

# THE LANCET

## Global Health

### Supplementary appendix

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**Table S1. Analysis of Exclusions.**

Variable	Unit	Excluded*	Included	P value
N		88,837*	402,668	
Male sex	No. (% , 95% CI)	32,839 (37.0, 36.6–37.3)	129,620 (32.2, 32.0–32.3)	0.059
Age	Median (IQR)	33 (28–40)	34 (28–41)	0.64
State	No. (% , 95% CI)			<0.0001
	Benue	11,144 (12.5, 12.3–12.8)	100,569 (25.0, 24.8–25.1)	
	Delta	3,393 (3.8, 3.7–3.9)	14,906 (3.7, 3.6–3.8)	
	Ekiti	243 (0.3, 0.2–0.3)	2,269 (0.6, 0.5–0.6)	
	Enugu	5,490 (6.2, 6.0–6.3)	15,577 (3.9, 3.8–3.9)	
	FCT	9,598 (10.8, 10.6–11.0)	32,964 (8.2, 8.1–8.3)	
	Gombe	2,754 (3.1, 3.0–3.2)	11,251 (2.8, 2.7–2.8)	
	Imo	6,562 (7.4, 7.2–7.6)	11,227 (2.8, 2.7–2.8)	
	Kaduna	1,859 (2.1, 2.0–2.2)	22,759 (5.7, 5.6–5.7)	
	Katsina	464 (0.5, 0.5–0.6)	4,686 (1.2, 1.1–1.2)	
	Kogi	1,122 (1.3, 1.2–1.3)	8,256 (2.1, 2.0–2.1)	
	Lagos	6,033 (6.8, 6.6–7.0)	30,994 (7.7, 7.6–7.8)	
	Nasarawa	6,419 (7.2, 7.1–7.4)	25,047 (6.2, 6.1–6.3)	
	Ogun	1,575 (1.8, 1.7–1.9)	10,713 (2.7, 2.6–2.7)	
	Ondo	784 (0.9, 0.8–0.9)	6,651 (1.7, 1.6–1.7)	
	Osun	508 (0.6, 0.5–0.6)	4,539 (1.1, 1.1–1.2)	
	Oyo	1,688 (1.9, 1.8–2.0)	11,473 (2.8, 2.8–2.9)	
	Plateau	2,125 (2.4, 2.3–2.5)	14,443 (3.6, 3.5–3.6)	
	Rivers	27,076 (30.5, 30.2–30.8)	74,344 (18.5, 18.3–18.6)	

Demographic differences between included and excluded patients; age was analyzed using Wilcoxon rank-sum test

for clustered data. Categorical variables were analyzed using Rao-Scott  $\chi^2$  test.

\* Patients younger than 18 or older than 99 (n = 29,707) were not included due to exclusion based on age.

**Table S2. Low-Level Viremia and Subsequent Virologic Non-Suppression or Virologic Failure.**

	≥1 VL Result in Reference Range	≥1 Subsequent VL after Reference Result	Subsequent Virologic Suppression ≤50 cp/mL	Subsequent Virologic Non-Suppression	≥2 Subsequent VL after Reference Result	Subsequent Virologic Failure
<b>Reference Range</b>						
≤50 cp/mL	190,639 (96.4)	175,626 (92.1)	151,512 (86.3)	13,894 (7.9)	97,674 (51.2)	1,426 (1.5)
LLV 51–999 cp/mL	69,405 (35.1)	55,161 (79.5)	43,436 (78.7)	5,595 (10.1)	29,958 (43.2)	819 (2.7)
51–199	50,039 (25.3)	38,410 (76.8)	29,524 (76.9)	3,282 (8.5)	20,398 (40.8)	430 (2.1)
200–399	14,601 (7.4)	10,989 (75.3)	7,656 (69.7)	1,091 (9.9)	6,034 (41.3)	171 (2.8)
400–999	13,552 (6.9)	10,261 (75.7)	6,970 (67.9)	1,287 (12.5)	5,524 (40.8)	219 (4.0)
≥1,000 cp/mL	19,199 (9.7)	11,399 (59.4)	7,862 (69.0)	2,232 (19.6)	--	--
All Ranges	--	197,729	--	19,199 (9.7)	112,316 (56.8)	2,232 (2.0)

Virologic non-suppression defined as ≥1,000 cp/mL at the next VL result following the relevant VL result; VF

defined as two consecutive non-suppressed results following the relevant VL result. LLV=low-level viremia.

VF=virologic failure. cp/mL=copies/mL. VL=viral load.

**Table S3. Prevalence of Virologic Suppression, Low-Level Viremia, and Virologic Non-Suppression at First Viral Load  $\geq$ 24 Weeks after ART Initiation.**

Age at ART initiation—yr	Virologic Suppression $\leq$ 50 cp/mL, no. (%)	LLV 51–199 cp/mL, no. (%)	LLV 200–399 cp/mL, no. (%)	LLV 400–999 cp/mL, no. (%)	LLV 51–999 cp/mL, no. (%)	VLNS $\geq$ 1,000 cp/mL, no. (%)
<b>First- and Second-Line ART: Males and Females (n = 402,668)</b>						
Total	292,137 (72.6)	40,830 (10.1)	11,767 (2.9)	11,883 (3.0)	64,480 (16.0)	46,051 (11.4)
<b>First-Line: Males and Females (n = 399,684, 99.3%)</b>						
18-19 (n=7,065)	4,953 (70.1)	704 (10.0)	205 (2.9)	227 (3.2)	1,136 (16.1)	976 (13.8)
20-29 (n=116,524)	86,279 (74.0)	10,716 (9.2)	3,144 (2.7)	3,328 (2.9)	17,188 (14.8)	13,057 (11.2)
30-39 (n=150,320)	109,391 (72.8)	14,771 (9.8)	4,332 (2.9)	4,352 (2.9)	23,455 (15.6)	17,474 (11.6)
40-49 (n=81,842)	58,547 (71.5)	9,007 (11.0)	2,520 (3.1)	2,469 (3.0)	13,996 (17.1)	9,299 (11.4)
50-999 (n=43,933)	31,271 (71.2)	5,240 (11.9)	1,445 (3.3)	1,372 (3.1)	8,057 (18.3)	4,605 (10.5)
Total (n=399,684)	290,441 (72.7)	40,438 (10.1)	11,646 (2.9)	11,748 (2.9)	63,832 (16.0)	45,411 (11.4)
<b>First-line: Males (n = 128,633, 32.2%)</b>						
18-19 (n=1,959)	1,416 (72.3)	225 (11.5)	52 (2.7)	52 (2.7)	329 (16.8)	214 (10.9)
20-29 (n=28,504)	21,696 (76.1)	2,741 (9.6)	709 (2.5)	766 (2.7)	4,216 (14.8)	2,592 (9.1)
30-39 (n=45,688)	32,460 (71.0)	5,202 (11.4)	1,437 (3.1)	1,381 (3.0)	8,020 (17.6)	5,208 (11.4)
40-49 (n=34,165)	23,712 (69.4)	4,155 (12.2)	1,111 (3.3)	1,037 (3.0)	6,303 (18.4)	4,150 (12.1)
50-999 (n=18,317)	12,622 (68.9)	2,368 (12.9)	650 (3.5)	573 (3.1)	3,591 (19.6)	2,104 (11.5)
Total (n=128,633)	91,906 (71.4)	14,691 (11.4)	3,959 (3.1)	3,809 (3.0)	22,459 (17.5)	14,268 (11.1)
<b>First-line: Females (n=271,051, 67.8%)</b>						
18-19 (n=5,106)	3,537 (69.3)	479 (9.4)	153 (3.0)	175 (3.4)	807 (15.8)	762 (14.9)
20-29 (n=88,020)	64,583 (73.4)	7,975 (9.1)	2,435 (2.8)	2,562 (2.9)	12,972 (14.7)	10,465 (11.9)
30-39 (n=104,632)	76,931 (73.5)	9,569 (9.1)	2,895 (2.8)	2,971 (2.8)	15,435 (14.8)	12,266 (11.7)
40-49 (n=47,677)	34,835 (73.1)	4,852 (10.2)	1,409 (3.0)	1,432 (3.0)	7,693 (16.1)	5,149 (10.8)
50-999 (n=25,616)	18,649 (72.8)	2,872 (11.2)	795 (3.1)	799 (3.1)	4,466 (17.4)	2,501 (9.8)
Total (n=271,051)	198,535 (73.2)	25,747 (9.5)	7,687 (2.8)	7,939 (2.9)	41,373 (15.3)	31,143 (11.5)
<b>Second-line: Males and Females (n=2,984, 0.7%)</b>						
18-19 (n=58)	31 (53.4)	6 (10.3)	1 (1.7)	2 (3.4)	9 (15.5)	18 (31.0)
20-29 (n=437)	242 (55.4)	57 (13.0)	10 (2.3)	21 (4.8)	88 (20.1)	107 (24.5)
30-39 (n=1,088)	597 (54.9)	137 (12.6)	51 (4.7)	46 (4.2)	234 (21.5)	257 (23.6)
40-49 (n=895)	514 (57.4)	117 (13.1)	37 (4.1)	41 (4.6)	195 (21.8)	186 (20.8)
50-999 (n=506)	312 (61.7)	75 (14.8)	22 (4.3)	25 (4.9)	122 (24.1)	72 (14.2)
Total (n=2,984)	1,696 (56.8)	392 (13.1)	121 (4.1)	135 (4.5)	648 (21.7)	640 (21.4)
<b>Second-line: Males (n=987, 33.1%)</b>						
18-19 (n=26)	14 (53.8)	4 (15.4)	0 (0.0)	0 (0.0)	4 (15.4)	8 (30.8)
20-29 (n=98)	48 (49.0)	15 (15.3)	2 (2.0)	4 (4.1)	21 (21.4)	29 (29.6)
30-39 (n=239)	125 (52.3)	34 (14.2)	7 (2.9)	9 (3.8)	50 (20.9)	64 (26.8)
40-49 (n=351)	187 (53.3)	47 (13.4)	17 (4.8)	15 (4.3)	79 (22.5)	85 (24.2)
50-999 (n=273)	150 (54.9)	49 (17.9)	14 (5.1)	15 (5.5)	78 (28.6)	45 (16.5)
Total (n=987)	524 (53.1)	149 (15.1)	40 (4.1)	43 (4.4)	232 (23.5)	231 (23.4)
<b>Second-line: Females (n=1,997, 66.9%)</b>						
18-19 (n=32)	17 (53.1)	2 (6.2)	1 (3.1)	2 (6.2)	5 (15.6)	10 (31.2)
20-29 (n=339)	194 (57.2)	42 (12.4)	8 (2.4)	17 (5.0)	67 (19.8)	78 (23.0)
30-39 (n=849)	472 (55.6)	103 (12.1)	44 (5.2)	37 (4.4)	184 (21.7)	193 (22.7)
40-49 (n=544)	327 (60.1)	70 (12.9)	20 (3.7)	26 (4.8)	116 (21.3)	101 (18.6)
50-999 (n=233)	162 (69.5)	26 (11.2)	8 (3.4)	10 (4.3)	44 (18.9)	27 (11.6)
Total (n=1,997)	1,172 (58.7)	243 (12.2)	81 (4.1)	92 (4.6)	416 (20.8)	409 (20.5)

First VL result on first- or second-line regimens  $\geq$ 24 weeks after ART initiation. ART=antiretroviral therapy. cp/mL=

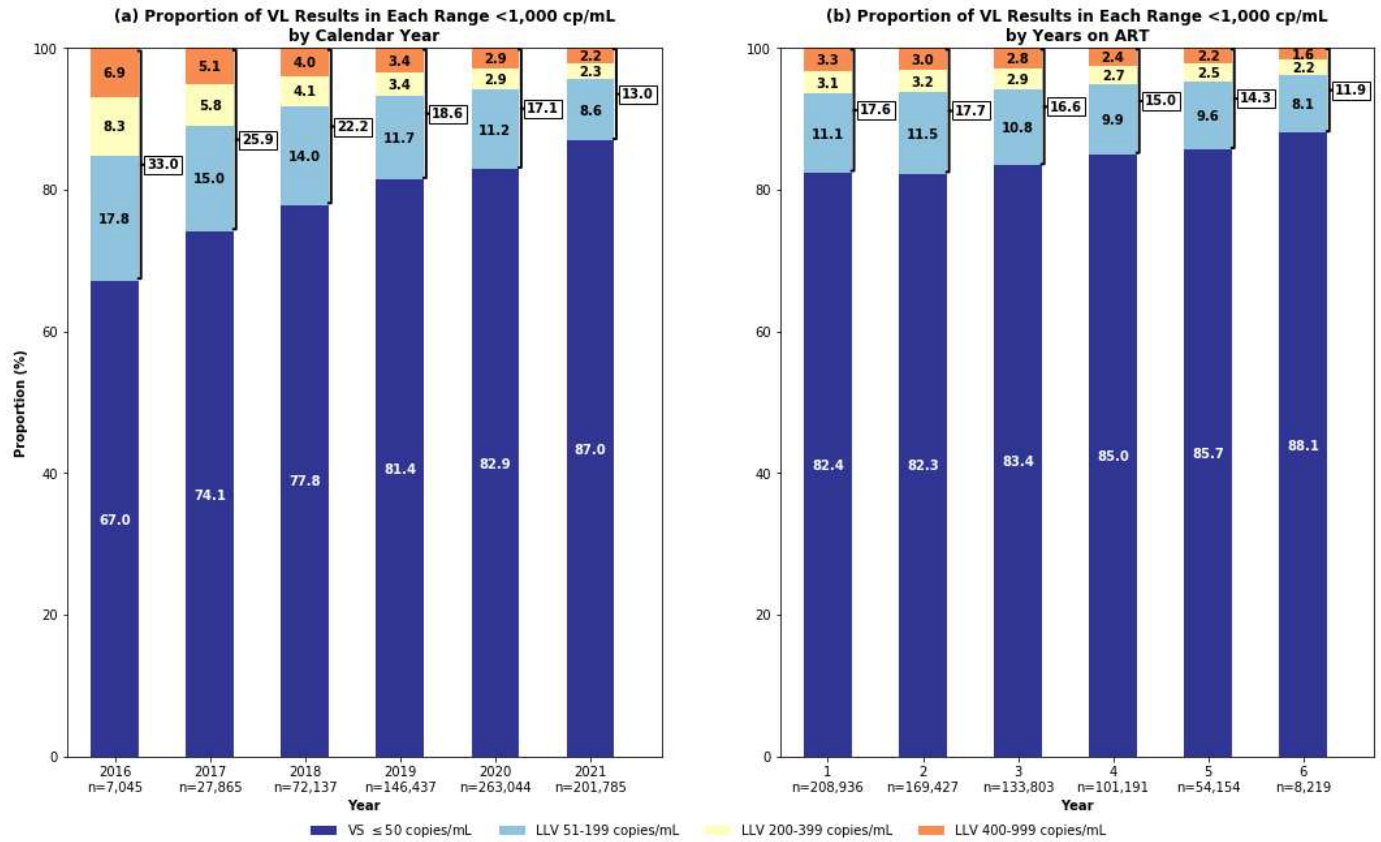
copies/mL. LLV=low-level viremia. VS=virologic suppression. VLNS=virologic non-suppression.

**Table S4.** Proportion (%) of Patients in Each Low-Level Viremia Range Among All Patients with Results in the Low-Level Viremia Range 51–999 copies per mL.

	<b>51–199 copies/mL</b>	<b>200–399 copies/mL</b>	<b>400–999 copies/mL</b>
<b>2016</b>	54.0	25.1	20.8
<b>2017</b>	57.9	22.6	19.5
<b>2018</b>	63.3	18.7	18.0
<b>2019</b>	63.1	18.6	18.3
<b>2020</b>	65.9	17.0	17.1
<b>2021</b>	65.9	17.3	16.8

cp/mL= copies/mL. LLV=low-level viremia.

**Figure S1. Viral Load Ranges Less Than 1,000 Copies/mL as a Proportion of All Viral Loads Less Than 1,000 Copies/mL, by Calendar Year and Years on ART\*.**



ART=antiretroviral therapy. cp/mL= copies/mL. LLV=low-level viremia. VS=virologic suppression.

\* Proportions were calculated using the first VL result of every year in order to avoid bias from repeated measurements within 1 year.

**Table S5. Unadjusted and Adjusted Relative Risks of Low-Level Viremia Among Patients on First-Line ART.**

	Log-binomial regression			
	Unadjusted RR (95% CI)	P value	Adjusted RR (95% CI)	P value
<b>Sex: male</b>	1.12 (1.06– 1.19)	0.0002	1.14 (1.10– 1.18)	<0.0001
<b>Age at ART initiation</b>				
<b>18–19</b>	0.89 (0.81– 0.97)	0.0094	0.93 (0.86– 1.00)	0.063
<b>20–29</b>	0.87 (0.83– 0.91)	<0.0001	0.90 (0.86– 0.93)	<0.0001
<b>30–39</b>	0.92 (0.89– 0.95)	<0.0001	0.93 (0.90– 0.96)	<0.0001
<b>40–49</b>	0.98 (0.96– 1.01)	0.11	0.98 (0.96– 1.00)	0.062
<b>≥50</b>	ref		ref	
<b>Initiated on DTG-based ART</b>	0.78 (0.74– 0.83)	<0.0001	0.83 (0.80– 0.87)	<0.0001
<b>Time on ART, years</b>	1.10 (1.08– 1.13)	<0.0001	1.07 (1.06– 1.09)	<0.0001
<b>First VL ≥12 months after ART initiation</b>	0.97 (0.92– 1.03)	0.31	--	--
<b>Documented dispense ratio ≥51%</b>	0.97 (0.94– 0.99)	0.022	1.03 (0.99– 1.05)	0.065

Log-binomial regression analysis, unadjusted and adjusted relative risks. Confidence intervals were calculated with cluster-robust standard errors to account for clustering at the facility level.

ART=antiretroviral therapy. cp/mL= copies/mL. CI=confidence interval. RR= relative risk. LLV=low-level viremia.

VS=virologic suppression. VLNS=virologic non-suppression.



**Table S6. Adjusted Relative Risks of Virologic Non-Suppression and Virologic Failure Among Patients on First-Line ART, with LLV and INSTI Exposure Treated as Dichotomous Variables.**

Variable	Virologic Non-Suppression		Virologic Failure	
	Adjusted RR (95% CI)	P value	Adjusted RR (95% CI)	P value
Male sex	1.05 (1.01–1.10)	0.041	1.07 (0.97–1.19)	0.18
Age at ART initiation - yr				
18–19	1.29 (1.14–1.46)	<0.0001	1.71 (1.23–2.38)	0.0014
20–29	1.17 (1.09–1.25)	<0.0001	1.30 (1.10–1.55)	0.0024
30–39	1.13 (1.06–1.19)	<0.0001	1.22 (1.04–1.42)	0.013
40–49	1.04 (0.98–1.10)	0.17	1.05 (0.91–1.22)	0.50
≥50	ref	--		
Time on ART - yr	1.30 (1.26–1.34)	<0.0001	1.22 (1.14–1.30)	<0.0001
First VL ≥12 months after ART initiation	0.70 (0.67–0.74)	<0.0001	0.67 (0.59–0.76)	<0.0001
Documented dispense ratio ≥51%	--	--	0.85 (0.74–0.96)	0.012
INSTI exposure (cumulative)	0.73 (0.68–0.79)	<0.0001	0.40 (0.35–0.47)	<0.0001
LLV (51–999 cp/mL) at first VL result	1.61 (1.55–1.67)	<0.0001	2.20 (1.98–2.43)	<0.0001

Log-binomial analysis and adjusted relative risks using first on-treatment viral load after at least 24 weeks of ART.

Confidence intervals were calculated using cluster-robust standard errors to account for clustering at the facility level. Only patients with 3 or more VL measurements (n=112,316) were included in analysis of virologic failure, defined as 2 consecutive VL results ≥1,000 cp/mL.

**Table S7. Viral Load Results Preceding Virologic Non-Suppression and Virologic Failure**

	Range of Preceding Viral Load Result*				
	Virologic Suppression ≤50 cp/mL, no. (%)	LLV 51–199 cp/mL, no. (%)	LLV 200–399 cp/mL, no. (%)	LLV 400–999 cp/mL, no.(%)	LLV 51–999 cp/mL, no. (%)
Experienced VLNS (n=19,199, 9.7%)	13,752 (71.6)	3,172 (16.5)	1,040 (5.4)	1,235 (6.4)	5,447 (28.4)
Experienced VF (n=2,232, 2.0%)	1,419 (63.6)	425 (19.0)	169 (7.6)	219 (9.8)	813 (36.4)

Analysis of virologic non-suppression included all patients who met outcomes analysis inclusion criteria

(n=197,729); analysis of virologic failure only included patients who met these criteria and who had ≥3 VL results

(n=112,316).

LLV=low-level viremia. VLNS= virologic non-suppression. VF= virologic failure. cp/mL=copies/mL.

\*For patients who experienced virologic failure, the VL result shown is that preceding the first of the two non-suppressed measurements

**Table S8. Unadjusted and Adjusted Relative Risks of Virologic Suppression and Virologic Failure Following Virologic Non-Suppression.**

	Virologic Suppression ≤50 cp/mL (n=7,862)				Virologic Failure (n=2,232)			
	Unadjusted RR (95% CI)	P value	Adjusted RR (95% CI)	P value	Unadjusted RR (95% CI)	P value	Adjusted RR (95% CI)	P value
<b>Sex: male</b>	0.93 (0.90–0.97)	0.0005	0.94 (0.91–0.98)	0.0028	1.04 (0.95–1.13)	0.40	--	--
<b>Age at ART initiation - yr</b>								
<b>18–19</b>	0.99 (0.87–1.12)	0.84	--	--	1.37 (1.05–1.78)	0.019	1.37 (1.05–1.78)	0.021
<b>20–29</b>	1.02 (0.96–1.08)	0.56	--	--	1.08 (0.94–1.24)	0.27	1.07 (0.93–1.23)	0.34
<b>30–39</b>	1.00 (0.95–1.06)	0.99	--	--	1.06 (0.93–1.21)	0.40	1.05 (0.92–1.20)	0.49
<b>40–49</b>	1.02 (0.97–1.08)	0.46	--	--	0.98 (0.85–1.12)	0.77	0.97 (0.84–1.11)	0.66
<b>≥50</b>	ref	--	--	--	ref	--	ref	--
<b>Time on ART - yr</b>	1.00 (0.98–1.01)	0.68	--	--	1.02 (0.98–1.06)	0.35	--	--
<b>First VL ≥12 months after ART initiation</b>	1.05 (1.02–1.09)	0.0033	1.03 (1.00–1.07)	0.045	0.92 (0.85–1.00)	0.056	0.93 (0.85–1.01)	0.085
<b>Documented dispense ratio ≥51%</b>	1.02 (0.99–1.06)	0.22	--	--	0.89 (0.81–0.99)	0.028	0.92 (0.84–1.02)	0.10
<b>On DTG-based ART at time of VLNS</b>	1.12 (1.08–1.16)	<0.0001	1.11 (1.07–1.14)	<0.0001	0.75 (0.68–0.82)	<0.0001	0.76 (0.70–0.83)	<0.0001
<b>LLV 51–999 at first VL</b>	0.82 (0.79–0.85)	<0.0001	0.83 (0.80–0.86)	<0.0001	1.34 (1.22–1.47)	<0.0001	1.32 (1.21–1.44)	<0.0001

Factors associated with virologic suppression ≤50 cp/mL and virologic failure following an episode of virologic non-suppression, patients with ≥1 VL after VLNS result only (n=11,399).

VL=viral load. INSTI=integrase strand transfer inhibitor. LLV=low-level viremia. VLNS=virologic non-suppression.

cp/mL=copies/mL. RR=relative risk.

**Table S9. Nigeria Low-Level Viremia Investigation Group**

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