



Agence autonome de l'Inserm

Formation Continue en Santé et Santé des Populations
Le 31 mars 2016



Impact de la Recherche sur la Santé : l'exemple des Pays du Sud

aviesan
alliance nationale
pour les sciences de la vie et de la santé

**ITMO Microbiologie
et maladies infectieuses**

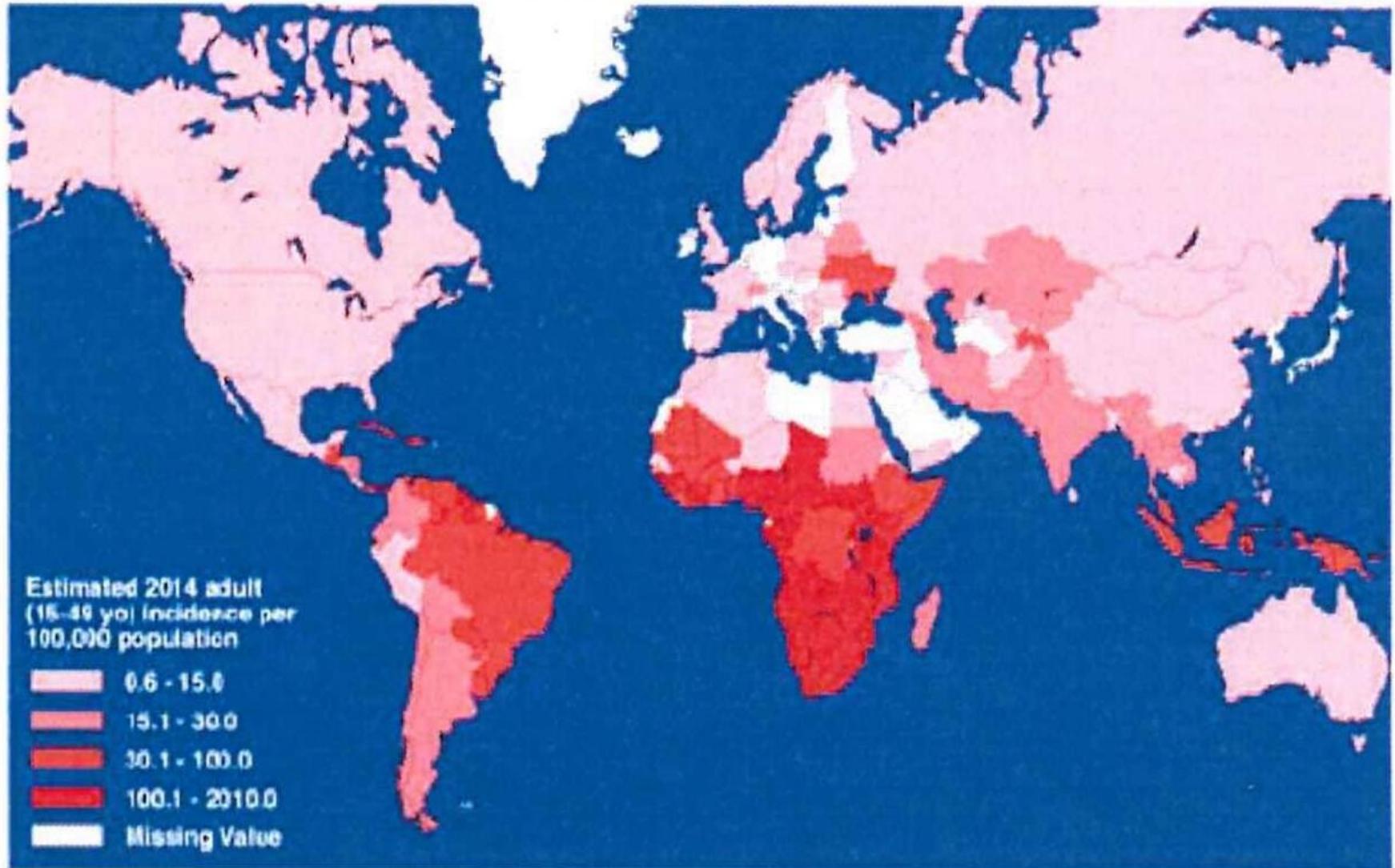
Pr. Jean-François DELFRAISSY
Director of ANRS/I3M
Internal Medicine Department
CHU Bicêtre – Paris XI - ANRS

Hôpitaux universitaires
Paris-Sud
Antoine-Béclère Bicêtre Paul-Brousse
ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

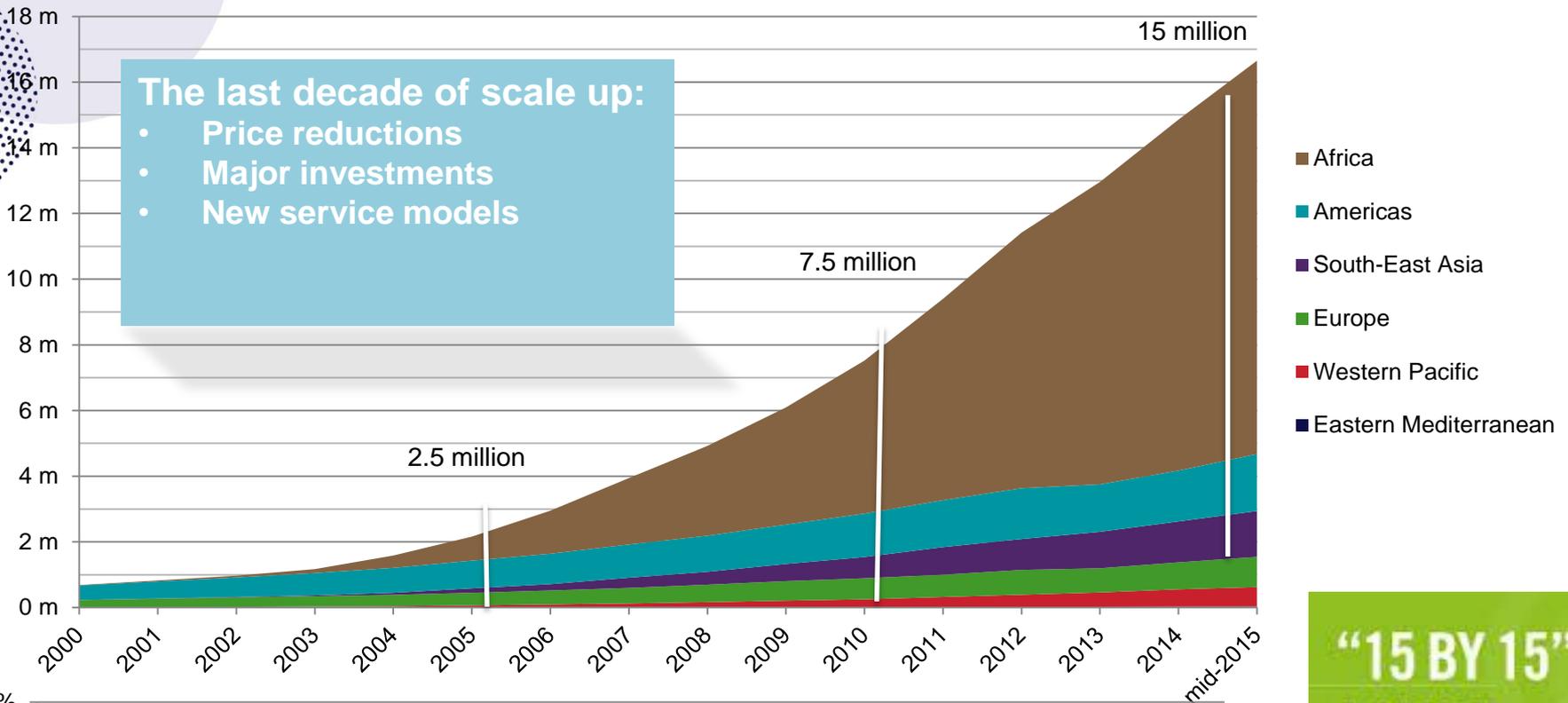
Ending the HIV/AIDS Pandemic

2030 ?

Adult HIV Incidence Rate by Country



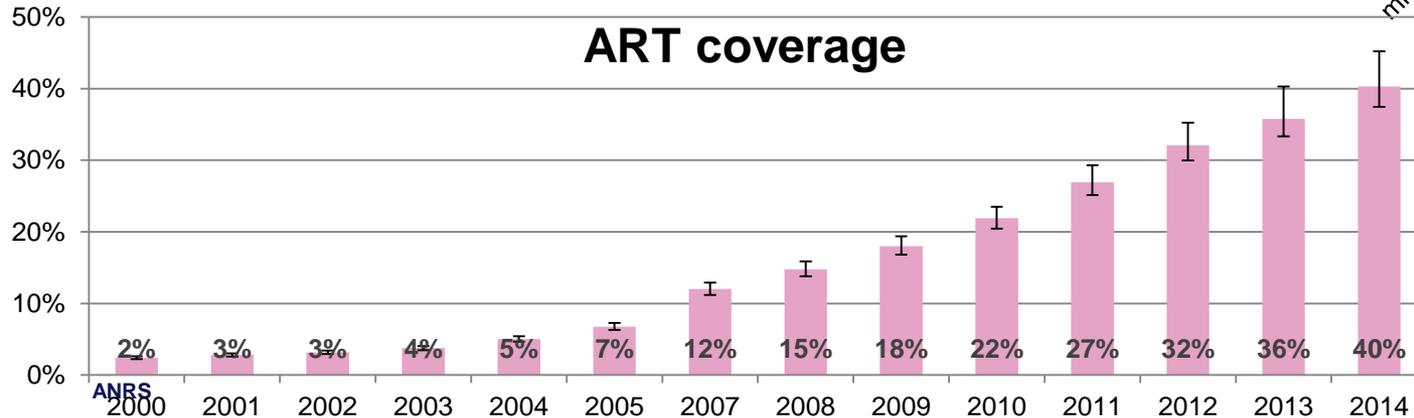
Progress in access to antiretroviral therapy: 2000–2015



“15 BY 15”
A GLOBAL TARGET ACHIEVED

UNAIDS

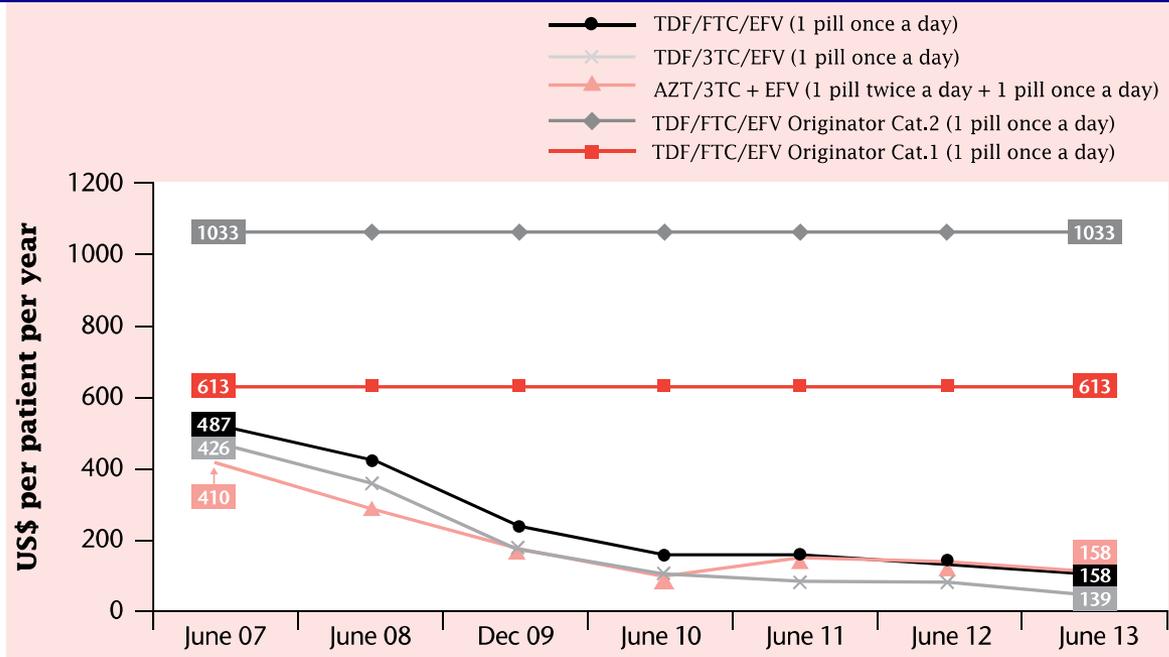
ART coverage



MDG main results and new targets...

Key parameters	2005	2015	2020	2030
New HIV infections	3 million	2 million [↓ 35%]	500,000	200,000
AIDS-associated deaths	2.4 million	1.2 million [↓ 50%]	400,000	200,000
PLHIV accessing ART	1.5 million	15 million [↑ 10x]	30 million	ALL
Investments for global HIV response (US\$)	7 billion	20 billion [↑ 3x]	32 billion	29 billion

A unique engagement of patients representatives for the universal access to treatment



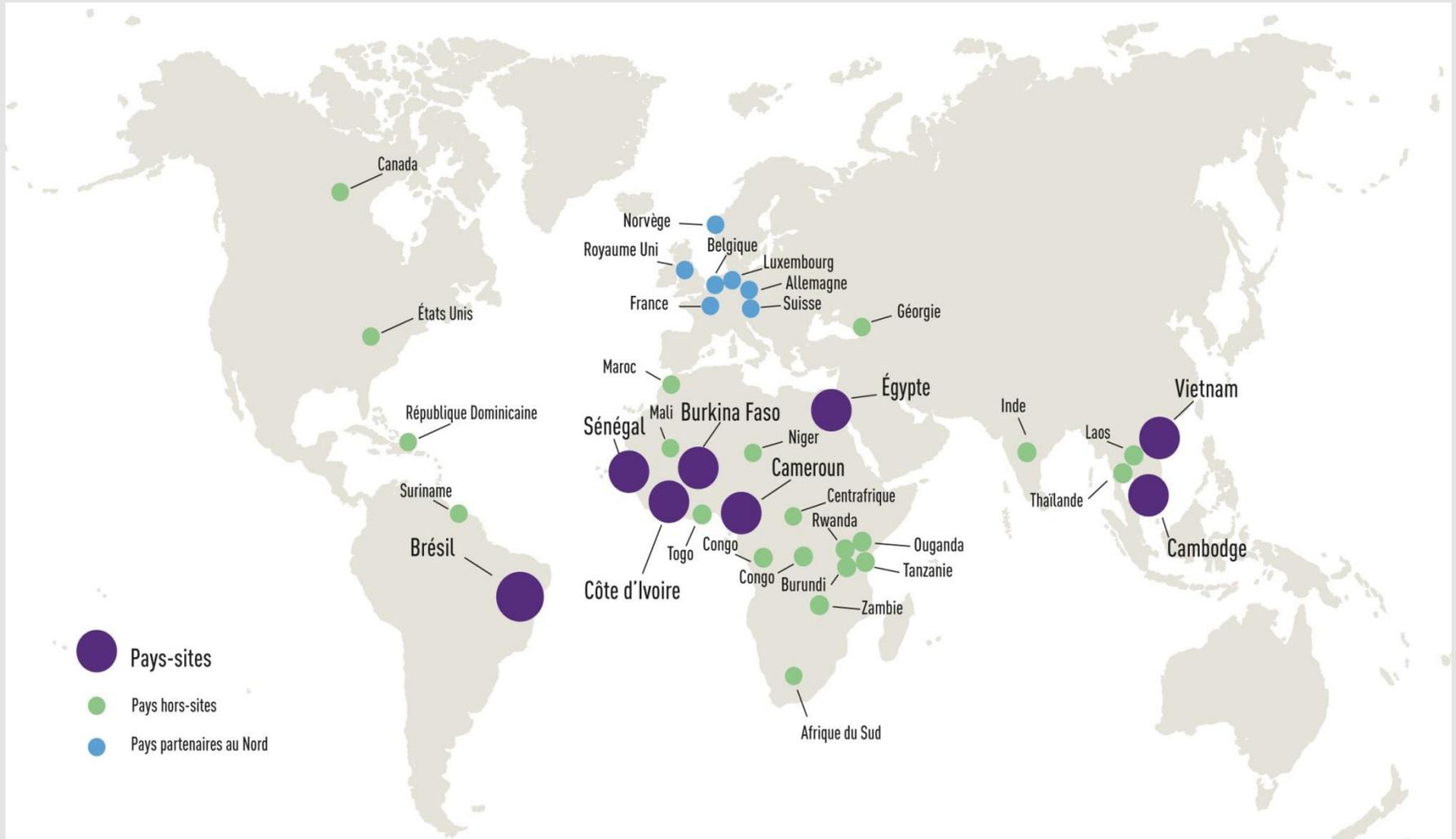
Evolution of 1st line treatment price (MSF)

Generic competition and activists pressure = drastic reduction of ARV prices in resource-limited countries but still too few combination available + 2nd/3rd line treatments prices too high !

Today: The revolution of Hepatitis C treatment!

New fight to achieve universal access at an affordable price to save lives...

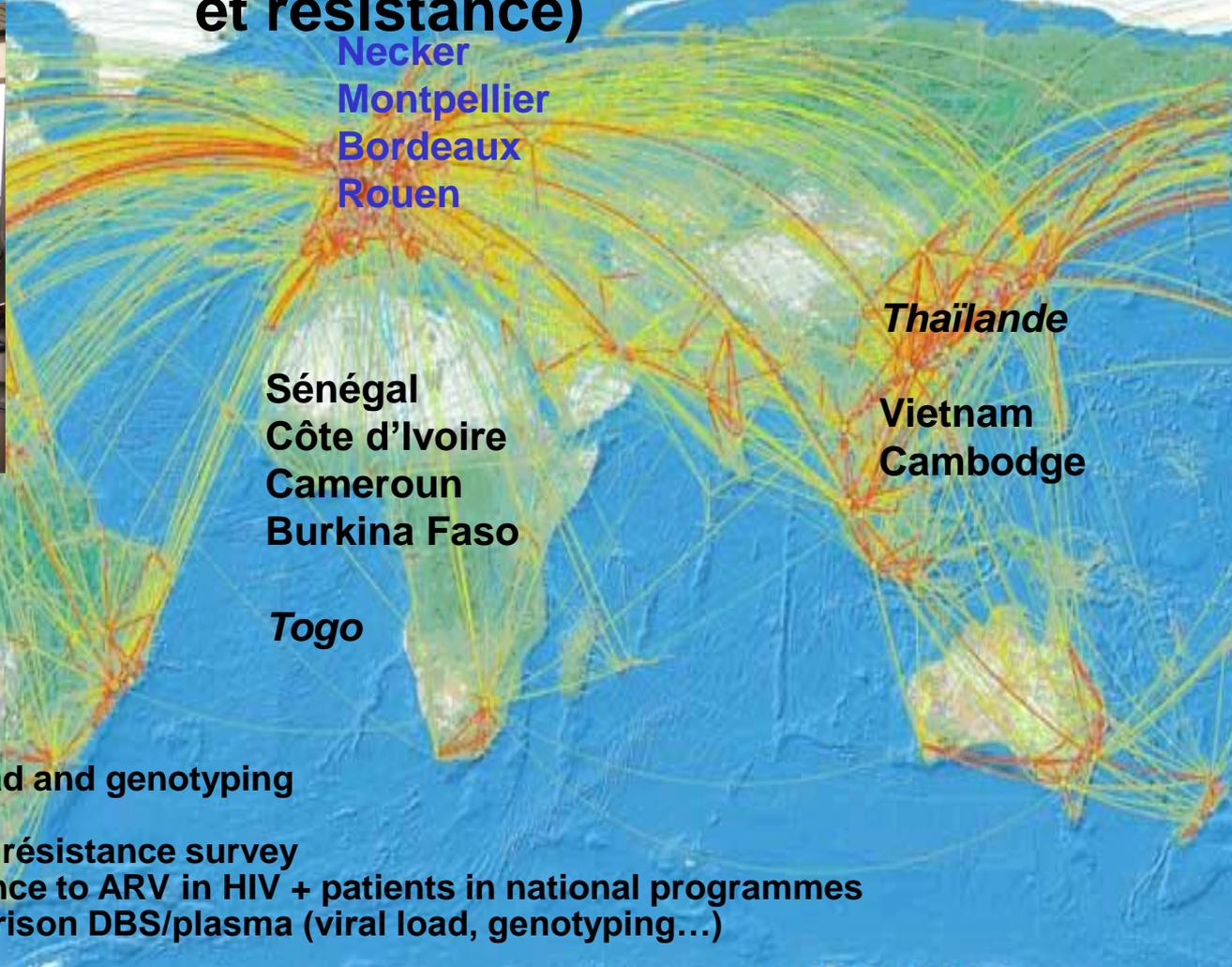
Les Sites ANRS (N=8) et les Pays partenaires



Caractéristiques des programmes sur les sites

Travail en réseau (projets multi-sites)

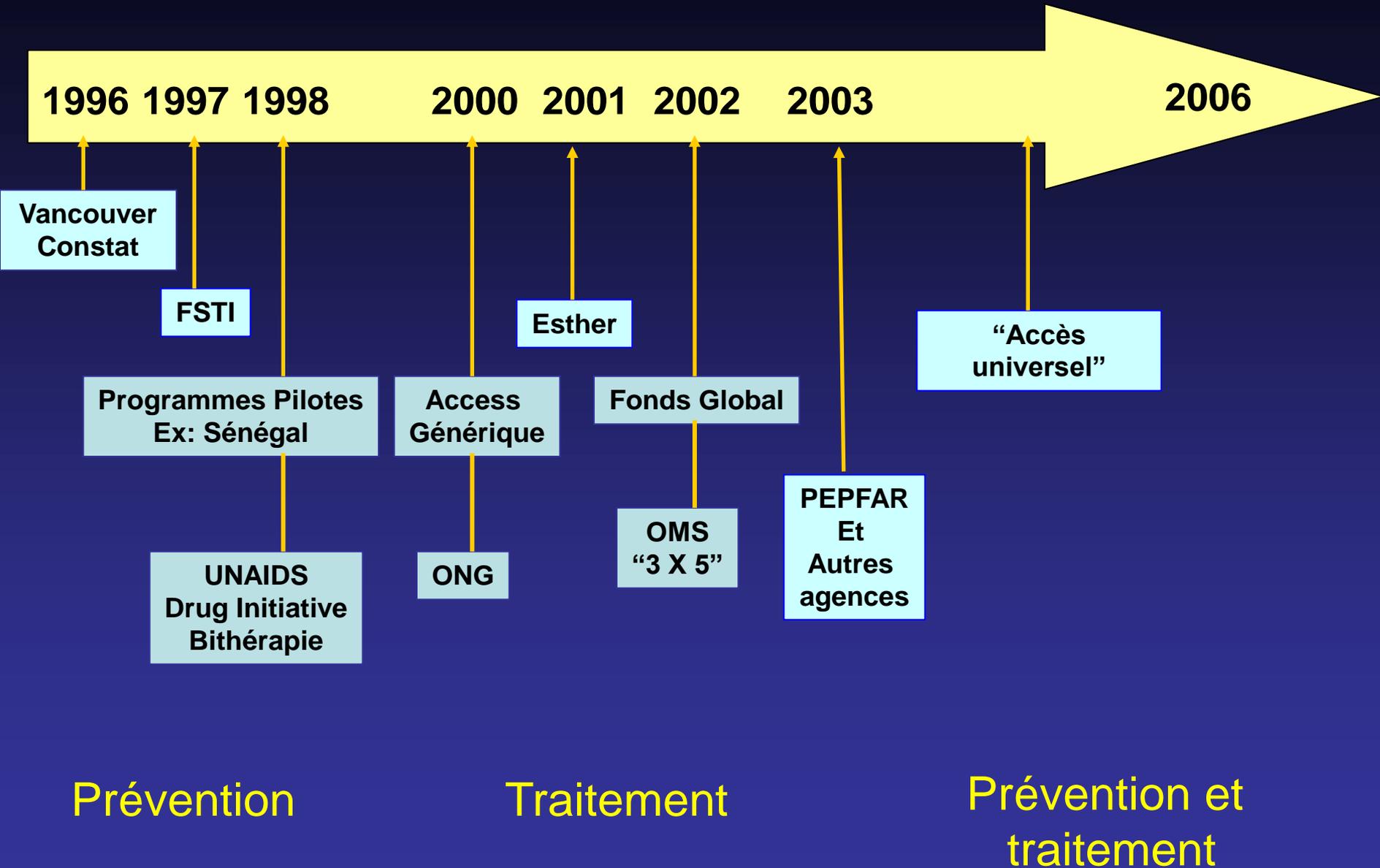
Groupe de travail nord/sud en virologie (quantification VIH et résistance)



Quality Control: viral load and genotyping

- 1) ANRS 12134: primary résistance survey
- 2) ANRS 12 186: resistance to ARV in HIV + patients in national programmes
- 3) ANRS 12 235: Comparison DBS/plasma (viral load, genotyping...)

Accès au traitement dans les Pays du Sud



« ARV therapy in sub saharan Africa :
-Complicated combination regimens
-Expensive and dangerous
-Severe side effects
-Adherence
-Rapid developpment of drug
resistance in the community».

Instead of promoting expensive and
dangerous ARV therapies...
PREVENTION »

E.Katabira, D Mabey ,et al Lancet,1998

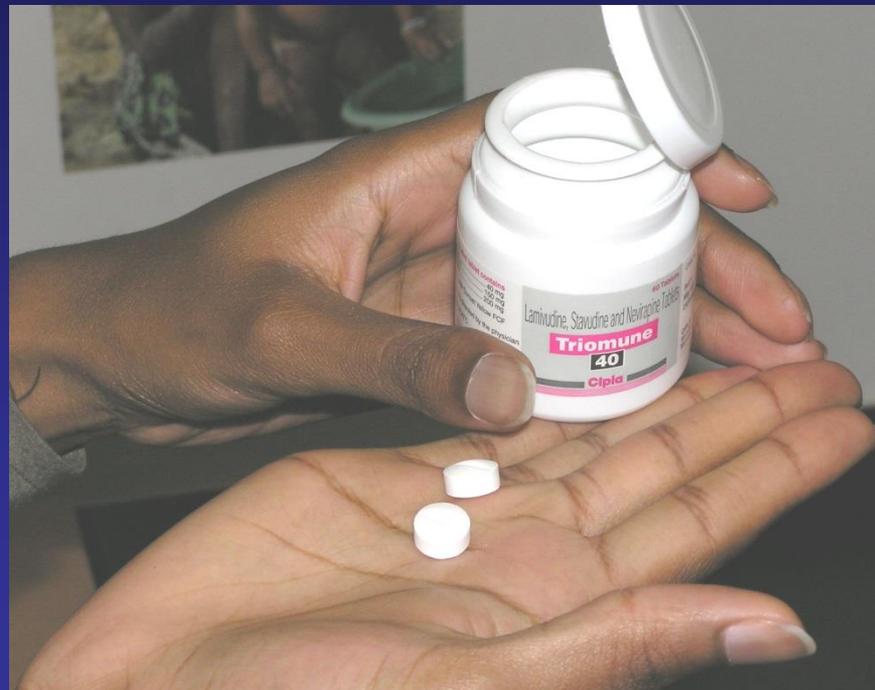
Effectiveness and safety of a generic fixed-dose combination of nevirapine, stavudine, and lamivudine in HIV-1-infected adults in Cameroon: open-label multicentre trial

Christian Laurent, Charles Kouanfack, Sinata Koulla-Shiro, Nathalie Nkoué, Anke Bourgeois, Alexandra Calmy, Bernadette Lactouck, Viviane Nzeusseu, Rose Mougnotou, Gilles Peytavin, Florian Liégeois, Eric Nerrienet, Michèle Tardy, Martine Peeters, Isabelle Andrieux-Meyer, Léopold Zekeng, Michel Kazatchkine, Eitel Mpoudi-Ngolé, Eric Delaporte, for the ANRS 1274 study group



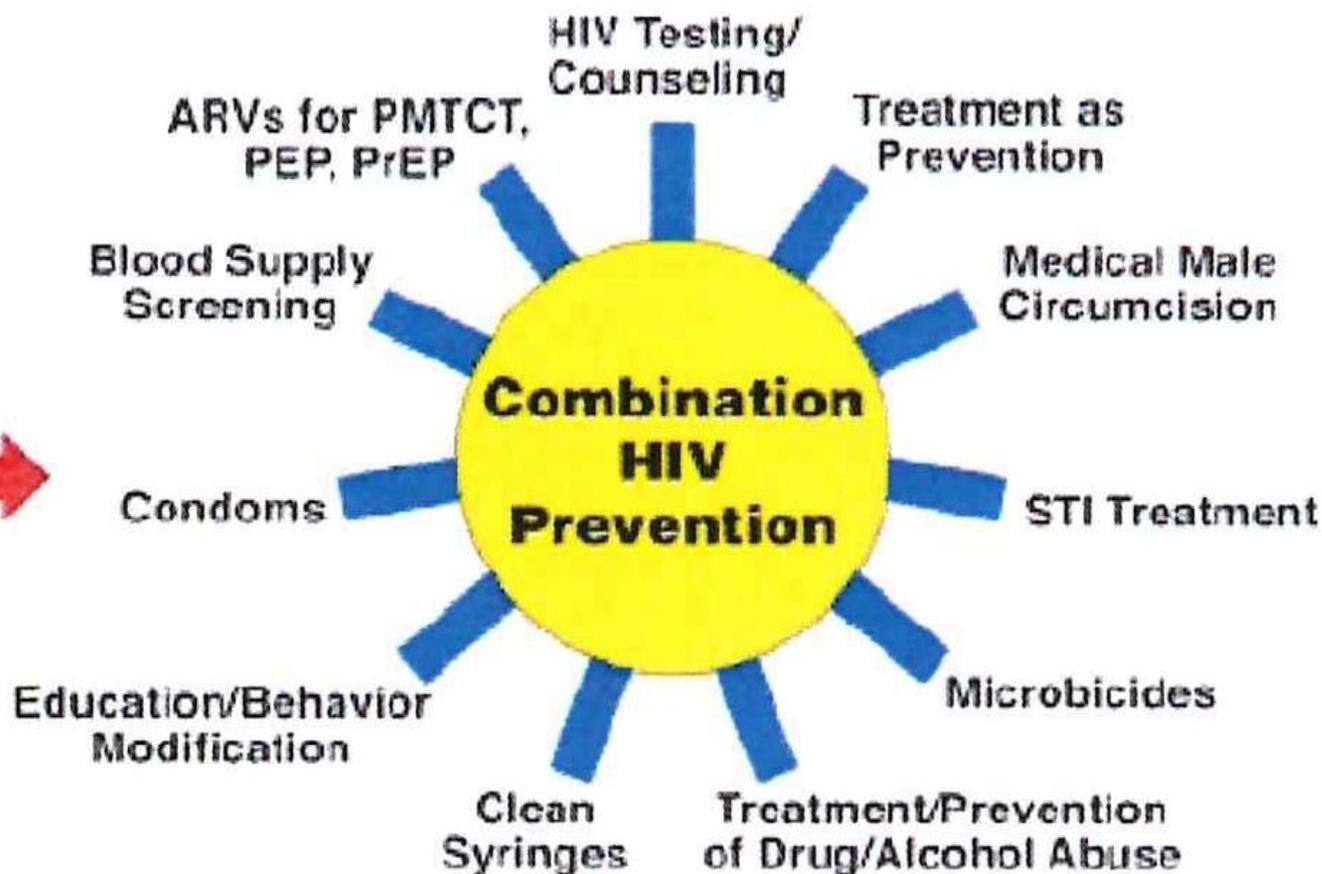
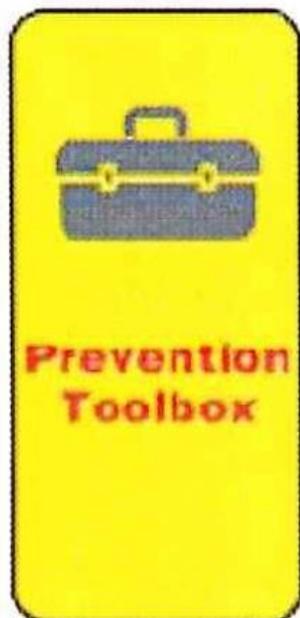
Lancet 2004; 364: 29-34

[See Comment page 3](#)



Tailored Prevention Using HIV Prevention Toolbox

Provision of Tailored Prevention Services

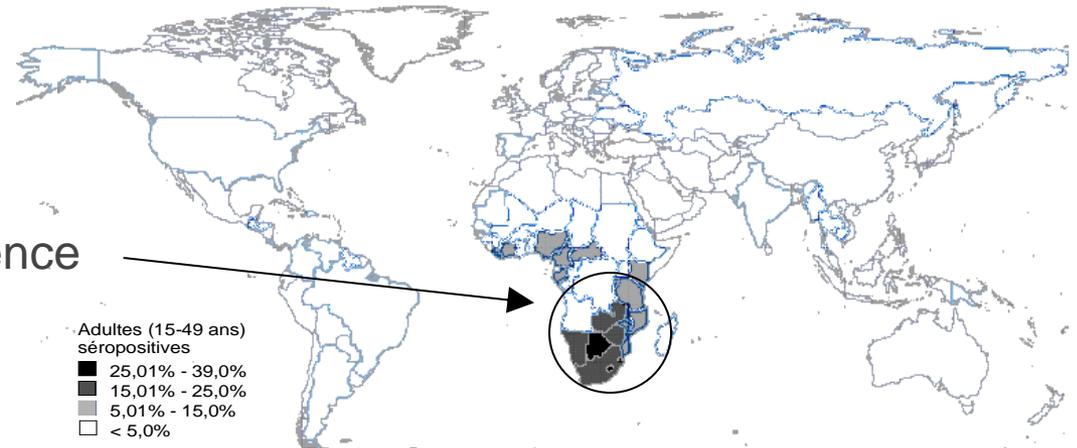


Male circumcision (MC) and HIV prevention 1/3

Main scientific facts

- 2005-2007: 3 RCT (South Africa – **ANRS-1265**, Uganda, Kenya)
- MC reduces the female-to-male transmission of HIV by about 60%
- MC explains the HIV heterogeneity in Africa
- 2007: WHO-UNAIDS recommendation
- Adapted to Eastern and Southern Africa
- Effectiveness: 10 MC to prevent 3 HIV infections in 10-20 years
- Cost: about 80 euros per MC
- High acceptability
- High potential impact

About 50% worldwide HIV incidence



Male circumcision (MC) and HIV prevention 2/3

Large scale study (ANRS-12126) 2008-2011 (B.Auvert)

- Township of Orange Farm in South Africa in 2008:
110 000 adults, MC prevalence = 12%, HIV prevalence = 20%
- Roll-out of Voluntary Medical MC (VMMC)
- Community based campaign against HIV
- 25 000 VMMC with HIV testing and counseling
- Results in 2012:
 - MC prevalence reaches 50% (60% among young men)
 - Reduction of HIV prevalence among men
 - No effect on risky sexual behavior and condom use
 - Women have a positively view of MC
 - Women with circumcised partners are less infected with HIV

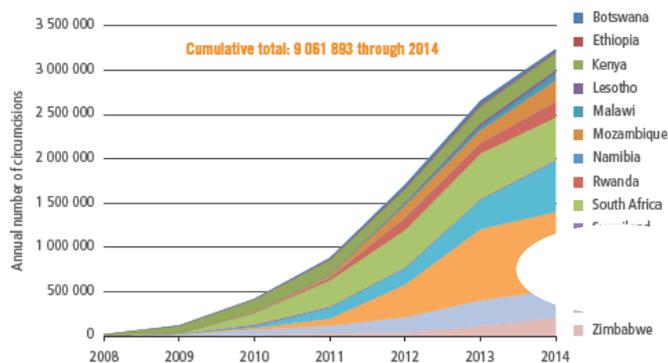


Male circumcision (MC) and HIV prevention 3/3

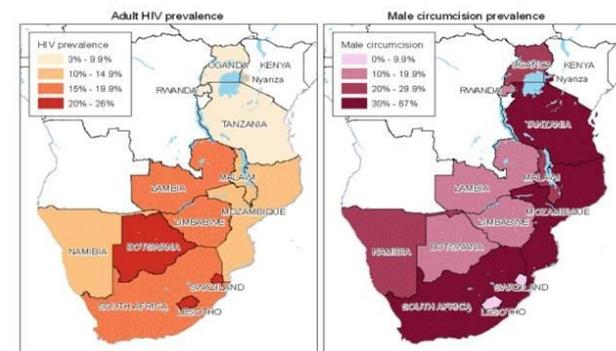
Roll-out in Africa since 2008

- Roll-out in 14 priority countries in Eastern and Southern Africa with low MC prevalence and high HIV prevalence
- Goal: 80% coverage among adults (21 million VMMC are needed)
- Funding: PEPFAR (USA), the Global Fund, African countries
- Complementary to ARV:
ARV for **HIV-positive**, VMMC is effective for **HIV-negative**
- Competition for funding with ARV!
- About 10 million VMMC done in 2008-2015 (50% of the goal)
- WHO stated in 2014: “The feasibility of scaling up this intervention”

Figure. Annual numbers of voluntary medical male circumcisions performed for HIV prevention in 14 countries of East and Southern Africa, 2008–2014

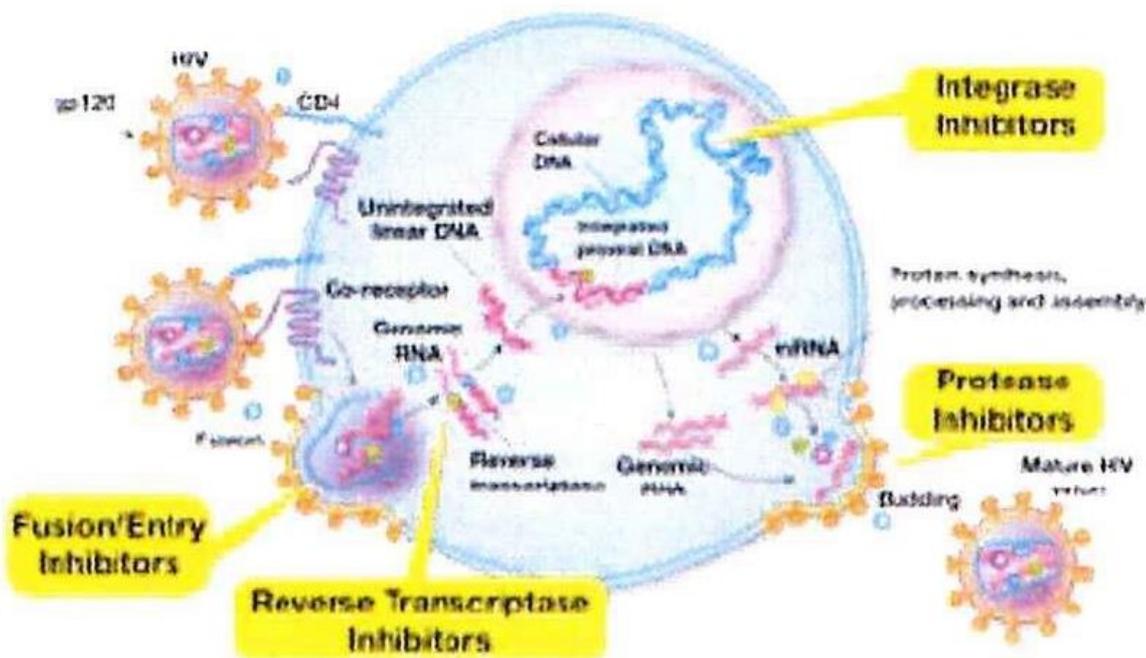


Source: Global AIDS Response Progress Reporting from national programmes WHO/UNAIDS/UNICEF.



Male circumcision target countries

Prevention Modalities Built upon Antiretroviral Therapy



- Prevention of Mother-to-Child Transmission
- Pre-Exposure Prophylaxis
- Post-Exposure Prophylaxis
- Treatment as Prevention



The
**New England
Journal of Medicine**

PUBLISHED WEEKLY BY THE NEW ENGLAND JOURNAL OF MEDICINE AND SOCIETY

Volume 331

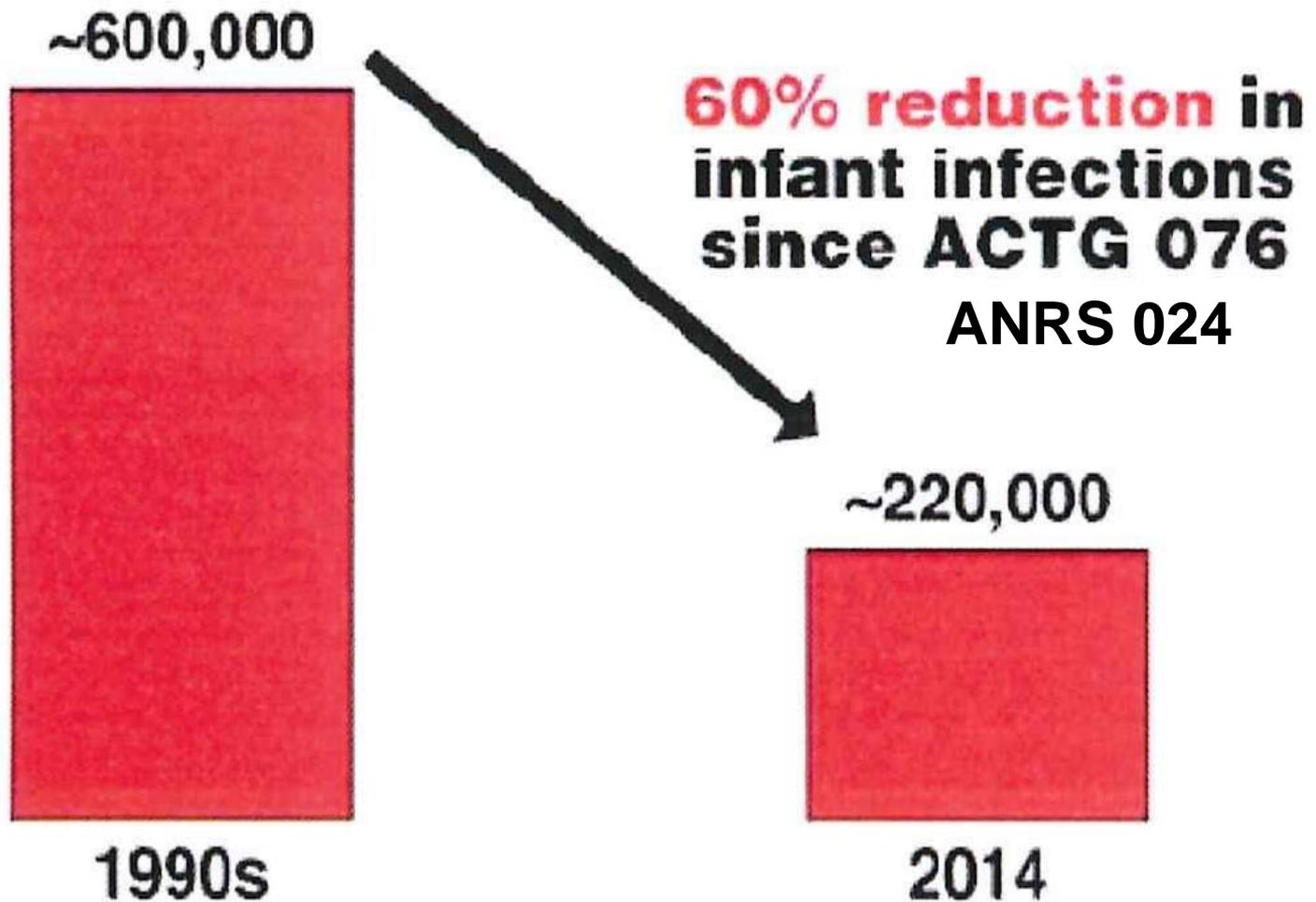
November 3, 1994

Number 18

**Reduction of Maternal-Infant
Transmission of Human
Immunodeficiency Virus Type 1
with Zidovudine Treatment**

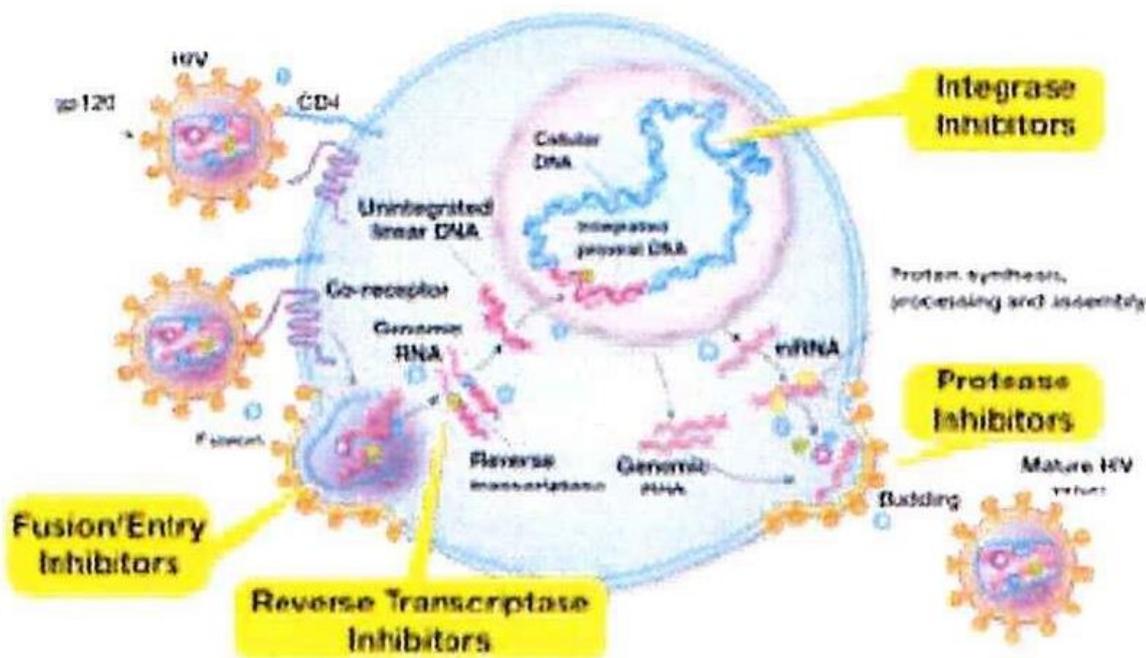
EM Connor, et al. - **ACTG 076** ANRS 024

Children Newly Infected with HIV Globally, 1990s to 2014



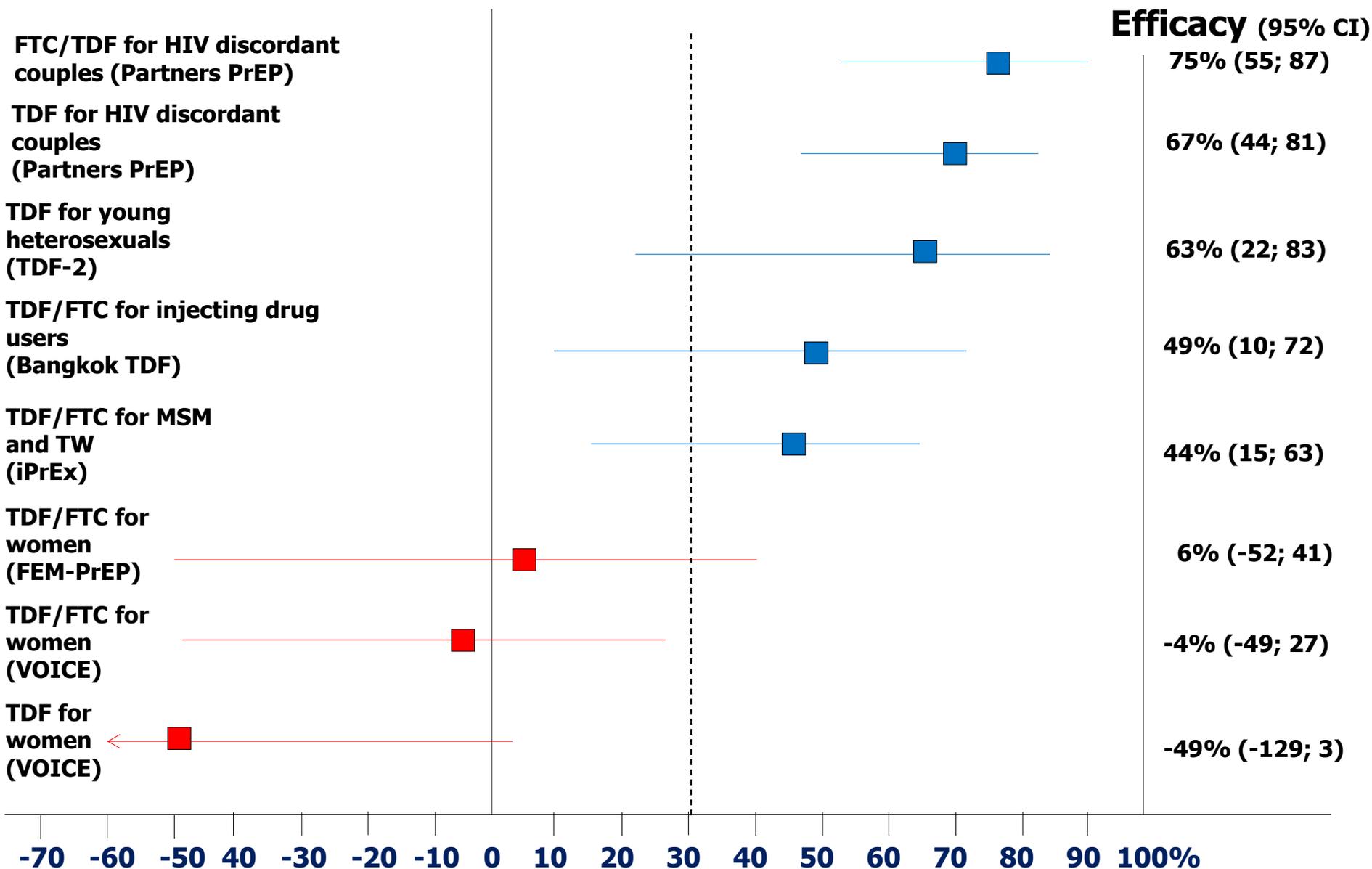
Source: UNAIDS

Prevention Modalities Built upon Antiretroviral Therapy



- Prevention of Mother-to-Child Transmission
- Pre-Exposure Prophylaxis
- Post-Exposure Prophylaxis
- Treatment as Prevention

Conflicting Results with Daily Oral PrEP





ipergay

ANRS

Intervention Préventive
de l'Exposition aux Risques
avec et pour les Gays

IPERGAY

Study Design

Effectiveness of “on demand” PrEP Randomized placebo-controlled trial

- High risk MSM
- Condomless anal sex with >2 partners

Full prevention services *
TDF/FTC before and after sex
(n = 950)

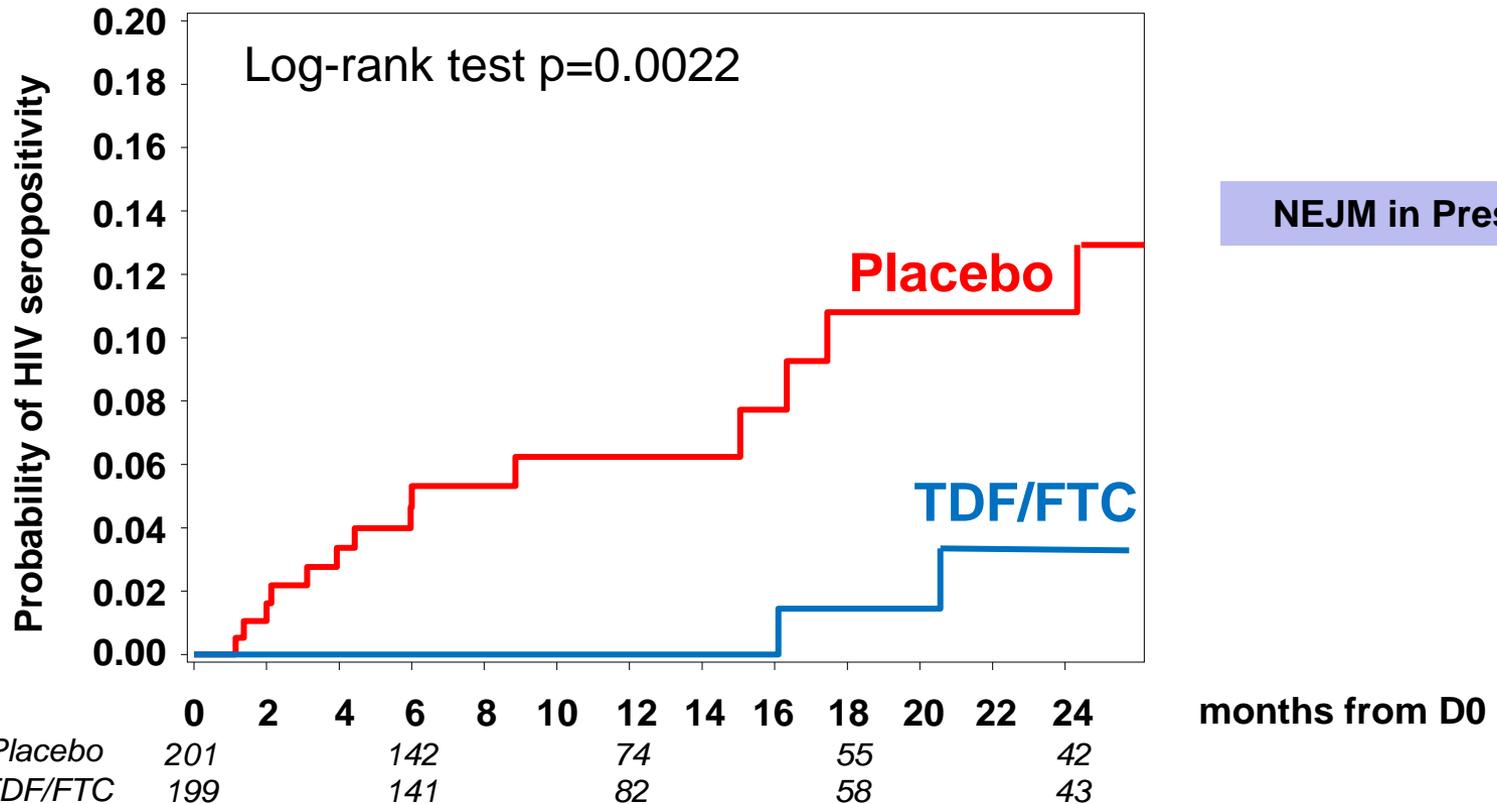
Full prevention services *
placebo before and after sex
(n = 950)

- Counseling, testing for STI, condoms, vaccination, PEP

Primary endpoint: HIV infection

Incidence of HIV infection: 3/100 PY, 50% efficacy, ~ 2000 pts

KM Estimates of Time to HIV-1 Infection (mITT Population)

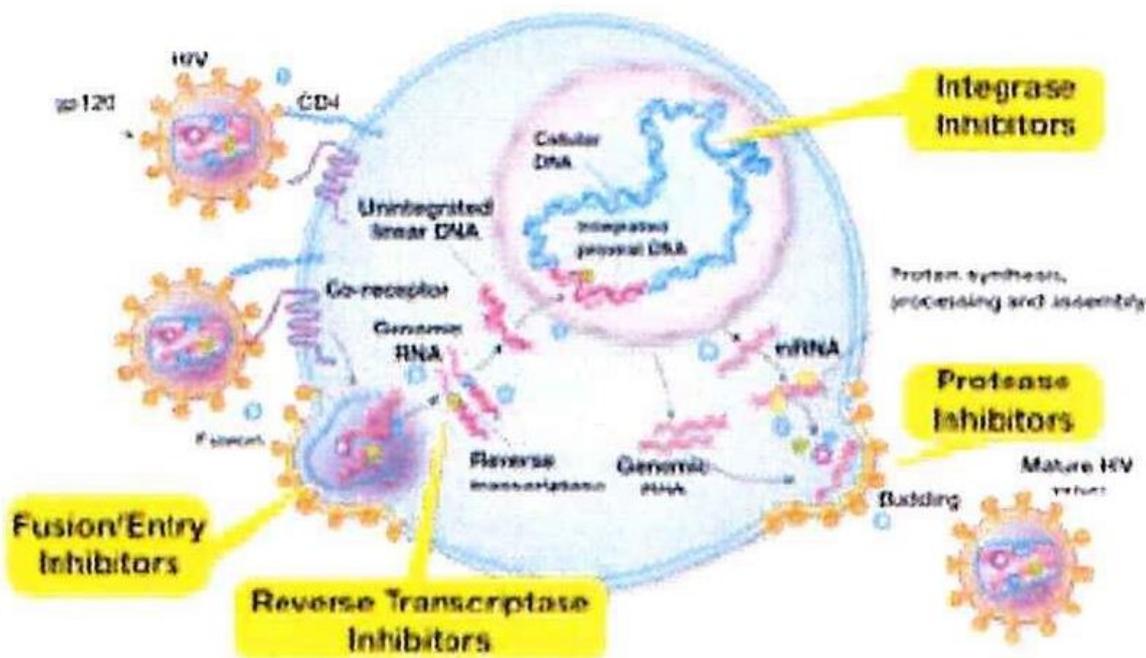


Mean follow-up of 13 months: 16 subjects infected

14 in placebo arm (incidence: 6.6 /100 PY) and **2 in TDF/FTC arm** (incidence: 0.9 /100PY)

86% relative reduction in the incidence of HIV-1 (95% CI : 40-98, $p=0.0019$)

Prevention Modalities Built upon Antiretroviral Therapy



- Prevention of Mother-to-Child Transmission
- Pre-Exposure Prophylaxis
- Post-Exposure Prophylaxis
- Treatment as Prevention

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

AUGUST 27, 2015

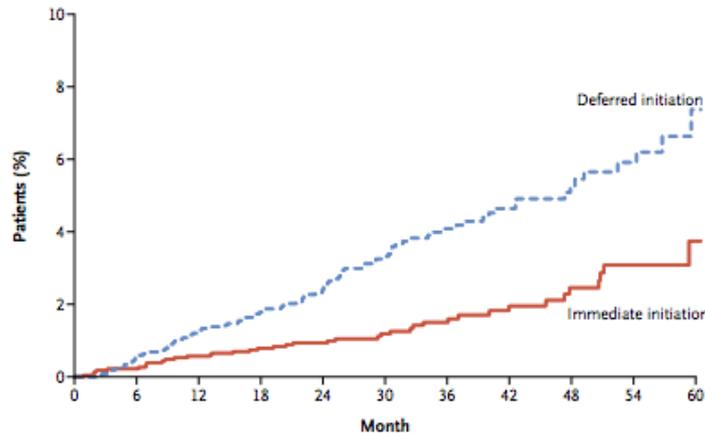
VOL. 373 NO. 9



Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection

The INSIGHT START Study Group*

A Time to First Primary Event



No. at Risk	
Immediate initiation	2326 2302 2279 2163 1801 1437 1031 757 541 336 110
Deferred initiation	2359 2326 2281 2135 1803 1417 1021 729 520 334 103
Estimated Percentage	
Immediate initiation	0.2 0.6 0.8 0.9 1.2 1.5 2.0 2.5 3.1 3.7
Deferred initiation	0.5 1.2 1.8 2.4 3.3 4.1 4.6 5.3 5.9 7.4

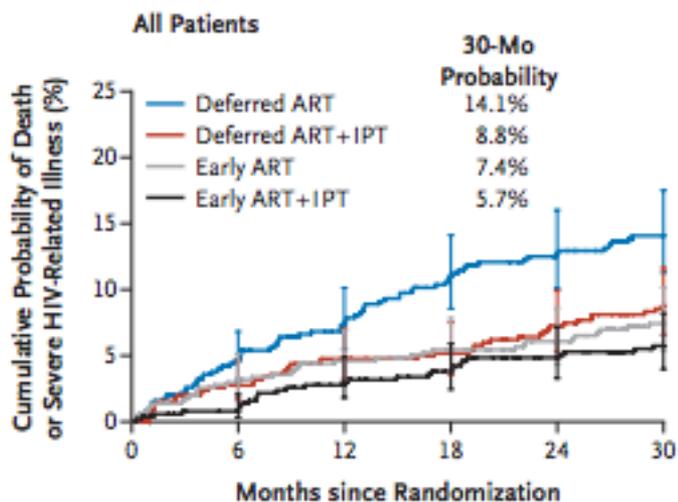
- N= >4,600 adults in 35 countries
- Risk of developing serious illness or death reduced by 53% among HIV+ patients starting ART at CD4 count above 500, compared to CD4 of 350

ORIGINAL ARTICLE

A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa

The TEMPRANO ANRS 12136 Study Group*

A Primary Outcome



No. at Risk

	0	6	12	18	24	30
Deferred ART	511	473	448	418	400	366
Deferred ART+IPT	512	489	473	459	440	419
Early ART	515	481	463	452	432	403
Early ART+IPT	518	501	478	459	445	418

Temprano Trial Shows Health Benefits of Early ART

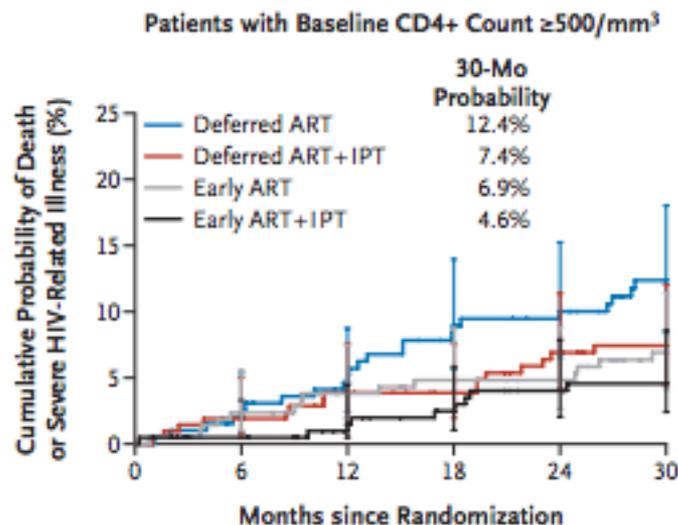


February 2015

Early ART and IPT in HIV-Infected African Adults With High CD4 Count (**Temprano Trial**)

C Danel, D Gabillard, JB Ntakpe, et al.

- RCT of over 2,000 patients in Côte d'Ivoire
- Early ART (as compared to delayed treatment) reduces risk of death and serious illness (e.g., TB and bacterial infections) **by 44%**



No. at Risk

	0	6	12	18	24	30
Deferred ART	201	190	181	168	162	145
Deferred ART+IPT	212	204	197	191	182	174
Early ART	222	205	193	189	185	171
Early ART+IPT	214	205	197	190	184	171

The ANRS 12249 TasP trial



- Cluster randomized trial (2011-2016) evaluating the feasibility, acceptability and efficacy of immediate ART on HIV incidence in rural KwaZulu-Natal, South Africa (*Iwuji C et al, Trials 2013; Orne-Gliemann et al, BMC Publ H 2015*)

Home-based HIV-testing (6 monthly rounds)

Trial area population: 22,000 individuals

Referral to TasP clinic if identified HIV+

TasP clinics (1/cluster)

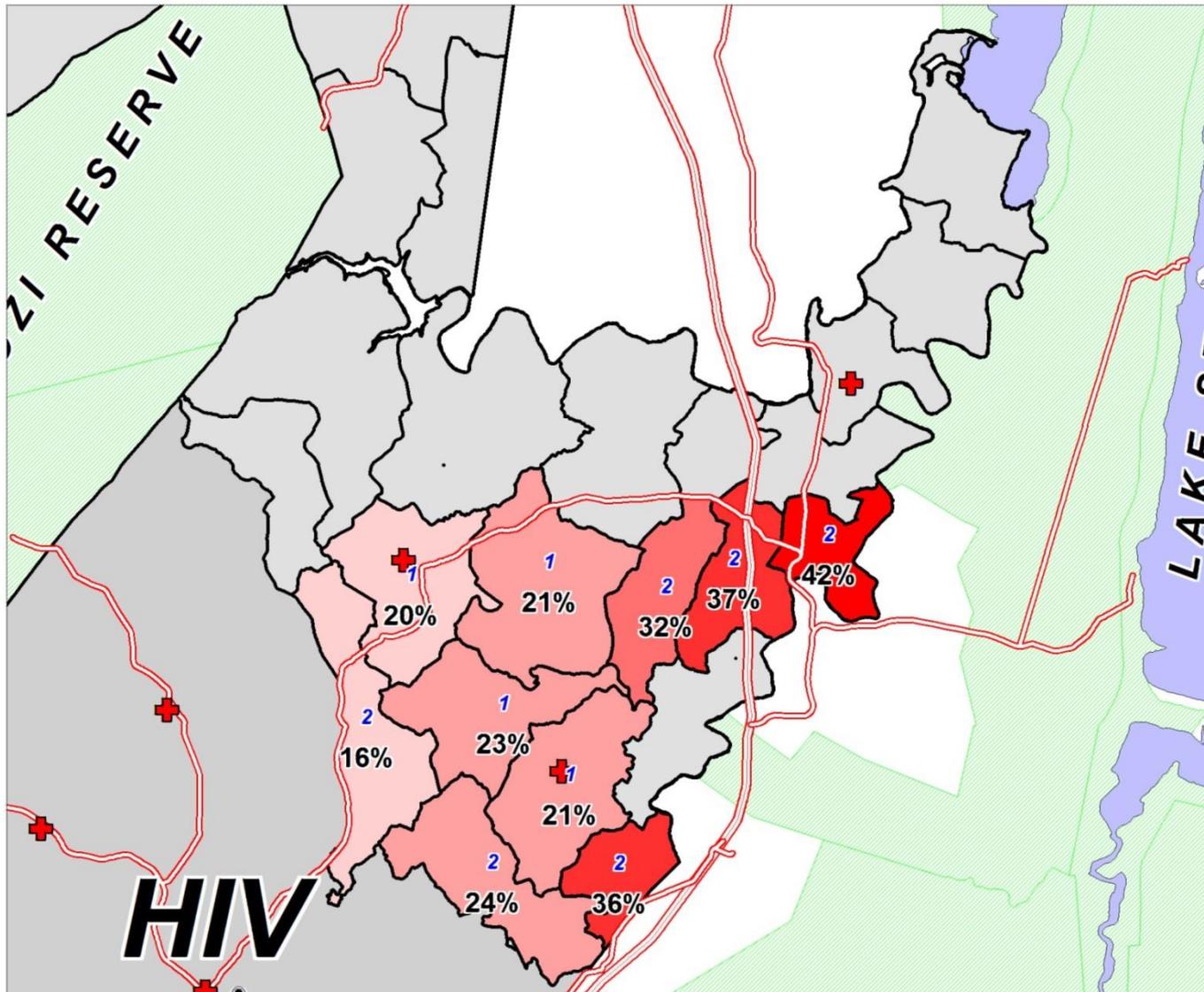
11 Intervention clusters: Treat all HIV+ individuals regardless of CD4 count /clinical stage

11 Control clusters: Treat all HIV+ individuals according to South African guidelines

DoH clinic (3 clinics in trial area)

Treat all HIV+ individuals according to South African guidelines

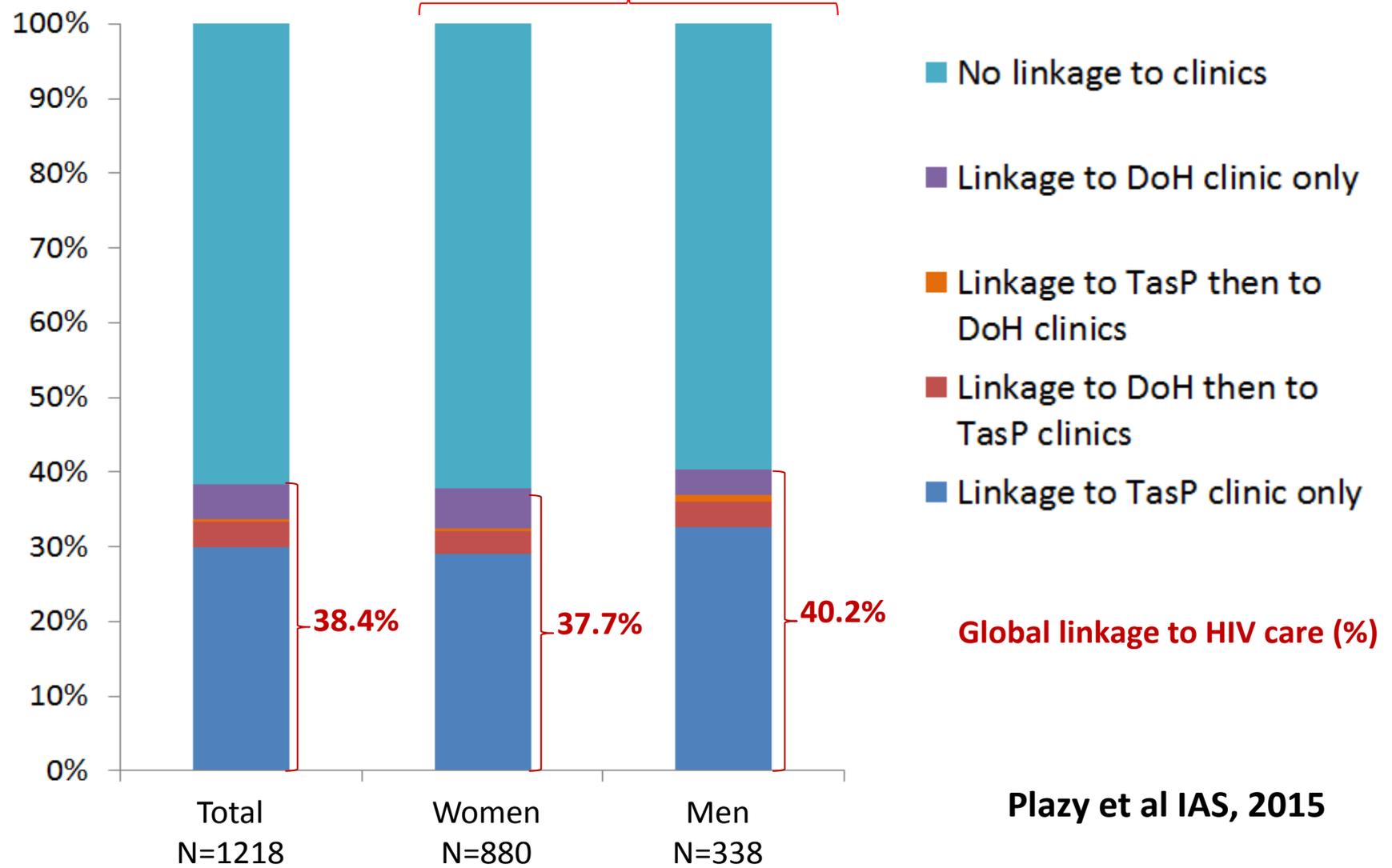
HIV prevalence by cluster – Initial 10 clusters



Rates of linkage to HIV care within 3 months of referral by sex



P=0.42



Plazy et al IAS, 2015



GUIDELINES

GUIDELINE ON WHEN
TO START ANTIRETROVIRAL
THERAPY AND
ON PRE-EXPOSURE
PROPHYLAXIS FOR HIV

SEPTEMBER 2015



- ART should be initiated in all adults living with HIV at any CD4 cell count

Temprano +++

- Treatment as Prevention
START, TASP ?

- Oral PrEP should be offered as an additional prevention choice for people at substantial risk of HIV infection

Proud, IPERGAY +++

- PREP in France – Nov 2015, a major political decision

Role of ANRS ?

« Paris sans SIDA »

2016 Paris

Blueprint to End AIDS



1. Diagnose and link to care
2. Treat with ART, retain in care, prevent transmission
3. Facilitate access to PrEP and PEP

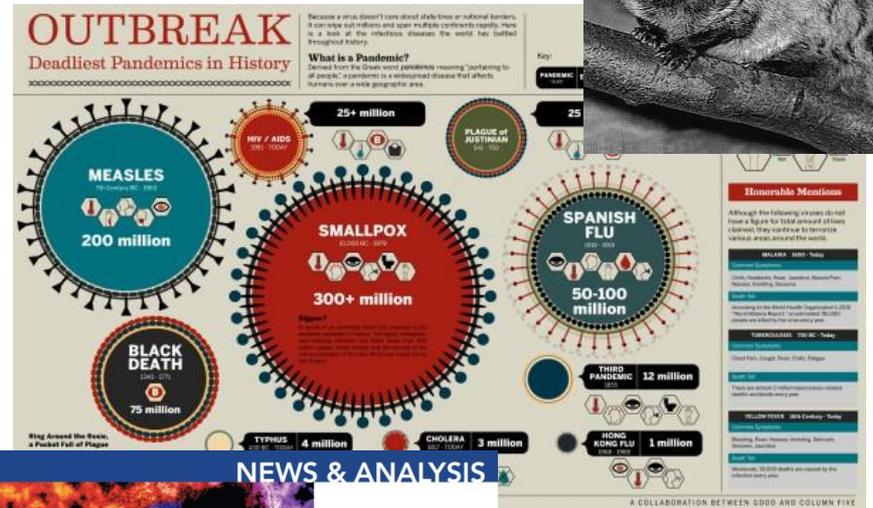


Reduce new
infections from 4 000
in 2014 to 1000 by 2020

PREVENIR ANRS TRIAL

Outbreaks: a constant repetition

SARS 2003
 Chikungunya 2005
 H1N1 pandemic 2009
 MERS-CoV 2013
 Ebola 2014
 Zika 2015



NEWS & ANALYSIS

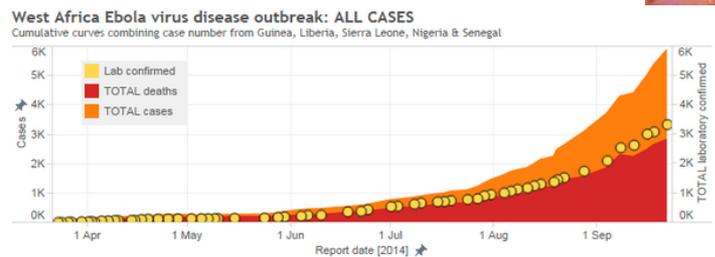
This work by Mautner's team in *The New England Journal of Medicine (NEJM)*. In a paper published in the 14 March issue of *Nature*, a team led by Bart Hagman of Erasmus MC in Rotterdam, the Netherlands, also identified the virus's receptor, a well-known protein called DPP4 that sits on the surface of cells deep inside the human lung.

So far, the virus appears to circulate primarily in the Arabian Peninsula. Besides the nine patients from Saudi Arabia, there were two from Qatar, and the first two confirmed cases are now known to have occurred almost a year ago during an outbreak in Jordan. (They weren't identified and reported until last fall.) Three U.K. residents were also infected—two fatally—in January and February, but the first one of those had traveled to Saudi Arabia and Pakistan before falling ill and presumably picked up the virus on the way. That two of his family members became infected suggests that the virus spreads from human to

West Nile in the New World
Clostridium difficile 027
 Dengue fever
Escherichia coli
 Influenza viruses



Unknown pathogen
ZIKA !!!



THE EBOLA CRISIS



Mortality 70% !

AUGUST – SEPTEMBER 2014

BRIEF REPORT

Emergence of Zaire Ebola Virus Disease in Guinea — Preliminary Report

Sylvain Baize, Ph.D., Delphine Pannetier, Ph.D., Lisa Oestereich, M.Sc.,
Toni Rieger, Ph.D., Lamine Koivogui, Ph.D., N’Faly Magassouba, Ph.D.,
Barrè Soropogui, M.Sc., Mamadou Saliou Sow, M.D., Sakoba Keïta, M.D.,
Hilde De Clerck, M.D., Amanda Tiffany, M.P.H., Gemma Dominguez, B.Sc.,
Mathieu Loua, M.D., Alexis Traoré, M.D., Moussa Kolié, M.D.,
Emmanuel Roland Malano, M.D., Emmanuel Heleze, M.D., Anne Bocquin, M.Sc.,
Stephane Mély, M.Sc., Hervé Raoul, Ph.D., Valérie Caro, Ph.D.,
Dániel Cadar, D.V.M., Ph.D., Martin Gabriel, M.D., Meike Pahlmann, Ph.D.,
Dennis Tappe, M.D., Jonas Schmidt-Chanasit, M.D., Benido Impouma, M.D.,
Abdoul Karim Diallo, M.D., Pierre Formenty, D.V.M., M.P.H.,
Michel Van Herp, M.D., M.P.H., and Stephan Günther, M.D.

BSL 4 Laboratory Jean Mérieux-Inserm, Lyon



REACTing: a multidisciplinary network (2013-....)

Research and ACTion targeting emerging infectious disease

- **Endorsed by Ministries of Health and Research**
- **Objectives**
 - **Improve research preparedness:** governance, research tools and priorities, links between disciplines, regulatory issues, criteria of research emergency. **Funding**
 - **Timely initiation of research projects and funding**
 - **From basic science to social and human sciences**
- **Sponsored by Inserm for Aviesan**

REACTing : The French Response to infectious disease crises

Lancet, April 2016 (in press) JF Delfraissy, Y Yazdanpanah, Y Lévy



Favipiravir in patients with Ebola Virus Disease: early results of the JIKI trial in Guinea



(Inserm C1463 - EEUU H2020 666092)

Daouda SISSOKO, Elin FOLKESSON, M'lebing ABDOUL,
Abdoul Habib BEAVOGUI, Stephan GUNTHER, Susan SHEPHERD,
Christine DANIEL, France MENTRE, Xavier ANGLARET, Denis MALVY

Inserm U897, University of Bordeaux, France
Médecins Sans Frontières (MSF), Belgium
Alliance for International Medical Action (ALIMA), France
Centre de Formation et de Recherche en Santé Rurale de Maférinayah, Guinea
Bernhard-Nocht-Institut für Tropenmedizin, Germany
Inserm U1137, Paris Diderot University, France

All authors declared no conflict of interest



RESEARCH ARTICLE

Experimental Treatment with Favipiravir for Ebola Virus Disease (the JIKI Trial): A Historically Controlled, Single-Arm Proof-of-Concept Trial in Guinea

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Evaluation of Convalescent Plasma for Ebola Virus Disease in Guinea

J. van Griensven, T. Edwards, X. de Lamballerie, M.G. Semple, P. Gallian, S. Baize, P.W. Horby, H. Raoul, N. Magassouba, A. Antierens, C. Lomas, O. Faye, A.A. Sall, K. Fransen, J. Buyze, R. Ravinetto, P. Tiberghien, Y. Claeys, M. De Crop, L. Lynen, E.I. Bah, P.G. Smith, A. Delamou, A. De Weggheleire, and N. Haba, for the Ebola-Tx Consortium*

Post-Ebogui Cohort - Guinea Oct 2015

- To implement a cohort of adults and children declared free of EVD aiming at describing the:

Clinical and immuno-virological perspective

- Clinical symptoms and sequelae, co-infections
- EBOV clearance in the different body fluids (blood, saliva, maternal breast milk, urines, feces, cervicovaginal secretions, semen)
- Kinetics of IgM and IgG & Genetic factors

Psychological perspective

- Psychological consequences of Ebola disease (individual and family)

Social and anthropological perspective

- Analysis of social effects of EVD (through a description of stigma experience and typology of survivors' socio-sanitary impairment situations)
 - Subjective experience of illness and cure, impact on health workers
- To conduct an in-depth immunological ancillary study on a sub-sample of the main study (PostEbogui-Immuno, INSERM)



Center for Disease Control and Prevention

MWR

Morbidity and Mortality Weekly Report

September 15, 2016 / Vol. 64

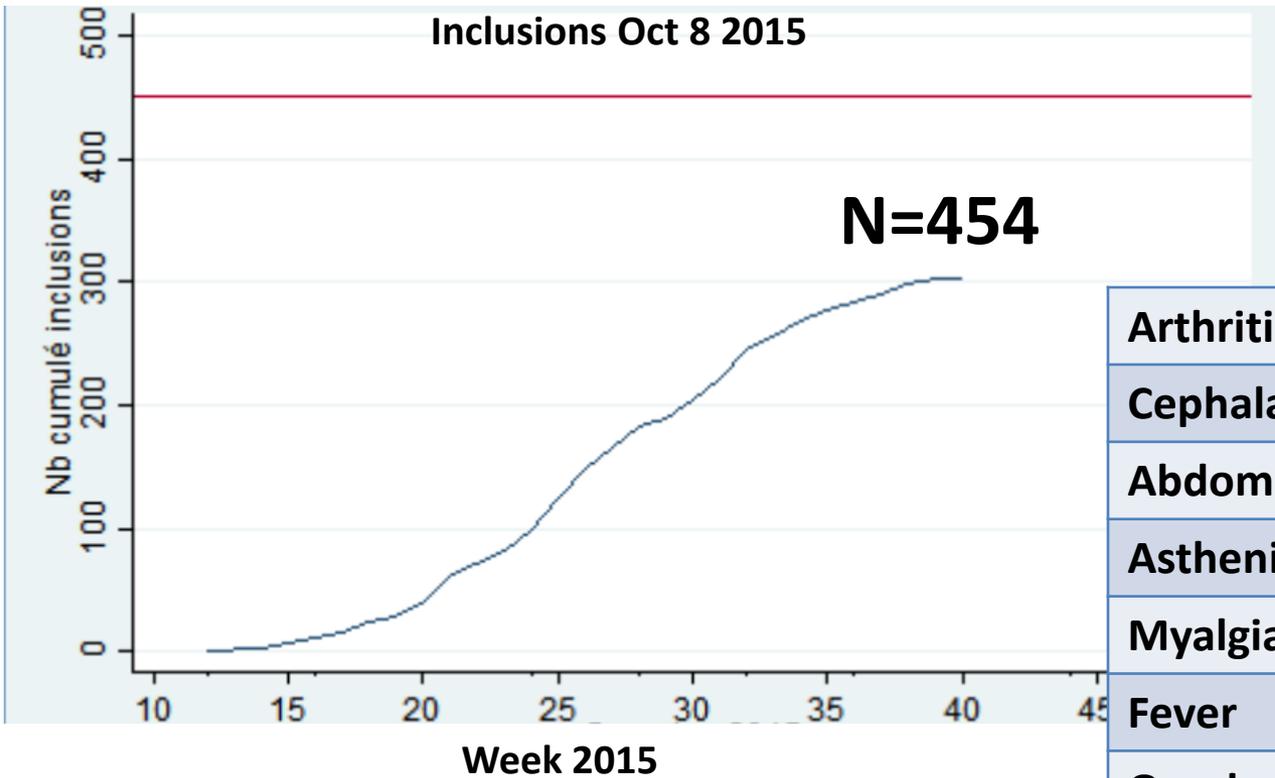
MMWR

Possible Sexual Transmission of Ebola Virus — Liberia, 2015

Christie, MIA¹, Gloria J. Davies-Wayne, MPH², Thierry Cordier-Lasalle, DESS², David J. Blackley, DrPH¹, A. Scott Lane Williams, MD, PhD¹, Shivam A. Shinde, MBBS², Moses Badio, MSc³, Terrence Lo, DrPH¹, Suzanne E. Mate, PhD⁴, Jasmal R. Wiley, PhD⁴, Jeffrey R. Kugelman, PhD⁴, Gustavo Palacios, PhD⁴, Michael R. Holbrook, PhD⁵, Krisztina B. Janusz, PhD⁵, Neeltje van Doremalen, PhD⁵, Vincent J. Munster, PhD⁵, James Pettitt, MS⁵, Randal J. Schoepp, PhD⁴, Leeroy Ampidou, MD⁶, Karsor K. Kollie, MPH³, Sonpon B. Sieh³, Alex Gasasira, MBChB², Fatorma Bolay, PhD⁷, Francis N. K. Tolbert G. Nyenswah, MPH³, Kevin M. De Cock, MD¹

Post-Ebogui Cohort - Guinea Dec 2015

Eric Delaporte, IRD



EBOV PCR positive in semen : 31% of patients at M3, M6

N = 160 patients

Arthritis	124	17%
Cephalalgia	90	13%
Abdominal pain	62	9%
Asthenia	54	8%
Myalgias	54	8%
Fever	53	7%
Ocular Problems	42	6%

Among the 304 patients

- 5 unexplained deaths
- 3 pregnancies

Among 42 patients with ocular problems

- 21 investigated
- 11 uveitis



Social and Human Sciences:

- Social Mobilisation and community engagement for the Ebola vaccine trial in Guinea and favipiravir trial
- Ebola Epidemic and social production of trust in Senegal; *IRD; CNRS; UCAD and Ministry of Health, Senegal*
- Rumors, disputes and controversies: perspectives from the digital world; IRD; McGill University; Columbia University; WHO

EDITORIALS



Time for global action on Zika virus epidemic

Our response to infectious disease epidemics must be faster and smarter

Daniel R Lucey *adjunct professor of medicine*

Department of Medicine, Infectious Diseases, Georgetown University Medical Center, Washington, DC, USA

Association between Zika virus and microcephaly in French Polynesia, 2013–15: a retrospective study



Simon Cauchemez, Marianne Besnard, Priscillia Bompard, Timothée Dub, Prisca Guillemette-Artur, Dominique Eyrolle-Guignot, Henrik Salje, Maria D Van Kerkhove, Véronique Abadie, Catherine Garel, Arnaud Fontanet, Henri-Pierre Mallet**

Summary

Background The emergence of Zika virus in the Americas has coincided with increased reports of babies born with microcephaly. On Feb 1, 2016, WHO declared the suspected link between Zika virus and microcephaly to be a Public Health Emergency of International Concern. This association, however, has not been precisely quantified.

Published Online
March 15, 2016
[http://dx.doi.org/10.1016/S0140-6736\(16\)00651-6](http://dx.doi.org/10.1016/S0140-6736(16)00651-6)

Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study



Van-Mai Cao-Lormeau*, Alexandre Blake*, Sandrine Mons, Stéphane Lastère, Claudine Roche, Jessica Vanhomwegen, Timothée Dub, Laure Baudouin, Anita Teissier, Philippe Larre, Anne-Laure Vial, Christophe Decam, Valérie Choumet, Susan K Halstead, Hugh J Willison, Lucile Musset, Jean-Claude Manuguerra, Philippe Despres, Emmanuel Fournier, Henri-Pierre Mallet, Didier Musso, Arnaud Fontanet*, Jean Neil*, Frédéric Ghawché*

Summary

Background Between October, 2013, and April, 2014, French Polynesia experienced the largest Zika virus outbreak ever described at that time. During the same period, an increase in Guillain-Barré syndrome was reported, suggesting a possible association between Zika virus and Guillain-Barré syndrome. We aimed to assess the role of Zika virus and dengue virus infection in developing Guillain-Barré syndrome.

Published Online
February 29, 2016
[http://dx.doi.org/10.1016/S0140-6736\(16\)00562-6](http://dx.doi.org/10.1016/S0140-6736(16)00562-6)
See Online Comment

www.thelancet.com Published online February 29, 2016 [http://dx.doi.org/10.1016/S0140-6736\(16\)00562-6](http://dx.doi.org/10.1016/S0140-6736(16)00562-6)

Acute myelitis due to Zika virus infection



Sylvie Mécharles, Cécile Herrmann, Pascale Poullain, Tuan-Huy Tran, Nathalie Deschamps, Grégory Mathon, Anne Landais, Sébastien Breurec, Annie Lannuzel

www.thelancet.com Published online March 3, 2016 [http://dx.doi.org/10.1016/S0140-6736\(16\)00644-9](http://dx.doi.org/10.1016/S0140-6736(16)00644-9)

Zika virus detection in urine from patients with Guillain-Barré syndrome on Martinique, January 2016

B Rozé¹, F Najioullah^{2,3}, J Fergé⁴, K Apetse⁵, Y Brouste⁶, R Cesaire^{2,3}, C Fagour⁷, L Fagour², P Hochedez^{1,3}, S Jeannin⁸, J Joux⁸, H Mehdaoui⁴, R Valentino⁴, A Signate⁸, A Cabié^{1,3,9}, on behalf of the GBS Zika Working Group¹⁰

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4. Intensive Care Unit, University Hospital of Martinique, Fort de France, France
5. Electrophysiological Department, University Hospital of Martinique, Fort de France, France
6. Emergency Department, University Hospital of Martinique, Fort de France, France
7. Diabetology Department, University Hospital of Martinique, Fort de France, France
8. Neurology Department, University Hospital of Martinique, Fort de France, France
9. INSERM CIC1428, Fort de France, France
10. The members of the group are listed at the end of the article

Correspondence: Benoît Rozé (benoit.roze@chu-fortdefrance.fr)

REACTing 2011-2016

éditorial

Virologie

Virologie 2012, 16 (1):3-5

Recherches en situation d'émergence infectieuse : la réponse à la crise se prépare dans l'intercriste

Bernadette Murgue¹
Jean François Delfraissy²

¹ Adjointe, Institut de microbiologie et maladies infectieuses, Institut national de la santé et de la recherche médicale (Inserm), 101, rue de Tolbiac, 75654 Paris, Cedex 13, France
<bernadette.murgue@inserm.fr>

² Directeur de l'Institut de microbiologie et maladies infectieuses

REACTing : the French response to infectious disease crises



Lancet, April 2016 (in press) JF Delfraissy, Y Yazdanpanah, Y Lévy

« Quatrième priorité, la recherche dans toutes les disciplines, des sciences du vivant aux sciences humaines et à la démographie.

Parce que l'anticipation en matière de recherche est cruciale et que les crises à venir se préparent dès à présent, la France a constitué un consortium mutualisant les moyens de ses instituts, baptisé REACTing : chargé de préparer la recherche sur les menaces sanitaires émergentes, ce consortium bénéficiera d'une allocation de 8 millions d'euros, pour mettre en œuvre un programme de recherche sur Zika et sur Ebola. Une dotation annuelle de 1 million d'euro lui permettra de fonctionner de manière pérenne. »

**Allocution du Président de la République, M. François Hollande
Conférence de Haut Niveau sur la Sécurité Sanitaire Internationale, Lyon – Mars 2016**

Lessons Learned

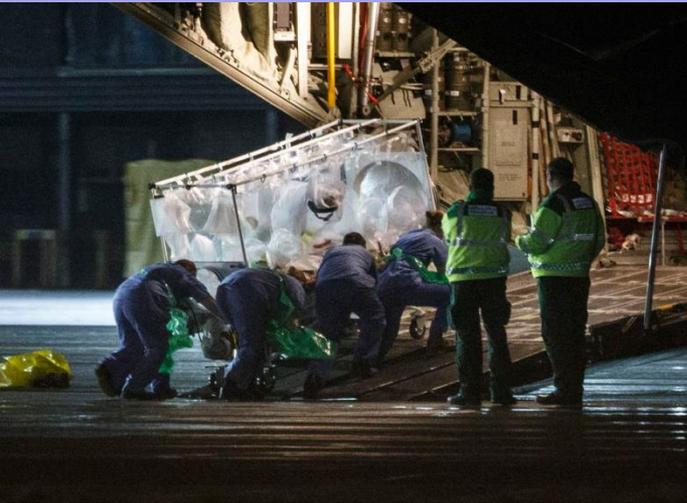
1. Clinical Trials -> Prevention trials
 - Top to bottom decisions
 - Scientific priority
 - No specific call /Specific working group
2. Prevention Research: Highly cost /Cost effective
 - Temprano 6 M€
 - IPERGAY 3M€
 - Start 34M€
 - HPTN 72 M€
 - ANRS is the « trigger » for « tour de table »
3. Science Driven or guidelines driven ?
4. High international visibility for the French Community



Back up

L'infirmière écossaise guérie d'Ebola à nouveau gravement malade

14 octobre 2015 à 18:53



Dr Jacob: « This is the original Ebola virus she had many months ago which has been inside the brain, replicating at a very low level, and has now re-emerged to cause this clinical illness of meningitis »

Pauline first admitted to the isolation unit (HLIU) at the Royal Free in December 2014 after contracting the disease in Sierra Leone.

Discharged in January 2015 after making a recovery.

Readmitted on 8th October 2015 to the HLIU after developing meningitis

She received symptomatic treatment and the experimental antiviral drug GS-5734

Discharged from its care on November 11, 2015

Ebola, a call for action



Ebola: time to act

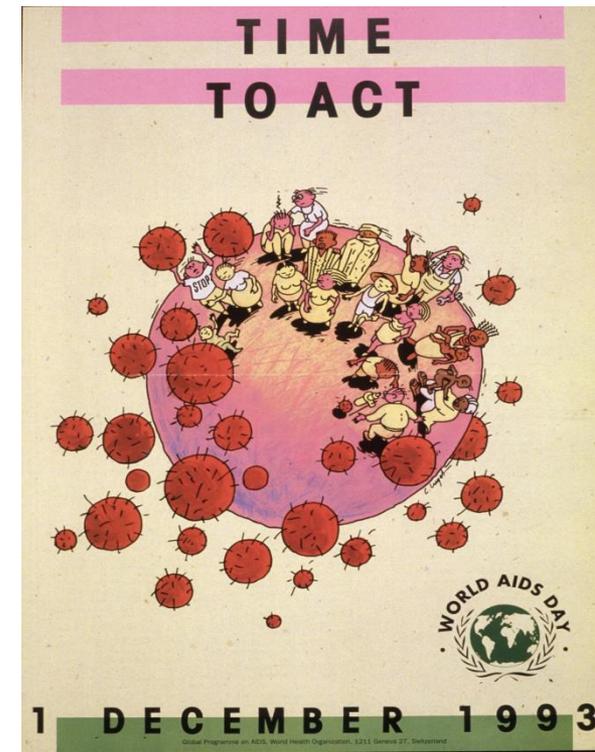
Governments and research organizations must mobilize to end the West African outbreak.

11 SEPTEMBER 2014 | VOL 513 | NATURE | 143

Ebola: learn from the past

Drawing on his experiences in previous outbreaks, David L. Heymann calls for rapid diagnosis, patient isolation, community engagement and clinical trials.

16 OCTOBER 2014 | VOL 514 | NATURE | 299



SPECIAL REPORT

The Neglected Dimension of Global Security — A Framework for Countering Infectious-Disease Crises

Peter Sands, M.P.A., Carmen Mundaca-Shah, M.D., Dr.P.H., and Victor J. Dzau, M.D.

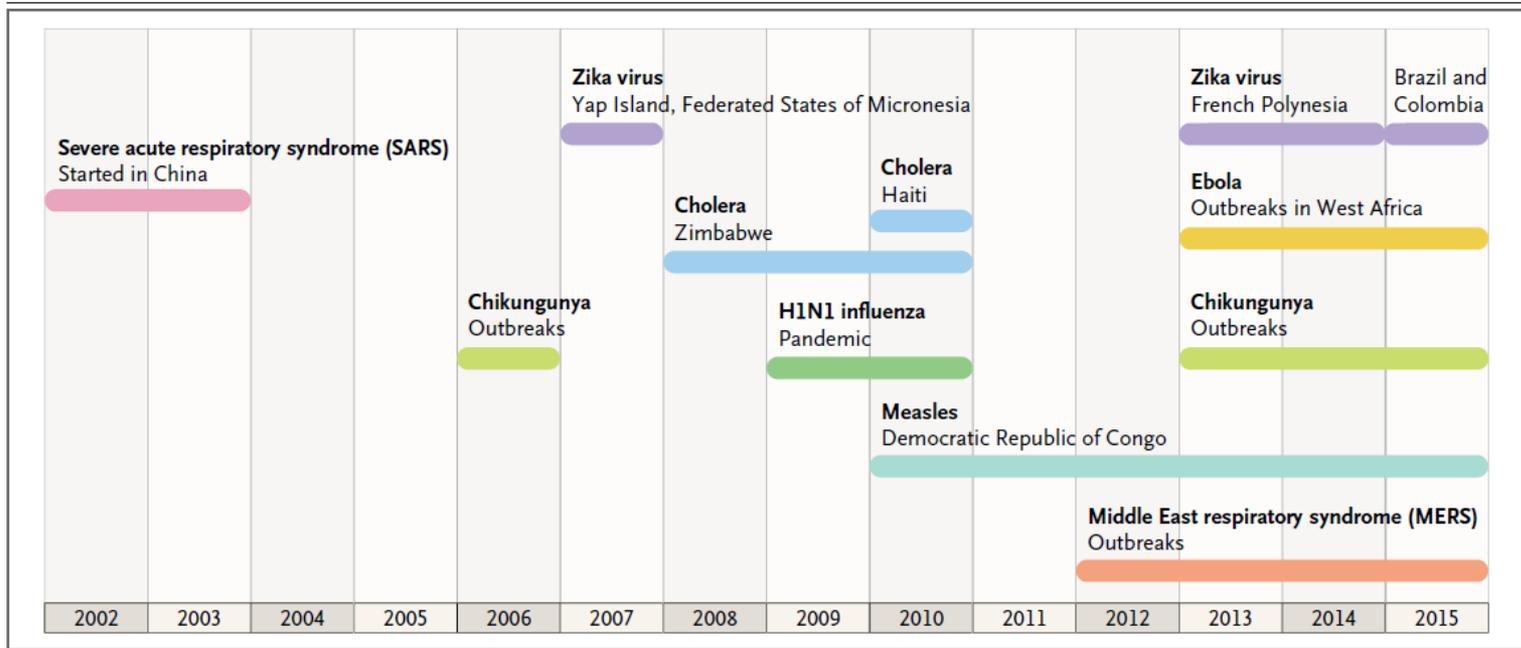


Figure 1. Major Emerging and Reemerging Infectious-Disease Outbreaks, Epidemics, and Pandemics, 2002 through 2015.

WHO ARV Guidelines Evolution 2002 to 2015

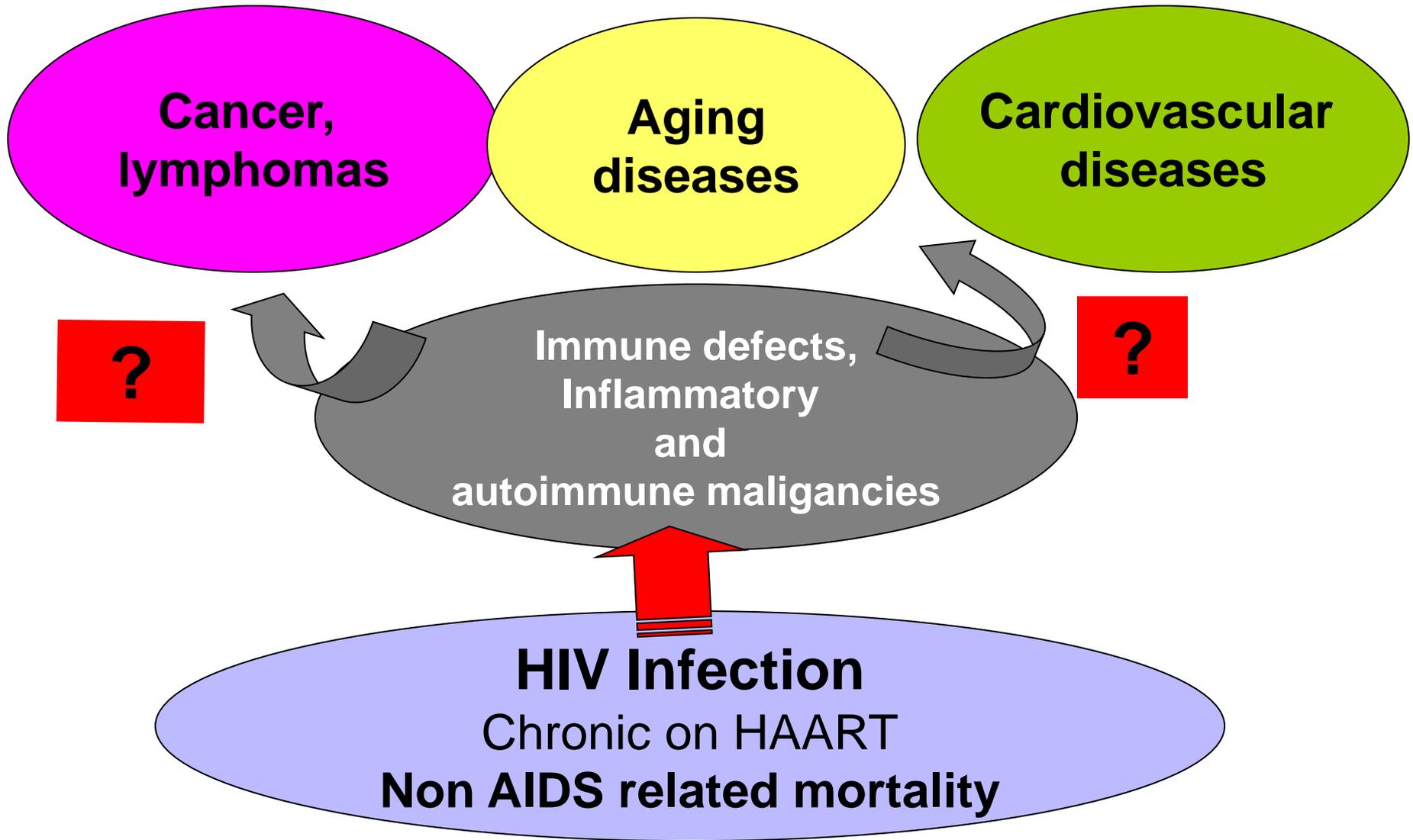
Topic	2002	2003	2006	2010	2013	2015*
When to start	CD4 ≤200	CD4 ≤ 200	CD4 ≤ 200 - Consider 350 - CD4 ≤ 350 for TB	CD4 ≤ 350 -Regardless CD4 for TB and HBV	CD4 ≤ 500 - Regardless CD4 for TB, HBV PW and SDC - CD4 ≤ 350 as priority	Towards treatment initiation at any CD4 cell count
Earlier initiation						
1st Line ART	8 options - AZT preferred	4 options - AZT preferred	8 options - AZT or TDF preferred - d4T dose reduction	6 options & FDCs - AZT or TDF preferred - d4T phase	1 preferred option & FDCs - TDF and EFV preferred across all pops	Continue with FDC approach and phased introduction of new options (DTG, EFV 400)
Simpler treatment						
2nd Line ART	Boosted and non-boosted PIs	Boosted PIs -IDV/r LPV/r, SQV/r	Boosted PI - ATV/r, DRV/r, FPV/r LPV/r, SQV/r	Boosted PI - Heat stable FDC: ATV/r, LPV/r	Boosted PIs - Heat stable FDC: ATV/r, LPV/r	Add more heat stable PI options (DRV/r) and strategies (NRTI sparing regimens)
Less toxic, more robust regimens						
3rd Line ART	None	None	None	DRV/r, RAL, ETV	DRV/r, RAL, ETV	Encourage HIV DR to guide
Viral Load Testing	No	No (Desirable)	Yes (Tertiary centers)	Yes (Phase in approach)	Yes (preferred for monitoring, use of PoC, DBS)	Support for scale up of VL using all technologies
Better and simpler monitoringz						

Bilan du programme de l'OMS "3 by 5"

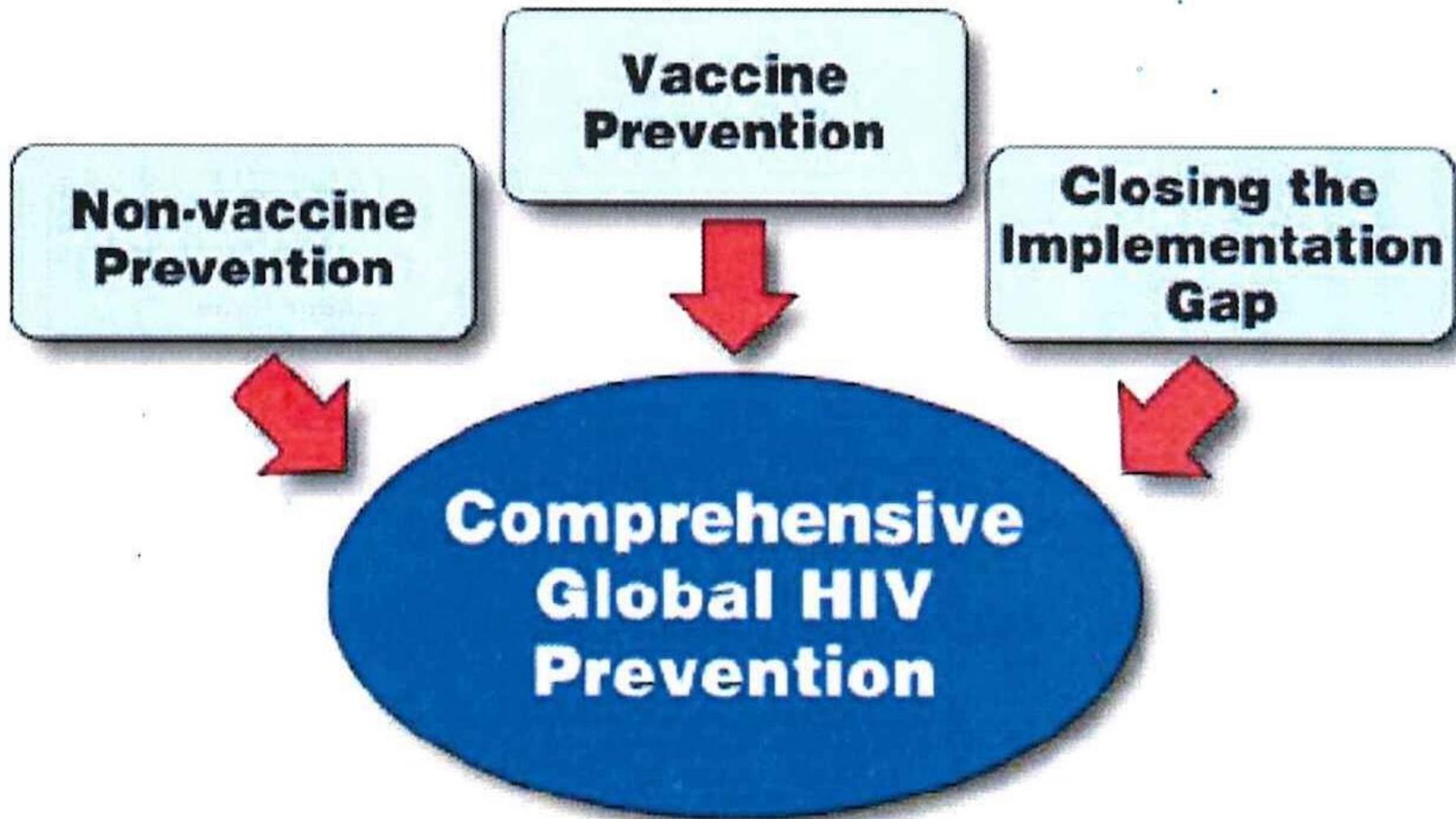
Couverture des besoins en traitement antirétroviral dans les pays à niveaux de ressource faible et moyen – Juin 2006

Région géographique	Nb de personnes sous ARV	Nb de personnes avec indication d'ARV	Taux de couverture
Afrique sub-saharienne	1 040 000	4 600 000	23 %
Amérique latine et Caraïbes	345 000	460 000	75 %
Asie du sud, de l'est et du sud-est	235 000	1 440 000	16 %
Europe de l'est et Asie centrale	24 000	190 000	13 %
Afrique du nord et Moyen-orient	4 000	75 000	5 %
Total	1 650 000	6 800 000	24 %

New Challenges: HIV and emerging new diseases...



Learning from each others beyond HIV/AIDS.....



Early Antiretroviral Therapy and Isoniazid Preventive Therapy in HIV-Infected African Adults With High CD4 Count :

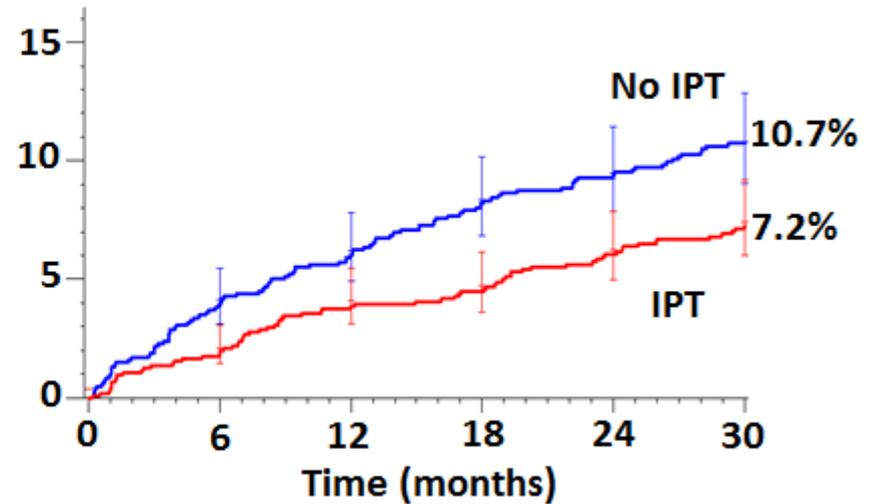
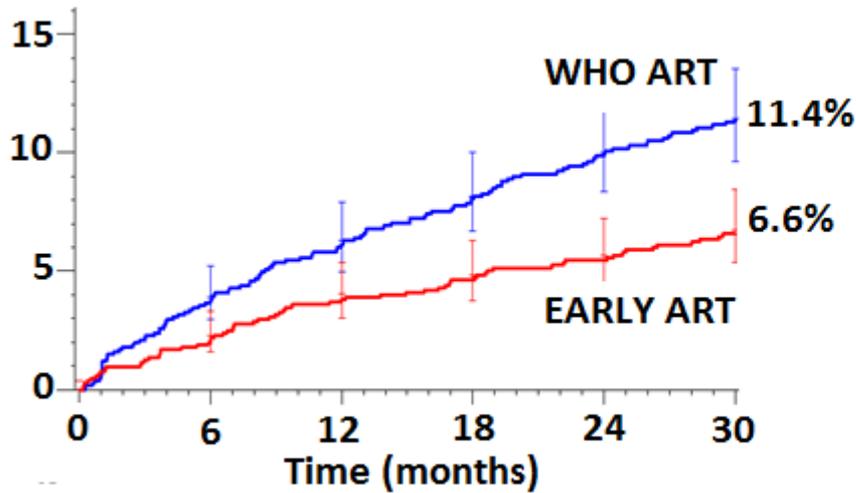
Temprano ANRS 12136 Trial

Christine DANEL, Raoul MOH, Delphine GABILLARD, Anani BADJE,
Jerome LE CARROU, Gerard M. KOUAME, Jean Baptiste NTAKPE,
Hervé MENAN, Serge P. EHOLIE, Xavier ANGLARET

Inserm U897, University of Bordeaux, France
Department of demato-infectiology, Felix Houphouët Boigny University , Abidjan, Côte d'Ivoire
CeDRS laboratory, & Department of Infectious and Tropical Diseases, Treichville University Hospital,
Abidjan, Côte d'Ivoire
Programme PACCI / ANRS research site in Côte d'Ivoire

Christine Danel has no financial relationships with commercial entities to disclose.

Severe HIV morbidity (N=2056)



	n	Rate /100 PY	95% CI	aHR	95%CI	p
Early ART	64	2.8	(2.1; 3.4)	0.56	(0.41; 0.76)	<i>0.0002</i>
WHO ART	111	4.9	(4.0; 5.9)			
IPT	71	3.0	(2.3; 3.7)	0.65	(0.48; 0.88)	<i>0.005</i>
No IPT	104	4.7	(3.8; 5.6)			

No significant interaction between early ART and IPT (p=0.45)

N: number of patients with at least one episode of severe morbidity

aHR: adjusted Hazard Ratio (adjusted by other strategy and by center)



World Health
Organization

GUIDELINES

GUIDELINE ON WHEN TO START ANTIRETROVIRAL THERAPY AND ON PRE-EXPOSURE PROPHYLAXIS FOR HIV

SEPTEMBER 2015

- ART should be initiated in all adults living with HIV at any CD4 cell count
Temprano +++
- Treatment as Prevention
TASP ?
- Oral PrEP should be offered as an additional prevention choice for people at substantial risk of HIV infection
IPERGAY +++
- PREP in France
December 1.2015? A difficult political decision
Role of ANRS ?

ACKNOWLEDGMENTS

- **Clinical and research teams**
- **Chairs of Coordinated working groups, PIs**
- **ANRS staff**
- **Patients NGOs, more specifically TRT5, AIDES, Sidaction**
- **INSERM, Institut Pasteur, IRD, CNRS, Hospitals**
- **Expertise France**
- **Pharmaceutical Industry**
- **Foundations : BMG Foundation, Total, MSD...**
- **Patients**
- **X Anglaret, B Auvert, D Costagliola, F Dabis, JM Molina**

More than 30 years ago: Alarming signals of an emerging epidemic

dimanche 1 juillet 2001

Pneumocystis Pneumonia --- Los Angeles

Page:1



MS Gottlieb, HM Schanker, PT Fan, A Saxon, JD Weisman.

June 5, 1981 / Vol. 30/ No. 21

Epidemiologic Notes and Reports

***Pneumocystis* Pneumonia --- Los Angeles**

In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.



**RARE CANCER SEEN
IN 41 HOMOSEXUALS**

**Outbreak Occurs Among Men
in New York and California
— 8 Died Inside 2 Years**

By LAWRENCE K. ALTMAN.

1981 July 4;30:305-8

Kaposi's Sarcoma and *Pneumocystis* Pneumonia Among Homosexual Men — New York City and California

During the past 30 months, Kaposi's sarcoma (KS), an uncommonly reported malignancy in the United States, has been diagnosed in 26 homosexual men (20 in New York City [NYC]; 6 in California). The 26 patients range in age from 26-61 years (mean 39 years). Eight of these patients died (7 in NYC, 1 in California)—all 8 within 24 months after KS was diagnosed. The diagnoses in all 26 cases were based on histopathological examination of skin lesions, lymph nodes, or tumor in other organs. Twenty-five of the 26 patients were white, 1 was black. Presenting complaints from 20 of these patients are shown in Table 1.

Mobilization of virologists by epidemiologists and clinicians

ARV chart 2015/16



HIV PHARMACY ASSOCIATION



Drug names		Recommended adult dose *	Total daily pills
------------	--	--------------------------	-------------------

Fixed dose combinations §			
Atripla (efavirenz 600 mg + emtricitabine 200 mg + tenofovir 300 mg)		One tablet, once-daily. Take at night and not with a high fat meal. See info on separate drugs.	1
Eviplera (rilpivirine 25 mg + emtricitabine 200 mg + tenofovir 300 mg)		One tablet, once-daily, with food (390 kcal). See separate drug info.	1
Stribild (elvitegravir 150 mg + cobicistat 150 mg + emtricitabine 200 mg + tenofovir 300 mg)		One tablet, once-daily, take with food. See info on separate drugs.	1
Triumeq (dolutegravir 50 mg + abacavir 600 mg + lamivudine 300 mg)		One tablet, once-daily. Take with or without food. See info on separate drugs.	1

Nukes: nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs)

Dual nukes

Truvada (tenofovir 300 mg + emtricitabine 200 mg)		One tablet, once-daily.	1
Kivexa (abacavir 600 mg + lamivudine 300 mg)		One tablet, once-daily.	1

Single nukes

lamivudine (3TC) ** (Epivir [pictured] - or generic)		1 x 300 mg or 2 x 150 mg (150 mg shown), (taken as a once-daily or twice-daily dose).	1 if 300 mg 2 if 150 mg
abacavir (Ziagen, Epzicom)		2 x 300 mg tablets (taken as a once-daily or twice-daily dose).	2
emtricitabine (FTC) (Emtriva)		1 x 200 mg capsule, once-daily.	1
tenofovir DF (Viread)		1 x 300 mg tablet, once-daily.	1

§ New fixed dose combinations and coformulations might become available during 2015/16.
* Different doses and formulations are sometimes used - always check the dose with your doctor and pharmacist.

** Generic versions of lamivudine, nevirapine and efavirenz may be a different colour and shape.

°° Elvitegravir is only available as a separate drug on expanded access from the manufacturer.

∞ PK boosters: ritonavir is the most widely used pharmacokinetic (PK) booster. Cobicistat can only be used to boost atazanavir, darunavir and elvitegravir.

Some drugs are not recommended for first-line therapy. Smaller pills are for children or if larger pills are difficult to swallow. Some syrups are available. Pictures approximate to actual size.

Drug names		Recommended adult dose *	Total daily pills
------------	--	--------------------------	-------------------

NNRTIs: non-nucleoside reverse transcriptase inhibitors (non-nukes)			
efavirenz ** (Sustiva) 600 mg or 200 mg		200 mg 1 x 600 tablet (or 3 x 200 caps) once-daily; at night, not with high fat meal.	1 tablet (or 3 capsules)
nevirapine ** 200 mg and nevirapine 400 mg (Viramune PR)	 	200 mg 400 mg 200 mg once-daily for first 14 days. Then 1 x 200 mg tablet, twice-daily or 2 x 200 mg once-daily; OR 1 x 400 mg prolonged release tablet once-daily (pic on right).	1 or 2 (based on 200 mg or 400 mg)
etravirine (Intencele)		1 x 200 mg tablet, twice daily, take with food. Dispersible in water.	2
rilpivirine § (Edurant)		1 x 25 mg tablet, once-daily, take with main meal (500 kcal).	1

INIs: integrase inhibitors

raltegravir (Isentress)		1 x 400 mg tablet, twice-daily. Take with or without food.	2
elvitegravir (Vitekta) °° (see also Stribild). Expanded access only.	 	1 x 85 mg or 1 x 150 mg tablet, once-daily in boosted PI. Take with food.	1
dolutegravir (Tivicay) *		1 x 50 mg tablet, once-daily (or 1 x 50 mg twice -daily). With food if twice-daily but with or without otherwise.	1 or 2

CCR5 inhibitors (entry inhibitor)

maraviroc * (Celsentri, Selzentry)		150 mg or 300 mg or 600 mg, as directed, depending on other ARVs in the combination.	1 or 2 or 4
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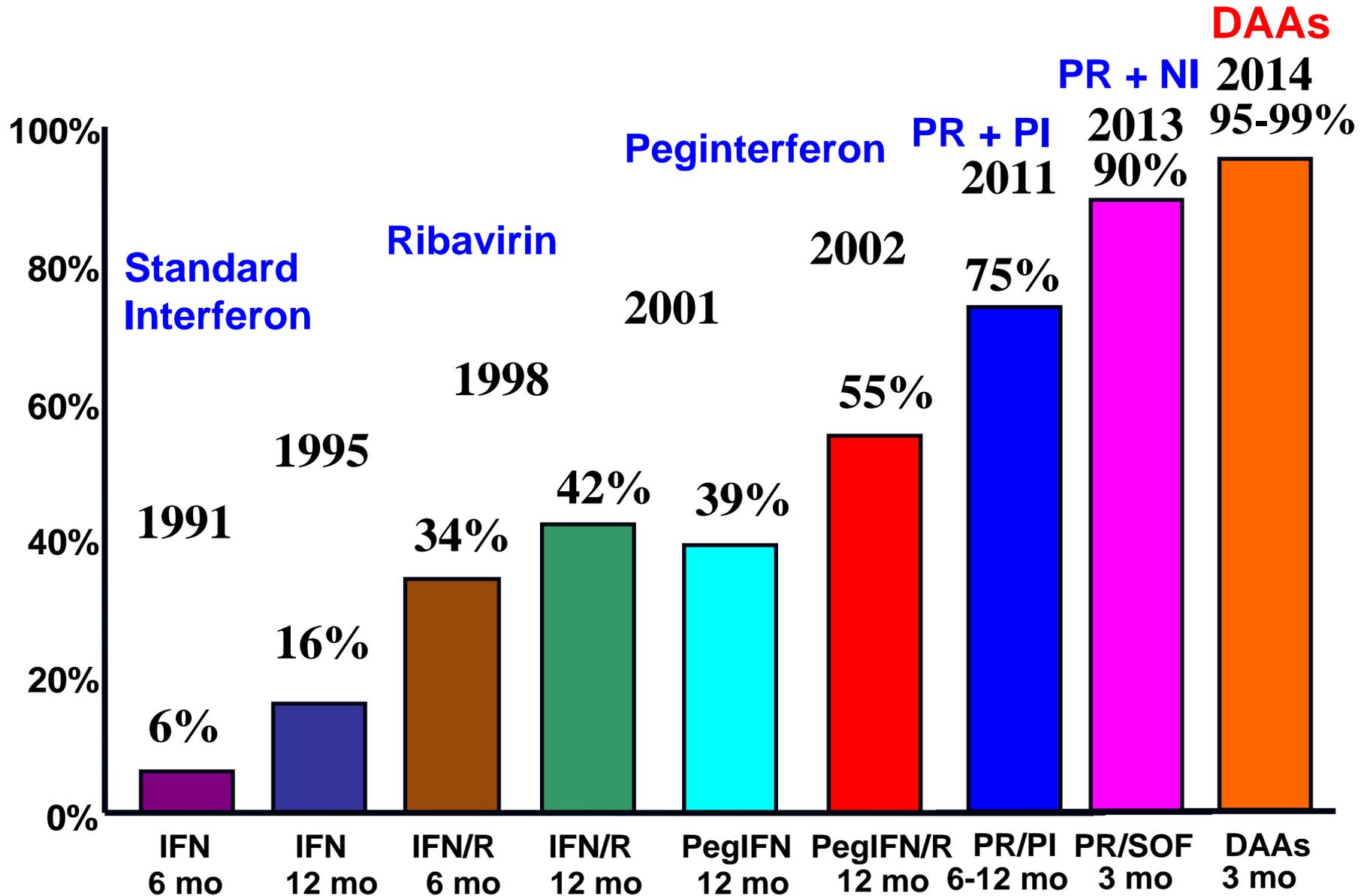
b/PI: boosted protease inhibitors

atazanavir * § (Reyataz)		1 x 300 mg cap + booster, once-daily. Take with food. 150 mg and 200 mg capsules also available.	1 (+ 1 booster)
darunavir * § (Prezista)		1 x 800 mg + booster once-daily (or 1 x 600 mg + 100 mg booster twice-daily if resistance). Take with food.	1 or 2 (+ 1 or 2 boosters based on dose)

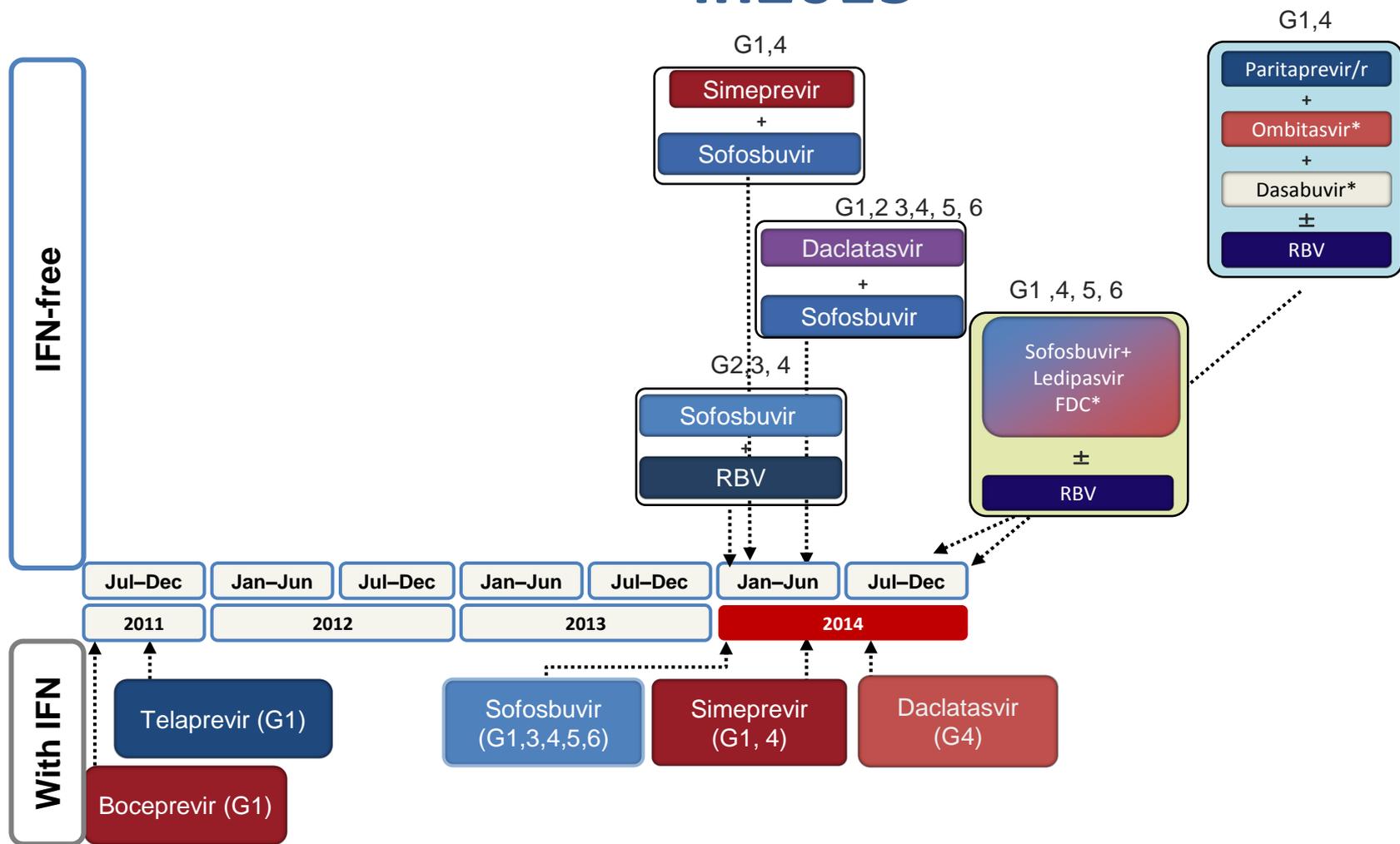
PK (pharmacokinetic) boosters ∞

cobicistat (c) § (Tybost)		150 mg tablet, once daily. Used to boost atazanavir, darunavir and elvitegravir.	depends on boosted drug
ritonavir (r) * (Norvir)		100 mg tablets used at different doses to boost other PIs.	depends on PI

HCV treatment: where do we come from ?



DAA Combinations approved by EMA in 2015





HCV Treatment update

- Myanmar : Only pegifn rbv available to date, sofosbuvir is not registered nor filed, Harvoni is filed, special drug import permit under negotiation for SOF and DCV.
- Pakistan: 141 people on treatment since May 2015, sofosbuvir originator (300 USD/bottle) ribavirin
- India: first patient started on SOF/PR on July 7th,
- Mozambique: sofosbuvir is not registered, special drug import permit under negotiation for SOF and DVC.
- Kenya : sofosbuvir registration submitted.
- Uganda: sofosbuvir registration submitted
- Treatment access is slow, complicated, and still extremely limited in October 2015 in resource limited settings, with concerns about anti-diversion rules, and long delays/drug registration and drug orders

Drugs for EBOLA

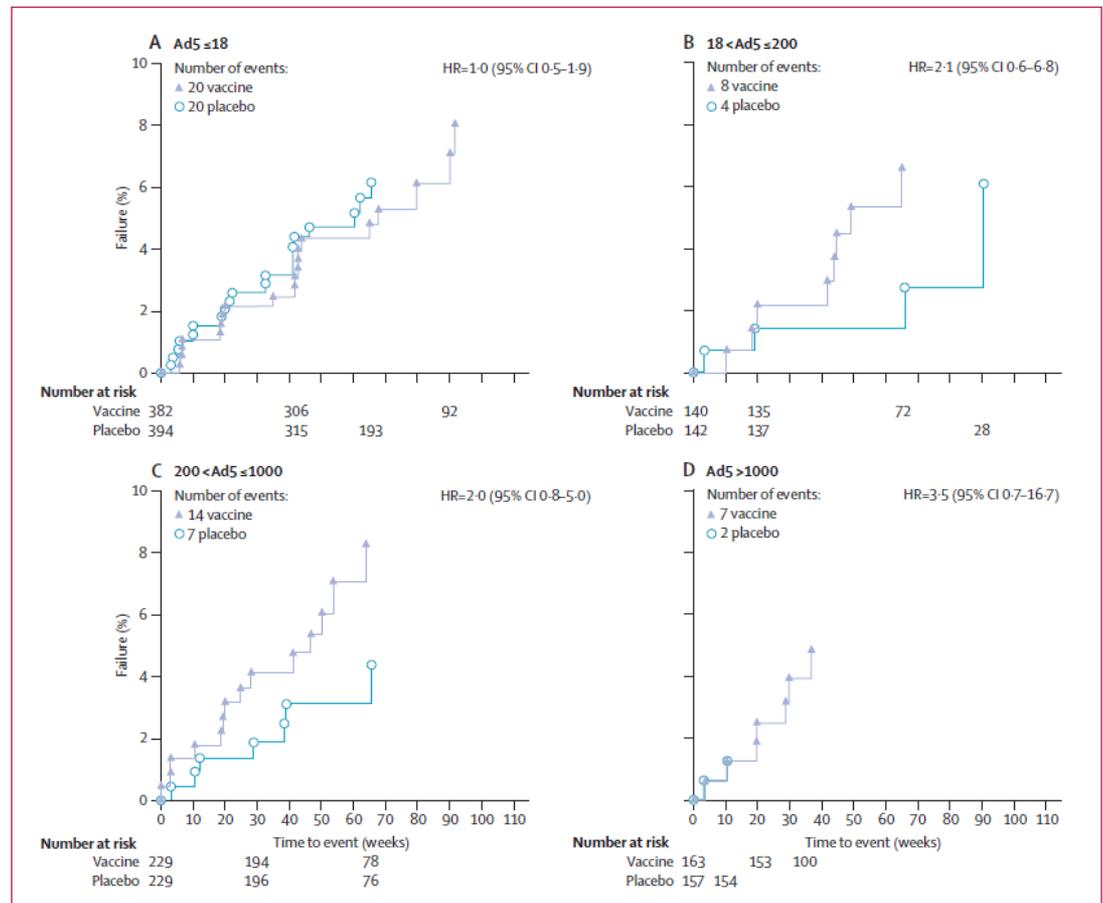
- **Drugs under clinical evaluation :**
 - Favipiravir: Guinea – Trial completed – considered as standard of care in Guinea
 - Brincidofovir: Liberia – Trial halted, product deprioritized
 - Zmapp: « cocktail » of 3 monoclonal antibodies (Liberia, Sierra Leone)
 - TKM-100802 (si-RNA); Sierra Leone – Trial completed, product deprioritized
 - Interferon: trial initiated in Donka (Guinea): not recruiting (n=9)
- **Drugs for which clinical evaluation is envisaged:**
 - BCX-4430: adenosine analogue that disrupts viral RNA-dependent RNA polymerase function by chain termination
 - MIL-177: cocktail of 3 Mabs (same sequences as Zmapp)
 - **Antiviral from Gilead**

Efficacy assessment of a cell-mediated immunity HIV-1 vaccine (the Step Study): a double-blind, randomised, placebo-controlled, test-of-concept trial

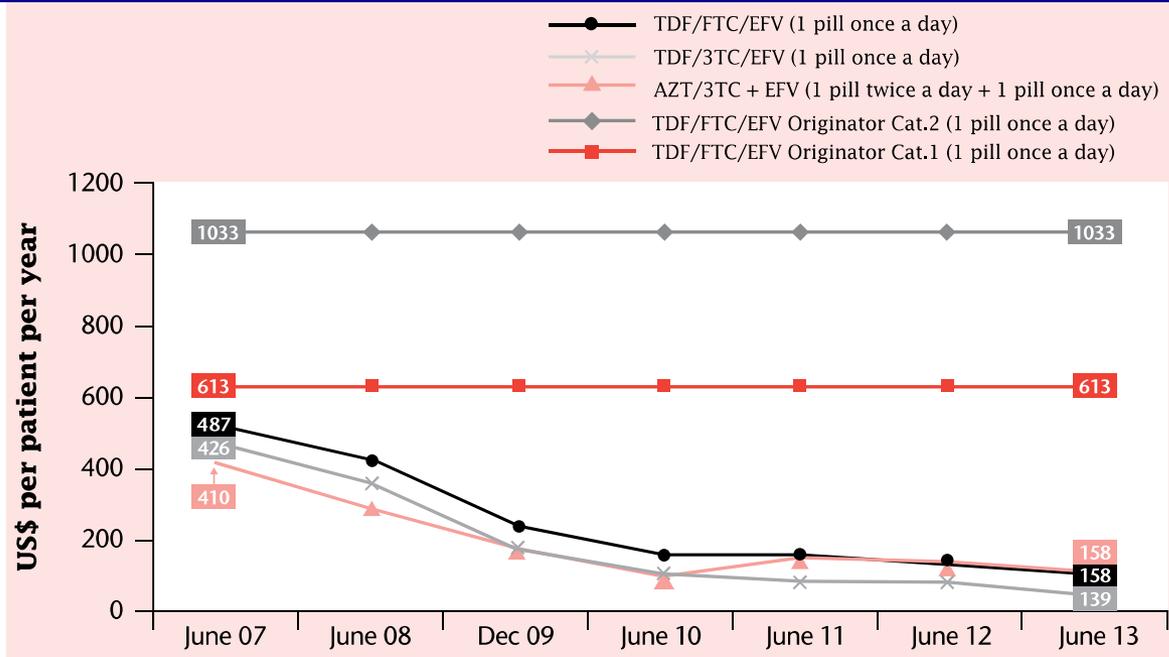
Susan P Buchbinder, Devan V Mehrotra, Ann Duerr, Daniel W Fitzgerald, Robin Mogg, David Li, Peter B Gilbert, Javier R Lama, Michael Marmor, Carlos del Rio, M Juliana McElrath, Danilo R Casimiro, Keith M Gottesdiener, Jeffrey A Chodakewitz, Lawrence Corey, Michael N Robertson, and the Step Study Protocol Team*

THE
LANCET

November 2008



A unique engagement of patients representatives for the universal access to treatment



Evolution of 1st line treatment price (MSF)

Generic competition and activists pressure = drastic reduction of ARV prices in resource-limited countries but still too few combination available + 2nd/3rd line treatments prices too high !

Today: The revolution of Hepatitis C treatment!

New fight to achieve universal access at an affordable price to save lives...

HIV/AIDS, still one priority among others in the Global Health era...

Infectious diseases

AIDS, Tuberculosis, malaria, hepatitis

Diarrhoeal diseases in infants

Respiratory infections

Emerging/re-emerging infectious diseases (influenza, encephalitis, antimicrobial resistance, Ebola...)

Maternal & child health

Alcohol, Tobacco

Climatic change

Lack of health professionals

Urbanization

Non communicable diseases

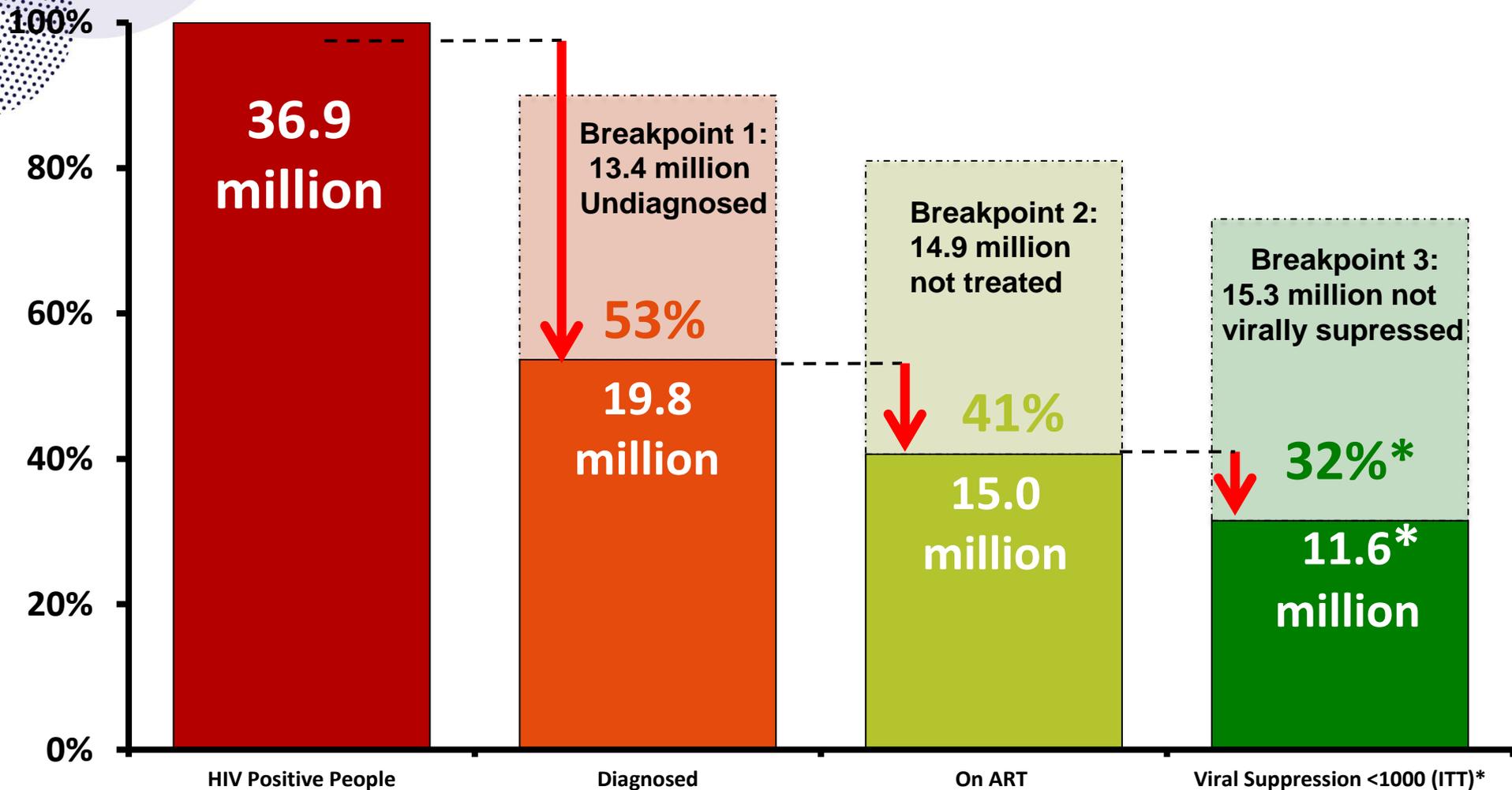
Now the most important cause of death globally:

- 1) Cardiovascular diseases: 17.3 millions death/year;
- 2) Cancers: 7,6 millions
- 3) Diabetes: 1,3 million

GLOBAL
HEALTH 2035

To invest in HIV Science is to invest on Global Health...

Global estimates (2014-2015) vs the gap to reach 90-90-90 targets



Ref: On ART = March 2015. How Aids Changed Everything. Fact Sheet. UNAIDS 2015. MDG 6: 15 YEARS, 15 LESSONS OF HOPE FROM THE AIDS RESPONSE July 2015. * Average viral suppression% Intention to Treat LMIC rate from a Systematic Review by McMahon J. et al. Viral suppression after 12 months of antiretroviral therapy in low-and middle-income countries: a systematic review." *Bulletin of the World Health Organization* 91.5 (2013): 377-385.

ANRS Research Sites involved in EBOLA

➤ Sub-Saharan Africa

Cameroon,

Burkina Faso,

Côte d'Ivoire,

Senegal

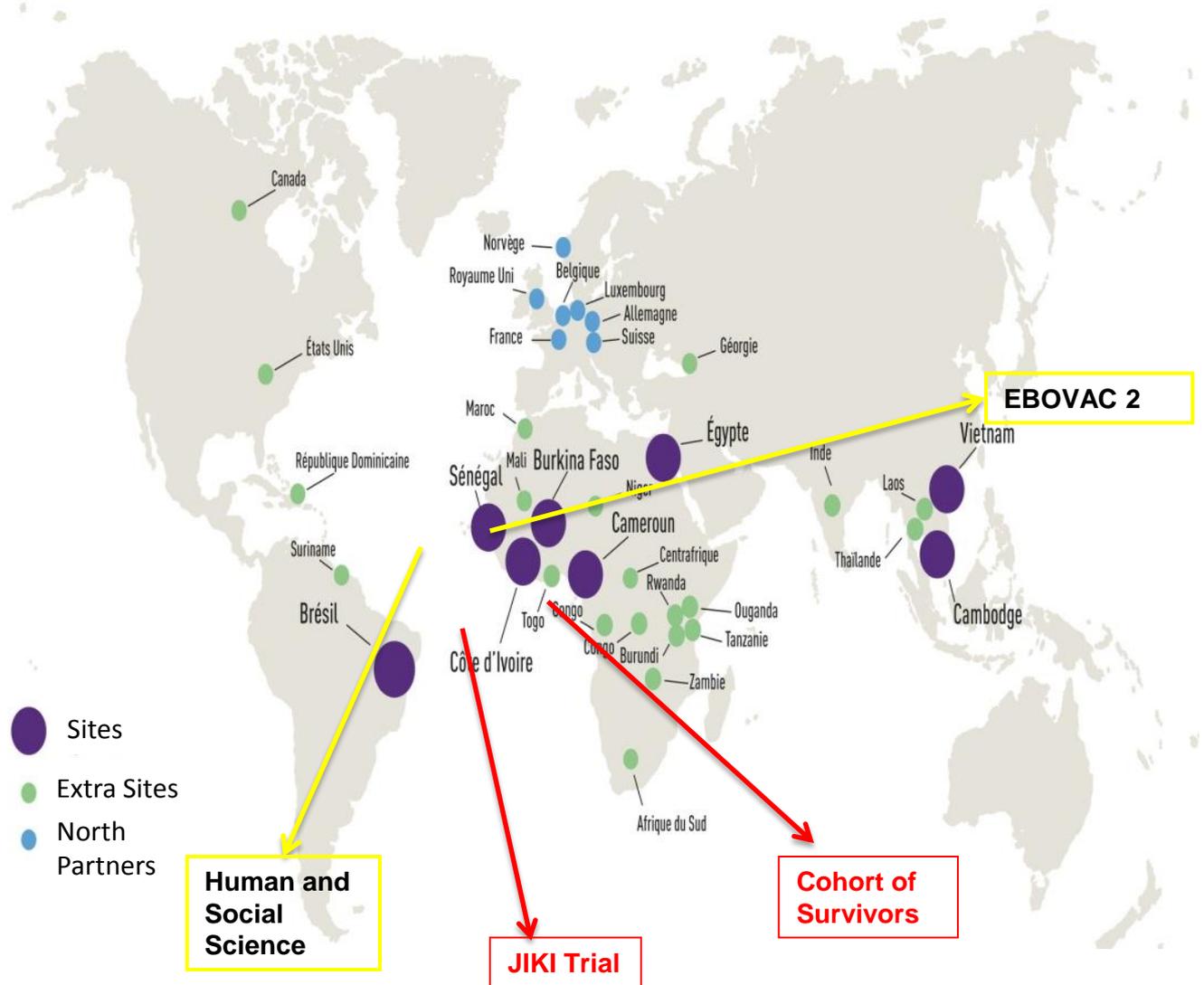
➤ South –East Asia

Cambodia,

Vietnam

➤ Egypt

➤ Brazil

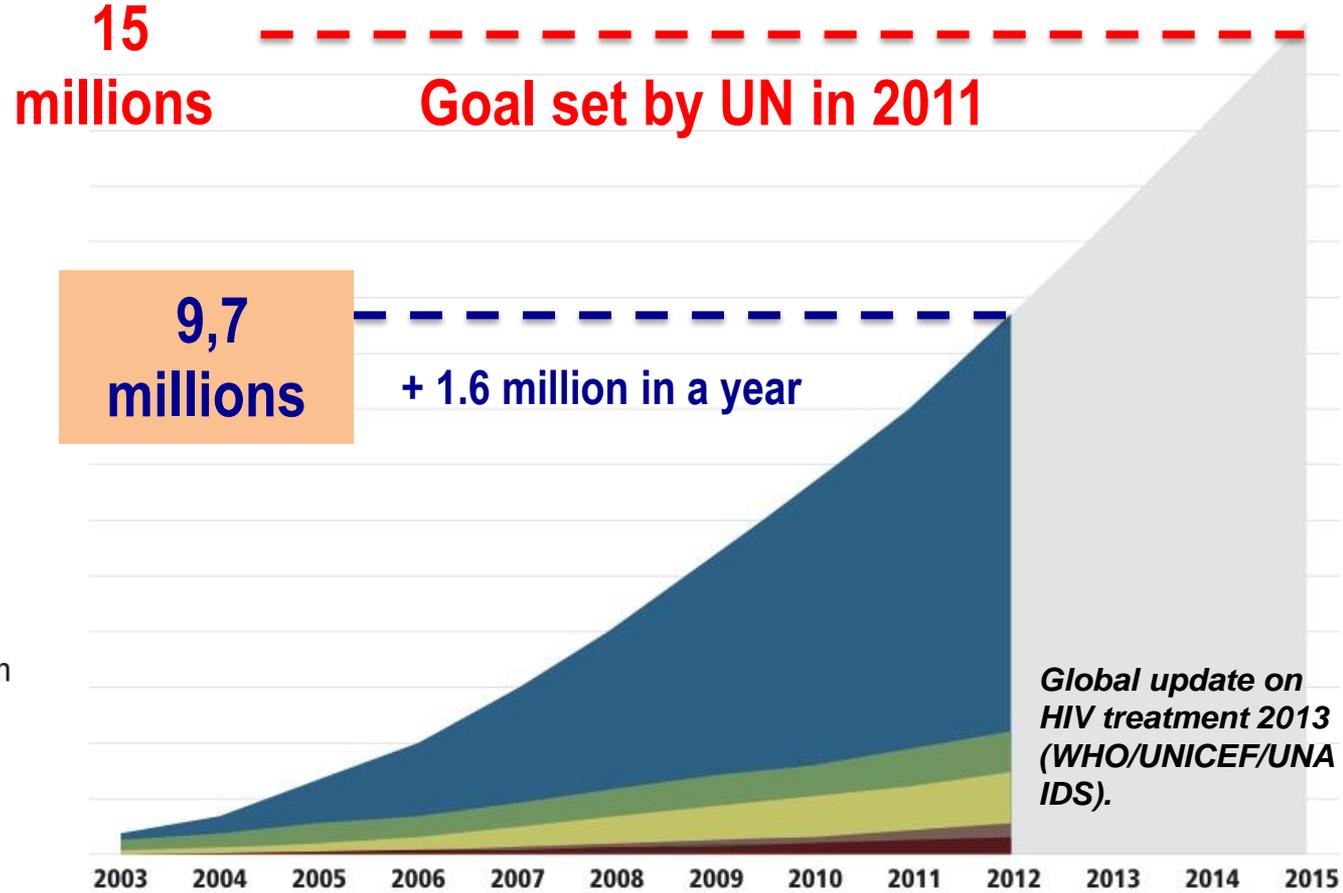


Progress in access to antiretroviral therapy in low-and middle-income countries

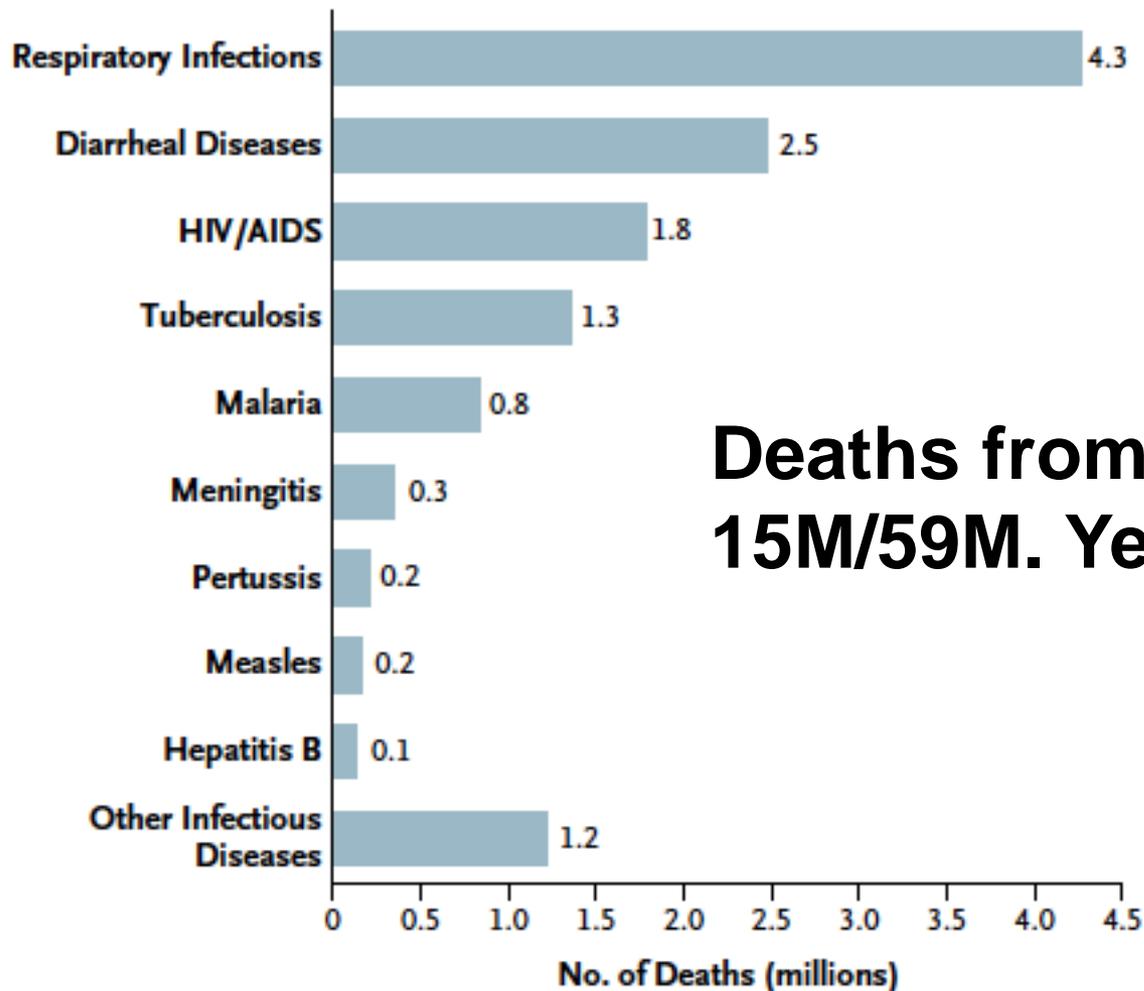
34,2 millions of PLWHIV
(23,5 in sub Saharan Africa)

- African Region
- Region of the Americas
- South-East Asia Region
- European Region
- Eastern Mediterranean Region
- Western Pacific Region

4,2 millions death avoided thanks to ARVs!



2013 OMS treatment guidelines: 26 millions HIV+ people now eligible for treatment initiation



Deaths from Infectious Diseases 15M/59M. Year (25%)

Figure 1. Leading Causes of Global Deaths from Infectious Diseases.

Of an estimated 58.8 million annual deaths worldwide, approximately 15.0 million (25.5%) are believed to be caused by infectious diseases. Cause-specific mortality estimates are provided by the World Health Organization.^{43,44} The data do not include deaths from secondary infectious causes, such as rheumatic fever and rheumatic heart disease, liver cancer and cirrhosis, or other chronic diseases.

N Engl J Med 2012;366:454-61.

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Aviesan Sud

- **Participants:** : IMMI, Institut Pasteur, Fondation Mérieux, IRD, CIRAD, Inserm, ITMOs Santé publique, Cancer, Technologies pour le santé, *CNRS, Universités*
- **Périmètre géographique, thématique,...**
- **Objectifs:**
- Offrir une plateforme d'échanges et de discussion pour aboutir à une vision plus large et plus objective de la recherche en partenariat, que celle de chacun des organismes partenaires
- Stratégie commune de collaboration
 - Géographique: masse critique sur sites limités
 - Scientifique: thèmes prioritaires
 - Formation, capacity building
- Règles éthiques de partenariat
- Définition des priorités scientifiques: approche multidisciplinaire
- Intégration européenne



Le Réseau International Pasteur : un exemple de partenariat avec le sud



32 instituts sur 5 continents ...



Le Réseau Pasteur: un engagement important dans la lutte contre les maladies infectieuses ...



La surveillance des maladies infectieuses (grippe, polio, TB, paludisme, résistance aux antibiotiques...)

- un réseau mondial de laboratoires accrédités par les Ministères de la santé (50 LNR CNR) et par l'OMS (10 CCOMS)...



Le Recherche et ses applications (physiopathologies, screening moléculaire, génomique, recherche sur les vecteurs, recherche vaccinale....)

L'investigation de et la réponse aux épidémies :

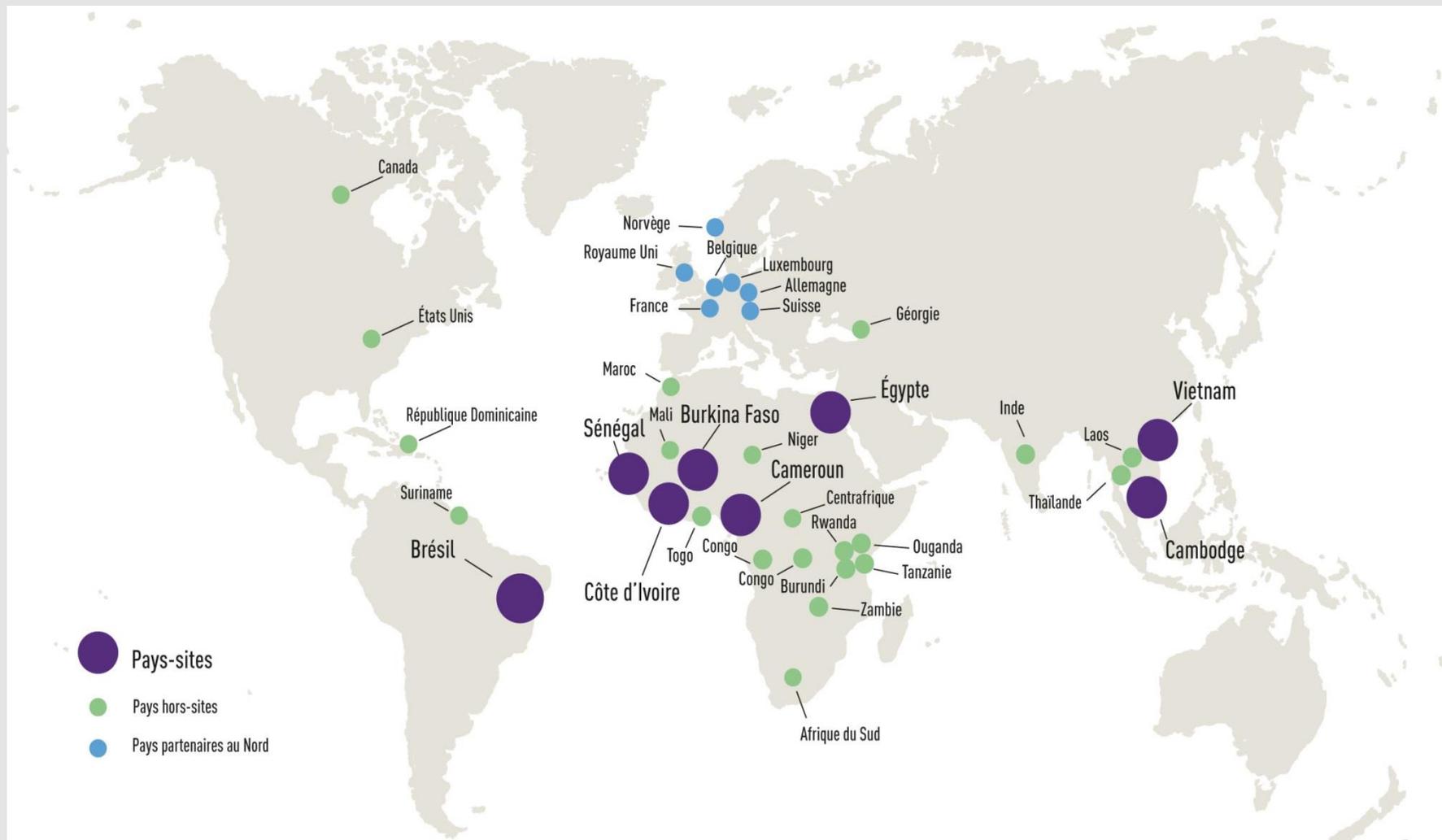
- IP et IP Dakar pour la dengue-3 en Côte d'Ivoire (2008)
- L'IP Guyane au Paraguay : épidémie de dengue
- IP Dakar pour la dengue hémorragique au Cap Vert (2009)

La vaccination : l'évaluation des campagnes de vaccination, l'étude des maladies à prévention vaccinale, les centres de vaccination





Les Sites ANRS (N=8) et les Pays partenaires



Les sites : principes généraux

Articulation avec les programmes nationaux

HCV risk factors

- Iatrogenic
- Intra-familial

Factors associated with HCV clearance

- epidemiology
- lipids
- virology
- immunology

Treatment efficacy

- Acute phase
- Chronic infection

Mathematical modeling

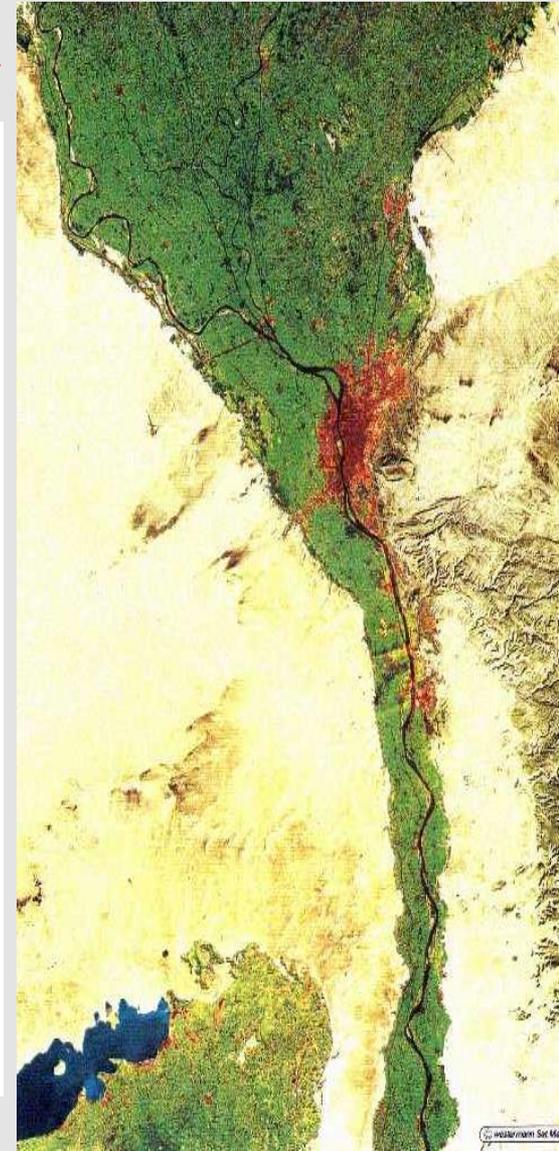
- Prediction
- cost-effectiveness

EGYPTIAN NATIONAL CONTROL STRATEGY FOR VIRAL HEPATITIS 2008-2012



April 2008

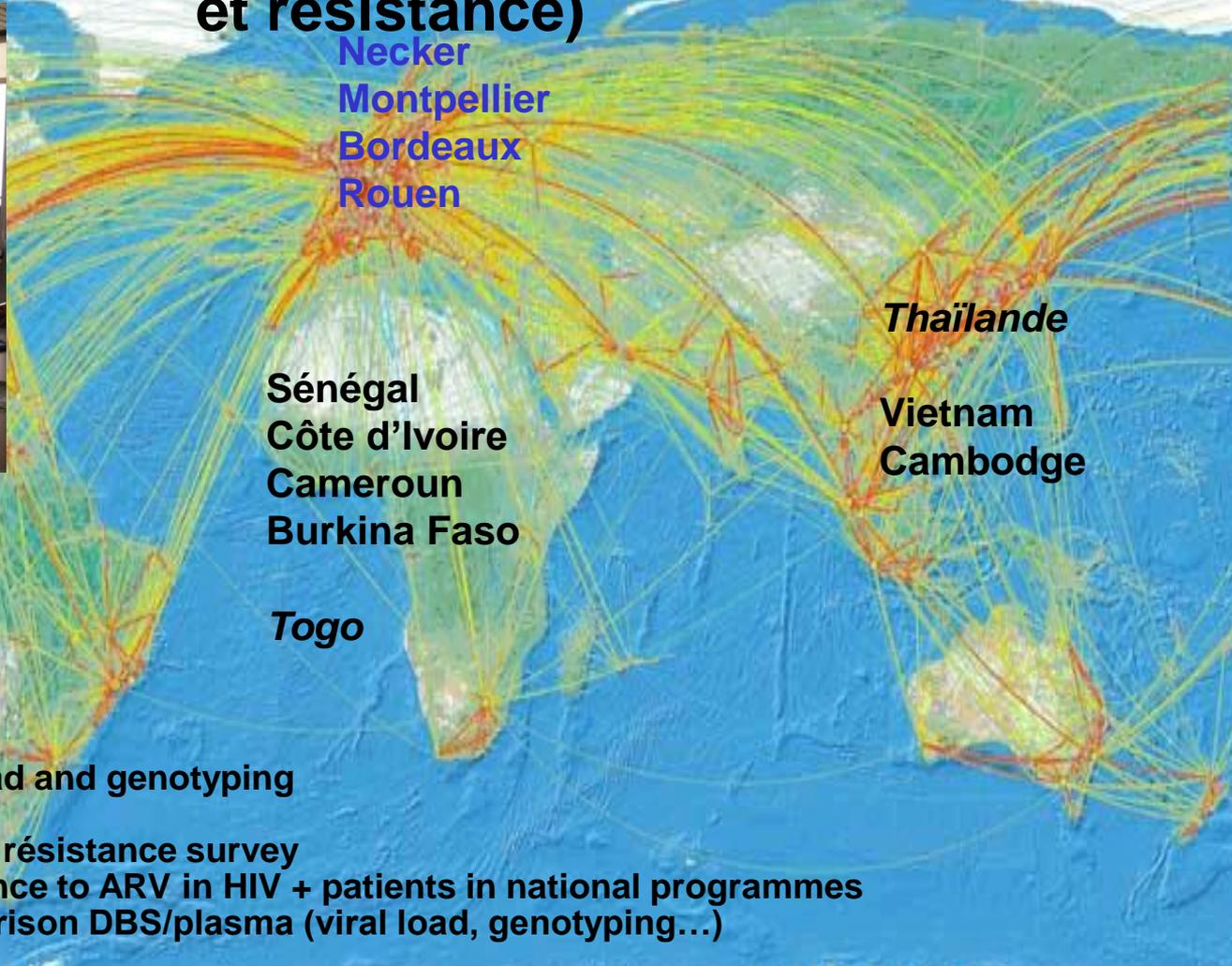
Arab Republic of Egypt, Ministry of Health and Population
National Committee for the Control of Viral Hepatitis



Caractéristiques des programmes sur les sites

Travail en réseau (projets multi-sites)

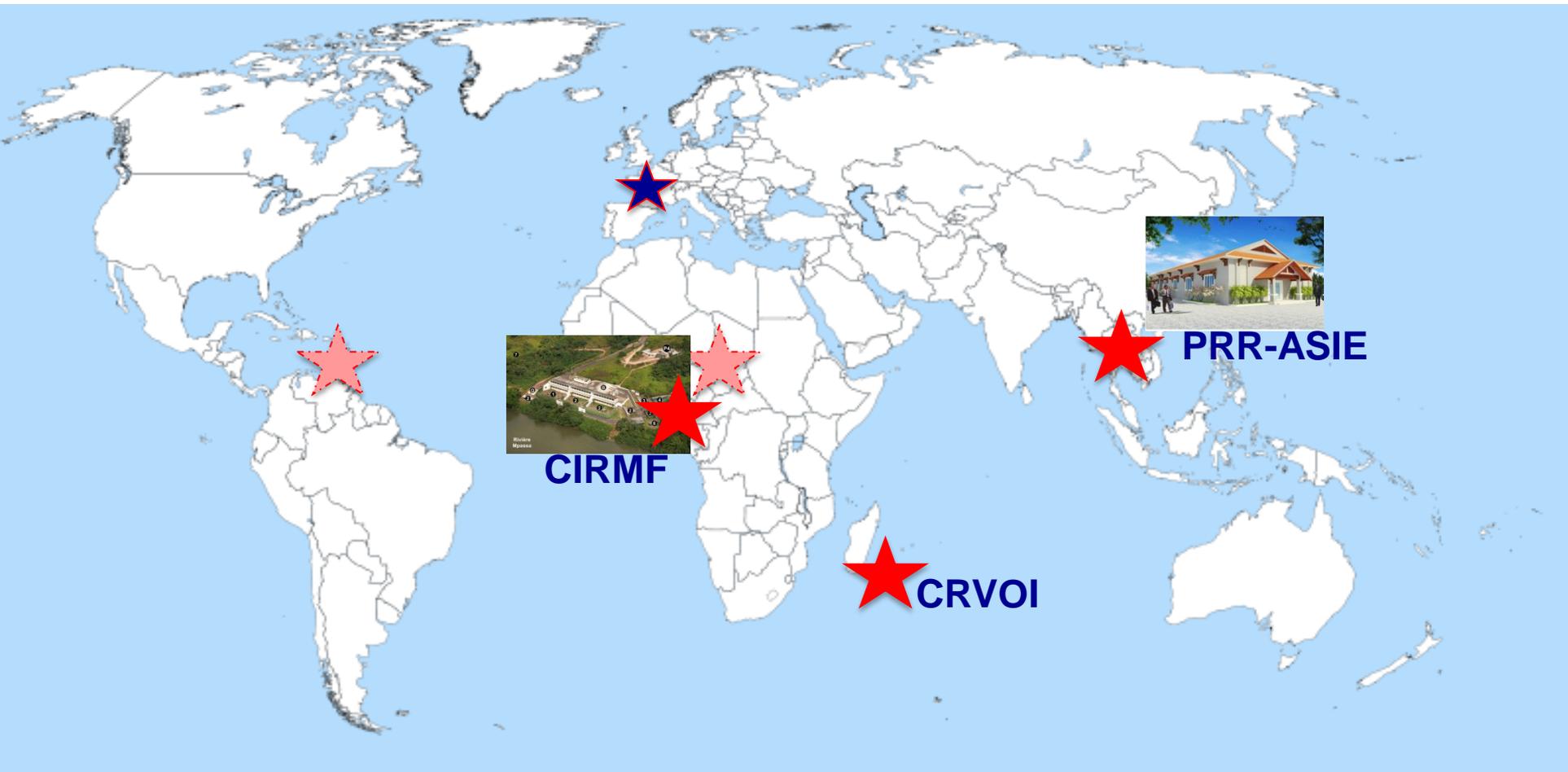
Groupe de travail nord/sud en virologie (quantification VIH et résistance)



Quality Control: viral load and genotyping

- 1) ANRS 12134: primary résistance survey
- 2) ANRS 12 186: resistance to ARV in HIV + patients in national programmes
- 3) ANRS 12 235: Comparison DBS/plasma (viral load, genotyping...)

A network of platforms for infectious diseases



 **Future platform**

REACTing

- **Not focused on one particular disease**
 - Emerging human, zoonotic infections, non infectious diseases
- **Not focused on a particular area of research**
 - Surveillance, modelling, economics, communication etc.
- **Not focused on northern or southern countries**
 - Platforms, surveillance etc. in Southern countries

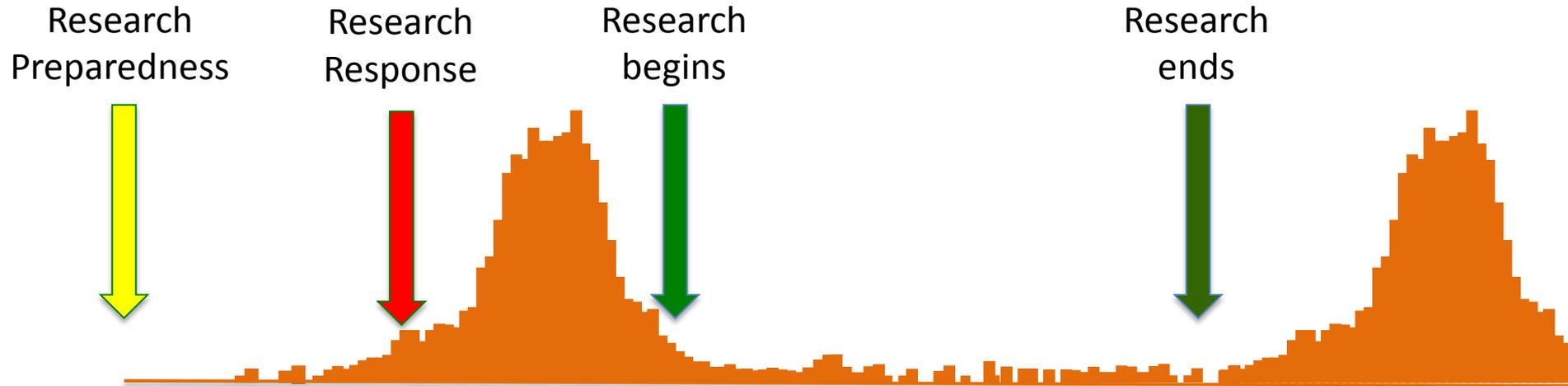
REACTing : The French Response to infectious disease crises

Lancet, April 2016 (in press) JF Delfraissy, Y Yazdanpanah, Y Lévy



REACTing

Research in a crisis situation



During the crisis : too late !

French Response to Ebola Crisis

A coordinated response – five pillars :

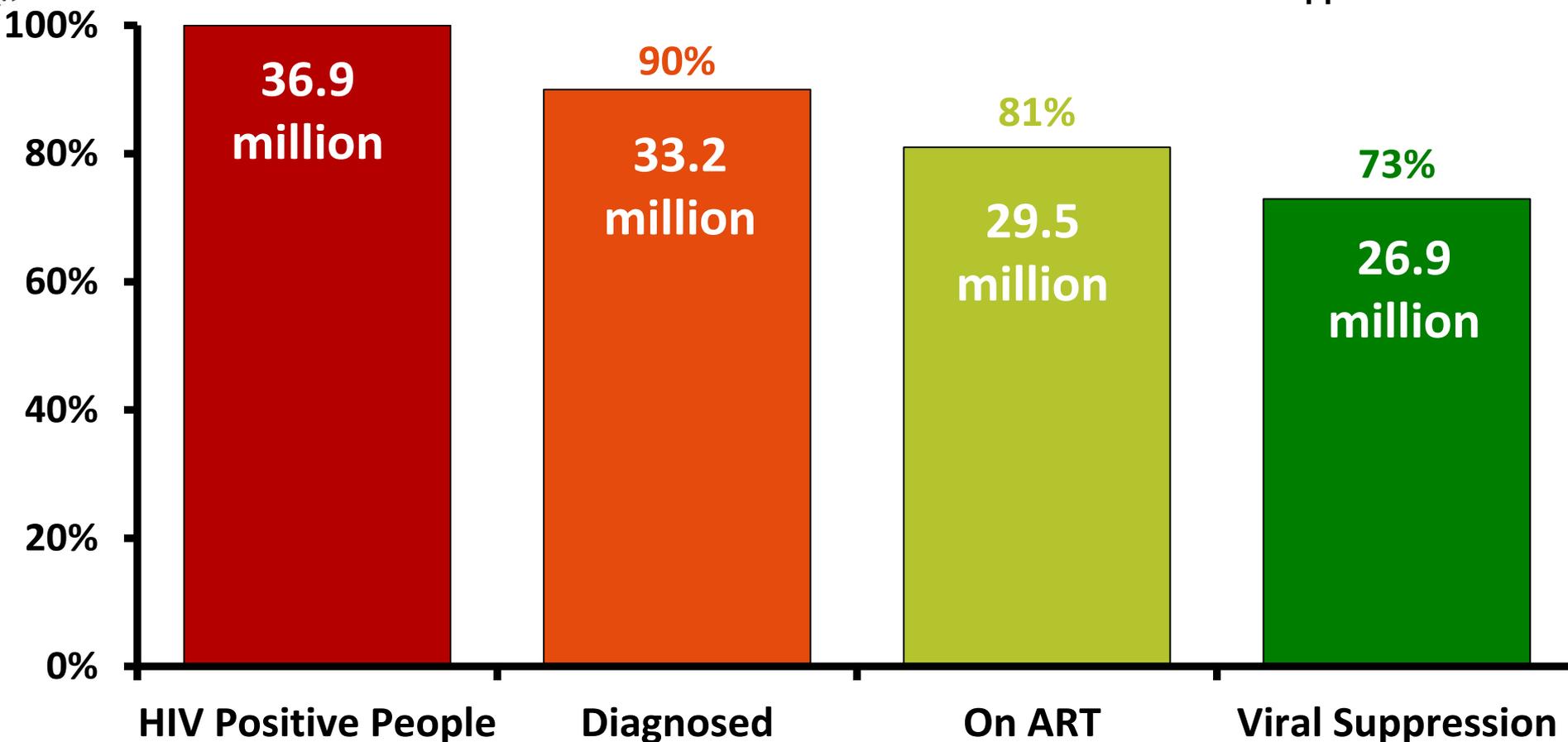
- ✓ **Support political coordination in Guinea**
 - ✓ 1 Expert with the National Coordinator, Surge capacity in Conakry (5 pers. including 2 medical officers), UNMEER
- ✓ **HWs mobilization, training, and protection**
 - Mobilization of 268 French staff (incl. 127 medical staff), training of 164 Guinean medical staff and 80 International, dedicated treatment unit (10 hospitalized 3 positives cases), intra/international evacuation capability
- ✓ **Research, Diagnosis and Treatment**
 - Laboratories with Pasteur Institute and Kplan and ETUs
- ✓ **Sensitization, education and prevention**
 - Integrated approach at the local level
- ✓ **Disease control measures:** Conakry, Bamako, Paris, Malabo

Global estimates (2014-2015) to reach the 90-90-90 target

Target 1:
90% of HIV+
people diagnosed

Target 2:
90% of diagnosed
people on ART

Target 3:
90% of people on
ART with HIV RNA
suppression



Issues in France for HIV Epidemic

- Diagnosis is **THE** major issue, whatever the risk group
 - How to reach those who never test
 - How to take advantage of the different tools and testing offers
- Earlier treatment unlikely to control the epidemic in MSM (and other high risk individuals)
 - Implementation of PREP will be a key component
 - May improve access to test



The
**New England
Journal of Medicine**

Volume 365

August 11, 2011

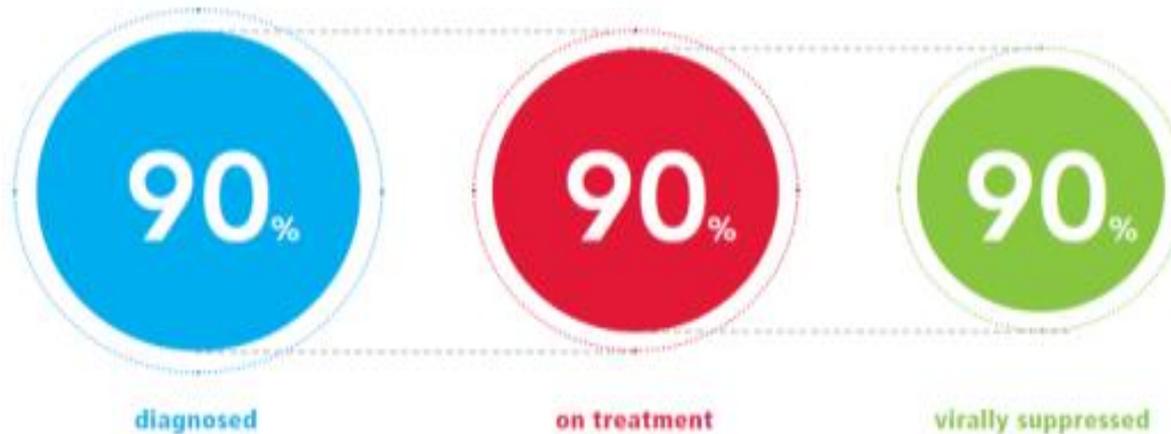
Number 6

Prevention of HIV-1 Infection with Early Antiretroviral Therapy

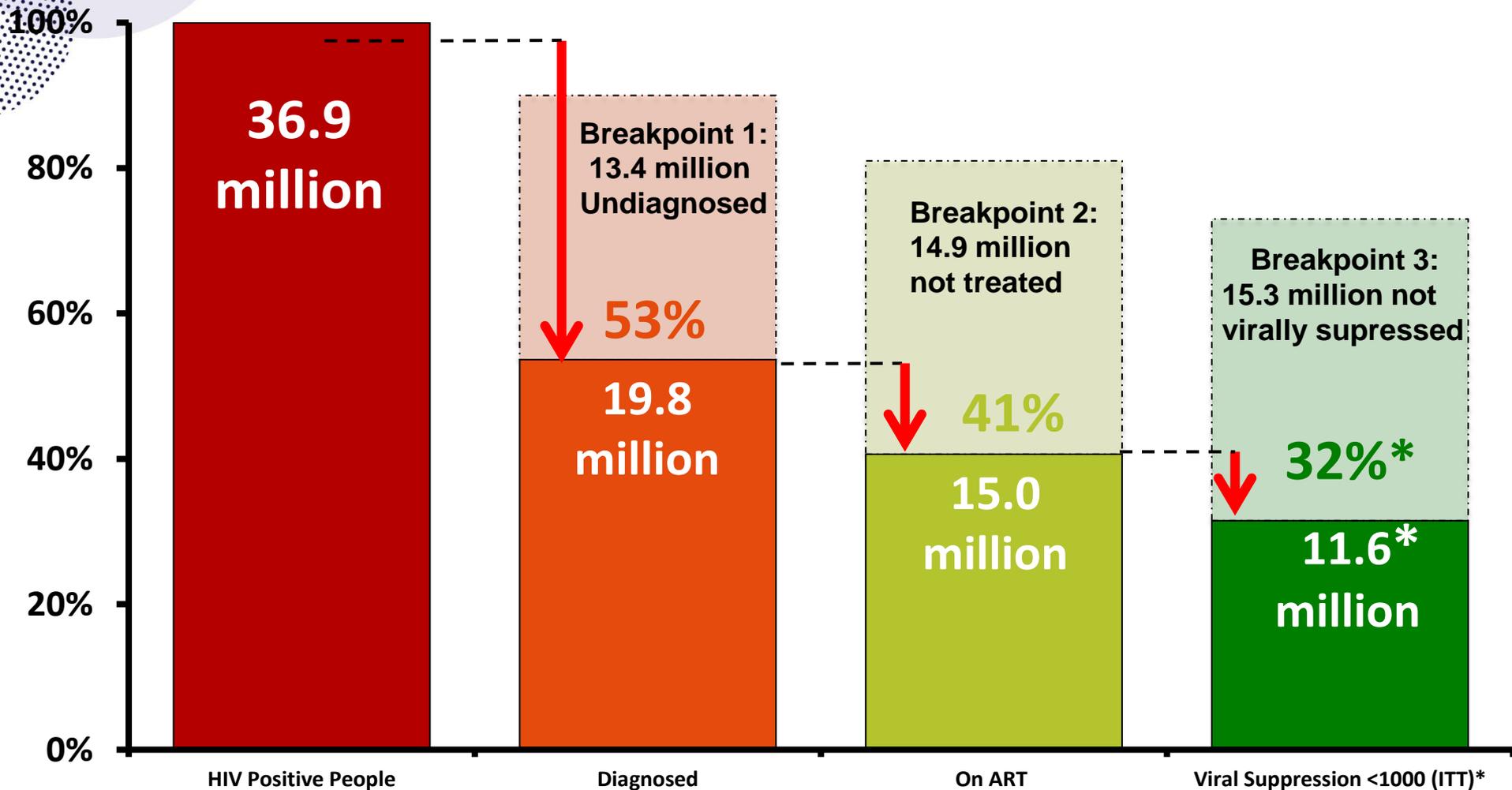
HPTN 052 Study Team

- **1,763 HIV-serodiscordant couples in 9 countries**
- **96% reduction in HIV transmission when ART started in HIV-infected partner at CD4 count of 350-550 compared to <250**

The 90/90/90: A new and ambitious target was established to end AIDS epidemic by 2030



Global estimates (2014-2015) vs the gap to reach 90-90-90 targets



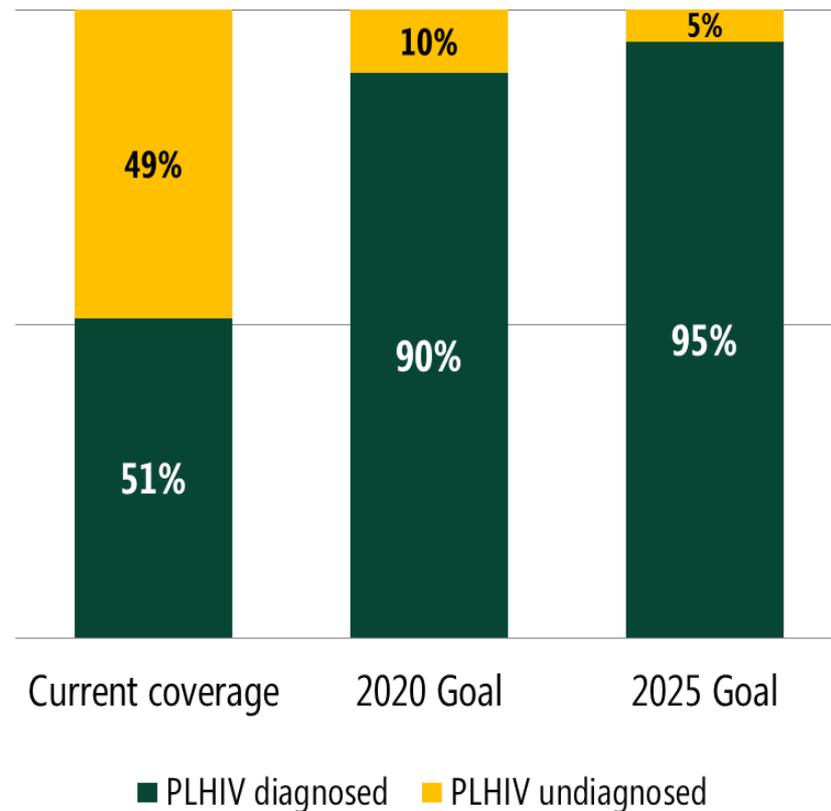
Ref: On ART = March 2015. How Aids Changed Everything. Fact Sheet. UNAIDS 2015. MDG 6: 15 YEARS, 15 LESSONS OF HOPE FROM THE AIDS RESPONSE July 2015. * Average viral suppression% Intention to Treat LMIC rate from a Systematic Review by McMahon J. et al. Viral suppression after 12 months of antiretroviral therapy in low-and middle-income countries: a systematic review." *Bulletin of the World Health Organization* 91.5 (2013): 377-385.

Increasing access to HIV testing

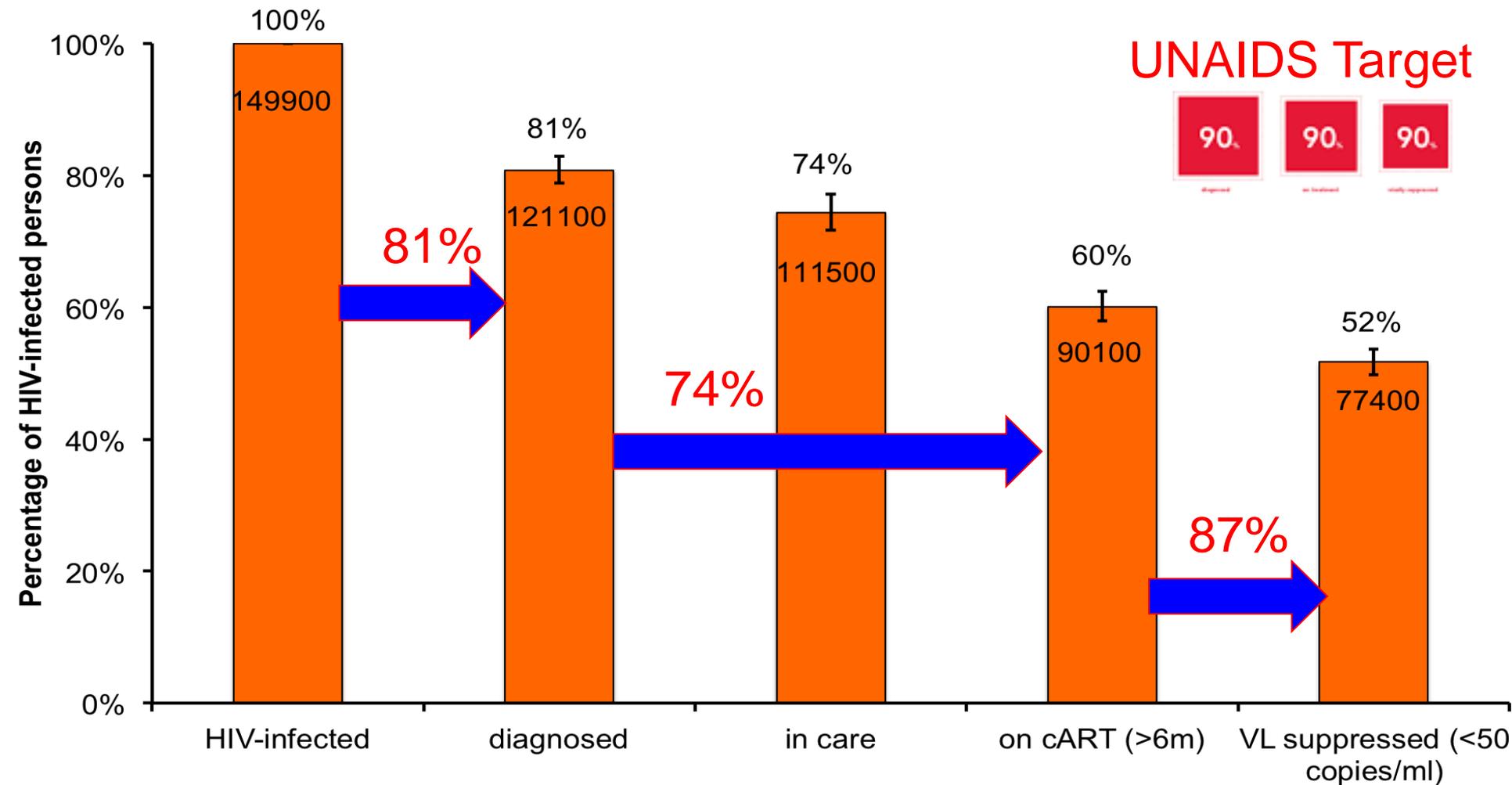
Aproximately 50% of PLHIV do not know their status

Innovations in HIV Testing

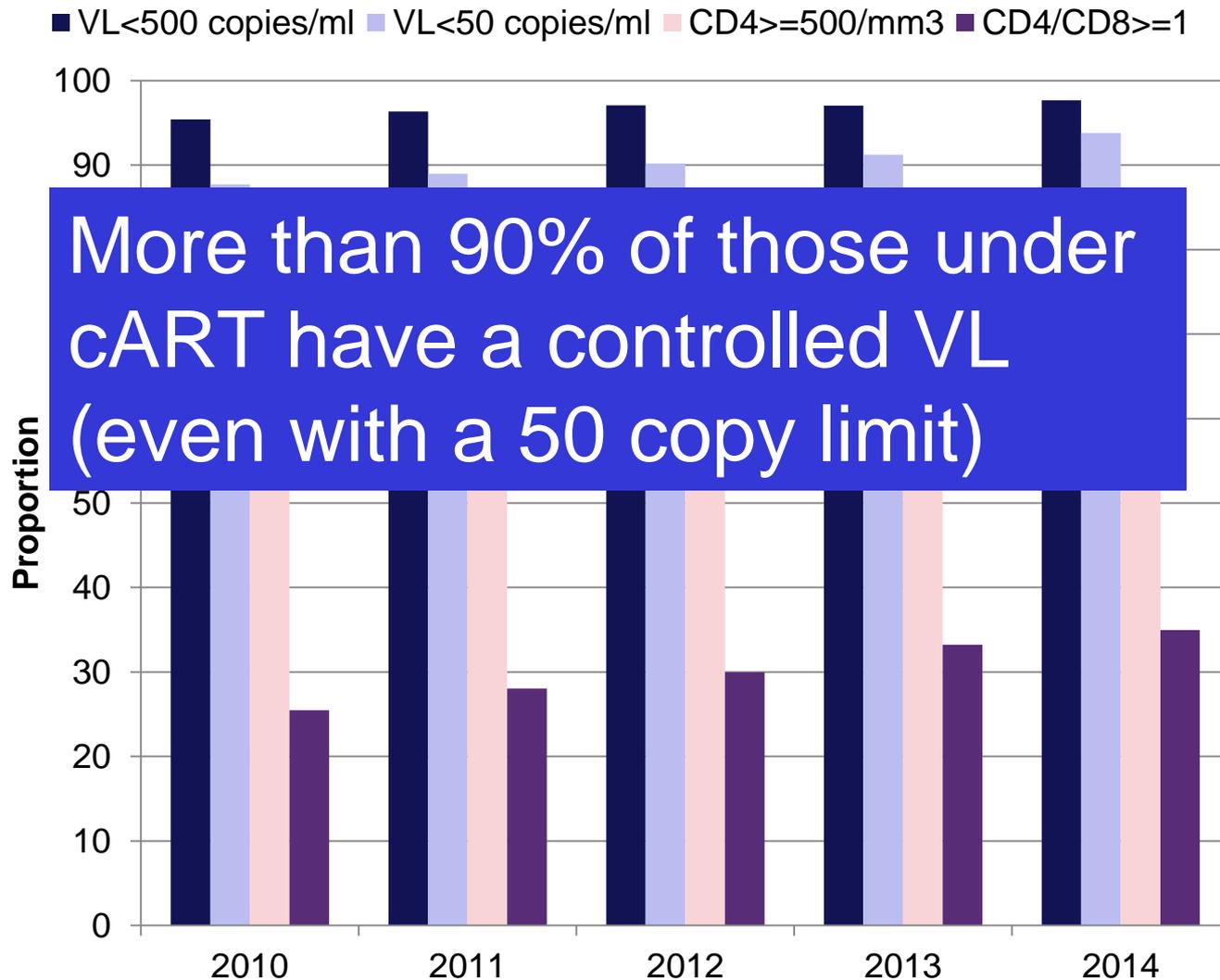
- Self testing
- Birth testing and integrated HIV testing for kids
- Targeted testing in low prevalence epidemics
- HTC within disease campaigns



Engagement in HIV Care in France in 2010



VL, CD4 and CD4/CD8 ratio in individuals under cART for at least 6 months – ANRS CO 4



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