

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	<ul style="list-style-type: none"> • Immediate (same day as HIV diagnosis) initiation: <ul style="list-style-type: none"> – Acute symptomatic infection – Severe or prolonged symptoms – Neurological disease – Age ≥ 50 years – CD4 count < 350 cells/μL – Pregnancy
DHHS ²	<ul style="list-style-type: none"> • Immediate initiation of ART for all PLHIV, regardless of CD4 count • The following conditions increase the urgency to initiate therapy: <ul style="list-style-type: none"> – Pregnancy – AIDS-defining conditions, including HIV-associated dementia and AIDS-associated malignancies – Acute opportunistic infections – Lower CD4 counts (eg. <200 cells/mm³) – HIV-associated nephropathy – Acute/early infection – HIV/hepatitis B virus co-infection – HIV/hepatitis C virus co-infection
WHO ³	<ul style="list-style-type: none"> • 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}	<ul style="list-style-type: none"> • Initiate ART as soon as possible after HIV diagnosis** <ul style="list-style-type: none"> – 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/mm³ 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 care³



- May decrease anxiety and increase trust⁴

- May decrease transmission risk⁵



- May reduce HIV reservoirs during acute HIV infection⁶
- May reduce drug resistance at VF⁷
- May reduce immune impairment and prevent disease progression⁸

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 out¹⁰



- Potentially less time to address barriers to ART and adherence¹¹
- 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

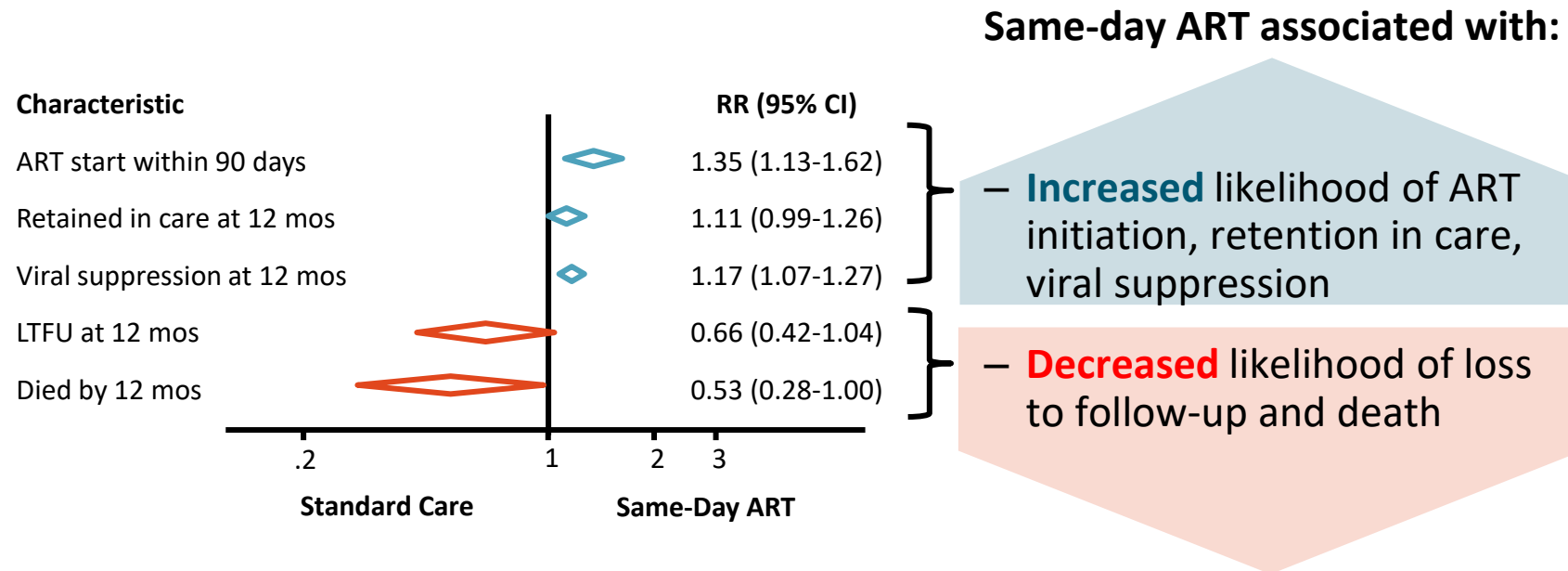
Nathan Ford^{a,b}, Chantal Migone^a, Alexandra Calmy^c,
Bernhard Kerschberger^d, Steve Kanfers^e, Sabin Nsanzimana^{f,g},
Edward J. Mills^h, Graeme Meintjesⁱ, Marco Vitoria^a,
Meg Doherty^a and Zara Shubber^j

AIDS 2018, 32:17–23

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

Improved Clinical Outcomes With Rapid ART Initiation

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



- 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.

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

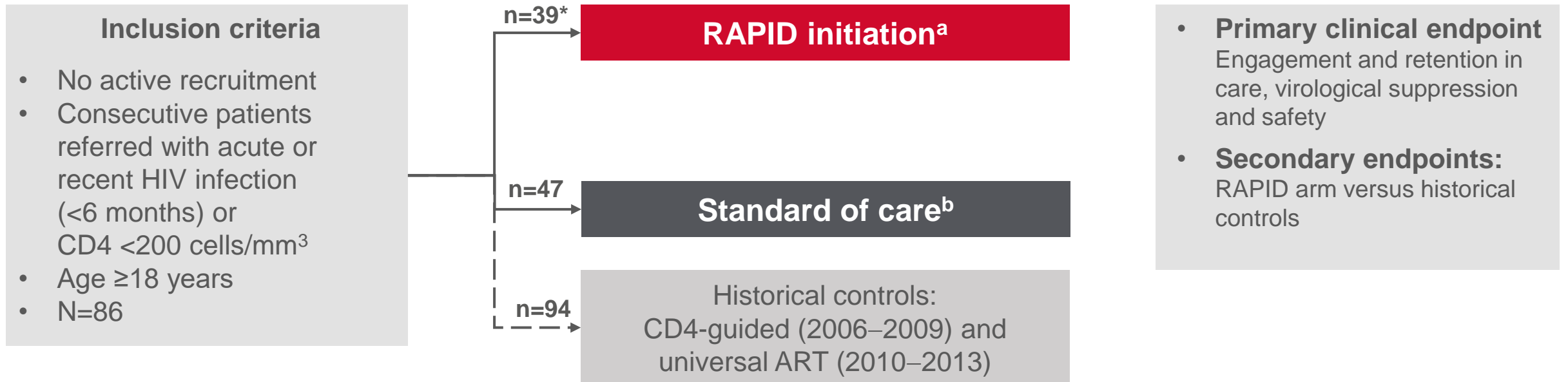
What are patients' perceived benefits of same day cART ?

- 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 ?

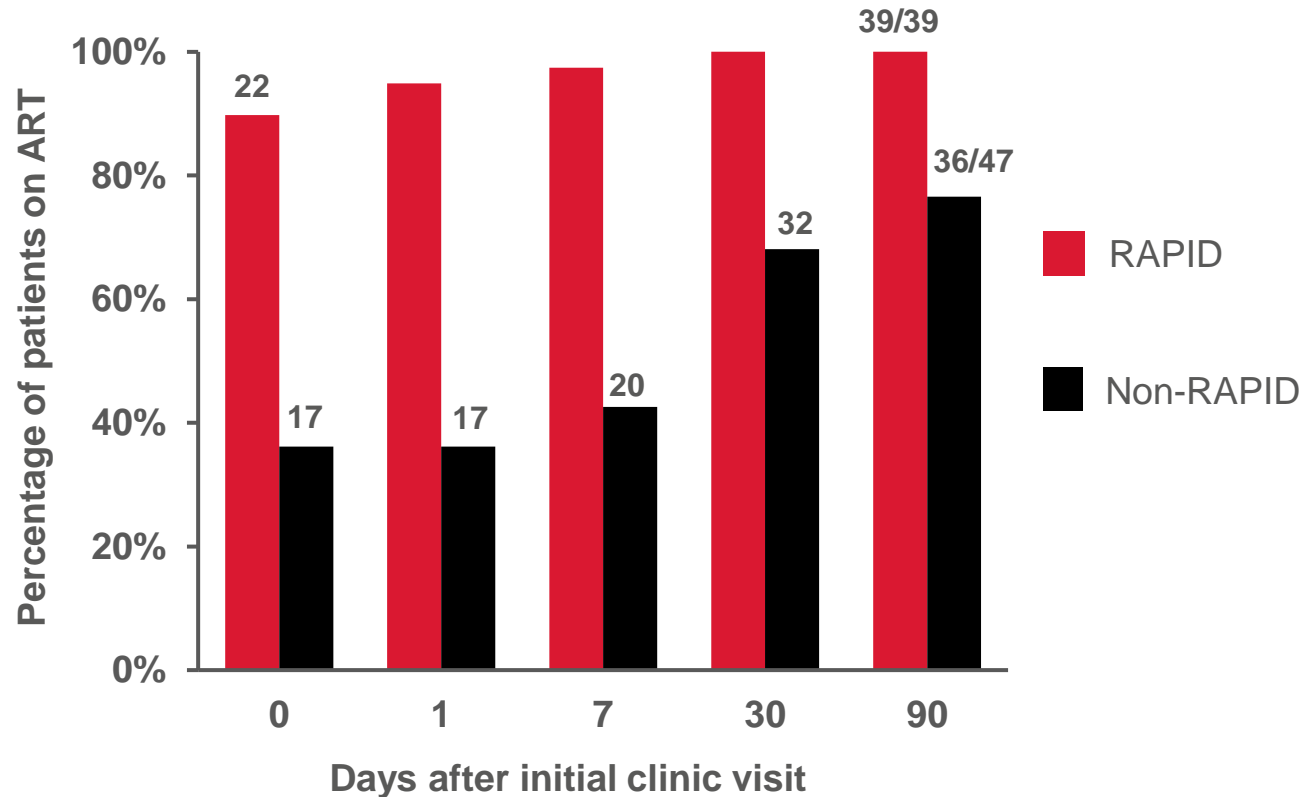
RAPID ART INITIATION VERSUS CLINICAL STANDARD MODEL OF CARE IN PEOPLE WITH NEWLY DIAGNOSED HIV

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



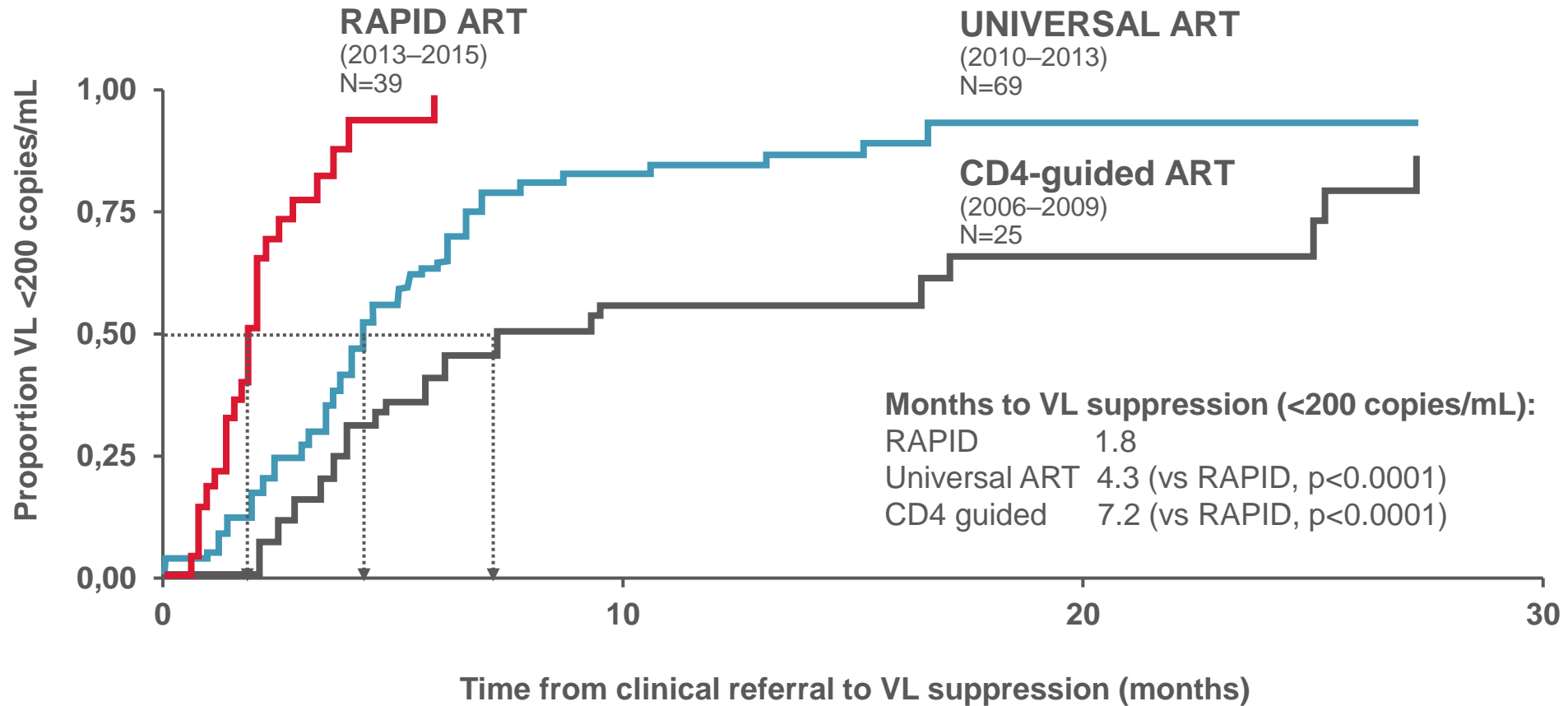
^aRAPID care initiation protocol included: 1) same-day access to an HIV provider; 2) same-day medical visit outline (including education re: HIV infection, risk reduction and sexual health, and benefits of ART); 3) accelerated insurance approval process; 4) pre-approved regimens; 5) 5-day starter packs (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). ^bIn 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.

UPTAKE OF ART WHEN OFFERED IMMEDIATELY AFTER DIAGNOSIS



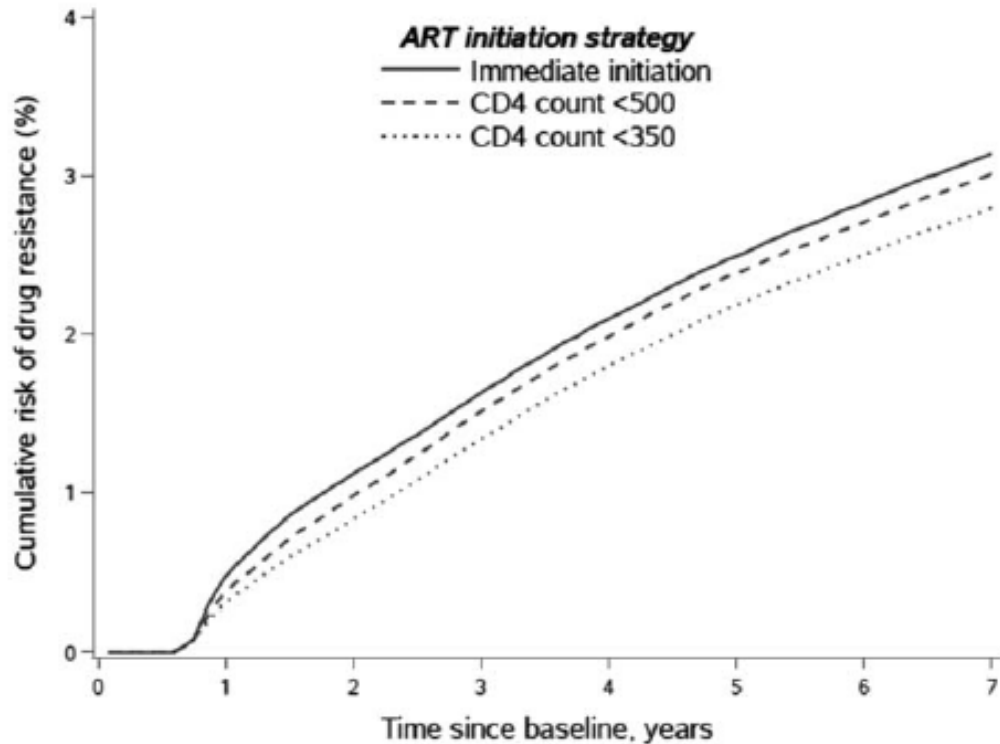
- **95%** of patients chose to begin ART within a day of it being offered
- Slower uptake among non-RAPID patients is related to the deferral of the offer to start ART
- Data are for patients with a new HIV diagnosis who attended their first San Francisco General Hospital HIV Clinic between 2013 and 2015

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



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/mm³

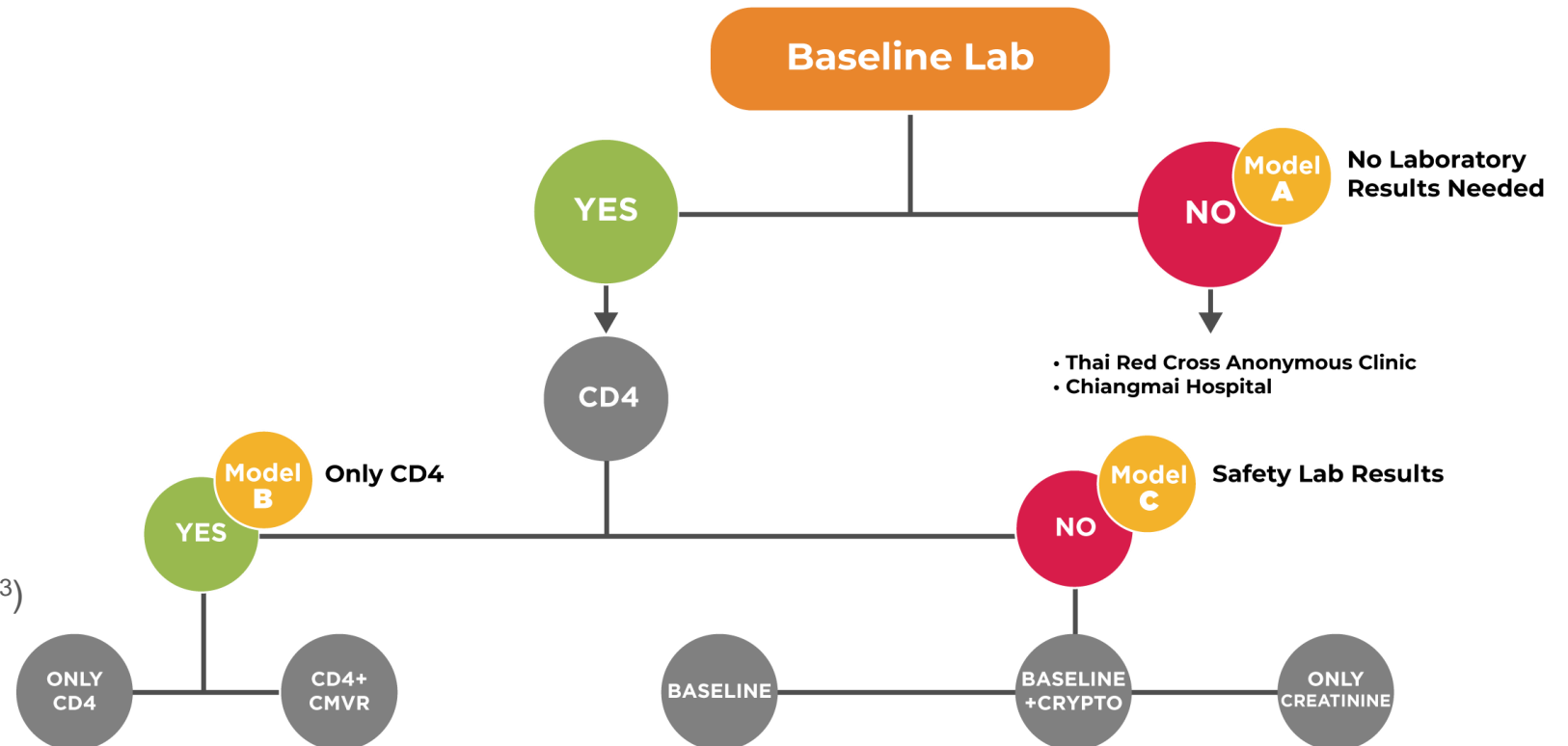
ART start	Risk at 7 years, % (95% CI)
Immediate	1.6 (1.2, 2.3)
CD4 <500 cells/mm ³	1.9 (1.4, 2.4)
CD4 <350 cells/mm ³	1.6 (1.2, 2.1)

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

IMMEDIATE ART: ANALYSIS OF THREE MODELS OF CARE IN THAILAND

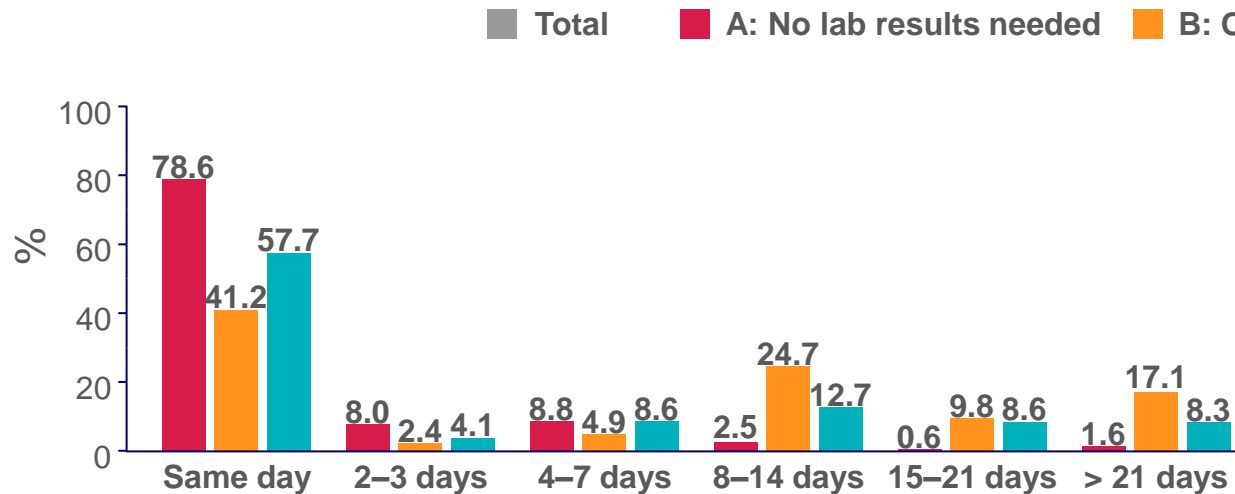
- **Aim:** assess the acceptability and effectiveness of ART initiated on the same day of the HIV diagnosis in the context of local resources and available same-day tests
- **First-line ART:** EFV+FTC/TDF
- **Baseline tests:**
 - Creatinine
 - Urinalysis
 - CD4 count
 - HBsAg
 - Anti-HCV
 - Syphilis serology
 - ALT
 - Chest X-ray
 - Cryptococcal antigen (CD<100 cells/mm³)

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



IMMEDIATE ART: RESULTS FROM THREE MODELS OF CARE IN THAILAND

Time between HIV diagnosis and ART initiation

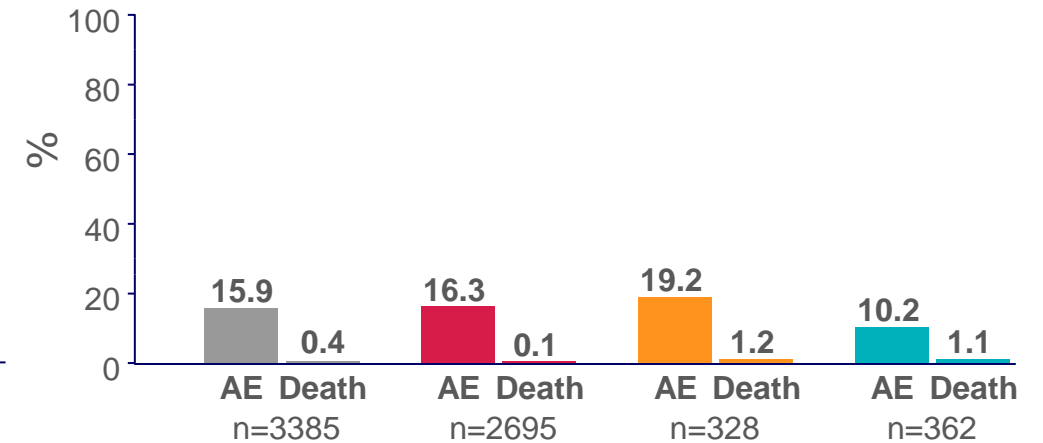


Median time (IQR)

- 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

Rapid ART Defined by the DHHS as a Key Component to Help End the HIV Epidemic

February 2019

Ending the HIV Epidemic: A Plan for America

HHS is proposing a once-in-a-generation opportunity to eliminate new HIV infections in our nation. The multi-year program will infuse 48 counties, Washington, D.C., San Juan, Puerto Rico, as well as 7 states that have a substantial rural HIV burden with the additional expertise, technology, and resources needed to end the HIV epidemic in the United States. Our four strategies – diagnose, treat, protect, and respond – will be implemented across the entire U.S. within 10 years.

GOAL: Our goal is ambitious and the pathway is clear – employ strategic practices in the *places* focused on the right *people* to:

- 75% reduction in new HIV infections in 5 years and at least 90% reduction in 10 years.**
- Diagnose** all people with HIV as early as possible after infection.
- Treat** the infection rapidly and effectively to achieve sustained viral suppression.
- Protect** people at risk for HIV using potent and proven prevention interventions, including PrEP, a medication that can prevent HIV infections.
- Respond** rapidly to detect and respond to growing HIV clusters and prevent new HIV infections.
- HIV HealthForce** will establish local teams committed to the success of the Initiative in each jurisdiction.

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?**



Word cloud of "Thank You" in various languages and scripts, including:

- Arabic: شكر, شكرا
- Bengali: তুমাকে ধন্যবাদ
- Burmese: ကျေးဇူးတင်
- Chinese: 谢谢
- Dutch: dank u, dank je
- English: thank you, thank you
- French: merci
- German: danke
- Hebrew: תודה
- Hindi: धन्यवाद
- Indonesian: terima kasih
- Italian: grazie
- Japanese: ありがとう
- Korean: 고맙습니다
- Latin: gratias agere, gratias
- Malayalam: നന്ദി
- Malay: terima kasih
- Marathi: धन्यवाद
- Polish: dziękuję
- Russian: спасибо
- Sanskrit: नमो
- Spanish: gracias
- Tamil: தודה
- Telugu: ధన్యవాదం
- Thai: ขอบคุณ
- Ukrainian: дякую
- Urdu: شکریہ
- Vietnamese: cảm ơn
- Welsh: diolch
- Yiddish: דאַנק
- Zulu: khangulani