

# Viral suppression in the era of transition to dolutegravir-based therapy in Cameroon

## Children at high risk of virological failure due to the lowly transition in pediatrics

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### Abstract

This study aimed to compare viral suppression (VS) between children, adolescents, and adults in the frame of transition to dolutegravir (DTG)-based antiretroviral therapy (ART) in the Cameroonian context. A comparative cross-sectional study was conducted from January 2021 through May 2022 amongst ART-experienced patients received at the Chantal BIYA International Reference Centre in Yaounde-Cameroon, for viral load (VL) monitoring. VS was defined as VL < 1000 copies/mL and viral undetectability as VL < 50 copies/mL. Chi-square and multivariate binary logistic regression models were used to identify factors associated with VS. Data were analyzed using SPSS v.20.0 (SPSS Inc., Chicago, Illinois), with  $P < .05$  considered significant. A total of 9034 patients (72.2% females) were enrolled. In all, there were 8585 (95.0%) adults, 227 (2.5%) adolescents, and 222 (2.5%) children; 1627 (18.0%) were on non-nucleoside reverse transcriptase-based, 290 (3.2%) on PI-based, and 7117 (78.8%) on DTG-based ART. Of those on DTG-based ART, only 82 (1.2%) were children, 138 (1.9%) adolescents, and 6897 (96.9%) adults. Median (interquartile range) duration on ART was 24 (12–72) months (24 months on Tenofovir + Lamivudine + Dolutegravir [TLD], 36 months on other first lines, and 84 months on protease inhibitors boosted with ritonavir-based regimens). Overall, VS was 89.8% (95% confidence interval: 89.2–90.5) and viral undetectability was 75.7% (95% confidence interval: 74.8–76.7). Based on ART regimen, VS on Non-nucleoside reverse transcriptase-based, protease inhibitors boosted with ritonavir-based, and DTG-based therapy was respectively 86.4%, 59.7%, and 91.8%,  $P < .0001$ . Based on ART duration, VS was respectively 51.7% ( $\leq 24$  months) versus 48.3% ( $\geq 25$  months),  $P < .0001$ . By gender, VS was 90.9% (5929) in females versus 87.0% (2183) in males,  $P < .0001$ ; by age-range, VS moved from 64.8% (144) in children, 74.4% (169) adolescents, to 90.8% (7799) adults,  $P < .0001$ . Following multivariate analysis, VS was associated with adulthood, female gender, TLD regimens, and combination antiretroviral therapy duration > 24 months ( $P < .05$ ). In Cameroon, ART response indicates encouraging rates of VS (about 9/10) and viral undetectability (about 3/4), driven essentially by access to TLD based regimens. However, ART response was very poor in children, underscoring the need for scaling-up pediatric DTG-based regimens.

**Abbreviations:** 3TC = lamivudine, ART = antiretroviral therapy, CIRCB = Chantal BIYA International Reference Centre for research on HIV/AIDS prevention and management, DTG = dolutegravir, IQR = interquartile range, NNRTI = non-nucleoside reverse transcriptase, RLS = resource-limited settings, SSA = Sub-Saharan Africa, TDF = tenofovir disoproxil fumarate, TLD = Tenofovir + Lamivudine + Dolutegravir, UNAIDS = joint united nations programme on HIV/AIDS, VL = viral load, VS = viral suppression, WHO = World Health Organization.

**Keywords:** ART duration, Cameroon, dolutegravir, HIV, viral suppression

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The authors have no conflicts of interest to disclose.

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## 1. Introduction

HIV infection remains a global health concern, especially in Sub-Saharan Africa (SSA) where about 2/3 of the world's epidemiological burden is concentrated.<sup>[1]</sup> Despite efforts made to fight the disease, AIDS has caused over 35 million deaths, with SSA being highly affected (about 27 million deaths) according to the world health organization.<sup>[2]</sup> To reduce the global incidence of HIV and its associated morbidity/mortality, World Health Organization consolidated guidelines on the use of antiretroviral drugs for HIV treatment and prevention are recommended for resource-limited settings (RLS) such as SSA.<sup>[3]</sup> In these settings, combination antiretroviral therapies (ART) are available as first, second and third-line regimens, with a transition to dolutegravir (DTG)-based therapy as a first-line regimen in several countries, including Cameroon where the transition was launched in 2020.<sup>[4]</sup>

The ambitious 95-95-95 target of the Joint United Nations Programme on HIV/AIDS (UNAIDS) to eliminate AIDS calls for 95% of all people living with HIV to know their HIV status, 95% of all people with diagnosed HIV infection to receive sustained ART, and 95% of all people receiving ART to have viral suppression (VS) by 2025.<sup>[2,5]</sup> Achieving these targets remains challenging for most RLS like Cameroon due to the suboptimal healthcare systems, characterized by frequent drug stockouts, use of drugs with a poor genetic barrier to resistance, poor viral load coverage, and high rate of attrition or nonadherence to ART.<sup>[6]</sup> Of note, at the end of 2020, 81% of infected people knew their HIV status, 67% of those diagnosed were receiving ART, and 73% of patients on ART had achieved VS.<sup>[7]</sup> Despite the progress recorded by then, the performance was below the expected targets of 90-90-90 for 2020.<sup>[7]</sup>

Based on evidence from pretreatment HIV drug resistance surveillance surveys (i.e., critical threshold of 10%), current first-line ART regimens in most RLS consist of tenofovir disoproxil fumarate (TDF), lamivudine (3TC) and efavirenz combination referred to as Tenofovir + Lamivudine + Efavirenz,<sup>[8]</sup> and/or TDF, 3TC and DTG combination referred to as Tenofovir + Lamivudine + Dolutegravir (TLD).<sup>[9,10]</sup> Furthermore, TLD is also recommended for use as a second-line regimen for patients failing on efavirenz- or nevirapine-containing first-line regimens or any other non-DTG-containing first-line regimen. Of note, supportive evidence underscore the use of TLD as preferred first-line ART due to its high potency (rapid tailoring of viral load [VL]),<sup>[9]</sup> its higher genetic barrier to resistance (requires 3–4 the emergence of drug resistance mutations) compared to non-nucleoside reverse transcriptase (NNRTIs) (1 drug resistance mutation) and first-generation integrase-strand transfer inhibitors. Regarding drug intake, TLD appears more convenient and associated with fewer drug interactions.<sup>[9]</sup> Thus, the ongoing transition to TLD may represent a game changer in the ART paradigm of RLS, thereby suggesting the need for

investigations in real-life conditions, in order to design interventions for ART optimization in the entire target population (children, adolescents and adults) living in these settings.

In Cameroon, a study conducted in 2019 revealed challenges in achieving the third UNAIDS target (about 80% overall VS), with very poor response in the population of adolescents (about 50% VS rate only).<sup>[4]</sup> This highlights gaps in achieving the previously set 90% target by 2020 in Cameroon, which might constraint programmatic efforts in reaching the expected 95% targets by 2025.<sup>[2,5]</sup> This prompts the need to closely monitor response to treatment in the course of transitioning to TLD at country level. Since the transition to TLD in 2020, little is known about the use of TLD in different target populations and the response to TLD as compared to other recommended regimens used in the national ART program in Cameroon. Data availability on patients who are virally suppressed and those who had attained viral undetectability are scarce. As such, strides aimed at achieving the 3<sup>rd</sup> 95% UNAIDS target by 2025 to curb the transmission of HIV infection at population-level cannot be adequately assessed. With the advent of DTG-containing regimens and the frame of wide transition to these new regimens, we sought to investigate the proportions of VS and viral undetectability among HIV-infected children, adolescents, and adults receiving ART in Cameroon, and to determine factors associated with virological response taking into account age-range, gender, ART regimens, and duration on ART.

## 2. Methods

### 2.1. Study design

A comparative cross-sectional study was conducted among, children (0–9 years), adolescents (10–19 years), and adults (≥ 20 years) routinely monitored for viral load at the Chantal BIYA International Reference Centre for research on HIV/AIDS prevention and management (CIRCB) in Yaounde, Cameroon. Data was queried from the institutional database from January 2021 to May 2022. This study period was purposely selected to match with the effective scale-up of “TLD” as the preferred first-line regimen at national-level.”

### 2.2. Description of the study site

CIRCB is one of the main national reference laboratories designated by the Ministry of Public Health on the management and prevention of HIV/AIDS, with a focus on, but not limited to, HIV confirmatory diagnosis, viral load measurements, CD4 count, HIV DR genotypic testing, HIV early infant diagnosis, as well as complementary HIV/AIDS biochemical and haematological analyses. CIRCB participates in HIV/AIDS external quality assurance programs ([http://circb.cm/btc\\_circb/web/](http://circb.cm/btc_circb/web/)).

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**Table 1****Population characteristics according to ART combination.**

| Variable                                | Overall†<br>N = 9034 | TDF + 3TC + DTG‡<br>N = 7117 (78.8) | Other 1st line ARV‡<br>N = 1627 (18.0) | ATVr or LPVr Based ARV‡<br>N = 290 (3.2) | P value* |
|-----------------------------------------|----------------------|-------------------------------------|----------------------------------------|------------------------------------------|----------|
| Gender, n (%)                           |                      |                                     |                                        |                                          |          |
| Male                                    | 2508 (27.8)          | 2003 (79.9)                         | 386 (15.4)                             | 119 (4.7)                                | <.0001   |
| Female                                  | 6526 (72.2)          | 5114 (78.4)                         | 1241 (19.0)                            | 171 (2.6)                                |          |
| Age in yr, median (IQR)                 | 39 (32–48)           | 40 (32–48)                          | 37 (29–46)                             | 38 (17–48)                               | <.0001   |
| Age groups, n (%)                       |                      |                                     |                                        |                                          |          |
| Children                                | 222 (2.5)            | 82 (36.9)                           | 85 (38.3)                              | 55 (24.8)                                |          |
| Adolescents                             | 227 (2.5)            | 138 (60.8)                          | 58 (25.5)                              | 31 (13.7)                                | <.0001   |
| Adults                                  | 8585 (95.0)          | 6897 (80.3)                         | 1484 (17.3)                            | 204 (2.4)                                |          |
| Duration on cART in month, median (IQR) | 24 (12–72)           | 24 (12–72)                          | 36 (12–72)                             | 84 (24–156)                              | <.0001   |
| Duration on cART in mo                  |                      |                                     |                                        |                                          |          |
| 6–12                                    | 4013 (44.4)          | 3271 (81.5)                         | 672 (16.7)                             | 70 (1.7)                                 | <.0001   |
| 13–24                                   | 655 (7.3)            | 522 (79.7)                          | 123 (18.8)                             | 10 (1.5)                                 |          |
| 25–36                                   | 672 (7.4)            | 553 (82.3)                          | 105 (15.6)                             | 14 (2.1)                                 |          |
| ≥ 48                                    | 3694 (40.9)          | 2771 (75.0)                         | 727 (19.7)                             | 196 (5.3)                                |          |

Other first-line ARV [ABC + 3TC + EFV (n = 13), ABC + 3TC + NVP (n = 2), AZT + 3TC + EFV (n = 36), AZT + 3TC + NVP (n = 14), TDF + 3TC + NVP (n = 51), TDF + 3TC + EFV (1511)], dLopinavir based (n = 173) and atazanavir based (n = 117).

3TC = lamivudine, ART = antiretroviral therapy, ARV = antiretroviral, ATVr = ritonavir boosted atazanavir, cART: combined antiretroviral therapy, EFV = efavirenz, IQR = interquartile range, LPVr = ritonavir boosted lopinavir, TDF = tenofovir disoproxil fumarate.

\* P value for virological success at < 1000 copies/mL.

† Percentages in this column represent column percentage.

‡ Percentages in this column represents row percentage.

### 2.3. Viral load quantification and results interpretation

Briefly, 4 mL of whole blood was collected in Ethylenediaminetetraacetic acid (EDTA)-containing tubes. Centrifugation of 1 EDTA tube was performed to obtain plasma, which was then divided into two (2) 700 µL aliquots and stored at – 20°C before analysis for viral load by Real Time PCR on the ABBOTT m2000rt platform, as per the manufacturer's instructions (<http://www.abbottmolecular.com/products/infectious-diseases/realtime-pcr/hiv-1-assay>). A protocol using 0.6 mL of plasma was used for RNA extraction, with < 40 copies/mL and > 10,000,000 copies/mL as the lower and higher detection limits, respectively.

### 2.4. Eligibility criteria

Patients with complete information; age, date of sample collection, date of ART initiation, and ART regimen together with VL result (s) were enrolled. Patients on ART for < 6 months or those reported to be non-adherent to treatment were excluded.

### 2.5. Operational definitions

Virological response was interpreted as thus; VS (VL < 1000 copies/mL),<sup>[11]</sup> virological failure, VF (VL ≥ 1000 copies/mL),<sup>[11]</sup> and undetectable viral load as VL < 50 copies/mL.<sup>[11,12]</sup>

### 2.6. Data analysis

Data analysis was done using SPSS version 20.0 (SPSS Inc., Chicago, Illinois), with a statistical significance set at  $P < .05$ . Confidence intervals, proportions, and frequencies were computed, and data were summarized using Tables. The chi-square test was used to evaluate association between categorical variables.

Multivariable logistic regression was used to control for potential confounders, taking into consideration age, gender, ART regimen, and duration on ART. The independent variables included in the model were those with a  $P$  value ≤ .2 with the dependent variable in bivariate analysis.

### 2.7. Ethics approval and consent to participate

This study was approved by the ethics institutional review board of the faculty of health sciences of the University of Buea as part of academic research project (ref. No:2022/026). Administrative approval was provided by the CIRCB Directorate General (ref. No: 0736/022), in collaboration with the National AIDS Control Committee and the Ministry of Public health. Data were collected from the laboratory records and confidentiality/privacy of all sample identities were duly observed using specimens identified numbers.

## 3. Results

### 3.1. Participants characteristics

A total of 9034 patients were enrolled, with the majority being females (6526; 72.2%). The median (interquartile range [IQR]) age, year of ART initiation, and duration on treatment was 39 (IQR: 32–48), 2014 (IQR: 2011–2016), and 24 (IQR: 12–72) months, respectively. Most patients were adults (8585; 95.0%). A significant proportion of the study participants, 78.8% (7117/9034) were on TDF + 3TC + DTG,  $P < .0001$ . Children showed a lower treatment coverage with TLD (82; 36.9%), followed by adolescents (138; 60.8%),  $P < .0001$ . Additionally, more men (79.9%) were on TLD and the median (IQR) duration under this regimen was 24 (12–72) months,  $P < .0001$  (Table 1).

### 3.2. Viral suppression in different study participants

The overall VS proportion (VL < 1000 copies/mL) obtained was 89.8% (8112/9034) with an optimal viral undetectability (<50 copies/mL) of 75.7% (6840/9034),  $P < .0001$  (Table 2). According to gender, VS proportion was higher among females, 90.9% (5929/6526) against 87.0% (2183/2508) in males; similarly, the proportion of viral undetectability was equally higher in females, 77.9% (5082/6526) against 70.1% (1758/2508) in males,  $P < .0001$  (Table 2). According to age distribution, VS was statistically significantly different, ranging from 64.8% in children, 74.4% in adolescents to 90.8% among adults,  $P < .0001$  (Table 2). According to ART regimens, VS was

significantly higher among patients on TDF + 3TC + DTG at 91.8% (6533/7117) as compared to those on other first-line regimens, 86.4% (1406/1627).

Of note, patients on protease inhibitors boosted with ritonavir-based therapy presented the lowest proportion of VS, 59.7% (173/290),  $P < .0001$  (Table 2). According to duration on ART, VS was 90.4% (3626/4013) at 12 months (M12), 87.6% (574/655) at 24 months (M24), 87.9% (591/672) at 36 months (M36), and 89.9% (3321/3694) from 48 months and above ( $\geq$  M48),  $P < .0001$  (Table 2).

It should also be noted that, taking in to consideration gender and age group, the best viral suppression performance was observed among patients on TLD (92.7% and 89.5% among females and males, respectively, and 73.2%, 80.4% and 92.3% among children, adolescents and adults respectively;  $P < .05$ ) (Table 3).

### 3.3. Factors associated with viral suppression

After adjusting gender, age categories, ART combination (TLD and other ART), and ART duration (considering 24 months

**Table 2**

**Participants characteristics and viral suppression levels.**

| Variable                                | Overall† N = 9034 | <50 copies/mL‡ N = 6840 (75.7%) | 50–999 copies/mL‡ N = 1272 (14.1%) | <1000 copies/mL‡ N = 8112 (89.8%) | ≥1000 copies/mL‡ N = 922 (10.2%) | P value*    |
|-----------------------------------------|-------------------|---------------------------------|------------------------------------|-----------------------------------|----------------------------------|-------------|
| Gender, n (%)                           |                   |                                 |                                    |                                   |                                  |             |
| Male                                    | 2508 (27.8)       | 1758 (70.1)                     | 425 (16.9)                         | 2183 (87.0)                       | 325 (13.0)                       | $P < .0001$ |
| Female                                  | 6526 (72.2)       | 5082 (77.9)                     | 847 (13.0)                         | 5929 (90.9)                       | 597 (9.1)                        |             |
| Age in yr, median (IQR)                 | 39 (32–48)        | 40 (32–48)                      | 39 (31–48)                         | 40 (32–48)                        | 37 (27–45)                       | $P < .0001$ |
| Age groups, n (%)                       |                   |                                 |                                    |                                   |                                  |             |
| Children                                | 222 (2.5)         | 104 (46.8)                      | 40 (18.0)                          | 144 (64.9)                        | 78 (35.1)                        | $P < .0001$ |
| Adolescents                             | 227 (2.5)         | 138 (60.8)                      | 31 (13.7)                          | 169 (74.4)                        | 58 (25.5)                        |             |
| Adults                                  | 8585 (95.0)       | 6598 (76.9)                     | 1201 (14.0)                        | 7799 (90.8)                       | 786 (9.1)                        |             |
| Duration on cART in month, median (IQR) | 24 (12–72)        | 24 (12–72)                      | 12 (12–60)                         | 18 (12–66)                        | 24 (12–72)                       | $P < .0001$ |
| Duration on cART in mo                  |                   |                                 |                                    |                                   |                                  |             |
| 6–12                                    | 4013 (44.4)       | 2957 (73.7)                     | 669 (16.7)                         | 3626 (90.4)                       | 387 (9.6)                        | $P < .0001$ |
| 13–24                                   | 655 (7.3)         | 478 (73.0)                      | 96 (14.7)                          | 574 (87.6)                        | 81 (12.4)                        |             |
| 25–36                                   | 672 (7.4)         | 501 (74.6)                      | 90 (13.4)                          | 591 (87.9)                        | 81 (12.1)                        |             |
| ≥48                                     | 3694 (40.9)       | 2904 (78.6)                     | 417 (11.3)                         | 3321 (89.9)                       | 373 (10.1)                       |             |
| ART combination, n (%)                  |                   |                                 |                                    |                                   |                                  |             |
| TDF + 3TC + DTG                         | 7117 (78.8)       | 5538 (77.8)                     | 995 (14.0)                         | 6533 (91.8)                       | 584 (8.2)                        | $P < .0001$ |
| Other 1st line ARV                      | 1627 (18.0)       | 1180 (72.5)                     | 226 (13.9)                         | 1406 (86.4)                       | 221 (13.6)                       |             |
| ATVr or LPVr based ARV                  | 290 (3.2)         | 122 (42.1)                      | 51 (17.6)                          | 173 (59.7)                        | 117 (40.3)                       |             |

3TC = lamivudine, ART = antiretroviral therapy, ARV = antiretroviral, ATVr = ritonavir boosted atazanavir, cART = combined antiretroviral therapy, DTG = dolutegravir, EFV = efavirenz, IQR = interquartile range, LPVr = ritonavir boosted lopinavir, TDF = tenofovir disoproxil fumarate.

Other first-line ARV [ABC + 3TC + EFV (n = 13), ABC + 3TC + NVP (n = 2), AZT + 3TC + EFV (n = 36), AZT + 3TC + NVP (n = 14), TDF + 3TC + NVP (n = 51), TDF + 3TC + EFV (1511)], Lopinavir based (n = 173) and atazanavir based (n = 117).

\* P value for virological success at < 1000 copies/M.

† Percentages in this column represent column percentage.

‡ Percentages in this column represents row percentage.

**Table 3**

**Viral suppression according to TLD coverage by age.**

| Variables      |                 | Overall†    | Viral load‡                       |                                  | OR (95% CI)      | P value*  |
|----------------|-----------------|-------------|-----------------------------------|----------------------------------|------------------|-----------|
|                |                 | N = 9034    | <1000 copies/mL; N = 8112 (89.8%) | ≥1000 copies/mL; N = 922 (10.2%) |                  |           |
| Gender         |                 |             |                                   |                                  |                  |           |
| Male           | TDF + 3TC + DTG | 2003 (79.9) | 1794 (89.5)                       | 210 (10.5)                       | 1                | $< .0001$ |
|                | Other ART       | 505 (20.1)  | 389 (77.2)                        | 115 (22.8)                       | 0.39 (0.30–0.50) |           |
| Female         | TDF + 3TC + DTG | 5114 (78.4) | 4743 (92.7)                       | 371 (7.3)                        | 1                | $< .0001$ |
|                | Other ART       | 1412 (21.6) | 1186 (84.0)                       | 226 (16.0)                       | 0.41 (0.34–0.49) |           |
| Age categories |                 |             |                                   |                                  |                  |           |
| Children       | TDF + 3TC + DTG | 82 (36.9)   | 60 (73.2)                         | 22 (26.8)                        | 1                | .043      |
|                | Other ART       | 140 (63.1)  | 83 (59.7)                         | 56 (40.3)                        | 0.54 (0.29–0.98) |           |
| Adolescents    | TDF + 3TC + DTG | 138 (60.8)  | 111 (80.4)                        | 27 (19.6)                        | 1                | .010      |
|                | Other ART       | 89 (39.2)   | 58 (65.2)                         | 31 (34.8)                        | 0.45 (0.24–0.83) |           |
| Adults         | TDF + 3TC + DTG | 6897 (80.3) | 6364 (92.3)                       | 533 (7.7)                        | 1                | $< .0001$ |
|                | Other ART       | 1688 (19.7) | 1437 (85.1)                       | 251 (14.9)                       | 0.47 (0.40–0.56) |           |

Other ART: ARV [ABC + 3TC + EFV (n = 13), ABC + 3TC + NVP (n = 2), AZT + 3TC + EFV (n = 36), AZT + 3TC + NVP (n = 14), TDF + 3TC + NVP (n = 51), TDF + 3TC + EFV (1511)], Lopinavir based (n = 173) and atazanavir based (n = 117).

3TC = lamivudine, ART = antiretroviral therapy, ARV = antiretroviral, ATVr = ritonavir boosted atazanavir, CI = confidence interval, DTG = dolutegravir, EFV = efavirenz, IQR = interquartile range, LPVr = ritonavir boosted lopinavir, OR = odds ratio, TDF = tenofovir disoproxil fumarate, TLD = Tenofovir + Lamivudine + Dolutegravir.

\* P value for virological success at < 1000 copies/M.

† Percentages in this column represent column percentage.

‡ Percentages in this column represents row percentage.



as the median duration), the adult age group ( $\geq 20$  years old) was independently associated with a higher proportion of VS than other age groups (adjusted odd-ratio (aOR): 3.72). Men were less likely to be virally suppressed compared to women (aOR:0.65). Patients on other ART regimens were less likely to be virally suppressed compared to patients on TLD (aOR:0.47). Also, patients on ART duration  $\geq 25$  months were less likely to be virally suppressed compared to patients who have been on ART for 6 to 24 (aOR: 0.76) (Table 4).

#### 4. Discussion

The overall proportion of VS ( $< 1000$  copies/mL) was 89.8%, with females registering a higher VS (90.9%). Children showed a higher and quite worrisome virological failure (VF) proportion of 35.1%, and those on TLD based regimens showed more sustained VS of 91.8% compared to those on non-TLD regimens (86.4% for other first-line regimens and 59.7% for ATVr or LPVr Based ART).

The 89.8% VS obtained here is about 5% away from the 3<sup>rd</sup> 95% target set by UNAIDS for 2025<sup>[5]</sup> but close to the current 90% performance achievement reported globally.<sup>[8]</sup> The proportion of patients with undetectable viraemia, ( $< 50$  copies/mL) was 75.8%, indicating the effectiveness of viral undetectability in ensuring viral untransmissibility in RLS like Cameroon is still a challenge, thus highlighting the need to continue reinforcing an integrated approach where condom uses, access to ART, and awareness of HIV prevention methods play a role in reducing transmission.

Even though the findings here are far below the achievements reported from many western countries,<sup>[13]</sup> our findings, however, provide great hope in the control of HIV transmission even in difficult-to-reach settings with highly potent ART regimens like TLD.<sup>[13]</sup> With the integration of DTG in the first-line of treatment, the degree of viral failure has dropped from 20.6% prior to TLD era to about 10%, which falls within the current range in other RLS where a 3.7% to 26.0% prevalence have been reported.<sup>[14]</sup> In 2016, the UNAIDS welcomed new goals, targets, and commitments of the 2016 United Nations General Assembly Political Declaration on Ending the AIDS epidemic by 2030. Following these new commitments and the transition to TLD in 2020, the availability and scalability of TLD based ART coverage in Cameroon improved, thus underscoring the positive impact TLD based regimes has had in polling down VF among PLHIV. To this end, health systems in RLS are encouraged to

make multiple efforts to provide a wider access to TLD in the near future.

Previous studies in Cameroon reported VS proportions between 72.1 and 90.2%,<sup>[4,15–18]</sup> with disparities attributed to differences in the study periods, population characteristics, and duration on ART. For instance, the 89.8% reported in our current findings is higher than the countrywide population-based HIV impact assessment study, which reported an 80% VS in a study conducted prior to transitioning to DTG-based ART.<sup>[18]</sup> As aforementioned, the lower VS proportions in previous studies in Cameroon were linked to the use of efavirenz- or NVP-based regimens that were in use then, thus calling for a wider phase-out or use of NNRTI-sparing ART combinations for the benefit of wider TLD coverage following transition from NNRTI-containing regimens.<sup>[19,20]</sup> Of note, a high proportion of adults switching to TLD achieved VS despite substantial baseline NRTI resistance, and the majority had low-level viraemia ( $\leq 100$  copies/mL),<sup>[19,20]</sup> with caution mainly for those with previous exposure to first-generation integrase inhibitors (Raltegravir).<sup>[21–28]</sup>

The poor proportion of VS in children and adolescents could be attributed to suboptimal adherence and inadequate psychological support, which increases the risks of virological failure in this group.<sup>[29,30]</sup> The very poor VS performance in children, in particular, is a cause for concern, especially in a context as this where the availability and coverage of pediatric DTG-based therapy recorded the lowest coverage of merely about 37% compared to older populations. The need to improve the availability and access to pediatric DTG formulation in Cameroon and similar RLS cannot be overemphasized,<sup>[31,32]</sup> as this is going to aid redress the problem of pediatrics Virological failure.

It has been reported that men are more likely to experience VF than females,<sup>[33–35]</sup> supported mainly by their limited attendance of health care services, which leads to poor adherence,<sup>[27–30]</sup> with an increased risk of VF and mortality.<sup>[36–39]</sup> While TLD showed a higher virological response, protease inhibitors boosted with ritonavir-based regimens need to be monitored closely as they are often used with recycled NRTIs in several RLS.<sup>[36]</sup> Also, duration on ART was associated with VS and this is likely due to tolerability overtime despite possible risks of HIV drug resistance emergence.<sup>[14,15,28,41]</sup> In a nutshell, the switch to DTG in 2020 in Cameroon shows encouraging performance with reducing resistance profiling, thereby supporting its fast track strides for achieving the 95% VS target.<sup>[38–40]</sup>

**Table 4**  
Factors associated with viral suppression.

| Variables             | OR (95% CI)      | P value* | aOR (95% CI)     | P value* |
|-----------------------|------------------|----------|------------------|----------|
| Gender                |                  |          |                  |          |
| Female                | 1                |          | 1                |          |
| Male                  | 0.65 (0.56–0.75) | <.0001   | 0.69 (0.60–0.81) | <.0001   |
| Age categories, N (%) |                  |          |                  |          |
| 0–10                  | 1                |          | 1                |          |
| 11–19.                | 1.57 (1.05–2.36) | .028     | 1.28 (0.84–1.94) | .242     |
| $\geq 20$             | 5.39 (4.05–7.16) | <.0001   | 3.72 (2.76–5.02) | <.0001   |
| ART combination       |                  |          |                  |          |
| TDF + 3TC + DTG       | 1                | <.0001   | 1                | <.0001   |
| Other ART             | 0.42 (0.36–0.48) |          | 0.47 (0.40–0.55) |          |
| ART Duration (mo)     |                  |          |                  |          |
| $\leq 24$             | 1                | .46      | 1                | .024     |
| $\geq 25$             | 0.78 (0.62–0.99) |          | 0.76 (0.59–0.96) |          |

Other ART: ARV [ABC + 3TC + EFV (n = 13), ABC + 3TC + NVP (n = 2), AZT + 3TC + EFV (n = 36), AZT + 3TC + NVP (n = 14), TDF + 3TC + NVP (n = 51), TDF + 3TC + EFV (1511)], Lopinavir based (n = 173) and atazanavir based (n = 117).

3TC = lamivudine, ART = antiretroviral therapy, aOR = adjusted odds ratio, CI = confidence interval, DTG = dolutegravir, OR = odds ratio, TDF = tenofovir disoproxil fumarate.

\* P value for virological success at  $< 1000$  copies/mL.

The lower representation of children and adolescents seemingly represents a bias to assess VS achievement in this key group. Notwithstanding, the representation here reflects the real-life population distribution of HIV epidemics at country level.<sup>[41]</sup> To mitigate this potential bias, statistical adjustments were implemented. The cross-sectional design could not allow assessing long-term outcomes, which supports conducting studies on the long-term benefits of TLD which is currently unknown.

## 5. Conclusion

In this study participants receiving ART in Cameroon, about 9 out of 10 patients on combination antiretroviral therapy have achieved VS, with poorer outcomes among children and adolescents. Of note, 3-quarter (3/4) have achieved an undetectable VL, might indicate the prevention of HIV transmission at community-level. High rate of viral suppression is independently associated to TLD based regimens, adults (especially females). The current limited access to pediatric DTG-containing therapies calls for urgent actions to improve on VS in these vulnerable populations living mainly in SSA settings.

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