HIV Treatment and Prevention for Sexual and Gender Minority Patients

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TEST FOR HIV

HIV tests determine the next prevention step, PrEP or HIV treatment.

86% of people with HIV know they have it.
TARGET: 95%

PREVENT

People without HIV, but at risk for it, can take PrEP as prescribed to prevent getting HIV.

TREAT

People who know they have HIV should take medicine daily to control the virus.

HAVE PREP PRESCRIPTION 18%

TARGET 50%

HAVE HIV UNDER CONTROL 63%

TARGET 95%

Multifactorial Drivers of SGM HIV/STI Risk

Biology

- Anal intercourse ↑susceptibility to HIV and STI
- Role versatility: receptive can be insertive, ↑ efficiency

Individual Behavior

- Number of partners over time

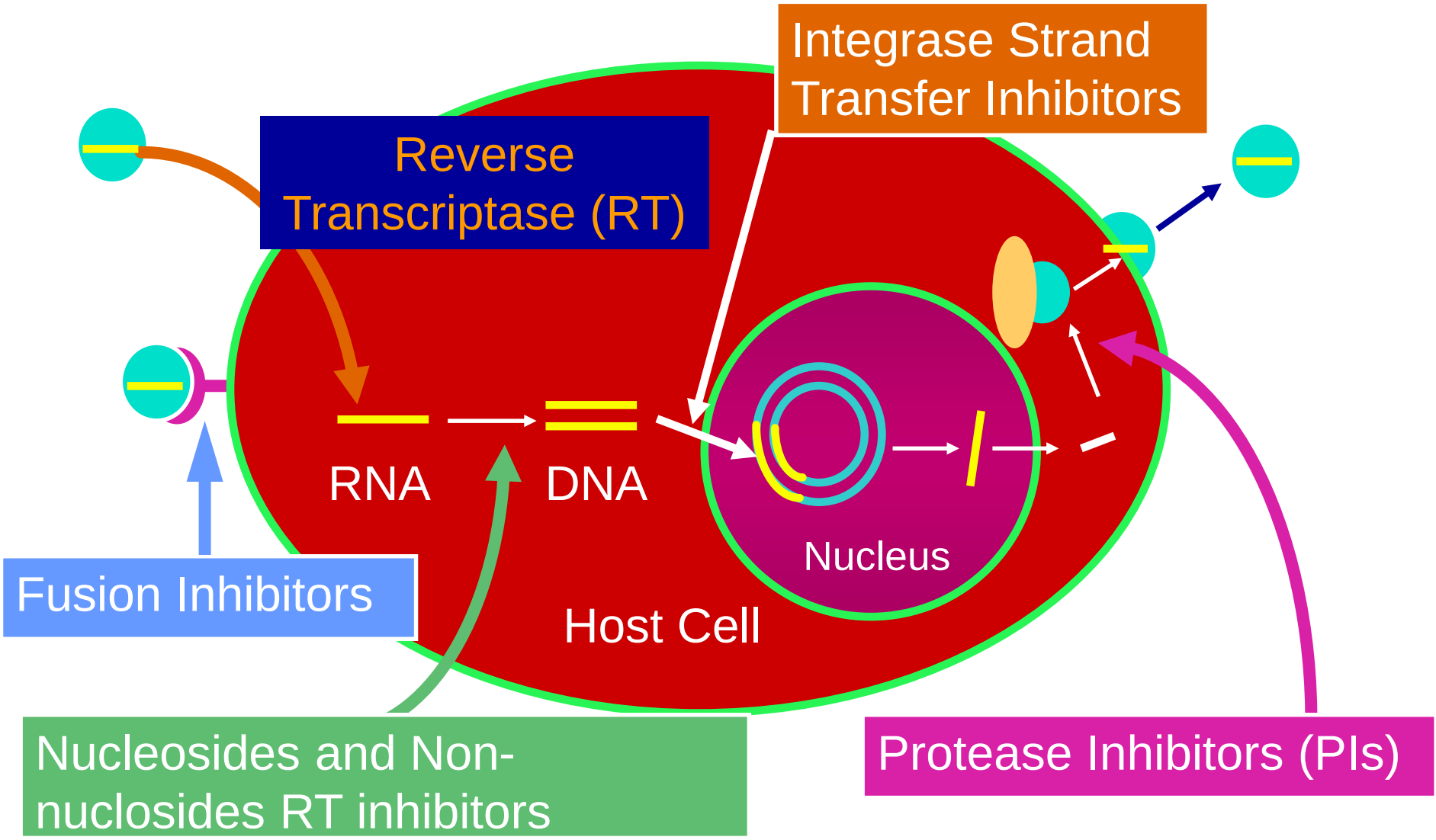
Social Networks (↑ risk of encountering HIV/STI)

- Sexual venues, e.g. bathhouses, social media
- Assortative mixing in sub-groups, e.g. racial minorities

Structural/Societal

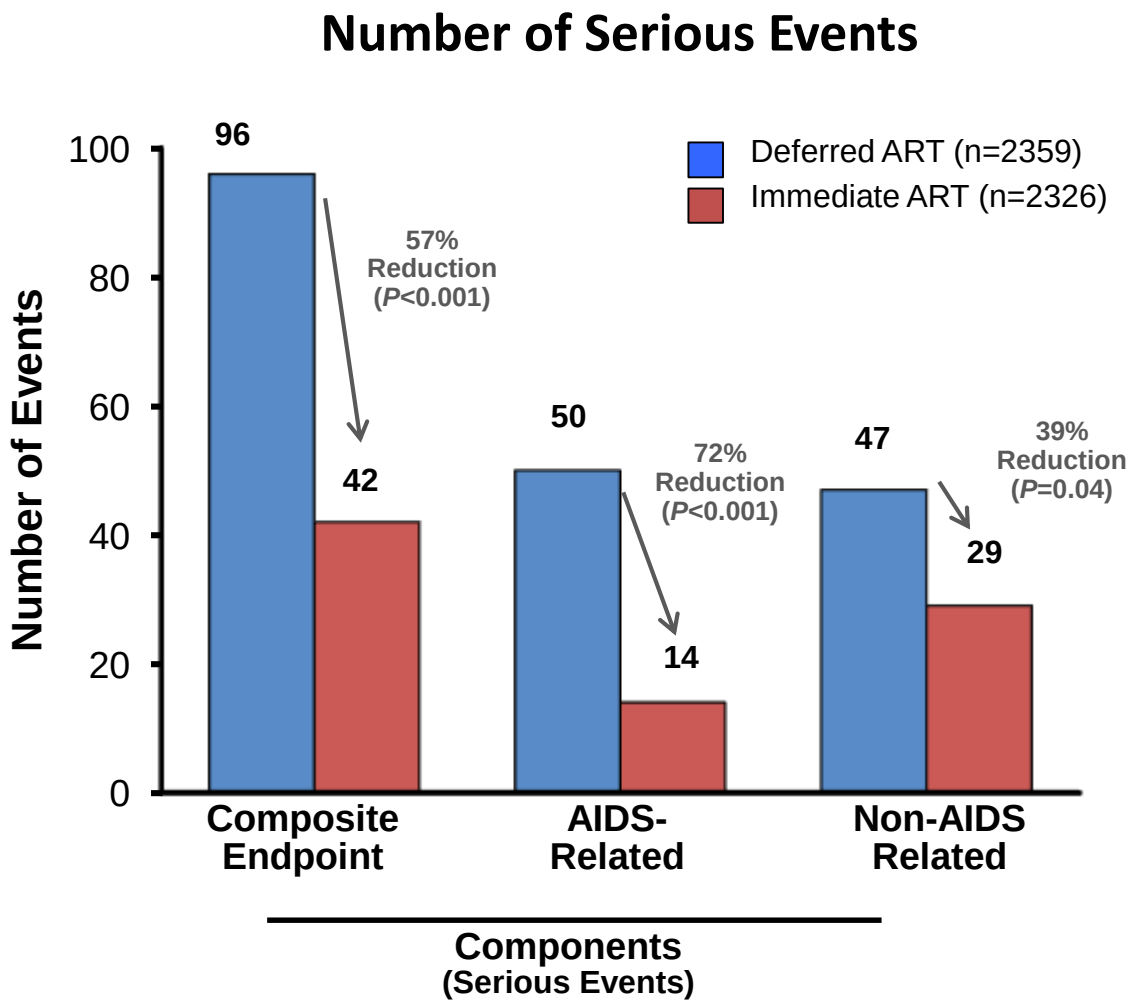
- Lack of acceptance → early developmental stress → syndemics → depression, lack of self-efficacy, and risk
- Criminalization and discrimination in health care settings delay receipt of timely health services

HIV Life Cycle and Antiretroviral Classes



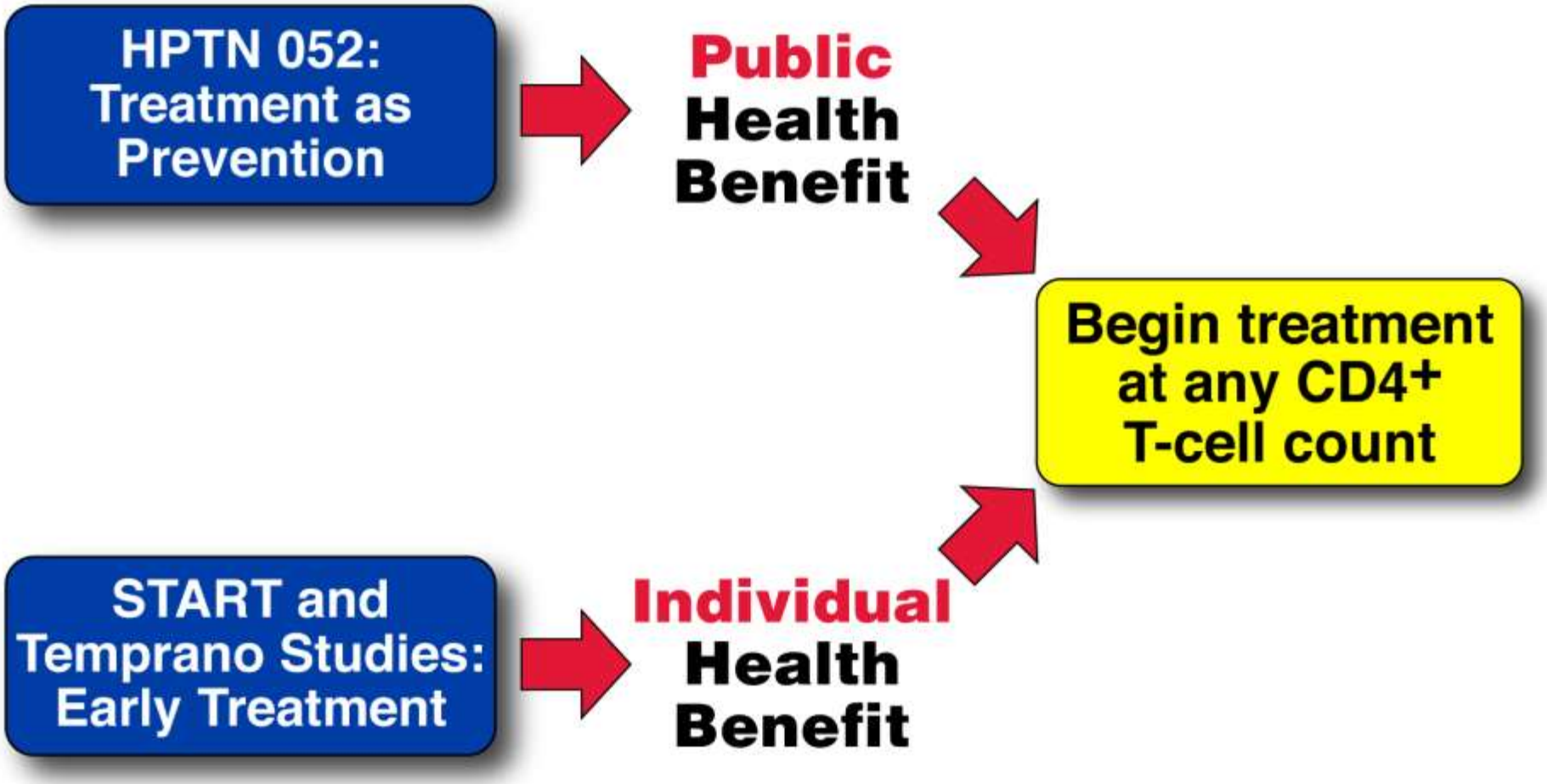
HIV Therapy Recommended Regardless of CD4: START Trial

- HIV-infected adults with CD4 >500
- Randomized to immediate or deferred ART
- Greatest benefit: age >50, VL >50,000, CD4:CD8 <0.5, Framingham score >10%



Lundgren J, et al. INSIGHT START Study Group. *N Engl J Med.* 2015. Borges et al, CROI 2016, #160; Molina J et al, International AIDS Conference 2016, Abstract THAB0201

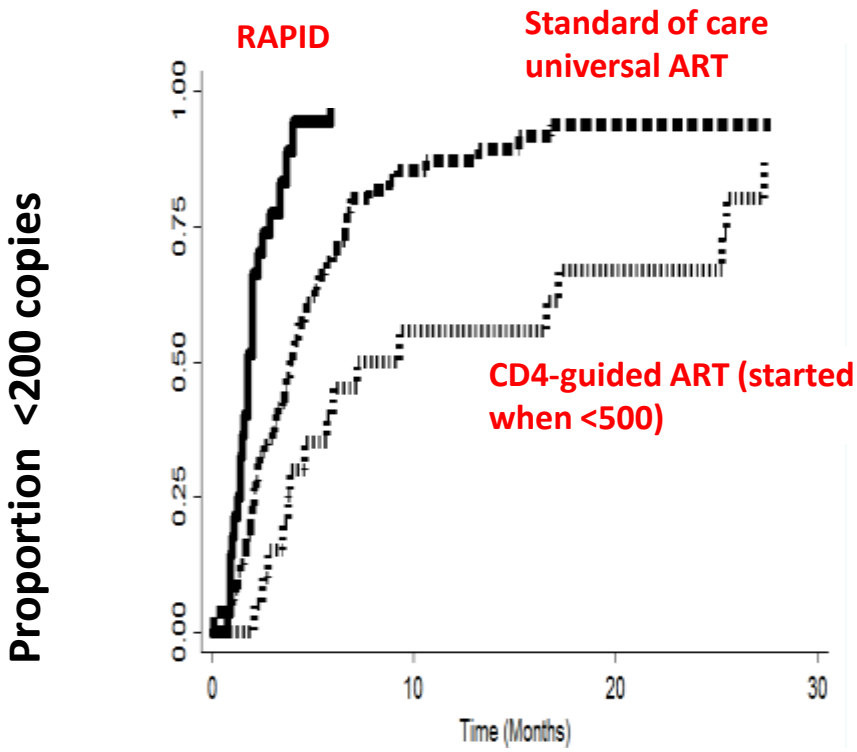
The Paradigm: Treat as soon as ready



Same day Initiation of ART: San Francisco

- 86 people with HIV referred to SFGH with recent infection (<6 mo) or CD4 <200
- RAPID group (n=39): ART (usually DTG + TDF/FTC) on day of dx, usually 1st dose in clinic.
  - Baseline CD4 474 (3-1391)
- Standard of care universal ART (n=47): ART started median of 21 d.
  - Baseline CD4 417 (11-1194)

Time to VL suppression

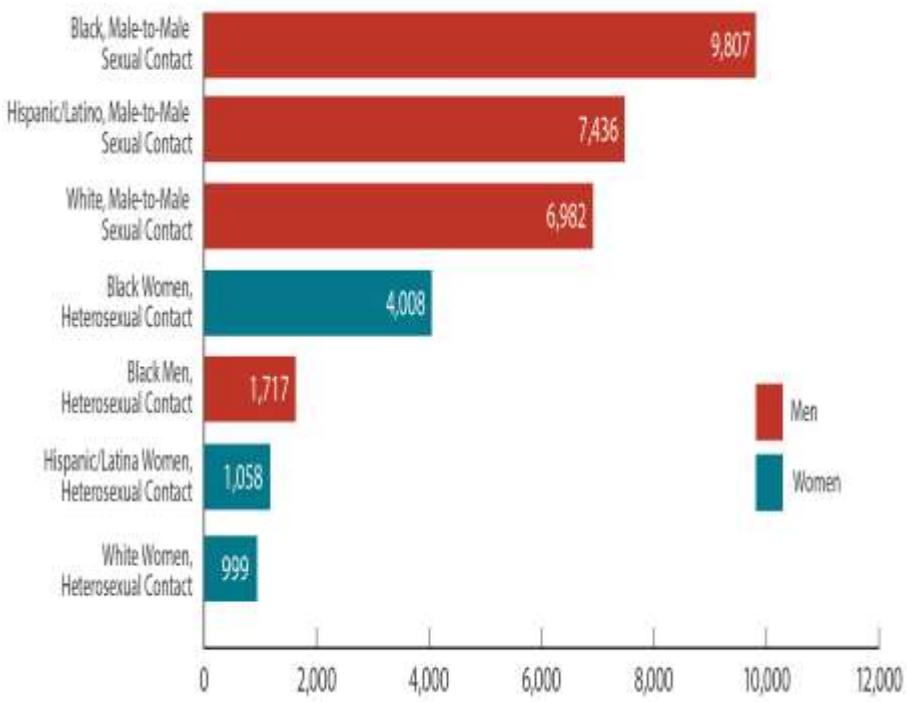


Median time from referral to viral suppression, 1.8 mo in RAPID vs. 4.3 mo. in Standard p<0.001

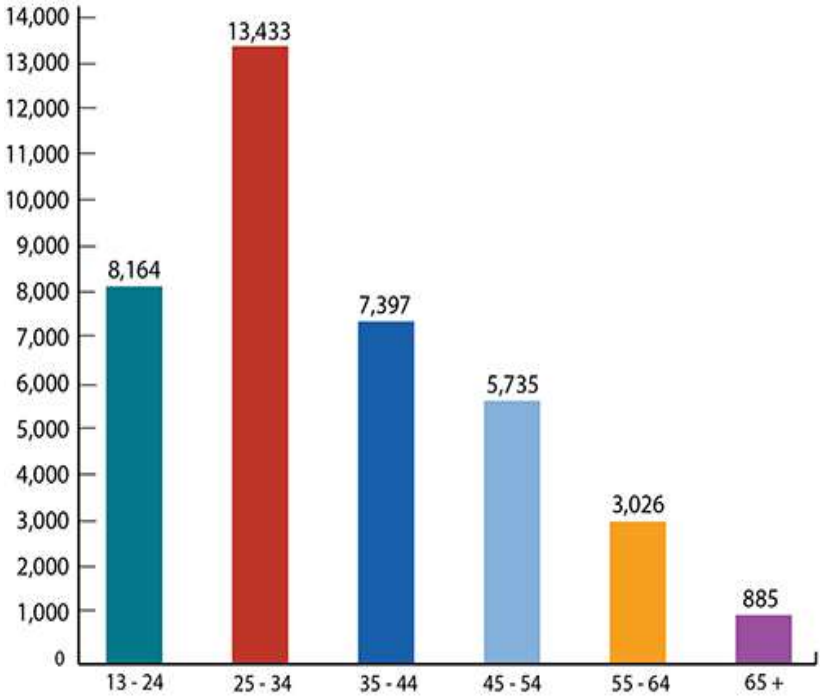
C Pilcher et al, JAIDS, 2016

Current snapshot of HIV in the US

New HIV diagnoses for the most-affected populations, 2017



New HIV diagnoses by age, 2017



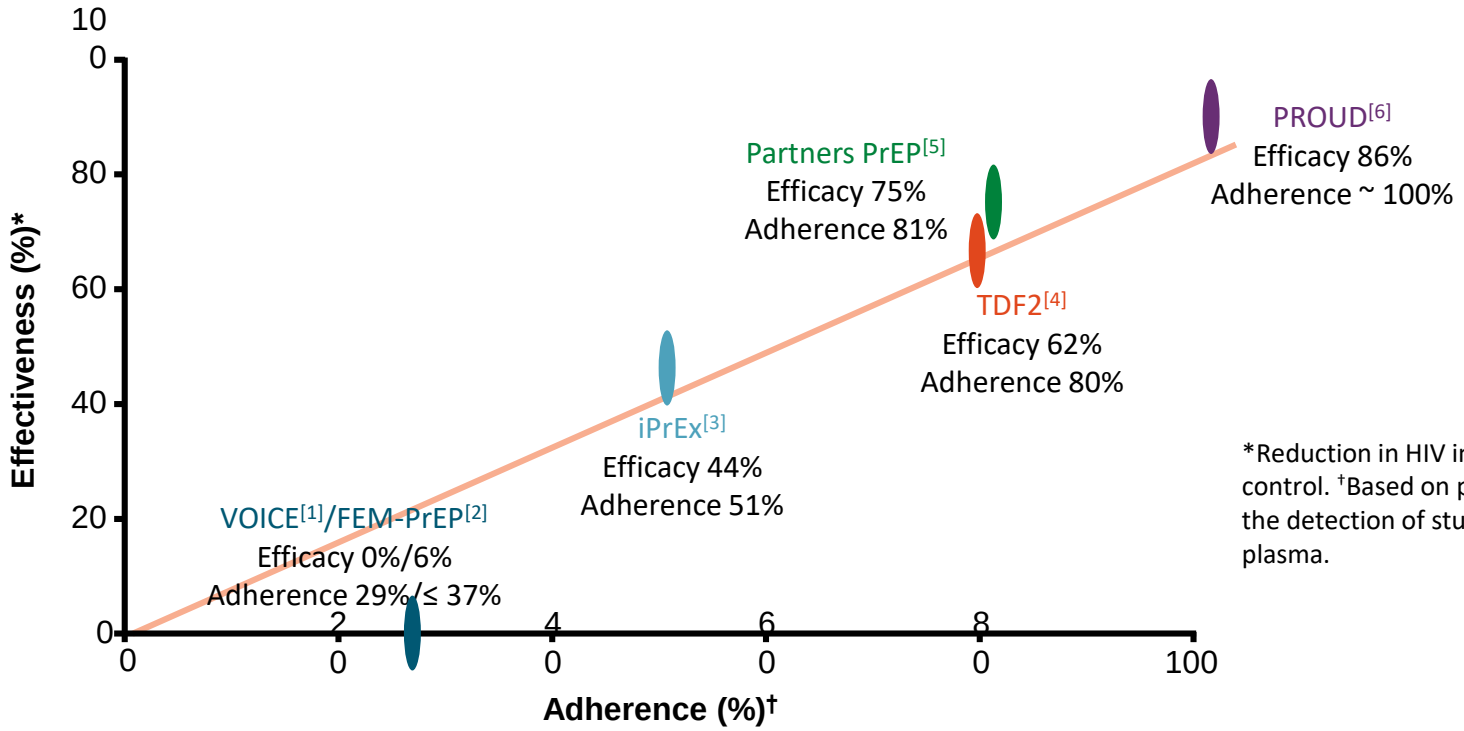
CDC. HIV in the United States and dependent areas. 2019.

Exposure risk per contact with HIV-infected source

Percutaneous (blood)[1]	0.3%
Mucocutaneous (blood)[2]	0.09%
Receptive anal intercourse[3]	1 - 2%
Insertive anal intercourse[4]	0.06%
Receptive vaginal intercourse[5]	0.1 – 0.2%
Insertive vaginal intercourse[6]	0.03 – 0.14%
Receptive oral (male)[7]	0.06%
Female-female orogenital[8]	4 case reports
IDU needle sharing[9]	0.67%
Vertical (no prophylaxis)[10]	24%

1. Bell DM. Am J Med 1997;102(suppl 5B):9-15; 2. Ippolito G et al. Arch Int Med 1993;153:1451-8; 3. Am J Epidemiology 1999;150:306-11; 4. Am J Epidemiology 1999;150:306-11; 5. MMWR 47;RR-17, 1998; 6. NEJM 336(15):1072-8. (rates in Europe & U.S); 7. Am J Epidemiology 1999;150:306-11; 8. Rothenberg RB et al. AIDS 1998;12:2095-2105; 9. MMWR 47;RR-17, 1998; 10. ACTG 076

Daily Oral TDF/FTC PrEP Trials: Effectiveness Improves With Adherence



*Reduction in HIV incidence vs control. †Based on pill counts or the detection of study drug in plasma.

1. Marrazzo. NEJM. 2015;372:509. 2. Van Damme. NEJM. 2012;367:411. 3. Grant. NEJM. 2010;363:2587.
4. Thigpen. NEJM. 2012;367:423. 5. Baeten. NEJM. 2012;367:399. 6. McCormack. Lancet. 2016;387:53.

Is TDF/FTC PrEP Safe?

- Meta-analysis of randomized, placebo-controlled PrEP studies demonstrated that the risk of adverse events not increased for TDF-based PrEP vs placebo[1]
- Reversible changes in creatinine, ↑ in older pts.
- Bone safety:

  -Small net decrease in spine and total hip BMD with TDF/FTC vs placebo, but no difference in fracture rate
  -BMD recovered following PrEP discontinuation
- Not 100% effective, but close to it
  - 7 infections in patients who were adherent.

1. Fonner VA, et al. AIDS. 2016;30:1973-1983. 2. Mulligan K, et al. Clin Infect Dis. 2015;61:57580.
3. Grant R, et al. CROI 2016. Abstract 48LB.

Risk Compensation, Adherence, Coverage

Best Case

"Risky" person is highly adherent to PrEP

No HIV transmission

Worst Case

"Risky" person is not adherent to PrEP

HIV transmission; Select for resistance

Risk Compensation (not often relevant)

Possible, but uncommon in studies

What about real-life setting (no more placebos)?

Match Counseling Messages and Prevention Intervention to Risk

CDC Guidance for PrEP Use

MSM	Heterosexual Women/Men	Injection Drug Users
▪ Any male sex partner in past 6 mos ▪ Not in monogamous relationship with a recently tested, HIV-negative man *And ≥ 1 of These Criteria* ▪ Any anal sex without a condom in past 6 mos ▪ Bacterial STI (syphilis, gonorrhea, or chlamydia) in	▪ Any sex with opposite sex partner in previous 6 mos ▪ Not in monogamous relationship with a recently tested, HIV-negative partner *And ≥ 1 of These Criteria* ▪ Is a bisexual male ▪ Infrequent condom use with ≥ 1 partner(s) with unknown HIV status at substantial risk of HIV infection (PWID or bisexual male) ▪ Is in ongoing relationship with HIV-positive partner ▪ Bacterial STI (syphilis, gonorrhea in females/males) in last 6 mos	▪ Any injection of drugs not prescribed by a clinician in past 6 mos *And ≥ 1 of These Criteria* ▪ Any sharing of injection/drug preparation equipment in past 6 mos ▪ Risk of sexual acquisition

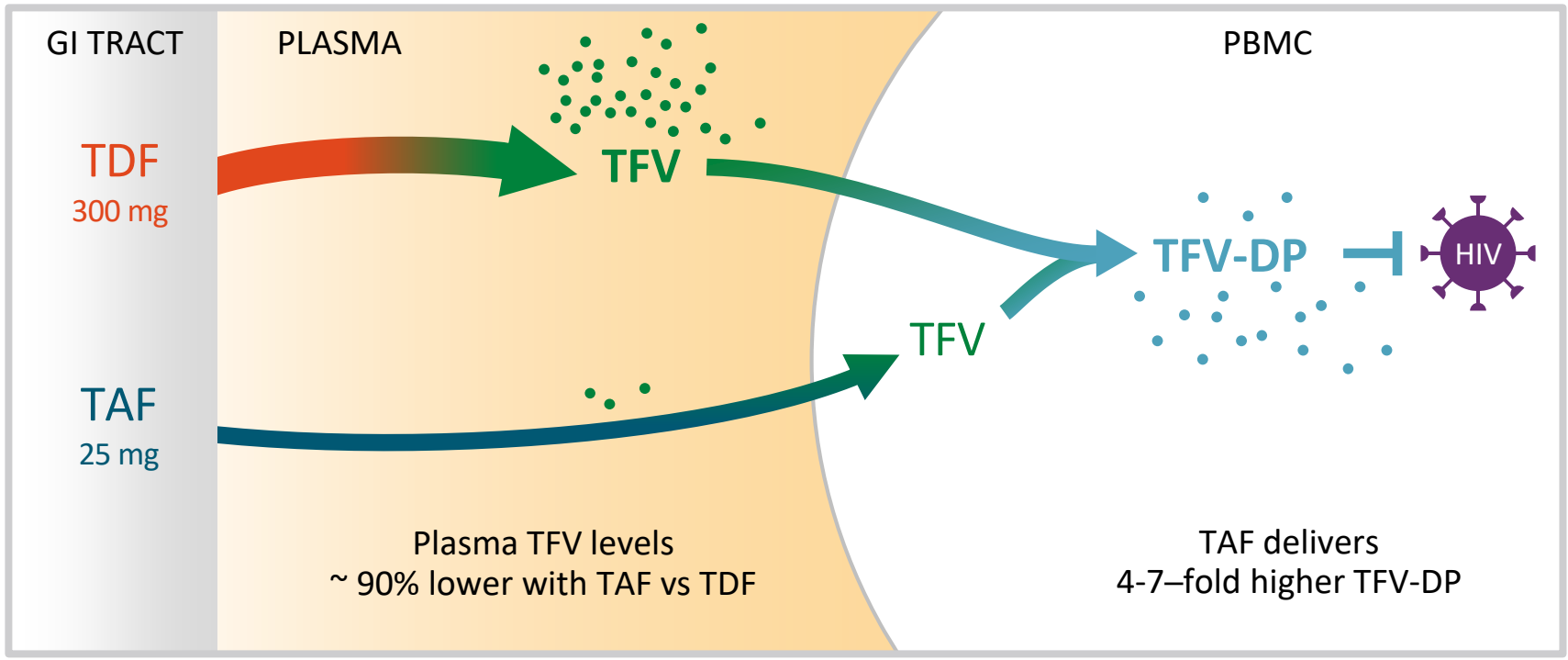
In any category, individual expected to be an adult or adolescent weighing > 35 kg with no acute or established HIV infection.

CDC

USPHS/CDC Guidelines on Prescribing PrEP

- Determine Eligibility (negative HIV test, at high-risk for HIV acquisition, renal function, screen/treat for STIs, screen/vaccinate for Hep B, HCV Ab; pregnancy test)
- Prescribe tenofovir-emtricitabine 1 tablet by mouth daily
- Provide condoms and risk-reduction counseling
- Monitor closely (q 2-3 mo: HIV test, risk assessment/counseling; q 6 mo: renal function, STI screen (q 3 months for some populations?)
- www.cdc.gov/hiv/pdf/PrEPguidelines2017.pdf

Higher TFV-DP Levels in PBMCs With TAF vs TDF

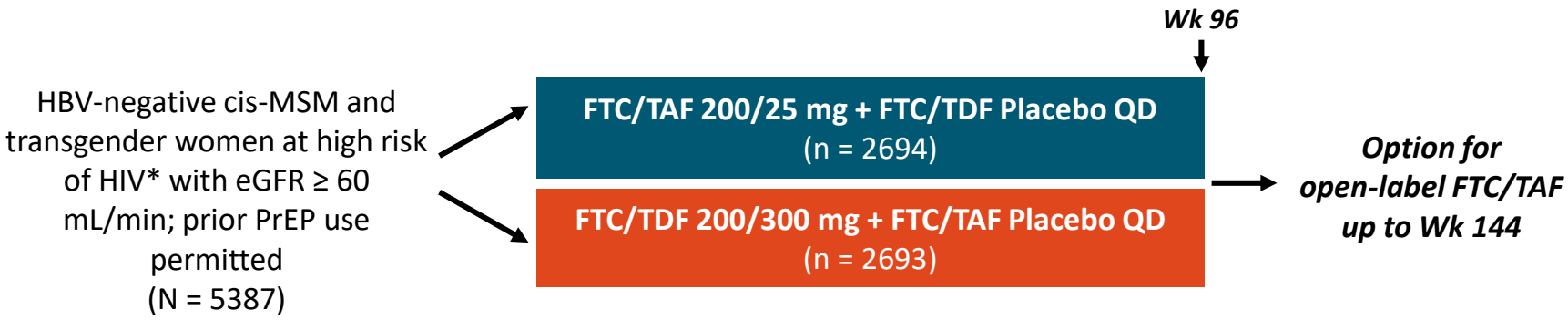


Ruane. JAIDS. 2013;63:449. Sax. JAIDS. 2014;67:52. Sax. Lancet. 2015;385:2606.

Slide credit: clinicaloptions.com

DISCOVER: FTC/TAF vs FTC/TDF for HIV Prevention

- International, randomized, double-blind, active-controlled phase III study



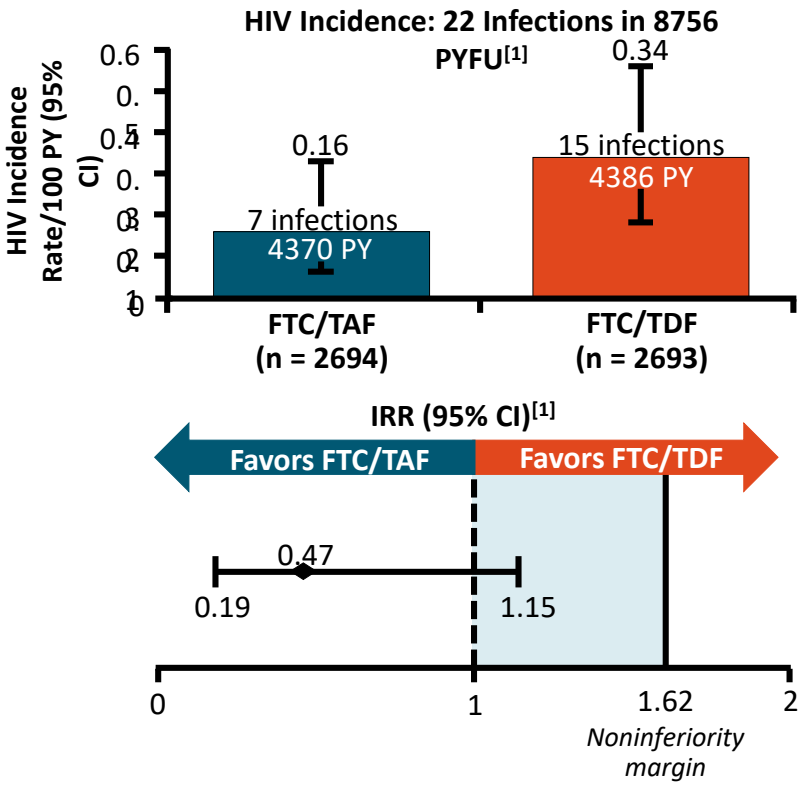
*Defined as ≥ 2 episodes of condomless anal sex within past 12 wks or rectal gonorrhea, chlamydia, or syphilis within past 24 wks. Prevention services (eg, risk reduction, condoms/lubricant) and adherence counseling provided at entry and every 12 wks.

- Primary endpoint: HIV incidence/100 PY
  - Noninferiority upper bound of 95% CI for IRR of FTC/TAF vs FTC/TDF: < 1.62
  - Expected incidence 1.44/100 PY based on prior studies

- Secondary endpoints: safety, including renal biomarkers and BMD substudy
- Critiques: insufficient enrollment of POC
- No parallel study of cisgender women and transgender men

Hare. CROI 2019. Abstr 104LB. NCT02842086.

DISCOVER: FTC/TAF Noninferior to FTC/TDF for HIV Prevention in Primary Analysis



- Primary analysis conducted when 100% completed Wk 48, 50% completed Wk 96[1]
- Noninferiority of FTC/TAF maintained:
  - In sensitivity analysis excluding 5 suspected baseline infections[1]
    - IRR: 0.55 (95% CI: 0.20-1.48)
  - Through Wk 96 analysis[2]
    - IRR: 0.54 (95% CI: 0.23-1.26)

1. Hare. CROI 2019. Abstr 104LB. 2. Ruane. EACS 2019. Abstr PE3/16.

Clinical Decisions Regarding PrEP Choice

Clinical feature	Favors
Pre-existing renal or bone disease/risk factors	TAF/FTC
Patient is MSM or transgender women without a vagina	TDF/FTC or TAF/FTC
Patient has receptive vaginal sex*	TDF/FTC
Patient has hyperlipidemia and/or is obese	TDF/FTC

*efficacy trial in African cisgender women underway

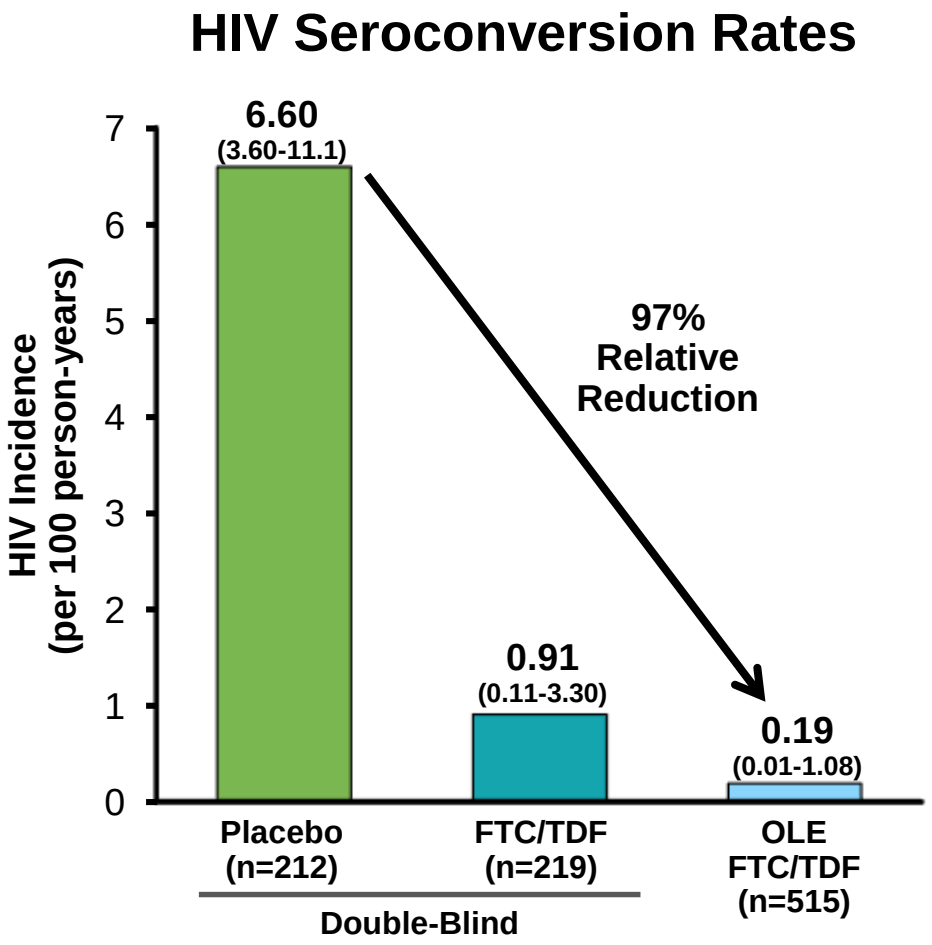
Considerations for On-Demand PrEP

- Off-label in the US (approved by WHO)
- Only efficacy data are from studies in MSM
- Not recommended for cis-gender or trans-gender women
  - Cis-gender women: lower drug concentrations in vaginal vs rectal tissue[1]
  - Transgender women: lower drug concentrations in transgender women using estrogens vs cis gender men[2]
- On-demand PrEP for MSM requires careful consideration, patient discussion
  - Frequency of sex acts, ability to plan ahead for medication use

1. Cottrell. J Infect Dis. 2016;214:55. 2. Shieh. HIVR4P 2018. Abstract OA23.03

ANRS Ipergay Trial Open-Label Extension Study: Efficacy of On-Demand PrEP in High-Risk MSM

- French/Canadian MSM
- 2 pills within 24 hours of sex, and a pill a day X 2 days after
- Generally well tolerated
  - Drug-related GI AEs (10%)
  - 33% acquired a new STD
- Estimated efficacy
  - 97% relative reduction in HIV transmission versus placebo
  - Rare infections in non-adherent or pts acutely infected when they started PrEP
- **On demand PrEP can work, but pts were sexually active and adherent (18 pills/month)**



Molina J-M, et al. *JAIDS*. 2016;19(suppl 5):42. Abstract WEAC0102.

Sex and Racial Disparities in US FTC/TDF PrEP Use Expansion From 2012 to 2016

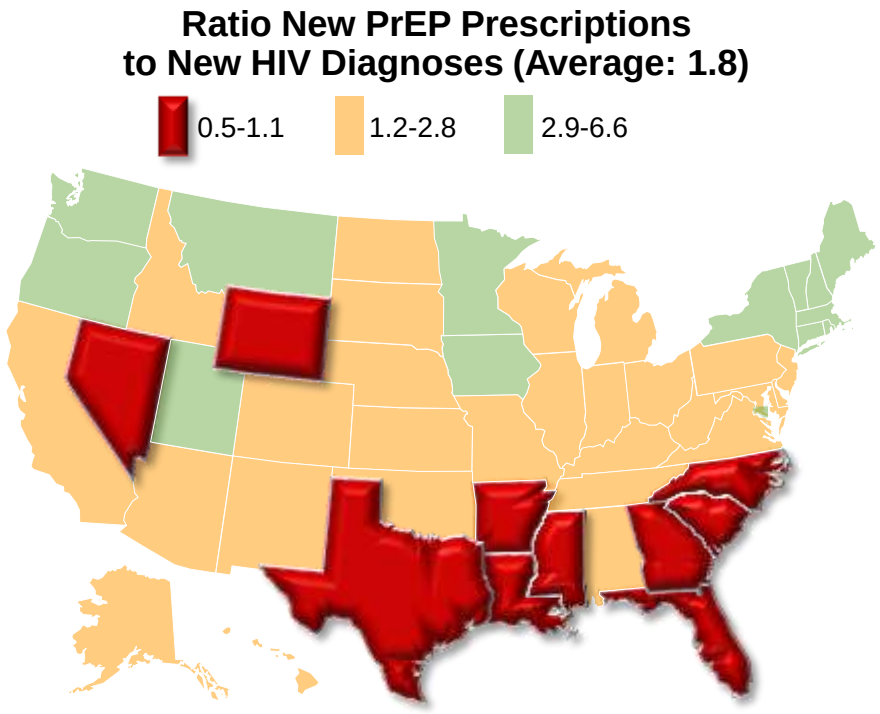
- Electronic patient-level data from 82% of US retail pharmacies with FTC/TDF dispensed for PrEP
  - January 2013 to March 2016
- 67,403 individuals initiated FTC/TDF PrEP
- Quarter-by-quarter growth in utilization 770% overall
  - 72% among women
  - 1350% among men
- In 2015 and Q1 2016, likelihood of initiating PrEP 3.4 and 4.2 times higher for white vs black or Latino women, respectively
  - Likelihood 8.1 and 6.6 times higher for white vs black or Latino men, respectively

FTC/TDF PrEP Start by Race/ Ethnicity Within Sex Subgroups, %	Women	Men
White	65	76
Black	17	9
Latino	15	11
Asian	3	3

Bush. Glasgow 2016. Abstract O314.

Active PrEP Prescriptions in the United States (Q4 2017)

- Number of active PrEP prescriptions for Q4 2017 (n=70,395)
- Only <10% of the 1.2 million people indicated for PrEP are potentially receiving protection
  - Individuals in the Southern United States
    - Account for 52% of new HIV infections
    - Had lower levels of PrEP use relative to new HIV infections



Active PrEP use: ≥1 day of PrEP use in a 3-month period.

Siegler AJ, et al. *Ann Epidemiol*. 2018;28.

Why Some MSM are not using PrEP

- National on-line sample of US MSM recruited on 2 sex networking sites (n=4698)
- 75% condomless anal sex ≥2x in past 3 mo
- Most (85%) had not used PrEP, 22% were unaware of PrEP
- Major barriers to PrEP uptake: structural factors (cost, access, insurance), anticipated side effects, and low perceived risk
  - Anticipated side effects: older MSM
  - Access concerns: black MSM, less educated MSM, MSM born outside of the US

Reasons for not Using PrEP Among Informed Non-Users (n=2926)

	Respond. (%)
Concerns about:	
Costs	40
Potential side effects	31
Effects on insurance	20
Medical provider's reaction	18
Reaction of sexual partner	5
Do not know where to access PrEP	31
Do not feel at risk	19
Did not think it would be effective	5

Mayer KH, et al. *J Int AIDS Soc*. 2017;20(suppl 4). Abstract MOPEC0648.

Tailoring PrEP for Key Populations

HPTN 073 Black MSM

Culturally-Tailored
Client-centered care coordination (C4)

ATN 110/113

- YMSM 15-22 y.o.
- PreP + Individual vs. group behavioral intervention (Hosek et al)

HPTN 073: PrEP for Black MSM

- Evaluating PrEP acceptance, initiation, adherence, safety among black MSM in LA, DC, Chapel Hill, NC
  - PrEP coupled with client-centered care coordination (C4): individualized prevention counseling, support, and service coordination; participants followed for 12 mos
  - 226 HIV-uninfected black MSM; 40.2% younger than 25 yrs of age
- **Of 178 who accepted PrEP in study, 5 acquired HIV (incidence: 2.9; 95% CI: 0.9-6.8)** vs 3 of those who never accepted PrEP (incidence: 7.7; 95% CI: 6-22.5)

  -several discontinued PrEP prior to seroconversion
- 2.9% incidence is still too high, but HPTN 073 showed client-centered care coordination beneficial and PrEP acceptable, feasible with high uptake among black MSM

Wheeler. AIDS 2016. Abstract WEAC0104. Wheeler. J Int AIDS Soc. 2019;in press. https://www.hptn.org/research/studies/hptn073.

PrEP Barriers Among Adolescents

- ATN 110/113 showed **adherence is a challenge among adolescents**, decreasing PrEP efficacy vs adults
  - Because adherence was highest during first 3 mos when clinic visits were monthly, it may make sense to **have more frequent contact with youth** when they initiate PrEP
  - Nonetheless, PrEP is approved for all weighing >30 Kg.
- Laws regarding consent vary by state concerning consent, confidentiality, parental disclosure, and reporting
  - In some states, emancipated minor laws allow for direct provision of PrEP to the adolescent without parental engagement (e.g., Florida, Massachusetts)
  - Parental insurance coverage can result in unintended disclosure
- Specific considerations are needed made for LGBTQ adolescents to reduce stigma and health disparities

Hosek. JAMA Pediatr. 2017;171:1063.

Transgender People and PrEP

- 11 HIV infections among transgender women (TGW) in iPrEX who got PrEP, 10 infections in placebo group
  - None of the TGW who became infected had detectable drug at visit where HIV was first detected
  - Lack of protection for 11 in PrEP group “seems to be primarily a result of low adherence”
- **PrEP protective in subgroup of TGW with high adherence**
- PrEP meds do not alter feminizing hormone levels, but high dose estrogens mildly decrease tenofovir levels, making adherence to daily regimen important.
- Much less known about transgender men (TGM), but a recent national survey found that some TGMSM had high levels of HIV risk and low levels of PrEP knowledge, suggesting a major unmet need exists

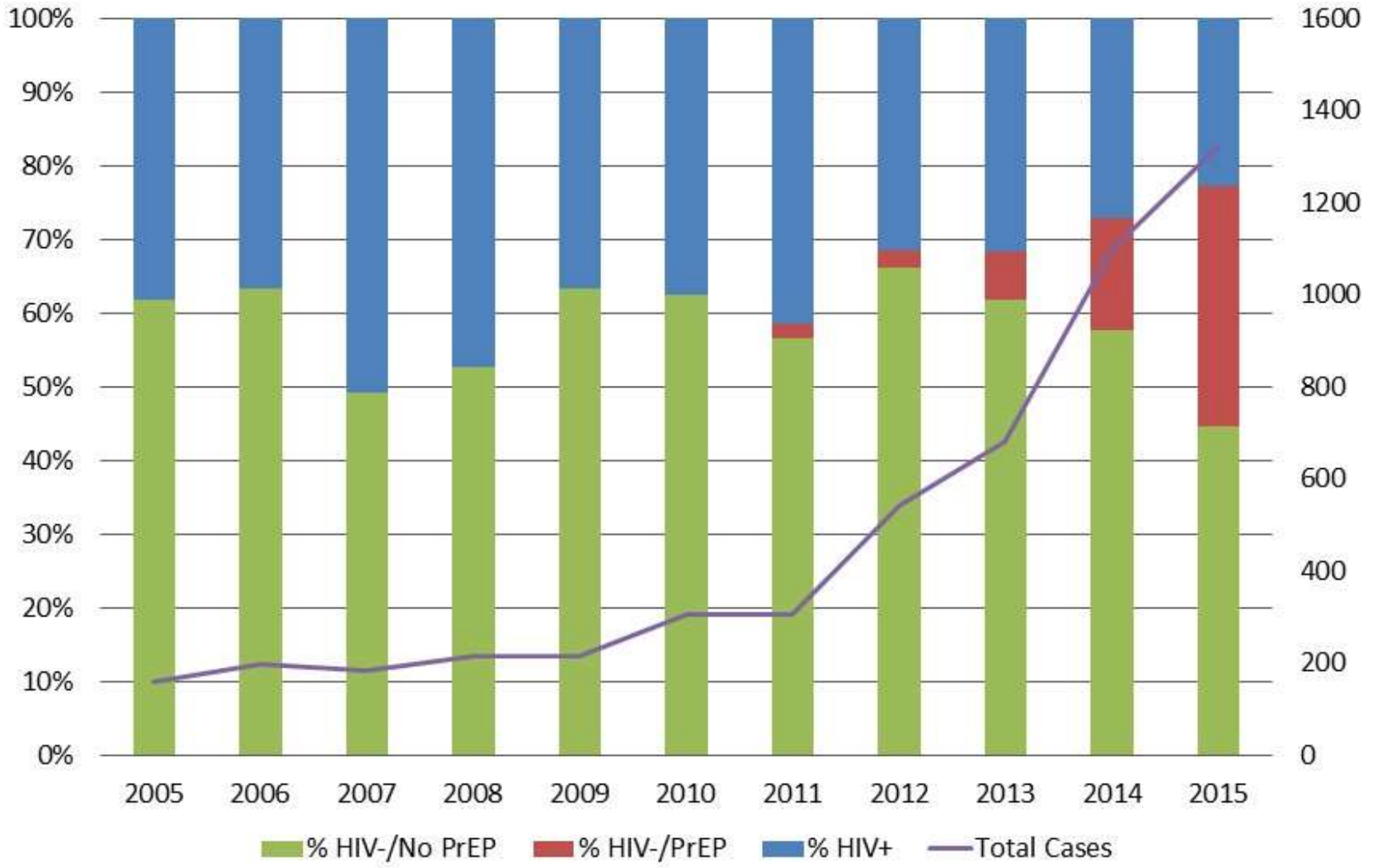
Deutsch et al, *The Lancet*. 2015; Reisner et al, JIAS, 2019

PrEP and “risk compensation”

- Fear for increase in risky behavior in persons using PrEP
- Increase in STI incidence

- Older fear around introduction of biomedical sexual health interventions:
  - penicillin in the 1950’s
  - oral contraceptives in the 1960’s
  - HPV vaccination in the 2000’s

Frequency of Bacterial STI infection, by HIV status and PrEP Use, among Male Patients, Fenway Health



Mayer, OFID, 2017

STI Incidence Before/After PrEP among MSM

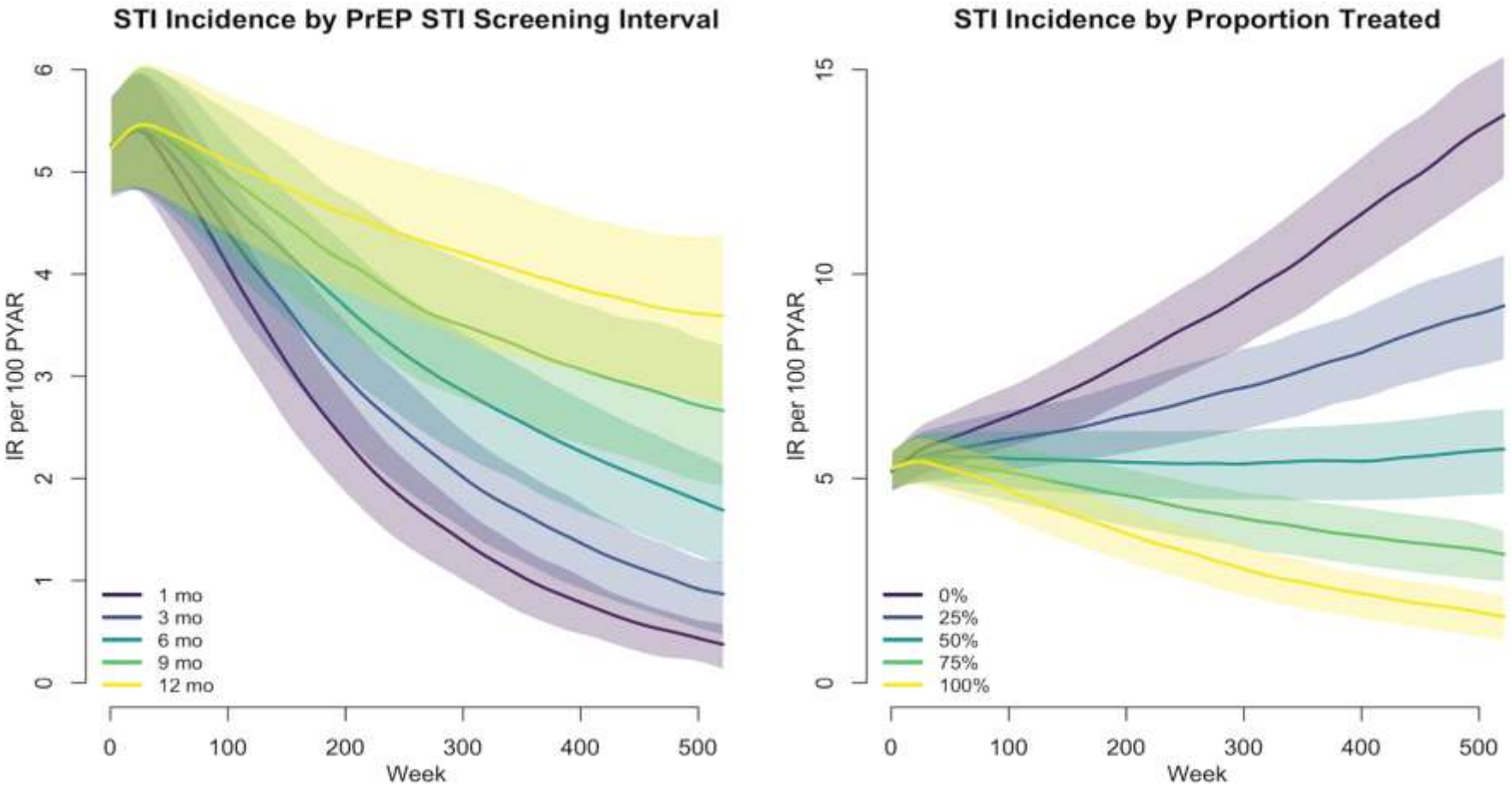
- 1378 participants of the PrEPX study in Australia with pre-enrollment testing data
- Mean follow-up of 1.1 years

	STI Incidence 1 year before Per 100 PY	STI Incidence Post Entry Per 100 PY	Incidence Rate ratio (95% CI)	Adjusted IRR* (95%CI)
All	69.5	98.4	1.41 (1.29-1.56)	**1.12** (1.02-1.23)
PrEP-Exp (n=541)	92.4	104.1	1.13 (0.99-1.28)	**1.05** (0.92-1.19)
PrEP-Naive (n=837)	55.1	94.2	1.71 (1.49-1.96)	**1.21** (1.06-1.39)

*Adjusted for testing frequency

Traeger M. et al, JAMA 2019;321:1380

Incidence of Gonorrhea and Chlamydia among MSM using PrEP



Over the next decade, 40% of NG and CT infections would be averted (40% PrEP coverage)

Jenness et al CID 2017

CDC: PrEP Persistence in the United States (2012-2016)

- PrEP persistence assessed using commercial and Medicaid insurance databases (2012-2016)
  - Non-persistence: >30-day gap from end of 30-day PrEP supply to refill of PrEP prescription
  - Most PrEP users were male and >24 years of age
- Medicaid insured PrEP users persisted for less time than commercially insured PrEP users
- Commercially insured non-persistent PrEP users: more likely to be younger, female, rural.
- Medicaid insured non-persistent PrEP users
  - More likely to be of younger age, female, and black

*Inclusion criteria : 18 to 64 years of age (continuously enrolled in health plan
6 months before/after PrEP prescription date)

*P<0.001 and P<0.05.

Huang YL, et al. NHPC. Atlanta, 2019. Abstract 5214.

PrEP Pricing

- Currently, both meds cost the same (20K/year)
- Generic TDF/FTC should be available from one manufacturer in Sept, 2020→modest ↓ cost
- 6 months later, any generic manufacturer can produce TDF/FTC, which should lower costs substantially
- Questions include:

  -impact on drug assistance programs

  -340B pricing

Financing Models for PrEP: A Patchwork of Funding and Delivery Mechanisms…

	Drug Access	PrEP Clinical Visits & Lab Costs	Counseling and Linkage
Uninsured	Manufacturer Patient Assistance Program PrEP Drug Assistance Programs or "PrEP DAPs" (state funded) Community Health Centers; Family Planning Clinics; STD Clinics using 340B savings	PrEP DAPs (state funded) CDC prevention funds to pay for HIV/STD testing Community Health Centers; Family Planning Clinics; STD Clinics using 340B savings	PrEP DAPs (state funded) CDC prevention grants and 340B savings Community Health Centers; Family Planning Clinics; STD Clinics using 340B savings
Insured	Covered by payers; co-pay assistance through manufacturer assistance program	Largely covered, but with patient co-pays PrEP DAPs pay for lab/clinical visit co-pays (state funded)	Not well covered by public or private insurance

Purview paradox: contradictory beliefs about which providers will prescribe PrEP

(Krakower, AIDS and Behavior, 2014)

HIV providers:

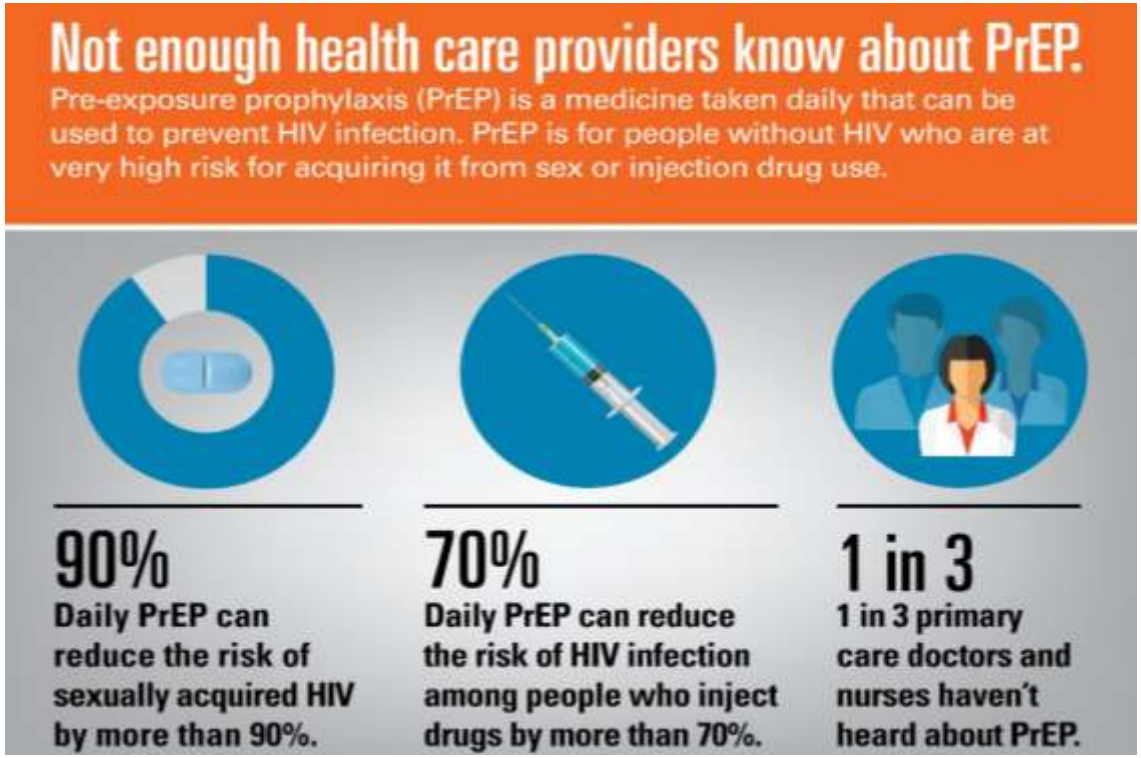
Primary care providers are in the best position to prescribe PrEP

Primary care providers:

It would not be feasible to prescribe PrEP

Expanding PrEP Service Providers

- Expanding service delivery locations and to other providers – primary care, NP, pharmacy
  - Addresses stigma, geographic barriers



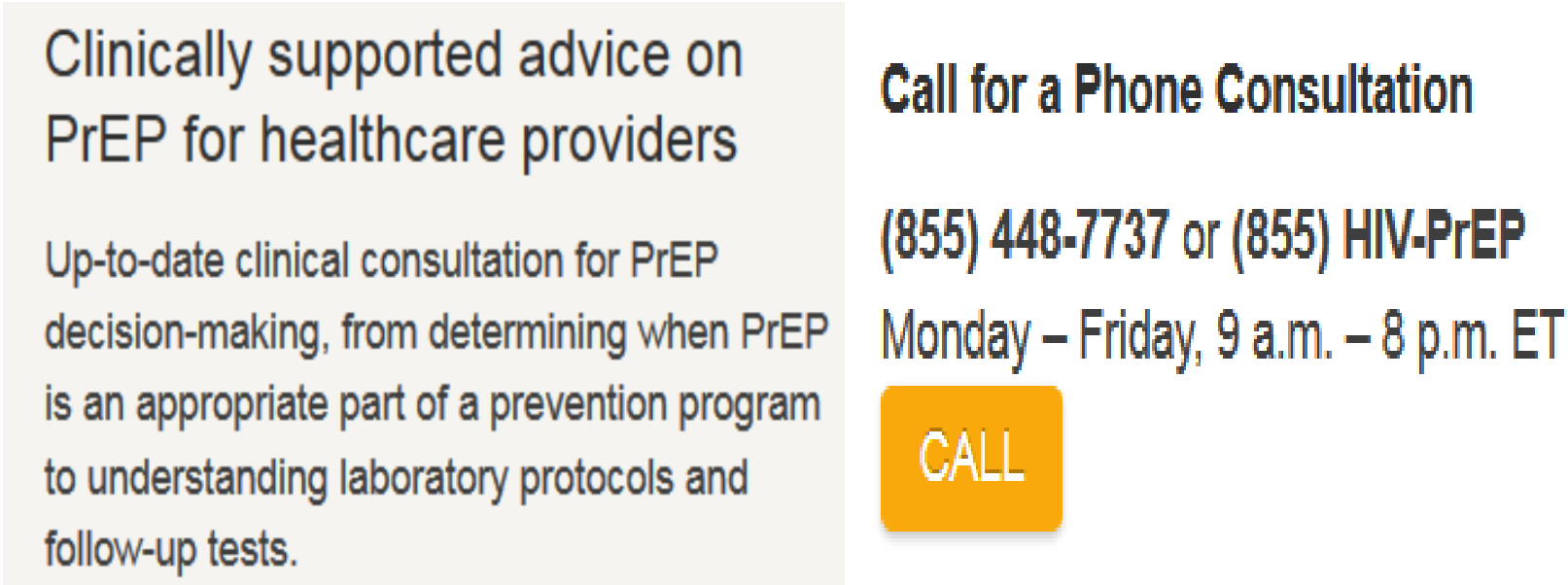
CDC. Vital Signs. 2015.

Online PrEP Tools

- Various online tools providing range of service levels from full PrEP service provision to directories for assistance finding a PrEP provider
  - Eg, *Nurx*, *PlushCare*, PleasePrEPMe
- With some online tools, individuals still need a location to access lab services
- Insurance coverage still needed
- These approaches may addresses stigma-related barriers by allowing anonymity in PrEP and empowering PrEP users
- Could be particularly useful for younger, tech-saavy populations

Provider Hotline, Provider Education

- PrEPline: CDC and UCSF Clinical Consultation Center
  - http://nccc.ucsf.edu



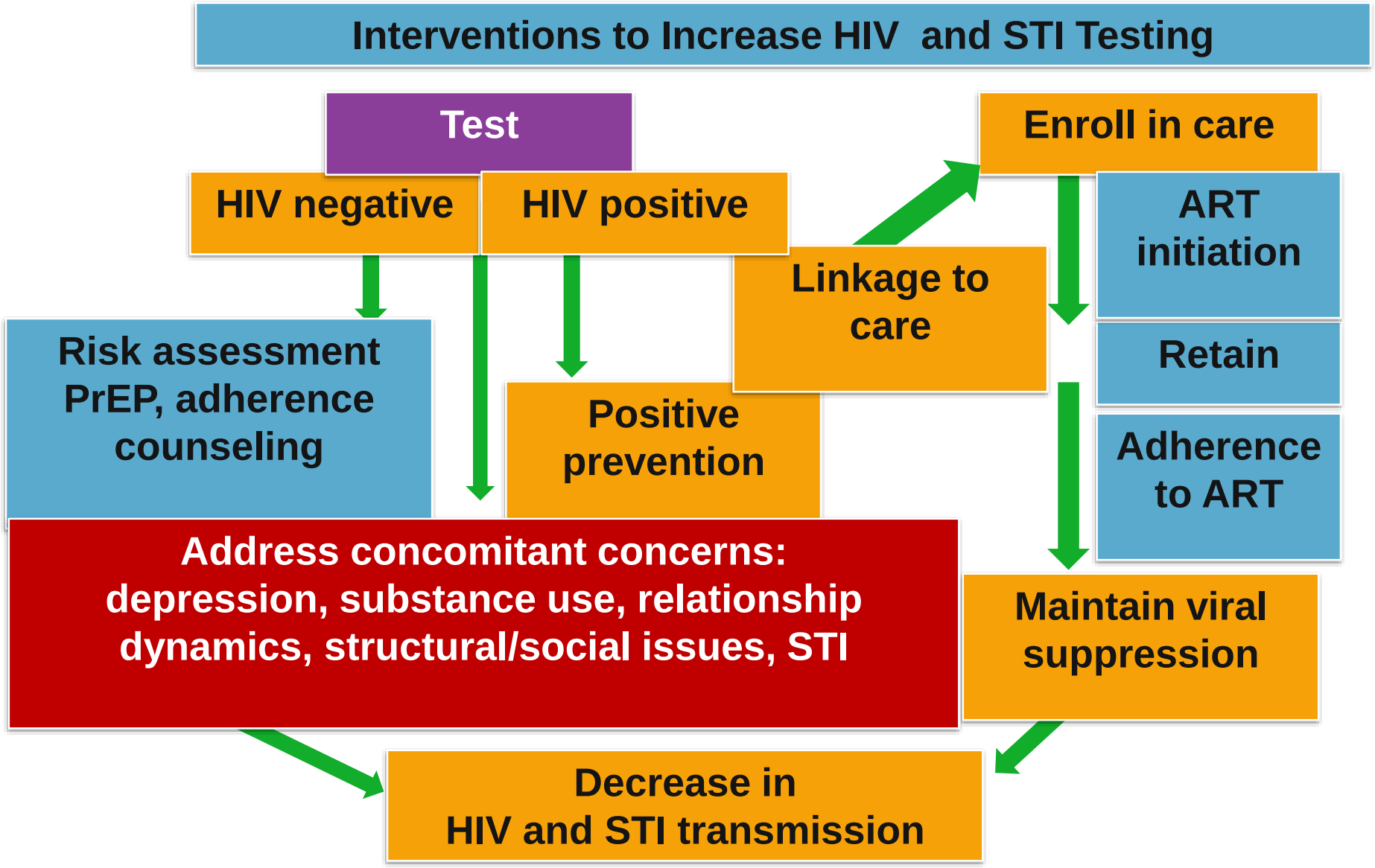
PrEP ECHO: www.lgbthealtheducation.org

AVAC
Global Advocacy for HIV Prevention

The Years Ahead in Biomedical HIV Prevention Research

Status of select biomedical HIV prevention clinical trials

Need to Address more than PrEP and U=U



Contact/Resources

- Amy Killelea, NASTAD (akillelea@nastad.org)
- NASTAD PrEP Resources – https://www.nastad.org/prepcost-resources/additional-resources
- PrEPcost.org – NASTAD's online plan assessment tool for PrEP
- AIDSVu PrEP Mapping – https://aidsvu.org/prep/
- CDC PrEP Guidelines – https://www.cdc.gov/hiv/risk/prep/index.html

Thank you

Kevin Ard
Alex Keuroghlian

Amy Killilea

Aaron Siegler
Patrick Sullivan

FENWAY HEALTH

NIAID, NIMH, NIDA, NICHD, CDC, HRSA, Mass DPH, Gilead