



# AHCCCS Pharmacy and Therapeutics Committee

16 January 2018



# Introductions & Minutes Approval

- Dr. Sara Salek, CMO, AHCCCS
  - Meeting Minutes 12 October 2017
  - Review
  - Approve or Amend

# P&T Operational Policy Overview

- Dr. Sara Salek, CMO, AHCCCS



# HIV/PrEP Presentation

- Dr. Ann Khalsa
  - Conflict of Interest Disclosure
    - Dr. Khalsa has financial interest, affiliation or is employed by organizations that may have a direct interest in the business before the AHCCCS P&T committee as follows:
      - ❑ Janssen Therapeutics – speaker
      - ❑ ViiV Therapeutics- Advisory Board
      - ❑ Thera Technologies- Speaker, Advisory Board
      - ❑ Gilead Sciences- Speaker, Advisory Board, Research

# HIV Treatment & Prevention Overview in 2018

**Ann Khalsa, MD, AAHIVS**

Medical Director

McDowell Health Care Center



# Goals of HIV Treatment

**1980s:**

Prevent AIDS deaths

**1990s:**

Control viral replication

**2000s:**

Prevent resistance

Decrease drug side effects

Decrease pill burden

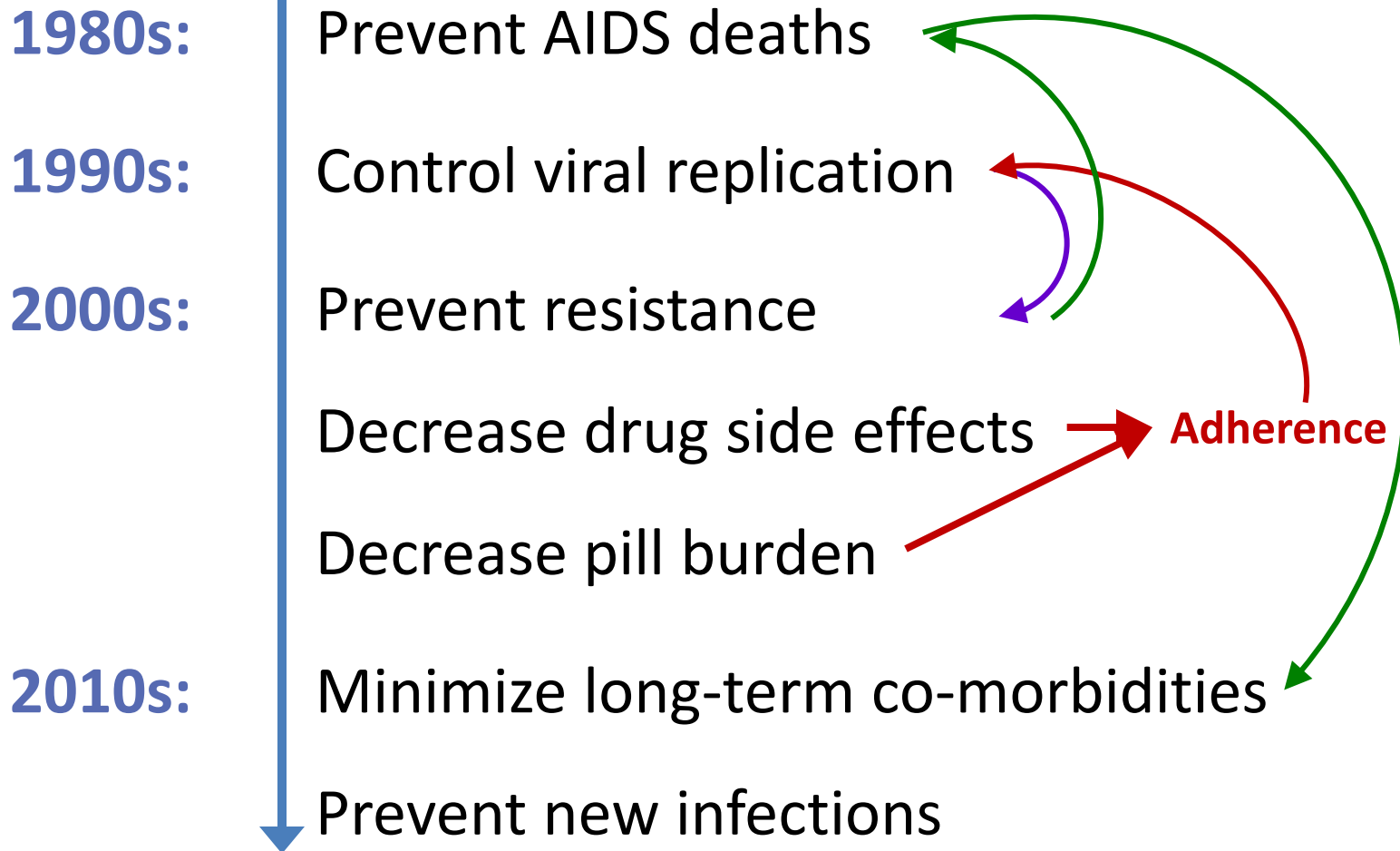
**2010s:**

Minimize long-term co-morbidities

Prevent new infections



# Goals of HIV Treatment



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**2010s:**

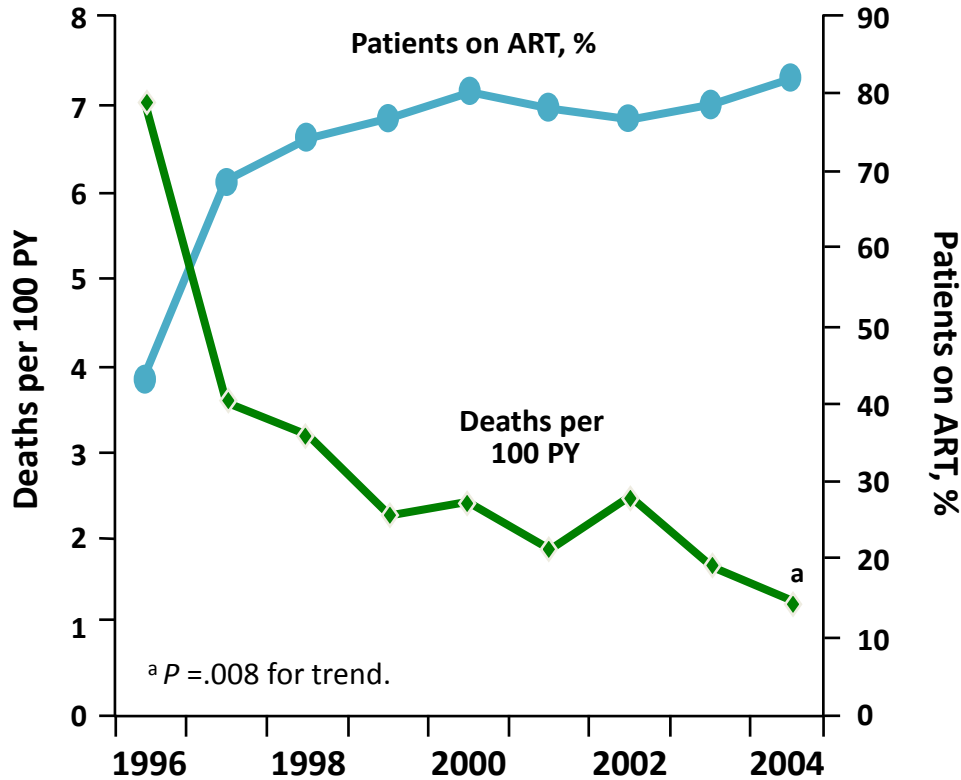
Minimize long-term co-morbidities

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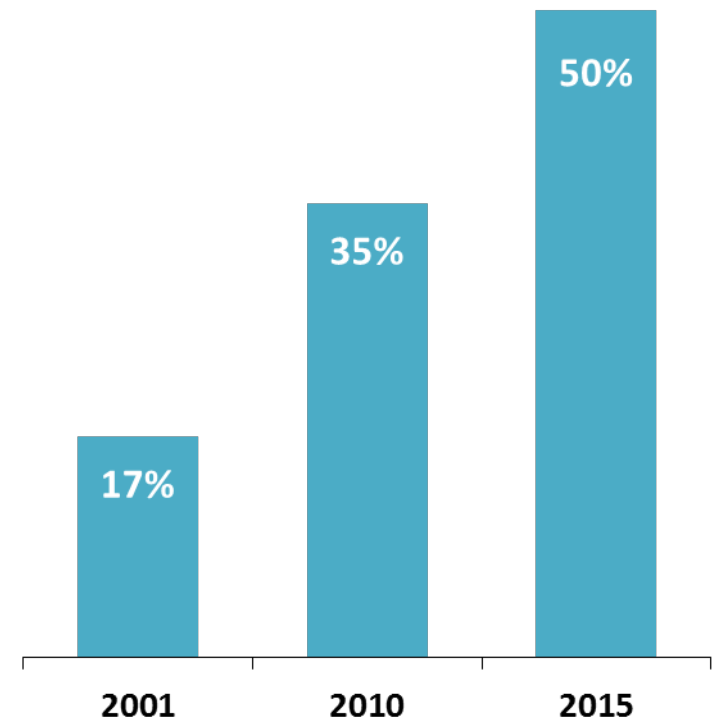


# HIV-Positive Patients Living Longer

## Declining death rates on ART



## Increasing Prevalence >50 YO



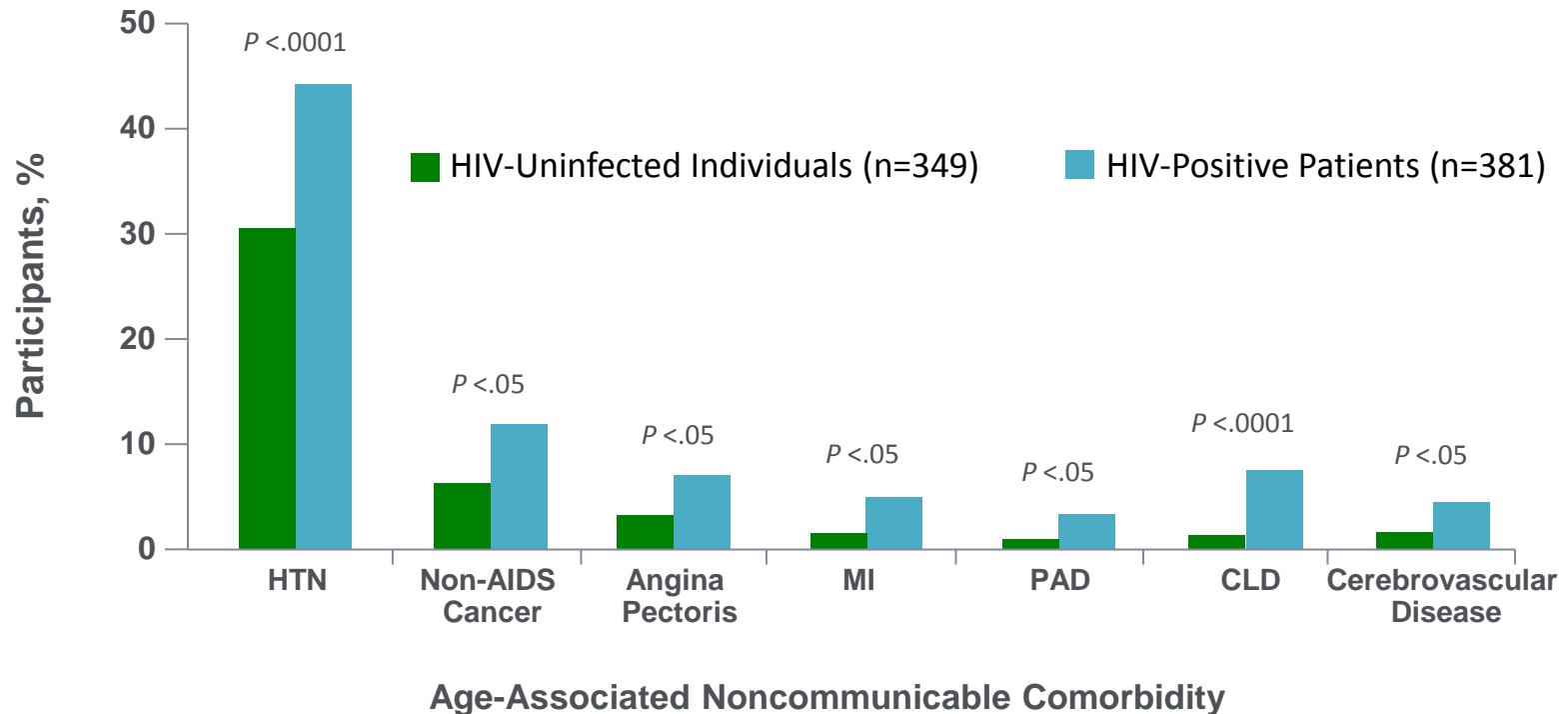
- In the United States, a 20-year-old HIV-positive patient can now expect to live into his/her early 70s<sup>5</sup>

ART, antiretroviral therapy; PY, person years.

<sup>1</sup> Palella FJ, et al. *J Acquir Immune Defic Syndr*. 2006;43:27-34; <sup>2</sup> Centers for Disease Control and Prevention (CDC). *HIV/AIDS Surveillance Report: Cases of HIV Infection and AIDS in the United States and Dependent Areas*. 2005; <sup>3</sup> CDC. *Diagnoses of HIV Infection in the United States and Dependent Areas*. 2011; <sup>4</sup> Effros RB, et al. *Clin Infect Dis*. 2008;47:542-553; <sup>5</sup> Samji H, et al. *PLoS ONE* 2013; 8:e81355.

# Comorbidities More Prevalent In HIV+ Persons

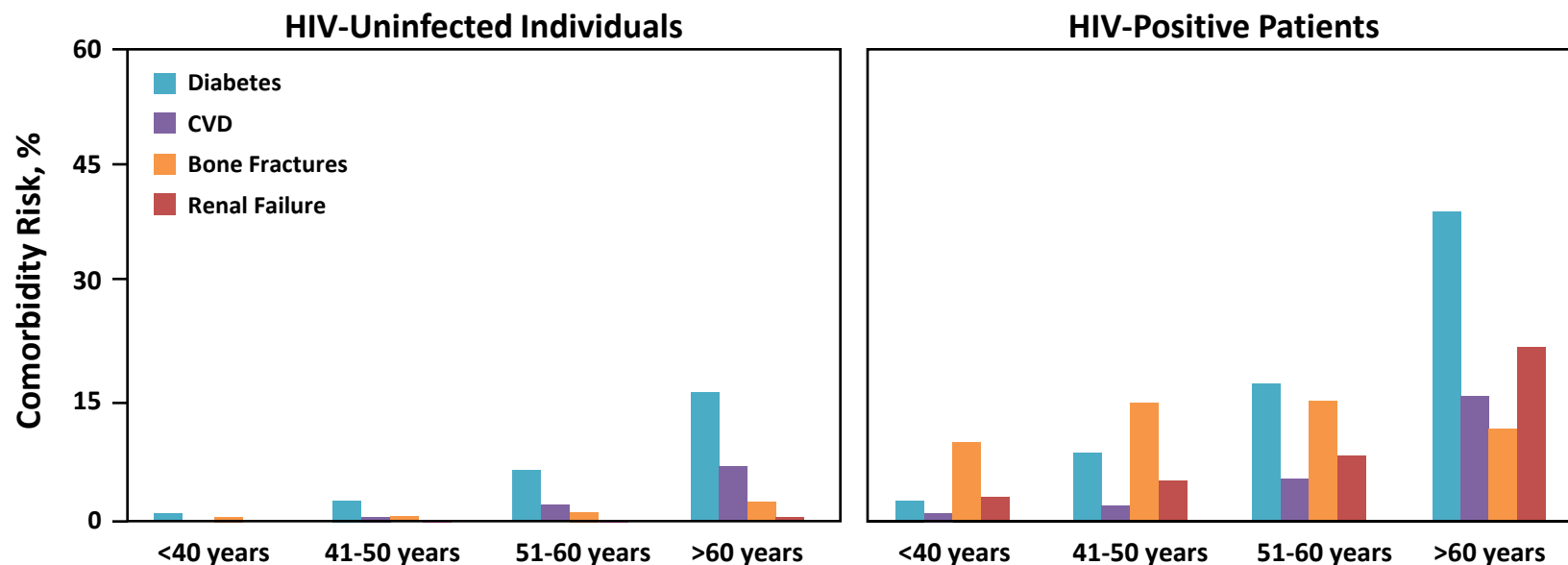
Subjects  $\geq 45$  Years With Age-Associated Noncommunicable Comorbidities  
AGE<sub>h</sub>IV Study, 2010-2012)<sup>2</sup>



- Similarities between aging and the courses of HIV and AIDS suggest that HIV infection may compress certain aging processes, thereby accelerating comorbidities and frailty<sup>1</sup>
- Duration of ART use (OR 1.24 per 5 additional years of ART use) and lower nadir CD4 cell count (OR 1.12 per 100 fewer cells) were associated with an increased risk of a higher number of comorbidities

# Comorbidities Earlier & Increased In HIV+

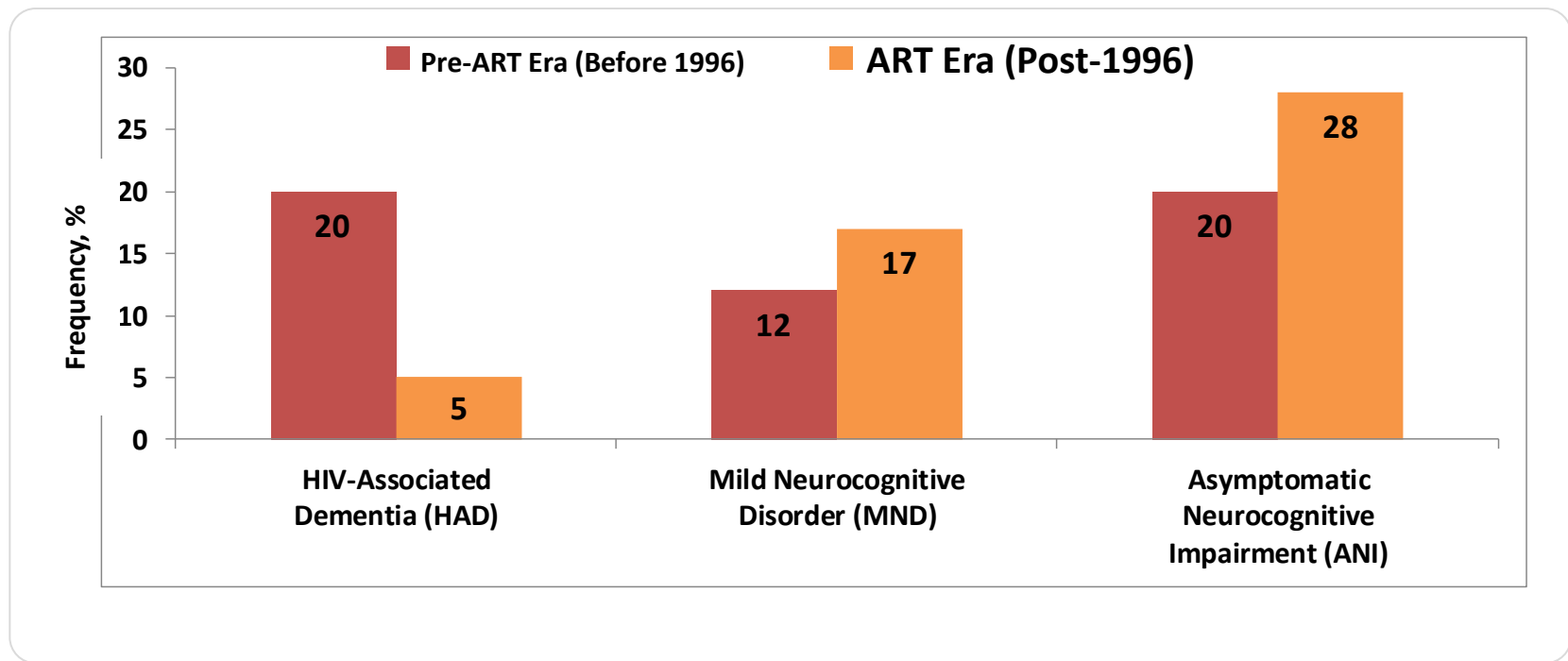
Prevalence of Noninfectious Comorbidities in a Cohort of 2854 HIV-Positive Patients and 8562 HIV-Uninfected Individuals, by HIV Serostatus and Age, 2009<sup>1</sup>



- HIV-positive patients are more susceptible to developing CVD, bone fractures, and renal failure than HIV-uninfected individuals<sup>2</sup>
- These comorbidities often develop earlier in HIV-positive patients<sup>2</sup>

# Increasing Rates of Neurocognitive Impairment

- HAND is the result of neural damage caused by HIV replication and immune activation<sup>1</sup>
- HAND is fairly prevalent, even in patients with low viral loads and high CD4 cell counts<sup>2</sup>
- Rapid initiation of ART can arrest and sometimes reverse severe HAND, but milder forms of cognitive impairment persist because they are more difficult to identify and treat<sup>2,3</sup>



HAND, HIV-associated neurocognitive disorders.

<sup>1</sup> Letendre S. *Top Antivir Med.* 2011;19:137-142; <sup>2</sup> McArthur JC, et al. *Ann Neurol.* 2010;67:699-714. <sup>3</sup> New York State Department of Health AIDS Institute. *Cognitive disorders and HIV/AIDS: HIV-associated dementia and delirium.* 2007.

## Recommended Initial Regimens for Most People with HIV

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.

### INSTI + 2 NRTIs:

- DTG + ABC/3TC<sup>a</sup> (AI)—if HLA-B\*5701 negative
- DTG + tenofovir<sup>b</sup>/FTC<sup>a</sup> (AI for both TAF/FTC and TDF/FTC)
- EVG/c/tenofovir<sup>b</sup>/FTC (AI for both TAF/FTC and TDF/FTC)
- RAL<sup>c</sup> + tenofovir<sup>b</sup>/FTC<sup>a</sup> (AI for TDF/FTC, All for TAF/FTC)

## Recommended Initial Regimens in Certain Clinical Situations

These regimens are effective and tolerable, but have some disadvantages when compared with the regimens listed above, or have less supporting data from randomized clinical trials. However, in certain clinical situations, one of these regimens may be preferred (see [Table 7](#) for examples).

### Boosted PI + 2 NRTIs: (In general, boosted DRV is preferred over boosted ATV)

- (DRV/c or DRV/r) + tenofovir<sup>b</sup>/FTC<sup>a</sup> (AI for DRV/r and All for DRV/c)
- (ATV/c or ATV/r) + tenofovir<sup>b</sup>/FTC<sup>a</sup> (BI)
- (DRV/c or DRV/r) + ABC/3TC<sup>a</sup> —if HLA-B\*5701–negative (BI)
- (ATV/c or ATV/r) + ABC/3TC<sup>a</sup> —if HLA-B\*5701–negative and HIV RNA <100,000 copies/mL (CI for ATV/r and CIII for ATV/c)

### NNRTI + 2 NRTIs:

- EFV + tenofovir<sup>b</sup>/FTC<sup>a</sup> (BI for EFV/TDF/FTC and BII for EFV + TAF/FTC)
- RPV/tenofovir<sup>b</sup>/FTC<sup>a</sup> (BI)—if HIV RNA <100,000 copies/mL and CD4 >200 cells/mm<sup>3</sup>

### INSTI + 2 NRTIs:

- RAL<sup>c</sup> + ABC/3TC<sup>a</sup> (CII)—if HLA-B\*5701–negative and HIV RNA < 100,000 copies/mL

### Regimens to Consider when ABC, TAF, and TDF Cannot be Used:<sup>d</sup>

- DRV/r + RAL (BID) (CI)—if HIV RNA <100,000 copies/mL and CD4 >200 cells/mm<sup>3</sup>
- LPV/r + 3TC<sup>a</sup> (BID)<sup>e</sup> (CI)

<sup>a</sup> 3TC may be substituted for FTC, or vice versa, if a non–fixed-dose NRTI combination is desired.

<sup>b</sup> TAF and TDF are two forms of tenofovir approved by the FDA. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

<sup>c</sup> RAL can be given as 400 mg BID or 1200 mg (two 600-mg tablets) once daily.

<sup>d</sup> Several other NRTI-limiting treatment strategies are under investigation. See the section titled Selected Strategies That Are Under Evaluation and Not Yet Recommended below for discussion regarding these regimens.

<sup>e</sup> LPV/r plus 3TC is the only boosted PI plus 3TC regimen with published 48-week data in a randomized controlled trial in ART-naïve patients. Limitations of LPV/r plus 3TC include twice-daily dosing, high pill burden, and greater rates of gastrointestinal side effects than other PIs.

## US DHHS ARV Guidelines 10/17/17 Update

### Regimen:

**2-NRTI + 3<sup>rd</sup> Rx:**

### Agents:

- **NRTI: TFV >ABC**

**TFV: TAF >TDF**

- **3<sup>rd</sup> Rx: INSTI pref'd**

**PI: DRV, ± ATV**

**NN: ± EVF or RPV**

[https://aidsinfo.nih.gov/contentfiles/lvguidelines/AA\\_Tables.pdf](https://aidsinfo.nih.gov/contentfiles/lvguidelines/AA_Tables.pdf)  
Table 7 - 1/8/2018.

# DHHS ART Guidelines - Prescribing Considerations

ISSUE	NOT TO USE	PREFERRED
Adherence*	Multi-tab Rx	STR: Triumeq (DTG-ABC), Odefsey/Complera (RPV), Genvoya/Stribild (EVG/c), Atripla (EFV), BIC-F/TAF, DRV/c-F/TAF
Food Req	All except	EFV, DTG, RAL, BIC-F/TAF
PPI Use	RPV, ATV	
Risk Resist*	EFV, RPV, RAL, EVG, ABC	DTG, BIC, DRV, TFV
CKD	TDF, ATV	TAF
CVD	ABC, LPV/r, DRV	DTG, BIC, RAL, RPV
↑QTc	EFV, RPV	
HLD	PI-r/c, EVG/c, EFV	
Osteopor.	TDF	TAF or ABC
Dementia	EFV	DTG, DRV
Psych.Dx	EFV, RPV, +/- INSTI	
HBV		TAF/TDF + 3TC/FTC
CD4 <200	RPV, DRV-RAL (2-Rx)	3-Rx
VL >100K	RPV, EFV-EPZ, ATV-EPZ, DRV-RAL (2Rx)	3-Rx

ARV Classes: Nuc RT Inh, NonNuc RT Inh, Protease Inh, Integrase Inh

# Pt Example: 55yo w/ HTN, CKD, HLD, GERD

ISSUE	NOT TO USE	PREFERRED
<b>Adherence*</b>	<b>Multi-tab Rx</b>	<b>STR:</b> Triumeq (DTG-ABC), Odefsey/Complera (RPV), Genvoya/Stribild (EVG/c), Atripla (EFV), <b>BIC-F/TAF</b> , <b>DRVc-F/TAF</b>
Food Req	All except	EFV, DTG, RAL, BIC-F/TAF
<b>PPI Use</b>	<b>RPV, ATV</b>	
<b>Risk Resist*</b>	<b>EFV, RPV, RAL, EVG, ABC</b>	<b>DTG, BIC, DRV, TFV</b>
<b>CKD</b>	<b>TDF, ATV</b>	<b>TAF</b>
<b>CVD</b>	<b>ABC, LPV/r, DRV</b>	<b>DTG, BIC, RAL, RPV</b>
↑QTc	EFV, RPV	
<b>HLD</b>	<b>PI-r/c, EVG/c, EFV</b>	
<i>Osteopor.</i>	<b>TDF</b>	<b>TAF or ABC</b>
Dementia	EFV	DTG, DRV
Psych.Dx	EFV, RPV, +/- INSTI	
HBV		TAF/TDF + 3TC/FTC
CD4 <200	RPV, DRV-RAL (2-Rx)	3-Rx
VL >100K	RPV, EFV-EPZ, ATV-EPZ, DRV-RAL (2Rx)	3-Rx

**TAF-FTC  
+ INSTI (DTG, BIC)**

ARV Classes: Nuc RT Inh, NonNuc RT Inh, Protease Inh, Integrase Inh

# ARV Regimen Switching After VL Suppression

- Switch Reasons:
  - Simplify regimen by ↓ pill burden &/or dosing frequency
  - Improve tolerability and ↓ short- or long-term toxicity
  - Prevent or mitigate drug-drug interactions
  - Eliminate food or fluid requirements
  - Optimize ARV safety during pregnancy
- Switch Strategies:
  - Account for any possible archived or transmitted resistance
  - Within class for tolerability (e.g. EFV → RPV, TDF → TAF) or co-formulation availability (e.g. DRV-rtv → DRV/cobi)
  - Between Class (e.g. PI or NNRTI → INSTI)
  - NEW 2-RX MAINTENANCE:
    - 3TC + Boosted PI , or 3TC/FTC + INSTI
    - INSTI + NNRTI: “Juluca” (DTG + RPV)
    - Boosted PI + INSTI (e.g. DRV + RAL)



# Rapid Initiation of ART (“fast start”)

**At the IAS 2017 conference, the World Health Organization (WHO) launched guidelines on management of advanced HIV disease and rapid initiation of ART<sup>1</sup>**

All people living with HIV should be offered rapid initiation of ART ( $\leq 7$  days of a positive HIV diagnosis)

ART initiation should be offered on the same day for people who are ready to start

- A UK pilot study assessed the acceptability and feasibility for rapid initiation of ART in 149 newly diagnosed HIV patients during the period July 2016-Jan 2017<sup>2</sup>
- Of 136 patients attending their first scheduled Dr appointment, 78% (106/136) started ART at that visit, with 29% (31/106) initiating ART within 2 days of diagnosis

## UK Pilot Study<sup>2</sup>: Rapid Initiation of ART After HIV Diagnosis

Median Time (IQR)	Standard of Care*	Pilot Study	P-value
HIV diagnosis to 1 <sup>st</sup> Dr appointment	16 days (14-21)	6 days (2-12)	<0.05
HIV diagnosis to ART initiation	26 days (16-55)	7 days (3-16)	<0.05

\*From May-Sept 2015. Standard time from HIV diagnosis to 1<sup>st</sup> Dr appointment was targeted at 2 weeks

**This pilot study demonstrated that rapid ART initiation is acceptable and deliverable for patients with newly diagnosed HIV**

# Goals of HIV Treatment

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Prevent AIDS deaths

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Control viral replication

**2000s:**

Prevent resistance

Decrease drug side effects

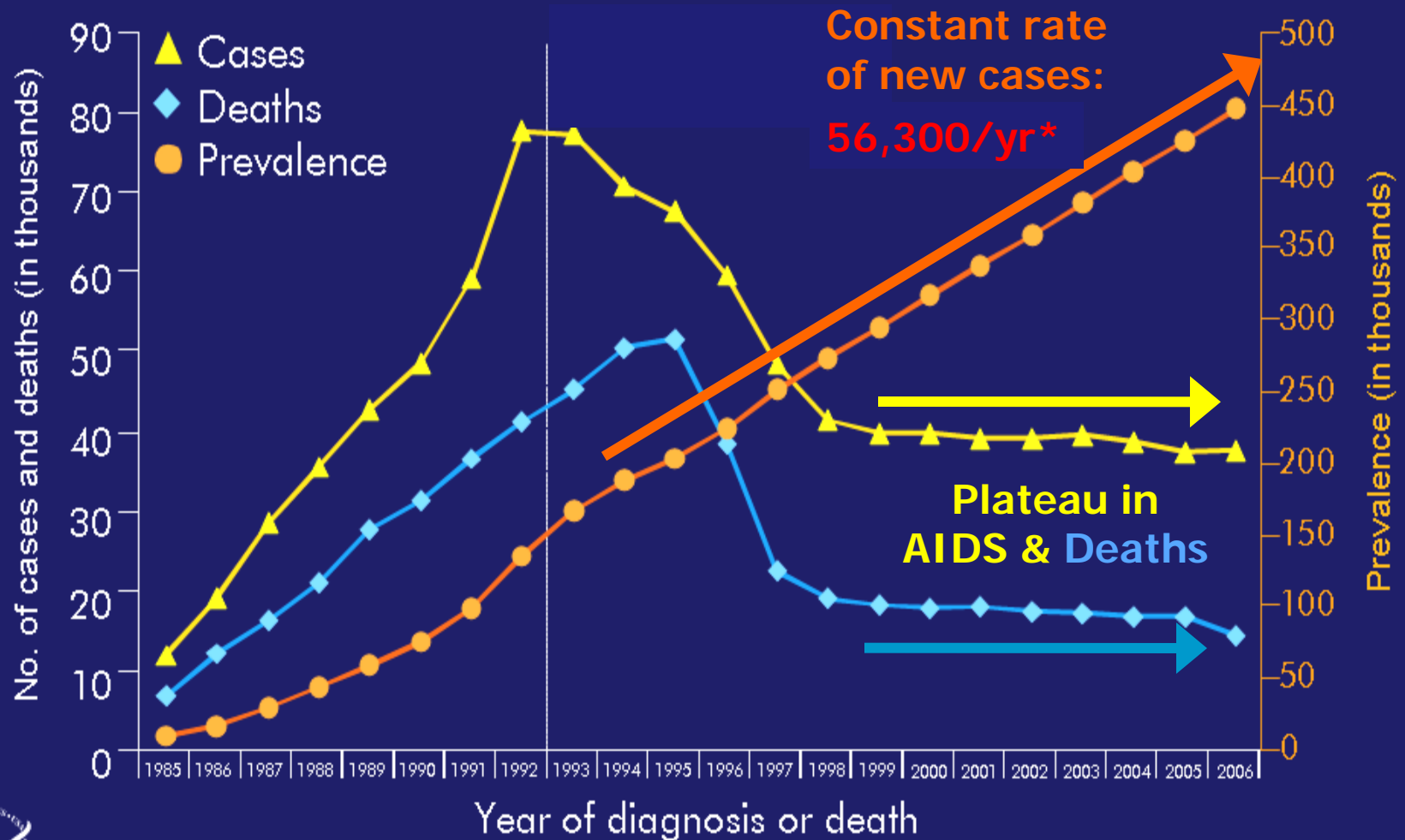
Decrease pill burden

**2010s:**

Minimize long-term co-morbidities

Prevent new infections

# Continued Expansion of HIV Epidemic



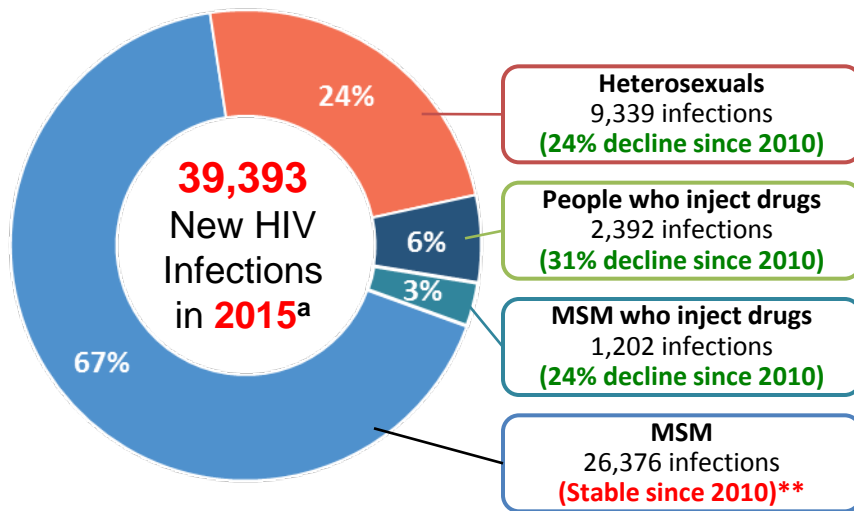
Note. Data have been adjusted for reporting delays.

\* CDC August 2008: Revised calculation from ID of recent vs long-standing infections on remnant specimens: Hall HI, et al. JAMA 2008;300:520-529.

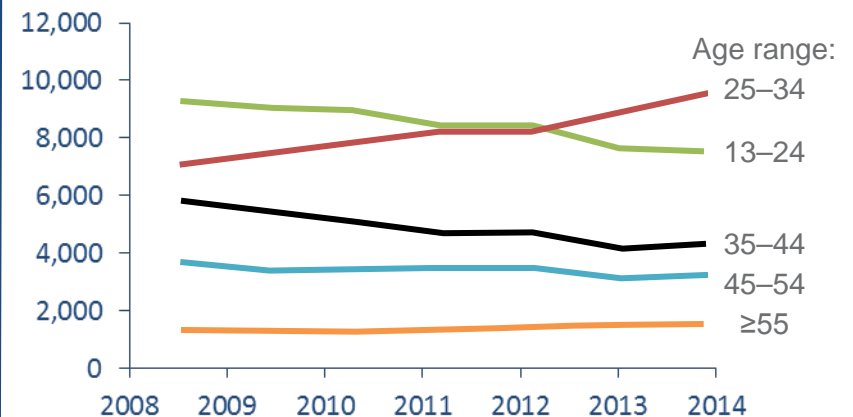


# Uneven Progress in Reducing New HIV Infections

New HIV Infections, by Transmission Category, United States, 2015<sup>1</sup>



Estimated HIV Incidence Among MSM, by Age, United States, 2008–2014<sup>2,3</sup>



- Total new HIV infections declined 10% in the US from 2010 to 2015<sup>1</sup>
- \*\* MSM were the only group that did not experience an overall decline from 2010 to 2015<sup>1</sup>

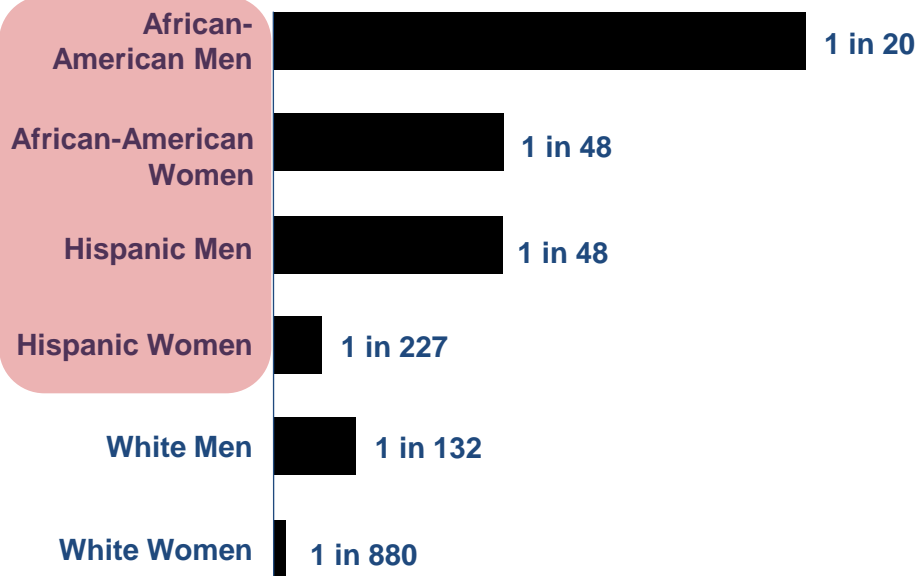
1. Centers for Disease Control and Prevention. HIV Surveillance Report, 2015; vol. 27.

2. Singh S, et al. CROI 2017. Seattle, WA. #30.

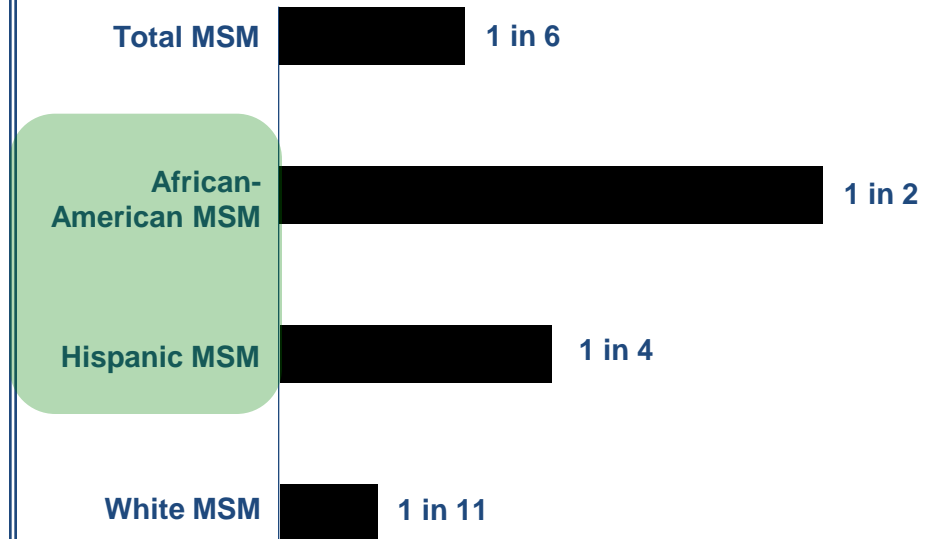
3. Adapted from CDC at [https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/hiv-incidence-fact-sheet\\_508.pdf](https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/hiv-incidence-fact-sheet_508.pdf). Accessed May 2017.

# Lifetime Risk of HIV Diagnosis: Increased for Minorities & MSM

Lifetime Risk of  
HIV Diagnosis by Race/Ethnicity<sup>1</sup>



Lifetime Risk of HIV Diagnosis Among  
MSM by Race/Ethnicity<sup>1</sup>



1. Hess K, et al. CROI 2016. Boston, MA. #52. Adapted from CDC at <https://www.cdc.gov/nchhstp/newsroom/2016/croi-2016.html#Graphics2>. Accessed May 2017; 2. White House Office of National AIDS Policy. National HIV/AIDS Strategy for the United States: Updated to 2020. 2015. Available at: <https://www.aids.gov/federal-resources/national-hiv-aids-strategy/nhas-update.pdf>. Accessed May 2017.

# HIV Prevalence Rates in AZ, 2014

## by Race / Ethnicity



The rate of black males living with an HIV diagnosis is 2.5 times that of white males.



The rate of Hispanic/Latino males living with an HIV diagnosis is 1.2 times that of white males.

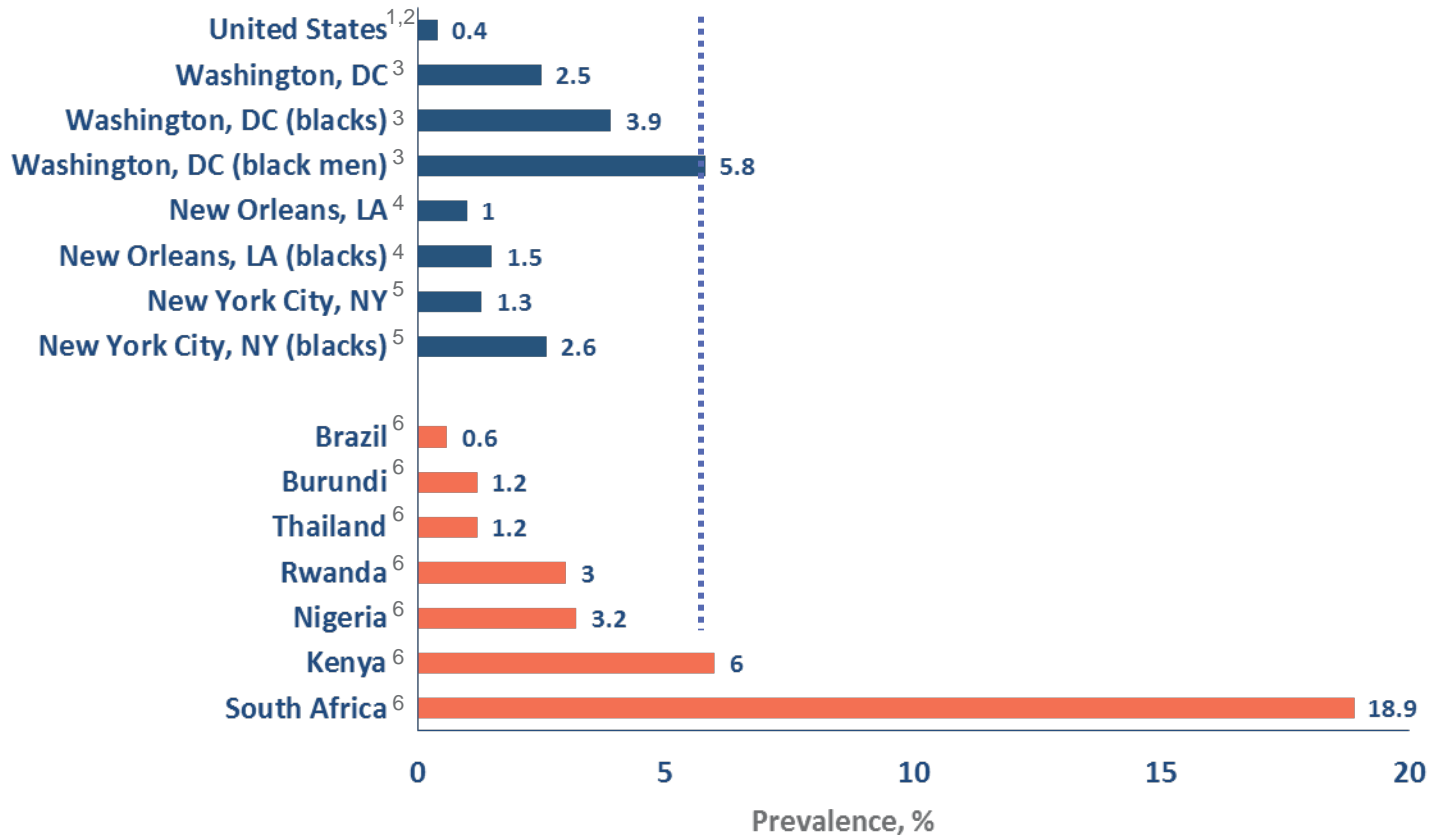


The rate of black females living with an HIV diagnosis is 11.3 times that of white females.



The rate of Hispanic/Latina females living with an HIV diagnosis is 1.5 times that of white females.

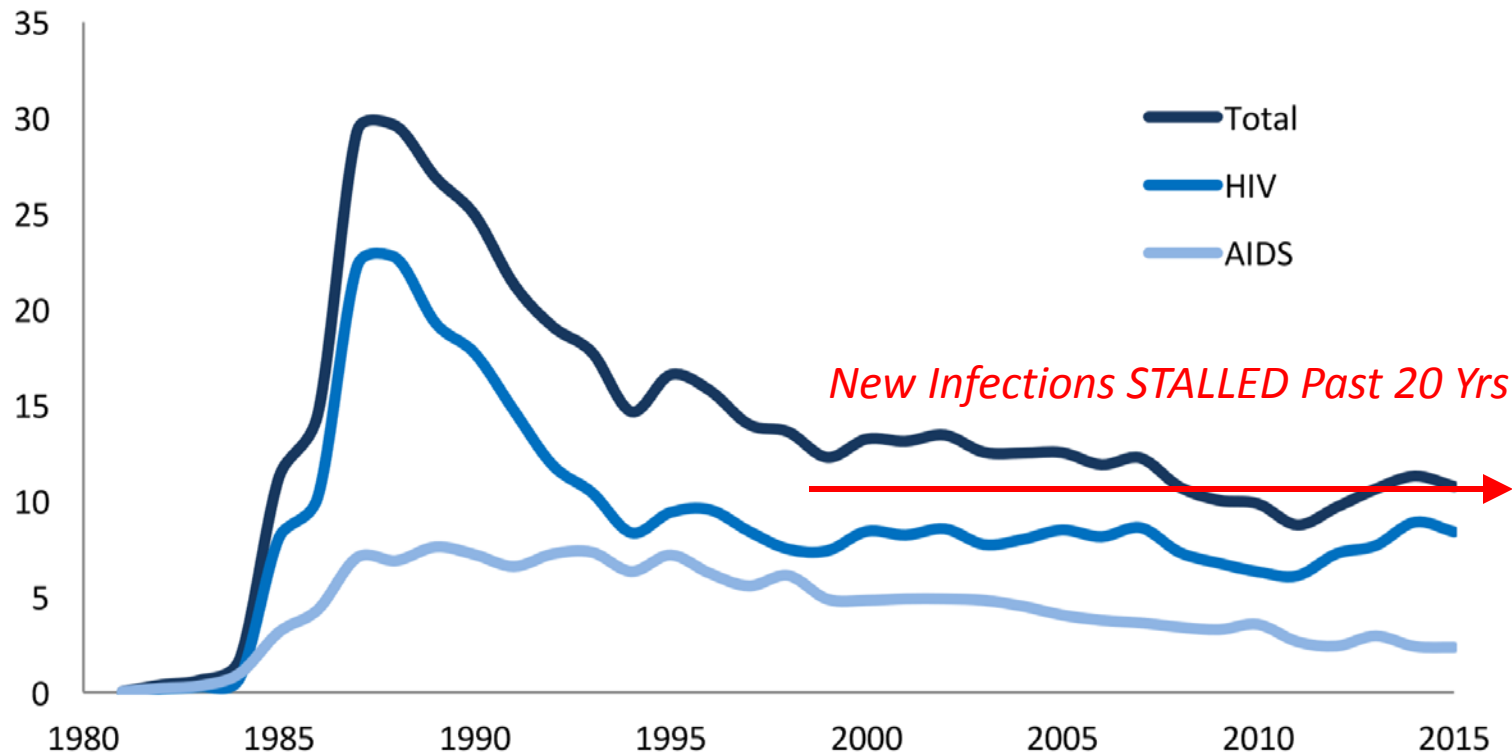
# HIV Prevalence in Certain US Populations Higher Than Some High Prevalence Nations



1. Centers for Disease Control and Prevention. HIV Surveillance Report, 2014; vol. 26. <http://www.cdc.gov/hiv/library/reports/surveillance/>. Published November 2015. Accessed May 2017; 2. U.S. Census Bureau. Population estimates. <http://www.census.gov/programs-surveys/popest/data/data-sets.2013.html>. Accessed May 2017; 3. Annual Epidemiology and Surveillance Reports for the District of Columbia. HIV/AIDS, Hepatitis, STD and TB Administration (HAHSTA) Annual Report 2014; 4. AIDSVu. <https://aidsvu.org/state/louisiana/new-orleans/>. Accessed May 2017; 5. AIDSVu. <https://aidsvu.org/state/new-york/new-york-city/>. Accessed May 2017; 6. Prevalence of HIV, World Bank Group. <http://data.worldbank.org/indicator/SH.DYN.AIDS.ZS>. Accessed May 2017.

# Arizona's HIV/AIDS Epidemic Overview

Figure 1: Arizona HIV/AIDS incidence rate per 100,000, 1980-2015

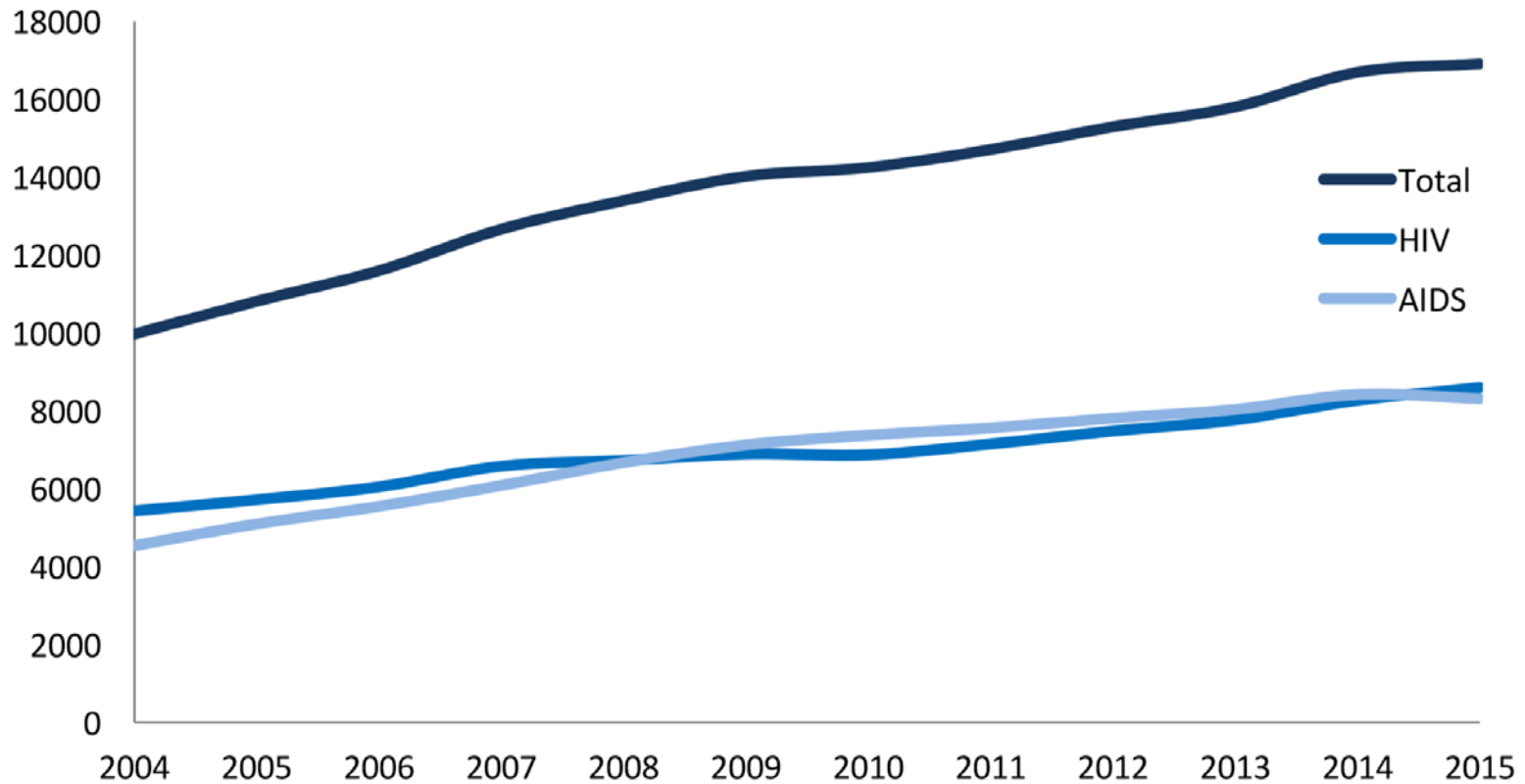


HIV/AIDS rates declined through the 1990s. By 1999, the rate was 51% lower than in 1990. The rate for 2015 (10.74 per 100,000) is slightly lower than 2014 (11.29 per 100,000).



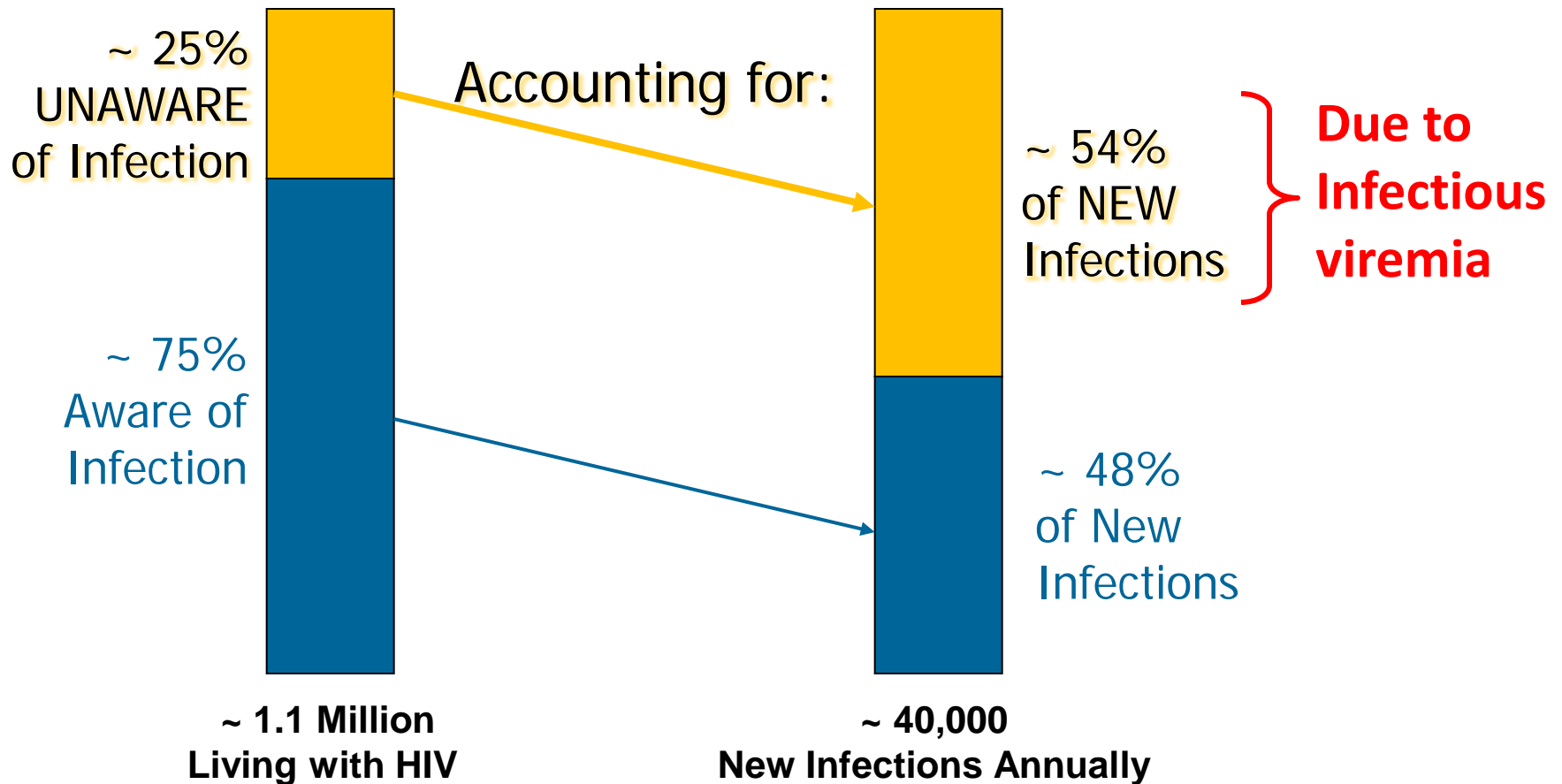
# Arizona's HIV/AIDS Epidemic Overview

Figure 2: Arizona HIV/AIDS prevalence counts, 2004-2015



# HIV Awareness & Transmission:

## Opportunity to Prevent Unknown Transmission

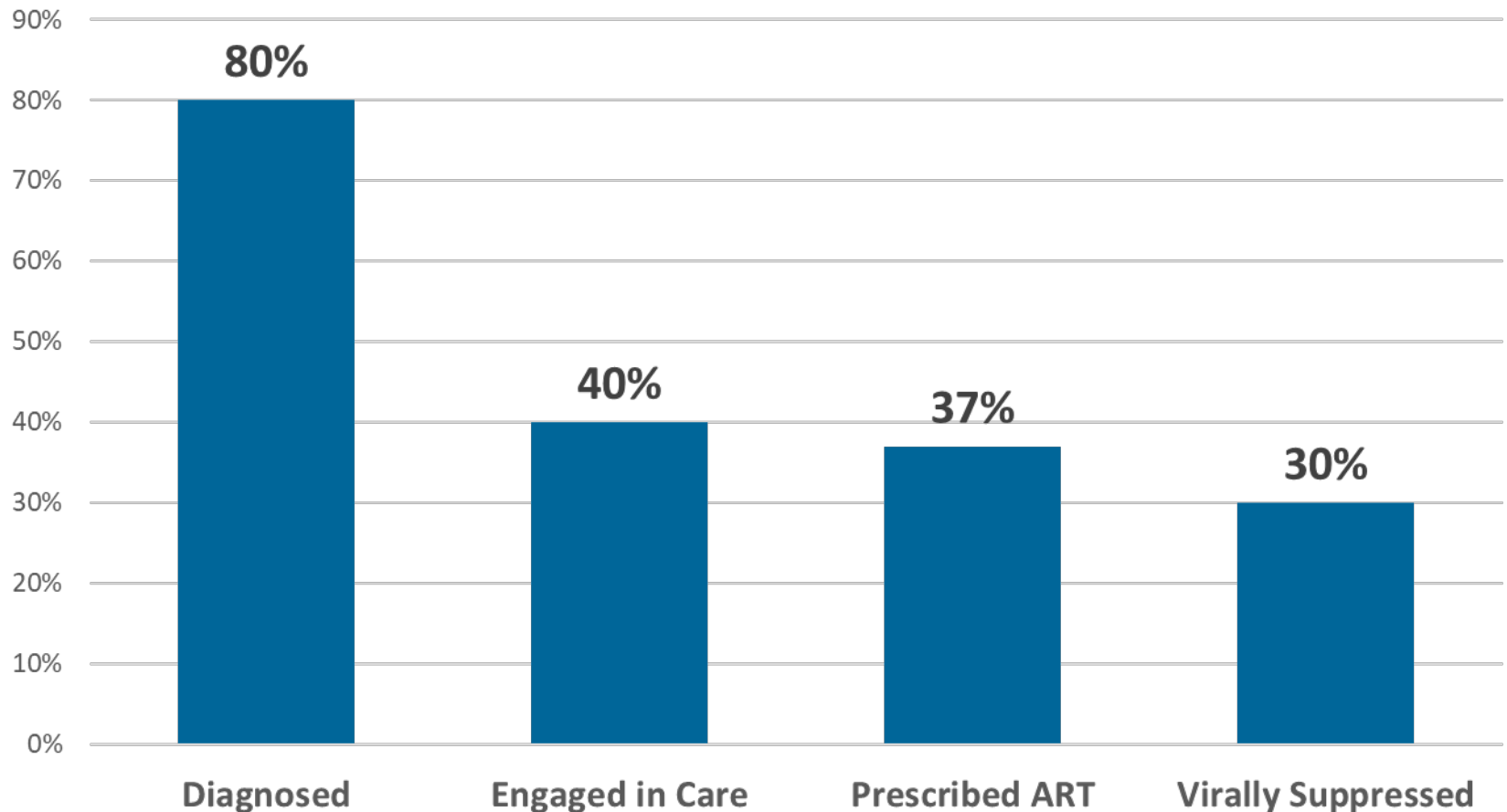


# HIV Care Continuum: US 2011

**GOAL: 90%**  
**2014: 85%**

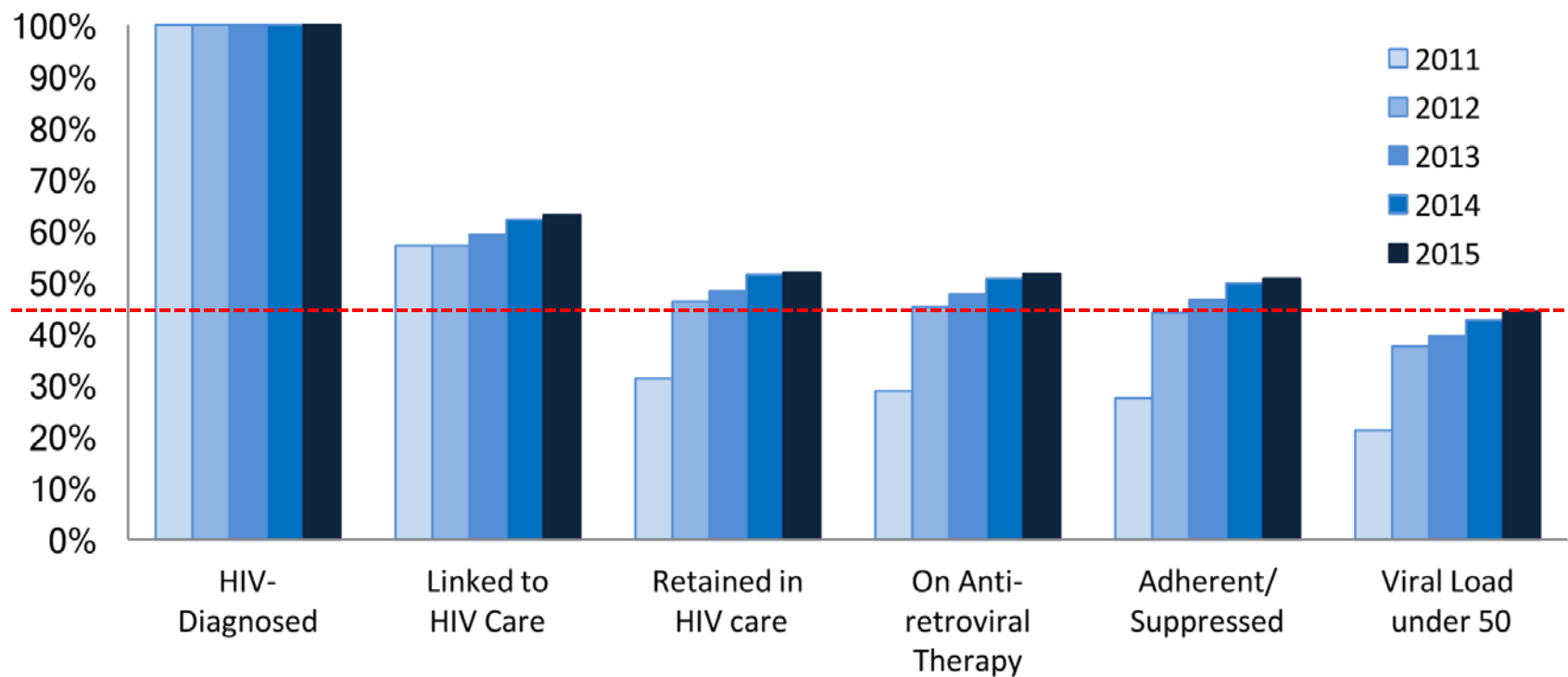
**90%**

**90%**  
**49%**



# HIV/AIDS Continuum of Care

Figure 14: Arizona, 2011-2015



## World AIDS Day 12/1/2014

The Fast-Track Cities Initiative (FTCI) is a global partnership between the City of Paris, Joint United Nations Program on HIV/AIDS (UNAIDS), United Nations Human Settlement Program (UN-Habitat), and the International Association of Providers of AIDS Care (IAPAC), in collaboration with the local, national, regional and international partners and stakeholders.

**90%**  
of people living  
with HIV (PLHIV)  
**KNOWING THEIR  
HIV STATUS**

**90%**  
of PLHIV who  
know their  
HIV+ status  
**ARE ON ARV TX**

**90%**  
of PLHIV  
on ARV Tx  
**ACHIEVING  
VIRAL SUPPRESSION**

**0%**  
**ZERO  
DISCRIMINATION  
AND STIGMA  
against PLHIV**

### AFRICA

Abidjan (Côte d'Ivoire)  
Accra (Ghana)  
Algiers (Algeria)  
Bamako (Mali)  
Bangui (CAR)  
Blantyre (Malawi)  
Brazzaville (Congo)  
Casablanca (Morocco)  
Cotonou (Benin)  
Dakar (Senegal)  
Dar es Salaam (Tanzania)  
Djibouti (Djibouti)  
Douala (Cameroon)  
Durban (South Africa)  
Entebbe (Uganda)  
Freetown (Sierra Leone)  
Johannesburg (South Africa)

Kigali (Rwanda)  
Kinshasa (DRC)  
Lagos (Nigeria)  
Libreville (Gabon)  
Lilongwe (Malawi)  
Lubumbashi (DRC)  
Lusaka (Zambia)  
Makeni (Sierra Leone)  
Maputo (Mozambique)  
Maseru (Lesotho)  
Nairobi (Kenya)  
Ouagadougou (Burkina Faso)  
Ouesso (Rep. of Congo)  
Pretoria (South Africa)  
Windhoek (Namibia)  
Yaoundé (Cameroon)

### LATIN AMERICA / CARIBBEAN

Buenos Aires (Argentina)  
Curitiba (Brazil)  
Havana (Cuba)  
Kingston (Jamaica)  
Mexico City (Mexico)  
Montevideo (Uruguay)  
Panama City (Panama)  
Port-au-Prince (Haiti)

Quito (Ecuador)  
Rio de Janeiro (Brazil)  
Salvador de Bahia (Brazil)  
São Paulo (Brazil)  
Santa Fe (Honduras)  
Santiago (Chile)  
San Miguelito (Panama)

### EUROPE

Amsterdam (Netherlands)  
Athens (Greece)  
Barcelona (Spain)  
Berlin (Germany)  
Brighton and Hove (England)  
Brussels (Belgium)  
Bucharest (Romania)  
Cascais (Portugal)  
Geneva (Switzerland)

Kyiv (Ukraine)  
Lisbon (Portugal)  
Madrid (Spain)  
Odessa (Ukraine)  
Paris (France)  
Porto (Portugal)  
Seville (Spain)  
Valencia (Spain)  
Vienna (Austria)

### ASIA / ASIA-PACIFIC

Almaty (Kazakhstan)  
Bangkok (Thailand)  
Delhi (India)

Jakarta (Indonesia)  
Melbourne (Australia)  
Mumbai (India)

### NORTH AMERICA

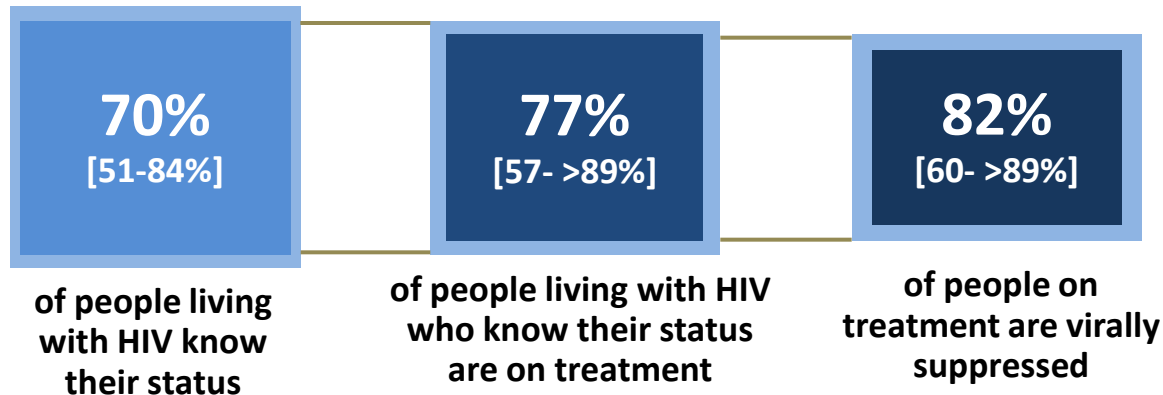
Atlanta (USA)  
Baltimore (USA)  
Birmingham (USA)  
Boston (USA)  
Chicago (USA)  
Denver (USA)  
Mexico City (Mexico)  
Miami (USA)  
Montréal (Canada)

New York City (USA)  
New Orleans (USA)  
Oakland (USA)  
Phoenix (USA)  
Providence (USA)  
San Antonio (USA)  
San Francisco (USA)  
Washington, DC (USA)



# ENDING AIDS Worldwide

## Progress towards the 90-90-90 Targets, Global 2016



### **Countries which have achieved the 90-90-90 targets**

Botswana, Cambodia, Denmark, Iceland, Singapore, Sweden, United Kingdom

- ***“Global attainment of all three 90s by 2020 is both feasible and reachable if gaps across the HIV testing and treatment cascade are aggressively addressed”***
- ***In 2016, 53% of people living with HIV were accessing ART***
  - ***“contributed to a 32% global decline in AIDS-related deaths and a 16% global decline in new HIV infections between 2010 and 2016”***



# Getting Phoenix to 90-90-90-0

## 90% AWARENESS OF STATUS

- Routine HIV testing
- Rapid testing by CBOs
- Opt-out testing in hospitals/clinics
- Combo HIV/HEP-C Testing

## 90% ON HIV MEDS

- Empower people to get in care or back in care
- Identify and address barriers/gaps to getting care (internal, external)
- Promote health literacy

## 90% VIRALLY SUPPRESSED

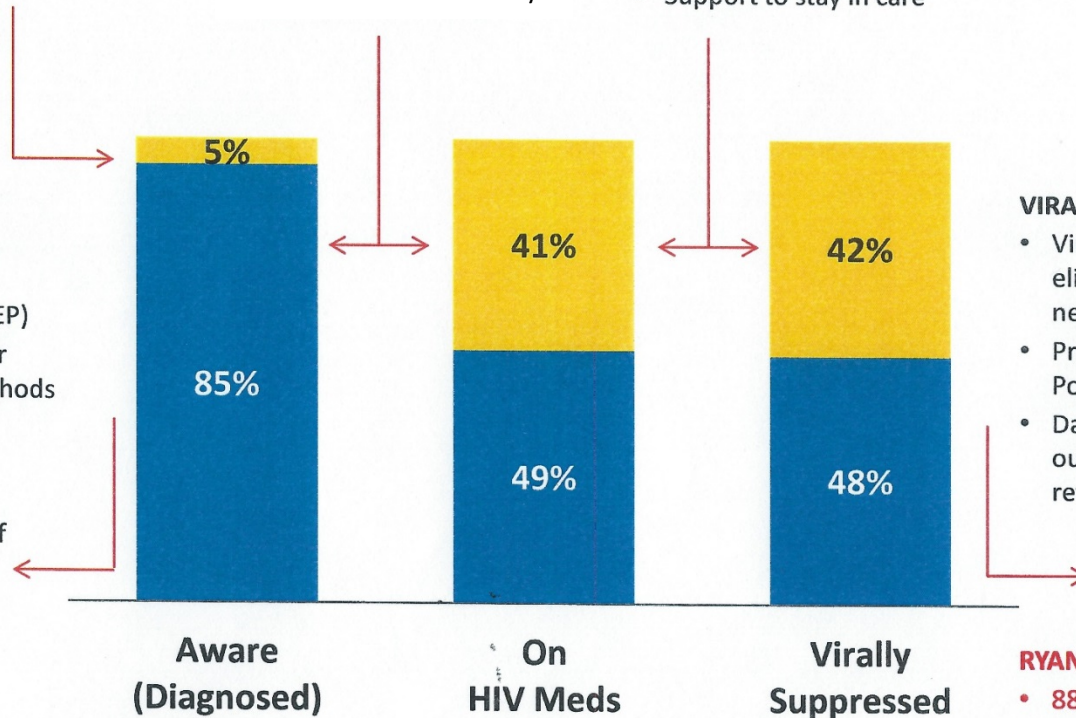
- Individualized adherence plans
- Encouragement to achieve and maintain viral suppression
- Support to stay in care

## 0% FEAR AND STIGMA

- Client empowerment training
- Provider training
- Cultural humility training
- Media campaigns

## KEEP NEGATIVE!

- Act on opioid epidemic
- Pre-Exposure Prophylaxis (PrEP)
- Condoms, other prevention methods
- Behavioral Interventions
- Address social determinants of health



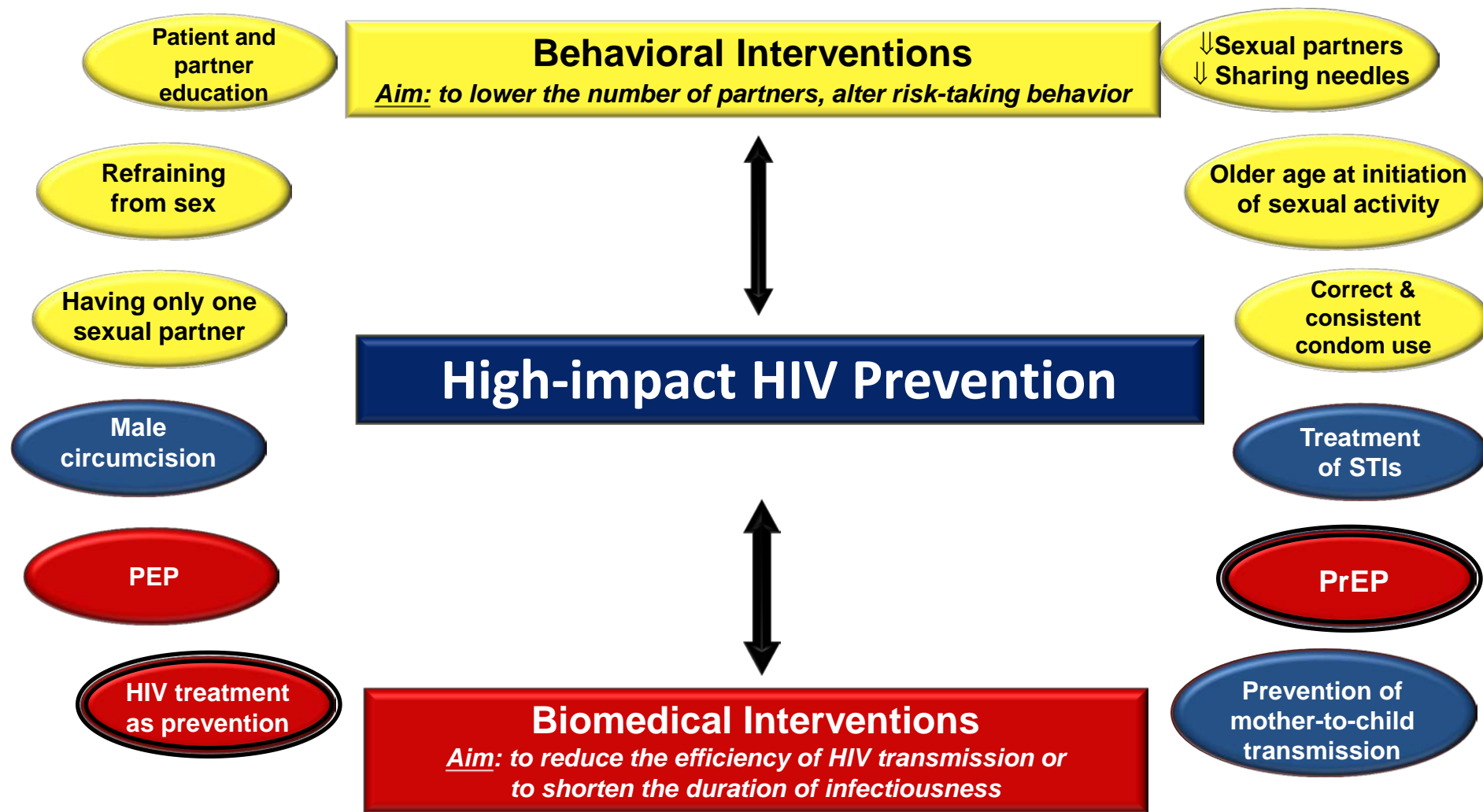
## VIRAL SUPPRESSION!

- Viral suppression eliminates 3 to 5 new HIV cases
- Prevention for Positives activities
- Data-to-Care to find out of care people, return to care

## RYAN WHITE CARE WORKS!

- 88% On HIV Meds
- 81% Virally Suppressed

# Preventing New Infections: Multi-Pronged Approach

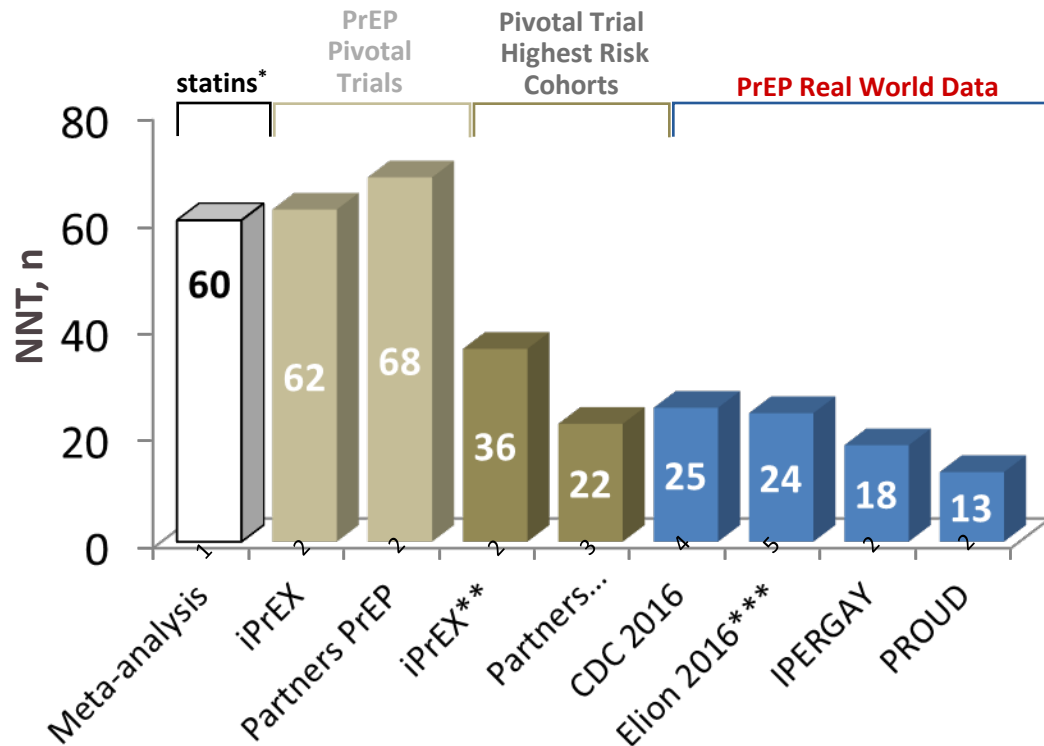




# Why Not Just Condoms?

- Has been recommended in the US since 1920s
  - Still high rates of STIs, teen & “oops” pregnancies
- Behavior change difficult!
  - Smoking cessation, weight loss, diabetic diet
  - Social stigma around sex (especially racial, sexual (LGBTQ), religious)
  - Lack of practiced, empowered condom negotiation
- Has been recommended 30+ yrs HIV epidemic
  - Still new infections
- HIV epidemic declines ONLY w/ TasP + PrEP
- Cost of PrEP <<< cost of HIV care (Rx, co-morbidities, etc.)

# Number Needed to Treat (NNT) to Prevent Outcome



\*Among primary prevention patients at moderate to moderately high risk of cardiovascular disease.

\*\*analysis in a high risk cohort as compared to all subjects in the study

\*\*\*Among Black MSM

- The NNT to prevent an HIV infection while using TRUVADA for PrEP in pivotal trials was 68 (Partners PrEP) and 62 (iPrEX trial)<sup>2</sup>. The number was lower in those with the highest risk.
- PrEP use in high-risk populations shows an even greater impact with NNTs ranging from 13 to 25 in real-world application studies<sup>2-4</sup>.
- As an industry comparison, we can look at statin use, whose NNT for cardio-protection was found to be 60<sup>1</sup> for those at intermediate risk

**The NNT for PrEP use is clinically similar to,  
and in some cases much lower than, the NNT for statins.**

1. Thavendiranathan P, et al. *Arch Intern Med*. 2006;166:2307-2313
2. <https://www.nice.org.uk/advice/esnm78/chapter/key-points-from-the-evidence> accessed March 27, 2017
3. Murnane P, et al. *AIDS*. 2013 August 24; 27(13)
4. Jenness SM, et al. *J Infect Dis*. 2016;214:1800-1807
5. Elion R, et al. International Workshop on HIV Prevention 2016. Oral, Oct. 15, 2016

# A Snapshot of STIs and HIV in the US



Rates of **STIs** are on the rise in the US<sup>1</sup>

From 2014 to 2015:

- Chlamydia: **5.9%** ↑
- Gonorrhea: **12.8%** ↑
- Syphilis<sup>a</sup>: **19%** ↑

The overall rate of diagnoses of **HIV infection** has decreased in the United States by 13% from 2010 through 2015<sup>2</sup>, but disparities still exist

In 2015<sup>1</sup>:

- **39,393 new HIV infections<sup>b</sup>**
- **Highest rates seen in:**
  - Persons aged **20–29 years**
  - **Blacks/African Americans**, followed by **Hispanics/Latinos**
- **67%** of the diagnosed HIV infections were attributed to **male-to-male, non-IDU sexual contact**
- **Southern states** comprised **52%** of all new HIV diagnoses

IDU, injection drug user; STI, sexually transmitted infection.

a. Primary and secondary syphilis. b. Data has been statistically adjusted to account for missing transmission category.

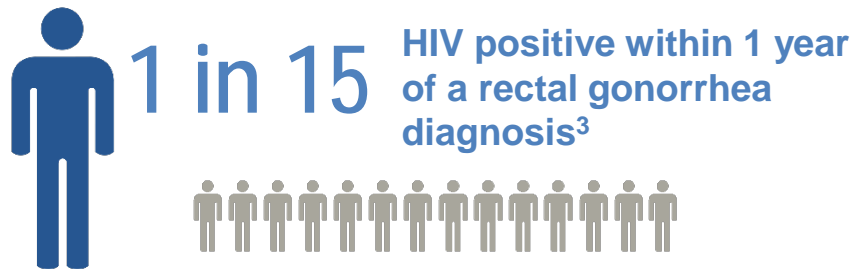
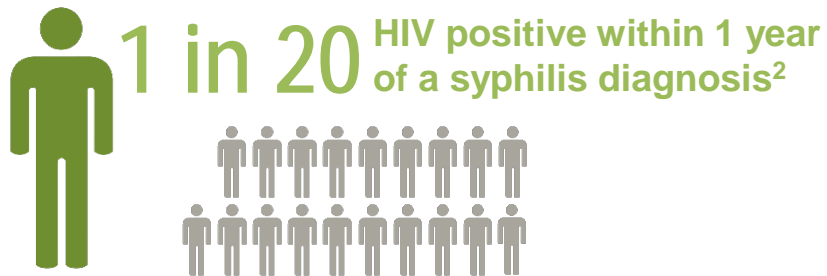
1. Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance 2015*. Atlanta: US Department of Health and Human Services; 2016. 2. Centers for Disease Control and Prevention. *HIV Surveillance Report*, 2015; vol. 27.

# STIs Increase Susceptibility for HIV Acquisition

- STIs that cause ulcers or inflammation greatly increase the efficiency of HIV transmission by increasing both the infectiousness of, and the susceptibility to HIV infection<sup>1</sup>

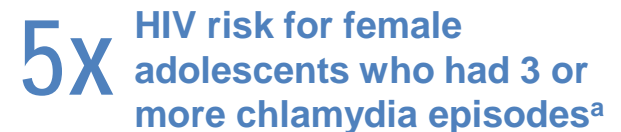
## STI Diagnosis in MSM

(New York City HIV/AIDS and STD Surveillance Registries, 2000-2010<sup>2</sup> or New York City Public STD Clinics<sup>3</sup>)



## STI Diagnosis in Adolescents

(Philadelphia High School STD Screening Program, 2003-2010)<sup>4</sup>



a. Compared with those with none.

1. Galvin SR, et al. *Nat Rev Microbiol.* 2004;2:33-42. 2. Pathela P, et al. *Clin Infect Dis.* 2015;61:281-287.

3. Pathela P, et al. *Clin Infect Dis.* 2013;57:1203-1209. 4. Newbern EC, et al. *Am J Public Health.* 2013;103:1874-1881.

# Adolescent Cognitive and Behavioral Development Affect Sexual Behavior

Adolescents' **heightened propensity for risky behavior** is thought to reflect **maturational imbalance** between cognitive control systems & affective reward processing.<sup>1</sup>



## Cognitive<sup>2</sup>

- Myth of invulnerability
- Lack of knowledge of STIs and associated signs/symptoms
- Fear of disclosure of sexual activity to parent/guardian

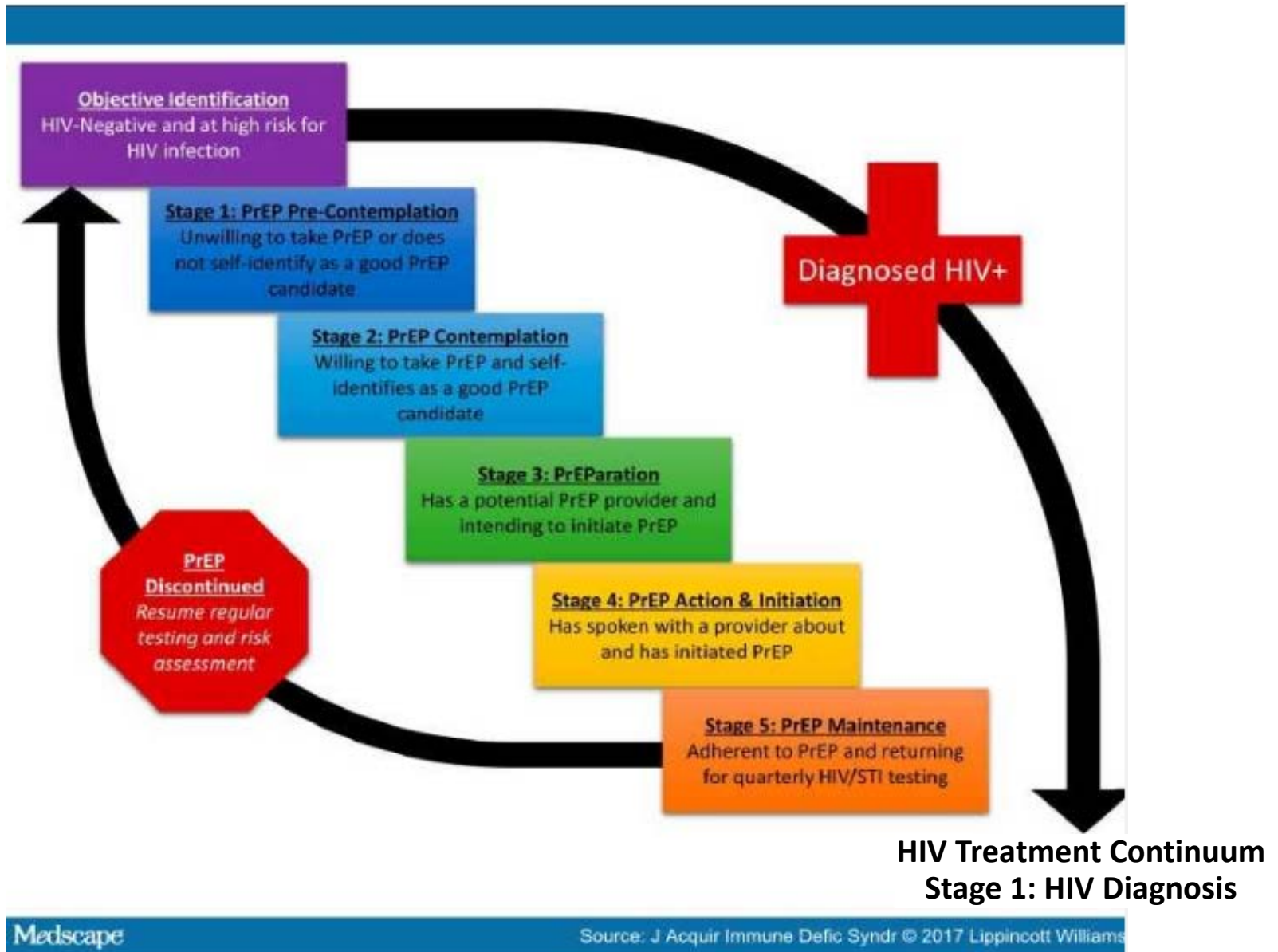


## Behavioral<sup>2</sup>

- Multiple partners, new partner in past 3 months, older partners, bisexual partners, partners who have been incarcerated
- Known sex with HIV-positive partner or partner with a history of IDU
- Inconsistent or lack of use of barrier method
- Oral contraceptive use (increases risk of chlamydia)
- Past history of STIs

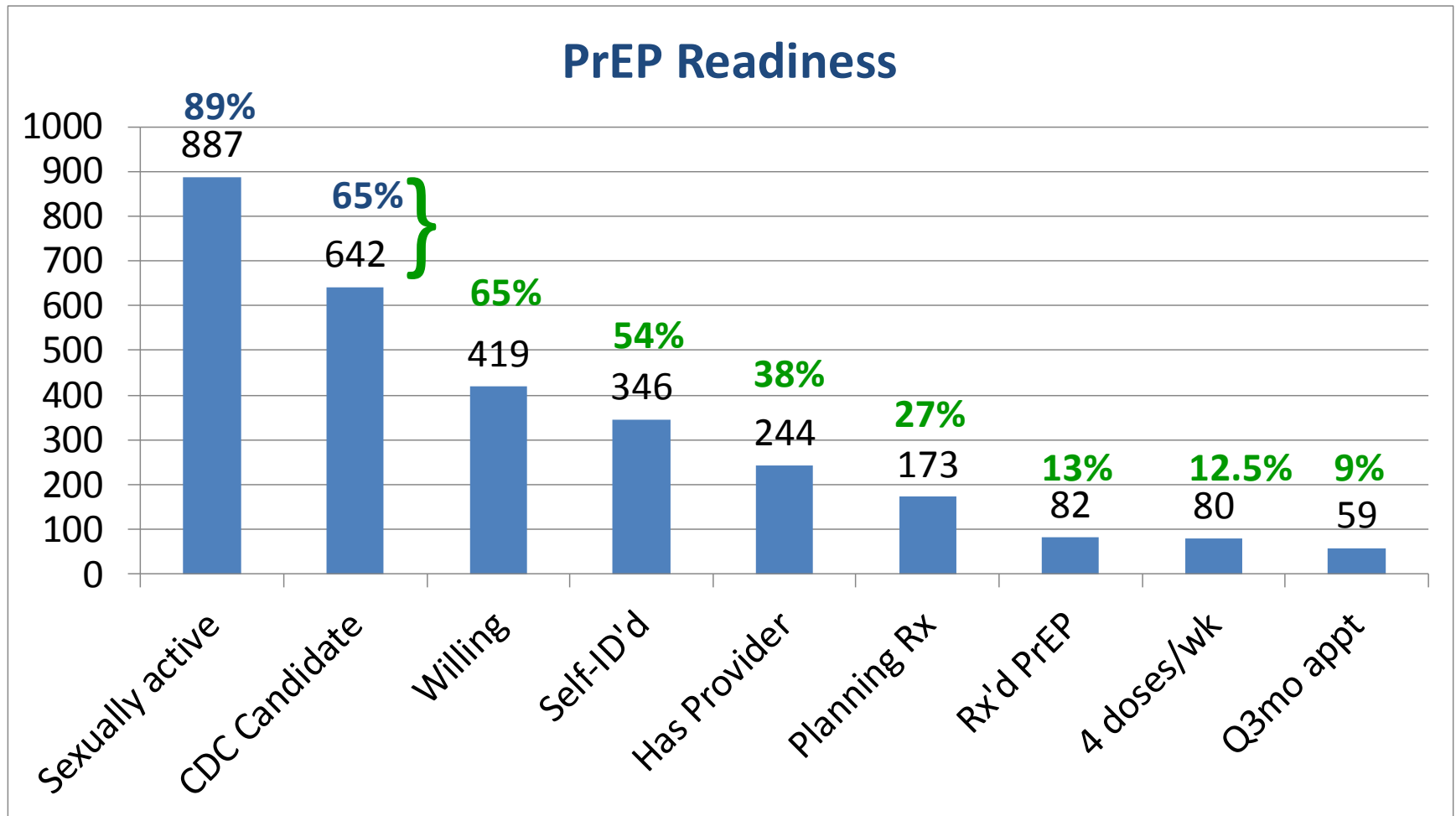
# PrEP Stages of Readiness

Prevention



# PrEP Continuum of Care

*"One Thousand Strong" N=995 HIV- US GBMSM*



# Health Guidelines for HIV Prevention:

## Recommend PrEP, Counseling, Risk Reduction

	CDC <sup>1</sup>	WHO <sup>2</sup>	IAS-USA <sup>3,4</sup>	ACOG <sup>5</sup>
Provides criteria for determining a person's risk of HIV infection and eligibility for PrEP	✓	✓	✓	✓
Includes PrEP as a prevention option for HIV-1-negative adults at high risk for HIV infection	✓	✓	✓	✓
Emphasizes the importance of counseling on adherence and comprehensive HIV risk reduction	✓	✓	✓	✓
Recommends confirming HIV-1-negative status prior to starting PrEP	✓	✓	✓	✓
Recommends that ongoing use of PrEP be guided by regular risk assessment		✓	✓	✓

**ACOG, American College of Obstetricians and Gynecologists; CDC, Centers for Disease Control and Prevention; IAS-USA, International AIDS Society-USA; WHO, World Health Organization.**

1. USPHS. Pre-exposure prophylaxis for the prevention of HIV-1 infection in the United States–2014. <http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf>. Accessed April 2017;
2. WHO. Guideline on When to Start Antiretroviral Therapy and on Pre-exposure Prophylaxis for HIV-1. <http://www.who.int/hiv/pub/guidelines/earlyrelease-arv/en>. Accessed April 2017;
3. Günthard FH, et al. *JAMA*. 2016;316:191-210;
4. Marrazzo JM, et al. *JAMA*. 2014;312:390-409; 5. Pre-exposure Prophylaxis for the prevention of HIV-1. Committee Opinion No. 59
5. American College of Obstetricians and Gynecologists. *Obstet Gynecol*. 2014;123: 1133-6.



## Summary of Guidance for PrEP Use

	Men Who Have Sex With Men	Heterosexual Women and Men	Injection Drug Users
<b>Detecting substantial risk of acquiring HIV infection:</b>	<ul style="list-style-type: none"> <li>Sexual partner with HIV</li> <li>Recent bacterial STD</li> <li>High number of sex partners</li> <li>History of inconsistent or no condom use</li> <li>Commercial sex work</li> <li>Lives in high-prevalence area or network</li> </ul>	<ul style="list-style-type: none"> <li>Sexual partner with HIV</li> <li>Recent bacterial STD</li> <li>High number of sex partners</li> <li>Commercial sex work</li> <li>Lives in high-prevalence area or network</li> </ul>	<ul style="list-style-type: none"> <li>HIV-positive injecting partner</li> <li>Sharing injection equipment</li> <li>Recent drug treatment (but currently injecting)</li> </ul>
<b>Clinically eligible:</b>	<ul style="list-style-type: none"> <li>Documented negative HIV test before prescribing PrEP</li> <li>No signs/symptoms of acute HIV infection</li> <li>Normal renal function, no contraindicated medications</li> <li>Documented hepatitis B virus infection and vaccination status</li> </ul>		
<b>Prescription</b>	Daily, continuing, oral doses of TDF/FTC (Truvada), ≤90 day supply		
<b>Other services:</b>	<ul style="list-style-type: none"> <li>Follow-up visits at least every 3 months to provide:</li> <li>HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STD symptom assessment</li> <li>At 3 months and every 6 months after, assess renal function</li> <li>Every 6 months test for bacterial STDs</li> </ul>		
	<ul style="list-style-type: none"> <li>Do oral/rectal STD testing</li> </ul>	<ul style="list-style-type: none"> <li>Assess pregnancy intent</li> <li>Pregnancy test every 3 months</li> </ul>	<ul style="list-style-type: none"> <li>Access to clean needles/syringes and drug treatment services</li> </ul>

Source: US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States —2014: a clinical practice guideline.

# Daily PrEP Efficacy Results: Clinical Trials and Real World Data

Clinical trial	Participants	Number	Drug	mITT <sup>a</sup> efficacy of % reduction in acquisition of HIV infection <sup>a</sup>		Adherence-adjusted efficacy based on TDF detection in blood <sup>b</sup>	
				%	(95% CI)	%	(95% CI)
<b>iPrEx</b>	<b>MSM</b>	<b>2499</b>	<b>TVD<sup>c</sup></b>	<b>42</b>	<b>(18-60)</b>	<b>92</b>	<b>(40-99)</b>
<b>Partners PrEP</b>	<b>HIV discordant couples</b>	<b>4747</b>	TDF	67	(44-81)	86	(67-94)
			<b>TVD<sup>c</sup></b>	<b>75</b>	<b>(55-87)</b>	<b>90</b>	<b>(58-98)</b>
<b>TDF 2</b>	<b>Heterosexually active men and women</b>	<b>1200</b>	<b>TVD<sup>c</sup></b>	<b>62</b>	<b>(22-83)</b>	<b>84</b>	<b>NS</b>
<b>Bangkok Tenofovir Study</b>	IDU	2413	TDF	49	(10-72)	74	(2-91)
<b>Fem-PrEP</b>	Heterosexually active women	1951	TVD <sup>c</sup>	6 <sup>e</sup>	.59-1.52	< 40%	-----
<b>VOICE</b>	Heterosexually active women	5029	TVD <sup>c</sup>	- 4 <sup>e</sup>	0.97-2.3	<30%	-----

a. Modified Intent to Treat

b. Excluded only those enrolled patients later found to be infected at randomization and those with no follow-up visit or HIV test

c. TVD = FTC/TDF

d. On-demand" regimen constitutes: FTC/TDF or 2 placebo < 24 hrs prior to sexual intercourse exposure 1 FTC/TDF or placebo dose 24 hrs after; and a final dose 48 hrs after

e. Not statistically significant

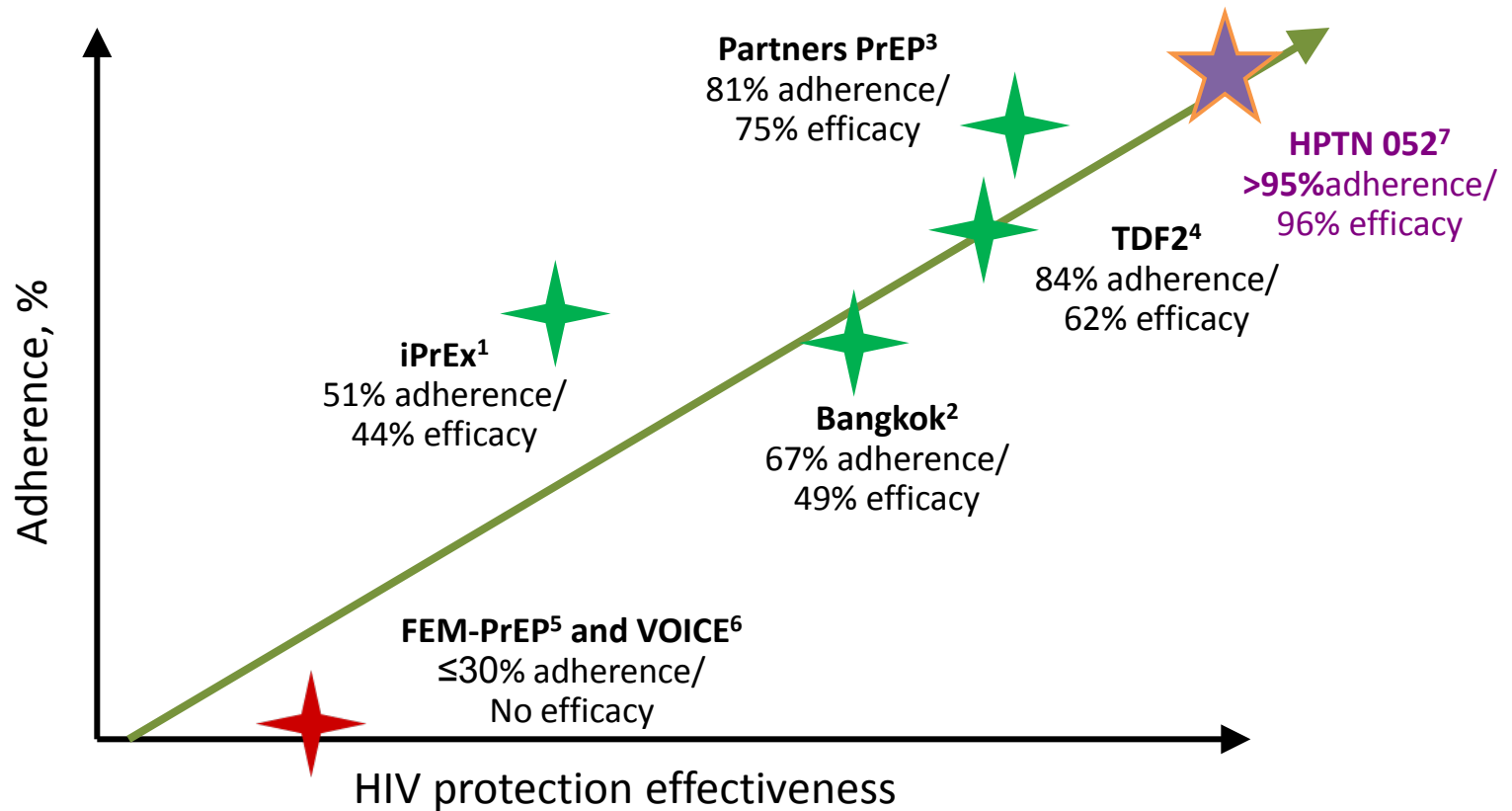
\* Considered "Real World" data

Volk, J et al. CID Sept 9, 2015.

McCormack S, et al. CROI 2015; Seattle, WA. #22LB

US Public Health Services. Preexposure Prophylaxis For The Prevention of HIV Infection In The United States, 2014. <http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf>.

# HIV Prevention Efficacy Correlates With Adherence To **PrEP** Or **TasP**



**TasP:** HPTN 052, 1763 couples, suppressive ART, prevented HIV transmission (29 linked infections, only 1 infection among treated couples)

# Truvada Prescribing Guidelines

- Dosing: Truvada 200/300 mg: 1 PO daily
  - Must strictly adhere to daily dosing – efficacy associated with adherence
  - Recommended as part of comprehensive prevention strategy
- Must confirm HIV negative status
  - Acute symptoms, or recent exposures need delayed PrEP, or possibly use of PEP
  - Resistance has ONLY been seen in cases of unrecognized baseline HIV infection
- Must confirm Hepatitis B infection status
- Truvada side effects:
  - RENAL: Mild, reversible, non-progressive decrease in estimated creatinine clearance, rare proximal renal tubulopathy. Monitor serum Cr and urine protein.
  - BONE: Small, reversible decrease in BMD. No bone fractures shown for PrEP.
  - SKIN: Rare reversible hyperpigmentation, especially in dark-skinned individuals.

# Risk Evaluation and Mitigation Strategy

[www.truvadapreprems.com](http://www.truvadapreprems.com)

## TRUVADA for a Pre-exposure Prophylaxis (PrEP) Indication

This is a **Risk Evaluation and Mitigation Strategy (REMS)** Web site. TRUVADA for a PrEP indication—in combination with safer sex practices—can help reduce the risk of sexually acquired HIV-1 infection as part of a comprehensive HIV-1 prevention strategy in adults at high risk. TRUVADA for a PrEP indication does not replace existing prophylaxis strategies.

[Review factors that can help healthcare providers identify individuals at high risk for sexually acquired HIV-1 and important prescribing considerations](#)

[Review the online training for prescribers](#) →

[Report completion of training for TRUVADA for a PrEP indication](#) →

[Participate in a Knowledge, Attitude, and Behavior \(KAB\) survey to assess the use and understanding of TRUVADA for PrEP](#) →

### REMS Information

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks.

To make sure TRUVADA for a PrEP indication is prescribed and taken safely, Gilead has worked with the FDA to develop materials for the REMS program to educate and inform healthcare providers and uninfected individuals at high risk for acquiring HIV-1.

[Access REMS resources](#) →

## REMS Materials

On this page, you'll find downloadable resources for you and uninfected individuals. You will need Adobe Acrobat installed on your computer to view these resources. If you do not have it and would like to download it, please [click here](#).

### DEAR HEALTHCARE PROVIDER LETTER



Information for healthcare providers on the new TRUVADA indication for pre-exposure prophylaxis (PrEP)

[Download](#) →

### TRAINING GUIDE FOR HEALTHCARE PROVIDERS



A comprehensive overview of TRUVADA for a PrEP indication

[Download](#) →

### IMPORTANT SAFETY INFORMATION FOR HEALTHCARE PROVIDERS



Important safety information about TRUVADA for a PrEP indication

[Download](#) →

**AND MORE**

# Checklist for Prescribers:

## Initiation of TRUVADA® for Pre-exposure Prophylaxis (PrEP)

Individual Label

Instructions: Complete checklist at each visit and file in individual's medical record.

I have completed the following prior to prescribing TRUVADA for a pre-exposure prophylaxis (PrEP) indication for the individual who is about to start or is taking TRUVADA for a PrEP indication:

### Lab Tests/Evaluation

- R/O HIV infection → ☐ Completed high risk evaluation of uninfected individual
- ☐ Confirmed a negative HIV-1 test immediately prior to initiating TRUVADA for a PrEP indication
- If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposure is suspected, delay starting PrEP for at least 1 month and reconfirm HIV-1 status or use a test approved by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection. (Note: TRUVADA for a PrEP indication is contraindicated in individuals with unknown HIV-1 status or who are HIV-1 positive)
- Eval HBV infection → ☐ Performed HBV screening test
- Eval renal function → ☐ Confirmed estimated creatinine clearance (CrCl) >60 mL/min prior to initiation and periodically during treatment. In patients at risk for renal dysfunction, assess estimated CrCl, serum phosphorus, urine glucose, and urine protein before initiation of TRUVADA and periodically while TRUVADA is being used. If a decrease in estimated CrCl is observed in uninfected individuals while using TRUVADA for a PrEP indication, evaluate potential causes and reassess potential risks and benefits of continued use
- ☐ Confirmed that the uninfected individual at high risk is not taking other HIV-1 medications or HBV medications
- ☐ Evaluated risk/benefit for women who may be pregnant or may want to become pregnant

### Counseling/Follow-up

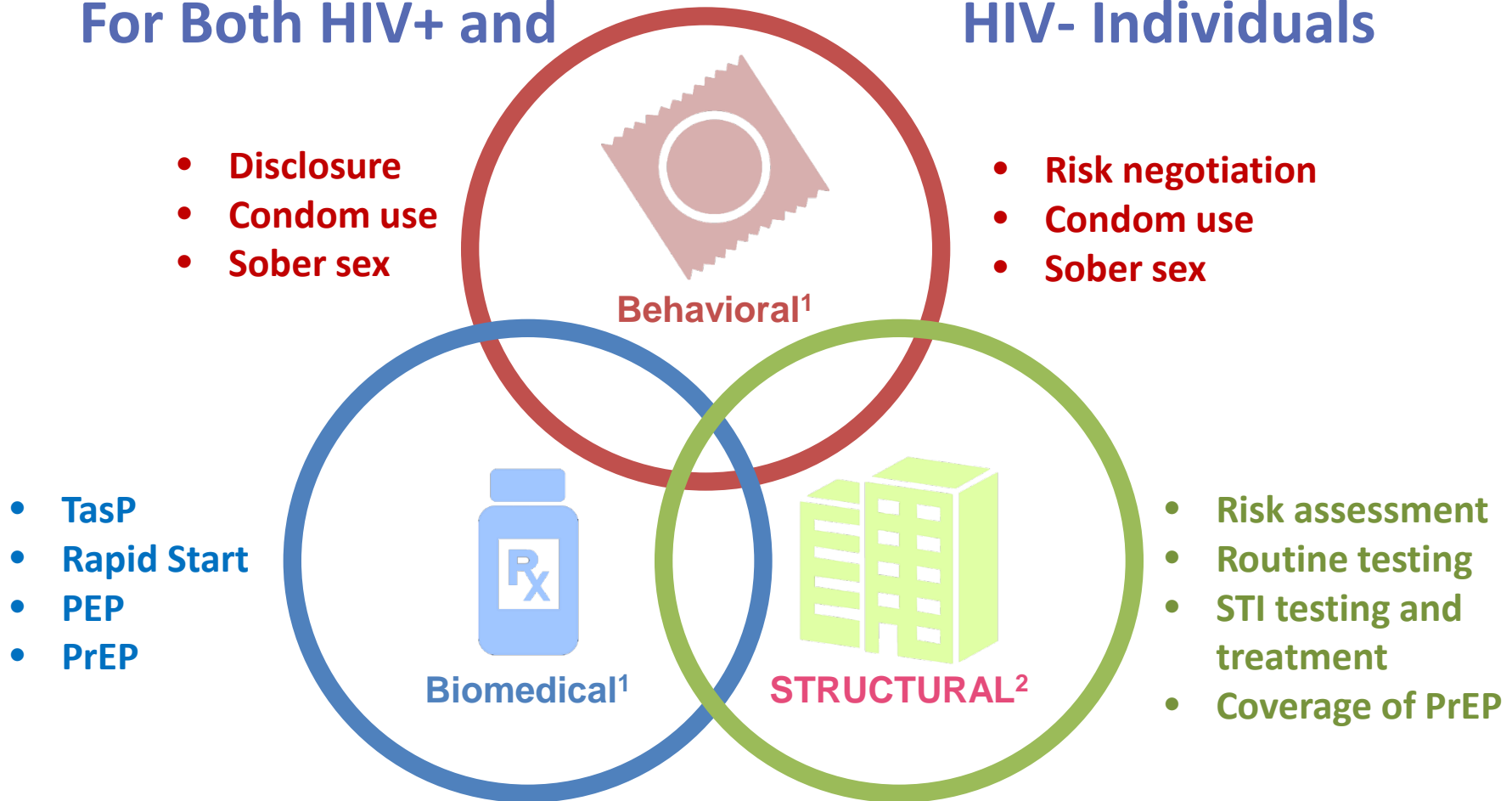
- F/U every 3 mos → ☐ Discussed known safety risks with use of TRUVADA for a PrEP indication
- ☐ Counseled on the importance of scheduled follow-up every 2 to 3 months, including regular HIV-1 screening tests (at least every 3 months), while taking TRUVADA for a PrEP indication to reconfirm HIV-1-negative status



# Reducing the HIV Epidemic Requires Multiple Interventions

For Both HIV+ and

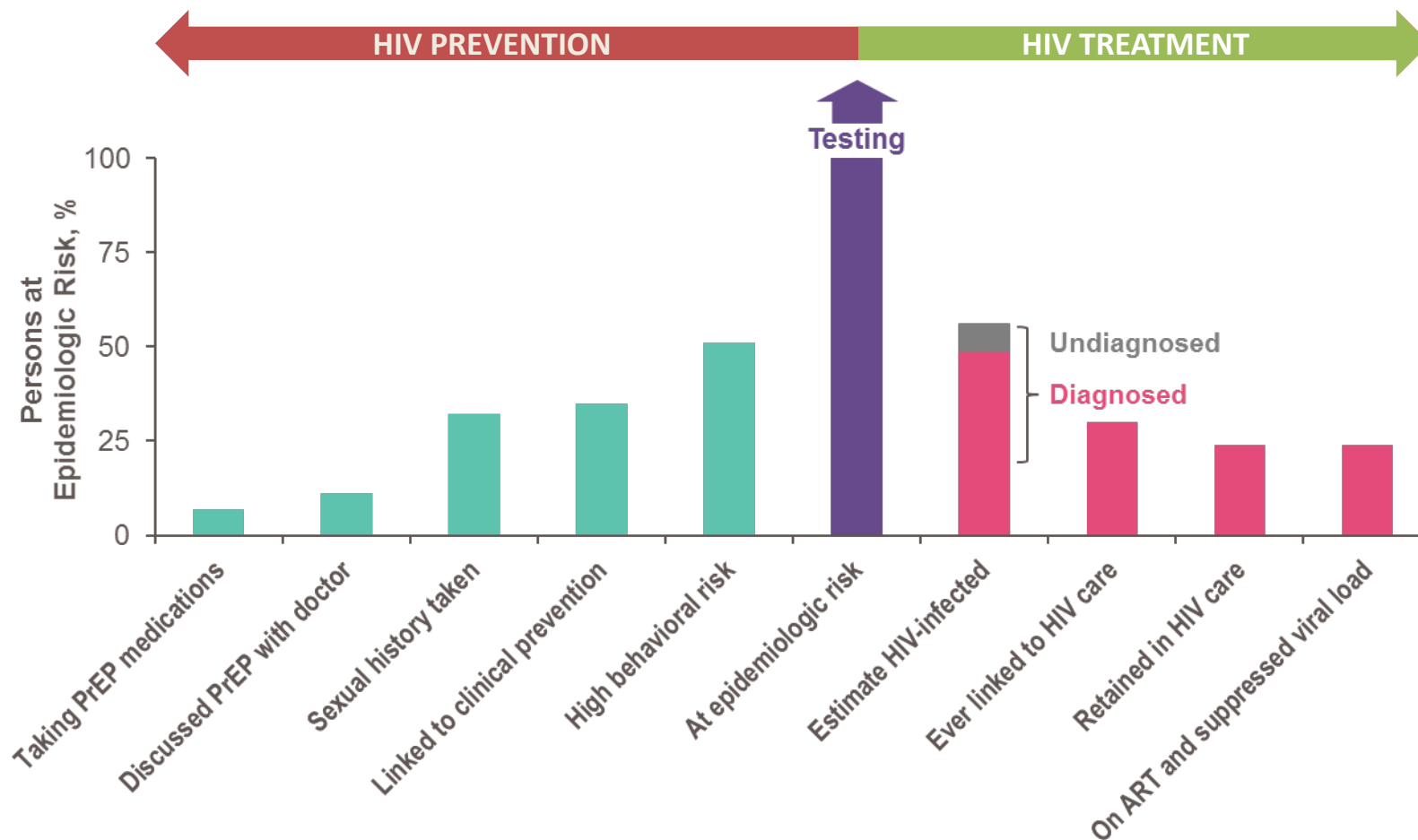
HIV- Individuals



1. Cohen M, et al. *J Int AIDS Soc.* 2008;11:4.

2. White House Office of National AIDS Policy. National HIV/AIDS Strategy for the United States: updated to 2020. Published July 2015.

# GOAL: Changing the HIV Epidemic Through Testing, Prevention, and Treatment



- Proactive integration and optimization of treatment in HIV-positive individuals and prevention in HIV-negative individuals will improve our ability to control the HIV epidemic



# Magellan Drug Class Reviews

*Lara Frick, PharmD, Magellan*



# Magellan Class Reviews

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## *Classes for Review*

- Glucocorticoids, Inhaled

## *New Products to Magellan PDL classes - COPD*

- Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol)

# Glucocorticoids, Inhaled

## *Class Overview: Single Agent Glucocorticoid Products*

- beclomethasone HFA - (QVAR, QVAR RediHaler)
- budesonide powder - (Pulmicort FlexHaler)
- budesonide solution - (Pulmicort Respules)
- ciclesonide aerosol - (Alvesco)
- flunisolide HFA - (Aerospan)
- fluticasone furoate powder – (Arnuity Ellipta)
- fluticasone propionate aerosol – (Flovent HFA)
- fluticasone propionate powder – (ArmonAir Respiclick, Flovent Diskus)
- mometasone furoate aerosol – (Asmanex HFA)
- mometasone furoate powder – (Asmanex Twisthaler)

# Glucocorticoids, Inhaled

## *Class Overview: Glucocorticoid/Long-Acting Beta<sub>2</sub> (LABA) Combination Products*

- budesonide/formoterol aerosol - (Symbicort)
- fluticasone furoate/vilanterol powder - (Breo Ellipta)
- fluticasone propionate/salmeterol aerosol - (Advair HFA)
- fluticasone propionate/salmeterol powder - (Advair Diskus, AirDuo RespiClick)
- mometasone/formoterol aerosol - (Dulera)

## *Class Overview: Glucocorticoid/Long-Acting Anticholinergic/Long-Acting Beta<sub>2</sub> (LABA) Combination Products*

- fluticasone furoate/umeclidinium/vilanterol powder - (Trelegy Ellipta)

# Glucocorticoids, Inhaled

- Prevalence and incidence of asthma in the U.S. continues to rise, affecting approximately 8.4% of the population
- Clinical studies have demonstrated the efficacy of inhaled corticosteroids (ICS) in improving lung function, reducing symptoms, reducing frequency and severity of exacerbations, plus improving the quality of life of patients with asthma
- The 2007 National Heart, Lung, and Blood Institute, (NHLBI), and the 2017 Global Initiative for Asthma (GINA) guidelines denote inhaled glucocorticoids as currently the most effective anti-inflammatory medications for the treatment of persistent asthma
- The 2017 GINA guidelines offer a control-based management plan which adjusts treatment through a continuous cycle of assessment and review of the patient's response to therapy as it relates to symptom control, future risk of exacerbations, and side effects

# Glucocorticoids, Inhaled

- The products listed in the class overview are not indicated for the relief of acute bronchospasm. Patients with asthma should be prescribed a rescue/reliever agent for instances of bronchospasm
- One of the newer agents in this class, fluticasone furoate/umeclidinium/vilanterol (Trelegy Ellipta) is not approved for use in asthma
- For asthma therapy, the combination products should only be prescribed for patients not adequately controlled on a single-agent asthma control medication, such as an inhaled corticosteroid (ICS), or for patients whose severity of asthma symptoms warrants initiation of treatment with both an ICS and a long-acting beta<sub>2</sub> agonist (LABA)
- At the initial diagnosis and periodically (and during exacerbations); patient's forced expiratory volume in 1 second (FEV<sub>1</sub>) should be evaluated for treatment progress/success

# Glucocorticoids, Inhaled

- In asthma therapy, corticosteroids suppress cytokine generation, recruitment of airway eosinophils, and release of inflammatory mediators, reducing airway hyper-responsiveness
- Long-acting beta<sub>2</sub> agonists (LABAs), lead to bronchial relaxation and a decrease in the release of mediators of immediate hypersensitivity from mast cells
- Anticholinergic agents (LAMAs), antagonizes the action of released acetylcholine causing bronchodilation
- Delivery system selection as well as the patients' ability to properly use the device are important factors in the clinical success of ICS therapy
- Metered dose inhalers (MDIs) are pressurized spray inhalers, available in suspension and solution

# Glucocorticoids, Inhaled

- MDIs deliver approximately 15% to 35% of the administered dose to the lungs
- Spacer chambers may be used with most MDIs to make them easier to use and help deliver a greater amount of medicine to the airway
- Products in this review with MDI devices include Advair HFA, Aerospan, Alvesco, Asmanex HFA, Dulera, Flovent HFA, QVAR, QVAR Redihaler, and Symbicort. QVAR Redihaler differs from conventional MDIs as it is breath activated, and should not be used with a spacer or volume holding chamber
- Dry-powder inhalers (DPIs) are breath-actuated devices that release the medicine in the form of a dry powder upon inhalation



# Glucocorticoids, Inhaled

- While DPIs minimize some of the difficulties in coordinating MDI usage, they have a tendency to result in more dosage variation at low inspiratory flow rates ( $< 20$  L/min)
- Products in this review with DPI devices include Advair Diskus, AirDuo RespiClick, ArmonAir RespiClick, Arnuity Ellipta, Asmanex Twisthaler, Breo Ellipta, Flovent Diskus, Pulmicort Flexhaler, and Trelegy Ellipta
- Products in this review that are nebulized include budesonide and Pulmicort respules
- Several of the products listed also carry indications in the treatment of chronic obstructive pulmonary disease (COPD). Their indications and efficacy will be discussed during the COPD therapeutic class review (Trelegy Ellipta is only indicated for COPD)

# Glucocorticoids, Inhaled

Single Agents	Indication	Age Indication
Aerospan	asthma maintenance therapy	patients 6 years and older
Alvesco	asthma maintenance therapy	patients 12 years and older
ArmonAir RespiClick	asthma maintenance therapy	patients 12 years and older
Arnuity Ellipta	asthma maintenance therapy	patients 12 years and older
Asmanex HFA	asthma maintenance therapy	patients 12 years and older
Asmanex Twisthaler	asthma maintenance therapy	patients 4 years and older
Flovent Diskus	asthma maintenance therapy	patients 4 years and older
Flovent HFA	asthma maintenance therapy	patients 4 years and older

# Glucocorticoids, Inhaled

Single Agents	Indication	Age Indication
Pulmicort Flexhaler	asthma maintenance therapy	patients 6 years and older
Pulmicort Respules	asthma maintenance therapy	patients 12 months to 8 years
QVAR	asthma maintenance therapy	patients 5 years and older
QVAR Redihaler	asthma maintenance therapy	patients 4 years and older

# Glucocorticoids, Inhaled

Combination Agents	Indication	Age Indication
AirDuo RespiClick	asthma maintenance therapy	patients 12 years and older
Advair Diskus	asthma maintenance therapy	patients 4 years and older
Advair HFA	asthma maintenance therapy	patients 12 years and older
Breo Ellipta	asthma maintenance therapy	patients 18 years and older
Dulera	asthma maintenance therapy	patients 12 years and older
Symbicort	asthma maintenance therapy	patients 6 years and older

# Glucocorticoids, Inhaled

- When used in equivalent dosages, efficacy among all ICS is similar
- There are differences among the agents in dosage frequency and the number of inhalations needed for each dose. Most are recommended for twice daily use
- Arnuity Ellipta, Breo Ellipta and Asmanex Twisthaler can be dosed once daily.
- Alvesco, QVAR and QVAR Redihaler are either converted during absorption (beclomethasone) or in the lung (ciclesonide)
- FDA cautions on the use of LABA products in asthma, also apply to the combination ICS/LABA products but no longer is a 'boxed' warning
- The FDA recommends against the use of LABA without the use of an ICS, and for the shortest duration possible to maintain asthma control

## *New Drug to Class: Glucocorticoids, Inhaled*

*Trelegy Ellipta (fluticasone  
furoate/umeclidinium/vilanterol)*



# Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol)

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- Trelegy Ellipta is the first approved triple agent inhaler (fluticasone furoate/umeclidinium/vilanterol)
- Trelegy Ellipta is approved for the long-term maintenance treatment of COPD (only)
- It is a fixed dose combination of an inhaled corticosteroid, anticholinergic, and long-acting beta2-adrenergic agonist (LABA); indicated in patients currently on a fixed-dose combination of fluticasone furoate/vilanterol who require additional bronchodilation or for patients already taking umeclidinium and fluticasone furoate/vilanterol
- Trelegy Ellipta is not indicated for the relief of acute bronchospasm or asthma

# Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol)

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- Trelegy Ellipta is supplied as prefilled with blister strips of powder for oral inhalation. One strip contains fluticasone furoate 100 mcg per blister and the other contains umeclidinium/vilanterol 62.5/25 mcg per blister
- Dosage is one oral inhalation using the two blister strips once daily
- Contraindications include severe hypersensitivity to milk proteins or other ingredients
- Warnings are similar to those for other inhaled steroids, anticholinergics and LABAs, including a boxed warning for risk of asthma-related death due to the LABA component.



# Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol)

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- Glaucoma, increased intraocular pressure, and cataracts have been reported with inhaled anticholinergics and corticosteroids. Monitoring is warranted
- Caution should be used in patients with narrow-angle glaucoma and with urinary retention.
- Trelegy Ellipta may have a cardiovascular effect (e.g., tachycardia, increased blood pressure, arrhythmias) or produce significant hypokalemia or hyperglycemia
- Trelegy Ellipta should be used cautiously in patients with diabetes, convulsive disorders, thyrotoxicosis, and those sensitive to sympathomimetic amines

# Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol)

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- The most common adverse effects include headache, back pain, dysgeusia, diarrhea, cough, oropharyngeal pain, and gastroenteritis
- There are no comparative data available
- Efficacy of Trelegy Ellipta is based on co-administration of its components in 2 multicenter, randomized, double-blind, parallel-group, 12-week confirmatory trials (Trial 1, n=206; Trial 2, n=206)
- Patients were randomized to either umeclidinium and fluticasone furoate/vilanterol or placebo and fluticasone furoate/vilanterol.
- The primary endpoint was the change from baseline in trough forced expiratory volume in 1 second (FEV<sub>1</sub>) at day 85

# Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol)

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- In Trial 1 and 2, the addition of umeclidinium to fluticasone furoate/vilanterol demonstrated a statistically significant increase in mean trough FEV<sub>1</sub> versus placebo measured at day 85
- Less average rescue medication was used with the addition of umeclidinium in both trials
- The effect on exacerbations was not measured in clinical trials comparing the addition of umeclidinium or placebo to fluticasone furoate/vilanterol

# Glucocorticoids, Inhaled

## *Product Updates:*

- Symbicort is now approved for in asthma for patients 6 years of age and older (previously for 12 years of age and older)
- AirDuo RespiClick is now available as a generic
- QVAR Redihaler (beclomethasone dipropionate HFA) has been approved for the maintenance treatment of asthma as prophylactic therapy in patients 4 years of age and older
  - It is not approved for the relief of acute bronchospasm.
  - Approved as a 40 and 80 mcg/actuation breath-actuated inhalation aerosol with dose counter (120 actuations per canister)

# Glucocorticoids, Inhaled

## *Product Updates:*

- Dosage for QVAR Redihaler is based on age, prior asthma therapy and disease severity
- Dosing ranges from 40 mcg twice daily to 320 mcg twice daily.
- Contraindications, warnings and adverse reactions are similar to other products in the class. No comparative clinical data available
- *Teva discontinued QVAR MDI upon launch of the QVAR Redihaler. Availability is limited to existing supplies*

# Glucocorticoids, Inhaled

## *Guideline Updates:*

- The 2017 update to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines observe that combination bronchodilator use may be more appropriate in patients with less advanced disease, but data does not definitively show LAMA/LABA treatment to be more effective than ICS/LABA

# Glucocorticoids, Inhaled

## 2017 GINA Guidelines Step Approach

Adults and Pediatrics 6 Years and Older

Step 1	As-needed reliever medication <ul style="list-style-type: none"><li>• Recommended: SABA</li><li>• Alternative Controller: consider addition of low dose ICS (controller option)</li></ul>
Step 2	One controller AND an as-needed reliever medication <ul style="list-style-type: none"><li>• Preferred controller: low-dose ICS + SABA</li><li>• Alternative controllers: leukotriene modifier or low dose theophylline* (if over 12 years)</li></ul>
Step 3	One or 2 controllers and an as-needed reliever medication <ul style="list-style-type: none"><li>• Preferred for adolescents and adults: low-dose ICS AND a LABA as maintenance plus as-needed SABA OR ICS/formoterol maintenance and reliever therapy<sup>†</sup></li><li>• Preferred for children 6 to 11 years of age: medium dose ICS + as-needed SABA</li><li>• Alternative controllers: medium- or high-dose ICS, OR low-dose ICS + leukotriene modifier, OR low-dose ICS + sustained-release theophylline*</li><li>• Sublingual immunotherapy (SLIT) may be considered in adults with allergic rhinitis or house dust mite sensitivity and exacerbations despite ICS use</li></ul>

# Glucocorticoids, Inhaled

## 2017 GINA Guidelines Step Approach

Adults and Pediatrics 6 Years and Older

Step 4	<p>Two or more controllers AND an as-needed reliever medication</p> <ul style="list-style-type: none"><li>• Preferred for adolescents and adults: medium/high-dose ICS + LABA plus as-needed SABA OR ICS/ formoterol maintenance and reliever therapy</li><li>• Preferred for children 6 to 11 years of age: referral to expert for assessment and advice</li><li>• Alternative controllers: For adults and adolescents: high dose ICS + leukotriene modifier, OR high-dose ICS + sustained release theophylline*, OR adding tiotropium</li><li>• Sublingual immunotherapy (SLIT) may be considered in adults with allergic rhinitis or house dust mite sensitivity and exacerbations despite ICS use</li></ul>
Step 5	<p>Higher level of care and/or add-on treatment</p> <ul style="list-style-type: none"><li>• In addition to Step 4 treatment, refer for add-on treatment: Tiotropium, monoclonal antibody treatment (omalizumab [anti-IgE therapy], mepolizumab or reslizumab [anti-IL-5 therapy]), low dose oral corticosteroids, or sputum guided therapy</li></ul>



# Executive Session



# P&T Public Vote on Recommendations



# Biosimilar Update

*Suzi Berman, RPh*



# BIOSIMILAR UPDATE

- There is no Biosimilar update for this P&T meeting.
- *As a reminder – per AHCCCS Policy 310-V: AHCCCS Contractors shall not transition to a biosimilar drug until AHCCCS has determined that the biosimilar drug is overall more cost-effective to the state than the continued use of the brand name drug.*

# New Drug Reviews

## *Non-Supplemental Rebate Classes*

*Lara Frick, PharmD, Magellan*



# Four New Products

- Gocovri - amantadine extended-release
- Vyzulta - latanoprostene bunod
- Solosec - secnidazole
- Xhance - fluticasone propionate

# Gocovri (amantadine extended-release)

- Amantadine extended-release (Gocovri) is indicated for the treatment of dyskinesia in adult patients with Parkinson's disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications
- Gocovri is available as 68.5 mg and 137 mg extended-release capsules
- Recommended starting dose is 137 mg once daily at bedtime for one week, increasing to 274 mg once daily at bedtime
- Capsules should not be crushed, chewed, or divided. If needed, Capsules can be opened and contents sprinkled on a teaspoonful of soft food like applesauce and swallowed immediately

# Gocovri (amantadine extended-release)

- Gocovri is contraindicated in patients with end-stage renal disease
- If moderate renal impairment, recommended initial dose is 68.5 mg at bedtime, increased to a maximum of 137 mg. If severe renal impairment, recommended dose is 68.5 mg at bedtime.
- Warnings include somnolence, suicidality and depression, hallucinations and psychotic behavior, dizziness and orthostatic hypotension, withdrawal-emergent hyperpyrexia and confusion, and impulse control/compulsive behaviors
- Common adverse reactions were hallucination, dizziness, dry mouth, peripheral edema, constipation, fall and orthostatic hypotension
- There are no comparative clinical data available



# Gocovri (amantadine extended-release)

- Efficacy and safety of Gocovri were evaluated in two key double-blind, placebo-controlled, phase 3 studies of similar design and population, EASE LID and EASE LID 3 with 198 combined patients
- Two other studies, EASED, a phase 2/3 dose-finding study, and EASE LID 2, a 105-week open-label safety study, were also conducted
- Inclusion criteria were Parkinson's disease patients using levodopa between the ages of 30 to 85 years with at least 1 hour of troublesome dyskinesia time during the day, and at least mild functional impact because of dyskinesia (assessed by Movement Disorder Society–Unified Parkinson's Disease Rating Scale [MDS-UPDRS])

# Gocovri (amantadine extended-release)

- For both the EASE LID and EASE LID-3 trials there was a significant reduction in dyskinesia issues, (UDysRS total score), from baseline in the Gocovri group compared to the placebo group
- Patients also saw a positive change from baseline in ON time without troublesome dyskinesia as well as a decrease in OFF time versus the placebo group
- Gocovri is available through prior authorization based on medical necessity
- Recommendation is to not add this drug to the AHCCCS Drug List

# • Vyzulta (latanaprostene bunod) •

- Latanoprostene bunod (Vyzulta) is a ophthalmic prostaglandin analog approved for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension
- Vyzulta is dosed as 1 drop in the conjunctival sac of the affected eye(s) once daily in the evening
- Do not administer more than once daily as more frequent administration may lessen the IOP lowering effect
- Administer each ophthalmic drug at least 5 minutes apart if more than 1 ophthalmic product is used
- Vyzulta is available as a 5 mL 0.024% solution in a 7.5 mL bottle

# • Vyzulta (latanaprostene bunod) •

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- There are no contraindications for Vyzulta
- Macular edema and bacterial keratitis have been reported
- Vyzulta should be used with caution in patients with known risk factors for macular edema
- Cases of bacterial keratitis are related patients inadvertently contaminating bottles of the product
- Most common ocular adverse events include conjunctival hyperemia, eye irritation, eye pain and instillation site pain
- Increased pigmentation of the iris and periorbital tissue and growth of eyelashes can occur

# • Vyzulta (latanaprostene bunod) •

- The safety and efficacy of Vyzulta was evaluated in three clinical trials: Voyager, Lunar and Apollo
- VOYAGER was a phase 2, multinational, randomized, investigator-masked, parallel-group, dose-ranging study, assessing the efficacy and safety of Vyzulta compared to latanoprost 0.005% in 413 adults with open angle glaucoma or ocular hypertension
- Participants were randomized 1:1:1:1:1 to Vyzulta 0.006%, 0.012%, 0.024%, or 0.04% or to latanoprost 0.005% once daily
- Primary endpoint was the reduction in mean diurnal IOP at day 28. Vyzulta 0.024% led to statistically significantly greater reductions in diurnal IOP than latanoprost at day 28

# • Vyzulta (latanaprostene bunod) •

- LUNAR was a phase 3, multinational, randomized, double-masked, parallel-group, non-inferiority study, assessing the efficacy and safety of Vyzulta compared to timolol, in 420 adults with open angle glaucoma or ocular hypertension
- Participants were randomized 2:1 to Vyzulta 0.024% once daily or timolol 0.5% twice daily
- Primary endpoint was the mean IOP at nine different time points
- Vyzulta was found to be non-inferior to timolol at all time points and led to statistically significantly greater reductions in IOP at most efficacy time points

# • Vyzulta (latanaprostene bunod) •

- APOLLO was a phase 3, multinational, randomized, double-masked, parallel-group study, assessing the efficacy and safety of Vyzulta compared to timolol in 420 adults with open angle glaucoma or ocular hypertension
- Participants were randomized 2:1 to Vyzulta 0.024% once daily or timolol 0.5% twice daily
- Primary endpoint was the mean IOP at 9 different time points
- Vyzulta led to statistically significantly greater reductions in IOP at all efficacy 9 time points
- Adverse effects were found to be similar between treatment groups

# Vyzulta (latanaprostene bunod)

- Vyzulta is available through prior authorization based on medical necessity
- Recommendation is to not add this drug to the AHCCCS Drug List



# Solosec (secnidazole)

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- Secnidazole (Solosec) is a nitroimidazole antimicrobial indicated for the treatment of bacterial vaginosis (BV) in adult women
- Secnidazole should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria in order to reduce the risk of drug-resistant bacteria
- Solosec comes as a 2 gram granule unit-of-use foil packet dosed as one packet per dose taken without regard to meals
- Contents may be sprinkled onto applesauce, yogurt, or pudding and should be consumed within 30 minutes without chewing or crunching the granules. Granules are not intended to be dissolved in liquid

# Solosec (secnidazole)

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- Contraindications include history of hypersensitivity to product components
- Warnings include possible development of vulvo-vaginal candidiasis and potential risk for carcinogenicity based on animal studies
- Common adverse reactions observed are vulvo-vaginal candidiasis, headache, nausea, dysgeusia, vomiting, diarrhea, abdominal pain, and vulvovaginal pruritus
- There is no comparative clinical data available

# Solosec (secnidazole)

- Safety and efficacy of Solosec was evaluated in a phase 3 placebo-controlled trial that included 189 non-pregnant women (ages 18 to 54) with a clinical diagnosis of BV based on Amsel criteria
- Patients were randomized (2:1) to a single oral dose of secnidazole 2 grams or placebo
- Primary efficacy endpoint of clinical outcome response was defined as normal vaginal discharge assessed between day 21 to 30 after the study dose and was achieved in 53.3% of patients treated with Solosec versus 19.3% given placebo
- While resistance to Solosec was not tested, data suggests cross-resistance between secnidazole and metronidazole *in vitro*

# Solosec (secnidazole)

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- Solosec is available through prior authorization based on medical necessity
- Recommendation is to not add this drug to the AHCCCS Drug List

# Xhance (fluticasone propionate)

- Fluticasone propionate (Xhance) is an intranasal corticosteroid indicated for the treatment of nasal polyps in patients 18 years and older
- Each Xhance spray delivers 93 mcg fluticasone propionate and comes in a 16 ml spray bottle delivering 120 actuations
- Recommended dosing is 1 spray per nostril twice a day. Some patients will require 2 sprays per nostril twice a day to be effective
- Medication is delivered into the nose by actuating the pump spray into one nostril while simultaneously blowing into the mouthpiece of the device

# Xhance (fluticasone propionate)

- Efficacy was shown in two randomized, double-blind, parallel-group, multicenter, placebo-controlled, dose-ranging trials in 646 adults 18 years and older with nasal polyps and associated moderate to severe nasal congestion
- Subjects were randomized 1:1:1:1 to receive 93 mcg, 186 mcg, or 372 mcg twice daily or placebo for a 16 week period. At baseline 90.6% of patients reported previous use of a topical steroid nasal spray for the treatment of nasal polyps and 53.6% reported previous sinus surgery or polypectomy
- Efficacy was demonstrated for the two higher dosage groups, 186-mcg twice daily dosing and 372 mcg twice daily
- Onset of action was generally seen within 2 weeks for both the higher doses

# Xhance (fluticasone propionate)

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- Contraindications are for hypersensitivity to any ingredients
- Warnings include local nasal effects, including nasal erosions, nasal ulcerations and nasal septal perforations
- Patients should be closely monitored for glaucoma and cataracts, immunosuppression, hypercorticism and adrenal suppression
- Patients on doses likely to cause immunosuppression should avoid exposure to chicken pox or measles
- Patients should also be assessed for possible decrease in bone mineral density at therapy start and periodically thereafter
- There is no comparative clinical data available with other products

# Xhance (fluticasone propionate)

- Xhance is available through prior authorization based on medical necessity
- Recommendation is to not add this drug to the AHCCCS Drug List





# P&T Public Vote

## *New Drugs in Non-Supplemental Classes*

# Agenda Items For The Next Meeting

## Tuesday April 17, 2018

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Please send agenda items to:

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# P&T Meeting Dates

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- **Next Meeting Dates:**
  - Tuesday 17 April 2018
- **Future 2018 Meeting Dates:**
  - Tuesday 17 July 2018
  - Tuesday 22 October 2018

# Thank You.

