Rapid Start
Panel Discussion
A Coordinated Team Approach

Friday
September 13, 2019
Estimated HIV Incidence among Persons Aged ≥13 Years

2010–2016—United States

Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Bars indicate the range of the lower and upper bounds of the 95% confidence intervals for the point estimate.
Estimated HIV Incidence among Persons Aged ≥13 Years, by Race/Ethnicity
2010–2016—United States

Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Hispanics/Latinos can be of any race.
* Difference from the 2010 estimate was deemed statistically significant (P < .05).
† Estimates should be used with caution because they do not meet the standard of reliability.
Estimated HIV Incidence among Persons Aged ≥13 Years, by Age
2010–2016—United States

Note. Estimates were derived from a CD4 depletion model using HIV surveillance data.
* Difference from the 2010 estimate was deemed statistically significant (P < .05).
Care Continuum US

Receipt of HIV Medical Care, Retention in Care, and Viral Suppression among Persons Aged ≥ 13 Years Living with Diagnosed HIV Infection, by Sex, 2016 - 41 States and the District of Columbia

- Total: 74.2%
- Male: 74.2%
- Female: 74.0%

- Receipt of care: 57.6%
- Retained in care: 61.5%
- Viral suppression: 57.6%

- Percentages for Viral Suppression: 62.2% for Male, 59.4% for Female
Retention in HIV Medical Care among Persons Aged ≥13 Years Living with Diagnosed HIV Infection, 2016—U.S. Census Bureau Estimates of Residence

Total = 57.6%

Note. Retained in continuous medical care was defined as ≥2 tests (CD4 or VL) ≥3 months apart in 2016. Residence was based on most recent known address as of year-end 2016.
Viral Suppression among Persons Aged ≥13 Years Living with Diagnosed HIV Infection, 2016—41 States and the District of Columbia

Total = 61.5%

Note. Viral suppression was defined as <200 copies/mL on the most recent VL test in 2016. Residence was based on most recent known address as of year-end 2016.
Background

- For the past five years, clinical guidelines for treatment of HIV recommend ART initiation in all HIV-positive individuals regardless of their CD4 cell count.\(^1\)\(^-\)\(^3\)

- These updates are further supported by randomized controlled trials and observational studies that have shown that initiation of ART at high CD4 cell counts (\(\geq 500\) cells/mm\(^3\))\(^4\)\(^-\)\(^5\):
  - Reduces the risk of serious AIDS and non-AIDS events
  - Reduces mortality in people living with HIV

- Additional studies have shown that **rapid initiation**, defined as starting therapy on the first day to within 1 week of diagnosis, results in\(^6\)\(^-\)\(^14\):
  - Shorter time to viral suppression
  - Increased retention in care
  - Increased rates of viral suppression
  - Decreased mortality

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Research Supporting Early Treatment Initiation

Early ART is Preferred over Delayed

- START Global
- TEMPRANO Ivory Coast

Rapid ART Programs Demonstrate Benefits

- RapIT South Africa
- Same-Day ART Haiti
- Same-Day ART Bangkok
- Retrospective Cohort China
- SLATE South Africa and Kenya

- RAPID San Francisco
- Acute HIV Consortium North Carolina - Duke/UNC
- REACH Atlanta - Emory/Grady
- CrescentCare Start Initiative New Orleans
- JumpstART Program New York City
Figure 1. Relative hazard of mortality with combination antiretroviral therapy in randomized clinical trials [8–13]. ...
Same-Day ART (Port-au-Prince, Haiti)

Results: Standard vs Same-Day ART Start

<table>
<thead>
<tr>
<th>Metric</th>
<th>Standard Start (n=285)</th>
<th>Same Day Start (n=279)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completed CD4 count</td>
<td>100%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Initiated ART</td>
<td>92%</td>
<td>100%</td>
<td>0.014</td>
</tr>
<tr>
<td>Alive and in Care at 12 months</td>
<td>72%</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>Alive with undetectable VL</td>
<td>44%</td>
<td>53%</td>
<td>0.015</td>
</tr>
<tr>
<td>Died</td>
<td>6%</td>
<td>3%</td>
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</tbody>
</table>

Same-day ART improved retention with virologic suppression and decreased mortality

RAPID Study (San Francisco)

**RAPID Program Interventions**

- Same-day access to an HIV provider
- Same-day medical visit including:
  - HIV education, risk reduction, sexual health and benefits of ART
  - Possible contraindications of ART discussed
  - Baseline laboratory tests drawn but not typically available prior to ART start
    - Included: CD4 cell count, HIV viral load, renal and liver function tests, hepatitis serologies, HLA B*5701 testing, HIV resistance genotyping
  - Accelerated insurance approval process
  - Preapproved ART regimens
  - Five day starter packs if needed were available
  - Directly observed administration of first dose
  - Telephone follow-up by RAPID nurses within the first 7 days
RAPID Study (San Francisco)

Standard vs. RAPID Models

**HIV+ Diagnosis**
- Disclosure
- HIV education
- Counseling
- Referral
- Scheduling

**1st Clinic Visit**
- Registered
- Insurance
- Assess housing, substance use, mental health needs
- HIV education
- Counseling
- Labs

**1st Primary Care Provider Visit**
- Medical evaluation
- Assess preparedness

**ART Start**
- Prescription
- Pharmacy pick-up

**ART Management**
- Viral load monitoring
- Adherence
- Retention

**RAPID Visit: ART Start**
- Disclosure, counseling
- Registration
- Insurance
- Assess housing, substance use, mental health needs
- Labs
- HIV education
- Counseling
- Medical evaluation
- Assess preparedness
- ART dispensed
- Telephone follow-up

**Primary Care Provider Visits: ART Management**
- Viral load monitoring
- ART management
- Adherence
- Retention
RAPID Study (San Francisco)

Results – Patients on ART by Days After Initial Visit

Day 0 = took their first dose in the clinic on their first visit
Day 1 = took their first dose within 24 hours of their first visit

[Bar chart showing percent of patients on ART by days after initial clinic visit for RAPID and Non-RAPID groups]
RAPID Study (San Francisco)

Results – Time to Viral Suppression

![Graph showing time to viral suppression for RAPID ART (2013-2015) with N=39, UNIVERSAL ART (2010-2013) with N=69, and CD4-guided ART (2006-2009) with N=25. The graph plots the proportion of VL < 200 copies/mL against time from clinical referral (months).](image-url)
Citywide RAPID Program, confirmed diagnoses and linked to care in ≤ 5 days between 2013 to 2016
- ART included (FTC/TDF or FTC/TAF) + (INSTI or DRV/r)

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Diagnosed, n</td>
<td>399</td>
<td>329</td>
<td>295</td>
<td>265</td>
<td>-</td>
</tr>
<tr>
<td>In Care within 1 year (%)</td>
<td>372 (93)</td>
<td>318 (97)</td>
<td>282 (96)</td>
<td>258 (97)</td>
<td>-</td>
</tr>
<tr>
<td>Diagnosis to 1st Care Visit (days*)</td>
<td>8</td>
<td>7</td>
<td>7</td>
<td>5</td>
<td>-38%</td>
</tr>
<tr>
<td>1st Care Visit to ART (days*)</td>
<td>27</td>
<td>17</td>
<td>6</td>
<td>1</td>
<td>-96%</td>
</tr>
<tr>
<td>ART to VL &lt;200 c/mL (days*)</td>
<td>70</td>
<td>53</td>
<td>50</td>
<td>38</td>
<td>-46%</td>
</tr>
<tr>
<td>Diagnosis to VL &lt;200 c/mL (days*)</td>
<td>134</td>
<td>92</td>
<td>77</td>
<td>61</td>
<td>-54%</td>
</tr>
</tbody>
</table>

Time from diagnosis to virologic suppression was cut by more than half from 134 days to 61 days. This benefit persisted in traditionally vulnerable populations, including racial/ethnic minorities and the homeless.
RAPID ART Program for HIV Diagnoses (RAPID) in San Francisco

- Linkage to care within 5 working days
- Labs, counseling, medical/psychosocial assessment, ART start at first care visit
  - (INSTI or DRV/RTV) + FTC/TDF*
- HIV clinics identified using HIV surveillance data, RAPID Provider Directory identified best clinic for each patient
- 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
- Time to ART start and first viral suppression decreased in vulnerable populations, including racial/ethnic minorities and homeless patients
  - Disparities still exist for some outcomes

*4-drug regimen optional if HIV infection suspected to have occurred while on PrEP.

Primary Endpoint: Time to Viral Suppression

REACH - Rapid Entry and ART Clinic for HIV (Atlanta - Emory University/Grady Health System)

41 days (21,72)
67 days (34,126)

Proportion VL <200 copies/mL

Days to viral suppression

Day 0 40 80 120 160 200
Pre-REACH 117 81 50 33 22 0
Post-REACH 90 47 16 8 3 0

Colasanti, J. et al. CROI 2018. Boston, MA. Poster 1109

Adjusted for Art Naive, INSTI use, baseline log10 HIV RNA

aHR = 1.83 (1.28, 2.61)
IAS-USA: Laboratory Recommendations

- Labs below should be drawn before beginning ART, but treatment may be started before results are available

**Laboratory tests for ART initiation:**

- HIV-1 RNA level
- CD4 cell count
- HIV genotype for NRTI, NNRTI, and PI
- Laboratory tests to exclude active viral hepatitis
- Chemistries

Result of testing for HLA-B*5701 allele should be available if an abacavir-containing regimen is anticipated

Unless preexisting kidney or liver damage or high likelihood of transmitted drug resistance exists, the results of these tests should not delay start of ART
### Rapid Initiation of ART: Key Regimen Considerations

<table>
<thead>
<tr>
<th>NRTI Backbone</th>
<th>3rd agent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FTC/TAF</strong></td>
<td><strong>NNRTIs</strong></td>
</tr>
<tr>
<td>- No dose adjustment eGFR ≥ 30 mL/min&lt;sup&gt;1&lt;/sup&gt;</td>
<td>- Generally not recommended due to potential for transmitted resistance&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>FTC/TDF</strong></td>
<td></td>
</tr>
<tr>
<td>- Dose adjust eGFR &lt; 50 mL/min&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td><strong>ABC/3TC</strong></td>
<td></td>
</tr>
<tr>
<td>- Not appropriate for rapid initiation&lt;sup&gt;3,4&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>- Requires HLA-B&lt;sup&gt;*&lt;/sup&gt;5701</td>
<td></td>
</tr>
<tr>
<td>- Inadequate HBV activity; requires HBsAg</td>
<td></td>
</tr>
<tr>
<td>- Not recommended for eGFR &lt; 50 mL/min&lt;sup&gt;5&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

Considerations when initiating rapid ART when laboratory results are pending

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5. Epitom Prescribing Information. April 2018.
Rapid ART Initiation Recommendations

- ART initiation, including rapid start, is recommended for all infected ambulatory patients committed to starting ART* or for those with unclear HIV diagnosis

<table>
<thead>
<tr>
<th>Recommended Regimens for Rapid ART Initiation</th>
</tr>
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<tbody>
<tr>
<td>BIC/FTC/TAF</td>
</tr>
<tr>
<td>DTG + FTC** + TAF†</td>
</tr>
<tr>
<td>Boosted DRV + FTC** + TAF†</td>
</tr>
</tbody>
</table>

Regimens containing NNRTIs or ABC‡‡ should not be used for rapid ART initiation

- Structural barriers that delay receipt of ART should be removed to allow newly diagnosed persons to receive ART at the first clinic visit after diagnosis, if they and their clinician determine that this approach is appropriate

*Unless the patient has symptoms that suggest an opportunistic infection for which immediate ART is contraindicated
**(or 3TC) †(or TDF)
‡‡Patients requiring ABC should not begin until the result of testing for the HLAB* 5701 allele is available

# Choosing Integrase Inhibitors

<table>
<thead>
<tr>
<th>Agent</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
</table>
| **Bictegravir** | • STR once daily  
  • Available with TAF  
  • Few drug or food interactions  
  • Potentially high barrier to resistance | • Least amount of data  
  • Only available as STR with TAF/FTC |
| **Dolutegravir** | • Only non-TFV QD STR  
  • High barrier to resistance  
  • Few drug or food interactions  
  • Active against some RAL- and EVG-resistant viruses | • STR only with ABC/3TC  
  • Increases metformin levels |
| **Elvitegravir** | • STR once daily  
  • Available with TAF and TDF | • Requires COBI boosting  
  • COBI drug interactions |
| **Raltegravir** | • Longest experience  
  • Few drug or food interactions | • Multiple pills  
  • No STR |
Rapid ART Initiation Recommendations

- ART initiation, including rapid start, is recommended for all infected ambulatory patients committed to starting ART* or for those with unclear HIV diagnosis (e.g., discordant serologic or rapid test results)

- Structural barriers that delay receipt of ART should be removed to allow newly diagnosed persons to receive ART at the first clinic visit after diagnosis, if they and their clinician determine that this approach is appropriate

- All elements of conventional treatment initiation must be in place at the treatment site but provided in a way that ensures immediate access

*Unless the patient has symptoms that suggest an opportunistic infection for which immediate ART is contraindicated

Rapid ART Initiation – Potential Benefits and Limitations

Potential Benefits

- Better clinical outcomes due to less time off ART
- Engagement opportunity to increase retention in care
- Shorter time to treatment decreases anxiety, increases trust
- Public health benefit: decreased transmission risk

Potential Limitations

- ART may not be optimized (HBV, renal insufficiency)
- OIs requiring delayed ART may not be ruled out
- Less time to address barriers to ART and adherence
- Risk of resistance if low barrier regimen used
- Requires change in work-flow with rapid access (access, appointment scheduling, staffing)

Implementation research is needed to better understand benefits and limitations in real world settings
“And Now the Rest of the Story”

(Paul Harvey)

• Retention
  • Valid contact information
  • Appointment reminders: paper, phone, text – best practices

• Adherence
  • Counseling - everyone
  • Reminders – calls, texts
  • Smart phone alerts
How can we do better?

• Dr. Avery ........
• Dr. Gripshover ........
• Jen- McMillian-Smith ........
• Amy Hirsch ........
• Audience ........
Randomized clinical trials show that deferring therapy based on CD4 count results in increased morbidity and mortality.

Rapid ART initiation is recommended in US and international HIV Guidelines.

Randomized clinical trials and observational trials evaluating rapid ART initiation show clinical benefits for patients, including:
- Shorter time to viral suppression
- Increased rates of viral suppression
- Increased retention in care
- Decreased mortality

Public health benefits of decreased transmission may be realized with earlier suppression of HIV viral load.