ASLM 2018

AFRICAN SOCIETY FOR LABORATORY MEDICINE

Role of the National Reference laboratory in HIV

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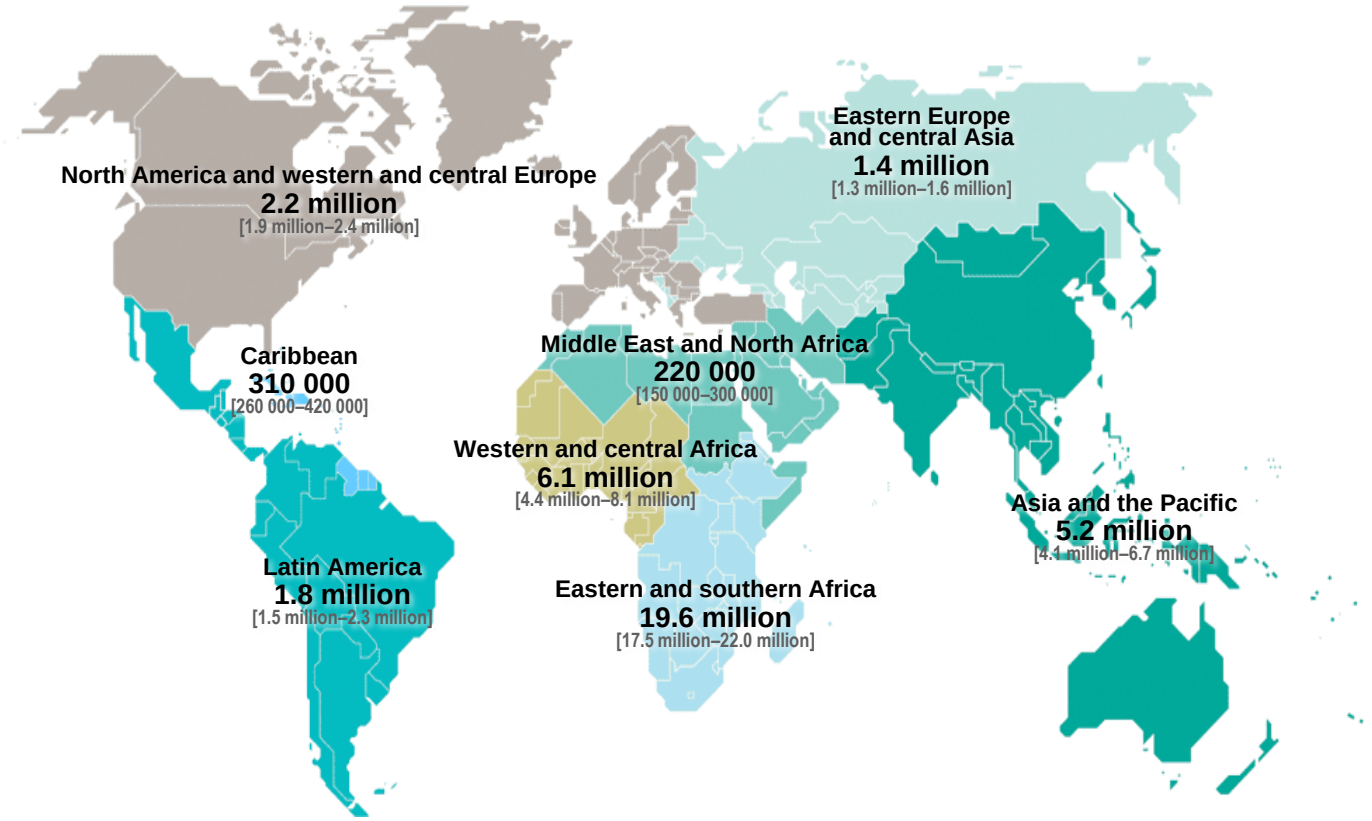
des racines pour la vie — roots for life

Adults and children estimated to be living with HIV | 2017 (UNAIDS)

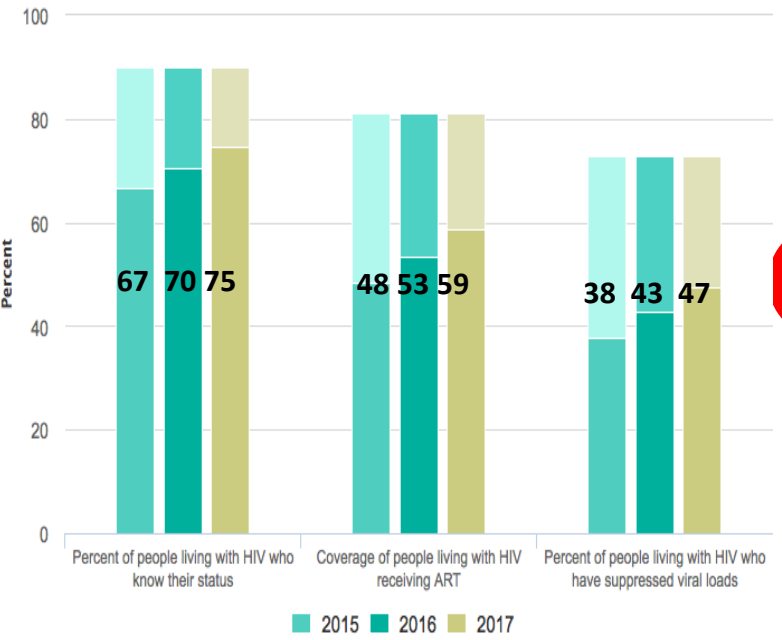


Total: 36.9 million [31.1 million–43.9 million]

UNADS targets for HIV

90% By 2020, 90% of all people living with HIV will know their HIV status

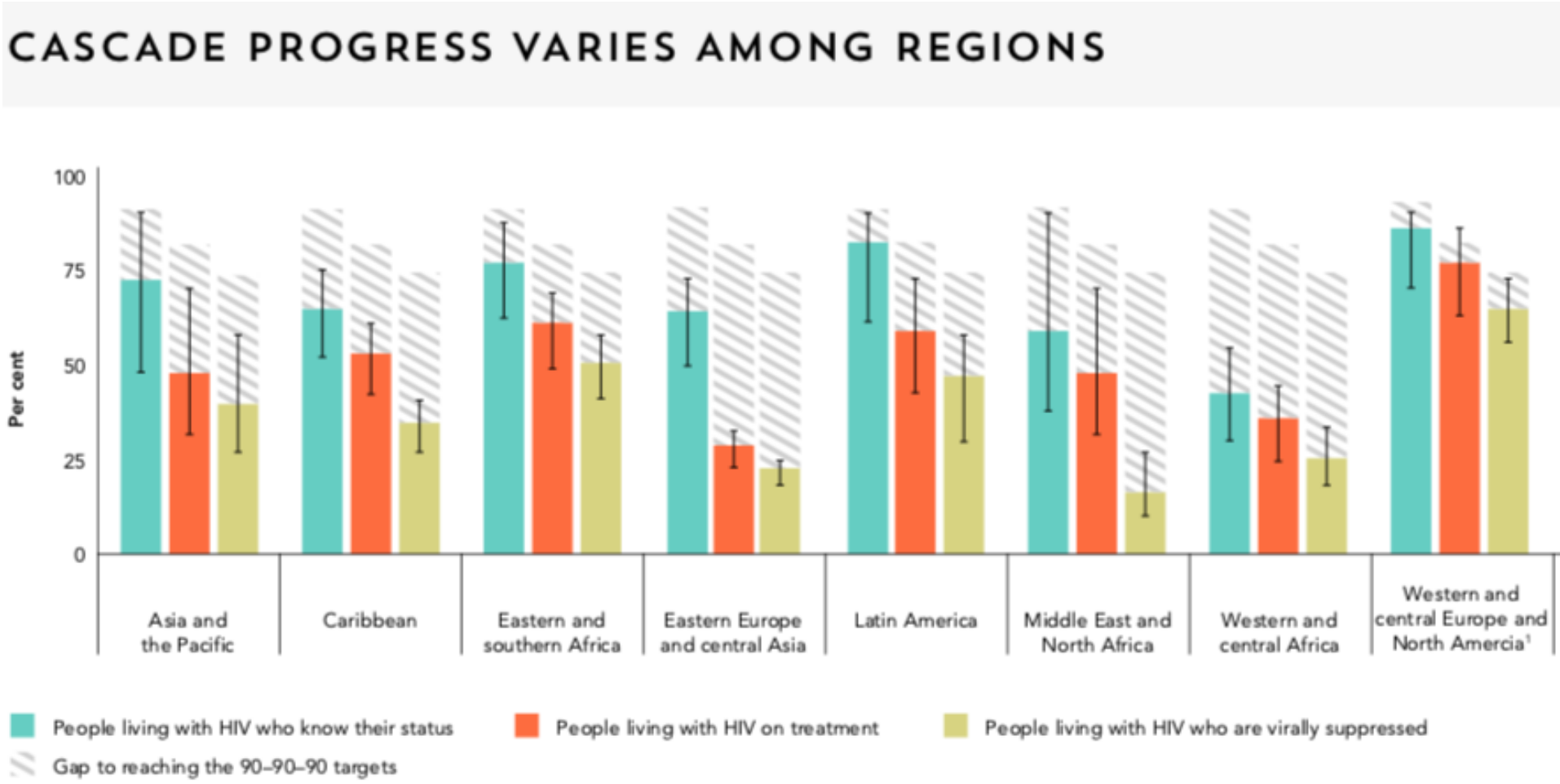
90% By 2020, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy



Source: UNAIDS special analysis, 2018

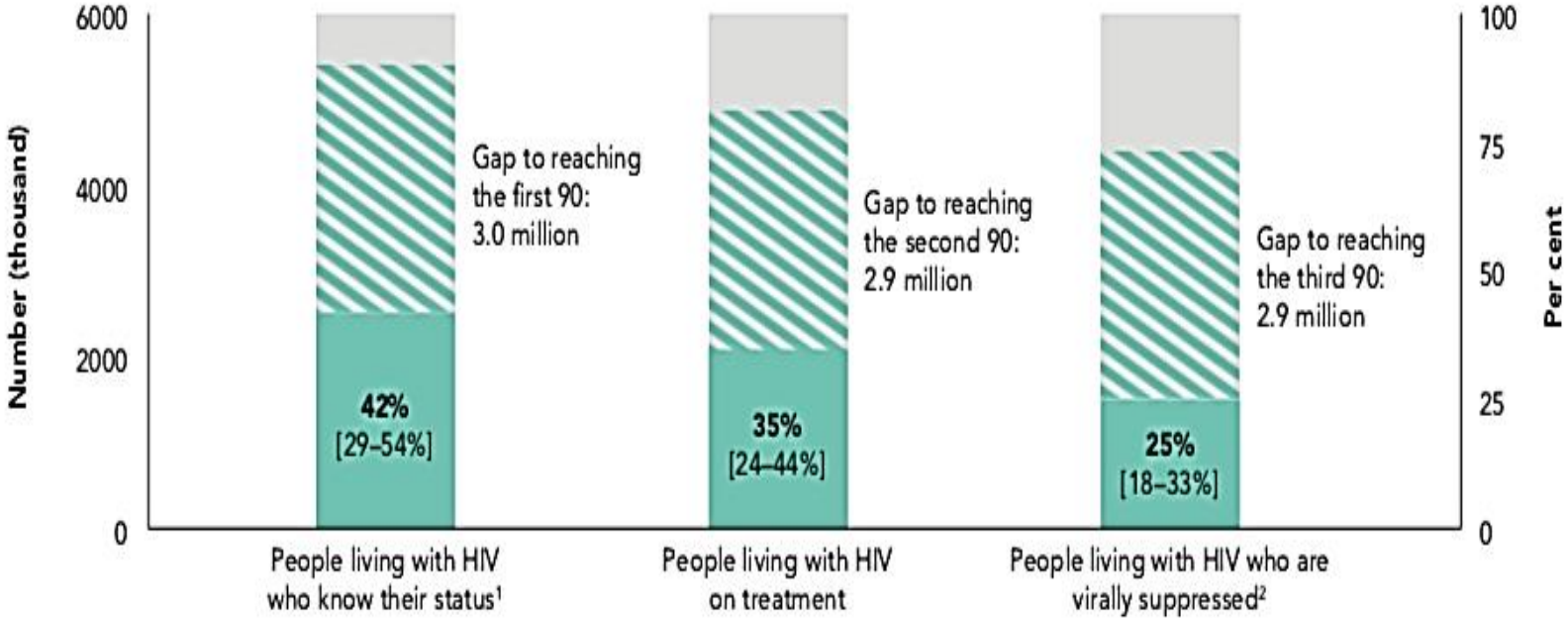
90% By 2020, 90% of all people receiving antiretroviral therapy will have viral suppression

UNADS targets for HIV



2017 (UNAIDS)

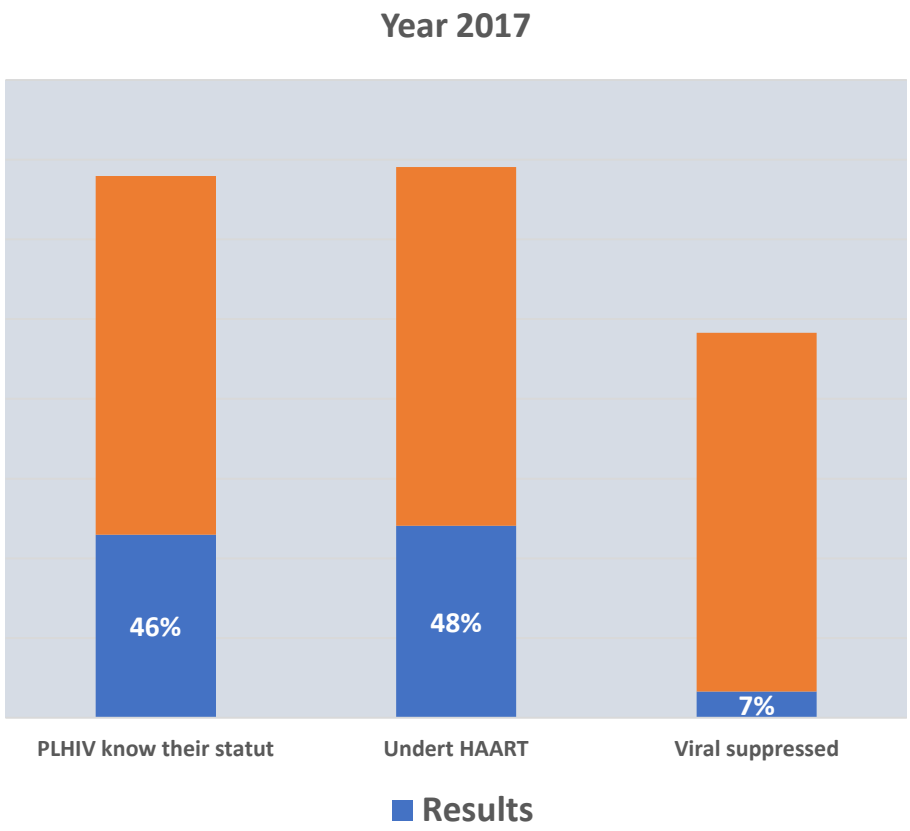
UNADS targets for HIV

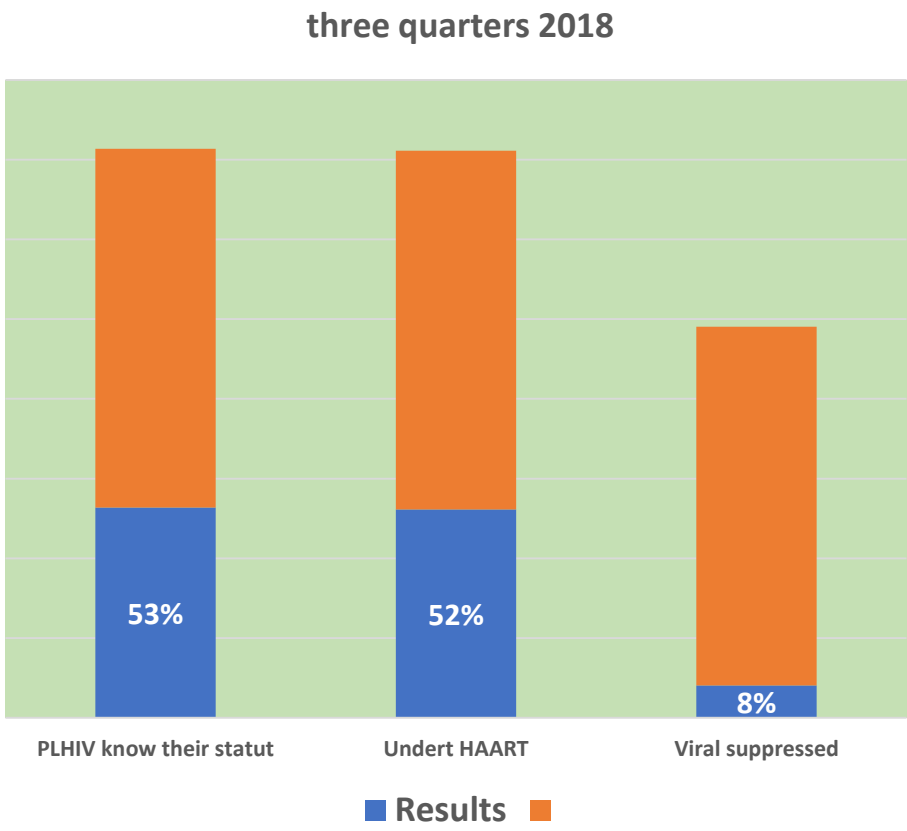


Western and Central Africa (ONUSIDA 2017)

Weighted mean retention rates as reported were 79.1%, 75.0% and 61.6 % at 6, 12, and 24 months, respectively. (Rosen S et al, 2007).

Targets 90 90 90 in Mali

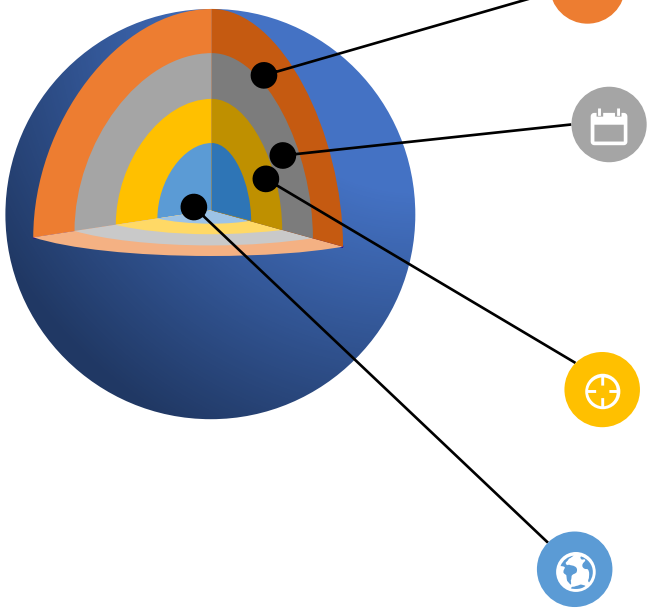




Report (CSLS/MoH)

NRL-Monitoring

Mission according to national policy



Participate to biologist straining and research

Realize the virology exam (early infants diagnosis, VL, genotyping etc….)

Develop and ensure the implementation of the laboratory external quality control system

Coordinate and ensure virological monitoring

Availability of Viral load device

01 NRL

02 8 Hospitals, including 4 in region

03 1 research institute, 1 association lab
1 private laboratory

04 10 District Hospitals: Alere q for EID
11 District Hospitals: GeneXpert for TB

All samples are taken at the sites of care.

NRL-Monitoring

To improve the 3rd target 90 in 2018

We use two platform with automated extraction:

Cobas **Abbott**

VL 2017

11 481

VL 2018

13 548

we made efforts

NRL-Monitoring

01 To improve the 3rd target 90 in 2018

Viral load (VL) are done at 90% at the NRL by 5 people

Samples transfer from regions to the NRL:

- samples do not always arrive in the right conditions
- about 30% of non-compliance plasma by cold chain breaking

We have just started DBS using three months ago.

Flow chart

In our NRL

Despite high rates LFU, but those monitored were undetectable at 87.7% in 12 months

J Antimicrob Chemother
doi:10.1093/jac/dky382

Journal of Antimicrobial Chemotherapy

Impact of HIV-1 primary drug resistance on the efficacy of a first-line antiretroviral regimen in the blood of newly diagnosed individuals in Bamako, Mali

Abdelaye Keita[1,2], Youssouf Sereme[2], Sylvie Pillet[2,3], Souleymane Coulibaly[1], Fodié Diallo[4], Bruno Pozzetto[2,3], Tenin Aoua Thiero[1] and Thomas Bourlet[2,3,*]

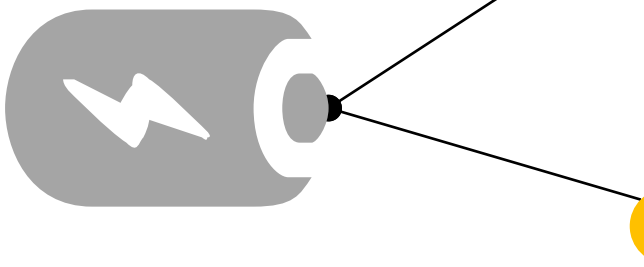
119 patients included

- 10 deceased (8.4%)
- 65 were followed-up for 12 months[1] (54.6%)
  - Undetectable VL
    - *Month 3*
    - *Month 6*
    - *Month 12*
  - Detectable VL at month 12
    - *Viral escape*
    - *No viral control under AR*
- 44 were lost to follow-up (37.0%)

	Month 3	*Month 6*	*Month 12*	*Viral escape*	*No viral control under AR*
Number (%)	20 (30.7)	47 (72.3)	57 (87.7)	2 (3.1)	6 (9.2)
Gain[1] of CD4+T cells count per ml (median)	+ 16	+ 14	+ 329	+ 342	+ 361

[1] after ART initiation; VL, viral load; ART, antiretroviral therapy

NRL- Resistance mutations



RESISTANCE

is a major concern in the HIV therapeutic management with ART weak genetic barrier (NNRTI)

Hamers et al, 2013

POLYMORPHISM

The impact of pol gene mutations at non-B strains on therapeutic efficacy is not fully understood

Holguin al, 2006

Wainberg et al, 2004 et Martinez et al, 2009

Primary resistance rate : 15,9%

NRL Results

		At ART initiation				
Patient ID	Gender	Age (years)	ART regimen	Clinical stage	PDRM	Drug resistance profile
013	F	36	TDF FTC EFV	3	V106I V179I	ETR[2]
019	F	46	TDF FTC EFV	3	E138A	ETR[2]
027	F	27	TDF FTC EFV	3	K103N	EFV NVP
038	F	24	3TC TDF EFV	2	K103N	EFV NVP
043	F	37	TDF FTC EFV	2	M184V T215Y K103E Y181C	ZDV 3TC FTC EFV NVP ETR RPV
046	F	33	TDF FTC EFV	3	K103N	EFV NVP
087	F	38	3TC TDF EFV	1	E138A	RPV ETR[2]
098	M	42	3TC TDF EFV	3	E138A	RPV ETR[2]
103	M	34	TDF FTC EFV	3	M184V Y181C	3TC FTC EFV NVP
104	M	54	3TC TDF LPV	3	V179T	ETR[1]
115	F	39	3TC TDF EFV	1	K103N	EFV NVP

The E138k polymorphic mutation that affects ETR, which is not yet used in the therapeutic regimen in Mali

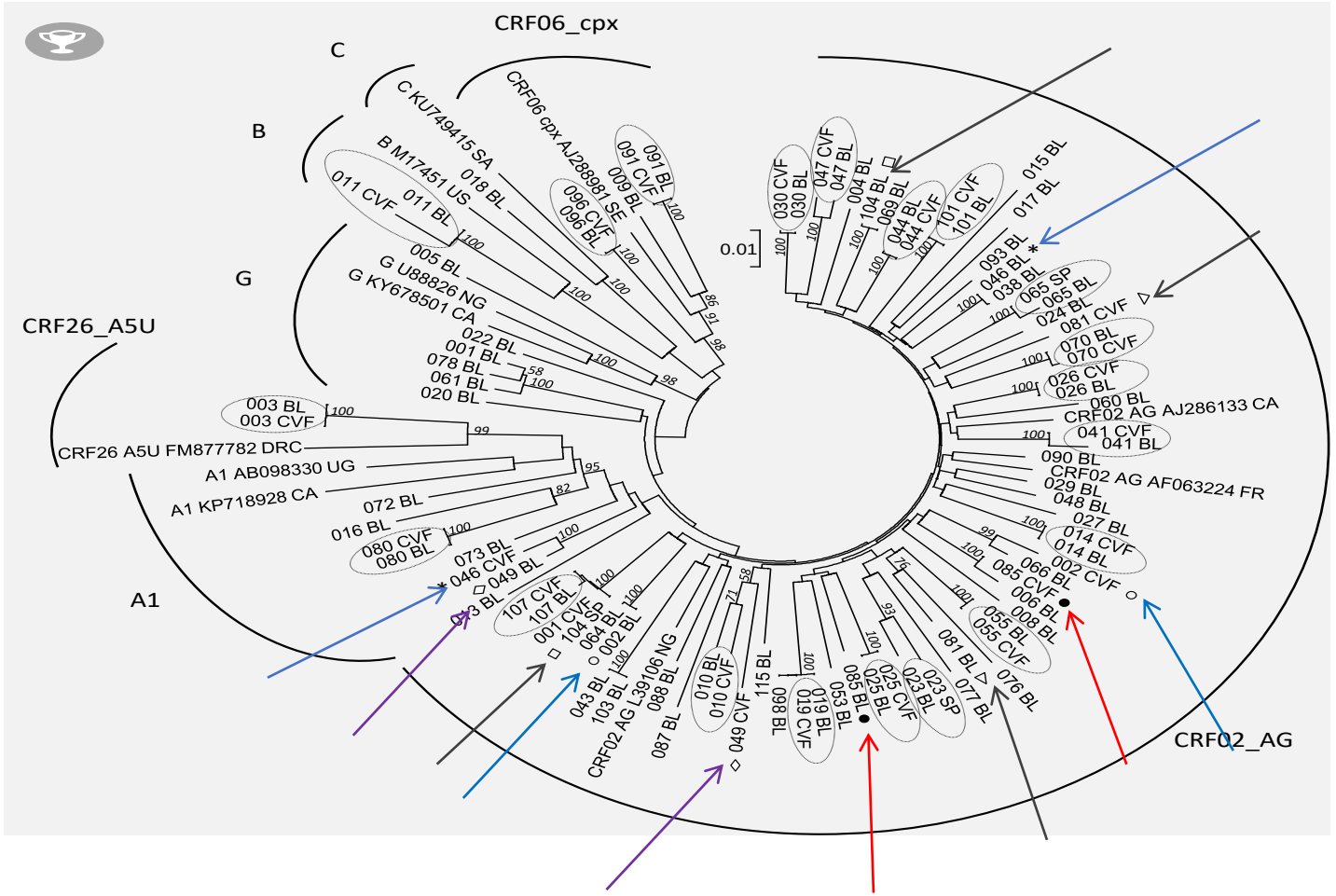
Acquired resistance rate : 3,1%

NRL Results

Patient ID	At ART inititation: Gender	Age (years)	ART regimen	CD4 gain[1]	HIV-1 RNA viral load (logcopies/ml): Before ART	M3[2]	M6[2]	M12[2]	Genotyping assay: Drug mutation (before ART/at M12)	Drug resistance profile at M12
no viral control										
011	F	29	3TC TDF EFV	-823	5.70	3.88	2.22	3.92	None/none	Wild-type
015	F	34	3TC TDF EFV	-427	3.98	3.81	1.85	4.38	None/K65E	TDF
038	F	24	3TC TDF EFV	183	6.14	3.75	1.85	5.36	K103N/K103N	EFV NVP
060	F	38	3TC TDF EFV	26	4.35	2.80	1.90	3.91	None/none	Wild-type
117	M	26	3TC TDF EFV	363	5.14	3.98	3.82	3.82	None/none	Wild-type
118	M	25	3TC TDF EFV	804	5.60	2.42	ND	1.88	None/NA	Unknown
viral rebound									None/L74V	ABC
002	F	37	3TC ABC LPV	72	4.69	2.47	1.6	2.60		
003	F	52	3TC TDF EFV	350	5.21	2.31	1.6	2.07	None/NA	Unknown

Mutations occur in patients on treatment: K65E and L74V

Phylogenetic analysis from blood sequences and genital secretions obtained at screening time



NRL-Resistance

01 Primary resistance rate : 15, 3% (2014)

TDRM: 7,9% (2008 Derrache A. et al), 11,5% (2010 Haidara A et al)

02 Residual VL and risk of transmission by persons under HAART

Viral rebound

Treatment efficacy on mucous reservoirs

Difficulties

1. Lack of coordination and monitoring of activities of other laboratories carrying out the viral load

   - Viral load devices are often available but little or no use

2. No strategy definition of virological monitoring

   - GeneXpert available in some district hospital
   - Alere q hiv1/2 available in some district hospital
   - M2000rt available in some national or regional hospital

3. Insufficient maintenance of available equipment

   insufficient funding

Difficulties

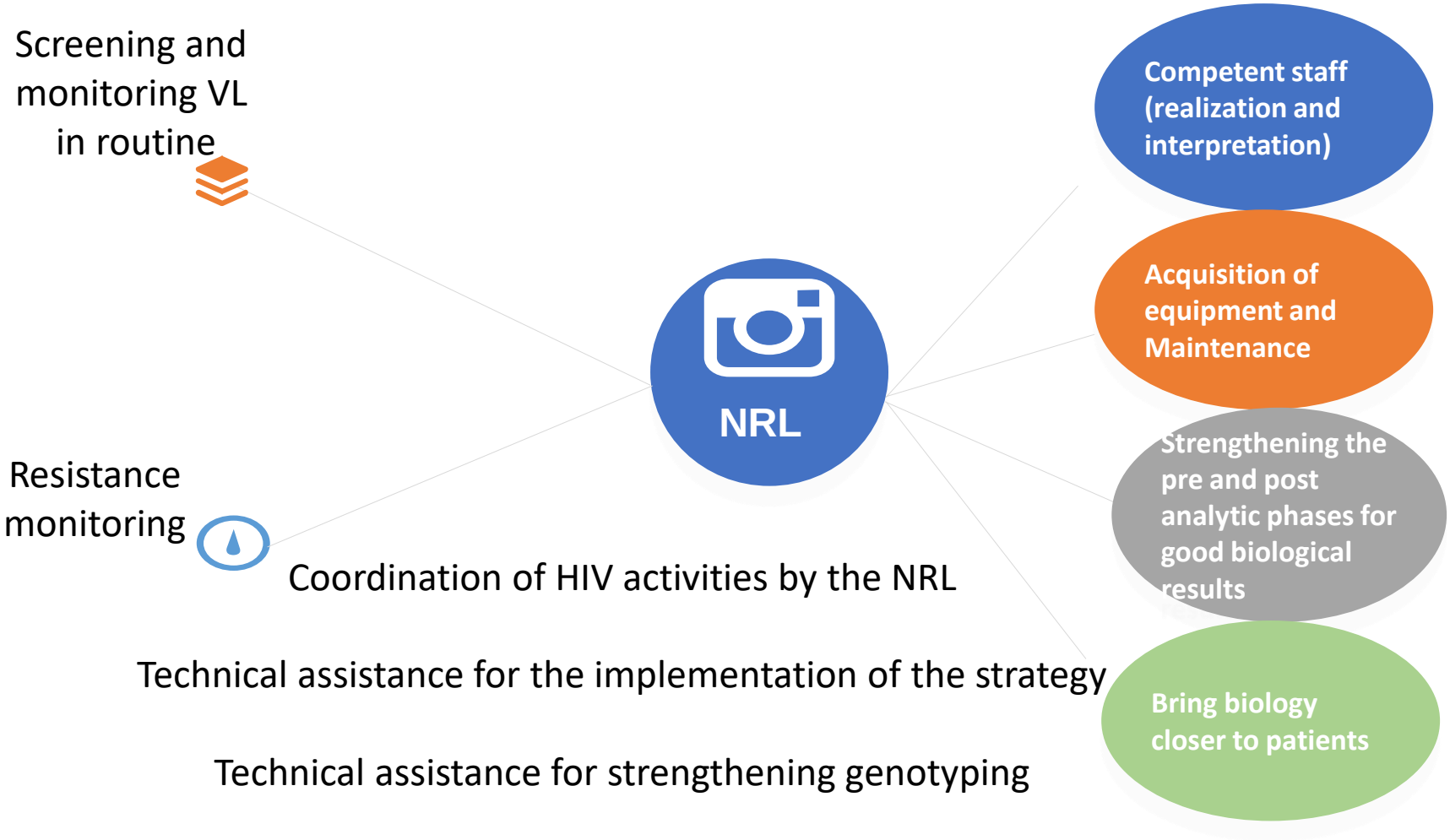
4 No external quality control for the laboratories carrying out the VL

- EQA only for screening
- Insufficient funding
- Lack of coordination

5 Viral load is not performed for all patients

6 Resistance testing is not widely available in resource-limited countries like Mali.

Challenges


Screening and monitoring VL in routine
Resistance monitoring
NRL
Coordination of HIV activities by the NRL
Technical assistance for the implementation of the strategy
Technical assistance for strengthening genotyping
Competent staff (realization and interpretation)
Acquisition of equipment and Maintenance
Strengthening the pre and post analytic phases for good biological results
Bring biology closer to patients

Conclusion

- Good sample, transported under the right conditions is essential to have a consistent and timely result
- Coordination of HIV activities is essential for successful UNAIDS goals
- HIV virological monitorring decentralization, supported by a national external quality system, would enable populations to access viral loads
- The NRL is essential in the ongoing monitoring of UNAIDS 3rd 90 and the achievement of the genotype.

THANK YOU FOR YOUR ATTENTION