HIV Update 2018

Danny Toub MD  dannyt@srhealth.org
April 14, 2018 HIV/AIDS Review
Case #1
- 19 yo white MSM
- SSU student
- 12/1/17: Preliminary+
- 12/4/17: Started ART
- In care, fully suppressed

Case #2
- 19 yo AA man
- Homeless, SUD, MH issues
- 1/12/18: ER: HIV+/Syphilis+
- 2/23/18: PCN IM x1
- Not yet seen HIV specialist
Learning Objectives

- Apply in practice the latest treatment guidelines and recommendations for HIV testing, the prevention of HIV transmission and the appropriate use of PrEP;

- Employ strategies for optimizing antiretroviral treatment for both treatment-naive and -experienced adults with HIV infection

- Incorporate best practices for addressing the complications and comorbidities which may arise in the care of individuals living with HIV
Overview

- Epidemiology
- Prevention/Transmission/Testing/Stigma
- HIV Treatment: Primary Care/ART
HIV Epidemiology
<table>
<thead>
<tr>
<th>Who is most disproportionately affected by HIV in the US?</th>
</tr>
</thead>
<tbody>
<tr>
<td>African-Americans</td>
</tr>
<tr>
<td>Latinos</td>
</tr>
<tr>
<td>Poor people</td>
</tr>
</tbody>
</table>
Rates of Diagnoses of HIV Infection among Adults and Adolescents by Race/Ethnicity, 2010–2015—United States

- Black/African American
- Multiple races
- Hispanic/Latino
- Native Hawaiian/other Pacific Islander

*Hispanics/Latinos can be of any race.*
Estimated HIV Incidence and Population among Persons Aged ≥13 Years, by Race/Ethnicity, 2015—United States

- American Indian/Alaska Native: 1% Population, 1% Incidence
- Asian: 2% Population, 6% Incidence
- Black/African American: 12% Population, 42% Incidence
- Hispanic/Latino: 16% Population, 26% Incidence
- Native Hawaiian/Other Pacific Islander: <1% Population
- White: 26% Population, 64% Incidence
- Multiple races: 2% Population, 3% Incidence

N = 268,671,725
N = 38,500

Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Hispanics/Latinos can be of any race.
† Estimate should be used with caution because it does not meet the standard of reliability.
‡ Incidence estimate is not provided for Native Hawaiians/other Pacific Islanders because it does not meet the minimum standard of reliability.
New HIV Diagnoses, 2016

39,782
DIAGNOSES IN 2016

26,570
GAY AND BISEXUAL MEN

9,578
HETEROSEXUALS

3,425
PEOPLE WHO INJECT DRUGS (PWID)
HIV Diagnoses

In 2016, 39,782 people received an HIV diagnosis. The annual number of HIV diagnoses declined 5% between 2011 and 2015.

New HIV Diagnoses in the United States for the Most-Affected Subpopulations, 2016

<table>
<thead>
<tr>
<th>Subpopulation</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black, Male-to-Male Sexual Contact</td>
<td>10,223</td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latino, Male-to-Male Sexual</td>
<td>7,425</td>
<td></td>
</tr>
<tr>
<td>White, Male-to-Male Sexual Contact</td>
<td>7,390</td>
<td></td>
</tr>
<tr>
<td>Black Women, Heterosexual Contact</td>
<td>4,189</td>
<td></td>
</tr>
<tr>
<td>Black Men, Heterosexual Contact</td>
<td>1,926</td>
<td></td>
</tr>
<tr>
<td>White Women, Heterosexual Contact</td>
<td>1,032</td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latina Women, Heterosexual</td>
<td>1,025</td>
<td></td>
</tr>
</tbody>
</table>


Subpopulations representing 2% or less of HIV diagnoses are not reflected in this chart.
Trends in HIV Diagnoses

- Decreased 8% among US population
- Remained stable among all MSM
  - 22% increase among Hispanic/Latino MSM
- Increased 19% among all 25-34 year olds
  - 32% increase among MSM aged 25-34
Rate of HIV Diagnoses Among Adults and Adolescents in the US by State, 2016

HIV/AIDS Mortality and Poverty

HIV Prevention: PreExposure Prophylaxis (PrEP)
What is the best way for HIV negative people to use ART to stay negative?

<table>
<thead>
<tr>
<th>Option</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily PrEP (PreExposure Prophylaxis)</td>
</tr>
<tr>
<td>On Demand PrEP</td>
</tr>
<tr>
<td>Daily nPEP (non-occupational PostExposure Prophylaxis)</td>
</tr>
<tr>
<td>On Demand nPEP</td>
</tr>
<tr>
<td>Ask their partners to take ART</td>
</tr>
</tbody>
</table>
HIV Prevention: PrEP

What is PrEP, or Pre-Exposure Prophylaxis?

Pre = before

Exposure = coming into contact with HIV

Prophylaxis = treatment to prevent an infection from happening

Approximately 1.2 MILLION PEOPLE are at high risk for HIV and could benefit from comprehensive HIV prevention strategies, including PrEP.

PrEP is when people at high risk for HIV take HIV medicine daily to lower their chances of getting infected.

AIDSVU.ORG SOURCE: U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION AIDSVU
HIV Prevention: PrEP

There were over 77,000 PrEP users in 2016.

That’s a 73% increase year over year since 2012.
HIV Prevention: PrEP Candidates


<table>
<thead>
<tr>
<th></th>
<th>MSM</th>
<th>Heterosexual Women and Men</th>
<th>Injection Drug Users</th>
</tr>
</thead>
</table>
| Potential indicators of substantial risk of acquiring HIV infection | - HIV-positive sexual partner  
- Recent bacterial STI (GC/CT/Syphilis)  
- High number of sex partners  
- History of inconsistent or no condom use  
- Commercial sex work  
- HIV-positive sexual partner  
- Recent bacterial STI (GC/Syphilis)  
- High number of sex partners  
- History of inconsistent or no condom use  
- Commercial sex work  
- In high prevalence area or network  
- HIV-positive injecting partner  
- Sharing injection equipment  | | |
| Clinically eligible     | - Documented negative HIV test result; no signs of acute HIV infection  
- Normal renal function; no contraindicated medications  
- Documented hepatitis B virus infection and vaccination status | | |
Indications for PrEP in MSM


- Adult man
  - Without acute or established HIV infection
  - Any male sex partners in past 6 mos
  - Not in a monogamous partnership with a recently tested, HIV-negative man
- AND at least 1 of the following:
  - Any anal sex without condoms (receptive or insertive) in past 6 mos
  - A bacterial STI (syphilis, gonorrhea, or chlamydia) diagnosed or reported in past 6 months
# HIV Prevention: PrEP Approaches


<table>
<thead>
<tr>
<th>Prescription</th>
<th>Other Services</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ TDF/FTC (300/200 mg) QD; continuing, oral dose, ≤ 90-day supply</td>
<td>▪ Follow-up visits at least every 3 mos to provide HIV test, medication adherence counseling, behavioral risk reduction support, AE assessment, STI symptom assessment</td>
</tr>
<tr>
<td>▪ TDF alone can be considered as an alternative regimen in IDUs and heterosexually active adults</td>
<td>▪ At 3 mos and every 6 mos thereafter, assess renal function</td>
</tr>
<tr>
<td>▪ <strong>Not recommended:</strong> other ARVs, coitally timed PrEP, or other noncontinuous daily use</td>
<td>▪ Every 3-6 mos, test for bacterial STIs</td>
</tr>
</tbody>
</table>

**MSM**
- Do oral/rectal STI testing

**Heterosexual Women**
- Assess pregnancy intent
- Pregnancy test every 3 mos

**Injection Drug Users**
- Access to clean needles/syringes and drug treatment services
Lab Monitoring for patients on PrEP

<table>
<thead>
<tr>
<th>PrEP</th>
<th>Baseline</th>
<th>1 week</th>
<th>1 month</th>
<th>Every 3 months</th>
<th>Every 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office visit</td>
<td><strong>Z71.7</strong></td>
<td>Phone call PrEP Navigator</td>
<td>Z71.7, Z79.899</td>
<td>Z71.7, Z79.899</td>
<td></td>
</tr>
<tr>
<td>HIV Ag/Ab and HCG</td>
<td>Z30.49</td>
<td>Z30.49</td>
<td>Z30.49</td>
<td>Z30.49</td>
<td>Z79.899</td>
</tr>
<tr>
<td>CMP</td>
<td>Z01.812</td>
<td></td>
<td></td>
<td></td>
<td>Z79.899</td>
</tr>
<tr>
<td>UA, Phosphorus</td>
<td>Z01.812</td>
<td></td>
<td></td>
<td>Z79.899</td>
<td></td>
</tr>
<tr>
<td>HCV Ab</td>
<td>Z20.5</td>
<td></td>
<td></td>
<td>Z20.5</td>
<td></td>
</tr>
<tr>
<td>HBsAg, HBsAb/cAb</td>
<td>Z01.812, Z20.5</td>
<td></td>
<td></td>
<td>Z30.49, Z11.3, Z20.2</td>
<td></td>
</tr>
<tr>
<td>GC/CT urine, GC/CT rectal, GC oral, RPR</td>
<td>Z30.49, Z11.3, Z20.2</td>
<td></td>
<td></td>
<td>Z30.49, Z11.3, Z20.2</td>
<td></td>
</tr>
</tbody>
</table>
PrEP Works

HIV is nearly impossible to get
-if men take PrEP $\geq 4x$/week,
-if women take PrEP 6-7x/wk

PrEP is safe
## ESTIMATED NUMBER OF ADULTS WHO COULD POTENTIALLY BENEFIT FROM PREP, UNITED STATES, 2015

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

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

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bayareaaetc.org
Coverage more important than adherence for MSM

www.PleasePrEPMe.org/PrEPNavigatorManual
PrEP Online

www.nurx.com/PrEP

http://prep.plushcare.com
HIV Prevention: On demand PrEP

- IPERGAY extension study
- Median 18 pills/month
- 97% reduction in new HIV infections
- Rates of condomless sex rose from 77% to 86%
- Incidence of bacterial STIs did not change

Molina et Al. Lancet HIV 2017; 4: e402–10
HIV Prevention: On demand PEP

- 2013–2017 (Toronto) relatively low-risk pts (PrEP referrals)

- Rx 28d TDF/FTC/dolutegravir: “start ASAP” if the patient had what they deemed to be an exposure that might transmit HIV.

- 4 of the 30 initiated PEP on their own, all ≤ 10h of exposure. Each reported good tx adherence and had close FU.

- All who started PEP were seen in clinic ≤1 w for clinical evaluation and labs. No new HIV+. 21.8 person-years of FU

AIDS. 2018 Feb 6. HIV Post-Exposure Prophylaxis-in-Pocket ("PIP") for individuals with low frequency, high risk, HIV exposures.
HIV prevention pill is not reaching most who could potentially benefit – especially African Americans and Latinos

44% of people who could potentially benefit from PrEP are African American – approximately 500,000 people…

...but only 1% of those – 7,000 African Americans – were prescribed PrEP*

25% of people who could potentially benefit from PrEP are Latino – nearly 300,000 people…

...but only 3% of those – 7,600 Latinos – were prescribed PrEP*

*Prescription data in this analysis limited to those filled at retail pharmacies or mail order services from September 2015 – August 2016; racial and ethnic information not available for one-third of the prescription data.
www.PleasePrEPMe.org

HIV Prevention Research in SF:
www.PowerToPreventHIV.org/our-research

- Vaginal Ring (MTN 036) (Dapirivirine)


- Broadly Neutralizing Antibodies: Antibody Mediated Prevention (AMP) Study: (HVTN 704/HPTN 085)

- HIV Vaccine (HPX2004)
What are the chances of someone with fully suppressed HIV (undetectable viral load) transmitting HIV to someone else?

0.3% (1 in 300 chance)

3% (3 in 100 chance)

Effectively zero (about the same chance as me getting hit by lightning today)

Zero
CDC: Undetectable = Untransmittable

"people who take ART daily as prescribed and achieve and maintain an undetectable viral load have effectively no risk of sexually transmitting the virus to an HIV-negative partner"
No HIV Transmission in 75K sex acts

The PARTNER study (2016)

- 1,000 mixed status couples
- All HIV+ partners virally suppressed on effective treatment
- 58,000 sex acts without a condom
- 0 transmissions of HIV

Viral suppression from ART prevents HIV transmission

PARTNER study

Opposites Attract
(IAS, 2017)

LATEST FINDINGS
358 +/- GAY COUPLES
17,000 ACTS OF CONDOMLESS SEX
UVL = SAFE

Source: Kirby Institute, Opposites Attract 2017
"U=U has already been successful in influencing public opinion, causing more people with HIV (and their friends and families) to comprehend that they can live long, healthy lives, have children, and never have to worry about passing on their infection to others."

The Lancet (November, 2017)
HIV Testing

As part of our commitment to your health, we promote screenings for HIV, Hepatitis, Diabetes, Heart Disease, and Cancer for all patients.

ALL WHO ENTER OUR DOORS ARE HEARD, VALUED & RESPECTED
Whom to screen?

Human Immunodeficiency Virus (HIV) Infection. Screening
Release Date: April 2013

Recommendation Summary

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade (What's This?)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adolescents and Adults 15-65 Years Old</td>
<td>The USPSTF recommends that clinicians screen for HIV infection in adolescents and adults aged 15 to 65 years. Younger adolescents and older adults who are at increased risk should also be screened. Go to the Clinical Considerations for more information about screening intervals.</td>
<td>A</td>
</tr>
<tr>
<td>Pregnant Women</td>
<td>The USPSTF recommends that clinicians screen all pregnant women for HIV, including those who present in labor who are untested and whose HIV status is unknown.</td>
<td>A</td>
</tr>
</tbody>
</table>

Supporting Documents

- Screening for HIV in Adults and Adolescents: Final Evidence Review
  PDF Version
- Screening for HIV in Pregnant Women: Final Evidence Review
  PDF Version
- Screening for HIV in Pregnant Women: Evidence Summary
  PDF Version
- Screening for HIV in Adolescents and Adults: Evidence Summary
  PDF Version

Draft Research Plan

Draft Research Plan for Human Immunodeficiency Virus (HIV) Infection in Nonpregnant Adolescents and Adults: Screening

This opportunity for public comment expired on March 22, 2017 at 8:00 PM EST
New CDC Recommendations for HIV Testing in Laboratories
A step-by-step account of the approach

CDC’s new recommendations for HIV testing in laboratories capitalize on the latest available technologies to help diagnose HIV infections earlier – as much as 3-4 weeks sooner than the previous testing approach. Early diagnosis is critical since many new infections are transmitted by people in the earliest (“acute”) stage of infection.

By putting the latest testing technology to work in laboratories across the United States, we can help address a critical gap in the nation’s HIV prevention efforts.

Step 1: “Fourth generation” HIV test
Detecting HIV sooner
Detected HIV in the blood earlier than previously recommended antibody tests by identifying the HIV-1 p24 antigen, a viral protein which appears in the blood sooner than antibodies.

Negative

Diagnosis
HIV-negative

False Positive

Negative

Diagnosis
Acute HIV-1 Infection

Positive

Diagnosis
HIV Infection

Step 2: HIV-1/HIV-2 antibody differentiation immunoassay
Diagnosing HIV-1 vs. HIV-2
Produces results faster than the previously recommended Western Blot.
Distinguishes between HIV-1 and HIV-2, which the previously recommended Western Blot cannot do – this distinction can have important treatment implications for a patient.

Negative or Indeterminate

Positive

Step 3: Nucleic Acid Test (NAT)
Acute HIV-1 infection or “false positive”?
Ensures accurate detection of early infection or indicates a false positive from the fourth generation test.

Interpret Test Results as HIV-1 or HIV-2

This graphic is designed to illustrate key concepts of the new testing approach in laboratories. For more detail, please see the full guidelines here: http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf.

www.cdc.gov/nchhstp/newsroom

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

JUNE 2014
HIV Testing:  [www.cdc.gov/vitalsigns/pdf/2017-12-vitalsigns.pdf]

Many people have HIV for years before they know it.

In 2015, nearly 40,000 people in the US received an HIV diagnosis:

1 in 2 had been living with HIV 3 years or more
1 in 4 had been living with HIV 7 years or more
1 in 5 already had the most advanced stage of HIV (AIDS)

7 in 10 people at high risk who weren’t tested for HIV in the past year saw a healthcare provider during that time.

More than 75% of them weren’t offered a test.
Diagnosed Infection among Persons Aged ≥13 Years Living with Diagnosed or Undiagnosed HIV Infection, by Age, 2014—United States

Note. Estimates were derived using HIV surveillance and CD4 data for persons aged ≥13 years at diagnosis in the 50 states and the District of Columbia.
Undiagnosed HIV Infections, 2015

44% of persons with undiagnosed HIV infections are blacks/African Americans

26% of persons with undiagnosed HIV infections are Hispanics/Latinos

Engagement in Care:

People living with HIV and not in care are linked to over 9 out of 10 of new HIV transmissions.²

Missing 2 HIV care appointments within 2 years of diagnosis increases the risk of death by 3.6 times.³

HIV Stigma: www.HIVIsNOTaCrime.com

- SB 239: California Law 10/2017: modernized outdated criminalization laws around HIV transmission

- www.HelpFightHIV.org
IT'S ALL ABOUT RELATIONSHIPS
What is the single best non-ART biomedical intervention to help people with HIV live longer?

When poll is active, respond at PollEv.com/dannytoub401

Text DANNYTOUB401 to 37607 once to join

- Vaccinations
- DASH diet
  - Exercise: 150 min/wk of moderate intensity aerobic exercise and muscle-strengthening activities 2d/week
- Cancer screenings
- Tobacco cessation
## HIV Primary Care: Vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>CD4&lt;200</th>
<th>CD4&gt;=200</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>One dose inactivated influenza vaccine annually</td>
<td>uheasdrfheasdhheasnhhhe</td>
</tr>
<tr>
<td>Diphtheria, Tetanus, Pertussis</td>
<td>Substitute one time dose of DTaP for Td booster, then boost with Td every 10 years</td>
<td>If born in 1957 or after and have not gotten this vaccine or have immunity to these diseases</td>
</tr>
<tr>
<td>MMR</td>
<td>Contraindicated</td>
<td>Two doses, if no evidence of immunity</td>
</tr>
<tr>
<td>Varicella</td>
<td>Contraindicated</td>
<td></td>
</tr>
<tr>
<td>Zoster (RZV preferred over ZVL)</td>
<td></td>
<td>No recommendation</td>
</tr>
<tr>
<td>Human papillomavirus</td>
<td></td>
<td>Three doses through age 26</td>
</tr>
<tr>
<td>Pneumococcal polysaccharide (PPV-23)</td>
<td>Two doses at least 5 years apart with additional dose at age 65 if at least 5 yrs from the 2nd dose</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal conjugate (PCV-13)</td>
<td></td>
<td>One dose given either at least 8 weeks before or at least one year after PPV-23</td>
</tr>
<tr>
<td>Meningococcal ACWY</td>
<td></td>
<td>Two doses &gt;8 months apart, then every 5 years</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td></td>
<td>Two doses</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td></td>
<td>Three doses</td>
</tr>
</tbody>
</table>

www.cdc.gov/vaccines/adults/rec-vac/health-conditions/hiv.html
HIV Primary Care: Cancer Prevention

- ART (Kaposi’s Sarcoma, NHL)
- Quit smoking (lung, oral,…)
- Cure HCV
- HBV vaccine
- ART for HBV
- HPV vaccine
- Cervical pap smears,
+/- anal pap smears

https://anchorstudy.org/about
HIV Primary Care: Cardiovascular Disease Prevention

- Tobacco, Diet, Exercise
- Abacavir (10 yrs)
  - NA-ACCORD data (JAIDS. 2018 Feb 6)
  - CROI 2018: mechanism
- Aspirin/Statins?
  - Consider HIV equivalent to DM on ACC/AHA ASCVD Risk Calculator
  - REPRIEVE (Randomized Trial to Prevent Vascular Events in HIV): enrolling 6,500 patients; 6y study; 1st RCT to see if statins prevent CV events in PLWH: Pitavastatin vs therapeutic lifestyle changes

www.cdc.gov/tobacco/campaign/tips/diseases/smoking-and-hiv.html

bayareaaetc.org
### When is it best for someone with HIV to start taking ART?

<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>After baseline labs (CD4, HIV Viral load, resistance test, etc)</td>
</tr>
<tr>
<td>After preliminary reactive HIV test</td>
</tr>
<tr>
<td>After confirmatory HIV test</td>
</tr>
<tr>
<td>After visit with HIV case manager</td>
</tr>
<tr>
<td>Once CD4 &lt; 500</td>
</tr>
<tr>
<td>Once HIV viral load &gt; 200</td>
</tr>
</tbody>
</table>
ART: Rapid Starts

- World Health Organization 2017 Guidelines:
  - “all PLHIV should be offered rapid initiation of ART, defined as within seven days of a positive HIV diagnosis, providing there are no contraindications.”
  - “ART initiation should be offered on the same day for people who are ready to start.“

- DHHS 2017 ART Guidelines
  - “Same day ART initiation is investigational”
ART: RAPID in SF

- Time to first virologic suppression decreased > 50% from 134 days to 61 days and time from care linkage to ART start decreased 96% from 27 days to 1 day

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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Diagnosed, n</td>
<td>399</td>
<td>329</td>
<td>295</td>
<td>265</td>
<td>-</td>
</tr>
<tr>
<td>Started ART, n (%)</td>
<td>311 (78)</td>
<td>276 (84)</td>
<td>244 (83)</td>
<td>215 (81)</td>
<td>-</td>
</tr>
<tr>
<td>Met RAPID definition, n (%)</td>
<td>23 (6)</td>
<td>45 (14)</td>
<td>50 (17)</td>
<td>80 (30)</td>
<td>-</td>
</tr>
<tr>
<td>In care within 1 yr, n (%)</td>
<td>372 (93)</td>
<td>318 (97)</td>
<td>282 (96)</td>
<td>258 (97)</td>
<td>-</td>
</tr>
<tr>
<td>Median time from diagnosis to care entry, d</td>
<td>8</td>
<td>7</td>
<td>7</td>
<td>5</td>
<td>-38</td>
</tr>
<tr>
<td>Median time from first care visit to ART initiation, d</td>
<td>27</td>
<td>17</td>
<td>6</td>
<td>1</td>
<td>-96</td>
</tr>
<tr>
<td>Median time from ART start to HIV-1 RNA &lt; 200 c/mL, d</td>
<td>70</td>
<td>53</td>
<td>50</td>
<td>38</td>
<td>-46</td>
</tr>
<tr>
<td>Median time from diagnosis to HIV-1 RNA &lt; 200 c/mL, d</td>
<td>134</td>
<td>92</td>
<td>77</td>
<td>61</td>
<td>-54</td>
</tr>
</tbody>
</table>

- Time to ART start and first viral suppression decreased vulnerable populations, including racial/ethnic minorities and homeless pts, although disparities still exist for some outcomes
### FDA Approved ART, 2018

#### NRTI (nucleoside analogs)
- Tenofovir alafenamide TAF
- Tenofovir TDF
- Abacavir ABC
- Emtricitabine FTC
- Lamivudine 3TC
- Stavudine D4T
- Didanosine DDI
- Zalcitabine DDC
- Zidovudine ZDV

#### NNRTI (non-nucleosides)
- Rilpivirine RPV
- Etravirine ETR
- Efavirenz EFV
- Nevirapine NVP
- Delavirdine DLV

#### Integrase Inhibitors (INSTIs)
- Dolutegravir DTG
- Elvitegravir EVG
- Raltegravir RAL
- Bictegravir BIC

#### Protease Inhibitors
- Darunavir DRV
- Atazanavir ATV
- Ritonavir RTV
- Cobicistat Cobi
- Lopinavir LPV
- Fosamprenavir FPV
- Amprenavir APV
- Tipranavir TPV
- Nelfinavir NFV
- Saquinavir SQV
- Indinavir IDV

#### CCR5 Inhibitors
- Maraviroc MVC

#### Fusion Inhibitors
- Enfuvirtide T-20

#### Post-Attachment Inhibitors
- Ibalizumab
INSTIs

Protease Inhibitors
# Recommended Regimens 1<sup>st</sup> Line ART

<table>
<thead>
<tr>
<th>DHHS</th>
<th>IAS-USA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dolutegravir/abacavir/lamivudine</td>
<td>Dolutegravir/abacavir/lamivudine</td>
</tr>
<tr>
<td>Dolutegravir/emtricitabine/tenofovir (TAF or TDF)</td>
<td>Dolutegravir/emtricitabine/tenofovir AF</td>
</tr>
<tr>
<td>Elvitegravir/cobicistat/emtricitabine/tenofovir (TAF or TDF)</td>
<td>Elvitegravir/cobicistat/emtricitabine/tenofovir AF</td>
</tr>
<tr>
<td>Raltegravir/emtricitabine/tenofovir (TAF or TDF)</td>
<td>Raltegravir/emtricitabine/tenofovir AF</td>
</tr>
</tbody>
</table>

Recommendations may differ according to renal function, HLA-B*5701 status, HBsAg status, osteoporosis status, other comorbidities.
ART: What to Start Certain Clinical Situations (DHHS Guidelines 10/2017)

<table>
<thead>
<tr>
<th>Recommended Initial Regimens in Certain Clinical Situations</th>
</tr>
</thead>
<tbody>
<tr>
<td>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).</td>
</tr>
</tbody>
</table>

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

- (DRV/c or DRV/r) + tenofovir²/FTC³ (AI for DRV/r and All for DRV/c)
- (ATV/c or ATV/r) + tenofovir²/FTC³ (BII)
- (DRV/c or DRV/r) + ABC/3TC³ — if HLA-B*5701—negative (BII)
- (ATV/c or ATV/r) + ABC/3TC³ — 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 + tenofovir²/FTC³ (BII for EFV/TDF/FTC and BII for EFV + TAF/FTC)
- RPV/tenofovir²/FTC³ (BII)— if HIV RNA <100,000 copies/mL and CD4 >200 cells/mm³

**INSTI + 2 NRTIs:**

- RAL² + ABC/3TC³ (CII)— if HLA-B*5701—negative and HIV RNA < 100,000 copies/mL

**Regimens to Consider when ABC, TAF, and TDF Cannot be Used:**

- DRV/r + RAL (BID) (CI)— if HIV RNA <100,000 copies/mL and CD4 >200 cells/mm³
## Selecting INSTI Regimens

<table>
<thead>
<tr>
<th>Agent</th>
<th>Backbone</th>
<th>Single Tablet Regimen?</th>
<th>Barrier to Resistance?</th>
<th>Food Requirements?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bictegravir</td>
<td>FTC/TAF</td>
<td>Yes</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>Dolutegavir</td>
<td>ABC/3TC</td>
<td>Yes</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>FTC/ Tenofovir (TAF or TDF)</td>
<td></td>
<td>High</td>
<td></td>
</tr>
<tr>
<td></td>
<td>FTC/TDF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rilpivirine</td>
<td>Yes</td>
<td>High</td>
<td>Unknown</td>
</tr>
<tr>
<td>Elvitegravir/cobicistat</td>
<td>FTC/Tenofovir (TAF or TDF)</td>
<td>Yes</td>
<td>Low/moderate</td>
<td>Yes</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>FTC/Tenofovir (TAF or TDF)</td>
<td></td>
<td>Low/moderate</td>
<td></td>
</tr>
</tbody>
</table>
# Selecting INSTI Regimens

<table>
<thead>
<tr>
<th>Agent</th>
<th>Backbone</th>
<th>CrCl</th>
<th>Special Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bictegravir</td>
<td>FTC/TAF</td>
<td>$\geq 30 \text{ mL/min}$</td>
<td></td>
</tr>
<tr>
<td>Dolutegavir</td>
<td>ABC/3TC</td>
<td>$\geq 50 \text{ mL/min}$</td>
<td>High CVD risk; C/I if HLA-B*5701</td>
</tr>
<tr>
<td></td>
<td>FT/ Tenofovir AF</td>
<td>$\geq 30 \text{ mL/min}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>FTC/Tenofovir DF</td>
<td>$\geq 50 \text{ mL/min}$</td>
<td>Osteoporosis</td>
</tr>
<tr>
<td></td>
<td>Rilpivirine</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td>Elvitegravir/</td>
<td>FTC/Tenofovir AF</td>
<td>$\geq 30 \text{ mL/min}$</td>
<td>Dyslipidemia</td>
</tr>
<tr>
<td>cobicistat</td>
<td>FTC/Tenofovir DF</td>
<td>$\geq 70 \text{ mL/min}$</td>
<td>Dyslipidemia, Osteoporosis</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>FTC/Tenofovir AF</td>
<td>$\geq 30 \text{ mL/min}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>FTC/Tenofovir DF</td>
<td>$\geq 50 \text{ mL/min}$</td>
<td>Osteoporosis</td>
</tr>
</tbody>
</table>
**Selecting INSTI Regimens: Drug Interactions:**  [www.hiv-druginteractions.org](http://www.hiv-druginteractions.org)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Backbone</th>
<th>Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bictegravir</td>
<td>FTC/TAF</td>
<td>Metformin</td>
</tr>
<tr>
<td>Dolutegavir</td>
<td>ABC/3TC; FTC/Tenofovir; Rilpivirine</td>
<td>Metformin, Metformin, PPIs</td>
</tr>
<tr>
<td>Elvitegravir/cobicistat</td>
<td>FTC/Tenofovir (TAF or TDF)</td>
<td>Statins, Corticosteroids (Inhaled/Injected/systemic)</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>FTC/Tenofovir (TAF or TDF)</td>
<td></td>
</tr>
</tbody>
</table>

All INSTIs: polyvalent cations (Calcium, Magnesium), Rifampin
## ART: Dual-Therapy Regimens Being Studied

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Treatment Setting</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTG + 3TC</td>
<td>Maintenance</td>
<td>- ASPIRE* (randomized phase III)[1]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- ANRS 167 LAMIDOL* (single-arm phase II)[2]</td>
</tr>
<tr>
<td></td>
<td>Initial</td>
<td>- GEMINI 1 &amp; 2 (randomized phase III)[3,4]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- PADDLE* (single-arm phase IV)[5,6]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- ACTG A5353* (single-arm phase II)[7]</td>
</tr>
<tr>
<td>DTG + DRV/RTV</td>
<td>Maintenance</td>
<td>- DUALIS (randomized phase III)[8]</td>
</tr>
<tr>
<td>DRV/RTV + 3TC</td>
<td>Maintenance</td>
<td>- DUAL-GESIDA* (randomized phase IV)[9]</td>
</tr>
<tr>
<td></td>
<td>Initial</td>
<td>- ANDES* (randomized phase IV)[10]</td>
</tr>
<tr>
<td>ATV/RTV + 3TC</td>
<td>Maintenance</td>
<td>- SALT* (randomized phase IV)[11]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- ATLAS-M* (randomized phase IV)[12]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- LATTE-2* (randomized phase IIb)[16]</td>
</tr>
</tbody>
</table>

ART: Simplification

- To manage adverse events
- To manage or prevent drug toxicity
- To simplify regimen (number of doses or pills)
- To address food restrictions
- To address drug interactions
- To plan for pregnancy
- To reduce cost
- To address new HBV coinfection
Dolutegravir/rilpivirine single tablet regimen: for maintenance

- Once-daily single-tablet regimen FDA approved 11/21/17
- First 2-drug STR FDA approved for use as a complete regimen
- Indications: for patient who have:
  - 1) been virologically suppressed for ≥ 6 mos
  - 2) no hx of tx failure and no resistance to DTG or RPV
- Must be taken with a meal
- Separate dose of DTG/RPV and antacid/polyvalent cation–containing medications; Avoid PPIs (eg, omeprazole, pantoprazole)
- Monitor for adverse effects pts with CrCl < 30 mL/min
- DHHS: Consider use when NRTIs not desirable
Bictegravir/emtricitabine/tenofovir AF single tablet regimen

- FDA approved 2/7/18 INSTI, once daily 50 mg, unboosted
- Active against many INSTI resistance mutations (in vitro)
- Performed comparably to dolutegravir for treatment naïve
  - (GS-1489: DOL/ABC/3TC; GS-1490: DOL/TAF/FTC)
- Switch from PI-based regimens OK (380-1878)
- Indications:
  - For treatment-naive pts
  - For pts VL< 50 ≥ 3m, no hx tx failure; no resistance to components
- Drug-drug interactions: CYP3A4 metabolized
  - Contraindicated with rifampin, dofetilide;
  - May increase metformin concentrations
  - Polyvalent cation–containing meds (antacids) may decrease BIC
- Not recommended for pts with estimated CrCl < 30 mL/min
- DHHS Guidelines 3/27/18 Update: recommended initial regimen (A1)
Ibalizumab infusions for multidrug-resistant (MDR) HIV

- New class: Post-attachment inhibitor
- FDA approved 3/6/18
- 15-30 minute infusion IV every 2 weeks
- Indications: in combination with other ART in heavily tx-experienced adults with MDR HIV failing current ART
- No cross-resistance with other HIV drug classes
Darunavir/cobicistat/emtricitabine/tenofovir AF single tablet regimen

- Approved in Europe 9/25/17
- Anticipate US FDA approval 2018

- EMERALD study:
  - N=1,141; 48wks:
  - Switch to this new PI-based STR is safe/effective
Which current ART are generic?

- **NRTIs:**
  - Abacavir (ABC)
  - Lamivudine (3TC)
  - ABC/3TC
  - Zidovudine (ZDV), ZDV/3TC, ABC/ZDV/3TC
  - Tenofovir DF 300mg/ lamivudine 300mg /efavirenz 400mg STR (Symfi Lo) FDA approved 2/5/18
  - Tenofovir DF 300mg/lamivudine 300mg coformulation (Cimduo); FDA approved 2/5/18

- **NNRTIs:** Nevirapine

- **PIs:** Atazanavir, ritonavir
Doravirine

- FDA action by 10/23/18 for:
  - doravirine and
  - coformulation of doravirine/tenofovir DF/lamivudine
- NNRTI, once-daily dosing (100 mg), active in vitro against common NNRTI resistance mutations (including K103N, Y181C, E138K)
- No food or PPI restrictions
- Phase 2: Doravirine + TDF/FTC: HIV RNA suppression matches efavirenz, fewer adverse events
HIV Drug Pipeline

- **2019:**
  - Cabotegravir/rilpivirine LA: results expected late 2018
    - treatment naïve: FLAIR;
    - switch: ATLAS, ATLAS-2M;
  - Dolutegravir/lamivudine:
    - treatment naïve: GEMINI 1&2;
    - switch: TANGO
  - Generic darunavir

- **2020-2021**
  - Generic emtricitabine and FTC/TDF/efavirenz STR

- ???: One pill once a week drug delivery systems
  (Nature Communications volume 9, Article number: 2 (2018))
HIV Cure

The only man cured of HIV.
Timothy Ray Brown
Thank you! Questions?