

# The Eras of the HIV Epidemic

1930-1980

1981-1986

1987-1995

1996-2005

2006-2011

2012+

**ACT UP**

**AIDS EMERGENCY FUND**

**UNAIDS**  
UNICEF • UNDP • UNFPA • UNDPF  
UNESCO • WHO • WORLD BANK

**3 million by 2005**

**HAART**

**3rd Gen.**

**HAART**

**Margrethe (Grethe) P. Rask**  
Born: 1930, Thisted, Denmark  
Died: 12 December 1977 (aged 47), Copenhagen, Denmark  
Years: 1968-1977

**Gaetan Dugas**  
Born: February 20, 1953

**INIRASE**  
Didanosine (dideoxyinosine) (didanosine) (ddI)  
200 mg

**3 million by 2005**

**HAART**

**3rd Gen.**

**HAART**



# 3<sup>rd</sup> Generation Future HAART: 2012 +

## THE FUTURE OF ANTIRETROVIRAL THERAPY

- **New drugs**

- INSTI: Elvitegravir, Dolutegravir
- NNRTI: Lersivirine
- NRTI: GS-7340 (TDF-prodrug)

- **New combinations**

- INSTI-NRTI: TDF-FTC-EVG-Cobi
- PI/cobi: DRV-Cobicistat booster
- PI/c-NRTI: DRV-Cobi-TDF<sub>pro</sub>-FTC

- **New strategies**

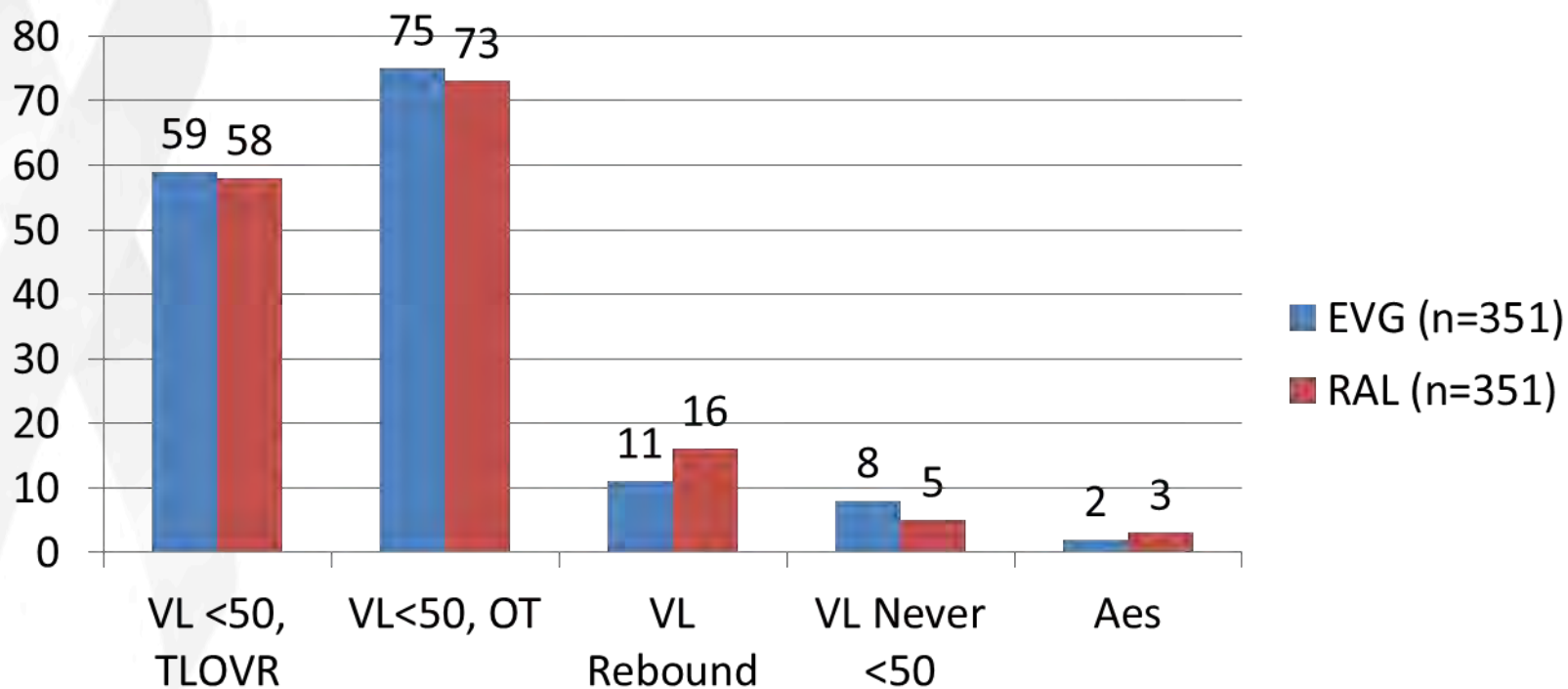
- **New classes**

- **Future needs**

# 3<sup>rd</sup> Generation Future HAART: 2012 +

## New Drugs: INSTI Elvitegravir: once daily therapy

### EVR Non-Inferior to RAL at Week 48



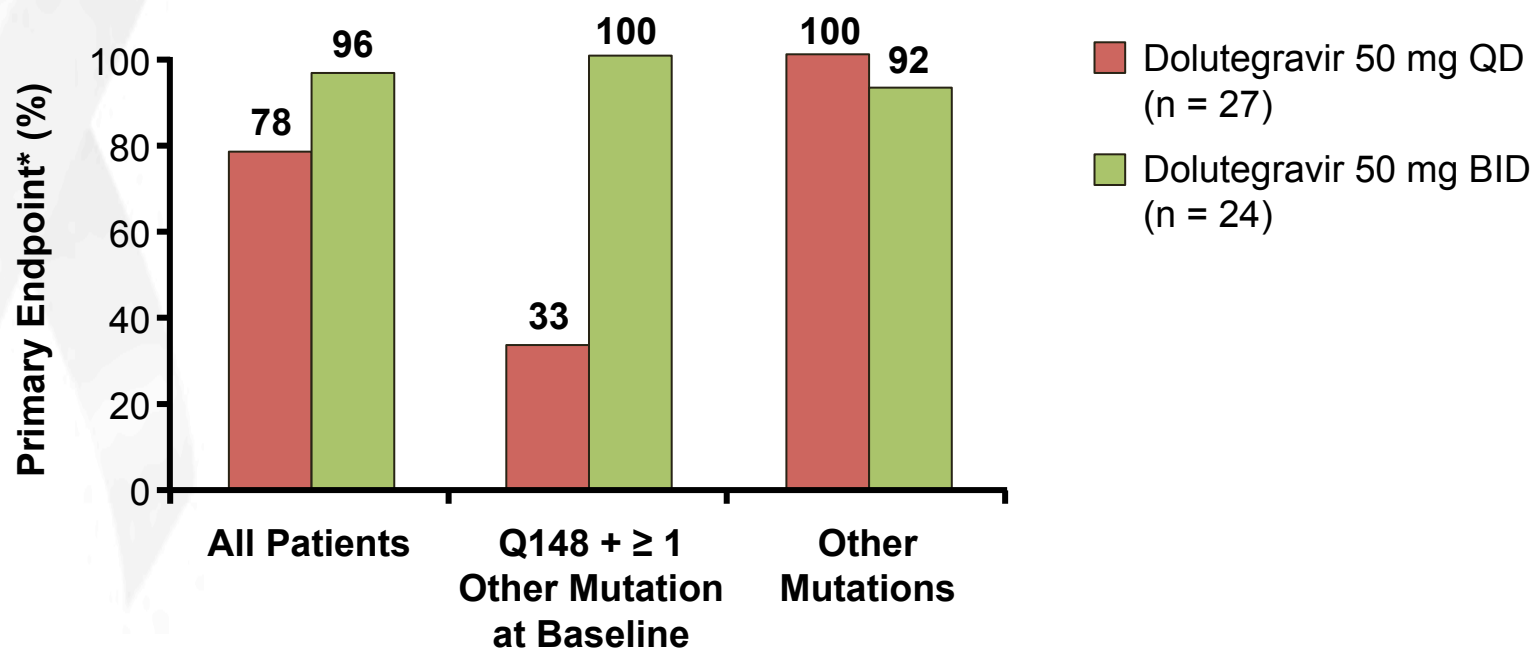
\*TLOVR: Difference: 1.1% (95% CI: -6.0 to 8.2;  $P = .001$ ).

Noninferiority: lower limit of 95% CI for difference between arms  $\geq -10\%$ .

## 3<sup>rd</sup> Generation Future HAART: 2012 +

**New Drugs: INSTI Dolutegravir: active against resistance**

**VIKING: Dolutegravir “Functional Monotherapy”  
in Pts With RAL Resistance**



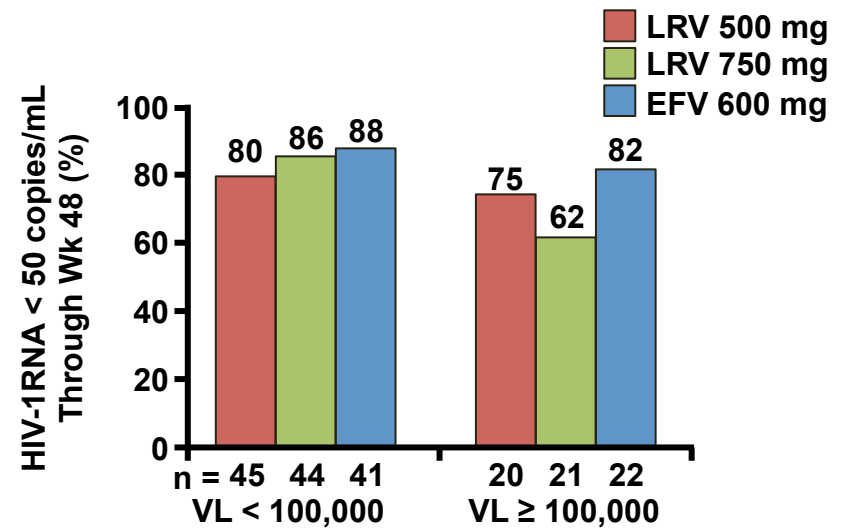
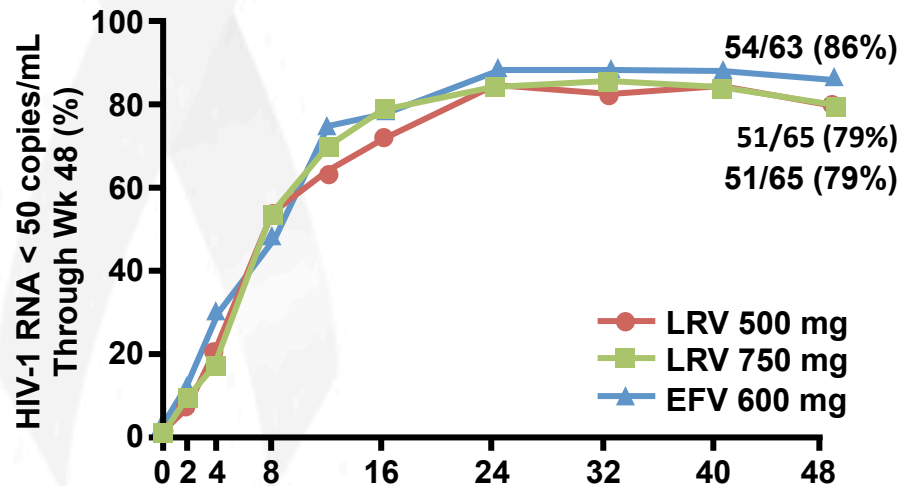
\*HIV-1 RNA < 400 copies/mL or  $\geq$  0.7 log<sub>10</sub> copies/mL reduction from baseline at Day 11.

Eron J. CROI 2011, Abstract 151LB.

# 3<sup>rd</sup> Generation Future HAART: 2012 +

**New Drugs: NNRTI Lersivirine:  
once daily without psych or CNS**

Lersivirine vs Efavirenz with TDF/FTC in ART-Naive Pts

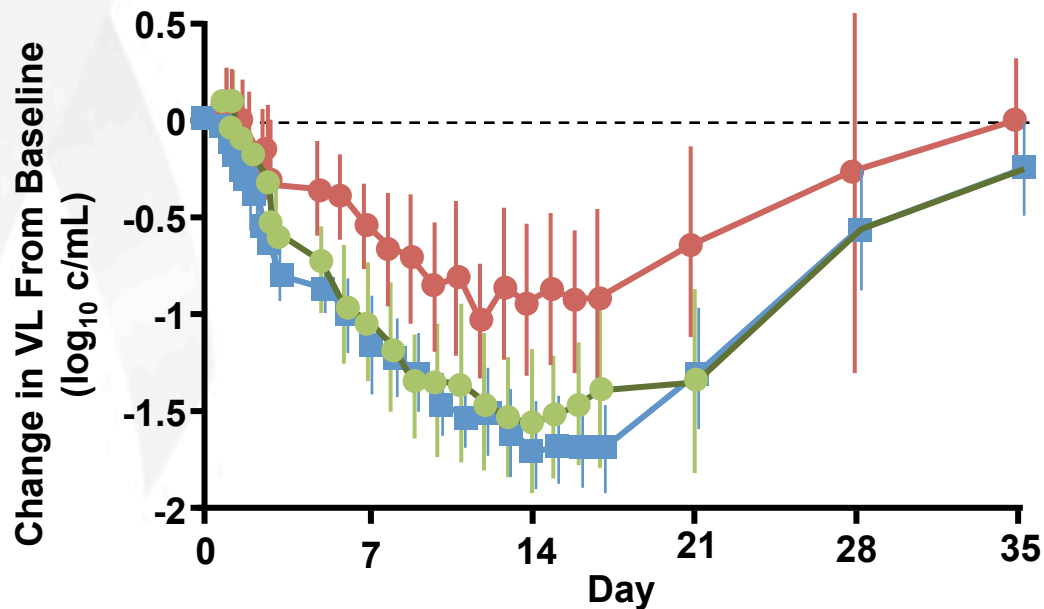


Vernazza P, et al. IAS 2011. Abstract TUAB0101.

# 3<sup>rd</sup> Generation Future HAART: 2012 +

## New Drugs: GS-7340 TDF Prodrug

- 14-day monotherapy in HIV+ patients:
  - Lower TDF plasma concentrations
  - Higher intracellular concentrations
  - Greater VL reduction

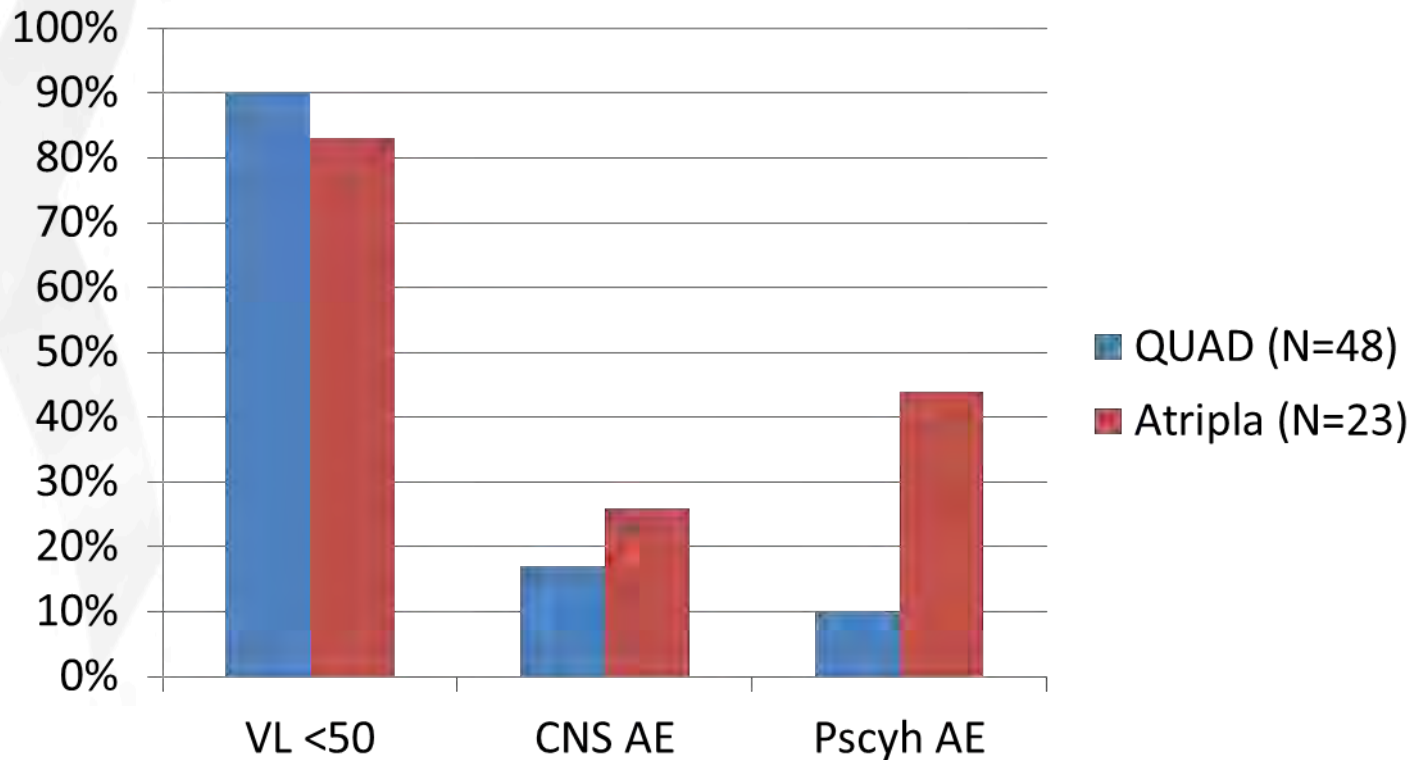


TDF 300 mg QD (n = 10)  
GS-7340 50 mg QD (n = 10)  
GS-7340 150 mg QD (n = 10)

# 3<sup>rd</sup> Generation Future HAART: 2012 +

## New Combinations: 3<sup>rd</sup> STR: The “Quad”: TDF-FTC-EVR-Cobi

TDF-FTC-EVR/Cobi -vs- TDF-FTC-EFV  
Week 48 results in Tx-Naïve Patients



Cohen AIDS 2011; 25:F7-12

## 3<sup>rd</sup> Generation Future HAART: 2012 +

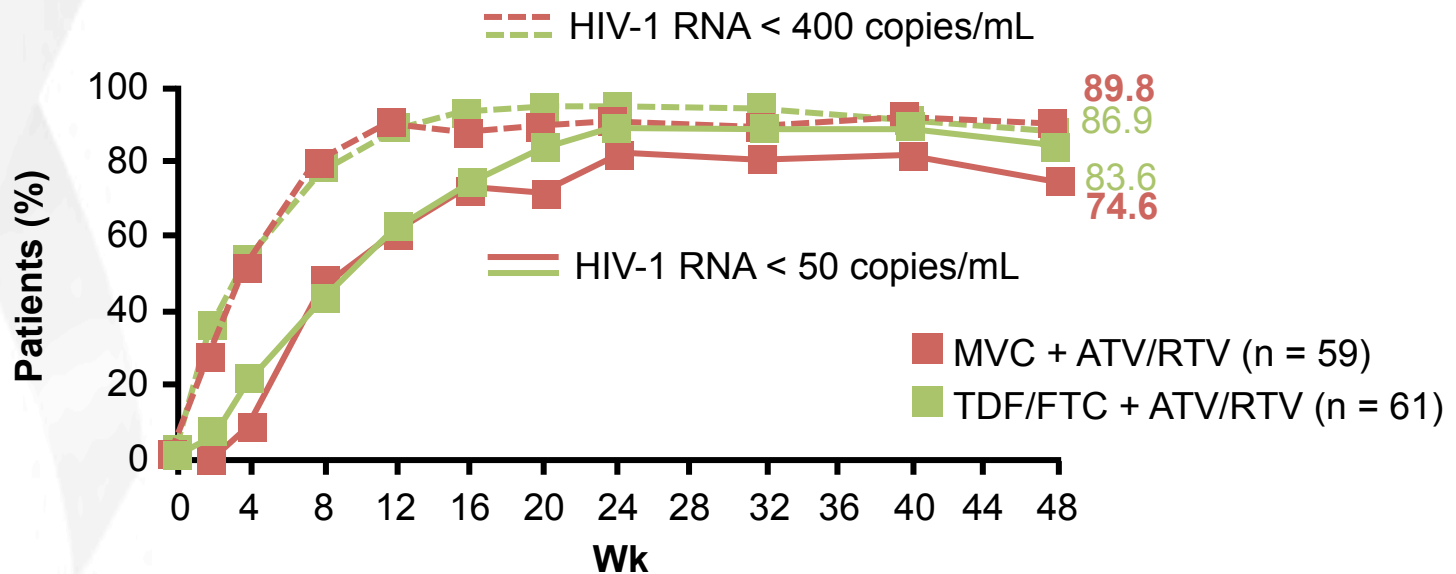
### THE FUTURE OF ANTIRETROVIRAL THERAPY

- New drugs
- New combinations
- **New strategies**
  - NRTI-sparing regimens
  - 2-drug potent regimens: INSTI-PI/r
- **New classes**
  - Mono-clonal antibody
  - Zinc fingers
- **Future needs**
  - HIV Vaccine
  - “Functional” cure

# 3<sup>rd</sup> Generation Future HAART: 2012 +

New strategies: NRTI-Sparing “2-Drug” CCR5-PI/r regimen

MVC vs TDF/FTC With ATV/RTV in ART-Naive Patients

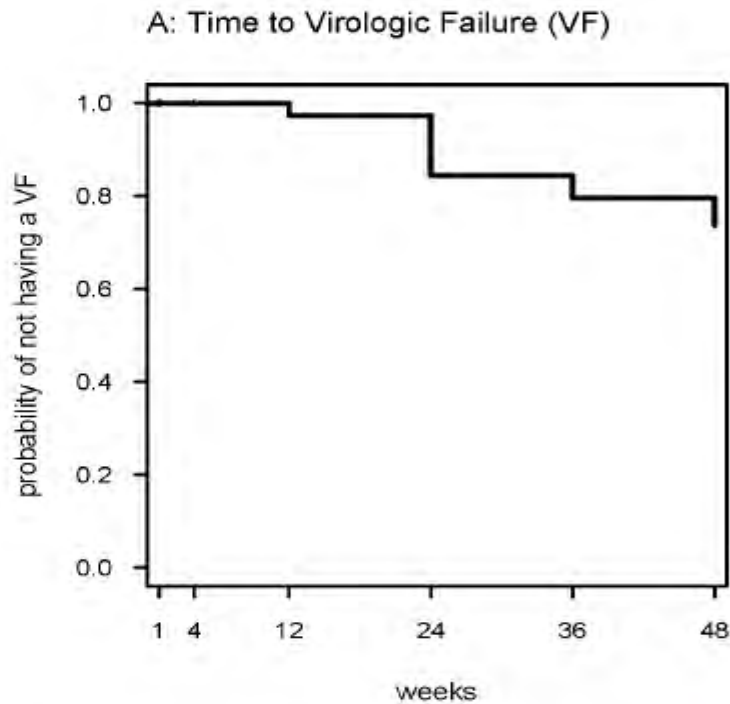


Portsmouth S, et al. IAS 2011. Abstract TUAB0103.

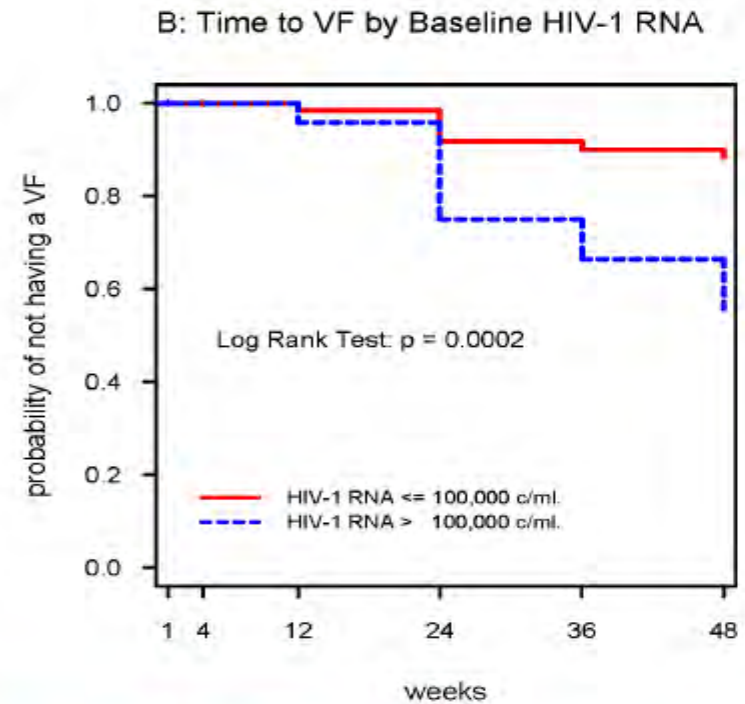
# 3<sup>rd</sup> Generation Future HAART: 2012 +

## New strategies: NRTI-Sparing “2-Drug” INSTI-PI/r regimen

ACTG A5262: DRV/r + RAL in Tx-Naïve: Faster failure at higher VL



n with VF: 0 0 3 14 5 6  
n at risk: 112 111 110 105 89 81

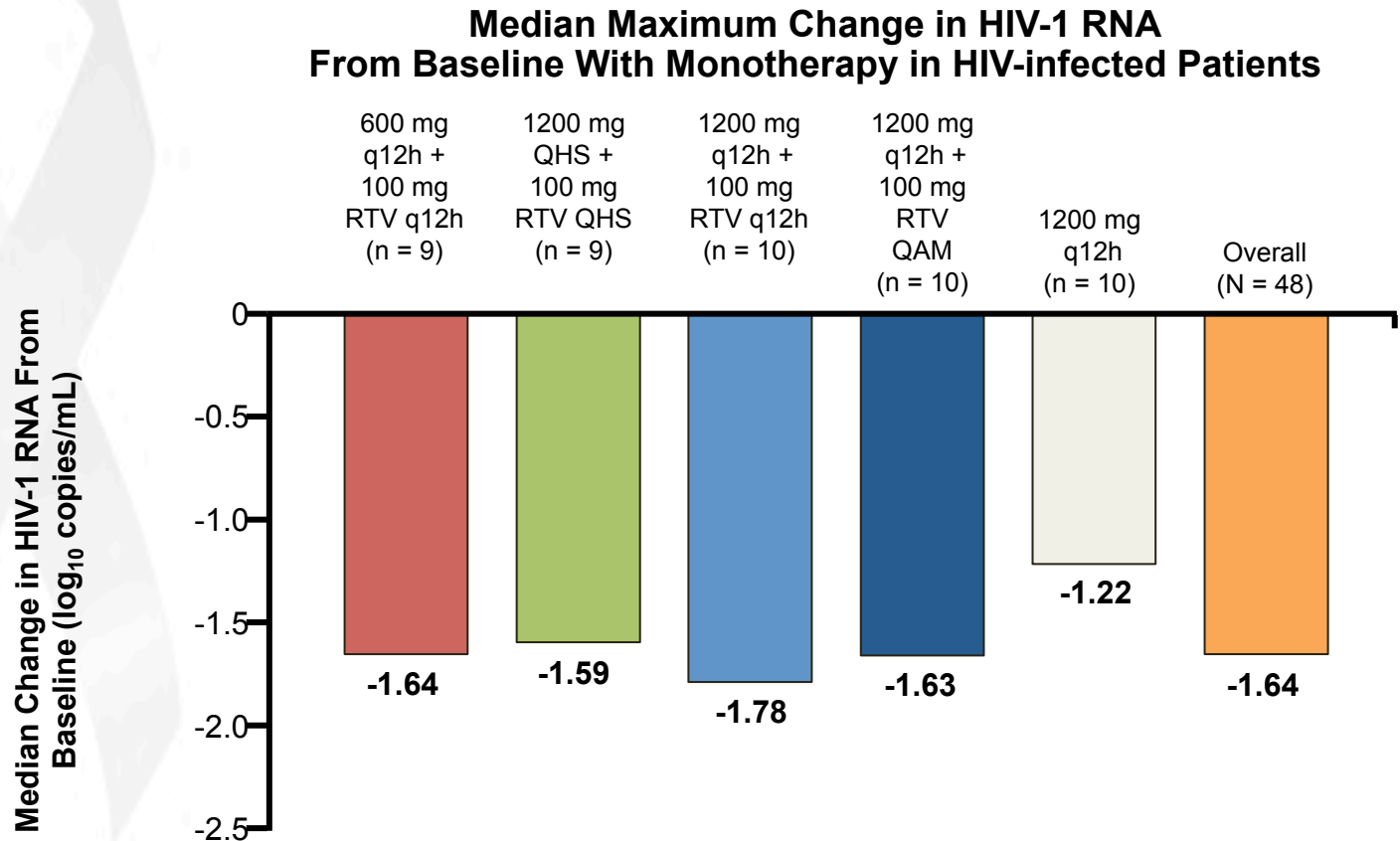


HIV-1 RNA ≤ 100,000 c/ml.:  
n with VF: 0 0 1 4 1 1  
n at risk: 63 63 62 59 54 50

HIV-1 RNA > 100,000 c/ml.:  
n with VF: 0 0 2 10 4 5  
n at risk: 49 48 48 46 35 31

# 3<sup>rd</sup> Generation Future HAART: 2012 +

## New Classes: BMS-663068: Oral Attachment Inhibitor



Envelope polymorphisms may reduce baseline susceptibility

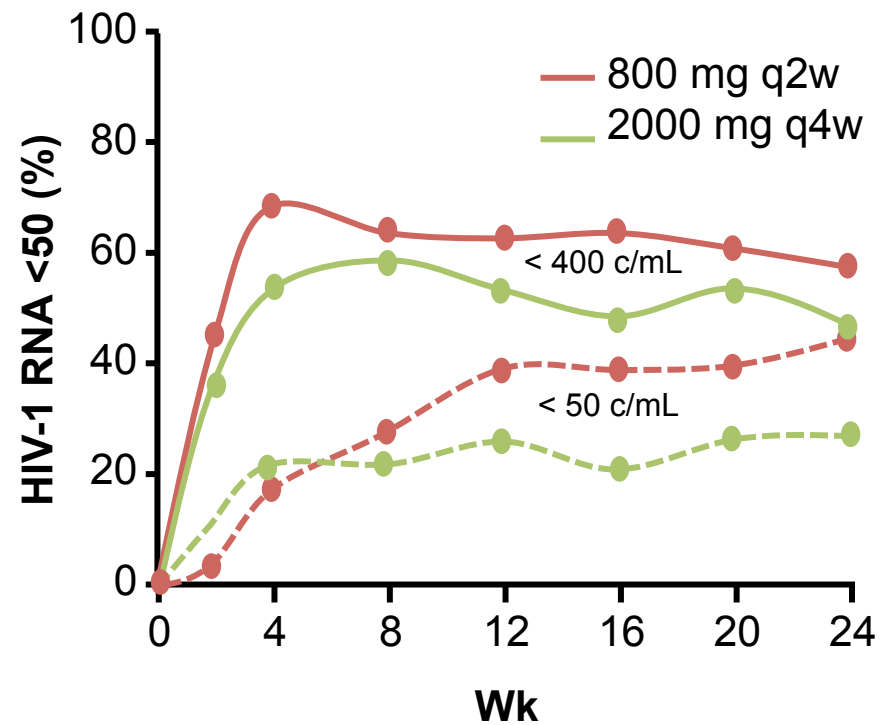
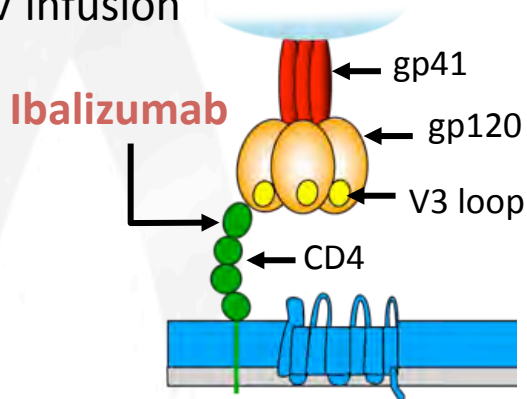
Nettles R, et al. CROI 2011. Abstract 49.

# 3<sup>rd</sup> Generation Future HAART: 2012 +

## New Classes: Ibalizumab: IV Entry Inhibitor

### Ibalizumab + OBR in Treatment-Experienced Patients

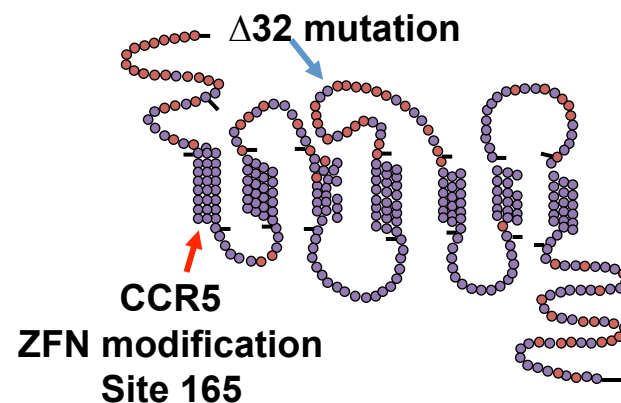
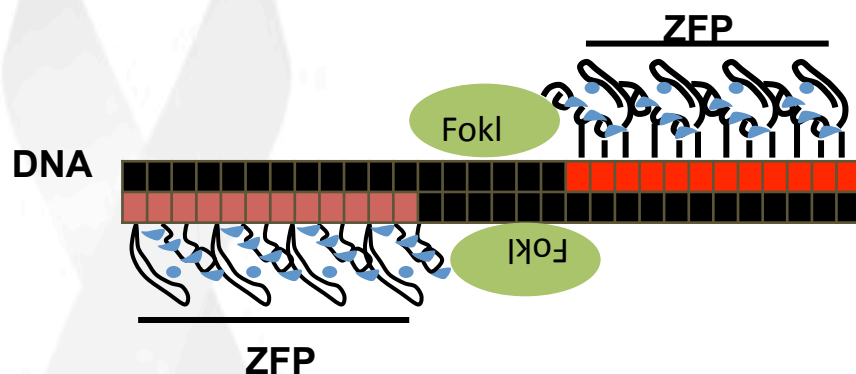
- Monoclonal antibody to non-HIV binding epitope of CD4
- Blocks HIV-1 entry into cell
- IV infusion



Khanlou H, et al. ICAAC 2011. Abstract H2-794b.

# 3<sup>rd</sup> Generation Future HAART: 2012 +

## New Classes: Zinc Finger Nuclease (ZFN) Disruption of CCR5 Gene in Autologous CD4+ Cells



### Mechanism:

- T: ZFN cleavage results in double-stranded DNA break with nonhomologous end repair leading to permanent CCR5 gene modification
- Treated CD4+ cells anticipated to be resistant to HIV infection

### Early HIV-infected patient studies :

- Engraftment with rapid clonal expansion and persistence of ZFN-modified cells in circulation and rectal mucosa
- Median ~100 cells/mm<sup>3</sup> increase in CD4+ count after 1 year
- Most AEs mild; no SAEs by median 337 d

# 3<sup>rd</sup> Generation Future HAART: 2012 +

## New Classes: Investigational Targets

- LEDGF/p75 Inhibitors
  - Cellular tethering factor for integration
  - In-vitro identification of inhibitory peptides
- Gag Inhibitors
  - Viral factor for particle assembly at cell membrane
  - In-vitro identification of inhibitory molecules
- CXCR4 Zinc Finger Nucleases
  - Cell culture-mouse model proof of concept tested
- Capsid Assembly Inhibitors
  - Formation of viral core
  - In-vitro identification of inhibitory molecules

## 3<sup>rd</sup> Generation Future HAART: 2012 +

### Future Needs: Potential for HIV Vaccine

- Concept proven: Thai RV144 study: 31% protection
- Human studies on-going to determine correlates of immunity from elite controllers:
  - Broadly reacting neutralizing antibodies
  - Specific neutralizing envelope epitopes
  - Precise B-cell clonal expansion
- Animal studies on-going to elucidate immune response

Comments, A. Fauci, NIH, 2011

# 3<sup>rd</sup> Generation Future HAART: 2012 +

## Future Needs: Functional Cure -vs- Microbial Eradication

### Early Treatment:

- Smaller latent reservoir
- Subsequent therapeutic vaccination boosting of immune control



### Novel Therapies:

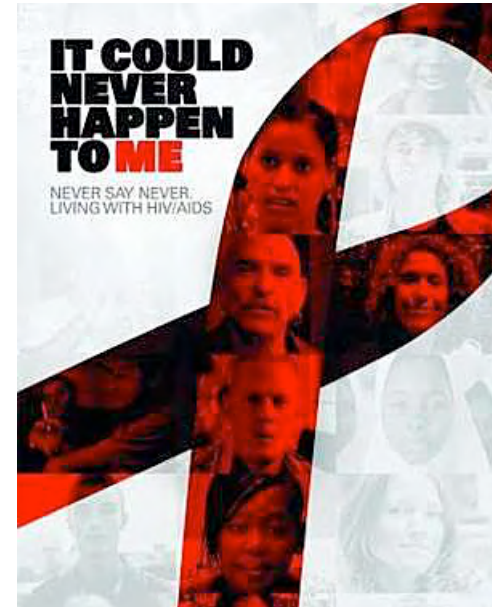
- Therapies to eliminate latent reservoir
- Gene therapy to inactivate or excise incorporated virus

Comments, A. Fauci, NIH, 2011

# Challenges Facing the Global AIDS Pandemic: 2012 +

## Expanded Prevention Efforts

Condoms and prevention

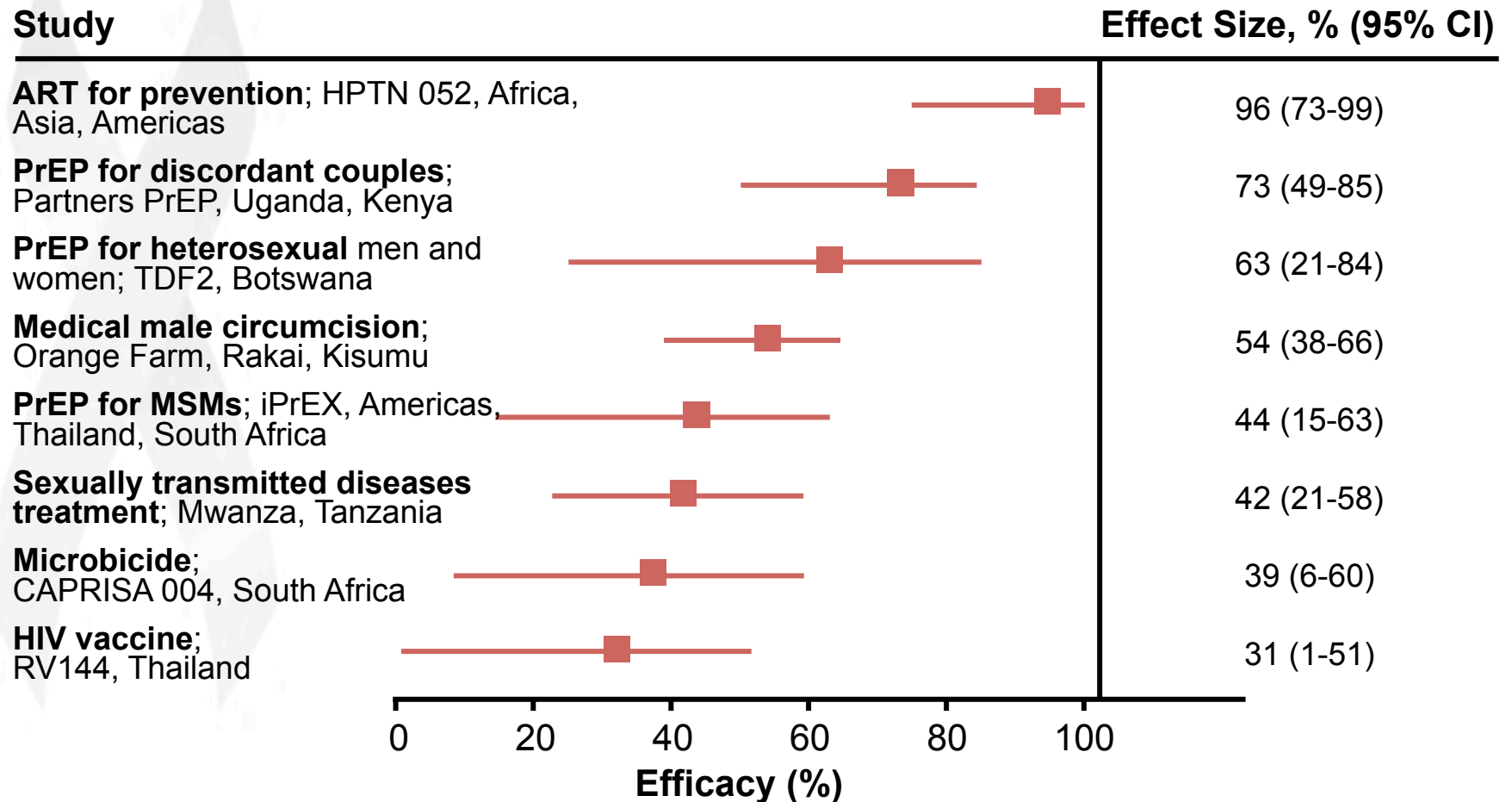


Uganda mobile male circumcision clinic

# Challenges Facing the Global AIDS Pandemic: 2012 +

## Multi-Pronged Prevention Approach

### Efficacy of HIV Prevention Strategies From Randomized Clinical Trials



Abdool Karim SS, et al. Lancet. 2011;[Epub ahead of print].

# Challenges Facing the Global AIDS Pandemic: 2012 +



## Gender Inequality

**GIVING WOMEN POWER OVER AIDS**

*Microbi- what? Microbicides!*

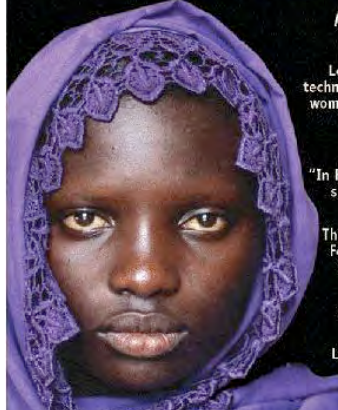
Learn about this new technology that will give women power over AIDS

Join us for a remarkable forum and photo exhibit, "In Her Mother's Shoes" showing February 20 through 23

The forum is Thursday February 22nd, 2007 11:30am -12:30pm

Bellevue Community College Room L100

Sponsored by: The Northwest Microbicide Coalition, Americans for UNFPA, World Neighbors, and others. To learn more, go to [www.global-campaign.org](http://www.global-campaign.org)





# Challenges Facing the Global AIDS Pandemic: 2012 +

## Maternal Child Health



# Challenges Facing the Global AIDS Pandemic: 2012 +

## Comprehensive Reduction Of Women's Vulnerability

 % HIV prevalence, 15-24 years old  
 % with secondary school education



Receiving treatment, % of total



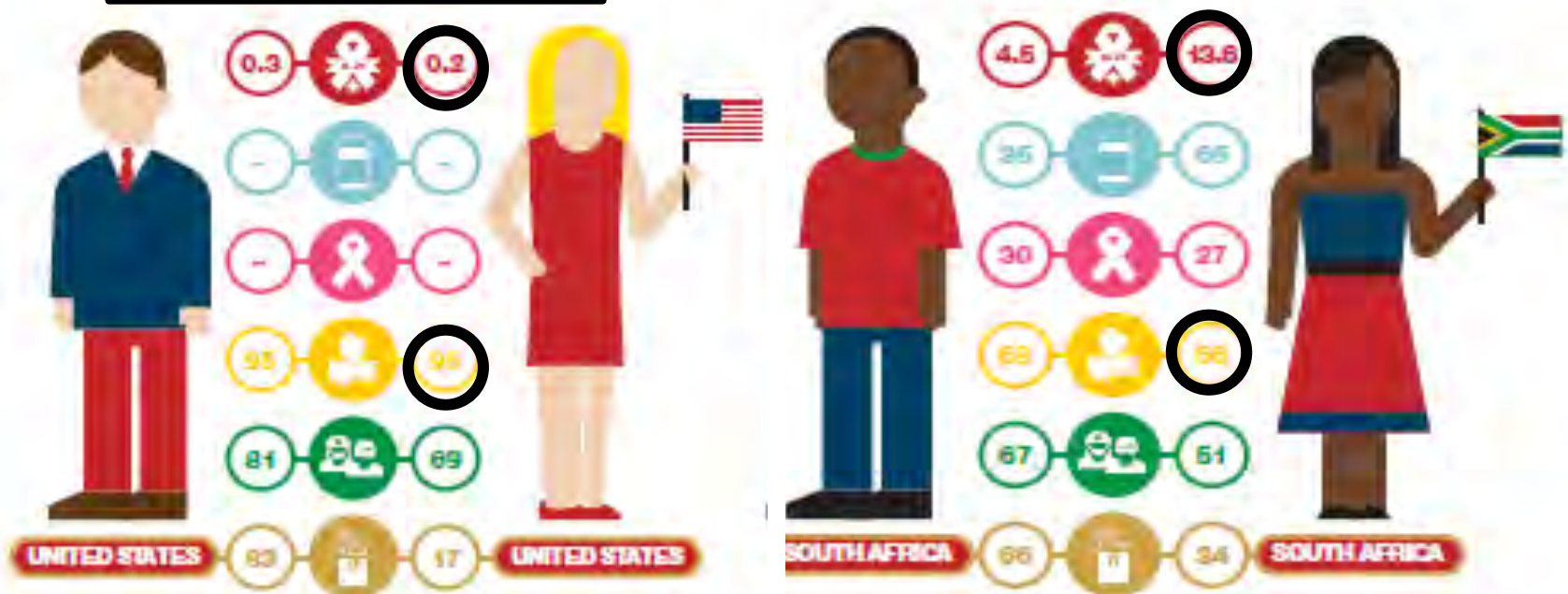
% who have knowledge of HIV



% labour force participation



% seats in parliament



# Challenges Facing the Global AIDS Pandemic: 2012 +

## Stigma and Discrimination

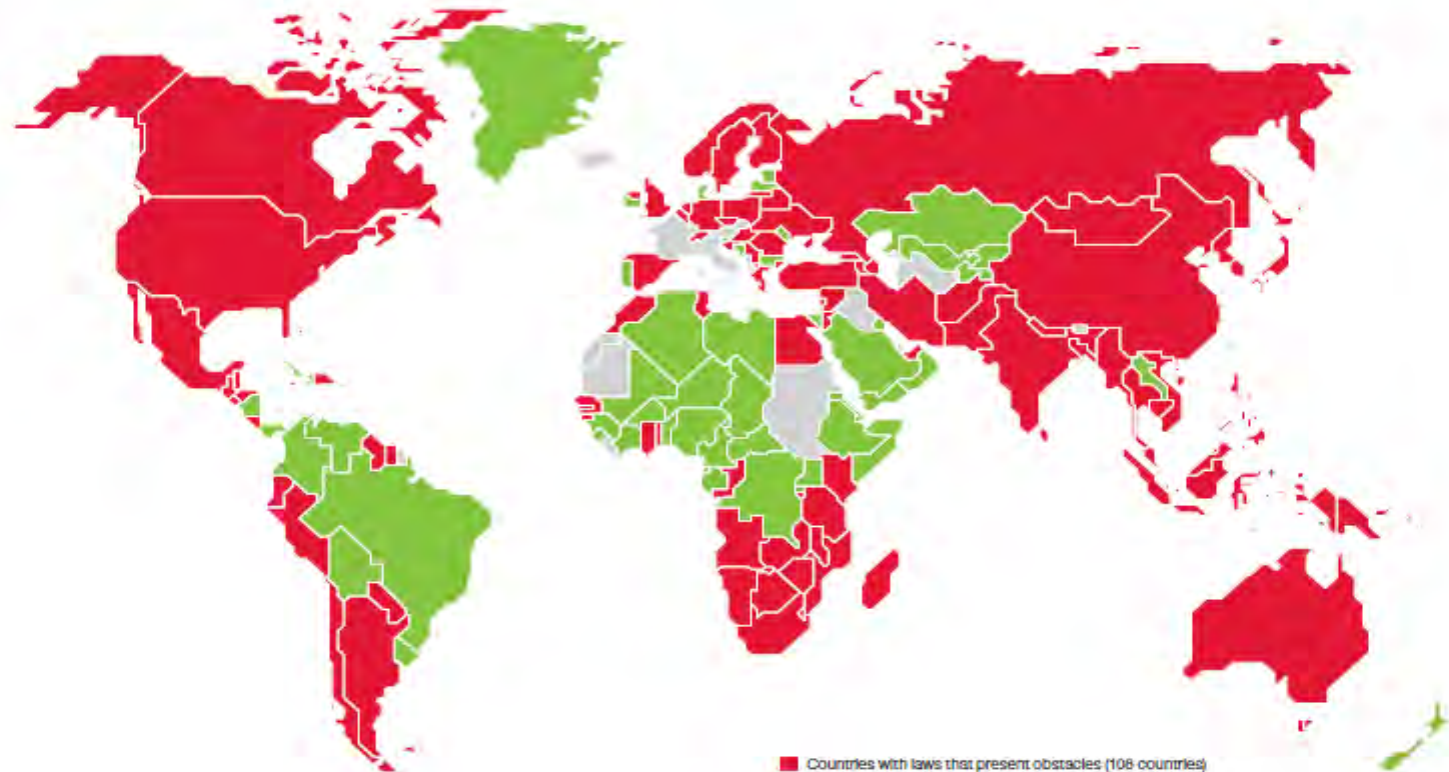
Stigma and discrimination



# Challenges Facing the Global AIDS Pandemic: 2012 +

## Country Policies That Impede Access To HIV Services

Countries with laws, regulations or policies that present obstacles for populations at higher risk or other vulnerable subpopulations to access prevention, treatment, care and support



[http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2011/20110607\\_IC2069\\_30Outlook\\_en.pdf](http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2011/20110607_IC2069_30Outlook_en.pdf)

# Challenges Facing the Global AIDS Pandemic: 2012 +

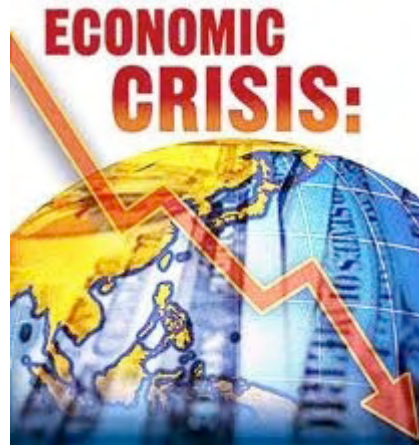
## Health Infrastructure



# Challenges Facing the Global AIDS Pandemic: 2012 +

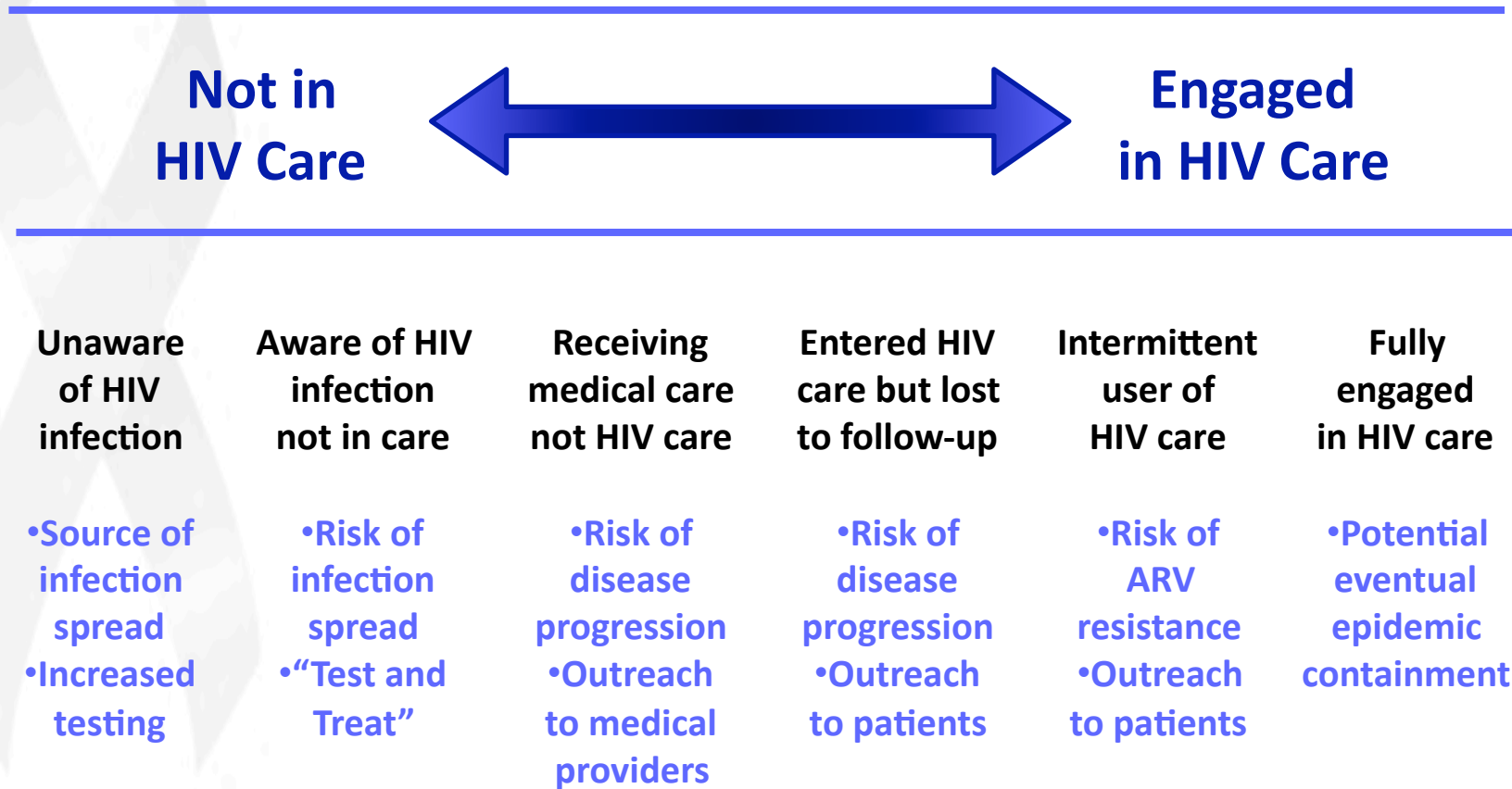
## External Factors:

- Competing health problems
- Global financial downturn
- Donor fatigue and shifting priorities



# Challenges Facing the Global AIDS Pandemic: 2012 +

## Patient Engagement in HIV Care



Adapted from Gardner Clin Inf Dis 2011;52:181



# The Eras of the HIV Epidemic

1930-1980

1981-1986

1987-1995

1996-2005

2006-2011

2012+

The collage is a comprehensive visual history of HIV/AIDS, organized into five eras. It features a variety of content:

- 1930-1980:** Images of primates, a chemical structure of Zidovudine (AZT), a map of Africa, and a portrait of Margrethe (Grethe) P. Rask.
- 1981-1986:** A CDC MMWR Weekly Report, a person in a hospital bed, and a portrait of Gaëtan Dugas.
- 1987-1995:** A red ribbon, the text "ACT UP", the AIDS Coalition to Unleash Power logo, and the AIDS Emergency Fund logo.
- 1996-2005:** A large red ribbon, the UNAIDS logo, a portrait of a man, and a box of INVIRASE (zalcitabine).
- 2006-2011:** A hand holding pills, a person using a rapid HIV test, and a "3 million by 2005" target graphic.
- 2012+:** A woman's face, a globe with a red ribbon, and a person looking through a microscope.

Scientific and medical elements include chemical structures, graphs showing viral load and CD4 counts, Kaplan-Meier survival curves, and diagrams of HIV transmission and treatment mechanisms like "Pharmacokinetic Boosting".