HIV Drug resistance in Senegal

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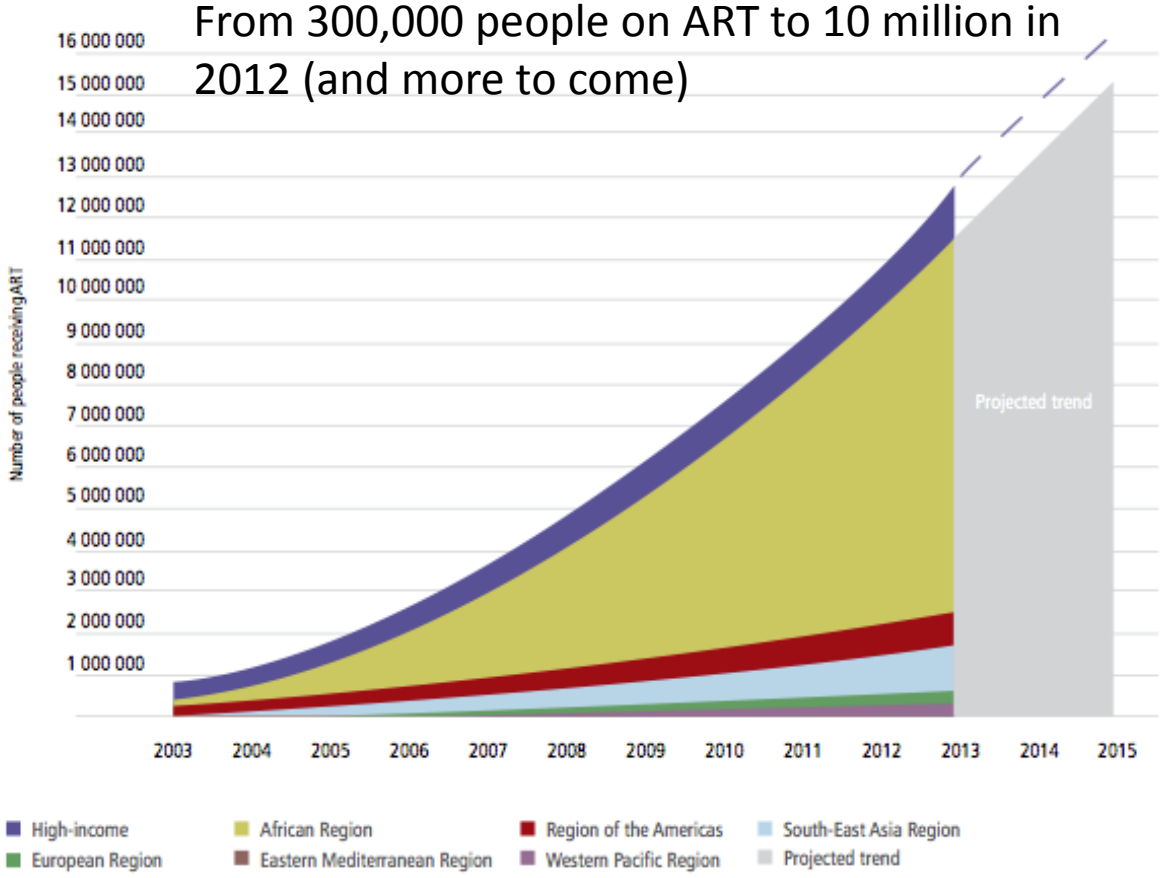
Outline

1. Introduction
2. Background on HIV Epidemiological situation
3. Acquired drug resistance in Adults
4. Acquired drug resistance in children
5. Transmitted drug resistance
6. HIV-2 drug resistance
7. Summary

Introduction

Actual and projected numbers of people receiving antiretroviral therapy in low- and middle-income countries by WHO region and in high-income countries across WHO regions, 2003–2015[a]



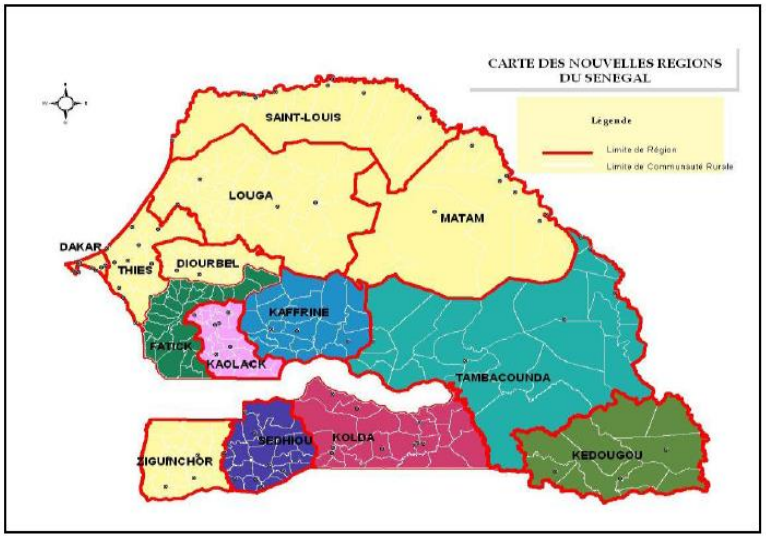
[a]Country income classification by the World Bank at the time of the 2011 Political Declaration on HIV and AIDS.

Source: Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS)

Despite benefits that rapid scale-up has had on AIDS-related morbidity and mortality,

Potential for widespread emergence and transmission of HIV drug resistance (HIVDR) to antiretrovirals (ARVs) has been a major ongoing concern of public health experts.

Background Senegal



HIV Epidemic : Prevalence

high

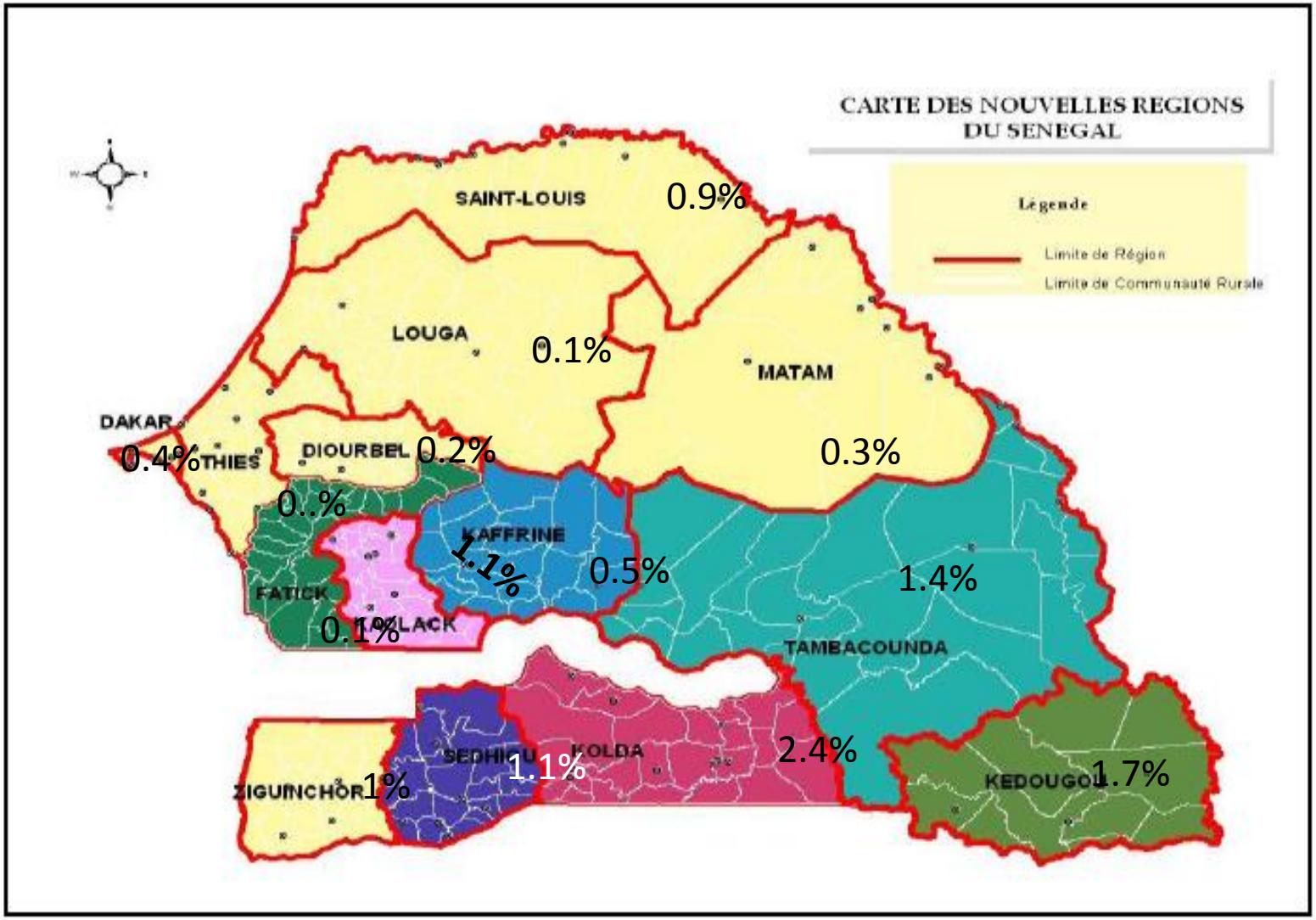
- SW (18.5-19.8 %)
- MSM (21.5-21.8 %)
- IDU (9.4 %)

low

- General Population (0.7%)
- Pregnant Women (0.7 %)

(DHS, 2006-2010)

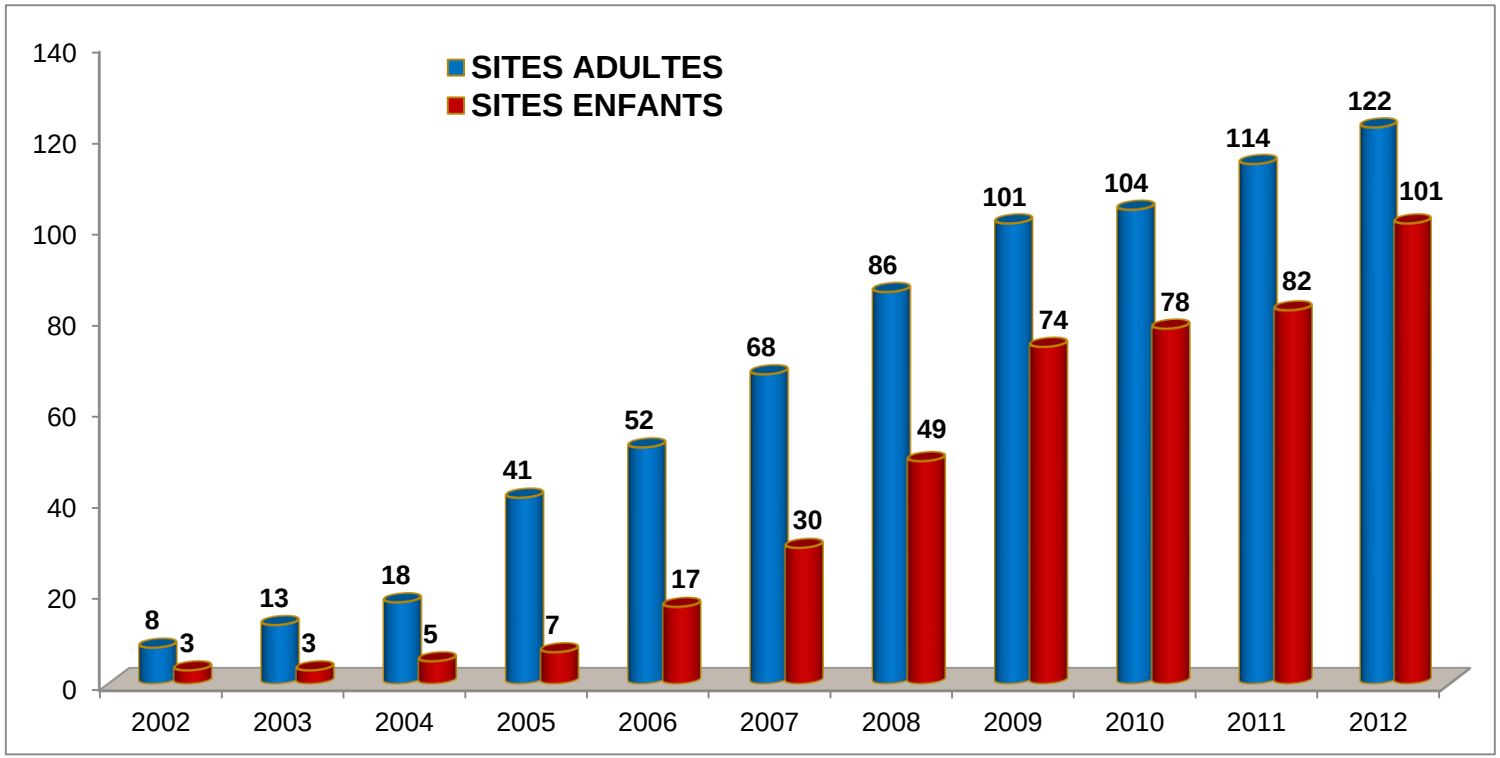
Disparities in HIV Prevalence from North to South



Background ART

❖ Senegal

✓ **ISAARV, 18352 of HIV patients on ART=> 78% of coverage[2]**



Sites monitoring from 2002 to 2012

Background ART

- ARVs free of charge
- diagnostic tests immunovirological monitoring since 2003
- Virological monitoring centralized in Dakar
- Viral load: D0, M6 and then every 6 months
- Virological rebound => Resistance Genotyping

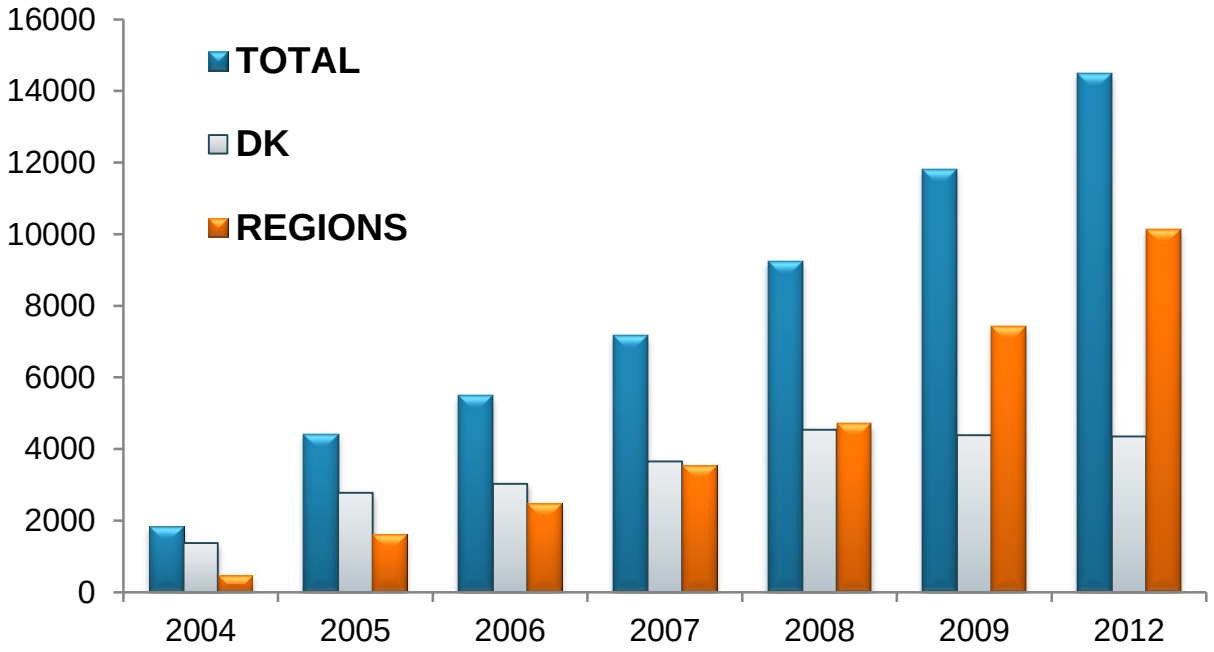
- Patient Cohorts in Resarch projects: Regular virological monitoring
- Patients Public health : +/- regular monitoring

Background : CD4 and viral load

- CD4 system
  - 86 CD4
- Viral load
  - 4 machines
  - Referal samples using DBS challenging
  - Procurement system (Central warehouse by two years international tenders)
  - Currently, reagents and consumables are obtained from distributors in Dakar, which increases the courier costs
  - Timely planning of procurement could be key
- Regional Laboratories
  - Limited space is a key factor
  - Re-organisation of labs was conducted to improve workflow and reduce contamination risk.

Background ART coverage

Senegal ISAARV ➔1998 (national initiative)

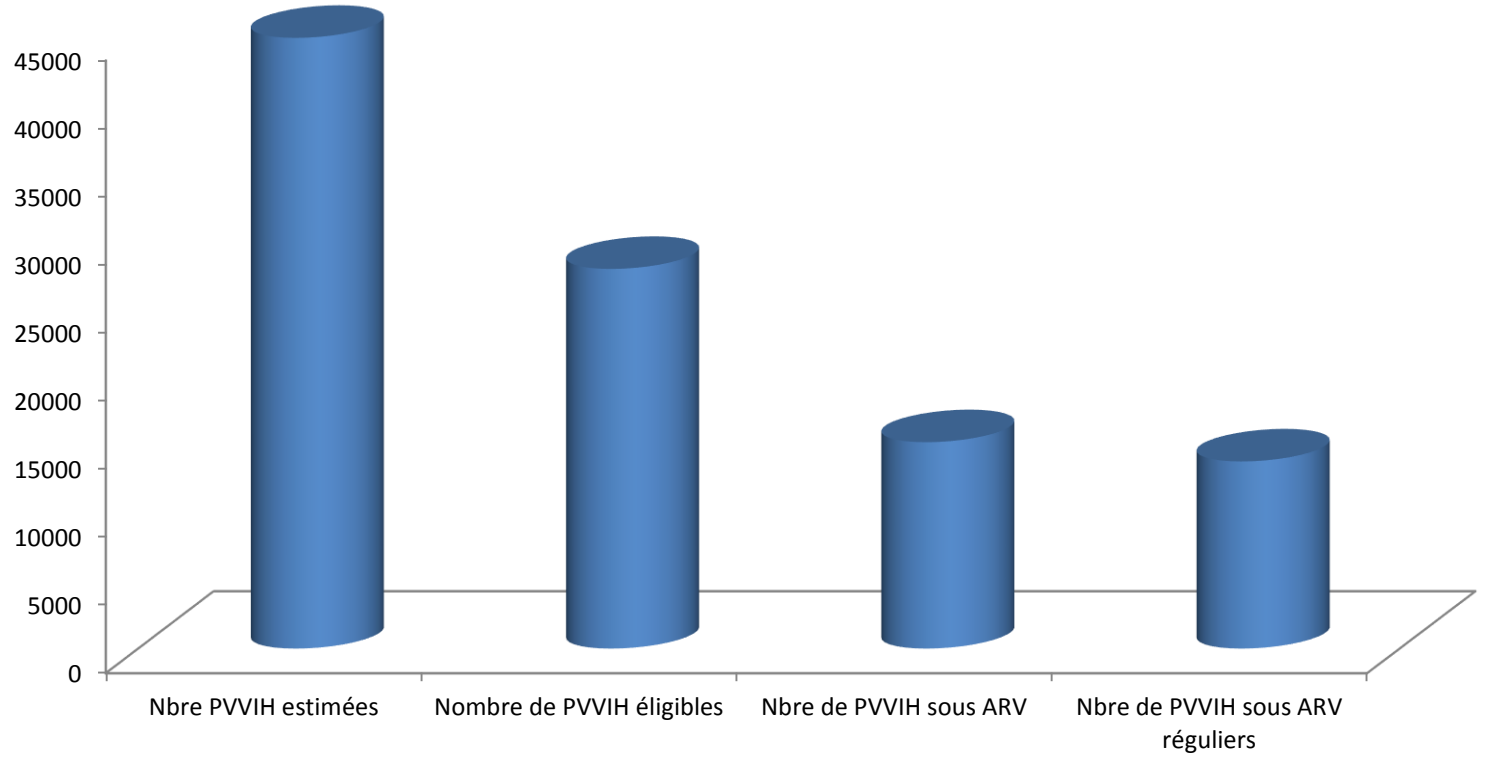


In 2004, 74% of patients were followed in Dakar

Since 2008, inversion of that trend

In 2012, 70% of new inclusions on ART in regions

ART coverage in 2013 : cascade



Coverage in 2013

71% for adults (31% H et 69% F)

29% for children

Antiretroviral treatment

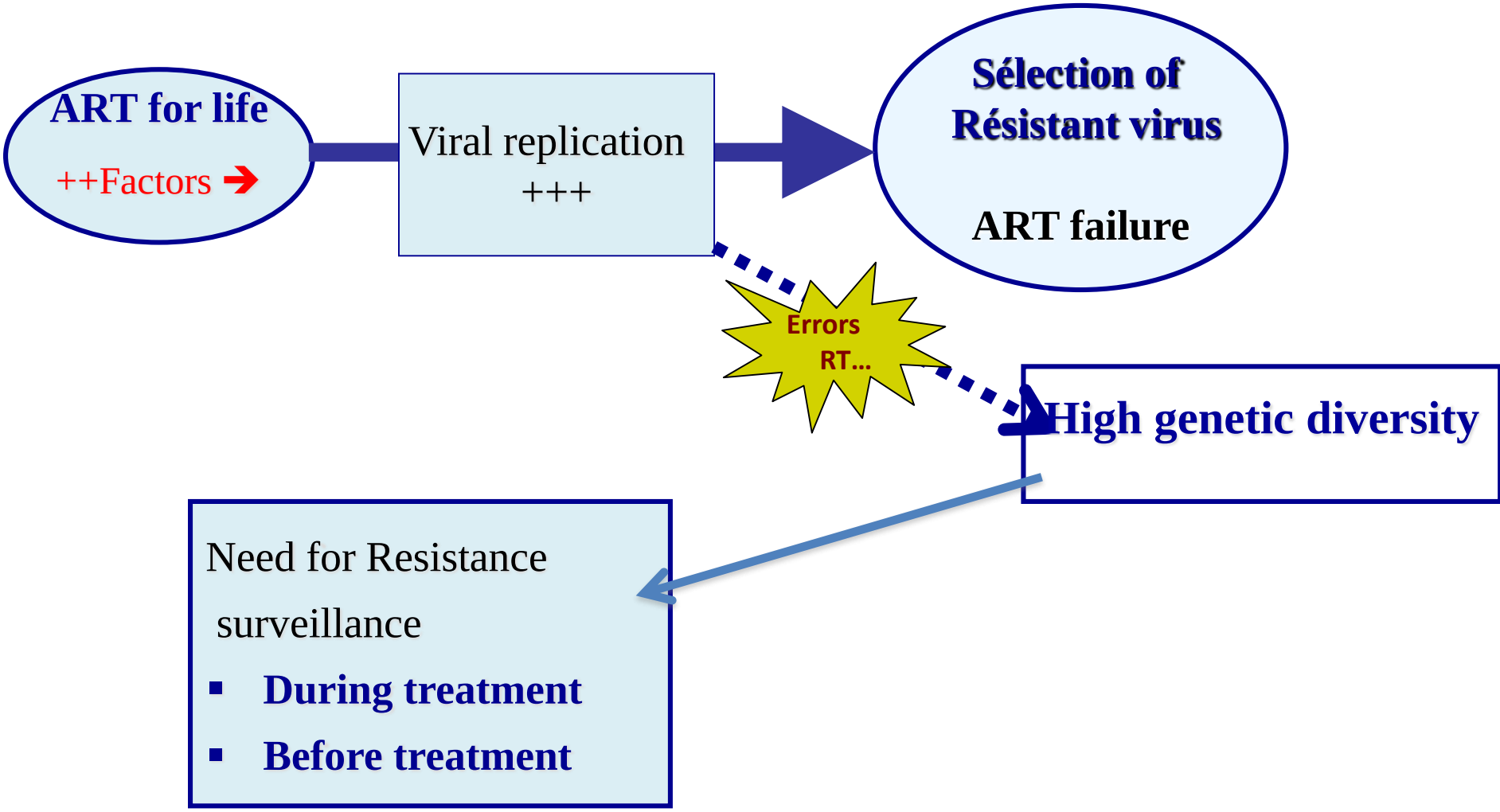
Antiretroviral therapy (ART)

improves the health and well-being of people living with HIV

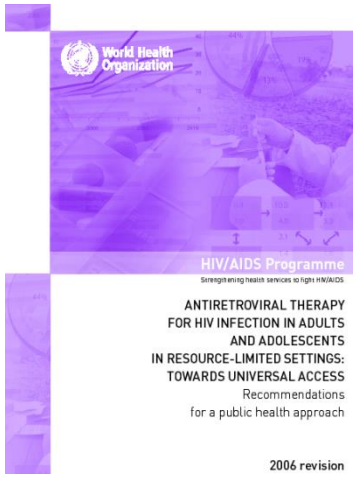
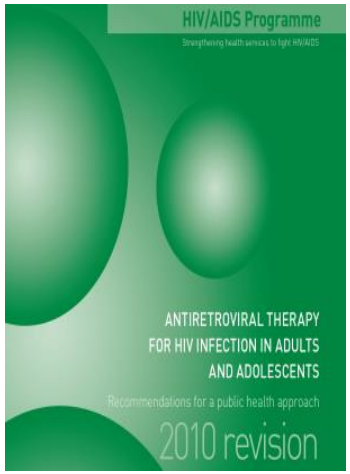
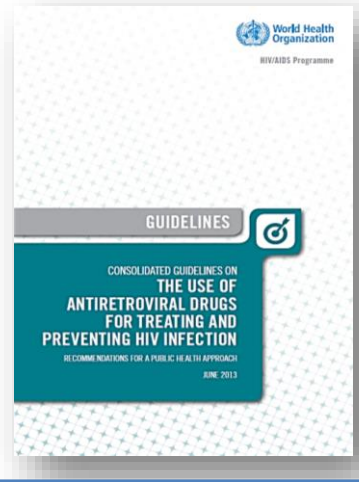
stops further HIV transmission but

Needs good laboratory in the Health System to keep the ART benefits

Without Good lab monitoring ➔ Emergence of HIVDR



ART monitoring in RLS
WHO : Recommandations

2002	2006	2010	2013
			
CD4+/-VL -	CD4 + VL +/- TF : 10 000 copies/ml	VL 6 months if possible VL for Failure confirmation TF 5 000 copies	VL : need for early TF detection TF : 1 000 copies CD4 at 500 for initiation

Acquired Resistance in Senegal

Structured cohorts : ANRS 1215/1290

- **Vergne L et coll. 2003** **11.8% après 18 mois de suivi**
- **Low rate of genotypic HIV-1 drug-resistant strains in the Senegalese government initiative of access to antiretroviral therapy. AIDS. 2003 Jul;17 Suppl 3:S31-8.**

Laurent C et coll. 2005. **12.5% après 30 mois**

Long-term benefits of highly active antiretroviral therapy in Senegalese HIV-1-infected adults. J Acquir Immune Defic Syndr. 2005 Jan 1;38(1):14-7.

De Beaudrap P et coll. **3% (M12), 6% (M24) et 18% (M60)**

27% en 24 mois en seconde ligne

Risk of virological failure and drug resistance during first and second-line antiretroviral therapy in a 10-year cohort in Senegal: results from the ANRS 1215 cohort. J Acquir Immune Defic Syndr. 2013 Apr 1;62(4):381-7

Cohorte ANRS 1215/1290

- lessons Learned
- ARV resistance not very different from the northern countries
- Possibility of reducing the emergence of resistance mutations to ARVs if correct monitoring is undertaking
- Results => scaling and decentralizing ART
- Level of HIVDR through public health approach

Acquired drug resistance in Public Health System

HIV DR in Public health system in Dakar

Journal of Clinical Microbiology
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J Clin Microbiol. 2013 February; 51(2): 578–584.
doi: 10.1128/JCM.02452-12
PMCID: PMC3553863

HIV-1 Genetic Diversity and Drug Resistance among Senegalese Patients in the Public Health System

Moussa Thiam,[a] Halimatou Diop-Ndiaye,[a] Aminata Diaw Diouf,[a] Nicole Vidal,[b] Ousseynou Ndiaye,[a] Ibrahima Ndiaye,[c] Ndeye Fatou Ngom-Gueye,[d] Sada Diallo,[a] Oumy Diop Diongue,[a] Makhtar Camara,[a] Abdoulaye Seck,[a] Souleymane Mboup,[a] and Coumba Toure-Kane[a]

HIV DR in Public health system in Dakar

- Cross-sectional study in 72 patients with virologic failure
- Followed CTA and SMIT (CHU Fann)
- CV> 3 log10 copies / ml (Abbott RealTime HIV-1)

- Median follow-up 40 months [12-123]
- Median viral load was 4.73 log10 copies / ml
- 1st line: 2 NRTI + EFV / NVP 54/72 (75%
- 2nd line: 2 NRTI + 1IP / r 18/72 (25%)
- 57 (76.4%): at least one ARV resistance mutation
  - 72.2% in 1st line
  - 88.9% in the second line ARV treatment

HIV DR in Public health system in Dakar

- **Mutations confering Resistance to NRTI**
  - **TAMs = 50,79%**
  - **M184V/I = 34,92%**
- **Mutations confering Resistance to NNRTI**
  - **K103N (46,27%),**
  - **V108, Y181 et K101**
- **Mutations confering Resistance to PI**
  - **M46I et L76V (24% each)**

HIV DR in Public health system in Dakar

- **Projet ANRS 12186: First line ART treatment**

Extraordinary Heterogeneity of Virological Outcomes in Patients Receiving Highly Antiretroviral Therapy and Monitored With the World Health Organization Public Health Approach in Sub-Saharan Africa and Southeast Asia

Avelin F. Aghokeng,[1,2] Marjorie Monleau,[2] Sabrina Eymard-Duvernay,[2] Anoumou Dagnra,[3] Dramane Kania,[4] Nicole Ngo-Giang-Huong,[5] Thomas D. Toni,[6] Coumba Touré-Kane,[7] Lien X. T. Truong,[8] Eric Delaporte,[2] Marie-Laure Chaix,[9] Martine Peeters,[2] and Ahidjo Ayouba;[2] for the ANRS 12186 Study Group[a]

Virological outcome in countries using the WHO public health approach - ANRS 12186

(2009 – 2012)

Objectives

To determine the proportion of patients failing ART (VL≥1000 copies/ml) and the frequency of drug resistance.

Population

HIV-1 infected adults receiving ARV since 12 and 24 months in national programs of Burkina Faso, Cameroon, Cote D'Ivoire, Togo, Senegal (Africa), and Thailand and Vietnam (Asia).

Virological outcome in countries using the WHO public health approach - ANRS 12186

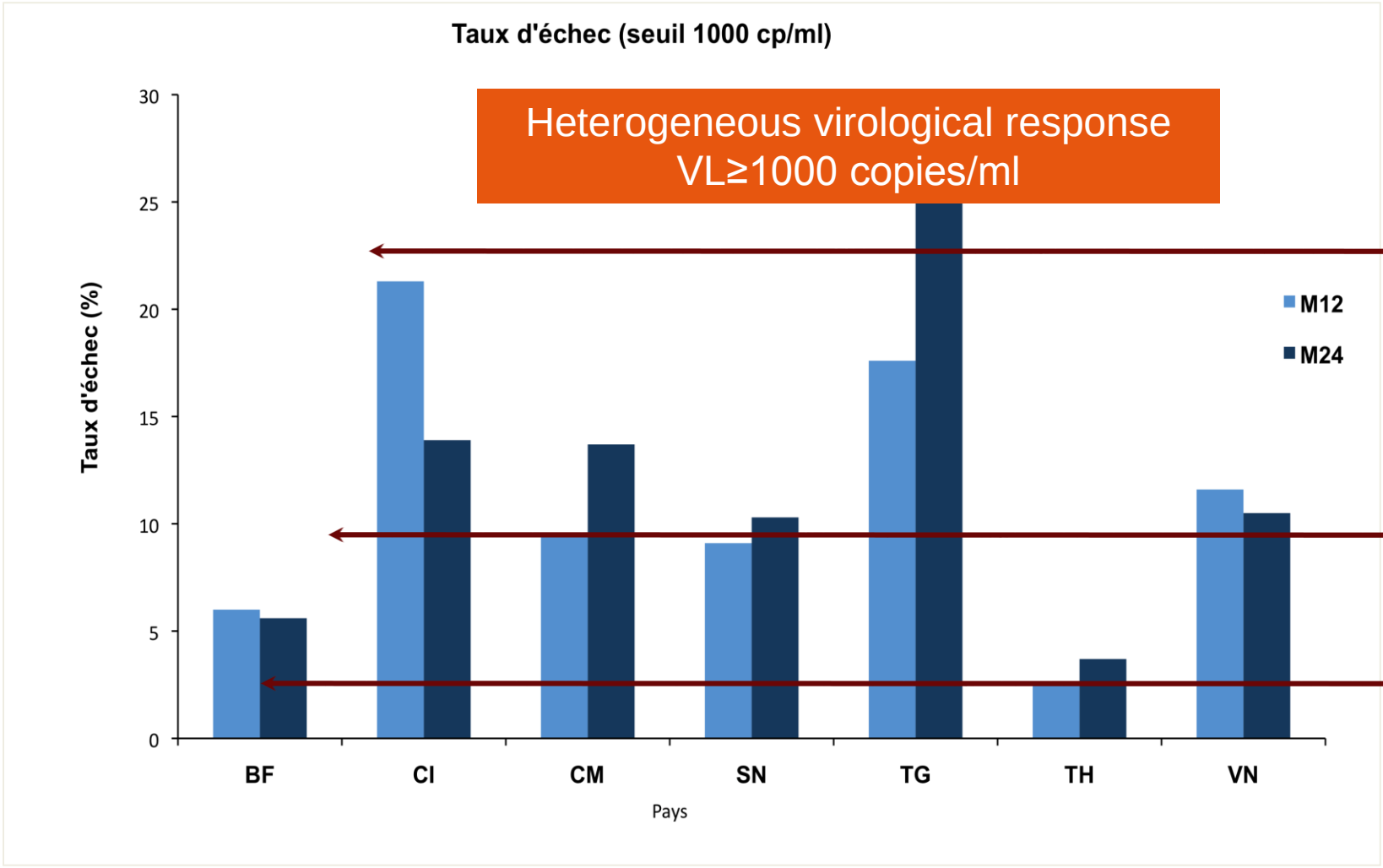
Study type & period

Cross-sectional evaluation conducted from October 2009 to December 2011.

Population size and details

- Overall, 3935 patients recruited, 2060 at month 12 and 1875 at month 24.
- Median ages: 32 to 42 years, and median CD4: 99 to 172 cells/μl.
- Main ART regimens included stavudine/zidovudine plus lamivudine plus nevirapine/efavirenz.

Virological outcome in countries using the WHO public health approach - ANRS 12186



Virological outcome in countries using the WHO public health approach - ANRS 12186

- **Projet ANRS 12186: First line ART**
- **Sites: CTA, SMIT, CPS, Roi Baudouin**

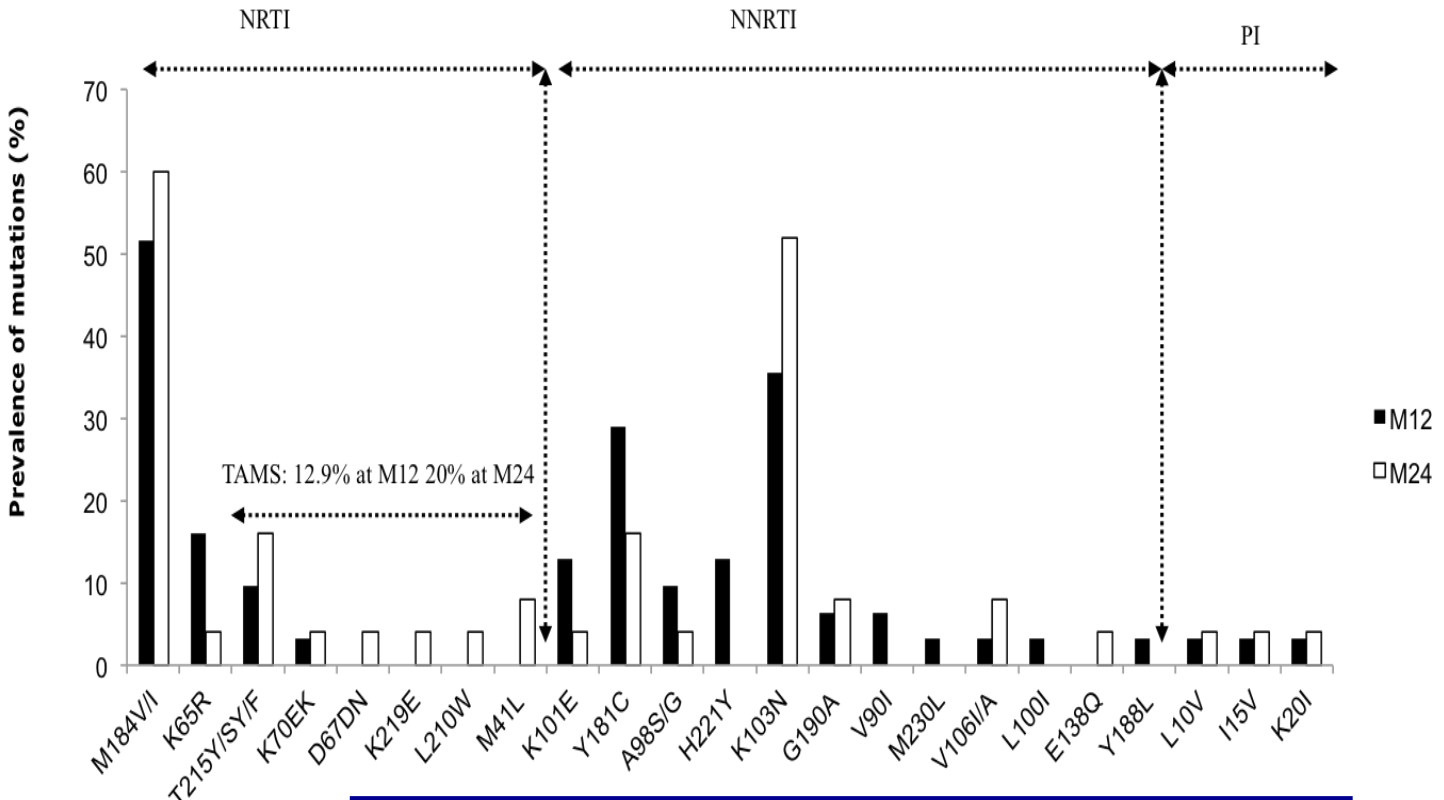
N=635	Virological failure	Resistance in VF	global Resistance rate
M12 (262)	7,9% (24/262)	70,8% (17/24)	6,5% (17/262)
M24 (168)	10,7% (18/168)	83,3% (15/83)	8,9% (15/168)

Virological outcome in countries using the WHO public health approach - ANRS 12186

Patients	ARV regimen	M24					
M12							
1	NVP 3TC d4T	1	EFV 3TC d4T/AZT	ABC	41LM 100I 103N 184V 215F	6,8	CRF09
2	EFV 3TC TDF	2	NVP 3TC AZT	ABC	103N 184V 210LRW 215Y	5,4	CRF02
3	EFV 3TC AZT	3	NVP 3TC d4T	ABC	67DN 179IV 181C 184V 215Y	5,2	CRF06
4	EFV 3TC d4T	4	NVP 3TC d4T/AZT	ABC	41L 98G 103NS 181C 184V 215Y	5,4	CRF06
5	NVP 3TC d4T	5	EFV 3TC d4T	ABC	67N 75M 103N 184V 190AG 215F	4,3	CRF01
6	NVP 3TC d4T	6	NVP 3TC d4T	ABC	75M 77L 101KQ 179I 184V 190A 210W 215Y	5,0	CRF01
7	NVP/EFV 3TC T	7	EFV 3TC AZT	ABC TDF	41L 103N 184V 210LW 215Y	5,9	CRF06
8	NVP 3TC d4T	8	NVP 3TC d4T	ABC TDF	41L 67N 70KR 98G 103R 179E 184V 188L 215F 219KQ	5,1	CRF02
9	NVP 3TC d4T	9	EFV 3TC AZT	ABC TDF	41L 103N 184V 188L 210W 215Y	3,8	CRF02
10	NVP 3TC d4T	10	NVP 3TC d4T/AZT	ABC TDF	67DN 101E 184V 190A 210W 215Y	5,5	CRF02
11	EFV 3TC d4T	11	NVP 3TC d4T	ABC ETR	67N 70R 90I 101E 181C 184IMV 190A 210W 219E	5,1	CRF02
12	NVP 3TC d4T	12	NVP 3TC d4T	ABC ETR	41L 75T 181C 184V 215Y 221Y	4,5	CRF02
13	NVP 3TC d4T	13	NVP 3TC d4T	ABC ETR	67DN 181C 184V 215F 221Y	4,6	CRF01
14	NVP 3TC d4T	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

Virological outcome in countries using the WHO public health approach - ANRS 12186

Senegal



Mutation NRTI: M184V/I, K65R, TAMs
Mutation NNRTI : K103N, Y181C

MAJOR ARTICLE HIV/AIDS

Extraordinary Heterogeneity of Virological Outcomes in Patients Receiving Highly Antiretroviral Therapy and Monitored With the World Health Organization Public Health Approach in Sub-Saharan Africa and Southeast Asia

Avelin F. Aghokeng,[1,2] Marjorie Monleau,[2] Sabrina Eymard-Duvernay,[2] Anoumou Dagnra,[3] Dramane Kania,[4] Nicole Ngo-Giang-Huong,[5] Thomas D. Toni,[6] Coumba Touré-Kane,[7] Lien X. T. Truong,[8] Eric Delaporte,[2] Marie-Laure Chaix,[9] Martine Peeters,[2] and Ahidjo Ayouba;[2] for the ANRS 12186 Study Group[a]

[1]Virology Laboratory, CREMER/IMPM/IRD, Yaoundé, Cameroon; [2]UMI 233 TransVIHMI, IRD and Université de Montpellier 1, Montpellier; [3]Centre National de Référence VIH-IST/PNLS, BIOLIM, FMMP/UL, Lomé, Togo; [4]Laboratoire de Virologie, Centre Muraz, Bobo-Dioulasso, Burkina Faso; [5]IRD UMI 174-PHPT and Chiang Mai University, Chiang Mai, Thailand; [6]Programme PAC-CI, Abidjan, Cote d'Ivoire; [7]Laboratoire de Bactériologie-Virologie, Dakar, Senegal; [8]Laboratoire de VIH/SIDA, Institut Pasteur, Ho Chi Minh City, Vietnam; and [9]Université Paris Descartes, EA 3620, AP-HP, Laboratoire de Virologie, CHU Necker-Enfants Malades, Paris, France

(See the Editorial Commentary by Katzenstein on pages 110–2.)

Publication: Clin Infect Dis. 2014 Jan;58(1):99-109

Commentaire: David Katzenstein (Stanford Univ.)

UNAIDS Science now

HIV this month. Issue no. 11. November 2013

Welcome to the 11th issue of **HIV this month**! In this issue, we cover the following topics:

Extraordinary Heterogeneity of Virological Outcomes in Patients Receiving Highly Antiretroviral Therapy and Monitored With the World Health Organization Public Health Approach in Sub-Saharan Africa and Southeast Asia.

Aghokeng AF, Monleau M, Eymard-Duvernay S, Dagnra A, Kania D, Ngo-Giang-Huong N, Toni TD, Touré-Kane C, Truong LX, Delaporte E, Chaix ML, Peeters M, Ayouba A; for the ANRS 12186 Study Group. Clin Infect Dis. 2013 Oct 23. [Epub ahead of print]

***Editor's notes**: As the number of people taking antiretroviral therapy (ART) increases, more attention will be needed to sustaining programme quality and effectiveness. The proportion of people taking ART who have suppressed HIV viral load is a key measure of treatment success. This survey of ART programmes in seven countries found wide variation in the proportion of patients with HIV viral load ≥1 000 copies per ml. This illustrates the value of viral load monitoring as a measure of programme quality. Among individuals with HIV viral load ≥1 000 copies per ml, most but not all had drug-resistant virus. This illustrates the difficulty of rational management of "treatment failure" where resistance cannot be determined. Of more concern are few patients who had resistance to drugs they apparently had never taken. This underlines the importance of careful ART stewardship to maximize the benefits of ART at population level.*

Acquired resistance in decentralized settings

Project named DECVISEN (GF)

- **Mbour (70 Km from Dakar)**
  - **166 patients (115 Women et 51 Males)**
  - **162 (97.6%) First line**
    - **AZT+3TC + NVP =65.1%**
    - **AZT+3TC + EFV = 22.3%**
  - **4 (2.4%) sous 2 INTI + LPV/r**
  - **VL plus genotyping Plasma**

Study population

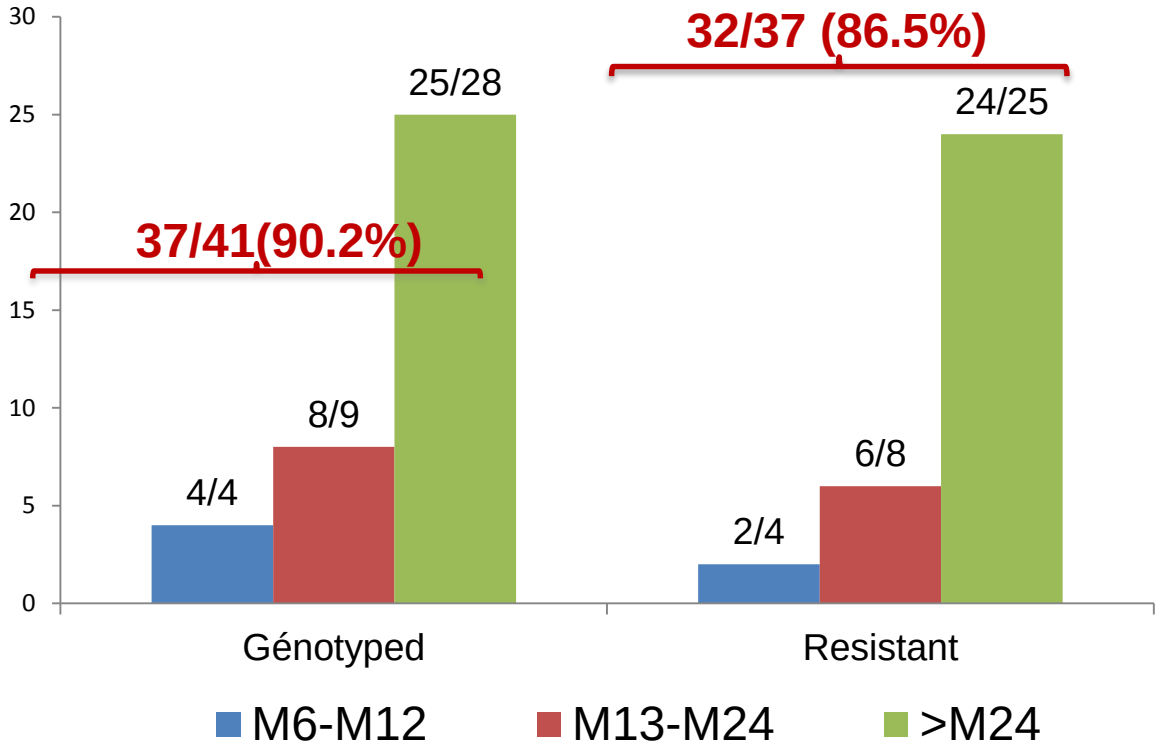
- N = 159 patients, median age = 41 years [20-74 years]
- Sex ratio F/H = 2.24
- Median of follow-up = 33 months (6-148 months)

	6-12 months	13-24 months	> 24 months	Total
AZT+3TC+EFV/NVP	09	37	96	142
TDF+3TC+EFV/NVP	07	05	03	15
Others	01	-	01	02
Total	17	42	100	159

HIV Drug Resistance

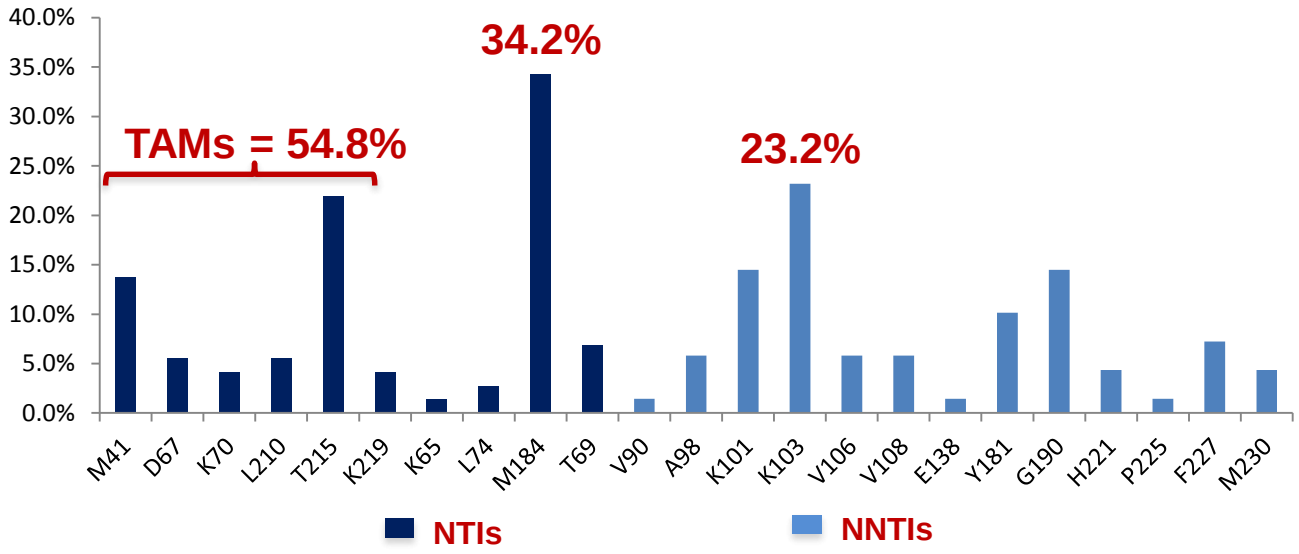
	6-12 month	13-24 month	> 24 month	Total
< 300 cps/ml	13	33	68	114
[300-1000 cps/ml[	-	-	04	04
≥ 1000 cps/ml	04 (23.5%)	09 (21.4%)	28 (28%)	41 (25.8%)
Total	17	42	100	159

Virologic failu
(CV ≥ 1000
cps/ml)



HIV Drug Resistance

- **Drug resistance rate = 20.1% (32/159)**
  - **Resistance to NRTIs : 27/32 (84.4%)**
  - **Resistance to NNRTIs : 32/32 (100%)**



- **Drug Prediction resistance for 2nde line treatment**

NRTIs : (71.9%; 23/32) for ABC and (59.4%; 19/32) for DDI

NNRTIs : (53.1%; 17/32) for ETR/RPV

HIVDR using DBS

Research Article

Dried blood spots for HIV-1 drug resistance genotyping in decentralized settings in Senegal

Abou Abdallah Malick Diouara[1], Halimatou Diop-Ndiaye[1], Khady Kebe-Fall[1], Edmond Tchiakpè[1], Ousseynou Ndiaye[1], Ahidjo Ayouba[2], Martine Peeters[2], Souleymane Mboup[1], Coumba Toure Kane[1,*]

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Issue

Journal of Medical Virology
Volume 86, Issue 1, pages 45–51, January 2014

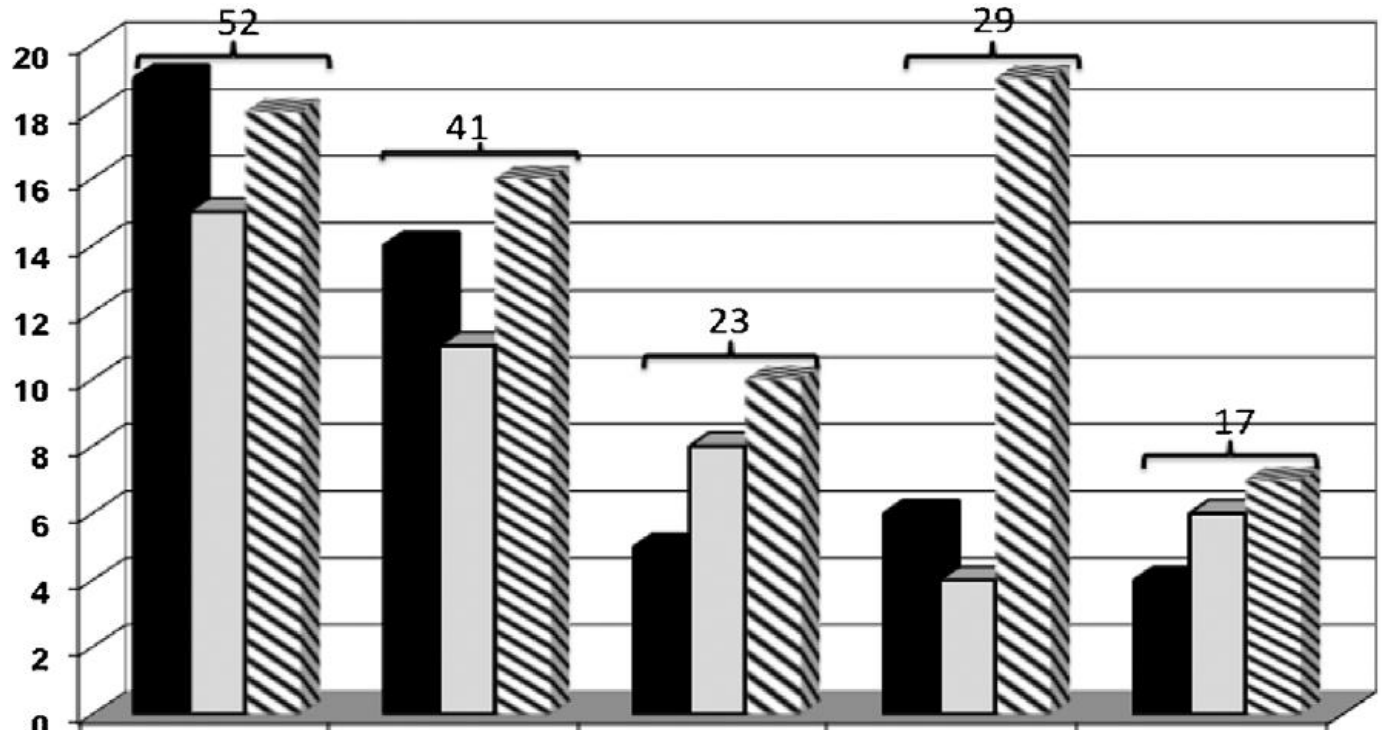
- **HIVDR on DBS**
- **231 patients under First line ART from 10 régions in Sénégal**
- **AZT-3TC-NVP/EFV 80.9%; 187/231)**

HIVDR using DBS

- **Median follow-up 18-month (6-68 months)**
- **Virological failure 23.8% (55/231)**
- **Global resistance rate 17.7% (41/231**

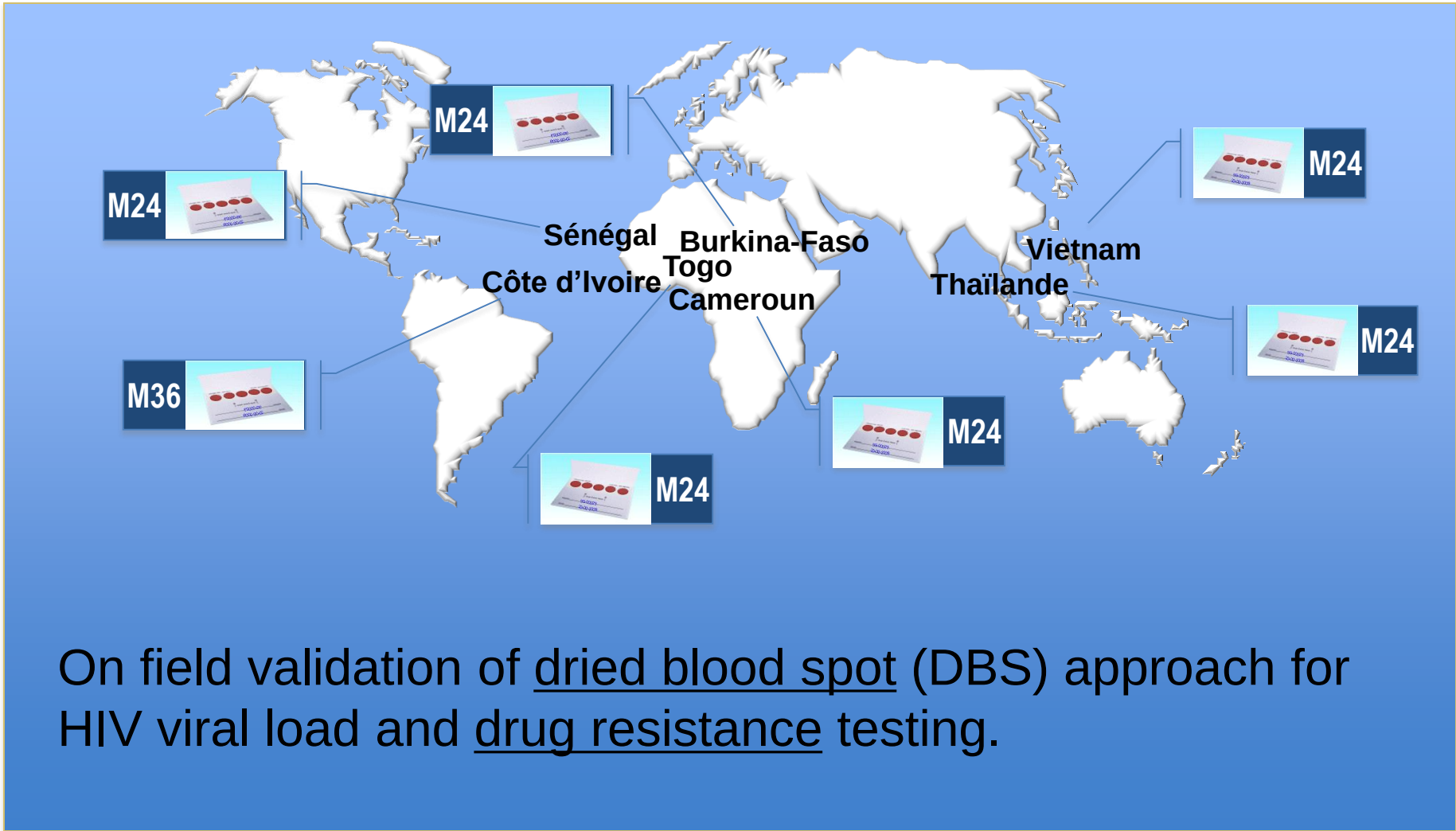
	M6–M12	M13–M24	>M24	Total
All	84	59	88	231
VL $\geq 3 \log_{10}$ copies/ml	19	17	19	55
Genotyped	19	15	18	52
Any DRM	14	11	16	41

HIVDR using DBS



	Genotyped	any DRM	M184V/I	TAMS	K103N
M6-M12	19	14	5	6	4
M13-M24	15	11	8	4	6
>M24	18	16	10	19	7

Improving access to virological monitoring in RLC using alternative tools – ANRS12235 (DBS)



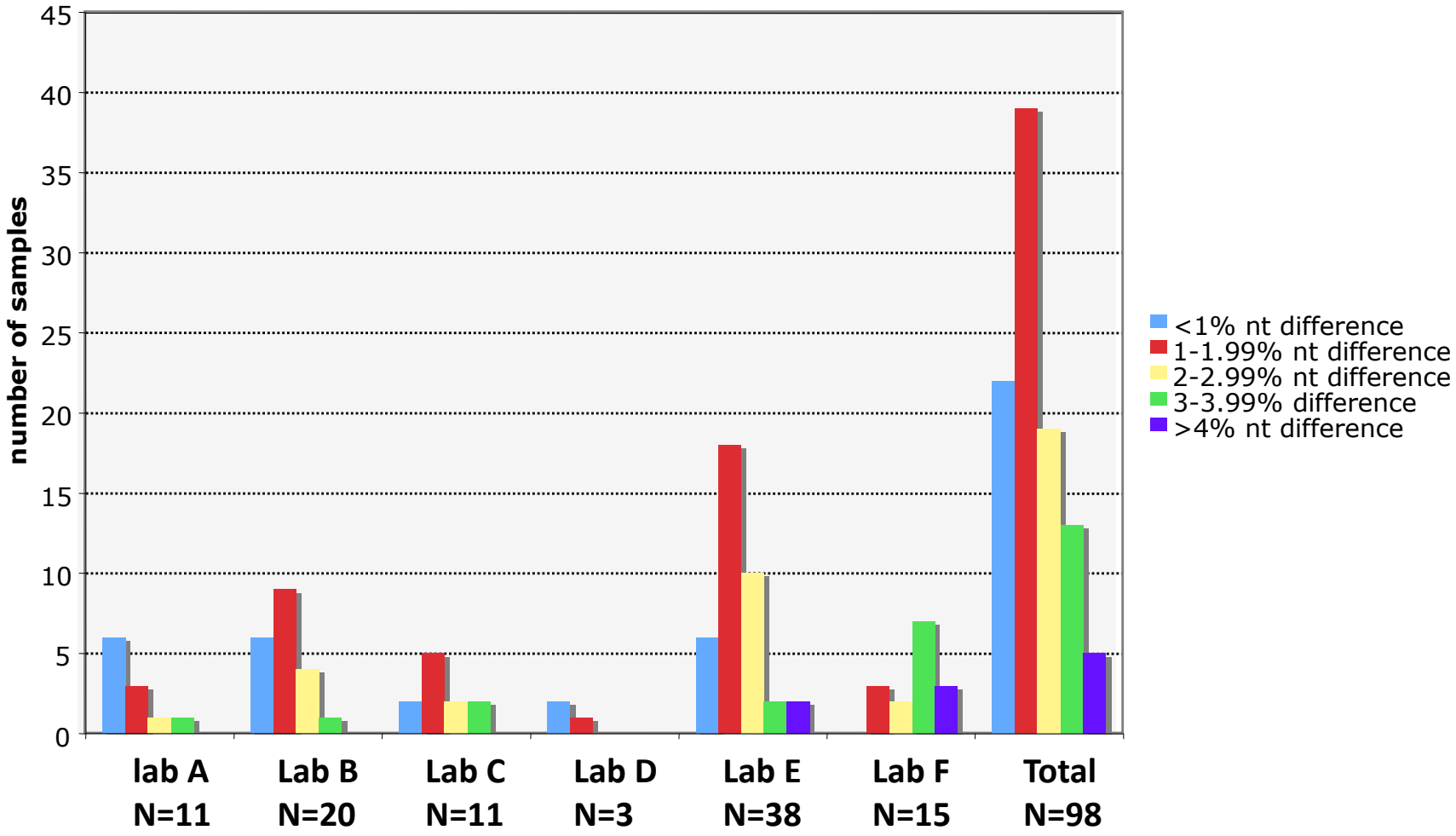
On field validation of dried blood spot (DBS) approach for HIV viral load and drug resistance testing.

DBS – ANRS12235

Viral load assay	Plasma-DBS pairs *(n=382)*	Plasma VL≥1000 cp/ml *(n=155)*	False negative[α]	False positive[β]	Sensitivity *(95% CI)*[δ]	Specificity *(95% CI)*
m2000rt assay	*173*					
Lab B	60	24 (40%)	0/24	1/36	**100** (85.8-100)	**97.2** (85.5-99.9)
Lab C	53	13 (25%)	0/13	7/40	**100** (75.3-100)	**82.5** (67.2-92.7)
Lab D	60	12 (20%)	3/12	1/48	**75.0** (42.8-94.5)	**97.9** (88.9-99.9)
G2 Generic assay	*118*					
Lab A	60	16 (27%)	1/16	17/44	**93.8** (69.8-99.8)	**61.4** (45.5-75.6)
Lab F	58	23 (40%)	2/23	14/35	**91.3** (72.0-98.9)	**60.0** (42.1-76.1)
Nuclisens assay	*91*					
Lab E	91	67 (74%)	10/67	1/24	**85.1** (74.3-92.6)	**95.8** (78.9-99.9)

DBS – ANRS12235

Number of samples with nucleotide (nt) difference



DBS – ANRS12235

Number of samples with DRM missed at VL detection and/or genotyping for the different sites

study site	Plasma VL >1,000	DBS VL <1,000	DRM in FN* DBS samples	Discordant DRM Plasma/DBS
Lab A	16/60	1/16	0/1	1/11
Lab B	24/60	0/24	-	4/20
Lab C	13/53	0/13	-	3/11 (1 no DRM at all)
Lab D	12/60	3/12	2/3	1/3
Lab E	67/91	10/67	10/10	5/38 (1 no DRM at all)
Lab F	23/58	2/23	2/2	9/15 (8 no DRM at all)

Main outcome

- DBS can reliably replace plasma specimen f
plasma collection, processing and transportati
- Selection of adequate technique according t
essential.
- Quality monitoring is also important.

1. **90% (139/155) of VF were correctly identified using DBS.**
2. **80% (77/96) of HIVDR interpretations were correct.**

Publication: J Clin Microbiol. 2014 Jan.

Resistance using DBS: WAHO projet

International AIDS Society

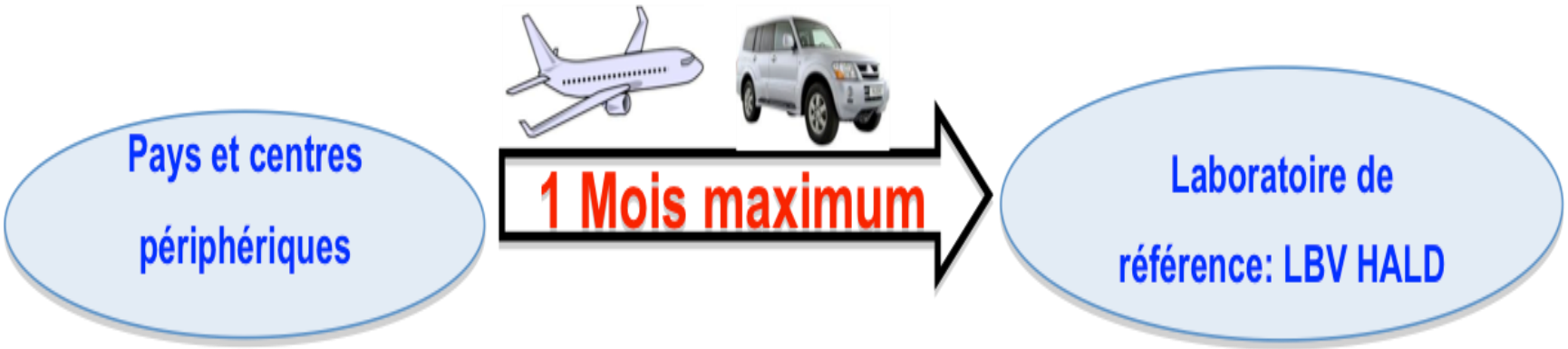
Research article

Antiretroviral treatment outcome in HIV-1-infected patients routinely followed up in capital cities and remote areas of Senegal, Mali and Guinea-Conakry

Abou Abdallah Malick Diouara[1], Halimatou Diop Ndiaye[1], Ibrehima Guindo[2], Nestor Bangoura[†,3], Mohamed Cissé[3], Tchiakpe Edmond[1], Flabou Bougoudogo[2], Souleymame Mboup[1], Martine Peeters[4], Ahidjo Ayouba[4] and Ndèye Coumba Touré Kane[§,1]

[§]Correspondingauthor: Ndèye CT Kane, Université Cheikh Anta Diop, Dakar, and Laboratoire de Bactériologie-Virologie, Hôpital Aristide Le Dantec, 30 Avenue

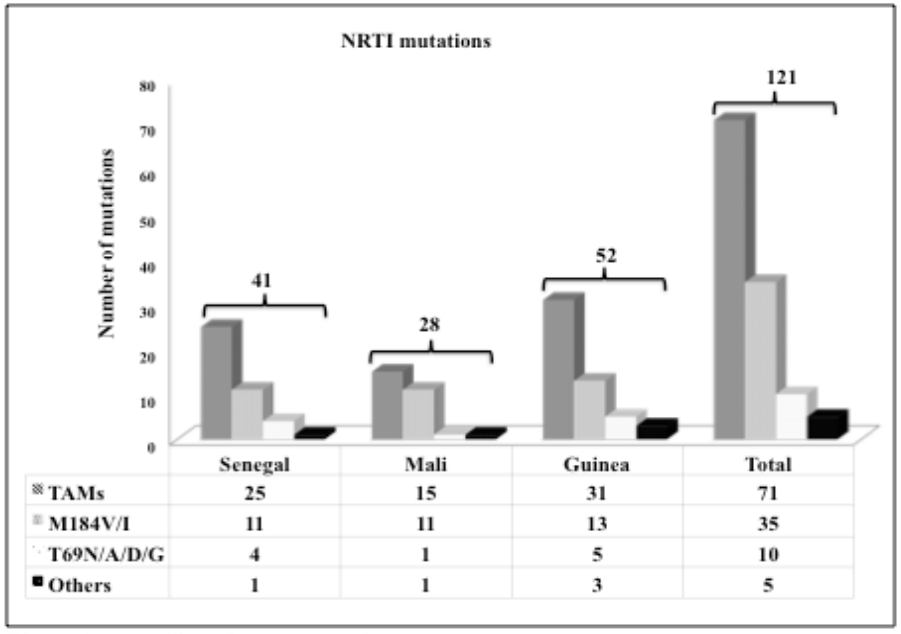
- **Multicentric study**
- **Guinée, Mali, Sénégal**



Resistance using DBS

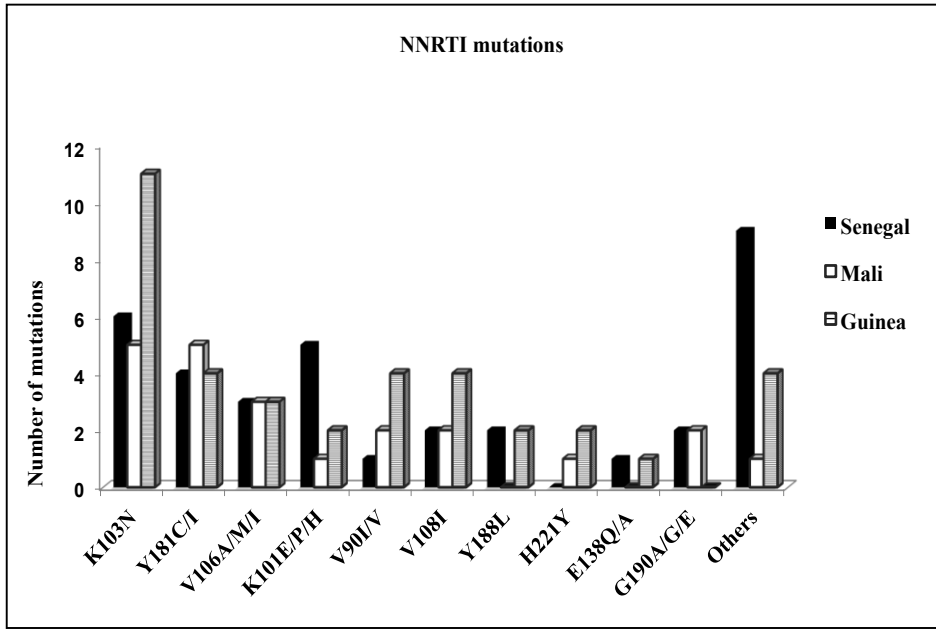
Countries	Senegal	Mali	Guinea	Total
Samples collection sites	7	6	4	17
Number of patients enrolled	119	152	136	407
Female (Percent)	94 (78.9%)	102 (67.1%)	83 (61%)	279 (68.5%)
Median age (Years)	42 [IQR: 18-65]	41 [IQR: 18-66]	38 [IQR: 18-61]	40 [IQR: 18-66]
Fist line therapy (2 NRTI+ 1 NNRTI)	114 (95.7%)	136 (89.4%)	129 (94.8%)	379 (93.1%)
AZT+3TC+NVP/EFV	109	66	80	255
D4T+3TC+NVP/EFV	1	43	47	91
Other fist-line combinations	4	27	2	33
Second line therapy (2 NRTI+ 1 PI)	5	16	7	28
Median time on ART	32 [IQR: 6-112]	39 [IQR: 6-136]	35 [IQR: 6-108]	36 [IQR: 6-136]
VL≥ technical cut off (800 Copies/mL)	31	17	33	81
Median of Viral load	3.63 [IQR: 3-5.48]	3.94 [IQR: 2.97-6.18]	3.64 [IQR: 3.07-6.75]	3.68 [IQR: 2.97-6.75]
Virological failure (VL≥3Log$_{10}$ Copies/mL)	31 (26%)	16 (10.5%)	33 (24.2%)	80 (19.6%)
Genotyped	27 (87%)	15 (93.7%)	28 (84.8%)	70 (87.5%)
Any DRM	19	14	19	52
DRM in patients with virological failure	70.3% (n=19/27)	93.3% (n=14/15)	67.8% (n=19/28)	74.2% (n=52/70)
Global DRM	15.9% (n=19/119)	9.2% (n=14/152)	13.9% (n=19/136)	12.7% (n=52/407)

Resistance using DBS



	Senegal	Mali	Guinea	Total
TAMs	25	15	31	71
M184V/I	11	11	13	35
T69N/A/D/G	4	1	5	10
Others	1	1	3	5

Figure 1a: NRTI's resistance mutation prevalence



Transmitted of HIVDR

Threshold survey

AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 25, Number 11, 2009

DOI: 10.1089/aid.2009.0142

Low Prevalence of HIV Type 1 Drug Resistance Mutations in Untreated, Recently Infected Patients from Burkina Faso, Côte d'Ivoire, Senegal, Thailand, and Vietnam: The ANRS 12134 Study

Ahidjo Ayouba,[1] Truong T.X. Lien,[2] Janin Nouhin,[3] Laurence Vergne,[4,*] Avelin Fobang Aghokeng,[4] Nicole Ngo-Giang-Huong,[5] Halimatou Diop,[6] Coumba Touré Kane,[6] Diane Valéa,[7] François Rouet,[7] Dominique Joulia-Ekaza,[8] Thomas D'Aquin Toni,[8] Eric Nerrienet,[3] Eitel Mpoudi Ngole,[4] Eric Delaporte,[1] Dominique Costagliola,[9] Martine Peeters,[1] and Marie-Laure Chaix[10]

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%

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

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Vietnam (*Ho Chi M*)	2006-07	VCT	**63**	<5%	<5%	<5%

Ayouba et al., Aids Res. 2009 / Aghokeng et al., Antiviral Th 2009/ Nouhin et al., 2009.

AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 26, Number 10, 2010

DOI: 10.1089/aid.2009.0295

Antiretroviral Drug Resistance Mutations in Antiretroviral-Naive Patients from Senegal

Halimatou Diop-Ndiaye,[1] Coumba Toure-Kane,[1] Nafissatou Leye,[1] Ndeye Fatou Ngom-Gueye,[2] Céline Montavon,[3] Martine Peeters,[3] and Souleymane Mboup[1]

- 200 sequences analyzed
- 1998-2001: 96 samples at D0 with median CD4 = 102
- 2003-2005: Monitoring of resistance (CD4> 350
- 2007: ANRS 12134 (CD4> 500)

Survey in Dakar

Low level of HIVDR at ART initiation after > 10 years of ARV circulation

Mutation	Année	Sous-type	ARV concernés	Classe d'ARV
V75S	1998	CRF11_cpx	aucun mais position de résistance	INTI
K65R	1999	C	tous les INTI sauf AZT	INTI
K219N	1999	CRF02_AG	aucun mais position de résistance	INTI
M41L	2001	CRF02_AG	TAM	INTI
M46L	1999	C	tous les IP sauf DRV et SQV	IP
G73S	2005	CRF02_AG	tous les IP sauf DRV, NFV et TPV	IP
I54T	2007	CRF09_cpx/CRF02_AG	LPV et ATZ	IP

HIV DR in children

Resistance after PMTC failure

International AIDS Society

Short report

The case for addressing primary resistance mutations to non-nucleoside reverse transcriptase inhibitors to treat children born from mothers living with HIV in sub-Saharan Africa

Khady Kébé[1], Laurent Bélec[2,3], Halimatou Diop Ndiaye[1], Sokhna Bousso Gueye[1], Abou Abdallah Malick Diouara[1], Safiétou Ngom[1], Ndéye Rama Diagne Gueye[4], Ngagne Mbaye[5], Haby Signaté Sy[4], Souleymane Mboup[1] and Coumba Touré Kane[6,1]

[6]Corresponding author: Coumba Touré Kane, Université Cheikh AntaDiop, Dakar, and Laboratoire de Bactériologie-Virologie, CHU Aristide Le Dantec, Dakar, Sénégal

25 chilredn
Median Age : 5.5 months

Prophylaxie

Résistance 6,5 Higher (p<0.05)

Resistance rate :32%
Resistance to NNRTI : 8

Mutations:
K103N, Y181C, K101E

Kebe et al 2014

Enfant	Age (mois)	Prophylaxie mère	Prophylaxie enfant	Mutations de résistance aux INNTI	Mutations de résistance aux INTI
#4569	3	AZT-3TC-NVP	AZT-NVP	**K103N**	**D67N**
#4001	8	AZT-3TC-NVP	Non	**V90I, Y188L**	-
#7078	3	AZT-3TC-NVP	NVP	**K103N, Y181C**	-
#5254	1,5	AZT-NVP	AZT-NVP	**K101E, V106M**	-
#6118	4	AZT-3TC-NVP	AZT-NVP	**K101E, V106M, P225S**	**D67N**
#5237	8	D4T-3TC-NVP	AZT-NVP	**Y181C, H221Y**	-
#7405	3	Non	NVP	**K103N**	-
#3994	3	NVP	AZT-NVP	-	-
#7225	1,5	AZT-3TC-NVP	NVP	-	-
#5222	12	AZT-3TC-NVP	AZT-NVP	-	-
#7041	1,5	AZT-3TC-NVP	No	-	-
#6179	5	AZT-3TC-NVP	No	-	-
#6453	5	D4T-3TC-NVP	AZT-NVP	-	-
#3988	3	Non	Non	-	-
#7278	8	Non	Non	-	-
#7137	3	Non	Non	-	-
#7399	1,5	Non	Non	-	-
#7561	4	Non	Non	-	-
#5947	8	Non	Non	**K101E**	-
#6250	3	Non	Non	-	-
#6467	3	Non	Non	-	-
#6048	1,5	Non	Non	-	-
#6546	12	Non	Non	-	-
#6028	1,5	Non	Non	-	-
#5687	5	Non	Non	-	-

Children under first line ART

AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 28, Number 00, 2012

DOI: 10.1089/aid.2011.0300

High Rate Of Antiretroviral Drug Resistance Mutations in HIV Type 1-Infected Senegalese Children in Virological Failure on First-Line Treatment According to the World Health Organization Guidelines

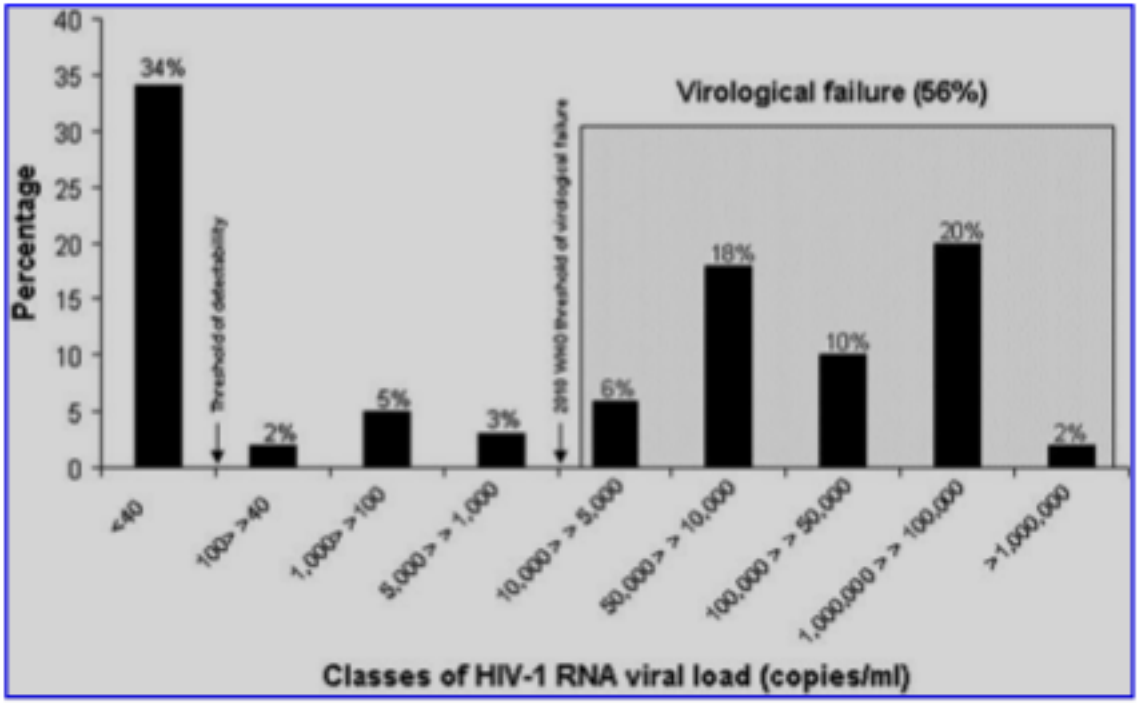
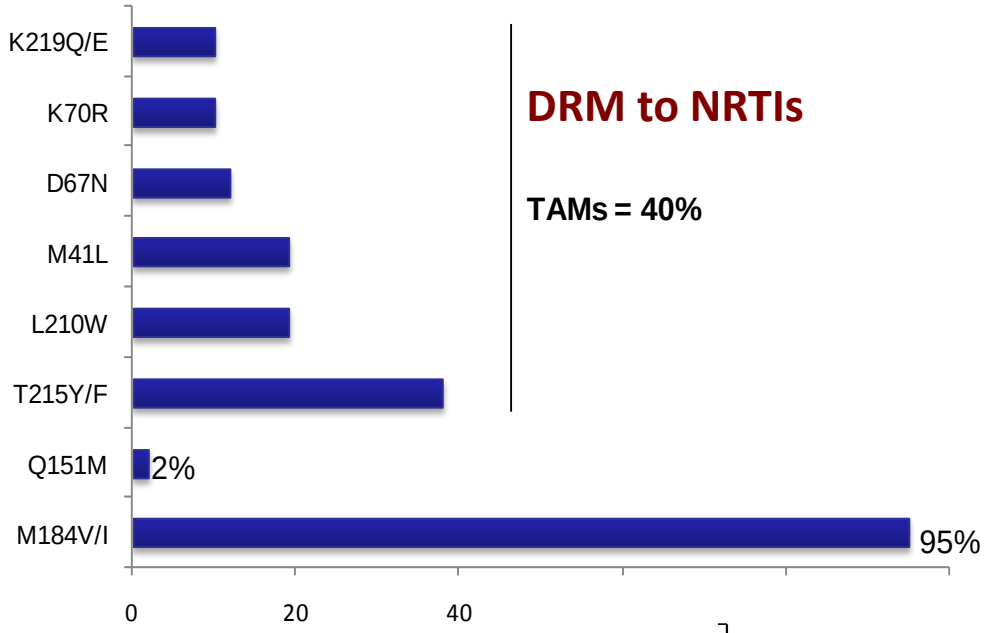


FIG. 1. Distribution of plasma HIV-1 RNA viral load in 125 children receiving first-line antiretroviral treatment according to the WHO recommendations, and followed-up in the Hôpital d'Enfants Albert Royer of Dakar, Senegal. The threshold of HIV-1 RNA load detection of the Abbott m2000 RealTime HIV-1 assay (40 copies/ml) and the threshold of virological failure according to the 2010 revised (5,000 or 3.7 log10 copies/ml) WHO criteria are indicated.

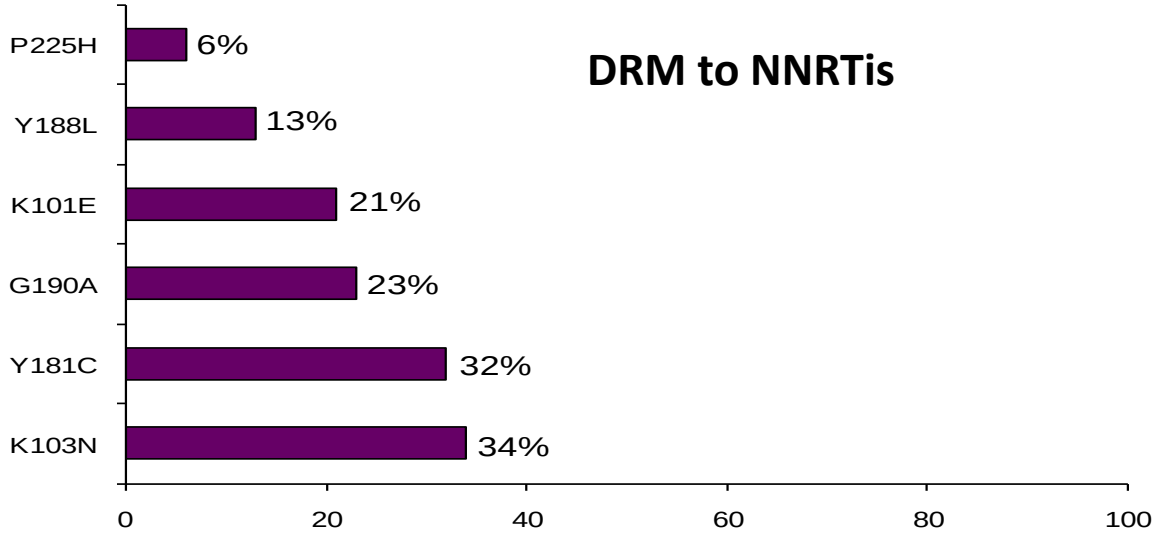
Kebe et al 2013

Children under first line ART



DRM to NRTIs

TAMs = 40%



DRM to NNRTis

Kebe et al 2013

HIV-2

HIV-2

- **HIV-2**
  - **resistant to the nonnucleoside reverse-transcriptase inhibitors and to**
  - **less susceptible than HIV-1 to some protease inhibitors (PIs).**
- **Senegal HIV-2 and HIV1/2 → 2NRTIs and PI**

HIV-2

- 23 patients ➔ Multiclass DRM (NRTI and PI) 30% of patients
- 52% to at least 1 ARV class.
  - M184V 43% K65R, 9% Q151M 9%
  - TAMS (M41L, D67N, K70R, L210W, and T215Y/F) not observed
    - exception of K70R, together with K65R and Q151M in 1 patient.
  - 8 ➔ PI mutations associated with indinavir resistance, including K7R, I54M, V62A, I82F, L90M, L99F
  - 4 patients had strains with multiple PI resistance–associated mutations.
- The duration of ARV associated with the development of drug resistance (P = .02).
- 9 (82%) of 11 patients ➔ detectable ARV resistance had undetectable plasma HIV-2 RNA loads (<1.4 log10 copies/mL)

Goetlieb et al 2013

Summary Senegal : HIVDR Surveillance: 3 priority surveys

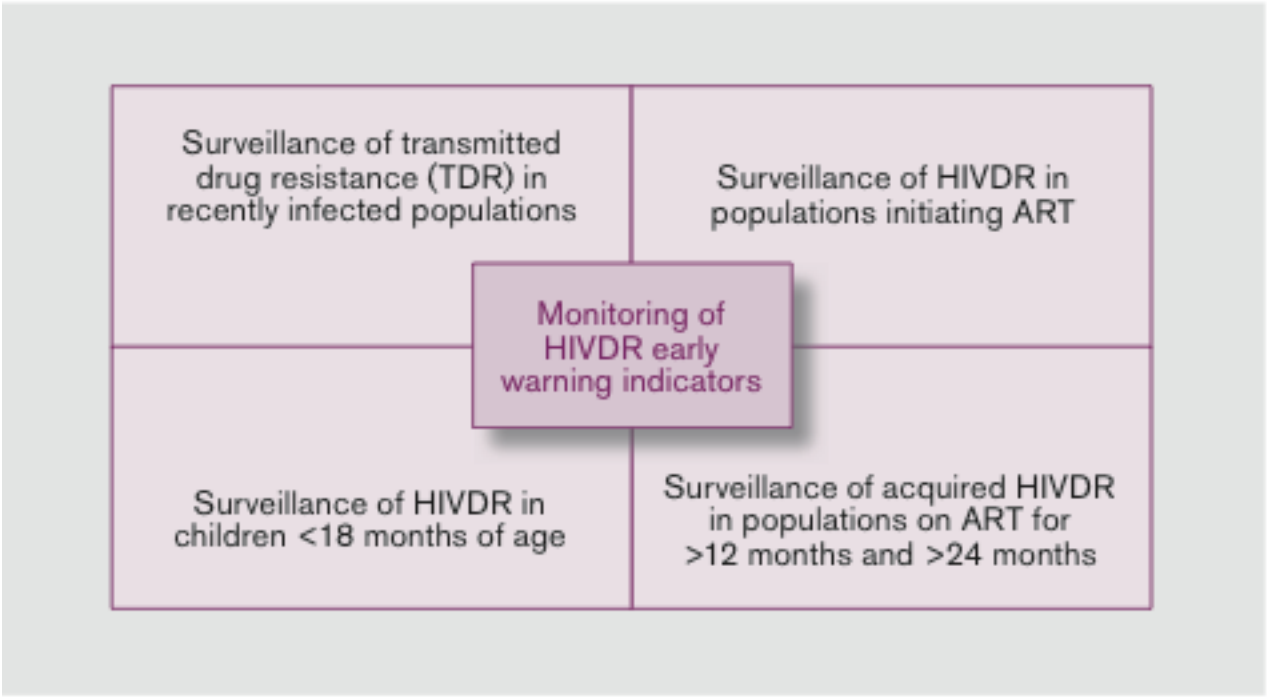
Survey	Frequency	Cost (K USD)
Pre-treatment HIVDR (PDR)	Every 3 years	238 K
Acquired HIVDR (ADR) (Adult and paediatric)	Every 3 years	336 K
EWI	Yearly	Integrated in M&E

2 additional surveys

Survey	Cost (K USD)
Pediatric < 18 months	135 K
Transmitted HIVDR (TDR)	182 K

Summary

Figure 1. WHO 2012 HIV drug resistance surveillance and monitoring strategy



Summary

- **ART more efficient Gain → Optimal lab monitoring**
  - **Resources (financial, human and hardware)**
  - **Need of innovative approaches**
  - **Good Procurement System**
  - **HIVDR**
    - **Genotyping national → or South-South cooperation and North-South (Networking +++)**

Thank you
Merci

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Centre Régional de Recherche et de Formation à la Prise en Charge Clinique de Fann

Conseil National de Lutte contre le Sida

Le Fonds mondial

De lutte contre le sida, la tuberculose et le paludisme