

Update From the 2019 Conference on Retroviruses and Opportunistic Infections

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IAS-USA

Learning Objectives

After attending this presentation, learners will be able to describe the results of selected studies presented at the 2019 Conference on Retroviruses and Opportunistic Infections (CROI) including:

- Studies on antiretroviral strategies
- Information concerning end-organ diseases
- Diagnosis and management of opportunistic infections

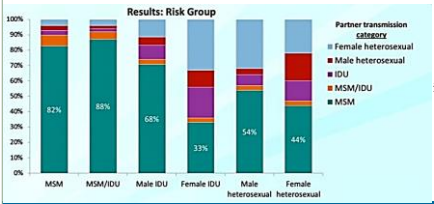
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Epidemiology

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HIV Transmission in the US- Role of Genetic analysis?

- Analysis of 41,294 HIV pol sequences submitted for resistance testing.
- Construct a HIV transmission network of genetically linked persons, then examine the characteristics of the persons linked



"Interventions that reduce transmissions involving MSM are likely to reduce HIV acquisition among other risk groups as well"

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Oster #68

Ending the HIV Epidemic in the United States

The Washington Post
January 10, 2016

OPINIONS

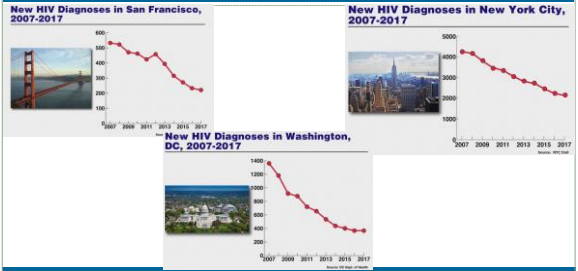
No More Excuses. We Have the Tools to End the HIV/AIDS Pandemic.
Anthony S. Fauci

ENDING THE HIV EPIDEMIC: A PLAN FOR THE UNITED STATES
SPECIAL PRESENTATION

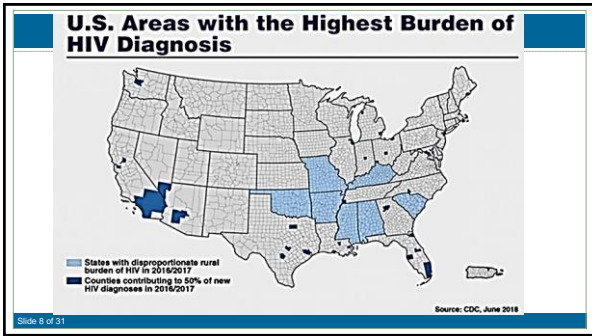
ANTHONY S. FAUCI
National Institute of Allergy and Infectious Diseases, National Institute of Health, US Department of Health and Human Services, Bethesda, MD, USA

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Control of HIV is Possible



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Plan to End US HIV Epidemic- Targeted DTPR

Goal:

- 75% reduction in new HIV infections in 5 years and at least 90% reduction in 10 years.

- Diagnose** all people with HIV as early as possible after infection.
- Treat** the infection rapidly and effectively to achieve sustained viral suppression.
- Protect** people at risk for HIV using potent and proven prevention interventions, including PrEP, a medication that can prevent HIV infections.
- Respond** rapidly to detect and respond to growing HIV clusters and prevent new HIV infections.

- Target 48 counties, DC, San Juan and 7 States with high rural burdens
- Increase Suppression rate from 60% to 90%
- Increase PrEP use in at risk to at least 50%
- Identify and respond to transmission clusters

“New money”
 Budget proposes \$120M more for RW; cuts to PEPFAR, TB, Medicaid

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Ending an HIV Epidemic- going “all in” with the PopART Study

PopART Intervention Package

- 52,500 persons enrolled in 21 communities in Zambia and S. Africa
- 640 Community HIV-care Providers (CHiPs) trained and supported to provide PopART intervention
- Early analysis showed condom use increased if flavored; ~1/4 of men got circumcised; and time to ART shortened

Facilitated by CHiPs

Service promotion and referral for HIV care for HIV vire including PMCT - VMMC - TB - STI

Universal testing: annual door-to-door HBT

Universal treatment for HIV vire irrespective of CD4 count

Follow-up on referral

Support for: Retention in care Adherence to treatment

CHiPs: Community HIV-care Providers

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Universal Community Based Testing & Treatment May (or May Not) Reduce HIV Incidence – HPTN071 PopART

- PopART in Arms A & B, SOC testing in Arm C; Universal ART in Arm A vs. National Standard ART in Arms B & C

	Arm A PopART+uART	Arm B PopART+sART	Arm C SOC+sART
GM community incidence rates	1.45% ↓	1.06% ↓	1.55%
Incidence vs. Arm C	7%	30%	N/A
P compared to SOC	0.51	0.006	

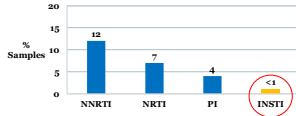
PopART services and SOC treatment worked, but PopART and universal ART did not

Hays #92LB

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Drug Resistance Among Newly Diagnosed Patients: 2013 – 2016

- CDC analyzed sequences of 36,288 (32% of infections) newly diagnosed, resistance testing within 12 weeks diagnosis
- Drug resistance detected in 19%¹



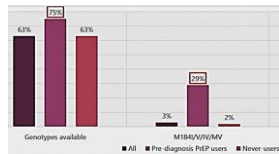
- Separate analysis N.Y. State: < 1% transmitted INSTI resistance²

¹ McClung # 526 ² Wang # 528

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Drug Resistance Among Former PrEP Users - NYC

- CDC guidelines recommend HIV NAAT in symptomatic PrEP candidates, despite >25% asymptomatic in acute HIV
- In 91 PrEP users in NYC high frequency of 3TC/FTC resistance at HIV diagnosis¹



- 93% of patients had no NAAT within 30D prior to PrEP

¹Mistra #107

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Antiretroviral Therapy

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Point of Care Viral Load Testing and Task Shifting – STREAM Study

POC VL + RN Counsel vs. Lab VL + NP Visit

- Endpoint – In care with HIV RNA < 200 @ 12 months
- Open label, randomized, 390 patients

	Intervention Arm	Standard-of-care Arm	Absolute Risk Difference	Non-inferiority (1-side 95% CI) P value	Superiority (2-side 95% CI) P value
Viral suppression (<200 copies/mL) and Retention in care at study clinic	89.7% (175/195)	75.9% (148/195)	13.9%	(≥7.6) <0.001	(6.4-21.2) <0.001

Drain #53 LB

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Does Initial Therapy with an INSTI Cause Disproportionate Weight Gain?

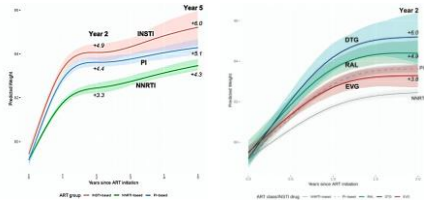
- A5257 – RAL produced more weight gain than DRV/r or ATV/r, but RAL better tolerated
- Spring 1 – DTG produced more weight gain than EFV, but DTG virologic efficacy superior
- Cabotegravir LA in **HIV uninfected** did not cause weight gain*

* Landovitz #34LB

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Analysis of Weight Gain in Treatment Naives

- Naïve patients starting ART 2007 - 2016
- 17 centers, 24,001 patients: 11,825 NNRTI, 7,436 PI, 4,740 INI

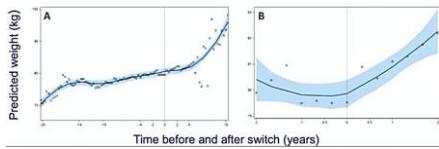


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Bourgi # 679

Does Switching to INSTI Cause Weight Gain?

- Analysis of weight trajectory before and after switching PI (¾) or NNRTI (¼) to INSTI
- 691 Patients started ART 1997 – 2017, VL <200 c/mL, then switch to INSTI (42% RAL, 30% EVG, 28% DTG)



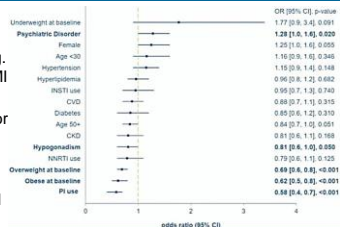
- In WIHS women switch to INSTI also associated with weight gain²

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¹ Lake #669² Kerchberger #672

What if You Look Specifically at Those Who Gain a lot of Weight?

- 3,468 from 9 clinics who changed ART while suppressed Aug. '13 – July '17, had BMI before and after.
- Analyze risk factors for ≥ 3% annual weight gain
- **Psychiatric disorder only significant +, PI use protective?**



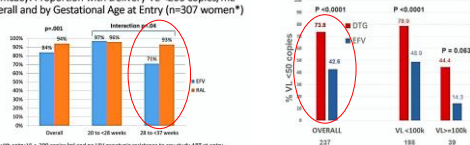
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McComsey #671

ART Efficacy in Pregnancy

- P1081 – RAL vs. EFV week 20–30 gestation¹
- DOLPHIN2 – same day DTG vs. EFV ≥ 28 weeks²

Efficacy: Proportion with Delivery VL <200 copies/mL Overall and by Gestational Age at Entry (n=307 women*)



*Women with entry VL ≥ 200 copies/mL and no HIV genotypic resistance to any study ART at entry

- In DOLPHIN2 there were 3 M:C transmissions and 4 stillbirths, all in DTG arm – not DTG related

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¹ Mirochnick #39 ² Khoo #40

End Organ Disease

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Is Long-Term, Controlled HIV a Risk for Sudden Cardiac Death?

- Review of 43,413 patients with HIV in VACS, excluding non-sudden cardiac death, age <18 or >90, Dialysis, Cancer, O2 dependent
- Compared to uninfected VACS controls

Results: 3,036 likely SCD

Risk Factors: CD4 <200, +HIV RNA, tobacco, HCV, obesity, anemia, alcohol use disorder, COPD

In those with CD4 ≥ 500 + uHIV RNA = no increased risk SCD

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Frieberg #32

Is Sudden Cardiac Death Cardiac, and if so is it Atherosclerotic?

- Among 179 SCD in patients with HIV and an autopsy, 47 judged SCD prior to autopsy
- Causes of Death Revealed by Autopsy

Cause	Frequency
Non-Cardiac	24 (16 O.D.)
Cardiac	23 (Cardiac Fibrosis common)
Arrhythmic	22
Cardiomyopathy	5
AMI	2

In San Francisco, drug overdose is the most common cause of "SCD", although cardiac fibrosis with arrhythmia is also common

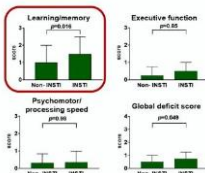
Tseng #33

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Are INSTI Causing Cognitive Impairment?

- Retrospective, cross-sectional study of about 100 pts on INSTI and 100 on non-INSTI regimens who had undetectable HIV RNA
- Did Neuropsychological testing and MRI brain volumes
- 2/3 both groups smokers, 1/2 + UDS, non-INSTI had been on regimen about 5x as long as INSTI

Domain deficit scores for non-INSTI versus INSTI



INSTI also associated with reduced grey matter volume¹

1. O'Halloran #442 2. Chan #440

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Probiotic Treatment for Systemic Inflammation- A5350 Visbiome Study

- Visbiome (commercial probiotic) or placebo for 24 weeks in 93 patients on stable ART
- At 24 wks no significant difference in CD4, CD4/CD8 ratio, sCD14, D-dimer
- Visbiome had modest effects on gut microbiome

Overton #35

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Tuberculosis

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Latent TB Infection - Screening

- PREVENT: Screen child contacts of 973 adult TB patients in villages in Lesotho
- Community Based HW screened children, linked to care and IPT
- SOC villages relied on health facilities

	CBHW	SOC	p
# Children	216	164	NS
Screened	204	101	NS

Hirsch - Moverman #79

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LTBI - Treatment

- PK analysis of 3 months INH/Rifapentine + DTG¹
61 HIV+, suppressed VL, need LTBI Rx
Results: DTG trough ↓50%, AUC ↓29% but at all time points (DTG) >300ng/mL and most likely therapeutic
- INH preventive treatment in 2nd and 3rd trimester was safe²

1. Dooley #80, 2. Salazar-Austin #77

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Tuberculosis- Treatment Highlights

- Can DRV/r be given with Rifampin if dose doubled?
Open label, randomized trial!
Results: good PK, but excess liver toxicity. If Rifampin must be used then DRV/r is not a good option
Since TAF and COBI contraindicated, acceptable regimens remain based on EFV 600mg or RAL 800mg BID, both with TDF/3TC
- Bedaquiline + Delamanid for MDR TB have "only" additive QTc prolongation.²
Avoid other QTc prolonging medications (clofazamine, moxifloxacin, etc.)
- EFV+RIF+DMPA PK study showed 12% with low MPA troughs at 12 weeks.³
Dose DMPA Q 8-10 wks

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1.2. Maartens #81,#84 3. Mngqibisa #78

CROI 2020

Boston
March 8-11



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Question-and-Answer

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