ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE
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Innovation and Integration of Laboratory and Clinical Systems
Reshaping the Future of HIV, TB, Malaria, Flu,
Neglected Tropical Diseases and Emerging Pathogens in Africa

Virological and HIV drug resistance outcomes of antiretroviral therapy in Central and West Africa:

challenges to improve treatment monitoring in contexts of generalized HIV epidemic

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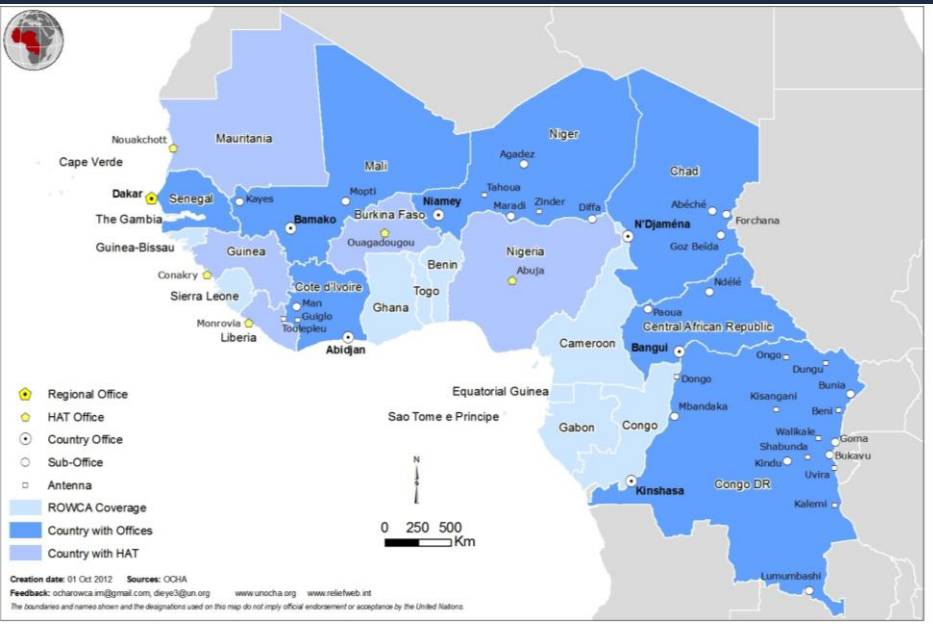
HIV infection in West-Central Africa



Country scorecard: Adult access to antiretroviral therapy, 2013

≥40%

Botswana
Burundi
Burkina Faso
Cabo Verde
Eritrea
Ethiopia
Gabon
Kenya
Malawi
Namibia
Rwanda
South Africa
Swaziland
Uganda
United Republic of Tanzania (the)
Zambia
Zimbabwe

25–39%

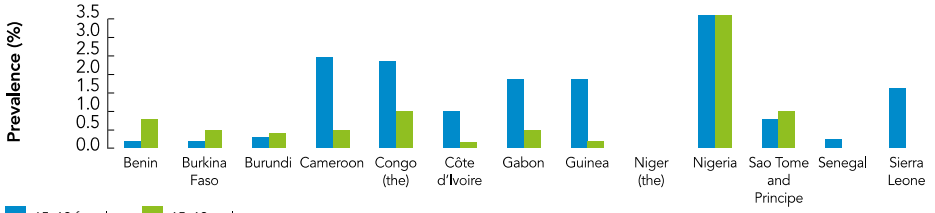
Angola
Benin
Cameroon
Congo (the)
Côte d'Ivoire
Gambia
Ghana
Lesotho
Mali
Mozambique
Niger (the)
Senegal
Togo

<25%

Central African Republic (the)
Chad
Democratic Republic of the Congo (the)
Guinea
Guinea-Bissau
Liberia
Madagascar
Mauritius
Nigeria
Sao Tome and Principe
Sierra Leone
South Sudan

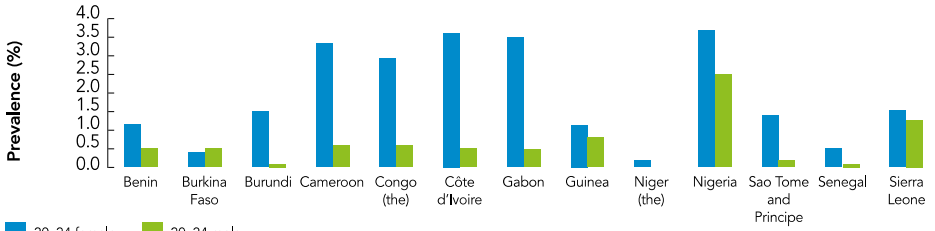
Source: UNAIDS 2013 estimates

HIV prevalence among young people aged 15–19 in west and central Africa



Source: most recent population-based survey.

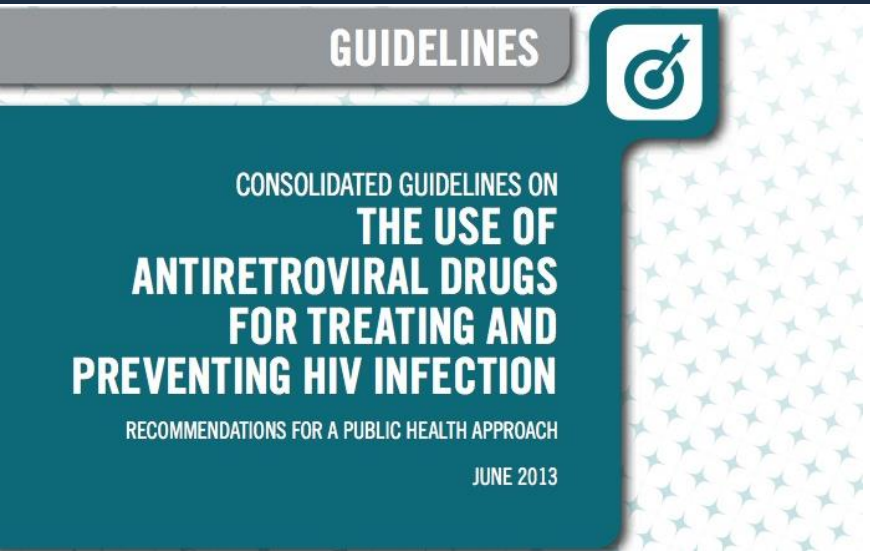
HIV prevalence among young people aged 20–24 in west and central Africa



Source: most recent population-based survey.

Source: UNAIDS 2013 estimates

ART access & Monitoring in WCA



Viral load recommended, but not routinely available

ART initiation	CD4 cell count	Haemoglobin test for AZT[d] Pregnancy test Blood pressure measurement Urine dipsticks for glycosuria and estimated glomerular filtration rate (eGFR) and serum creatinine for TDF[e] Alanine aminotransferase for NVP[f]
Receiving ART	CD4 cell count (every 6 months) HIV viral load (at 6months after initiating ART and every 12 months thereafter)	Urine dipstick for glycosuria and serum creatinine for TDF[c]
Treatment failure	CD4 cell count HIV viral load	HBV (HBsAg) serology[a] (before switching ART regimen if this testing was not done or if the result was negative at baseline)

First-line ART	Preferred first-line regimens	Alternative first-line regimens[a b]
Adults (including pregnant and breastfeeding women and adults with TB and HBV coinfection)	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV AZT + 3TC + NVP TDF + 3TC (or FTC) + NVP
Adolescents (10 to 19 years) ≥35 kg		AZT + 3TC + EFV AZT + 3TC + NVP TDF + 3TC (or FTC) + NVP ABC + 3TC + EFV (or NVP)
Children 3 years to less than 10 years and adolescents <35 kg	ABC + 3TC + EFV	ABC + 3TC + NVP AZT + 3TC + EFV AZT + 3TC + NVP TDF + 3TC (or FTC) + EFV TDF + 3TC (or FTC) + NVP
Children <3 years	ABC or AZT + 3TC + LPV/r	ABC + 3TC + NVP AZT + 3TC + NVP

Essentially 2NRTIs + NNRTI
First-line regimens >95% of ART

Virological Response to 1st line ART

Data from a few recent studies: **ADULTS**

Country	**Location**	**ART duration** (months)	**Design**	**VL threshold** (copies/ml)	**Failure rate** (%)	**HIVDR** (%)	**Author.,** Date
Cameroon	Urban	12	CS	1000	**16.4**	**4.4**	Kouanfack, 2009
Cameroon	Urban	12	WHO-M	1000	**9.2**	**5.3**	Billong, 2013
Cote d'Ivoire	Urban	12	Cohort	300	**25.0**	**12.0**	Messou, 2013
Nigeria	Urban	12	WHO-M	1000	**10.4**	**5.2**	Ugbena, 2012
Togo	Urban	12	CS	1000	**30.8**	**24.5**	Dagnra, 2011

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Cameroon	Urban	**24**	CS	1000	**22.5**	**16.8**	Kouanfack, 2009
CAR	Urban	**24**	CS	1000	**28.5**	**-/-**	Péré, 2012
Cote d'Ivoire	Urban	**24**	Cohort	300	**27.0**	**19.0**	Messou, 2013
DRC	Urban	**25**	CS	1000	**14.6**	**11.7**	Muwonga, 2011
Cameroon	Urban	**36**	CS	1000	**17.6**	**14.0**	Aghokeng, 2013

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Virological Response to 1st line ART

Data from a few recent studies: **Rural sites**

Country	**Age group**	**ART duration** (months)	**Design**	**VL threshold** (copies/ml)	**Failure rate** (%)	**HIVDR** (%)	**Author.,** Date
Gabon	Adults	33	CS	1000	**41.3**	**21.3**	Zoufaly, 2013
Cameroon	Adults	24	CS	1000	**38.6**	**25.0**	Rouet, 2006
Cameroon	Children	40	CS	200	**53.0**	**-/-**	Germanaud, 2010

Virological Response to 1st line ART

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Virological Response to 1st line ART

Data from a few recent studies: **Children**

Country	**Age group**	**ART duration** (months)	**Design**	**VL threshold** (copies/ml)	**Failure rate** (%)	**HIVDR** (%)	**Author.,** Date
Cameroon	<18 yrs	40	CS	200	**53.0**	**-/-**	Zoufaly, 2013
Cote d'Ivoire	6.5 yrs	36	Cohort	300	**50**	**-/-**	Rouet, 2006
Mali	2.5 yrs	6	Cohort	400	**44.0**	**22.5**	Germanaud, 2010
Senegal	7 yrs	20	CS	1000	**56.0**	**38.5**	Kebe, 2013

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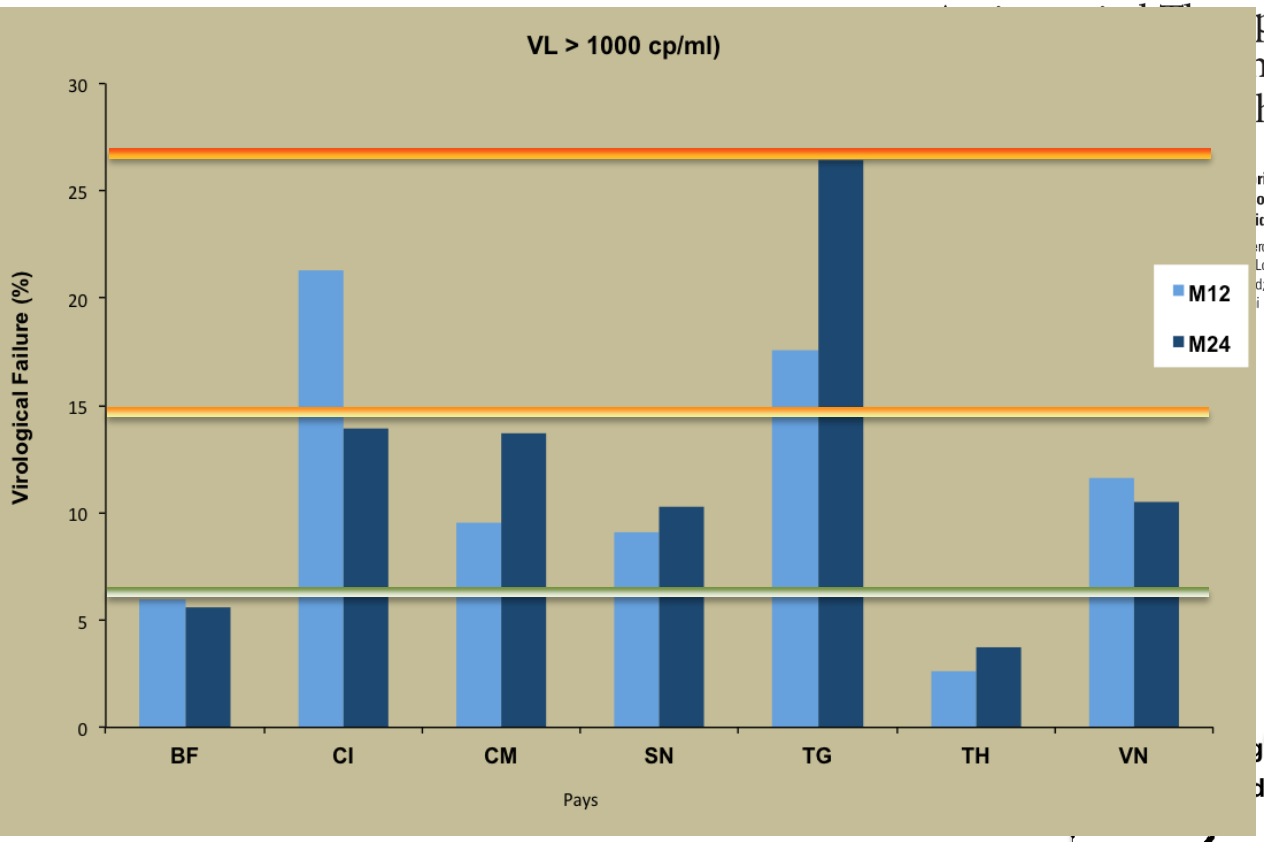
ANRS Virology Group: 12186 Study

MAJOR ARTICLE HIV/AIDS

Extraordinary Heterogeneity of Virological Outcomes in Patients Receiving Highly py and Monitored With the nization Public Health haran Africa and Southeast Asia

rina Eymard-Duvernay,[2] Anoumou Dagnra,[3] Dramane Kania,[4] oumba Touré-Kane,[7] Lien X. T. Truong,[8] Eric Delaporte,[2] idjo Ayouba;[2] for the ANRS 12186 Study Group[a]

eroon; [2]UMI 233 TransVIHMI, IRD and Université de Montpellier 1, Montpellier; [3]Centre Lomé, Togo; [4]Laboratoire de Virologie, Centre Muraz, Bobo-Dioulasso, Burkina Faso; [5]IRD UMI d; [6]Programme PAC-CI, Abidjan, Cote d'Ivoire; [7]Laboratoire de Bactériologie-Virologie, Dakar, i Minh City, Vietnam; and [9]Université Paris Descartes, EA 3620, AP-HP, Laboratoire de



Drug Resistance Mutations

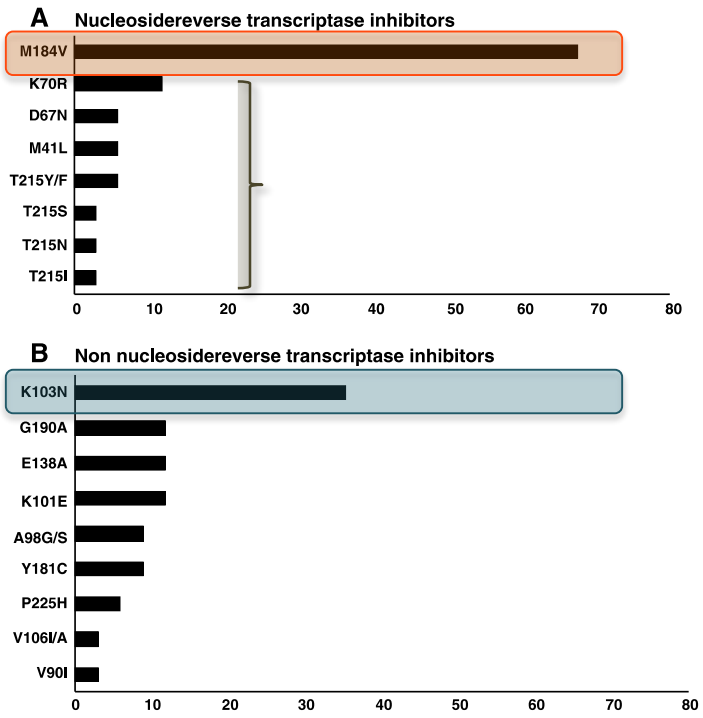


FIG. 2. Percentage of patients whose viruses showed resistance-associated mutations to nucleoside reverse transcriptase inhibitors (NRTI) **(A)**, nonnucleoside reverse transcriptase inhibitors (NNRTI) **(B)**, or protease inhibitors (PI) **(C)**, out of 45 patients followed up at "Hôpital de Jour" and treated by antiretroviral drugs whose laboratory monitoring from July 2009 to October 2009 demonstrated detectable plasma HIV-1 RNA load.

Péré H. et al., 2012 (CAR)

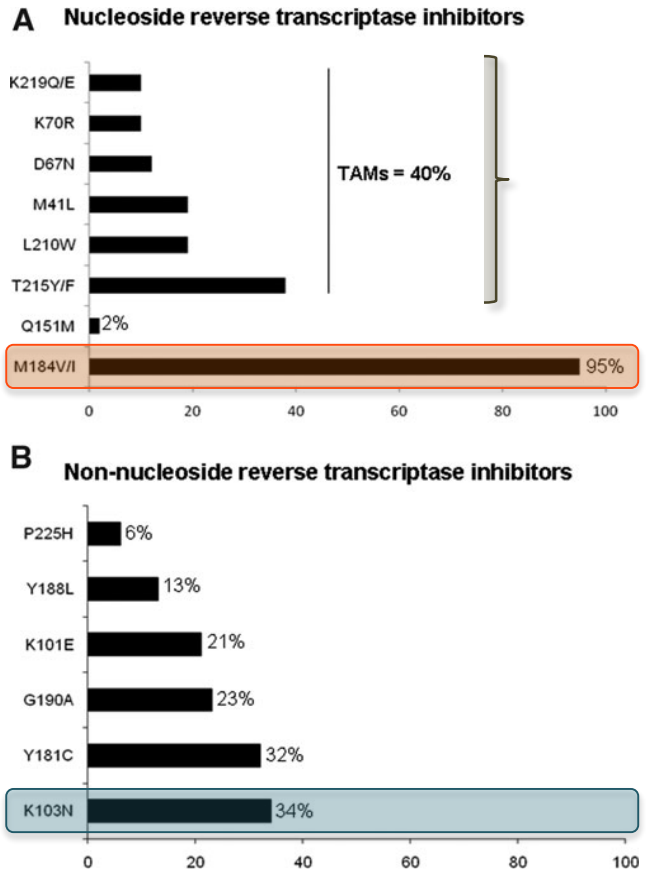


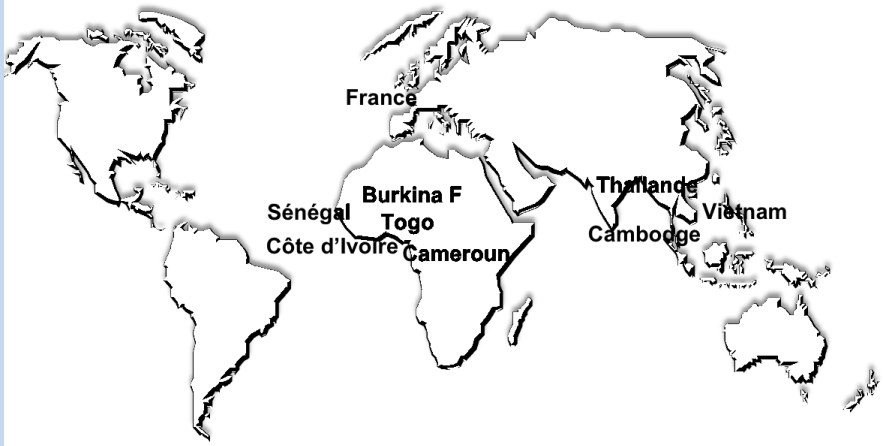
FIG. 2. Percentages of resistance-associated mutations to nucleoside reverse transcriptase inhibitors **(A)** and to non-nucleoside reverse transcriptase inhibitors **(B)** observed in children followed-up at the Hôpital d'Enfants Albert Royer of Dakar, Senegal, who were receiving a first-line antiretroviral regimen for a median time of 26 months, and whose plasma HIV-1 RNA load was ≥ 3.0 $\log_{10}$ copies/ml. Forty-nine (94%) children were in virological failure according to the 2010 revised criteria. TAMs, thymidine-analogue mutations.

Kebe K. et al., 2013 (Senegal)

Drug Resistance Mutations

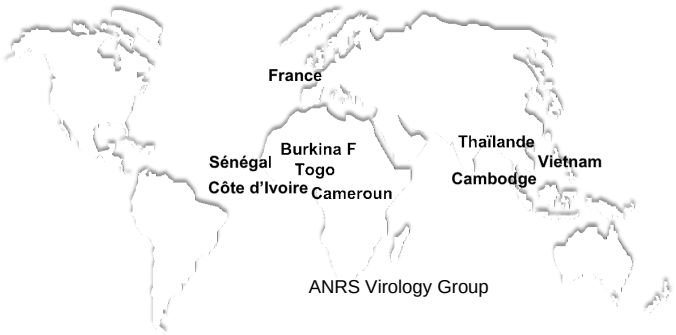
Patients	ARV regimen	Affected ARVs	RT resistance mutations	VL, Log10 copies/ml	Subtype
M12					
1	NVP 3TC d4T	ABC	41L 103S 184V 190A 215Y	5,2	CRF02
2	EFV 3TC TDF	DDI	65R 90I 100I 103N 184I	5,2	CRF06
3	EFV 3TC AZT	ABC DDI	74LV 101P 103N 184V	6,3	CRF02
4	EFV 3TC d4T	ABC DDI	74ILV 100IL 103N 184V 215F	5,6	CRF02
5	NVP 3TC d4T	DDI FTC	65R 101E 181C	3,8	C
6	NVP 3TC d4T	DDI FTC	65R 67E 101Q 181C 190A	5,4	CRF02
7	NVP/EFV 3TC TDF	DDI ETR	65R 98G 106I 115F 181C 184V 188L	6,0	C
8	NVP 3TC d4T	ABC DDI ETR	74V 103N 181C 184V 221HY	5,6	CRF02
9	NVP 3TC d4T	ABC DDI ETR	69N 70R 74LV 108IV 181C 184V 221Y	3,8	CRF01
10	NVP 3TC d4T	ABC ETR TDF	41LM 67DN 70R 98G 103KN 181C 184V 215F 219EQ 221Y 230LM	5,5	CRF02
11	EFV 3TC d4T	ABC ETR RPV	41LM 103N 138Q 179E 184V 215Y 238R	5,0	CRF01
12	NVP 3TC d4T	DDI ETR FTC	65R 69d 90I 181C 190A 219R	5,5	CRF02
13	NVP 3TC d4T	DDI ETR FTC	65R 181C 190A 221HR 230MV	3,4	CRF01
14	NVP 3TC d4T	DDI ETR RPV	65KR 103N 181V 184MV 221Y	5,0	CRF02
M24					
1	EFV 3TC d4T/AZT	ABC	41LM 100I 103N 184V 215F	6,8	CRF09
2	NVP 3TC AZT	ABC	103N 184V 210LRW 215Y	5,4	CRF02
3	NVP 3TC d4T	ABC	67DN 179IV 181C 184V 215Y	5,2	CRF06
4	NVP 3TC d4T/AZT	ABC	41L 98G 103NS 181C 184V 215Y	5,4	CRF06
5	EFV 3TC d4T	ABC	67N 75M 103N 184V 190AG 215F	4,3	CRF01
6	NVP 3TC d4T	ABC	75M 77L 101KQ 179I 184V 190A 210W 215Y	5,0	CRF01
7	EFV 3TC AZT	ABC TDF	41L 103N 184V 210LW 215Y	5,9	CRF06
8	NVP 3TC d4T	ABC TDF	41L 67N 70KR 98G 103R 179E 184V 188L 215F 219KQ	5,1	CRF02
9	EFV 3TC AZT	ABC TDF	41L 103N 184V 188L 210W 215Y	3,8	CRF02
10	NVP 3TC d4T/AZT	ABC TDF	67DN 101E 184V 190A 210W 215Y	5,5	CRF02
11	NVP 3TC d4T	ABC ETR	67N 70R 90I 101E 181C 184IMV 190A 210W 219E	5,1	CRF02
12	NVP 3TC d4T	ABC ETR	41L 75T 181C 184V 215Y 221Y	4,5	CRF02
13	NVP 3TC d4T	ABC ETR	67DN 181C 184V 215F 221Y	4,6	CRF01
14	NVP 3TC d4T	ABC ETR	67DN 101E 179I 184V 190A 215F	4,2	CRF01
22	NVP 3TC d4T	DDI ETR	65R 69d 101E 106I 181C 190A 219R 221Y	4,0	U
15	EFV 3TC d4T	ABC DDI TDF	67G 69N 70R 74I 100I 103N 179I 184V 215F 219E	5,5	CRF22
16	NVP 3TC d4T/AZT	ABC DDI TDF	41L 74V 101Q 181C 184V 210W 215Y	4,5	CRF06
17	NVP 3TC AZT	ABC TDF ETR	41L 67DN 70KR 98AG 103R 179E 181C 184V 215FY 219EK 221HY	4,0	CRF14
18	NVP 3TC AZT	ABC TDF ETR	41LM 67G 70A 181C 184V 210LW 215Y 221Y	4,0	CRF36
19	NVP 3TC d4T/AZT	ABC TDF ETR	41L 67DN 98G 106I 181C 184V 210W 215Y 221Y	5,5	CRF06
20	NVP 3TC d4T	ABC TDF ETR	41L 44D 67N 75M 101E 179I 181I 184V 210W 215Y	4,7	CRF01
21	NVP 3TC d4T	ABC TDF ETR	41L 75M 77L 98G 101EQ 179T 181C 184V 190A 210W 215Y 219N	4,9	CRF01
23	NVP 3TC d4T/AZT	ABC DDI TDF ETR	41L 67N 74V 103N 181C 184V 210RW 215F 221Y	4,8	CRF02
24	NVP 3TC d4T/AZT	ABC DDI TDF ETR	41L 44D 74LV 103N 179IV 181C 184V 210W 215Y 221Y	5,9	CRF02
25	NVP 3TC d4T	ABC DDI TDF ETR	67DN 74LV 106IV 181C 184V 190AG 210M 215F 219N 230L	4,3	CRF01
26	NVP 3TC d4T	ABC DDI TDF ETR	67DN 74V 179I 181C 184V 210W 215F 219KN 221Y 230L	6,2	CRF01
27	NVP 3TC d4T/AZT	ABC DDI TDF RPV	41L 74V 106A 179E 184V 210W 215Y 221Y	6,1	CRF02
28	NVP 3TC d4T	ABC TDF ETR RPV	41LM 98G 103N 138Q 184V 210LRW 215Y	5,1	CRF02

ARV: antiretroviral; RT: reverse transcriptase; VL: viral load; d4T: Stavudine, 3TC: Lamivudine, AZT: Zidovudine, TDF: tenofovir, ABC: abacavir; ddI: didanosine; ETR: Etravirine; RPV: rilpivirine; NVP: Nevirapine, EFV: Efavirenz.



Accumulation of HIV DRM

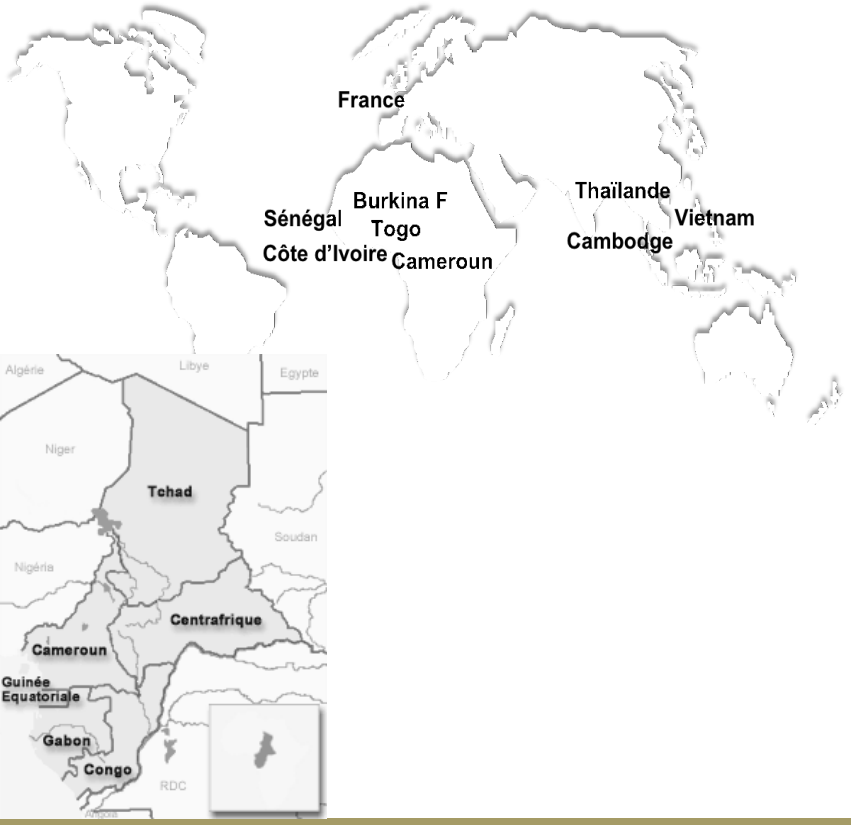
Transmitted Drug Resistance



Surveillance of transmitted HIV-1 DR in Africa and Asia (2006-2009) – ANRS12134

Country	Year	Population	Sample size	PI	NRTI	NNRTI
Chad (*Ndjamena*)	2006-07	ANC, <25	**59**	<5%	<5%	<5%
Burkina Faso (*Bobo*)	2006-07	ANC, <25	**51**	<5%	<5%	<5%
Cameroun (*Yaoundé*)	2006-07	ANC, <25	**59**	<5%	<5%	5%-15%
Cameroun (*Douala*)	2006-07	ANC, <25	**67**	<5%	5%-15%	<5%
Cote d'Ivoire (*Abidjan*)	2006-07	ANC, <25	**48**	<5%	<5%	<5%
Senegal (*Dakar*)	2006-07	VCT	**48**	<5%	<5%	<5%
Cambodia (*Phnom P*)	2006-07	VCT	**67**	<5%	<5%	<5%
Thailand (*Chiang Mai*)	2006-07	ANC, <25	**56**	<5%	<5%	<5%
Vietnam (*Ho Chi M*)	2006-07	VCT	**63**	<5%	<5%	<5%

Drug Resistance in ART Naive



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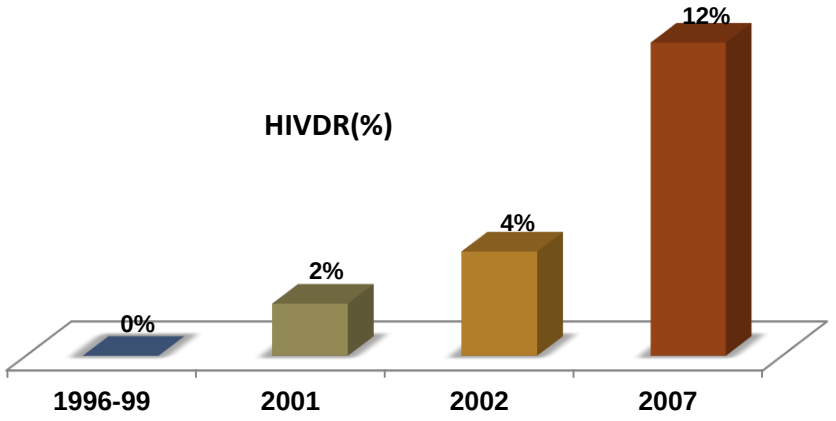
Scale-up of antiretroviral treatment in sub-Saharan Africa is accompanied by increasing HIV-1 drug resistance mutations in drug-naive patients

Avelin F. Aghokeng[a,c], Charles Kouanfack[b], Christian Laurent[c], Eugenie Ebong[a], Arrah Atem-Tambe[a], Christelle Butel[c], Celine Montavon[a,c], Eitel Mpoudi-Ngole[a], Eric Delaporte[c] and Martine Peeters[c]



Additional studies needed with new WHO protocols

Challenges & way forward

1. Programmatic factors

- Adherence to treatment
- Lost to follow-up
- Drug stock-outs
- Cost reduction
- Access to care services

2. Improved Virological Monitoring

- **Better access to routine viral load is essential**
- **Field friendly tools as DBS exist**
- **Point-of-care will support rural areas**

3. Prevent HIV drug resistance

- **Low genetic barrier drugs is a concern**
- **Viral load access may prevent accumulation of DRM and better switches to 2nd lines.**
- **Surveillance studies should be promoted**

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- Eric Delaporte
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- Amandine
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IRD

- Eitel Mpoudi-Ngole
- Ginette Edoul
- Jenny Domyeum
- Landry Tsoumtsa
- Thomas
- Clarisse
- …

Cremer

ANRS Virology group

- Vincent Calvez
- Diane Descamps
- Avelin F Aghokeng
- Martine Peeters
- Marie-Laure Chaix
- Toni Thomas d'Aquin
- Françoise Brun-Vézinet
- Xuan Lien
- Coumba Touré Kane
- Diane Descamps
- Nicole N'Go
- Kania Dramane
- Janin Nouhin
- François Rouet
- Hervé Fleury
- J-Christophe Plantier
- Ahidjo Ayouba
- Florian Liégeois
- Anoumou Dagnra
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- Brigitte Bazin
- Claire Rekacewicz

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