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Transition to dolutegravir-based ART in 35 low- and middle-income countries: a global survey of HIV care clinics

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Objective: We studied the transition to dolutegravir-containing antiretroviral therapy (ART) at HIV treatment clinics within the International epidemiology Databases to Evaluate AIDS (IeDEA).

Design: Site-level survey conducted in 2020–2021 among HIV clinics in low- and middle-income countries (LMICs).

Methods: We assessed the status of dolutegravir rollout and viral load and drug resistance testing practices for persons on ART switching to dolutegravir-based regimens. We used generalized estimating equations to assess associations between clinic rollout of both first- and second-line dolutegravir-based ART regimens (dual rollout) and site-level factors.

Results: Of 179 surveyed clinics, 175 (98%) participated; 137 (78%) from Africa, 30 (17%) from the Asia-Pacific, and 8 (5%) from Latin America. Most clinics (80%) were in low- or lower-middle-income countries, and there were a mix of primary-, secondary- and tertiary-level clinics. Ninety percent reported rollout of first-line dolutegravir, 59%

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of second-line, 94% of first- or second-line and 55% of dual rollout. The adjusted odds of dual rollout were higher among tertiary-level [adjusted odds ratio (aOR) 4.00; 95% confidence interval (CI) 1.39–11.47] and secondary-level clinics (aOR 3.66; 95% CI 2.19–6.11) than in primary-level clinics. Over half (59%) of clinics that introduced first- or second-line dolutegravir-based ART required recent viral load testing before switching to dolutegravir, and 15% performed genotypic resistance testing at switch.

Conclusions: Dolutegravir-based ART was rolled out at nearly all IeDEA clinics in LMICs, yet many switched persons to dolutegravir without recent viral load testing and drug resistance testing was rarely performed. Without such testing, drug resistance among persons switching to dolutegravir may go undetected.

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Keywords: antiretroviral therapy, dolutegravir, drug resistance testing, HIV, low- and middle-income countries, viral load

Introduction

The integrase strand transfer inhibitor (INSTI) dolutegravir was approved in 2013 in the United States and in early 2014 in the European Union. Dolutegravir is an antiretroviral drug with a higher barrier to drug resistance than nonnucleoside reverse transcriptase inhibitors (NNRTI), is well tolerated and associated with rapid viral suppression in treatment naïve people with HIV (PWH) [1–5]. Commonly prescribed in many high-income settings since 2015, an agreement in 2017 for a generic fixed-dose combination regimen containing tenofovir disoproxil fumarate, lamivudine and dolutegravir (TLD) [6] made this regimen more affordable in resource-limited settings.

The advent of dolutegravir was timely. By 2016, NNRTI pretreatment resistance had surpassed 10% in Southern and Eastern Africa and was approaching this level in Latin America and the Caribbean [7]; 10% represents the point at which the World Health Organization (WHO) recommends a change in the first-line antiretroviral therapy (ART) regimen [8]. In its 2017 HIV Drug Resistance Report [7], WHO argued for the "strategic use of increasingly affordable drugs with higher barriers to the development of resistance (e.g. dolutegravir)". A recent modelling study that examined the impact of scaling up dolutegravir-based ART in South Africa found that widespread use of dolutegravir-based first-line ART will likely curb the spread of NNRTI resistance [9].

The introduction of dolutegravir in resource-limited settings was complicated by concerns of a possible association between foetal in-utero exposure and neural tube defects [10]. This led the WHO in its July 2018 interim guidance to initially caution its use in women and adolescent girls of child-bearing age [11]. Subsequent studies found the risk for neural tube disorders was lower than previously suggested [12], and modelling suggested the benefits of dolutegravir outweighed the risks [13,14]. In July 2019, the WHO recommended dolutegravir as the preferred drug for first-line and second-line ART in all populations, including pregnant women and those of

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child-bearing age [15]. Since then, dolutegravir-based ART has been recommended by countries globally with about 100 countries including dolutegravir in their treatment guidelines by mid-2022 [16].

The extent and pace of transition to dolutegravir-based first- and second-line ART in low- and middle-income countries (LMICs) remains unclear. Previous studies that assessed the early uptake of dolutegravir in ART regimens focussed on gender difference in early uptake either in a small subset of LMICs countries [17,18], or in a single country [19]. The WHO recommendations may take time to be implemented in national guidelines, may be adopted in only some countries, and within countries, may not be uniformly implemented across all treatment facilities. We examined the transition to dolutegravir in a large sample of HIV treatment and care clinics in LMICs. Specifically, we determined the proportion of clinics that reported rollout of dolutegravir as part of first- or second-line ART, and examined the role of viral load measurements and genotypic drug resistance testing for PWH on ART who switch to dolutegravir-based ART.

Methods

Data sources

The International epidemiology Databases to Evaluate AIDS (IeDEA) research consortium collects de-identified routine clinical data from over 2.2 million people living with and at risk for HIV enrolled in participating HIV treatment and care sites in 44 countries across seven geographic regions: the Asia-Pacific; the Caribbean, Central and South America (Latin America); Central Africa; East Africa; Southern Africa; West Africa; and North America [20–22]. In addition to collecting routine patient-level data, IeDEA conducts periodic cross-sectional site assessment surveys among participating clinics to better understand and assess clinic characteristics, current clinical practices and support services available to enrolled PWH [23].

We analysed data from an IeDEA site assessment survey, conducted between September 2020 and March 2021 among sites actively contributing data to the consortium. It included all clinics that were actively contributing longitudinal patient data to IeDEA in 2020 for all regions, except Southern Africa, where due to a large number of clinics, purposive random sampling was used to include 15% of 213 participating clinics [23]. The survey included questions to characterize the clinic population's residence and age, and the availability of viral load and genotypic drug resistance testing as part of routine patient care. It also explored the status of dolutegravir-based first- and second-line ART introduction, the impetus for dolutegravir rollout (e.g., national or local/sub-national initiative), and viral load and genotypic drug resistance testing practices for PWH on ART who switch to dolutegravir-based ART. The survey questionnaire (see Supplementary File, http://links.lww.com/QAD/D305) was available in English and French for completion on paper, or online using REDCap (Research Electronic Data Capture) [24,25].

Inclusion criteria

We included all surveyed clinics from countries classified by the World Bank for year 2020 as either low-, lower-middle-, or upper-middle-income. We excluded clinics that did not initiate the survey questionnaire.

Definitions

We obtained national HIV prevalence estimates for 2020 from UNAIDS [26] and for countries not available in the UNAIDS data (i.e., China and Mozambique) from other sources [27,28]. We classified countries and their clinics into three groups: those with a low national HIV prevalence ($<1\%$), a medium prevalence ($1-4.9\%$), and a high prevalence ($\geq 5\%$). We categorized participating clinics as either primary- (e.g., health centres), secondary- (e.g., district hospitals) or tertiary-level (e.g., regional, provincial or university hospitals) clinics.

The survey explored the current status of dolutegravir rollout for first- and second-line ART regimens at each clinic and assessed the availability of HIV viral load assay and HIV-1 genotypic drug resistance testing in 2019 as part of routine care. The location where testing was typically performed was defined as either onsite (i.e., at the HIV clinic or in the same health facility) or only offsite. The survey assessed whether viral load testing was required to transition a person to dolutegravir-based ART and the timeliness of such testing (e.g., within the previous six months, within the previous 12 months, or varies by client group), and whether HIV genotypic drug resistance testing was performed at switch to dolutegravir-based ART.

Statistical analysis

We used descriptive statistics to summarize clinic-level characteristics, including the age of PWH served (e.g., paediatric (≤ 9 years), adolescents ($10-24$ years), adults (≥ 20 years)), the residence of the PWH population served (e.g., predominantly urban, predominately rural, or mixed urban/rural), availability of viral load and genotypic drug resistance testing (e.g., onsite, offsite or not available) and the impetus for dolutegravir rollout (e.g., national or local initiative), stratified by IeDEA region. We also used descriptive statistics to summarize reported rollout of dolutegravir-based ART for first-line, second-line and for both first- and second-line regimens (i.e. dual rollout). Among those clinics that reported rollout of first- or second-line dolutegravir-based ART, we summarized viral load and genotypic drug resistance testing practices for persons switching to dolutegravir-based ART. Descriptive statistics were stratified by World Bank country income group, national HIV prevalence category, and clinic level.

We used generalized estimating equations, with clinics clustered by country, to assess the association of World Bank country income group, national HIV prevalence category, clinic level, residence of the PWH population served and availability of HIV genotypic drug resistance testing with the probability of a clinic reporting rollout of both first- and second-line dolutegravir-based ART regimens (dual rollout). We calculated p-values for each model variable using a likelihood ratio test and calculated adjusted odds ratios for each association. All statistical analyses and descriptive mapping were performed using R Statistical Software (v4.3.3; R Core Team 2024) [29] and RStudio (version 2023.12.1) [30].

Ethical consideration

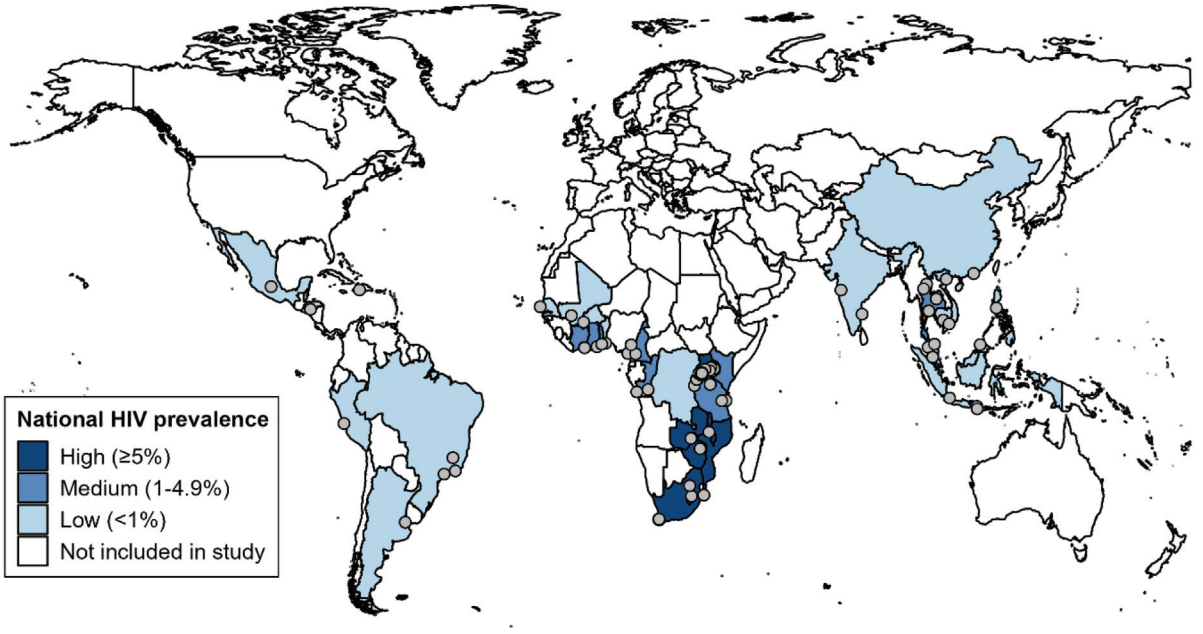
The survey was designated a nonhuman subjects operational/quality improvement project by the Vanderbilt University Medical Center (VUMC) Institutional Review Board (#200013) [24]. Informed consent was not required because the survey did not collect patient-level data; only clinic-level data was collected. We invited colleagues from clinics that provided survey data to collaborate on the drafting of this manuscript.

Results

The survey was sent to 179 clinics in 35 LMICs, of which four clinics in two Southern Africa countries did not complete the survey (2%). Of the 175 facilities included in this study, 137 (78%) were from 21 countries in the four African regions of IeDEA, 30 (17%) were from eight countries in the Asia-Pacific region and 8 (5%) were from six countries in Latin America (Fig. 1).

Site characteristics

About half of the clinics were from countries with a medium HIV prevalence (47% of clinics), half were from lower-middle-income countries (51%) and half were primary-level clinics (53%) (Table 1). Nearly half of clinics reported serving a mixed population of clients



Latin America	West Africa	Central Africa	Southern Africa	East Africa	Asia-Pacific
Argentina (1)	Benin (2)	Burundi (3)	Lesotho (1)	Kenya (42)	Cambodia (2)
Brazil (3)	Burkina Faso (1)	Cameroon (3)	Malawi (2)	Tanzania (3)	China (1)
Haiti (1)	Côte d'Ivoire (7)	Dem. Rep. Congo (1)	Mozambique (1)	Uganda (29)	India (3)
Honduras (1)	Ghana (1)	Republic of Congo (2)	South Africa (14)		Indonesia (4)
Mexico (1)	Mali (1)	Rwanda (12)	Zambia (5)		Malaysia (6)
Peru (1)	Senegal (1)		Zimbabwe (5)		Philippines (1)
	Togo (1)				Thailand (8)
					Vietnam (5)

Fig. 1. Location of 175 HIV clinics in low- and middle-income countries participating in the survey. The grey dots on the map represent the location of surveyed clinics and the number of surveyed clinics per country are included in parentheses in the table.

Table 1. Characteristics of 175 HIV clinics participating in the survey.

	Total	Asia-Pacific	Latin America	Central Africa	East Africa	Southern Africa	West Africa
	175 (100)	30 (17)	8 (5)	21 (12)	74 (42)	28 (16)	14 (8)
Country income group							
Low	51 (29)	0 (0)	0 (0)	16 (76)	29 (39)	3 (11)	3 (21)
Lower-middle	89 (51)	15 (50)	2 (25)	5 (24)	45 (61)	11 (39)	11 (79)
Upper-middle	35 (20)	15 (50)	6 (75)	0 (0)	0 (0)	14 (50)	0 (0)
National HIV prevalence							
Low (<1)	35 (20)	22 (73)	7 (88)	1 (5)	0 (0)	0 (0)	5 (36)
Medium (1–4.9)	83 (47)	8 (27)	1 (12)	20 (95)	45 (61)	0 (0)	9 (64)
High (≥5)	57 (33)	0 (0)	0 (0)	0 (0)	29 (39)	28 (100)	0 (0)
Clinic level							
Primary	93 (53)	4 (13)	0 (0)	12 (57)	54 (73)	20 (71)	3 (21)
Secondary	17 (10)	0 (0)	0 (0)	0 (0)	13 (18)	2 (7)	2 (14)
Tertiary	65 (37)	26 (87)	8 (100)	9 (43)	7 (9)	6 (21)	9 (64)
Residence of population served							
Predominantly urban	49 (28)	10 (33)	8 (100)	7 (33)	1 (1)	16 (57)	7 (50)
Predominantly rural	42 (24)	0 (0)	0 (0)	2 (10)	37 (50)	3 (11)	0 (0)
Mixed urban/rural	84 (48)	20 (67)	0 (0)	12 (57)	36 (49)	9 (32)	7 (50)
Age of population served							
Pediatric only (≤9 years)	22 (13)	10 (33)	1 (12)	0 (0)	1 (1)	3 (11)	7 (50)
Adults only (≥20 years)	17 (10)	9 (30)	2 (25)	0 (0)	3 (4)	1 (4)	2 (14)
Adolescents only (10–24 years)	1 (1)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Pediatric and adults	135 (77)	10 (33)	5 (62)	21 (100)	70 (95)	24 (86)	5 (36)
Adolescents (10–24 years) served							
Yes	165 (94)	25 (83)	7 (88)	21 (100)	71 (96)	28 (100)	13 (93)
No	10 (6)	5 (17)	1 (12)	0 (0)	3 (4)	0 (0)	1 (7)
Viral load testing							
Available onsite[a]	73 (42)	24 (80)	6 (75)	8 (38)	9 (12)	15 (54)	11 (79)
Available only offsite	97 (55)	5 (17)	2 (25)	12 (57)	62 (84)	13 (46)	3 (21)
Not available	5 (3)	1 (3)	0 (0)	1 (5)	3 (4)	0 (0)	0 (0)
Genotypic resistance testing							
Available onsite[a]	27 (15)	12 (40)	5 (62)	0 (0)	2 (3)	6 (21)	2 (14)
Available only offsite	112 (64)	14 (47)	1 (12)	17 (81)	57 (77)	14 (50)	9 (64)
Not available	36 (21)	4 (13)	2 (25)	4 (19)	15 (20)	8 (29)	3 (21)
Impetus for dolutegravir first- or second-line rollout							
National initiative	144 (82)	7 (23)	6 (75)	20 (95)	70 (95)	27 (96)	14 (100)
Local initiative	16 (9)	12 (40)	0 (0)	0 (0)	3 (4)	1 (4)	0 (0)
No initiative reported	4 (2)	1 (3)	1 (12)	1 (5)	1 (1)	0 (0)	0 (0)
No first- or second-line rollout	11 (6)	10 (33)	1 (12)	0 (0)	0 (0)	0 (0)	0 (0)

Number of clinics (%) are shown unless otherwise indicated.
[a]In the HIV clinic or in the same health facility.

from both urban and rural settings (48%) and more than three quarters (77%) served both paediatric (≤9 years) and adult (≥20 years) PWH; overall 94% of all clinics served adolescents (10–24 years). Almost all clinics reported having viral load testing available (97%) and more than three quarters (79%) reported having genotypic drug resistance testing available as part of routine patient care. Most clinics (82%) reported that dolutegravir first- or second-line rollout was part of a national initiative and about a tenth (9%) as part of a local-level initiative; 2% did not report an initiative and 6% did not report first- or second-line rollout of dolutegravir-based ART. Aside from Southern Africa, no other African region had clinics in an upper-middle-income country. In contrast, there were no clinics from low-income countries in the Asia-Pacific and Latin America. All clinics in Southern Africa and over a third (39%) in East Africa had a high national HIV prevalence, and most clinics in Central, East and Southern Africa were primary-level clinics. While most clinics in Africa and Latin America reported rollout of first- or second-line dolutegravir-based ART was part of a national initiative, in the Asia-Pacific more than half reported it was part of a local initiative.

Rollout of dolutegravir-based ART

Rollout of dolutegravir for first-line ART was reported by 157 (90%) clinics and for second-line ART by 104 (59%) clinics; 164 (94%) clinics reported rollout of first- or second-line ART. First-line rollout of dolutegravir-based ART was reported by all clinics with high (100%) national HIV prevalence or low (100%) country income (Fig. 2). In contrast, fewer than two-thirds of these clinics reported second-line rollout of dolutegravir-based ART. Among clinics with low national HIV prevalence or upper-middle-income, reported rollout of dolutegravir in second-line ART regimens was at least as common as reported rollout in first-line regimens. The reported rollout of first-line dolutegravir-based regimens was higher among primary- (99%) and secondary-level clinics (100%) than among tertiary-level clinics (74%). In contrast, the reported rollout of second-line dolutegravir-based regimens was higher among secondary- (88%)

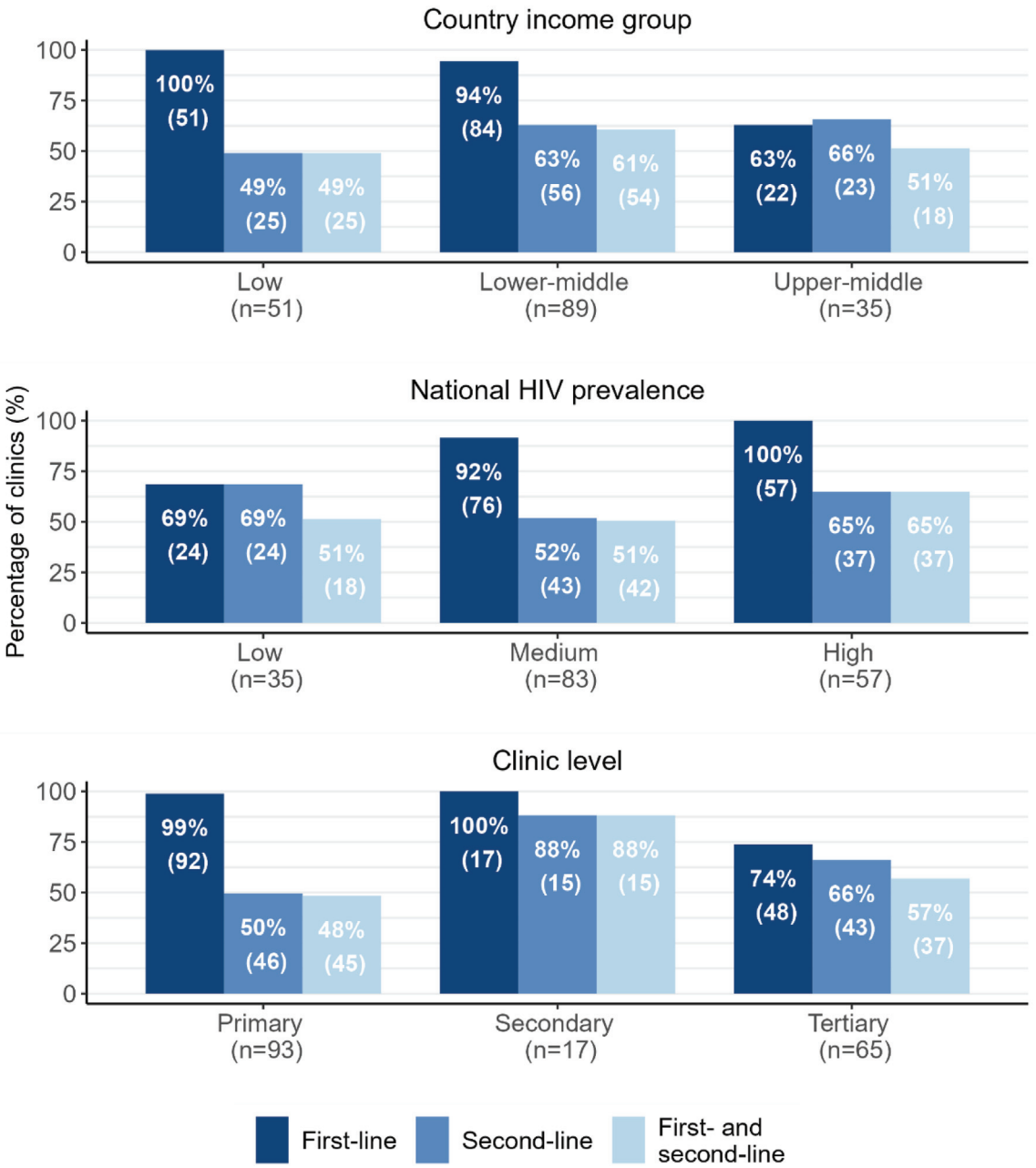


Fig. 2. Reported rollout of dolutegravir-based ART for first-line, second-line and for both first- and second-line regimens among 175 surveyed HIV clinics by country income, HIV prevalence and clinic level.

and tertiary-level (66%) clinics than primary-level (50%) clinics.

Dual rollout of dolutegravir-based ART regimens (i.e., for both first- and second-line ART) was reported by 97 (55%) clinics (Fig. 2) in 29 countries. More than three quarters of secondary-level (88%) and more than half of tertiary-level (57%) clinics reported dual rollout, whereas dual rollout was reported by less than half of primary-level (48%) clinics. The regression analysis for dual rollout of dolutegravir-based ART regimens suggested an association with clinic level (Fig. 3). The adjusted odds of dual rollout were higher among tertiary-level clinics [adjusted odds ratio (aOR) 4.00; 95% confidence interval (CI) 1.39–11.47] and secondary-level clinics (aOR 3.66; 95% CI 2.19–6.11) clinics than primary-level clinics. There was only weak evidence (P-value >0.1) of an association with national HIV prevalence and the residence of the PWH population served, and no evidence of an association with other covariates in the model.

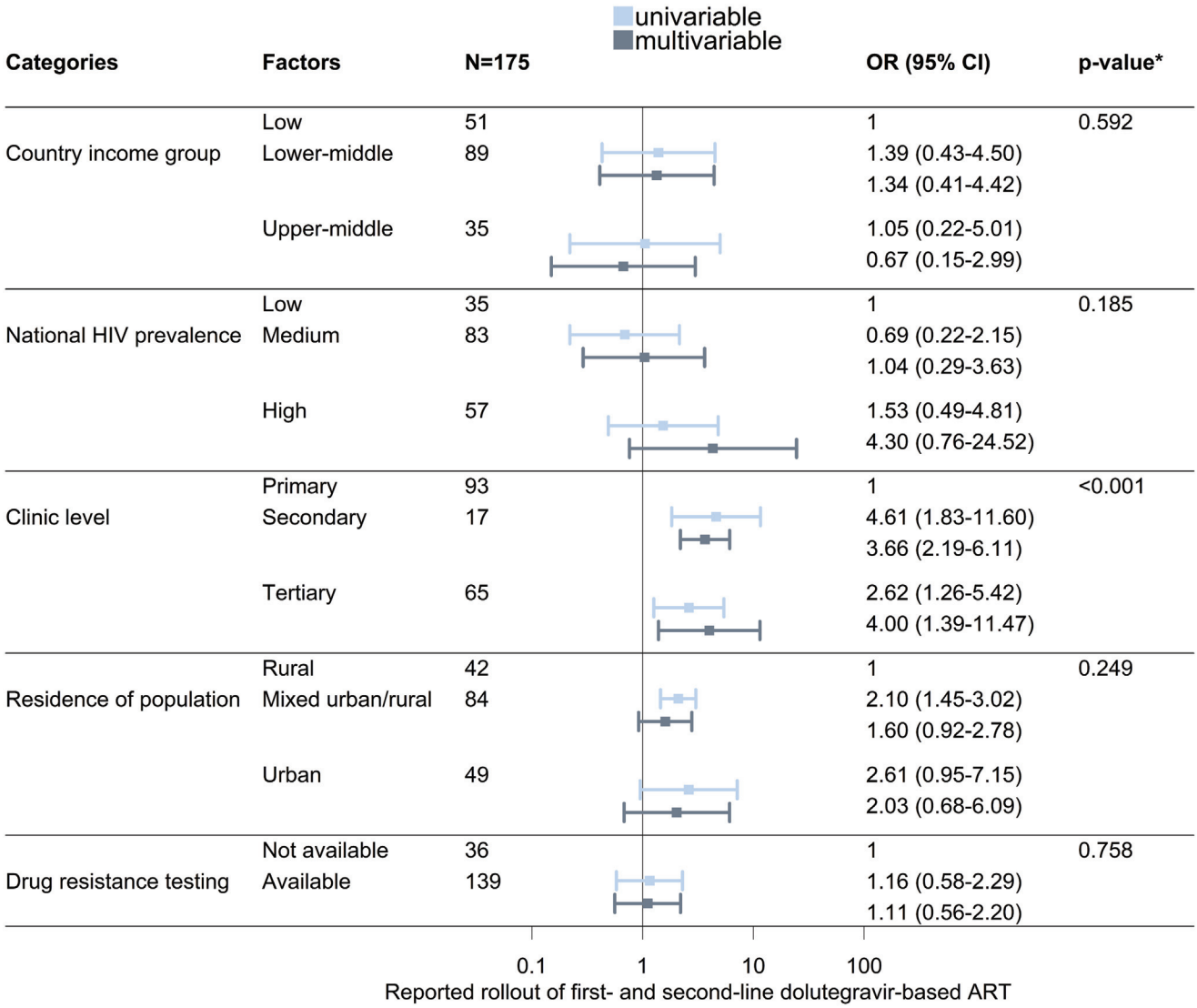


Fig. 3. Univariable and multivariable logistic regression of reported rollout of dolutegravir-based ART for both first- and second-line regimens among 175 HIV clinics. *Likelihood ratio test. ART, antiretroviral therapy; CI, confidence interval; OR, odds ratio.

Viral load and drug resistance testing practices at switch to dolutegravir

All 164 clinics that reported introducing first- or second-line dolutegravir-based ART, reported having viral load testing available as part of routine care (Table 2). Of these clinics, 59% required testing within the six months before a PWH on ART switched to dolutegravir-based ART; this requirement was more common among clinics in low-income countries or in countries with a high HIV prevalence than in other countries. While 80% of these 164 clinics reported having genotypic resistance testing available as part of routine care, only 15% reported performing resistance testing at the time a PWH switched to dolutegravir-based ART. Such testing was more common in clinics from upper-middle-income countries, in low prevalence countries and in tertiary-level clinics.

Discussion

This study of 175 HIV treatment and care clinics in 35 LMICs is the first, to our knowledge, that describes clinic-level rollout of dolutegravir-based ART by treatment line in resource-limited settings. Although previous patient-level studies in LMICs found early uptake of dolutegravir-based ART varied by sex [17–19], our clinic-level study found that rollout of dolutegravir regimens in LMICs varied across ART treatment lines. By the end of 2020 and the beginning of 2021, we found most clinics reported rollout of dolutegravir in first-line ART regimens; fewer reported rollout in second-line regimens. About half of clinics reported rolling out dolutegravir-based ART across both treatment lines, with the regression analysis showing a positive association with

Table 2. Viral load and genotypic drug resistance testing practices at switch to dolutegravir among 164 surveyed HIV clinics that reported rollout of first- or second-line dolutegravir-based ART.

		Country income group			National HIV prevalence			Clinic level		
	Total $N=164$ (100%)	Low $n=51$ (31%)	Lower-middle $n=86$ (52%)	Upper-middle $n=27$ (17%)	Low (<1%) $n=30$ (18%)	Medium (1–4.9%) $n=77$ (47%)	High (≥5%) $n=57$ (35%)	Primary $n=93$ (57%)	Secondary $n=17$ (10%)	Tertiary $n=54$ (33%)
Viral load monitoring										
Required within previous 6 months	96 (59)	36 (71)	44 (51)	16 (59)	19 (63)	36 (47)	41 (72)	56 (60)	7 (41)	33 (61)
Required within previous 12 months	27 (16)	3 (6)	19 (22)	5 (19)	1 (3)	14 (18)	12 (21)	19 (21)	6 (35)	2 (4)
Required, varies by client group	11 (7)	0 (0)	9 (11)	2 (7)	1 (3)	8 (10)	2 (4)	5 (5)	4 (24)	2 (4)
Available, not required	30 (18)	12 (23)	14 (16)	4 (15)	9 (30)	19 (25)	2 (4)	13 (14)	0 (0)	17 (31)
Unavailable	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Genotypic drug resistance testing										
Performed	24 (15)	6 (12)	10 (12)	8 (30)	7 (23)	9 (12)	8 (14)	9 (10)	3 (18)	12 (22)
Available, not performed	107 (65)	33 (65)	60 (70)	14 (51)	19 (64)	53 (69)	35 (61)	64 (69)	13 (76)	30 (56)
Unavailable	33 (20)	12 (23)	16 (18)	5 (19)	4 (13)	15 (19)	14 (25)	20 (21)	1 (6)	12 (22)

Number of clinics (%) are shown unless otherwise indicated.

higher clinic levels. Over half of clinics that rolled out dolutegravir in first- or second-line ART regimens reported requiring PWH to have a recent viral load measurement before switching to dolutegravir-based ART, but less than a fifth reported performing genotypic drug resistance testing at such a switch.

A scoping review identified several factors at different levels influencing the uptake of and compliance with clinical guidelines in LMIC settings, including organizational and institutional factors, and highlighted the importance of interactions with high income countries [31]. Funding from international donors (e.g., the US President's Emergency Plan for AIDS Relief; PEPFAR) may have contributed to the universal rollout of first-line dolutegravir-based ART and the higher level of recent viral load testing reportedly required at regimen switch among clinics in countries with a high HIV prevalence and in low-income countries. The rollout of first-line dolutegravir-based ART in most clinics is reassuring; however the shortfall in second-line rollout could be of concern, as it suggests that many who fail first-line NNRTI-based therapies may lack access to dolutegravir-based second-line ART regimens.

These results should be interpreted in light of the evidence and global recommendations available at the time on dolutegravir-based first- and second-line ART. By the time of the survey in late 2020, clinical trials and a network meta-analysis had documented that, compared to efavirenz, dolutegravir-based first-line ART had higher rates of viral suppression, fewer ART discontinuations and reduced emergence of drug-resistance to nucleoside reverse transcriptase inhibitors (NRTIs) [1–5]. In contrast, the evidence supporting the use of dolutegravir-based ART for second-line regimens was more limited. The DAWNING trial [32] had only just reported that dolutegravir-based ART was more efficacious in suppressing viral replication than boosted lopinavir in PWH who had experienced virological failure on a NNRTI-based first-line regimen, and that dolutegravir had a more favourable safety profile. Unsurprisingly, the July 2019 updated WHO recommendations were "strong" for dolutegravir-based first-line ART, but "conditional" for the use of dolutegravir in second-line ART, which may have been reflected in national and local HIV treatment guidelines.

Other reasons for the limited roll-out of dolutegravir for second-line ART at the time of the survey may relate to the cost of adding another second-line regimen to the existing one based on a boosted protease inhibitor [33]. Since 2019, the WHO has recommended a dolutegravir-based ART that contains zidovudine as the preferred second-line regimen for many PWH failing an NNRTI-based first-line ART regimen with a tenofovir-based NRTI backbone [15]. This regimen is not only more expensive to purchase than first-line TLD, but is also less-well tolerated and requires more frequent dosing and laboratory monitoring to identify side effects [34,35]. Indeed, clinics based in middle-income countries and secondary- and tertiary-level clinics, which generally are better resourced, were more likely to roll out dolutegravir for second-line ART than clinics from low-income countries or primary-level clinics. A previous study in IeDEA suggested that higher retention rates in secondary- versus primary-level facilities likely reflect enhanced staffing, resources and services available in higher-level care [36]. Similarly, secondary- and tertiary-level clinics in our study were likely better placed to provide management-intensive second-line dolutegravir-based ART regimens. Recent trial results suggest that TLD may also be an effective second-line ART regimen [37–41]. Some national ART guidelines reflect these findings in their current recommendations [42]. Given our study's finding of near universal rollout of first-line

dolutegravir-based ART regimens, such a shift in ART recommendations may expand clinic-level rollout of dolutegravir in second-line ART regimens.

The genetic barrier to resistance is high for dolutegravir [43,44], but the resistance risk may increase in some situations. A recent collaborative analysis of eight cohort studies from Europe, Canada and South Africa found that among PWH experiencing viremia on dolutegravir-based ART, dolutegravir resistance mutations were more common on dolutegravir monotherapy or dual therapy, and in the presence of NRTI resistance [45]. Other recent data indicate that switching PWH with unsuppressed viral load is associated with a greater risk of virological failure and probably of dolutegravir resistance [46]. In our survey, a substantial minority of clinics (41%) that rolled out dolutegravir-based ART did not require a viral load measurement within six months before switching to dolutegravir. This is in line with several observational studies of patient-level data in IeDEA that found less than half of PWH in low- or lower-middle-income countries received viral load testing within six months of ART initiation following implementation of Treat-All policies [47–49]. Of note, availability of viral load monitoring has greatly increased since the 2017 survey of the IeDEA consortium, when only about half of facilities surveyed in low- and lower-middle-income countries reported having viral load testing available as part of routine care [50]. Our results confirm that genotypic drug resistance testing at switch is rarely performed in LMICs, despite many clinics reporting having access to such tests. There is concern that increasing levels of pretreatment resistance to dolutegravir may jeopardize the success of ART programmes in the years to come [51].

Our study had several limitations. Firstly, HIV clinics participating in IeDEA may not be representative of HIV treatment and care facilities within a country or region. Secondly, since our survey was conducted just over a year after the WHO updated guidelines recommending dolutegravir-based ART first- and second-line regimens for all adults and adolescents, some clinics may still have been in the process of planning for dolutegravir rollout. Thirdly, as our survey did not explicitly define first- and second-line therapies, some clinics may have used first-line ART for second-line therapy. In addition, as the survey was conducted during 2020 and 2021, our findings may have been influenced by the COVID-19 pandemic, which impacted care provision at IeDEA facilities [52–54]. Despite these limitations, this study provides essential data on the rollout of dolutegravir-based ART in first- and second-line ART by clinics from geographically and economically diverse settings across different clinic levels and countries with varying HIV burdens. This information is needed to better understand and contextualize progress in the dolutegravir rollout and to inform modelling efforts that assess the impact of dolutegravir-based ART on reducing HIV drug resistance in resource-limited settings. While observational studies have previously investigated patient-level rollout of dolutegravir-based ART, to our knowledge, this is the first study that describes clinic-level rollout across both first- and second-line ART in a large sample of HIV care facilities in LMICs.

Conclusion

The introduction of dolutegravir at IeDEA clinics in LMICs has been remarkably quick. Within two years of the WHO recommending dolutegravir, 90% of 175 HIV treatment and care clinics in 35 LMICs had introduced it in first-line and more than half in second-line ART. All clinics that introduced dolutegravir in ART regimens had access to viral load testing, however about 40% did not require a recent measurement before switching PWH to a dolutegravir-based regimen, and genotypic drug resistance testing at switch was rarely performed. As rollout of second-line dolutegravir-based ART regimens expands, an increasing number of PWH may be switched with an unsuppressed viral load, possibly increasing the risk of accumulating drug resistance to dolutegravir and other drugs used in the treatment of HIV.

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Conflicts of interest

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