RAPID ART INITIATION

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# International Guidelines Recommend ART Initiation Regardless of CD4 Cell Count and Immediately in Certain Clinical Scenarios

<table>
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<th>Guideline</th>
<th>Recommendations</th>
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| EACS<sup>1</sup> | • Immediate (same day as HIV diagnosis) initiation:  
− Acute symptomatic infection  
− Severe or prolonged symptoms  
− Neurological disease  
− Age ≥ 50 years  
− CD4 count < 350 cells/µL  
− Pregnancy  
• Immediate initiation of ART for all PLHIV, regardless of CD4 count  
• The following conditions increase the urgency to initiate therapy:  
− Pregnancy  
− AIDS-defining conditions, including HIV-associated dementia and AIDS-associated malignancies  
− Acute opportunistic infections  
− Lower CD4 counts (e.g., <200 cells/mm<sup>3</sup>)  
− HIV-associated nephropathy  
− Acute/early infection  
− HIV/hepatitis B virus co-infection  
− HIV/hepatitis C virus co-infection  |
| DHHS<sup>2</sup> |  
| WHO<sup>3</sup> | • Rapid initiation (within 7 days)* should be offered to all PLHIV following a confirmed HIV diagnosis and clinical assessment  
• ART initiation should be offered on the same day to people who are ready to start  |
| IAS-USA<sup>4,5</sup> | • Initiate ART as soon as possible after HIV diagnosis**  
− Rapid start (including same day as diagnosis) ART, unless the patient is not ready to commit to starting therapy  |

*Priority for treatment initiation in people with advanced HIV disease (i.e. CD4 cell count <200 cells/mm<sup>3</sup> or a WHO clinical stage 3 or 4 event);**ART should be started as soon as possible (but within 2 weeks) after diagnosis of most opportunistic diseases.

BENEFITS AND LIMITATIONS OF RAPID ART INITIATION WITHIN THE FIRST WEEK OF DIAGNOSIS

**Potential benefits**

- May allow better clinical outcomes due to less time off ART\(^1,2\)
- Engagement opportunity to increase retention in care\(^3\)
- May decrease anxiety and increase trust\(^4\)
- May decrease transmission risk\(^5\)
- May reduce HIV reservoirs during acute HIV infection\(^6\)
- May reduce drug resistance at VF\(^7\)
- May reduce immune impairment and prevent disease progression\(^8\)

Disclaimer: these benefits have been demonstrated in select patient populations and may not apply to all clinical scenarios; the definition of rapid ART may vary across countries.

**Potential limitations**

- ART may not be optimised as BL test results may not be available (eg. HBV, renal function)\(^9\)
- OIs requiring delayed ART may not be ruled out\(^10\)
- Potentially less time to address barriers to ART and adherence\(^11\)
- Risk of resistance if a low-barrier regimen is used\(^11,12\)
- May impact a change in workflow with rapid access (access, appointment scheduling, staffing)\(^4\)

ART, antiretroviral therapy; BL, baseline; HBV, hepatitis B virus; OI, opportunistic infection; VF, virological failure.

FOCUS ON SELECTED RANDOMISED CLINICAL TRIALS OF RAPID ART INITIATION

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<tr>
<th>Table Title</th>
<th>Reference</th>
<th>Authors</th>
<th>Journal/Year</th>
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Benefits and risks of rapid initiation of antiretroviral therapy

Nathan Ford\textsuperscript{a, b}, Chantal Migone\textsuperscript{a}, Alexandra Calmy\textsuperscript{c}, Bernhard Kerschberger\textsuperscript{d}, Steve Kanters\textsuperscript{e}, Sabin Nsanzimana\textsuperscript{f,g}, Edward J. Mills\textsuperscript{h}, Graeme Meintjes\textsuperscript{i}, Marco Vitoria\textsuperscript{a}, Meg Doherty\textsuperscript{a} and Zara Shubber\textsuperscript{j}

\textit{AIDS} 2018, 32:17–23

Rapid =
Same day OR next day
OR within 7 days OR within 3 months
Improved Clinical Outcomes With Rapid ART Initiation

- Systematic review of rapid ART initiation (including 4 RCTs)\(^1\)

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<tr>
<th>Characteristic</th>
<th>RR (95% CI)</th>
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<tr>
<td>ART start within 90 days</td>
<td>1.35 (1.13-1.62)</td>
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<tr>
<td>Retained in care at 12 mos</td>
<td>1.11 (0.99-1.26)</td>
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<tr>
<td>Viral suppression at 12 mos</td>
<td>1.17 (1.07-1.27)</td>
</tr>
<tr>
<td>LTFU at 12 mos</td>
<td>0.66 (0.42-1.04)</td>
</tr>
<tr>
<td>Died by 12 mos</td>
<td>0.53 (0.28-1.00)</td>
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- In addition, earlier ART initiation reduces the viral reservoir in the individual\(^{2-5}\)

What are patients’ concerns with same day cART initiation?

- limited time to process information
- limited time to disclose HIV status
- seek partner’s approval prior to starting cART only in pregnant women (Africa, Thailand)
- concerns about side-effects
- challenge of adherence to lifelong therapy
- pill burden not specifically related to same day cART

Ford et al, AIDS 2018
What are patients’ perceived benefits of same day cART?

• prevention of onward transmission (among both pregnant women and MSM)

• starting cART as soon as possible would reduce the risk of stigma
IS IT FEASIBLE IN ROUTINE CARE?
Clinic-based cohort study of consecutive patients (diagnosed June 2013–December 2014) in the US public health setting

Inclusion criteria
- No active recruitment
- Consecutive patients referred with acute or recent HIV infection (<6 months) or CD4 <200 cells/mm$^3$
- Age ≥18 years
- N=86

RAPID ART INITIATION VERSUS CLINICAL STANDARD MODEL OF CARE IN PEOPLE WITH NEWLY DIAGNOSED HIV

*RAPID care initiation protocol included: 1) same-day access to an HIV provider; 2) same-day medical visit outline (including education re: HIV infection, risk reduction and sexual health, and benefits of ART); 3) accelerated insurance approval process; 4) pre-approved regimens; 5) 5-day starter packs (available if needed for ART to be initiated while insurance benefits are being arranged); 6) observed administration of a first dose; 7) telephone follow-up (varied between 1 and 7 days). In the standard of care approach, the HIV clinic team addressed medical (symptoms), social (housing, insurance, food access, immigration status) and psychological (counselling, mental health, substance use) concerns.*37 patients (94.9%) in RAPID began ART within 24 hours.

San Francisco RAPID Study

UPTAKE OF ART WHEN OFFERED IMMEDIATELY AFTER DIAGNOSIS

- 95% of patients chose to begin ART within a day of it being offered
- Slower uptake among non-RAPID patients is related to the deferral of the offer to start ART
- Data are for patients with a new HIV diagnosis who attended their first San Francisco General Hospital HIV Clinic between 2013 and 2015
TIME TO VIROLOGICAL SUPPRESSION WAS SIGNIFICANTLY SHORTER USING RAPID VS STANDARD MODEL OF CARE (IN HISTORICAL CONTROLS)

ART, antiretroviral therapy; VL, viral load.

VIROLOGICAL RESISTANCE DEVELOPMENT WITH SAME-DAY ART

Risk of acquired drug resistance up to 7 years after baseline by ART initiation strategy (HIV-CAUSAL collaboration, 2000–2015)

Estimates of virological resistance in individuals with baseline CD4 count >500 cells/mm$^3$

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<tr>
<th>ART start</th>
<th>Risk at 7 years, % (95% CI)</th>
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<tr>
<td>Immediate</td>
<td>1.6 (1.2, 2.3)</td>
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<tr>
<td>CD4 &lt;500 cells/mm$^3$</td>
<td>1.9 (1.4, 2.4)</td>
</tr>
<tr>
<td>CD4 &lt;350 cells/mm$^3$</td>
<td>1.6 (1.2, 2.1)</td>
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Same-day ART initiation was not associated with an increased risk of resistance versus deferred start.

ART, antiretroviral therapy; CI, confidence interval.
**IMMEDIATE ART: ANALYSIS OF THREE MODELS OF CARE IN THAILAND**

- **Aim:** assess the acceptability and effectiveness of ART initiated on the same day of the HIV diagnosis in the context of local resources and available same-day tests

- **First-line ART:** EFV+FTC/TDF

- **Baseline tests:**
  - Creatinine
  - Urinalysis
  - CD4 count
  - HBsAg
  - Anti-HCV
  - Syphilis serology
  - ALT
  - Chest X-ray
  - Cryptococcal antigen (CD<100 cells/mm³)

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**All HIV care centres systematically perform a clinical examination and chest X-ray before starting ART:**

- 3 models of immediate ART provision identified

**Model A**
- No Laboratory Results Needed
- Thai Red Cross Anonymous Clinic
- Chiangmai Hospital

**Model B**
- Only CD4
- Model B

**Model C**
- Safety Lab Results

**Baseline Lab**
- CD4
- YES
- Model B
- Only CD4
- YES
- Model C
- Safety Lab Results

**ONLY CD4**
- CD4+ CMV
- BASELINE
- BASELINE + CRYPTO
- ONLY CREATININE

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ART, antiretroviral therapy; EFV, efavirenz; FTC, emtricitabine; TDF, tenofovir disoproxil fumarate.
Same-day ART initiation in HIV/STI testing centre in Bangkok, Thailand

Immediate ART: Results from three models of care in Thailand

Time between HIV diagnosis and ART initiation

- Model A: No lab results needed
- Model B: Only CD4
- Model C: Safety lab results

Median time (IQR)
- Model A = 0 (0–0)
- Model B = 7 (0–15)
- Model C = 0 (0–8)

Adverse events and deaths

- Deaths: Total: p<0.001
- Model A vs Model B: p=0.006
- Model A vs Model C: p=0.012
- Model B vs Model C: p=1.000

- Adverse events: Total: p<0.001
- Model A vs Model B: p=0.026
- Model A vs Model C: p=0.083
- Model B vs Model C: p=0.001

Not using baseline laboratory results facilitated faster ART initiation with no increase in severe AEs or deaths

AE, adverse event; ART, antiretroviral therapy; IQR, interquartile ratio.
Adapted from Seekaew P, IAS 2019. WEAB0102.
Rapid ART Defined by the DHHS as a Key Component to Help End the HIV Epidemic

Are you ready?