Rapid Start

Panel Discussion

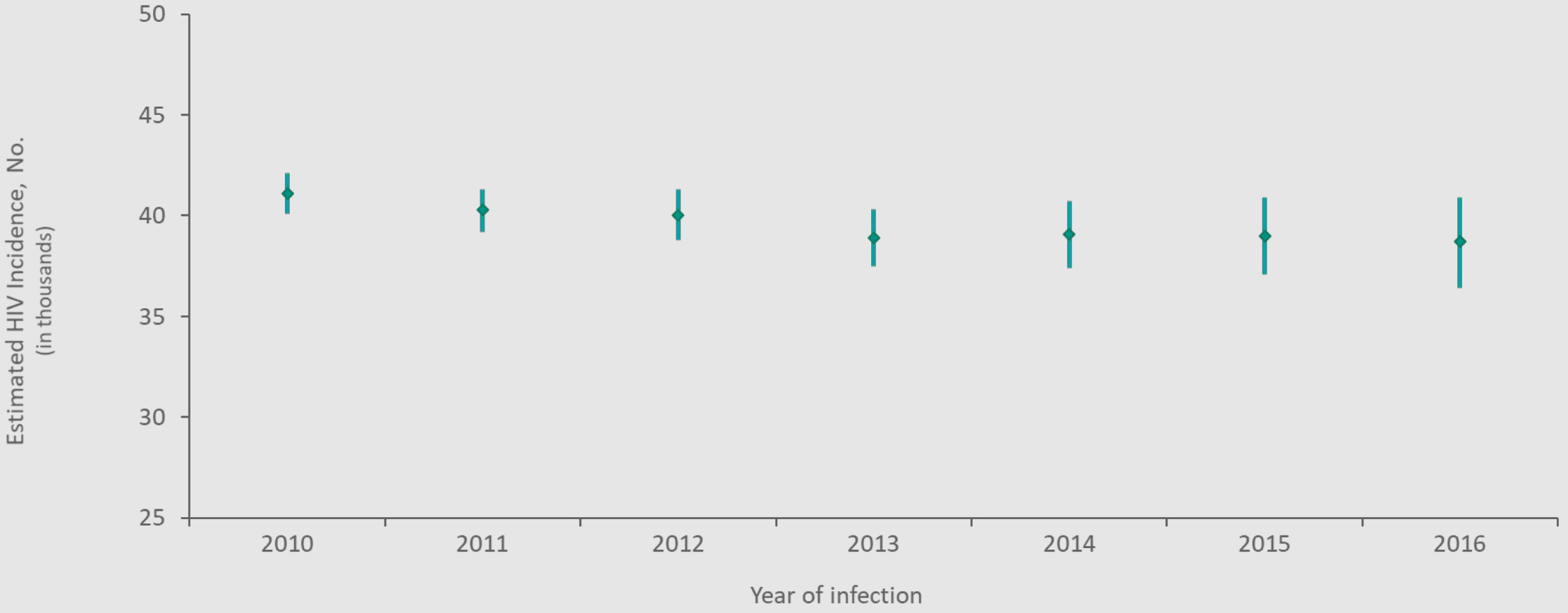
A Coordinated Team Approach

Friday

September 13, 2019

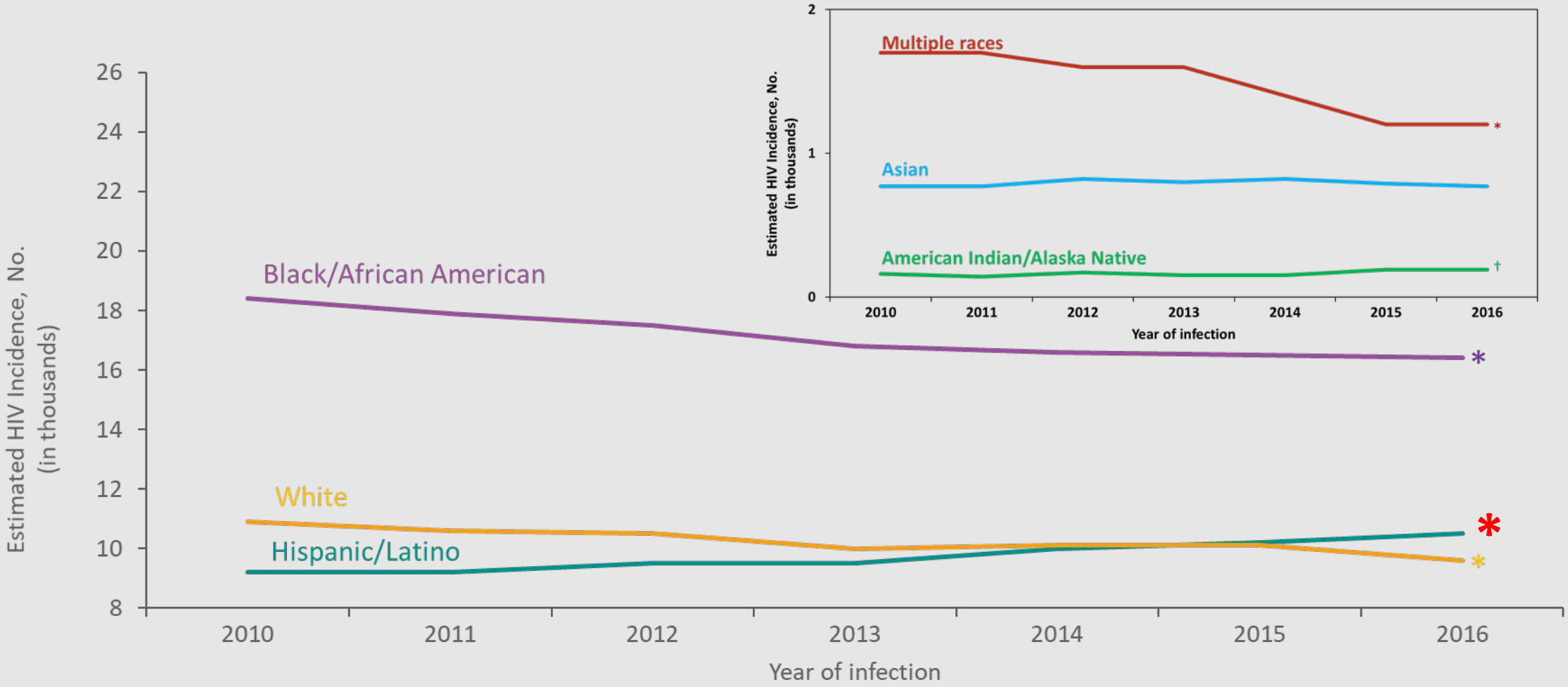
Estimated HIV Incidence among Persons Aged ≥13 Years

2010–2016—United States



Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Bars indicate the range of the lower and upper bounds of the 95% confidence intervals for the point estimate.

Estimated HIV Incidence among Persons Aged ≥13 Years, by Race/Ethnicity 2010–2016—United States

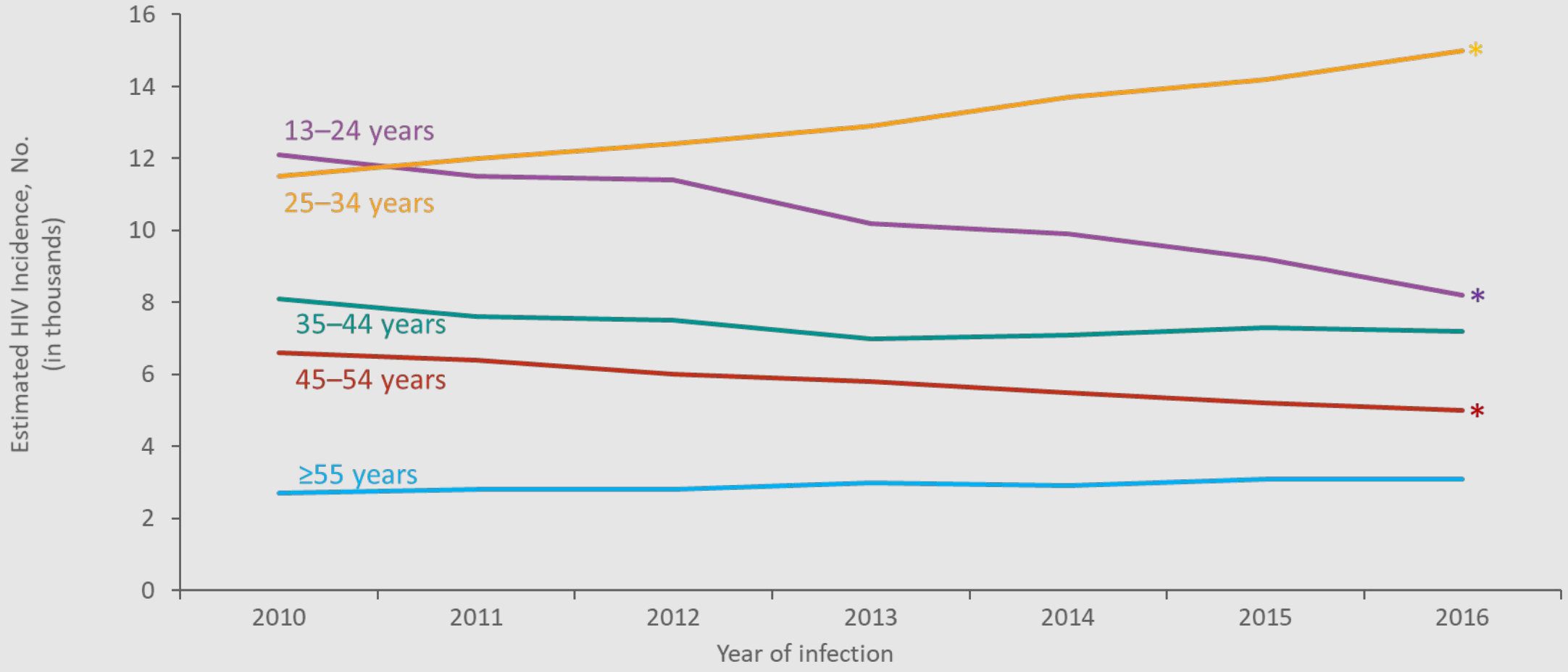


Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Hispanics/Latinos can be of any race.

* Difference from the 2010 estimate was deemed statistically significant ($P < .05$).

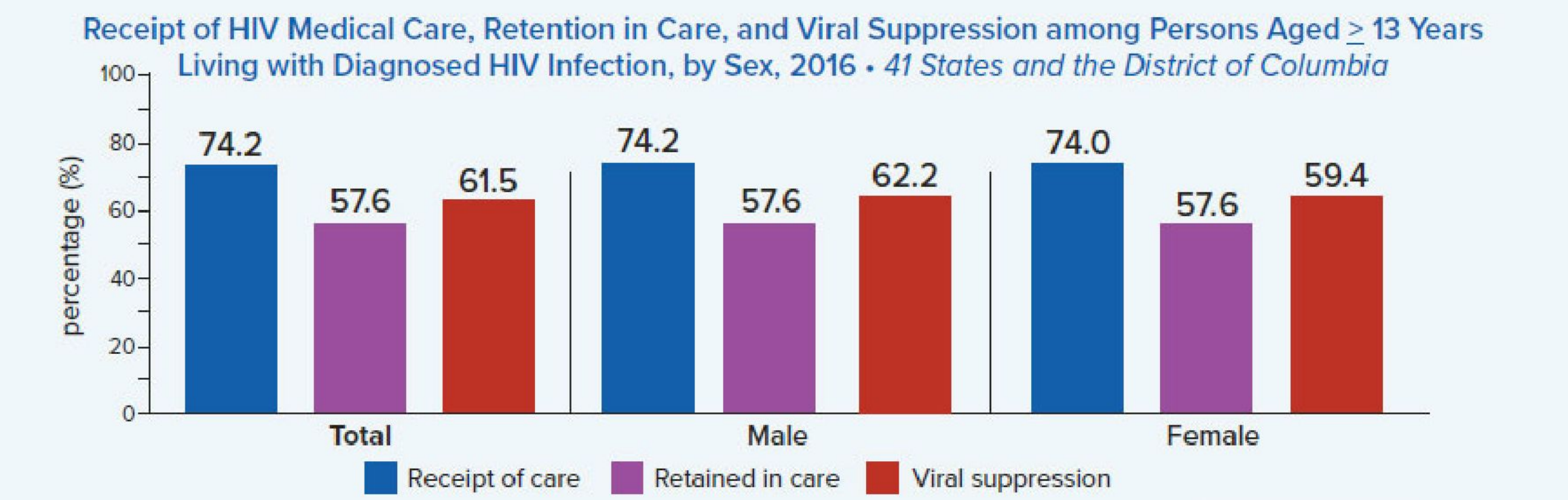
† Estimates should be used with caution because they do not meet the standard of reliability.

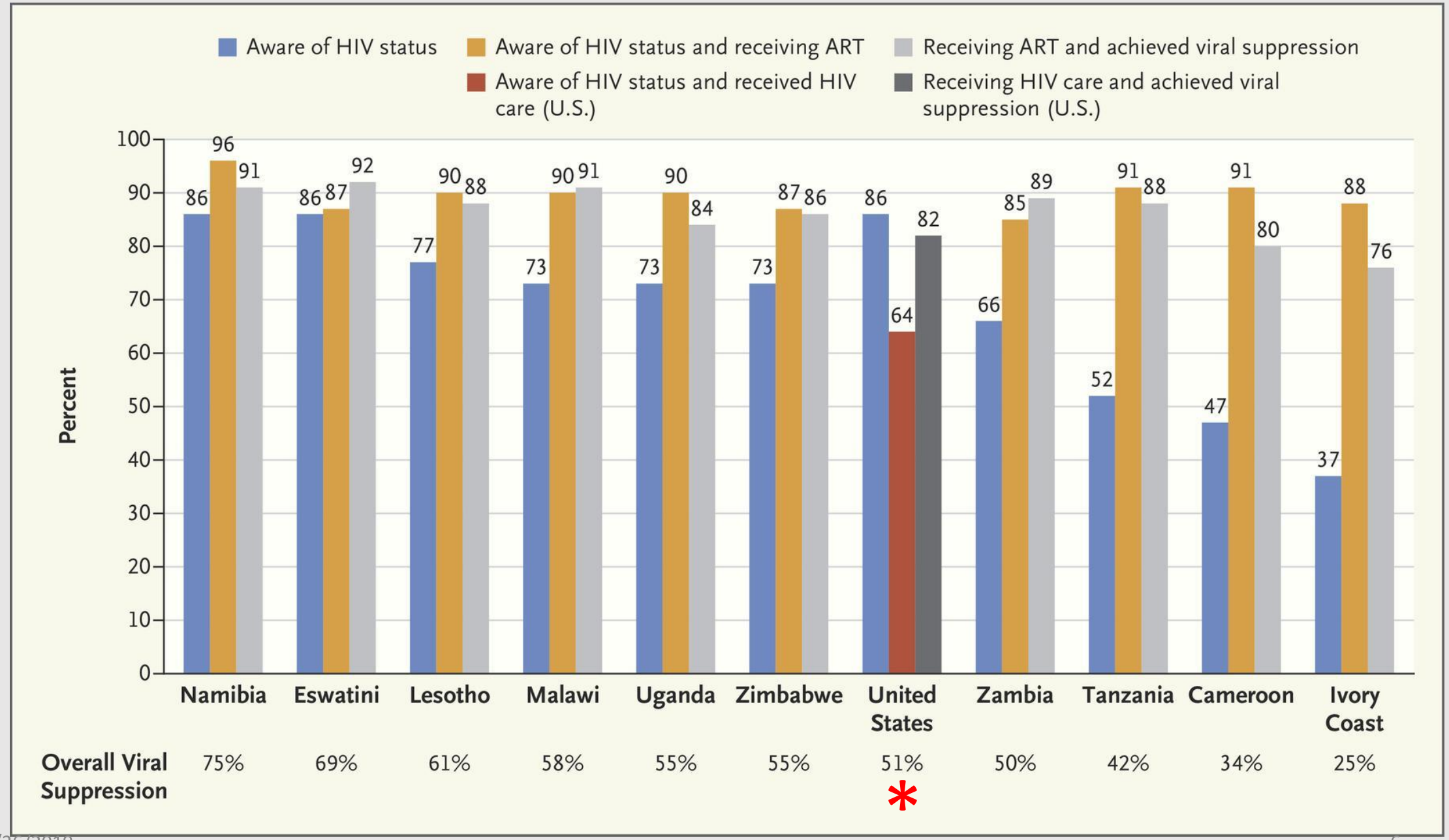
Estimated HIV Incidence among Persons Aged ≥13 Years, by Age 2010–2016—United States



Note. Estimates were derived from a CD4 depletion model using HIV surveillance data.
* Difference from the 2010 estimate was deemed statistically significant (P < .05).

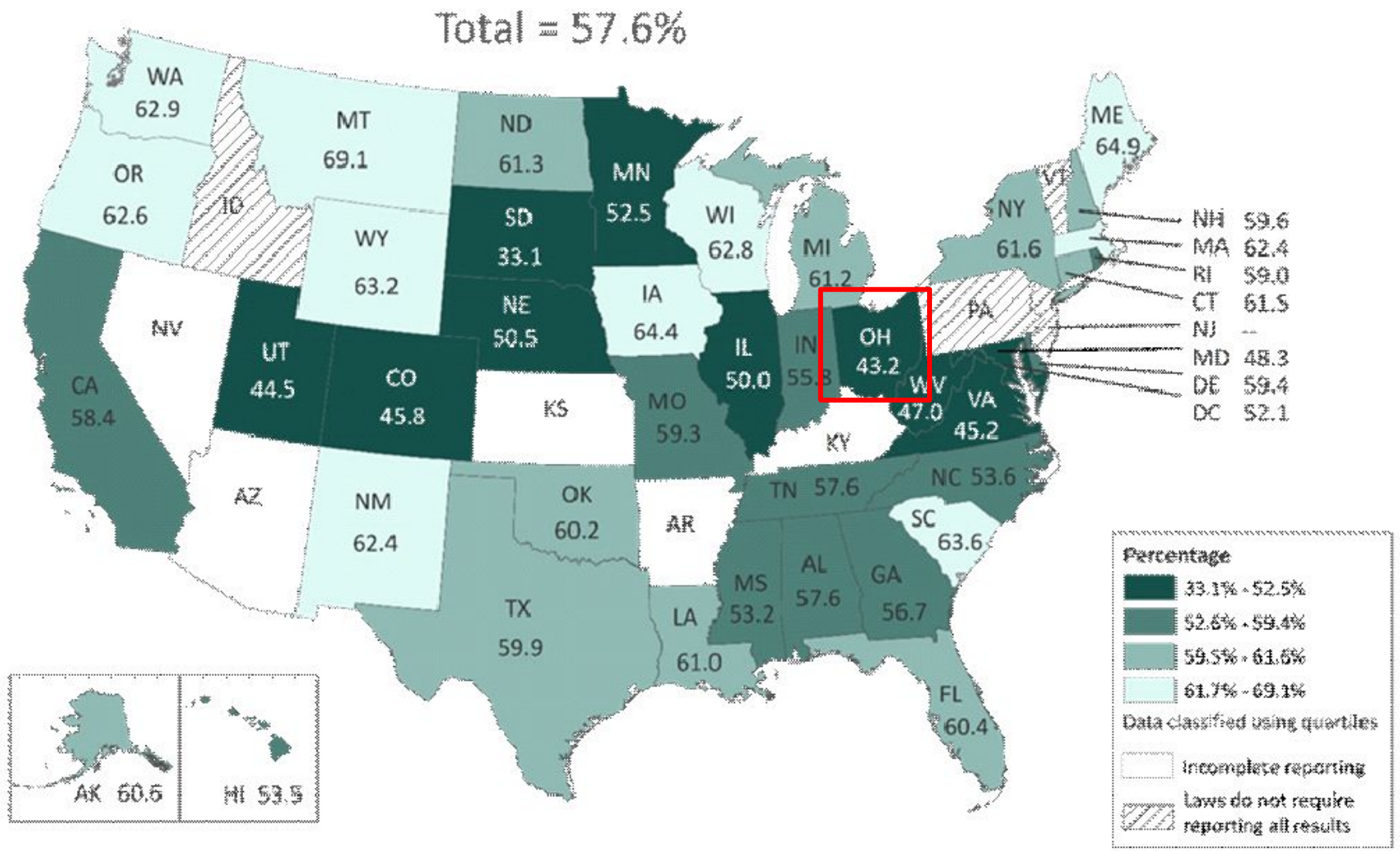
Care Continuum US





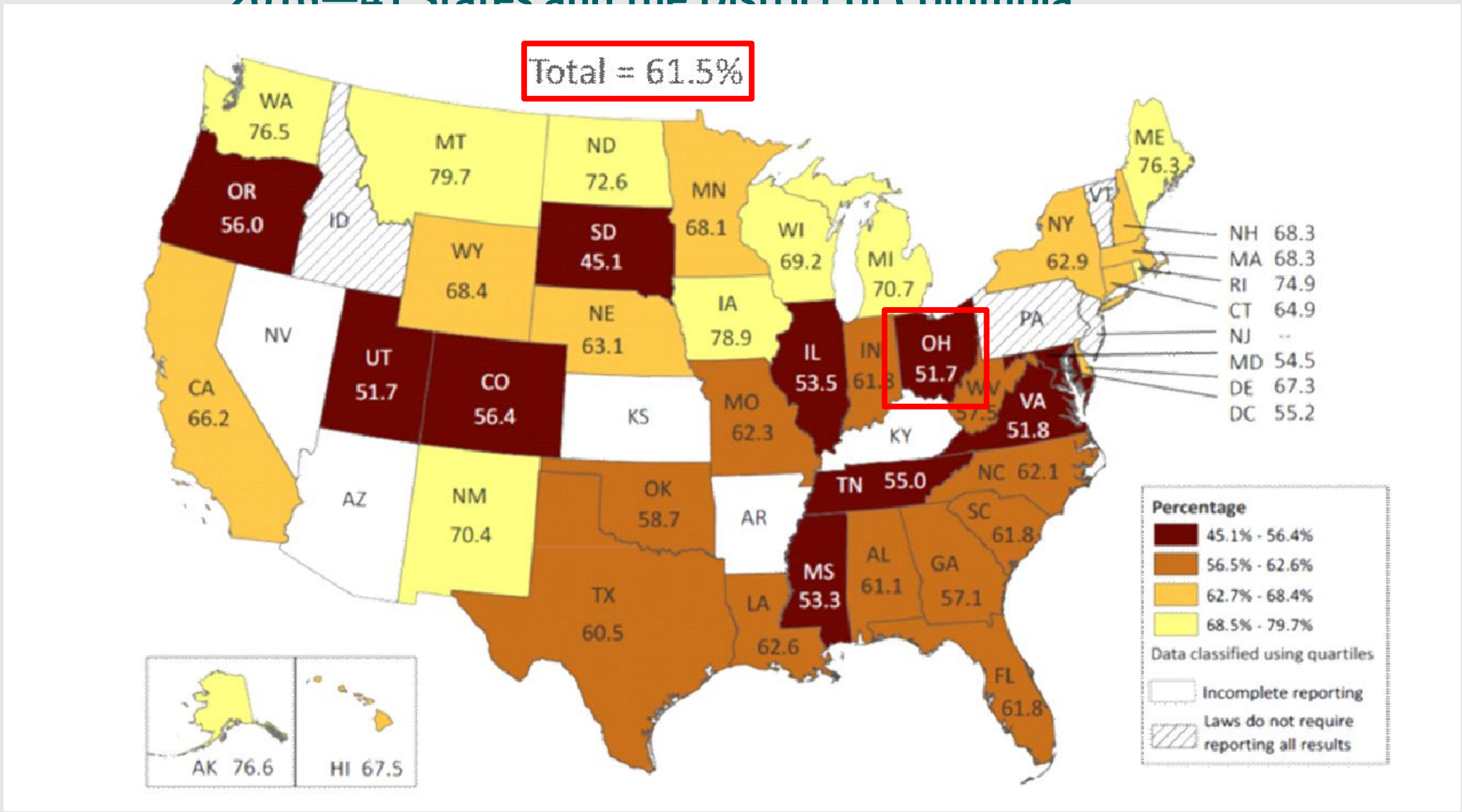
N Engl J Med 2019; 380:1985-1987

Retention in HIV Medical Care among Persons Aged ≥13 Years Living with Diagnosed HIV



Note. Retained in continuous medical care was defined as ≥2 tests (CD4 or VL) ≥3 months apart in 2016. Residence was based on most recent known address as of year-end 2016.

Viral Suppression among Persons Aged ≥13 Years Living with Diagnosed HIV Infection, 2016—41 States and the District of Columbia



Note. Viral suppression was defined as <200 copies/mL on the most recent VL test in 2016. Residence was based on most recent known address as of year-end 2016.

Background

- For the past five years, clinical guidelines for treatment of HIV recommend ART initiation in all HIV-positive individuals regardless of their CD4 cell count[1-3]
- These updates are further supported by randomized controlled trials and observational studies that have shown that initiation of ART at high CD4 cell counts (≥500 cells/mm^3):[4-5]
  - Reduces the risk of serious AIDS and non-AIDS events
  - Reduces mortality in people living with HIV
- Additional studies have shown that **rapid initiation**, defined as starting therapy on the first day to within 1 week of diagnosis, results in:[6-14]
  - Shorter time to viral suppression
  - Increased retention in care
  - Increased rates of viral suppression
  - Decreased mortality

1. Panel on Antiretroviral Guidelines for Adults and Adolescents, Oct 2017. https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf
2. WHO, 2016, Diagnosis, Treatment and Care for Key Populations. 2016; Available at: http://apps.who.int/iris/bitstream/10665/246200/1/9789241511124-eng.pdf?ua=1
3. EACS Guidelines, Version 9.0, October 2017. http://www.eacsociety.org/guidelines/eacs-guidelines/eacs-guidelines.html
4. The INSIGHT START Study Group. N Engl J Med 2015;373:795-807
5. Temprano ANRS Study Group. N Eng J Med. 2015;373:808-822
6. Ford N, et al. AIDS 2018;32:17-23
7. Rosen S, et al. PLOS Medicine 2016;13(5):e1002015
8. Koenig S, et al. PLOS Medicine 2017;14(7):e1002357
9. Seekaew P, et al. AIDS 2018. Amsterdam, NL. THAC0403
10. Zhao Y, et al. CID 2018;66(5):727–34
11. Rosen S, et al. AIDS 2018. Amsterdam, NL. LBPEE0049
12. Pilcher C, et al. JAIDS 2017;74:44-51
13. Colasanti J, et al. CROI 2018. Boston, MA. 1109
14. Halperin J, et al. AIDS Pt Care STDs 2018;32:39-41

Research Supporting Early Treatment Initiation

Early ART is Preferred over Delayed

- START *Global*
- TEMPRANO *Ivory Coast*

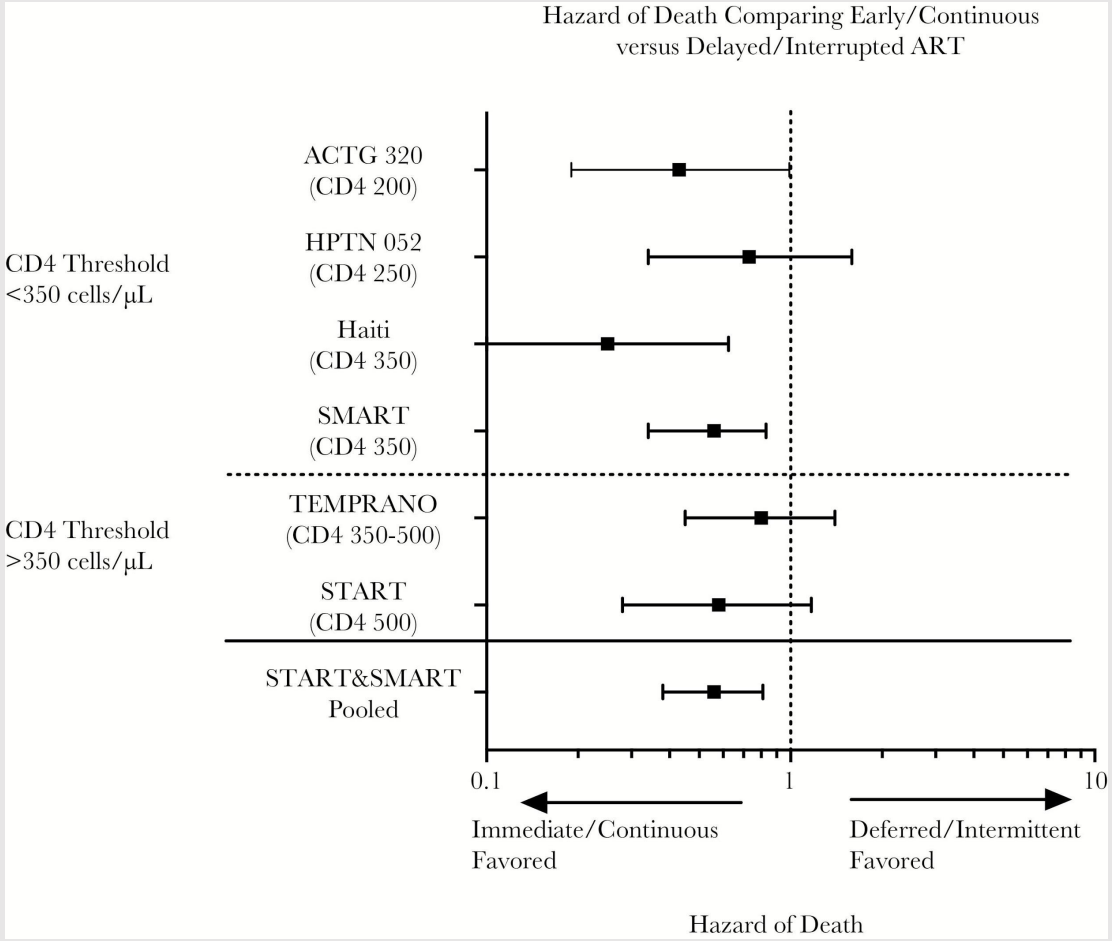
Rapid ART Programs Demonstrate Benefits

- RapIT *South Africa*
- Same-Day ART *Haiti*
- Same-Day ART *Bangkok*
- Retrospective Cohort *China*
- SLATE South Africa and Kenya
- RAPID *San Francisco*
- Acute HIV Consortium *North Carolina - Duke/UNC*
- REACH *Atlanta* - Emory/Grady
- CrescentCare Start Initiative *New Orleans*
- JumpstART Program *New York City*

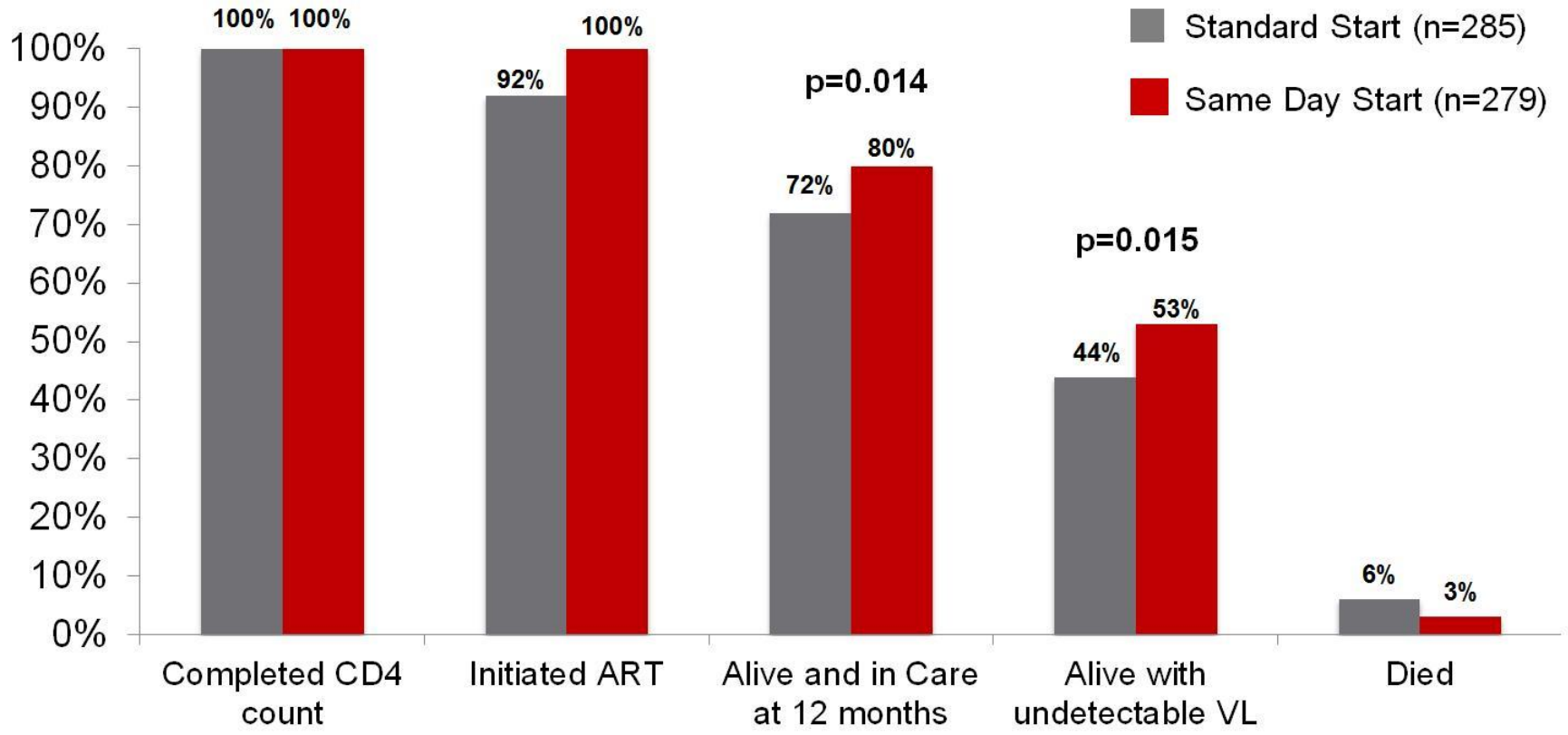
Smart and Start Trials

Benefits of Early Continuous Therapy

Figure 1. Relative hazard of mortality with combination antiretroviral therapy in randomized clinical trials [8–13]. ...



Results: Standard vs Same-Day ART Start



Same-day ART improved retention with virologic suppression and decreased mortality

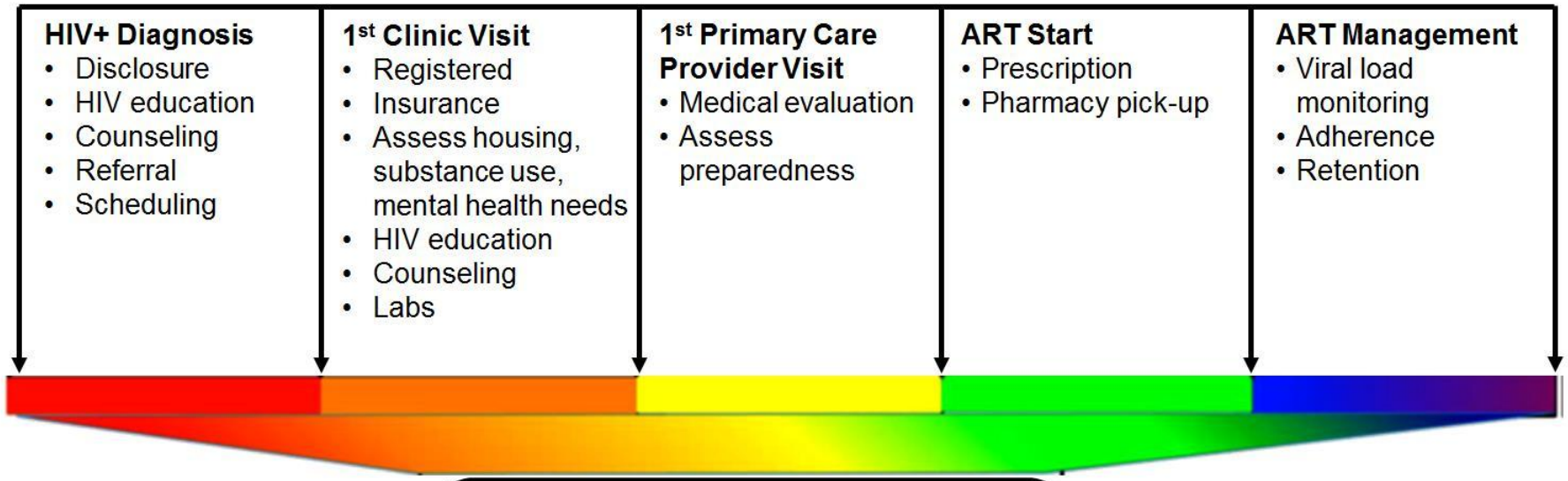
Koenig S, et al. PLOS Medicine. https://doi.org/10.1371/journal.pmed.1002357 July 25, 2017

RAPID Program Interventions

- Same-day access to an HIV provider
- Same-day medical visit including:
  - HIV education, risk reduction, sexual health and benefits of ART
  - Possible contraindications of ART discussed
  - Baseline laboratory tests drawn but not typically available prior to ART start
    - Included: CD4 cell count, HIV viral load, renal and liver function tests, hepatitis serologies, HLA B*5701 testing, HIV resistance genotyping
  - Accelerated insurance approval process
  - Preapproved ART regimens
  - Five day starter packs if needed were available
  - Directly observed administration of first dose
  - Telephone follow-up by RAPID nurses within the first 7 days

Pilcher C, et al. JAIDS 2017;74:44-51

Standard vs. RAPID Models

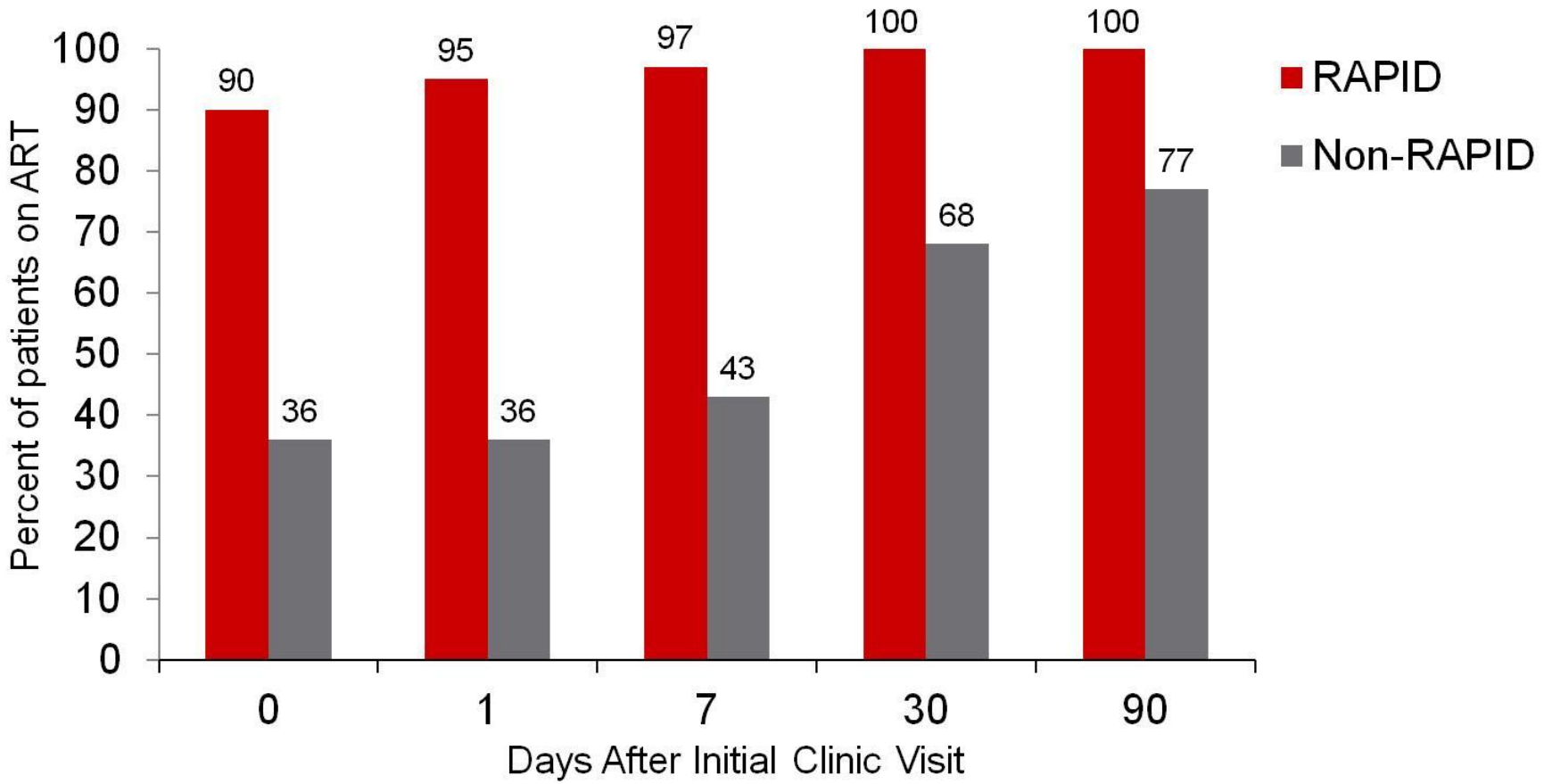


RAPID Visit: ART Start
- Disclosure, counseling
- Registration
- Insurance
- Assess housing, substance use, mental health needs
- Labs
- HIV education
- Counseling
- Medical evaluation
- Assess preparedness
- ART dispensed
- Telephone follow-up

Primary Care Provider Visits: ART Management
- Viral load monitoring
- ART management
- Adherence
- Retention

Pilcher C, et al. JAIDS 2017;74:44-51

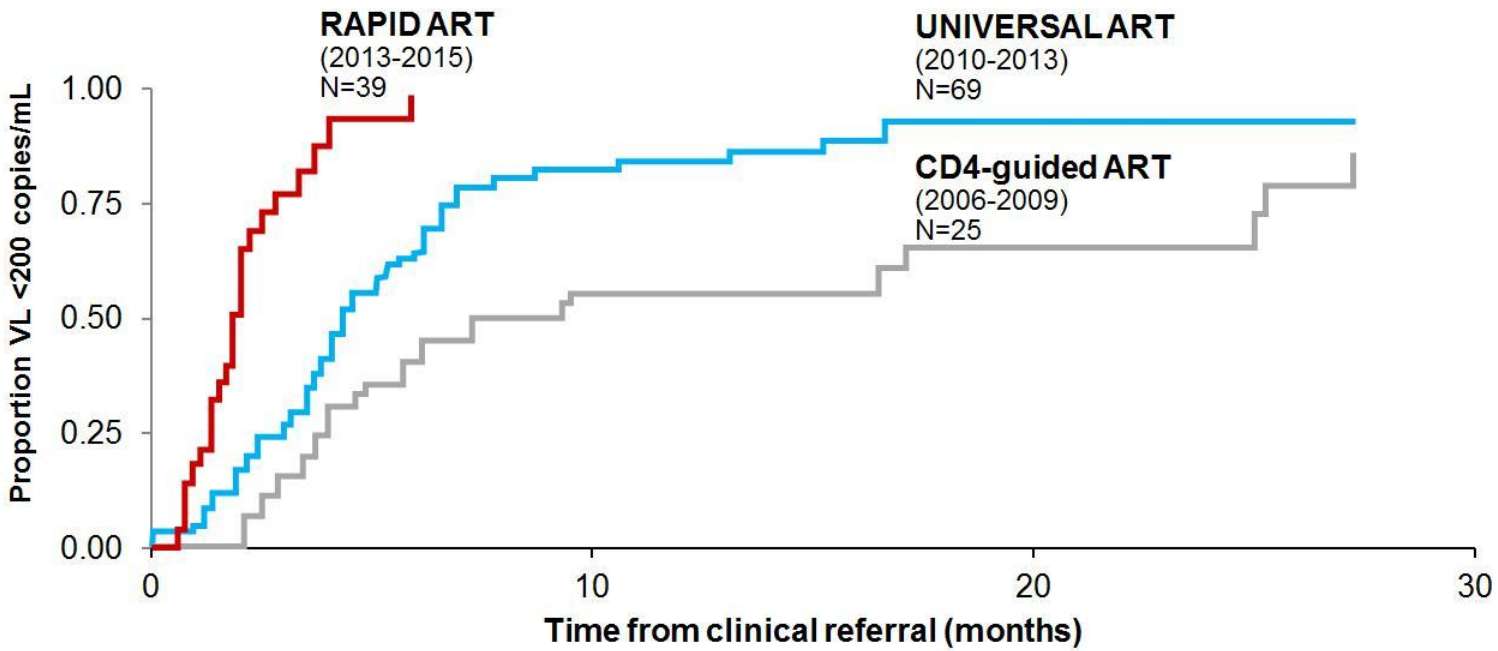
Results – Patients on ART by Days After Initial Visit



Day 0 = took their first dose in the clinic on their first visit
Day 1 = took their first dose within 24 hours of their first visit

Pilcher C, et al. JAIDS 2017;74:44-51

Results – Time to Viral Suppression



Pilcher C, et al. JAIDS 2017;74:44-51

Rapid ART Program Initiative for HIV Diagnoses (RAPID)

Citywide RAPID protocol, confirmed diagnoses and linked to care in ≤ 5 days between 2013 to 2016

- ART included (FTC/TDF or FTC/TAF) + (INSTI or DRV/r)

	2013	2014	2015	2016	%Δ 2013 - 2016
Diagnosed, n	399	329	295	265	-
In Care within 1 year (%)	372 (93)	318 (97)	282 (96)	258 (97)	-
Diagnosis to 1st Care Visit (days*)	8	7	7	5	-38%
1st Care Visit to ART (days*)	27	17	6	1	-96%
ART to VL <200 c/mL (days*)	70	53	50	38	-46%
Diagnosis to VL <200 c/mL (days*)	134	92	77	61	-54%

Time from diagnosis to virologic suppression was cut by more than half from 134 days to 61 days. This benefit persisted in traditionally vulnerable populations, including racial/ethnic minorities and the homeless

* Median

Bacon O, et al. CROI 2018. Boston, MA. Oral 93

Bacon O, et al. CROI 2018. Boston, MA. Oral 93

RAPID ART Program for HIV Diagnoses (RAPID) in San Francisco

- Linkage to care within 5 working days
- Labs, counseling, medical/ psychosocial assessment, ART start at first care visit
  - (INSTI or DRV/RTV) + FTC/TDF*
- HIV clinics identified using HIV surveillance data, RAPID Provider Directory identified best clinic for each patient

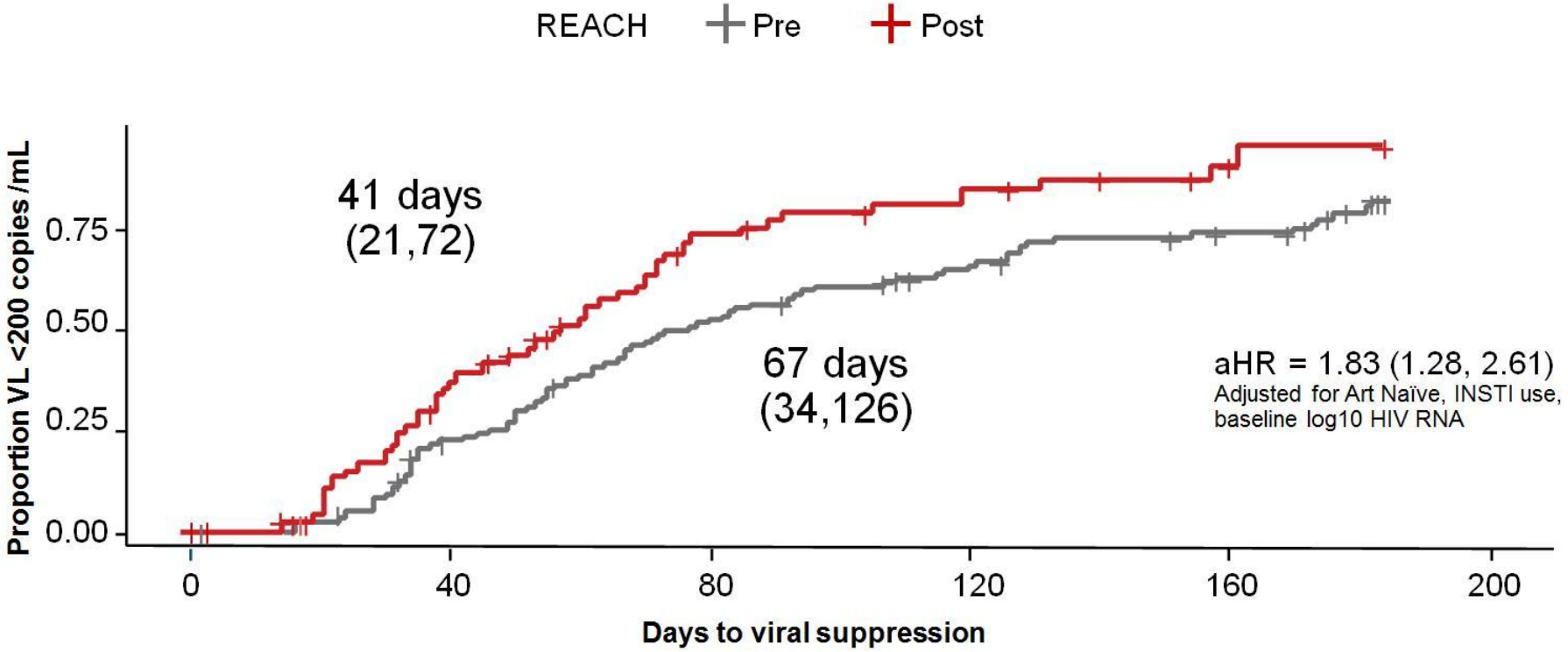
*4-drug regimen optional if HIV infection suspected to have occurred while on PrEP.

- Time to first virologic suppression decreased > 50% from 134 days to 61 days and time from care linkage to ART start decreased 96% from 27 days to 1 day
- Time to ART start and first viral suppression decreased in vulnerable populations, including racial/ethnic minorities and homeless patients
  - Disparities still exist for some outcomes

Bacon O, et al. CROI 2018. Abstract O93.

REACH - Rapid Entry and ART Clinic for HIV (Atlanta - Emory University/Grady Health System)

Primary Endpoint: Time to Viral Suppression



Patients at Risk	Day	0	40	80	120	160	200
	Pre-REACH	117	81	50	33	22	0
	Post-REACH	90	47	16	8	3	0

Colasanti J, et al. CROI 2018. Boston, MA. Poster 1109

IAS-USA: Laboratory Recommendations

- Labs below should be drawn before beginning ART, but treatment may be started before results are available

Laboratory tests for ART initiation:
• HIV-1 RNA level
• CD4 cell count
• HIV genotype for NRTI, NNRTI, and PI
• Laboratory tests to exclude active viral hepatitis
• Chemistries

Result of testing for HLA-B*5701 allele should be available if an abacavir-containing regimen is anticipated

Unless preexisting kidney or liver damage or high likelihood of transmitted drug resistance exists, the results of these tests should not delay start of ART

Saag M, et al. JAMA 2018;320(4):379-396. https://www.iasusa.org/guidelines

Rapid Initiation of ART: Key Regimen Considerations

NRTI Backbone	3rd agent
▪ **FTC/TAF** – No dose adjustment eGFR ≥ 30 mL/min[1] ▪ **FTC/TDF** – Dose adjust eGFR < 50 mL/min[2] ▪ **ABC/3TC** – Not appropriate for rapid initiation[3,4] ▪ Requires HLA-B*5701 ▪ Inadequate HBV activity; requires HBsAg ▪ Not recommended for eGFR < 50 mL/min[5]	▪ **NNRTIs** – Generally not recommended due to potential for transmitted resistance[3]

Considerations when initiating rapid ART when laboratory results are pending

1. Descovy Prescribing Information. Sept 2017.
2. Truvada Prescribing Information. May 2018
3. Saag M, et al. JAMA 2018;320(4):379-396. https://www.iasusa.org/guidelines
4. SFDPH. Rapid ART Program Initiative. March 2018. Available at: https://www.gettingtozerosf.org/wp-content/uploads/2017/05/RAPID_Provider_final_v2_high-res-1.pdf
5. Epzicom Prescribing Information. April 2018.

Rapid ART Initiation Recommendations

- ART initiation, including rapid start, is recommended for all infected ambulatory patients committed to starting ART* or for those with unclear HIV diagnosis

Recommended Regimens for Rapid ART Initiation
BIC/FTC/TAF
DTG + FTC** + TAF†
Boosted DRV + FTC** + TAF†

Regimens containing NNRTIs or ABC†† should not be used for rapid ART initiation

- Structural barriers that delay receipt of ART should be removed to allow newly diagnosed persons to receive ART at the first clinic visit after diagnosis, if they and their clinician determine that this approach is appropriate

*Unless the patient has symptoms that suggest an opportunistic infection for which immediate ART is contraindicated
**(or 3TC) †(or TDF)
††Patients requiring ABC should not begin until the result of testing for the HLAB* 5701 allele is available

Saag M, et al. JAMA 2018;320(4):379-396. https://www.iasusa.org/guidelines

Choosing Integrase Inhibitors

Agent	Advantages	Disadvantages
Bictegravir	▪ STR once daily ▪ Available with TAF ▪ Few drug or food interactions ▪ Potentially high barrier to resistance	▪ Least amount of data ▪ Only available as STR with TAF/FTC
Dolutegravir	▪ Only non-TFV QD STR ▪ High barrier to resistance ▪ Few drug or food interactions ▪ Active against some RAL- and EVG-resistant viruses	▪ STR only with ABC/3TC ▪ Increases metformin levels
Elvitegravir	▪ STR once daily ▪ Available with TAF and TDF	▪ Requires COBI boosting ▪ COBI drug interactions
Raltegravir	▪ Longest experience ▪ Few drug or food interactions	▪ Multiple pills ▪ No STR

Rapid ART Initiation Recommendations

- **ART initiation, including rapid start, is recommended for all infected ambulatory patients committed to starting ART* or for those with unclear HIV diagnosis** (eg, discordant serologic or rapid test results)
- Structural barriers that delay receipt of ART should be removed to allow newly diagnosed persons to receive ART at the first clinic visit after diagnosis, if they and their clinician determine that this approach is appropriate
- All elements of conventional treatment initiation must be in place at the treatment site but provided in a way that ensures immediate access

*Unless the patient has symptoms that suggest an opportunistic infection for which immediate ART is contraindicated

Saag M, et al. JAMA 2018;320(4):379-396. https://www.iasusa.org/guidelines

Rapid ART Initiation – Potential Benefits and Limitations

Potential Benefits

- Better clinical outcomes due to less time off ART
- Engagement opportunity to increase retention in care
- Shorter time to treatment decreases anxiety, increases trust
- Public health benefit: decreased transmission risk

Potential Limitations

- ART may not be optimized (HBV, renal insufficiency)
- OIs requiring delayed ART may not be ruled out
- Less time to address barriers to ART and adherence
- Risk of resistance if low barrier regimen used
- Requires change in work-flow with rapid access (access, appointment scheduling, staffing)

Implementation research is needed to better understand benefits and limitations in real world settings

“And Now the Rest of the Story”

(Paul Harvey)

- Retention
  - Valid contact information
  - Appointment reminders: paper, phone, text – best practices
- Adherence
  - Counseling - everyone
  - Reminders – calls, texts
  - Smart phone alerts

How can we do better?

- Dr. Avery……..
- Dr. Gripshover……..
- Jen- McMillian-Smith……..
- Amy Hirsch……..
- Audience……..

Summary

- Randomized clinical trials show that deferring therapy based on CD4 count results in increased morbidity and mortality
- Rapid ART initiation is recommended in US and international HIV Guidelines
- Randomized clinical trials and observational trials evaluating rapid ART initiation show clinical benefits for patients, including:
  - Shorter time to viral suppression
  - Increased rates of viral suppression
  - Increased retention in care
  - Decreased mortality
- Public health benefits of decreased transmission may be realized with earlier suppression of HIV viral load