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Table S1: Search strategy

Database	Search strategy	Results
PubMed	(("resistan*"[Title]) AND ("HIV"[Title] OR "human immunodeficiency virus"[Title] OR "AIDS"[Title] OR "acquired immunodeficiency syndrome"[Title]) AND ("child*"[Title/Abstract] OR "adolecen*"[Title/Abstract] OR "infant*"[Title/Abstract] OR "newborn*"[Title/Abstract] OR "pediatri*"[Title/Abstract])) NOT ("Case Reports"[Publication Type] OR "Comment"[Publication Type] OR "Editorial"[Publication Type] OR "Review"[Publication Type] OR "Meta-analysis"[Publication Type])) AND (humans[Filter]) up to 28 June 2024	461
Embase	('hiv'/exp OR 'aids'/exp OR hiv:ti OR 'human immunodeficiency virus':ti OR aids:ti OR 'acquired immunodeficiency syndrome':ti) AND resistan*:ti AND (child*:ab,ti OR adolescent*:ab,ti OR infant*:ab,ti OR newborn*:ab,ti OR pediatr*:ab,ti) AND [article]/lim AND [humans]/lim AND [english]/lim up to 28 June 2024	945
Web Of Science	TI=(resistan*) AND (TI=(child* or adolescen* or infan* or newborn* or pediatri*) OR AB=(child* or adolescen* or infan* or newborn* or pediatri*)) AND TI=(aids OR "acquired immunodeficiency syndrome" OR HIV OR "human immunodeficiency virus") up to 28 June 2024	876

Table S2: Countries included in analysis listed by income level

(In the order of data extraction process)

First author	Study performed country	Region	World Bank Income level	Median	Age
				sampling year	(month)
Lindström, 2010	Malawi	Southern Africa	Low income	2007	3.3
Lindström, 2010	Malawi	Southern Africa	Low income	2007	3.3
Towler, 2010	Uganda	Eastern Africa	Low income	2005	51.5
Towler, 2008	Uganda	Eastern Africa	Low income	/	1.4
Fogel, 2011	Malawi	Southern Africa	Low income	2008	3
Van Dyke, 2016	United States	North America	High income	2011	37.2
Kurle, 2007	India	Asia	Lower middle income	/	0.7
Kurle, 2007	India	Asia	Lower middle income	/	6
Vignoles, 2009	Argentina	South America	Upper middle income	2005	51.2
Gibb, 2002	UK, Italy, Spain	Europe	/	1999	6
Nelson, 2015	Malawi	Southern Africa	Low income	2007	3.62
Nelson, 2015	Malawi	Southern Africa	Low income	2007	3.62
Nelson, 2015	Malawi	Southern Africa	Low income	2007	8.63
Louis, 2019	Haiti	North America	Lower middle income	2013	6.5
Boerma, 2016	Nigeria	Western and Central Africa	Lower middle income	2012	57.6
Bennett, 2020	Zambian	Southern Africa	Lower middle income	2017	5
Inzaule, 2018	Nigeria	Western and Central Africa	Lower middle income	2015	5.1
Crowell, 2017	Mali	Western and Central Africa	Low income	2012	31.2
Salou, 2016	Тодо	western and Central Africa	Low income	2012	5
Kityo, 2016	Uganda	Eastern Africa	Low income	2010	58.8
Dow, 2017	Tanzania	Eastern Africa	Lower middle income	2013	3.73
Hunt, 2011	Southern Africa	Southern Africa	Upper middle income	2006	24
Zeh, 2011	Kenya	Eastern Africa	Lower middle income	2005	6
Nii-Trebi, 2013	Ghana	Western and Central Africa	Lower middle income	2009	60
Neubert, 2016	Germany	Europe	High income	2005	24
Taylor, 2011	Southern Africa	Southern Africa	Upper middle income	2005	8
Fofana, 2023	Mali and Benin	Western and Central Africa	/	2019	31.2
Hunt, 2019	Southern Africa	Southern Africa	Upper middle income	2012	1.2
Parker, 2003	United States	North America	High income	1998	3
Parker, 2003	United States	North America	High income	1998	3
Karchava, 2006	United States	North America	High income	2001	6
Frange, 2018	France	Europe	High income	2012	26
Ngo-Giang-	Europe and Thailand	Asia	/	2003	79.2
Huong, 2016			· ·	2010	100
Tadesse, 2019	Ethiopia	Eastern Africa	Low income	2018	108
Jordan, 2022	Namibia	Southern Africa	Upper middle income	2016	18
Soeria-Atmadja, 2020	Ugandan	Eastern Africa	Low income	2015	74.4
Aulicino. 2019	Argentina	South America	Upper middle income	2010	2.3
	U		r r		

Abidi, 2021	Pakistan	Asia	Lower middle income	2019	36
Kovacs, 2005	United States	North America	High income	/	2.6
Delaugerre, 2009	France	Europe	High income	2001	0.97
Ikomey, 2017	Cameroon	Western and Central Africa	Lower middle income	2015	30
de Andrade, 2017	Brazil	South America	Upper middle income	2013	44.4
Kuhn, 2015	Southern Africa	Southern Africa	Upper middle income	2011	4.43
Kuhn, 2015	Southern Africa	Southern Africa	Upper middle income	2011	24
Fokam, 2011	Cameroon	Western and Central Africa	Lower middle income	2010	72
Han, 2009	China	Asia	Upper middle income	2006	6
Eshleman, 2001	Uganda	Eastern Africa	Low income	2000	1.63
Martinson, 2007	Southern Africa	Southern Africa	Upper middle income	2002	6
Vaz, 2012	Mozambique	Southern Africa	Low income	2008	25.2
Olusola, 2021	Nigeria	Western and Central Africa	Lower middle income	2016	76.8
Guimarães, 2015	Brazil	South America	Upper middle income	2013	108
Masquelier, 2001	France	Europe	High income	1995	6
Jordan, 2017	5 sub-Saharan African countries (Mozambique, Swaziland, Southern Africa, Uganda, and Zimbabwe)	Southern Africa		2012	4
Jordan, 2017	Mozambique	Southern Africa	Low income	2012	4
Jordan, 2017	Swaziland	Southern Africa	Lower middle income	2012	4
Jordan, 2017	Uganda	Eastern Africa	Low income	2012	4
Jordan, 2017	Zimbabwe	Southern Africa	Lower middle income	2012	4
Yeganeh, 2018	Southern Africa, Brazil, Argentina	South America	Upper middle income	2008	3
Neogi, 2012	India	Asia	Lower middle income	2009	96
de Azevedo, 2022	Brazil	South America	Upper middle income	2004	6
de Azevedo, 2022	Brazil	South America	Upper middle income	2010	12
Rogo, 2015	United States	North America	High income	2001	180
Chalermchockchar oenkit, 2009	Thailand	Asia	Upper middle income	2002	1
Phung, 2015	Vietnam	Asia	Lower middle income	2010	50
Antunes, 2015	Mozambique	Southern Africa	Low income	2011	7
Almeida, 2009	Brazil	South America	Upper middle income	2002	21.5
Fogel, 2013	Southern Africa, Tanzania,	Southern Africa	/	2012	18
	Uganda, and Zimbabwe				-
Chaix, 2007	Coîte d'Ivoire	Western and Central Africa	Lower middle income	2006	3
Jarchi, 2019	Iran	Asia	Lower middle income	2017	144
Green,2006	Italy,Brazil,UK,Spain,Ger	Europe	/	2001	114
Boender, 2016		Factorn Africa	Low income	2010	64.8
,	Uganda	Lastern Annea	Low meene	2010	01.0
Towler, 2010	Uganda	Eastern Africa	Low income	2005	/

Coetzer, 2013	Cambodia	Asia	Lower middle income	2007	96
Rossouw, 2015	Southern Africa	Southern Africa	Upper middle income	2010	56.3
Chaix, 2005	Côte d'Ivoire	Western and Central Africa	Lower middle income	2002	76.2
Machado, 2004	Brazil	South America	Upper middle income	2000	7.6
Rodríguez-Galet,	Equatorial Guinea	Western and Central Africa	Upper middle income	2020	6
2023					
Rubio-Garrido,	the Democratic Republic of	Western and Central Africa	Low income	2017	48
2021	Congo Southarn Ethionia	Eastorn Africa	Lowincomo	2016	144
Massara Kninda	the Control African	Wastern and Cantral A fries		2010	144
2017	Republic	western and Central Africa	Low income	2015	144
Kebe, 2013	Senegalese	Western and Central Africa	Lower middle income	2010	84
Crowell, 2017	Mali	Western and Central Africa	Low income	2012	31.2
Stoddart, 2014	Southern African	Southern Africa	Upper middle income	2011	96
Aboulker 2004	France Spain Germany	Europe	/	2000	2.5
100000000, 2000	Italy, UK	Larop	,	2000	2.0
Puthanakit, 2010	Thailand	Asia	Upper middle income	2005	109.2
Nyandiko, 2022	Kenya	Asia	Lower middle income	2011	96
Taylor, 2011	Southern Africa.	Southern Africa	Upper middle income	2005	7.3
Fofana, 2023	Mali and Benin	Western and Central Africa	/	2019	120
Contreras, 2013	United States	North America	High income	2003	75.6
Delaugerre, 2007	France	Europe	High income	2002	144
Agwu, 2014	United States, Puerto Rico	North America	/	2006	121.2
Inzaule, 2016	Kenya	Eastern Africa	Lower middle income	2006	6
Kityo, 2017	Ugnda	Eastern Africa	Low income	2010	58.8
Soeria-Atmadja,	Ugandan	Eastern Africa	Low income	2015	74.4
2020					
Jittamala, 2009	Thailand	Asia	Upper middle income	2004	85.2
Abidi, 2021	Pakistan	Asia	Lower middle income	2019	36
Chohan, 2015	Kenya	Eastern Africa	Lower middle income	2008	45.6
Shet, 2013	India	Asia	Lower middle income	2009	120
Theodore, 2011	Ugandan	Eastern Africa	Low income	2010	64.8
Yan, 2022	China	Asia	Upper middle income	2020	84
Zhao, 2011	China	Asia	Upper middle income	2007	166.8
Bratholm, 2010	Tanzanian	Eastern Africa	Lower middle income	2009	60
Gupta, 2010	Zambian	Southern Africa	Lower middle income	2004	94.8
Beghin, 2020	Southern African	Southern Africa	Upper middle income	2008	8.6
Beghin, 2020	Southern African	Southern Africa	Upper middle income	2008	54
Ventosa-Cubillo,	Panama	South America	High income	2018	144
2023					
Muri, 2017	Tanzania	Eastern Africa	Lower middle income	2016	132
Vaz, 2018	Mozambique	Southern Africa	Low income	2013	103
Makadzange, 2015	Zimbabwe	Southern Africa	Lower middle income	2012	136.8
Yendewa, 2021	Sierra Leone	Western and Central Africa	Low income	2019	108
Brice, 2020	Mali	Western and Central Africa	Low income	2013	118.8
Vaz, 2009	Mozambique	Southern Africa	Low income	2005	49
Sylla, 2019	Mali	Western and Central Africa 5	Low income	2013	150

Vaz, 2012	Mozambique	Southern Africa	Low income	2008	25.2
Brindeiro, 2002	Brazil	South America	Upper middle income	1999	68.28
Adje-Toure, 2008	Côte d'Ivoire	Western and Central Africa	Lower middle income	2001	84
Tagnouokam	Cameroon	Western and Central Africa	Lower middle income	2009	4.2
Ngoupo, 2021					
Amani-Bossé,	Burkina Faso, Côte d'	Western and Central Africa	/	2012	13.9
2017	Ivoire	Destana Africa	T	2006	(1.9
Anoua, 2011	Uganda	Eastern Africa	Low income	2006	64.8
Ahoua, 2011	Uganda	Eastern Africa	Low income	2006	66
Mutwa, 2014	Rwanda	Eastern Africa	Low income	2010	129.6
Rogo, 2015	United States	North America	High income	2001	/
Mulder, 2011	Spain	Europe	High income	2001	182.4
Fitzgibbon, 2001	United States	North America	High income	2004	94.8
Francesca, 2019	Switzerland	Europe	High income	1999	168
Ross, 2015	North America, Europe	North America, Europe, Southern	/	2007	108
	and Southern Africa	Africa			
Ross, 2015	Southern Africa, Mexico,	Southern Africa, North America,	/	2007	16
1 1 2007	Argentina and Portugal	Europe	T	2002	00
Lwembe, 2007	Kenya	Eastern Africa	Lower middle income	2003	90
Al Hajjar, 2012	Saudi Arab	Asia	High income	2008	84
Makatini, 2019	Southern Africa	Southern Africa	Upper middle income	2014	96
Camara-Cissé,	Côte d'Ivoire	Western and Central Africa	Lower middle income	2012	132
2021	D 1			2002	00.4
Dumans, 2009	Brazil	South America	Upper middle income	2002	80.4
Fokam, 2011	Cameroon	Western and Central Africa	Lower middle income	2010	72
Green, 2012	Southern Africa	Southern Africa	Upper middle income	2009	94.8
Pillay, 2014	Southern Africa	Southern Africa	Upper middle income	2012	122.4
Hunt, 2023	Southern Africa	Southern Africa	Upper middle income	2018	154.8
Fofana, 2018	Benin	Western and Central Africa	Lower middle income	2016	120
Servais, 2002	Belgian	Europe	High income	1999	114
Ramkissoon, 2015	Jamaica	North America	Upper middle income	2015	120
Saravanan, 2017	India	Asia	Lower middle income	2012	109.2
Bismara, 2012	Brazil	South America	Upper middle income	2012	90
Khanh Thu et	Vietnam	Asia	Lower middle income	2019	2
Lehman et					
al(2015)	Kenya, America	Africa, North America	/	2007	4.7
Fisher et al(2015)	Southern Africa	Southern Africa	Upper middle income	2008	3.4
Ronen et al(2017)	Kenya	Eastern Africa	Lower middle income	2007	6
Fokam et al(2018)	Cameroon	Western and Central Africa	Lower middle income	2015	72
Abuogi et al(2023)	Kenya	Eastern Africa	Lower middle income	2020	9
Djiyou et al(2023)	Cameroon	Western and Central Africa	Lower middle income	2021	192
Khamadi et					
al(2023)	Tanzania	Eastern Africa	Lower middle income	2020	144
Charpentier et al(2012)	the Central African Republic	Western and Central Africa	Low income	2009	96
Bouassa et al(2019)	the Central African Republic	Western and Central Africa	Low income	2008	132

Pang et al(2024)	China	Asia	Upper middle income	2024	
Sivay et al(2024)	Russia	Europe	Upper middle income	2020	60
Tambuyzer et al(2016)	Thailand, Argentina, United States, South Africa	/	/	2010	144
Lange et al(2015)	South Africa	Southern Africa	Upper middle income	2015	8
Gopalan et al(2019)	India	Asia	Lower middle income	2014	96
Szubert et al(2017)	Uganda, Zimbabwe	/	/	2008	72

Table S3A: PICO Summary of included studies for treatment-naive children prevalence analysis

Study	Patient/Population	Intervention	Comparison	Outcome
J. Lidstrom, 2010	Infant patients with utero HIV-1 infection	6 weeks of PMTCT drugs : sdNVP+AZT	6 weeks of PMTCT drugs: sdNVP+AZT+NVP	Overall HIV-1 pretreatment drug resistance
J. Lidstrom, 2010	Infants infected with HIV in utero in Malawi, aged 0 to 14 weeks	6 weeks of PMTCT drugs : sdNVP+AZT	6 weeks of PMTCT drugs : sdNVP+AZT+NVP	Overall HIV-1 pretreatment drug resistance
J. Lidstrom, 2010	Infants infected with HIV in utero in Malawi, aged 0 to 14 weeks	6 weeks of PMTCT drugs: sdNVP+AZT+NVP	6 weeks of PMTCT drugs sdNVP+AZT	Overall HIV-1 pretreatment drug resistance
W. I. Towler, 2010	HIV-infected children in Uganda	sdNVP to prevent MTCT exposure; d4T+3TC+NVP	Children previously exposed to sdNVP compared with those who were not exposed	Overall HIV-1 pretreatment drug resistance, specific mutation resistance prevalence
J. D. Church, 2008	Newborn infants in Uganda from 2005 to 2008	PMTCT drugs:sdNVP at birth for the infant and the mother in labor, extended NVP prophylaxis up to 6 weeks of age for the infant	Control Group: Infants who received sdNVP only Intervention Group: Infants who received sdNVP plus daily NVP up to 6 weeks of age	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence
J. Fogel, 2011	Neonates to 14-week-old infants in Malawi	36 weeks of PMTCT drugs: extended NVP arm for infants. sdNVP+ZDV for 1 week, sdNVP+NVP up to 14 weeks of age, sdNVP+NVP+ZDV up to 14 weeks of age	Infants receiving sdNVP +ZDV for 1 week	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence
R. B. V. Dyke, 2016	Children and adolescents in the United States with perinatal HIV infection, enrolled in the study between 2007 and 2009	NRTI/PI/NNRTI/ EI/FI/ INSTI	Reference laboratory overall antiretroviral resistance rates	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence
S. N. Kurle, 2007	Neonates infected with HIV-1 subtype C in India within 48 hours and 2 months of birth	neonates exposed to sdNVP for PMTCT of HIV	Neonates infected with HIV-1 subtype C not exposed to SD-NVP (hypothetical control group)	Overall HIV-1 pretreatment drug resistance, specific mutation resistance prevalence
S. N. Kurle, 2007	Neonates infected with HIV-1 subtype C in India within 48 hours and 2 months of birth	neonates exposed to sdNVP for PMTCT of HIV	Neonates infected with HIV-1 subtype C not exposed to SD-NVP (hypothetical control group)	Overall HIV-1 pretreatment drug resistance, specific mutation resistance prevalence
M. Vignoles, 2009	Vertically HIV-1-infected children in Argentina, aged 0 to 17 years, newly diagnosed and initiating their first HAART regimen between December 2004 and July 2006.	Administration of HAART, including various combinations of antiretroviral drugs, with some children receiving maternal/infant ARV prophylaxis: AZT, AZT+sdNVP	Not explicitly mentioned in the study, but the baseline characteristics of the patients (prior to HAART initiation) can serve as a form of comparison.	Specific mutation resistance prevalence
D. M. Gibb, 2003	Untreated HIV-1 infected children	Administration of different combinations of antiretroviral drugs including ZDV, 3TC, ABC, and NFV. A minority of participants had documented exposure to antiretroviral	Comparison among different antiretroviral regimens	Different regimens resistance prevalence

		therapy before birth		
J. A E. Nelson, 2015	Neonates and infants up to 48 weeks of age living in	7days PMTCT drugs: Infant: sdNVP at delivery, a week of	No additional intervention	Overall HIV-1 pretreatment drug resistance,
	Lilongwe, Malawi	AZT/3TC postpartum		different regimens resistance prevalence
J. A E. Nelson, 2015	Neonates and infants up to 48 weeks of age living in	Infant: sdNVP at delivery, a week of AZT/3TC	No additional intervention	Overall HIV-1 pretreatment drug resistance,
	Lilongwe, Malawi	postpartum;		different regimens resistance prevalence
		Mother: sdNVP at delivery, a week of AZT/3TC		
		postpartum; ART (AZT/3TC/NVP, AZT/3TC/nelfinivir, or		
		AZT/3TC/ritonavir-boosted lopinavir) for 28 weeks		
J. A E. Nelson, 2015	Neonates and infants up to 48 weeks of age living in	Infant: sdNVP at delivery, a week of AZT/3TC postpartum;	No additional intervention	Overall HIV-1 pretreatment drug resistance,
	Lilongwe, Malawi	daily NVP prophylaxis for 28 weeks		different regimens resistance prevalence
F. J. Louis, 2019	Children <18 months old who acquired HIV infection	Genotyping of HIV-1 to detect drug resistance mutations in	Comparisons could be made to historical	specific mutation resistance prevalence
	through mother-to-child transmission in Haiti during the	children exposed to ART	data or studies conducted in different	
	period of January 1, 2013 to December 31, 2014.		settings.	
R. S. Boerma, 2016	Children aged 1 to 12 years from Lagos, Nigeria, who	Initiation of ART, typically an NNRTI (such as NVP) plus	No specific control group, but compared	Overall HIV-1 pretreatment drug resistance
	were untreated for HIV and had no prior exposure to	two NRTIs (such as AZT, and 3TC)	treatment outcomes between children with	prevalence
	PMTCT drugs, recruited between 2012 and 2013 for a		and without pre-treatment HIV drug	
	24-month follow-up study		resistance (PDR).	
S. J. TOWNSEND,	HIV-1 infected mothers and their infants aged 0 to 15	Prophylaxis:	the study compared resistance profiles	Overall HIV-1 pretreatment drug resistance
2020	months in Lusaka, Zambia, from 2015 to 2018	NVP/Other/None/Missing	between mothers and infants who were on	prevalence
			different ART regimens	
S. C. Inzaule, 2018	HIV-infected infants aged up to 18 months from	PMTCT drugs: Sd-NVP/	HIV-infected infants who were not	Overall HIV-1 pretreatment drug resistance
	Nigeria, with samples collected between June 2014 and	extended prophylaxis	exposed to PMTCT medication	prevalence
	July 2015 across all six geopolitical regions.			
C. S. Crowell, 2017	HIV-1 infected children less than 10 years of age	HIV exposure	Baseline NNRTI resistance among	Overall HIV-1 pretreatment drug resistance
	initiating antiretroviral therapy (ART) in Mali.		children receiving NNRTI-based ART	prevalence
			versus those without baseline NNRTI	
			resistance receiving PI-based ART	
M. Salou, 2016	Children diagnosed with HIV who are less than 18	Different types of antiretroviral exposure	No maternal ART and no neonatal	Different regimens resistance prevalence
	months old in Togo	Infant: no ARV exposure/exposed to both neonatal	prophylaxis	
		prophylaxis and maternal ARV/neonatal prophylaxis.		
		Neonatal exposure consisted of NVP,		
		AZT or NVP+AZT.		
		Mother: short-time prophylaxis: AZT, NVP, AZT/3TC		
		(3TC); AZT/NVP or AZT/efavirenz cART:		
		AZT/3TC/NVP, AZT/3TC/EFV stavdine/3TC/NVP,		
		TDF/3TC/EFV		
C. Kityo, 2016	HIV-infected children less than 12 years old recruited at	PMTCT drugs:	Children without prior ART exposure	Overall HIV-1 pretreatment drug resistance,

	three clinics in Uganda between January 2010 and	sdNVP, sdNVP+AZT		different regimens resistance prevalence,
	August 2011.			specific mutation resistance prevalence
D. E. Dow, 2017	HIV-exposed infants aged approximately 3 months in	Maternal regimen: sdNVP Option A (daily zidovudine	Infants not exposed to NVP or infants	Overall HIV-1 pretreatment drug resistance,
	Northern Tanzania.	(AZT) as early as 14 weeks of gestation, sdNVP onset of	whose mothers did not receive any form of	different regimens resistance prevalence,
		labor, aAZT+3TC 7 days postpartum)	PMTCT intervention	specific mutation resistance prevalence
		Infant regimen: NVP given /NVP not given		
G. M. Hunt, 2011	HIV-positive infants aged 2 years or younger who were	Mother and Infant: sdNVP	The study did not include a formal control	Overall HIV-1 pretreatment drug resistance,
	born in South Africa and had been exposed to single-		group. However, comparisons could be	specific mutation resistance prevalence
	dose nevirapine (sdNVP) before initiating antiretroviral		made indirectly between different age	
	therapy (ART). Infants were categorized into different		groups of infants to assess the impact of	
	age groups: 0-6 months, 6-12 months, 12-18 months,		sdNVP exposure over time	
	and 18-24 months.			
C. Zeh, 2011	Neonates to 6 months old in Kisumu, Kenya, whose	Mother: AZT/3TC/ NVP or NFV from 34 weeks gestation	No direct control group, but a comparison	Overall HIV-1 pretreatment drug resistance,
	HIV-infected mothers received triple antiretroviral	to 6 months postpartum	between NVP-based and NFV-based	different regimens resistance prevalence,
	prophylaxis from the 34th week of gestation through 6	Infant: sdNVP at birth, breastfeeding 6 months	regimens within the intervention group	specific mutation resistance prevalence
	months of breastfeeding.			
N. I. Nii-Trebi, 2013	101 HIV-1 infected patients (adults ${\geq}15$ years old and	Antiretroviral therapy (ART) with NRTIs (AZT, d4T,	ART-naive individuals (newly diagnosed	Overall HIV-1 pretreatment drug resistance,
	children) in Koforidua, Eastern Region, Ghana, during	3TC), NNRTIs (NVP, EFV), and PIs (NFV)	cases without prior ART exposure)	different regimens resistance prevalence,
	February 2009 to January 2010			specific mutation resistance prevalence
J. Neubert, 2016	HIV-1-infected children treated at the University	Children who received or did not receive ART to prevent	Comparison with data from other	Overall HIV-1 pretreatment drug resistance,
	Hospital Düsseldorf, Germany, between January 2005	MTCT, and subsequently started on antiretroviral therapy	countries, such as Spain and the United	specific mutation resistance prevalence
	and December 2015	including NRTIs, NNRTIs, and PIs	States, regarding HIV-1-infected children	
B. S. Taylor, 2011	HIV-infected children less than two years old in South	Initiation of ART with RTV or LPV/r	Comparison of LPV/r treatment to RTV	Overall HIV-1 pretreatment drug resistance,
	Africa who were exposed to NVP for PMTCT		treatment	different regimens resistance prevalence,
				specific mutation resistance prevalence
D. B. Fofana, 2023	HIV-positive children (ages not specified but typically	Integrase strand transfer inhibitors (INSTIs) including	HIV-positive children who have not been	Different regimens resistance prevalence,
	considered 0-18 years) in West Africa (Benin and Mali)	RAL, EVG, DTG, BIC, and CAB	treated with INSTIs (INSTI-naïve) or have	specific mutation resistance prevalence
			received other types of antiretroviral	
			therapy (ART).	
G. M. Hunt, 2019	Neonates (4-8 weeks old) in South Africa, studied in	Maternal ART plus infant NVP +/- AZT,	Infants with no or unknown PMTCT	HIV-1 pretreatment drug resistance, different
	2010, 2011-2012, and 2012-2013	Infant NVP+/-AZT,	exposure compared to infants with known	regimens resistance prevalence, specific
		Any other ARV combination,	PMTCT exposure	mutation resistance prevalence
		No/unknown exposure		
M. M. Parker, 2003	Neonates (infants younger than 60 days of age) born in	Infants exposed to antiretroviral drugs prenatally (including	Infants without documented prenatal	Overall HIV-1 pretreatment drug resistance
	New York State, USA, in 1998 and 1999	AZT, 3TC, NVP, and PIs)	antiretroviral exposure	
M. M. Parker, 2003	Neonates (infants younger than 60 days of age) born in	PMTCT exposure	Infants without documented prenatal	Overall HIV-1 pretreatment drug resistance
	New York State, USA, in 1998 and 1999		antiretroviral exposure	

M. Karchava, 2006	Infants born in New York State and diagnosed as HIV- positive within 24 weeks of age between 2001 and 2002	Infants exposed to antiretroviral drugs (ARVs), including prenatal, intrapartum, and neonatal (up to 6 weeks postnatal) ARV exposure	Comparison with data from 1998-1999 to assess trends in drug resistance.	Overall HIV-1 pretreatment drug resistance
P. Frange, 2018	Children newly diagnosed with HIV-1 infection in France between 2006 and 2017	Previous exposure to in utero or postnatal antiretroviral prophylaxis, including only NRTI, including NRTI+PI, including NRTI+NNRTI, including NRTI+NNRTI+PI+NI	No prior exposure to antiretroviral prophylaxis for PMTCT	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence
N. Ngo-Giang-Huong, 2016	HIV-infected children under 18 years old who initiated cART between 1998 and 2008 in international multi- center settings, primarily Europe and Africa	Initial cART regimens including NNRTIs plus at least two NRTIs or unboosted PIs plus at least two NRTIs, with some children having pre-treatment drug resistance	Children without PDR or with "PDR and fully active cART" as a control group	Different regimens resistance prevalence
B. T. Tadesse, 2019	Children aged 0 to 18 years diagnosed with HIV infection in Ethiopia during the period of 2017 to 2019	Children who have not previously received antiretroviral therapy (cART-naive)	No direct comparator group is specified, but the results can be compared with other studies or data from different regions or time periods	Overall HIV-1 pretreatment drug resistance
M. R. Jordan, 2022	Infants less than 18 months old, newly diagnosed with HIV and treatment-naive in Namibia in 2016	Some infants may have received prophylactic treatment with NVP+AZT for 6 weeks. Neonates (<1 month) were prescribed RAL+AZT+3TC; infants 4 weeks to 2 months of age were given zidovudine (AZT) + lamivudine (3TC) and ritonavir-boosted lopinavir; for infants 3 to 35 months old, ABC could substitute AZT	No direct control group, but comparison can be made with infants who have received ART or with data from other countries	Overall HIV-1 pretreatment drug resistance
S. S. Soeria-Atmadja, 2020	ART-naïve children aged 3-12 years living in urban Uganda during the period 2015-2016, some of whom may have been exposed to antiretrovirals through PMTCT programs	Initiation of efavirenz-based ART consisting of two NRTIs and efavirenz	Comparison of children with baseline PDR versus those without PDR	Overall HIV-1 pretreatment drug resistance
P. C. Aulicino, 2019	Newborns to 2.3-month-old infants born in Argentina between 2007 and 2014	Infant prophylaxis: short-course ZDV, ZDV+NVP (+3TC) at birth, zidovudine monotherapy Maternal ART: NNRTI-based cART, PI-based cART 28, Breastfeeding	Infants who were not exposed to ARVs (ARV-unexposed group)	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence
S. H. Abidi, 2021	Children aged 0-15 years diagnosed with HIV-1 during the 2019 extensive pediatric HIV-1 outbreak in Larkana, Pakistan	Antiretroviral therapy (ART) regimens containing NNRTIs (e.g., efavirenz) and NRTIs (e.g., zidovudine)	ART-naive individuals (children who have not yet started ART)	Overall HIV-1 pretreatment drug resistance prevalence, specific mutation resistance prevalence
A. Kovacs, 2005	Infants aged ≤120 days	Administration of didanosine (ddI) following at least 24 hours of zidovudine (ZDV) treatment	Comparison between infants receiving ddI + placebo and infants receiving ddI + ZDV	Overall HIV-1 pretreatment drug resistance prevalence, different regimens resistance prevalence, specific mutation resistance prevalence

C. Delaugerre, 2009	Neonates born in France between 1997 and 2004 whose	Mother: AZT+3TC+DDI/NVP/LPV/IDV	Comparison of the effects of different	Overall HIV-1 pretreatment drug resistance,
	mothers received antiretroviral prophylaxis during	Infant: AZT+3TC	antiretroviral drug combinations, and	different regimens resistance prevalence,
	pregnancy		potentially neonates who did not receive	specific mutation resistance prevalence
			antiretroviral prophylaxis as an indirect	
			comparison	
G. M. Ikomey, 2017	Untreated, immunocompetent HIV-1 positive children	Mother:	No specific comparison group; baseline	Overall HIV-1 pretreatment drug resistance,
	aged 9 months to 6 years in Yaoundé, Cameroon, during	cART naïve,	data for drug-naïve children	specific mutation resistance prevalence
	2015-2016	cART exposed during pregnancy		
		Infant: unknown		
S. D. d. Andrade,	Children aged neonates to adolescents (median age 3.7	Antiretrovirals received during pregnancy,	Comparison between children exposed to	Overall HIV-1 pretreatment drug resistance,
2017	years) diagnosed with HIV-1 between 2010 and 2015 in	Intra-partum prophylaxis with ZDV,	PMTCT and those not exposed	different regimens resistance prevalence,
	Manaus, Amazonas State, Brazil, who are antiretroviral-	Postnatal infant prophylaxis with ZDV		specific mutation resistance prevalence
	naive (28.2% exposed to PMTCT)			
L. Kuhn, 2015	Newly diagnosed HIV-infected children under 2 years	Maternal antiretroviral regimen: cART, Zidovudine/	Without documented antiretroviral	Overall HIV-1 pretreatment drug resistance,
	old, recruited in Johannesburg, South Africa	nevirapine, Zidovudine alone, Nevirapine alone	exposure	different regimens resistance prevalence,
		Infant prophylaxis: Nevirapine alone, Zidovudine/		specific mutation resistance prevalence
		nevirapine		
L. Kuhn, 2015	Newly diagnosed HIV-infected children under 2 years	Maternal antiretroviral regimen:	With documented antiretroviral exposure	Overall HIV-1 pretreatment drug resistance,
	old, recruited in Johannesburg, South Africa	Infant prophylaxis		different regimens resistance prevalence,
				specific mutation resistance prevalence
J. Fokam, 2011	This study involved 92 HIV-1-infected children aged	The interventions included standard first-line ART	The study compared drug-naive children	Overall HIV-1 pretreatment drug resistance,
	between 3 months and 12 years in Yaoundé, Cameroon	regimens such as AZT/3TC/NVP and a fixed-dose	with those experiencing first-line ART	specific mutation resistance prevalence
	(from June 2009 to February 2011), including 41 drug-	combination of d4T/3TC/NVP	failure	
	naive and 51 first-line antiretroviral treatment-failing			
	children			
J. Han, 2009	HIV-1-infected pregnant women in China who are	sdNVP	Comparison between sdNVP and ZDV-	Overall HIV-1 pretreatment drug resistance,
	ART-naïve	ZDV-sdNVP	sdNVP regimens	different regimens resistance prevalence
S. H. Eshleman, 2001	HIV-1-positive pregnant women and their infants in	Single-dose nevirapine (NVP) to prevent HIV-1 vertical	Self-comparison within the same	Overall HIV-1 pretreatment drug resistance,
	Uganda	transmission	intervention group (women and infants	specific mutation resistance prevalence
			receiving NVP)	
N. A. Martinson, 2007	HIV-1 infected infants aged neonates to 12 weeks old in	Single-dose nevirapine (sd-NVP) administered to mothers	Potentially infants not exposed to sd-NVP	Overall HIV-1 pretreatment drug resistance,
	South Africa (Soweto and Durban) before 2007	at the onset of labor and to newborns	or infants without detectable resistance	specific mutation resistance prevalence
P. Vaz, 2012	HIV-infected children aged 0-15 years initiating ART at	Standard first-line ART regimens including ZDV+	Baseline characteristics and ART	Overall HIV-1 pretreatment drug resistance,
	the main pediatric ART referral center in Maputo,	3TC+NVP, d4T+3TC+NVP, and d4T+3TC+LPV/r	outcomes compared to outcomes at 12	specific mutation resistance prevalence
	Mozambique between 2007 and 2008		months post-initiation	
F. I. Olusola, 2021	ART-naïve HIV-infected children less than 15 years old	Sequencing of the HIV-1 pol gene to identify mutations	The prevalence of PDR in ART-naïve	Overall HIV-1 pretreatment drug resistance,
	residing in Ibadan, Nigeria, around the year 2021	conferring resistance to NNRTIs and NRTIs in ART-naïve	children compared to historical data or	specific mutation resistance prevalence

		children	other populations	
P. M. de S. Guimara [~] es, 2015	Adults and children recently diagnosed with HIV in São Paulo, Brazil, between 2012 and 2014	Evaluation of transmitted drug resistance (TDR) among antiretroviral therapy-naïve individuals	No specific comparison group mentioned, but the study compared TDR prevalence against historical data and other studies	Overall HIV-1 pretreatment drug resistance, specific mutation resistance prevalence
B. Masquelier, 2001	HIV-1 infected neonates born in France	Mothers who received zidovudine as part of their antiretroviral therapy regimen during pregnancy	For comparison purposes, neonates born to mothers who did not receive zidovudine or those who received alternative antiretroviral regimens during pregnancy	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence
M. R. Jordan, 2017	Children under 18 months old in Sub-Saharan African countries (Mozambique, Swaziland, South Africa, Uganda, and Zimbabwe) diagnosed with HIV through early infant diagnosis between 2011 and 2014	Maternal and neonatal ARV drug exposure as part of PMTCT programs. Non-nucleoside reverse transcriptase inhibitors (NNRTIs): NVP, EFV, ETR, RPV Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs/TIs): AZT, d4T, FTC, TDF	Children without documented maternal or neonatal ARV exposure and those with unknown exposure histories	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence
M. R. Jordan, 2017	Children under 18 months old in Mozambique diagnosed with HIV through early infant diagnosis between 2011 and 2014	Maternal and neonatal ARV drug exposure as part of PMTCT programs. Non-nucleoside reverse transcriptase inhibitors (NNRTIs): NVP, EFV, ETR, RPV Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs/TIs): AZT, d4T, FTC, TDF	Children without documented maternal or neonatal ARV exposure and those with unknown exposure histories	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence
M. R. Jordan, 2017	Children under 18 months old in Sub-Saharan African countries Swaziland diagnosed with HIV through early infant diagnosis between 2011 and 2014	Maternal and neonatal ARV drug exposure as part of PMTCT programs. Non-nucleoside reverse transcriptase inhibitors (NNRTIs): NVP, EFV, ETR, RPV Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs/TIs): AZT, d4T, FTC, TDF	Children without documented maternal or neonatal ARV exposure and those with unknown exposure histories	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence
M. R. Jordan, 2017	Children under 18 months old in Sub-Saharan African countries Uganda diagnosed with HIV through early infant diagnosis between 2011 and 2014	Maternal and neonatal ARV drug exposure as part of PMTCT programs. Non-nucleoside reverse transcriptase inhibitors (NNRTIs): NVP, EFV, ETR, RPV Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs/TIs): AZT, d4T, FTC, TDF	Children without documented maternal or neonatal ARV exposure and those with unknown exposure histories	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence
M. R. Jordan, 2017	Children under 18 months old in Sub-Saharan African countries Zimbabwe diagnosed with HIV through early infant diagnosis between 2011 and 2014	Maternal and neonatal ARV drug exposure as part of PMTCT programs. Non-nucleoside reverse transcriptase inhibitors (NNRTIs): NVP, EFV, ETR, RPV Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs/TIs): AZT, d4T, FTC, TDF	Children without documented maternal or neonatal ARV exposure and those with unknown exposure histories	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence
N. Yeganeh, 2018	Pregnant women and their newborns in South Africa, Brazil, and Argentina between April 2004 and January 2011	group A: AZT 6 weeks group B: AZT 6 weeks + NVP 1 week group C: AZT 6 weeks+NFV+3TC 6 weeks	Untreated mother-infant pairs and those treated with different ART regimens	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence

		Infant prophylaxis medications: ZDV, ZDV+NVP, ZDV+NFV+3TC		
U. Neogi, 2012	Children and adolescents aged 2 to 16 years old, perinatally infected with HIV-1 subtype C, and antiretroviral therapy-naïve, from Bangalore, India, between 2007 and 2011	Participants were antiretroviral therapy-naïve, with some potentially exposed to nevirapine as part of PMTCT strategies	There was no specific control group in this study	Overall HIV-1 pretreatment drug resistance, specific mutation resistance prevalence
S. S. D. d. Azevedo, 2022	Treatment-naïve children and adolescents (neonates to 19 years old) infected with HIV-1 through vertical transmission in the Rio de Janeiro State, Brazil, between 2001 and 2007.	Maternal antiretroviral therapy for PMTCT, starting with zidovudine monotherapy and later transitioning to combination ART including NRTIs and NNRTIs	Comparative analysis of TDRM prevalence between the time periods 2008 and 2012	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence
S. S. D. d. Azevedo, 2022	Treatment-naïve children and adolescents (neonates to 19 years old) infected with HIV-1 through vertical transmission in the Rio de Janeiro State, Brazil, between 2008 and 2012.	Maternal antiretroviral therapy for PMTCT, starting with zidovudine monotherapy and later transitioning to combination ART including NRTIs and NNRTIs	Comparative analysis of TDRM prevalence between the time periods 2001 and 2007	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence
T. Rogo, 2015	HIV-infected children attending the only pediatric HIV clinic in Rhode Island between 1991 and 2012, ranging in age from neonates to adolescents	Antiretroviral therapy (ART), including NNRTIs, NRTIs, and PIs	ART-naïve children serving as a comparison group to ART-experienced children	Overall HIV-1 pretreatment drug resistance, specific mutation resistance prevalence
A. Chalermchockcharoen kit, 2009	HIV-positive pregnant women and their infants in Thailand	Mother: AZT+NVP Infant: sdNVP at birth	No specific control group mentioned, but the study likely compares the outcomes to historical data or theoretical scenarios without the intervention	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence
T. T. B. Phung, 2015	HIV-1 infected children aged 1 month to 12 years (mean age of 50 months) from 21 provinces in Northern Vietnam, recruited between December 2009 and December 2011	Genotyping of antiretroviral-naïve children to detect drug resistance mutations without specifying any intervention or drug regimen	Historical data on drug resistance rates in other populations in Vietnam	Overall HIV-1 pretreatment drug resistance, specific mutation resistance prevalence
F. Antunes, 2015	6 to 48-week-old children in Maputo, Mozambique, enrolled between July 2011 and March 2012	Infant: ARV prophylaxis: AZT, sd-NVP + daily NVP Mothers: antepartum daily AZT as early as 14 weeks of gestation, sd-NVP at onset of labor and twice daily AZT + 3TC for 7 days postpartum	The study did not include an explicit control group but analyzed various factors related to the development of NVP resistance	Overall HIV-1 pretreatment drug resistance, specific mutation resistance prevalence
F. J. Almeida, 2009	HIV-1-infected children in São Paulo, Brazil, who were born to mothers who were not treated with antiretroviral therapy during pregnancy	Children receiving or not receiving HAART	Comparison: ARV-naive children versus children failing HAART. Control Group: ARV-naive children (without prior antiretroviral exposure)	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence

J. M. Fogel, 2013	Infants aged 0 to 6 months from South Africa, Tanzania, Uganda, and Zimbabwe who were enrolled in the study between 2010 and 2013.	Mothers received sdNVP and infants received sdNVP+ZDV/3TC for PMTCT Infants received extended nevirapine prophylaxis (daily NVP until 6 weeks of age) followed by NVP or placebo until 6 months of age.	Infants received no additional extended NVP prophylaxis	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence
M. Chaix, 2007	Pregnant women aged 15-49 years old, residing in Abidjan, Côte d'Ivoire, who are HIV positive and participated in the ANRS 1201/1202 Ditrame Plus study between 2006 and 2007.	mother: AZT+NVP at ≥36 weeks infant: AZT+sdNVP 7days	Comparison between women who received sdNVP alone and those who received sdNVP + ZDV, as well as infants who received sdNVP alone versus those who received sdNVP + ZDV	Overall HIV-1 pretreatment drug resistance, specific mutation resistance prevalence
M. Jarchi, 2019	Children under 12 years old in Iran, diagnosed between June 2014 and January 2019.	Genotypic testing for transmitted drug resistance (TDR) mutations in the pol gene of HIV-1 in treatment-naïve children	Not applicable, as there is no direct comparison group	Overall HIV-1 pretreatment drug resistance, specific mutation resistance prevalence
H. H. K. Thu, 2024	HIV-1 infected children under 18 months old from the Central Highlands and Southern regions of Vietnam during the period 2017–2021	mother: two nucleoside reverse transcriptase inhibitors (NRTIs) plus one non-nucleoside reverse transcriptase infant: sdNVP	Infants born to mothers who did not receive any PMTCT intervention or different ART Regimen	Specific mutation resistance prevalence
D. A. Lehman, 2012	Infants exposed to sdNVP	Infants subsequently treated with NVP-HAART	Infants without detectable nevirapine resistance mutations serve as the reference group	Overall HIV-1 pretreatment drug resistance, specific mutation resistance prevalence
R. G. FISHER, 2015	Infants less than 3 years old in South Africa	Dual AZT and NVP prophylaxis regimen for prevention of HIV mother-to-child transmission (PMTCT)	Conventional bulk sequencing versus next- generation sequencing (NGS) using Ion PGM and MiSeq platforms	different regimens resistance prevalence, specific mutation resistance prevalence
K. Ronen, 2017	Neonates to 6-week-old infants in Ethiopia who participated in the study aimed at preventing mother-to- child transmission of HIV between February 2001 and March 2007	Infants received nevirapine prophylaxis (either sdNVP or ED-NVP) starting from Day 8 of life for up to 6 weeks	Infants receiving single-dose nevirapine (SD-NVP) served as the comparator group	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence
J. Fokam, 2018	Eighteen HIV-1 vertically infected children, seven of whom were born to mothers who received PMTCT interventions, and eleven born to mothers without PMTCT exposure	Next-generation sequencing (NGS) for determining HIV-1 drug resistance and viral tropism, AZT+3TC+NVP were used in PMTCT-exposed infants	Comparative analysis of drug resistance mutations and viral tropism between Sanger sequencing and NGS	Overall HIV-1 pretreatment drug resistance, different regimens resistance prevalence, specific mutation resistance prevalence

Abbreviations, DRMs = drug resistance mutations; ART antiretroviral therapy; cART = combination antiretroviral therapy; NRTIs = nucleoside reverse transcriptase inhibitors; NVP = nevirapine; PI = protease inhibitor; LPV/r = lopinavir/ritonavir; INSTIs = integrase strand transfer inhibitors; d4T = stavudine; 3TC = lamivudine ; DBS = dried blood spots; VF = virological failure; PDR = pretreatment HIV drug resistance; VL = viral load; PMTCT = mother-to-child transmission; RAMs = resistance-associated mutations; ZDV = Zidovudine; NFV = nelfinavir; RTIs = reverse transcriptase inhibitors; TAMs = thymidine analogue mutations; HAART = Highly Active Antiretroviral Therapy.

Table S3B: PICO Summary of included studies for treatment-experienced children prevalence analysis

Study	Patient/Population	Intervention	Comparison	Outcome
Hannah Green, 2006	HIV-1-infected children aged 3 months to 18 years from six countries (Italy, Brazil, UK, Spain, Germany, Portugal) enrolled between June 2000 and July 2003. The majority (97%) acquired HIV through PMTCT. All children had VF with HIV-1 RNA >2,000 copies/ml.	Children were randomized to receive genotypic resistance testing at the time of switching ART due to VF. Resistance testing was performed using the Virtual Phenotype TM, and results were used to guide subsequent ART regimens. NRTIs:15(17%); NRTIs+NNRTIs:10(11%); NRTIs+Pis:17(20%); NRTIs+NNRTIs+Pis:17(20%)	The control group did not receive resistance testing. Instead, their ART regimens were switched based on clinical judgment without the guidance of genotypic resistance testing.	Primary outcomes included the change in HIV-1 RNA viral load at 48 and 96 weeks, the proportion of patients with undetectable viral loads, and changes in CD4+ T-cell percentages.
T. Sonia Boender, 2016	HIV-1-positive adults and children in Uganda who were on NNRTI-based first-line ART and experienced virological failure between 2010 and 2011.	Continuation of first-line NNRTI-based ART with the following regimens: Nevirapine-based ART: $d4T + 3TC +$ NVP or AZT + 3TC + NVP; Efavirenz-based ART: AZT + 3TC + EFV or TDF + FTC + EFV Participants with VL \geq 1000 copies/mL underwent genotypic resistance testing to monitor the accumulation of DRMs.	Comparison of DRM accumulation rates and predicted drug susceptibility between adults and children, as well as between those on nevirapine-based versus efavirenz-based ART regimens.	Rate of DRM accumulation per year and the decline in susceptibility to NNRTIs and NRTIs following continued virological failure.
W. I. Towler, 2010	HIV-1-infected children in Uganda who received ART as part of a prospective observational study between 2004 and 2006. The study included children with and without prior single-dose nevirapine exposure.	The children received a cART regimen consisting of d4T, 3TC, and NVP. Children weighing <9 kg received syrup formulations, while those >9 kg received a fixed-dose combination tablet (Triomune).	Comparison between children with prior sdNVP exposure and those without it in terms of the presence and development of DRMs before and after ART initiation.	DRM accumulation, virological suppression, NRTI/NNRTI resistance emergence
Doreen Kamori, 2023	HIV-1-positive children (≤15 years old) and adults in Tanzania, who were not part of PMTCT programs and were enrolled after confirmed virological failure in 2020.	Participants were on ART regimens, including: - Dolutegravir-based regimen: TDF + 3TC + DTG - PI-based regimen: Various combinations including LPV/r, ATV/r with NRTIs like TDF and 3TC.	Comparison of DRM accumulation and resistance profiles between participants on dolutegravir-based regimens and those on PI-based regimens.	Prevalence of HIV DRMs and the patterns of resistance among participants, including the emergence of resistance to dolutegravir and PIs.
Mia Coetzer, 2013	HIV-infected Cambodian children under 15 years of age who have been on first-line ART for at least 6 months, monitored at the Angkor Hospital for Children in 2011.	Continuation of first-line ART, primarily consisting of stavudine, lamivudine, and nevirapine, with routine monitoring of viral load and CD4 counts. DRMs were determined using the IAS-USA 2011 list.	Children with extensive drug resistance mutations (\geq 4 mutations) versus those with fewer mutations.	Prevalence and patterns of DRMs, resistance levels, number of mutations, and predicted susceptibility to second-line ART
Theresa M Rossouw, 2015	HIV-1 infected children in South Africa, primarily under 3 years of age, who initiated PI-based ART and subsequently experienced virological failure between 2008 and 2012. The cohort included children with advanced clinical disease, severe malnutrition, and a high tuberculosis co-infection rate.	PI-based ART, primarily using regimens including LPV/r, with a focus on children who received ritonavir as a single protease inhibitor (RTV-sPI) during co-treatment for TB. Genotypic drug resistance testing was performed after virological failure.	Children with major PI mutations versus those without, and comparisons of different ART dosing strategies (RTV-sPI, double-dose LPV/r, super-boosted LPV/r).	Prevalence of major PI mutations, associated factors such as duration of ART and TB co- treatment, and the projected susceptibility of the virus to various ART drugs.

Marie-Laure Chaix, 2005	HIV-1-infected children in Côte d'Ivoire, enrolled in the ANRS 1278 cohort between October 2000 and September 2003. The study involved 115 children with a median age of 6.35 years (range: 1.2–15 years) who received HAART for at least 6 months.	Administration of HAART, consisting of 2 NRTIs combined with either nelfinavir (70.5%) or efavirenz (29.5%). NRTIs used included ZDV, 3TC, d4T, and ddI. Genotypic resistance tests were performed in cases of virologic failure (defined as viral load \geq 3 log10 copies/mL) after at least 6 months of HAART.	Nelfinavir-based versus efavirenz-based regimens, and virologic success versus failure.	Frequency of DRMs, resistance to 3TC, NNRTIS, PIs, and overall prevalence of drug- resistant viruses.
Elizabeth S Machado, 2004	HIV-1-infected children in Brazil, receiving antiretroviral therapy according to Brazilian Ministry of Health guidelines between November 1999 and January 2002. The study included 75 children up to 14 years of age.	Two groups based on treatment history: 1) Dual therapy group, receiving two NRTIs; 2) Triple therapy group, receiving two NRTIs combined with a PI or a NNRTI. Genotypic resistance tests were performed on plasma samples, targeting reverse transcriptase and protease genes.	ual therapy versus triple therapy, with further subdivision by prior ARV exposure, and B versus non-B subtypes in terms of DRMs and treatment response.	Frequency of DRMs, impact on virologic/immunologic responses, cross-resistance, subtype influence on CD4+ recovery, and prior NRTI exposure effects.
Ana Rodríguez- Galet, 2023	HIV-infected children (≤12 years old) and adults in Equatorial Guinea, including 57 children/adolescents and 187 adults in 2019-2020.	ART regimens used in the study population, primarily focusing on NRTIs (AZT, 3TC, TDF, FTC, D4T, ABC), NNRTIs (EFV, NVP), PIs (LPV/r), and INSTIs (DTG). Monitoring included DRMs and virological failure.	ART-naïve versus ART-treated children, and effectiveness of different ART regimens, including resistance to various drug classes.	Prevalence of DRMs in both ART-naïve and ART-treated populations, virological failure rates (defined as viral load >1000 copies/mL), and the impact on predicted antiretroviral drug susceptibility.
M. Rubio- Garrido, 2021	HIV-infected children and adolescents in Democratic Republic of Congo, who were receiving ART in 2016. The study included 71 participants with a median age of 14 years.	Continuation of ART with the following regimens: NRTI-based ART: AZT + 3TC + NVP or TDF + FTC + EFV NNRTI-based ART: EFV + 3TC + AZT or ABC + 3TC + LPV/r Participants with viral load (VL) \geq 1000 copies/mL underwent genotypic resistance testing to monitor the accumulation of DRMs.	Comparison of DRMs between different drug classes and across different ART regimens. The study also examined the impact of ART exposure time on the development of DRMs.	Prevalence of major DRMs to NRTIs, NNRTIs, PIs, and INSTIs. The study found high levels of resistance, particularly to NNRTIs and NRTIS.
Birkneh Tilahun Tadesse, 2018	HIV-infected children under 18 years of age in Southern Ethiopia, enrolled in the Ethiopia Pediatric HIV Cohort (EPHIC) between 2015 and 2017, who were experiencing virologic treatment failure after being on cART for more than 5 months.	Continuation of first-line NNRTI-based ART with the following regimens: - Nevirapine-based ART: $d4T + 3TC + NVP$ or $AZT + 3TC + NVP$ - Efavirenz-based ART: $AZT + 3TC + EFV$ or $TDF + FTC + EFV$ Participants with VL ≥ 1000 copies/mL underwent genotypic resistance testing to monitor the accumulation of DRMs.	Comparison of DRMs between different drug classes (NRTIs, NNRTIs) among children failing first-line ART. The study also compared the prevalence and impact of DRMs on second-line treatment options.	Prevalence of DRMs, particularly dual-class resistance (NRTIs and NNRTIs), and the impact on the effectiveness of recommended second-line ART regimens.
Christian Diamant Mossoro- Kpinde, 2017	HIV-1-infected children in the Central African Republic, aged 4– 17 years, who had been on ART for at least 6 months in 2013. The study included 220 children, with a median age of 12 years.	Continuation of WHO-recommended first-line and second- line ART regimens: - First-line ART: AZT + 3TC + NVP, AZT + 3TC + EFV, d4T + 3TC + EFV, d4T + 3TC + LPV/r	Comparison of DRMs between children on first-line ART versus second-line ART. The study also compared the resistance profiles of viruses to NRTIs, NNRTIs, and	Prevalence of DRMs, particularly resistance to NRTIs, NNRTIs, and PIs. The study observed high levels of virological failure and drug resistance among the children, leading to the

		- Second-line ART: AZT + 3TC + LPV/r, d4T + 3TC +	PIs among the children.	need for potential third-line regimens.
		LPV/r		
		Participants with VL ≥ 1000 copies/mL underwent		
		genotypic resistance testing to monitor DRMs.		
Khady Kebe,	HIV-1-infected children in Senegalese, aged less than 15 years,	Continuation of WHO-recommended first-line ART	No direct comparison group mentioned in	Virological failure rates, prevalence of drug-
2013	treated with NRTI and NNRTI based first-line ART for at least 6	regimens, including:	the provided text, but the study evaluates	resistant mutations, resistance patterns to
	months according to WHO recommendations. 125 children were	- AZT + 3TC + NVP	VF based on the 2010 revised WHO	NRTIs, NNRTIs, and PIs, multi-class
	included, with a median age of 7 years.	- AZT + 3TC + EFV	criteria (HIV-1 RNA ≥ 3.7 log10	resistance occurrences
		- d4T + 3TC + NVP	copies/ml).	
		- d4T + 3TC + EFV		
		Participants with a viral load ≥3.0 log10 copies/mL		
		underwent genotypic resistance testing to monitor DRMs.		
Claudia S.	HIV-infected children under 10 years of age in Mali in 2010. The	Initiation of ART, with regimens including:	Comparison of virological failure rates and	Prevalence of baseline NNRTI resistance,
Crowell,	study included 120 children, with a median age of 2.6 years.	- NNRTI-based ART: Mainly EFV or NVP combined	DRMs among children initiated on	virological failure rates at 6 months, and the
2017		with NRTIs such as AZT, 3TC, and ABC.	NNRTI-based versus PI-based ART. The	association between baseline resistance and
		- PI-based ART: Mainly LPV/r combined with NRTIs.	study also analyzed the impact of baseline	treatment outcomes.
		Baseline resistance testing was performed, and	NNRTI resistance on treatment outcomes.	
		participants with VL ≥1000 copies/mL at 6 months		
		underwent further genotypic resistance testing.		
Cheryl A.	South African children < 15 years old with known treatment	Continuation of first-line ART regimens:	Comparison between children failing	Cross-resistance to didanosine, effectiveness
Stoddart,	history, who were exposed to a $d4T+3TC$ (n = 279) or a	- ABC + 3TC + EFV/NVP/LPV/r	ABC-based regimens and those failing	of didanosine in second-line regimens,
2014	ABC+3TC-based regimen $(n = 91)$ in 2012	- d4T + 3TC + EFV/NVP/LPV/r	d4T-based regimens.	recommendation for zidovudine-based second-
		Second-line ART: Didanosine-based regimen upon		line regimens
		virological failure.		
J-P	HIV-1-positive children under 12 weeks were eligible if they had	Continuation of HAART with stavudine (d4T) +	Not applicable (non-randomized, open-	Safety, efficacy (CD4 count, viral load), drug
Aboulker,	evidence of definitive HIV-1 infection, they were a part of	didanosine (ddl) + nelfinavir (NFV). Participants were	label study).	resistance, virological failure, acquisition of
2004	PMTCT programs and initiated HAART (stavudine, didanosine,	followed up for 72 weeks with monitoring for CD4 counts,		resistance mutations, regimen tolerability.
	nelfinavir) at a median age of 2.5 months in a multicenter study	viral load, and emergence of drug resistance mutations.		
	across France, Spain, Germany, Italy ,UK in 1999.			
T Puthanakit,	HIV-infected children in Thailand, enrolled in 2002, under 18	Continuation of NNRTI-based ART with the following	Different NNRTI-based regimens (NVP	Prevalence of DRMs, resistance to NRTIs,
2010	years old, who failed first-line NNRTI-based ART (nevirapine or	regimens:	vs. EFV), and their association with	resistance to NNRTIs, effectiveness of second-
	efavirenz) and underwent genotypic resistance testing within 12	- Nevirapine-based ART: d4T + 3TC + NVP or AZT +	virological failure.	line regimens
	months before switching to second-line therapy.	3TC + NVP		
		- Efavirenz-based ART: AZT + 3TC + EFV		
		Participants with VL ≥ 1000 copies/mL underwent		
		genotypic resistance testing to monitor DRMs.		

Winstone	HIV-1-infected children and adolescents in Western Kenya who	Continuation of first-line NNRTI-based ART with the	Different ART regimens and their	Prevalence of DRMs, particularly resistance to
Nyandiko,	were perinatally infected, under 14 years of age or beginning	following regimens:	association with virological failure and	NRTIs and NNRTIs, and the impact on
2022	NNRTI-based 1st-line ART in 2010. The study included 480	- ABC + 3TC + EFV/NVP	clinical outcomes, including the impact of	second-line ART outcomes.
	participants, with a median age of 8 years.	- AZT + 3TC + EFV/NVP	DRMs on second-line ART effectiveness.	
		- D4T + 3TC + EFV/NVP		
		Participants with VL >1000 copies/mL underwent		
		genotypic resistance testing to monitor DRMs.		
Barbara S.	HIV-1-infected children (<24 months of age) and adolescents	Initiation of PI-based ART, primarily with the following	LPV/r-based ART versus RTV-based	Prevalence of DRMs, particularly PI-related
Taylor, 2011	in Johannesburg and South Africa, either prior to ART start or	regimens:	ART, including virological outcomes and	mutations, and the impact on virological
	after ART start if they had recently initiated ART, were receiving	- LPV/r-based ART: Used for children over 6 months of	resistance profiles.	suppression.
	a first-line PI-based regimen, and had not had any changes to this	age and those not receiving TB treatment.		
	first-line regimen.	- RTV-based ART: Used for children under 6 months of		
		age or those receiving TB treatment.		
		Genotypic resistance testing was conducted for children		
		who did not achieve HIV-1 plasma RNA <400 copies/ml		
		by 52 weeks.		
Djeneba B.	HIV-1-infected children aged less than 15 years in West African,	The ART regimens included:	Comparison of integrase RAMs between	Prevalence of natural polymorphisms and
Fofana, 2023	Mali and Benin. The study involved 107 children, with a median	- NNRTI-based: 3TC + (ZDV or ABC) + NVP or EFV	ART-naïve and ART-treated children. The	RAMs associated with integrase inhibitors.
	age of 10 years for ART-treated children.	- NRTI+PI-based: TDF + (3TC or FTC or ABC) + LPV/r	study also compared the prevalence of	
		Genotypic sequencing was conducted on DBS collected	integrase polymorphisms between these	
		from ART-treated children with virological failure.	groups.	
German A.	Perinatally HIV-infected children and adolescents who received	Analysis of the prevalence of resistance-associated	Children with versus without RAM,	Prevalence of etravirine among the cohort and
Contreras,	routine care at UTHealth Houston in the United States in 2009.	mutations to etravirine (RAM) among children and	association with previous NNRTI use	the identification of risk factors associated
2013	The study involved 66 patients with a history of ART and	adolescents. The ART regimens included:	(especially nevirapine), and prevalence	with RAM.
	resistance testing.	- NRTI-based regimens: with history of exposure to	across different birth cohorts and ethnic	
		NRTIs.	groups.	
		- Protease inhibitor-based regimens: with history of		
		exposure to PIs.		
		- NNRTI-based regimens: specifically including		
		nevirapine or efavirenz, with some patients exposed to both		
		drugs.		
		The study also evaluated the factors associated with the		
		presence of RAM, such as CD4% and history of NNRTI		
		use.		

Constance	HIV-1-infected children treated with ART who experienced	Analysis of genotypic resistance profiles following	Children with versus without resistance to	Prevalence of drug resistance, resistance to
Delaugerre.	virological failure (defined as HIV-1 RNA > 500 copies/mL) at	virological failure. This included the detection of resistance	ART drugs and resistance to different	NRTIs, resistance to NNRTIs, resistance to
2007	Necker Hospital. Paris. France in 2007. The population included	mutations to NRTIs. NNRTIs, and PIs. The study focused	ART classes (NRTIs, NNRTIs, PIs).	PIs association with viral load association
	children born between 1983 and 2003 with a median age of 12	on identifying risk factors associated with resistance	including factors like age gender and	with the number of PIs gender differences
	vears.	including the number of prior ART drugs, viral load, and	ART history.	triple-class resistance.
		demographic factors like gender.		r r r r r r r r r r r r r r r r r r r
Allison L	HIV-1-infected children and youth enrolled in the LEGACY	Recycling of NNRTI-based regimens despite documented	Participants who recycled NNRTIs versus	Virologic suppression (VL < 400 copies/mL)
Agwu, 2014	cohort across the United States and Puerto Rico in 2005, with	NNRTI-R. This involved restarting NNRTI therapy after a	those who did not, focusing on adherence.	at 24 weeks post-recycling. CD4 count
5	documented NNRTI resistance (NNRTI-R). The study included	median of 402 days from the first detection of NNRTI-R,	CD4 count, specific NNRTI mutations	changes, and the development of additional
	133 participants with a median age of 10.1 years, predominantly	with a median duration of 370 days on the recycled	(e.g., K103N), and virologic suppression	NNRTI-R mutations.
	Black, non-Hispanic, and infected perinatally.	regimen.	outcomes.	
Seth C.	HIV-1-infected infants in the Kisumu Breastfeeding Study	Mother: NFV/ZDV/3TC from 34 weeks of gestation to 6	Infants with versus without the K65R	Development of K65R mutation, association
Inzaule, 2016	(KiBS) in Kenya in 2003, whose mothers were on a triple-	months post-partum	mutation, focusing on CD4 cell counts,	with lower baseline CD4 counts, early
,	antiretroviral regimen of zidovudine (AZT), lamivudine (3TC),	children: sdNVP within 72h of birth, then breastfeeding	timing of DRM emergence, and presence	emergence of DRMs, multiclass drug
	and either nevirapine (NVP) or nelfinavir (NFV) during		of multiclass resistance.	resistance, disappearance of K65R by 6 to 9
	breastfeeding. The study involved 24 infants who acquired HIV-1			months, impact on future NRTI-based ART
	during the study period.			responses.
Cissy Kityo,	HIV-1-infected children aged ≤12 years in Uganda in 2010,	The study evaluated the impact of PDR on virological	Children with and without PDR were	Association between PDR and increased
2017	initiating first-line ART between January 2010 and August 2011.	outcomes. Children initiated on first-line ART, primarily	compared in terms of VF and the	likelihood of VF and ADR, prevalence of VF
	The study enrolled 317 children from three Joint Clinical	NNRTI-based regimens, with follow-up for 24 months,	accumulation of additional resistance	within 24 months, PDR as a strong predictor
	Research Center (JCRC) Regional Centers of Excellence (RCEs)	including viral load (VL) monitoring and genotypic	mutations (ADR).	of VF and ADR.
	in Kampala, Mbale, and Fort Portal, Uganda.	resistance testing.		
Sandra	ART-naïve Ugandan children aged 3-12 years, initiating	The study assessed the prevalence of PDR and its	Children with and without PDR were	Baseline PDR prevalence, association with
Soeria-	efavirenz-based ART between February 2015 and February 2016.	association with virological outcomes after 24 weeks of	compared regarding virological	odds of viremia, accumulation of new DRMs,
Atmadja,	The study included 99 children from an urban cohort, primarily	efavirenz-based ART. Baseline and 24-week assessments	suppression, the development of acquired	viral suppression rates by week 24.
2020	from families living within a 50 km radius of Kampala, Uganda.	included VL and genotypic drug resistance testing for	drug resistance, and accumulation of new	
		NRTI and NNRTI.	drug resistance mutations (DRMs) after 24	
			weeks of treatment.	
Podjanee	HIV-1-infected children aged less than 18 years who were	NNRTI-based antiretroviral therapy, primarily using	NVP-based regimens (d4T+3TC+NVP)	Virologic failure rates, comparison of failure
Jittamala,	antiretroviral drug-naive before initiation of NNRTI-based ART	nevirapine (NVP)-based regimens, with some children	versus EFV-based regimens	risk between NVP-based and EFV-based
2009	in 2017, except for exposure to antiretroviral prophylaxis for	receiving efavirenz (EFV)-based regimens. Clinical,	(3TC+d4T+AZT).	regimens, common resistance mutations
	mother-to-child transmission. The study involved 202 children	immunologic, and virologic outcomes were assessed, with		identified.
	from Thailand, enrolled from four hospitals between August 2002	HIV RNA and CD4 monitored every 6 months.		
	and October 2006.			

Syed Hani Abidi, 2021 Bhavna H. Chohan, 2015	Children aged 0-15 years who were part of an extensive HIV-1 outbreak in Pakistan, between April and June 2019. A total of 401 blood samples were collected, with 344 samples successfully sequenced for HIV-1 subtype and drug resistance mutation analysis. HIV-1-infected Kenyan infants less than 5 months old who were not previously exposed to NVP for PMTCT in 2007. A total of 22 infants initiated on NVP-based ART were followed for 12	Phylogenetic and drug-resistance analysis of HIV-1 sequences, specifically focusing on subtype distribution, transmission clusters, and DRM. Bayesian and maximum- likelihood phylogenetic methods were used to determine subtype distribution, identify clusters, and estimate the time to the most recent common ancestor (tMRCA). Nevirapine-based antiretroviral therapy (NVP-ART) was administered to the infants in a dose-escalation strategy, combined with two NRTIs, either lamivudine and	HIV-1 sequences from the outbreak versus sequences from high-risk groups in Pakistan (PWID and MSM), focusing on phylogenetic relationships and DRMs. Development of NVP resistance in NVP- unexposed infants over 12 months, focusing on resistance association with	Clusters of HIV-1 transmission, presence of drug resistance mutations, common HIV-1 strains (CRF02_AG, subtype A1), resistance in RT genes, potential challenges for treatment due to resistant strains NVP resistance development, detection timeline (3 to 6 months), association with higher viral loads, virologic failure,
	months.	zidovudine (NVP/3TC/AZT) or lamivudine and abacavir (NVP/3TC/ABC).	virologic failure, viral load, HIV-1 subtype, and adherence.	comparison of viral loads in infants with and without NVP resistance.
Anita Shet, 2013	HIV-1-infected children in India less than 16 years old on first- line ART in 2007. A total of 80 children were included, with 68 achieving virologic suppression and 12 experiencing virologic failure.	First-line ART including pediatric fixed-dose combination pills. The ART regimens were based on NRTIs and NNRTIS. 2 NRTI (zidovudine/stavudine + lamivudine) + 1 NNRTI (nevirapine or efavirenz)	Children on first-line ART with virologic suppression versus those with virologic failure, focusing on associated drug resistance mutations.	Virologic suppression rate, presence of resistance-associated mutations, M184V mutation, thymidine analogue mutations (M41L, T215Y/F/I), NNRTI mutations (K103N/R, Y181C, G190A).
Theodore D, 2011	HIV-1-infected Ugandan children (n=120) starting ART in 2010.	First-line ART, including regimens based on NVP or EFV combined with 3TC and either ZDV) or D4T.NVP/3TC/ZDV 19 (16%), NVP/3TC/D4T 17 (14%), EFV/3TC/ZDV 73 (61%), EFV/3TC/ZDV 7(6%), 4 (3%) children ABC/ZDV/3TC for concurrent anti-tuberculosis therapy, then changed to NVP/ZDV/3TC after 154-237 days of ARV therapy	Comparison of virologic outcomes in children with early virological failure (EVF) versus those without EVF, and the evolution of ARV resistance mutations over time.	Extended virologic failure (EVF), persistent viremia, reverse transcriptase mutations (M184V, NNRTI-associated mutations), thymidine analog mutations (TAMs) after 12 months of virologic failure.
Liting Yan, 2022	HIV-1-infected children and adolescents less than 15 years old in China in 2019, receiving long-term antiretroviral therapy (ART) from five different centers, with a median ART duration of 10 years.	Genotypic resistance testing for those identified with virological failure (VF) (viral load (VL) \geq 400 copies/mL) after long-term ART.ZDV + 3TC + NVP/EFV 17 (18.3) TDF + 3TC + EFV 13 (14.0) ZDV + 3TC + LPV/r 21 (22.6) ABC + 3TC + LPV/r 26 (27.9) TDF + 3TC + LPV/r 13 (14.0) ABC + ZDV + 3TC + LPV/r 3 (3.2)	Comparison between participants with DRMs and those without, based on various factors such as age at ART initiation, ART regimen, and HIV subtype.	Major DRM presence, NNRTI resistance, NRTI resistance, PI resistance, younger age at ART initiation, subtype B association, NNRTI-based regimen association, continued virologic failure, accumulation of major mutations.
Yan Zhao, 2011	HIV-1-infected children from rural China experiencing virologic failure to first-line antiretroviral therapy regimens and who were part of a national pediatric antiretroviral therapy program in 2005.	Switching to a second-line antiretroviral therapy regimen after experiencing virologic failure on the first-line regimen.Regimen at enrollment of resistance test, AZT/D4T + 3TC + NVP, AZT/D4T + 3TC + EFV, AZT/D4T + ddI + NVP. Second-line regimen, ABC + 3TC + LPV/r, AZT + 3TC + LPV/r, ABC + 3TC + AZT +	Comparison between the effectiveness of second-line regimens (including boosted protease inhibitors) after switching from failing first-line regimens, focusing on drug resistance profiles before and after the switch.	Resistance to nevirapine, resistance to efavirenz, undetectable viral loads after switching to second-line therapy, increases in CD4 counts.

		LPV/r		
Clara	HIV-1-infected children under 15 years who received long-term	First-line NNRTI-based ART regimen with regular	Comparison between virologically	Virological suppression drug resistance
Bratholm,	antiretroviral treatment at Havdom Lutheran Hospital in rural	monitoring of virological response and genotypic resistance	suppressed children and those with	mutations, resistance to NRTIs and NNRTIs
2010	Tanzania in 2009.	testing for those with viral load >200 copies/mL.	clinically relevant drug resistance	,
		zidovudine/lamivudine/nevirapine 7(36%),	mutations after long-term ART.	
		stavudine/lamivudine/nevirapine 7(36%),	-	
		zidovudine/lamivudine/efavirenz 4 (21%),		
		stavudine/lamivudine/efavirenz 1(5%).		
Ravindra K.	HIV-1-infected Zambian children on adult fixed-dose	Administration of adult fixed-dose combination	Children with previous ART exposure	Viral suppression, virologic failure, NNRTI
Gupta, 2010	combination cART (stavudine, lamivudine, nevirapine) in 2003	antiretroviral therapy (cART) consisting of	versus those without, and children with	resistance, M184V mutations, thymidine
	with a median age of 8 years.	D4T+3TC+NVP (Triomune30), dosed according to WHO	different levels of drug resistance.	analogue mutations (TAM), resistance to
		guidelines.		NNRTI and lamivudine.
Jean-	HIV-1-infected South African children under 2 years old in 2014	Treatment with NRTI + 1 PI regimen	NRTI + 1 PL regimens at initiation of	Virologic suppression rates CD4% increases
Christophe	This group includes infants and toddlers who were diagnosed	- Initial cART Regimens: Loninavir/ritonavir + Stavudine	cART versus subsequent treatments	and development of drug resistance mutations
Beghin, 2020	with HIV and initiated on combination antiretroviral therapy	+ Lamivudine Lopinavir/ritonavir + Zidovudine +	including the impact of switching from	focusing on the effectiveness and resistance
	(cART) shortly after diagnosis.	Lamivudine.	Stavudine or Zidovudine to Abacavir or	profiles associated with NRTI + 1 PI
		- Updated Regimens in 2014: Lopinavir/ritonavir +	Tenofovir on virologic suppression,	regimens.
		Abacavir + Lamivudine, Lopinavir/ritonavir + Zidovudine	CD4% recovery, and drug resistance	-
		+ Lamivudine, Lopinavir/ritonavir + Tenofovir +	development.	
		Lamivudine, Efavirenz + Abacavir + Zidovudine, Efavirenz		
		+ Abacavir + Lamivudine, Efavirenz + Lopinavir/ritonavir		
		+ Abacavir + Zidovudine.		
Jean-	HIV-1-infected South African children under 2 years old in 2014.	Treatment with NRTI + NNRTI regimen.	Different NRTI + NNRTI regimens at	Virologic suppression rates, CD4% increases,
Christophe	This population consists of very young children, including those	- Initial cART Regimens: Lopinavir/ritonavir + Stavudine	cART initiation, including switches	and development of drug resistance mutations,
Beghin, 2020	diagnosed at birth or within the first few months of life. The	+ Lamivudine, Efavirenz + Stavudine + Lamivudine,	between Stavudine and Tenofovir or	focusing on the effectiveness and resistance
	children are from diverse backgrounds, receiving treatment in	Efavirenz + Abacavir + Lamivudine.	Zidovudine and Abacavir, focusing on	profiles associated with NRTI + NNRTI
	various healthcare facilities across South Africa.	- Updated Regimens in 2014: Lopinavir/ritonavir +	virologic response and immune recovery.	regimens.
		Abacavir + Lamivudine, Lopinavir/ritonavir + Zidovudine	It also compares NNRTI-based regimens	
		+ Lamivudine, Lopinavir/ritonavir + Tenofovir +	(especially Efavirenz) versus PI-based	
		Lamivudine, Lopinavir/ritonavir + Abacavir + Zidovudine,	regimens for maintaining viral	
		Etavirenz + Abacavir + Lamivudine, Efavirenz + Tenofovir	suppression, improving CD4 counts, and	
		+ Lamivudine, Efavirenz + Stavudine + Lamivudine.	minimizing resistance development.	

Judit	HIV-1-infected children aged less than 18 years in Panama, who	The ART regimens included: - NNRTI-based: 3TC + (ZDV	Integrase RAMs and polymorphisms	Prevalence of natural polymorphisms and
Ventosa-	were part of a the mother-to-child transmission of HIVprogram.	or ABC) + NVP or EFV - NRTI+PI-based: TDF + (3TC or	between ART-naïve and ART-treated	RAMs associated with integrase inhibitors.
Cubillo,	The study involved 107 children, with a median age of 10 years	FTC or ABC) + LPV/r. Genotypic sequencing was	children.	
2023	for ART-treated children.	conducted on DBS collected from ART-treated children		
		with virological failure.		
Lukas Muri,	HIV-1-infected children and adolescents aged 18 years or less,	The ART regimens included NNRTI-based and PI-based	Comparison of virologic failure and	Virologic failure, prevalence of HIV-DRM,
2017	from rural Tanzania, attending the paediatric HIV Clinic of	treatments. Initial regimens consisted mostly of ZDV/3TC	acquisition of DRMs between children on	multiclass resistances.
	Ifakara in 2016. The study involved 213 children on ART for at	with NNRTI (54.9%) or d4T/3TC with NVP (39%). 15%	NNRTI-based and PI-based ART	
	least 12 months. The median age was 11 years, and the median	of the children were on a PI-based regimen at the time of	regimens.	
	time on ART was 4.45 years. Some children had prior ART	investigation.		
	exposure, excluding PMTCT.			
Paula Vaz,	HIV-1-infected children aged 1 to 14 years on ART for ${\geq}12$	Children were treated with first-line ART regimens,	Children with virologic failure (VL ≥ 1000	Virologic failure, drug resistance mutations,
2018	months from Mozambique in 2013. The study involved 715	primarily using fixed-dose combinations containing d4T,	copies/mL) versus those with suppressed	compromised efficacy of second-line ART,
	children, with a mean age of 103 months and a mean time on	3TC, and NVP. Viral load testing was performed, and for	viral loads, including prevalence of drug	effectiveness of drugs in the regimen.
	ART of 60 months. Approximately 20.1% had a history of	those with ≥ 1000 copies/mL, genotyping was conducted to	resistance mutations and effectiveness of	
	exposure to the PMTCT of HIV. Children were included if they	assess drug resistance mutations.	standard second-line ART regimens.	
	had been on ART for at least 12 months.			
A.T.	HIV-1-infected children and adolescents aged 0-19 years in	The intervention primarily involved first-line ART	Different age groups (children vs.	Virologic failure, drug resistance mutations,
Makadzange,	Zimbabwe in 2012, enrolled between 2004 and 2011. The	regimens, with a significant proportion of the participants	adolescents) in terms of virologic and	compromised efficacy of second-line ART,
2015	participants were part of a public ART program at Parirenyatwa	on a Nevirapine-based regimen (82.6%). Zidovudine and	immunologic outcomes, impact of age at	effectiveness of drugs in the regimen.
	Hospital Family Care Center (PHFCC), Harare. The median age	Stavudine were also commonly used in the NRTI	ART initiation and duration of ART on	
	at ART initiation was 8 years. The study included children with a	backbone. Protease inhibitors were used for infants and in	virologic failure, and outcomes based on	
	history of advanced clinical disease (WHO stages 3 and 4), with	cases of treatment failure, with all children and adolescents	Nevirapine versus other ART regimens.	
	many participants having experienced severe immunosuppression.	on a PI-based regimen receiving Lopinavir/ritonavir. The		
		median time on ART was 2.9 years.		
George A.	HIV-1-infected children, adolescents, and pregnant women in	ART regimens included: NRTI + NNRTI-based (TDF +	Drug resistance mutations across different	Prevalence of drug resistance mutations to
Yendewa,	Sierra Leone in 2019. This study involved 96 children (age 2-9	3TC + EFV, AZT+ 3TC+ EFV, AZT+ 3TC+ NVP, AZT+	age groups and ART regimens, and	NRTIs, NNRTIs, and PIs.
2021	years, median age 5), 47 adolescents (age 10-18 years, median	3TC+ LPV/r) and NRTI + PI-based (ABC+ $3TC+$ EFV,	prevalence of RAMs between ART-naïve	
	age 13), and 54 pregnant women (age >18 years, median age 26).	ABC+ 3TC+ NVP, ABC+ 3TC+ LPV/r). Genotypic	and ART-experienced patients.	
	All children and adolescents acquired HIV through mother-to-	sequencing was conducted on plasma samples collected		
	child transmission, and 72.2% of the pregnant women were ART-	from ART-experienced patients.		
	experienced.			
Josephine	HIV-1-infected children in Mali, with ages ranging from infancy	The ART regimens included: 2 NRTIs + 1 NNRTI (most	Presence of RAMs and defective viral	HIV-1 resistance in DNA, resistance to NRTIs
Brice, 2020	to under 20 years old, involved in a cross-sectional study	commonly, combinations such as Zidovudine +	populations between children with	and NNRTIs.
	conducted from August 2013 to April 2014. The children were	Lamivudine + Nevirapine, or Abacavir + Lamivudine +	different ART regimens, including the	
	part of the Prevention of Mother-to-Child Transmission (PMTCT)	Efavirenz) and 2 NRTIs + 1 PI (commonly Abacavir +	genotypic susceptibility score (GSS) for	
	program and had been on ART for more than 6 months with	Lamivudine + Lopinavir). Genotypic resistance testing was	each regimen.	

	virological suppression (HIV-1 RNA \leq 50 copies/mL). The median age at the time of inclusion was 9.9 years, and the median duration of ART was 5.5 years.	performed on DNA from dried blood spots (DBS).		
Vaz, Paula, 2009	HIV-1-infected children under 15 years old in Mozambique, treated between December 2003 and September 2007. The study involved 512 children who received first-line ART for at least 6 months, with a median age of 49 months at treatment initiation. Among them, some had a history of perinatal prophylaxis (PMTCT) and 135 children experienced virological failure (VF)	The ART regimen included NNRTI-based therapy: Nevirapine combined with 2 NRTIs (Stavudine or Zidovudine and Lamivudine). Genotypic resistance testing was performed on available samples from children with virological failure.	Presence and pattern of resistance mutations between children with virologic failure (VF) treated for different durations, including extended resistance to drugs not previously administered, and resistance patterns in children with shorter versus	Resistance to Lamivudine and Nevirapine, extended spectrum of resistance, resistance to Abacavir, Tenofovir, and Etravirine.
M. Sylla, 2019	defined as HIV-1 RNA >50 copies/mL. The study involved HIV-1-infected children less than 18 years of age who were infected with HIV-1 and receiving second-line ART for at least 6 months in Mali, receiving second-line ART. These children were enrolled from November 2013 to August 2014 at Gabriel Touré Hospital in Bamako. All children included in the study were experiencing virological failure (VF), defined as a viral load \geq 1000 copies/mL after 6 months on second-line ART.	The intervention involved sequencing the protease and reverse transcriptase genes from children experiencing VF on second-line ART. The first-line regimens: d4T + 3TC + NVP, AZT + 3TC + NVP. second-line regimens: ABC + 3TC + LPV/r, ddI + ABC + LPV/r	longer treatment durations. The study compared the prevalence and patterns of drug resistance mutations in the children, focusing on mutations associated with NRTIs, NNRTIs, and PIs.	Resistance to NRTIs, NNRTIs, and PIs, common presence of the M184V mutation, continued activity of LPV/r despite second- line ART failure.
P. Vaz, 2012	HIV-1-infected children aged ≤13 years in Mozambique, enrolled between 2007 and 2008 at the Pediatric Day Hospital (HDP) in Maputo. This study involved 119 children, with a median age of 25.2 months. 50% were aged <18 months, and 13 children had maternal or child PMTCT exposure. All children were in WHO clinical stages III or IV at the time of ART initiation, and 48% were severely immunocompromised.	First-line ART regimens included: ZDV or d4T in combination with 3TC and either NVP or EFV. A small number of children (2 of 119) received a boosted PI regimen (Lopinavir/ritonavir + ZDV + 3TC).	Virological outcomes at 12 months after ART initiation, comparing children with HIV drug resistance mutations and viral load suppression (<1000 copies/mL) versus those with virologic failure (VF).	Viral suppression at 12 months, presence of HIVDR mutations, dual class resistance (NRTI and NNRTI), predictors including maternal ARV exposure for PMTCT, baseline HIVDR.
Patricia A. Brindeiro, 2002	HIV-1-infected children aged 2 to 14 years in Brazil (specifically in Rio de Janeiro and São Paulo), from April 1999. All children were vertically infected with HIV. Most children were undergoing highly active antiretroviral treatment with some on dual-nucleoside reverse transcriptase inhibitor therapy. A significant number of children had virological failure. No specific information is provided on whether the children were exposed to PMTCT.	The study involved testing genotypic and phenotypic resistance to ARV therapy in children who were failing their treatment. Plasma samples were collected for HIV-1 pol gene sequencing and phenotyping. The children were receiving various ARV regimens, including dual-NRTI therapy and HAART, with specific drugs like AZT, 3TC, and various PIs such as ritonavir and NFV.	Genotypic resistance patterns and phenotypic resistance profiles in children infected with different HIV-1 clades (B versus non-B), focusing on resistance mutations and their impact on treatment outcomes.	Primary mutations conferring resistance to ARV drugs, differences in secondary resistance mutations between B and non-B subtypes.

Christiane Adjé-Touré, 2008	HIV-1-infected children aged 0–15 years in Côte d'Ivoire, between 1998 and 2003. A total of 134 children were included in the study who had initiated ART and remained on treatment for approximately 1 year. The median age was 7 years, and 25% were less than 4 years old at treatment initiation. PMTCT was not explicitly mentioned.	The study involved ART regimens primarily consisting of two reverse transcriptase inhibitors (ZDV, ddI, d4T, 3TC) combined with either one protease inhibitor (nelfinavir) or one NNRTI (efavirenz).	The study compared the virologic and immunologic responses to ART, as well as the development of drug resistance among children receiving these regimens.	Changes in viral load, CD4 T cell percentage, incidence of drug resistance.
Paul Alain Tagnouokam -Ngoup, 2021	HIV-1-infected children under 15 years old in Cameroon, enrolled in the ANRS 12225-PEDIACAM cohort study between November 2007 and October 2011. The cohort included 210 children born to HIV-infected mothers, with 155 included in the final analysis. The median age at cART initiation was 4.2 months. Approximately 61.3% received PMTCT prophylaxis at birth, and 47.1% were born to mothers who received PMTCT prophylaxis.	The study primarily focused on the administration of cART with regimens including AZT/3TC/LVP/r, 3TC/D4T/LVP/r, AZT/3TC/NVP, and 3TC/D4T/NVP. Follow-up included regular viral load measurements and drug resistance testing for five years.	Comparison was made between different ART regimens (e.g., LPV/r-containing regimens vs. NVP-containing regimens) and their effectiveness in preventing VF and drug resistance.	Occurrence of virological failure, presence of drug resistance mutations, duration between cART initiation and VF.
Clarisse Amani- Bosse, 2017	HIV-1-infected children under the age of 2 years, residing in Côte d'Ivoire and Burkina Faso in 2010. These children were ART- naive except for PMTCT exposure. The study cohort consisted of 156 children, with a median age of 13.9 months at ART initiation, and included children who had experienced virological failure.	History of antiretroviral drug exposure, n (%) : Prenatal maternal ART 19 (12.2) PMTCT and postnatal maternal ART 11 (7.1) . PMTCT only 50 (32.1) Postnatal maternal ART only 18 (11.5) No previous exposure to any PMTCT or maternal ART 58 (37.2). First-line NRTI backbone, n (%) ZDV-3TC 142 (91.0) ABC-3TC 14 (9.0).	Outcomes based on variables such as access to tap water, main caregiver (mother vs. father), and socio-economic factors, and the difference in virological suppression rates between children with versus without prior PMTCT exposure.	Development of antiretroviral resistance mutations among those with virological failure, identification of risk factors for virological failure.
Laurence Ahoua, 2011	The study involved HIV-1-infected children aged less than 15 years from rural Uganda. The children were part of a cohort initiated on ART between 2005 and 2006. The majority of the children were 5 years old at the start of the therapy, and most had advanced stages of the disease (clinical stage 3 or 4). Some children had previously been exposed to PMTCT interventions, including single-dose nevirapine.	The intervention included initiating cART regimens. The majority of children were on a regimen that included NNRTI-based therapy, primarily using NVP with a combination of 3TC and either AZT or d4T. Adjustments were made based on clinical responses, and some children switched to PI-based regimens due to drug resistance or toxicity. ART regimen (%): AZT 3TC NVP 54 (77.1), d4T 3TC NVP 16 (22.9).	Virological and immunological responses between children who maintained viral suppression versus those with virological failure, including a comparison of drug resistance patterns and mutations associated with resistance to NNRTIs and NRTIs.	Virological suppression (HIV RNA < 400 copies/mL), immunological response (CD4 count and percentage), prevalence of drug resistance mutations.
Laurence Ahoua, 2011	The study involved HIV-1-infected children aged less than 15 years from rural Uganda. The children were part of a cohort initiated on ART between 2005 and 2006. Most of the children were 5 years old at the start of the therapy, and most had advanced stages of the disease (clinical stage 3 or 4). Some children had previously been exposed to PMTCT interventions,	The intervention included initiating cART regimens. The majority of children were on a regimen that included NNRTI-based therapy, primarily using NVP with a combination of 3TC and either AZT or d4T. Adjustments were made based on clinical responses, and some children switched to PI-based regimens due to drug resistance or	Differences in virological and immunological responses between children who maintained viral suppression versus those with virological failure, and drug resistance patterns, including mutations associated with NNRTI and	Virological suppression (HIV RNA < 400 copies/mL), immunological response (CD4 count and percentage), prevalence of drug resistance mutations at 12 and 24 months.

	including single-dose nevirapine.	toxicity. ART regimen (%): AZT 3TC NVP 25 (78.1), d4T 3TC NVP 7 (21.9).	NRTI resistance.	
Philippe R.	HIV-1-infected children and adolescents aged 1 to 18 years in	cART which included either NNRTI-based regimens	No direct comparison group. However, the	Long-term effectiveness of cART, virologic
Mutwa, 2014	Rwanda in 2009. The study was conducted between September	(AZT/3TC/NVP, d4t/3TC/NVP) or PI-based regimens	study evaluated outcomes based on	failure, genotypic drug resistance mutations,
	2009 and October 2010. Participants were perinatally infected and	(AZT/3TC/EFV, d4T/3TC/EFV) based on Rwandan	different cART regimens and factors such	clinical condition, immunologic criteria.
	were on combination antiretroviral therapy (cART) for a median	national guidelines.	as CD4 count at cART initiation, regimen	
	of 3.4 years. Some had prior exposure to PMTCT, including single-dose nevirabine.		changes, and exposure to PMTCT.	
Tanya Rogo,	The study involved HIV-1-infected children attending the only	The study focused on ART regimens given to these	The study compared virologic outcomes	Drug resistance, virologic failure, missed
2015	pediatric HIV clinic in USA between 1991 and 2012. The cohort	children, which included various combinations of NRTIs,	and the development of drug resistance	appointments and doses.
	consisted of 56 children, including ART-naive and ART-	NNRTIs, and PIs. ART regimens were individualized, and	between different ART regimens, as well	
	experienced individuals. 64% of the children were perinatally	the study investigated the development of DRMs over time.	as between children with different	
	infected, with ages at diagnosis ranging from less than 1 year to		adherence levels, caregiver support, and	
	over 5 years. A significant proportion (20%) were refugees, and		disclosure of HIV status. It also compared	
	73% were Black or Hispanic. The study also included children		ART-naive children to ART-experienced	
	who experienced virologic failure (57% of ART-experienced		children regarding the prevalence of	
	children).		DRMs.	
Miguel de	HIV-1-infected children under 18 months, primarily from Spain,	The study involved the administration of ART, including	Comparison of drug resistance mutations	Drug resistance mutations, transmitted DRMs
Mulder, 2011	with data collected between 1993 and 2009. The majority were	regimens based on NNRTIs, NRTIs, and PIs. The	between ART-naive and ART-experienced	in ART-naive children, resistance mutations in
	perinatally infected, with a high percentage presenting moderate	resistance analysis was conducted on specimens collected	children, as well as between children	ART-experienced children
	to severe AIDS symptoms. Of these, 85% were receiving ART at	from plasma, PBMCs, and DNA, with sequences analyzed	infected with different HIV-1 subtypes (B	
	the time of sample collection. A subset was infected through	for drug resistance mutations. Treatment regimens varied,	and non-B variants). The study also	
	PMTC1, with about 96% being perinatally infected. Among the	and some children were treated with multiple regimens	compared the prevalence of drug	
	The schort included both APT paive and APT experienced	over time.	resistance in children on various ART	
	children with 61.6% having received four or more different ART		regimens.	
	regimens during their follow-up			
Joseph	HIV-1-infected children, primarily from the Pediatric AIDS	Nelfinavir-containing regimens combined with various	No direct comparison group was indicated	Virological response, emergence of drug
E.Fitzgibbon,	Program at Robert Wood Johnson Medical School, New	RTIs, including AZT, 3TC, d4T,ddI, and NNRTIs like	in this study; however, the study did assess	resistance mutations in protease and reverse
2001	Brunswick, NJ, USA. The study included 17 children with a mean	NVP and DLV. The specific drugs used in combination	the emergence of drug resistance	transcriptase genes, resistance mutations
	age of 7.9 years (ranging from 1 to 17 years). All children were	with nelfinavir varied among the participants. Current	mutations following the initiation of	including D30N, L90M, and M184V.
	experienced with reverse transcriptase inhibitors (RTIs) prior to	therapy: Nelfinavir.	nelfinavir therapy.	
	the study, and two had previous exposure to PIs. There is no			
	mention of whether the children were involved in a PMTCT			

	program or had experienced VF prior to the study.			
Compagno Francesca, 2019	HIV-1-infected children aged under 15 years in Switzerland, part of the Swiss Mother and Child HIV Cohort Study (MoCHIV), born between 1989 and 2009. The study included 22 mother-child pairs, where 95% of mothers were treatment-naïve before pregnancy. The study also accounted for whether ART was administered during pregnancy, with a focus on the rate of VF and DRMs.	cART, including various ART regimens provided to the mothers during pregnancy or at delivery, with a focus on assessing the impact of maternal ART on the emergence of drug-resistant mutations in the children. The intervention also included the monitoring and analysis of HIV-1 genotypes and drug resistance profiles in both mothers and children.	The study compared the rate of transmitted drug resistance mutations (HIV-DRM) versus selected drug resistance mutations (HIV-DRM) in the children. It also looked at the effects of ART administration versus no ART during pregnancy on these outcomes.	Prevalence of HIV-DRM and HIV-DRM in the children, with an emphasis on understanding the timing of these mutations' emergence and their impact on virological failure and treatment efficacy.
Lisa L. Ross, 2015	HIV-infected children from North America, Europe, and South Africa, enrolled in 2004, aged 2 to 18 years. Majority of children were ART-experienced before the study, with some having prior exposure to PIs.	ART experience: 3 NRTIs. Children received either unboosted fosamprenavir (FPV) or FPV/ritonavir (FPV/RTV) regimens, with 13 children on FPV and 65 on FPV/RTV.	Not specifically defined; indirect comparison with standard ART regimens in similar populations.	The incidence of virologic failure (VF) and treatment-emergent mutations in HIV-1 were observed over 48 weeks.
Lisa L. Ross, 2015	HIV-infected children from South Africa, Mexico, Argentina, and Portugal, enrolled in 2003, aged 4 weeks to <2 years. 30% were ART-naïve at study start, and the rest were ART-experienced, but most were PI-naïve.	All children received FPV/RTV with 2 NRTIs.	Not specifically defined; indirect comparison with standard ART regimens in similar populations.	Treatment-emergent mutations.
R. Lwembe, 2007	HIV-1-infected children in Kenya and Nairobi, aged 1-7 years, born to HIV-1-infected mothers unable to care for them, studied between 2001 and 2004. All were vertically infected with non- subtype B HIV-1 (subtypes A1, C, D, CRF02_AG) and had no prior ART or blood transfusion exposure. PMTCT history is unclear, but nevirapine for PMTCT was not yet in use in Kenya by 2002. These children experienced virological failure after initiating ART.	VariousARTregimensincludingzidovudine/lamivudine/nevirapine,zidovudine/didanosine/efavirenz,anddidanosine/lamivudine/abacavir.Somechildrenalsoreceived multipleARTregimensover the study period.	Comparison of ART-naïve children with those who received different ART regimens in terms of the emergence and patterns of RAMs, particularly RTI and NNRTI resistance.	Persistence of vertically transmitted NNRTI- resistance mutations in the absence of drug pressure, the emergence of RTI-resistance mutations during treatment, and differences in the patterns of drug resistance between non- subtype B and subtype B HIV-1-infected children.
S. H. Al Hajjar, 2012	HIV-infected children aged under 15 years, living in Saudi Arabia and Riyadh, enrolled between July 2006 and January 2009. The study focused on those experiencing VF following first-line highly active antiretroviral therapy. The study included children with a median age of 7 years. There was no specific mention of PMTCT. Among the children, 48% experienced persistent viral load >1000 copies/mL.	The study population received first-line HAART as per the recommended guidelines. The therapy involved various antiretroviral drugs including PIs and RTIs. Genotypic resistance tests were performed on children with virologic failure to optimize subsequent treatment regimens.	Not explicitly provided in the study, as it was a retrospective analysis focusing on the prevalence and patterns of antiretroviral resistance in the study population.	Drug resistance prevalence, adherence issues, common mutations in protease and reverse transcriptase regions, cross-resistance to NRTIs.

Z. Makatini, 2019	Children perinatally infected with HIV in South Africa, attending Dr George Mukhari Academic Hospital (DGMAH) from 2011 to 2017. The schert included 22 shildren with a median are of 3	Children were managed with a PI-based cART regimen. The most common PI regimen was LPV/r with various NRTI healthones including APC + $2TC$ A ZT + $2TC$ A ZT	Emergence of drug resistance mutations in children exposed to PI-based regimens	Major PI resistance mutations observed, frequent mutations included V82A, M46I/L, and I54V, loss of PI activity.
	vears at cART initiation (IOR 1.25-8.6 years) and all were below	+ ABC and dAT + 3TC. All children had evidence of major	antiretroviral options (e.g. atazanavir	
	16 years of age at the time of study. Most children were on a	PI resistance mutations after virological failure on first- or	darunavir) with a focus on resistance	
	folling regimen for a median of 22 months (IOP 6.66 months)	second line regimens	natterns and their impact on treatment	
	and had VE. The study included children exposed to PMTCT	second-nine regimens.	options	
	regimens, specifically single dose PTV and 2TC monotherapy		options.	
M. Comoro	HIV 1 infacted abildram in Câte d'Ivaire studied between 2012	The study focused on evaluating registence to PTIs in	Provalance of registence mutations in the	Pasistance to PTIs among HIV 1 infected
Cisso 2021	2012 The study included 61 abildren all under 18 years of age	abildran undergoing APT. Construit resistance to KTIS in	reverse transcriptese gene among children	abildron including NPTIs and NNPTIs with
C1556, 2021	with a madian age of 11 years at virological failure. The shildren	performed using the ANPS algorithm to assess resistance	on APT focusing on NPTIs and NNPTIs	common mutations M184V for NPTIs and
	were from a national schort at the Abidian Integrated Disalinian	performed using the ANKS algorithm to assess resistance	resistance profiles and specific mutations	V102N/S for NNPTIa
	Passagrah Captra. The majority of children had been on APT for a	approximate and the reverse transcription gene. The most	with additional phylogenetic analysis of	K10510/5 101 ININK115.
	modian duration of 6 years, with the treatment angoing for at least	focus on NPTIs and NNPTIs. Children were treated with	HIV 1 viral subtypes	
	6 months No specific information was provided regarding	some process of NPTIs and NNPTIs such as $ZDV + 2TC$	III v-1 vital subtypes.	
	avposure to PMTCT interventions. However, the study achert	\pm EEV ADC \pm 2TC \pm EEV and TDE \pm 2TC \pm EEV		
	included abildram from the first MTCT provention program. All	+ EFV, ABC $+$ STC $+$ EFV, and TDF $+$ STC $+$ EFV.		
	abildran had experienced VE with viral loads greater than 1000			
	conies/mI			
А Т	HIV 1 infacted abildram and adults in Provil with complex	DI treatment affectiveness in two different HIV 1 subtunes	Pate of acquisition of major and minor PL	Differences in the acquisition of resistance
A. I.	collected between 1008 and 2005. The study involved 24 shildren	(P and E1). The treatment regimens included various Pla	Rate of acquisition of major and minor Pi-	principal participal participad p
2000	inforted with subtures E1, 00 shildren with subtures P, 141 adults	(B and F1). The treatment regimens included various F1s	associated resistance initiations and	mutations between subtypes.
2009	with subtras D, and 00 adults with subtras E1. Definite wars on	such as KTV, IDV, SQV, and LPV, with differences in	polymorphisms in Hiv -1 subtypes B and E1 analyzing the americanae of specific	
	APT and superiorsed VE after at least 2 months of DI treatment	exposure times and resistance mutation acquisition.	F1, analyzing the emergence of specific	
	AKT and experienced VF after at least 5 months of PT freatment.		nutations in freated versus unfreated	
	exposure times		patients.	
I Fokam	The study focused on 164 infants (mean age was 72 months in	Diagnostic evaluation of congenital toxonlasmosis using	Not explicitly stated as a comparison	Prevalence of drug resistance
2011	both groups (drug paive and those failing first line treatment	serological tests (IgM IgA IgG) PCP and attempts to	group but findings were compared to	revalence of drug resistance
2011	with a range difference (min max: 3 144 months and 12 144	isolate the parasite from various samples (CSE blood	Africa cohorts where systematic prepatal	
	months, respectively) from the Cameroon between 1001 and	urino) 2TC A ZT NVR 51 (26) 2TC DAT NVR 20 (15)	Affica conorts where systematic prenatal	
	2005 These infants were confirmed or suspected of having	$\begin{array}{c} \text{arme}_{J,S} = C AZI \text{ivel SI} (20), \text{SIC} D4I \text{ivel 29} (13), \\ \text{SIC} AZT EEV \\ \text{S} (A) \text{SIC} DAT EEV \\ \text{A} (2) \text{SIC} AZT ABC \\ \end{array}$	were implemented Differences in clinical	
	congenital toxonlasmosis. None of the mothers received treatment	2 (1) 3TC DAT NVP 2 (1) NVP ATT (3TC or DAT) 2 (1)	severity were analyzed	
	for Toxonlasma gondii during programacy (PMTCT not applied)	2(1), 51C D41 IVVI 2(1), IVVF AZI (51C 0I D41) 2(1), 2TC (D4T NVD) or (ABC A7T) 2(1)	severity were analyzed.	
	Most infants did not receive postnatal treatment when their sorum	$\sum_{i=1}^{n} \sum_{i=1}^{n} \sum_{i=1}^{n} \sum_{j=1}^{n} \sum_{i=1}^{n} \sum_{i=1}^{n} \sum_{i=1}^{n} \sum_{i=1}^{n} \sum_{i$		
	was obtained			
	was obtained.			

T. N. Green, 2012	HIV-1-infected children aged less than 15 years in South Africa, recruited from King Edward VIII hospital in Durban, KwaZulu-Natal. The study was conducted between August 2008 and January 2010. The study included both HAART-failing children (n=51) and HAART-naive children (n=43). Some HAART-naive children had been exposed to antiretroviral therapy for the PMTCT. The median age of HAART-failing children was 7.9 years, while HAART-naive children had a median age of 0.9 years.	The intervention primarily involved HAART regimens, including two NRTIs plus one NNRTI for most children (80.5% of HAART-failing children). Some children (19.5%) were receiving two NRTIs plus one PI. The median duration of HAART prior to study recruitment was 28.6 months.	The study compared drug resistance mutations and coreceptor usage between HAART-failing and HAART-naive children. It assessed the prevalence of drug resistance mutations and the usage of CXCR4 (X4) or dual (R5X4)/mixed (R5, X4) (D/M)-tropic viruses in both groups.	Prevalence of drug resistance mutations, presence of TAMs.
S. Pillay, 2014	The study was conducted on 101 children aged \leq 15 years in rural KwaZulu-Natal, South Africa, who were experiencing VF after being on first-line ART. The study period was between August 2011 and December 2012. The children had been on ART for a median of 3.3 years (IQR 2.5-4.4), and the majority were on an NNRTI-based regimen (73 out of 89 successfully genotyped children). The median age at ART initiation was 7 years (IQR 3.7-9.6), and the median age at genotyping was 10.2 years (IQR 7.7-12.9). There was no specific mention of PMTCT drug exposure in the cohort.	The children were on either an NNRTI-based regimen $(3TC + d4T/ABC + EFV/NVP)$ or a PI-based regimen $(3TC + d4T/ABC + LPV/r)$ at the time of genotyping. The study focused on identifying DRMs associated with these regimens.	The study compared the prevalence and patterns of DRMs in children failing NNRTI-based regimens versus those failing PI-based regimens. Additionally, it looked at the presence of TAMs and other DRMs, including the Q151M complex and major PI mutations.	Prevalence of NRTI and NNRTI resistance mutations, and presence of major PI resistance mutations.
G. M. Hunt, 2023	HIV-positive children aged ≤ 19 years in South Africa, receiving ART from public health facilities, between March 2017 and March 2019. The study included 899 participants from 40 facilities across eight provinces. The median age was 12.9 years, and participants had been on ART for a median of 1.0 years. About 37.6% had documented exposure to PMTCT, and all participants had VF with at least one viral load ≥ 1000 copies/mL.	Participants were treated with PI-based regimens (ritonavir- boosted lopinavir or atazanavir), NNRTI-based regimens (primarily efavirenz), or NRTI-based regimens. The intervention included genotypic resistance testing using next-generation sequencing technologies.	The study compared the prevalence of drug resistance among children on different ART regimens (PI-based, NNRTI-based, NRTI-based) with virological failure.	Prevalence of HIV drug resistance, resistance to NNRTIS, NRTIS, and PIS, dual-class resistance, efficacy of PI-based regimens in NNRTI-failing patients.
D. B. Fofana, 2018	HIV-infected children in Benin, Cotonou, during 2015-2016, with a median age of 10 years (IQR 6–13). 53% were male. These children were on ART for a median of 5 years (IQR 3–7). All participants were experiencing VF defined as two consecutive VL of >1000 copies/mL. No specific mention of PMTCT exposure.	Participants were on NNRTI-based or boosted PI-based ART regimens. Resistance testing was conducted on dried blood spots using genotypic methods. NNRTI-based regimens, first-line: 3TC ZDV NVP, 3TC ZDV EFV, 3TC ABC NVP, 3TC ABC EFV, 3TC TDF EFV. PI-based regimens, first-line: 3TC ZDV LPV/r.	Not applicable (the study focused on identifying resistance profiles and treatment outcomes in the population without a direct comparative intervention).	Prevalence of DRMs for NRTIs, NNRTIs, and dual-class resistance, resistance to PIs and integrase inhibitors, undetectable ARV concentrations associated with VF.
J. Servais, 2002	HIV-1-infected children aged 3 to 16 years in Belgium, enrolled in a multicenter observational study from 1997 to 2000. All children had acquired HIV through PMTCT, with a majority having advanced disease. The study included 21 children, 18 of whom were of African origin. Virological failure was defined as a	Switching children from a failing PI-based HAART regimen to a second-line regimen. First-line treatments predominantly involved ritonavir (RTV) with two NRTIs. The second-line regimen involved single or dual PI-based therapy, mainly with NFV or ritonavir-saquinavir (RTV-	The study compared the effectiveness of the second-line PI-based therapy after virological failure of the first PI-based regimen. Genotypic and phenotypic resistance testing was used to predict the	Virologic response, change in viral load after switching to second-line therapy, presence of resistance mutations, cross-resistance between protease inhibitors.

	<1 log10 decrease in viral load compared with pretreatment values. Most children had prior exposure to NRTIs before starting their first PI-based therapy.	SQV), and in some cases, the addition of NVP.	response to the second-line therapy.	
A. P. Ramkissoon, 2015	HIV-1-infected pediatric patients in Jamaica, with a median age of 10 years, attending the Kingston Pediatric and Perinatal HIV/AIDS Programme. The study includes 55 children, with 75% on first-line ART (NRTI/NNRTI-based regimen) and 25% on second-line ART (PI-based regimen). All participants have been on ART for at least 24 months, and nearly all (98%) experienced virological failure. PMTCT programs were implemented, with 98% of HIV-exposed infants receiving ART.	First-line ART: NRTI/NNRTI-based regimen (AZT+3TC+NVP, LPV/r+NRTI). Second-line ART: PI- based regimen (ritonavir-boosted lopinavir). The study investigates drug resistance mutations in these pediatric patients.	Between the frequency and type of resistance mutations in pediatric patients on first-line vs. second-line ART. The study also compares the mutation patterns in Jamaican pediatric patients with those in the adult population.	Frequency of drug resistance mutations, virological failure, common mutations affecting NRTIs and NNRTIs (M184V, T215Y, K103N, Y181C, G190A), resistance to protease inhibitors in patients on second- line therapy.
Shanmugam Saravanan, 2017	HIV-1-infected children aged less than 15 years in India, who have been exposed to ART for at least 24 months. The study involved 55 children, with a median age of 10 years. Most children (75%) were on first-line ART with an NRTI/NNRTI- based regimen (Zidovudine + Lamivudine + Nevirapine). The remaining 25% were on second-line ART with a PI-based regimen (Lopinavir/ritonavir + NRTI backbone). The cohort likely included children who had undergone PMTCT, as indicated by the high prevalence of ART exposure. All but one of the children experienced virological failure (98%).	The primary intervention was ART with either first-line NNRTI-based regimens or second-line PI-based regimens. For the first-line regimen, the most common combination was Zidovudine + Lamivudine + Nevirapine. The second- line regimen typically included Lopinavir/ritonavir with an NRTI backbone. Treatment history: d4T + 3TC + NVP, d4T + 3TC + EFV, AZT +3TC + NVP, AZT +3TC + EFV, IDV +3TC + NVP, ABC +3TC + NVP, TDF +3TC + EFV/NVP, TDF/3TC/RTV + ATV.	RAMs in reverse transcriptase and protease genes among children on first- line NNRTI-based regimens versus second-line PI-based regimens, focusing on the prevalence and specific mutations conferring drug resistance.	Prevalence of DRMs associated with ART regimens, frequency of RAMs in reverse transcriptase and protease genes, significant resistance to NRTIs and NNRTIs, compromised efficacy of ART regimens.
Bismara BA, 2012	The study involved 61 vertically HIV-1-infected children from Brazil, specifically followed at the Immunodeficiency Clinic at the State University of Campinas, São Paulo, Brazil. The children had a median age of 7.5 years, with 60.6% being male. The study was conducted in 2012, and all children had been on HAART for at least 6 months. Most had already experienced VF, with a viral load higher than 10,000 copies/ml.	The intervention included ART regimens using a combination of drugs such as zidovudine, lamivudine, and nelfinavir. The study specifically focused on identifying drug-resistance mutations in the HIV-1 polymerase gene, particularly in the protease and reverse transcriptase regions. ZDV, 3TC, DDC, NEF.	Prevalence of drug-resistance mutations in the studied HIV-1-infected children and established resistance profiles from other studies. The study also compared the mutation frequencies between different subtypes (B, F, and recombinant forms).	Resistance to at least one antiretroviral drug, common mutations in reverse transcriptase gene (M184V, M41L, D67N, T215Y, L210W), common mutations in protease gene (L63P, M36I, L90M).
Abuogi L, 2023	HIV-1-infected children aged 1–14 years in Kisumu County, Kenya, enrolled from March 2019 to December 2020. The study included a total of 704 children, with a median age of 9 years (IQR 7, 12). Among the participants, 344 (49%) were female. Some children had exposure to antiretrovirals as part of PMTCT.	Point-of-care viral load testing every three months combined with targeted genotypic drug resistance testing for children with VF (HIV RNA \geq 1000 copies/mL). The intervention included a multidisciplinary committee review of DRT results to offer tailored treatment recommendations.	Standard-of-care management following national guidelines for children with VF. This typically included enhanced adherence counseling and repeat VL testing after three months of confirmed adherence. DRT was less commonly used and required approval by a regional HIV	Detection of major HIV drug resistance mutations, viral suppression, loss to follow-up, mortality, association with history of VF, and duration on ART.

			Technical Working Group, primarily for those failing a PI-containing regimen or with persistent VF.	
Djiyou ABD, 2023	HIV-1-infected adolescents aged 10-19 years in Cameroon, 2021, receiving ART for at least 6 months. The majority of participants (89.7%) were infected perinatally, and they were followed up in an urban hospital setting. Participants were categorized based on their viral load: those with low-level viraemia (VL 200-999 copies/mL) and those with virological failure (VL \geq 1000 copies/mL).	ART regimens included TDF-3TC-EFV, ABC-3TC-EFV, TDF-3TC-DTG, TDF-3TC-LPV/r, ABC-3TC-LPV/r, and TDF-3TC-ATV/r.	Comparison of HIV drug resistance between adolescents with low-level viraemia and those with confirmed VF.	Presence of HIV drug resistance mutations, resistance to specific drug classes, risk associated with functional monotherapy.
Khamadi SA, 2023	HIV-infected children and adolescents aged 1-19 years, living in the Southern Highland zone of Tanzania. The study includes participants on ART for more than 6 months between 2019 and 2021. The median age is 12 years, with 54% female. The study also notes participants receiving ART through PMTCT programs and those experiencing VF.	The intervention includes 290 (41.0%) participants were on an ART regimen with an abacavir ABC/3TC backbone, 54 (7.6%) were on an AZT/3TC backbone, and 363 (51.3%) were on a TDF/3TC backbone regimen, including 339 (93.4%) who were on TDF/3TC/DTG.	Different ART regimens (NNRTI-based, PI-based, and INSTI-based) to evaluate their effectiveness in achieving viral suppression and in managing drug resistance mutations.	Prevalence of viral suppression (VS) (<1000 copies/mL) and the occurrence of HIV drug resistance mutations (HIVDRMs).
C. Charpentier, 2012	HIV-1-infected children from the Central African Republic, studied between April and June 2009. The study involved 242 children, with a median age of 8 years (range: 4 months to 18 years). Among these children, 165 were receiving ART, including first-line, second-line, and third-line regimens. Most children were infected through PMTCT. The study assessed virological failure and resistance profiles after a median of 18 months on first-line ART and 30 months on second-/third-line ART.	Children were receiving ART regimens based on WHO recommendations. The majority of children were on a first- line regimen, primarily consisting of a combination of d4T, 3TC, and NVP. A smaller group of children was on second- line or third-line regimens, including PIs such as LPV or IDV.	Virological failure and the prevalence of drug resistance mutations between children on first-line ART regimens and those on second-/third-line regimens. The study also assessed the difference in resistance patterns to NRTIs and NNRTIs between these groups.	Detection of HIV-1 RNA, virological failure, presence of drug-resistance mutations, major resistance mutations (excluding M184V), resistance mutations to NRTIs or NNRTIS.
Mboumba Bouassa RS, 2019	HIV-1-infected children aged 5-19 years (median age 11 years), in Central African Republic (Bangui). Most were born to HIV- infected mothers who failed PMTCT. All participants were in virological failure, defined as viral load > 1000 copies/mL, and were cART-experienced but INSTI-naive (no prior exposure to integrase strand transfer inhibitors).	Fourteen of them received a combination of ZDV + d4T + NVP, two children received ZDV + 3TC + EFV and one child received a PI-based combination composed of d4T + 3TC + lopinavir boosted by LPV/r.	The study compared the prevalence of DRMs in the integrase gene among children failing first- and second-line WHO-recommended ART regimens, evaluating the susceptibility of their HIV-1 strains to INSTIs. This was contrasted against the effectiveness of other antiretrovirals in use, particularly NRTIs, NNRTIs, and PIs.	Susceptibility to INSTIs, presence of major resistance mutations (E138K and E138T), potential effectiveness of INSTIs (particularly dolutegravir) in optimized regimens.

Pang X, 2024	The study involved 491 HIV-1-infected children and adolescents from Guangxi, China, under the age of 18. These individuals were undergoing prolonged ART and experiencing virologic failure. The median treatment duration was 7.4 years, and the study population predominantly contracted HIV through mother-to- child transmission (86.62%). Most participants were on ART regimens containing NNRTIs and NRTIs, with some having	The intervention examined was the continued administration of various ART regimens, primarily involving NNRTIs (Nevirapine) and NRTIs (Lamivudine, Zidovudine). The study focused on understanding the prevalence and patterns of DRMs among this population.	The study compared the emergence of drug resistance mutations between different ART regimens and their effectiveness. It also examined the differences in DRMs based on various factors like gender, HIV subtype (CRF01_AE, CRF08_BC), pretreatment	Prevalence of HIV drug resistance mutations (DRMs), resistance to NNRTIs and NRTIs, key mutations (M184V/I, K103N), associated risk factors (male sex, CRF01_AE subtype, low pretreatment CD4+ T cells, high viral load).
Sivay MV,	viral loads (>1000 copies/mL). This study was conducted in four Siberian regions of Russia	The intervention involved ART regimens. For children,	The study compared DRMs between	Prevalence of HIV drug resistance mutations
2024	(Altai, Krasnoyarsk, Novosibirsk, Omsk) from 2019 to 2021. It involved 815 HIV-infected individuals, including 96 children (0- 14 years old) and 719 adults (\geq 15 years old). The median age of	INSTI-based therapy was the most common (51.1%), followed by PI-based (24.9%) and NNRTI-based (20.5%). For adults, NNRTI-based ART was the most common	different ART regimens and among patients with varying epidemiological characteristics. Factors such as viral load	(DRMs), resistance to NNRTIs and NRTIs, key mutations (M184V/I, K103N), associated factors (male sex, CRF01_AE subtype, low
	the patients was 37 years. The study population included individuals who had been diagnosed with HIV for a median of 5 years. Some of the participants were infected through perinatal transmission (11.9%) while others were through heterosexual contact or persons who inject drugs. All children in the study received ART to PMTCT.	(51.4%), followed by INSTI-based (18.1%) and PI-based (17.5%). ART adherence was assessed using self-reported data. The most common ART regimens included ABC + 3TC + RAL for children and TDF + 3TC + NVP/EFV/ETR for adults.	levels, CD4 cell counts, and region of residence were analyzed to determine their association with the presence of DRMs.	pretreatment CD4+ T cells, high viral load).
Tambuyzer L, 2016	The study involved HIV-1-infected children and adolescents aged 6 to <18 years who were treatment-experienced. The participants were from multiple countries, including Thailand, Argentina, the USA, and South Africa in 2008. A total of 101 patients (41 children and 60 adolescents) were enrolled, with a median baseline viral load of 3.6 log10 copies/ml for children and 4.0 log10 copies/ml for adolescents. Patients had previously used at least two ARVs, including NRTIs, NNRTIs, and PIs. The study assessed those currently failing virologically (confirmed plasma viral load >500 copies/ml) at the start of the study.	The intervention included the administration of etravirine (5.2 mg/kg twice daily) along with an optimized background regimen consisting of a boosted PI, NRTIs, and optional enfuvirtide and/or raltegravir. Etravirine was chosen based on its resistance profile and previous usage of NNRTIs in the population.	The study compared the presence and emergence of resistance-associated mutations between VFs and responders, focusing on mutations related to etravirine and other NNRTIS. Both population sequencing and deep sequencing were utilized to detect minority variants and emerging mutations.	The study found that 40.6% of the patients experienced virological failure by week 48. The emergence of resistance to etravirine was observed, with specific RAMs, such as Y181C, L100I, and E138A, being detected. The study concluded that etravirine resistance patterns in children and adolescents were similar to those observed in adults, and the presence of minority variants was not consistently associated with treatment failure.
Lange CM, 2015	HIV-1-infected children in South Africa, involved in the CHER trial. The study includes children who were infected despite receiving nevirapine prophylaxis for the PMTCT. The children were aged less than 12 weeks at ART initiation. Baseline drug resistance was analyzed, and the children had virological failure while on PI-based ART.	Early ART with a regimen including AZT, 3TC, and LPV/r. ART was initiated within the first 12 weeks of life, and the treatment continued for various periods. Some children also received ritonavir to achieve VL with LPV due to tuberculosis treatment.	Presence of DRMs detected by single genome sequencing and bulk sequencing. The focus was on identifying multiclass drug resistance, particularly in children with early virological failure after PI- based ART.	Virological failure rate by week 48, emergence of resistance to etravirine, specific resistance- associated mutations (RAMs) (Y181C, L100I, E138A), comparison of etravirine resistance patterns in children/adolescents and adults, association of minority variants with treatment failure.

B. P.	The study involved HIV-1-infected children aged ≤16 years in	The intervention involved initiating NNRTI-based ART	Virological nonresponders and responders.	Prevalence of treatment-relevant DRMs.
Gopalan,	Bangalore, India, between January 2012 and March 2016. All	regimens. Specifically, the children received either	The study compared the presence and	
2019	children were vertically infected and initiated on NNRTI-based	Nevirapine or Efavirenz combined with NRTIs such as	frequency of DRMs in cell-associated	
	ART. The study focused on those who had been on continuous	AZT+3TC, d4T+3TC, or TDF+3TC. The study also	DNA and cell-free RNA between these	
	ART for ≥ 2 years and had available pre and post ART samples.	examined the presence of DRMs in cell-associated DNA	groups. It also compared the predictive	
	The population included both virological nonresponders (children	and cell-free RNA at different time points (baseline, month	value of NGS analysis of cell-associated	
	with VL \geq 200 copies/mL at two consecutive time points within 2	six of ART, and at virological failure) using next-	DNA at six months of ART with Sanger	
	years of ART initiation) and responders (children who maintained	generation sequencing and Sanger sequencing.		
	VL < 200 copies/mL for two or more years after six months of	virological failure.		
	ART initiation). The analysis also looked at the presence of			
	PMTCT exposure, but specific details about PMTCT were not			
	highlighted.			
A. J. Szubert,	HIV-infected children from Uganda and Zimbabwe, aged 3	The intervention included ART regimens initiated based on	Comparison was between children	Long-term virological response, accumulation
2017	months to 17 years, recruited between March 2007 and November	WHO 2006 guidelines. Children were randomized to	monitored with CD4 counts versus those	of resistance mutations, effectiveness of ART
	2008. The study involved 1,206 children with a median age of 6	receive either 2NRTIs plus an NNRTI (mainly lamivudine	without CD4 counts, and between the	regimens without real-time viral load
	years at ART initiation. The majority had advanced HIV disease	and abacavir plus nevirapine or efavirenz) or a 3NRTI	different ART regimens. The study also	monitoring, viral load suppression below
	with a median CD4% of 12%. The study also included children	regimen as long-term ART. Viral load was not monitored	compared the virological suppression	1,000 copies/mL after 4 years, resistance to
	born to mothers who may have received PMTCT interventions,	in real-time, and CD4 counts were monitored in some	rates, drug resistance patterns, and the	second-line drugs, importance of confirming
	though specific details about PMTCT exposure were not	children. The study focused on evaluating virological	development of resistance mutations over	virological failure before switching therapies.
	extensively discussed. Children were followed for a median of 4	outcomes, drug resistance, and long-term virological	time among the different monitoring	
	years.	suppression without regular viral load monitoring.	strategies.	

Abbreviations, DRMs = drug resistance mutations; ART antiretroviral therapy; cART = combination antiretroviral therapy; NRTIs = nucleoside reverse transcriptase inhibitors; NVP = nevirapine; PI = protease inhibitor; LPV/r = lopinavir/ritonavir; INSTIs = integrase strand transfer inhibitors; d4T = stavudine; 3TC = lamivudine ; DBS = dried blood spots; VF = virological failure; PDR = pretreatment HIV drug resistance; VL = viral load; PMTCT = mother-to-child transmission; RAMs = resistance-associated mutations; ZDV = Zidovudine; NFV = nelfinavir; RTIs = reverse transcriptase inhibitors; TAMs = thymidine analogue mutations; HAART = Highly Active Antiretroviral Therapy.

Table S4A: Quality assessment of included DR studies for treatment-naive children prevalence analysis

Q1. Was the study's target population a close representation of the national population in relation to relevant variables?

- Q2. Was some form of random selection used to select the sample, OR was a census undertaken?
- Q3. Was the likelihood of nonresponse bias minimal?
- Q4. Were data collected directly from the subjects (as opposed to a proxy)?
- Q5. Was an acceptable case definition used in the study?
- Q6. Was the study instrument that measured the parameter of interest shown to have validity and reliability?
- Q7. Was the same mode of data collection used for all subjects?
- Q8. Was the length of the shortest prevalence period for the parameter of interest appropriate?
- Q9. Were the numerator(s) and denominator(s) for the parameter of interest appropriate

TOTAL SCORE: Poor (0-3), Fair (4-6), Good (7-9).

Quality assessment of naive children studies

Study	Overall Quality Rating	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
J. Lidstrom, 2010	Fair	N	N	Y	Y	Y	Y	N	Y	Y
W. I. Towler, 2010	Good	N	N	Y	Y	Y	Y	Y	Y	Y
Jessica D. Church, 2008	Good	NR	Y	Y	Y	Y	Y	N	Y	Y
Jessica Fogel, 2011	Fair	NR	N	Y	Y	Y	Y	N	Y	Y
Russell B. Van Dyke, 2016	Good	Y	Y	Y	Y	Y	Y	Y	Y	Y
SwaraliN Kurle, 2007	Fair	N	N	Y	Y	Y	Y	N	Y	N
Moira Vignoles, 2009	Fair	N	N	Y	Y	Y	Y	Y	Y	N
Diana M Gibb, 2003	Fair	NR	N	N	Y	Y	NR	Y	Y	Y
Julie A E Nelson, 2015	Fair	NR	N	Y	Y	Y	Y	N	Y	Y
Frantz Jean Louis, 2019	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Ragna S Boerma, 2016	Fair	N	N	Y	Y	Y	Y	Y	Y	N
Sydney J. TOWNSEND, 2020	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Seth C. Inzaule, 2018	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Claudia S. Crowell, 2017	Fair	N	Y	N	Y	Y	Y	N	Y	Y
Mounerou Salou, 2016	Good	Y	Y	N	Y	Y	Y	Y	Y	Y
Cissy Kityo, 2016	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Dorothy E. Dow, 2017	Fair	N	N	Y	Y	Y	Y	Y	Y	N
Gillian M. Hunt, 2011	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Clement Zeh, 2011	Fair	N	N	Y	Y	Y	Y	Y	Y	N
Nicholas I. Nii-Trebi, 2013	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Jennifer Neubert, 2016	Good	N	Y	Y	Y	Y	Y	N	Y	Y
Barbara S. Taylor, 2011	Fair	N	Y	N	Y	Y	Y	Y	Y	N
Djeneba B. Fofana, 2023	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Gillian M. Hunt, 2019	Good	Y	Y	Y	Y	Y	Y	Y	Y	Y
Monica M Parker, 2003	Fair	N	N	Y	Y	Y	Y	N	Y	Y
Marine Karchava, 2006	Fair	N	N	Y	Y	Y	N	Y	Y	N
Pierre Frange, 2018	Good	N	N	Y	Y	Y	Y	Y	Y	Y
Nicole Ngo-Giang-Huong, 2016	Fair	NR	N	Y	Y	Y	Y	Y	Y	N
Birkneh Tilahun Tadesse, 2019	Good	N	N	Y	Y	Y	Y	Y	Y	Y

Michael R Jordan, 2022	Fair	N	N	Y	Y	Y	Y	Ν	Y	Y
Sandra Soeria-Atmadja, 2020	Fair	N	N	Y	Y	Y	Y	Y	Y	N
Paula C. Aulicino, 2019	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Syed Hani Abidi, 2021	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Andrea Kovacs, 2005	Fair	N	N	Y	Y	Y	N	Y	Y	Y
Study	Overall Quality Rating	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
Constance Delaugerre, 2009	Fair	Y	N	Y	Y	Y	Y	N	Y	N
George Mondinde Ikomey, 2017	Good	N	N	Y	Y	Y	Y	Y	Y	Y
Solange Dourado de Andrade, 2017	Fair	N	N	Y	Y	Y	Y	Y	Y	NR
Louise Kuhn, 2015	Good	N	Y	Y	Y	Y	Y	Y	Y	N
Joseph Fokam, 2011	Fair	N	N	Y	Y	Y	Y	Y	Y	N
J Han, 2009	Good	N	Y	Y	Y	Y	Y	N	Y	Y
Susan H. Eshleman, 2001	Fair	NR	N	Y	Y	Y	Y	N	Y	N
Neil A. Martinson, 2007	Good	N	Y	Y	Y	Y	Y	Y	Y	N
P. Vaz, 2012	Fair	N	N	Y	Y	Y	Y	Y	Y	N
Fiyinfoluwa I. Olusola, 2021	Good	N	Y	N	Y	Y	Y	Y	Y	Y
Paula Morena de Souza Guimara [~] es,	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
2015										
Bernard Masquelier, 2001	Fair	N	N	Y	Y	Y	N	Y	Y	N
Michael R Jordan, 2017	Good	N	Y	N	Y	Y	Y	Y	Y	Y
Nava Yeganeh, 2018	Fair	N	N	Y	Y	Y	Y	N	Y	Y
Ujjwal Neogi, 2012	Fair	N	N	Y	Y	Y	Y	Y	N	Y
Suwellen Sardinha Dias de Azevedo,	Good	N	Y	N	Y	Y	Y	Y	Y	Y
2022										
Tanya Rogo, 2015	Good	N	Y	N	Y	Y	Y	Y	Y	Y
Amphan Chalermchockcharoenkit,	Fair	N	N	N	Y	Y	Y	Y	Y	Y
2009										
Thuy Thi Bich Phung, 2015	Fair	N	N	N	Y	Y	Y	Y	Y	Y
Francisco Antunes, 2015	Fair	N	Y	N	Y	Y	Y	N	Y	Y
Flávia J. Almeida, 2009	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Jessica M. Fogel, 2013	Good	N	N	Y	Y	Y	Y	Y	Y	Y
Marie-Laure Chaix, 2007	Fair	N	Y	N	Y	Y	N	N	Y	Y
Maryam Jarchi, 2019	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
L. Tambuyzer, 2016	Fair	N	N	N	Y	Y	Y	N	Y	N
D. A. Lehman, 2012	Fair	N	NR	N	Y	Y	N	Y	Y	Y
R. G. Fisher, 2015	Fair	N	NR	Y	Y	Y	N	Y	N	Y
J. Fokam, 2018	Fair	N	N	Y	Y	N	N	N	Y	Y
C. M. Lange, 2015	Good	N	Y	Y	Y	Y	Y	Y	N	Y
D. Persaud, 2011	Fair	Y	Y	N	Y	Y	N	Y	Y	N

Table S4B: Quality assessment of included DR studies for treatment-experienced children prevalence analysis

Study	Overall Quality Rating	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
Hannah Green, 2006	Good	Y	Y	Y	Y	Y	N	Y	Y	Y
T. Sonia Boender, 2016	Good	N	Y	Y	Y	Y	Y	Y	Y	N
W. I. Towler, 2010	Fair	N	Ν	Y	Y	Y	Y	Y	Y	Ν
Doreen Kamori, 2023	Good	Y	Y	Y	Y	Y	Y	N	Y	Y
Mia Coetzer, 2013	Fair	N	Ν	Y	Y	Y	Y	N	Y	N
Theresa M Rossouw, 2015	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Marie-Laure Chaix, 2005	Fair	N	N	Ν	Y	Y	Y	Y	Y	Y
Elizabeth S Machado, 2004	Fair	N	Ν	Y	Y	Y	Y	N	Y	Y
Ana Rodríguez-Galet, 2023	Good	N	Ν	Y	Y	Y	Y	Y	Y	Y
M. Rubio-Garrido, 2021	Fair	N	Y	N	Y	Y	Y	N	Y	Y
Birkneh Tilahun Tadesse, 2018	Good	Y	Y	Y	Y	Y	Y	Y	Y	Y
Christian Diamant Mossoro-	Fair	N	Y	Ν	Y	Y	Y	Y	Y	N
Kpinde, 2017										
Khady Kebe, 2013	Good	N	Y	N	Y	Y	Y	Y	Y	Y
Claudia S. Crowell, 2017	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Cheryl A. Stoddart, 2014	Fair	N	N	Y	Y	Y	Y	Y	Y	N
J-P Aboulker, 2004	Fair	Y	N	Y	Y	Y	N	Y	Y	N
T Puthanakit, 2010	Good	Y	Y	N	Y	Y	N	Y	Y	Y
Winstone Nyandiko, 2022	Fair	N	Y	N	Y	Y	Y	Y	Y	N
Barbara S. Taylor, 2011	Fair	N	Ν	Ν	Y	Y	Y	Y	Y	Y
Djeneba B. Fofana, 2023	Good	NR	Ν	Y	Y	Y	Y	Y	Y	Y
German A. Contreras, 2013	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Constance Delaugerre, 2007	Fair	N	Y	Y	Y	Y	N	N	Y	N
Allison L. Agwu, 2014	Good	Y	N	Y	Y	Y	Y	Y	Y	Y
Seth C. Inzaule, 2016	Fair	NR	Ν	Y	Y	Y	Y	Y	Y	N
Cissy Kityo, 2017	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Sandra Soeria-Atmadja, 2020	Good	N	N	Y	Y	Y	Y	Y	Y	Y
Podjanee Jittamala, 2009	Fair	N	Y	N	Y	Y	N	Y	Y	N
Syed Hani Abidi, 2021	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Bhavna H. Chohan, 2015	Fair	N	N	Y	Y	Y	N	Y	Y	Y
Anita Shet, 2013	Good	N	Y	Y	Y	Y	N	Y	Y	Y
Theodore D, 2011	Fair	N	Ν	Ν	Y	Y	Y	N	Y	Y
Liting Yan, 2022	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Yan Zhao, 2011	Fair	N	Ν	Y	Y	Y	Y	N	Y	Y
Clara Bratholm, 2010	Fair	N	N	Y	Y	Y	Y	Y	Y	N
Ravindra K. Gupta, 2010	Fair	N	Y	N	Y	Y	Y	N	Y	Y
Jean-Christophe Beghin, 2020	Good	N	Y	N	Y	Y	Y	Y	Y	Y
Judit Ventosa-Cubillo, 2023	Fair	N	Ν	Y	Y	Y	Y	Y	Y	N
Lukas Muri, 2017	Good	N	Y	Ν	Y	Y	Y	Y	Y	Y
Paula Vaz, 2018	Good	Y	Y	Ν	Y	Y	Y	Y	Y	Y
A.T. Makadzange, 2015	Fair	N	Y	N	Y	Y	Y	Y	Y	N
George A. Yendewa, 2021	Good	N	Y	N	Y	Y	Y	Y	Y	Y
Josephine Brice, 2020	Good	N	Y	Y	Y	Y	Y	Y	Y	Y
Vaz, Paula, 2009	Fair	N	Ν	N	Y	Y	N	Y	Y	Y
M. Sylla, 2019	Fair	N	Y	N	Y	Y	Y	N	Y	Y
P. Vaz, 2012	Good	N	Y	Y	Y	Y	Y	Y	Y	Y

Patricia A. Brindeiro, 2002	Fair	N	Y	Y	Y	Y	Y	N	Y	N
Study	Overall Quality Rating	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
Christiane Adjé-Touré, 2008	Fair	NR	Ν	N	Y	Y	NR	Y	Y	Y
Paul Alain Tagnouokam-Ngoup,	Good	N	Y	N	Y	Y	Y	Y	Y	Y
2021										
Clarisse Amani-Bosse, 2017	Good	N	Y	N	Y	Y	Y	Y	Y	Y
Laurence Ahoua, 2011	Fair	N	Y	N	Y	Y	N	Y	Y	Y
Philippe R. Mutwa, 2014	Fair	N	Ν	N	Y	Y	Y	Y	Y	Y
Tanya Rogo, 2015	Good	N	Y	N	Y	Y	Y	Y	Y	Y
Miguel de Mulder, 2011	Fair	Y	Y	N	Y	Y	Y	N	Y	N
Joseph E.Fitzgibbon, 2004	Fair	N	Ν	Y	Y	Y	N	Y	Y	N
Compagno Francesca, 2019	Fair	NR	Ν	Y	Y	Y	Y	N	Y	Y
Lisa L. Ross, 2015	Good	Y	Y	N	Y	Y	N	Y	Y	Y
R. Lwembe, 2007	Fair	NR	N	Y	Y	Y	Y	Y	Y	N
S. H. Al Hajjar, 2012	Good	N	Y	Y	Y	Y	NR	Y	Y	Y
Z. Makatini, 2019	Fair	N	Y	Y	Y	Y	Y	NR	Y	N
M. Camara-Cisse, 2021	Good	N	Y	Y	Y	Y	N	Y	Y	Y
A. T. Dumans, 2009	Fair	NR	N	Y	Y	Y	N	Y	Y	N
J. Fokam, 2011	Good	N	Ν	Y	Y	Y	Y	Y	Y	Y
T. N. Green, 2012	Fair	N	Ν	Y	Y	Y	Y	Y	Y	N
S. Pillay, 2014	Fair	N	Ν	Y	Y	Y	Y	N	Y	Y
G. M. Hunt, 2023	Good	Y	Y	Y	Y	Y	Y	Y	Y	Y
D. B. Fofana, 2018	Good	N	Y	Y	Y	Y	N	Y	Y	Y
J. Servais, 2002	Fair	N	Ν	Y	Y	Y	NR	Y	Y	N
A. P. Ramkissoon, 2015	Good	N	Y	N	Y	Y	Y	Y	Y	Y
Shanmugam Saravanan, 2017	Fair	NR	Ν	Y	Y	Y	Y	Y	Y	N
Bismara BA, 2012	Fair	N	Ν	Y	Y	Y	N	Y	Y	Y
B. P. Gopalan, 2019	Good	N	Y	Y	Y	Y	Y	Y	Y	N
A. J. Szubert, 2017	Good	Y	N	Y	Y	Y	Y	Y	N	Y
C. Charpentier, 2012	Fair	N	Y	N	Y	Y	N	Y	Y	N
Abuogi L, 2023	Good	N	Y	Y	Y	Y	Y	Y	N	Y
Djiyou ABD, 2023	Fair	N	Y	N	Y	Y	Y	Y	N	Y
Khamadi SA, 2023	Good	N	Y	N	Y	Y	Y	Y	Y	Y
Pang X, 2024	Fair	N	Ν	Y	Y	Y	N	Y	Y	Y
Sivay MV, 2024	Good	Y	N	Y	Y	Y	Y	Y	N	Y
Thu HHK, 2024	Good	Y	N	N	Y	Y	Y	Y	Y	N
Mboumba Bouassa RS, 2019	Fair	N	Y	N	Y	Y	Y	Y	Y	Ν

Table S5A: Pooled	prevalence of d	drug resistance	among treatment-	naive c	hildren a	lfter í	2015
			······				

	Number of	Number of HIV-infected	Number of Individuals with	Prevalence of DR (95% Confidence	Hetero	geneity	p value for subgroup
	datasets	individuals	DR	Interval)	<i>I</i> ² (%)	p value	difference
Overall	11	904	361	25.40 (11.80-41.79)	94	< 0.01	
Region*							< 0.01
Asia	3	170	83	36.20 (11.08-65.93)	92	< 0.01	
Eastern Africa	2	147	26	17.58 (11.75-24.25)	0	0.37	
Southern Africa	1	49	33	67.35 (51.46-80.05)	-	-	
Western and Central Africa	5	538	219	15.67 (0.79-40.82)	96	< 0.01	
World Bank Income Level							0.07
Low income	2	147	26	17.58 (11.75-24.25)	0	0.37	
Lower middle income	8	713	335	33.86 (17.20-52.70)	89	< 0.01	
Age group (years)							< 0.01
< 2	3	584	304	58.18 (45.81-70.00)	84	< 0.01	
≥2	11	320	57	13.85 (5.17-25.29)	81	< 0.01	
PMTCT experience							< 0.01
Yes	6	686	330	38.10 (17.37-61.27)	91	< 0.01	
no	5	218	31	11.37 (2.47-24.44)	81	< 0.01	

PMTCT= the prevention of mother-to-child transmission *median (range). Several datasets are generated from the same study.

Table S5B: Pooled	prevalence of drug	g resistance amon	g treatment-ex	perienced o	children a	fter 20	015

	Number of	Number of	Number of	Prevalence of DR (95%	Heter	ogeneity	p value for
	datasets	HIV-infected individuals	Individuals with DR	Confidence Interval)	P	p value	subgroup difference
Overall	20	2644	1808	67.93 (55.59-79.15)	97%	< 0.01	
Region							< 0.01
South America	1	62	36	58.06 (44.85-70.49)	-	-	
North America	1	41	39	95.12 (83.47-99.40)	-	-	
Europe	1	96	71	73.96 (64.00-82.38)	-	-	
Asia	3	760	390	55.72 (37.88-72.83)	93	< 0.01	
Eastern Africa	6	599	368	68.32 (46.63-86.56)	96	< 0.01	
Southern Africa	2	819	716	84.21 (64.78-97.34)	58	0.12	
Western and Central Africa	6	267	206	63.65 (30.02-91.35)	96	< 0.01	
Income level							0.17
Low income	4	273	165	63.68 (36.06-87.27)	96	< 0.01	
Lower middle income	7	795	478	74.10 (57.96-87.50)	96	< 0.01	
Upper middle income	7	1483	1129	76.25 (63.92-86.76)	97	< 0.01	
High income	1	62	36	58.06 (36.06-87.27)	-	-	
Age group (Years)							< 0.01
< 7	7	733	353	55.06 (40.16-69.53)	91	< 0.01	
≥ 7	12	1515	1247	75.49 (58.55-89.21)	94	< 0.01	
Antiretroviral treatment time							0.77
< 3 years	8	1067	583	62.03 (46.63-76.32)	94	< 0.01	
\geq 3 years	8	519	325	66.61 (38.68-89.54)	96	< 0.01	
Proportion of viral failure							0.36
100%	8	861	548	64.41 (39.19-86.13)	96	< 0.01	
50%-99%	6	1031	872	78.24 (65.61-88.73)	89	< 0.01	
< 50%	3	218	130	67.38 (24.93-97.53)	98	< 0.01	
Unknown	3	534	258	56.20 (32.67-78.35)	94	< 0.01	
ART regimen#							< 0.01
NRTI+NNRTI	4	527	270	58.00 (29.29-84.08)	97	< 0.01	
NRTI+NNRTI/PI	10	1681	1304	80.59 (71.86-88.08)	95	< 0.01	
NNRTI+PI	1	199	93	46.73 (39.65-53.92)	-	-	
NRTI+PI	1	10	7	70.00 (34.75-93.33)	-	-	
NRTI+NNRTI+PI	3	131	63	36.51 (0.15-88.10)	97	< 0.01	
NRTI+NNRTI/PI/INSTI	1	96	71	73.96 (64.00-82.38)	-	-	

DR= drug resistance; WHO= World Health Organization; CDC= National Centers for Disease Control; PMTCT= the prevention of mother-to-child transmission *median (range). #ART regimes are defined as the maximum proportion of all treatment among each dataset. Several datasets are generated from the same study.

Table S6A: Meta regression analysis for the variation of the prevalence of treatment-naive HIV infected children

			Univariate analysis		Multivariate analysis				
Variables(reference)	No. of datasets	P value	Coefficient (95% confidence interval)	R2, %	P value	Adjusted coefficient (95% confidence interval)			
Region	69	0.0319		11.58					
Asia	10	Ref			Ref				
Eastern Africa	11	0.1374	0.1659 (-0.0530-0.3849)		0.4092	0.0988 (-0.1358-0.3333)			
Europe	5	0.8644	-0.0238 (-0.2968-0.2493)		0.6303	-0.0795 (-0.4030-0.2441)			
North America	7	0.2586	0.1421 (-0.1044-0.3886)		0.0252	0.3250 (0.0405-0.6096)			
South America	8	0.4367	-0.1003 (-0.3373-0.1366)		0.3854	-0.1089 (-0.3547-0.1370)			
Southern Africa	18	0.0282	0.2269 (0.0282-0.4256)		0.4261	0.0927 (-0.1356-0.3209)			
Western and Central Africa	10	0.7423	0.0381 (-0.1888-0.2649)		0.7651	0.0526 (-0.1051-0.2104)			
Sample Year	69	0.1352	0.0088 (-0.0028-0.0204)	2.41					
Age	69	0.0001	-0.0031 (-0.0047-0.0015)	18.58	0.0005	-0.0038 (-0.0060-0.0017)			
Income Level	63	0.4238		0.00					
High income	11	Ref			Ref				
Low income	15	0.1765	0.1419 (-0.0638-0.3476)						
Lower middle income	20	0.2954	0.1044 (-0.0912-0.3001)						
Upper middle income	17	0.8412	0.0205 (-0.1802-0.2213)						
CD4 count	22	0.6686		0.00					
<500	8	Ref			Ref				
≥500	14	0.6686	-0.0497 (-0.2774-0.1779)						
HIV-RNA	27	0.1464		5.02					
< 5	9	Ref			Ref				
≥5	18	0.1464	-0.1527 (-0.3589-0.0534)						
PMTCT	69	0.0045		10.71					
No	23	Ref			Ref				
Yes	46	0.0045	0.1844 (0.0571-0.3116)		0.5133	0.0526 (-0.1051-0.2104)			
WHO Stage	10	0.6442		0.00					
≥50%	4	Ref			Ref				
>50%	6	0.6442	-0.0385 (-0.2021-0.1250)						
Male	36	0.1961		2.57					
≤50%	23	0.1961	0.1106 (-0.0571-0.2782)		Ref				
>50%	14	Ref							

Table S6B: Meta regression analysis for the variation of the prevalence of treatment-experienced HIV-infected children

	Univaria	te analysis			Multivariate analysis			
Variables(reference)	No. of	P value	Coefficient (95% confidence	R2, %	P value	Adjusted coefficient (95%		
	datasets		interval)			confidence interval)		
Region	79	0.5774		0.00				
Asia	12	Ref			Ref			
Eastern Africa	17	0.1818	-0.1634 (-0.4032-0.0764)		0.2411	-0.1488 (-0.3975-0.1000)		
Europe	6	0.2520	-0.1861 (-0.5045-0.1323)		0.1124	-0.2540 (-0.5677-0.0596)		
North America	7	0.0816	-0.2693 (-0.5724-0.0337)		0.0966	-0.2890 (-0.6299-0.0519)		
South America	5	0.8959	-0.0225 (-0.3591-0.3142)		0.3672	-0.1702 (-0.5401-0.1997)		
Southern Africa	15	0.6532	-0.0562 (-0.3015-0.1890)		0.9033	0.0155 (-0.2340-0.2650)		
Western and Central Africa	17	0.2535	-0.1392 (-0.3780-0.0997)		0.1886	-0.1716 (-0.4274-0.0842)		
Sample Year	81	0.9517	-0.0004 (-0.0118-0.0111)	0.00				
Age	78	0.0198	0.0018 (0.0003-0.0033)	6.40	< 0.0001	0.9477 (0.6830-1.2123)		
Male	72	0.0866		3.03				
≤50%	20	0.0866	-0.1380 (-0.2958-0.0198)		0.5781	-0.0535 (-0.2422-0.1351)		
>50%	52	Ref			Ref			
Income Level	75	0.2395		1.81				
High income	11	Ref						
Low income	18	0.5939	0.0598 (-0.1600-0.2796)					
Lower middle income	24	0.8263	0.0234 (-0.1855-0.2323)					
Upper middle income	22	0.1025	0.1763 (-0.0353-0.3880)					
CD4 count	36	0.6618		0.00				
<500	18	Ref						
≥500	18	0.6618	0.0525 (-0.1826-0.2785)					
HIV-RNA	41	0.3510	`	0.00				
<5	24	Ref						
≥5	17	0.3510	-0.1032 (-0.3201-0.1137)					
WHO Stage	35	0.5425		0.00				
≤50%	18	Ref						
>50%	17	0.5425	-0.0664 (-0.2799-0.1472)	7.40				
Viral failure	81	0.0307						
< 50%	28	Ref			Ref			
50-99%	15	0.2246	0.1209 (-0.0742-0.3159)		0.1873	0.1513 (-0.0736-0.3761)		
100%	28	0.0094	0.2152 (0.0528-0.3776)		0.1070	0.1505 (-0.0325-0.3336)		
Unkown	10	0.0213	0.2615 (0.0390-0.4841)		0.0607	0.2433 (-0.0109-0.4976)		
ART duration	72	0.6533	0.0006 (-0.0020-0.0032)	0.00				

Figure S1: Demonstration of countries and regions included in the study



Figure S2A: Forest plot of the drug resistance prevalence among treatment-naive groups

Study E	vents	Total		Proportion	95%-CI	Weight
Lindström et al(2010)	28	43		0.6512	[0.4907: 0.7899]	1.4%
Lindström et al(2010)	37	45		0.8222	[0.6795; 0.9200]	1.4%
Towler et al(2010)	2	74		0.0270	[0.0033; 0.0942]	1.5%
Church et al(2008)	33	49		0.6735	[0.5246; 0.8005]	1.5%
Fogel et al(2011)	78	108		0.7222	[0.6278; 0.8041]	1.5%
Van Dyke et al(2016)	175	234		0.7479	[0.6872; 0.8022]	1.5%
Kurle et al(2007)	2	19		0.1053	[0.0130; 0.3314]	1.3%
Vignoles et al(2007)	0	35	-	0.4615	[0.1922; 0.7487]	1.2%
Gibb et al(2003)	4	105		0.0381	[0.0105: 0.0947]	1.5%
Nelson et al(2015)	3	28		0.1071	[0.0227: 0.2823]	1.4%
Nelson et al(2015)	1	16		0.0625	[0.0016; 0.3023]	1.3%
Nelson et al(2015)	4	13		0.3077	[0.0909; 0.6143]	1.2%
Louis et al(2019)	217	304		0.7138	[0.6594; 0.7640]	1.5%
Boerma et al(2016)	13	82		0.1585	[0.0872; 0.2558]	1.5%
Bennett et al(2020)	33	49		0.6735	[0.5246; 0.8005]	1.5%
Inzaule et al(2018)	205	430		0.4767	[0.4287; 0.5251]	1.6%
Salou et al (2016)	121	201	-	0.6020	[0.5507, 0.6702]	1.5%
Dow et al (2017)	34	65		0.1004	[0.3954: 0.6485]	1.5%
Hunt et al(2011)	80	255	*	0.3137	[0.2573: 0.3746]	1.5%
Zeh et al(2011)	16	32		0.5000	[0.3189; 0.6811]	1.4%
Nii-Trebi et al(2013)	5	10		0.5000	[0.1871; 0.8129]	1.2%
Neubert et al(2016)	7	24		0.2917	[0.1262; 0.5109]	1.4%
Taylor et al(2011)	39	155		0.2516	[0.1854; 0.3275]	1.5%
Fofana et al(2023)	0	44		0.0000	[0.0000; 0.0804]	1.4%
Hunt et al(2019)	112	220		0.5091	[0.4410; 0.5769]	1.5%
Parker et al(2003)	5	49		0.1020	[0.0340; 0.2223]	1.5%
Parker et al(2003)	6	38		0.1579	[0.0602; 0.3125]	1.4%
France et al(2006)	16	42		0.1905	[0.0660; 0.3412]	1.4%
Ngo-Giang-Huong et al(2016)	37	476		0.1903	[0.1130, 0.2900]	1.5%
Tadesse et al(2019)	8	57		0.1404	[0.0626: 0.2579]	1.5%
Soeria-Atmadia et al(2020)	18	90		0.2000	[0.1231; 0.2975]	1.5%
Aulicino et al(2019)	34	115		0.2957	[0.2142; 0.3879]	1.5%
Abidi et al(2021)	15	50	— — •	0.3000	[0.1786; 0.4461]	1.5%
Kovacs et al(2005)	11	44		0.2500	[0.1319; 0.4034]	1.4%
Delaugerre et al(2009)	12	60		0.2000	[0.1078; 0.3233]	1.5%
Ikomey et al(2017)	11	37		0.2973	[0.1587; 0.4698]	1.4%
Kubp et al(2017)	19	155		0.1624	[0.1007; 0.2419]	1.5%
Kuhn et al (2015)	18	75		0.2400	[0 1489: 0 3525]	1.5%
Fokam et al(2011)	2	41		0.0488	[0.0060; 0.1653]	1.4%
Han et al(2009)	2	14		0.1429	[0.0178; 0.4281]	1.2%
Eshleman et al(2001)	11	24	· · · · ·	0.4583	[0.2555; 0.6718]	1.4%
Martinson et al(2007)	24	53		0.4528	[0.3156; 0.5955]	1.5%
Vaz et al(2012)	6	112	-	0.0536	[0.0199; 0.1130]	1.5%
Olusola et al(2021)	3	12		0.2500	[0.0549; 0.5719]	1.2%
Guimaraes et al(2015) Masquelier et al(2001)	07	31		0.1935	[0.0745; 0.3747]	1.4%
lordan et al(2017)	529	1048		0.2039	[0.0870, 0.3790]	1.4%
Jordan et al(2017)	86	224		0.3839	[0.3199: 0.4510]	1.5%
Yeganeh et al(2018)	13	123		0.1057	[0.0575; 0.1740]	1.5%
Neogi et al(2012)	6	105		0.0571	[0.0213; 0.1202]	1.5%
de Azevedo et al(2022)	9	38		0.2368	[0.1144; 0.4024]	1.4%
de Azevedo et al(2022)	10	97		0.1031	[0.0506; 0.1814]	1.5%
Rogo et al(2015)	1	16		0.0625	[0.0016; 0.3023]	1.3%
Chalermchockcharoenkit et al(2009)	2	10		0.2000	[0.0252; 0.5561]	1.2%
Phung et al(2015) Phung et al(2015)	2	65		0.0233	[0.0026; 0.0615]	1.5%
Antunes et al(2015)	43	79		0.0308	[0.0037, 0.1000]	1.5%
Almeida et al(2009)	-0	24		0.0000	[0.0000; 0.1425]	1.4%
Fogel et al(2013)	1	18		0.0556	[0.0014; 0.2729]	1.3%
Chaix et al(2007)	6	26		0.2308	[0.0897; 0.4365]	1.4%
Jarchi et al(2019)	2	15		0.1333	[0.0166; 0.4046]	1.3%
Khanh Thu et al(2024)	66	105		0.6286	[0.5288; 0.7209]	1.5%
Lehman et al(2015)	12	20		0.6000	[0.3605; 0.8088]	1.3%
Fisher et al(2015)	7	15		0.4667	[0.2127; 0.7341]	1.3%
Konen et al(2017) Eckam et al(2018)	19	43		0.4419	[0.2908; 0.6012]	1.4%
	0	15		0.0000	[0.0000, 0.2180]	1.3%
Random effects model Heterogeneity: $I^2 = 96\%$, $\tau^2 = 0.0666$, $p = 0$)	6914		0.2631	[0.2076; 0.3225]	100.0%

0

0.2 0.4 0.6 0.8

Figure S2B: Forest plot of the drug resistance prevalence among treatment-experienced groups

Study	Events	lotal	Pro	port
Boender et al(2016)	50	56		0.89
Towler et al(2010)	12	12		1.00
Kamori et al(2023)	72	92		0.78
Coetzer et al(2013)	50	51		0.9
Rossouw et al(2015)	65	65		1.0
	03	20		0.7
Chaix et al(2005)	21	38		0.7
Machado et al(2004)	28	37		0.7
Rodríguez-Galet et al(2023)	27	38		0.7
Rubio-Garrido et al(2021)	18	27	· · · · · ·	0.6
Tadesse et al(2018)	73	90		0.8
Mossoro-Kninde et al(2017)	54	58		0.9
Kebe et al (2013)	18	52		0.0
	40	07		0.5
Crowell et al(2017)	29	37		0.70
Stoddart et al(2014)	354	370		0.9
Aboulker et al(2004)	6	20		0.30
Puthanakit et al(2010)	118	120	-+	0.9
Nyandiko et al(2022)	119	128		0.9
Taylor et al(2011)	32	41	·	0.7
Fofana et al(2023)	0	31	-	0.0
Controrpo et al(2012)	22	66		0.0
Contreras et al(2013)	23	00		0.3
Delaugerre et al(2007)	82	119	- · · · · · · · · · · · · · · · · · · ·	0.6
Agwu et al(2014)	117	117		1.0
Inzaule et al(2016)	16	24		0.6
Kitvo et al(2017)	67	84		0.7
Soeria-Atmadia et al(2020)	22	02		0.2
littamala at al(2000)	20	20		0.0
	38	39	-	0.9
Abidi et al(2021)	114	2/1		0.4
Chohan et al(2015)	7	19		0.3
Shet et al(2013)	12	70		0.1
Theodore et al(2011)	16	120	- H -	0.1
Yan et al(2022)	68	93		07
$Z_{\text{bac}} \text{ of } al(2011)$	76	76		1.0
	10	10		0.5
Bratholm et al(2010)	11	19		0.5
Gupta et al(2010)	22	26		0.8
Beghin et al(2020)	16	29	· · · ·	0.5
Beghin et al(2020)	19	64		0.2
Ventosa-Cubillo et al(2023)	36	62		0.5
Muri ot al(2017)	47	52		0.0
1/2	-+/	040		0.9
vaz et al(2018)	238	248		0.9
Makadzange et al(2015)	69	102		0.6
Yendewa et al(2021)	51	64	·	0.7
Vaz et al(2009)	77	84		0.9
Vaz et al(2012)	10	113		0.0
Brindeiro et al(2002)	50	52		0.9
Adie-Toure et al(2008)	47	68		0.6
Tagnouokam Ngouno et al(2021)	40	57		0.7
Amani Basaá at al(2017)	40	20		0.7
Amani-Bosse et al(2017)	21	20		0.7
Anoua et al(2011)	13	17		0.7
Ahoua et al(2011)	16	17		0.9
Mutwa et al(2014)	50	52		0.9
Rogo et al(2015)	19	26		0.7
Mulder et al(2011)	66	157		0.4
Fitzgibbon et al(2004)	8	17		0.4
Fitzgibboli et al(2004)	10	22		0.4
Francesca et al(2019)	10	22		0.7
Ross et al(2015)	9	25		0.3
Ross et al(2015)	2	54	.	0.0
Lwembe et al(2007)	4	12		0.3
Hajjar et al(2012)	21	22		0.9
Makatini et al(2019)	21	22		0.9
Camara-Cissé et al(2021)	18	61		0.7
Dumana at $a/(2000)$	40	01		0.7
Dumans et al(2009)	59	90		0.6
нокат et al(2011)	45	50	— •	0.9
Green et al(2012)	35	41		0.8
Pillay et al(2014)	81	89		0.9
Hunt et al(2023)	709	809		0.8
Fofana et al(2018)	40	53		0.0
Servais et al/2002)	24	21		1.0
	21	21		1.0
Ramkissoon et al(2015)	39	41		0.9
Saravanan et al(2017)	91	97		0.9
Bismara et al(2012)	60	61	-+	0.9
Abuogi et al(2023)	93	199		0.4
Diivou et al(2023)	43	54		07
Khamadi at al(2022)	40	74		0.0
	60	74		0.8
Unarpentier et al(2012)	59	69		0.8
Bouassa et al(2019)	12	18		0.6
Pang et al(2024)	208	396		0.5
Sivay et al(2024)	71	96		0.7
	41	101	i	04
Tambuyzer et al(2016)	7	10		0.7
Tambuyzer et al(2016)		10		0.7
Tambuyzer et al(2016) Lange et al(2015)	-			
Tambuyzer et al(2016) Lange et al(2015) Gopalan et al(2019)	26	30		0.0
Tambuyzer et al(2016) Lange et al(2015) Gopalan et al(2019) Szubert et al(2017)	26 559	30 1132		0.4

Proportion	95%-CI	Weight
0.8929	[0.7812; 0.9597]	1.3%
1.0000	[0.7354; 1.0000]	1.1%
0.7826	[0.6844; 0.8619]	1.3%
1 0000	[0.8955; 0.9995]	1.2%
0.7105	[0.5410: 0.8458]	1.2%
0.7568	[0.5880; 0.8823]	1.2%
0.7105	[0.5410; 0.8458]	1.2%
0.6667	[0.4604; 0.8348]	1.2%
0.8111	[0.7149; 0.8859]	1.3%
0.9310	[0.8327; 0.9809]	1.3%
0.9231	[0.8146; 0.9786]	1.2%
0.9568	[0.0173, 0.9017] [0.9307, 0.9751]	1.2%
0.3000	[0.1189; 0.5428]	1.2%
0.9833	[0.9411; 0.9980]	1.3%
0.9297	[0.8707; 0.9673]	1.3%
0.7805	[0.6239; 0.8944]	1.2%
0.0000	[0.0000; 0.1122]	1.2%
0.5465	[0.2353, 0.4756]	1.3%
1.0000	[0.9690: 1.0000]	1.3%
0.6667	[0.4468; 0.8437]	1.2%
0.7976	[0.6959; 0.8775]	1.3%
0.2500	[0.1655; 0.3511]	1.3%
0.9744	[0.8652; 0.9994]	1.2%
0.4207	[0.3612; 0.4819]	1.3%
0.3004	[0.1629, 0.6164]	1.2%
0 1333	[0.0310, 0.2000] [0.0782 0.2075]	1.3%
0.7312	[0.6292; 0.8179]	1.3%
1.0000	[0.9526; 1.0000]	1.3%
0.5789	[0.3350; 0.7975]	1.2%
0.8462	[0.6513; 0.9564]	1.2%
0.0017	[0.3569; 0.7355]	1.2%
0.5806	[0.4485: 0.7049]	1.3%
0.9038	[0.7897; 0.9680]	1.2%
0.9597	[0.9271; 0.9805]	1.3%
0.6765	[0.5766; 0.7658]	1.3%
0.7969	[0.6777; 0.8872]	1.3%
0.0885	[0.0433; 0.1567]	1.3%
0.9615	[0.8679; 0.9953]	1.2%
0.6912	[0.5674; 0.7976]	1.3%
0.7018	[0.5660; 0.8157]	1.3%
0.7500	[0.5513; 0.8931]	1.2%
0.7047	[0.3010, 0.9319] [0.7131, 0.9985]	1.1%
0.9615	[0.8679; 0.9953]	1.2%
0.7308	[0.5221; 0.8843]	1.2%
0.4204	[0.3422; 0.5017]	1.3%
0.4706	[0.2298; 0.7219]	1.1%
0.7273	[0.4978; 0.8927]	1.2%
0.3000	[0.1797, 0.3748] [0.0045; 0.1275]	1.2%
0.3333	[0.0992: 0.6511]	1.1%
0.9545	[0.7716; 0.9988]	1.2%
0.9545	[0.7716; 0.9988]	1.2%
0.7869	[0.6632; 0.8814]	1.3%
0.6556	[0.5480; 0.7526]	1.3%
0.9000	[0.7819, 0.9007] [0.7083, 0.9443]	1.2%
0.9101	[0.8305: 0.9604]	1.3%
0.8764	[0.8517; 0.8983]	1.3%
0.9245	[0.8179; 0.9791]	1.2%
1.0000	[0.8389; 1.0000]	1.2%
0.9512	[0.8347; 0.9940]	1.2%
0.9836	[0.9120; 0.9996]	1.3%
0.4673	[0.3965; 0.5392]	1.3%
0.7963	[0.6647; 0.8937]	1.2%
0.8108	[0.7030; 0.8925]	1.3%
0.8551	[0.7496; 0.9283] [0.4099: 0.86661	1.3%
0.5253	[0.4748; 0.5753]	1.3%
0.7396	[0.6400; 0.8238]	1.3%
0.4059	[0.3093; 0.5082]	1.3%
0.7000	[0.3475; 0.9333]	1.0%
0.800/	[0.0928; 0.9624]	1.2%
0.4300	[0.4040, 0.0204]	1.5 /0

0.7416 [0.6774; 0.8013] 100.0%

Figure S3A: Sensitivity analysis for the variation of the prevalence of treatment-naive groups

Study		Proportion	95%-CI	P-value	Tau2	Tau	12
Omitting Lindström et al(2010) -	<u>.</u>	0.26	[0.20; 0.32]		0.0654	0.2558	96%
Omitting Lindström et al(2010) -	+	0.26	[0.20; 0.31]		0.0627	0.2504	96%
Omitting Towler et al(2010) -		0.27	[0.21; 0.33]		0.0656	0.2561	96%
Omitting Church et al(2008) –	-	0.26	[0.20; 0.32]		0.0651	0.2552	96%
Omitting Fogel et al(2011) – Omitting Van Dyke, et al(2016) –		0.26	[0.20; 0.32]		0.0636	0.2533	90%
Omitting Kurle et al(2007)	- 10 - 1	0.20	[0.20, 0.31] [0.21, 0.33]		0.0671	0.2590	97%
Omitting Kurle et al(2007) –		0.26	[0.21; 0.32]	· .	0.0670	0.2589	97%
Omitting Vignoles et al(2009) -		0.27	[0.21; 0.33]		0.0646	0.2541	96%
Omitting Gibb et al(2003) -		0.27	[0.21; 0.33]	· .	0.0658	0.2565	96%
Omitting Nelson et al(2015) -		0.27	[0.21; 0.33]		0.0671	0.2590	96%
Omitting Nelson et al(2015) –	-	0.27	[0.21; 0.33]		0.0668	0.2584	96%
Omitting Nelson et al (2015) –	-	0.26	[0.21; 0.32]		0.0674	0.2597	97%
Omitting Louis et al(2019) –		0.20	[0.20; 0.32]		0.0674	0.2533	90%
Omitting Beennett et al(2010)	-	0.20	[0.21, 0.33]	•	0.0651	0.2552	96%
Omitting Inzaule et al(2018) –	<u>.</u>	0.26	[0.20; 0.32]		0.0669	0.2587	96%
Omitting Salou et al(2016) -	<u>i</u>	0.26	[0.20; 0.32]		0.0658	0.2565	96%
Omitting Kityo et al(2016) -	-	0.27	[0.21; 0.33]		0.0669	0.2586	96%
Omitting Dow et al(2017) -	-	0.26	[0.20; 0.32]		0.0666	0.2581	96%
Omitting Hunt et al(2011) –	-	0.26	[0.21; 0.32]	i i	0.0677	0.2601	97%
Omitting Zeh et al(2011) –	-	0.26	[0.20; 0.32]	÷.	0.0668	0.2585	97%
Omitting Nul- Irebi et al(2013) -		0.26	[0.21; 0.32]	•	0.0659	0.2580	97%
Omitting Taylor et al(2010)		0.20	[0.21, 0.32]		0.0677	0.2599	97%
Omitting Fofana et al(2023)	1	0.27	[0.21; 0.33]		0.0643	0.2537	96%
Omitting Hunt et al(2019) –	-	0.26	[0.20; 0.32]		0.0667	0.2582	96%
Omitting Parker et al(2003) -		0.27	[0.21; 0.33]		0.0670	0.2588	96%
Omitting Parker et al(2003) -		0.26	[0.21; 0.33]	×	0.0674	0.2596	96%
Omitting Karchava et al(2006) –		0.26	[0.21; 0.32]		0.0675	0.2598	97%
Omitting Frange et al(2018) –		0.26	[0.21; 0.32]		0.0675	0.2599	96%
Omitting Ngo-Glang-Huong et al(2016)		0.27	[0.21; 0.33]		0.0605	0.2579	96%
Omitting Speria-Atmadia et al(2020)		0.26	[0.21, 0.33] [0.21, 0.32]		0.0676	0.2599	96%
Omitting Aulicino et al(2019) –	<u> </u>	0.26	[0.21; 0.32]		0.0677	0.2601	97%
Omitting Abidi et al(2021) –	•	0.26	[0.21; 0.32]		0.0676	0.2600	97%
Omitting Kovacs et al(2005) -	<u> </u>	0.26	[0.21; 0.32]		0.0676	0.2600	97%
Omitting Delaugerre et al(2009)		0.26	[0.21; 0.32]		0.0676	0.2599	97%
Omitting Ikomey et al(2017) –	<u>.</u>	0.26	[0.21; 0.32]		0.0676	0.2600	97%
Omitting Andrade et al(2017) –		0.26	[0.21; 0.33]		0.0674	0.2596	96%
Omitting Kuhn et al(2015) –		0.20	[0.20, 0.32] [0.21, 0.32]		0.0676	0.2572	90%
Omitting Fokam et al(2013)	- in -	0.20	[0.21; 0.32]		0.0663	0.2575	96%
Omitting Han et al(2009)	<u> </u>	0.26	[0.21; 0.32]		0.0673	0.2594	97%
Omitting Eshleman et al(2001) -	<u>.</u>	0.26	[0.20; 0.32]		0.0671	0.2590	97%
Omitting Martinson et al(2007) -		0.26	[0.20; 0.32]		0.0671	0.2590	97%
Omitting Vaz et al(2012) -		0.27	[0.21; 0.33]		0.0662	0.2572	96%
Omitting Olusola et al (2021) –		0.26	[0.21; 0.32]	•	0.0675	0.2597	97%
Omitting Guimaraes et al(2015) –		0.26	[0.21; 0.32]	•	0.0675	0.2598	97%
Omitting Jordan et al(2007)		0.20	[0.21, 0.32] [0.20, 0.32]	•	0.0675	0.2583	96%
Omitting Jordan et al(2017) –	- i-	0.26	[0.21: 0.32]		0.0675	0.2597	97%
Omitting Yeganeh et al(2018) -	-	0.27	[0.21; 0.33]		0.0670	0.2588	96%
Omitting Neogi et al(2012) -	<u> </u>	0.27	[0.21; 0.33]		0.0662	0.2574	96%
Omitting de Azevedo et al(2022) -	-	0.26	[0.21; 0.32]		0.0676	0.2600	97%
Omitting de Azevedo et al(2022) –		0.27	[0.21; 0.33]	•	0.0669	0.2587	96%
Omitting Rogo et al(2015) –		0.27	[0.21; 0.33]		0.0654	0.2584	96%
Omitting Phung et al(2015)		0.20	[0.21, 0.32] [0.21, 0.33]		0.0674	0.2590	97%
Omitting Phung et al(2015)	i.	0.27	[0.21: 0.33]		0.0657	0.2564	96%
Omitting Antunes et al(2015) -	<u>i</u>	0.26	[0.20; 0.32]		0.0664	0.2577	96%
Omitting Almeida et al(2009) -		0.27	[0.21; 0.33]		0.0650	0.2549	96%
Omitting Fogel et al(2013) -		0.27	[0.21; 0.33]		0.0667	0.2582	96%
Omitting Chaix et al(2007) -	<u>.</u>	0.26	[0.21; 0.32]		0.0676	0.2599	97%
Omitting Jarchi et al(2019) –	-	0.26	[0.21; 0.32]		0.0673	0.2594	97%
Omitting Knann Thu et al(2024) –		0.26	[0.20; 0.32]		0.0655	0.2560	96%
Omitting Eenman et al(2015)	-	0.20	[0.20, 0.32]		0.0670	0.2580	97%
Omitting Ronen et al(2017) –	÷	0.26	[0.20: 0.32]		0.0672	0.2591	97%
Omitting Fokam et al(2018)	-	0.27	[0.21; 0.33]		0.0655	0.2560	96%
Random effects model	$\overset{\cdot}{\frown}$	0.26	[0.21; 0.32]		0.0666	0.2580	96%
-0.3-0.2-0.1 0 0.1 0.2	0.3						

Figure S3B: Sensitivity analysis for the variation of the prevalence of treatment-experienced groups

Study		Proportion	95%-CI	P-value Tau2	Tau	12
Omitting Boender et al(2016)	+	0.74	[0.67; 0.80]	. 0.0950	0.3082	97%
Omitting Towler et al(2010)	*	0.74	[0.67; 0.80]	. 0.0938	0.3062	97%
Omitting Kamori et al(2023)	=	0.74	[0.68; 0.80]	. 0.0955	0.3090	97%
Omitting Rossouw et al(2015)	-	0.74	[0.67; 0.80]	0.0925	0.3041	97%
Omitting Chaix et al(2005)		0.74	[0.68; 0.80]	. 0.0954	0.3089	97%
Omitting Machado et al(2004)	+	0.74	[0.68; 0.80]	. 0.0954	0.3089	97%
Omitting Rodríguez-Galet et al(2023)		0.74	[0.68; 0.80]	. 0.0954	0.3089	97%
Omitting Rubio-Garrido et al(2021)	=	0.74	[0.68; 0.80]	. 0.0953	0.3088	97%
Omitting Mossoro-Kpinde et al(2017)		0.74	[0.67: 0.80]	0.0946	0.3076	97%
Omitting Kebe et al(2013)	÷	0.74	[0.67; 0.80]	. 0.0947	0.3077	97%
Omitting Crowell et al(2017)	+	0.74	[0.68; 0.80]	. 0.0954	0.3089	97%
Omitting Stoddart et al(2014)		0.74	[0.67; 0.80]	. 0.0940	0.3066	97%
Omitting Aboulker et al(2004)	=	0.75	[0.68; 0.81]	. 0.0932	0.3053	97%
Omitting Nvandiko et al(2022)		0.74	[0.67: 0.80]	. 0.0945	0.3075	97%
Omitting Taylor et al(2011)	÷	0.74	[0.68; 0.80]	. 0.0954	0.3089	97%
Omitting Fofana et al(2023)		0.75	[0.69; 0.81]	. 0.0847	0.2911	97%
Omitting Contreras et al(2013)		0.75	[0.68; 0.81]	. 0.0934	0.3056	97%
Omitting Delaugerre et al(2007)	三	0.74	[0.68; 0.80]	. 0.0955	0.3090	97%
Omitting Inzaule et al(2014)		0.74	[0.68: 0.80]	. 0.0953	0.3087	97%
Omitting Kityo et al(2017)	+	0.74	[0.68; 0.80]	. 0.0954	0.3089	97%
Omitting Soeria-Atmadja et al(2020)		0.75	[0.68; 0.81]	. 0.0920	0.3034	97%
Omitting Jittamala et al(2009)	-	0.74	[0.67; 0.80]	. 0.0939	0.3065	97%
Omitting Abidi et al(2021)	=	0.75	[0.68; 0.81]	. 0.0940	0.3066	97%
Omitting Shet et al(2013)		0.75	[0.66, 0.61]	0.0936	0.3003	97%
Omitting Theodore et al(2011)		0.75	[0.69: 0.81]	. 0.0896	0.2994	97%
Omitting Yan et al(2022)	-	0.74	[0.68; 0.80]	. 0.0955	0.3090	97%
Omitting Zhao et al(2011)	+	0.74	[0.67; 0.80]	. 0.0924	0.3039	97%
Omitting Bratholm et al(2010)	<u>+</u>	0.74	[0.68; 0.80]	. 0.0950	0.3083	97%
Omitting Gupta et al(2010)	=	0.74	[0.68; 0.80]	. 0.0952	0.3086	97%
Omitting Beghin et al(2020)		0.74	[0.68, 0.80]	0.0928	0.3046	97%
Omitting Ventosa-Cubillo et al(2023)		0.74	[0.68; 0.80]	. 0.0951	0.3084	97%
Omitting Muri et al(2017)	+	0.74	[0.67; 0.80]	. 0.0949	0.3080	97%
Omitting Vaz et al(2018)		0.74	[0.67; 0.80]	. 0.0940	0.3065	97%
Omitting Makadzange et al(2015)		0.74	[0.68; 0.80]	. 0.0954	0.3089	97%
Omitting Vaz et al(2009)		0.74	[0.68; 0.80]	0.0954	0.3089	97%
Omitting Vaz et al(2012)		0.75	[0.69: 0.81]	. 0.0883	0.2972	97%
Omitting Brindeiro et al(2002)	+	0.74	[0.67; 0.80]	. 0.0941	0.3068	97%
Omitting Adje-Toure et al(2008)		0.74	[0.68; 0.80]	. 0.0954	0.3089	97%
Omitting Tagnouokam Ngoupo et al(2021)	=	0.74	[0.68; 0.80]	. 0.0954	0.3089	97%
Omitting Amani-Bosse et al(2017)		0.74	[0.68; 0.80]	0.0954	0.3089	97%
Omitting Ahoua et al(2011)		0.74	[0.67; 0.80]	. 0.0947	0.3077	97%
Omitting Mutwa et al(2014)	÷	0.74	[0.67; 0.80]	. 0.0941	0.3068	97%
Omitting Rogo et al(2015)	<u>+</u>	0.74	[0.68; 0.80]	. 0.0954	0.3089	97%
Omitting Mulder et al(2011)		0.75	[0.68; 0.81]	. 0.0940	0.3067	97%
Omitting Francesca et al(2004)		0.74	[0.68: 0.80]	0.094	0.3088	97%
Omitting Ross et al(2015)		0.75	[0.68; 0.81]	. 0.0937	0.3061	97%
Omitting Ross et al(2015)		0.75	[0.69; 0.81]	. 0.0868	0.2946	97%
Omitting Lwembe et al(2007)	-	0.75	[0.68; 0.80]	. 0.0937	0.3061	97%
Omitting Hajjar et al(2012)		0.74	[0.67; 0.80]	. 0.0945	0.3074	97%
Omitting Makatini et al(2019) Omitting Camara–Cissé et al(2021)		0.74	[0.67; 0.80]	0.0945	0.3074	97%
Omitting Dumans et al(2009)		0.74	[0.68; 0.80]	. 0.0954	0.3088	97%
Omitting Fokam et al(2011)	÷	0.74	[0.67; 0.80]	. 0.0949	0.3081	97%
Omitting Green et al(2012)	*	0.74	[0.67; 0.80]	. 0.0952	0.3086	97%
Omitting Pillay et al (2014)		0.74	[0.67; 0.80]	. 0.0948	0.3079	97%
Omitting Funt et al(2023) Omitting Fofana et al(2018)		0.74	[0.67; 0.80]	0.095	0.3083	97%
Omitting Servais et al(2002)		0.74	[0.67: 0.80]	. 0.0933	0.3054	97%
Omitting Ramkissoon et al(2015)	÷.	0.74	[0.67; 0.80]	. 0.0944	0.3072	97%
Omitting Saravanan et al(2017)	*	0.74	[0.67; 0.80]	. 0.0944	0.3073	97%
Omitting Bismara et al(2012)	±	0.74	[0.67; 0.80]	. 0.0935	0.3058	97%
Omitting Abuogi et al(2023)		0.74	[0.68; 0.80]	0.0944	0.3073	97%
Omitting Khamadi et al(2023)	÷	0.74	[0.68: 0.80]	. 0.0954	0.3088	97%
Omitting Charpentier et al(2012)		0.74	[0.67; 0.80]	. 0.0952	0.3086	97%
Omitting Bouassa et al(2019)	+	0.74	[0.68; 0.80]	. 0.0953	0.3087	97%
Omitting Pang et al(2024)		0.74	[0.68; 0.80]	. 0.0948	0.3079	97%
Omitting Tambuyzer et al(2016)		0.74	[0.68: 0.81]	. 0.0955	0.3090	97%
Omitting Lange et al(2015)		0.75	[0.68: 0.80]	0.0952	0.3086	97%
Omitting Gopalan et al(2019)	÷	0.74	[0.67; 0.80]	. 0.0952	0.3085	97%
Omitting Szubert et al(2017)	-	0.74	[0.68; 0.80]	. 0.0946	0.3076	97%
Devidence officiale model			10 00. 0 00.		0.0000	070/
Random effects model		0.74	[0.68; 0.80]	. 0.0942	0.3069	97%
	-0.5 0 0.5					

Figure S4A: Forest plot of the NNRTI mutation prevalence among treatment-naive groups

Study	Events Tota	I	Proportion	95%-CI	Weight
Region = Southern Africa Lindström et al(2010) Lindström et al(2010) Fogel et al(2011) Nelson et al(2015) Nelson et al(2015) Bennett et al(2015) Hunt et al(2011) Taylor et al(2011) Hunt et al(2011) Hunt et al(2011) Hunt et al(2019) Jordan et al(2012) Kuhn et al(2015) Kuhn et al(2015) Martinson et al(2007) Vaz et al(2012) Jordan et al(2017) Yeganeh et al(2017) Fisher et al(2015) Fisher et al(2015) Random effects model Heterogeneity: $r^2 = 97\%$, $r^2 = 0.0737$, p	28 43 37 45 78 100 3 28 1 16 4 17 32 46 27 255 33 155 33 155 33 155 33 155 131 220 130 199 88 155 18 75 24 53 5 112 516 1046 12 122 36 75 1 18 6 16 2805 < 0.01		0.6512 0.7222 0.1721 0.0625 0.3077 0.6531 0.1059 0.2129 0.5091 0.5697 0.2400 0.4528 0.0446 0.4924 0.0976 0.4557 0.5556 0.4000 0.3657	$\begin{matrix} [0.4907; 0.7899]\\ [0.6795; 0.9200]\\ [0.6278; 0.8041]\\ [0.0227; 0.2823]\\ [0.006; 0.3023]\\ [0.0909; 0.6143]\\ [0.5036; 0.7833]\\ [0.709; 0.1503]\\ [0.513; 0.2858]\\ [0.4410; 0.5769]\\ [0.4410; 0.5769]\\ [0.4859; 0.7224]\\ [0.4859; 0.6470]\\ [0.1489; 0.3525]\\ [0.3136; 0.5855]\\ [0.3146; 0.5855]\\ [0.3146; 0.5854]\\ [0.147; 0.5311]\\ [0.0471; 0.1011]\\ [0.4514; 0.1642]\\ [0.6341; 0.5717]\\ [0.1634; 0.6771]\\ [0.2494; 0.4901] \end{matrix}$	$\begin{array}{c} 1.4\%\\ 1.4\%\\ 1.5\%\\ 1.4\%\\ 1.5\%\\ 1.5\%\\ 1.5\%\\ 1.5\%\\ 1.5\%\\ 1.5\%\\ 1.5\%\\ 1.5\%\\ 1.5\%\\ 1.5\%\\ 1.5\%\\ 1.5\%\\ 1.5\%\\ 1.5\%\\ 1.5\%\\ 1.3\%\\ 29.0\%\end{array}$
$\label{eq:response} \begin{array}{l} \mbox{Region} = \mbox{Eastern Africa} \\ \mbox{Towler et al}(2010) \\ \mbox{Church et al}(2010) \\ \mbox{Course} \\ \mbox{Rescaled} \\ \mbox{Rescaled} \\ \mbox{Course} \\ \mbox{Course} \\ \mbox{Course} \\ \mbox{Course} \\ \mbox{Course} \\ \mbox{Rescaled} \\ Res$	1 74 33 46 21 275 34 66 6 32 8 57 16 90 11 24 80 224 1 16 10 20 19 43 975 < 0.01		0.0135 0.6735 0.0753 0.5231 0.1875 0.1404 0.1778 0.4583 0.3571 0.0556 0.5000 0.4419 0.2703	[0.0003; 0.0730] [0.5246; 0.8005] [0.0472; 0.1128] [0.3954; 0.6485] [0.0721; 0.3644] [0.1052; 0.2726] [0.2555; 0.6718] [0.2944; 0.4237] [0.2720; 0.7280] [0.270; 0.7280] [0.270; 0.7280] [0.2908; 0.6012] [0.1485; 0.4116]	1.5% 1.5% 1.5% 1.4% 1.5% 1.5% 1.3% 1.3% 1.3% 1.4% 1.3%
Region = North America Van Dyke et al(2016) Louis et al(2019) Parker et al(2003) Parker et al(2003) Karchava et al(2006) Rogo et al(2015) Lehman et al(2015) Random effects model Heterogeneity: $l^2 = 97\%$, $r^2 = 0.0959$, p	105 234 210 304 2 49 1 38 5 42 1 16 10 20 703 < 0.01		0.4487 0.6908 0.0408 0.0263 0.1190 0.0625 0.5000 0.2375	[0.3839; 0.5149] [0.6355; 0.7423] [0.0050; 0.1398] [0.0007; 0.1381] [0.0398; 0.2563] [0.0016; 0.3023] [0.2720; 0.7280] [0.2720; 0.7280]	1.5% 1.5% 1.4% 1.4% 1.3% 1.3% 10.0%
Region = Asia Kurle et al(2007) Kurle et al(2007) Ngo-Giang-Huong et al(2016) Han et al(2009) Neogi et al(2012) Chalermchockcharoenkit et al(2009) Phung et al(2015) Jarchi et al(2019) Khanh Thu et al(2024) Random effects model Heterogeneity: $l^2 = 95\%$, $\tau^2 = 0.0546$, p	2 19 6 13 17 476 2 14 5 100 2 10 2 65 2 15 60 100 822 < 0.01		0.1053 0.4615 0.0357 0.1429 0.0476 0.2000 0.0308 0.1333 0.5714 0.1556	[0.0130; 0.3314] [0.1922; 0.7487] [0.0209; 0.0566] [0.0178; 0.4281] [0.0156; 0.1076] [0.0252; 0.5561] [0.0037; 0.1068] [0.0166; 0.4046] [0.4711; 0.6676] [0.0478; 0.3018]	1.3% 1.2% 1.6% 1.2% 1.5% 1.5% 1.3% 1.5% 1.5%
Region = Western and Central Afri Boerma et al(2016) Inzaule et al(2018) Crowell et al(2017) Salou et al(2017) Salou et al(2013) Ikomey et al(2013) Ikomey et al(2011) Olusola et al(2021) Chaix et al(2007) Fokam et al(2007) Fokam et al(2008) Random effects model Heterogeneity: $l^2 = 93\%$, $l^2 = 0.0462$, p	ca 13 82 194 430 27 120 120 201 5 10 11 37 2 41 3 12 6 26 0 16 974 < 0.01		0.1585 0.4512 0.2250 0.5970 0.5000 0.2973 0.0488 0.2500 0.2308 0.0000 0.2539	[0.0872; 0.2558] [0.4034; 0.4996] [0.1538; 0.3102] [0.5257; 0.6654] [0.1871; 0.8129] [0.1887; 0.4698] [0.0600; 0.1653] [0.0549; 0.4719] [0.0897; 0.4365] [0.0900; 0.2180] [0.1346; 0.3936]	1.5% 1.5% 1.5% 1.2% 1.4% 1.4% 1.2% 1.4% 1.3%
Region = Europe Neubert et al(2016) Frange et al(2018) Ngo-Giang-Huong et al(2016) Delaugerre et al(2009) Masquelier et al(2001) Random effects model Heterogeneity: $l^2 = 71\%$, $r^2 = 0.0094$, p	3 24 5 84 17 476 2 60 7 34 678 < 0.01		0.1250 0.0595 0.0357 0.0333 0.2059 0.0695	[0.0266; 0.3236] [0.0196; 0.1335] [0.0209; 0.0566] [0.0041; 0.1153] [0.0870; 0.3790] [0.0234; 0.1339]	1.4% 1.5% 1.6% 1.5% 1.4% 7.3%
Region = South America Aulicino et al(2019) Andrade et al(2017) Guimarães et al(2015) Yeganeh et al(2018) de Azevedo et al(2022) de Azevedo et al(2022) Almeida et al(2009) Random effects model Heterogeneity: $l^2 = 74\%$, $\tau^2 = 0.0100$, p	25 115 16 117 1 31 12 123 3 35 5 97 0 24 545 < 0.01		0.2174 0.1368 0.0323 0.0976 0.0789 0.0515 0.0000 0.0855	[0.1459; 0.3040] [0.0802; 0.2126] [0.0008; 0.1670] [0.0514; 0.1642] [0.0166; 0.2138] [0.0169; 0.1162] [0.0000; 0.1425] [0.0402; 0.1437]	1.5% 1.5% 1.4% 1.5% 1.4% 1.5% 1.4% 10.2%
Random effects model Heterogeneity: $l^2 = 97\%$, $\tau^2 = 0.0675$, <i>p</i> Test for subgroup differences: $\chi_6^2 = 32.94$	7505 = 0 4, df = 6 (p < 0.0	5	0.2364	[0.1826; 0.2945]	100.0%

Figure S4B: Forest plot of the NNRTI mutation prevalence among treatment-experienced groups

Study	Events	Total	P	roportion	95%-CI	Weight
Region1 = Europe	20	96		0.2256 10	2204: 0 42521	1 20/
Aboulker et al (2006)	28	20		0.3256 [0	0.0000 0 1684	1.3%
Delaugerre et al(2007)	49	119		0.4118 [0	0.3224; 0.5057]	1.3%
Mulder et al(2011)	35	157		0.2229 [0	0.1605; 0.2962]	1.3%
Francesca et al(2019) Servais et al(2002)	21	22		1.0000 [0	0.1073; 0.5022]	1.2%
Sivay et al(2024)	57	96		0.5938 [0	.4887; 0.6929]	1.3%
Random effects model		521		0.3998 [0	.1347; 0.6997]	8.6%
Heterogeneity: $T = 95\%$, $\tau = 0.1560$), p < 0.01					
Region1 = Eastern Africa	19	56		0.9571 0	7279.0 02621	1 20/
Towler et al(2010)	12	12		1.0000 [0	0.7354; 1.0000]	1.1%
Kamori et al(2023)	64	92		0.6957 [0	0.5910; 0.7873]	1.3%
Tadesse et al(2018)	72	90		0.8000 [0	0.7025; 0.8769]	1.3%
Kityo et al(2017)	64	84		0.7619 [0	0.6565; 0.8481]	1.3%
Soeria-Atmadja et al(2020)	22	92		0.2391 [0	0.1563; 0.3394]	1.3%
Chohan et al(2015)	12	19		0.3684 [0	0.1629; 0.6164]	1.2%
Bratholm et al(2010)	11	19		0.5789 [0	0.3350; 0.7975]	1.2%
Muri et al(2017)	47	52		0.9038 [0	0.7897; 0.9680]	1.2%
Ahoua et al(2011) Aboua et al(2011)	12	17		0.7059 [0	0.4404; 0.8969]	1.2%
Mutwa et al(2014)	49	52		0.9423 [0	0.8405; 0.9879]	1.2%
Lwembe et al(2007)	4	12		0.3333 [0	0.0992; 0.6511]	1.1%
Abuogi et al(2023) Khamadi et al(2023)	87	199		0.4372 [0	0.3672; 0.5091]	1.3%
Random effects model	00	1031		0.6048 [0	.4482; 0.7517]	20.6%
Heterogeneity: $I^{+} = 96\%$, $\tau^{-} = 0.0952$	2, p < 0.01					
Region1 = Asia	50	E1		0.0004 10	1 8055 · 0 0005	1 20/
Puthanakit et al(2013)	117	120		0.9804 [0		1.2%
Nyandiko et al(2022)	119	128	-	0.9297 [0	0.8707; 0.9673]	1.3%
Jittamala et al(2009)	37	39		0.9487 [0	0.8268; 0.9937]	1.2%
Yan et al(2022)	59	93		0.6344 [0	0.5281: 0.7319	1.3%
Zhao et al(2011)	38	76		0.5000 [0	.3830; 0.6170]	1.3%
Hajjar et al(2012) Saravanan et al(2017)	0	22		0.0000 [0	0.0000; 0.1544]	1.2%
Pang et al(2024)	192	396		0.4848 [0	0.4346; 0.5353]	1.3%
Tambuyzer et al(2016)	75	101		0.7426 [0	0.6460; 0.8244]	1.3%
Random effects model Heterogeneity: $I^2 = 98\%$, $\tau^2 = 0.1759$), p < 0.01	1193		0.6886 [0	.4391; 0.8917]	13.8%
Desilent - Desilent Africa						
Region1 = Southern Africa Rossouw et al(2015)	29	65		0 4462 [0	3227 0 57471	1.3%
Stoddart et al(2014)	265	370		0.7162 [0	0.6673; 0.7616]	1.3%
Taylor et al(2011)	5	41		0.1220 [0	0.0408; 0.2620]	1.2%
Beghin et al(2010)	13	20		0.4483 [0	2645: 0.6431	1.2%
Beghin et al(2020)	13	64		0.2031 [0	0.1128; 0.3223]	1.3%
Vaz et al(2018)	69	248	*	0.2782 [0	0.2234; 0.3384]	1.3%
Vaz et al(2009)	26	84		0.2549 [0	0.1738; 0.3508]	1.3%
Vaz et al(2012)	9	113		0.0796 [0	0.0371; 0.1458]	1.3%
Makatini et al(2019)	14	22		0.6364 [0	0.4066; 0.8280]	1.2%
Pillay et al(2012)	64	41		0.4146 [0	0.2632; 0.5789]	1.2%
Hunt et al(2023)	625	809		0.7726 [0	0.7421; 0.8010]	1.3%
Tambuyzer et al(2016)	75	101	- 	0.7426 [0	0.6460; 0.8244]	1.3%
Random effects model	'	2214		0.5145 [0	.3664; 0.6613]	19.8%
Heterogeneity: $I^2 = 98\%$, $\tau^2 = 0.0842$	e, p < 0.01					
Region1 = Western and Central	Africa					
Chaix et al(2005)	14	38		0.3684 [0	0.2181; 0.5401]	1.2%
Rubio-Garrido et al(2023)	18	27		0.6667 [0	0.4604: 0.8348	1.2%
Mossoro-Kpinde et al(2017)	28	58		0.4828 [0	0.3495; 0.6178]	1.3%
Kebe et al(2013)	48	52		0.9231 [0	0.8146; 0.9786]	1.2%
Yendewa et al(2021)	49	64		0.7656 [0	0.6431: 0.8625	1.3%
Brice et al (2020)	49	91		0.5385 [0	0.4308; 0.6436]	1.3%
Sylla et al (2019) Adie-Toure et al (2009)	10	33		0.3030 [0	0.1559; 0.4871]	1.2%
Tagnouokam Ngoupo et al(2021)	14	57		0.2632 [0	0.1554; 0.3966]	1.2%
Amani-Bossé et al(2017)	4	28		0.1429 [0	0.0403; 0.3267]	1.2%
Camara-Cisse et al(2021) Fokam et al(2011)	34	61 50		0.8800 0	0.4245; 0.6845]	1.3%
Fofana et al(2018)	45	53		0.8491 [0	0.7241; 0.9325]	1.2%
Djiyou et al(2023)	41	54		0.7593 [0	0.6236; 0.8651]	1.2%
Bouassa et al(2012)	59	69 18		0.8551 [0	.7490; 0.9283] .4099: 0.86661	1.3%
Random effects model		896		0.5940 [0	.4706; 0.7120]	22.2%
Heterogeneity: $I^{*} = 93\%$, $\tau^{e} = 0.0631$, p < 0.01					
Region1 = North America	12.2		_	0.0.17	0050 5	
Contreras et al(2013) Aqui et al(2014)	23	66 117		0.3485 [0	9690 1 0000	1.3%
Rogo et al(2015)	15	26		0.5769 [0	0.3692; 0.7665]	1.2%
Fitzgibbon et al(2004)	4	17		0.2353 [0	0.0681; 0.4990]	1.2%
Ross et al(2015) Ross et al(2015)	1	25 54		0.0400 [0	0.0010; 0.2035]	1.2%
Ramkissoon et al(2015)	28	41		0.6829 [0	0.5191; 0.8192]	1.2%
Tambuyzer et al(2016)	75	101		0.7426 [0	0.6460; 0.8244]	1.3%
Heterogeneity: $l^2 = 98\%$, $\tau^2 = 0.1987$	', p < 0.01	-1-41		0.4010 [0		3.070
Region1 = South Amorica						
Ventosa-Cubillo et al(2023)	23	62		0.3710 [0	0.2516; 0.5031]	1.3%
Brindeiro et al(2002)	50	52		0.9615 [0	0.8679; 0.9953]	1.2%
Tambuyzer et al(2012)	8	61 101		0.7426 0	0.0584; 0.2422]	1.3%
Random effects model		276		0.5716 [0	.1758; 0.9203]	5.0%
Heterogeneity: $I^2 = 98\%$, $\tau^2 = 0.1774$, p < 0.01					
Random effects model		6578	\diamond	0.5639 [0	.4876; 0.6388]	100.0%
Heterogeneity: $I^2 = 97\%$, $\tau^2 = 0.1119$ Test for subgroup differences: $\tau^2 = 2$	p = 0	(n = 0 =				
		J- 0.7				

Figure S5A: Forest plot of the NRTI mutation prevalence among treatment-naive groups

Study	Events Total		Proportion 95%-C	l Weight
Region = Southern Africa Lindström et al(2010) Bennett et al(2010) Bennett et al(2010) Hunt et al(2011) Taylor et al(2011) Hunt et al(2011) Jordan et al(2012) Kuhn et al(2015) Vaz et al(2015) Vaz et al(2015) Jordan et al(2017) Yeganeh et al(2018) Antunes et al(2015) Fisher et al(2015) Random effects model Heterogeneity: $J^2 = 91\%$, $\tau^2 = 0.0300$, p	0 43 0 45 6 49 19 255 11 155 10 220 41 198 23 155 8 75 1 112 71 1048 2 123 33 79 5 15 2572 < 0.01		0.0000 [0.0000; 0.0822 0.0000 [0.0000; 0.0787 0.1224 [0.0463; 0.2477 0.0745 [0.0455; 0.1139 0.0710 [0.0360; 0.1234 0.0455 [0.0220; 0.0820 0.2071 [0.1529; 0.2702 0.1484 [0.0964; 0.2143 0.1067 [0.0472; 0.1994 0.0089 [0.0002; 0.0487 0.0677 [0.0533; 0.0847 0.0163 [0.0020; 0.0575 0.4177 [0.3077; 0.5341 0.3333 [0.1182; 0.6162 0.0850 [0.0373; 0.1478	1.6% 1.7% 1.7% 1.9% 2.9%
Region = Eastern Africa Towler et al(2010) Kityo et al(2016) Dow et al(2017) Zeh et al(2017) Tadesse et al(2019) Soeria-Atmadja et al(2020) Jordan et al(2017) Lehman et al(2015) Random effects model Heterogeneity: J^2 = 84%, τ^2 = 0.0254, p	1 74 16 279 12 65 14 32 3 57 4 90 19 224 2 20 841 < 0.01	 ↓↓++	0.0135 [0.0003; 0.0730 0.0573 [0.0331; 0.0915 0.1846 [0.0992; 0.3003 0.4375 [0.2636; 0.6234 0.0526 [0.0110; 0.1462 0.0444 [0.0122; 0.1099 0.0848 [0.0518; 0.1293 0.1000 [0.0123; 0.3170 0.0957 [0.0345; 0.1800	1.8% 1.9% 1.7% 1.5% 1.5% 1.7% 1.8% 1.8% 1.8% 1.3.8%
Region = North America Van Dyke et al(2016) Louis et al(2019) Parker et al(2003) Parker et al(2003) Karchava et al(2006) Kovacs et al(2005) Rogo et al(2015) Lehman et al(2015) Random effects model Heterogeneity: I^2 = 96%, τ^2 = 0.0656, p	142 234 123 304 1 49 6 38 3 42 11 44 0 16 2 20 747 <0.01	*	- 0.6068 [0.5411; 0.6698 0.4046 [0.3490; 0.4621 0.0204 [0.0005; 0.1085 0.1579 [0.0602; 0.3125 0.0714 [0.0150; 0.1948 0.2500 [0.1319; 0.4034 0.0000 [0.0000; 0.2059 0.1000 [0.0123; 0.3170 0.1770 [0.0547; 0.3437	1.9% 1.9% 1.7% 1.6% 1.6% 1.6% 1.3% 1.3% 1.4% 13.1%
Region = Asia Kurle et al(2007) Kurle et al(2007) Ngo-Giang-Huong et al(2016) Han et al(2009) Neogi et al(2012) Chalermchockcharoenkit et al(2009) Phung et al(2015) Jarchi et al(2019) Khanh Thu et al(2024) Random effects model Heterogeneity: l^2 = 0.0028, p	0 19 0 13 28 476 0 14 2 105 0 10 2 65 2 15 11 105 822 = 0.14		0.0000 [0.0000; 0.1765 0.0000 [0.0000; 0.2471 0.0588 [0.0394; 0.0839 0.0000 [0.0000; 0.2316 0.0190 [0.0002; 0.0671 0.0000 [0.0000; 0.3085 0.0308 [0.0037; 0.1068 0.1333 [0.0166; 0.4046 0.1048 [0.0535; 0.1797 0.0320 [0.0104; 0.0613	1.3% 1.2% 2.0% 1.2% 1.2% 1.1% 1.1% 1.2% 1.1% 1.2% 1.3% 1.3% 1.3% 1.3% 1.3% 1.3% 1.3%
Region = Europe Gibb et al(2003) Neubert et al(2016) Frange et al(2018) Ngo-Giang-Huong et al(2016) Delaugerre et al(2009) Random effects model Heterogeneity: $l^2 = 72\%$, $\tau^2 = 0.0103$, p	4 105 5 24 3 84 28 476 10 60 749 < 0.01		0.0381 [0.0105; 0.0947 0.2083 [0.0713; 0.4215 0.0357 [0.0074; 0.1008 0.0588 [0.0394; 0.0839 0.1667 [0.0829; 0.2852 0.0784 [0.0298; 0.1449] 1.8%] 1.4%] 1.8%] 2.0%] 1.7%] 8.7%
Region = Western and Central Afric Boerma et al(2016) Inzaule et al(2017) Salou et al(2017) Salou et al(2016) Nii-Trebi et al(2013) Ikomey et al(2017) Fokam et al(2011) Olusola et al(2021) Fokam et al(2018) Random effects model Heterogeneity: $J^2 = 86\%, \tau^2 = 0.0117, p$	ca 7 82 94 430 4 120 22 201 0 10 1 37 1 41 1 12 0 15 948 < 0.01		0.0854 [0.0350; 0.1680 0.2186 [0.1804; 0.2607 0.0333 [0.0092; 0.0831 0.1095 [0.0699; 0.1610 0.0000 [0.0000; 0.3085 0.0270 [0.0007; 0.1416 0.0244 [0.0006; 0.1286 0.0833 [0.0021; 0.388 0.0000 [0.0020; 0.2180 0.0620 [0.0220; 0.1160	1.8% 1.9% 1.8% 1.9% 1.1% 1.6% 1.1% 1.2%
Region = South America Aulicino et al(2019) Andrade et al(2017) Guimarães et al(2015) Yeganeh et al(2018) de Azevedo et al(2022) de Azevedo et al(2022) Almeida et al(2009) Random effects model Heterogeneity: f^2 = 79%, τ^2 = 0.0137, ρ	14 115 2 117 3 31 2 123 8 38 5 97 0 24 545 < 0.01		0.1217 [0.0682; 0.1958 0.0171 [0.0021; 0.0604 0.0968 [0.0204; 0.2575 0.0163 [0.0020; 0.0575 0.2105 [0.0955; 0.3732 0.0515 [0.0169; 0.1162 0.0000 [0.0000; 0.1425 0.0559 [0.0159; 0.1137	1.8% 1.8% 1.5% 1.9% 1.6% 1.8% 1.4% 1.9%
Random effects model Heterogeneity: $l^2 = 93\%$, $\tau^2 = 0.0270$, p Test for subgroup differences: $\chi_6^2 = 7.35$,	7224 < 0.01 df = 6 (p = 0.29)	0 0.1 0.2 0.3 0.4 0.5 0.6	0.0804 [0.0556; 0.1087	j 100.0%

Figure S5B: Forest plot of the NRTI mutation prevalence among treatment-experienced groups

Study E	vents	Total		Proportion	95%-CI	Weight
Region1 = Europe Green et al (2006) Aboulker et al(2004) Delaugerre et al(2007) Mulder et al(2017) Francesca et al(2019) Servais et al(2019) Servais et al(2020) Sivay et al(2024) Random effects model Heterogeneity: $l^2 = 97\%$, $t^2 = 0.1248$, p	84 5 77 54 11 21 81	86 20 119 157 22 21 96 521	**	0.9767 0.2500 0.6471 0.3439 0.5000 1.0000 0.8438 0.7022	[0.9185; 0.9972] [0.0866; 0.4910] [0.5542; 0.7324] [0.2701; 0.4239] [0.8282; 0.7178] [0.8389; 1.0000] [0.7554; 0.9098] [0.4332; 0.9142]	1.3% 1.2% 1.3% 1.3% 1.2% 1.2% 1.3% 8.9%
Region = Lasen Annea Boender et al (2016) Towler et al (2010) Kamori et al (2023) Tadesse et al (2013) Inzaule et al (2013) Kityo et al (2017) Soeria-Atmadja et al (2020) Chohan et al (2015) Theodore et al (2011) Bratholm et al (2010) Muri et al (2017) Ahoua et al (2011) Ahoua et al (2011) Mutwa et al (2011) Mutwa et al (2011) Abua et al (2011) Abua et al (2011) Khamadi et al (2023) Random effects model Heterogeneity: $I^2 = 96\%$, $t^2 = 0.0996$, p	43 12 49 64 16 63 11 2 14 11 42 13 16 47 3 700 50	56 12 92 90 24 84 92 19 129 52 17 17 52 12 199 74 1031		0.7679 0.5326 0.7111 0.6667 0.7500 0.1196 0.1053 0.1167 0.5789 0.8077 0.7647 0.90412 0.9038 0.2500 0.3518 0.6757 0.5992	$\begin{matrix} [0.6358; 0.8702] \\ [0.7354; 1.0000] \\ [0.4256; 0.6374] \\ [0.4606; 0.8018] \\ [0.4468; 0.8437] \\ [0.6436; 0.8381] \\ [0.612; 0.2039] \\ [0.0130; 0.3314] \\ [0.6633; 0.1880] \\ [0.3635; 0.7975] \\ [0.6747; 0.9037] \\ [0.701; 0.9031] \\ [0.7397; 0.9680] \\ [0.5498; 0.5719] \\ [0.2568; 0.4224] \\ [0.5568; 0.4726] \\ [0.4393; 0.7496] \end{matrix}$	1.3% 1.1% 1.3% 1.2% 1.3% 1.2% 1.3% 1.2% 1.3% 1.2% 1.3% 1.3% 1.3% 21.3%
Region1 = Asia Coetzer et al(2013) Puthanakit et al(2010) Nyandiko et al(2022) Jittamala et al(2009) Shet et al(2013) Yan et al(2022) Zhao et al(2011) Hajjar et al(2012) Saravanan et al(2017) Pang et al(2024) Tambuyzer et al(2016) Random effects model Heterogeneity: I^2 = 98%, r^2 = 0.0996, p	49 118 114 34 11 45 59 21 80 138 82	51 120 128 39 70 93 76 22 97 396 101 1193	* * *	0.9608 0.9833 0.8906 0.8718 0.1571 0.4839 0.7763 0.9545 0.8247 0.3485 0.8119 0.7623	$\begin{array}{l} [0.8654; 0.9952] \\ (0.9411; 0.9980] \\ (0.8233; 0.9389] \\ (0.7257; 0.9570] \\ (0.811; 0.2638] \\ (0.3789; 0.5899] \\ (0.6662; 0.8640] \\ (0.7716; 0.9988] \\ (0.7343; 0.8945] \\ (0.3016; 0.3977] \\ (0.5219; 0.8828] \\ (0.5824; 0.9047] \end{array}$	1.3% 1.3% 1.3% 1.3% 1.3% 1.3% 1.2% 1.3% 1.4% 1.3% 1.4%
Region1 = Southern Africa Rossouw et al(2015) Stoddart et al(2014) Taylor et al(2011) Beghin et al(2020) Beghin et al(2020) Vaz et al(2018) Makadzinage et al(2015) Vaz et al(2019) Green et al(2012) Pillay et al(2014) Hunt et al(2023) Tambuyzer et al(2016) Random effects model Heterogeneity. $f^2 = 98\%, t^2 = 0.1101, \mu$	63 354 30 10 9 220 41 74 10 17 29 73 563 82	65 370 41 29 64 248 102 84 113 22 41 89 809 101 2178		0.9692 0.9568 0.7317 0.3448 0.1406 0.8871 0.4020 0.8810 0.0885 0.7727 0.7073 0.8202 0.6959 0.8119 0.6790		1.3% 1.4% 1.2% 1.3% 1.3% 1.3% 1.3% 1.3% 1.3% 1.3% 1.3
Region1 = Western and Central A Chaix et al(2005) Rodríguez-Calet et al(2023) Rubio-Garrído et al(2021) Mossoro-Kpinde et al(2021) Kebe et al(2013) Crowell et al(2017) Yendewa et al(2021) Brice et al (2020) Sylla et al (2019) Adje-Toure et al(2008) Tagnouckam Ngoupo et al(2021) Amani-Bossé et al(2017) Camara-Cissé et al(2021) Fokam et al(2011) Fokam et al(2011) Dijvou et al(2023) Charpentier et al(2012) Bouassa et al(2012) Bouassa et al(2019) Random effects model Heterogeneity. f^2 = 87%, t^2 = 0.0281, p	frica 30 21 15 27 47 26 29 30 20 30 30 30 30 30 38 13 42 45 37 35 58 11	38 38 52 37 64 91 33 68 67 28 61 50 53 54 9 18 896		0.7895 0.5526 0.5556 0.9038 0.7027 0.4531 0.3297 0.6061 0.4643 0.6685 0.9000 0.6981 0.6481 0.6481 0.6481 0.6481	[0.6268; 0.9045] [0.3630; 0.7138] [0.3533; 0.7452] [0.3533; 0.7452] [0.3533; 0.613] [0.5302; 0.8413] [0.3282; 0.5825] [0.2347; 0.4361] [0.4214; 0.7709] [0.5294; 0.7860] [0.5294; 0.7860] [0.5294; 0.7860] [0.5294; 0.7860] [0.5294; 0.7860] [0.5294; 0.7860] [0.5294; 0.7860] [0.5294; 0.7860] [0.5528; 0.7192]	1.3% 1.2% 1.3% 1.3% 1.3% 1.3% 1.3% 1.3% 1.3% 1.3
Region1 = South America Machado et al(2004) Ventosa-Cubillo et al(2023) Brindeiro et al(2002) Bismara et al(2012) Tambuyzer et al(2016) Random effects model Heterogeneity: l^2 = 87%, t^2 = 0.0289, p	28 36 50 42 82	37 62 52 61 101 313	****	0.7568 0.5806 0.9615 0.6885 0.8119 0.7754	[0.5880; 0.8823] [0.4485; 0.7049] [0.8679; 0.9953] [0.5571; 0.8010] [0.7219; 0.8828] [0.6270; 0.8958]	1.3% 1.3% 1.3% 1.3% 1.3% 6.5%
Region1 = North America Rogo et al(2015) Filzgibbon et al(2004) Ross et al(2015) Ramkisson et al(2015) Tambuyzer et al(2015) Random effects model Heterogeneity: r^2 = 97% r^2 = 0.1157. z	13 4 4 1 24 82	26 17 25 54 41 101 264		0.5000 0.2353 0.1600 0.0185 0.5854 0.8119 0.3633	[0.2993; 0.7007] [0.0681; 0.4990] [0.0454; 0.3608] [0.005; 0.0989] [0.4211; 0.7368] [0.7219; 0.8828] [0.1196; 0.6493]	1.2% 1.2% 1.3% 1.3% 1.3% 7.5%
Random effects model Heterogeneity: $l^2 = 97\%$, $\tau^2 = 0.0868$, μ Test for subgroup differences: $\chi_6^2 = 8.95$	o = 0 9, df =	6396 6 (p = 0	0.17) 0.2 0.4 0.6 0.8	0.6519	[0.5848; 0.7162]	100.0%

Figure S6A: Forest plot of the PI mutation prevalence among treatment-naive groups

Study	Events Total		Proportion	95%-CI	Weight
Region = North America Van Dyke et al(2016) Louis et al(2019) Parker et al(2003) Parker et al(2003) Karchava et al(2006) Random effects model Heterogeneity: $I^2 = 97\%$, $\tau^2 = 0.03$	80 234 10 304 1 49 2 38 1 42 667		0.3419 0.0329 0.0204 0.0526 0.0238 0.0754	[0.2813; 0.4065] [0.0159; 0.0597] [0.0005; 0.1085] [0.0064; 0.1775] [0.0066; 0.1257] [0.0060; 0.1989]	3.3% 3.3% 2.4% 2.2% 2.3% 13.6%
Region = Western and Centra Boerma et al(2016) Inzaule et al(2018) Crowell et al(2017) Nii-Trebi et al(2017) Ikomey et al(2017) Fokam et al(2018) Random effects model Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p =$	Al Africa 0 82 2 430 0 120 0 10 0 37 0 15 694 = 0.97	B	0.0000 0.0047 0.0000 0.0000 0.0000 0.0000 0.0000	[0.0000; 0.0440] [0.0006; 0.0167] [0.0000; 0.0303] [0.0000; 0.3085] [0.0000; 0.0949] [0.0000; 0.2180] [0.0000; 0.0007]	2.8% 3.4% 3.0% 1.1% 2.2% 1.4% 14.0%
Region = Southern Africa Bennett et al(2020) Hunt et al(2011) Taylor et al(2011) Jordan et al(2012) Kuhn et al(2015) Kuhn et al(2015) Yeganeh et al(2015) Fisher et al(2015) Random effects model Heterogeneity: $/^2 = 45\%$, $\tau^2 = 0.00$	2 49 4 255 2 155 3 198 2 155 1 75 2 123 7 79 2 15 1104		0.0408 0.0157 0.0129 0.0152 0.0129 0.0133 0.0163 0.0886 0.1333 0.0182	[0.0050; 0.1398] [0.0043; 0.0397] [0.0016; 0.0458] [0.0016; 0.0458] [0.0003; 0.0458] [0.0003; 0.0721] [0.0020; 0.0575] [0.0364; 0.1741] [0.0166; 0.4046] [0.0082; 0.0312]	2.4% 3.3% 3.1% 3.2% 3.1% 2.7% 3.0% 2.8% 1.4% 25.1%
Region = Eastern Africa Kityo et al(2016) Dow et al(2017) Tadesse et al(2019) Random effects model Heterogeneity: $l^2 = 0\%$, $\tau^2 = 0$, $p =$	0 279 0 65 0 57 401	⊨ ■ }	0.0000 0.0000 0.0000 0.0000	[0.0000; 0.0131] [0.0000; 0.0552] [0.0000; 0.0627] [0.0000; 0.0031]	3.3% 2.6% 2.6% 8.5%
Region = Europe Neubert et al(2016) Frange et al(2018) Ngo-Giang-Huong et al(2016) Delaugerre et al(2009) Random effects model Heterogeneity: $I^2 = 21\%$, $\tau^2 = < 0$.	1 24 0 84 3 476 1 60 644 0001, <i>p</i> = 0.29		0.0417 0.0000 0.0063 0.0167 0.0022	[0.0011; 0.2112] [0.0000; 0.0430] [0.0013; 0.0183] [0.0004; 0.0894] [0.0000; 0.0099]	1.8% 2.8% 3.4% 2.6% 10.7%
Region = Asia Ngo-Giang-Huong et al(2016) Abidi et al(2021) Han et al(2009) Phung et al(2015) Random effects model Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0.000$	3 476 0 50 0 14 2 86 626 02, p = 0.52	н	0.0063 0.0000 0.0000 0.0233 0.0012	[0.0013; 0.0183] [0.0000; 0.0711] [0.0000; 0.2316] [0.0028; 0.0815] [0.0000; 0.0099]	3.4% 2.5% 1.4% 2.8% 10.1%
Region = South America Aulicino et al(2019) Andrade et al(2017) Guimarães et al(2015) Yeganeh et al(2018) de Azevedo et al(2022) de Azevedo et al(2022) Almeida et al(2009) Random effects model Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p =$	4 115 4 117 2 31 2 123 0 38 2 97 0 24 545		0.0348 0.0342 0.0645 0.0163 0.0000 0.0206 0.0000 0.0204	[0.0096; 0.0867] [0.0094; 0.0852] [0.0079; 0.2142] [0.0020; 0.0575] [0.0000; 0.0925] [0.0025; 0.0725] [0.0000; 0.1425] [0.00084; 0.0360]	3.0% 3.0% 2.1% 3.0% 2.2% 2.9% 1.8% 18.0%
Random effects model Heterogeneity: $l^2 = 87\%$, $\tau^2 = 0.01$ Test for subgroup differences: $\chi_6^2 =$	4681 108, <i>p</i> < 0.01 : 31.71, df = 6 (<i>p</i> < 0.01)	♦ 0 0.1 0.2 0.3 0.4	0.0150 4	[0.0053; 0.0280]	100.0%

Figure S6B: Forest plot of the PI mutation prevalence among treatment-experienced groups

Study	Events Total		Proportion	95%-CI Weight
Region1 = Europe Green et al (2006) Aboulker et al(2004) Delaugerre et al(2007) Mulder et al(2011) Francesca et al(2019) Servais et al(2020) Sivay et al(2024) Random effects model Heterogeneity: I^2 = 96%, τ^2 = 0.141	$\begin{array}{cccccccccccccccccccccccccccccccccccc$		0.6047 [0.48 0.3000 [0.11 0.3529 [0.26 0.2357 [0.17 0.3182 [0.13 1.0000 [0.83 0.0417 [0.15	34: 0.7085] 1.7% 89: 0.5428] 1.5% 76: 0.4458] 1.7% 87: 0.5487] 1.6% 89: 1.0000 1.5% 89: 1.0000 1.5% 15: 0.1033] 1.7% 19; 0.6961] 11.4%
Region1 = Eastern Africa Kamori et al(2023) Tadesse et al(2018) Kityo et al(2017) Bratholm et al(2010) Muri et al(2017) Abuogi et al(2023) Khamadi et al(2023) Random effects model Heterogeneity: $I^2 = 62\%, \tau^2 = 0.005$	7 92 1 90 0 84 0 19 0 52 10 199 1 74 610 1, p = 0.01		0.0761 [0.03 0.0111 [0.00 0.0000 [0.00 0.0000 [0.00 0.0503 [0.02 0.0503 [0.02 0.0135 [0.00	11; 0.1505] 1.7% 03; 0.0604] 1.7% 00; 0.0430] 1.7% 00; 0.1765] 1.5% 00; 0.0685] 1.6% 44; 0.0905] 1.7% 03; 0.0730] 1.7% 13; 0.0416] 11.6%
Region1 = Southern Africa Rossouw et al(2015) Stoddart et al(2014) Taylor et al(2011) Beghin et al(2020) Beghin et al(2020) Vaz et al(2018) Makadzange et al(2015) Makatini et al(2019) Pillay et al(2014) Hunt et al(2023) Tambuyzer et al(2016) Lange et al(2015) Random effects model Heterogeneity: l^2 = 97%, t^2 = 0.106	32 65 109 370 14 41 3 29 9 64 4 248 4 102 21 22 1 89 64 809 46 101 2 10 1950 1, p < 0.01		0.4923 [0.36 0.2946 [0.24 0.3415 [0.22 0.1034 [0.02 0.1034 [0.02 0.0161 [0.00 0.0392 [0.01 0.9545 [0.77 0.0112 [0.00 0.4751 [0.35 0.2000 [0.02 0.2213 [0.08	60; 0.6193] 1.7% 86; 0.3439] 1.7% 08; 0.5059] 1.6% 19; 0.2735] 1.6% 64; 0.2502] 1.7% 08; 0.0948] 1.7% 08; 0.0941 1.7% 08; 0.0974 1.7% 08; 0.0974 1.7% 06; 0.0576 1.7% 06; 0.5576 1.7% 52; 0.5561] 1.4% 31; 0.3990] 19.7%
Region1 = Western and Centra Chaix et al(2005) Rodriguez-Galet et al(2023) Rubio-Garrido et al(2021) Mossoro-Kpinde et al(2017) Kebe et al(2017) Yendewa et al(2017) Brice et al (2020) Sylla et al (2019) Adje-Toure et al(2008) Tagnouckam Ngoupo et al(2021) Amani-Bossé et al(2017) Fokam et al(2011) Fofana et al(2011) Fofana et al(2013) Charpentier et al(2012) Bouassa et al(2019) Random effects model Heterogeneity: $l^2 = 90\%$, $\tau^2 = 0.061$	I Africa 22 38 1 38 2 27 11 58 0 52 0 37 4 64 5 91 17 33 20 68 3 57 1 28 4 50 1 53 6 54 4 69 12 18 835 0, p < 0.01		$\begin{array}{c} 0.5789 & [0.40 \\ 0.0263 & [0.00 \\ 0.0741 & [0.00 \\ 0.0897 & [0.09 \\ 0.0000 & [0.00 \\ 0.0625 & [0.01 \\ 0.0549 & [0.01 \\ 0.05152 & [0.33 \\ 0.2941 & [0.18 \\ 0.0526 & [0.01 \\ 0.0357 & [0.00 \\ 0.0357 & [0.00 \\ 0.0357 & [0.00 \\ 0.0189 & [0.00 \\ 0.1111 & [0.04 \\ 0.6667 & [0.40 \\ 0.1215 & [0.04 \\ 0.041$	82: 0.7369] 1.6% 07; 0.1381] 1.6% 91; 0.2429] 1.6% 87; 0.3141] 1.7% 00; 0.0685] 1.6% 73; 0.1524] 1.7% 81; 0.1236] 1.7% 98; 0.4171] 1.7% 98; 0.4171] 1.7% 00; 0.0949] 1.6% 73; 0.1524] 1.7% 98; 0.4171] 1.7% 09; 0.1835] 1.6% 05; 0.1007] 1.7% 19; 0.2263] 1.7% 99; 0.8666] 1.5% 94; 0.2165] 27.7%
Region1 = South America Machado et al(2004) Ventosa-Cubillo et al(2023) Brindeiro et al(2002) Dumans et al(2009) Bismara et al(2012) Tambuyzer et al(2016) Random effects model Heterogeneity: $l^2 = 96\%$, $\tau^2 = 0.112$	0 37 3 62 23 52 59 90 31 61 46 101 403 5, p < 0.01	₩- ₩- ₩- ₩- ₩- ₩- ₩- ₩- ₩- ₩- ₩- ₩- ₩- ₩	0.0000 [0.00 0.0484 [0.01 0.4423 [0.30 0.6556 [0.54 0.5082 [0.37 0.4554 [0.35 0.3064 [0.09	00: 0.0949] 1.6% 01: 0.1350] 1.7% 47: 0.5867] 1.6% 80: 0.7526] 1.7% 70: 0.6386] 1.7% 60: 0.5576] 1.7% 05: 0.5788] 10.0%
Region1 = Asia Shet et al(2013) Yan et al(2022) Zhao et al(2011) Hajjar et al(2012) Pang et al(2024) Tambuyzer et al(2016) Random effects model Heterogeneity: $l^2 = 98\%, \tau^2 = 0.171$	0 70 3 93 0 76 17 22 4 396 46 101 758 7, p < 0.01		0.0000 [0.00 0.0323 [0.00 0.0000 [0.00 0.7727 [0.54 0.0101 [0.00 0.4554 [0.35 0.1211 [0.00	00; 0.0513] 1.7% 67; 0.0914] 1.7% 00; 0.0474] 1.7% 63; 0.9218] 1.6% 28; 0.0257] 1.7% 60; 0.5576] 1.7% 00; 0.4133] 10.0%
Region1 = North AmericaRogo et al(2015)Fitzgibbon et al(2004)Ross et al(2015)Ross et al(2015)Ramkissoon et al(2015)Tambuyzer et al(2016)Random effects modelHeterogeneity: $I^2 = 93\%$, $\tau^2 = 0.058$	6 26 7 17 4 25 0 54 4 41 46 101 264 5, <i>p</i> < 0.01		0.2308 [0.08 0.4118 [0.18 0.1600 [0.04 0.0000 [0.00 0.0976 [0.02 0.4554 [0.38 0.1882 [0.05	97; 0.4365] 1.6% 44; 0.6708] 1.5% 54; 0.3608] 1.6% 00; 0.0660] 1.7% 60; 0.5576] 1.7% 07; 0.3783] 9.6%
Random effects model Heterogeneity: $l^2 = 96\%$, $\tau^2 = 0.100$ Test for subgroup differences: $\chi_6^2 = 3$	5341 5, <i>p</i> < 0.01 36.19, df = 6 (<i>p</i> < 0.01)	0 0.2 0.4 0.6 0.8	0.1714 [0.11	22; 0.2394] 100.0%

Test for subgroup differences: χ_6^2 = 36.19, df = 6 (p < 0.01)

Figure S7A: Forest plot of the INST mutation prevalence among treatment-naive groups



Figure S7B: Forest plot of the INST mutation prevalence among treatment-experienced groups

Study	Events	Total		Proportion	95%-CI	Weight
Region1 = Eastern Africa Boender et al(2016) Kamori et al(2023) Khamadi et al(2023) Random effects model Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, J	3 5 3 9 = 0.91	56 92 74 222		0.0536 0.0543 0.0405 0.0491	[0.0112; 0.1487] [0.0179; 0.1223] [0.0084; 0.1139] [0.0229; 0.0832]	8.3% 9.4% 9.0% 26.7%
Region1 = Western and Cer Rodríguez–Galet et al(2023) Rubio–Garrido et al(2021) Fofana et al(2023) Yendewa et al(2021) Fofana et al(2018) Djiyou et al(2023) Bouassa et al(2019) Random effects model Heterogeneity: $J^2 = 75\%$, $\tau^2 = 0.000$	ntral Afric 0 2 0 0 0 8 2 .0176, <i>p</i> <	38 27 31 64 53 54 18 285 0.01		- 0.0000 - 0.0741 0.0000 0.0000 0.1481 0.1111 0.0231	[0.0000; 0.0925] [0.0091; 0.2429] [0.0000; 0.1122] [0.0000; 0.0560] [0.0000; 0.0672] [0.0662; 0.2712] [0.0138; 0.3471] [0.0000; 0.0785]	7.2% 6.2% 6.6% 8.6% 8.1% 8.2% 5.0% 49.8%
Region1 = Asia Yan et al(2022)	0	93		0.0000	[0.0000; 0.0389]	9.5%
Region1 = South America Ventosa-Cubillo et al(2023)	4	62		0.0645	[0.0179; 0.1570]	<mark>8.5%</mark>
Region1 = Europe Francesca et al(2019)	1	22		0.0455	[0.0012; 0.2284]	5.6%
Random effects model Heterogeneity: $I^2 = 66\%$, $\tau^2 = 0$. Test for subgroup differences: χ	.0094, <i>p</i> < ² ₄ = 10.99,	684 0.01 df = 4 (p =	0.03) 0 0.05 0.1 0.15 0.2 0	0.0282	[0.0075; 0.0580]	100.0%

Figure S8A: Forest plot of the dual-class mutation prevalence among treatment-naive groups

Study	Events	Total						F	Proportion	95%-CI	Weight
Dual = NNRTI+NRTI											
Church et al(2008)	12	49							0.2449	[0.1334: 0.3887]	2.8%
Van Dyke et al(2016)	77	234			_				0.3291	[0.2692; 0.3933]	3.1%
Louis et al(2019)	121	304							0.3980	[0.3426: 0.4555]	3.1%
Inzaule et al(2018)	88	430			+				0.2047	[0.1675: 0.2459]	3.1%
Crowell et al(2017)	4	120			_				0.0333	[0.0092; 0.0831]	3.0%
Salou et al(2016)	21	201			-				0.1045	[0.0658; 0.1553]	3.1%
Kityo et al(2016)	9	279		+-					0.0323	[0.0149: 0.0604]	3.1%
Zeh et al(2011)	4	32			-1				0.1250	[0.0351; 0.2899]	2.6%
Neubert et al(2016)	2	24							0.0833	[0.0103; 0.2700]	2.5%
Hunt et al(2019)	10	220							0.0455	[0.0220; 0.0820]	3.1%
Parker et al(2003)	1	49		-					0.0204	[0.0005; 0.1085]	2.8%
Karchava et al(2006)	1	42		+					0.0238	[0.0006; 0.1257]	2.7%
Frange et al(2018)	1	84		+					0.0119	[0.0003; 0.0646]	3.0%
Tadesse et al(2019)	3	57		-+-	_				0.0526	[0.0110; 0.1462]	2.9%
Soeria-Atmadja et al(2020)	2	90		-+					0.0222	[0.0027; 0.0780]	3.0%
Aulicino et al(2019)	7	115							0.0609	[0.0248; 0.1214]	3.0%
Delaugerre et al(2009)	1	60		+ 1					0.0167	[0.0004; 0.0894]	2.9%
Ikomey et al(2017)	1	37			-				0.0270	[0.0007; 0.1416]	2.7%
Andrade et al(2017)	2	117		+					0.0171	[0.0021; 0.0604]	3.0%
Kuhn et al(2015)	18	155			•				0.1161	[0.0703; 0.1773]	3.1%
Fokam et al(2011)	1	41		+	-				0.0244	[0.0006; 0.1286]	2.7%
Vaz et al(2012)	1	112		+					0.0089	[0.0002; 0.0487]	3.0%
Yeganeh et al(2018)	3	123		+					0.0244	[0.0051; 0.0696]	3.0%
Yeganeh et al(2018)	3	123		-+					0.0244	[0.0051; 0.0696]	3.0%
de Azevedo et al(2022)	2	38		-+					0.0526	[0.0064; 0.1775]	2.7%
de Azevedo et al(2022)	1	97		+					0.0103	[0.0003; 0.0561]	3.0%
Phung et al(2015)	2	65		+					0.0308	[0.0037; 0.1068]	2.9%
Jarchi et al(2019)	2	15		-	+				0.1333	[0.0166; 0.4046]	2.2%
Khanh Thu et al(2024)	2	105		+					0.0190	[0.0023; 0.0671]	3.0%
Lehman et al(2015)	12	20					1		0.6000	[0.3605; 0.8088]	2.4%
Lehman et al(2015)	12	20				2			0.6000	[0.3605; 0.8088]	2.4%
Fisher et al(2015)	4	15		1	1		_		0.2667	[0.0779; 0.5510]	2.2%
Random effects model		3473		\diamond	>				0.0822	[0.0460; 0.1265]	91.1%
Heterogeneity: $I^2 = 94\%$, $\tau^2 =$	0.0358, p	< 0.01									
Dual = PI+NRTI											
Van Dyke et al(2016)	71	234				+			0.3034	[0.2452: 0.3667]	3.1%
Parker et al(2003)	1	49		-+					0.0204	[0.0005: 0.1085]	2.8%
Random effects model		283		~			_		0.1351	[0.0000: 0.5017]	5.9%
Heterogeneity: $I^2 = 96\%$, $\tau^2 =$	0.0821, p	< 0.01							0.1001	[010000, 010011]	0.070
Dual = INI+NRTI				_							
Frange et al(2018)	1	84		+					0.0119	[0.0003; 0.0646]	3.0%
Random effects model		3840		\diamond	>				0.0824	[0.0475; 0.1248]	100.0%
Heterogeneity: $l^2 = 94\%$, $\tau^2 =$	0.0363, p	< 0.01			T	1	1				
Test for subgroup differences:	$\chi^2_2 = 7.51$, df = 2 (j	o = 0.02)	0	0.2	0.4	0.6	0.8			

Figure S8B: Forest plot of the dual-class mutation prevalence among treatment-experienced groups

Nandom enects model	0004
Heterogeneity: $I^2 = 97\%$, $\tau^2 =$	0.0983, <i>p</i> < 0.01
Test for subgroup differences:	$\chi_2^2 = 6.15$, df = 2 (p = 0.05)

	Proportion	95%-CI	Weight
	1.0000 0.4674 0.9608 0.5000 0.4444 0.6889 0.3276 0.8077 0.7027 0.8906 0.2689 0.7500 0.1087 0.1429 0.3871 0.5789 0.1290 0.7885 0.0796 0.1071 0.3462 0.2941 0.2500 0.1967 0.2933 0.6415 0.8041 0.1475 0.2563 0.4259 0.6111 0.3005 0.7292 0.4655	$ \begin{bmatrix} 0.7354; 1.0000 \\ [0.3626; 0.5744] \\ [0.8654; 0.9952] \\ [0.3338; 0.6662] \\ [0.2548; 0.6467] \\ [0.5826; 0.7823] \\ [0.2101; 0.4634] \\ [0.6747; 0.9037] \\ [0.5302; 0.8413] \\ [0.6734; 0.9389] \\ [0.1918; 0.3579] \\ [0.6436; 0.8381] \\ [0.0534; 0.1908] \\ [0.0707; 0.2471] \\ [0.2878; 0.4938] \\ [0.3550; 0.7975] \\ [0.6530; 0.8894] \\ [0.371; 0.1458] \\ [0.0227; 0.2823] \\ [0.1721; 0.5567] \\ [0.1031; 0.5596] \\ [0.0549; 0.5719] \\ [0.1060; 0.3184] \\ [0.586; 0.6274] \\ [0.4980; 0.7686] \\ [0.7111; 0.8776] \\ [0.4980; 0.7686] \\ [0.7111; 0.8776] \\ [0.4980; 0.7686] \\ [0.7111; 0.8776] \\ [0.2923; 0.5679] \\ [0.3575; 0.8270] \\ [0.2557; 0.3483] \\ [0.3622; 0.5703] \\ \end{bmatrix} $	2.2% 2.6% 2.5% 2.5% 2.5% 2.5% 2.6% 2.6% 2.6% 2.6% 2.6% 2.6% 2.6% 2.6
	0.2500 0.4754 0.0101 0.1943	[0.0866; 0.4910] [0.3460; 0.6073] [0.0012; 0.0358] [0.0001; 0.5650]	2.3% 2.5% 2.6% 7.5%
	0.3902 0.1311 0.0101 0.1348	[0.2420; 0.5550] [0.0584; 0.2422] [0.0012; 0.0358] [0.0000; 0.4180]	2.5% 2.5% 2.6% 7.6%
0.2 0.4 0.6 0.8 1	0.4156	[0.3173; 0.5172]	100.0%

Figure S9A: Forest plot of the triple-class mutation prevalence among treatment-naive groups

Study	Events	Total		Proportion	95%-CI	Weight
Van Dyke et al(2016) Neubert et al(2016) Frange et al(2018) Frange et al(2018) Ngo-Giang-Huong et al(2016) Ngo-Giang-Huong et al(2016) Aulicino et al(2019) Andrade et al(2017) Phung et al(2015) Fisher et al(2015)	43 0 0 0 0 1 0 2 1	234 24 84 476 476 115 117 65 15		0.1838 0.0000 0.0000 0.0000 0.0000 0.0000 0.0087 0.0000 0.0308 0.0667	$\begin{bmatrix} 0.1363; 0.2394 \\ 0.0000; 0.1425 \\ 0.0000; 0.0430 \\ 0.0000; 0.0430 \\ 0.0000; 0.0077 \\ 0.0000; 0.0077 \\ 0.0000; 0.0077 \\ 0.0002; 0.0475 \\ 0.0000; 0.0310 \\ 0.0037; 0.1068 \\ 0.0017; 0.3195 \\ 0.0017; 0.001; 0.$	11.3% 7.6% 10.2% 10.2% 11.6% 11.6% 10.6% 10.7% 9.8% 6.3%
Random effects model Heterogeneity: $I^2 = 94\%$, $\tau^2 = 0.01$	81, p < 0	1690 .01	0 0.05 0.1 0.15 0.2 0.25 0.3	0.0094	[0.0000; 0.0404]	100.0%

Figure S9B: Forest plot of the triple-class mutation prevalence among treatment-experienced groups

Study	Events	Total
Rodríguez-Galet et al(2023)	1	38
Rubio-Garrido et al(2021)	2	27
Tadesse et al(2018)	1	90
Mossoro-Kpinde et al(2017)	8	58
Taylor et al(2011)	2	41
Delaugerre et al(2007)	27	119
Yan et al(2022)	3	93
Amani-Bossé et al(2017)	1	28
Rogo et al(2015)	3	26
Fitzgibbon et al(2004)	1	17
Fokam et al(2011)	3	50
Fofana et al(2018)	2	53
Bismara et al(2012)	8	61
Abuogi et al(2023)	8	199
Abuogi et al(2023)	8	199
Abuogi et al(2023)	8	199
Djiyou et al(2023)	6	54
Bouassa et al(2019)	9	18
Pang et al(2024)	3	396
Random effects model		1766
	A 4 4	0.01

Heterogeneity: $I^2 = 84\%$, $\tau^2 = 0.0147$, p < 0.01

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+							
<u>i</u>	+	-					
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					101		
100			3		100		
	_						
0.	1	0.2	0.3	0.4	0.5	0.6	0.7

Proportion	95%-CI	Weight
0.0263	[0.0007; 0.1381]	4.8%
0.0741	[0.0091; 0.2429]	4.3%
0.0111	[0.0003; 0.0604]	5.8%
0.1379	[0.0615; 0.2538]	5.4%
0.0488	[0.0060; 0.1653]	4.9%
0.2269	[0.1552; 0.3127]	6.1%
0.0323	[0.0067; 0.0914]	5.9%
0.0357	[0.0009; 0.1835]	4.3%
0.1154	[0.0245; 0.3015]	4.2%
0.0588	[0.0015; 0.2869]	3.5%
0.0600	[0.0125; 0.1655]	5.2%
0.0377	[0.0046; 0.1298]	5.3%
0.1311	[0.0584; 0.2422]	5.4%
0.0402	[0.0175; 0.0777]	6.4%
0.0402	[0.0175; 0.0777]	6.4%
0.0402	[0.0175; 0.0777]	6.4%
0.1111	[0.0419; 0.2263]	5.3%
0.5000	[0.2602; 0.7398]	3.6%
0.0076	[0.0016; 0.0220]	6.7%
0.0669	[0.0367; 0.1039]	100.0%

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PRISMA Checklist

Section and Topic	Item #	Checklist item	Page where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2-3
INTRODUCTION	<u> </u>		
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	
METHODS	<u> </u>		
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable details of automation tools used in the process.	6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	7
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5))	8
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	8
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	8
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta- analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used	8-9
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	8
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	8
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	8
RESULTS			
Study selection	Idy selection16aDescribe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.		9, Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	9
Study characteristics	17	Cite each included study and present its characteristics.	9, Table 1

Risk of bias in studies	18	Present assessments of risk of bias for each included study.	9, Table S3		
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.			
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	9-10		
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	10-12		
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	10-11		
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	11		
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	10-11		
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	9-12		
DISCUSSION					
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	12		
	23b	Discuss any limitations of the evidence included in the review.	14-15		
	23c	Discuss any limitations of the review processes used.	14-15		
	23d	Discuss implications of the results for practice, policy, and future research.	12-15		
OTHER INFORMATIO	N	<u>.</u>			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	7		
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	7		
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	7		
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	9		
Competing interests	26	Declare any competing interests of review authors.	16		
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	16		

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71