


# Disparities in dolutegravir utilisation in children, adolescents and young adults (0–24 years) living with HIV. An analysis of the IeDEA Pediatric West African cohort

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## ABSTRACT

**Introduction** We describe the 24-month incidence of Dolutegravir (DTG)-containing antiretroviral treatment (ART) initiation since its introduction in 2019 in West Africa.

**Methods** We included all patients aged 0–24 years on ART from nine clinics in Côte d'Ivoire (n=4), Ghana, Nigeria, Mali, Benin, and Burkina Faso. Baseline varied by clinic and was defined as date of first DTG prescription; patients were followed up until database closure/death/loss to follow-up (LTFU, no visit ≥7 months), whichever came first. We computed the cumulative incidence function for DTG initiation; associated factors were explored in a shared frailty model, accounting for clinic heterogeneity.

**Results** Since 2019, 3350 patients were included; 47.2% were female; 78.9% had been on ART ≥12 months. Median baseline age was 12.5 years (IQR 8.4–15.8). Median follow-up was 14 months (IQR 7–22). The overall cumulative incidence of DTG initiation reached 22.7% (95% CI 21.3 to 24.2) and 56.4% (95% CI 54.4 to 58.4) at 12 and 24 months, respectively. In univariate analyses, those aged <5 years and female were overall less likely to switch. Adjusted on ART line and available viral load (VL) at baseline, females aged >10 years were less likely to initiate DTG compared with males of the same age (adjusted HR among 10–14 years: 0.62, 95% CI 0.54 to 0.72; among ≥15 years: 0.43, 95% CI 0.36 to 0.50), as were those with detectable VL (>50 copies/mL) compared with those in viral suppression (aHR 0.86, 95% CI 0.77 to 0.97) and those on PIs compared with those on non-nucleoside reverse-transcriptase inhibitors (aHR after 12 months of roll-out: 0.75, 95% CI 0.65 to 0.86).

**Conclusion** Paediatric DTG uptake was incomplete and inequitable in west African settings: DTG use was least likely in children <5 years, females ≥10 years and those with detectable VL. Maintained monitoring and support of treatment practices is required to better ensure universal and equal uptake.

## WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Dolutegravir (DTG)-based antiretroviral treatment (ART) regimens have been recommended as the preferred first-line ART regimens for all individuals living with HIV by the World Health Organization (WHO) since 2018, with a specific caution for pregnant women. This was subsequently confirmed for all children with approved DTG dosing and adolescents since 2019.
- ⇒ The deployment of universal DTG for adults in west Africa has faced challenges including infrastructure challenges, disparities in healthcare systems, and initial perinatal safety concerns that significantly impacted women of childbearing age.
- ⇒ Specific data on DTG uptake in children, adolescents and young adults in west Africa is limited.

## INTRODUCTION

Dolutegravir (DTG) is an integrase strand transfer inhibitor that was first recommended by the World Health Organization (WHO) for antiretroviral therapy (ART) in adults in 2016.<sup>1</sup> Indeed, DTG-based regimens are highly effective, associated with higher viral suppression rates and higher genetic barrier, reducing potential drug resistance.<sup>2</sup> In 2018, the Tsepamo study in Botswana raised concerns about a potential association between neural tube defects in babies and the use of DTG by mothers at the time of conception.<sup>3</sup> Subsequently, the WHO revised recommendations, with a note of caution about using DTG among females of reproductive age.<sup>4</sup> Further data reported a weaker association between DTG and neural tube defects, and modelling studies supported the use of

### WHAT THIS STUDY ADDS

- ⇒ This study describes the dynamic of the DTG roll-out over the first 24 months and its correlates since 2019 in a large west African multicentric cohort of children, adolescents and young adults.
- ⇒ We observed a rapid scale-up of DTG among children, adolescents and young adults living with HIV in west Africa, despite the COVID-19 pandemic.
- ⇒ However, DTG uptake after 24 months was incomplete and inequitable, with adolescent girls and young women being less likely to initiate DTG compared with boys and young men, as were those with a detectable viral load (>50 copies/mL) compared with those in success.
- ⇒ Younger children <5 years old were also less likely to initiate DTG, explained by the later approval of paediatric formulations and their low availability.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ Maintained monitoring, training and updating guidance for healthcare workers is essential to ensure universal uptake to DTG, especially for girls and young women, for whom inequity begins at age 10 years.
- ⇒ Efforts to improve uptake to universal DTG in west Africa require multifaceted interventions including healthcare infrastructure improvement and facilitation of paediatric antiretroviral forecasting and planning.

DTG in all people living with HIV because the benefits outweighed the risks.<sup>5–7</sup>

In addition, DTG treatment was inaccessible for most children living with HIV, the only formulation available in Sub-Saharan Africa being the 50 mg film-coated tablet registered for use in people weighing >40 kg. Data from the Odyssey trial showed that 50 mg DTG tablets given once daily in children provide appropriate pharmacokinetic profiles comparable to adults.<sup>8,9</sup> As a result, the WHO 2019 DTG paediatric dosing guidelines also led to the US Food and Drug Administration (FDA) approval of 50 mg dosing down to 20 kg, widening the paediatric population eligible for DTG.<sup>4,10,11</sup> The Odyssey trial team also investigated the dosing of DTG among children receiving rifampicin-containing tuberculosis treatment (TB) treatment and found twice daily DTG was safe and sufficient, providing a practical ART option for children with HIV-associated TB.<sup>12</sup> Additional data from the trial, addressed the dosing of DTG in children weighing 3 kg to <20 kg and aged 4 weeks and above, and formulations are now available for children as young as 4 weeks of age.<sup>13</sup>

Thus, in 2019, the WHO strongly recommended DTG-containing ART regimens for all adults and adolescents living with HIV, including females of reproductive age regardless of contraception, and in infants and children with approved DTG dosing.<sup>14,15</sup>

Since 2019, west African HIV treatment programs have been transitioning to DTG giving priority to those who need it most (1. those not treated, 2. children receiving non-nucleoside reverse transcriptase inhibitors (NNRTI)-based regimens, 3. children who need

to start TB treatment and 4. children receiving LPV/r solid formulations with challenges in administration and achieving viral suppression). To ensure rapid scale-up, WHO recommends DTG switch should occur irrespective of the availability of a viral load (VL) test/result, and urge clinicians to ensure sufficient quantification and supply. Of note, paediatric DTG in a 10 mg scored formulation to be associated with optimised backbone antiretrovirals (ARVs) such as abacavir/ lamivudine 120/60 mg scored dispersible tablets became available in 2021 in west Africa; paediatric fixed-dose combinations (pALD) were not available during the study period. We sought to describe this early transition, since 2019, among children and adolescents aged 0–24 years in a large multicentre paediatric cohort in west Africa.

### METHODS

#### Study design and inclusion criteria

The International epidemiology Database to Evaluate AIDS (IeDEA) pediatric west African Database to evaluate AIDS (pWADA) is aimed at addressing evolving research questions in the field of HIV/AIDS care and treatment using routine data from multicentre HIV/AIDS children cohorts in west Africa.<sup>16,17</sup> This collaboration, initiated in July 2006, involves, in 2024, 10 paediatric referral HIV/AIDS clinics in seven countries: Benin (n=1), Burkina Faso (n=1), Côte d'Ivoire (n=4), Ghana (n=1), Mali (n=1), Nigeria (n=1) and Togo (n=1).

We included all children and adolescents aged 0–24 years enrolled in an IeDEA pWADA clinic, with at least one visit from January 2019, the time of DTG introduction in west Africa. Those followed up in clinics where DTG was not yet rolled out at the time of the study were excluded from the analysis.

#### Outcomes and key definitions

Baseline was site-specific, and defined as the date of the first documented prescription of DTG among patients aged 0–24 years in each site. For those who enrolled after the beginning of a DTG roll-out, baseline was date of enrolment. Our main outcome was dolutegravir initiation, which we defined as either transitioning to a DTG-containing regimen from another regimen, or newly initiating DTG-based ART. Start dates for DTG were based on clinician documentation of a new prescription. Competing events were death or loss-to-program. Loss-to-program included patients with a documented transfer to another clinic or those lost-to-follow-up (LTFU), defined as last clinical contact >7 months at database closeout date. Database closeout dates varied by site, ranging from 2020 to 2022; site-specific study periods are available in [table 1](#).

#### Statistical analysis

Patients were followed up from baseline until DTG initiation, a competing event (death, transfer or LTFU), or database closeout date, when they were censored.

**Table 1** Baseline characteristics of the nine sites rolling-out DTG and 3350 patients aged 0–24 years living with HIV and enrolled in the leDEA pediatric WestAfrica, 2019–2022

<b>Structural-level characteristics</b>						
	<b>N</b>	<b>Date of DTG introduction (baseline)</b>	<b>Date of database closure</b>	<b>Number of months of DTG roll-out</b>	<b>Time to first visit since DTG introduction, median (IQR)</b>	
Côte d'Ivoire, CEPREF	446	11 May 2019	14 June 2021	25	41	(18–74)
Côte d'Ivoire, CHU Cocody	396	27 March 2019	15 October 2021	31	22	(9–50)
Côte d'Ivoire, CHU Yopougon	406	3 July 2019	18 July 2022	37	30	(9–63)
Côte d'Ivoire, CIRBA	374	7 May 2019	29 March 2022	35	51	(17–126)
Burkina Faso	243	7 March 2019	15 April 2022	37	126	(61–224)
Benin	247	3 September 2019	8 August 2021	23	56	(15–107)
Mali	633	27 May 2020	10 July 2021	13	48	(26–71)
Ghana	305	25 September 2019	13 July 2021	22	49	(26–71)
Nigeria	300	22 February 2019	5 March 2022	36	49	(21–70)
<b>Patient-level characteristics</b>						
	<b>N</b>	<b>%</b>				
<b>Sex</b>						
Male	1770	52.8%				
Female	1580	47.2%				
<b>Age at baseline</b>						
< 2 years	104	3.1%				
4 years	245	7.3%				
5–9 years	768	22.9%				
10–14 years	1227	36.6%				
>15 years	1006	30.0%				
<b>ART regimen at baseline</b>						
ART-naive	287	8.6%				
NNRTI-based ART	2037	60.8%				
PI-based ART	962	28.7%				
Other ART regimens	64	1.9%				
<b>ART line at baseline</b>						
ART naive	287	8.6%				
first-line	1980	59.1%				
≥2 L	1083	32.3%				
<b>Time on ART</b>						
ART naive	287	8.6%				
<12 months	423	12.6%				
≥12 months	2640	78.8%				
<b>Viral load available</b>						
Success (% of available)	1319	59.4%				
Failure (% of available)	900	40.6%				
CEPREF: Research and training support centre CHU : University teaching hospital CIRBA: Integrated Bioclinical Research Centre of Abidjan ART, antiretroviral treatment ; DTG, dolutegravir ; NNRTI, non-nucleoside reverse transcriptase inhibitors; PI, protease inhibitor.						

First, we calculated crude cumulative incidence proportions over the first 24 months after DTG introduction, along with 95% CIs, for DTG initiation and competing events using the Aalen-Johansen estimator. Second, we used multi-level survival analysis to estimate HRs for time to DTG initiation.<sup>18</sup> We computed a Cox regression model with mixed effects, incorporating a clinic-specific random effect to account for within-clinic homogeneity in outcomes, and the shared frailty followed a gamma distribution. The model was adjusted for sex stratified by age at baseline, duration on ART, baseline virological status (VL unavailable, detectable VL  $\geq 50$  copies/mL or undetectable VL  $< 50$  copies/mL) and type of ART regimen immediately before DTG initiation according to time.

### Patient and public involvement

This study was conducted using programmatic data collected routinely. Patients were not involved in the analysis plan or result interpretation. Patients did not contribute to the writing or editing of this manuscript.

### Ethics approval

Each participating country formally agreed to contribute paediatric data, with local institutional review board and National Institute of Health approval to contribute to the analyses. Specific individual consent was not required as this was routine collected data.

## RESULTS

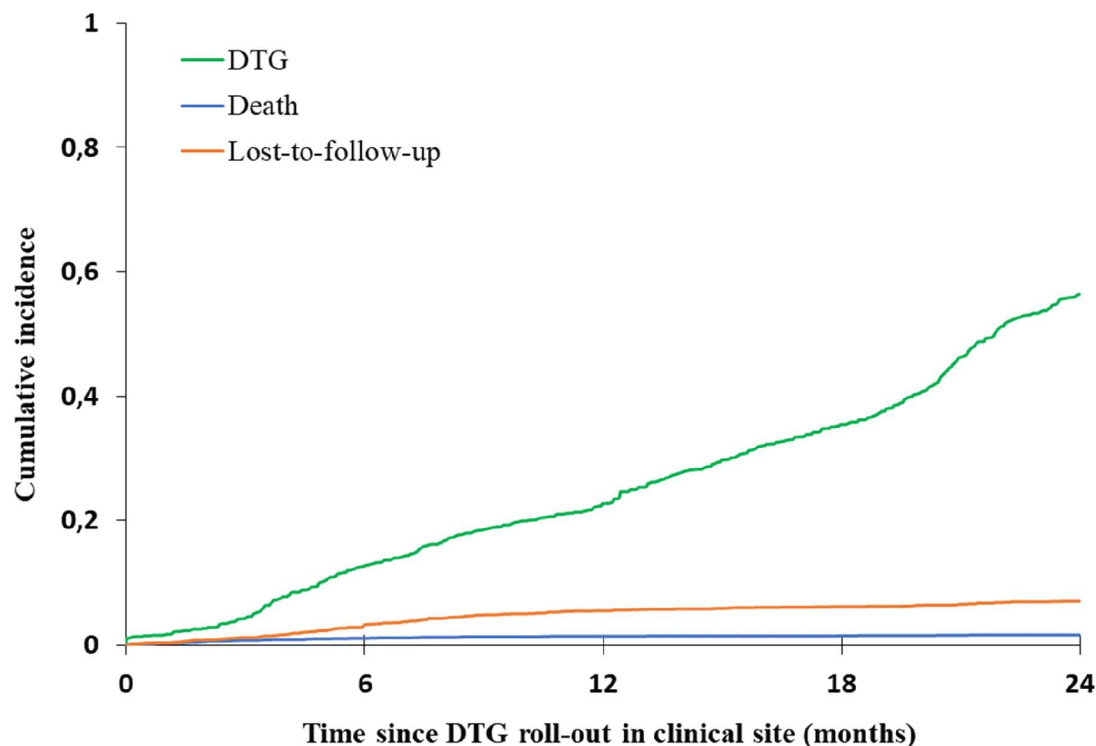
Between January 2019 and July 2022, of the 10 paediatric clinical sites contributing to the pWADA cohort, all except the site in Togo had initiated DTG roll-out. Documentation of DTG prescription was first in Nigeria (February 2019) and then in Burkina Faso and the Cocody University Hospital in Côte d'Ivoire (March 2019). Other Ivorian sites accessed DTG between May to July 2019, and the clinical sites in Benin and Ghana began roll-out in September 2019. Lastly, the Gabriel Toure Hospital in Mali began prescribing DTG in May 2020.

Of the 3891 children with at least one clinical visit since 2019, 3350 children and adolescents were eligible and included in this study, of whom 3063 (91.4%) were on ART and in active follow-up at baseline, and 287 (8.6%) ART-naïve were newly enrolled during the study period (online supplemental figure A). Overall, 47% were female and median age at baseline was 12.5 years (IQR 8.4–15.8). Overall baseline characteristics are presented in table 1. Overall, 59.1% were of first-line ART, although this varied by clinic (online supplemental table S1): in Benin, Burkina Faso and the Integrated Bioclinical Research Centre of Abidjan (CIRBA) in Côte d'Ivoire,  $> 50\%$  were already on second-line regimens, while 80.3% of patients in Ghana were still on first-line. Overall, 78.8% had been on ART  $> 12$  months, median time since ART initiation was 6.9 years (IQR 3.7–9.9). VL measurement was available at baseline for 66.2% of children, of whom 59.4% were in viral suppression (VL  $< 50$  copies/

ml). VL measurement at baseline varied across clinics and countries, ranging from 32.9% in Burkina Faso (of whom 47.5% were in viral suppression) to 90.9% at the Yopougon University Hospital, Côte d'Ivoire (of whom 55.0% were in viral suppression).

Overall, since 2019, 1496 (44.7%) patients initiated a DTG-containing regimen, 50 (1.5%) died and 213 (6.4%) were lost to the program. Median follow-up was 14.0 months (IQR 7.5–21.9). Cumulative incidence rates for DTG initiation are described in figure 1. The 6 month cumulative incidence rate for DTG initiation since roll-out in the clinic was 12.7% (95% CI: 11.5 to 13.9) and reached 56.4% (95% CI 54.4 to 58.4) by 24 months. DTG incidence varied greatly according to country (figure 2). The CIRBA clinic in Côte d'Ivoire was the only site to reach  $> 50\%$  within the first 12 months of DTG introduction (55.7%, 95% CI 50.5 to 60.6), followed by Mali (36.5%, 95% CI 32.6 to 40.4) and the Nigerian Institute for Medical Research (24.1%, 95% CI 19.2 to 29.2) in Nigeria, while all other clinics were below 20%. After 24 months of roll-out, the CIRBA still had the highest DTG initiation rate (71.4%, 95% CI 66.8 to 76.0), followed by the Yopougon University Hospital in Côte d'Ivoire (68.1%, 95% CI 63.4 to 72.5), the Research and training support centre clinic in Côte d'Ivoire (65.7%, 95% CI 59.3 to 71.4) and the Yaldago Ouedraogo Hospital in Burkina Faso (58.8%, 95% CI 51.8 to 65.1), while the other clinics remained below 50%. DTG initiation also varied by sex, with higher cumulative incidence among males compared with females at both 12 and 24 months (figure 3A). However, we note the gap closing towards the end of the follow-up period.

Factors associated with DTG initiation are presented in table 2 and figure 3. In univariate analyses, we found that DTG use was least likely in females, younger children ( $< 5$  years), those with detectable VL and those on protease inhibitor (PI)-based ART. In multivariate analyses, adjusted for all other variables, these associations remained: females were less likely to initiate DTG than their male counterparts. This association strongly depended on age, while there was no difference between sex among those aged  $< 10$  years, the adjusted aHR was 0.62 (95% CI 0.54 to 0.72) among those 10–14 years and 0.43 (95% CI 0.36 to 0.50) among those  $\geq 15$  years. We also found that DTG initiation was less likely among those with detectable VL (aHR 0.86, 95% CI 0.77 to 0.97) compared with those with VL  $< 50$  copies/mL. In the first year of DTG roll-out, ART-naïve children were more likely to initiate DTG compared with those on an NNRTI-based ART regimen (aHR 2.00, 95% CI 1.52 to 2.65); after the first year, those on a PI-based ART regimen were less likely to initiate DTG compared with those on an NNRTI-based ART regimen (aHR 0.75, 95% CI 0.65 to 0.86). We also found that those on ART  $\geq 12$  months were most likely to switch to DTG compared with those on ART for a shorter duration (aHR 1.29, 95% CI 1.11 to 1.51)



	6 months N= 2,681	12 months N=2,012	18 months N=1,361	24 months N=570
Cumulative incidence	12.7%	22.7%	35.5%	56.4%
95% Confidence Interval	[11.5-13.9]	[21.3-24.2]	[33.7-37.2]	[54.4-58.4]

**Figure 1** Overall cumulative incidence function of DTG initiation among the 3350 children, adolescents and young adults living with HIV and enrolled in the leDEA pediatric west African sites rolling out DTG.

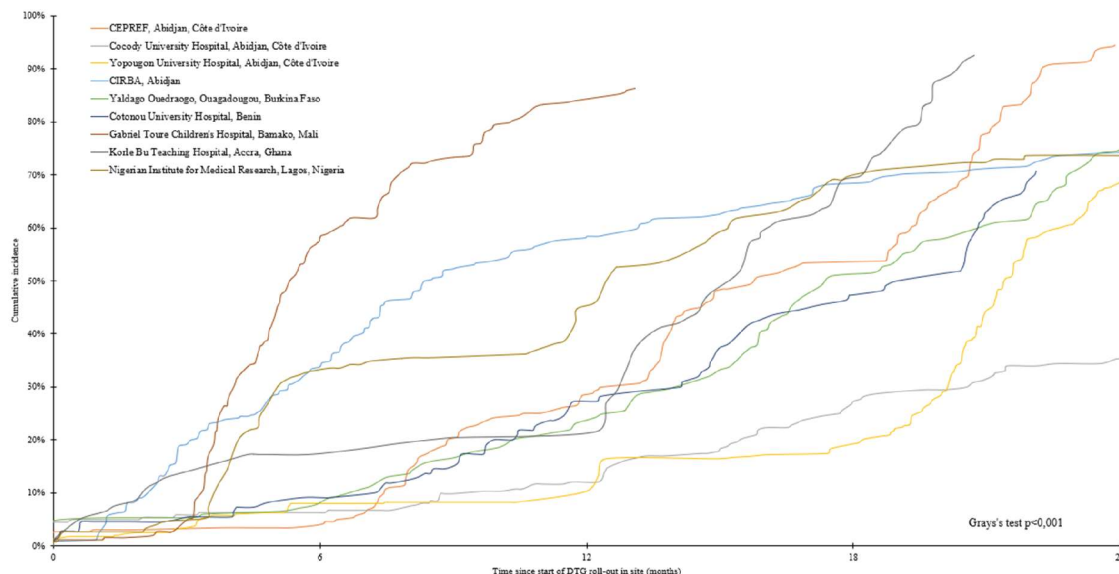
## DISCUSSION

Universal DTG-containing ART regimens were recommended by the WHO as preferred first-line ART since 2018 in adults and adolescents.<sup>4</sup> This study describes the dynamic of the DTG roll-out over 24 months and its correlates in a large west African cohort of children, adolescents and youth. DTG has been available since 2019 in nearly all clinical sites. Transition to DTG-containing ART regimens was less likely in children <10 years, in females ≥10 years and in those having a detectable VL at baseline. Furthermore, we observed a role of the previous ART regimen at time of DTG roll-out, where use of DTG in the first 12 months was less likely in those on PI-based ART.

First, in our cohort, six out of the seven participating countries had begun prescribing DTG in 2019, among which all but one site (9/10) began in the first semester of 2019. While this is delayed compared with other regions in sub-Saharan Africa, once available,<sup>19</sup> we observed a rapid scale-up of DTG roll-out in west Africa, noticeable despite the COVID-19 pandemic in March 2020. Despite the remarkable progress in the roll-out of DTG since 2019, this was also heterogeneous between countries and still incomplete 24 months after the WHO

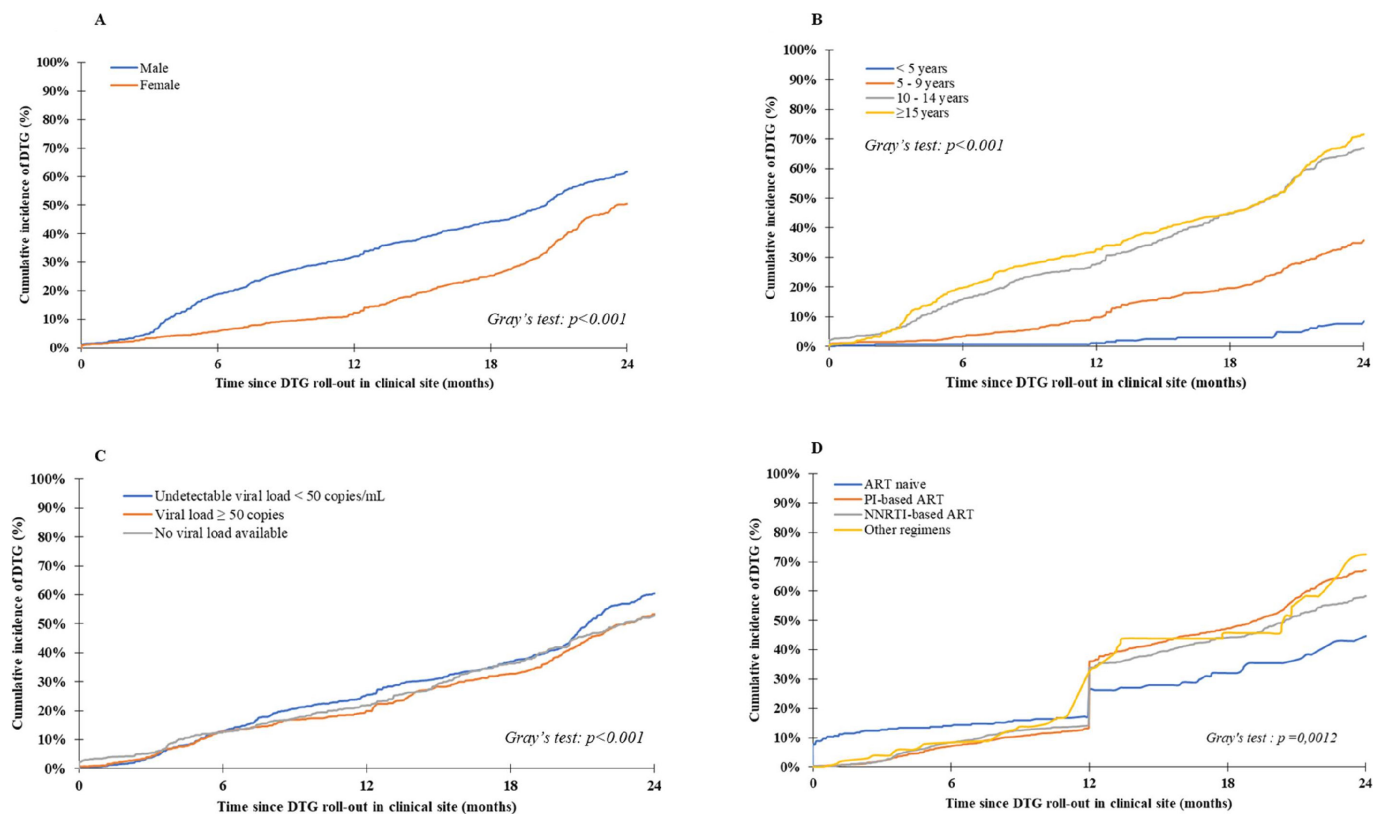
recommendations, as only four clinics reached >50% coverage. As detailed below, population characteristics could explain such differences in transitioning to DTG regimens, but also structural factors not captured in this analysis. We cannot exclude either, an effect of the COVID-19 pandemic that may also have jeopardised and slowed the DTG roll-out in the earlier years.<sup>20</sup>

Second, we observed sex disparities among adolescents and young adults ≥10 years, where DTG use was less likely in females compared with males of the same age. These disparities increased consistently with age. We assume that clinicians were reluctant in using DTG among female adolescents of childbearing potential because they were aware of the initial signal of neural tube defects reported from Botswana that led to a note of caution in the WHO recommendations in 2018.<sup>3,4</sup> Since most sites had begun DTG roll-out before the WHO recommended DTG to all, in July 2019, providing further reassurance on DTG due to the declining estimate of neural tube defect risk and observed efficacy, we hypothesise our observation is mostly related to the delay in disseminating such information at the field level.<sup>14</sup> Thus, the observed challenges in DTG use in adolescent and young females also reflects the fear of healthcare providers to address this concern



	6 months	12 months	18 months	24 months
<b>CEPREF, Abidjan, Côte d'Ivoire</b>				
Number at risk	417	335	260	20
Cumulative incidence	2.3%	17.4%	33.2%	65.7%
95% Confidence interval	[1.2-4.0]	[14.0-21.1]	[28.8-37.8]	[59.3-71.4]
<b>Cocody University Hospital, Abidjan, Côte d'Ivoire</b>				
Number at risk	333	282	237	207
Cumulative incidence	3.6%	7.0%	16.0%	20.7%
95% Confidence interval	[2.0-5.7]	[4.7-9.8]	[12.5-20.0]	[16.7-24.9]
<b>Yopougon University Hospital, Abidjan, Côte d'Ivoire</b>				
Number at risk	351	322	278	74
Cumulative incidence	7.4%	10.1%	19.0%	68.1%
95% Confidence interval	[5.1-10.2]	[7.4-13.3]	[15.3-23.0]	[63.4-72.5]
<b>CIRBA, Abidjan, Côte d'Ivoire</b>				
Number at risk	247	158	120	94
Cumulative incidence	32.3%	55.7%	65.5%	71.4%
95% Confidence interval	[27.6-37.0]	[50.5-60.6]	[60.4-70.1]	[66.8-76.0]
<b>Yaldago Ouedraogo, Ouagadougou, Burkina Faso</b>				
Number at risk	220	182	127	83
Cumulative incidence	5.4%	17.4%	39.2%	58.8%
95% Confidence interval	[3.0-8.8]	[12.8-22.6]	[32.7-45.7]	[51.8-65.1]
<b>Cotonou University Hospital, Benin</b>				
Number at risk	209	167	104	
Cumulative incidence	4.2%	13.0%	23.9%	
95% Confidence interval	[2.2-7.2]	[9.1-17.8]	[18.4-29.8]	
<b>Gabriel Toure Children's Hospital, Bamako, Mali</b>				
Number at risk	448	167		
Cumulative incidence	24.1%	36.5%		
95% Confidence interval	[20.1-27.6]	[32.6-40.4]		
<b>Korle Bu Teaching Hospital, Accra, Ghana</b>				
Number at risk	241	220	115	
Cumulative incidence	5.4%	6.6%	27.2%	
95% Confidence interval	[3.2-8.5]	[4.1-10.0]	[21.5-33.1]	
<b>Nigerian Institute for Medical Research, Lagos, Nigeria</b>				
Number at risk	227	185	139	120
Cumulative incidence	17.3%	24.1%	38.8%	41.3%
95% Confidence interval	[13.2-21.9]	[19.2-29.2]	[33.0-44.6]	[35.3-47.1]

**Figure 2** Cumulative incidence function of DTG initiation by clinic among the 3350 children, adolescents and young adults living with HIV and enrolled in the leDEA pediatric west African clinics rolling out DTG.



**Figure 3** Cumulative incidence function of DTG initiation among the 3350 children, adolescents and young adults living with HIV and enrolled in the leDEA paediatric west African clinics rolling out DTG by sex (A), baseline age (B), baseline viral load (C) and baseline ART regimen (D).

and their inability to offer contraceptive use in this population. Indeed, contraceptive uptake among adolescent girls and young women in Sub-Saharan Africa is low<sup>21 22</sup> and healthcare providers lack education or face bias in addressing these questions.<sup>23 24</sup> The gap between males and females in terms of DTG initiation tended to close towards the end of the follow-up period. But, this inequity for young females should be addressed urgently and women should be provided with information about benefits and risks to make an informed choice regarding the use of DTG or other ART. Similar studies in the adult population have also reported this trend.<sup>25 26</sup> We advocate that if healthcare providers and stakeholders continue to be educated on the evidence of DTG safety among women of childbearing potential, DTG use in adolescent girls and young women would increase and match that of their male counterparts.

Third, we report that children, adolescents and young adults with detectable VL were less likely to initiate DTG compared with those in viral suppression in our cohort. This is not in line with the paediatric ARV guidelines recommending that DTG transition should occur irrespective of the availability of VL test.<sup>15</sup> However, this result is likely driven by the adolescent and young adult population. This is most likely related to anticipated adherence challenges in children and adolescents and inadequate psychological support, which increases the risks of virological failure in this population.<sup>27</sup> Suboptimal adherence

to ART has long been identified as a major contributor to the development of drug resistance among people living with HIV.<sup>28 29</sup> Despite the higher genetic barrier in DTG, several studies have reported on the emergence of integrase inhibitor drug resistance and reduced efficacy<sup>30 31</sup> in patients on DTG receiving functional monotherapy. Viral failure in children and adolescents living with perinatally acquired HIV can be either the result of poor adherence, frequent in this population, or also often the consequence of pre-treatment drug resistance caused by suboptimal maternal ART regimens.<sup>32</sup> In the absence of drug resistance testing, clinicians are inclined to prioritise therapeutic education to improve adherence first, despite persistent challenges in this domain, before transitioning to DTG-containing ART regimens. But this can end in a lack of chance too if not switching those who have unknown drug resistance mutations. Affordable technologies for detecting HIV drug resistance among those failing ART would be needed to distinguish between children and adolescents living with HIV with HIV drug resistance and those who have suboptimal adherence in low-income settings. This would also be important and useful when monitoring patients on DTG, as evidence of pre-treatment resistance to DTG in children and adolescents emerge.<sup>33</sup>

Fourth, we report that ART-naïve patients were most likely to initiate DTG. This was an expected result since the WHO recommendations in the paediatric population

**Table 2** Factors associated with transition to DTG-containing ART regimen among the 3350 children, adolescents and young adults living with HIV and enrolled in the leDEA pediatric west African sites rolling out DTG, 2019–2022

	Univariate analysis		Multivariate analysis					
	HR	95% CI	Adjusted HR	95% CI				
Age (ref: <5 years)								
5–9 years	2.32	(1.75 to 3.09)	–	–				
10–14 years	5.55	(4.23 to 7.27)	–	–				
≥15 years	6.10	(4.63 to 8.02)	–	–				
Sex, female vs male	0.62	(0.57 to 0.69)						
Sex, according to age								
< 5 years, female vs male	–	–	1.09	(0.65 to 1.84)				
5–9 years, female vs male	–	–	0.84	(0.67 to 1.06)				
10–14 years, female vs male	–	–	0.62	(0.54 to 0.72)				
≥ 15 years, female vs male	–	–	0.43	(0.36 to 0.50)				
On ART >12 months vs ≤12 months	1.77	(1.53 to 2.04)	1.29	(1.11 to 1.51)				
Virological status at baseline (ref: undetectable: viral load <50 copies/mL)								
Detectable viral load	0.93	(0.83 to 1.04)	0.86	(0.77 to 0.97)				
Viral load unavailable	1.04	(0.92 to 1.19)	0.98	(0.86 to 1.12)				
<b>Baseline ART regimen (ref: NNRTI*-based ART)</b>								
	Within the first 12 months		> 12 months of follow-up		Within the first 12 months		> 12 months of follow-up	
	HR	95% CI	HR	95% CI	Adjusted HR	95% CI	Adjusted HR	95% CI
ART naive	2.00	(1.52 to 2.65)	0.54	(0.35 to 10.85)	4.13	(3.08 to 5.54)	1.07	(0.68 to 1.69)
PI†-based ART	0.97	(0.83 to 1.14)	1.51	(1.32 to 1.74)	0.92	(0.78 to 1.08)	0.75	(0.65 to 0.86)
Other ART regimens	1.34	(0.83 to 2.18)	1.39	(0.82 to 2.35)	0.94	(0.58 to 1.53)	0.66	(0.39 to 1.12)

Cox regression model with mixed effects, incorporating a clinic-specific random effect and the shared frailty followed a gamma distribution.  
 \*Non-nucleoside reverse transcriptase inhibitor.  
 †Protease inhibitor.  
 ART, antiretroviral therapy; NNRTI, non-nucleoside reverse transcriptase inhibitors; PI, protease inhibitor.

prioritise those not treated.<sup>14</sup> We also found that those on PI-based ART regimens were less likely to initiate DTG compared with those on NNRTI-based ART. Several reasons can explain this expected observation. First, concerns about the development of resistance, as described above, may have led clinicians to favour PI-based regimens if there were anticipated adherence challenges. Indeed, observations from the DAWNING study suggest that failure on PIs is less likely to lead to resistance in adults.<sup>34</sup> Second, countries that had existing stocks of lopinavir and ritonavir (LPV/r) pellets or granules were encouraged to consider utilising these stocks, in order to transition to DTG with minimal wastage.<sup>35</sup>

Fifth, we found that children, adolescents and young adults on ART ≥12 months were most likely to switch compared with those who had just enrolled into care and initiated ART. This observation is particularly interesting in light of the fact that ART-naive clients were also more likely to initiate on DTG, suggesting that DTG is being adopted across both treatment-experienced and naive populations. This dual trend underscores the growing

confidence in DTG as a first-line option for ART-naive clients as well as a preferred switch option for patients with longer ART histories.

Finally, we report in univariate analyses that DTG use was least likely in children <5 years. This was an expected result in the early years of our study, since paediatric DTG (pDTG, 10mg) was not widely available then. Cote d’Ivoire, Benin and Nigeria were the first countries to rollout paediatric formulations.<sup>36</sup> Furthermore, the TORPEDO study, carried out in Benin and Nigeria reported high acceptability and preference for pDTG.<sup>37</sup> However, our results report low transition in the population. While this is most probably explained by the fact that these younger children were on LPV/r, remaining in the system, it may also be a result of poor planning and stock-outs. This is of particular concern in terms of outcomes in these younger children living with HIV, who may remain at high risk of virological failure in the context of a slow transition to DTG-containing ART regimens.<sup>38</sup> As paediatric treatment optimisation is focused on the continued scale-up of pDTG, irrespective of VL,

and more recently the introduction of paediatric fixed-dose combination of abacavir-lamivudine-dolutegravir (pALD), it is essential for countries to ensure appropriate forecasting and supply, even for small quantities.

Our study had several limitations. First, the referral clinics involved in these analyses are not representative of their country, leading to a probable over-estimation of DTG roll-out progress. We also reported no DTG roll-out in Togo, although previous literature has reported on the beginning of DTG roll-out since October 2019.<sup>39</sup> Second, we report that DTG roll-out began in 2019, shortly before the COVID-19 pandemic, where healthcare provision may have been different from that of standard care, thus affecting structural factors associated with DTG initiation. Third, this study was carried out in the early years of DTG roll-out, with varying database closeout dates ranging from 2021–2022. This was also amidst perinatal safety concerns regarding the use of DTG among women of childbearing age and before pDTG was rolled out. We do not account for change in practices over time, however, this less complex model, avoids overfitting and associated limitations in external validity of results. Fourth, the actual reasons from the perspective of healthcare providers for not transitioning patients to DTG-based regimens are not documented. This could help inform strategies to address any barriers and facilitate better access to DTG regimens.

This study however, provides useful real-world evidence on the scale-up of DTG in children, adolescents and young adults increasing rapidly since 2019 in west Africa, but still incomplete after 24 months. While we anticipate that sex disparities and the slow transition among the youngest children may fade in the coming years, DTG uptake remains unequal. Lack of VL and wastage concerns should not be a barrier to DTG initiation. Implementation of DTG regimens should be accompanied by an accelerated scaling up of access to VL before, and after switch to DTG. Continued monitoring of DTG implementation, its outcomes and better planning of treatment option strategies are required to ensure universal access to all.

## ETHICS

This study was conducted using data from the IeDEA consortium, which collects and manages de-identified patient data from various sites across the globe for research purposes. Ethical approval for the conduct of this study was obtained from the institutional review boards (IRBs) or equivalent ethics committees of each participating country and institution, ensuring compliance with both national and international ethical guidelines for research involving human participants.

The following IRBs and ethics committees provided approval for the use of data in this study:

- ▶ Côte d'Ivoire, Comité National d'Ethique des Sciences de la Vie et de la Santé (CNESVS), IRB00009111, Expiration date: 02/17/2025

- ▶ Nigeria, National Inst Med Rsch (NIMR) IRB #1 – Biomedical, IRB00003224, Expiration date: 3/22/2026
- ▶ Mali, U Mali Faculty Med Pharmacy & Dentistry IRB #1 – USTTB, IRB00001983, Expiration date: 09/02/2025
- ▶ Burkina Faso, Comité d'Ethique pour la Recherche en Santé, IRB000013418, Expiration date: 02/17/2025
- ▶ Bénin, Comité National d'Ethique pour la Recherche en Santé (CNPERS), IRB00006860, Expiration date: 6/20/2027
- ▶ Togo, Comité de Bioethique pour la Recherche en Santé (CBRS), IRB00009547, Expiration date: 11/03/2026
- ▶ Ghana, U Ghana Med Sch/College of Hlth Sciences, IRB00006220, Expiration date: 11/15/2024

All data used were de-identified before analysis, ensuring that patient confidentiality and privacy were protected.

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**Contributors** SD and VL conceived the study and designed the methodology. KM was responsible for data collection and management. SD provided statistical expertise and analysed the data. JD, AD, MAF, SNG, MS, ET, KK, FTE, LBT and CY contributed data and were involved in the interpretation and analysis of the findings, providing input that informed the study's conclusions and implications. All authors contributed to the drafting of the manuscript, provided revisions, and approved the final version for submission. VL acts as guarantor. DeepPro was used at times for translations to the English language.

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## REFERENCES

- 1 *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach*. 2nd edn. Geneva: World Health Organization, 2016.
- 2 Phillips AN, Cambiano V, Nakagawa F, *et al*. Cost-effectiveness of public-health policy options in the presence of pretreatment NNRTI drug resistance in sub-Saharan Africa: a modelling study. *Lancet HIV* 2018;5:e146–54.
- 3 Zash R, Makhema J, Shapiro RL. Neural-Tube Defects with Dolutegravir Treatment from the Time of Conception. *N Engl J Med* 2018;379:979–81.
- 4 World Health Organisation. Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV. 2018.
- 5 Zash R, Holmes L, Diseko M, *et al*. Neural-Tube Defects and Antiretroviral Treatment Regimens in Botswana. *N Engl J Med* 2019;381:827–40.
- 6 Dugdale CM, Ciaranello AL, Bekker L-G, *et al*. Risks and Benefits of Dolutegravir- and Efavirenz-Based Strategies for South African Women With HIV of Child-Bearing Potential: A Modeling Study. *Ann Intern Med* 2019;170:614–25.
- 7 Phillips AN, Venter F, Havlir D, *et al*. Risks and benefits of dolutegravir-based antiretroviral drug regimens in sub-Saharan Africa: a modelling study. *Lancet HIV* 2019;6:e116–27.
- 8 Turkova A, White E, Mujuru HA, *et al*. Dolutegravir as First- or Second-Line Treatment for HIV-1 Infection in Children. *N Engl J Med* 2021;385:2531–43.
- 9 Bollen PDJ, Moore CL, Mujuru HA, *et al*. Simplified dolutegravir dosing for children with HIV weighing 20 kg or more: pharmacokinetic and safety substudies of the multicentre, randomised ODYSSEY trial. *Lancet HIV* 2020;7:e533–44.
- 10 Viani RM, Alvero C, Fenton T, *et al*. Safety, Pharmacokinetics and Efficacy of Dolutegravir in Treatment-experienced HIV-1 Infected Adolescents: Forty-eight-week Results from IMPAACT P1093. *Pediatr Infect Dis J* 2015;34:1207–13.
- 11 Bruzzese E, Lo Vecchio A, Smarrazzo A, *et al*. Dolutegravir-based anti-retroviral therapy is effective and safe in HIV-infected paediatric patients. *Ital J Pediatr* 2018;44:37.
- 12 Turkova A, Waalewijn H, Chan MK, *et al*. Dolutegravir twice-daily dosing in children with HIV-associated tuberculosis: a pharmacokinetic and safety study within the open-label, multicentre, randomised, non-inferiority ODYSSEY trial. *Lancet HIV* 2022;9:e627–37.
- 13 Waalewijn H, Chan MK, Bollen PDJ, *et al*. Dolutegravir dosing for children with HIV weighing less than 20 kg: pharmacokinetic and safety substudies nested in the open-label, multicentre, randomised, non-inferiority ODYSSEY trial. *Lancet HIV* 2022;9:e341–52.
- 14 World Health Organisation. Update of recommendations on first- and second-line antiretroviral regimens. Geneva, Switzerland World Health Organization; 2019.
- 15 *Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery and Monitoring: Recommendations for a Public Health Approach*. Geneva: World Health Organization, 2021.
- 16 Ekouevi DK, Azondekon A, Dicko F, *et al*. 12-month mortality and loss-to-program in antiretroviral-treated children: The leDEA pediatric West African Database to evaluate AIDS (pWADA), 2000–2008. *BMC Public Health* 2011;11:519.
- 17 Anaky M-F, Duvignac J, Wemin L, *et al*. Scaling up antiretroviral therapy for HIV-infected children in Côte d'Ivoire: determinants of survival and loss to programme. *Bull World Health Organ* 2010;88:490–9.
- 18 Austin PC. A Tutorial on Multilevel Survival Analysis: Methods, Models and Applications. *Int Stat Rev* 2017;85:185–203.
- 19 Desmonde S, Anderson K, Bwami J, *et al*. Global Transition to Dolutegravir-Based ART in Children and Adolescents 0–19 Years Living With HIV. 2024.
- 20 Ben Farhat J, Tiendrebeogo T, Malateste K, *et al*. Effects of the COVID-19 Pandemic on ART Initiation and Access to HIV Viral Load Monitoring in Adults Living With HIV in West Africa: A Regression Discontinuity Analysis. *J Acquir Immune Defic Syndr* 2024;96:114–20.
- 21 Mohammed A, Donkoh IE, Aboagye RG, *et al*. Access to quality contraceptive counselling among adolescent girls and young women in sub-Saharan Africa. *Contracept Reprod Med* 2024;9:16.
- 22 Radovich E, Dennis ML, Wong KLM, *et al*. Who Meets the Contraceptive Needs of Young Women in Sub-Saharan Africa? *J Adolesc Health* 2018;62:273–80.
- 23 Wollum A, Moucheraud C, Gipson JD, *et al*. Characterizing provider bias in contraceptive care in Tanzania and Burkina Faso: A mixed-methods study. *Soc Sci Med* 2024;348:116826.
- 24 Agu IC, Agu C, Mbachu C, *et al*. Impact of a capacity-building intervention on views and perceptions of healthcare providers towards the provision of adolescent sexual and reproductive health services in southeast Nigeria: a cross-sectional qualitative study. *BMJ Open* 2023;13:e073586.
- 25 Tiendrebeogo T, Malateste K, Poda A, *et al*. Sex-Based Disparities in the Transition to Dolutegravir-Based Antiretroviral Therapy in West African HIV Cohorts. *Open Forum Infect Dis* 2024;11:ofae139.
- 26 Romo ML, Patel RC, Edwards JK, *et al*. Disparities in Dolutegravir Uptake Affecting Females of Reproductive Age With HIV in Low- and Middle-Income Countries After Initial Concerns About Teratogenicity: An Observational Study. *Ann Intern Med* 2022;175:84–94.
- 27 Machila N, Libonda L, Habineza P, *et al*. Prevalence and predictors of virological failure in paediatric patients on HAART in sub-Saharan Africa: a systematic review and meta-analysis. *Pan Afr Med J* 2023;45:98.

- 28 Redd AD, Mukonda E, Hu N-C, *et al*. ART Adherence, Resistance, and Long-term HIV Viral Suppression in Postpartum Women. *Open Forum Infect Dis* 2020;7:ofaa346.
- 29 Malinga S, Khan A, Archary M. Breaking the unbreakable: A paediatric case of dolutegravir resistance from KwaZulu-Natal. *South Afr J HIV Med* 2023;24:1458.
- 30 Rhee S-Y, Grant PM, Tzou PL, *et al*. A systematic review of the genetic mechanisms of dolutegravir resistance. *J Antimicrob Chemother* 2019;74:3135–49.
- 31 Salou M, Butel C, Comlan AS, *et al*. Challenges of scale-up to dolutegravir-based regimens in sub-Saharan Africa. *AIDS* 2020;34:783–7.
- 32 Siberry GK, Amzel A, Ramos A, *et al*. Impact of Human Immunodeficiency Virus Drug Resistance on Treatment of Human Immunodeficiency Virus Infection in Children in Low- and Middle-Income Countries. *J Infect Dis* 2017;216:S838–42.
- 33 HIV drug resistance – brief report. 2024. Available: <https://www.who.int/publications-detail-redirect/9789240086319> [Accessed 13 May 2024].
- 34 Aboud M, Kaplan R, Lombaard J, *et al*. Dolutegravir versus ritonavir-boosted lopinavir both with dual nucleoside reverse transcriptase inhibitor therapy in adults with HIV-1 infection in whom first-line therapy has failed (DAWNING): an open-label, non-inferiority, phase 3b trial. *Lancet Infect Dis* 2019;19:253–64.
- 35 Clinton Health Access Initiative. Paediatric Dolutegravir 10 mg dispersible, scored tablets implementation memo. 2021.
- 36 Clinton Health Access Initiative, icap Globam Health. The Dolutegravir transition in west Africa best practices, lessons learned, next steps (a CQUIN & CHAI webinar). 2022.
- 37 Campbell J, Rathakrishnan D, Ngwatu B, *et al*. Outcomes from the transitioning children to optimal regimens of paediatric dolutegravir (TORPEDO) study at 6 months in Benin, Nigeria, and Uganda. Brisbane, Australia; 2023.
- 38 Fokam J, Nka AD, Mamgue Dzukam FY, *et al*. 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. *Medicine (Baltimore)* 2023;102:e33737.
- 39 Casalini C, D’Almeida Y, Nassam MA, *et al*. Targeted solutions to increase dolutegravir coverage, viral load testing coverage, and viral suppression among children living with HIV in Togo: An analysis of routine facility data. *PLoS One* 2023;18:e0296293.