

HIV: RAPID Start AND New Drugs

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Disclosures

- No disclosures or conflict of interest

What is PrEP?

What if I test positive?

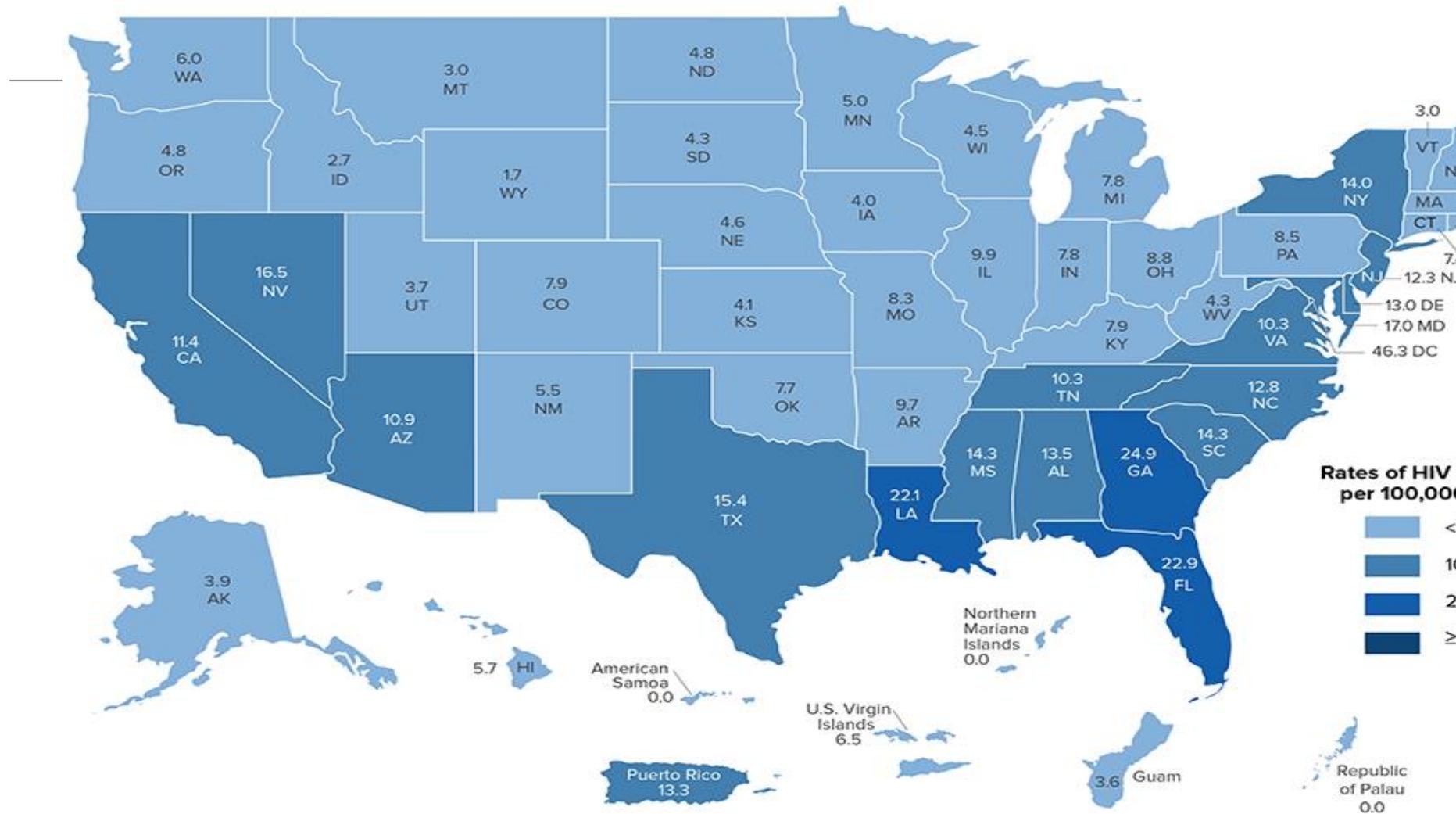
How many people are living with HIV?

Where can I get Tested?

Objectives

- To discuss an overview of RAPID Start ART
- To go over recently approved antiretrovirals (ART)
- To describe the use of 2-drug regimens in persons living with HIV

Rates of New HIV Diagnoses in the US,



UNAIDS Target by 2020 (TasP)

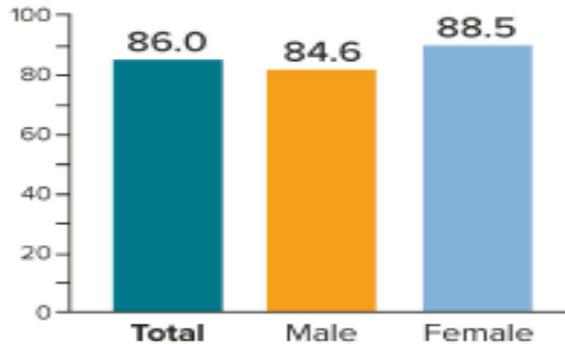


Same Day ART

- Decrease the time from diagnosis to treatment
- Redesign clinic structure, processes, etc. to treat people faster

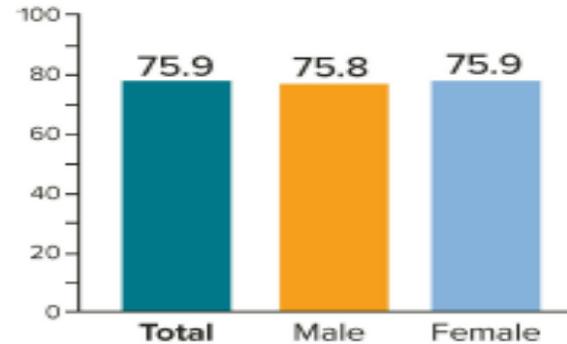
HIV: Continuum of Care

Persons Living with Diagnosed HIV Infection
HIV Care Continuum Outcomes, by Sex 2015 US



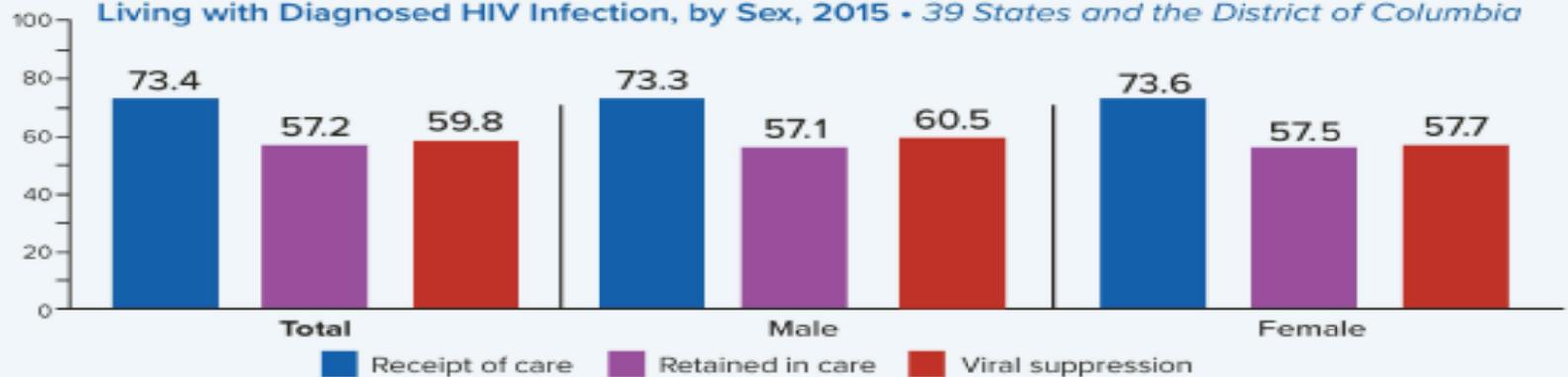
Note: Estimates derived by using HIV surveillance from NHSS and CD4 data for persons aged > 13 years.

Linkage to HIV Medical Care within 1 Month after HIV Diagnosis
during 2016 among Persons Aged > 13 Years, by Sex, 2016
39 States and the District of Columbia



Note: Linkage to HIV medical care was defined as having a CD4 or VL test \leq 1 month after HIV diagnosis

Receipt of HIV Medical Care, Retention in care, and Viral Suppression among Persons Aged \geq 13 Years
Living with Diagnosed HIV Infection, by Sex, 2015 • 39 States and the District of Columbia



Note: Receipt of medical care was defined as \geq 1 test (CD4 or VL in 2015). Retained in continuous medical care was defined as \geq 2 tests (CD4 or VL) \geq 3 months apart in 2015. Viral suppression was defined as $<$ 200 copies/mL on the most recent test in 2015.

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Division of HIV/AIDS Prevention



CASE #1

- 46 yo man presents to primary care clinic to discuss Lab results
 - HIV Ag/Ab screen and HIV confirmatory test sent 3 days prior positive
 - PMH significant for depression and hypertension
 - The PCP discusses the HIV test results with the patient
- 

What is the best strategy for the first visit with the Infectious Diseases (ID) Clinic

1. The patient meets with the provider and gets lab work done
2. The patient gets lab work done and schedules an appointment in ID clinic within 4 weeks. A team member is assigned to call the patient in one week
3. The patient meets with the nurse, provider and case manager
4. The patient schedules an appointment within 4 weeks in ID clinic. A team member is assigned to call the patient in 2 weeks

Rapid ART Initiation of Treatment (Rap

■ Primary outcome

- VS (≤ 400 copies/ml) within 10 months of study enrollment

■ Secondary outcomes

- Initiation of ART ≤ 90 days of study enrollment
- Retention in care
- Time to ART initiation
- Feasibility and acceptability of intervention

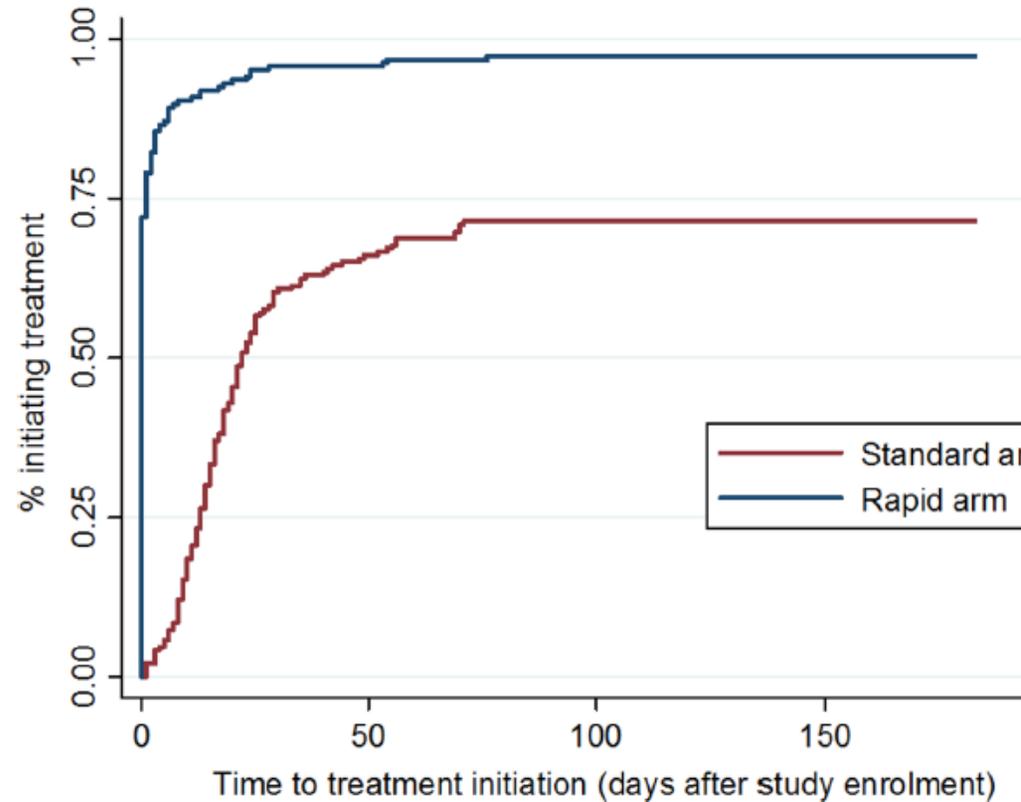


Fig 3. Time to ART initiation, by study arm. Cumulative incidence of ART initiation in each number of days since study enrollment.

Rapid ART Initiation of Treatment (Rap)

- 64% (119/187) patients initiated treatment and were virologically suppressed in the rapid arm at 10 months compared to 51% (96/190) in the standard arm (**primary outcome**)
- 81% (151/187) initiated ART ≤ 90 days and were retained in care at 10 months in the rapid arm compared to 64% (121/190) in the standard arm (**secondary outcome**)
- Single-visit ART initiation increased ART uptake by 36% and viral suppression by 13% in South Africa

Same-Day (Rapid) Start ART: US

- WHO recommended that Rapid ART initiation should be offered to all people living with HIV with a confirmed HIV diagnosis and clinical assessment in 2017
- In the US, San Francisco implemented a citywide RAPID ART program for newly diagnosed people
 - Of 265 newly diagnosed → 97% were linked to care (30% within 5 days) and 81% started ART
 - Time from diagnosis to VL <200 copies/ml decreased by more than 50% and time from first care to ART decreased from 27 days to 1 day
- The Atlanta experience
 - Time from diagnosis to VL <200 copies/ml decreased from 77 to 57 days and time to ART initiation decreased from 21 to 7 days

<http://www.who.int/hiv/pub/guidelines/advanced-HIV-dise>

Pilcher CD. J Acquir Immune Defic Syndr 2017. Colasanti J. C

Same Day ART

- WHO endorsed ART initiation within 7 days of new diagnosis
- IAS recommends Rapid ART for all infected ambulatory patients (**unless the patient has symptoms of an opportunistic infection**) or for those with an unclear HIV diagnosis

I'm a **Case Manager**.
I help you understand
HIV and can connect
you with HIV services.

I'm a **Pharmacist**.
I fill your prescriptions
and answer any
questions you have
about your
medicine.

I'm a **Health Care
Provider**. I run tests,
prescribe medicines,
and work with you to
select an HIV regimen.

We're your **Partner,
Friends, and Family**.
We offer support and
help you live a
healthy lifestyle.



It takes a team to stay healthy with HIV. Who's on your team?

Clinic and Practice Setting: Type of Ca

- HIV specialty care (no primary care provided)
- Primary care with HIV care integrated
- HIV specialty care with primary care integrated
- Other

} One-stop-shop approach

Additional Services Provided

- Mental health services
 - Dental services
 - Case management
 - Other
-
- In-house or somewhere else

HIV CARE CONTINUUM:

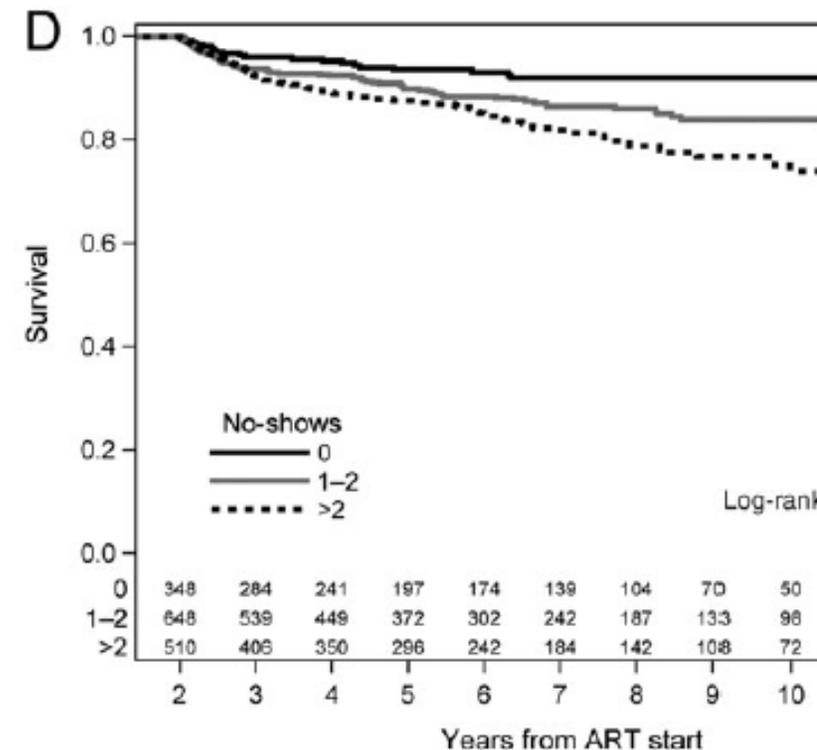
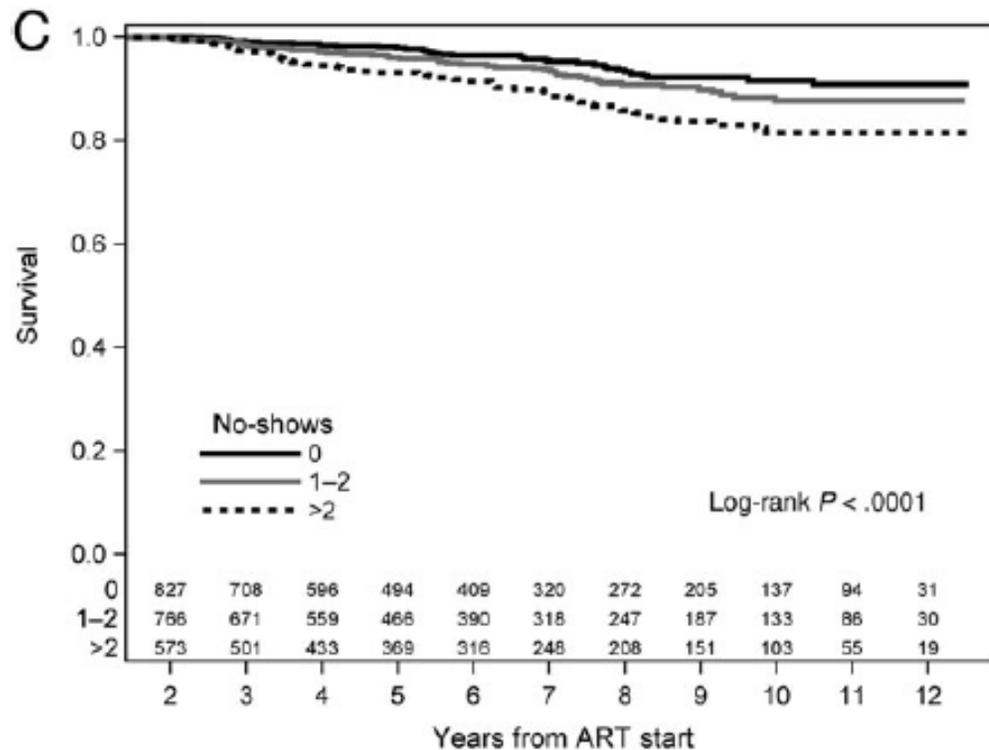
THE SERIES OF STEPS A PERSON WITH HIV TAKES FROM INITIAL DIAGNOSIS THROUGH THEIR SUCCESSFUL TREATMENT WITH HIV MEDICATION



- Primary care, Lab
- Case Management
- Mental Health
- Adherence Counseling

- Provider, Lab, Nursing
- Case Management
- Adherence Counseling
- Mental Health

Missed Clinic Visits are Independently Associated with All-Cause Mortality



Recent Depressive Symptoms are a RF for Unsuppressed HIV VL

Table 2. Risk Ratios and 95% Confidence Intervals for the Association Between Having Recent Depressive Symptoms and the Risk of an Adverse Event Over Time Along the Human Immunodeficiency Virus Treatment Cascade

Depressive Symptom Status	Detectable Viral Load ^a		Missed Human Immunodeficiency Virus Treatment ^b	
	Unadjusted	Adjusted ^b	Unadjusted	Adjusted Set 1 ^c
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
No depressive symptoms (PHQ-9 < 10)	1.00	1.00	1.00	1.00
Depressive symptoms (PHQ-9 ≥ 10)	1.37 (1.20, 1.56)	1.28 (1.07, 1.53)	1.24 (1.07, 1.39)	1.20 (1.05, 1.36)



Same-Day (Rapid) Start ART: Example Protocol

■ Day 1

- Upon notification, Confirm diagnosis and contact patient
- Patient meets with provider (initial education, symptom assessment/OI, risk behavior modification, med counseling, partner notification/PrEP and social worker (to assess imminent barriers to care, MH, SI/HI)
- Lab work including RT/PI genotype, CD4 count, HIV VL, hepatitis serology, SCR, UA
- ART initiation: BIC/TAF/FTC; DTG + TAF/FTC; or Boosted DRV + TAF/FTC

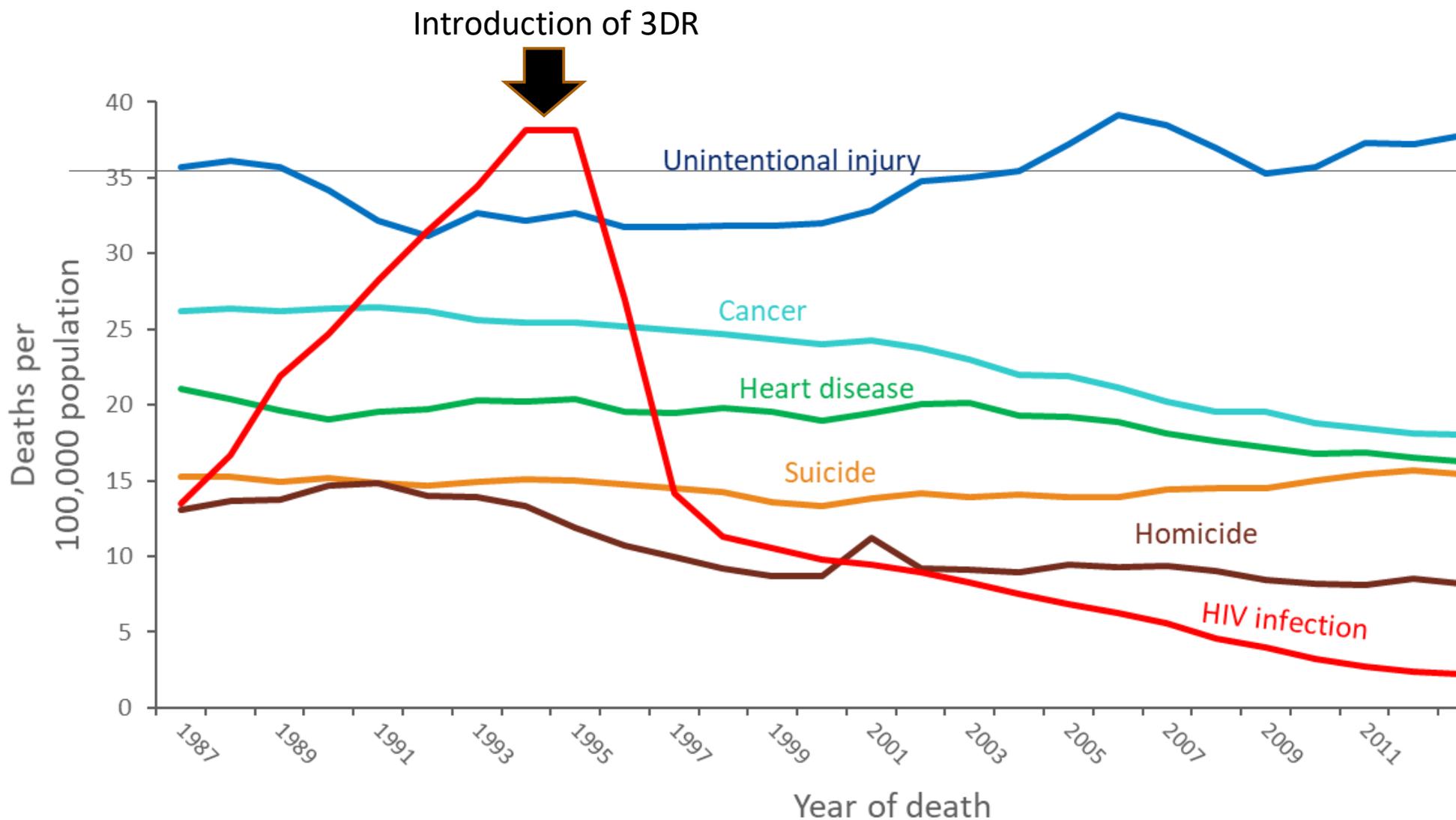
■ Day 14

- Telephone visit with PharmD for med reconciliation, drug interaction, side effects and adherence education
- Lab work: SCR, UA, HIV VL
- Social worker call if follow up on any resources needed and identified during visit on Day 1 and to assess for any ongoing barriers to care

■ Week 4-6

- Provider visit: assess med adherence, side effects, drug interactions, risk behavior modification and psychosocial issues
- Lab work: CD4 count, HIV VL, CBC, CMP, UA

Mortality Among Persons 25-44 Years old, USA: 1987-2015



Note: For comparison with data for 1999 and later years, data for 1987-1998 were modified to account



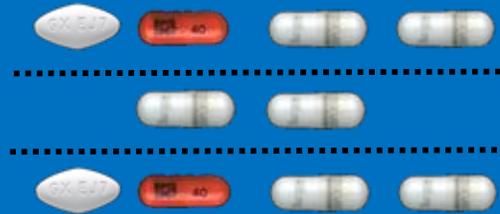
© 2015 CDC

FDA- Approved HIV Drugs in 2018/20

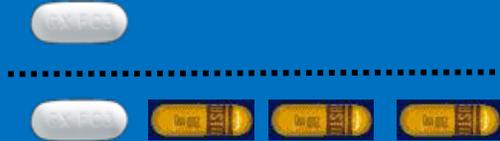
- BIC/TAF/FTC: February 7, 2018
 - Ibalizumab: March 6, 2018
 - DRV/C/FTC/TAF: July 12, 2018
 - Doravirine (or DRV/3TC/TDF): August 30, 2018
 - DTG/3TC: August 8, 2019
- 

Simplification of Therapy: 1996-2006

1996: d4T/3TC/IDV 10 tab, TID



1998: ZDV/3TC/EFZ 5 tab, BID



2002: ZDV/3TC/EFV 3 tab, BID



2004: TVD or EPZ /EFV 2 tab, QD



2006: ATRIPLA 1 tab, QD



CASE #2

- 65 yo man living with HIV since 2004. HLA B5701 positive
 - PMH significant for depression and Hypertension
 - Treated with AZT, 3TC, Nelfinavir, lopinavir, and ritonavir in the past. Currently on TDF/FTC/EFV undetectable
 - HBV negative
 - History of severe diarrhea with lopinavir/ritonavir; headaches with AZT
 - Seen in your clinic for routine follow up and is complaining of R hip pain
- 

CASE #2

- SCR 2.7 (baseline 1.2)
 - UA: 3+ protein
 - You discuss with him getting off tenofovir
- 

Which regimen would you recommend now?

- A. BIC/TAF/FTC
 - B. DTG + TAF/FTC
 - C. DTG/ABC/3TC
 - D. DTG/RPV
 - E. DTG + 3TC
 - F. DRV/C + DTG
 - G. DRV/C + TAF/FTC
- 

Which regimen would you recommend now?

- A. BIC/TAF/FTC
 - B. DTG + TAF/FTC
 - C. DTG/ABC/3TC
 - D. DTG/RPV
 - E. DTG + 3TC
 - F. DRV/C + DTG
 - G. DRV/C + TAF/FTC
- 

So Why 2-Drug Regimens?

- Concern about toxicities (like in this case), polypharmacy, patients co-morbid conditions (diabetes, depression, ..)
 - Cost?
 - High barrier agents (INSTIs)
- 

Are 2-Drug Regimens The Present?

- Not quite
 - Guidelines have recommendations on 2-drug regimes that may be used in treatment-naïve or switch
 - Need to take into account baseline genotypes/resistance information and medication adherence among other factors
- 

DHHS Guidelines on 2-Drug Regime

- Consider when ABC, TAF, and TDF cannot be used or are not optimal
 - ✓ DTG + 3TC or DRV/R + 3TC
 - ✓ DRV/R + RAL

Which of these people should get an HIV test?



All of them

HIV testing can save your life.

Question

A 3D rendering of the word "Question" in white, blocky letters. The letter "n" is partially obscured by a large, vibrant red question mark. The entire scene is set against a white background with a subtle reflection on the surface below. At the bottom of the image, there is a solid orange horizontal bar.

Same-Day (Rapid) Start ART: Other International Mod

■ Same-Day ART (SDART; Haiti)

- Same-day ART vs SOC (RCT; n=280 in each group)
- Inclusion: adult; WHO stage 1 or 2; CD4 ≤ 500
- Intervention: ART offered day 1
- Study: stopped due to significant results
- ✓ ART initiation rates
- ✓ Alive and in care at 12 months (80% vs 72%)
- ✓ Alive and undetectable (53% vs 44%)

■ Home-Based Testing (CASCADE; Lesotho)

Positive in-home-based test → same-day ART vs SOC

(RCT; n=137 in each group)

- Intervention: posttest counseling; pamphlet on ART adherence; POC CD4 and SCr; ART; follow-up at health facility in 14-28 days
- Primary outcome:
 - Increased rates of linkage to care (69% vs 43%) by 3 months
 - VS at 12 mon (51% vs 34%)
- Secondary Outcome: increased retention at 12 mon

■ Streamlined ART (START-ART; Uganda)

- 20 clinics randomized in groups of 5
- Multicomponent intervention
 - Opinion-leader-led training on benefits of ART
 - POC CD4 assay
 - Biannual feedback to the sites
- Primary endpoint: ART initiation within 14 days of clinical eligibility
- Secondary endpoints (intervention vs control)
 - ART same day: 71% vs 18% (RR 3.87)
 - ART 30 days: 85% vs. 57% (RR 1.49)
 - ART 90 days 90% vs. 70% (RR 1.27)
 - VS: 66% vs 58% (RR 1.13; missing data treated as failures)
 - Survival and retention: RR NS

Koenig SP. PloS Med 2017; Labhardt ND, Amanyire G. Lancet HIV 2016.