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Barcelona

What Do Advances in HIV Treatment Mean in the Context of Ending AIDS as a Public Health Threat by 2030?

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Conflict of interests

- I have received received honoraria, speakers' fees, and/or funds for research from:
  - Abbvie
  - Bristol-Myers-Squibb
  - Gilead Sciences
  - Janssen-Cilag
  - MSD
  - ViiV

The UNAIDS 2030 Fast-track

FAST-TRACK
ENDING THE AIDS EPIDEMIC BY 2030

United Nations A/70/L.52

General Assembly

Distr.: Limited
7 June 2016

Original: English

Seventieth session
Agenda item 11
Implementation of the Declaration of Commitment on HIV/AIDS and the political declarations on HIV/AIDS

Draft resolution submitted by the President of the General Assembly

Political Declaration on HIV and AIDS: On the Fast-Track to Accelerate the Fight against HIV and to End the AIDS Epidemic by 2030

The General Assembly,

Adopts the Political Declaration on HIV and AIDS annexed to the present resolution.

http://www.unaids.org/sites/default/files/media_asset/2016-political-declaration-HIV-AIDS_en.pdf

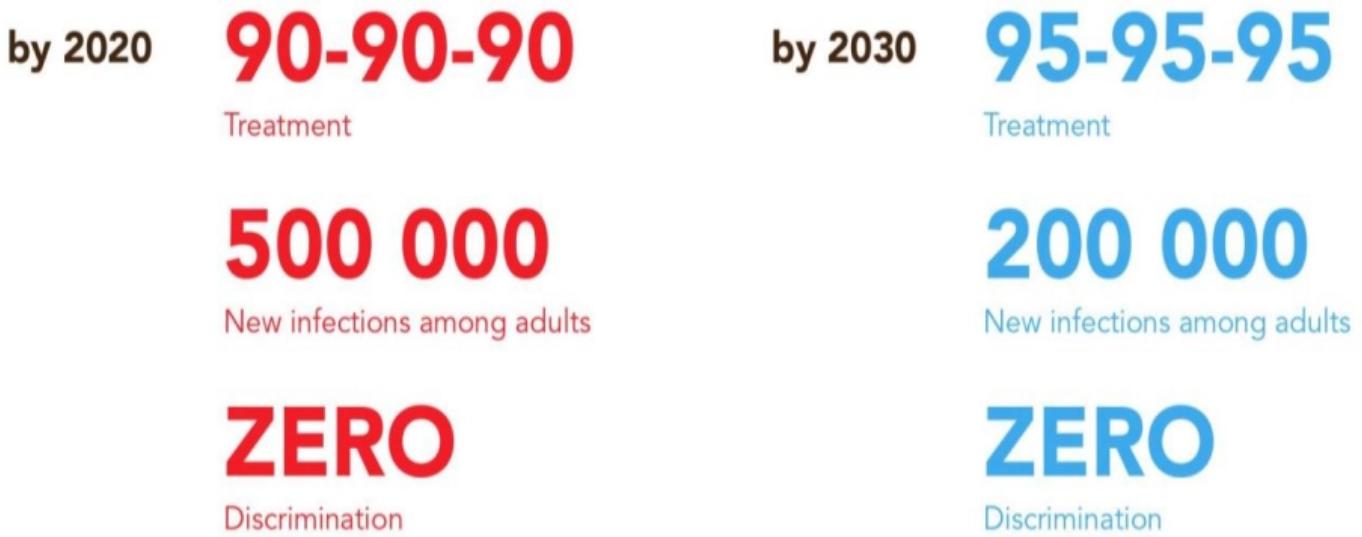
Ending the AIDS epidemic by 2030

HIV Cure/Eradication ≠ Ending AIDS epidemic

HIV infections may not disappear in the foreseeable future, but the AIDS epidemic can be ended as a global health threat.

http://www.unaids.org/sites/default/files/media_asset/2016-political-declaration-HIV-AIDS_en.pdf

Targets for ending the AIDS epidemic



- **90%** of people (children, adolescents and adults) living with **HIV know their status**
- **90%** of people living with HIV who know their status are **receiving treatment**
- **90%** of people on treatment have **suppressed viral loads.**
- Achieving the 90–90–90 by 2020 targets would still leave 27% of people living with HIV with unsuppressed viral loads in 2020

http://www.unaids.org/en/resources/documents/2014/FastTrackslidesPPT

The Fast-Track

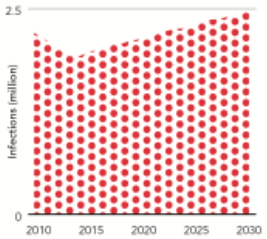
FAST-TRACK
ENDING THE AIDS EPIDEMIC BY 2030

NO SCALE-UP—maintain 2013 coverage levels

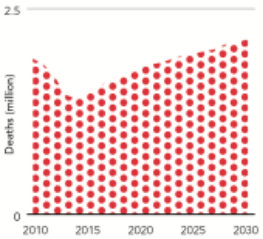
2015

RAPID SCALE-UP—achieve ambitious targets

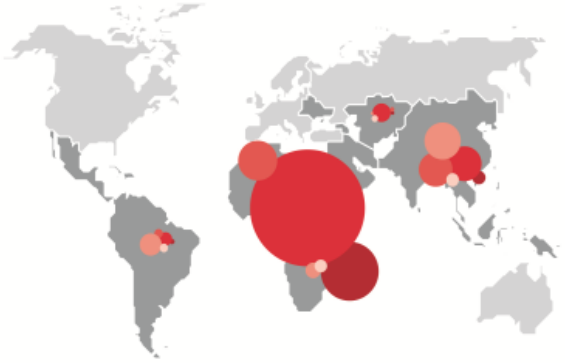
New HIV infections in low- and middle-income countries (millions)



AIDS-related deaths in low- and middle-income countries (millions)



New HIV infections in different population groups, low- and middle-income countries, 2030



Children
Heterosexual (including young women, excluding sex work)
Female sex workers and their clients
Men who have sex with men
People who inject drugs

2030

Without scale-up,
the AIDS epidemic will continue to outrun the response, increasing the long-term need for HIV treatment and increasing future costs.

MAJOR BENEFITS:

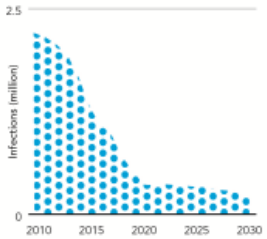
21 MILLION
AIDS-related deaths averted by 2030

28 MILLION
HIV infections averted by 2030

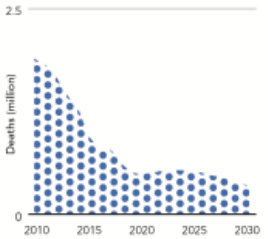
5.9 MILLION
infections among children averted by 2030

15– FOLD
return on HIV investments

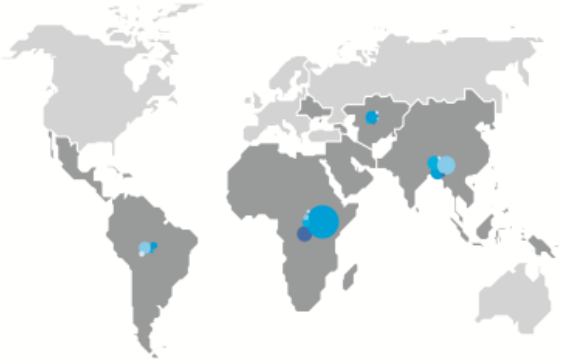
New HIV infections in low- and middle-income countries (millions)



AIDS-related deaths in low- and middle-income countries (millions)



New HIV infections in different population groups, low- and middle-income countries, 2030



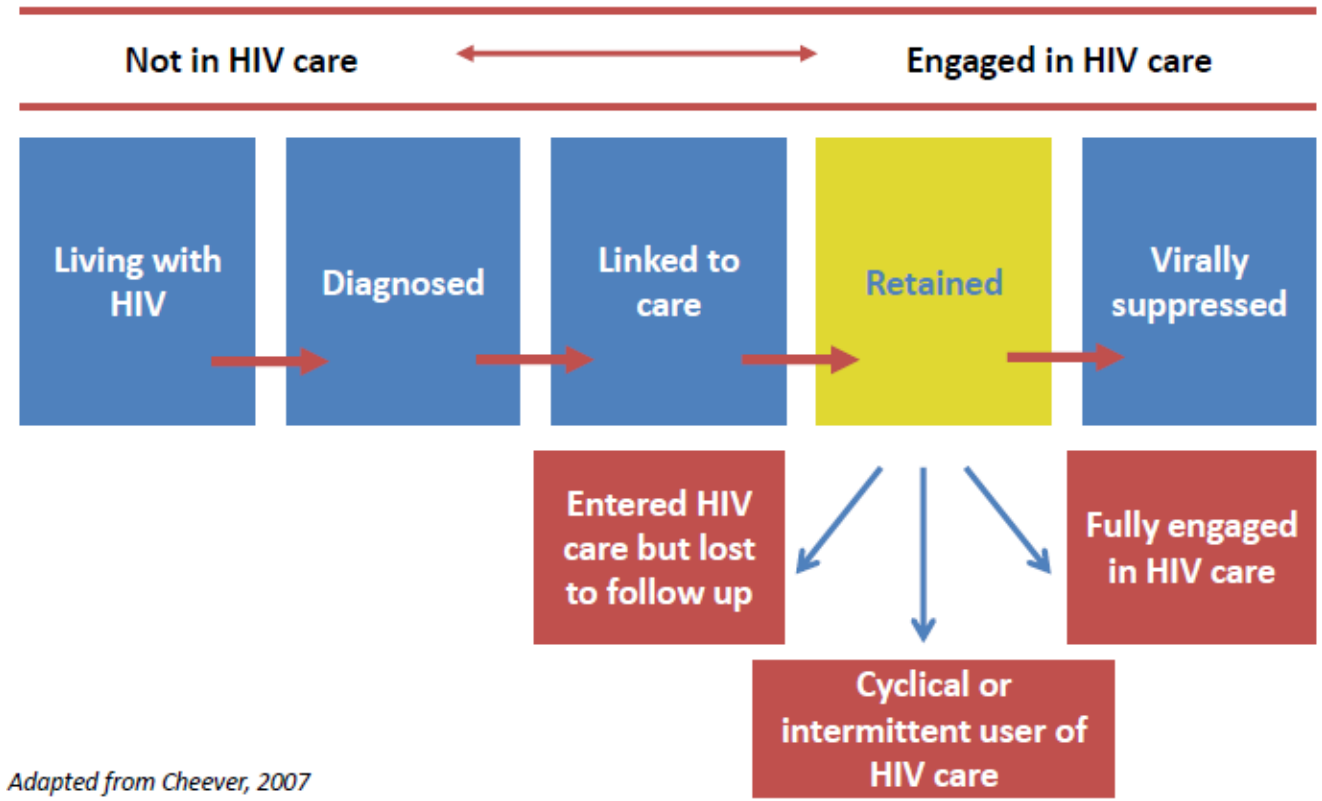
Children
Heterosexual (including young women, excluding sex work)
Female sex workers and their clients
Men who have sex with men
People who inject drugs

Rapid scale-up
of essential HIV prevention and treatment approaches will enable the response to outpace the epidemic.

2030

http://www.unaids.org/en/resources/documents/2014/FastTrackslidesPPT

Cascade of care/HIV Care continuum

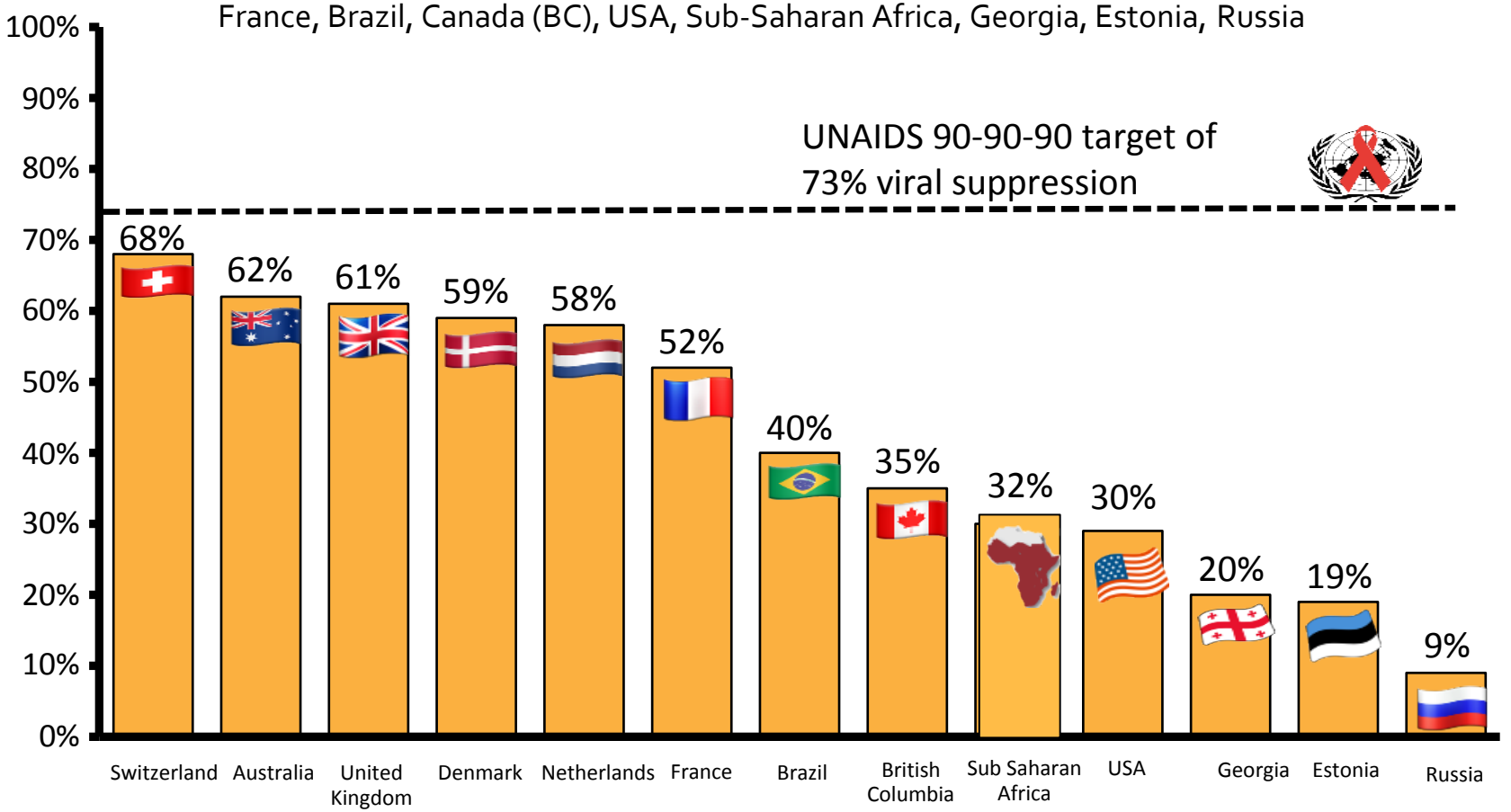


Adapted from Cheever, 2007

Apea V and Nixon E. BHIVA/BASHH 2014. Oral presentation

HIV treatment targets for 2020 with global 2013 estimates

Global HIV treatment cascades from 12 countries/regions: Switzerland, Australia, UK, Denmark, Netherlands, France, Brazil, Canada (BC), USA, Sub-Saharan Africa, Georgia, Estonia, Russia



- **No country or region analysed so far met the UNAIDS 90-90-90 coverage target of 73% of HIV positive people achieving undetectable HIV RNA**

Levi J et al. IAS 2015. Vancouver, Canada. Oral # MOAD0102

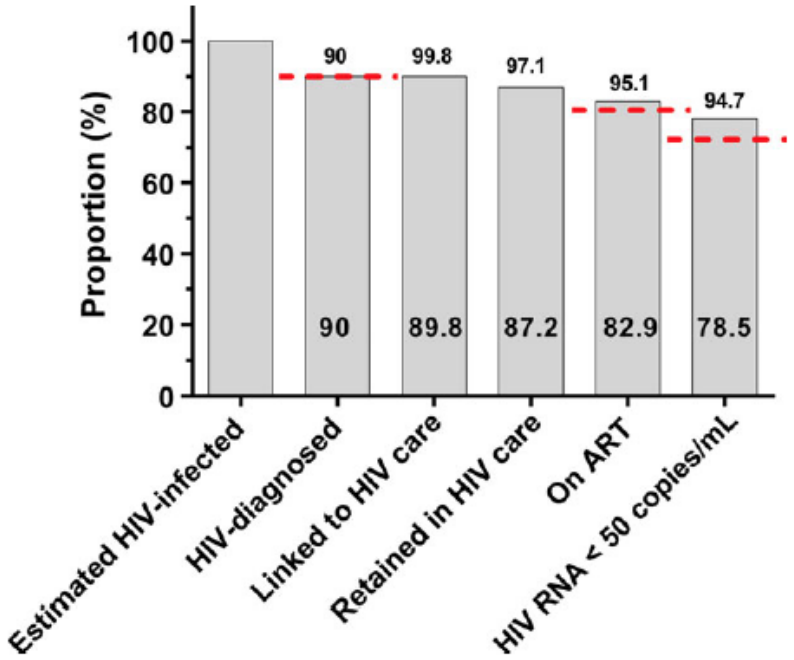
Targets for ending the AIDS epidemic

DOI: 10.1111/hiv.12431
HIV Medicine (2016)

SHORT COMMUNICATION

Sweden, the first country to achieve the Joint United Nations Programme on HIV/AIDS (UNAIDS)/World Health Organization (WHO) 90–90–90 continuum of HIV care targets

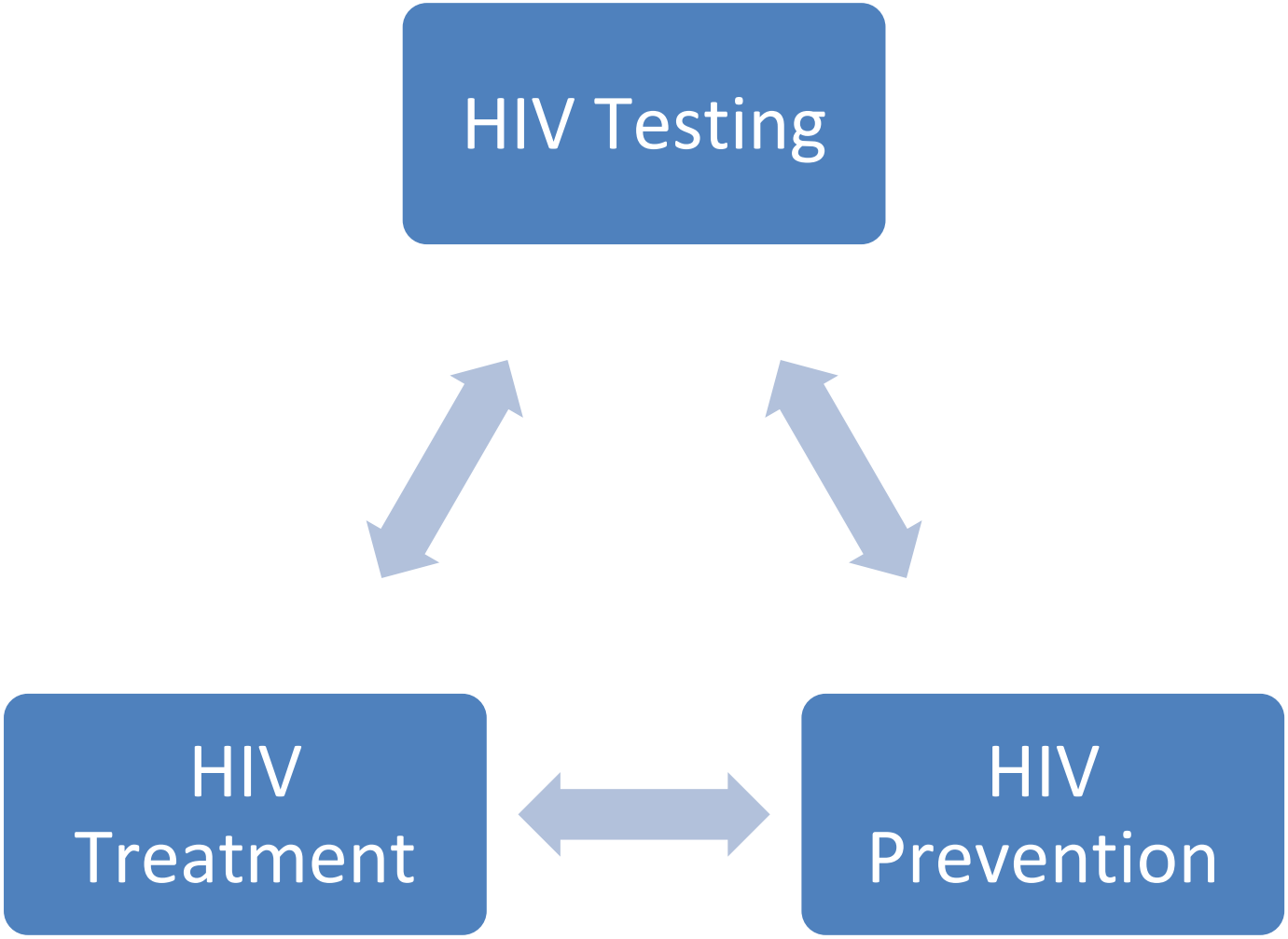
M Gisslén,[1] V Svedhem,[2] L Lindborg,[3] L Flamholc,[4] H Norrgren,[5] S Wendahl,[6] M Axelsson[7] and A Sönnerborg[2,8]



- Swedish InfCare HIV Cohort Study
- **6946** PLWHIV in Sweden 31st Dec 2015
- **Estimation that 10%** of people living with HIV remain undiagnosed
- 79% HIV suppression (>73% UNAIDS objetive for 2020)

Gisslén M et al. HIV Med 2016 August 18

Targets for ending the AIDS epidemic



HIV Testing

The optimal frequency of testing for those at ongoing risk is unknown due to lack of data

- Yearly testing though seems reasonable unless specific aspects of risk behaviour warrant more frequent testing (e.g. every 3–4 months)

Frequency of HIV testing should be based partly on the level of patient risk

A dialogue between the provider and the patient is essential

Universal opt-out testing is recommended for all sexually active individuals that present for medical care

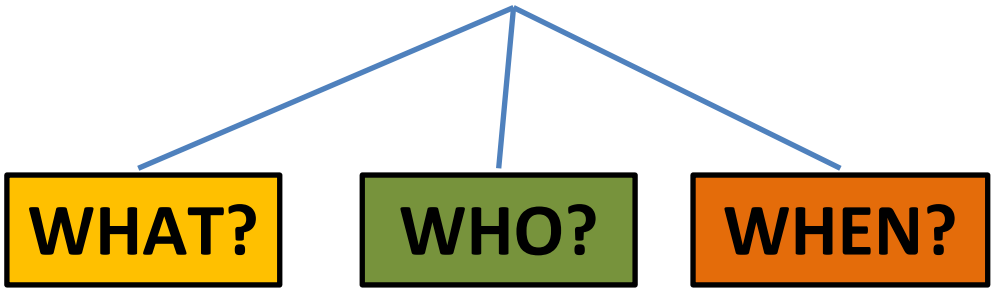
- All individuals who seek care in STI/genito-urinary/ dermato-venereology clinics should be offered an HIV test as part of the initial screening for STI
- Any pregnant woman, regardless of risk factors
- Indicator condition-guided (lymphoma, CIN, HZV, HEP…)
- People who voluntarily seek testing, especially if they have never been tested before

Gökengin D et al. Int J STD AIDS. 2014;25(10):695–704

Targets for ending the AIDS epidemic

- HIV testing
- **HIV prevention**
- **HIV treatment**

What Do Advances in HIV Treatment Mean in the Context of Ending AIDS as a Public Health Threat by 2030?

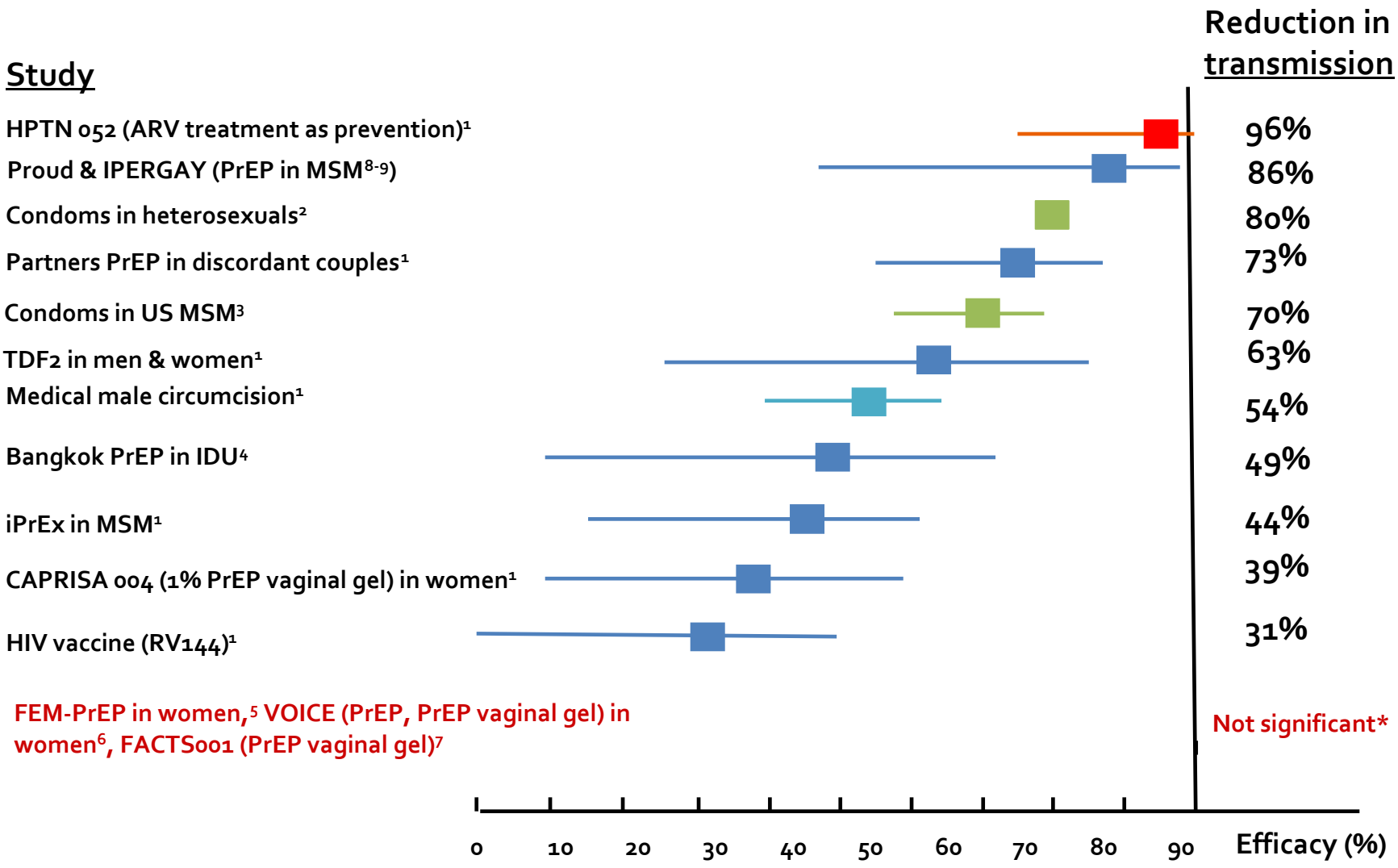


HIV Prevention

- Location and population (tailored to national circumstances)
- Key populations (MSM, transgender, prisons... but also young people)
- Women (especially young & adolescents in sub-Saharan Africa): more data on women in clinical trials

  - Comprehensive prevention (education on sexual and reproductive health, male circumcision, condoms, ARV-microbicides...)
  - TasP/"test and treat"
  - PrEP
  - PEP
  - Preventive vaccines

Relative efficacy and prevention strategies



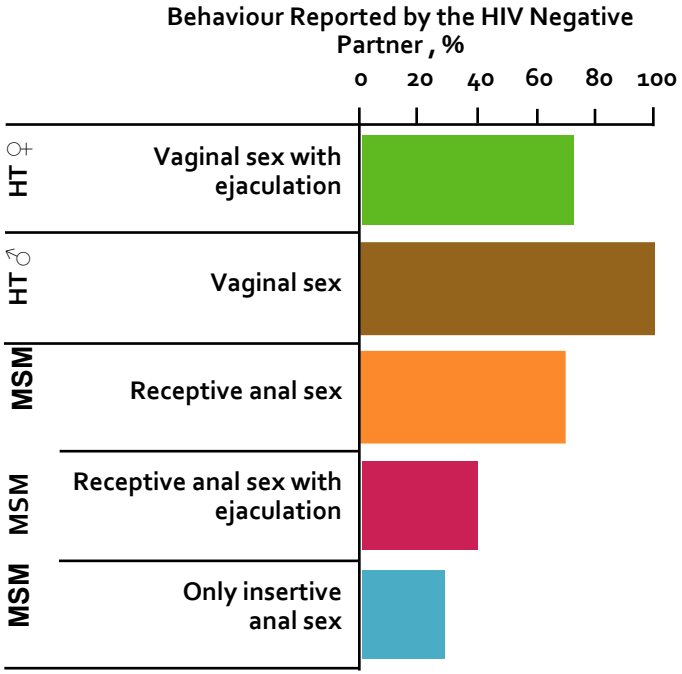
*__FEM-PrEP__: HR 0.94 __VOICE__: Oral PrEP: HR [1.49, 1.04], PrEP vaginal gel: HR 0.85 __HIV vaccine__: 31% reduction in transmission

1. Adapted from Karim SS and Karim QA. Lancet 2011;378:e23–25; 2. Weller S and Davis K. Cochrane Database Syst Rev 2002:CD003255; 3. Smith DK et al. JAIDS 2015;68:337–344; 4. Martin M et al. AIDS 2015;29:819–24; 5. van Damme L et al. NEJM 2012;367:411–422; 6. Marrazzo JM et al. CROI 2013. Atlanta, GA. #26LB; 7. Rees H et al. CROI 2015. Seattle, WA. #26LB; 8. McCormack S Lancet 2016;387:53-60; 9. Molina JM N Engl J Med 2015;373:2237-46

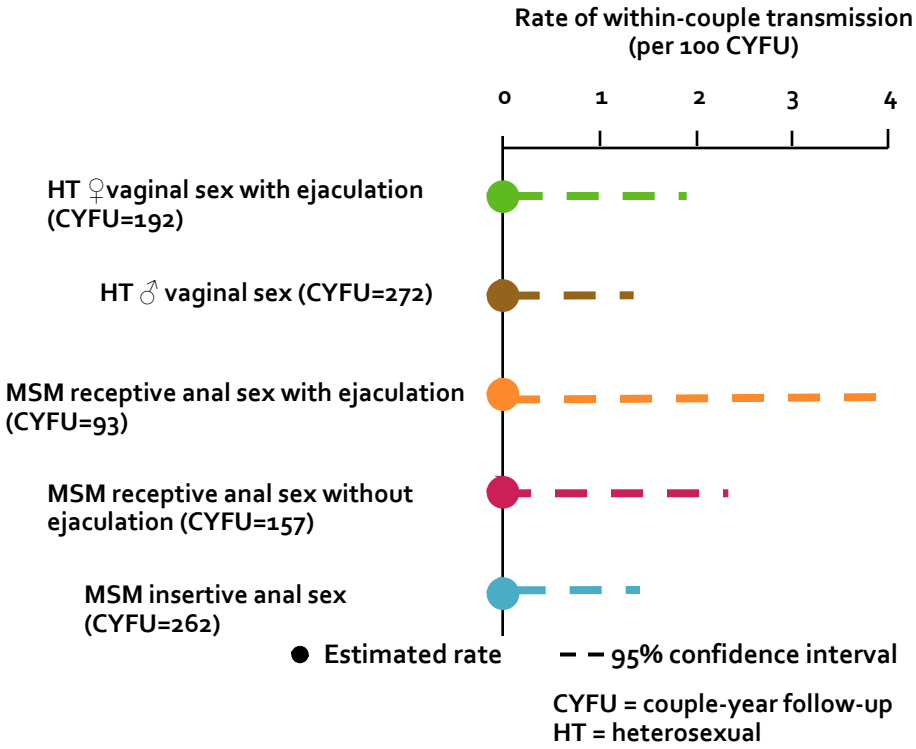
Condomless sex and rate of HIV transmission-Partner

Multicentre, European, observational study in HIV sero-different 767 couples, heterosexual (n=445) and MSM (n=282), HIV-positive with latest HIV VL <200 copies (within max past 12 months)

HIV-negative partners reporting penetrative sex acts



Rate of linked HIV transmission by behaviour of HIV-negative partner



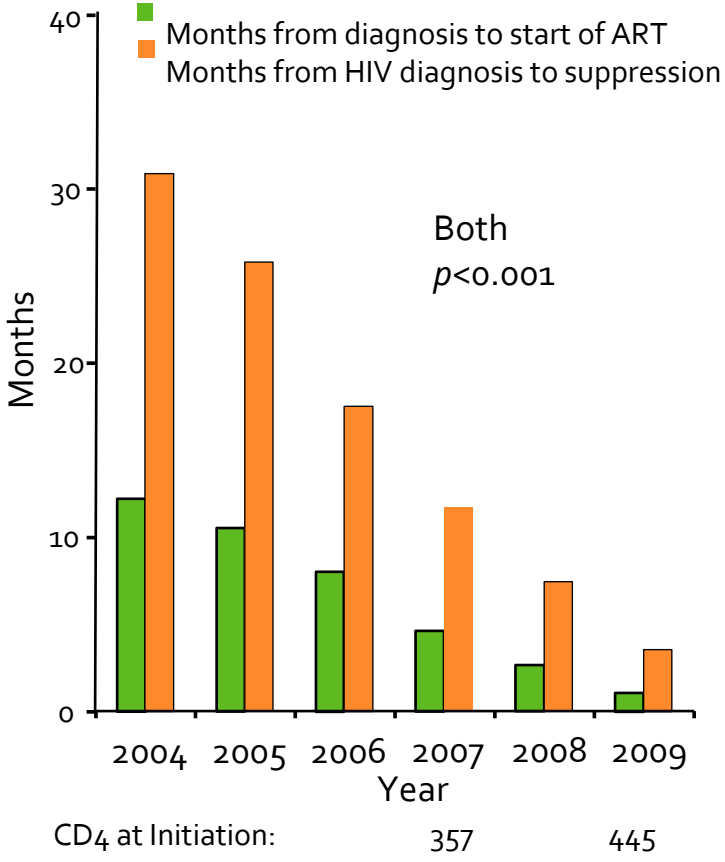
- Suppressive ART resulted in zero linked transmissions to HIV-negative partners with condomless sex, despite a substantial number of sex acts. Unlinked transmissions did occur
- Additional follow-up in MSM is forthcoming in the PARTNER2 study

Rodger AJ et al. JAMA 2016; 316:171-81

Early Diagnosis & Treatment of HIV S.Francisco

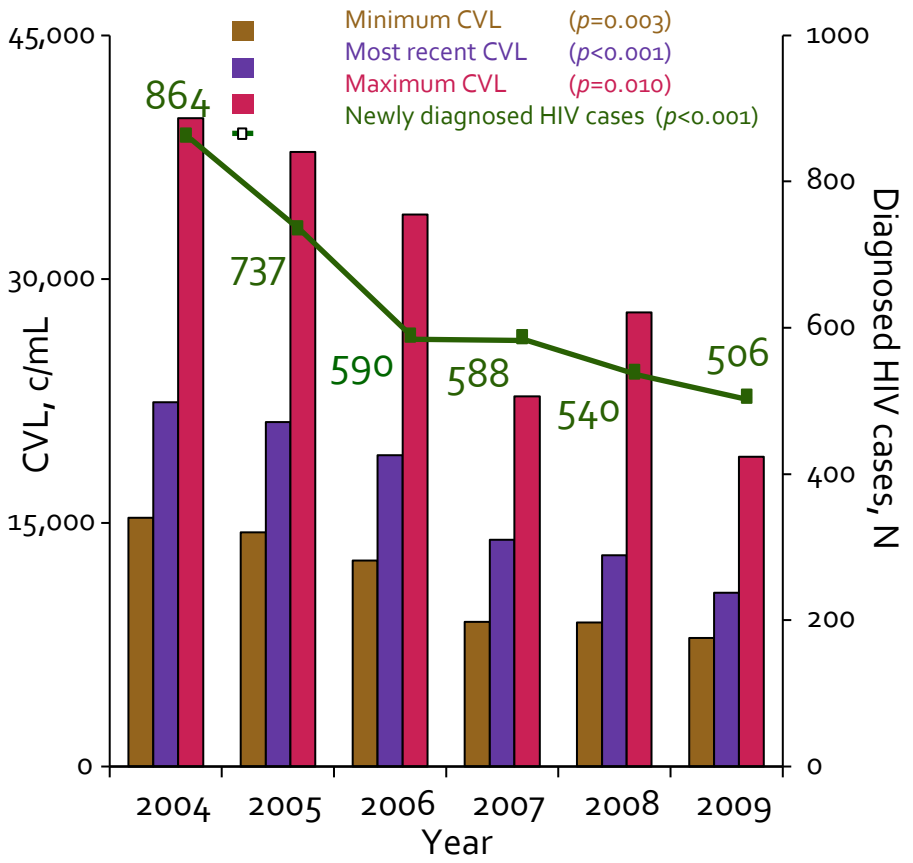
Earlier HIV diagnosis & initiation of therapy associated with lower community viral load (CVL) and reduced transmission

Mean months from diagnosis to ART initiation and to virological suppression



Time from ART initiation to virological suppression decreased from a mean of 18.8 months in 2004 to a mean of 2.8 months in 2009 (*P*<0.001)

Minimum, most recent, maximum CVL and newly diagnosed and reported HIV cases



Irrespective of CVL measure, the number of diagnosed HIV cases decreased over time (*P*<0.001)

Das M et al. CROI 2011. Boston, MA. #1022

Early Treatment of HIV

Study	Population	Treatment	Primary Clinical Outcome
HTPN 052[1]	1763 HIV serodiscordant couples	- Early ART - Deferred ART (CD4<250 or AIDS diagnosis)	41% RRR in AIDS-related clinical event or death HR 0.59 (95%CI 0.40-0.88)
TEMPRANO[2]	2056 patients	- Early ART +/- IPT - Deferred ART +/- IPT (CD4<350)	44% RRR in death or severe HIV-related illness HR 0.56 (95%CI 0.41-0.76)
INSIGHT START[3]	4685 patients	- Early ART - Deferred ART (CD4<350)	57% RRR in serious AIDS and non-AIDS related event HR 0.43 (95%CI 0.30-0.62)

HTPN 052 DSMB recommended study be stopped early after showing a 96% reduction of HIV transmission
START DSMB also recommended early termination

1. Cohen MS et al. NEJM 2011;365:493–505; 2. Denel C et al. NEJM 2015; 373:808-22. ; 3. Lundgren JD et al. NEJM 2015; 373:795-807

Early Treatment of HIV

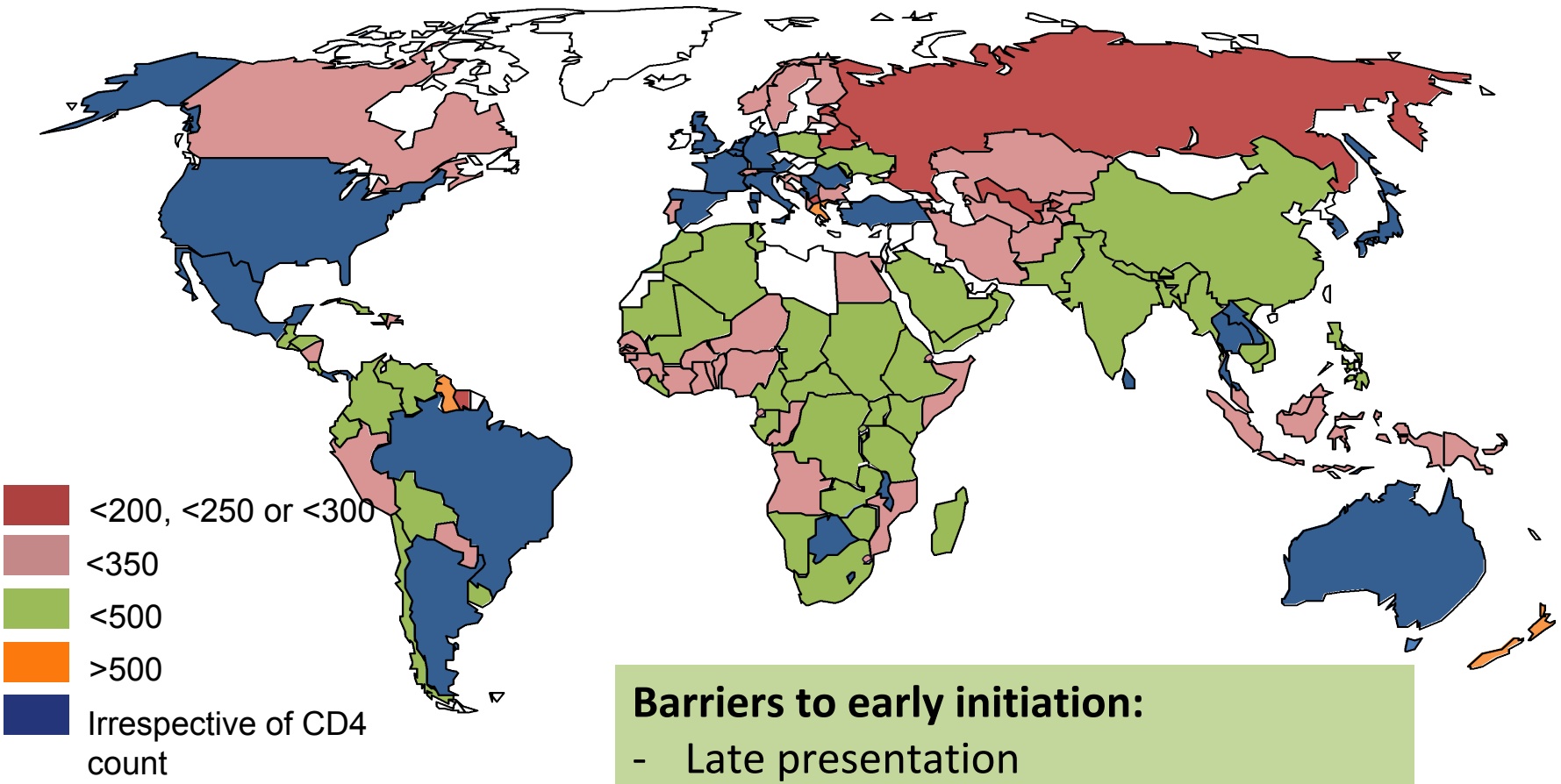
"Combination antiretroviral therapy (ART) should be recommended for all HIV-positive persons regardless of CD_4+ count."

- Individual benefit for the patient
- Population benefit reducing risk of transmission

- **Guidelines recommendations** (DHHS, EACS, BHIVA, IAS-USA, GeSIDA, WHO): treat **ALL** patients **at any CD4+ cell count**

Barriers to Early Treatment of HIV

2015 WHO Recommendation : Irrespective of CD4 count



Barriers to early initiation:

- Late presentation
- Access to testing
- Access to treatment
- Patient acceptance of treatment

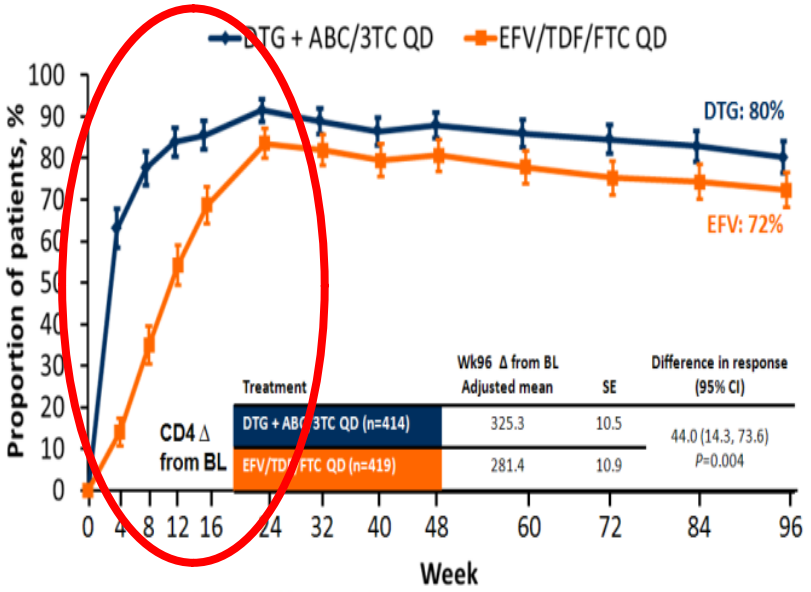
www.hivpolicywatch.org

HIV Treatment: What do we have?

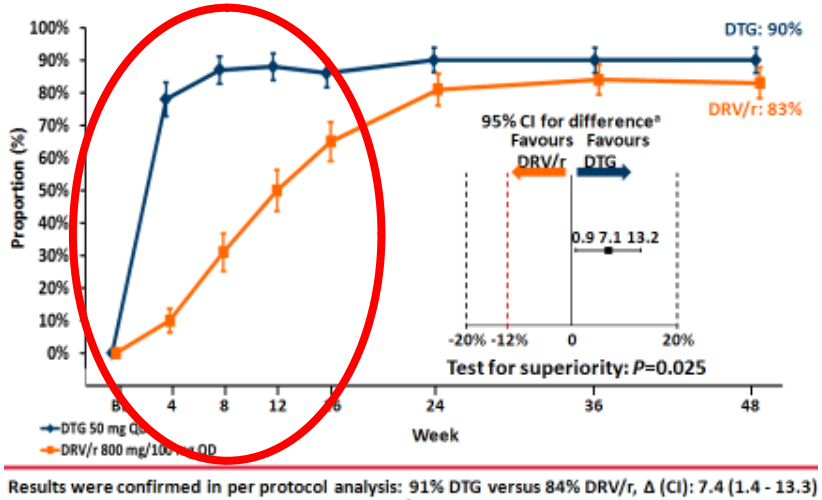
- New ART with better tolerability, potency, barrier to resistance and durability
- New strategies/combinations for naïve & experienced patients
- ARV that rapidly decrease viral load

INSTIs: Rapid decay in Viral Load

Single[1]



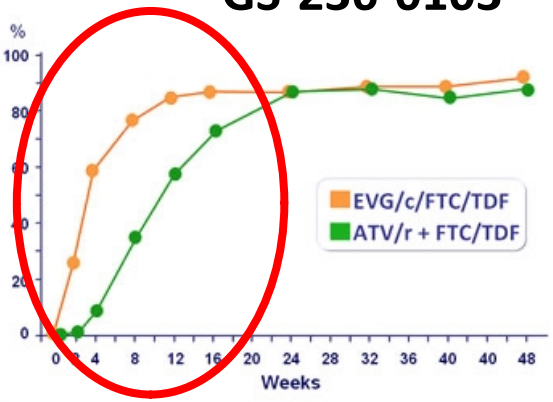
Flamingo[2]



Results were confirmed in per protocol analysis: 91% DTG versus 84% DRV/r, Δ (CI): 7.4 (1.4 - 13.3)

ARN VIH < 50 c/ml :

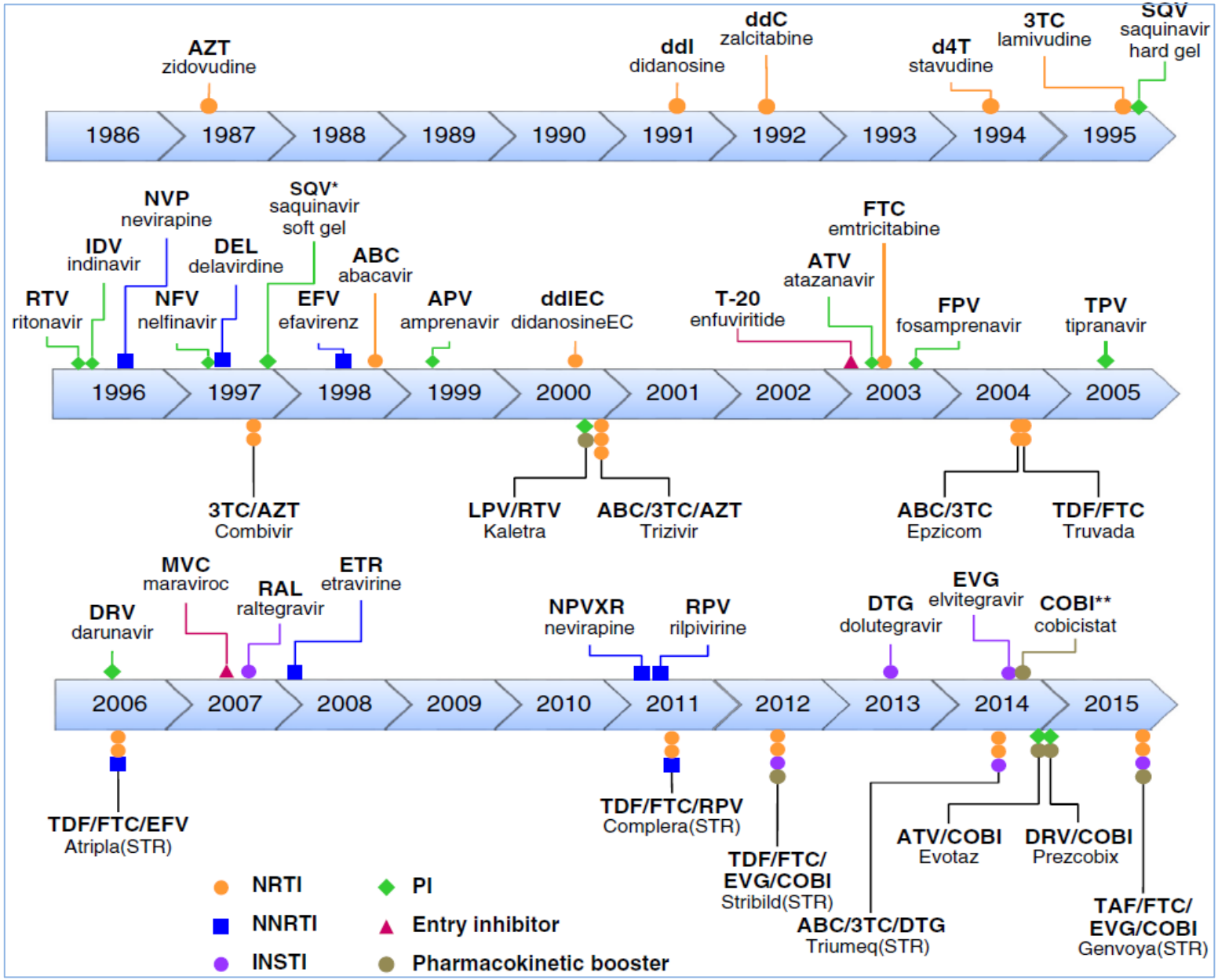
GS-236-0103[3]



Number of patients									
EVCG/c/FTC/TDF	353	353	353	353	353	353	353	353	353
ATV/r + FTC/TDF	355	355	355	355	355	355	355	355	355

1. Walmsley SL et al. NEJM 2013; 369:1807-18;
2. Clotet B et al.Lancet 2014; 383: 2222-31;
3. DeJesus E et al. Lancet 2012; 379: 2429-38

HIV Treatment: drugs and combinations in 3 decades



HIV Treatment: future drugs and combinations

- **NRTI**: TAF (new FDC) (P3); MK-8591 (LA) (P1)
- **NNRTI**: Doravirine (MK-1439) (P3)
- **INSTI**: RAL QD (P3); Bictegravir (GS-9883) (P3)
- **Entry Inhib:** Fostemsavir (BMS-663068) (P3); Combinectin (BMS-986197) (P1)
- **Maturation Inhib**: BMS-955176 (P2b)
- **Antibodies:** Ibalizumab(P3), PRO140 (P2-3), VRC01 (P2)
- **Long acting (LA)**: Cabotegravir LA (P2b); RPV LA (P2)...

TAF: New Fixed Dose Combinations (FDC)

Genvoya® (EGV 150 / cobi 150 / FTC 200 / TAF 10) **STR**

Descovy® (FTC 200 / TAF 25 or 10)

Odefsey® (RPV 25 / FTC 200 / TAF 25) **STR**

DRV 800 / cobi 150 / FTC 200 / TAF 10 **STR**

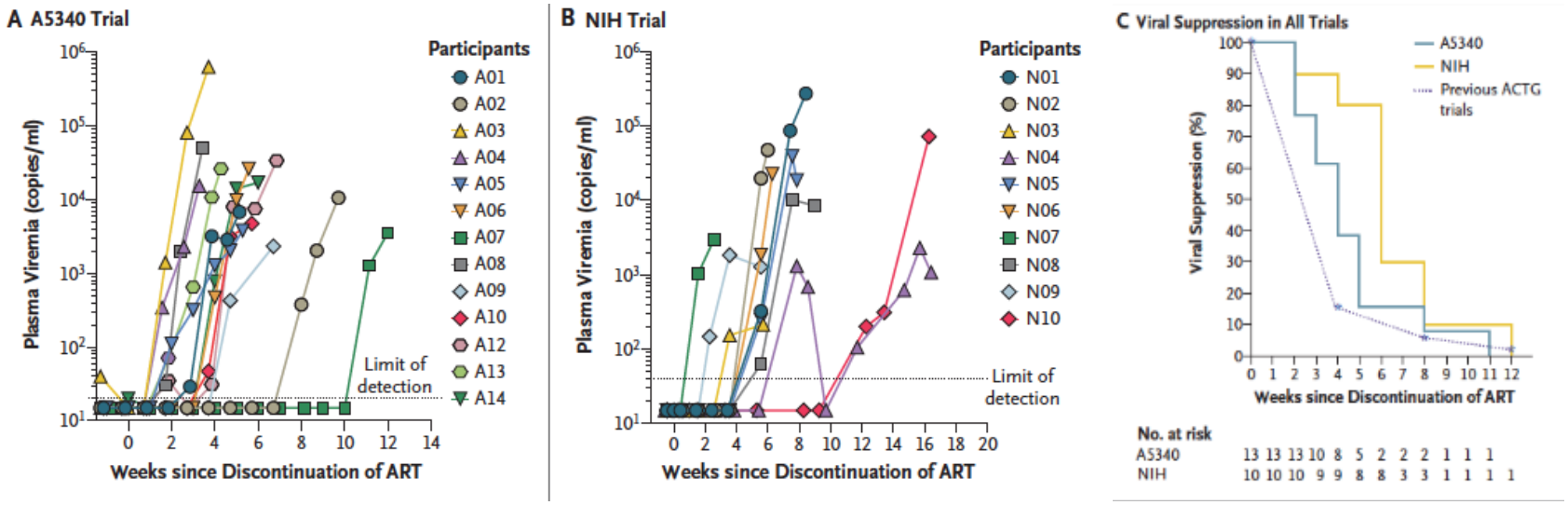
HIV Treatment: future drugs and combinations

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of HIV Antibody VRC01 on Viral Rebound after Treatment Interruption

VRC01 is a broadly neutralizing antibody (bNAbs) against HIV



CONCLUSIONS

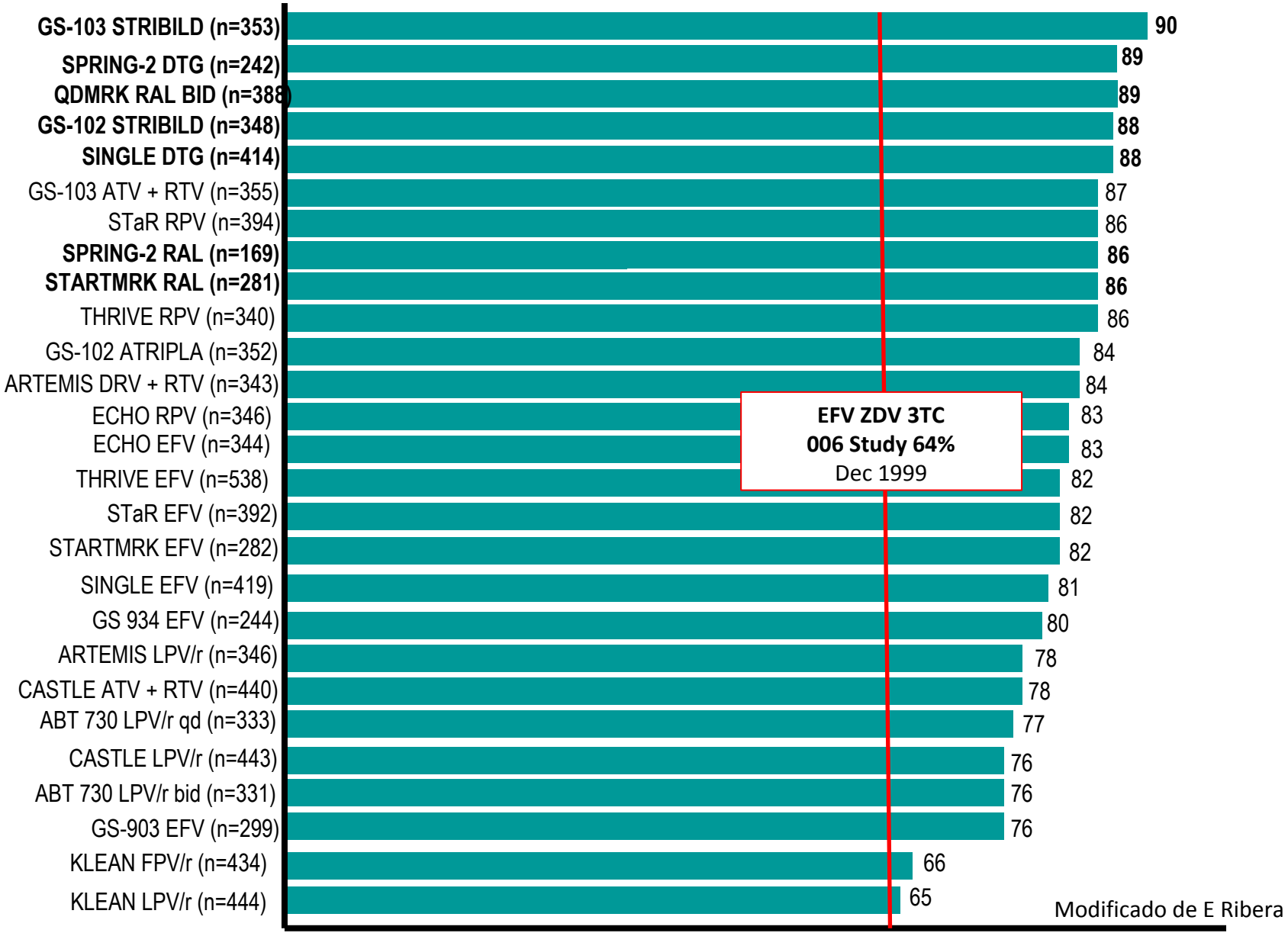
VRC01 slightly delayed plasma viral rebound in the trial participants, as compared with historical controls, but it did not maintain viral suppression by week 8. In the

Bar KJ et al. NEJM online first, November 9 2016

Long Acting Therapies

- MK-8591
- Combinectin (BMS-986197)
- Albuvirtide (fusion inhibitor)
- Tenofovir LA
- Cabotegravir LA
- Rilpivirine LA
- CAB LA + RPV LA (Latte-2, FLAIR, ATLAS)

HIV Treatment: Efficacy in Clinical Trials

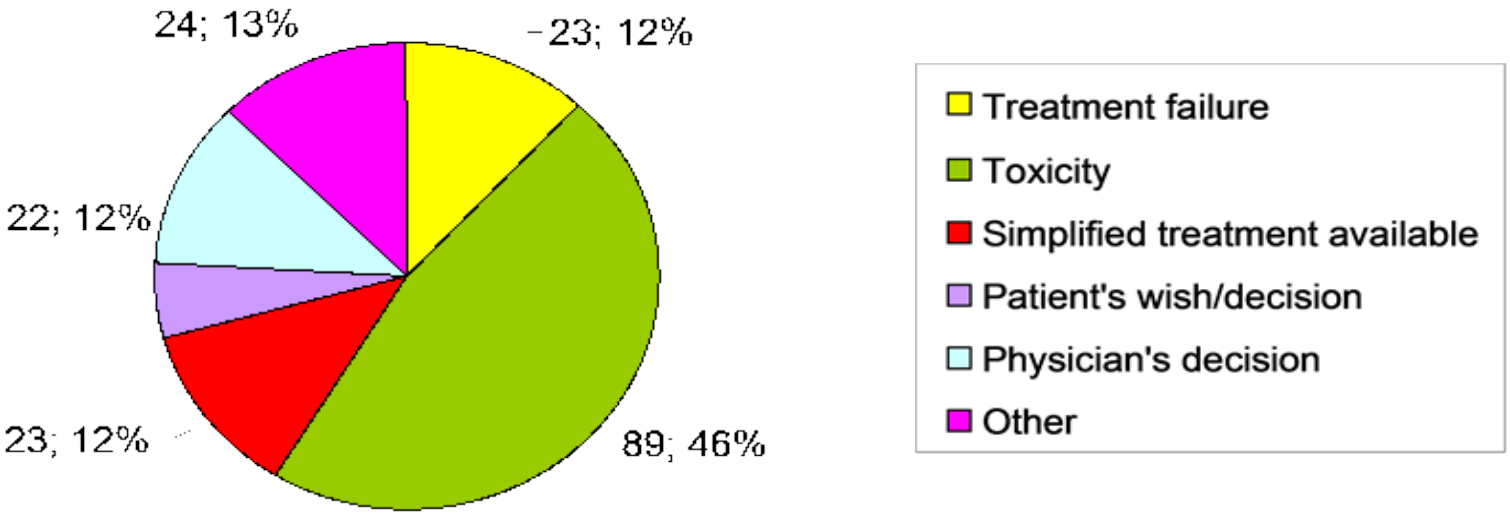


HIV Treatment: Effectiveness in real life

– Limitations to translate this high efficacy into high effectiveness in clinical practice:
  - Adherence
  - Adverse events
  - Drug-drug interactions

} Ageing HIV population!

Reasons for changing ART in the CORIS Cohort:



Jarrin I et al. Antivir Ther 2013; 18: 161-70.

Where can we improve/where are we going?

- **HIV testing**
  - enable more affordable point-of-care diagnosis
    - of HIV diagnosis
    - for HIV follow-up-VL
    - for related diseases
  - Increase testing

Where can we improve/where are we going?

- **HIV prevention**
  - Increase outreach of comprehensive prevention
  - TasP: treating all patients ASAP with better tolerated regimens.
  - PrEP: long-acting formulations, well tolerated and with high genetic barrier
  - PEP: well tolerated, easier (long-acting?)
  - Preventive vaccines

Where can we improve/where are we going?

- **HIV treatment**
  - Better tolerability (short/medium/long-term side effects) & less risk of DDI
  - New ARV from classic and new families
  - Long-acting formulations of ART (single and combinations)
  - Better drug formulations for children
  - New/more affordable second and third line therapies
  - Reducing costs of ART (generics?)
  - Therapeutic vaccines
  - Curative interventions

- Engaging people living with, at risk of and affected by HIV in the AIDS response

Advances in HIV Treatment to End AIDS Epidemic?

- Starting ART sooner
- Starting ART to all patients, regardless of CD4+
- Using ARV that rapidly decline viral load
- Using better tolerated and simpler ART regimens in order to increase retention to care, ART uptake and therefore viral suppression
  - classic and new targets
  - classic and new formulations (long acting)
  - for naïve and experienced patients
- Using ART in HIV-negative subjects wisely
  - PrEP
  - PEP

THANK YOU

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