Rapid ART:

Immediate ART initiation at HIV diagnosis and re-engagement in care

Immediate ART initiation:

- **Gets more people on treatment, and sooner, than waiting to start ART.**
- **Decreases time to virologic suppression by removing obstacles to care.**

San Francisco citywide RAPID initiative (2013-2018):[1]

- Faster time from HIV diagnosis to first HIV care visit, to ART initiation, and to virologic suppression.
- Faster ART initiation and viral suppression regardless of race/ethnicity, sex/gender, age, and housing status.

TIME TO HIV CARE, ART START, AND HIV SUPPRESSION

Median Days	2013	2014	2015	2016	2017	2018
Diagnosis to 1st care visit	8	7	7	5	4	2
1st care visit to ART start	27	17	7	1	0	0
ART start to VL <200 c/mL	76	54	53	42	46	35
Diagnosis to VL <200 c/mL	134	92	79	65	65	46

San Francisco General Hospital Ward 86 RAPID Program (2013-2017):[2]

- Highly acceptable to newly-diagnosed persons (98% accepted RAPID)
- Very high rate of viral suppression: 95.8% by 1 year

In San Francisco, RAPID has been implemented in community-based clinics, public health clinics, HMO clinics, hospitals, and private practices.

DHHS and IAS-USA Guidelines advise immediate ART[3,4]

ART should be started "immediately (or as soon as possible) after HIV diagnosis in order to increase the uptake of ART and linkage to care, decrease the time to viral suppression for individual patients, and improve the rate of virologic suppression among persons with HIV."

Immediate ART also benefits the community:

HPTN 052 study and PARTNER studies: NO linked transmissions in male-female or male-male serodifferent couples when the partner with HIV had stable viral suppression on ART.[5,6]

The CDC endorses ART for HIV prevention (also called "U=U"): "effectively no risk of sexually transmitting the virus" if the HIV viral load is continuously suppressed on ART.[7]

RAPID through one patient's eyes

It's one of the best things to do to put your mind at ease, that it's not as devastating as it could be to be HIV-positive ... ***It made me feel great that I live in a time that doesn't take weeks or months to get treatment*** *[instead of being] kept in doubt or guessing what are you going to do or ... dealing with the stress of that.*

So, it felt nice to just be able to say, "Oh, I can get treatment right away."

——RAPID patient

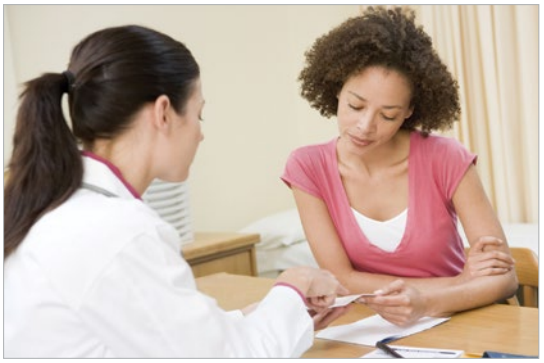
RAPID through one provider's eyes

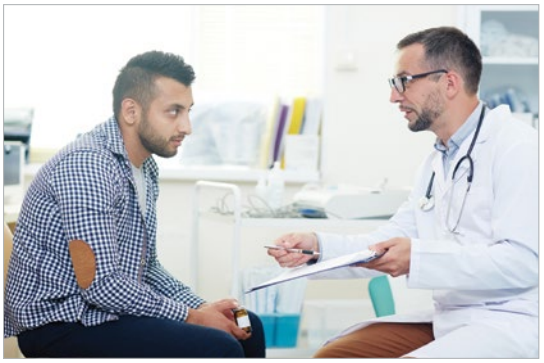
We talk all about the benefits to the client but we never talk about how much it makes it easier on the provider. ***I can't imagine ever disclosing again without being able to offer immediate treatment.***

——RAPID provider Pierre-Cédric Crouch, PhD, NP

RAPID implementation: Overview

GOAL: First care appointment within 0-5 days of new HIV diagnosis; start ART at first visit





- **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 interacting directly with 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 Programs
  - ❑ Starter packs of 5-7 days of medication are helpful but are not essential
  - ❑ Partner with a local specialty (HIV) pharmacy to expedite medication dispensing
- **Ideally the first visit will be in person.** If it's a Telehealth visit, a mechanism for obtaining initial lab tests should be in place.

* **Insurance coverage for ART medications is often the biggest barrier to RAPID ART start;** it is important to establish systems for rapid access to coverage for uninsured persons and to have benefits navigators or social workers with expertise in establishing insurance and medication coverage.

Immediate ART is appropriate for:

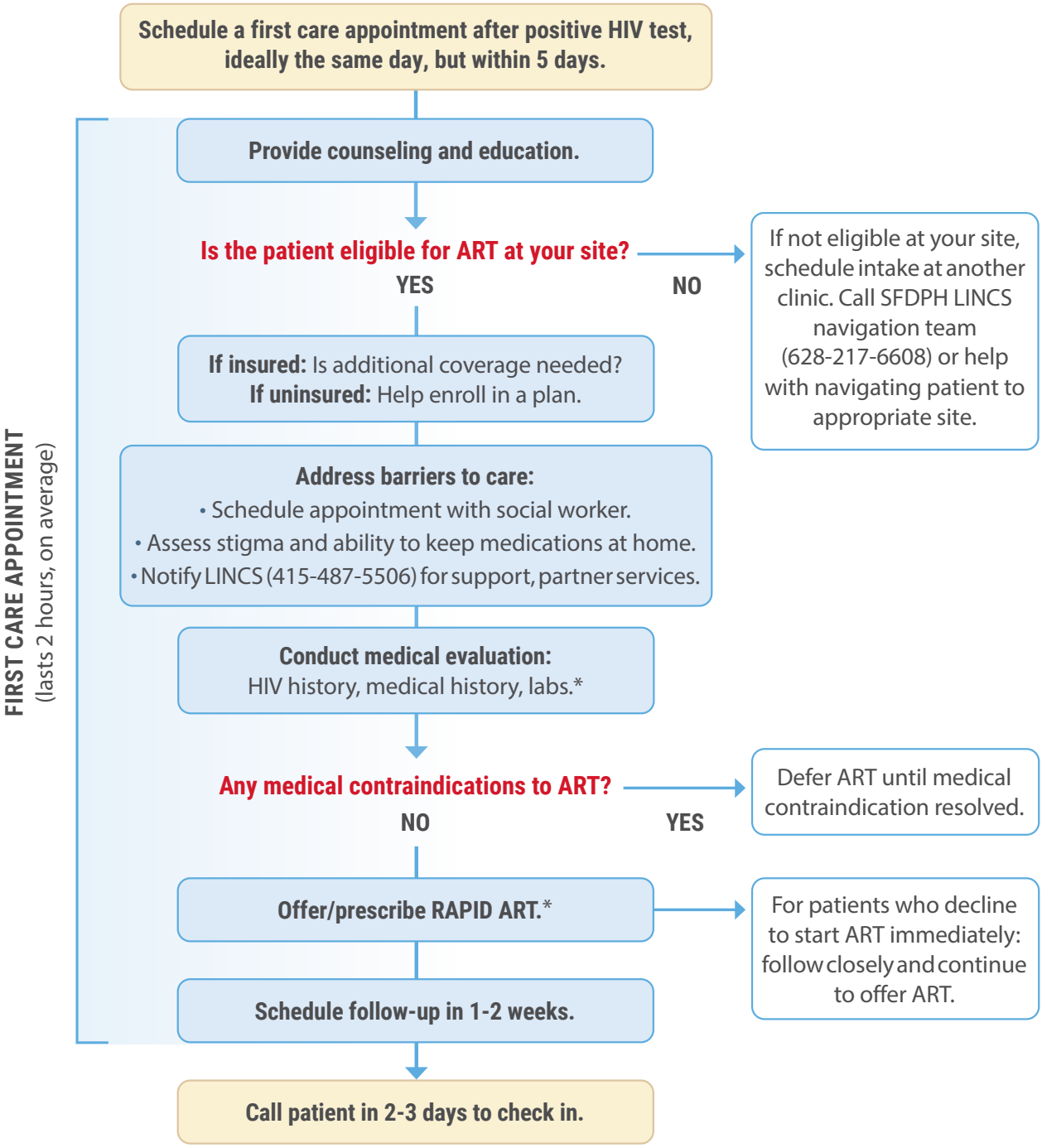
- **Anyone with a new HIV diagnosis unless there is a clear contraindication**
- **Persons with possible acute HIV** (see page 6)
- **People with HIV who are re-engaging in care:** Restart ART immediately if possible and if drug resistance can be predicated and accounted for in the new ART regimen. For more, see RAPID Restart, pages 9-10.

Immediate ART is not appropriate for:

- **Patients for whom immediate ART might be medically dangerous** (e.g., untreated central nervous system opportunistic infections such as cryptococcal meningitis)
- **Patients likely to have multiple ARV mutations** (e.g., treatment experienced with known or suspected resistance) for whom it would be difficult to design an ART regimen without current resistance test results

How to implement RAPID at your healthcare facility

RAPID CARE FOR PATIENTS TESTING HIV POSITIVE



* See pages 7-8 for labs and recommended treatment regimens.

RAPID intake can be done by Telehealth, if necessary; a mechanism for obtaining lab tests should be in place.

HIV testing

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

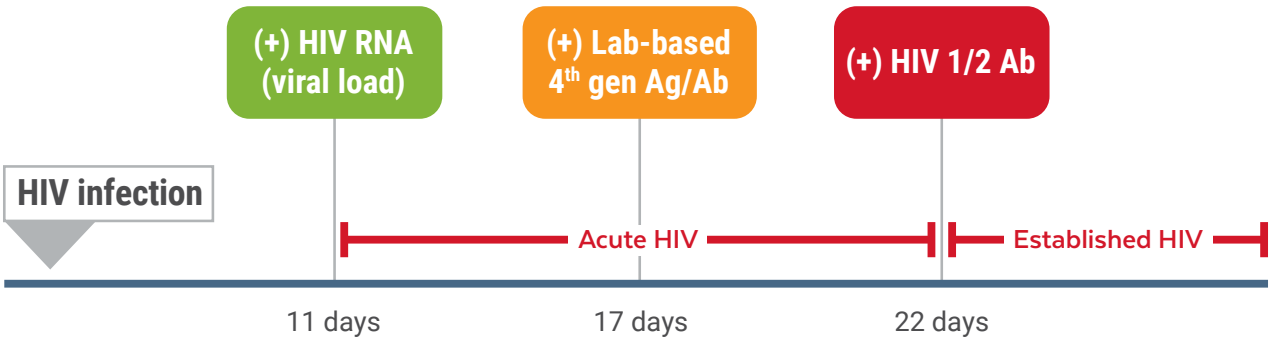
- A confirmed positive test will depend on the testing algorithm used:
  - reactive lab-based 4th generation Ag/Ab plus reactive differentiation Ab
  - reactive Ab plus reactive confirmatory Ab
  - 2 different reactive rapid fingerstick Ab tests

Occasionally, a patient will present with:

- **(+) HIV RNA (quantitative or qualitative) plus nonreactive Ab:** Indicates acute HIV infection; warrants immediate ART initiation before confirmatory test results are available.
- **Reactive lab-based 4th gen Ag/Ab test plus nonreactive differentiation Ab:** Indicates either acute HIV infection or false positive Ag/Ab test. If the patient is at risk for HIV infection, consider immediate ART initiation until result of the "tiebreaker" HIV RNA is available (ART can be stopped if RNA is negative).*
- **Reactive rapid (point-of-care) Ab test with confirmation test pending:** Indicates either HIV infection or false positive Ab test. If the patient is at risk for HIV infection, consider immediate ART initiation until result of confirmatory test is available. (ART can be stopped if the confirmatory test is negative.)*

* The decision to start ART should be made with shared decision-making and the patient's understanding that they may take ART for several days in the setting of a false positive initial HIV test.

HIV testing during acute vs. established infection: Average days until detection by different HIV assays



Interpreting HIV test results can be difficult; seek expert advice in cases with discordant test results or complicated clinical scenarios.

Recommended laboratory tests

❑ Confirmatory HIV testing (if needed)	❑ Hepatitis A IgG antibody
❑ HIV RNA (viral load)	❑ Hepatitis B serology (sAb, cAb, Ag)
❑ HIV genotype, including integrase	❑ Hepatitis C antibody
❑ CD4+ T cell count	❑ Pregnancy test (if indicated)
❑ HLA B*5701	❑ Syphilis screening
❑ Comprehensive metabolic panel (including creatinine and liver function)	❑ Gonorrhea and chlamydia NAAT at all sites of exposure (could be urine, vaginal, pharyngeal, rectal)
❑ **Also consider:** Quantiferon, Toxoplasma IgG antibody, and G6PD testing. *Can be deferred to subsequent blood draw.*	

RAPID ART regimens for new HIV diagnoses

Initial RAPID ART will be given before the results of baseline lab testing are available. Thus, it is important to choose RAPID regimens that are likely to be effective even if the most common transmitted resistance mutations are present and if the viral load is >100,000 c/mL. They should have minimal pill burden and side effects.

Recommended for most:

OPTION 1

Bictegravir/ TAF/FTC

OPTION 2

Dolutegravir 50 mg

+

TAF/FTC , TDF/FTC, or TDF/3TC

OPTION 3

Darunavir/cobicistat/ TAF/FTC

*Dosing for all options above = **1 pill of each per day***

*Can be modified once the results of baseline genotype, HLA B*5701, viral load, serum creatinine, and other tests are available.*

Abbreviations: 3TC: lamivudine; FTC: emtricitabine; TAF: tenofovir alafenamide; TDF: tenofovir disoproxyl fumarate

Patients with positive HIV test while on PrEP:

- **For oral PEP**: Take a thorough medication history to determine the last time that they took PrEP, and their PrEP-taking pattern.
  - If the patient took any oral PrEP in the weeks after date of suspected infection, consider starting an enhanced regimen consisting of an INSTI (dolutegravir or bictegravir) + boosted darunavir + TAF/FTC (or TDF/FTC, TDF/3TC) while awaiting results of the genotype.
- **For any history of long-acting cabotegravir PrEP**: darunavir/cobicistat/TAF/FTC while awaiting genotype results.

Pregnancy and RAPID ART:

For those who may become pregnant while taking ART:

Discuss possible risks/benefits of specific ARVs at conception and early pregnancy; choose ART through shared decision making.

For pregnant individuals:

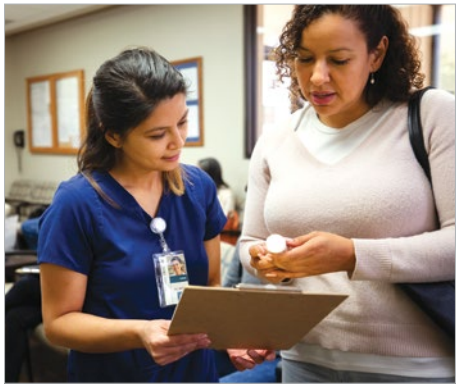
- Dolutegravir 50 mg once daily + (TAF/FTC, TDF/FTC, or TDF/3TC) once daily

ARVs to AVOID until results of genotype, HIV RNA, and HLA B*5701 are known:

- **NNRTIs (efavirenz, etravirine, rilpivirine, doravirine, nevirapine)**
  - Transmitted drug resistance to the NNRTI class is most common.
  - Rilpivirine is less potent if baseline viral load >100,000 c/mL.
- **Abacavir-containing regimens, including co-formulations (Epzicom®, Triumeq®)**
  - High risk of abacavir hypersensitivity reaction if HLA B*5701(+)
- **2-drug regimens**: **dolutegravir/3TC (Dovato®), dolutegravir/rilpivirine (Juluca®), cabotegravir + rilpivirine (Cabenuva®), boosted darunavir + 3TC, and others**
  - Risk of transmitted drug resistance and virologic failure; not well studied as RAPID regimens

RAPID Restart:

For persons re-engaging in care



Immediate ART restart (or initial start, if not previously treated) is appropriate for most persons with known HIV diagnoses who are not on ART, if:

- they are willing and there are no contraindications (see page 4),
- the ART and HIV resistance history is known or can be predicted (based on previous resistance testing, HIV viral load while on ART, and adherence history), and
- an appropriate ART regimen can be devised without information from current resistance test results

- Note that this includes nearly all persons who are re-engaging in care.
- ART restart is particularly urgent for persons with CD4 counts <200 cells/mm^3.
- RAPID Restart can be done via Telehealth, if indicated.

Provide robust clinical supports to optimize successful re-engagement in care and ART adherence, e.g.:

- Same-day evaluation by a social worker or counselor to assess and address barriers that caused the client to disengage from care
- Referral for mental health, substance use, or other services as needed
- Close follow up with the primary care provider

Laboratory tests:

HIV RNA, CD4, comprehensive metabolic panel, and other tests as indicated or if not previously done (see page 7).

HIV resistance test (generally a genotype) should be done, unless new acquired resistance is unlikely (may not be needed if patient had viral suppression at time of ART discontinuation). Include integrase genotype if patient has been on INSTI. ART can be modified, if indicated, when results are available. ***Note:*** Genotypes obtained when patients are off ARVs may not detect important mutations—consult with an HIV expert.

For patients who do not restart immediately:

- Follow closely (e.g., in 1-2 weeks) and restart ART at the earliest appropriate time.

RAPID Restart ART regimens

Select ART regimens on an individual basis and in consultation with an expert HIV clinician.

Common RAPID Restart ART scenarios:

- **Patient was taking a 1st or 2nd ART regimen, no suspected resistance, consider:** BIC/TAF/FTC; DTG + (TAF/FTC, TDF/FTC, or TDF/3TC); or DRV/c/TAF/FTC; or (unless contraindications) can restart the patient's previous regimen.
- **Patient has known or suspected history of virologic failure with ART resistance:** select the ART regimen based on the suspected resistance mutations. Consult with an HIV expert.
  - **If concern for NRTI resistance with/without NNRTI resistance, consider:** boosted PI + 2 NRTIs ± an integrase inhibitor (e.g., DRV/c/TAF/FTC ± DTG).
  - **If concern for NRTI resistance with/without INSTI resistance, consider:** boosted PI + 2 NRTIs ± a 2nd generation NNRTI (if no significant NNRTI resistance) (e.g., DRV/c/TAF/FTC ± doravirine).
  - **If more extensive resistance may be present, consider:** multi-class regimen with boosted DRV + an integrase inhibitor ± an NNRTI, fostemsavir, NRTIs, and/or other ARVs, depending on anticipated ARV activity.
- **Pregnancy:** If patient is pregnant or may become pregnant on RAPID Restart regimen, discuss possible risks and benefits of specific ARVs; select regimen through shared decision making.

ARVs to avoid for RAPID Restart:

- 2-ARV regimens, e.g., DTG/3TC, DTG/rilpivirine, cabotegravir + rilpivirine, others (high risk of virologic failure if resistance is present, not studied in this setting)
- Abacavir, unless HLA B*5701 is known to be negative

Abbreviations: 3TC: lamivudine; BIC: bictegravir; c: cobicistat; DRV: darunavir; DTG: dolutegravir; FTC: emtricitabine; TAF: tenofovir alafenamide; TDF: tenofovir disoproxyl fumarate

Counseling tips

1. Check in and offer support

- *What questions or concerns do you have as 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 is does not define you.*
- *Do you know anyone living with HIV? It's like other manageable conditions—you monitor it, take medications daily, and check in with your care team regularly.*

2. Destigmatize and normalize

- *People from every background and every profession are living full and healthy lives with HIV.*
- *Do you know how HIV is (and isn't) transmitted? People who take HIV medications daily and keep their viral load undetectable will not infect sexual partners.*
- *It is illegal to discriminate against anyone living with HIV.*

3. Medical management

- *To control your virus and keep yourself as healthy as possible, take your HIV medications every day. 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.*
- *For some people, long-acting injectable HIV medications may be a good option, after they are established in care.*
- *Most people have few or no side effects from HIV medications. If you have any side effects, let us know and we can help you minimize them.*

Take home messages for RAPID teams

RAPID appointments

- Ensure patients can access a care appointment as soon as possible, and within 5 days of HIV diagnosis.
- Draw baseline labs and offer ART to newly-diagnosed patients at the first visit.
- For returning-to-care patients, offer an immediate care appointment, and restart ART at the first visit.

Patient education and supports

- Discuss how ARVs work, the importance of daily adherence, and potential side effects.
- Offer robust clinical supports to all. Refer patients to mental health, substance use, and housing services as needed.
- Assess and address stigma and client's ability to take medications openly at home.

Follow up

- Follow up with the patient by phone in 2-3 days, and in the clinic in 1-2 weeks. Subsequent visits should be at 1 month and then at least quarterly until patient is well established in care and HIV viral load is suppressed.
- If patient declines RAPID ART start (or Restart), follow closely and continue to offer ART.
- Intervene immediately for missed visits and refer to LINCS navigation services (415-487-5506) if unable to locate.

We thank the RAPID team at Ward 86, SFGH, for contributing their experience in implementing RAPID.

REFERENCES: (1) San Francisco Department of Public Health Population Health Division. HIV Epidemiology Annual Report 2019. Sept. 2020. **(2)** Coffey S, et al. RAPID ART: High virologic suppression rates with immediate ART initiation in a vulnerable urban clinic population. *AIDS 2019*, 33(5):825-832. **(3)** HHS Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. September 21, 2022. **(4)** Saag MS, et al. Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults: 2018 Recommendations of the International Antiviral Society–USA Panel. *JAMA.* 2018;320(4):379-396. **(5)** Cohen MS, et al. Antiretroviral Therapy for the Prevention of HIV-1 Transmission. *New Engl J Med.* 2016 Sep 1;375(9):830-9. **(6)** Rodger AJ, et al. Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study. *Lancet.* 2019 Jun 15;393(10189):2428-2438. **(7)** CDC, Dear Colleague letter, Sept. 27, 2017. cdc.gov/nchhstp/dear_colleague/2017/dcl-092717-National-Gay-Mens-HIV-AIDS-Awareness-Day.html

GETTING TO ZERO SAN FRANCISCO

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