THE UNIVERSITY OF CHICAGO MEDICINE & BIOLOGICAL SCIENCES

Syndemic Approaches: Ending the HIV Epidemic

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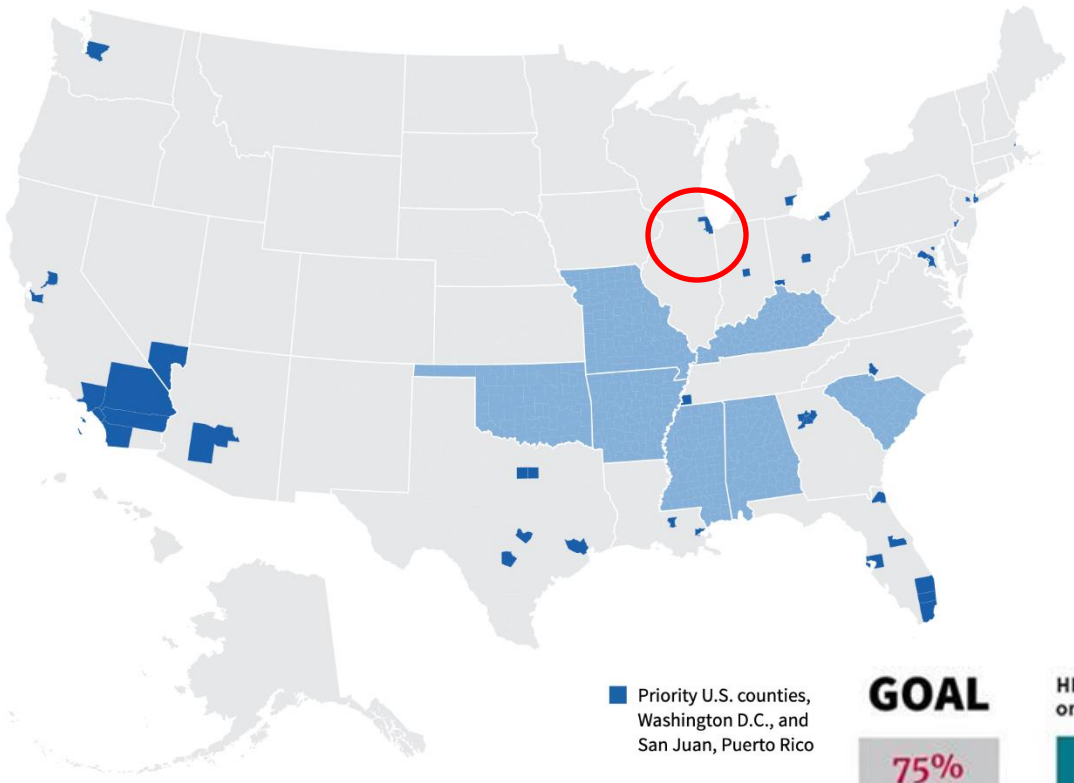
Disclosures

- No financial interest to disclose
- Served on an advisory board for Gilead Sciences, Inc.
- *This continuing education activity is managed by The St. Louis STI/HIV Prevention Training Center and accredited by Missouri State Medical Association (MSMA) in cooperation with the Chicago Department of Public Health*

Objectives

- Understand evidence, guidelines, and implementation of rapid initiation of antiretroviral therapy
- Recognize symptoms and diagnosis of acute HIV infection
- Recognize the importance of testing for HIV in persons presenting with a viral syndrome

Ending the HIV Epidemic



Priority U.S. counties, Washington D.C., and San Juan, Puerto Rico

GETTING TO ZERO ILLINOIS

GOAL

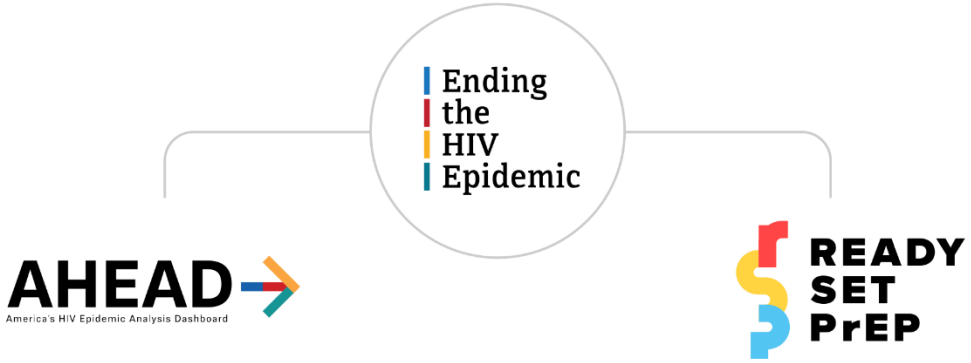
75% reduction in new HIV infections in 5 years and at least 90% reduction in 10 years.

HHS will work with each community to establish local teams on the ground to tailor and implement strategies to:

- **Diagnose** all people with HIV as early as possible.
- **Treat** people with HIV rapidly and effectively to reach sustained viral suppression.
- **Prevent** new HIV transmissions by using proven interventions, including pre-exposure prophylaxis (PrEP) and syringe services programs (SSPs).
- **Respond** quickly to potential HIV outbreaks to get needed prevention and treatment services to people who need them.

https://files.hiv.gov/s3fs-public/ending-the-hiv-epidemic-flyer.pdf

Ending the HIV Epidemic



Diagnose

Diagnose all people with HIV as early as possible after infection.

Treat

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

Prevent

Prevent new HIV transmissions by using proven interventions, including pre- exposure prophylaxis (PrEP) and syringe services programs (SSPs).

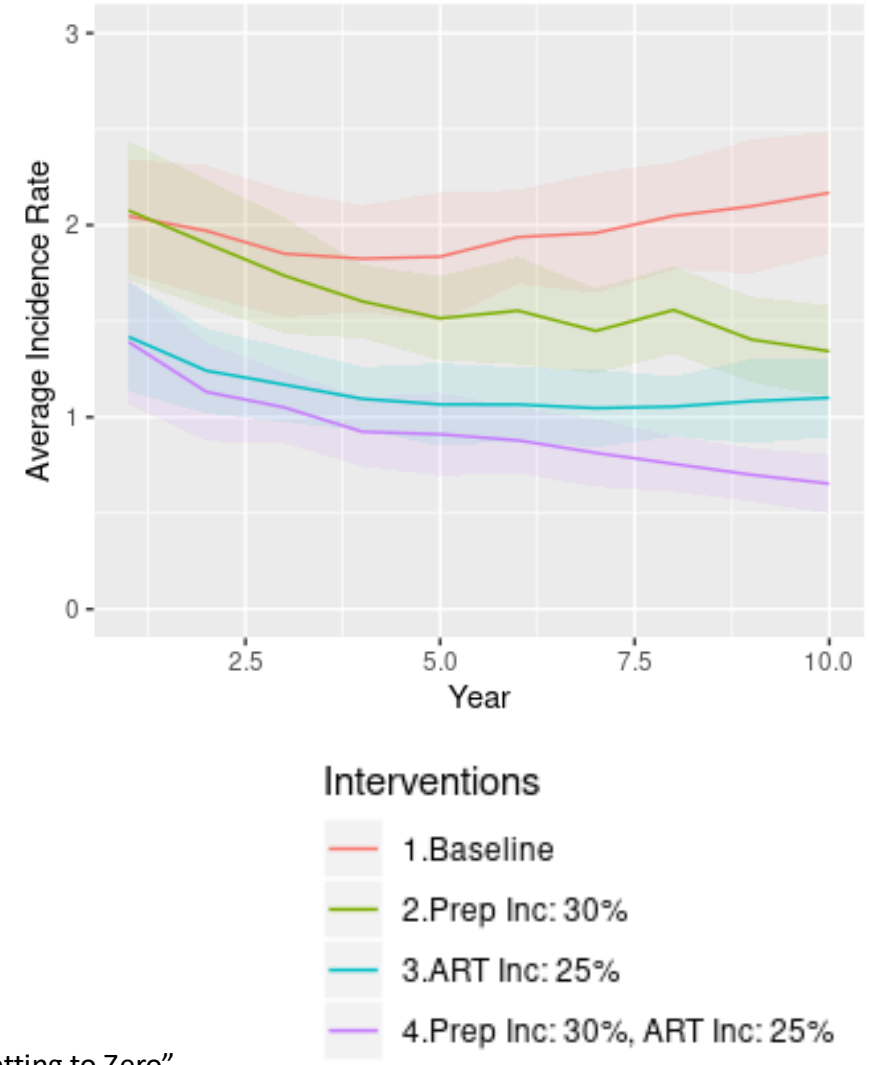
Respond

Respond quickly to potential HIV outbreaks to get needed prevention and treatment services to people who need them.

https://files.hiv.gov/s3fs-public/ending-the-hiv-epidemic-flyer.pdf

How do we get there?

- Modeling methods suggest simultaneously increasing PrEP and ART uptake is likely to be more effective than increasing only one
- But just doing those may not be enough
- And how?



Khanna et al. Triangulation of modeling approaches to formulate the "Getting to Zero" strategy in Illinois.

How do we get there?

B

		Atlanta (GA)	Baltimore (MD)	Los Ageles (CA)	Miami (FL)	New York City (NY)	Seattle (WA)
Protect	Syringe service programme						
	MOUD with buprenorphine						
	MOUD with methadone						
	Targeted PrEP for high-risk MSM						
Diagnose	Opt-out testing in ER						
	Opt-out testing in primary care						
	EMR testing offer reminder						
	Nurse-initiated rapid testing						
	MOUD-integrated rapid testing						
Treat	Case management (ARTAS)						
	Care coordination						
	Targeted care coordination						
	EMR ART engagement reminder						
	RAPID ART initiation						
	Enhanced personal contact						
	Relinkage programme						

Nosyk B et al. The Lancet HIV. 2020.

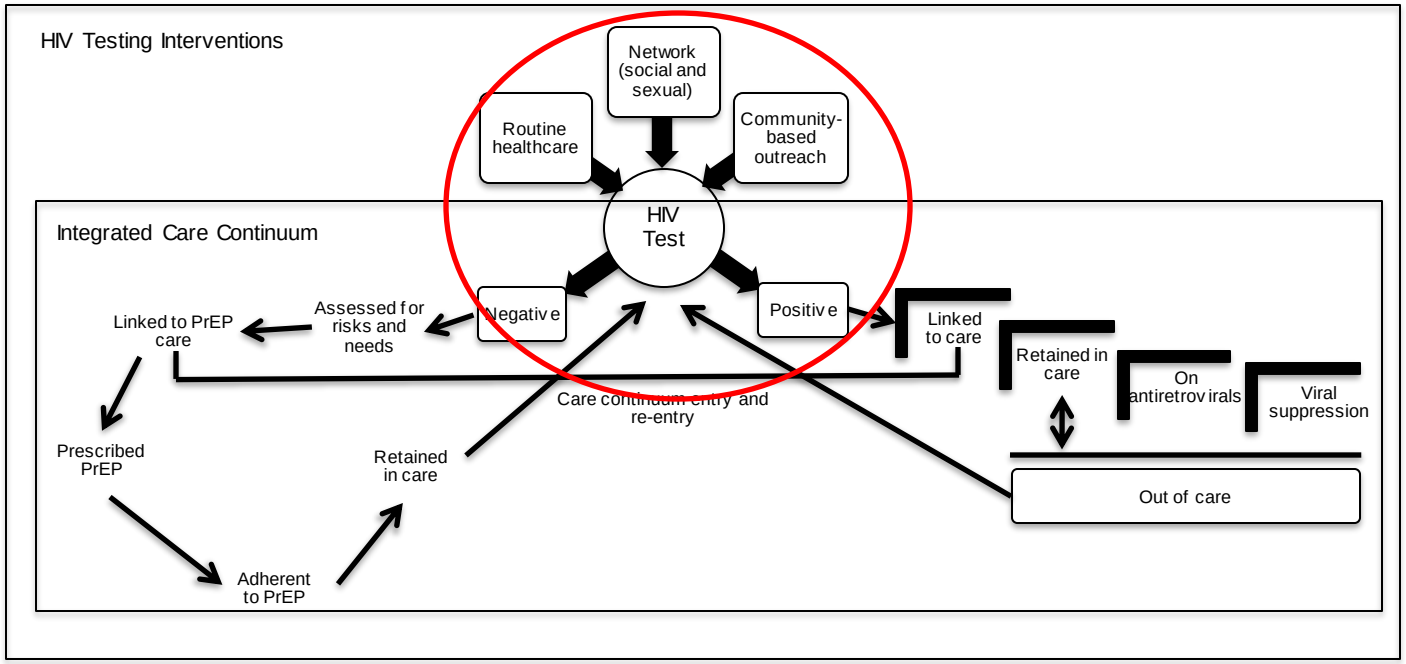
Diagnose

Diagnose all people with HIV as early as possible after infection.

Treat

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

HIV Testing as Care Continuum Entry



Adapted from McNulty, Schneider et al. AIDS 2018;. and Horn et al. J Int AIDS Soc. 2016; 19(1): 21263.

HIV Testing and the Continuum of Care

- Benefits of faster linkage to care and ART
- Evaluation of NHAS linkage to care guidelines 90 days → 30 days
  - Among those linked to care within 2–3 months after HIV diagnosis, 58.2% and 72.7% achieved viral suppression within 12 and 24 months, respectively, which was significantly lower than the percentage with viral suppression among persons linked to care within 1 month

CDC 2016; Jenness 2012; Pitasi 2020; Hall 2016

Early Antiretroviral Therapy (ART)

- Reduces morbidity and mortality
- Reduced risk of transmission to others
- Improved immunologic recovery
- Reduced HIV reservoir
- Reduced treatment delays

GETTING TO ZERO ILLINOIS

U = U
Undetectable means Untransmittable

Zolopa 2009; Lundgren 2015; Cohen 2016; Jain 2013; Ford 2018; New York State Clinical Guidelines Program 2015

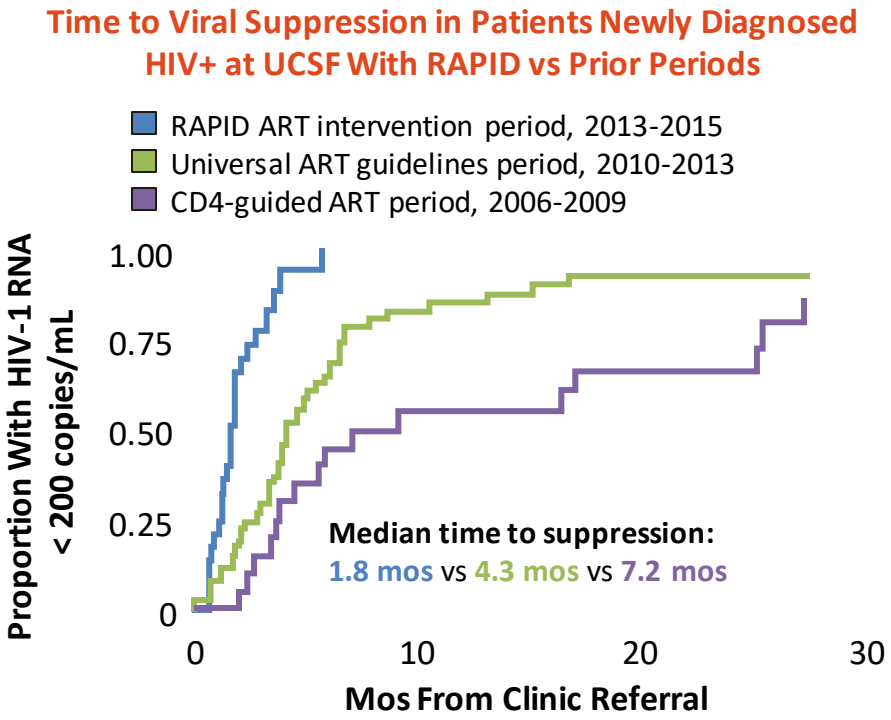
Rapid Initiation of ART

- Newer evidence suggests that faster time to linkage **and** starting medication (same day, within 72 hours to 7 days) results in:
  - Reduces loss to follow up
  - Faster viral suppression (including durable viral suppression)
  - Better retention in care
  - Trends towards less mortality
  - Expect less transmission to others

Pilcher 2017; Coffey 2019; Halperin 2018; Colasanti 2018; Koenig 2017; Rosen 2016; WHO 2017; Saag 2018; DHHS 2019; Bacon 2020

Pilot Study: Rapid ART Program Initiative for HIV Diagnoses (RAPID) in San Francisco

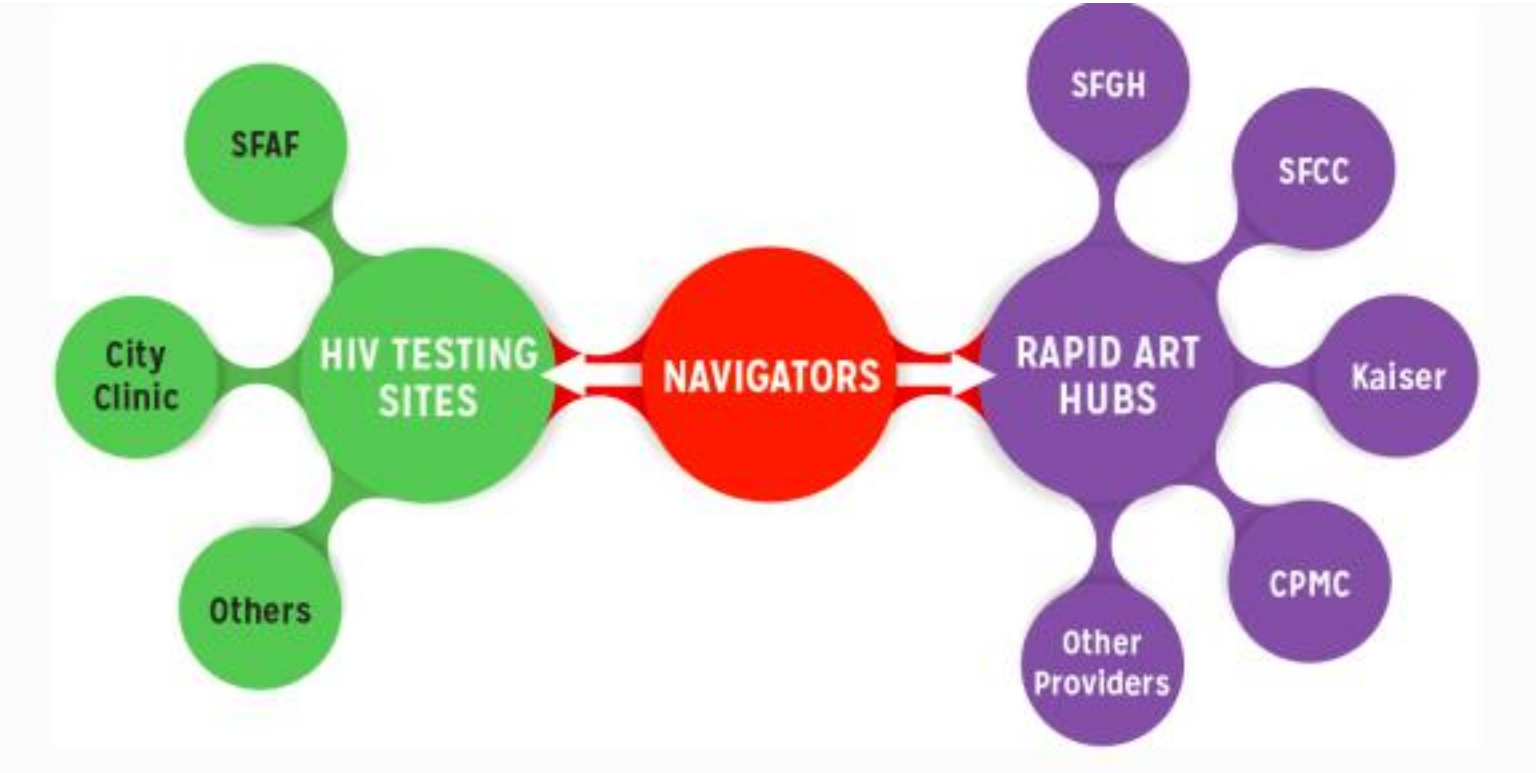
- Same-day (RAPID) ART initiation, including access to HIV provider, labs, and counseling
  - Most RAPID protocol patients received INSTI-based regimens
  - No resistance-driven ART changes in RAPID protocol patients after GT became available (25% had transmitted mutations, 22% of which were major NNRTI mutations)
- RAPID protocol led to faster HIV-1 RNA suppression vs historical cohorts with different ART initiation strategies



Pilcher. JAIDS. 2017;74:44.
Slide prepared by Dr. Gregory Hugn, Cook County Health, CORE Center

Slide credit: clinicaloptions.com

San Francisco: RAPID Program



Pilcher 2017; Coffey 2019; gettingtozerosf.org

Recommendations for Rapid ART

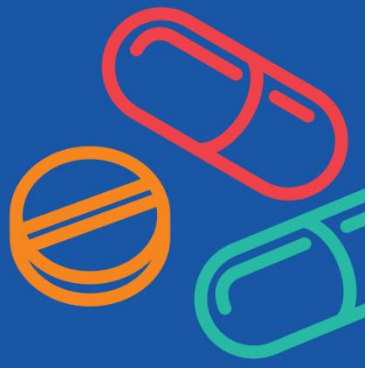
- DHHS
  - Recommended at time of diagnosis or soon afterward
    - Resource intensive
- WHO
  - Recommended for all PWH, including same day, if patient is ready
- IAS-USA
  - Start ART as soon as possible, including immediately after diagnosis, if patient is ready

*Rapid initiation defined as within 7 days of diagnosis. Priority should be given to patients with advanced disease.

DHHS Guidelines. December 2019; WHO Guidelines. July 2017; Saag. JAMA. 2018;320:379.
Adapted from slide prepared by Dr. Gregory Hugn, Cook County Health, CORE Center

Rapid ART

Starting antiretroviral therapy (ART) immediately after HIV diagnosis is recommended by U.S. federal guidelines. Rapid ART (aka immediate ART) can result in earlier HIV viral suppression, improved retention in care, and reduced HIV transmission.



INDICATIONS

Rapid ART is appropriate for:

- Individuals with a confirmed HIV diagnosis (i.e., HIV Ag, Ab, and/or HIV RNA viral load)
- Persons with suspected acute HIV infection, with or without confirmed HIV diagnosis (HIV Ag or Ab test results may be negative or indeterminate at the time of evaluation)

Rapid ART is not appropriate for:

- Persons with certain untreated opportunistic infections (OIs)—e.g., the CNS infections cryptococcal or TB meningitis; begin OI treatment before starting ART (consult with experts)

COMPRESSED HIV INTAKE

- Review of HIV test results
- Targeted health history
- HIV risk behaviors
- Date of last negative HIV test
- Use of PrEP or PEP
- Psychoemotional counseling, support
- HIV education (including ART benefits, possible adverse effects, adherence, preventing transmission)
- Targeted physical exam
- Benefits counseling, insurance enrollment or optimization

Baseline Labs

Offer ART

- If patient agrees and there are no contraindications, prescribe 30-day supply, give starter pack if available
- If patient declines immediate ART, follow up within 1-2 weeks, re-offer ART, continue HIV education

AIDS Education and Training Center Program. January 2023. AIDSETC.org

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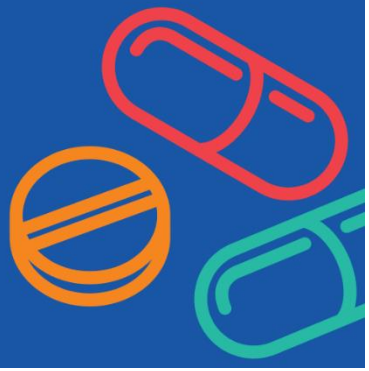


RECOMMENDED REGIMENS

These can be modified based on results of baseline labs.

- Dolutegravir (Tivicay), 50 mg once daily + [TAF/FTC (Descovy), TDF/FTC (Truvada), or TDF/3TC] 1 once daily
- Bictegravir/TAF/FTC (Biktarvy) 1 once daily
- Darunavir/cobicistat/TAF/FTC (Symtuza) 1 once daily

If **taking PrEP or PEP** at or since the time of HIV infection:

- Consider an enhanced regimen: boosted PI + integrase inhibitor + TAF/FTC (Descovy), TDF/FTC (Truvada), or TDF/3TC; seek consultation
- If on injectable cabotegravir PrEP, consider boosted PI + TAF/FTC (Descovy), TDF/FTC (Truvada), or TDF/3TC

If **pregnant** or trying to conceive (some antiretrovirals are notrecommended during pregnancy):

- Dolutegravir (Tivicay), 50 mg once daily + [TAF/FTC (Descovy), TDF/FTC (Truvada), or TDF/3TC] 1 once daily
- Other options may be appropriate; consult with expert

Abbreviations: 3TC: lamivudine; FTC: emtricitabine; PI: protease inhibitor; TAF: tenofovir alafenamide; TDF: tenofovir disoproxil fumarate; BID: twice daily

FOLLOW UP

Schedule a follow-up visit for 1-2 weeks, then at least monthly until well established in care

AIDS Education and Training Center Program. January 2023. AIDSETC.org

Rapid Initiation of ART for HIV Infection

Figure 1. Protocol for Rapid Antiretroviral Therapy Initiation

Identify Rapid ART Candidates	Counseling and Education	Assess and Refer	Baseline Lab Testing	Initiate ART	Payment Assistance?	Follow-Up	Adjust ART
Candidates have: • A new reactive POC HIV test result, new HIV diagnosis, acute HIV, or known HIV, *and* • No or limited prior ARV use, *and* • No medical conditions or OIs that require deferral of ART initiation	• HIV diagnosis • Disclosure • Adherence • Side effects and management of • Management of lifelong medications	• Health literacy • Identify and address medical and psychosocial barriers to treatment and adherence • As indicated, refer for substance use treatment, behavioral health services, housing assistance	• Confirm HIV diagnosis • Viral load • Resistance testing • CD4 count • HAV, HBV, HCV testing • Metabolic panel • STIs • Urinalysis • Pregnancy test for individuals of childbearing potential	• Choose a preferred regimen based on patient characteristics and preference • Initiate ART immediately—preferably on the same day—or within 72 hours • Administer the first dose on site if possible	• Assess need for payment assistance • Refer patients with no insurance to NYS UCP • Provide resources for payment assistance	• Contact the patient within 24 to 48 hours by phone (or other preferred method) • Assess medication tolerance and adherence • If feasible, schedule in-person visit with medical care provider within 7 days • Reinforce adherence	• Change or adjust the initial ART regimen based on results of initial lab and resistance testing

New York State Department of Health AIDS Institute: www.hivguidelines.org

Implementation of Rapid ART

Patient experience:

(1) immediate ART encounters were seen as supportive
(2) immediate ART was sensible/logical
(3) immediate ART offered emotional relief from fears and agency over one's health

Successful programs:

(1) presence of an implementation champion;
(2) comfort and competence prescribing RAPID ART;
(3) expedited access to ART medications;
(4) expertise in benefits, linkage, and care navigation;
(5) RAPID team member flexibility and organizations' adaptive capacity;
(6) patient-centered approach; and
(7) strong communication methods and culture

Koester et al. BMC Infectious Diseases 2022
Christopoulos et al. Open Forum Infectious Diseases 2021

Key Components of Rapid ART Programs

- Provision of client-centered services
- On-site testing or strong partnerships with testing programs
- Warm hand-offs and accessible linkage coordinators
- Accessible education on beginning ART
- Accelerated access to a medical visit with an HIV provider
- Early and sustained access to ART
  - Pre-approved ART regimens and starter pack of medications
- Accelerated insurance/payor approval and clinic enrollment
- Follow-up with continued education, patient navigation, and supportive services

https://targethiv.org/ta-org/building-rapid-start

Original Article

Implementing Rapid Initiation of Antiretroviral Therapy for Acute HIV Infection Within a Routine Testing and Linkage to Care Program in Chicago

Journal of the International Association of Providers of AIDS Care
Volume 19: 1-7

DOI: 10.1177/2325958220939754
journals.sagepub.com/home/jia
SAGE

McNulty et al., JIAPAC 2020

Acute HIV Infection

- Acute, or primary, HIV infection is the earliest stage of HIV infection associated with very high viral loads and risk of transmission
  - Also called the "window period" phase of seroconversion, where antibodies are not yet detectable

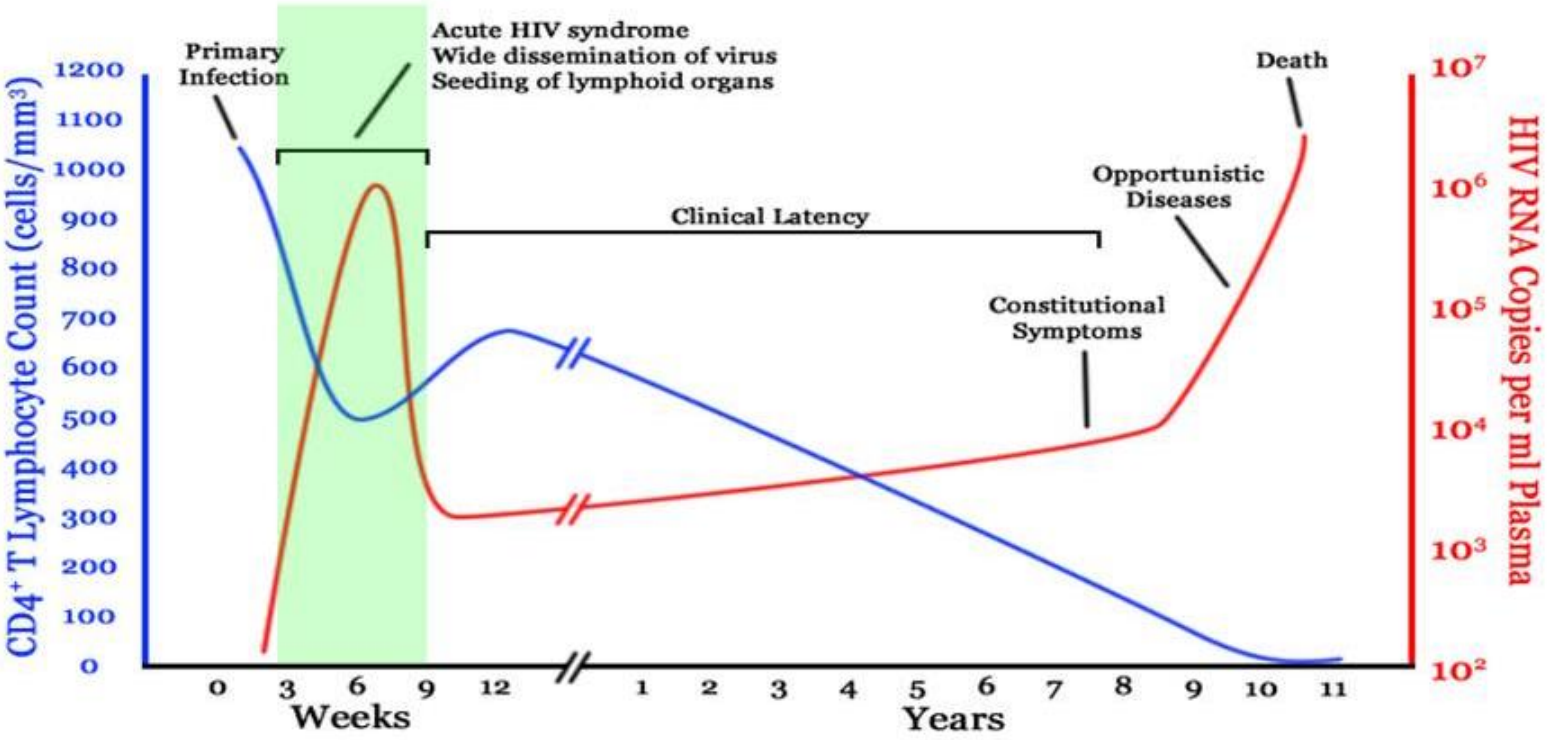
- Acute infection is defined as positive p24 antigen and viral load, but negative or indeterminate antibody detection

- Everyone has acute infection at some point
  - 50-75% of patients have symptoms of viral illness, but usually mild

- A smaller proportion of patients with have an acute HIV infection syndrome or primary HIV infection syndrome that is severe enough to bring them into care
  - Often have extremely viral loads and rapid progression of disease

CDC 2021; New York State Department of Health 2017; Pilcher 2004; Cohen 2010; Cohen 2011; Yerly 2001; Marzel 2015

Natural History of HIV Infection

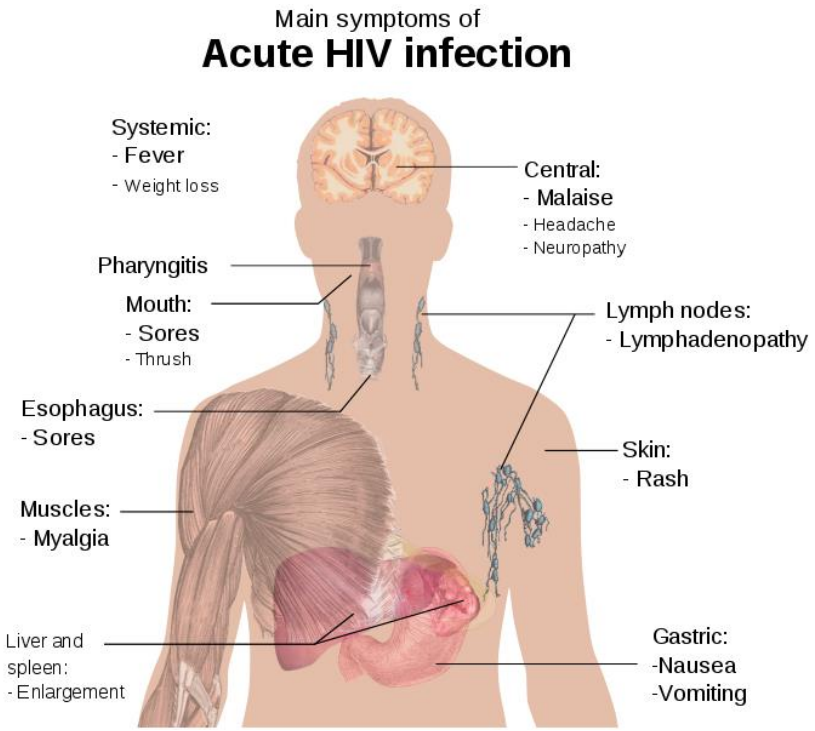


Hirschel, Infectious Disease Advisor

Symptoms of Acute HIV Infection

- Symptoms
  - Fever
  - Rash
  - Sore throat
  - Swollen lymph nodes
  - Diarrhea
  - Body aches

- Runny nose and cough are not usually symptoms of acute HIV



Hoenigl et al., 2016

Significance

- Early detection of HIV is important for improving patient health outcomes and decreasing transmission
- Viral load gives an indication of HIV in the body
  - Correlates with infectivity
- Viral loads are very high in acute infection, especially if symptomatic, compared to chronically infected patients
- 8-10 times higher risk of transmission during acute infection compared to chronic infection
- ≥ 25% of new transmissions may be from patients with acute infection (Swiss cohort study)

CDC 2021; New York State Department of Health 2017; Pilcher 2004; Cohen 2010; Cohen 2011; Yerly 2001; Marzel 2015

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Table 2. Care Continuum Outcomes Among Persons With Acute HIV Infection at 6 Health Care Sites in the Expanded Testing and Linkage to Care (X-TLC) Program.

Site (new HIV infections)	AHI (%[a])	Median days to linkage (IQR)	Received ART (%)	Median days to ART (IQR)	Median days to ≥ 2 log reduction (IQR)	Median days to VL ≤ 200 (IQR)	VS ever (%)	Retained in care[b] (%)	VS at end of follow-up (%[c])
A (22)	1 (4.5)	27 (27-27)	1 (100.0)	9 (9-9)	55 (55-55)	55 (55-55)	1 (100.0)	1 (100.0)	1 (100.0)
B (80)	6 (7.5)	11 (6-58)	6 (100.0)	21.5 (7-58)	48 (34-62)	132.5 (48-321)	4 (66.7)	4 (66.7)	4 (100.0)
C (29)	2 (7.1)	39 (39-39)	1 (50.0)	53 (53-53)	95 (95-95)	162 (162-162)	1 (50.0)	1 (50.0)	1 (100.0)
D (36)	4 (11.1)	3.5 (1.5-4.5)	3 (75.0)	4 (3-6)	31 (29-33)	31 (29-33)	3 (75.0)	3 (75.0)	3 (100.0)
E (80)	14 (17.5)	8.5 (4-18)	14 (100.0)	5.5 (4-21)	55 (47-131)	124 (55-162)	14 (100.0)	10 (71.4)	10 (100.0)
F (87)	6 (6.9)	14 (13-21)	6 (100.0)	25.5 (23-34)	92.5 (62-471)	329.5 (186-643)	6 (100.0)	4 (66.7)	4 (100.0)
Total (334)	33 (9.9)	11 (5-19.5)	31 (93.9)	15 (5-27)	58.5 (42-117)	131 (54-188)	29 (87.9)	23 (69.7)	23 (100.0)

- 6 sites identified AHIs
- Of 334 new HIV diagnoses, 33 (9.9%) individuals had acute HIV infection
- Median time to linkage was 11 (interquartile range [IQR]: 5-19.5) days, with 15 days (IQR 5-27) to initiation of antiretroviral therapy
- Clients achieved viral suppression at a median of 131 (IQR: 54-188) days
  - Of all, 69.7% were retained in care, all of whom were virally suppressed

McNulty et al., JIAPAC 2020

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	Acute (N = 33) frequency (%) or median (IQR)	New (N = 301) frequency (%) or median (IQR)	*P* value[a]
Baseline clinical factors	Median (IQR)	Median (IQR)	*P* value[a]
Viral load (copies/mL)	2.19 million (0.5-5.0); 6.34 $\log_{10}$	49972[b] (13167, 134544); 4.67 $\log_{10}$	<.0001
CD4 count (/μL)	440.5 (287.5-568.5)	277[c] (139-475)	.0027
Presenting symptoms			
Fever	22 (66.7)		
Gastrointestinal	22 (66.7)		
Myalgia	12 (36.4)		
Pharyngitis	7 (21.2)		
Rash	1 (3.0)		
No symptoms	1 (3.0)		
Initial ART			
2 NRTIs + INSTI	20 (60.6)		
2 NRTIs + INSTI + bPI	10 (30.3)		
Unknown	1 (3.0)		

- Sites required few additional resources to incorporate rapid initiation into existing processes.
- Integration into existing HIV screening programs is a promising strategy for scaling up this important intervention.

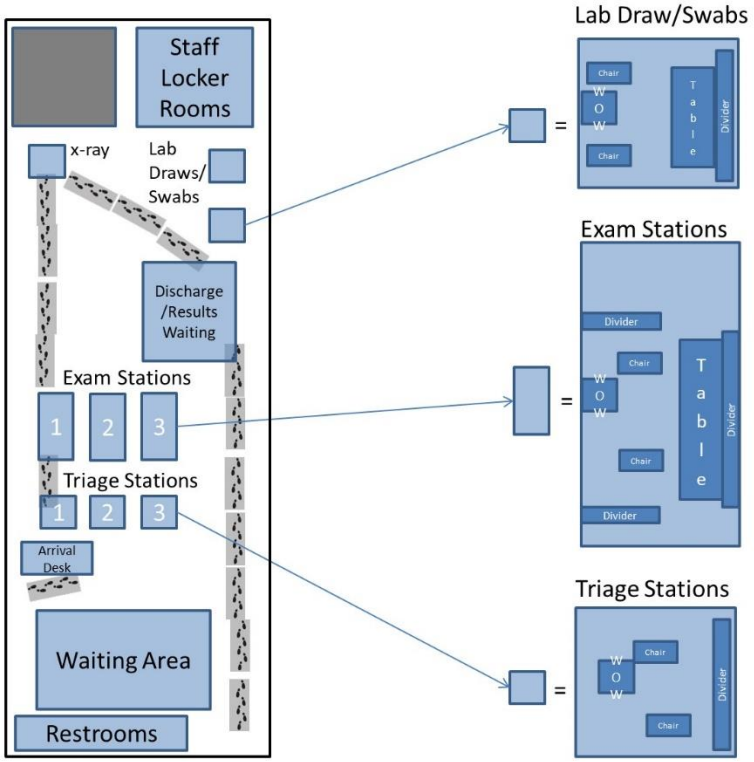
McNulty et al., JIAPAC 2020

Acute HIV Infection, ILI and COVID-19

Symptom	AHI	ILI	COVID-19
Fever/chills	X	X	X
Fatigue	X	X	X
Muscle/body aches	X	X	X
Headache	X	X	X
Sore throat	X	X	X
Swollen lymph nodes	X	X	
Rash	X		
Mouth sores	X		
Nasal congestion		X	X
Runny nose		X	X
Cough		X	X
Shortness of breath		X	X
Nausea, vomiting, diarrhea	X	X	X

Adapted from New York State Department of Health 2017; CDC 2021

COVID-19, ILI, and HIV Testing



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Stanford, et al. AIDS & Behavior, 2020
Stanford, et al. IDWeek, 2020

Research Letter

ONLINE FIRST

April 12, 2021

Incorporating HIV Screening With COVID-19 Testing in an Urban Emergency Department During the Pandemic

Kimberly A. Stanford, MD, MPH[1]; Moira C. McNulty, MD, MS[2]; Jessica R. Schmitt, LCSW, AM[2]; Dylan S. Eller, MPH[2]; Jessica P. Ridgway, MD, MS[2]; Kathleen V. Beavis, MD[3]; David L. Pitrak, MD[2]

» Author Affiliations | Article Information

JAMA Intern Med. Published online April 12, 2021. doi:10.1001/jamainternmed.2021.0839

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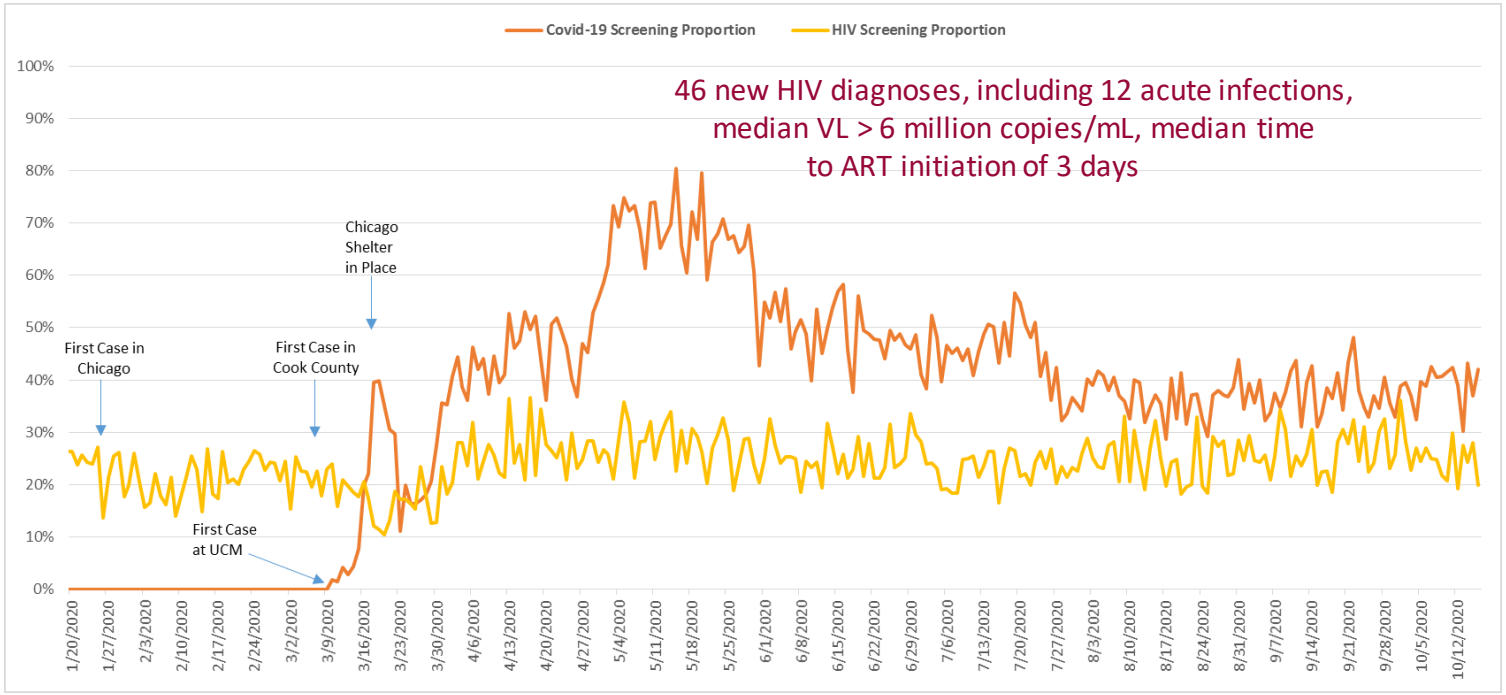
Stanford, et al. JAMA Internal Mediicne 2021
Slide courtesy of Dave Pitrak

Routine Screening for HIV During the COVID-19 Pandemic



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Stanford, et al. AIDS & Behavior, 2020
Stanford, et al. IDWeek, 2020
Slide courtesy of Dave Pitrak

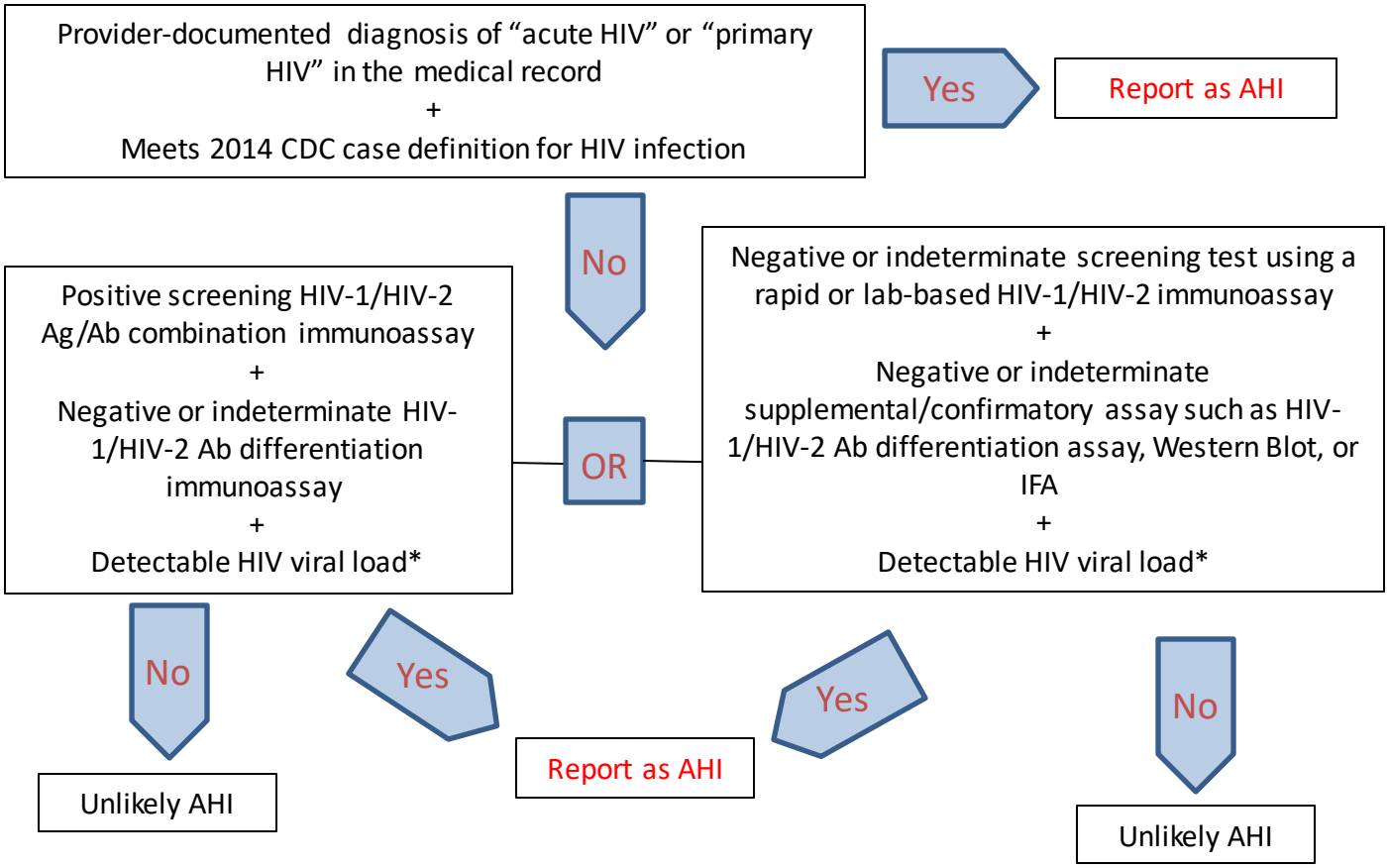
Increase in Diagnosis of AHI

- UCM performed 36,146 HIV screens (20,524) in the ED in 2020
- Sixteen patients were diagnosed with AHI after the first case of COVID-19 in Chicago (1/24/20), all in ED
- Rate of AHI diagnoses was significantly higher from 1/1/2020 to 1/31/2021 compared to the previous 4 years (14.4 per year versus 6.8 per year, Incidence Ratio (IR) 2.30, 95 % CI 1.23 to 4.31, p = 0.009)
- AHIs comprised 27.1 % (16/59) of all new diagnoses, the highest proportion ever observed

Year	AHI Dx	AHI Dx ED	New Dx	New Dx ED
2016	7	5	41	19
2017	7	7	37	22
2018	4	4	39	28
2019	9	9	56	39
2020	12	9	49	42
2021 (through 2/172020)	4	4	10	8

Stanford, et al. JAMA Internal Mediicne 2021

Revised Surveillance Case Definition for Acute HIV Infection



*Ideally nucleic acid test or HIV viral load is performed on the same specimen but no more than one month later.

https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6303a1.htm

Conclusions

- Need multi-pronged approach for EHE
- Improve early diagnosis of HIV, with rapid linkage/ART
- Rapid initiation of ART is safe and effective, one part of approach for EHE
  - Leads to earlier viral suppression and supports retention/engagement in care
- Can be scaled up within existing HIV care and testing programs
- Barriers in implementation, but not insurmountable

Thank You!