Rapid ART Program Initiative:

How immediate ART initiation improves health outcomes

Earlier treatment is better care[1,2]

START: HIV+ adults who started ART immediately with a CD4+ T cell count of ≥500 cells/mm^3, compared to those who deferred until their CD4+ T cell count fell to ≤350 cells/mm^3:

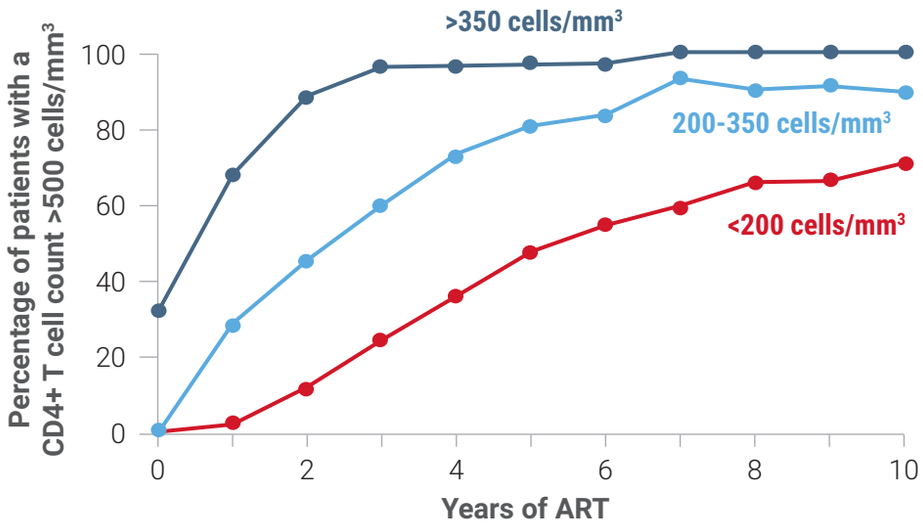
- were 0.43 times as likely to die from any cause.
- experienced a 72% reduction in the number of serious AIDS-related events.
- experienced a 39% reduction in the number of serious non-AIDS related events.

TEMPRANO: HIV+ adults who started ART immediately with a baseline CD4+ T cell count of <800 cells/mm^3, versus those who deferred at the same baseline count:

- were less likely to reach death (any cause), AIDS defining disease, non-AIDS defining cancer, or non-AIDS defining invasive bacterial disease (HR 0.56, 95% CI 0.41-0.76).
- This also applied to patients with CD4+ T cell counts ≥500 cells/mm^3 (HR 0.56, 95% CI 0.33-0.94).

Earlier ART improves CD4+ T cell recovery[3]

FIGURE 1. THE PERCENTAGE OF PATIENTS ON ART WITH A CD4+ T CELL COUNT IN THE NORMAL RANGE (>500 CELLS/mm^3) OVER TIME, STRATIFIED BY CD4+ T CELL COUNT BEFORE INITIATION OF THERAPY



25% of patients who start ART at CD4+ T cell counts <200 cells/mm^3 were unable to achieve CD4+ T cell counts >500 cells/mm^3 even after >7 years of suppressive ART.

Immediate ART also benefits the community:[4,5]

- **HPTN 052 study**: In 1763 serodiscordant couples, immediate ART reduced partner infection by 93% vs. delayed ART; no linked transmissions were observed when the index participant's HIV was stably suppressed on ART.
- **PARTNER study**: NO cases of HIV were transmitted [888 serodifferent couples (38% gay male couples) with an estimated 58,213 sex acts] by either anal or vaginal condomless sex if the HIV+ partner maintained a VL<200 copies/mL.

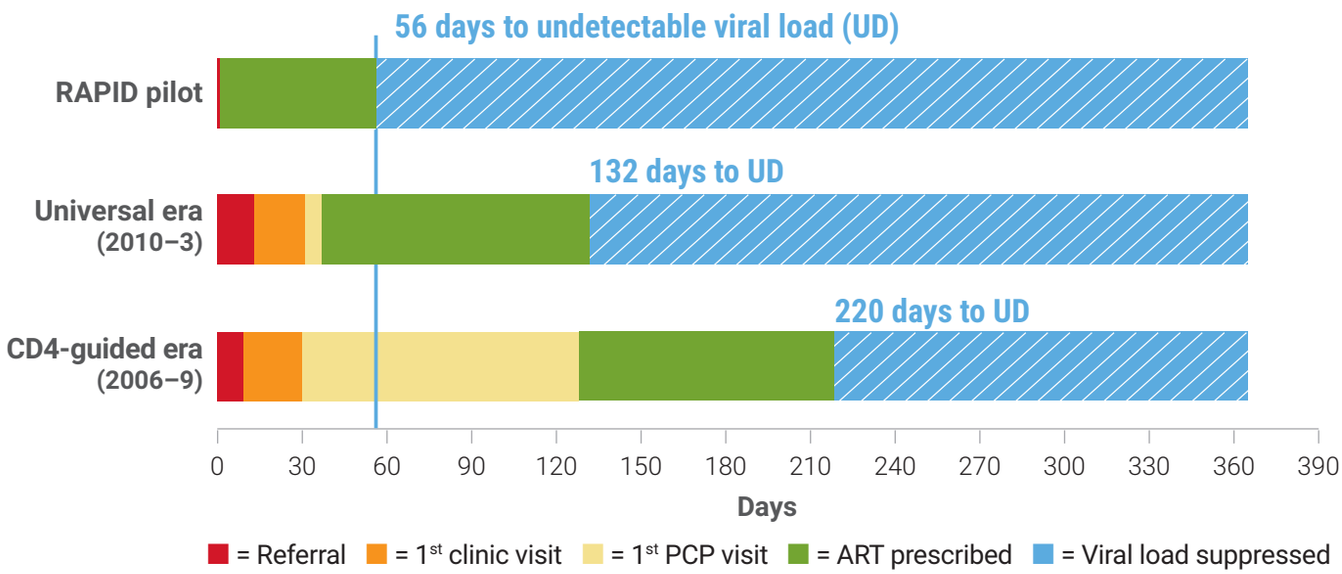
DHHS advises early use of ART[6]

- ART is recommended for all HIV-infected individuals, regardless of CD4+ T cell count, to reduce the morbidity and mortality associated with HIV infection.
- ART is also recommended for HIV-infected individuals to prevent HIV transmission.
- When initiating ART, educate patients regarding the benefits and considerations and address strategies to optimize adherence. Therapy should be initiated as soon as possible.

Immediate ART initiation...

Decreases the median time to virologic suppression by removing obstacles to care.*

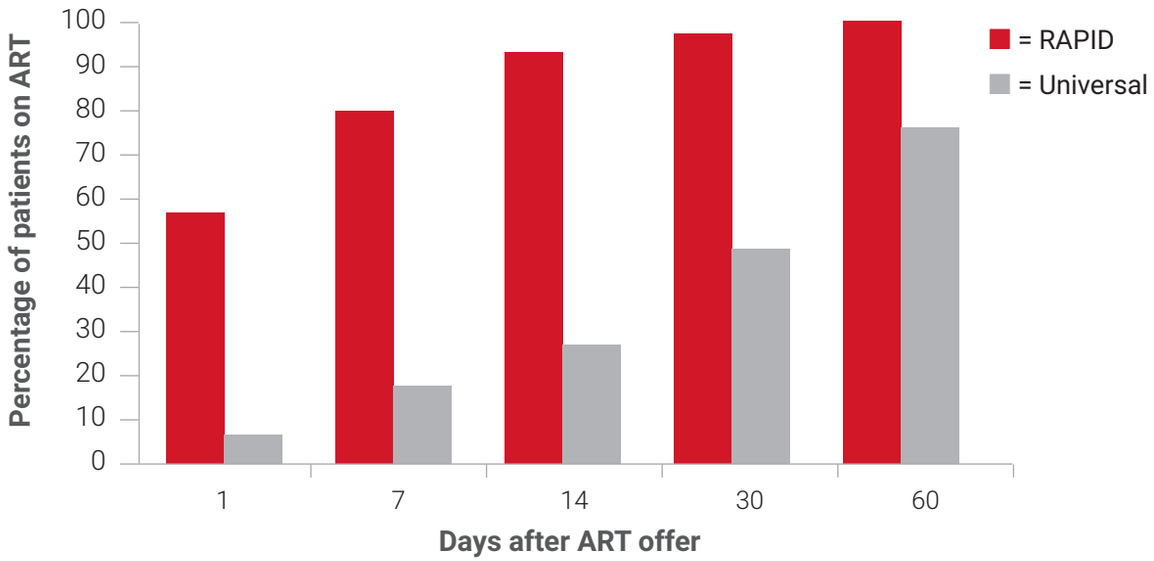
FIGURE 2. ENGAGEMENT TIMELINE[7]



* Results from clinic-based pilot 2013-2014.

Gets more people on treatment, and sooner, than waiting to start ART.[7]

FIGURE 3. ACCEPTANCE OF SAME DAY ART



RAPID through one patient's eyes

"I was prepared for a lot worse, and it was very simple."

"You still have to work through the lifestyle adjustments: you have to disclose, stay healthy, but they are things you have to do as a responsible person, to make sure that no one else gets it.

"But the agony and depression of uncertainty about how you are going to be treated, is it (the medication) going to work or not, how do you organize yourself to take so many pills, it's going to be a ball and chain…. I looked at the two pills in my hand and said: ok, just two. And then you feel like you aren't sick.

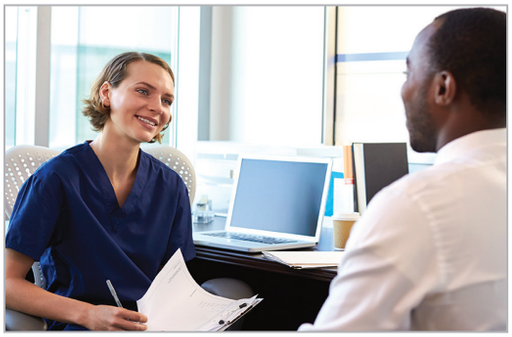
"Taking the medication didn't make me feel like I was terminally ill. I was prepared for a lot worse, and it was very simple."

—RAPID patient, male

RAPID Implementation: Overview

GOAL: Intake, first care appointment, and ART initiation within 0-5 days of new HIV Diagnosis

Average RAPID intake is 2-2.5 hours



- **Create a single point-of-contact for RAPID referrals**: e.g., a dedicated RAPID pager or knowledgeable front desk.
- **Form a committed team to handle RAPID roles** (Counseling, Benefits Navigation, Clinical/Prescription).
- **Educate entire clinic staff about RAPID,** even if they aren't "touching" the patient.
- **Minimize handoffs on Day 1**: Every handoff should be warm.
- **Develop a plan for medication access**:
  - ❑ Emergency ADAP
  - ❑ Presumptive Medi-Cal
  - ❑ Pharma Patient Assistance Cards
  - ❑ Starter packs of 5-7 days of medication can be helpful but not essential
  - ❑ Partner with a local specialty (HIV) pharmacy to expedite medication dispensing.
- **Start ART at first patient visit.**

Who is eligible for immediate ART?

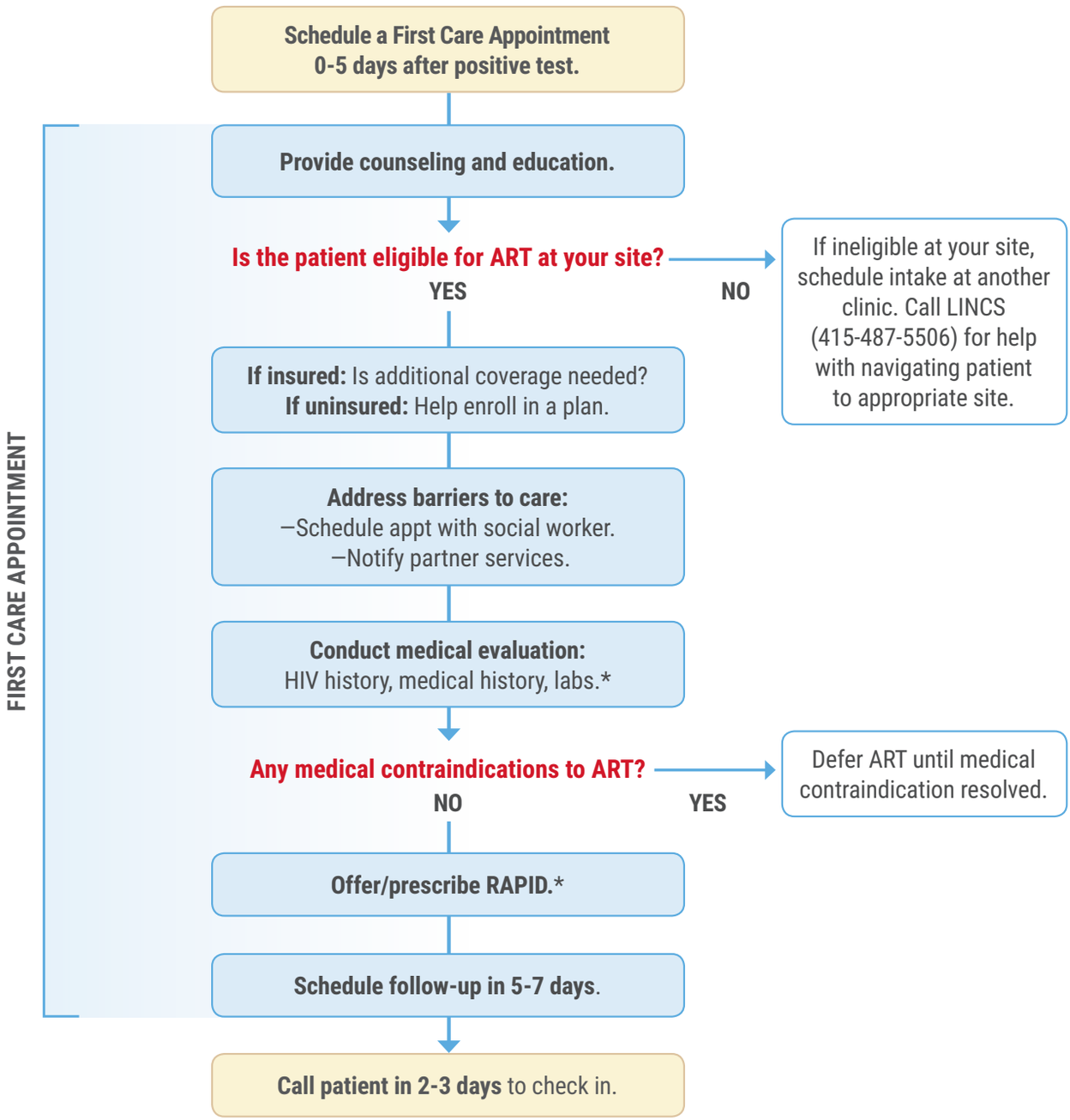
- Anyone with a new, confirmed HIV diagnosis unless there is a clear contraindication.
- HIV+ persons with an uncomplicated ART history (e.g., stopped first-line therapy for reasons other than regimen failure) may be considered for RAPID if concern for acquired resistance is low.

Who is *not* eligible for immediate ART?

- Patients for whom immediate ART might be medically dangerous (e.g., untreated Cryptococcal Meningitis)
- Patients likely to have multiple ARV mutations (e.g., treatment experienced with known or suspected resistance), for whom the results of resistance testing would likely influence regimen choice

How to implement RAPID at your healthcare facility

FIGURE 4. RAPID CARE FOR PATIENTS TESTING HIV POSITIVE



* See pages 6-7 for labs and recommended treatment regimens.

HIV Testing

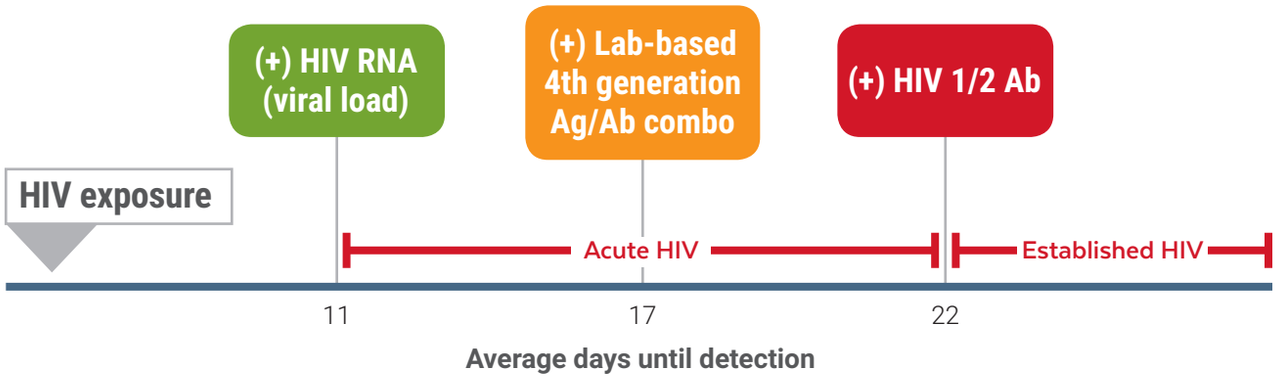
Usually, patients start RAPID with a confirmed positive HIV test.

- A confirmed positive test will depend on the testing algorithm used:
  - reactive lab-based 4th gen p24 antigen/antibody + reactive differentiation antibody
  - reactive antibody + reactive confirmatory antibody
  - 2 different reactive rapid fingerstick antibody tests

Occasionally, a patient will present with:

- **(+) HIV RNA (quantitative or qualitative) + negative antibody**: Indicates acute HIV infection, and warrants immediate ART initiation before confirmatory testing results are available.
- **Reactive lab-based 4th generation Ag/Ab test + nonreactive differentiation antibody**: Some of these are false-positives, especially in a low-risk setting. If the patient is at high risk for HIV infection, he or she may be referred for RAPID initiation before the results of the "tiebreaker" HIV RNA are available.

HIV testing during acute vs. established infection



What if my patient has a positive HIV test on PrEP?

- Take a thorough medication history to determine the last time that they took PrEP and their PrEP taking pattern.
- If the patient took any PrEP in the last 3 weeks, consider starting an enhanced regimen consisting of FTC/TDF (or FTC/TAF) + INSTI (DTG or RAL) + DRV/r while awaiting results from the genotype.

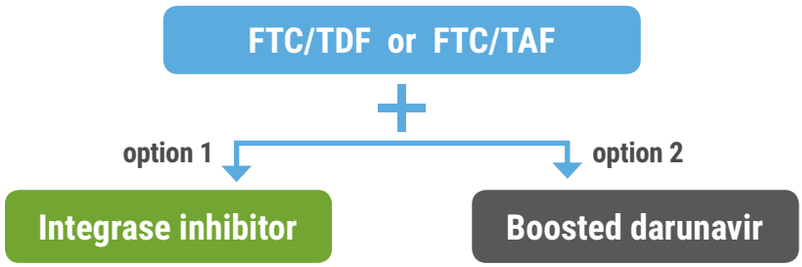
Recommended labs and regimens

TABLE 1. LABORATORY EVALUATION FOR RAPID PATIENTS

❑ Confirmatory HIV testing *(if needed)*	❑ HAV IgG antibody
❑ HIV viral load	❑ Hepatitis B serology
❑ HIV genotype, including integrase	❑ HCV antibody
❑ CD4+ T cell count	❑ 3-site STD test (urine, pharyngeal, rectal), gonorrhea & chlamydia NAAT, syphilis screening
❑ HLAB5701 polymorphism	
❑ Comprehensive metabolic panel (including creatinine and liver function)	❑ **Also consider:** QFT/ Toxoplasma IgG antibody and G6PD testing

FIGURE 5. RECOMMENDED RAPID TREATMENT REGIMENS

Initial RAPID ART will be given before the results of baseline lab testing are available. Therefore, RAPID regimens should be chosen that will likely be suppressive despite the most common transmitted resistance mutations and viral loads >100,000 c/mL, and that avoid abacavir. They should have minimal pill burden and side effects.



Can be modified once the results of baseline genotyping, HLAB5701, viral load, and serum creatinine are available.

ARVs to AVOID until results of genotype and HLAB5701 are known

1st and 2nd generation NNRTIs (efavirenz, nevirapine, etravirine, rilpivirine):

- NNRTI class is most associated with transmitted drug resistance.
- Efavirenz can have neuropsychiatric side effects.
- Nevirapine is associated with hepatotoxicity.
- Rilpivirine is less potent if baseline VL>100,000 c/mL.

Abacavir-containing regimens, including co-formulations (Epzicom®, Triumeq®):

- High risk of fatal abacavir hypersensitivity reaction if HLA-B5701(+)

Take home messages

- Ensure patients can access a care appointment within 0-5 days of HIV diagnosis.
- Draw baseline labs and offer antiretrovirals to newly-diagnosed patients at the first visit.
- Discuss how the medications work, the importance of daily adherence, and potential side effects.
- Follow-up with the patient in 2-3 days by phone, in 5-7 days in person for repeat labs, and schedule quarterly visits.
- Intervene immediately for missed visits and refer to LINCS (415-487-5506) if unable to locate.

COUNSELING TIPS

1. Check in and offer support

- Do you have any questions or concerns before we start the visit?
- How are you doing with this diagnosis? It's often overwhelming at first, but with time, you will realize that you have control of your HIV and that it does not define you.
- Do you know anyone living with HIV? It's like other manageable diseases—you monitor it, take medications daily, and check in with your team regularly.

2. Destigmatize and normalize

- People from every profession are working and living with HIV. It is illegal to discriminate against anyone living with HIV.
- Do you know how HIV is (and isn't) transmitted? People who take HIV medications daily and have an undetectable viral load for 6+ months are unlikely to infect sexual partners.

3. Medical management

- To control your virus and keep you as healthy as possible, take your HIV medications daily. Find a time that fits your daily routine to help ensure you don't miss doses.
- Use pill dispensers to keep track of your medications.
- Most people have few to no side effects from HIV medications. If you have any side effects, let us know and we can help you minimize them.

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REFERENCES: (1) Lundgren J and the START INSIGHT Study Team. Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. *New Engl J Med.* Aug 27 2015;373 (9):795-807. **(2)** TEMPRANO ANRS 12136 Study Group. A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa. *New Engl J Med.* 2015 Aug 27;373(9):808-22. **(3)** Adapted from: Kelley CF, Kitchen CM, Hunt PW, et al. Incomplete peripheral CD4+ cell count restoration in HIV-infected patients receiving long-term antiretroviral treatment. *Clin Infect Dis.* Mar 15 2009;48(6):787-794. **(4)** Cohen MS, Chen YQ, McCauley M, et al. Antiretroviral Therapy for the Prevention of HIV-1 Transmission. *New Engl J Med.* 2016 Sep 1;375(9):830-9. **(5)** Rodger A et al. HIV transmission risk through condomless sex if HIV+ partner on suppressive ART: PARTNER study. 21st Conference on Retroviruses and Opportunistic Infections, Boston, abstract 153LB, 2014. **(6)** Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents for HIV-1-infected adults and adolescents. Available at: aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/0 Accessed 29 August 2016. **(7)** Pilcher C, Hatano H, Dasgupta A, et al. Providing same day, observed ART to newly diagnosed HIV+ outpatients is associated with improved virologic suppression [abstract #WEAD0105LB]. In: Program and Abstracts of the 8th International AIDS Conference on Pathogenesis (Vancouver, Canada) 19-22 July 2015.

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