

## Update From CROI 2019: Ending AIDS by 2030

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IAS-USA

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### CROI Update 2019



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### AIDS Vaccine Development

The American team said their discovery may lead to a vaccine against AIDS.  
"We hope to have such a vaccine ready for testing in about two years," Heckler said.

Miami Herald - April 24, 1984

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### Prospects for the Rapid Development of an AIDS Vaccine



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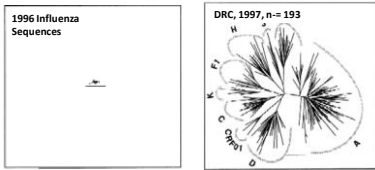
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### Relative Viral Diversity: HIV and Influenza A



Betty Korber, 2002

BRITISH MEDICAL BULLETIN

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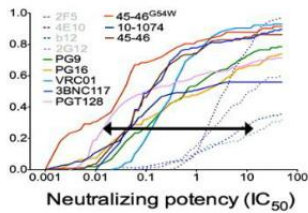
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### Despite the Genetic Diversity, Broadly Neutralizing Abs are Possible



Nussenzweig, CROI 2019

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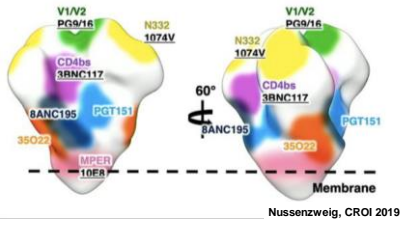
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### Mapping Broadly Neutralizing Epitopes




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### Only A Minority of People Make them and it is After Years of Exposure




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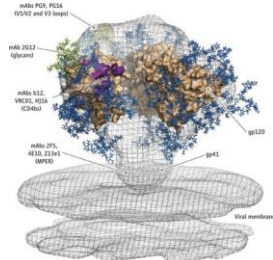
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### Neutralizing HIV antibodies.




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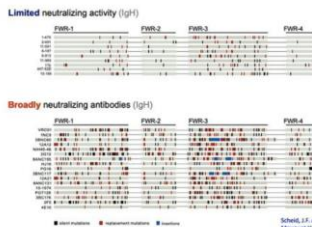
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## Broadly Neutralizing Antibodies Require Many Somatic Mutations



Nussenzweig, CROI 2019

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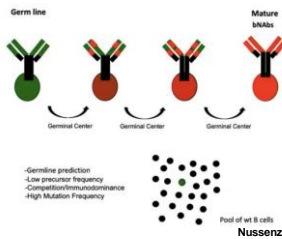
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## Sequential Immunization



Nussenzweig, CROI 2019

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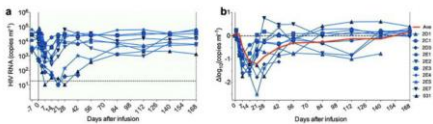
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## Monoclonal Abs Reduce Plasma HIV-1 RNA Levels



- Viral load decline of 0.8 – 2.5 log copies/ml (mean 1.48 copies/ml).
- Plasma viremia was significantly reduced for at least 4 weeks.
- Rebound viruses contained mutations within known antibody contact sites.

Nussenzweig, CROI 2019

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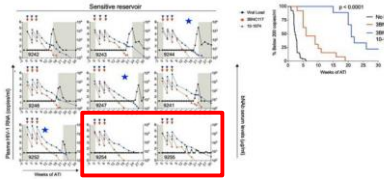
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## Nine Study Volunteers - Two BNAbs



Nussenzweig, CROI 2019

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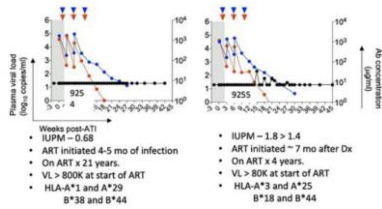
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## Two "Long term" Suppressors



Nussenzweig, CROI 2019

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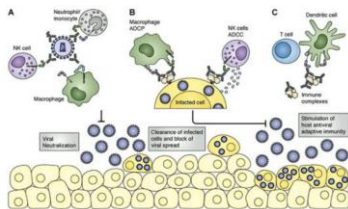
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## Antibodies Engage other Immune Effectors



Nussenzweig, CROI 2019

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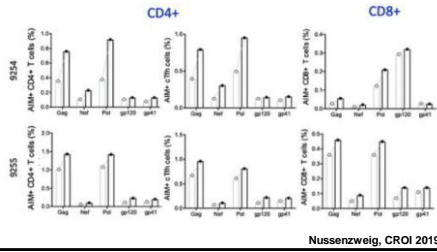
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## T-Cell Responses in Long Term Suppressors



Nussenzweig, CROI 2019

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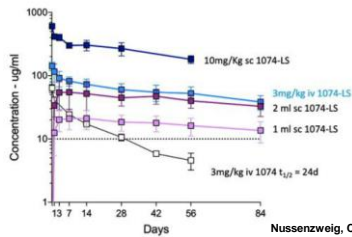
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## Preliminary PK Data – LS Variants



Nussenzweig, CROI 2019

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## HIV Vaccine Progress: 2019

- The good news
  - We know much more about what antigens broadly active neutralizing antibodies recognize
  - We know that some HIV-1 infected people can make them
  - We know that they suppress HIV *in vivo*
- The bad news
  - We have no clue about how to make HIV seronegative people make these antibodies with currently understood vaccines or immunization strategies

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## CROI Update 2019



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## Trump Pledges to end the HIV/AIDS Epidemic by 2030



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## CROI 2019: Another Cure

- Diagnosed with HIV-1 in 2003
- Developed Stage IV B Hodgkin lymphoma in 2013
- Placed on TDF/FTC/EFV->TDF/FTC/Raltegravir
- Received ABVD chemotherapy
- Failed multiple lines of chemotherapy
- Listed for BMT
- Unrelated high 9/10 HLA resolution match homozygous for CCR5-delta 32 deletion found

Gupta, CROI 2019; Nature 2019

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## Transplant Course

- Received 3.6 x 10<sup>6</sup> CD34+ stem cell/kg infusion
- Complicated post tx course including sepsis, GVHD
- Discharged on day 31
- Reactivated CMV->ganciclovir
- Reactivated EBV->Rituximab

Gupta, CROI 2019; Nature 2019

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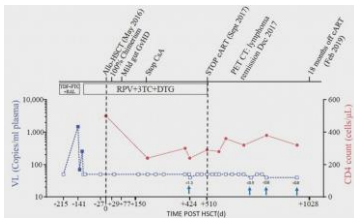
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## Post Transplant Course



Gupta, CROI 2019; Nature 2019

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### 'The London Patient'

### Timothy Brown

- Homozygous for wild type CCR5
- Infection with R5 using virus
- Hodgkin Lymphoma
- Single HSCT
- No irradiation
- Reduced intensity conditioning
- T cell depletion with aCD52
- Mild GVH
- 100% T cell donor chimerism

- Heterozygous for Δ32
- Infection with R5 using virus
- Acute Myelogenous Leukemia
- Two HSCT
- Total Body Irradiation
- Full intensity conditioning
- T cell depletion with ATG
- Mild GVH
- 100% T cell donor chimerism

Gupta, CROI 2019; Nature 2019

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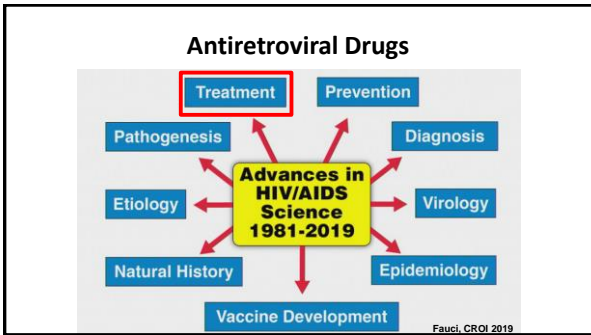
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### FDA-Approved Antiretroviral Drugs

<b>NRTIs</b> <ul style="list-style-type: none"> <li>■ 7 multi-drug combinations</li> <li>■ Abacavir</li> <li>■ Didanosine</li> <li>■ Emtricitabine</li> <li>■ Lamivudine</li> </ul>	<ul style="list-style-type: none"> <li>■ Stavudine</li> <li>■ Tenofovir (TDF, TAF)</li> <li>■ Zidovudine</li> </ul>	<b>Pharmacokinetic Enhancers</b> <ul style="list-style-type: none"> <li>■ Cobicistat</li> <li>■ Ritonavir</li> </ul>	<b>Single-Tablet Regimens</b> <ul style="list-style-type: none"> <li>■ Atripla</li> <li>■ Biktarvy</li> <li>■ Complera</li> <li>■ Delstrigo</li> <li>■ Genvoya</li> <li>■ Juluca</li> <li>■ Odefsey</li> <li>■ Stribild</li> <li>■ Symfi Lo</li> <li>■ Symtuza</li> <li>■ Trumeq</li> </ul>
<b>NNRTIs</b> <ul style="list-style-type: none"> <li>■ Delavirdine</li> <li>■ Doravirine</li> <li>■ Efavirenz</li> </ul>	<ul style="list-style-type: none"> <li>■ Etravirine</li> <li>■ Nevirapine</li> <li>■ Rilpivirine</li> </ul>	<b>PIs</b> <ul style="list-style-type: none"> <li>■ Atazanavir</li> <li>■ Darunavir</li> <li>■ Fosamprenavir</li> <li>■ Indinavir</li> <li>■ Lopinavir/Ritonavir</li> <li>■ Nelfinavir</li> <li>■ Ritonavir</li> <li>■ Saquinavir</li> <li>■ Tipranavir</li> </ul>	
<b>Integrase Inhibitors</b> <ul style="list-style-type: none"> <li>■ Bictegravir</li> <li>■ Dolutegravir</li> </ul>	<ul style="list-style-type: none"> <li>■ Elvitegravir</li> <li>■ Raltegravir</li> </ul>	<b>Entry Inhibitor</b> <ul style="list-style-type: none"> <li>■ Maraviroc</li> </ul>	<b>Fusion Inhibitor</b> <ul style="list-style-type: none"> <li>■ Enfuvirtide</li> </ul>
<b>Post-Attachment Inhibitor</b> <ul style="list-style-type: none"> <li>■ Ibalizumab</li> </ul>			

Source: AIDInfo.nih.gov, February 2019

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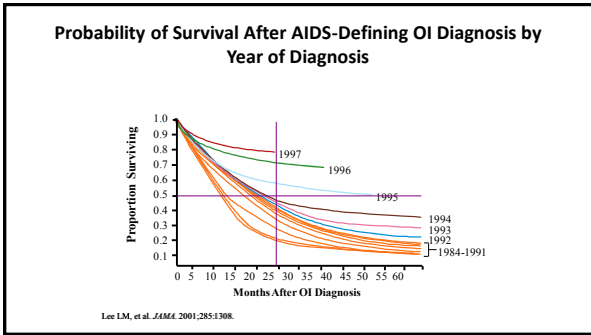
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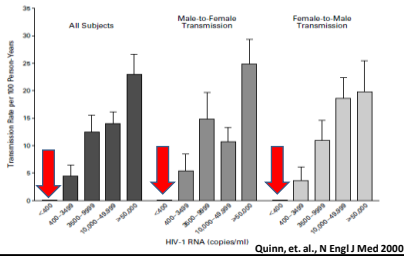
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### HIV-1 Seroconversion Risk by Plasma HIV-1 RNA Level




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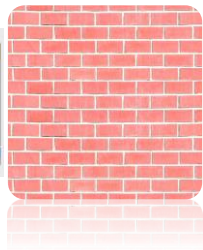
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### Drugs for Prevention: Whom to Treat?

FDA-Approved Antiretroviral Drugs		Pharmacokinetic	Single Tablet
<b>NRTIs</b>	<b>Integrase Inhibitors</b>	<b>Protease Inhibitors</b>	<b>Entry Inhibitor</b>
<b>NNRTIs</b>	<b>Post-Attachment Inhibitor</b>	<b>Pharmacokinetic</b>	<b>Single Tablet</b>
<b>CCR5 Inhibitor</b>	<b>Entry Inhibitor</b>	<b>Protease Inhibitor</b>	<b>Entry Inhibitor</b>




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### ART for Prevention

The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic

Julio G. Montaner, Robert Hogg, Evan Wood, Thomas Kerr, Mark Tyndall, Adrian E. Lew, P. Richard Harrigan *Lancet* 2009

➤ @ Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model

Reuben M. Granich, Charles F. Gilks, Christopher Dye, Kevin M. De Cock, Brian C. Williams *Lancet* 2009

Theoretical model evaluated in the context of a generalized heterosexual epidemic of the same intensity as South Africa. Indicates that universal and annual voluntary HIV testing followed by immediate ART (irrespective of clinical stage or CD4 cell count) could reduce new HIV cases by 95% within 10 years

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**The Pivotal** HPTN 052/ACTG 5245 Study

The New England Journal of Medicine

**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

**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 (83% lower risk)

No linked infections when HIV was stably suppressed by ART (i.e. undetectable viral load) in HIV+ partner

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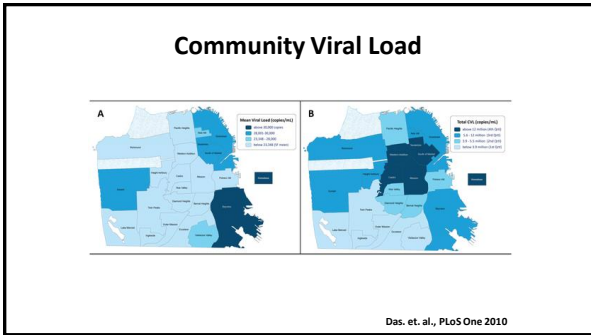
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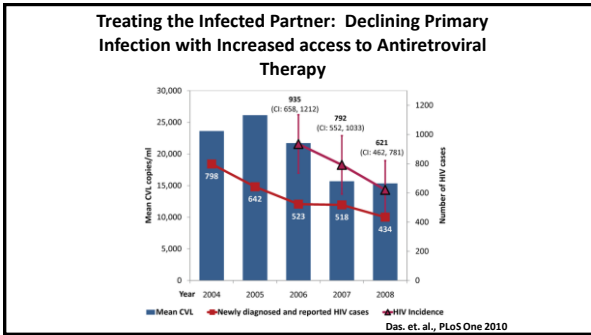
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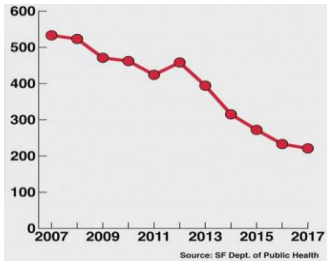
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### San Francisco: 2007 - 2017



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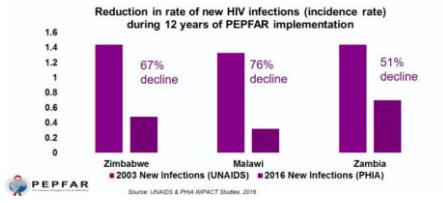
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### Since the Start of PEPFAR, New HIV Infections Have Declined 51-76%



Hillier, CROI, 2019

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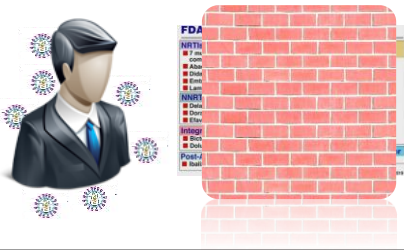
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### Drugs for Prevention: Whom to Treat?



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## PrEP in 2019

- Oral PrEP: Seven completed trials
  - MSM: 3/3 studies demonstrated reduction in transmission
  - Heterosexual women: 2/4 studies demonstrated reduction in transmission
- Dapivirine Ring
  - Reductions in women (except youngest age group)
- Longer acting oral and injectable PrEP in development

Hillier, CROI 2019

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## Ending AIDS by 2030: The Plan



Fauci, CROI 2019

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## What are Our Two Biggest Challenges to Reaching the 2030 Goal?

- A failure to follow the science and invest the money in ways that it is effective
- Mismatches between where we invest and where the epidemic is going

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### First the Positives....

- Invests \$291 million in the Ending AIDS Initiative
  - CDC and local health departments: Up \$140 million
  - Ryan White AIDS Care Program: Up \$120 million
  - Yes to needle exchange (despite Pence)

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### And Now the Negatives.....

Since the Start of PEPFAR, New HIV Infections Have Declined 51.76%

Reduction in rate of new HIV infections (incidence rate) during 12 years of PEPFAR implementation

Region	2005 New Infections (NAs)	2016 New Infections (NAs)	Decline (%)
Zimbabwe	~1.1	~0.4	57%
Botswana	~1.1	~0.3	70%
Zambia	~0.8	~0.4	51%

**PEPFAR: Cut By 1.35 Billion**

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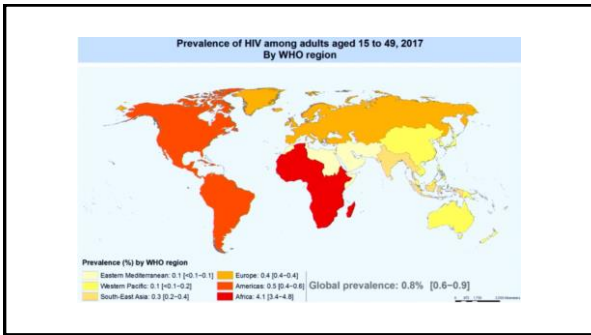
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**Trump wants to cut billions from the NIH. This is what we'll miss out on if he does.**

Is spending money at the NIH a good deal? The research is incredibly clear: Yes.

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### Health Care (not) For All

- Medicaid and ACA subsidies: Cut by \$777 billion over 10 years
  - Ending coverage for pre-existing conditions
  - Requiring additional documentation of citizenship, etc.
  - Re-imposing means tests
- Medicaid Expansion: Reversed
- Medicare: Cut by \$845 billion
  - Reduce support for graduate medical education
- Two Weeks Ago: DOJ decides to support a Texas Court decision that declared the entire ACA invalid

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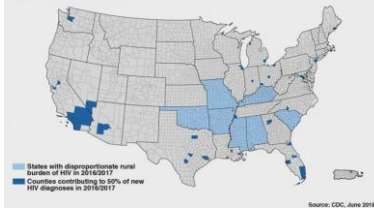
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### AIDS is no Longer a Bicoastal Problem

#### U.S. Areas with the Highest Burden of HIV Diagnosis




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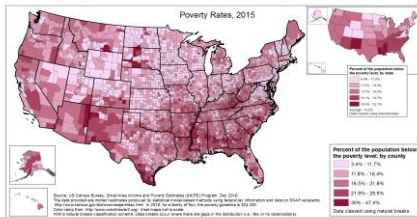
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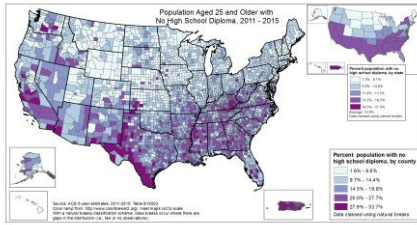
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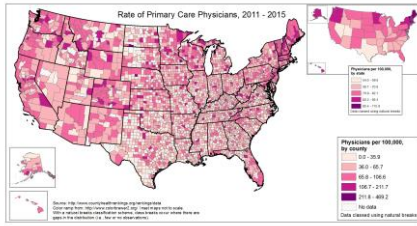
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### Ending AIDS: What Can We Do?

- Promote policies that have been shown to make a difference:
  - Access to health care for all
  - Invest in public health
  - Invest in research

**VOTE!**

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**Thank you!**



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**Question-and-Answer**

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IAS-USA

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