HIV Treatment and Prevention: What's New in 2018 and What's Coming?

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Disclosures

None

HIV Treatment and Prevention in 2018

- Epidemiology in Alaska and the US
- When to Start ART and What to Start
- Newest ARV's and ART Trends
- Latest on Pre-Exposure Prophylaxis (PrEP)
- Conclusions

National HIV Curriculum

www.hiv.uw.edu

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A free educational web site from the University of Washington and the AETC National Coordinating Resource Center.

Contributors

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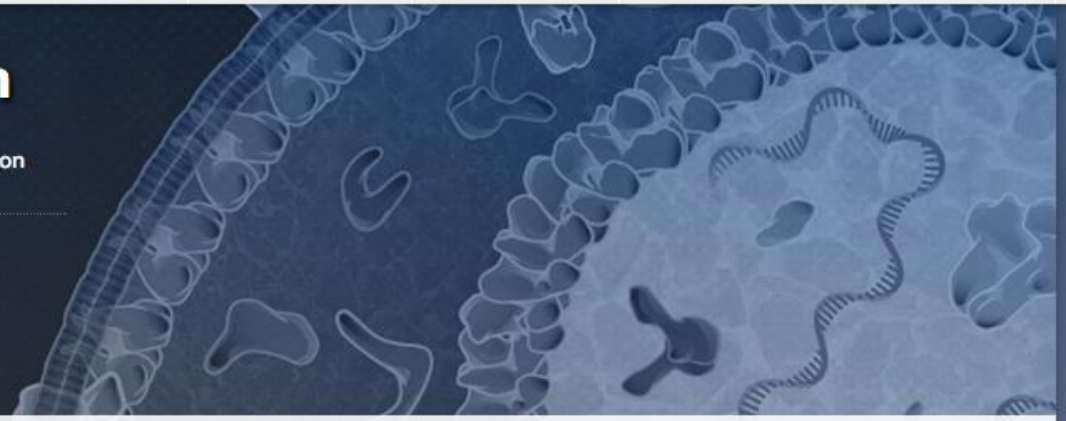
Health Resources and Services Administration



Course Modules

Screening and Diagnosis

This module is for any health care provider who would like to establish core competence in testing for HIV, recognizing acute HIV infection, and linking persons diagnosed with HIV to medical care.

Overview / Quick Reference ›
Rapidly access info about Screening and Diagnosis

Question Bank CNE/CME
Interactive board-review style questions with CE credit

Self-Study CNE/CME
Track your progress and receive CE credit

Clinical Challenges COMING SOON!
Expert opinions for challenging and controversial cases

Basic HIV Primary Care

The Basic HIV Primary Care module is intended for any clinician who may interact with persons who have HIV infection in a clinical setting, with an emphasis on the primary care management issues related HIV.

Overview / Quick Reference ›
Rapidly access info about Basic HIV Primary Care

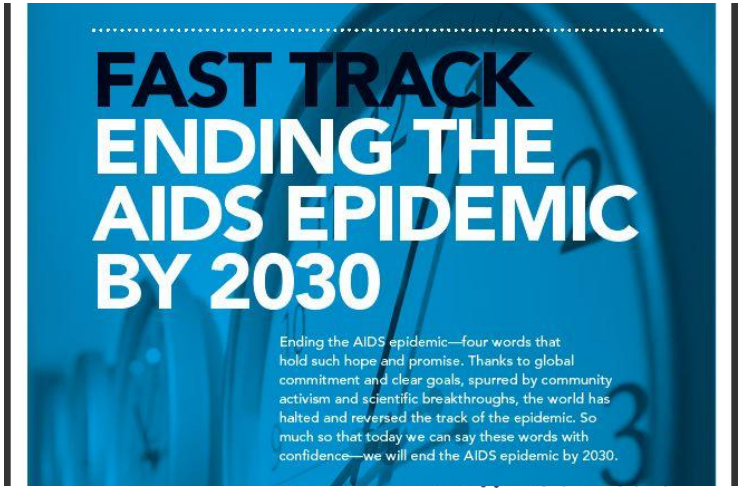
Question Bank CNE/CME
Interactive board-review style questions with CE credit

Self-Study CNE/CME
Track your progress and receive CE credit

Clinical Challenges COMING SOON!
Expert opinions for challenging and controversial cases

What are the current HIV care goals?

- UNAIDS “90-90-90” – 90% diagnosed, 90% receiving ART, 90% virally suppressed (by 2020)
- US HIV Strategy - 90% diagnosed, 85% linked to care, 90% retained in care, 80% virally suppressed, etc (by 2020)
- Certain jurisdictions, “Getting to Zero” – zero new infections, zero HIV-related deaths, zero stigma (by 2020)



People-First Language

- People-First Language is a way of reducing stigma and showing respect for individuals who are living with HIV by focusing on the person instead of the disease
- i.e. Instead of "HIV-infected person" use "person with HIV"

Update on HIV Epidemiology, Alaska & the U.S.

Newly Diagnosed HIV Cases in AK, 2017 (n=29)

Of 75 cases reported to the Alaska Section of Epidemiology in 2017, 29 were newly diagnosed in Alaska. Of those 29:

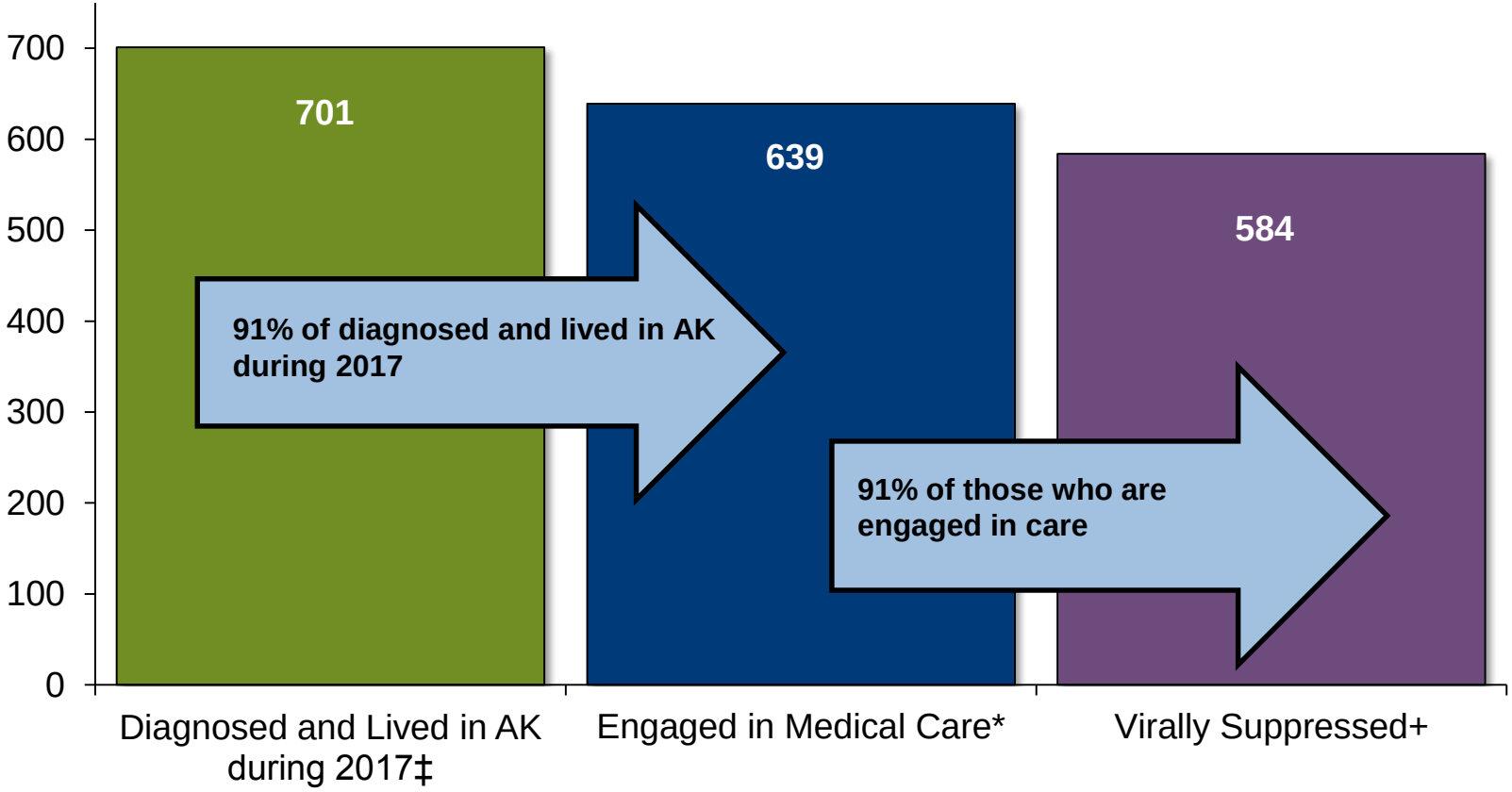
- 8 (28%) had advanced infection (CD4 count below 200 cells/mL or opportunistic infection)
- Zero are known to have died
- Demographics:
  - 72% male
  - 62% men who have sex with men (MSM); 24% Heterosexual
  - 45% AN/AI; 31% White; 14% Black
  - 69% 34 years old or younger at the time of diagnosis

Persons Living with HIV in AK as of end of 2017 (n=710)

Of 710 persons living with HIV in Alaska as of 12/31/2017:

- Demographics:
  - 75% male
  - 48% MSM; 27% Heterosexual
  - 42% White; 27% AN/AI; 14% Black
- 66% had an initial diagnosis in AK
- 91% of those living in AK during 2017 were engaged in medical care, and of those 91% were virally suppressed

HIV Care Continuum, Alaska — 2017 (n=701)



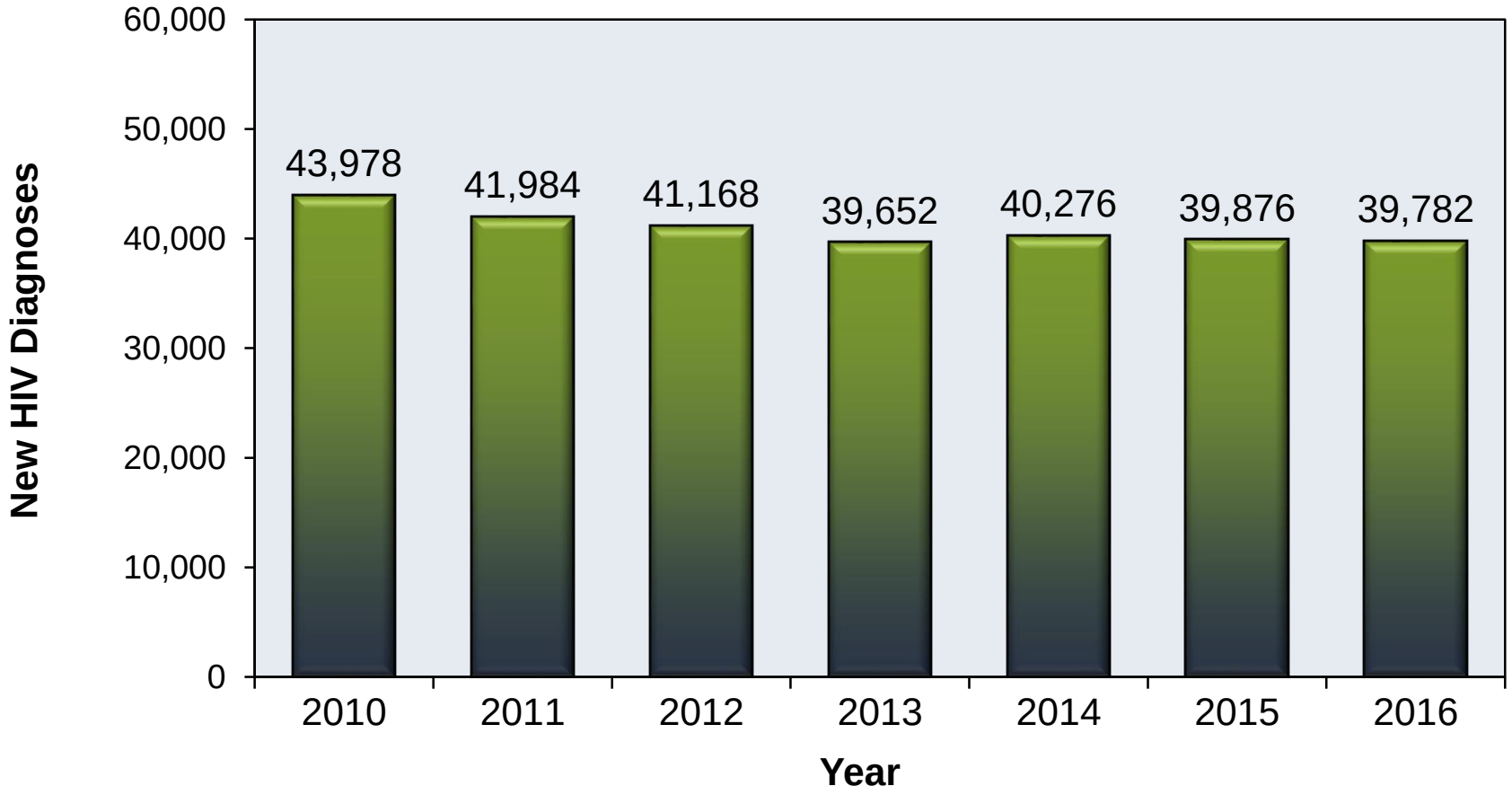
‡ Includes all cases who lived in Alaska (AK) during 2017; cases with unknown residence and no activity in the surveillance system for ten or more years were excluded (n=25).
** Received at least one CD4/Viral Load between Jan. 1 and Dec. 31, 2017.*
+ Viral Load ≤200 copies/mL.

ALASKA DIVISION OF Public Health

Turning to U.S. Data…

New Diagnoses of HIV Infection in the U.S. by Year, 2010-2016

***Positive news**: lifespan for a person with HIV who takes ART is near-normal and # of new infections per year is finally decreasing (slowly)…



Source: CDC. HIV Surveillance Report, 2016;vol. 28:1-125. November 2017.

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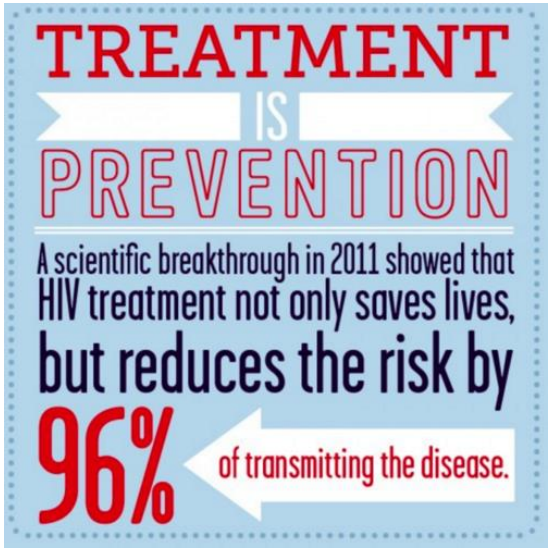
Why is Overall Incidence Finally Decreasing?

- Expanded testing
- Efforts at linkage and retention in care
- Pre-exposure prophylaxis (PrEP)
- **Treatment for all and “treatment as prevention”**

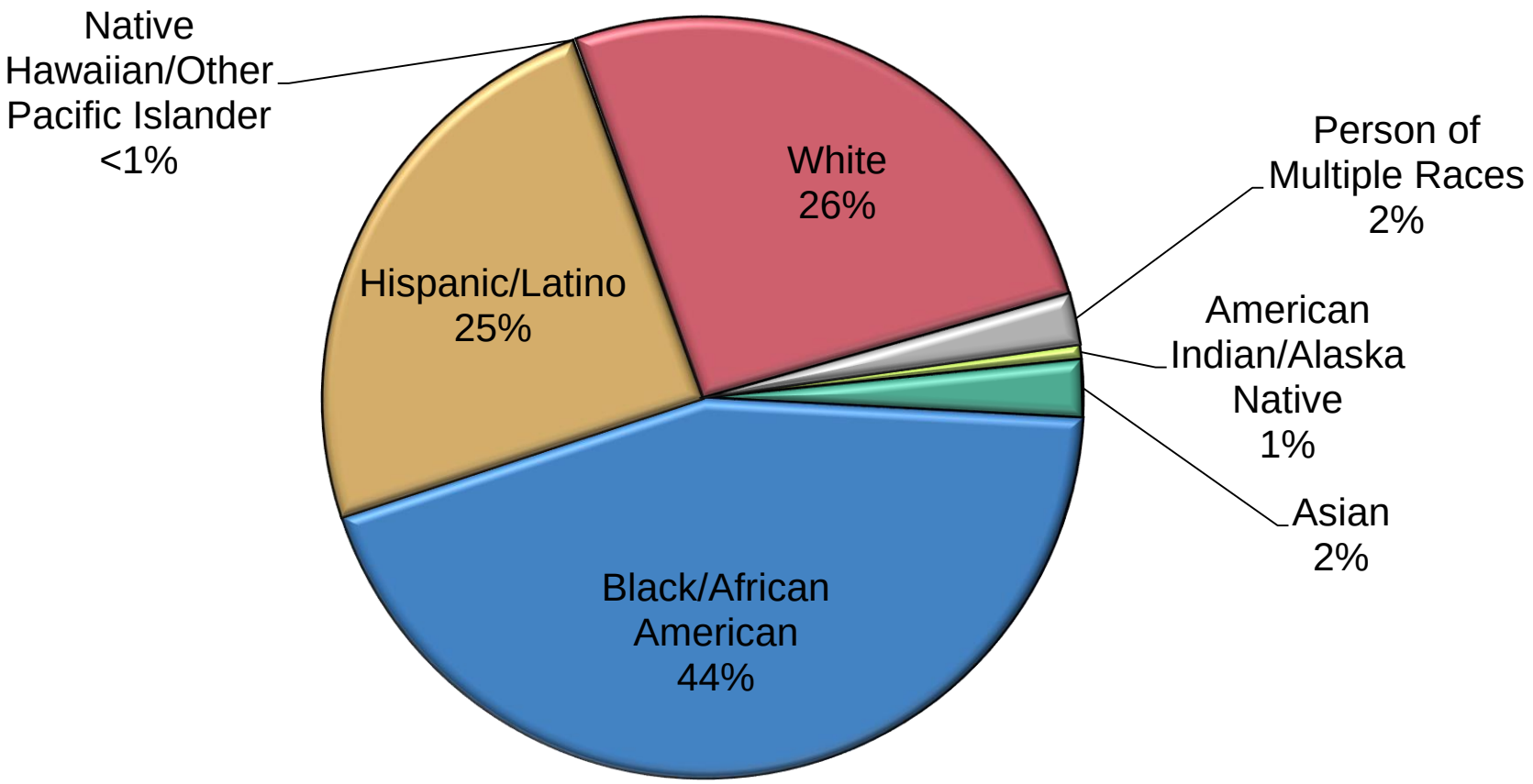


However, major problems remain…

- Many still with advanced infection at time of diagnosis
- Challenges to retention in care and medication adherence
- Limited access to mental health and addictions services
- **Disparities for certain demographic groups**
  - **Incidence for MSM has <u>not decreased</u>**
  - **Incidence for young MSM (age 25-34) <u>actually rising</u>**
  - **Lifetime risk of HIV for an African American MSM: <u>1 in 2</u>**

New Diagnoses of HIV Infection in U.S. by Race/Ethnicity, 2016

New Diagnoses of HIV Infection, by Race/Ethnicity



Source: CDC. HIV Surveillance Report, 2016;vol. 28:1-125. November 2017.

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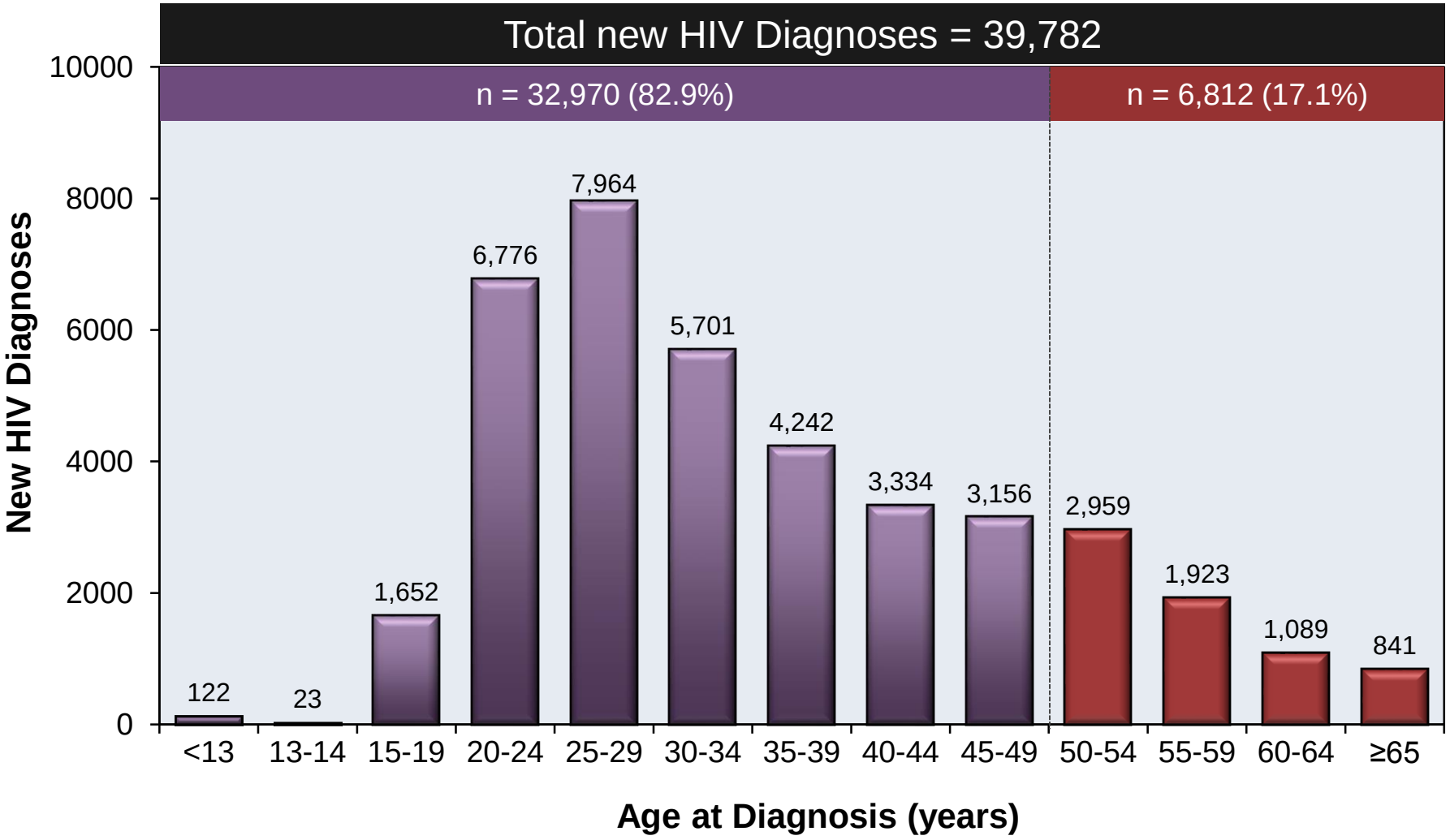
New Diagnoses of HIV Infection in United States (estimated) by Age Group at Time of Diagnosis, 2016



Source: CDC. HIV Surveillance Report, 2016;vol. 28:1-125. November 2017.

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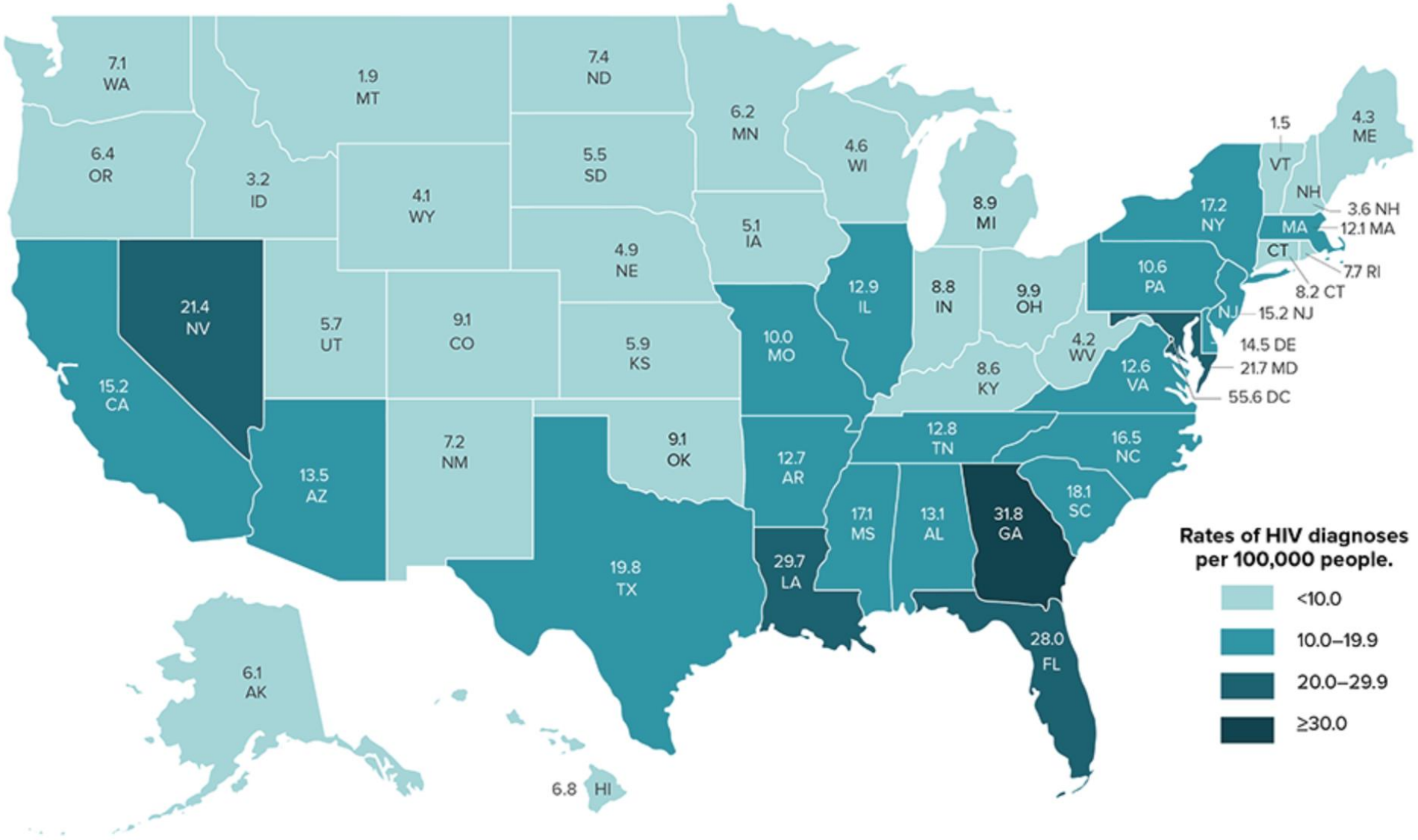
Rates of HIV Diagnoses Among Adults and Adolescents in the US by State, 2016



CDC Surveillance Report, 2017

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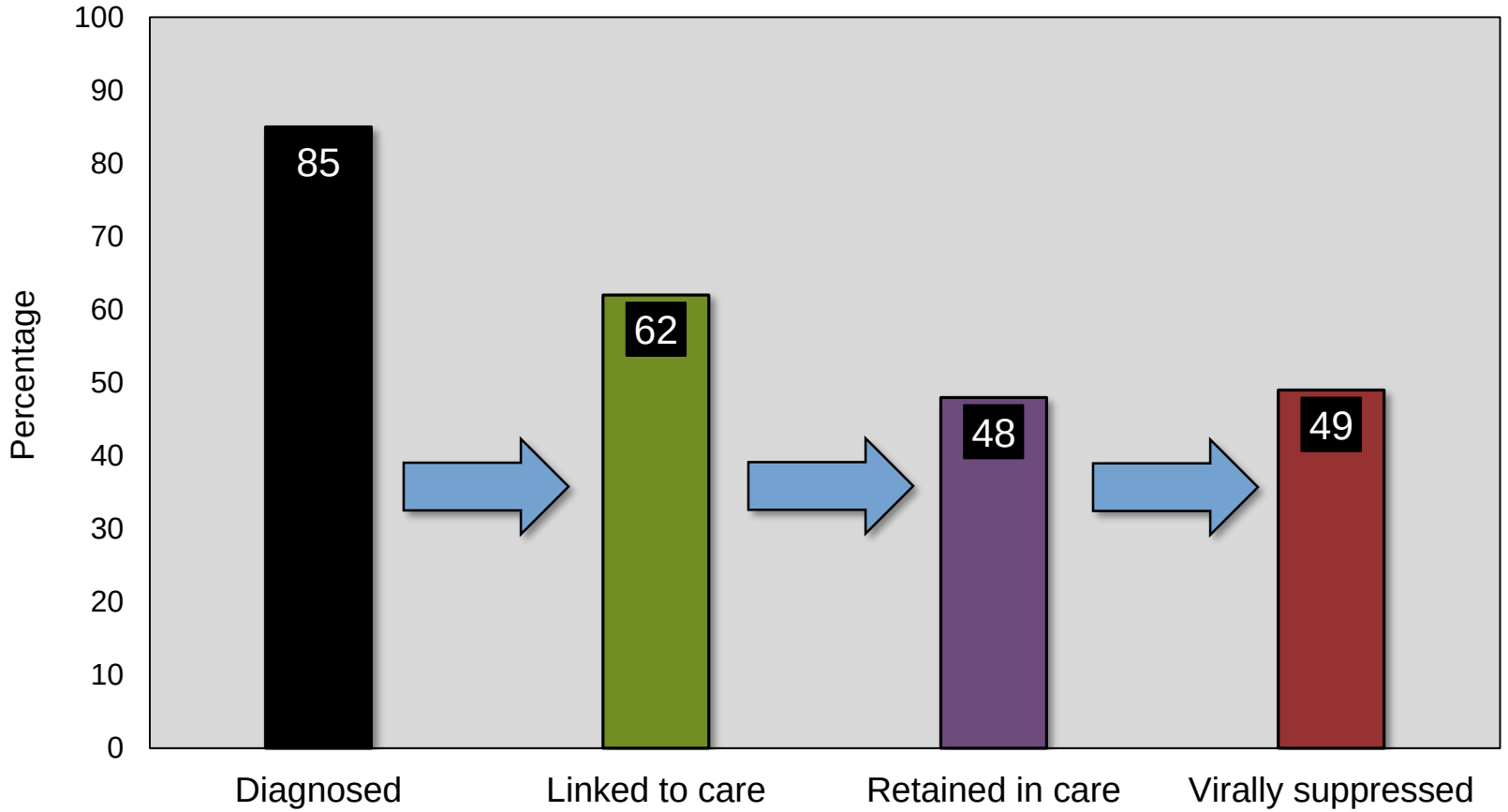
U.S. HIV Continuum of Care, 2014

Of the 1.2 million persons in the U.S. living with HIV…



*All percentages lower for certain demographic groups

Source: CDC Surveillance Report, 2017

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When to Start ART and What to Start

Case

- 27-year-old man with positive HIV 4th gen test 4 days ago
- CD4 count 710 cells/mL; HIV RNA 47,200 copies/mL
- Active intranasal meth; history of injection heroin and meth
- Expresses he is eager to start ART
- Reports difficulty swallowing pills
- Female partner does not have HIV
- *When would you offer ART? At this visit or wait?*

2018 DHHS ANTIRETROVIRAL THERAPY GUIDELINES

Initiating Antiretroviral Therapy in Treatment-Naïve Patients: When to Start

HHS Antiretroviral Therapy Guidelines: 2018
When to Start ART

Antiretroviral Therapy is Recommended for:	
All persons living with HIV, regardless of CD4 count, to reduce morbidity and mortality	**AI**
All persons living with HIV to prevent transmission	**AI**
On a case-by-case basis, ART may be deferred because of clinical and/or psychosocial factors, but therapy should be initiated as soon as possible.	
Conditions that increase the urgency of ART: pregnancy; opportunistic infection; CD4 count <200; HIV-associated dementia, malignancy, or nephropathy; HBV/HCV; acute HIV	

Source: HHS Antiretroviral Therapy Guidelines. 2018. AIDS Info

HIV Treatment as Prevention: The Evidence

Study	Methodology	# Linked Transmissions	HIV Transmission Risk
HPTN 052	ART early versus delayed	Zero	Risk reduction: 93-96%
PARTNER Study	888 serodifferent couples; 1,238 CYFU	Zero	Risk: 0.0/100 CY (0.0-0.3)
Opposites Attract	343 serodifferent male-male couples; 591 CYFU	Zero	Risk: 0.0/100 CY (0.0-0.16)

From CDC: *"People living with HIV who take HIV medicine as prescribed and get and keep an undetectable viral load have effectively no risk of transmitting HIV to their HIV-negative sexual partners."*

Sources: Cohen 2011, Cohen 2016, Roger 2016, Bavinton 2017

Undetectable = Untransmittable

Source: Prevention Access Campaign, www.preventionaccess.org

Would you start ART on the day of diagnosis?

- SF: “Getting to Zero Campaign” & “RAPID Initiative”
- All persons diagnosed with HIV linked to care within 5 days; ART started first visit (unless risk for fatal IRIS)
- Educated providers & trained linkage navigators across SF
- **Time from diagnosis to VL <200 copies decreased 54%;** also improved time to first visit and % in care at 1 year

Sources: Bacon O, CROI 2018; www.gettingtozerosf.org

2018 DHHS ANTIRETROVIRAL THERAPY GUIDELINES

Initiating Antiretroviral Therapy in Treatment-Naïve Patients: What to Start

DHHS Guidelines 2018
Recommended Initial Regimens for Most People With HIV

Components (Integrase with 2 NRTI's)	Trade Name	Pill
Dolutegravir-Abacavir-Lamivudine[+]	*Triumeq*	
Dolutegravir + TAF-Emtricitabine[#*]	*Tivicay + Descovy*	
Bictegravir-TAF-Emtricitabine[#]	*Biktarvy*	
Elvitegravir-Cobicistat-TAF-Emtricitabine[#*]	*Genvoya*	
Raltegravir + TAF-Emtricitabine[#*]	*Isentress + Descovy*	

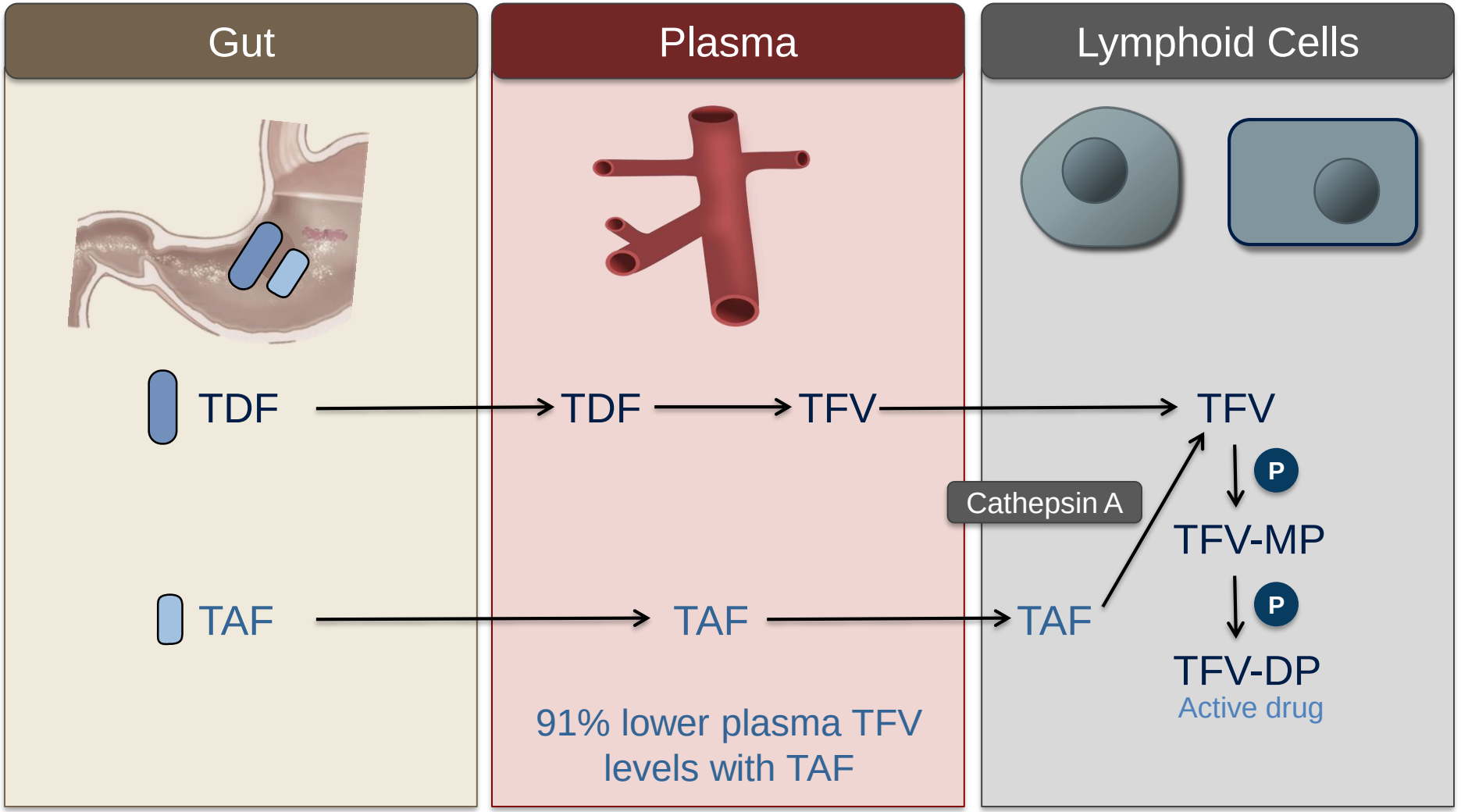
[+]Only if HLA-B*5701 negative; caution if history of ischemic CV disease
[#]TAF ok with creatinine clearance as low as 30 mL/min
*Options with TAF shown; TDF is also reasonable per HHS guidelines, though IAS-USA guidelines favor TAF

DHHS Guidelines 2018
Recommended Initial Regimens In Certain Clinical Situations

Components
Boosted PI plus 2 NRTI's
Darunavir (with a booster[+]) + 2 NRTI's*
Atazanavir (with a booster[+]) + 2 NRTI's*
NNRTI with 2 NRTI's
Efavirenz-TDF-Emtricitabine (*Atripla*)
Rilpivirine-TAF-Emtricitabine (*Odefsey*)[#]
Rilpivirine-TDF-Emtricitabine (*Complera*)[#]

[+]Booster can be a combined tablet with cobicistat or a separate ritonavir tablet
[*]NRTI combinations: TAF-emtricitabine, TDF-emtricitabine, or abacavir-lamivudine
[#]Rilpivirine-based options and boosted ataanavir with abacavir-lamivudine should not be started if CD4 count below 200 cells/mL or HIV RNA above 100,000 copies/mL

Tenofovir DF (TDF) versus Tenofovir alafenamide (TAF)



TDF = tenofovir disoproxil fumarate; TFV = tenofovir

Tenofovir alafenamide (TAF) Summary

- **Does TAF have efficacy similar to TDF?**
  YES
- **Does TAF have better side effect profile than TDF?**
  BMD: Yes; Renal: Yes; Lipids: No
- **Is TAF Safe with Mild-Moderate Renal Impairment?**
  Yes: safe in study with patients with CrCl 30-69 ml/min
- **Does TAF have adequate activity against HBV?**
  Yes; approved by FDA for treatment of HBV
- **Can TAF be used for PrEP, oPEP, or nPEP?**
  NOT NOW; maybe in future

Choosing between options

- Key questions:
  - CD4 count, viral load, resistance assay result
  - Comorbidities (viral hepatitis, CKD, CVD, etc)
  - HLA-B*5701 status
  - Drug interactions (including OTC's)
  - Food requirements
  - Pill preference (size, number)
  - Pregnancy
  - Ability to adhere

Source: HHS Guidelines, 2018 (www.aidsinfo.org)

Case

- 27-year-old man with positive HIV 4th gen test 4 days ago
- CD4 count 710 cells/mL; HIV RNA 47,200 copies/mL
- Active intranasal meth; history of injection heroin and meth
- Expresses he is eager to start ART
- Reports difficulty swallowing pills
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- *When would you offer ART? At this visit or wait?*
- *Which ART regimen would you recommend?*

DHHS Guidelines 2018
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Newest ARV's and ARV Trends

New ARV's

- Recently Approved by the FDA:
  - Bictegravir-TAF-emtricitabine (*Biktarvy*) - February 2018
  - Rilpivirine-dolutegravir (*Juluca*) – November 2017
  - Ibalizumab (*Trogarzo*) – March 2018

Bictegravir--Tenofovir Alafenamide-Emtricitabine (*Biktarvy)*
Single-Tablet Regimen

Biktarvy
[bik-TAR-vee]

Bictegravir-Tenofovir alafenamide-Emtricitabine

- INSTI
- NRTI
- NRTI

Summary of Phase 3 Studies
Bictegravir-Tenofovir alafenamide-Emtricitabine (*Biktarvy*)

- Phase 3 Trials in in Treatment Naïve Adults
  - 1489: Bictegravir-TAF-FTC versus Dolutegravir-ABC-3TC
  - 1490: Bictegravir-TAF-FTC versus Dolutegravir + TAF-FTC

- Phase 3 Trials in in Virologically Suppressed Adults
  - 1844: Switch to Bictegravir-TAF-FTC or continue Dolutegravir-ABC-3TC
  - 1878: Switch to Bictegravir-TAF-FTC or continue boosted PI + NRTIs
  - 1961: Switch to Bictegravir-TAF-FTC or continue boosted PI or boosted elvitegravir + NRTIs (trial in women)

Bictegravir-TAF-Emtricitabine (*Biktarvy*)
Indications

- BIKTARVY is indicated as a complete regimen for the treatment of HIV-1 infection in:

  1) Adults who have no ARV treatment history

  2) To replace the current ARV regimen if: virologically suppressed on a stable regimen for ≥3 months with no history of treatment failure and no known resistance to the individual components

Source: Biktarvy package insert, Gilead Sciences.

Bictegravir-TAF-Emtricitabine (*Biktarvy*)
Common Questions

- Food requirement? No
- Renal impairment? Ok with CrCl as low as 30 mL/min
- Effect on serum creatinine? Yes, maybe less than dolutegravir
- Tolerability? Similar to dolutegravir
- Interaction with cations? Yes
- Interaction with metformin? Yes, though less than dolutegravir
- Interaction with rifampin? Yes, contraindicated

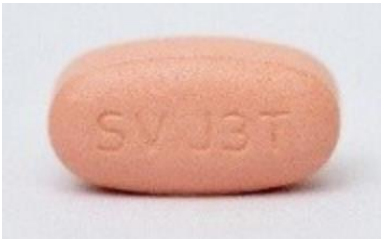
Biktarvy package insert.

Dolutegravir-Rilpivirine (*Juluca*)

FDA Approved Indication

Complete regimen to replace current ARV in those who are:

- Virologically suppressed (HIV-1 RNA <50 copies per mL)
- On a stable antiretroviral regimen for ≥6 months
- No history of treatment failure
- No known resistance to dolutegravir or rilpivirine



See Dr. Spach's ECHO talk:
11/30/17
www.hivecho.org

Source: *Juluca* Prescribing Information. ViiVhealthcare.com.

Other Trends in Antiretroviral Therapy

- Novel formulations and delivery systems in development
  - Injectables, implants, etc.
- Long-acting agents are coming
  - Oral and other formulations
- 2-drug ART for initial or maintenance therapy is promising
  - But not monotherapy – don't do it!

TAF implant
(betablog.org)

Phase I & II

MK-8591/EFdA
(NRTI)

Elsufavirine
(NNRTI)

Sifuvirtide
(Fusion inhibitor)

Cenicriviroc
(CCR5/CCR2 inhibitor)

VRC01
(Broadly neutralizing Ab)

GSK-3640254
(Maturation inhibitor)

GS-PI1
(Protease inhibitor)

GS-CA1
(Capsid inhibitor)

ABX464
(Rev inhibitor)

Late Phase (III & Beyond)

Oral

Cabotegravir
(INSTI)

*Doravirine
(NNRTI)

*DRV/c/TAF/FTC
(INSTI/NRTI's)

*Fostemsavir
(Attachment inhibitor)

DTG/3TC
(INSTI/NRTI)

Parenteral

Cabotegravir
(INSTI)

Rilpivirine-LA
(NNRTI)

Albuvirtide
(Fusion inhibitor)

PRO-140
(Monoclonal Ab/Entry inhibitor)

*FDA to review soon!

Adapted from: HIV Pipeline Report 2017 and other sources

Is Dual ART the Future?
Ongoing Trials (Selected List)

- **Initial ART**
  - Dolutegravir + 3TC (PADDLE, ACTG 5353, GEMINI)
  - Boosted darunavir + 3TC (ANDES)
  - Boosted darunavir + rilpivirine (PREZENT)

- **Maintenance ART**
  - Long-acting IM cabotegravir + rilpivirine (ATLAS, ATLAS-2M, FLAIR)
  - Boosted darunavir + dolutegravir (DUALIS)
  - Dolutegravir + rilpivirine (SWORD1&2)
  - Dolutegravir + 3TC (LAMIDOL, ASPIRE, TANGO)
  - Boosted darunavir + 3TC (DUAL GESIDA)

Source: clinicaltrials.gov

Update on Pre-Exposure Prophylaxis (PrEP)

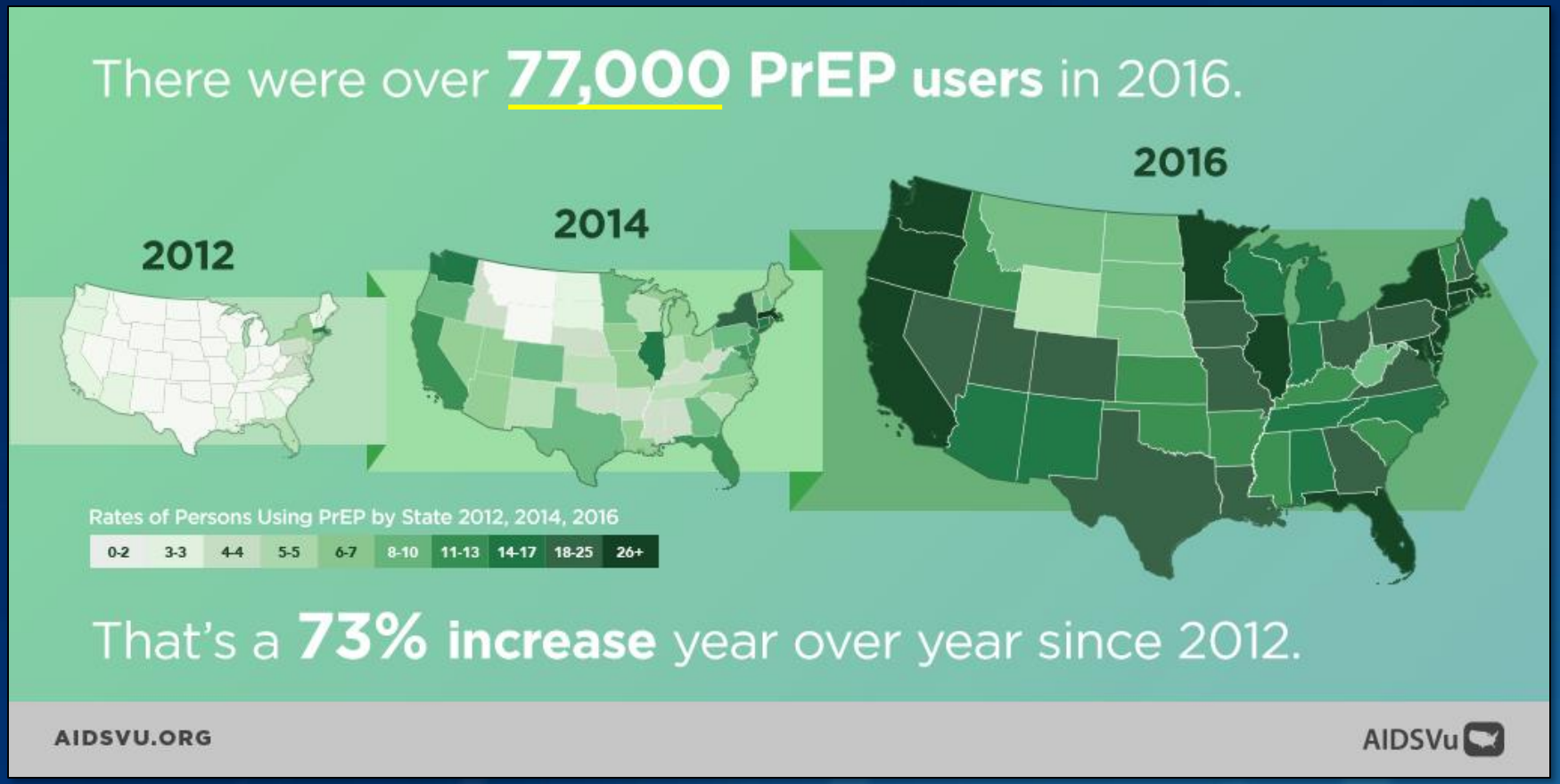
What is PrEP?

- A prevention strategy in which a **high-risk** individual takes a medication **regularly** (along with continued behavioral **risk-reduction** strategies) to prevent HIV infection
- Tenofovir-emtricitabine (*Truvada*) approved for HIV PrEP by the FDA in July 2012

www.nytimes.com

CDC PrEP Guidelines, 2017

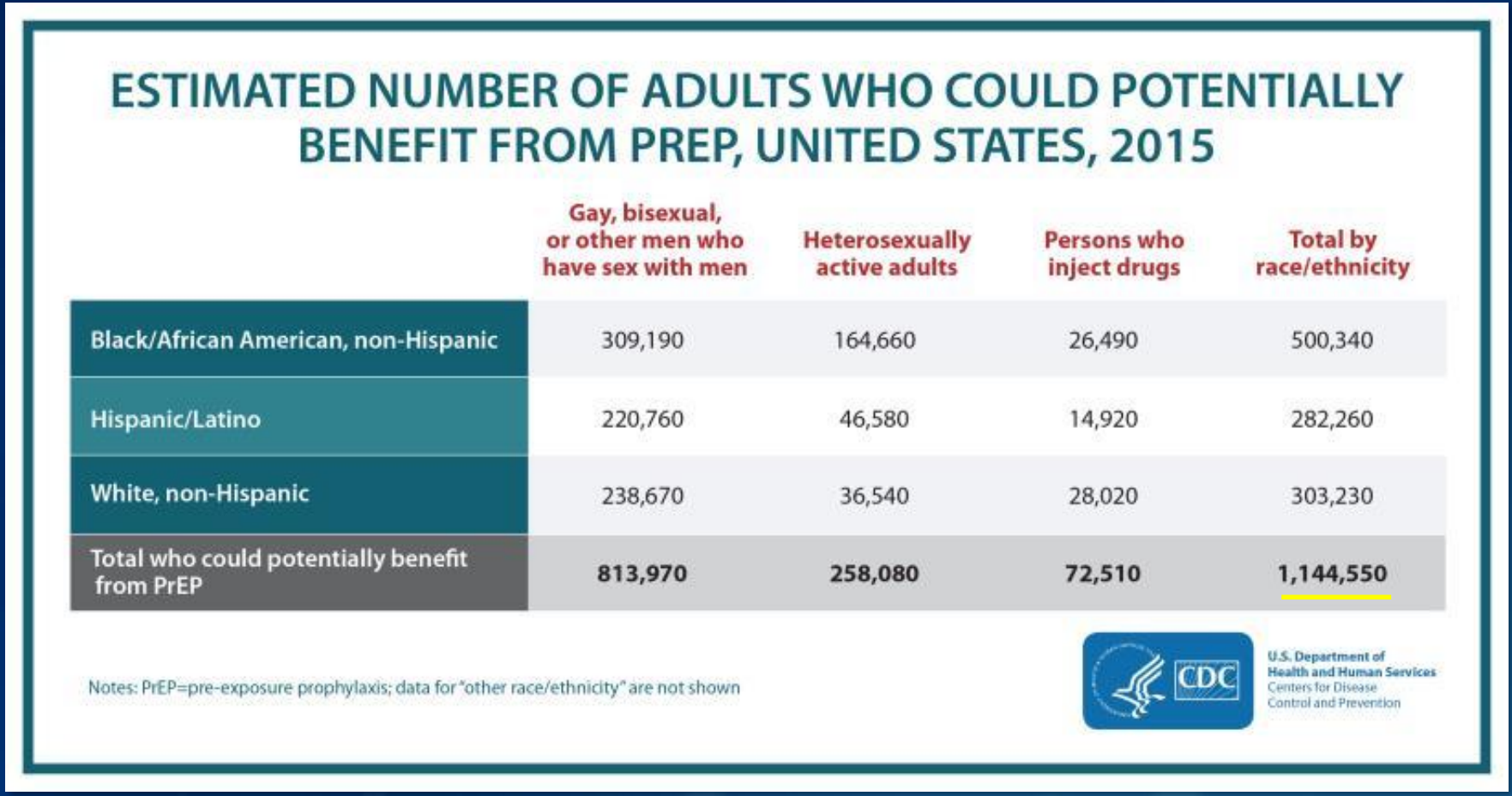
PrEP Uptake has Increased Dramatically



http://map.aidsvu.org/map

Slide courtesy of Dr. Christine Johnston

But PrEP is still underutilized…



ESTIMATED NUMBER OF ADULTS WHO COULD POTENTIALLY BENEFIT FROM PREP, UNITED STATES, 2015

	Gay, bisexual, or other men who have sex with men	Heterosexually active adults	Persons who inject drugs	Total by race/ethnicity
Black/African American, non-Hispanic	309,190	164,660	26,490	500,340
Hispanic/Latino	220,760	46,580	14,920	282,260
White, non-Hispanic	238,670	36,540	28,020	303,230
Total who could potentially benefit from PrEP	**813,970**	**258,080**	**72,510**	**1,144,550**

Notes: PrEP=pre-exposure prophylaxis; data for "other race/ethnicity" are not shown

CDC

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Smith et al, CROI 2018

Slide Courtesy of Dr. Christine Johnston

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PrEP efficacy and future directions

Pill

Gel

Vaginal film

Vaginal ring

Injectable

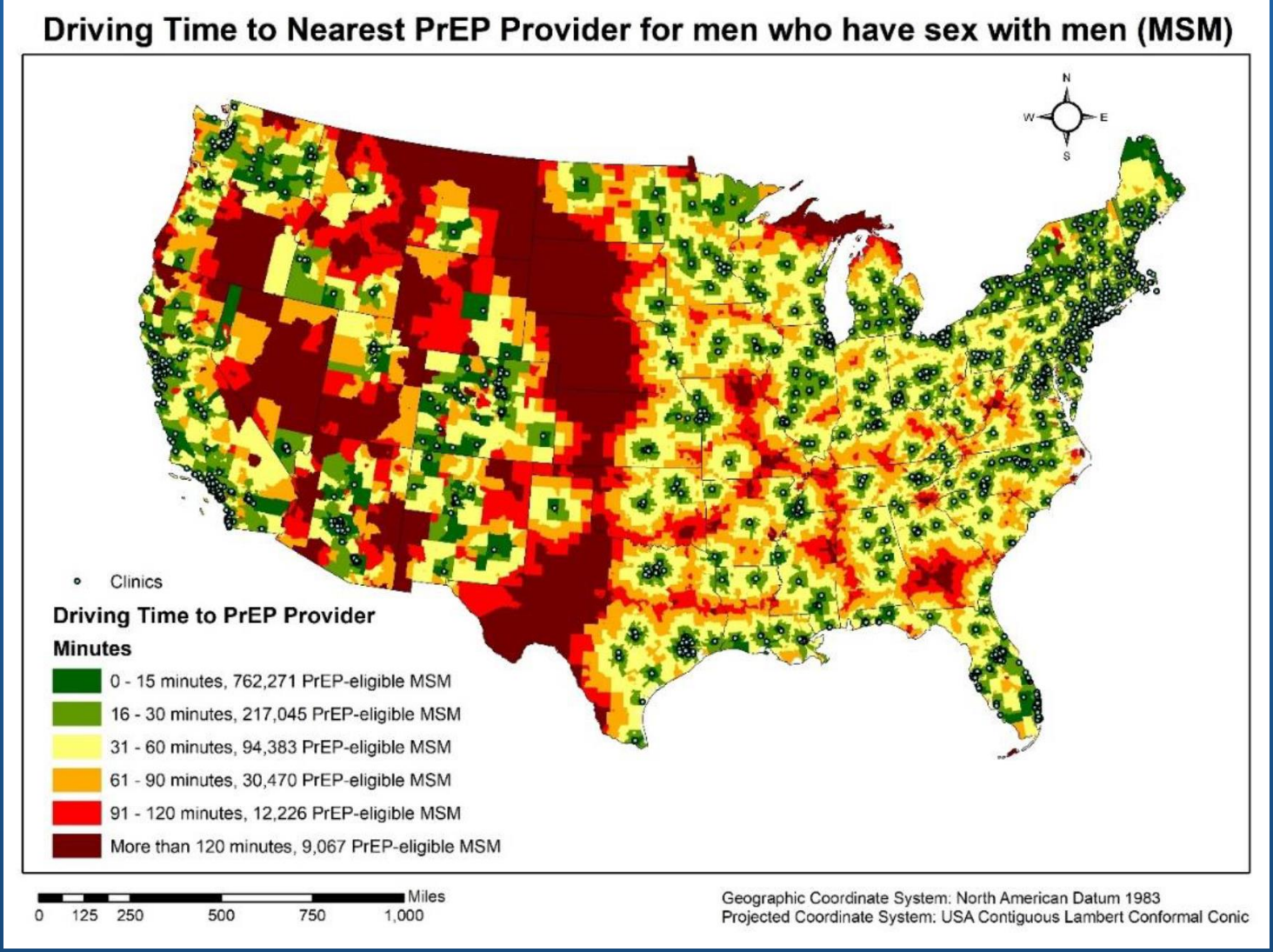
Number needed to treat (NNT) to prevent one case of HIV: **13-60**.[1]

An estimated **33%** of HIV infections in MSM would be prevented over 10 years with 40% uptake and 60% adherent.[2]

*One thing that is needed around the world = prevention **options**.*

Sources: 1. Grant, oral abstract TUAC0104 (IAS Conference 2016).
2. Jenness SM et al. J Infect Dis. 2016;14(12):1800-7.

PrEP “Deserts” in the U.S.



Source: Weiss K et al. CROI 2018.

Barriers to PrEP in the U.S. and Innovative Solutions

- Barriers
  - Cost/access, stigma, provider awareness and willingness to prescribe, awareness of at-risk individuals and willingness to ask, adherence
- Innovative solutions
  - Pharmacist-delivered PrEP, telemedicine visits, access through apps or websites, text message adherence support
  - Examples: Kelley Ross Pharmacy (Seattle), PrEPTECH (SF), PrEP Iowa, nurx.com, plushcare.com, etc.

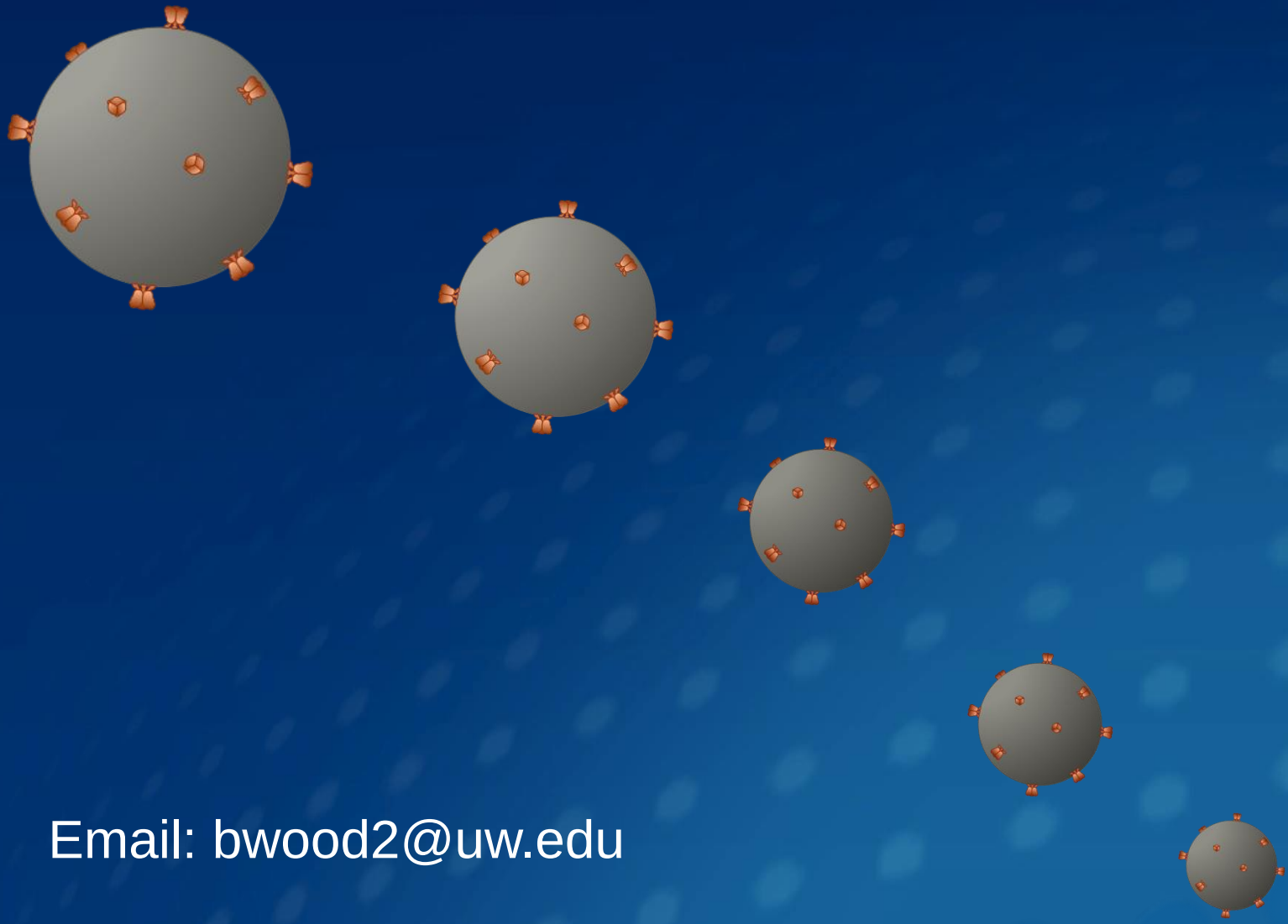
Other Notable Changes and Progress

- New vaccines and vaccine recommendations
- New data on abacavir and cardiovascular risk
- High risk of HIV in late pregnancy and post-partum
- Integrase inhibitors may cause weight gain
- Generic formulations of TDF approved
- Transplants from donors with HIV (or hep C)
- Doxycycline as PEP (or PrEP) can prevent bacterial STI's
- Promising cure study presented (but much more needed)

Summary

- There has been substantial progress towards HIV prevention and control in recent years
- With early ART for all and improved ART options, incidence is finally decreasing & people living near-normal lifespans
- Significant disparities remain, with many individuals undiagnosed or diagnosed late, certain groups still at elevated risk, PrEP underutilized, and stigma a huge issue
- What will it take to “Get to Zero?” Expanded testing, improved linkage and retention, dissemination of PrEP, improved adherence – talking about risk is key

Questions



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