RAPID ART INITIATION

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INTERNATIONAL GUIDELINES RECOMMEND ART INITIATION REGARDLESS OF CD4 CELL COUNT AND IMMEDIATELY IN CERTAIN CLINICAL SCENARIOS

Guideline	Recommendations
EACS[1]	• **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
DHHS[2]	• **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 (eg. <200 cells/mm^3) – HIV-associated nephropathy – Acute/early infection – HIV/hepatitis B virus co-infection – HIV/hepatitis C virus co-infection
WHO[3]	• **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[4,5]	• **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 (ie. CD4 cell count <200 cells/mm^3 or a WHO clinical stage 3 or 4 event)[3];**ART should be started as soon as possible (but within 2 weeks) after diagnosis of most opportunistic diseases.

ART, antiretroviral therapy; DHHS, Department of Health and Human Services; EACS, European AIDS Clinical Society; IAS-USA, International Antiviral Society–USA; PLHIV, people living with HIV; WHO, World Health Organization.

1. EACS Society Guidelines, Version 10.1, October 2020. Available at: https://www.eacsociety.org/files/guidelines-10.1_finaljan2021_1.pdf Last accessed: January 2021; 2. DHHS guidelines. Available at: aidsinfo.nih.gov/guidelines Last accessed: January 2021; 3. WHO Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy. Available at: apps.who.int/iris/bitstream/handle/10665/255884/9789241550062-eng.pdf;jsessionid=653173779EF17A65E9F759F03AB1827D?sequence=1 Last accessed: January 2021; 4. Saag M, et al. *JAMA* 2018;320:379–96; 5. IAS-USA Guidelines. Available at: www.iasusa.org/content/antiretroviral-drugs-treatment-and-prevention-hiv-infection-adults-2018-recommendations Last accessed: January 2021.

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]

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]

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.

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

1. Koenig S, et al. *PLoS Med* 2017;14:e1002357; 2. Zhao Y, et al. *Clin Infect Dis* 2018;66:727–34; 3. Koenig S, et al. *PLoS Med* 14:e1002357; 4. Nwokolo N, et al. BHIVA 2016, #P2; 5. Cohen MS, et al. *New Engl J Med* 2016;375:830–9; 6. Jain V, et al. *J Infect Dis* 2013;208:1202–11; 7. Palumbo PJ, et al. *JAIDS* 2018;77:484–91; 8. Holmberg SD, et al. *Clin Infect Dis* 2004;39:1699–704; 9. Boyd M, et al. *HIV Med* 2019;20(Suppl 1):3–11; 10. Ford N, et al. *AIDS* 2018;32:17–23; 11. Braithwaite RS, et al. *Clin Infect Dis* 2009;48:822–26; 12. Luber AD, et al. *MedGenMed* 2005;7:69.

FOCUS ON SELECTED RANDOMISED CLINICAL TRIALS OF RAPID ART INITIATION

Effects of a multicomponent intervention to streamline initiation of antiretroviral therapy in Africa: a stepped-wedge cluster-randomised trial *(Uganda)*

Amanyire G, et al.
Lancet HIV 2016;3:e539-e48

Initiating antiretroviral therapy for HIV at a patient's first clinic visit: The RapIT randomized clinical trial *(South Africa)*

Rosen S, et al.
PLoS Med 2016;13:e1002050.

Effect of offering same-day ART vs usual health facility referral during home-based HIV testing on linkage to care and viral suppression among adults with HIV in *Lesotho*: The CASCADE randomized clinical trial

Labhardt ND, et al.
JAMA 2018;319:1103–12

Same-day HIV testing with initiation of antiretroviral therapy versus standard care for persons living with HIV: A randomized unblinded trial *(Haiti)*

Koenig S, et al.
PLoS Med 2017;14:e1002357.

Benefits and risks of rapid initiation of antiretroviral therapy

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

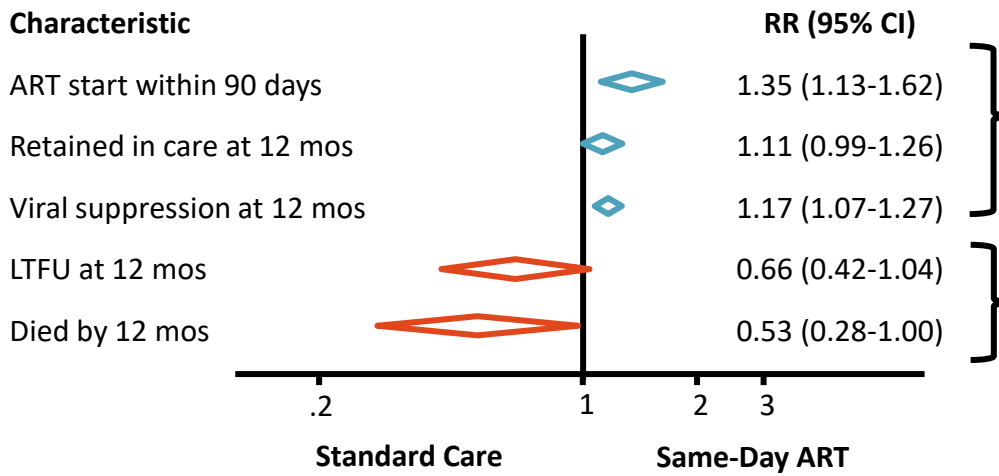
AIDS 2018, **32**:17–23

Rapid =
Same day OR next day
OR within 7 days OR within 3 months

Ford et al, AIDS 2018

Improved Clinical Outcomes With Rapid ART Initiation

- Systematic review of rapid ART initiation (including 4 RCTs)[1]



Same-day ART associated with:

- **Increased** likelihood of ART initiation, retention in care, viral suppression
- **Decreased** likelihood of loss to follow-up and death

- In addition, earlier ART initiation reduces the viral reservoir in the individual[2-5]

1. Ford. AIDS. 2018;32:17. 2. Tagarro. JAIDS. 2018;79:269. 3. Luo. BMC Infect Dis. 2019;19:257.
4. Jain. J Infect Dis. 2013;208:1202. 5. Buzon. J Virol. 2014;88:10056.

Ford et al, AIDS 2018

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

Ford et al, AIDS 2018

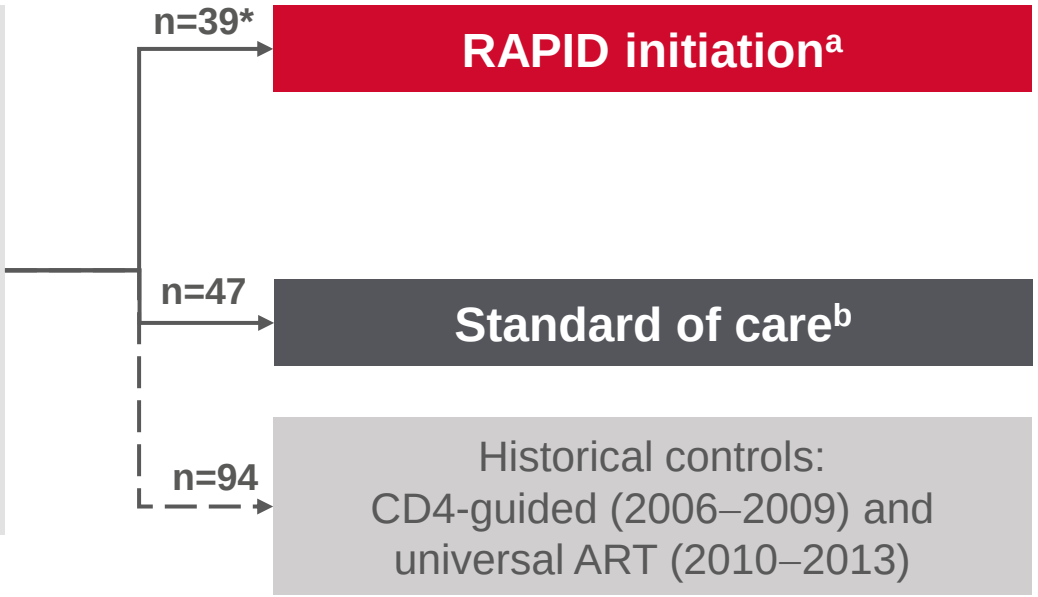
IS IT FEASIBLE IN ROUTINE CARE ?

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

Clinic-based cohort study of consecutive patients (diagnosed June 2013–December 2014) in the US public health setting

Inclusion criteria

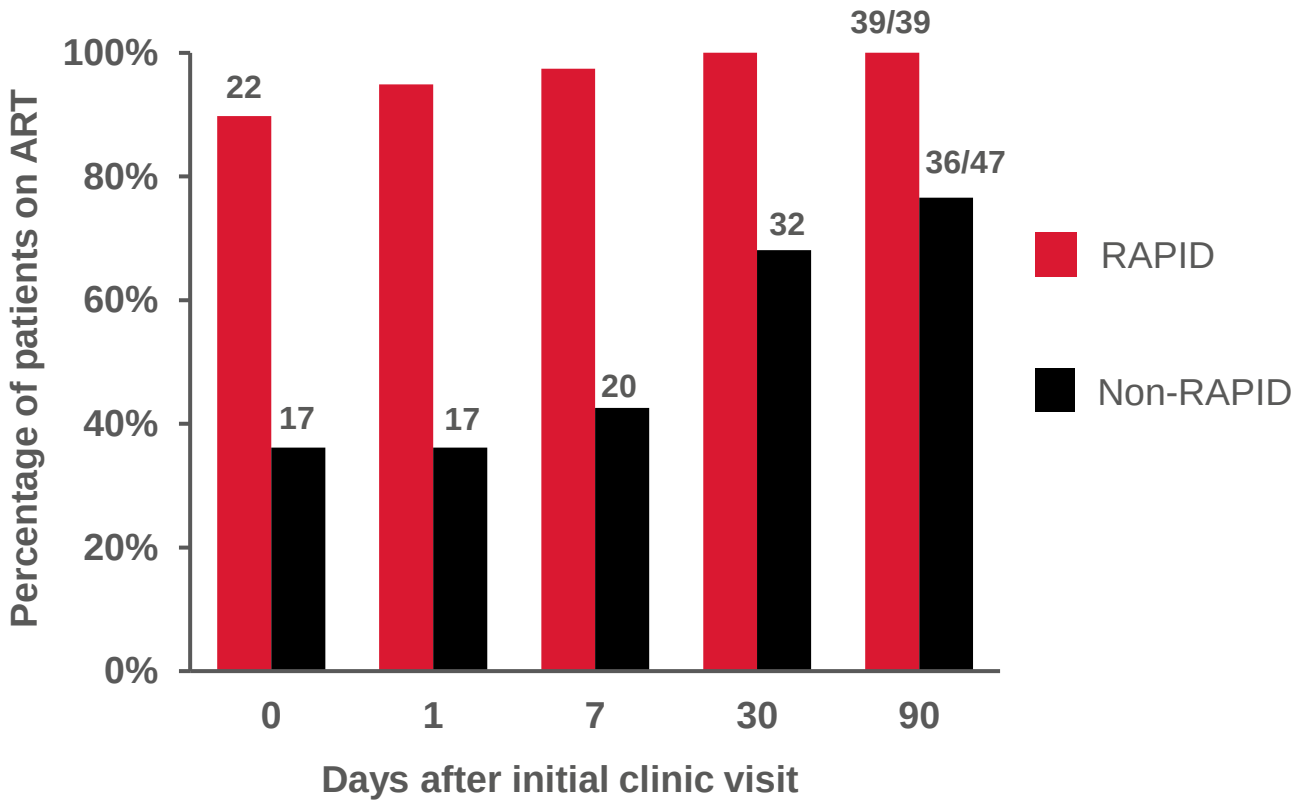
- No active recruitment
- Consecutive patients referred with acute or recent HIV infection (<6 months) or CD4 <200 cells/mm^3
- Age ≥18 years
- N=86



- **Primary clinical endpoint**
  Engagement and retention in care, virological suppression and safety
- **Secondary endpoints:**
  RAPID arm versus historical controls

[a]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). [b]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.
ART, antiretroviral therapy.
Pilcher C, et al. *JAIDS* 2017;74:44–51.

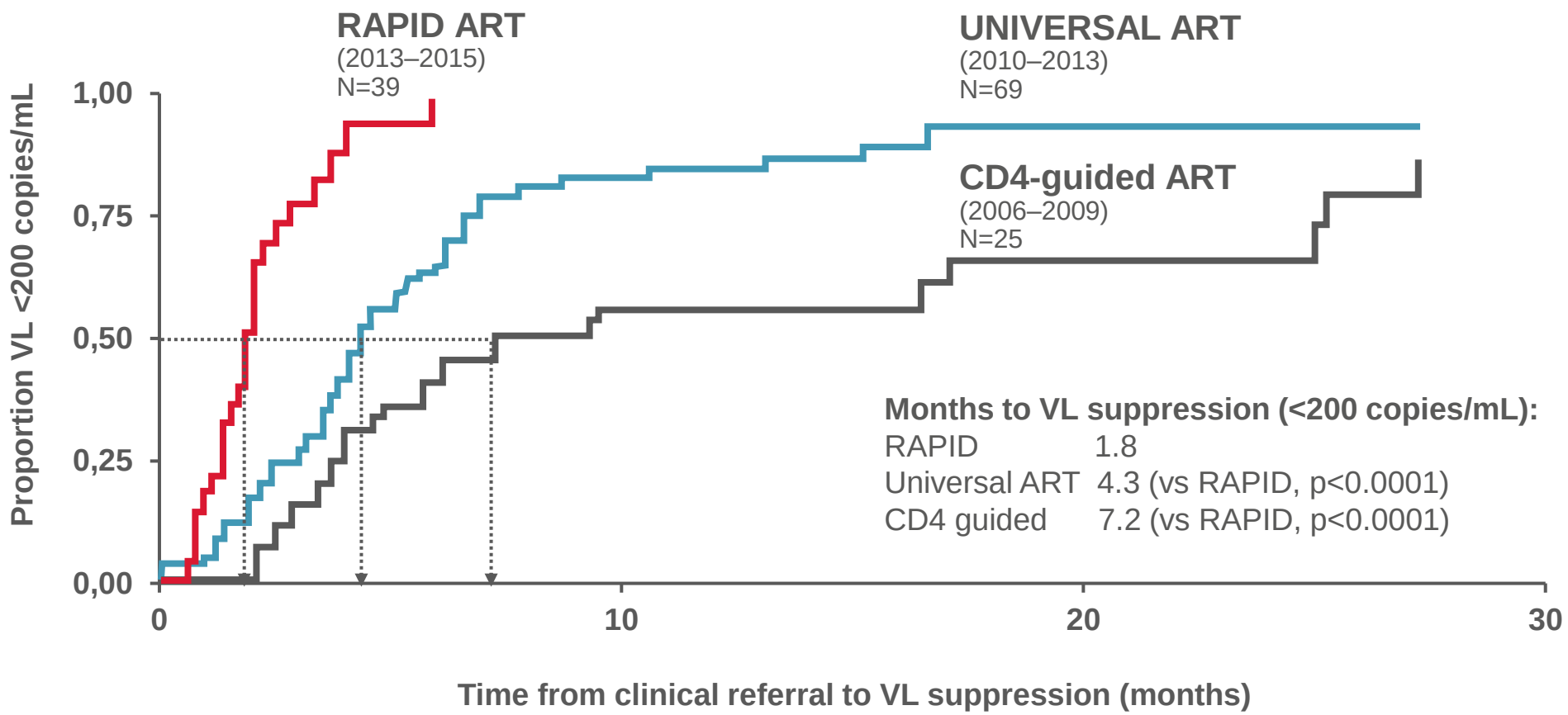
UPTAKE OF ART WHEN OFFERED IMMEDIATELY AFTER DIAGNOSIS



- **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

ART, antiretroviral therapy.
Pilcher C, et al. *JAIDS* 2017;74:44–51.

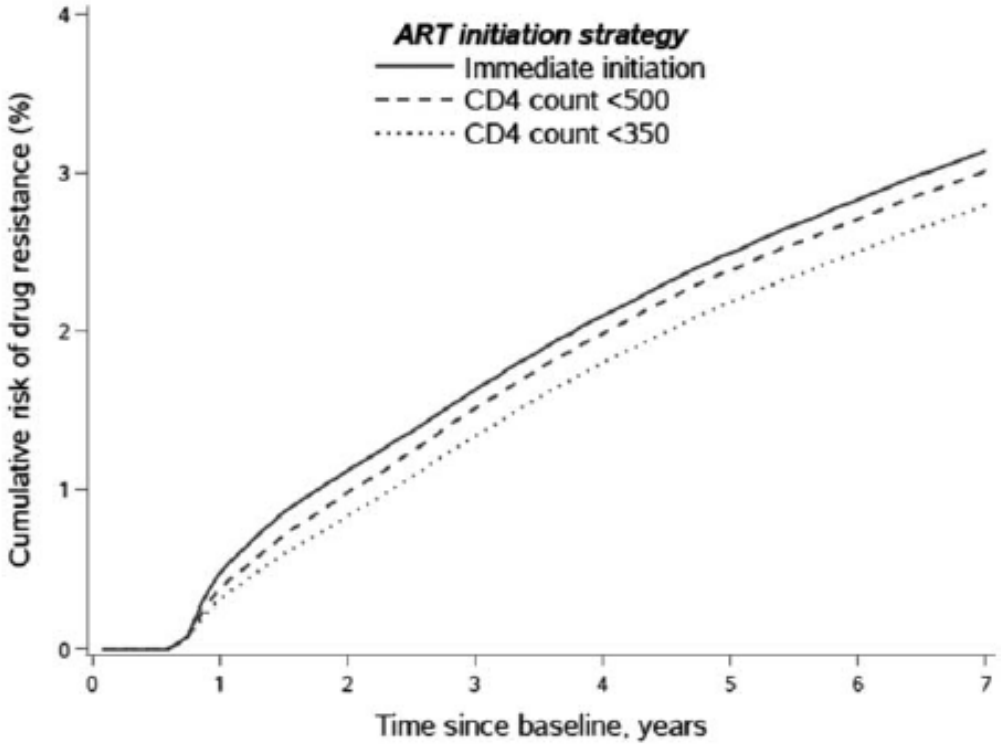
TIME TO VIROLOGICAL SUPPRESSION WAS SIGNIFICANTLY SHORTER USING RAPID VS STANDARD MODEL OF CARE (IN HISTORICAL CONTROLS)



ART, antiretroviral therapy; VL, viral load.
Pilcher C, et al. *JAIDS* 2017;74:44–51.

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

ART start	Risk at 7 years, % (95% CI)
Immediate	1.6 (1.2, 2.3)
CD4 <500 cells/mm^3	1.9 (1.4, 2.4)
CD4 <350 cells/mm^3	1.6 (1.2, 2.1)

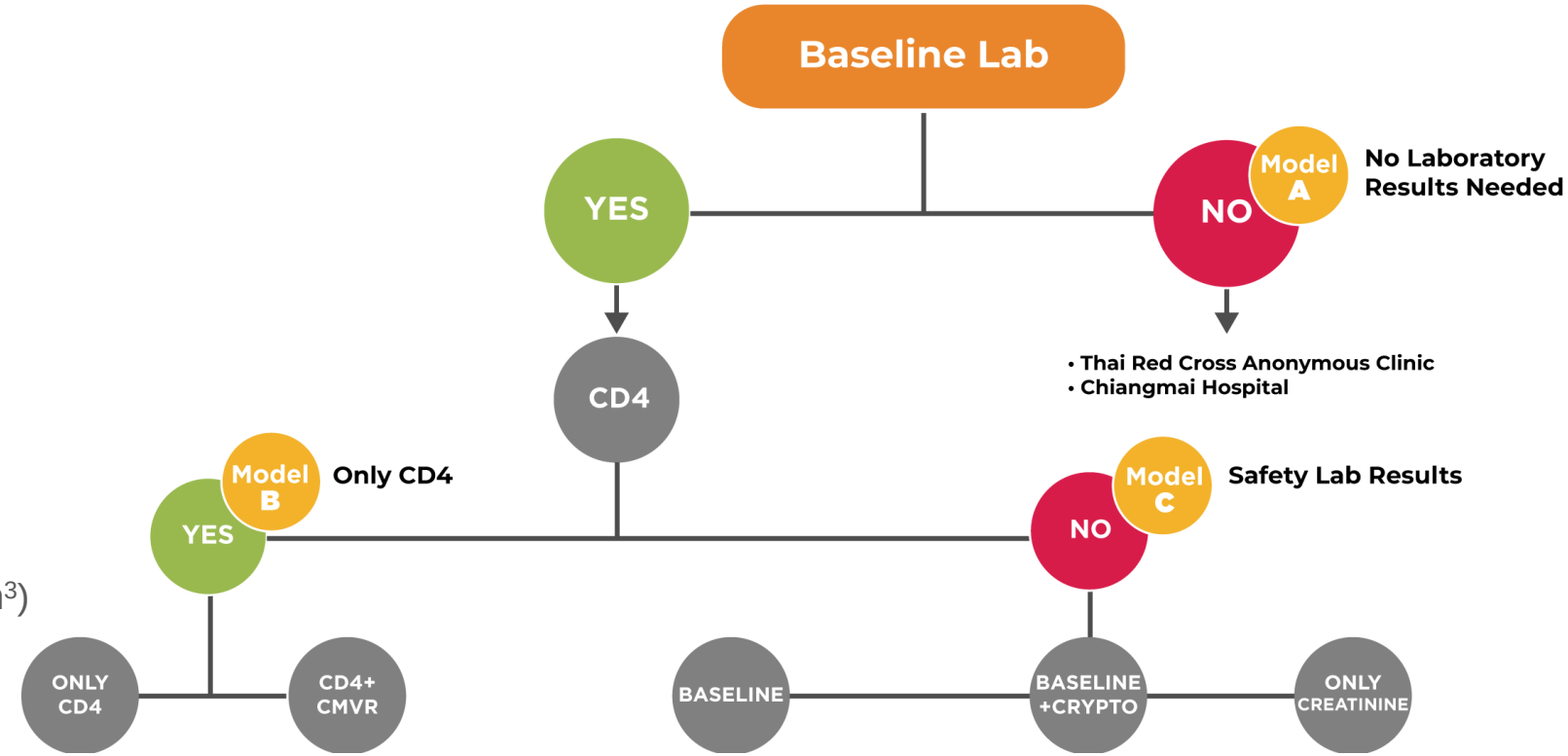
Same-day ART initiation was not associated with an increased risk of resistance versus deferred start

ART, antiretroviral therapy; CI, confidence interval.
Lodi S, et al. *AIDS* 2018;32:327–35.

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/mm^3)

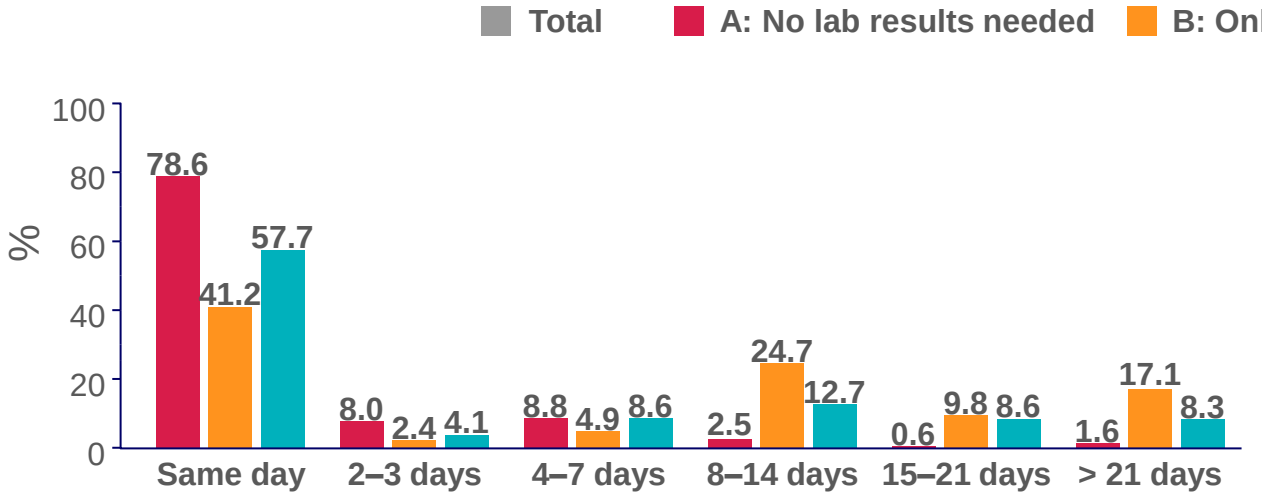
All HIV care centres systematically perform a clinical examination and chest X-ray before starting ART: 3 models of immediate ART provision identified



ART, antiretroviral therapy; EFV, efavirenz, FTC, emtricitabine; TDF, tenofovir disoproxil fumarate.
Seekaew P, IAS 2019. WEAB0102.

IMMEDIATE ART: RESULTS FROM THREE MODELS OF CARE IN THAILAND

Time between HIV diagnosis and ART initiation

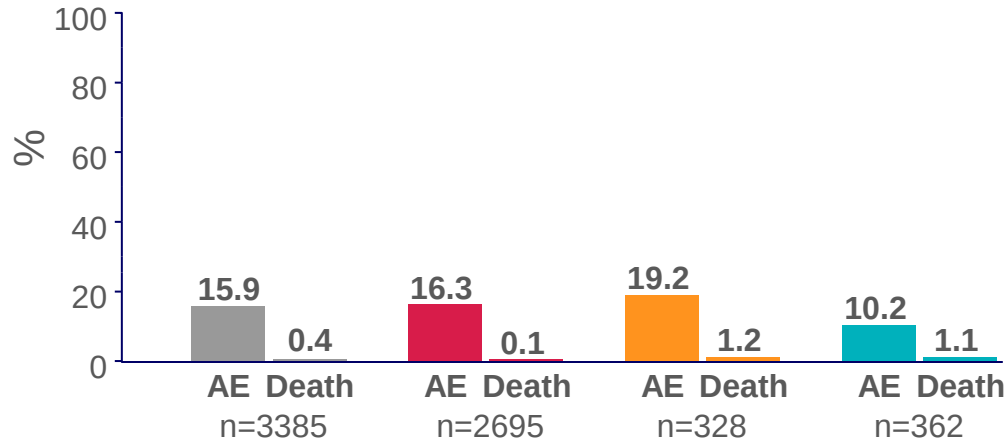


Median time (IQR)

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

- Model **A vs** Model **B:** p<0.001
- Model **B vs** Model **C:** p<0.001
- Model **C vs** Model **A:** p<0.001

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

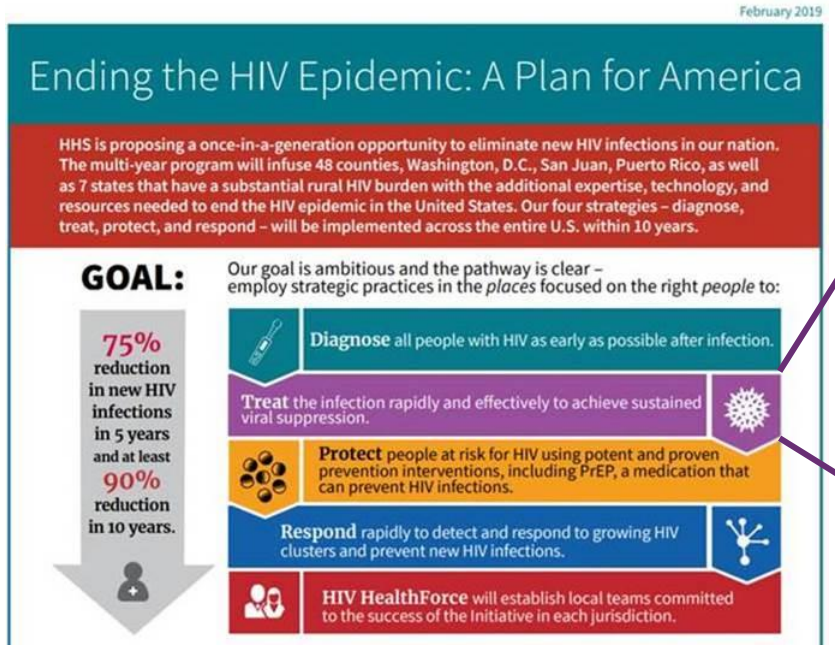
Adverse events

- 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



Treat the infection **rapidly and effectively** to achieve sustained viral suppression

DHHS. Ending the HIV Epidemic: A Plan for America. 2019. Accessed February 12, 2019.


ARE
YOU
READY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thank you
gracias
obrigado
danke
go raibh maith agat
спасибо
grazie
terima kasih
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