Immediate Antiretroviral Therapy Initiation

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OBJECTIVES

- To Understand the reasoning to Implement Immediate ART Initiation for newly diagnosed HIV infected persons.

- Review data on the Implementation of Immediate ART Initiation.

- Review the Implementation of Immediate ART Initiation in Miami

- Discuss potential barriers to the implementation of Immediate ART Initiation
Definition

- ART initiation at the time of diagnosis or as soon as possible

- ART be prescribed on the same day of the confirmed diagnosis or at their initial clinic visit, even if all baseline laboratory test results haven't returned
### DHHS
#### Changing Criteria for Initiating ART

<table>
<thead>
<tr>
<th>CD4 Count (cells/mL)</th>
<th>1998</th>
<th>2001</th>
<th>2006</th>
<th>2008</th>
<th>2009</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;500</td>
<td>Offer if VL &gt;20,000</td>
<td>Offer if VL &gt;55,000</td>
<td>Consider if VL &gt;100,000</td>
<td>Consider in certain groups</td>
<td>Consider in certain patients</td>
<td>Treat</td>
</tr>
<tr>
<td>&gt;350–500</td>
<td>Offer if VL &gt;20,000</td>
<td>Consider if VL &gt;55,000</td>
<td>Consider if VL &gt;100,000</td>
<td>Consider in certain groups</td>
<td>Consider in certain groups</td>
<td>Treat</td>
</tr>
<tr>
<td>200–350</td>
<td>Offer if VL &gt;20,000</td>
<td>Offer, but controversy existed</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>
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</table>

**VL**, viral load.

When to Start ARV

**When to Start Therapy**
*Balance Now Favors Earlier ART Initiation*

**EARLY ART**
- ↑ Potency, durability, simplicity, and safety of current regimens
- ↓ Emergence of resistance
- ↓ Toxicity with earlier therapy
- ↑ Subsequent treatment options
- ↓ Risk of uncontrolled viremia at all CD4 levels
- ↓ Transmission

**DELAYED ART**
- – Drug toxicity
- – Preservation of limited Rx options
- – Risk of resistance
- – Risk of transmission of resistant virus
- – Increased cost

Reasons for Rapid ARV

- Shifting guidelines (DHHS and WHO)
- High attrition rates between time of positive HIV test and ART initiation
- Delays in treatment are associated with
  - Increased mortality
  - Diminished CD4 recovery
  - Avoidable hospitalizations
  - Higher costs of treatment for opportunistic infections
  - HIV transmission
- Improved ART tolerability and durability
- Lower risk for viral resistance with current ART regimens
In 2013, the Ward 86 HIV Clinic at the University of California, San Francisco (UCSF) at San Francisco General Hospital (SFGH) became the first clinic in the United States to provide immediate antiretroviral therapy (ART) upon HIV diagnosis.

San Francisco Experience: Same-Day Observed ART Initiation Versus Standard of Care

**Standard of Care (n=47)**
- 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

**Same Day ART Initiation (n=39)**
- RAPID Visit: ART Start
  - Disclosure, counseling
  - Registration
  - Insurance
  - Assess housing, substance use, mental health needs
  - Labs
- Primary Care Provider Visits: ART Management
  - Viral load monitoring
  - ART management
  - Adherence
  - Retention

Clinic-based cohort (consecutive patients referred with new HIV diagnosis, 2013-2014). Same-day ART initiation cohort: patients with acute or recent infection (<6 months) or CD4 <200 cells/mm³. Intensive, same-day appointment included social needs assessment, medical provider evaluation, and a first ART dose offered after laboratories were drawn. 95% of patients began ART within 24 hours. Outcomes: time to viral suppression, acceptance of ART, drug toxicities, and resistance.

San Francisco Experience: Same-Day Observed ART Initiation Versus Standard of Care

- Significantly shorter time to viral suppression ($P<0.0001$)
  - Same-day ART versus universal ART (2010-2013) and CD4-guided ART (2006-2009)
- Similar rates of loss to follow-up
  - Same-day (10%) versus non-same-day ART (15%)
- Most same-day patients received INSTI-based regimens
  - Similar safety and tolerability with non-same day ART
  - No regimen modifications due to virologic failure
  - No cases of treatment-emergent resistance (35% had transmitted mutations, 24% with major NNRTI mutations)

Dolutegravir (69%), elvitegravir/cobicistat (18%), darunavir/r (10%), raltegravir (2%). Pitcher CD, et al. JAIDS. 2017;74:44-51.
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The study was stopped early by DSMB due to better outcomes in the same-day ART group.
RAPID Safety Data

• INSTI-based regimen in 87% (NS difference between arms)
  – Most common initial regimen in RAPID: DTG + TDF/FTC (67%)
• ART modifications more frequent among RAPID arm
  – 2 ART changes due to rash
  – 10 ART changes for simplification
  – No changes for VF
  – No changes based on genotype results
• Transmitted drug resistance (n=75 with genotype results)
  – 82% in RAPID vs 92% in non-RAPID obtained genotype results (NS)
    • Of those with a mutation, 35% with any major resistance mutation
    • Of those with a mutation, 24% with NNRTI resistance mutation

3TC, lamivudine; ABC, abacavir; DTG, dolutegravir; INSTI, integrase strand transfer inhibitor (integrase inhibitor); NNRTI, nonnucleoside/tide reverse transcriptase inhibitor; NS, nonsignificant; VF, virologic failure.
# REACH: Atlanta Georgia

**Rapid Entry and ART in Clinic for HIV**

## Goals

1. Facilitate provider appointment and ART access within 72 hours of patients’ first presenting to clinic for enrollment
2. Decrease time to viral suppression

## Health System Changes to Facilitate Program Implementation

<table>
<thead>
<tr>
<th>ACTION</th>
<th>LEVEL</th>
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<tbody>
<tr>
<td>Remove eligibility restrictions for clinic enrollment</td>
<td>EMA Ryan White office</td>
</tr>
<tr>
<td>Loosen administrative requirements for clinic enrollment</td>
<td>EMA Ryan White office; <strong>hospital system</strong></td>
</tr>
<tr>
<td>Remove TB skin test as requirement for clinic enrollment</td>
<td><strong>Clinic administration</strong></td>
</tr>
<tr>
<td>Enhance access to <em>New Patient</em> provider visits</td>
<td>Hospital system; clinic administration</td>
</tr>
<tr>
<td>Enhance provider education on <em>Rapid Starts</em></td>
<td><strong>Clinician</strong></td>
</tr>
<tr>
<td>Enhance support for accessing ART, regardless of payer</td>
<td><strong>Pharmacy administration</strong></td>
</tr>
<tr>
<td>Continue access to ongoing ART-adherence education</td>
<td><strong>Nursing</strong></td>
</tr>
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Evidence for Rapid ARV

- Demonstration projects from clinics in New Orleans, Los Angeles, and Atlanta have found that implementation of immediate ART programs led to earlier linkage to care and shorter time to virologic suppression than seen in historical controls.

- Current guidelines from the U.S. Department of Health and Human Services and the International Antiviral Society--USA endorse ART initiation at the time of diagnosis or as soon as possible afterwards.
Rapid ARV literature: Better outcomes, such as improved ART uptake, sustained ART adherence, and decreased time to virologic suppression


Test and Rapid Response Miami

United States HIV Prevalence 2015
Source: AIDSVu (www.aidsvu.org), Emory University, Rollins School of Public Health [accessed April 10, 2018].
Test and Rapid Response Miami- Treatment Setting
University of Miami/Jackson Memorial Hospital Medical Center/DOH

- Largest single-site HIV clinic in Florida
- 3200 HIV+ individual patients annually
- ~23% of the estimated 14,000 HIV (Miami)
- Minorities: 57.9% Black; 36.4% Hispanic
- Women: 37.6%
- Older population
  ~75% > 40
  ~50% > 50
- Interdisciplinary treatment
- Collaborations with the Miami HD

Pilot Program: Miami UM/JMMC Clinic March 2016
Statewide Guidance Issue September 2016
Miami Department of Health, testing agencies, funding agency, pharmacy, clinical settings
Referral and Linkage Process Miami Dade

Before Rapid ARV

- Pt. tests for HIV
- Returns in 10 days for results.
- Referred to provider agency.
- Case management appointment given 2 weeks (or more) away.
- Case manager assesses for financial eligibility & ADAP; refers to Doctor; appointment given for 2 weeks (or more) away.
- Doctor orders labs, patient is scheduled for return appointment in 2 weeks.
- Doctor writes script at return appt.
- Pt. takes script to pharmacy.

After T&T

- Pt. tests for HIV; preliminary results positive.
- Pt accepts Test and Treat.
- Pt. is escorted to case management agency where eligibility is established.
- Pt. is seen by doctor and labs done.
- Doctor writes script.
- Medical case manager escorts Pt. to on site pharmacy to obtain 30 day supply of medication.

< 7 days (most same or next day)

Up to 3 months or more
Test and Rapid Response Treatment Process

- 4 organizations collaborated to contribute to patient care:
  - Florida Department of Health (FLDOH)
  - South Florida AIDS Network (SFAN)
  - Jackson Memorial Medical Center (JMMC)
  - University of Miami-Division of Infectious Diseases (UM-ID)

- FLDOH made funds available to provide the first 30 days of medication to the patients
  - Greatly reduced the time elapsed in the traditional linkage process

- The Ryan White Part A added a billing code to allow the first medical visit and laboratory work
  - Established immediate patient eligibility to immediately see the doctor, receive a prescription and, get baseline laboratory work.

- SFAN and UM-ID provided protected time for case management and medical staff

- JHS performed laboratory tests
Traditional Linkage to Care vs. Test and Rapid Response Treatment Initiative

Time elapsed from a positive rapid HIV test to receipt of ART:

- Traditional Linkage Method: 49-73 days
- Test and Rapid Response Treatment: 1-7 days
PTs recruited from FDOH clinics and Field Testing

Alert notification emailed to the TNT Team

PT is escorted to SFAN and meets MCM. Eligibility for RW services

PT receives financial assessment and receives Jackson Card and PT number

During next 30 days PT works with MCM toward obtaining ART on long term basis and developing the Care Plan

MCM takes PT to Jackson Pharmacy and PT receives 30 day supply of ART.

Doctor provides physical exam writes prescription and gives to PT

PT Navigator arranges for patient to see the doctor and get labs.
The Miami Experience
Implementation of an Immediate HIV Treatment Initiation Program in a Public/Academic Medical Center
The Miami Experience
Demographics First 2 years

22% of the new cases had AIDS
Reduced time to ART

Days to ARV
03/01/16 - 02/28/18
Improved Clinical Outcomes – 2 years

Over 90% received ART within 7 days

Virological suppression (<200 copies/mL)
92% suppressed within 70 days of testing (average 50 days)
97% suppressed within the first 12 months

97% retention

CD4 T-cell count (24% had AIDS at diagnosis)

Fast CD4 T-cell count improvement at 3 months when compared with historical data

\[327.77 + 242.5 \text{ cells/mm}^3 \quad \text{vs} \quad 597.78 + 322.5 \text{ cells/mm}^3\]

Increase over 1 year

Baseline = 452 cells/mm\(^3\) \quad 12 \text{ months} = 668 \text{ cells/mm}^3

Under review
Program Implementation Highlights

- Pre planning - coordination of services among different co-located services handling initial testing, financial administration, clinic registration, navigation of the patient in the first visit, HIV provider availability, first visit clinical evaluation, next day reviews of labs and a subsequent clinic visit within two weeks.

- Our program in partnership with the Florida Department of Health did not require financial enrollment on the day of the positive HIV test.

- Patient Clinic navigator’s coordination of new patient care between case management, the clinic, and dispensing pharmacies allowed for the patient to transition into the existing patient flow involving sustained regular visits, labs, ART dispensation, and follow-up.
The Miami Test and Treat Rapid Response Program

The Miami Test and Treat Rapid Response Program: Present: Accomplishments/Publications


- Poschman K, Spencer EC, Goldberg D, Villamizar KA, Adams T, Beal JA. Impact of HIV test and treat initiative in antiretroviral-naive patients in Miami-Dade County, Florida. CROI; 2019; Seattle, WA.

- 460 patients
- 2 Navigators representing our demographics

Test Miami
Exceptional performance award
December 2018
Immediate Initiation of Antiretroviral Therapy in the Outpatient Clinic

Management Recommendations
Optimal implementation of a rapid ART program should include:

- Efficient and reliable identification of all persons with new HIV diagnosis (for example, referral from testing sites via a single point of contact such as a dedicated pager or specific staff person).

- Activation of a "rapid" multidisciplinary team (social work, eligibility/insurance specialist clinician) that can mobilize quickly to see the patient on a same-day basis.

- Capacity to provide follow-up care within 1-2 week.
Appropriate patients to offer immediate ART include:

- Individuals with confirmed new diagnoses of HIV infection.
- Persons with suspected acute HIV infection whose HIV diagnosis may not yet be confirmed (eg, the HIV antigen or antibody test results may be negative at the time of evaluation).
- Persons with positive results of rapid HIV antibody tests, before confirmatory test results are available, if the pretest probability of HIV infection is high (after counseling, immediate ART is offered with the understanding that, if confirmatory test results are negative, the patient would stop ART and start pre-exposure antiretroviral prophylaxis, if appropriate).
- Chronically infected patients who have never received ART.
- Chronically infected patients who return to care after being out of care and off ART, if they have a known wild-type virus or their viral resistance pattern is predictable (these persons may require individually-tailored regimens).
The Immediate ART Clinic Intake Visit

- Obtaining sufficient information from the history to determine whether immediate ART is indicated, whether the patient is willing to start ART, and what medications to use
- Beginning education about HIV, ART (eg, possible benefits of early ART, adherence), and preventing transmission to others
- Engaging the patient in committing to return to clinic for follow-up appointments
- Assistance with insurance enrollment or optimization
Recommended Laboratory Tests at Immediate ART Intake Visit

- Confirmatory HIV testing (if needed)
- HIV viral load
- CD4 cell count
- HIV genotype, including integrase genotype
- HLA-B*5701
- Metabolic panel (creatinine, electrolytes, glucose, liver function tests)
- Hepatitis A IgG
- Hepatitis B sAb, cAb, Ag
- HCV IgG
- STD testing: serum RPR or VDRL, chlamydia and gonorrhea NAAT tests (urine, pharynx, rectum, depending on sites of sexual exposure)
- Pregnancy test (if indicated)
- Consider: lipids, G6PD, toxoplasma IgG
Follow Up visit

- Phone check-in with a social worker, nurse, or clinician 2-3 days after the intake appointment
- Clinic follow-up appointment at 1-2 weeks
- At the follow-up appointment, clinicians should review baseline laboratory results with the patient, evaluate ART adherence, screen for side effects, and provide further counseling and education
Recommended Immediate ART Regimens for Naïve Patients

- Preferred regimens
  - Bictegravir/tenofovir alafenamide/emtricitabine (Biktarvy)
  - Dolutegravir* (Tivicay) + tenofovir alafenamide/emtricitabine (Descovy) or tenofovir disoproxil fumarate/emtricitabine (Truvada) or tenofovir disoproxil fumarate/lamivudine

- Alternative regimens
  - Darunavir (Prezista)/cobicistat/tenofovir alafenamide/emtricitabine (Symtuza)
  - Darunavir + ritonavir + tenofovir alafenamide/emtricitabine (Descovy) or tenofovir disoproxil fumarate/emtricitabine (Truvada) or tenofovir disoproxil fumarate/lamivudine
Recommended Immediate ART Regimens for patients that had been taking antiretroviral prophylaxis as pre- or postexposure prophylaxis (PrEP or PEP) at the time of HIV infection or since becoming infected with HIV

- Take a careful history to determine the last time the patient took PrEP or PEP medications.

- If we have concern that resistance to the antiretrovirals may have developed, we generally start a reinforced ART regimen consisting of an integrase inhibitor (dolutegravir or bictegravir) + boosted darunavir + a tenofovir/emtricitabine or tenofovir/lamivudine formulation while awaiting the results of the genotype assay.
Rapid ARV as one tool among many that may help us improve the HIV care continuum

The Expanding But Imperfect Toolkit

- Patient navigators
- ARTAS
- Clinic-based buprenorphine
- Enhanced personal contacts
- Clinic-based surveillance
- EMR alerts (virology fast track)
- RAPID-ENTRY ART INITIATION

ARTAS, antiretroviral treatment and access to services; EMR, electronic medical record; LRC, linkage to, retention in, and reengagement in HIV care.

Concluding Comments

What We Know

- Rapid entry/initiation of ART is safe
- Rapid entry/initiation improves
  - Time to viral suppression
  - Viral suppression at 12 months
  - Retention in care at 10–12 months (domestic and international studies)
  - Survival at 12 months (international studies)
- **Remaining question:** Longitudinal retention plus viral suppression at 12 months?
  The outcomes from existing cohorts certainly look promising

- Rapid entry/initiation is acceptable to patients and uptake is good
- Rapid entry/initiation is feasible in a variety of settings
- Population-level data demonstrate that HIV incidence decreases as the proportion of individuals virally suppressed increases
Remaining questions, future steps

- Which populations will benefit most from this approach?
  - Difficult-to-retain populations?
  - Late-stage vs early-stage disease?
- What is the effect on transmission within communities?
- What are the long-term benefits that rapid approaches bring to the HIV care continuum?
  - Longitudinal retention and viral suppression?
- What are the best implementation approaches?
  - Global vs domestic?
  - Ryan White vs FQHC vs insured populations?
Thank you