What’s New in 2017:
HIV Update

Donna E. Sweet, MD, AAHIVS, MACP
Professor of Medicine
The University of Kansas School of Medicine - Wichita
LGBT CARE:
MORE THAN JUST HIV
Lesbian and bisexual women are at increased risk for the following disorders:

» Overweight
» Obesity
» Tobacco use
» Alcohol use

• Clinicians should screen for these conditions regularly
• Provide appropriate referrals
The Following Annual Screenings Should be Offered to All Men Who Have Sex With Men...

• HIV
• Syphilis
• Chlamydia
• Gonorrhea
Pre-exposure Protocol against HIV infection...

is appropriate for some at risk individuals who can adhere to daily therapy
Is a rule that can help physicians to consider the appropriate screening services for transgender individuals.

“Screen What You Have”
Can benefit transgender individuals who are changing their physical appearance to their affirmed gender.
More than 1.2 million people in the US are living with HIV

1 in 8 of them don't know they are living with HIV

2005 to 2014, the annual number of new HIV diagnoses declined 19%.

Gay and bisexual men, particularly young African American gay and bisexual men, are most affected.

Still have around 40,000 new infections/year

https://www.cdc.gov/hiv/statistics/overview/ataglance.html
Rates of Diagnoses of HIV Infection among Adults and Adolescents, 2014—United States and 6 Dependent Areas

N = 44,609  Total Rate = 16.6

Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.
• 547 people are estimated to be living with HIV/AIDS in South Dakota

• 25 new HIV/AIDS cases were reported in 2015
  – 7 Females
  – 18 Males

• Disproportionately impacted by HIV/AIDS:
  – Blacks: 23% of living cases, 1% of the population
  – Native Americans: 16% of living cases, 9% of the population
SOUTH DAKOTA: 1 January – 31 May 2016: Provisional Data

HIV (including Stage III AIDS)

New cases in 2016

<table>
<thead>
<tr>
<th>Regions</th>
<th>Cases</th>
<th>Rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sioux Falls MSA</td>
<td>9</td>
<td>3.6</td>
</tr>
<tr>
<td>Rapid City MSA</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Northeast</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Southeast</td>
<td>2</td>
<td>1.8</td>
</tr>
<tr>
<td>Central</td>
<td>1</td>
<td>1.1</td>
</tr>
<tr>
<td>West</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>12</strong></td>
<td><strong>1.4</strong></td>
</tr>
</tbody>
</table>

*Rate: cases per 100,000 population

New HIV-AIDS cases 2016

<table>
<thead>
<tr>
<th>Regions</th>
<th>Cases</th>
<th>Rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>East River</td>
<td>12</td>
<td>4.7</td>
</tr>
<tr>
<td>West River</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>12</strong></td>
<td><strong>1.4</strong></td>
</tr>
</tbody>
</table>

South Dakota Late Testers

Persons who are diagnosed with AIDS within 12 months of their initial HIV diagnosis are known as “late testers”

2010 thru 2015: 32% of all cases were “late testers”.

"It never occurred to me I could have HIV."
Goals of the National HIV/AIDS Strategy

- Reduce The Number of New HIV/AIDS Infections
  - Test all Americans
  - Get them into care
  - Keep them in care
  - Get their HIV viral load to undetectable

- Increase access to care for people living with HIV/AIDS

- Reduce HIV related Health Disparities
Current Status: 90-90-90 Targets

**Global (2016):**
- Number of People Living With HIV: 37 million
- People With HIV Who Know Their Status: 70%
- People With HIV on Treatment: 53%
- People With HIV Who Are Virally Suppressed: 44%

**Eastern and Southern Africa (2016):**
- Number of People Living With HIV: 100,000
- People With HIV Who Know Their Status: 76%
- People With HIV on Treatment: 60%
- People With HIV Who Are Virally Suppressed: 50%

**Western and Central Europe and North America (2015):**
- Number of People Living With HIV: 2,000
- People With HIV Who Know Their Status: 85%
- People With HIV on Treatment: 76%
- People With HIV Who Are Virally Suppressed: 64%

**Current 90% achievement**
- Gap to reach 90% target
- Above target
Stage 3 (AIDS) Classifications, Deaths, and Persons Living with HIV Infection Ever Classified as Stage 3 (AIDS) 1985–2010—United States and 6 Dependent Areas

Diagnoses and deaths, No. (in thousands)

Year of diagnosis or death


Diagnoses
Deaths
Prevalence

1993 definition implementation

Note. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting. Deaths of persons with HIV infection, stage 3 (AIDS) may be due to any cause.
Risk of Death Associated with Deferral of ARV Therapy

<table>
<thead>
<tr>
<th>CD4 Count Threshold Analysis</th>
<th>Relative Risk of Death with Deferral of Antiretroviral Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>351-500 cells/mm(^3)</td>
<td>69%</td>
</tr>
<tr>
<td>More than 500 cells/mm(^3)</td>
<td>94%</td>
</tr>
</tbody>
</table>

**Study Background**
- Two parallel analyses involving total of 17,517 asymptomatic ARV-naïve patients
- Time period 1996-2005
- Analysis 1 (N = 8364 Patients): Initiate therapy at CD4 351-500 cells/m\(^3\) or Defer
- Analysis 2 (N = 9,155 Patients): Initiate therapy at CD4 > 500 cells/m\(^3\) or Defer

Life expectancy for HIV patients approaches that of general population.

HIV patients: 74 years
General population: 80 years

Median age of death for patients with HIV aged 25 years

2010 to 2015
73.9 years

1995 to 1996
34.5 years

GET TESTED!
Know Your Status
USPSTF Recommends an “A” grade for Routine HIV Screening: April 2013

- The USPSTF statement recommends clinicians screen for HIV in all adolescents and adults aged 15-65 years.
- It also recommends...
  - Repeat HIV screenings for those who are at increased risk for HIV infection, including men who have sex with men and people who inject drugs.
  - Younger adolescents and older adults who are at increased risk for HIV infection should also be screened.
- These updated USPSTF recommendations align with CDC’s 2006 guidelines which state that HIV testing should be a routine part of medical care for all American adults and adolescents.

http://www.cdc.gov/hiv/dhap/ehap/fyi/050113.html
Testing for HIV: Old Algorithm

• HIV enzyme immunoassay (EIA). If positive, confirmatory western blot (WB)

• Problem with old algorithm:
  – Western blot doesn’t turn positive until well after patient acquires infection (6-8 wks): “window period”
  – Reactive EIA & negative WB may be erroneously interpreted as negative test
  – Western blot no longer recommended

Immunoassay generations:
• 1\textsuperscript{st}: viral lysate Ags (detects IgG; includes WB, IFA)
• 2\textsuperscript{nd}: peptide/recombinant protein Ags (detects IgG)
• 3\textsuperscript{rd}: peptide/recombinant protein Ags (detects IgM, IgG)
• 4\textsuperscript{th}: peptide/recombinant protein Ags, p24 antibody (detects IgM, IgG, p24 antigen)
HIV Testing: Current Algorithm

To “close the window”, current testing algorithm:

Sensitive HIV-1/2 Immunoassay (4th Generation)

HIV-1/2 Ab Differentiation assay

Patient is infected

Advantages:

• RNA testing identifies patients with acute HIV
  • Averted missed diagnoses in 8 – 32% of HIV patients
  • All antibody-positive specimens tested for HIV-2
  • Same day turnaround

4th gen. immunoassay: HIV-1/HIV-2 antibodies and p24 antigen

Branson B, Stekler J. JID. 2012; MMWR June 21, 2013
Laboratory Testing for the Diagnosis of HIV Infection, Updated
CDC Recommendations, June 27, 2014.
Caveat emptor!

- Although current algorithm more likely to detect HIV during routine screening, if acute HIV suspected, check immunoassay (IA) and HIV RNA

- If IA negative and HIV RNA low (<10,000), repeat RNA testing to rule out a false positive result.

- If very recent exposure (<10-15 d), repeat testing 1-2 wks later, particularly if symptoms develop
Point-of-Contact (Rapid) 4th Generation HIV Testing

Alere Determine HIV-1/2 Ag/Ab Combo

- 4th generation for fingerstick or venous whole blood, serum or plasma
- Can be used to detect acute (early) HIV infection before antibody detection
- Distinguish between the detection of p24 antigen and HIV antibodies
- Results in about 20 minutes

We offer HIV testing to all patients.

If we fail to ask, ask us.
Routine Testing: The Benefits

Reduces HIV transmission

- HIV+ people who know their status reduce high-risk sex by about 50%
- Lower viral loads from ARVs also reduce transmission

Prolongs Life

- HIV treatment can increase survival by many years and improve quality of life

Preserves Resources

- Successful ART reduces overall care costs for HIV+ patients from $36,532 to $13,865 (U. of Alabama)
Reduced Community Viral Load (CVL) and New HIV Infections, San Francisco

Routine Testing: The Challenges

- Stigma and discrimination (jobs)
  Normalizing testing could decrease stigma
- Patient awareness
  Provider responsibility to inform, educate
- Lose possible benefit of counseling
- Perceived coercion, privacy, civil liberties
- Legal issues (state laws)
- Resources to pay for more testing and care
- Insurers’ disincentive to know
Perinatal HIV Transmission

- Without ARV drugs during pregnancy, risk of transmission from mother to infant is 1 in 4

- Pediatric AIDS Clinical Trials Group (PACTG) 076 found that by giving zidovudine (ZDV) to the pregnant woman during pregnancy, labor, and delivery, and to her newborn, transmission could be reduced to 8%

- The risk of perinatal transmission can now be less than 2% (1 in 50) with:
  - Highly effective ARV therapy (HAART)
  - Elective Cesarean section as appropriate
  - Formula feeding
### Current DHHS Recommendations: Initial ART in Pregnant Women

<table>
<thead>
<tr>
<th>Guideline Status</th>
<th>NRTIs</th>
<th>PIs</th>
<th>INSTIs</th>
<th>NNRTIs</th>
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</thead>
<tbody>
<tr>
<td>Preferred</td>
<td>3TC/ABC</td>
<td>ATV/RTV*</td>
<td>RAL* §</td>
<td></td>
</tr>
<tr>
<td></td>
<td>FTC/TDF</td>
<td>DRV/RTV*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3TC + TDF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alternative</td>
<td>3TC/ZDV</td>
<td>LPV/RTV* †</td>
<td>EFV*</td>
<td>RPV* ‡</td>
</tr>
<tr>
<td>Insufficient data to recommend</td>
<td>FTC/TAF</td>
<td>FPV</td>
<td>DTG</td>
<td>EVG/COBI</td>
</tr>
</tbody>
</table>

*In addition to preferred 2-NRTI backbone. †Must be used twice daily in pregnancy. ‡Only if pretreatment HIV-1 RNA ≤ 100,000 copies/mL and CD4+ cell count ≥ 200 cells/mm³. §If adherence concerns or potential for ART discontinuation postpartum, a PI is preferred over INSTI to reduce resistance risk.
Estimated Number of Perinatally Acquired AIDS Cases by Year of Diagnosis, 1985–2006—United States and Dependent Areas

Note. Data have been adjusted for reporting delays and cases without risk factor information were proportionally redistributed.
Births to HIV-Infected Women and Number of Perinatally Acquired HIV Infections* by Year of Birth, 1990-2006

Rate of Perinatal Transmission for years 2004-2006 = 0.7%

* HIV or AIDS at first diagnosis for a child exposed to HIV during mother’s pregnancy, at birth, and/or during breastfeeding.
Approach to Barriers to Routinization of HIV Testing

• Provider should strongly recommend testing as “Standard of Care”.
• Utilize existing indigenous staffing
  – “Empower Them”
• Get your EHR to help
  – “Pop-up reminders”
• Offer as Opt-out
  – No informal consent required
  – No required prevention counseling
• Written/Visual information in lobby and exam rooms.
  – “CDC materials”
Desired Outcome of Routine HIV Screening

- HIV Screening
- HIV Diagnosis
- Link to Care

- Improve Survival & Quality of Life
- Prevent New HIV Infections

Source: CDC
KEY POINTS!

- Test everyone aged 15-65 at least once
- Test at least annually for those at risk
- Confirm that your patient is linked to care
“The top doesn’t come off. It’s preventative medicine.”
Treatment as Prevention
Treatment as Prevention: HPTN 052–96% Reduction in HIV Transmission

Kaplan-Meier estimate for cumulative probabilities of linked HIV-1 transmission between partners among those in the early-therapy and delayed-therapy groups

- HIV serodiscordant couples randomized to receive either early or delayed ART
- Early ART was initiated in the HIV-infected partner at enrollment
- Delayed ART was initiated after 2 consecutive CD4 cell counts ≤250 cells/mm³ or the development of an AIDS-related illness

Number at Risk
<table>
<thead>
<tr>
<th></th>
<th>Early</th>
<th>Delayed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years Since Randomization</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>0</td>
<td>893</td>
<td>882</td>
</tr>
<tr>
<td>1</td>
<td>658</td>
<td>655</td>
</tr>
<tr>
<td>2</td>
<td>298</td>
<td>297</td>
</tr>
<tr>
<td>3</td>
<td>79</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>31</td>
<td>26</td>
</tr>
<tr>
<td>5</td>
<td>24</td>
<td>22</td>
</tr>
</tbody>
</table>

HPTN 052: HIV Transmission Reduced by 96% in Serodiscordant Couples

Total HIV-1 Transmission Events: 39
(4 in immediate arm and 35 in delayed arm; $P < .0001$)

Linked Transmissions: 28

Unlinked or TBD Transmissions: 11

Immediate Arm: 1
Delayed Arm: 27

Single transmission in patient in immediate ART arm believed to have occurred close to time therapy began and prior to suppression of VL

$P < .001$

Efficacy of HIV Prevention Strategies From Randomized Clinical Trials

- **Antiretroviral treatment for prevention**
  - HPTN 052 Africa, Asia, Americas\(^5\)
  - Effect size (95% CI): 96% (73–99)
- **PrEP for discordant couples**
  - Partners PrEP Uganda, Kenya\(^1\)
  - Effect size (95% CI): 73% (49–85)
- **PrEP for heterosexual men and women**
  - TDF2 Botswana\(^2\)
  - Effect size (95% CI): 63% (21–84)
- **Medical male circumcision**
  - Orange Farm,\(^6\) Rakai,\(^7\) Kisumu\(^8,9*\)
  - Effect size (95% CI): 54% (38–66)
- **PrEP for MSMs**
  - iPrEx Americas, Thailand, South Africa\(^4\)
  - Effect size (95% CI): 44% (15–63)
- **Sexually transmitted diseases treatment**
  - Mwanza Tanzania\(^10\)
  - Effect size (95% CI): 42% (21–58)
- **Microbicide**
  - CAPRISA 004 South Africa\(^3\)
  - Effect size (95% CI): 39% (6–60)
- **HIV vaccine**
  - RV144 Thailand\(^11\)
  - Effect size (95% CI): 31% (1–51)
• There is now evidence-based confirmation that the risk of HIV transmission from a person living with HIV (PLHIV), who is on Antiretroviral Therapy (ART) and has achieved an undetectable viral load in their blood for at least 6 months is negligible to non-existent.

• While HIV is not always transmitted even with a detectable viral load, when the partner with HIV has an undetectable viral load this both protects their own health and prevents new HIV infections.

https://www.preventionaccess.org/consensus
PrEP: A New Era in HIV Prevention
FTC/TDF (TRUVADA) FOR PrEP INDICATION

- FTC/TDF is indicated in combination with safer sex practices for PrEP to reduce the risk of sexually acquired HIV-1 in adults at high risk
- This indication is based on clinical trials in MSM at high risk for HIV-1 infection and in heterosexual serodiscordant couples

emtricitabine (FTC) 200 mg  
tenofovir disoproxil fumarate (TDF) 300 mg

Pill image is for illustration only.
PrEP Facts

Daily PrEP can reduce the risk of getting HIV from sex by more than 90%.

Daily PrEP can reduce the risk of getting HIV among people who inject drugs by more than 70%.

1 in 3 primary care doctors and nurses haven't heard about PrEP.

http://www.cdc.gov/vitalsigns/hivprep/index.html
CDC PrEP Guidance: Who is recommended for PrEP?

0 Daily oral PrEP is recommended for adults at **substantial risk** of acquiring HIV infection:
   0 Sexually active MSM
   0 Heterosexually active men and women
   0 Injection drug users

<table>
<thead>
<tr>
<th>Detecting substantial risk of acquiring HIV infection</th>
<th>MSM</th>
<th>Heterosexual Women and Men</th>
<th>Injection Drug Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-positive sexual partner</td>
<td></td>
<td>HIV-positive sexual partner</td>
<td>HIV-positive injecting partner</td>
</tr>
<tr>
<td>Recent bacterial STI</td>
<td></td>
<td>Recent bacterial STI</td>
<td>Sharing injection equipment</td>
</tr>
<tr>
<td>High number of sex partners</td>
<td></td>
<td>High number of sex partners</td>
<td>Recent drug treatment</td>
</tr>
<tr>
<td>History of inconsistent or no condom use</td>
<td></td>
<td>History of inconsistent or no condom use</td>
<td>(but currently injecting)</td>
</tr>
<tr>
<td>Commercial sex work</td>
<td></td>
<td>Commercial sex work</td>
<td></td>
</tr>
<tr>
<td>In high-prevalence area or network</td>
<td></td>
<td>In high-prevalence area or network</td>
<td></td>
</tr>
</tbody>
</table>

MSM=men who have sex with men; STI=sexually transmitted infection.

TRUVADA FOR PrEP SHOULD BE USED AS PART OF A COMPREHENSIVE PREVENTION STRATEGY

Safer sex practices, including consistent and correct use of condoms, and reducing sexual risk behavior

- Knowledge of their own HIV-1 status and that of their partner(s)

- Regular testing for HIV-1 and other STIs
- Counsel uninfected individuals to strictly adhere to their dosing schedule

- TRUVADA for PrEP is not always effective in preventing the acquisition of HIV-1
- The effectiveness of TRUVADA for PrEP in reducing the risk of acquiring HIV-1 is strongly correlated with adherence
The risk categories listed in the USPHS/CDC guidelines include:

**MSM:**
- HIV-positive sexual partner
- Recent bacterial STI
- High number of sex partners
- History of inconsistent or no condom use
- Commercial sex work

**Heterosexual Men and Women:**
- HIV-positive sexual partner
- Recent bacterial STI
- High number of sex partners
- History of inconsistent or no condom use
- Commercial sex work In high-prevalence area or network

TRUVADA FOR PrEP: REQUIREMENTS FOR INITIATION AND MONITORING FOR HIV-1 INFECTION

Confirm HIV-1 status prior to TRUVADA for PrEP initiation

- Confirm negative HIV-1 status immediately prior to initiation
- If signs or symptoms of acute HIV-1 infection (eg, fever, fatigue, myalgia, skin rash) are present and recent exposures (<1 month) are suspected, delay initiation for ≥1 month, then reconfirm HIV-1 status
- Alternatively, confirm negative HIV-1 status with a test approved by the FDA to aid diagnosis of acute or primary HIV-1 infection

Discontinue if an HIV-1 infection is suspected

- Screen uninfected individuals for HIV-1 infection at least every 3 months while they are taking TRUVADA for PrEP
- If symptoms of acute HIV-1 infection develop following a potential exposure event, discontinue TRUVADA for PrEP until negative HIV-1 status is confirmed using a test approved by the FDA to aid diagnosis of acute or primary HIV-1 infection

HIV-1 resistance may emerge in individuals with undetected HIV-1 infection who are taking only TRUVADA because this does not constitute a complete ART regimen for HIV-1 treatment.

ART, antiretroviral therapy.
TRUVADA Prescribing Information. Gilead Sciences, Inc. 2016.
Contraindications:

- Do not use TRUVADA for PrEP in individuals with unknown or positive HIV-1 status

Dosage and Administration:

- TRUVADA for PrEP in HIV-1 uninfected adults: one tablet once daily with or without food

HBV Testing

- It is recommended that all individuals be tested for the presence of chronic HBV before initiating TRUVADA
Drug for PrEP

No Descovy
HPTN 077: Cabotegravir for PrEP in Low-Risk Persons

- International, randomized, double-blind, placebo-controlled phase IIa study (N = 199)

**Men and women at low risk of HIV infection (N = 199)**

**Cohort 1**

- CAB 30 mg PO QD (n = 82)
- Placebo PO QD (n = 28)

**Cohort 2**

- CAB 30 mg PO QD (n = 69)
- Placebo PO QD (n = 20)

**Oral Phase**

- CAB 800 mg IM Q12W
- Placebo IM Q12W
- CAB 600 mg IM Q8W*
- Placebo IM Q8W*

**Injection Phase**

- All pts were followed to Wk 105

*Pts received 4-wk loading dose.

- Grade ≥ 2 AEs significantly different between CAB and PBO during injection phase: injection-site pain (34% vs 2%; P < .0001), headache (15% vs 2%; P = .03)
  - Most injection-site reactions mild/moderate; 1 discontinuation due to injection-related AE
- 1 seroconversion (CAB cohort 1): detected 48 wks after final injection; CAB levels undetectable
- Participants in cohort 2 (600 mg IM Q8W) consistently met prespecified PK targets; this dose will be assessed in phase III studies

When to Treat
# Changing Criteria for Antiretroviral Therapy Initiation in DHHS Guidelines

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 500</td>
<td>Offer if VL &gt; 20K</td>
<td>Offer if VL &gt; 20K</td>
<td>Consider if VL ≥ 100K</td>
<td>Consider in certain groups*</td>
<td>Consider†</td>
<td>Treat</td>
</tr>
<tr>
<td>350-500</td>
<td>Offer if VL &gt; 20K</td>
<td>Consider if VL &gt; 55K</td>
<td>Consider if VL ≥ 100K</td>
<td>Consider in certain groups*</td>
<td>Treat</td>
<td>Treat</td>
</tr>
<tr>
<td>200-350</td>
<td>Offer if VL &gt; 20K</td>
<td>Offer, but controversy exists</td>
<td>Offer after discussion with patient</td>
<td>Treat</td>
<td>Treat</td>
<td>Treat</td>
</tr>
<tr>
<td>&lt; 200 or symptomatic</td>
<td>Treat</td>
<td>Treat</td>
<td>Treat</td>
<td>Treat</td>
<td>Treat</td>
<td>Treat</td>
</tr>
</tbody>
</table>

*Pregnant women, patients with HIV-associated nephropathy, and patients with HBV that requires treatment.
†50% of panel members recommended starting antiretroviral therapy; 50% of members viewed treatment as optional.
# Key Findings From START Study

<table>
<thead>
<tr>
<th>Types of Events</th>
<th>Early ART Group, n=2,326</th>
<th>Deferred ART Group, n=2,359</th>
<th>Hazard Ratio in Early vs Deferred Group, 95% CI and P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opportunistic diseases</td>
<td>14</td>
<td>50</td>
<td>0.28 (0.15-0.50; P&lt;0.001)</td>
</tr>
<tr>
<td>Serious non-AIDS events (cardiovascular, liver, and kidney disease + non-AIDS-defining cancers) and death not attributable to AIDS</td>
<td>29</td>
<td>47</td>
<td>0.61 (0.38-0.97; P=0.04)</td>
</tr>
<tr>
<td>Cancer(^a)</td>
<td>14</td>
<td>39</td>
<td>0.36 (0.19-0.66; P=0.001)</td>
</tr>
</tbody>
</table>

\(^a\) Of the 53 cancer events, 26 (5 vs 21 in the early and deferred groups, respectively) were affected by immunodeficiency, whereas the remaining 27 (9 vs 18, respectively) were not.

**ART**, antiretroviral therapy
START: Cancer Events With Immediate vs Deferred ART

<table>
<thead>
<tr>
<th>Cancer Event, n</th>
<th>Immediate ART (n = 2326)</th>
<th>Deferred ART (n = 2359)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>14</td>
<td>39</td>
</tr>
<tr>
<td>Kaposi’s sarcoma</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Lymphoma, NHL + HL</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Anal cancer</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Cervical or testis cancer</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Other types*</td>
<td>4</td>
<td>9</td>
</tr>
</tbody>
</table>


Time to Cancer Event

Rate/100 PY: immediate, 0.20; deferred, 0.56 (HR: 0.36; 95% CI: 0.19-0.66; P = .001)


Slide credit: clinicaloptions.com
What to Use
## Licensure of Antiretroviral Agents by Year

<table>
<thead>
<tr>
<th>Year</th>
<th>Drug Name</th>
<th>Month/Year</th>
<th>Other Drugs/Combinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1987</td>
<td>zidovudine (Retrovir)</td>
<td>6/06</td>
<td>darunavir (Prezista)</td>
</tr>
<tr>
<td>1991</td>
<td>didanosine (Videx)</td>
<td>7/06</td>
<td>efavirenz/emtricitabine, tenofovir DF (Atripla)</td>
</tr>
<tr>
<td>1992</td>
<td>zalcitabine (Hivid)</td>
<td>8/07</td>
<td>maraviroc (Selzentry)</td>
</tr>
<tr>
<td>1994</td>
<td>stavudine (Zerit)</td>
<td>10/07</td>
<td>raltegravir (Isentress)</td>
</tr>
<tr>
<td>1995</td>
<td>lamivudine (Epivir)</td>
<td>1/08</td>
<td>etravirine (Intelence)</td>
</tr>
<tr>
<td></td>
<td>saquinavir (Invirase)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1996</td>
<td>ritonavir (Norvir)</td>
<td>5/20/11</td>
<td>rilpivirine (Edurant)</td>
</tr>
<tr>
<td></td>
<td>indinavir (Crixivan)</td>
<td>8/11/11</td>
<td>rilpivirine/ tenofovir/ emtricitabine (Complera)</td>
</tr>
<tr>
<td></td>
<td>nevirapine (Viramune)</td>
<td>7/16/12</td>
<td>emtricitabine/tenofovir</td>
</tr>
<tr>
<td>1997</td>
<td>nelfinavir (Viracept)</td>
<td>8/28/12</td>
<td>disoproxil fumarate (Truvada)</td>
</tr>
<tr>
<td></td>
<td>delavirdine (Rescriptor)</td>
<td>8/30/14</td>
<td>emtricitabine/tenofovir/ elvitegravir/ cobicistat. (Stribild)</td>
</tr>
<tr>
<td></td>
<td>efavirenz (Sustiva)</td>
<td>8/12/13</td>
<td>dolutegravir (Tivicay)</td>
</tr>
<tr>
<td></td>
<td>abacavir (Ziagen)</td>
<td>8/30/14</td>
<td>abacavir/dolutegravir/lamivudine (Triumeq)</td>
</tr>
<tr>
<td>1999</td>
<td>amprenavir (Agenerase)</td>
<td>8/30/14</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>lopinavir/ritonavir (Kaletra)</td>
<td>1/29/15</td>
<td>atazanavir 300 mg and cobicistat / 150 mg (Evotaz)</td>
</tr>
<tr>
<td>2001</td>
<td>tenofovir (Viread)</td>
<td>11/5/15</td>
<td>elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide.(Genvoya)</td>
</tr>
<tr>
<td>2003</td>
<td>enfuvirtide (Fuzeon)</td>
<td>3/1/16</td>
<td>rilpivirine+emtricitabine+tenofovir alafenamide (Odefsey)</td>
</tr>
<tr>
<td>6/03</td>
<td>atazanavir (Reyataz)</td>
<td>4/6/16</td>
<td>emtircitabine+tenofovir alafenamide (Descovy)</td>
</tr>
<tr>
<td>7/03</td>
<td>emtricitabine (Emtriva)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8/04</td>
<td>lamivudine/abacavir sulfate (Epzicom)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6/05</td>
<td>tipranavir (Aptivus)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Fixed dose combinations of existing drugs*
Recommended ART Regimens
(2 NRTI + 3rd drug)

• Protease Inhibitor-based
  – tenofovir (TDF)/emtricitabine + darunavir/r (Truvada/Prezcobix)

• Integrase Inhibitor-based
  – abacavir/lamivudine/dolutegravir (Triumeq)
  – tenofovir (TDF)/emtricitabine + dolutegravir (Truvada/Tivicay)
  – tenofovir (TAF)/emtricitabine/elvitegravir/cobicistat (Genvoya)
  – tenofovir (TDF)/emtricitabine/elvitegravir/cobicistat (Stribild)
  – tenofovir (TDF)/emtricitabine + raltegravir (Truvada/Isentress)
Antiretroviral Treatment: New TAF Drugs

<table>
<thead>
<tr>
<th>Non-TAF</th>
<th>TAF Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Stribild) emtricitabine/ tenofovir/ elvitegravir/ cobicistat</td>
<td>(Genvoya) FTC/TAF + EVG/COBI</td>
</tr>
<tr>
<td>(Complera) rilpivirine/ tenofovir/emtricitabine</td>
<td>(Odefsey) FTC/TAF + RPV</td>
</tr>
<tr>
<td>(Truvada) emtricitabine/tenofovir disoproxil fumarate</td>
<td>(Descovy) FTC/TAF</td>
</tr>
</tbody>
</table>
**LATTE-2: 96-Wk Results for Cabotegravir IM + Rilpivirine IM as Long-Acting Maintenance ART**

- **Cabotegravir:** INSTI formulated as PO tablet and for long-acting IM injection
- LATTE-2: phase IIb study in which pts randomized to **CAB 400 mg + RPV 600 mg IM Q4W, CAB 600 mg + RPV 900 mg IM Q8W,** or **CAB 30 mg + ABC/3TC 600/300 mg PO QD** after induction/virologic suppression with oral CAB + ABC/3TC (N = 309)

![Wk 96 Virologic Efficacy](chart.png)

- At 96 wks, ~ 30% pts receiving IM injection experienced ISR
  - 99% of ISRs mild/moderate
- AEs leading to withdrawal
  - Pooled Q4W/Q8W IM arms, 4%; PO arm, 2%
- Withdrawals between Wks 48 and 96: CAB IM arms, n = 4 (n = 1 for AE, n = 3 withdrew consent); CAB PO arm, n = 3 (all withdrew consent)
- No additional PDVF after Wk 48 in any arm
- ~ 88% of pts receiving IM CAB very satisfied to continue present treatment vs 43% receiving PO CAB

*HIV-1 RNA < 50 copies/mL.


Slide credit: [clinicaloptions.com](http://clinicaloptions.com)
Dual-Therapy Regimens for Initial ART

- **ANDES**: randomized phase IV study of DRV/RTV + 3TC vs DRV/RTV + TDF/3TC in ART-naive pts (N = 145)[1]
  - Baseline: 24% HIV-1 RNA > 100,000 c/mL
- **ACTG A5353**: single-arm phase II study of DTG + 3TC in ART-naive pts (N = 120)[2]
  - Baseline: 31% HIV-1 RNA > 100,000 c/mL

<table>
<thead>
<tr>
<th>HIV-1 RNA &lt; 400 c/mL (ITT) at Wk 24, n/N (%)</th>
<th>DRV/RTV + 3TC</th>
<th>DRV/RTV + TDF/3TC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>71/75 (95)</td>
<td>68/70 (97)</td>
</tr>
<tr>
<td>BL HIV-1 RNA &gt; 100,000 c/mL</td>
<td>20/20 (100)</td>
<td>15/15 (100)</td>
</tr>
</tbody>
</table>

- 1 virologic failure with DRV/RTV + TDF/3TC

**GEMINI 1/2 randomized phase III trials of DTG + 3TC ongoing[3,4]**

<table>
<thead>
<tr>
<th>Virologic Outcome at Wk 24, n (%)</th>
<th>Baseline HIV-1 RNA, c/mL</th>
<th>Total (N = 120)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt; 100,000 (n = 37)</td>
<td>≤ 100,000 (n = 83)</td>
</tr>
<tr>
<td>Success*</td>
<td>33 (89)</td>
<td>75 (90)</td>
</tr>
<tr>
<td>Nonsuccess</td>
<td>3 (8)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>No data</td>
<td>1 (3)</td>
<td>6 (7)</td>
</tr>
</tbody>
</table>

*HIV-1 RNA < 50 copies/mL.

- n = 3 with PDVF; n = 1 with emergent M184V and R263R/K mixture

The yearly total of primary and secondary syphilis cases more than doubled, from 8,724 to 16,663.

P&S Syphilis Cases per 100,000 population, 2015

- All men: 17.5
- Men who have sex with men: 309
- Men who have sex with women only: 2.9
- Women: 1.8

A disturbing trend

After national syphilis rates hit historic lows in 2001, they increased almost every year since, peaking in 2014 with the highest rate reported in 20 years.

- **22.7%** the syphilis case rate increase in women from 2013 to 2014
- **19,999** the number of syphilis cases reported in 2014 (compared to **6,103** in 2001)
- **37%** the congenital syphilis case rate increase from 2012 to 2014

Before 2013, increasing syphilis rates were mainly due to cases in men — particularly in men who have sex with men (MSM). But from 2013 to 2014, syphilis rates also increased in women. And more syphilis cases in women means more cases of congenital syphilis in babies. Serious health problems from syphilis, like syphilis of the eye, are increasing among both men and women.

Treatment

Hepatitis C
DAA’s Available

- sofosbuvir (Sovaldi)
- simeprevir (Olysio)
- ombitasvir / paritaprevir / ritonavir / dasabuvir (Vikera Pak)
- ledipasvir / sofosbuvir (Harvoni)
- daclatasvir (Daklinza)
- ombitasvir / pritaprevir / ritonavir (Technivie)
- elbasvir and grazoprevir (Zepatier)
- sofosbuvir/velpatasvir (Epclusa)
- glecaprevir/pibrentasvir (Mavyret)
The FDA has approved glecaprevir/pibrentasvir (GLE/PIB; Mavyret) for the treatment of all major HCV genotypes in patients with mild/no cirrhosis.

GLE/PIB can be used across all stages of chronic kidney disease (CKD), including dialysis.

https://www.univadis.com/viewarticle/mavyret-8-wk-hcv-regimen-wins-fda-approval-543784?u=g7Nnk16ewglkywbUIY1MK1ZSaeXLxHOJfnTlgs0eY1LvFJRGbRFdj6yhVfoVUN&utm_source=newsletter%20email&utm_medium=email&utm_campaign=ct-newsletter_wf-automated_fq-daily_cpedicalupdates_20170626&utm_content=1541824&utm_term=automated_daily
GLE/PIB (Mavyret) WAC price of $26,400 for 8-week course marks significant departure from prohibitive drug prices set for first-generation cures

- The U.S. Wholesale Acquisition Cost price for:
  - 12 weeks course of treatment has been set at $39,600.
  - 8-week course of treatment is set at a price of $26,400.

- This price is in stark contrast with the WACs set for its pangenotypic predecessors, including Gilead’s Vosevi and Epclusa (both $74,760 for 12 weeks of therapy), and is by far the lowest WAC of any direct acting antiviral (DAA) regimen currently available for HCV infection in the U.S.
The journey continues…