.44 - 3.88]	2.36 [2.19 - 2.53]	2.26 [2.11 - 2.42]
Kano	2.44 [2.33 - 2.55]	2.34 [2.24 - 2.43]	1.59 [1.51 - 1.67]	1.56 [1.49 - 1.64]
Kebbi	0.51 [0.43 - 0.6]	0.52 [0.44 - 0.61]	0.32 [0.27 - 0.37]	0.33 [0.28 - 0.38]
Kwara	2.68 [2.48 - 2.91]	2.55 [2.37 - 2.75]	1.68 [1.54 - 1.83]	1.65 [1.51 - 1.78]
Lagos	2.67 [2.57 - 2.78]	2.54 [2.45 - 2.63]	2.09 [2.01 - 2.18]	2.02 [1.95 - 2.1]
Niger	3.43 [3.29 - 3.58]	3.19 [3.07 - 3.31]	2.76 [2.64 - 2.89]	2.62 [2.51 - 2.73]
Sokoto	2.64 [2.44 - 2.86]	2.51 [2.34 - 2.7]	1.74 [1.61 - 1.89]	1.7 [1.58 - 1.84]
Yobe	3.28 [3.03 - 3.56]	3.06 [2.85 - 3.3]	2.21 [2.03 - 2.4]	2.13 [1.97 - 2.3]
Zamfara	3.68 [3.36 - 4.04]	3.4 [3.13 - 3.69]	2.02 [1.83 - 2.22]	1.96 [1.78 - 2.14]

Discussion

Our study found that male clients in younger age groups (0-24) who started treatment before 2020 and have been on treatment for less than one year, receiving care at small and medium facilities that are specialised to a secondary and tertiary level facilities that are publicly owned and located in the Edo, Borno and, Niger states had the highest association with VL non-suppression. Other studies have found similar results for the risk of viral non-suppression in younger age groups in Cambodia, Uganda, and South Carolina (USA) [6,8,18], and among males [19–21]. Our findings suggest that in some Nigerian states, the health seeking behavior of certain demographics can be improved or given more attention to by HIV care programs, specifically for younger-aged males. In that same regard, the quality of HIV healthcare programs can be improved across several states in Nigeria with consideration the facility types, size, and public ownership.

The increased risk of viral non-suppression among ART clients who received treatment at tertiary health facilities have not been observed in Ethiopia where higher risk of viral non-suppression was associated with primary health facilities in Ethiopia [22]. Small and medium facilities were identified to be associated with viral-non-suppression of HIV clients on treatment and this was consistent with findings that clients were more likely to miss consecutive visits at lower volume facilities. This could be due to smaller clinics being located within smaller communities, as a result, patients may avoid stigmatisation within their community and may not pick-up treatment as routinely as patients that attend clinics that are outside of their communities [23]. Such clients that would miss their drug pickup appointments more frequently, are reasonably expected to have non-suppressed viral loads. A possible circumvention of the stigmatisation within communities would be to offer clients that live within communities a referral to HIV care facilities that are located outside of their communities. However, consideration should be given to the distance needed for travel as well because although a distance less than one kilometre to the clinic was associated with higher IIT [23], mean distances above 4.7 km to clinics were associate with higher IIT [24].

Clients that received care at privately owned facilities have lower risk of a non-suppressed VL seeing that there are fewer clients represented in the private sector. However, clients receiving care at privately owned facilities were non-suppressed in higher proportion than those receiving care at public facilities. Nevertheless, given the higher number of virally non-suppressed clients at public facilities, those clients are at higher risk if of the unfavourable outcome. Another study has found

that HIV care was of greater quality at public facilities than private in Anambra state in Nigeria [25]. This may be reflected in our unadjusted, univariable results for the ownership of the facilities as well, which depicted that patients receiving care at private facilities were more likely to be virally non-suppressed.

ART clients who had their last VL test conducted within less than one year on treatment were less likely to be virally non-suppressed compared with clients who had their VL tested after one year on ART. Our finding was consistent with the Center for Disease Control and Prevention's finding that PLHIV on ART could be virally suppressed within six months of initiation, provided that they adhered to their medication [26]. Moreover, a greater likelihood of viral suppression was found among PLHIV who were initiated on treatment for less than one year compared with those on ART for more than one year [27]. This could suggest that greater attention to patients enrolled on ART for less than one year could be given to perhaps cultivate a habit of adhering to the treatment, which could result to better viral load outcomes. However, contrary to this, a shorter time on ART was identified as a factor associated with a non-suppressed VL in South Africa [28]. The contradictory findings in the literature could speak to the specific adherence patterns of the populations investigated and models that may be specific to the study settings. Also, elucidating that clients more engaged in care can have more opportunities for non-suppressed viral load test results, though, this does not necessarily mean that this population is more likely to be non-suppressed. Nevertheless, this advocates for support of newly enrolled clients into developing treatment-adherence habits because it is possible that in some clinical settings adherence habits are better developed earlier on due to more attentive healthcare programs. Therefore, improving HIV care may ultimately result in better treatment-adherence habits and consequential VL suppression.

A possible explanation for the clients receiving care in the Kwara and Niger states in the North-Central zone having higher risk of viral non-suppression could be linked to health-seeking behaviour such as non-use of the service, poor adherence to treatment, and possibly religious affiliation (for example Islamic religion predominant in northern Nigeria) where in certain circumstances women require permission to leave the premises of a household which can reduce access to healthcare [29,30]. Community refills (door-to-door) could be implemented in such communities, perhaps staffed by female health workers. On the other hand, in Borno and Yobe

states in the North-East zone of Nigeria, the incessant insecurity in the region has largely led to people often been displaced and this has largely impacted on the health-seeking behavior,

One of the limitations of our study was the inaccessibility of the longitudinal data set, leaving us unable to conduct a longitudinal study to explore the factors affecting viral non-suppression over time. We were therefore restricted to conducting a cross-sectional study. The study cohort was composed of clients that received care at USAID-supported facilities, therefore, it may not be a true representation of the risk of VL suppression throughout the country. In facilities that support is better, the results here could overestimate the contribution of some of the factors to VL non-suppression. Vice-versa, where support is lacking, the contribution of some of the factors presented here on VL non-suppression could be underestimated.

It is possible that some of the 21.6% of client records (eliminated from analysis) without a VL test on record are a consequence of poor adherence to treatment which could lead to viral load non-suppression that is not tested/recorded. This assumption is based on the concept that patients need to attend clinic visits to either receive treatment or have their VL samples collected and tested. Investigating the factors that are associated with an untested viral load could provide useful insight. At the same time, longitudinal studies into both viral load non-testing and viral load non-suppression may ultimately be of greatest use. Additional variables relating to the capacity of clinical facilities to conduct testing would reveal whether the lack of viral load testing is also affected by a low capacity.

Other unavailable variables that could be explored in future studies to identify their association with viral suppression are tuberculosis status, adherence level, ART drug regimen, side-effects, IIT, marital status, and education level, however, these variables would need to be provided and analysed longitudinally. The absence of VL suppression data for recently initiated clients may have also had an impact on the study seeing that they had to be excluded, therefore only the results of tested patients could be analysed, leaving out the results of those without a test.

Conclusions

Targeting males, below 35 that started treatment before 2020 and have been on treatment for less than three years, receiving care at tertiary health facility, small and medium facilities, publicly

owned, and in the Edo, Borno, Niger states for interventions could lead to improvements in VL suppression in Nigeria. The independent factors associated here with a non-suppressed VL can guide the improvement of ART program development and VL suppression of PLHIV in Nigeria.

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Data Statement: The data that support the findings of this study are owned by the Government of Nigeria and were used under license for the current study. Access to these data is subject to restrictions owing to privacy and ethics policies set by the Government of Nigeria so are not publicly available. Requests to access these data should be directed to Dauda.Sulaiman@thepalladiumgroup.com.

Ethics approval

The study used secondary data. Ethical approvals for this study were obtained in Nigeria and the United States. Informed consent was waived from all subjects or, if subjects are under 18, from a parent and/or legal guardian by the expedited institutional review board (IRB) approvals granted by both the National Health Research Ethics Committee of Nigeria (NHREC), reference number NHREC/01/01/2007, and the HML IRB in the United States, reference number 772EQH20. Data were anonymised and handled confidentially during all phases of the research. All methods were carried out in accordance with relevant guidelines and regulations. All experimental protocols were granted approval by the institutional review board (IRB) of the National Health Research Ethics Committee of Nigeria (NHREC), reference number NHREC/01/01/2007, and the HML IRB in the United States, reference number 772EQH20.

List of abbreviations

AIC:	Akaike information criterion
AOR:	Adjusted odds ratio
ARR:	Adjusted risk ratio
ART:	Antiretroviral therapy
ARV:	Antiretroviral
CI:	Confidence interval
Data.FI:	Data for Implementation
EMR:	Electronic medical records
FMOH:	Federal Ministry of health
HFR:	Health facility registry
HIV:	Human immunodeficiency virus
IIT:	Interruption in treatment
IP:	Implementing partner
MMD:	Multi-month dispensing
PEPFAR:	United States President's Emergency Plan for AIDS Relief
PLHIV:	People living with HIV
RADET:	Retention audit determination tool
UNAIDS:	Joint United Nations Programme on HIV/AIDS

USAID: United States Agency for International Development

VL: Viral load

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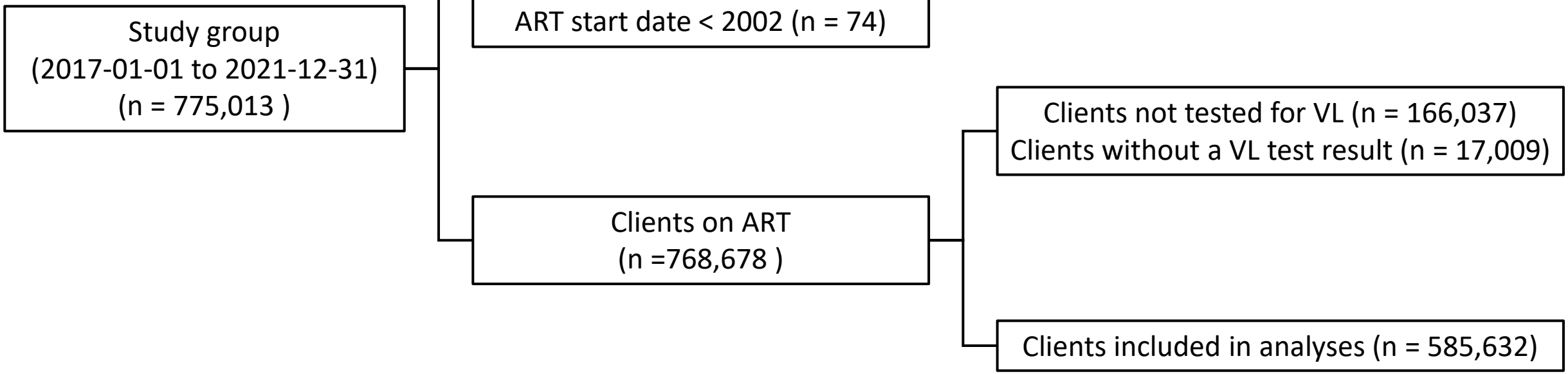
Study group
(2017-01-01 to 2021-12-31)
(n = 775,013)
Duplicate records (n = 5,973)
ART start date < DOB (n = 48)
Last pickup date < DOB (n = 240)
ART start date < 2002 (n = 74)
Clients on ART
(n =768,678)
Clients not tested for VL (n = 166,037)
Clients without a VL test result (n = 17,009)
Clients included in analyses (n = 585,632)

Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	#3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	#4	Present key elements of study design early in the paper	5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of	5

		recruitment, exposure, follow-up, and data collection	
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants.	5
	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	5
Bias	#9	Describe any efforts to address potential sources of bias	7
Study size	#10	Explain how the study size was arrived at	6
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	6
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	7
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	7
Statistical methods	#12c	Explain how missing data were addressed	5
Statistical methods	#12d	If applicable, describe analytical methods taking account of sampling strategy	6
Statistical methods	#12e	Describe any sensitivity analyses	8
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	6
Participants	#13b	Give reasons for non-participation at each stage	6
Participants	#13c	Consider use of a flow diagram	6

Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	9
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	5
Outcome data	#15	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	9
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11
Main results	#16b	Report category boundaries when continuous variables were categorized	6
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	#18	Summarise key results with reference to study objectives	13
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	15
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	14
Generalisability	#21	Discuss the generalisability (external validity) of the study results	16
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

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Factors associated with viral load non-suppression in people living with HIV on ART in Nigeria: cross-sectional analysis from 2017 to 2021

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Factors associated with viral load non-suppression in people living with HIV on ART in Nigeria: cross-sectional analysis from 2017 to 2021

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Abstract

Objectives Identify factors (demographic and clinical) associated with a non-suppressed viral load of PLHIV on antiretroviral therapy in Nigeria.

Design Cross-sectional study.

Setting Sixteen United States Agency for International Development (USAID) supported states in Nigeria.

Participants 585,632 people living with HIV (PLHIV) on antiretroviral therapy (ART).

Primary outcome measures Viral load (VL) non-suppression (defined as having a VL of at least 1,000 HIV ribonucleic acid copies per mL of plasma). Chi-square testing and multivariable modified Poisson regression with robust variance estimates were conducted on routinely collected ART program data.

Results Sixty-six percent of the study population were females. The largest age groups were 25-34 and 35–44, accounting for 32.1% and 31.1%, respectively. Males had a 9% greater likelihood (APR=1.09) of being non-suppressed. The age groups below 60+ (APR=0.67) had a higher likelihood of a non-suppressed VL, with the highest in the 0–14 age group (APR=2.38). Clients enrolled at tertiary and secondary level facilities had the greatest likelihood of a non-suppressed VL. Clients who started ART between 2010 and 2015 had the greatest likelihood of viral non-suppression (APR=6.19). A shorter time on ART (<1 year [APR=3.92]) was associated with a higher likelihood of a non-suppressed VL. Clients receiving care at private facilities had a lower likelihood of viral non-suppression in the adjusted model. Clients in the Edo (APR=2.66) and Niger (APR=2.54) states had the greatest likelihood of viral non-suppression.

Conclusions Targeting males, clients of younger age, those on treatment for less than 3 years, clients at tertiary and secondary health facilities, small and medium facilities, and clients in the Edo, Niger, and Borno states for interventions could lead to improvements in VL suppression in

Nigeria. The independent factors associated with a non-suppressed VL can guide improvements in ART program development and VL suppression of PLHIV on ART in Nigeria.

Strengths and limitations of the study

- The study used data from over 500,000 PLHIV enrolled on ART in 16 Nigeria states over four years between 2017 and 2021 which can allow the results to cover a broad portion of HIV healthcare in Nigeria in recent times.
- The data used was routinely collected by clinics, reflecting the actual state of HIV healthcare in Nigeria during the period of the study.
- The study included distal factors such as state, facility level, size, and ownership which can guide intervention at an infrastructural level.
- Variables such as education level and marital status/cohabiting, treatment adherence, opportunistic infections, and side effects were not available, and some of these factors could have been confounders of the predictors used in this study.

Introduction

In 2020, there were 37.7 million people living with HIV (PLHIV) globally; in 2021, 27.5 million (73%) had access to antiretroviral therapy (ART) [1]. In 2020, 66% of PLHIV were virally suppressed [1]. Nigeria is a country with one of the highest numbers of PLHIV in the world (1.9 million), with a prevalence rate of 1.4% and an incidence rate of 0.34 per 1,000 capita with approximately 74,000 individuals newly infected as estimated in 2021. It was also estimated that 86% of the PLHIV on ART in Nigeria were virally suppressed in 2021 [2]. The Nigeria National Guidelines for HIV Prevention, Treatment, and Care define virologic suppression as having a viral load (VL) below 1,000 HIV ribonucleic acid copies per mL of plasma [3] (viral load non-suppression is defined as having a VL of at least 1,000 HIV ribonucleic acid copies per mL of plasma). Given that an undetectable VL significantly reduces the transmission risk of HIV, suppressing the VL of 95% of PLHIV on ART is key to achieving epidemic control [4,5].

Globally, including in some Nigerian states, factors that were found to be predictors of viral suppression were age, sex, duration on ART [6–9], current ART regimen [10], and adherence to medications [11]. This study explored whether similar associations alongside other factors such as state and facility level existed in Nigeria using data over a period of four years from 16 States that

were not necessarily under investigation before, contributing to the body of knowledge and allowing better targeted interventions to improve HIV programs, the VL of clients, and epidemic control in the country.

The objective of this study was to determine which factors were associated with a non-suppressed VL in Nigeria using a large cross-sectional database of clients who received ART. We explored several variables—sex, age group, ART start year, time on ART, facility size, facility level, facility ownership, and state—to identify which factors were associated with viral non-suppression. The findings from the analysis can be used to guide HIV programs to conduct targeted intervention for the PLHIV on ART with the highest likelihood of having a non-suppressed VL.

Methods

Study design, setting, and population

The study was a cross-sectional analysis of clients who were enrolled on ART at 580 facilities across 16 States (Adamawa, Akwa Ibom, Bauchi, Bayelsa, Borno, Cross River, Edo, Jigawa, Kano, Kebbi, Kwara, Lagos, Niger, Sokoto, Yobe, Zamfara) in Nigeria that were supported by the United States Agency for International Development (USAID). The data set covered a period of 4 years, with the last drug pickup dates ranging from January 1, 2017 to December 31, 2021. The study was carried out to investigate the clinical and demographic factors associated with a non-suppressed VL among more than 500,000 HIV clients who had a VL test on record. The age of clients ranged between 0 and 101 with a median of 37 and a mean of 37.2.

Data Source and Management

The data were routinely collected by the USAID-supported implementing partners (IPs) through their quarterly data submissions using the retention and audit determination tool (RADET). Each IP submission was then combined into a single data set that was used for this study. The RADET dataset provides cross-sectional information for every client ever enrolled on ART at their last point of visit to the clinics supported by USAID and associated IPs. That is, longitudinal records for variables were not available nor ethically approved for studying, for example only the last recorded viral load test for each client was available. Depending on the purpose of the clinical visit of the clients, the data was collected to reflect the most recent clinical details of a particular client.

The data set received contained 775,013 non-longitudinal, cross-sectional client records with a last drug pickup date between January 1st, 2017, and December 31st, 2021. Due to missing unique client identifiers for 153,433 clients, a unique identifier was created for data deduplication using the date of birth, sex, database-provided unique identifier, and client hospital number. For clarification, unique identifiers were not provided for all clients, in such cases a client hospital number was captured instead. Data cleaning involved removing duplicate unique identifiers (n=5,973). Data which may have contained a typo, like records with a date of birth occurring after the ART start date (n=48) or after the date of last drug pickup (n=240) were removed. Clients with an ART start date earlier than 2002 (n=74) when the ART program started in Nigeria [12] were also excluded from the analysis. An additional 166,037 client records without a date of viral load sample collection were removed alongside a further 17,009 who did not receive their VL test results at the time of the data collection. After data cleaning, 585,632 client records were retained for downstream analyses (Figure 1) to isolate a cohort that was active during the latest VL suppression policy rolled out in Nigeria, which indicates that every client on treatment for 6 months is due for a VL test, and VL tests should be repeated every 12 months [13].

Figure 1. Data cleaning process, excluded data, and study population subset analyzed.

Variables engineered as predictors of a non-suppressed viral load

The age variable was calculated as the time difference (in years) between the date of VL sample collection and the date of birth of the client. Then, age group was reclassified into six groups: 0–14, 15–24, 25–34, 35–44, 45–59, and 60+ years. Similarly, the "duration on ART to last VL test" variable was created by calculating the time difference (in months) between the date of received current VL and the ART start date. The duration on ART was reclassified as <1 year, 1–3 years, and 3+ years, and labelled as "Time on ART". The "Facility Size" variable was calculated by determining the number of clients receiving care at the facility, then grouped as small ([0,25) percentiles), medium ([25,75) percentiles), or large ([75,100] percentiles). The number and distribution of clients into the small, medium, and large facilities is presented in Table 1.

Table 1. Summary of the distribution of facility size by the number of clients in care.

Facility Size	Number Of	Number Of Clients

	Facilities	Total	Min.	Max.	Mean	Median
Small	143	5,360	4	62	37	39
Medium	295	92,348	63	1,078	313	199
Large	146	487,924	1,088	13,585	3,342	2,879

The "Facility Level" variable was obtained from the Nigeria Health Facility Registry (HFR) [14]. The classification resulted in three levels of facilities: primary (operate at Local Government level), secondary (operate at State level), and tertiary (operate at Federal Government level) [15]. Similarly, the "Facility Ownership" variable was created by grouping the facilities in their respective ownership type (public or private) according to their classification in the Nigeria HFR system [14].

The "geopolitical zone" variable was created by grouping the 16 USAID-supported States into their nationally recognized geopolitical zones. This resulted in five geopolitical zone groupings: North-Central (Kwara and Niger States), North-East (Adamawa, Bauchi, Borno, and Yobe States), North-West (Jigawa, Kano, Kebbi, Sokoto, and Zamfara States), South-South (Akwa Ibom, Bayelsa, Cross River, and Edo States), and South-West (Lagos).

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Statistical analysis

For the 585,632 clients with a last VL test on record, the Pearson's chi-square test was used to examine the association of each variable with a non-suppressed VL at a client's last VL test date. Unadjusted and adjusted modified Poisson regression with robust variance estimates models were conducted to explore the association of variables with a non-suppressed VL (a VL above 1,000 ribonucleic acid copies per mL of plasma). Current ART status was excluded as a factor from the regression modelling because at the time of the VL test, all clients were active, even though they may now have a different status (interruption in treatment (IIT) defined as missing a drug-pickup appointment for longer than 28 days, deceased, transferred out, or stopped treatment). Similarly, the regimen line was excluded from the regression analysis because other regimen lines, aside

from the first-line regimen, are prescribed in the case of a non-suppressed VL or reaction or a reported side effect from the current ARVs. The regimen line was therefore dependent on the VL outcome investigated and it could not be used as an independent variable associated with VL non-suppression. The multi-month dispensing variable (MMD) was excluded from the regression models because the variable is not independent of the VL outcome. That is, eligibility criteria for MMD requires that clients are virally suppressed. Model selection was done using forward addition and backward elimination of variables where the Akaike's information criterion (AIC) was used to evaluate variable inclusion in the final model. The retained model with the lowest AIC (249,787.3) resulted in the exclusion of the geopolitical zone variable. The variables included in the models were sex, age group, ART start year, time on ART to last VL test, facility level, facility size, facility ownership and, state. The group accounting for the most clients in each of the independent variables analysed was set as the reference group for the respective variable. A two-tailed P value of $P<0.05$ was used to define statistical significance. Multicollinearity was tested using the generalized variance inflation factor (GVIF) for the set of variables used in the modified Poisson regression model, and none of the variables exhibited multicollinearity (having a GVIF below 1.4). All data processing and analysis were conducted using the R software for Statistical Computing v4.0. [16].

Results

Of the 585,632 clients included in the analysis, 35,549 (6.1%) were virologically non-suppressed while the remaining 93.9% were virologically suppressed (Table 2). Sixty-five percent of the clients were female, with 6.1% of both sexes virologically non-suppressed. Clients ages 25–34 and 35–44 were the largest age groups, accounting for 32.1% and 31.1% of the total number of clients in the analysis, respectively. Clients in the 0–14 age group was the smallest group (3.4%) and had the largest proportion of virally non-suppressed individuals (17.8%).

The Current ART status was recorded as active for 88.9% of the clients, with the remaining 11.1% being dead (1.7%), had stopped treatment (0.5%) had transferred out to another facility (3.1%), or had interrupted treatment (5.8%) (Table 2). Most clients (95.8%) were on the adult first-line ART regimen, with 94.5% of them being virally suppressed. Clients on the adult second-line and

paediatric first-line regimens each accounted for 2% of the clients in the study, with 81.7% and 82% of clients on the two regimen lines being virally suppressed, respectively.

Approximately forty-three percent of the clients were on ART for more than three years and 28.3% were on treatment for less than one year (Table 2). Clients who were on ART for less than three years had a higher proportion of viral suppression (94.5%) than those who were on ART for more than three years (both 93.1%).

A greater proportion of ART clients received treatment from a large volume facility (83.3%), with 94.4% of these clients being virally suppressed (Table 2). ART clients at the medium volume facilities comprised 15.8% of the total clients, with 91.4% of them being virally suppressed. Most clients were receiving ART at a secondary health facility (52.2%), followed by primary health facilities (35.7%) (Table 2). Clients receiving treatment at a tertiary (9.7%) or secondary health facility (7.0%) were non-suppressed in higher proportions compared with clients receiving ART at a primary health facility. Ninety-four percent of the clients received ARVs from a publicly owned facility, with 94% of them being virally suppressed (Table 2). Only 6% of the clients were receiving treatment from a privately owned facility, with 7.4% of these clients virally non-suppressed.

Akwa Ibom state had the highest proportion of client records (36.8%) with viral suppression rate of 96.9%. While Zamfara had the smallest proportion of clients (0.9%) with a viral suppression rate of 89.6%, Kebbi state had the highest proportion of virally suppressed client with 98.4% although, a smaller proportion of the clients (1.6%) in the study. The South-South zone served the highest proportion of clients in the cohort and highest suppression rate (54.2% and 95.6%, respectively). Similarly, North-Central Zone had the smallest proportion and lowest suppression rate (7.4% and 90.6%, respectively) (Table 2).

Table 2. Characteristics of the 517,012 clients with a viral load test on record at Nigerian facilities between 2017 and 2021.

Factors	Viral load		Total	p-value (<0.05)
	Suppressed	Non-Suppressed		
Sex				
Female	357 783 (93.9)	23 058 (6.1)	380 841 (65.0)	0.5
Male	192 300 (93.9)	12 491 (6.1)	204 791 (35.0)	0.5
Age Group				
0-14	16 450 (82.2)	3 561 (17.8)	20 011 (3.4)	
15-24	57 434 (92.9)	4 416 (7.1)	61 850 (10.6)	
25-34	177 648 (94.4)	10 580 (5.6)	188 228 (32.1)	
35-44	172 070 (94.5)	10 097 (5.5)	182 167 (31.1)	
45-59	106 743 (94.8)	5 813 (5.2)	112 556 (19.2)	
60+	19 738 (94.8)	1 082 (5.2)	20 820 (3.6)	
Art Start Year				
<2005	542 (94.4)	32 (5.6)	574 (0.1)	
[2005-2010)	40 276 (92.8)	3 113 (7.2)	43 389 (7.4)	
[2010-2015)	82 198 (91.1)	8 012 (8.9)	90 210 (15.4)	
[2015-2020)	220 451 (92.5)	17 808 (7.5)	238 259 (40.7)	
>2020	206 616 (96.9)	6 584 (3.1)	213 200 (36.4)	
Time On Art				
<1 year	156 702 (94.5)	9 085 (5.5)	165 787 (28.3)	
1-3 years	161 118 (94.6)	9 183 (5.4)	170 301 (29.1)	
3+ years	232 263 (93.1)	17 281 (6.9)	249 544 (42.6)	
Regimen Switch				
After VL test	269 102 (94.2)	16 696 (5.8)	285 798 (48.8)	
Before VL test	22 189 (78.5)	6 084 (21.5)	28 273 (4.8)	
Not Switched	258 792 (95.3)	12 769 (4.7)	271 561 (46.4)	
Current ART Regimen				
3TC-TDF-DTG	517 510 (95.6)	24 011 (4.4)	541 521 (92.5)	
3TC-TDF-EFV	8 893 (65.1)	4 759 (34.9)	13 652 (2.3)	
ABC-3TC-DTG	9 356 (87.0)	1 403 (13.0)	10 759 (1.8)	
Other	14 324 (72.7)	5 376 (27.3)	19 700 (3.4)	
ART dispensed (months)				
1-2	26 476 (67.9)	12 515 (32.1)	38 991 (6.7)	
3	99 879 (89.3)	11 911 (10.7)	111 790 (19.1)	
3+	423 728 (97.4)	11 123 (2.6)	434 851 (74.3)	
Current ART Status				
Active	501 083 (96.2)	19 544 (3.8)	520 627 (88.9)	
Dead	6 568 (67.1)	3 217 (32.9)	9 785 (1.7)	
IIT	25 849 (75.7)	8 313 (24.3)	34 162 (5.8)	
Stopped	1 911 (71.9)	747 (28.1)	2 658 (0.5)	
Transferred out	14 672 (79.7)	3 728 (20.3)	18 400 (3.1)	
Current Regimen Line				

Adult 1st Line	529 898 (94.5)	31 006 (5.5)	560 904 (95.8)
Adult 2nd Line	9 203 (81.7)	2 066 (18.3)	11 269 (1.9)
Adult 3rd Line	21 (58.3)	15 (41.7)	36 (0.006)
Peds 1st Line	10 850 (82.0)	2 382 (18.0)	13 232 (2.3)
Peds 2nd Line	97 (57.7)	71 (42.3)	168 (0.03)
Salvage	14 (60.9)	9 (39.1)	23 (0.004)
Facility Size			
Small	4 920 (91.8)	440 (8.2)	5 360 (0.9)
Medium	84 429 (91.4)	7 919 (8.6)	92 348 (15.8)
Large	460 734 (94.4)	27 190 (5.6)	487 924 (83.3)
Facility Level			
Primary	201 847 (96.5)	7 428 (3.5)	209 275 (35.7)
Secondary	284 415 (93.0)	21 275 (7.0)	305 690 (52.2)
Tertiary	63 821 (90.3)	6 846 (9.7)	70 667 (12.1)
Facility Ownership			
Private	31 279 (92.6)	2 486 (7.4)	33 765 (5.8)
Public	518 804 (94.0)	33 063 (6.0)	551 867 (94.2)
State			
Adamawa	38 183 (92.7)	3 020 (7.3)	41 203 (7.0)
Akwa Ibom	208 852 (96.9)	6 604 (3.1)	215 456 (36.8)
Bauchi	24 565 (93.8)	1 631 (6.2)	26 196 (4.5)
Bayelsa	11 046 (91.5)	1 025 (8.5)	12 071 (2.1)
Borno	14 595 (87.3)	2 122 (12.7)	16 717 (2.9)
Cross River	59 487 (95.4)	2 893 (4.6)	62 380 (10.7)
Edo	23 832 (87.3)	3 465 (12.7)	27 297 (4.7)
Jigawa	8 580 (88.8)	1 083 (11.2)	9 663 (1.7)
Kano	37 577 (92.8)	2 897 (7.2)	40 474 (6.9)
Kebbi	9 191 (98.4)	147 (1.6)	9 338 (1.6)
Kwara	8 308 (92.2)	705 (7.8)	9 013 (1.5)
Lagos	54 689 (92.2)	4 620 (7.8)	59 309 (10.1)
Niger	30 717 (90.2)	3 333 (9.8)	34 050 (5.8)
Sokoto	8 765 (92.3)	731 (7.7)	9 496 (1.6)
Yobe	7 032 (90.6)	730 (9.4)	7 762 (1.3)
Zamfara	4 664 (89.6)	543 (10.4)	5 207 (0.9)
Zone			
North-Central	39 025 (90.6)	4 038 (9.4)	43 063 (7.4)
North-East	84 375 (91.8)	7 503 (8.2)	91 878 (15.7)
North-West	68 777 (92.7)	5 401 (7.3)	74 178 (12.7)
South-South	303 217 (95.6)	13 987 (4.4)	317 204 (54.2)
South-West	54 689 (92.2)	4 620 (7.8)	59 309 (10.1)

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All factors used in the adjusted multivariable modified Poisson regression model were statistically significant, with a p-value below 0.05. Males (adjusted prevalence ratio [APR]=1.09, 95% CI: 1.06–1.11) were found to have 9% higher odds of being virally non-suppressed than females, however, the unadjusted modified Poisson regression did not identify a significant difference between the odds of viral non-suppression of females and males (Table 3). The adjusted model indicated that young people ages 0–24 were associated with higher likelihood of viral non-suppression compared with the 25–34 age group. Younger clients ages 0–14 years had the highest APR of viral non-suppression (APR = 2.38, 95% CI: 2.29–2.47).

Clients who started ART between 2010 and 2015 (APR = 6.19, CI: 5.9-6.51) had greater likelihood of viral non-suppression compared to clients that started before 2010 or after 2015. Compared with clients who were on ART for more than three years, those who were on treatment between 1 and 3 years had greater likelihood to be virally non-suppressed (APR=1.67, 95% CI: 1.62–1.72), whereas clients on ART for less than one year were found to have the greatest likelihood of viral non-suppression (APR=3.92, 95% CI: 3.77–4.08).

Clients receiving ARVs at tertiary health facilities were 68 % more likely to be virally non-suppressed (APR=1.68, 95% CI: 1.61 –1.76) than primary health facilities (Table 3). Moreover, clients receiving care at small (APR=1.63, 95% CI: 1.48–1.8) and medium (APR=1.47, 95% CI: 1.43–1.51) facilities were found to have the higher likelihood of viral non-suppression compared to large facilities. Clients receiving treatment at privately owned facilities (APR=0.87, CI: 0.84-0.91) had a lower likelihood of viral non-suppression than clients at publicly owned facilities.
Compared with the Akwa Ibom state, clients in the Edo (APR = 2.66, 95% CI: 2.54–2.79) and Niger (APR =2.54, 95% CI: 2.44–2.66) states had greater likelihood of VL non-suppression (Table 3). Clients in the Kebbi state had the lowest likelihood for VL non-suppression (APR = 0.34, 95% CI: 0.29–0.4).

Table 3. Factors associated with a non-suppressed viral load presented as unadjusted and adjusted prevalence ratios derived using modified Poisson regression. P-values were indicated when above 0.05.

	Univariable		Multivariable	
Factors	**UPR**	**p-value (<0.05)**	**APR**	**p-value (<0.05)**
Sex				
Female	1 [ref]		1 [ref]	
Male	1.01 [0.99 - 1.03]	0.51	1.09 [1.06 - 1.11]	
AgeGroup				
0-14	3.17 [3.05 - 3.29]		2.38 [2.29 - 2.47]	
15-24	1.27 [1.23 - 1.32]		1.29 [1.24 - 1.34]	
25-34	1 [ref]		1 [ref]	
35-44	0.99 [0.96 - 1.01]	0.31	0.86 [0.84 - 0.89]	
45-59	0.92 [0.89 - 0.95]		0.72 [0.7 - 0.75]	
60+	0.92 [0.87 - 0.98]		0.67 [0.63 - 0.72]	
ArtStartYear				
<2005	1.81 [1.28 - 2.55]		4.64 [3.27 - 6.59]	
[2005-2010)	2.32 [2.23 - 2.42]		5.34 [5.04 - 5.66]	
[2010-2015)	2.88 [2.78 - 2.97]		6.19 [5.9 - 6.51]	
[2015-2020)	2.42 [2.35 - 2.49]		4.08 [3.93 - 4.23]	
>2020	1 [ref]		1 [ref]	
Time On ART				
<1 year	0.79 [0.77 - 0.81]		3.92 [3.77 - 4.08]	
1-3 years	0.78 [0.76 - 0.8]		1.63 [1.58 - 1.69]	
3+ years	1 [ref]		1 [ref]	
Facility Size				
Small	1.47 [1.34 - 1.62]		1.63 [1.48 - 1.8]	
Medium	1.54 [1.5 - 1.58]		1.47 [1.43 - 1.51]	
Large	1 [ref]		1 [ref]	
Facility Level				
Primary	1 [ref]		1 [ref]	
Secondary	1.96 [1.91 - 2.01]		1.45 [1.4 - 1.49]	
Tertiary	2.73 [2.64 - 2.82]		1.68 [1.61 - 1.76]	
Facility Ownership				
Public	1 [ref]		1 [ref]	
Private	1.23 [1.18 - 1.28]		0.87 [0.84 - 0.91]	
State				
Adamawa	2.39 [2.29 - 2.5]		1.86 [1.78 - 1.94]	
Akwa Ibom	1 [ref]		1 [ref]	
Bauchi	2.03 [1.92 - 2.14]		1.56 [1.48 - 1.65]	
Bayelsa	2.77 [2.59 - 2.96]		2.02 [1.89 - 2.16]	
Borno	4.14 [3.94 - 4.35]		2.46 [2.33 - 2.6]	
Cross River	1.51 [1.45 - 1.58]		1.3 [1.24 - 1.36]	

Edo	4.14 [3.97 - 4.32]	2.66 [2.54 - 2.79]
Jigawa	3.66 [3.43 - 3.9]	2.19 [2.05 - 2.35]
Kano	2.34 [2.24 - 2.44]	1.55 [1.48 - 1.62]
Kebbi	0.51 [0.44 - 0.6]	0.34 [0.29 - 0.4]
Kwara	2.55 [2.36 - 2.76]	1.64 [1.51 - 1.77]
Lagos	2.54 [2.45 - 2.64]	1.98 [1.91 - 2.06]
Niger	3.19 [3.06 - 3.33]	2.54 [2.44 - 2.66]
Sokoto	2.51 [2.33 - 2.71]	1.69 [1.56 - 1.83]
Yobe	3.07 [2.84 - 3.31]	2.08 [1.92 - 2.25]
Zamfara	3.4 [3.12 - 3.71]	1.92 [1.76 - 2.11]

Some of the states such as Edo (766, 25.2%) and Borno (697, 26.3%), had the highest prevalence of VL non-suppression for clients on treatment less than one year (Table 4). However, those same states also had high prevalence of VL non-suppression of clients on ART for longer than three years. By contrast, Bayelsa had high prevalence of VL non-suppression for clients on ART for longer than one year.

Table 4. Cross table of the State variable by the number of years on ART.

	Years On ART [Non-suppressed/Total (%)]		
State	**<1 year**	**1-3 years**	**3+ years**
Akwa Ibom	2 566 / 86 893 (3)	2 180 / 87 555 (2.5)	1 858 / 41 008 (4.5)
Adamawa	762 / 8 207 (9.3)	713 / 8 490 (8.4)	1 545 / 24 506 (6.3)
Bauchi	451 / 6 935 (6.5)	321 / 4 001 (8)	859 / 15 260 (5.6)
Bayelsa	189 / 4 467 (4.2)	313 / 3 100 (10.1)	523 / 4 504 (11.6)
Borno	697 / 2 648 (26.3)	461 / 3 255 (14.2)	964 / 10 814 (8.9)
Cross River	627 / 14 601 (4.3)	866 / 22 022 (3.9)	1 400 / 25 757 (5.4)
Edo	766 / 3 045 (25.2)	727 / 5 145 (14.1)	1 972 / 19 107 (10.3)
Jigawa	173 / 1 075 (16.1)	241 / 1 965 (12.3)	669 / 6 623 (10.1)
Kano	372 / 5 171 (7.2)	662 / 6 956 (9.5)	1 863 / 28 347 (6.6)
Kebbi	29 / 1 842 (1.6)	34 / 2 279 (1.5)	84 / 5 217 (1.6)
Kwara	125 / 1 247 (10)	191 / 2 039 (9.4)	389 / 5 727 (6.8)
Lagos	1 038 / 15 290 (6.8)	1 193 / 11 901 (10)	2 389 / 32 118 (7.4)
Niger	955 / 10 923 (8.7)	792 / 6 695 (11.8)	1 586 / 16 432 (9.7)
Sokoto	130 / 1 674 (7.8)	193 / 2 198 (8.8)	408 / 5 624 (7.3)
Yobe	96 / 800 (12)	145 / 1 432 (10.1)	489 / 5 530 (8.8)
Zamfara	109 / 969 (11.2)	151 / 1 268 (11.9)	283 / 2 970 (9.5)

Discussion

Our study found that males, clients in younger age groups (0-24), those who started treatment before 2020, clients on treatment for less than one year, those receiving care at small and medium facilities, receiving care at secondary and tertiary level facilities, publicly owned facilities, and clients receiving care in the Edo, Niger and, Borno states had the highest association with VL non-suppression. Other studies have found similar results for the likelihood of viral non-suppression in younger age groups in Cambodia, Uganda, and South Carolina (USA) [6,8,17], and among males [18–20]. Our findings suggest that the health seeking behavior of certain demographics can be improved or given more attention to by HIV care programs. In that same regard, considerations should be given to the facility types, size, and public ownership.

The increased likelihood of viral non-suppression among ART clients who received treatment at tertiary health facilities have not been observed in Ethiopia where higher likelihood of viral non-suppression was associated with primary health facilities in Ethiopia [21]. Here, we found that small and medium facilities were associated with viral non-suppression of HIV clients on treatment and this was consistent with findings that clients were more likely to miss consecutive visits at lower volume facilities [22]. This could be due to smaller clinics being located within smaller communities, as a result, patients may avoid stigmatization within their community by not pick-up treatment as routinely as patients that attend clinics that are outside of their communities [22]. Such clients that would miss their drug pickup appointments more frequently to avoid stigma, are reasonably expected to have non-suppressed viral loads. A possible circumvention of the stigmatization within communities would be to offer clients a referral to HIV care facilities that are located outside of their communities. However, consideration should be given to the distance needed for travel as well because although a distance less than one kilometer to the clinic was associated with higher IIT in Rwanda [22], while mean distances above 4.7 km to clinics were associate with higher IIT in Malawi [23].

Clients that received care at privately owned facilities had lower likelihood of a non-suppressed VL when adjusting for the other variables included in the model. Nevertheless, another study had found that HIV care was of greater quality at public facilities than private in Anambra state in Nigeria [24]. This was also reflected in our unadjusted, univariable results.

ART clients who had their last VL test conducted within less than one year on treatment were less likely to be virally non-suppressed compared with clients who had their VL tested after one year on ART in the unadjusted model. Our finding was consistent with the Center for Disease Control and Prevention's finding that PLHIV on ART could be virally suppressed within six months of initiation, provided that they adhered to their medication [25]. Moreover, a greater likelihood of viral suppression was found among PLHIV who were on treatment for less than one year compared with those on ART for more than one year according to a study in Ethiopia [26]. This elucidates that clients more engaged in care can have more opportunities for non-suppressed viral load test results, though, this does not necessarily mean that this population is more likely to be non-suppressed. However, our adjusted model reflected the reverse, more specifically, a higher likelihood for clients on ART for less than 1 year to be virally non-suppressed. We attribute this to the high prevalence of virally non-suppressed clients in some of the states, such as Edo and Borno (Table 4). Similarly, a shorter time on ART was identified as a factor associated with a non-suppressed VL in South Africa [27]. This could suggest that although in general, clients on ART for longer than one year may need more attention, greater attention should be given to patients enrolled on ART for less than one year in states such as Edo and Borno, where non-suppression is more common in early initiates. Examples of interventions that could be implemented include enhanced/intensive adherence counselling, improved follow-up programs or more frequent follow-ups to perhaps cultivate a habit of adherence and retention in treatment, which could result in better viral load outcomes. The contradictory findings in the literature as well as those identified between the unadjusted and adjusted models could speak to the specific adherence patterns of the population investigated and models that may be specific to the study setting. Nevertheless, these findings motivate for support of newly enrolled clients, at least in some states, to develop treatment-adherence habits.

A possible explanation for the clients receiving care in the Kwara and Niger states in the North-Central zone having higher likelihood of viral non-suppression could be linked to health-seeking behavior such as non-use of the service, poor adherence to treatment, and possibly religious affiliation (for example Islamic religion predominant in northern Nigeria) where in certain circumstances women require permission to leave the premises of a household which can reduce

access to healthcare [28,29]. Community refills, regular visits from case managers, and enhanced adherence counselling could be implemented in such communities in a door-to-door manner, perhaps staffed by female health workers, to improve VL outcomes. On the other hand, in Borno and Yobe states in the North-East zone of Nigeria, the incessant insecurity in the region has largely led to people often been displaced and this has largely impacted on the health-seeking behavior,

One of the limitations of our study was the inaccessibility of the longitudinal data set. We were therefore restricted to conducting a cross-sectional study. The study cohort was composed of clients that received care at USAID-supported facilities, therefore, it may not be a true representation of the likelihood of VL non-suppression throughout the country. In facilities that support is better, the results here could overestimate the contribution of some of the factors to VL non-suppression. Vice-versa, where support is lacking, the contribution of some of the factors presented here on VL non-suppression could be underestimated.

It is possible that some of the 21.6% of client records (eliminated from analysis) without a VL test on record are a consequence of poor adherence to treatment which could lead to viral load non-suppression that is not tested/recorded. This assumption is based on the concept that patients need to attend clinic visits to either receive treatment or have their VL samples collected and tested. Investigating the factors that are associated with an untested viral load could provide useful insight. At the same time, longitudinal studies into both viral load non-testing and viral load non-suppression may ultimately be of greatest use. Additional variables relating to the capacity of clinical facilities to conduct testing would reveal whether the lack of viral load testing is also affected by a low capacity.

Other unavailable variables that could be explored in future studies to identify their association with viral suppression are tuberculosis status, adherence level, ART drug regimen, side-effects, IIT, marital status, and education level, however, these variables would need to be provided and analysed longitudinally. Ultimately, the factors reflected in this study may not be exhaustive. The absence of VL suppression data for recently initiated clients may have also had an impact on the study seeing that they had to be excluded, therefore only the results of tested patients could be analysed, leaving out the VL outcomes of those without a test.

Conclusions

Targeting males, those below 35 years of age, those who started treatment before 2020 and those on treatment for less than three years, receiving care at tertiary health facility, small and medium facilities, publicly owned, and in the Edo, Borno, and Niger states for interventions could lead to improvements in VL suppression in Nigeria. The independent factors associated here with a non-suppressed VL can guide the improvement of ART program development and VL suppression of PLHIV in Nigeria.

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Data Statement: The data that support the findings of this study are owned by the Government of Nigeria and were used under license for the current study. Access to these data is subject to restrictions owing to privacy and ethics policies set by the Government of Nigeria so are not publicly available. Requests to access these data should be directed to Dauda.Sulaiman@thepalladiumgroup.com.

Ethics approval

The study used secondary data. Ethical approvals for this study were obtained in Nigeria and the United States. Informed consent was waived from all subjects or, if subjects are under 18, from a parent and/or legal guardian by the expedited institutional review board (IRB) approvals granted by both the National Health Research Ethics Committee of Nigeria (NHREC), reference number NHREC/01/01/2007, and the HML IRB in the United States, reference number 772EQH20. Data were anonymized and handled confidentially during all phases of the research. All methods were carried out in accordance with relevant guidelines and regulations. All experimental protocols were granted approval by the institutional review board (IRB) of the National Health Research Ethics Committee of Nigeria (NHREC), reference number NHREC/01/01/2007, and the HML IRB in the United States, reference number 772EQH20.

List of abbreviations

AIC:	Akaike information criterion
APR:	Adjusted prevalence ratio
ART:	Antiretroviral therapy
ARV:	Antiretroviral
CI:	Confidence interval
Data.FI:	Data for Implementation
EMR:	Electronic medical records
FMOH:	Federal Ministry of health
HFR:	Health facility registry
HIV:	Human immunodeficiency virus
IIT:	Interruption in treatment
IP:	Implementing partner

MMD: Multi-month dispensing

PEPFAR: United States President's Emergency Plan for AIDS Relief

PLHIV: People living with HIV

RADET: Retention audit determination tool

UNAIDS: Joint United Nations Programme on HIV/AIDS

UPR: Unadjusted prevalence ratio

USAID: United States Agency for International Development

VL: Viral load

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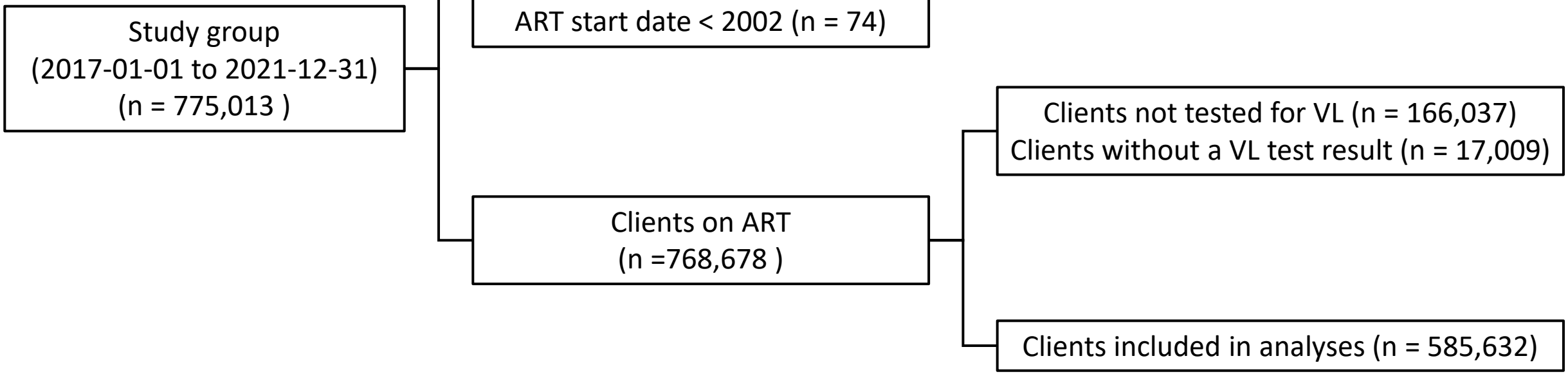
Study group
(2017-01-01 to 2021-12-31)
(n = 775,013)
Duplicate records (n = 5,973)
ART start date < DOB (n = 48)
Last pickup date < DOB (n = 240)
ART start date < 2002 (n = 74)
Clients on ART
(n =768,678)
Clients not tested for VL (n = 166,037)
Clients without a VL test result (n = 17,009)
Clients included in analyses (n = 585,632)

Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cross sectionalreporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary	3

		of what was done and what was found	
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	#3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	#4	Present key elements of study design early in the paper	5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants.	5-8
	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	5-6
Bias	#9	Describe any efforts to address potential sources of bias	7-8
Study size	#10	Explain how the study size was arrived at	6

Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	6-7
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	7-8
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	7-8
Statistical methods	#12c	Explain how missing data were addressed	6
Statistical methods	#12d	If applicable, describe analytical methods taking account of sampling strategy	6
Statistical methods	#12e	Describe any sensitivity analyses	8
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	6,10
Participants	#13b	Give reasons for non-participation at each stage	6
Participants	#13c	Consider use of a flow diagram	6
Descriptive data	#14a	Give characteristics of study participants (eg demographic,	10

		clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	5
Outcome data	#15	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	10
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-14
Main results	#16b	Report category boundaries when continuous variables were categorized	6-7
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	14
Discussion			
Key results	#18	Summarise key results with reference to study objectives	15
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	17

Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	15-17
Generalisability	#21	Discuss the generalisability (external validity) of the study results	17

Other Information

Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18