Making HIV Universal Test-and-Treat a Reality to Achieve SDG 3.3: The Role of Rapid Start of Antiretroviral Therapy

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Co-Director, Ending HIV in Alabama Scientific Working Group at UAB Center for AIDS Research
WHO Sustainable Development Goals

• Target 3.3: By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases

• Indicator 3.3.1: Number of new HIV infections per 1,000 uninfected population, by sex, age and key populations
1. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV, DHHS 2019
2. Initiation of ART in Early Symptomatic HIV infection. NEJM 2015
5. Pre-exposure Chemoprophylaxis for HIV Prevention in Men who Have Sex with Men. NEJM 2011; On Demand PrEP in Men at High Risk for HIV Prevention, NEJM 2015
HIV Viral Load and Transmissibility of HIV Infection
Undetectable Equals Untransmittable

RW Eisinger, CW Dieffenbach, and AS Fauci
## Analysis 2.2. Comparison 2 Rapid ART versus standard care: subgroup analysis by time of ART initiation, Outcome 2 Virological suppression at 12 months.

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Rapid ART</th>
<th>Standard of care</th>
<th>log[Risk Ratio] (SE)</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td></td>
<td>IV, Fixed, 95% CI</td>
<td></td>
<td>IV, Fixed, 95% CI</td>
</tr>
<tr>
<td><strong>2.2.1 Same-day ART</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Koenig 2017</td>
<td>0</td>
<td>0</td>
<td>0.2 (0.067)</td>
<td></td>
<td>57%</td>
<td>1.18 [1.04, 1.35]</td>
</tr>
<tr>
<td>Labhardt 2018</td>
<td>0</td>
<td>0</td>
<td>0.4 (0.146)</td>
<td></td>
<td>12.01%</td>
<td>1.47 [1.11, 1.95]</td>
</tr>
<tr>
<td>Rosen 2016</td>
<td>0</td>
<td>0</td>
<td>0.2 (0.091)</td>
<td></td>
<td>30.99%</td>
<td>1.26 [1.05, 1.5]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100%</td>
</tr>
<tr>
<td>Heterogeneity: Tau²=0; Chi²=1.89, df=2 (P=0.39); I²=0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z=4.22 (P&lt;0.0001)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **2.2.2 ART offered within 14 days** | | | | | | |
| Amanyire 2016     | 0         | 0                | 0.1 (0.052)          |            | 100%    | 1.13 [1.02, 1.25] |
| **Subtotal (95% CI)** | | | | | | 100% |
| Heterogeneity: Not applicable |
| Test for overall effect: Z=2.34 (P=0.02) |
| Test for subgroup differences: Chi²=1.56, df=1 (P=0.21), I²=35.95% |

Favours standard care 0.5 0.7 1 1.5 2 4 Favours rapid ART
### Rapid Start vs SOC: Mortality

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log[Risk Ratio]</th>
<th>SE</th>
<th>Weight</th>
<th>Risk Ratio IV, Fixed, 95% CI</th>
<th>Risk Ratio IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1.1.1 RCT</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Koerig 2017</td>
<td>-0.6675</td>
<td>0.3793</td>
<td>21.0%</td>
<td>0.51 [0.24, 1.08]</td>
<td></td>
</tr>
<tr>
<td>Labhardt 2018</td>
<td>1.0084</td>
<td>1.5445</td>
<td>1.3%</td>
<td>5.00 [0.24, 103.19]</td>
<td></td>
</tr>
<tr>
<td>Rosen 2016</td>
<td>-1.8331</td>
<td>1.5084</td>
<td>1.3%</td>
<td>0.15 [0.01, 2.79]</td>
<td></td>
</tr>
<tr>
<td>Stevens 2017</td>
<td>-0.3902</td>
<td>0.4844</td>
<td>14.1%</td>
<td>0.68 [0.27, 1.68]</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td></td>
<td></td>
<td>37.7%</td>
<td>0.59 [0.34, 1.02]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Chi² = 3.00, df = 3 (P = 0.39); I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.87 (P = 0.06)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **1.1.2 Cluster-RCT** | | | | |
|-----------------------|-----------------|-----|--------|------------------------------|------------------------------|
| Amanire 2016 (1)      | -0.4308         | 0.7833 | 4.9%   | 0.85 [0.14, 3.02]           |                              |
| Ekl 2017 (2)          | -0.1333         | 0.3965 | 19.3%  | 0.37 [0.40, 1.86]           |                              |
| McNairy 2017          | -0.2231         | 0.2823 | 38.1%  | 0.30 [0.46, 1.39]           |                              |
| **Subtotal (95% CI)** |    |        | 62.3%  | 0.81 [0.52, 1.24]           |                              |
| Heterogeneity: Chi² = 0.11, df = 2 (P = 0.95); I² = 0% |
| Test for overall effect: Z = 0.97 (P = 0.33) |

| **Total (95% CI)**    |    |        | 100.0% | 0.72 [0.51, 1.01]           |                              |
| Heterogeneity: Chi² = 3.90, df = 6 (P = 0.69); I² = 0% |
| Test for overall effect: Z = 1.92 (P = 0.06) |
| Test for subgroup differences: Chi² = 0.78, df = 1 (P = 0.38); I² = 0% |

Footnotes:
1. Based on a random sample of participants which was inverse probability weighted
2. CI/S
The US Experience

San Francisco: RAPID

Time to HIV RNA <200 copies/mL

- Same-Day (2013-14) (median: 1.8 months)
- Universal ART (2010-13) (median: 4.3 months)
- CD4-Guided ART (2006-09) (median: 7.2 months)

All comparisons to same-day ART (P<0.0001)

Birmingham: FAST TRACK

Proportion VL <200 copies/mL

- 46 Days (35, 72)
- 78 Days (59, 151)

New Orleans: Adolescents

Proportion With Viral Suppression

- 96.8 / 30 (31)
- 97.9 / 91 (93)
- 97.6 / 121 (124)

- 83.9 / 26 (31)
- 92.5 / 86 (93)
- 90.3 / 112 (124)

- 96.8 / 30 (31)
- 97.9 / 91 (93)
- 97.6 / 121 (124)

<table>
<thead>
<tr>
<th>Met Endpoint (%)</th>
<th>Age Group Comparison</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Achieved viral suppression</td>
<td>.7286</td>
</tr>
<tr>
<td></td>
<td>Sustained viral suppression after 12 mos</td>
<td>.1619</td>
</tr>
<tr>
<td></td>
<td>Engaged in care after 12 mos</td>
<td>.7286</td>
</tr>
</tbody>
</table>

RAPID ART BY THE GUIDELINES

**DHHS\(^1\) and IAS-USA\(^2\)**

- Encourage rapid initiation of ART, including same-day start if feasible
- Avoid ABC, DTG/3TC, and NNRTI-based regimens during rapid start
- Recommended regimens
  - BIC/FTC/TAF
  - DTG + (3TC or FTC) + (TAF or TDF)
  - DRV/(RTV or COBI) + (3TC or FTC) + (TAF or TDF)

**WHO\(^3\)**

- Immediate ART for all PWH
- Initiation should be considered within 7 days of diagnosis, ideally on the same day

**Considerations**

- Transmitted NNRTI or NRTI resistance more likely than PI or INSTI resistance
- Empiric HBV coverage
- Treatment suitable for patients with CrCl ≥ 30 mL/min
- OIs (Cryptococcal meningitis, TB meningitis)
- Pregnancy\(^4,\,5\) , Retention\(^6\)

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1. DHHS Guidelines. December 2019
3. WHO Guidelines for Managing Advanced HIV Disease and Rapid Initiation of Antiretroviral Therapy. 2017;
Rapid Start in Practice

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, counselling
- 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

Adapted from Pilcher et al JAIDS 2017
Assessing Barriers to Care and Treatment

- Poverty
- Stigma
- Forgetting!
- Medication Adverse Events
- Substance Use
- Mental Health
- Youth Discrimination
- Adherence
RAPID START PROMOTES EQUITY

- Black men are more likely to experience delays in ART initiation even after seeing a prescribing provider [1]
- Hispanic/Latino persons significantly less likely to receive ART after meeting clinical indications for treatment vs whites [2]
- Same-day immediate access to a provider can demonstrate commitment to a community
- Dázon Dixon Diallo from Sister Love: “See my brothers and sisters as your own. If you do, then of course you will see patients same-day, start same-day, and love same-day.”

“When I was first diagnosed, my first thought was not, ‘Am I going to die?’ because you know everyone is going to die. It was, ‘Can I give this to my boyfriend?’ That terrified me. I started medication on the day I was diagnosed, and I am now undetectable so the answer is: ‘No, I cannot.’”

“I have not had sex in 17 yrs, since the day I was diagnosed. U=U changes how I see myself and my risk to others. I just went on my first date.”

“U=U was the message I took home to my family. Ten yrs ago I came out; 5 yrs ago I was diagnosed. Over Christmas, I told my family that I was undetectable, on medication, and showed the U=U video. I feel good with my family, and I have not in a long time.”

Quotes courtesy Dr. Jason Halperin
Increased Diagnoses of Acute HIV through Routine ED Screening and Rapid LTC and initiation of ART during the COVID-19 Pandemic

Stanford, Schitt, Pitrak (presenting) et al. ID Week 2020.

- Of the 9 AHI patients, 7 were men (6 identified as MSM) and 2 were cis-gender women
- Median age was 25 years (range 21 to 28 years)
- The median viral load was > 6 million (range 115,000 to > 6 million) copies/mL
- Eight of 9 patients presented with an illness indistinguishable from COVID-19
  - Including 1 patient with co-infection
- All 9 patients were notified, LTC, and initiated on ART
  - Median of 1 day (0-38 days) from result of confirmatory PCR
  - Median 3 days (range 1-41 days) from presentation as a result of delayed reflex PCR testing due to high demands on lab personnel and scarcity of reagents due to COVID-19 testing volumes

<table>
<thead>
<tr>
<th>Year</th>
<th>AHI Dx</th>
<th>AHI Dx ED</th>
<th>New Dx</th>
<th>New Dx ED</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>7</td>
<td>5</td>
<td>41</td>
<td>19</td>
</tr>
<tr>
<td>2017</td>
<td>7</td>
<td>7</td>
<td>37</td>
<td>22</td>
</tr>
<tr>
<td>2018</td>
<td>4</td>
<td>4</td>
<td>39</td>
<td>28</td>
</tr>
<tr>
<td>2019</td>
<td>9</td>
<td>9</td>
<td>56</td>
<td>39</td>
</tr>
<tr>
<td>2020 (through 8/17/2020)</td>
<td>9</td>
<td>9</td>
<td>35</td>
<td>31</td>
</tr>
</tbody>
</table>

Update 10/16/20 12 12
CRITICAL COMPONENTS TO RAPID ART

Planning, coordination, teamwork, and funding critical to program design

- Cooperation and rapport between testing and rapid ART sites
- Warm hand-offs and accessible linkage coordinators
- Early and sustained access to ART
- Expedited insurance/payer source and clinic enrollments
- Same-day clinician visits
- Accessible education on beginning ART in advance of genotype/lab results
- Follow-up with continued education, patient navigation efforts, and contact with retention teams