

Demystifying Medicine 2019

Ending the HIV/AIDS Pandemic: Follow the Science

Anthony S. Fauci, M.D.
Director
National Institute of Allergy and
Infectious Diseases
National Institutes of Health
January 8, 2019




1

The Global HIV Pandemic



- In 2017:
 - 36.9 million people living with HIV
 - 1.8 million new HIV infections
 - 940,000 deaths from AIDS-related illnesses
- Since start of the pandemic:
 - 77.3 million infected with HIV
 - 35.4 million deaths from AIDS-related illnesses

AS Fauci/NIAID

2

HIV/AIDS in the United States

- 1.1 M people living with HIV, of whom 15% are unaware of their infection
- 703,413 people with stage 3 HIV infection (AIDS) have died
- 38,281 newly diagnosed HIV infections in 2017
- MSM, Blacks/African Americans bear the greatest burden of HIV
- Youths 13-24 years old accounted for 21% of new HIV diagnoses in 2017



Source: CDC, 11/2018

AS Fauci/NIAID

3

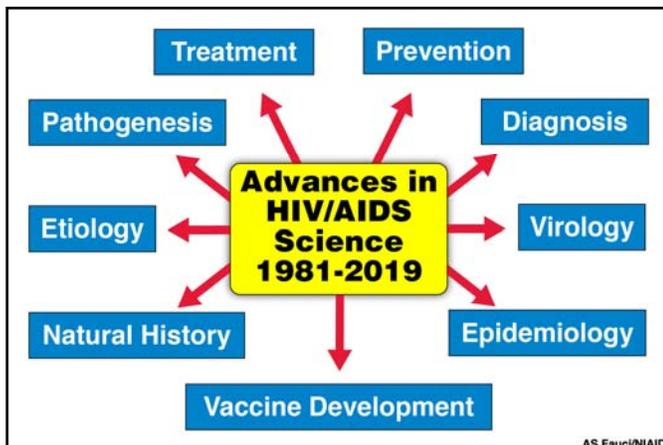


Ending the HIV-AIDS Pandemic – Follow the Science

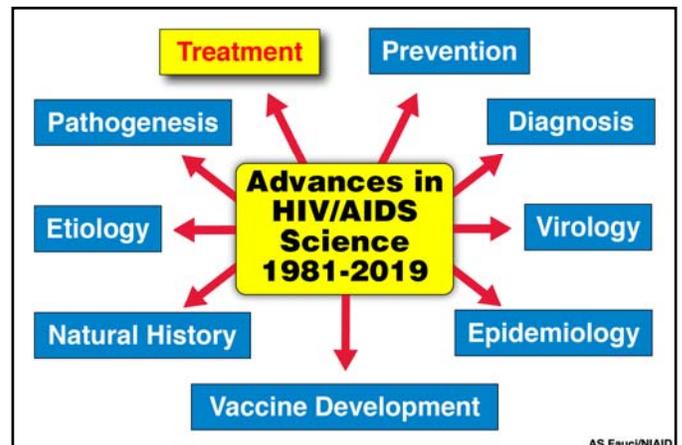
AS Fauci & HD Marston

AS Fauci/NIAID

4



5



6

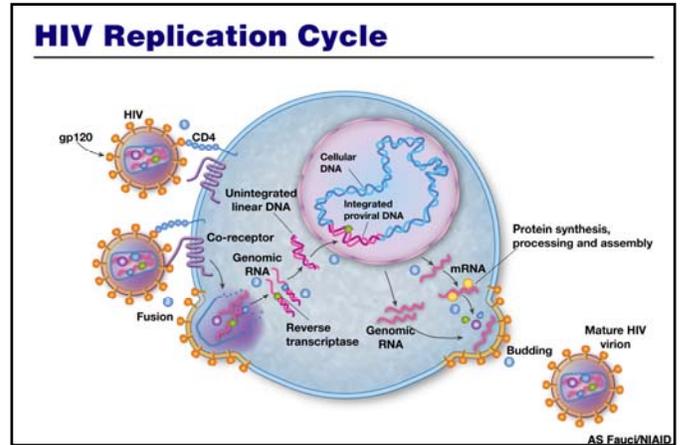
Rounds at NIH Clinical Center, Early 1980s – AIDS Patient



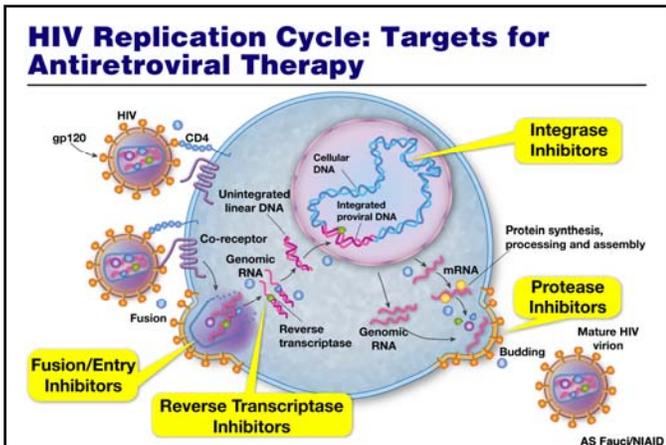
■ Median survival of AIDS patients: ~8-15 months

AS Fauci/NIAID

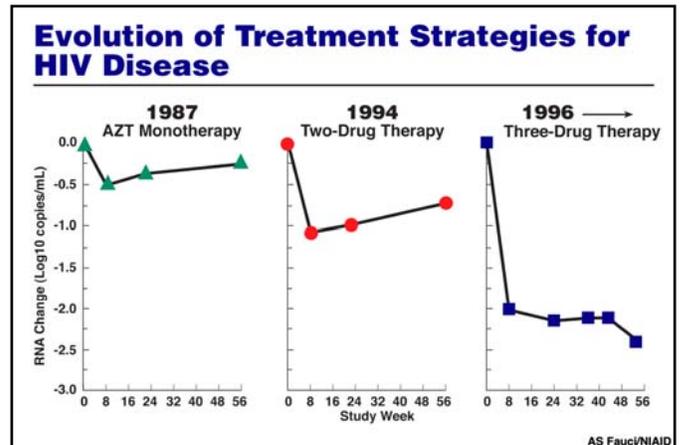
7



8



9



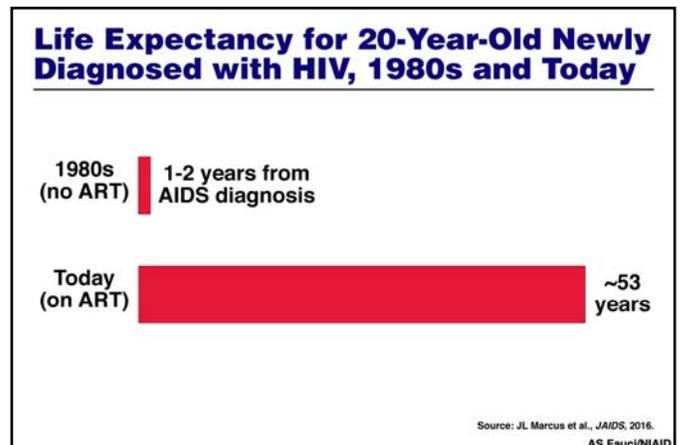
10

FDA-Approved Antiretroviral Drugs

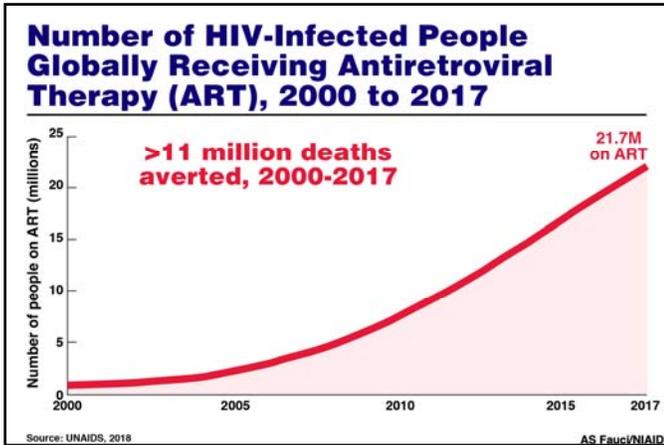
NRTIs ■ 7 multi-drug combinations ■ Abacavir ■ Didanosine ■ Emtricitabine ■ Lamivudine ■ Stavudine ■ Tenofovir (TDF, TAF) ■ Zidovudine	Pharmacokinetic Enhancers ■ Cobicistat ■ Ritonavir	Multi-Class Combinations ■ Atripla ■ Biktarvy ■ Complera ■ Delstrigo ■ Genvoya ■ Juluca ■ Odefsey ■ Stribild ■ Symfi ■ Symfi Lo ■ Symtuza ■ Triumeq
NNRTIs ■ Delavirdine ■ Doravirine ■ Efavirenz ■ Etravirine ■ Nevirapine ■ Rilpivirine	PIs ■ Atazanavir ■ Darunavir ■ Fosamprenavir ■ Indinavir ■ Lopinavir/Ritonavir ■ Nelfinavir ■ Ritonavir ■ Saquinavir ■ Tipranavir	Fusion Inhibitor ■ Enfuvirtide
Integrase Inhibitors ■ Bictegravir ■ Dolutegravir ■ Elvitegravir ■ Raltegravir	Entry Inhibitor ■ Maraviroc	
Post-Attachment Inhibitor ■ Ibalizumab		

AS Fauci/NIAID Source: AIDSinfo.nih.gov, Sept. 2018

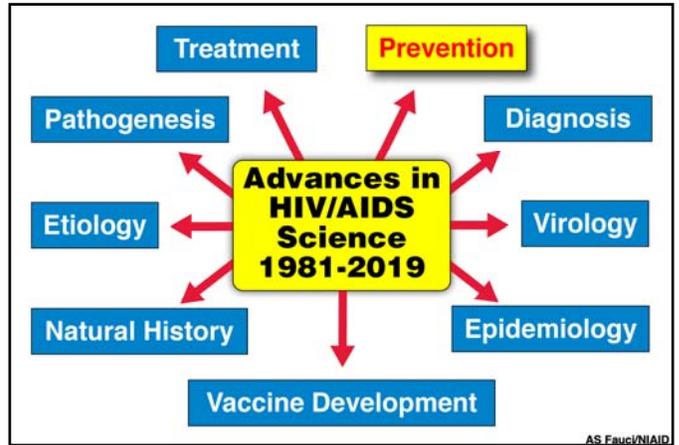
11



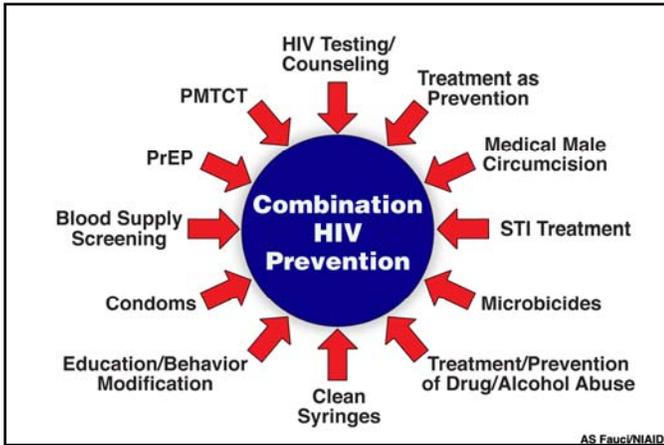
12



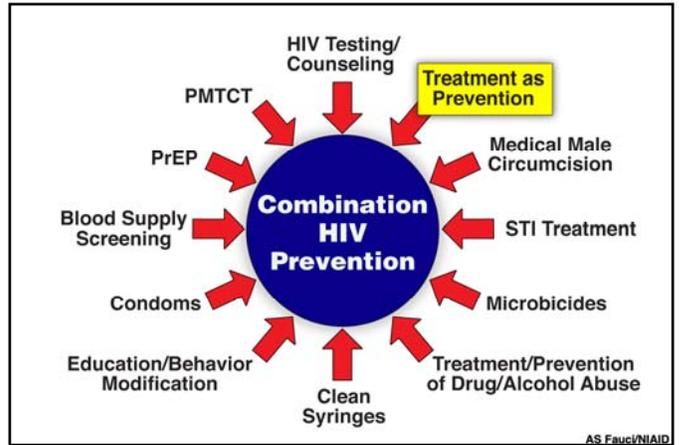
13



14



15



16

The Pivotal HPTN 052 Study

The New England Journal of Medicine

Vol. 364 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 New England Journal of Medicine

Vol. 376 September 1, 2016 Number 9

Antiretroviral Therapy for the Prevention of HIV-1 Transmission

HPTN 052 Study Team

- After 5+ years of follow-up, protective effect of early ART was sustained (93% lower risk)
- No linked infections when HIV was stably suppressed by ART (i.e. undetectable viral load) in HIV+ partner

AS Fauci/NIAID

17

- Between the PARTNER and Opposites Attract studies, nearly 35,000 acts of condomless anal intercourse were reported in gay male couples when the HIV-positive partner had an undetectable viral load and the HIV-negative partner was not taking PrEP
- Zero linked transmissions

Source: BR Bavinton et al., Lancet HIV, July 16, 2016. AS Fauci/NIAID

18

PARTNER 2 Study – No HIV Transmissions When HIV+ Partner Had Undetectable Viral Load



- 783 HIV-serodiscordant MSM couples in 14 European countries
- 76,991 condomless sex acts (incl. 70,743 acts of anal intercourse)
- No linked HIV transmissions with HIV+ partner on suppressive ART in 1,596 couple-years of followup

AS Fauci/NIAID

19



July 2018

Viral Suppression for HIV Treatment Success and Prevention of Sexual Transmission of HIV

The science related to the use of ART as an additional prevention tool is clear: there is no evidence that individuals who have successfully achieved and maintained viral suppression through ART transmit the virus sexually to their HIV-negative partner(s). The preventive benefits of ART should be appropriately emphasized in HIV treatment and prevention programmes.

AS Fauci/NIAID

20

U = U

AS Fauci/NIAID

21

Progress in San Francisco

Abstract 93  Boston, Massachusetts March 4-7, 2018

The RAPID ART Program Initiative for HIV Diagnoses (RAPID) in San Francisco

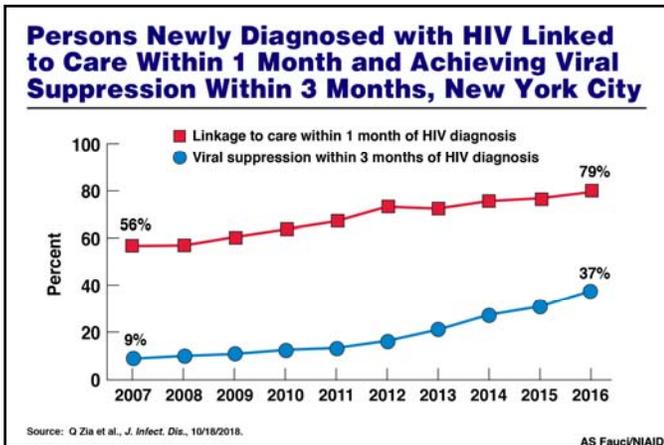
O Bacon et al.

From 2013 to 2016:

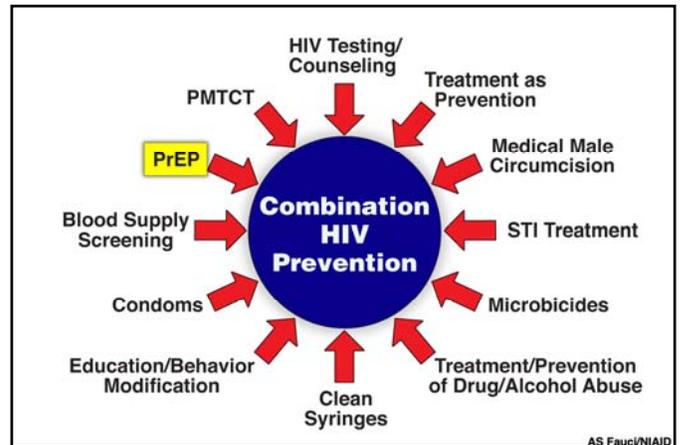
- Median time from diagnosis to VL <200 c/mL -- ↓ 54%, from 134 days to 61 days
- Median time from first care visit to ART -- ↓ 96%, from 27 days to 1 day

AS Fauci/NIAID

22



23



24

HIV Pre-Exposure Prophylaxis (PrEP)



One pill per day

↓

>95% effective in preventing HIV acquisition

AS Fauci/NIAID

25



HEALTH, LIFE & HIV

August 22, 2017

5,000 Cumulative Years of PrEP Use and No HIV Infections



- 4,991 started PrEP, 7/2012 through 2/2017 in Kaiser Permanente Northern California (KPNC) healthcare system
- No HIV infections during 5,104 person-years of PrEP use

AS Fauci/NIAID Source: JL Marcus et al. Clin Infect Dis. July 29, 2017

26



U.S. Preventive Services
TASK FORCE

November 20, 2018

Draft Recommendation Statement

Prevention of Human Immunodeficiency Virus (HIV) Infection: Pre-Exposure Prophylaxis

Draft: Recommendation Summary

Population	Recommendation	Grade
Persons at high risk of HIV acquisition	The USPSTF recommends that clinicians offer pre-exposure prophylaxis (PrEP) with effective antiretroviral therapy to persons who are at high risk of HIV acquisition.	A

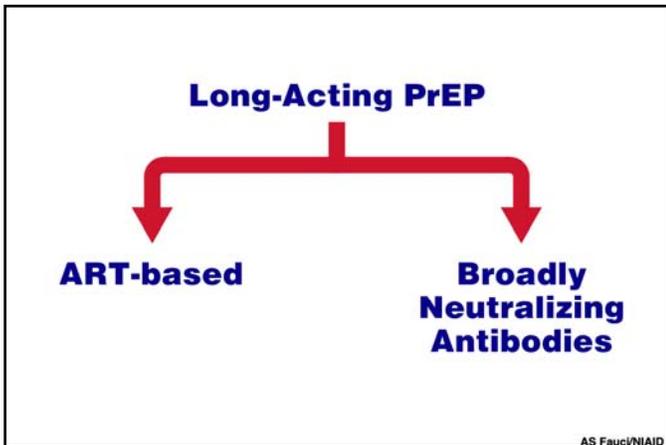
AS Fauci/NIAID

27

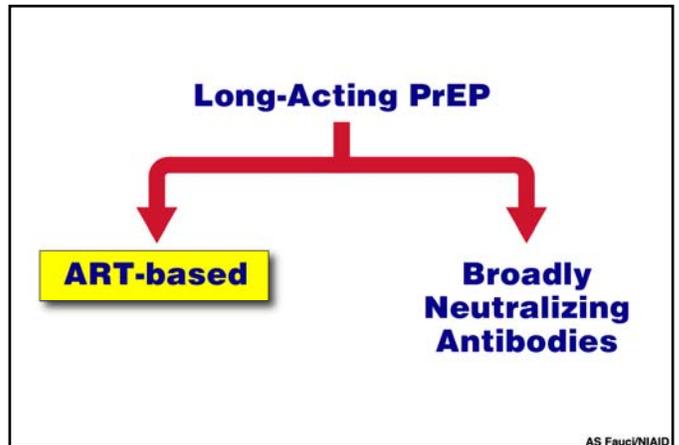
Long-Acting PrEP

AS Fauci/NIAID

28



29



30

Long-acting Antiretrovirals for Prevention



RCT of long-acting cabotegravir vs. TDF/FTC for PrEP

4500 MSM and TGW in multiple countries

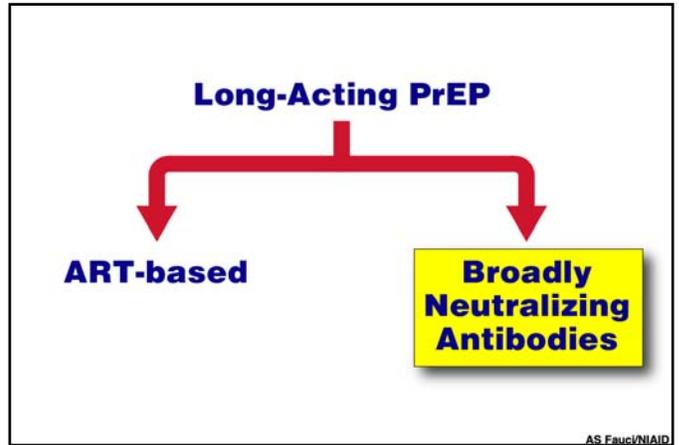


RCT of long-acting cabotegravir vs. TDF/FTC for PrEP

3200 women in Sub-Saharan Africa

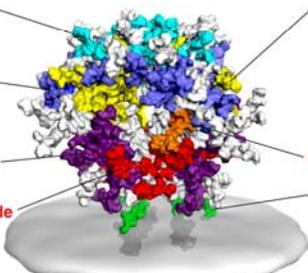
AS Fauci/NIAID

31



32

Broadly Neutralizing Antibodies Binding to Neutralization Epitopes on HIV Trimer



V1V2 glycan

- PGD
- PGDM1400
- PGT145
- VRC38.01
- CAP256-VRC26

V3 glycan

- 2G12
- TD-1074
- PGT121
- PGT128
- PGT135

Subunit interface

- 35022
- BANC195

Fusion peptide

- PGT151
- VRC34

CD4 binding site

- 3BNC117
- BANC131
- b12
- CH103
- HJ16
- IO3A
- VRC01
- VRC07-523
- VRC13.01
- VRC16.01
- NS

Silent face center

- VRC-PG05

Membrane Proximal External Region

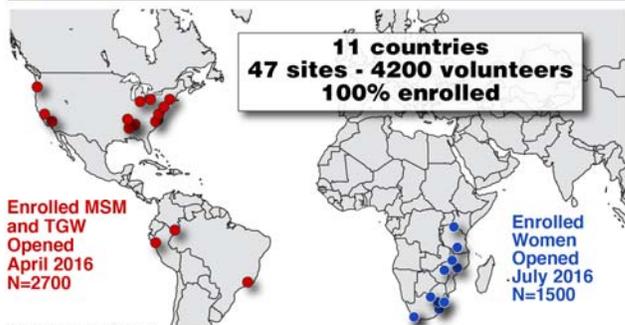
- 2F5
- 10E8
- 4E10
- DF511
- Z13e1

Image by J Stuckey, GY Chuang, VRC, NIAID, NIH. Adapted from: PD Kwong, JR Mascola, et al. *Immunity* 2018, YD Kwon, PD Kwong, et al. *Cell Reports* 2018, J Liu, S Subramaniam, et al. *Nature* 2008.

AS Fauci/NIAID

33

Antibody-Mediated Prevention (AMP) VRC01 mAb Phase 2b Studies in High-Risk Men and Women



11 countries
47 sites - 4200 volunteers
100% enrolled

Enrolled MSM and TGW
Opened April 2016
N=2700

Enrolled Women
Opened July 2016
N=1500

Courtesy Julie Ledgerwood, DO

AS Fauci/NIAID

34

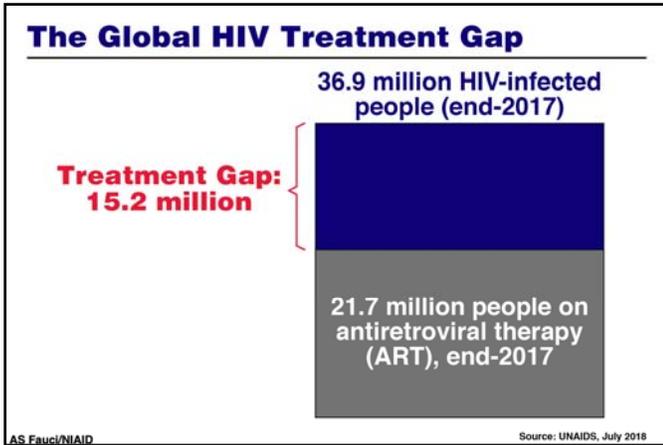
The Implementation Gap in Addressing the HIV/AIDS Pandemic

AS Fauci/NIAID

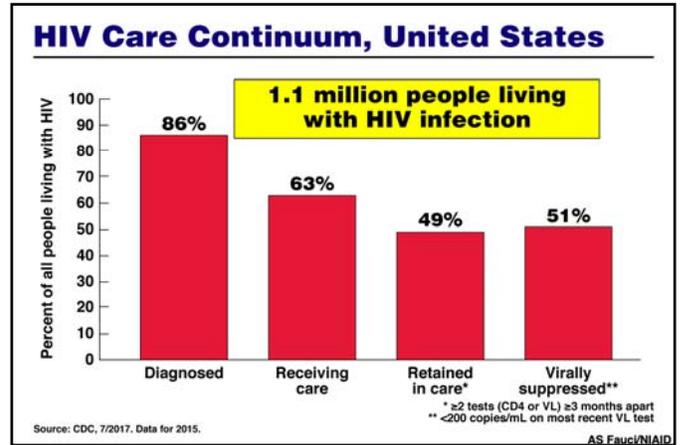
35



36



37



38

HIV Pre-Exposure Prophylaxis (PrEP) is Underutilized

- 1.1 million individuals in United States are at substantial risk for HIV and should be offered PrEP (CDC)
- Estimated number of current U.S. PrEP users: 220,000-225,000 (AVAC PrEPWatch, 8/2018)

The New England Journal of Medicine
VOLUME 379 October 4, 2018 NUMBER 14

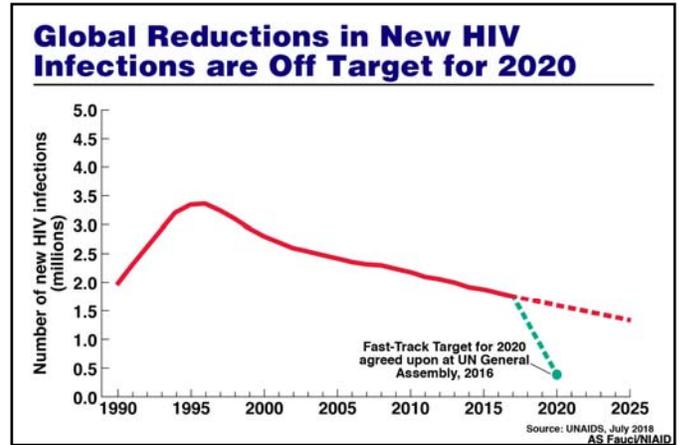
Being PrEPared — Preexposure Prophylaxis and HIV Disparities

RH Goldstein, CG Streed, SR Cahill

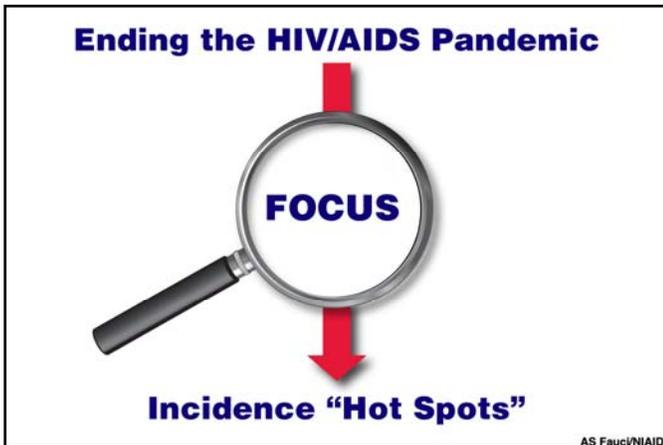
Beyond the cost of the medication, stigma and distrust of the medical system prevent at-risk people of color from obtaining and benefiting from PrEP.

AS Fauci/NIAID

39



40

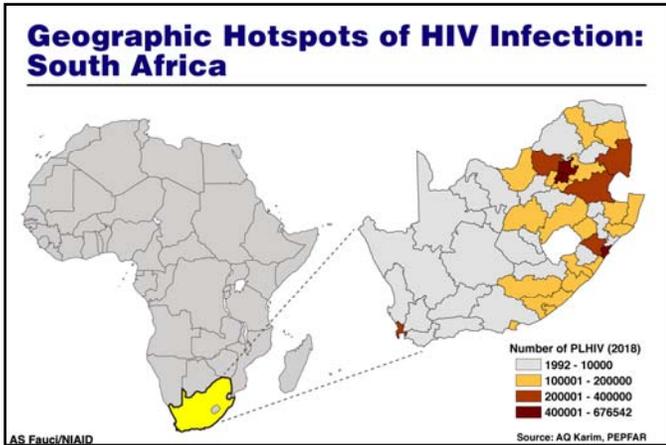


41

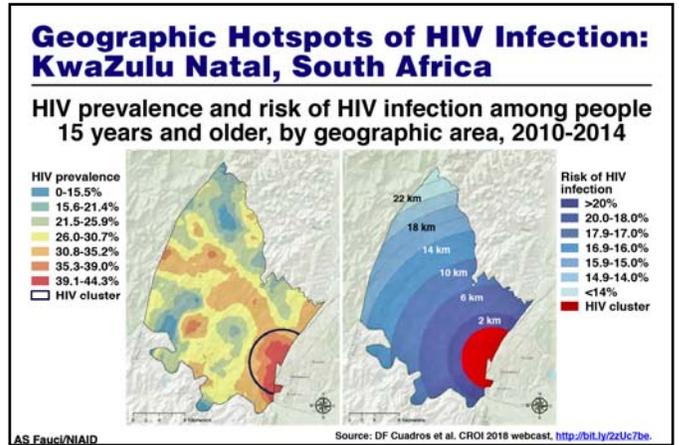
Geographic Hot Spots

AS Fauci/NIAID

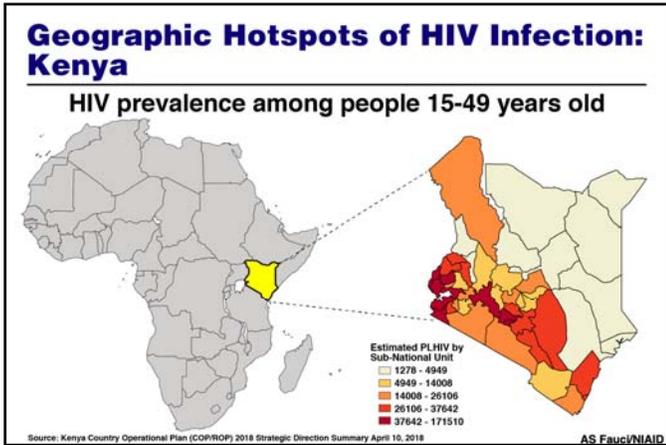
42



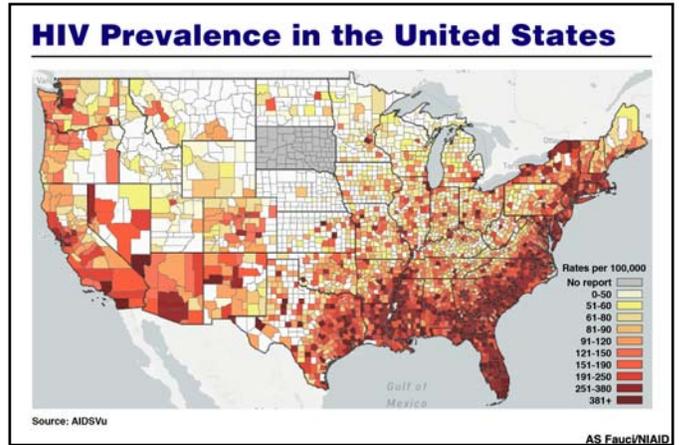
43



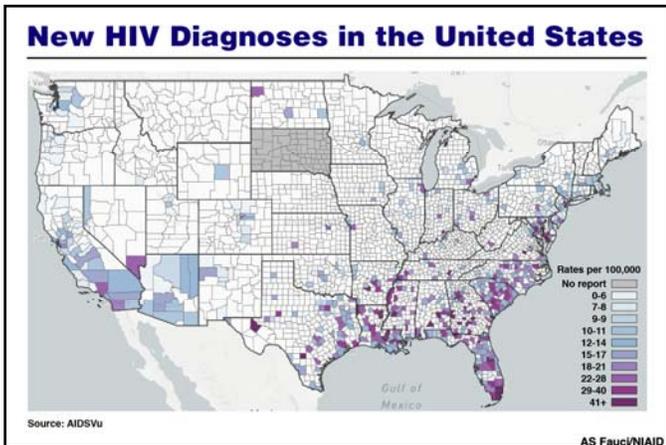
44



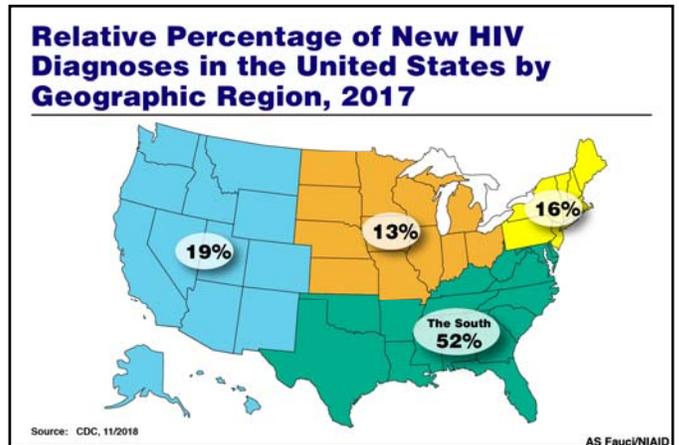
45



46



47

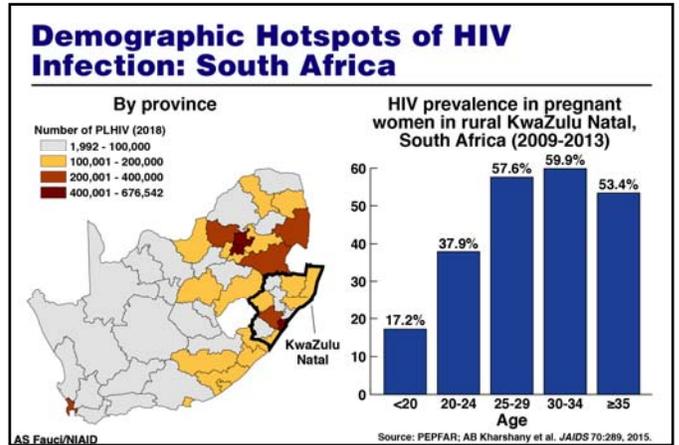


48

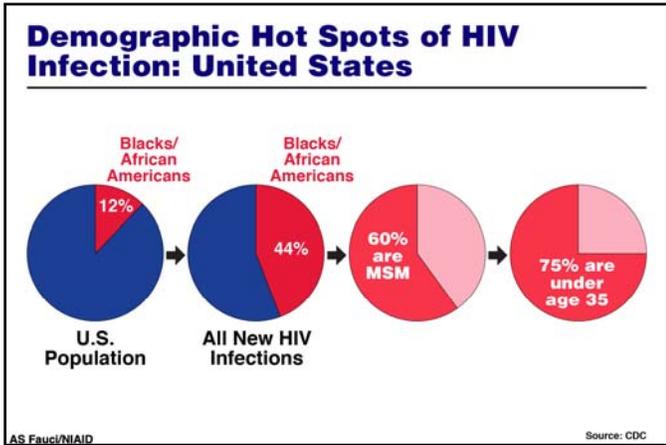
Demographic Hot Spots

AS Fauci/NIAID

49



50



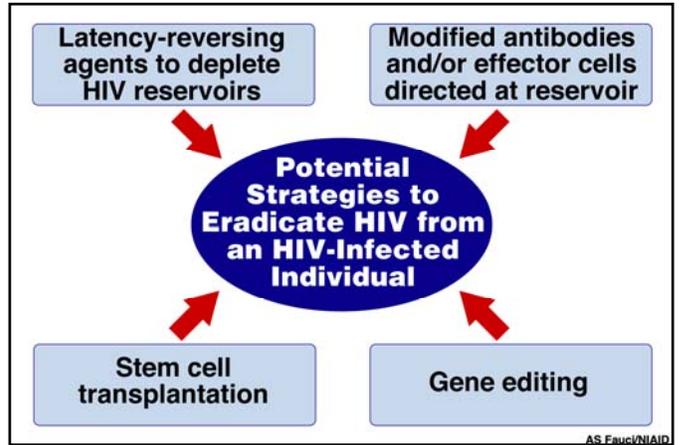
51

- ## Key Scientific Challenges Remaining for HIV Researchers
- Developing strategies for achieving sustained ART-free HIV remission
 - Developing a safe and effective preventive HIV vaccine
- AS Fauci/NIAID

52

- ## Key Scientific Challenges Remaining for HIV Researchers
- Developing strategies for achieving sustained ART-free HIV remission
 - Developing a safe and effective preventive HIV vaccine
- AS Fauci/NIAID

53



54

ART-Free Approaches Towards Durable Control of HIV Infection Requiring Intermittent or Continual Non-ART Intervention

- Therapeutic vaccination
- Passive transfer of broadly neutralizing anti-HIV monoclonal antibodies (bNAbs)

AS Fauci/NIAID

55

Key Scientific Challenges Remaining for HIV Researchers

- Developing strategies for achieving sustained ART-free HIV remission
- Developing a safe and effective preventive HIV vaccine

AS Fauci/NIAID

56

Towards an HIV Vaccine: A Dual Pathway

Empirically Test a Vaccine Candidate to Identify a Correlate of Immunity: The "Classical Approach" in Vaccinology

versus

Assume a Correlate of Immunity and Design a Vaccine to Induce this Correlate

AS Fauci/NIAID

57

Towards an HIV Vaccine: A Dual Pathway

Empirically Test a Vaccine Candidate to Identify a Correlate of Immunity: The "Classical Approach" in Vaccinology

versus

Assume a Correlate of Immunity and Design a Vaccine to Induce this Correlate

AS Fauci/NIAID

58

First Signal of Efficacy (31%) in an HIV Vaccine Clinical Trial – RV144



Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand

S Rerks-Ngarm, JH Kim, NL Michael, et al. for the MOPH-TAVEG Investigators

AS Fauci/NIAID

59

Strategies to Amplify RV144 Response

↑ **Strength**

↑ **Breadth**

↑ **Durability**

Potential approaches:

- Multiple boosts
- Modified vectors
- Adjuvants

AS Fauci/NIAID

60

Two NIAID-Supported HIV Vaccine Efficacy Trials Now Underway

- **HVTN 702, launched Nov. 2016**
 - Modified RV144 prime-boost regimen: HIV clade C gp120 with MF59 adjuvant
 - N=5,400 men and women in South Africa
- **HVTN 705 (Imbokodo), launched Nov. 2017**
 - Quadrivalent, Ad26-vectored mosaic vaccine + HIV clade C gp140
 - N=2,600 women in sub-Saharan Africa

AS Fauci/NIAID

61

Towards an HIV Vaccine: A Dual Pathway

Empirically Test a Vaccine Candidate to Identify a Correlate of Immunity: The "Classical Approach" in Vaccinology

versus

Assume a Correlate of Immunity and Design a Vaccine to Induce this Correlate

AS Fauci/NIAID

62

Assumption

↓

Broadly neutralizing antibodies induced by a vaccine will afford protection against acquisition of HIV

AS Fauci/NIAID

63

Broadly Neutralizing Antibodies Binding to Neutralization Epitopes on HIV Trimer

Image by J Stuckey, GY Chuang, VRC, NIAID, NIH. Adapted from: PD Kwong, JR Mascola, et al. Immunity 2018, YD Kwon, PD Kwong, et al. Cell Reports 2018, J Liu, S Subramaniam, et al. Nature 2008.

AS Fauci/NIAID

64

Major Sites of bNAb Recognition (Neutralizing Epitopes) on the HIV Envelope Trimer

Image by J Stuckey, GY Chuang, VRC, NIAID, NIH. Adapted from: PD Kwong, JR Mascola, et al. Immunity 2018, YD Kwon, PD Kwong, et al. Cell Reports 2018, J Liu, S Subramaniam, et al. Nature 2008.

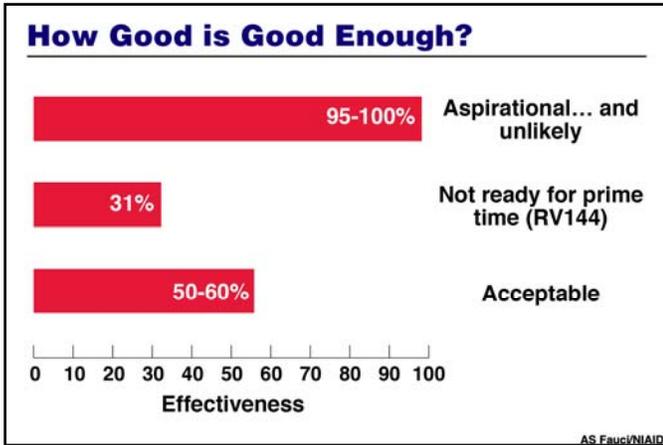
AS Fauci/NIAID

65

Fundamental Challenge: Convert HIV Neutralization Epitopes to Vaccines That Induce bNAbs

AS Fauci/NIAID

66



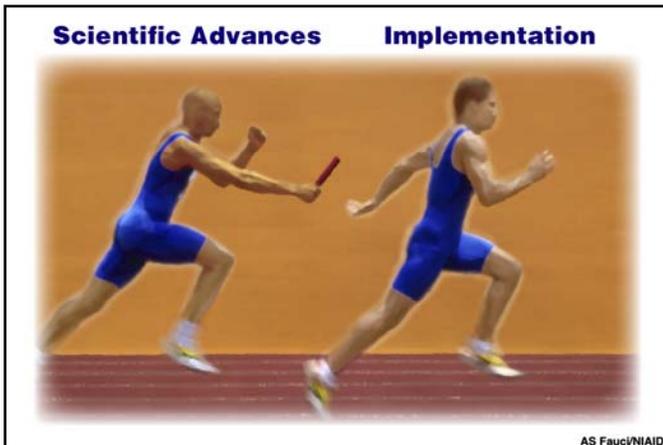
67

An HIV Vaccine with ~50% Efficacy Could be Highly Impactful

- With status quo of treatment and diagnosis, ~49 million new HIV cases projected between 2015 and 2035.
- The availability of an HIV vaccine could avert ~17 million of those cases.

AS Fauci/NIAID

68



69