HIV 101 and Renal Function

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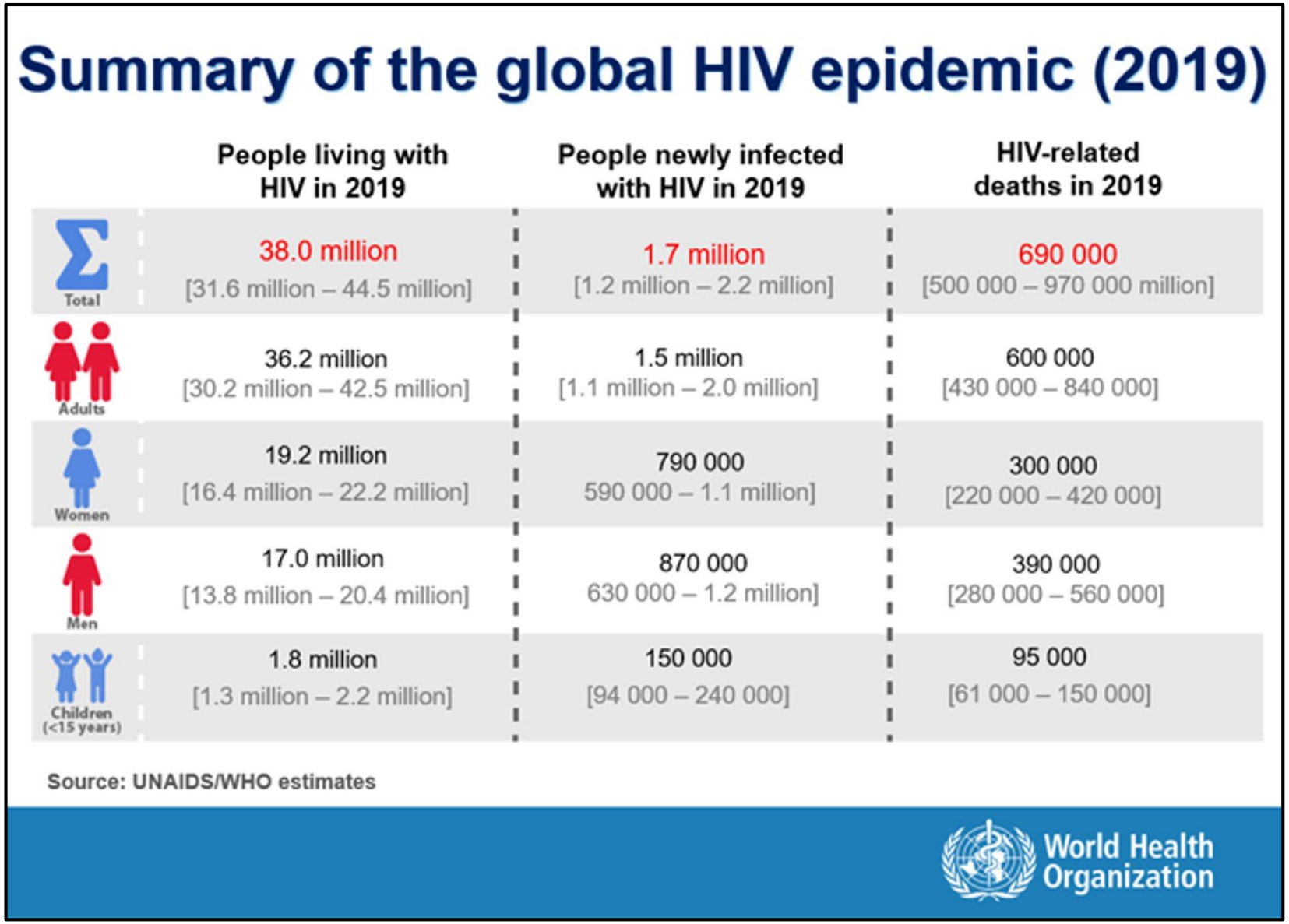
Disclaimer

This presentation is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $3,139,511.00 with zero percent financed with nongovernmental sources. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS or the U.S. Government.

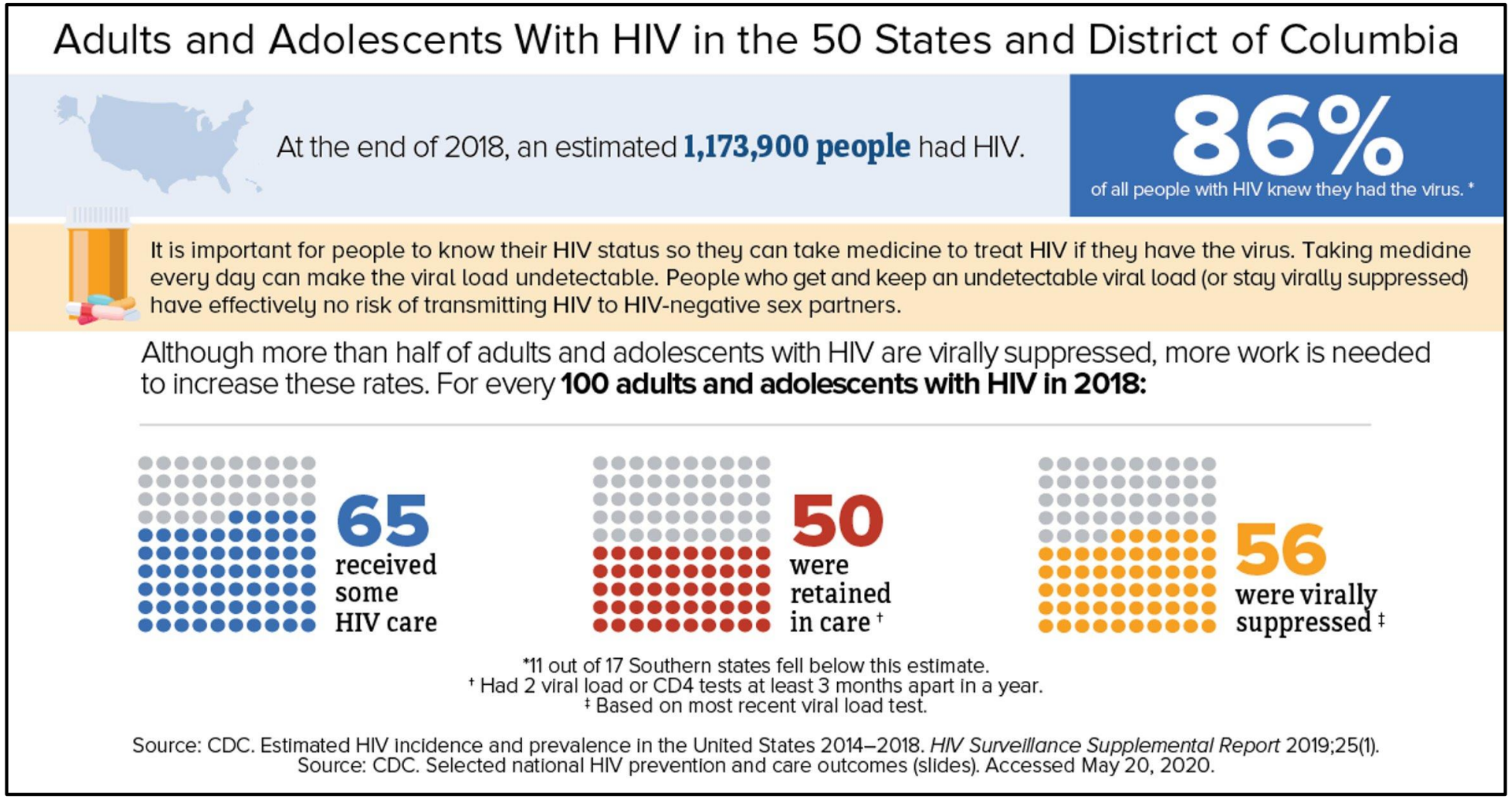
Outline of Topics

1. HIV epidemic overview
2. Antiretroviral therapy (ART) basics
3. Initiating ART
4. Primary care resources for people with HIV
5. Renal considerations with HIV
    A. Treatment toxicity
    B. HIV associated nephropathies
    C. AKI
    D. Comorbid CKD
6. Hemodialysis and HIV
7. Transplant and HIV

HIV Worldwide



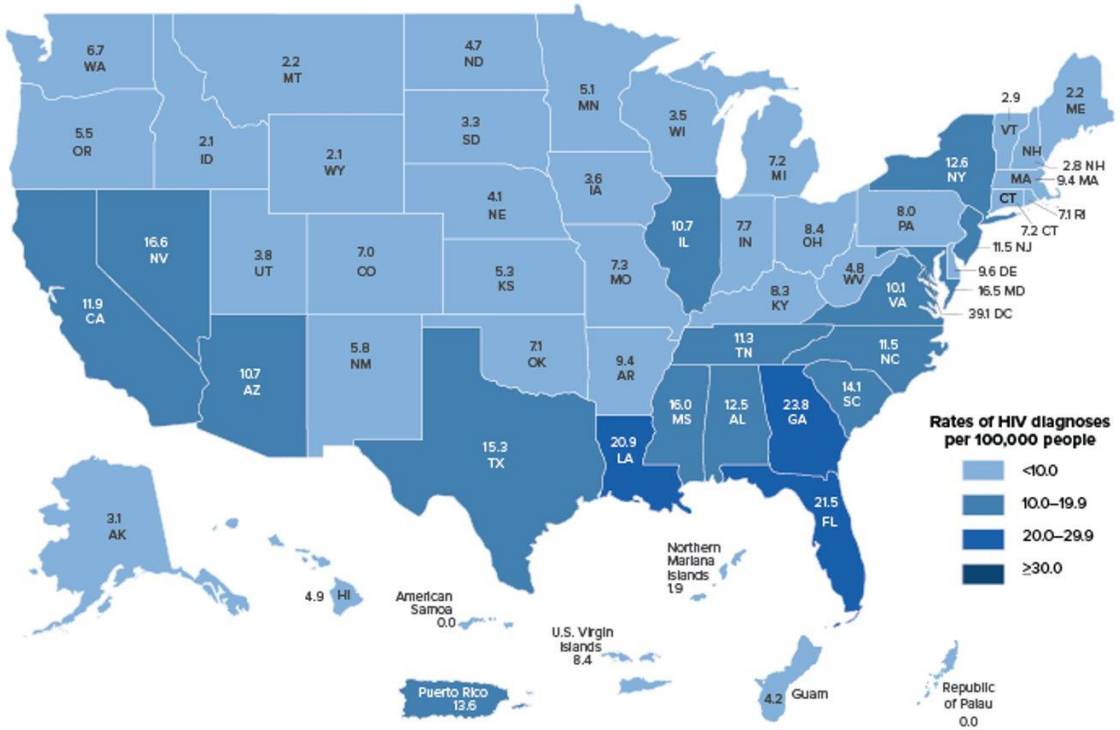
HIV in the United States



HIV Rates Vary Across the US

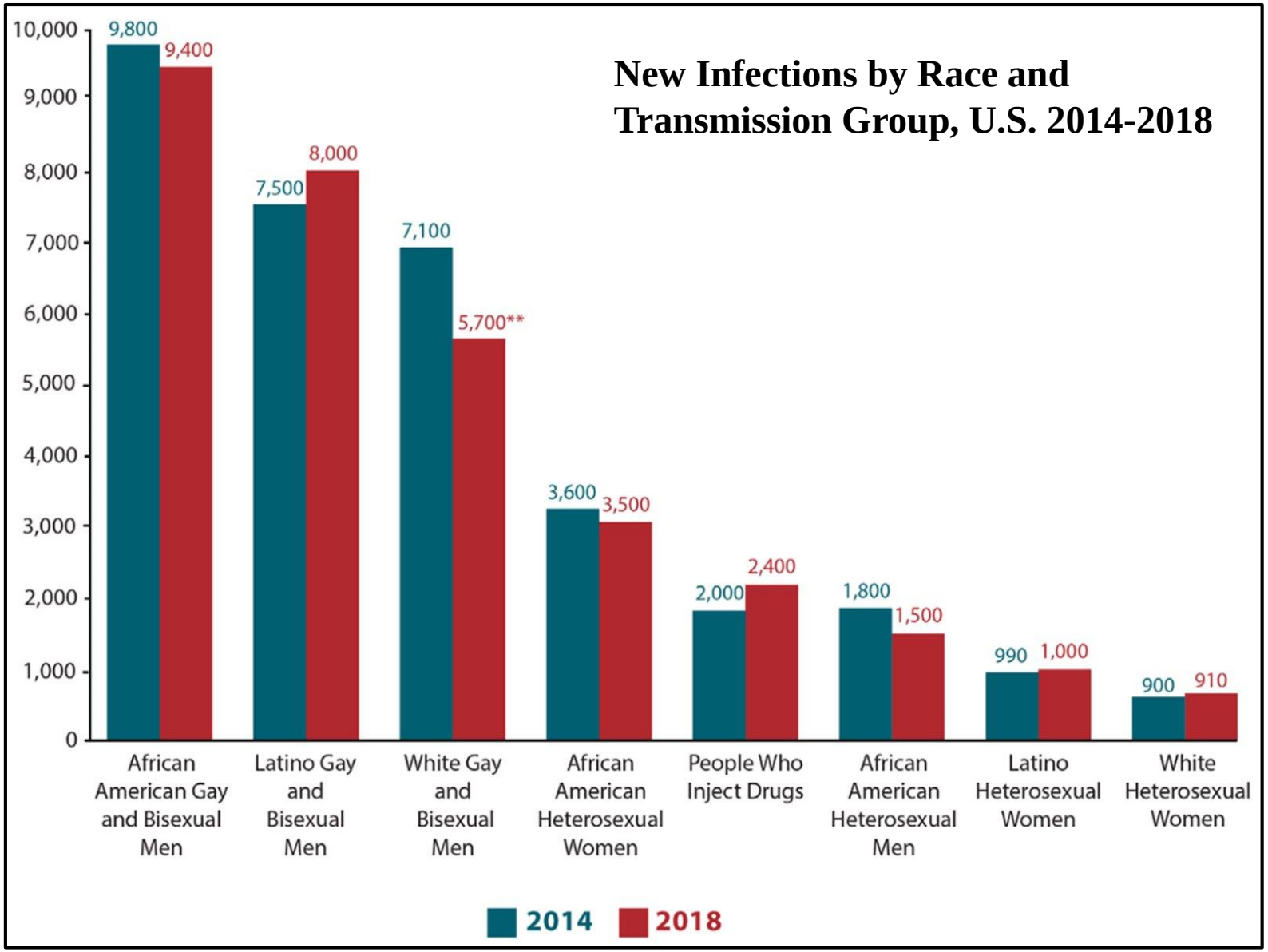
Rates of New HIV Diagnoses for Adults and Adolescents in the US and Dependent Areas, 2018

The highest rates of new HIV diagnoses were mainly in the South.



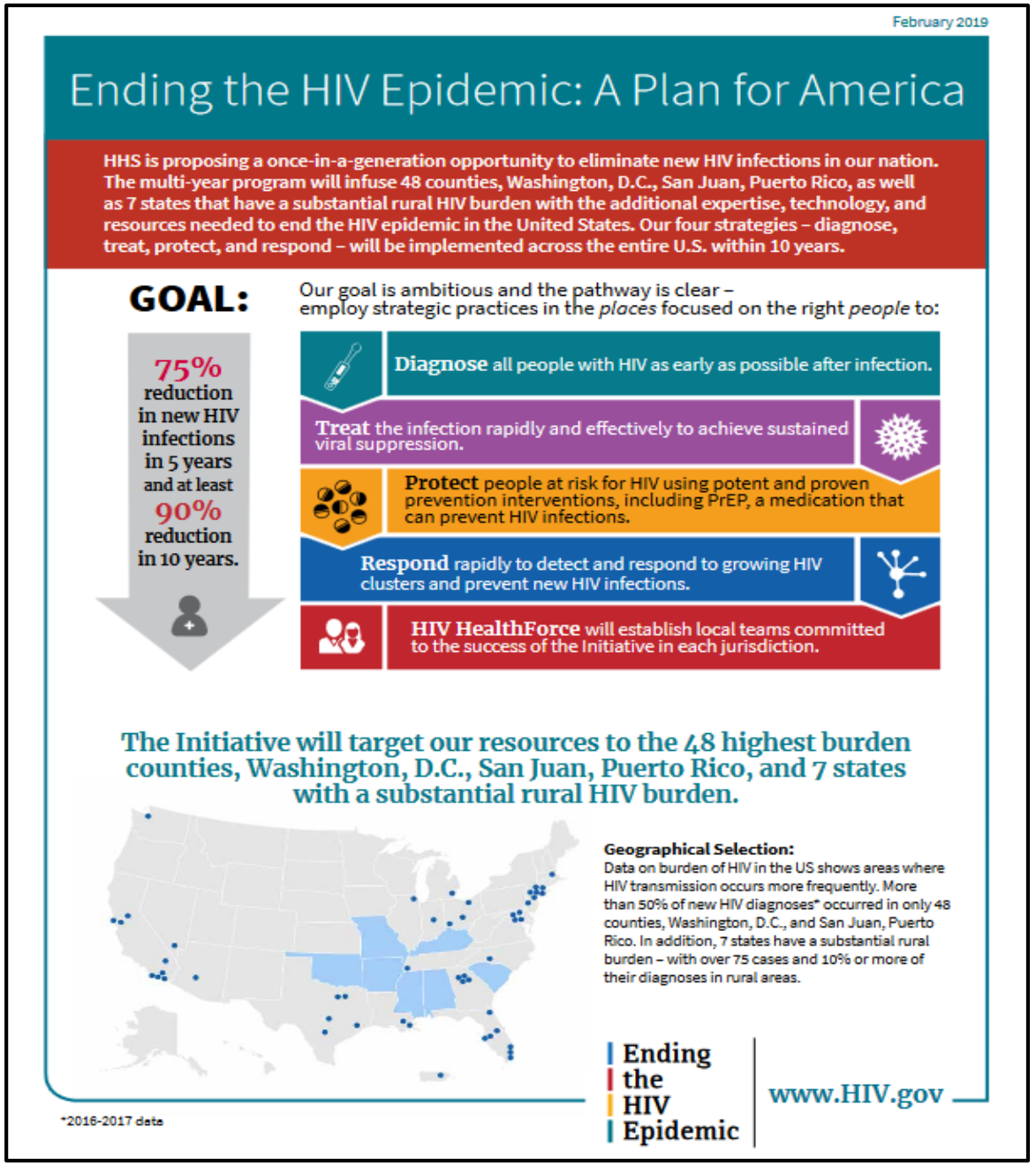
Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2018. *HIV Surveillance Report* 2020;31.

HIV Disparities



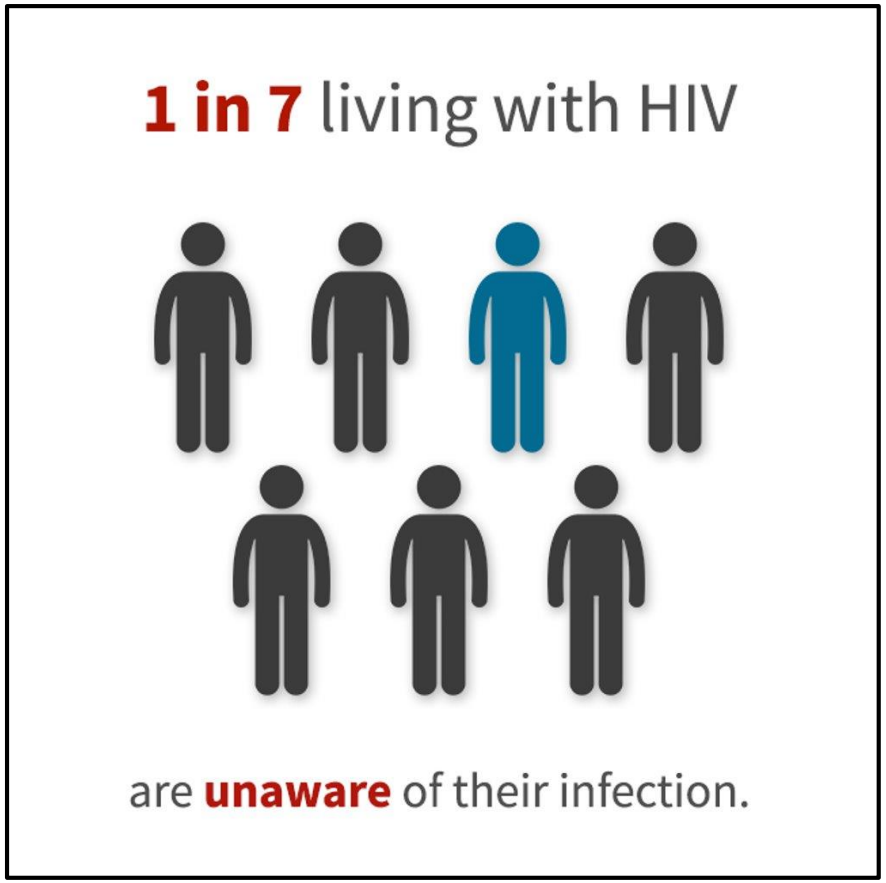
https://www.hiv.gov/hiv-basics/overview/data-and-trends/statistics

Ending the HIV Epidemic



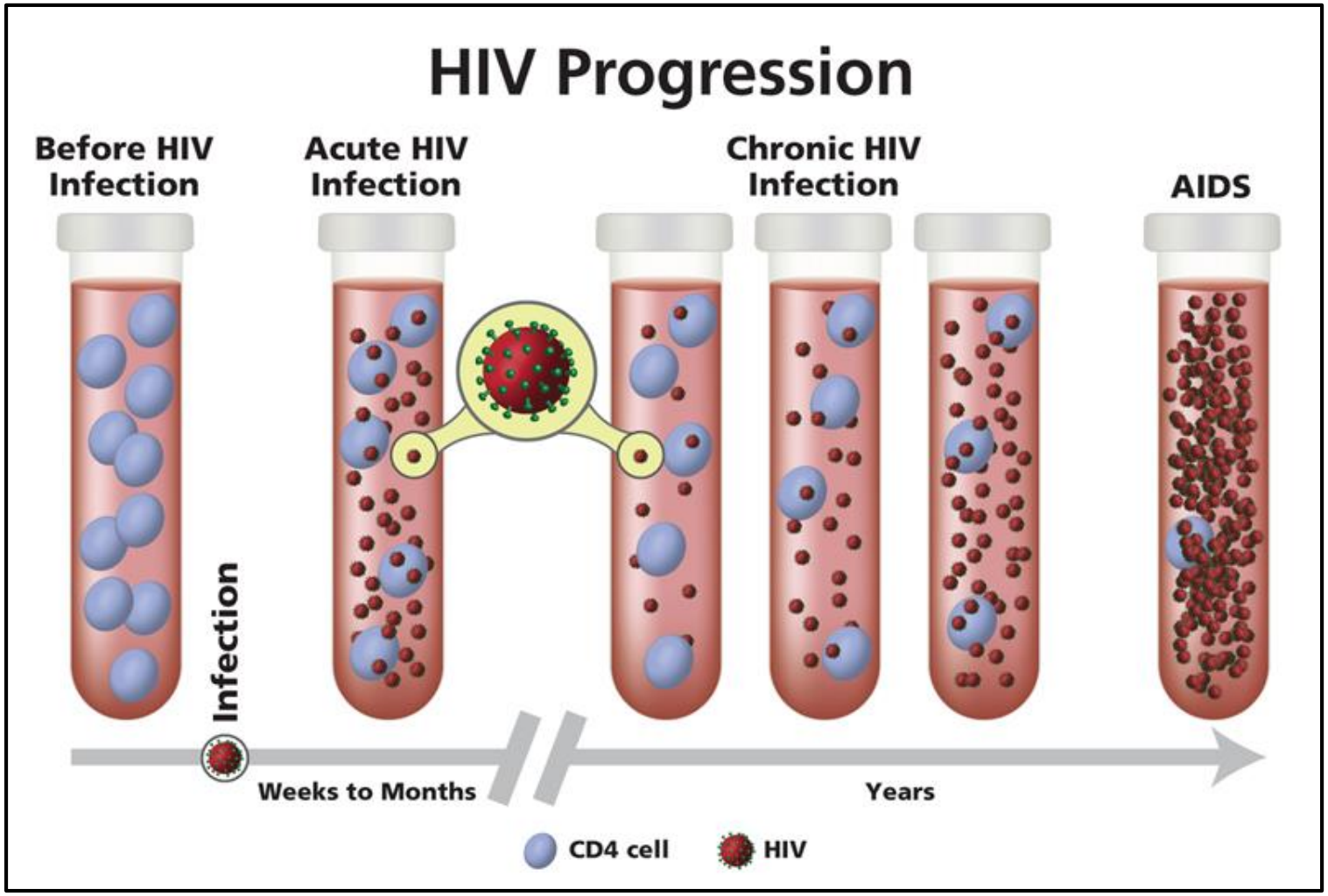
Importance of Testing

An estimated **1.2 million people in the United States aged 13 and older were living with HIV at the end of 2018**



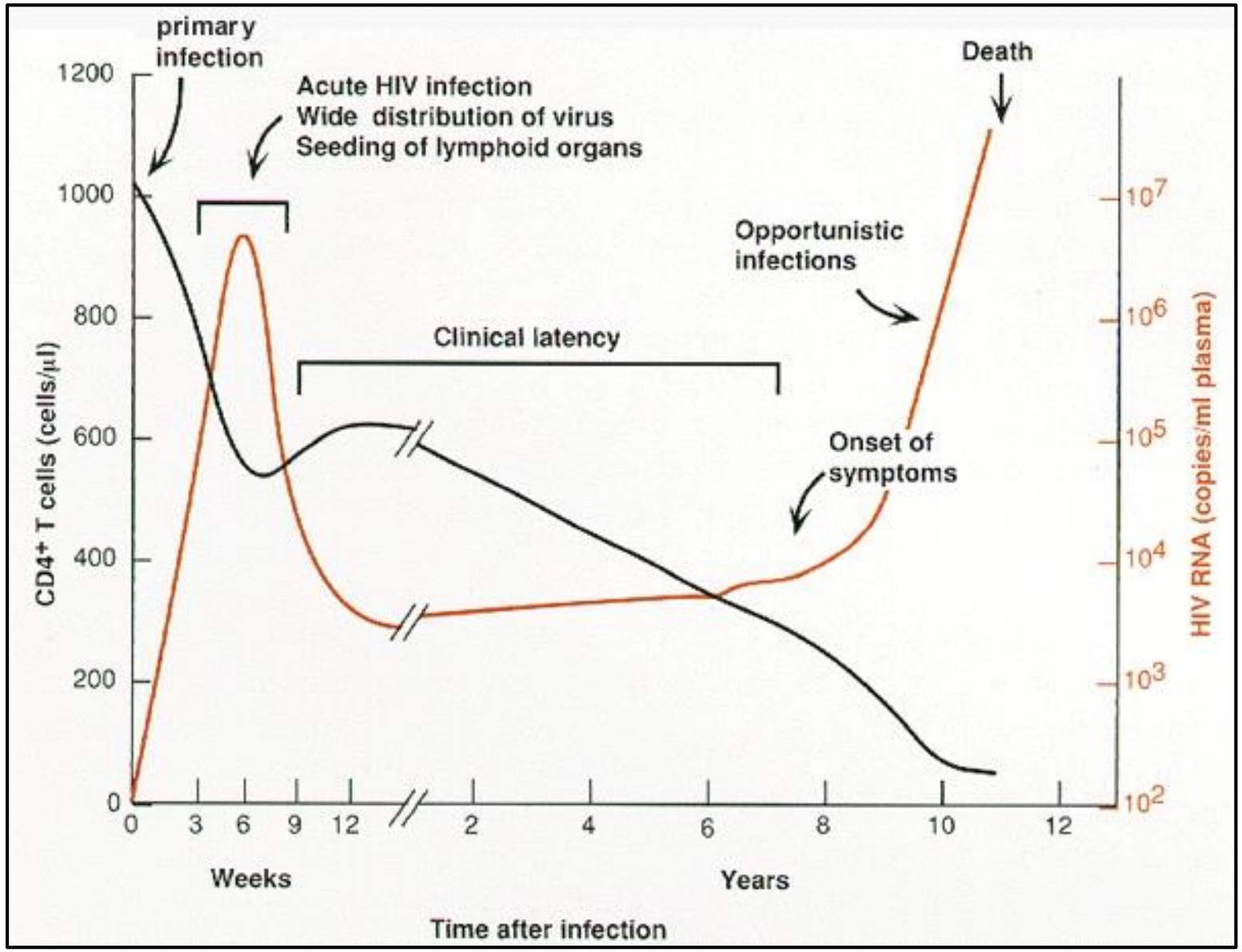
https://www.hiv.gov/hiv-basics/overview/data-and-trends/statistics

Untreated HIV Progression

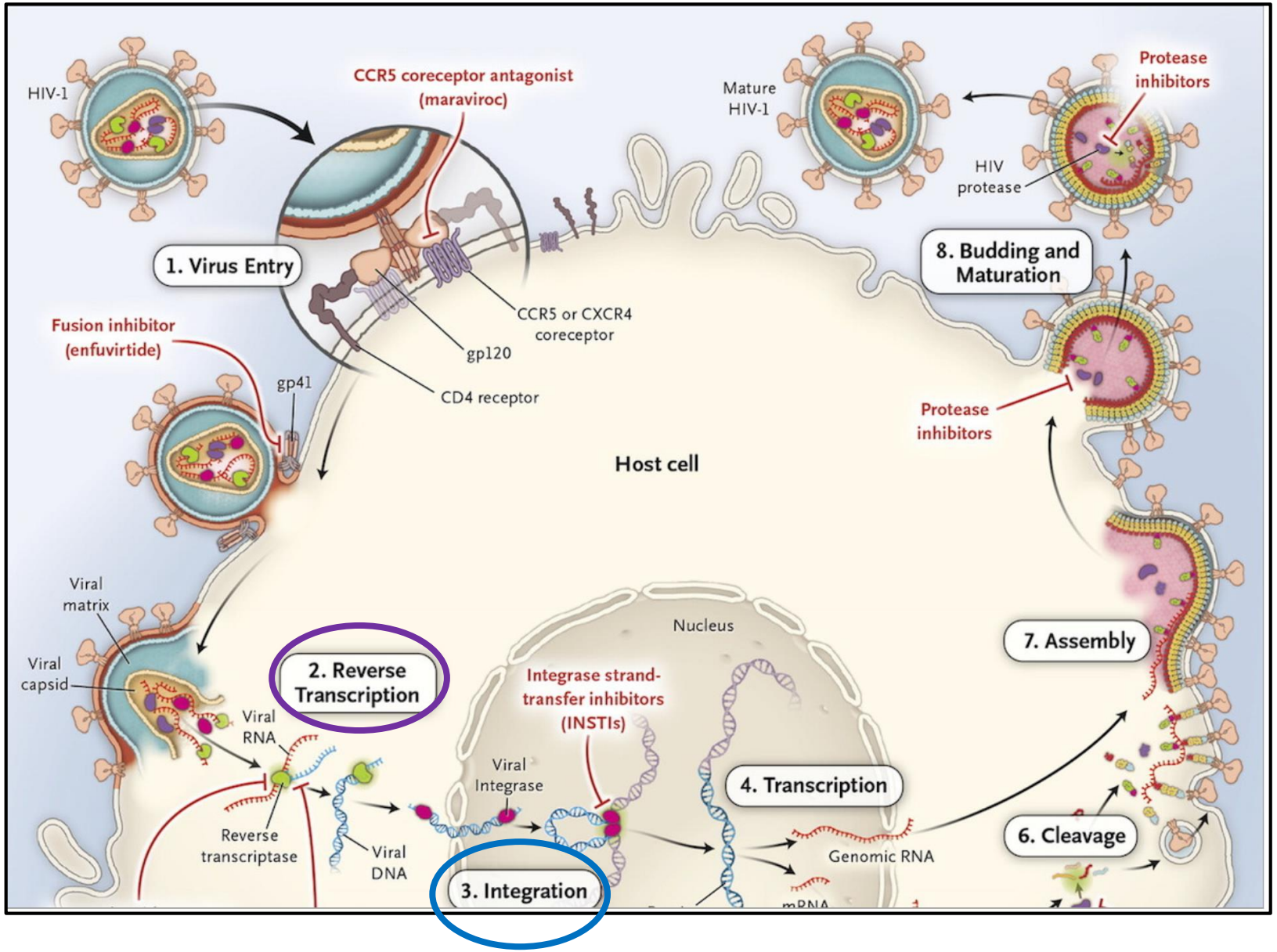


https://clinicalinfo.hiv.gov/en/glossary/hiv-progression

Course of Untreated HIV Infection



Coffin JM, Hughes SH, Varmus HE, editors. Retroviruses. Cold Spring Harbor (NY): Cold Spring Harbor Laboratory Press; 1997. Course of Infection with HIV and SIV. Available from: https://www.ncbi.nlm.nih.gov/books/NBK19374/



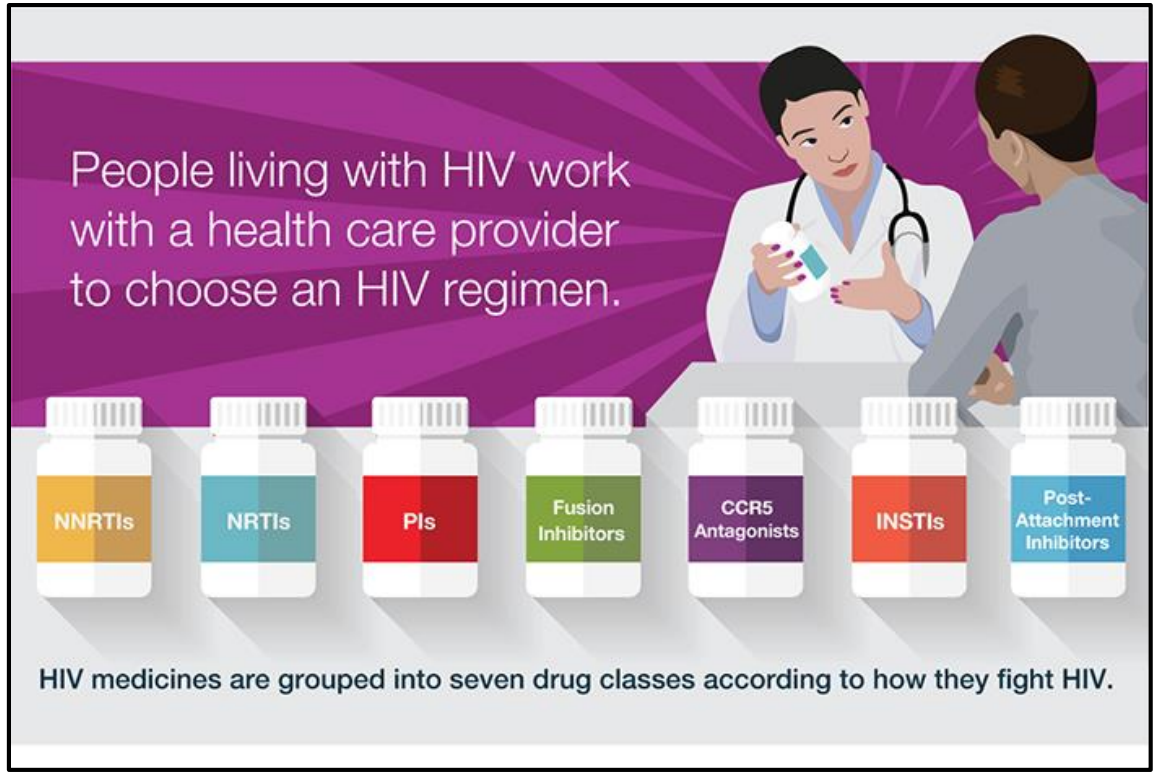
HIV: Life Cycle

- Medications from various classes target viral replication at different points in the HIV life cycle
- **Nucleoside reverse transcriptase inhibitors (NRTIs)** are the backbone of all first line antiretroviral therapy (ART)
- **Integrase strand-transfer inhibitors (INSTIs)** are the anchor drug in all first line HIV ART

NIH HIV Guidelines

https://clinicalinfo.hiv.gov/en/guidelines

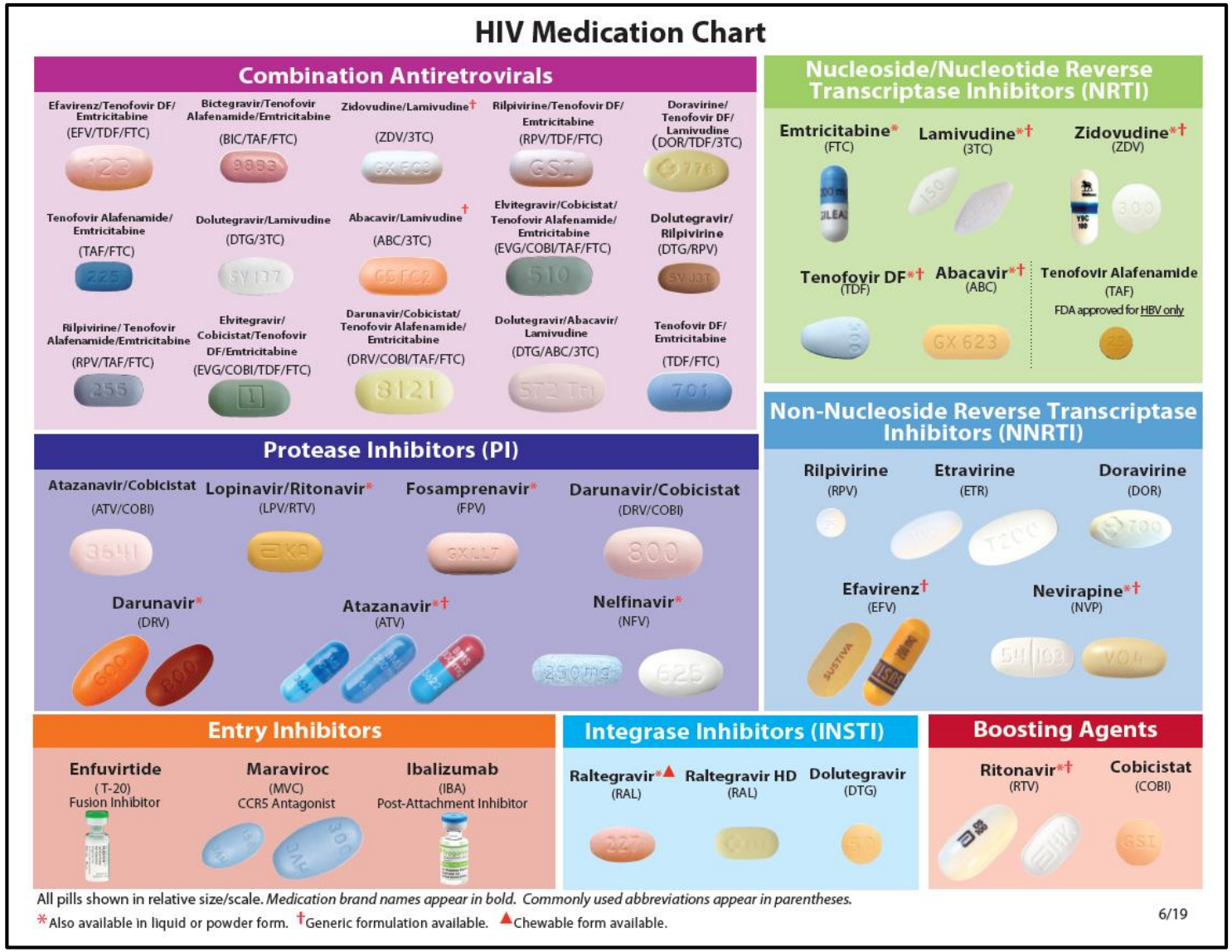
Different Classes of Antiretroviral Therapy (ART)



- **Non-nucleoside reverse transcriptase inhibitors (NNRTIs)**
- **Nucleoside reverse transcriptase inhibitors (NRTIs)**
- **Protease Inhibitors (PIs)**
- Fusion Inhibitors
- CCR5 Antagonists
- **Integrase Strand Transfer Inhibitors (INSTIs)**
- Post-attachment Inhibitors

Bold = more commonly used classes

https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-treatment-basics



Many medications!

- Most medications consist of **three** active medications, from at least two classes
  - Two newer ARTs with just two active medications (approved 2017, 2019)

- Many people with HIV are maintained on a single tablet that contains three drugs in one tablet

https://aidsetc.org/resource/hiv-medication-chart-pad

New Long-Acting Injectable Therapy - 2021

FDA NEWS RELEASE

FDA Approves First Extended-Release, Injectable Drug Regimen for Adults Living with HIV

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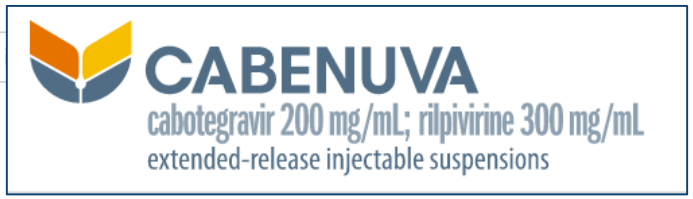


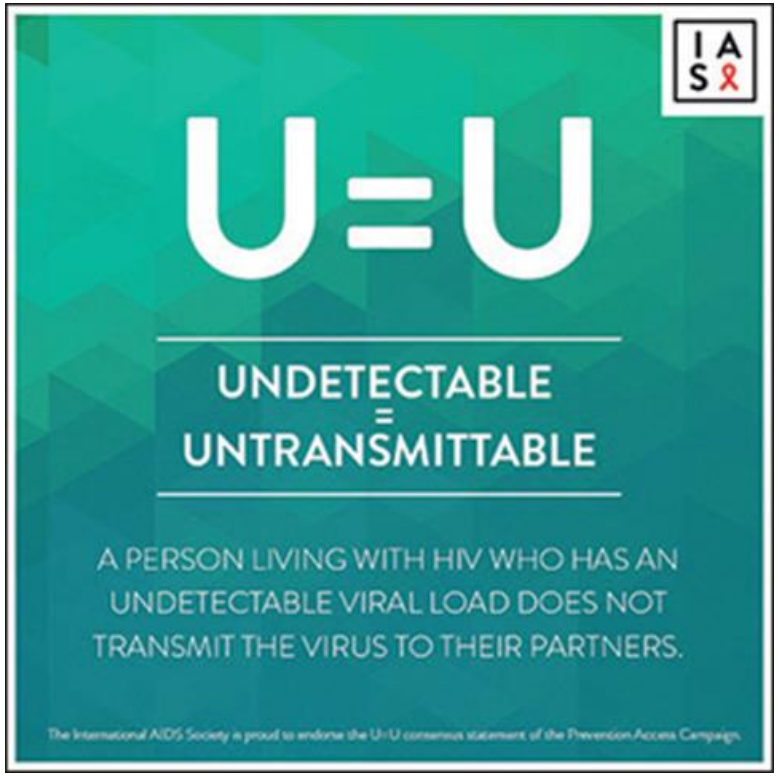
For Immediate Release: January 21, 2021

The U.S. Food and Drug Administration today approved Cabenuva (cabotegravir and rilpivirine, injectable formulation) as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults to replace a current antiretroviral regimen in those who are virologically suppressed on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine. This is the first FDA-approved injectable, complete

- No dosage adjustment necessary for patients with mild or moderate renal impairment CrCl > 30mL/min
- In severe renal impairment or end-stage renal disease, increased monitoring for adverse effects is recommended
- As cabotegravir and rilpivirine are greater than 99% protein bound, dialysis is not expected to alter exposures of cabotegravir or rilpivirine.

Guidelines for Starting ART

- Antiretroviral therapy (ART) is recommended for all persons with HIV (PWH) to reduce the risk of disease progression, HIV → AIDS
- ART also is recommended for PWH to prevent HIV transmission
    - **Undetectable = Untransmittable!**
- PWH starting ART should be willing and able to commit to treatment and understand the benefits and risks of therapy and the importance of consistent adherence
    - HIV mutates readily and non-adherence → drug resistance
- Goal is to start on treatment as soon as possible after diagnosis (start same day as diagnosis)



What to Start – NIH HIV Clinical Guidelines

Recommended Initial Regimens for Most People with HIV (in alphabetical order):

- **Bictegravir/tenofovir alafenamide/emtricitabine**

- **Dolutegravir/abacavir/lamivudine—only** for individuals who are HLA-B*5701 negative and without chronic hepatitis B virus (HBV) coinfection

- **Dolutegravir plus (emtricitabine or lamivudine) plus (tenofovir alafenamide or tenofovir disoproxil fumarate)**

What to Start – NIH HIV Clinical Guidelines, cont.

• **Dolutegravir/lamivudine -** except for individuals with HIV RNA >500,000 copies/mL, HBV co-infection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.

• **Raltegravir plus (emtricitabine or lamivudine) plus (tenofovir alafenamide [TAF] or tenofovir disoproxil fumarate [TDF])**

Primary Care Guidelines for Persons with HIV

Clinical Infectious Diseases

MAJOR ARTICLE

Primary Care Guidance for Persons With Human Immunodeficiency Virus: 2020 Update by the HIV Medicine Association of the Infectious Diseases Society of America

Melanie A. Thompson,[1,a] Michael A. Horberg,[2,a] Allison L. Agwu,[3] Jonathan A. Colasanti,[4] Mamta K. Jain,[5] William R. Short,[6] Tulika Singh,[7] and Judith A. Aberg[8]

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Advances in antiretroviral therapy (ART) have made it possible for persons with human immunodeficiency virus (HIV) to live a near expected life span, without progressing to AIDS or transmitting HIV to sexual partners or infants. There is, therefore, increasing emphasis on maintaining health throughout the life span. To receive optimal medical care and achieve desired outcomes, persons with HIV must be consistently engaged in care and able to access uninterrupted treatment, including ART. Comprehensive evidence-based HIV primary care guidance is, therefore, more important than ever. Creating a patient-centered, stigma-free care environment is essential for care engagement. Barriers to care must be decreased at the societal, health system, clinic, and individual levels. As the population ages and noncommunicable diseases arise, providing comprehensive healthcare for persons with HIV becomes increasingly complex, including management of multiple comorbidities and the associated challenges of polypharmacy, while not neglecting HIV-related health concerns. Clinicians must address issues specific to persons of childbearing potential, including care during preconception and pregnancy, and to children, adolescents, and transgender and gender-diverse individuals. This guidance from an expert panel of the HIV Medicine Association of the Infectious Diseases Society of America updates previous 2013 primary care guidelines.

Keywords. HIV primary care; HIV care engagement; HIV monitoring; HIV comorbidities; sexually transmitted infections.

Although substantial inequities exist by region and population, with continuous engagement in high-quality human immunodeficiency virus (HIV) care and uninterrupted access to antiretroviral therapy (ART), people with HIV now have the possibility of an expected life span that approaches that of persons not living with HIV, free of opportunistic diseases and without horizontal transmission to partners or vertical transmission to infants [1–4]. Ending the HIV epidemic, must be an overarching priority of HIV primary care. Ensuring stigma-free, culturally appropriate, and patient-centered care experiences is essential to maximize care engagement, treatment adherence, and viral suppression. While ART has become more potent, less toxic, and simpler, other aspects of HIV care have become increasingly complex as people with HIV live longer and experience increased comorbidities across the life span, requiring additional attention to issues

Thompson, M et al, Primary Care Guidelines for Persons With Human Immunodeficiency Virus: 2020 Update by the HIV Medicine Association of the Infectious Diseases Society of America, *Clinical Infectious Diseases*, 2020. https://doi.org/10.1093/cid/ciaa1391

Primary Care Guidelines - Baseline Renal Monitoring

Urinalysis and Calculated Creatinine Clearance:

- Baseline urinalysis and calculated CrCl or eGFR, especially in Black persons with HIV and those with advanced disease or comorbid conditions, because of an increased risk of nephropathy (*strong recommendation, high quality evidence*)

- Urinalysis and calculated creatinine clearance should also be performed prior to initiating drugs such as tenofovir due to potential for nephrotoxicity (*strong recommendation, moderate quality evidence*).

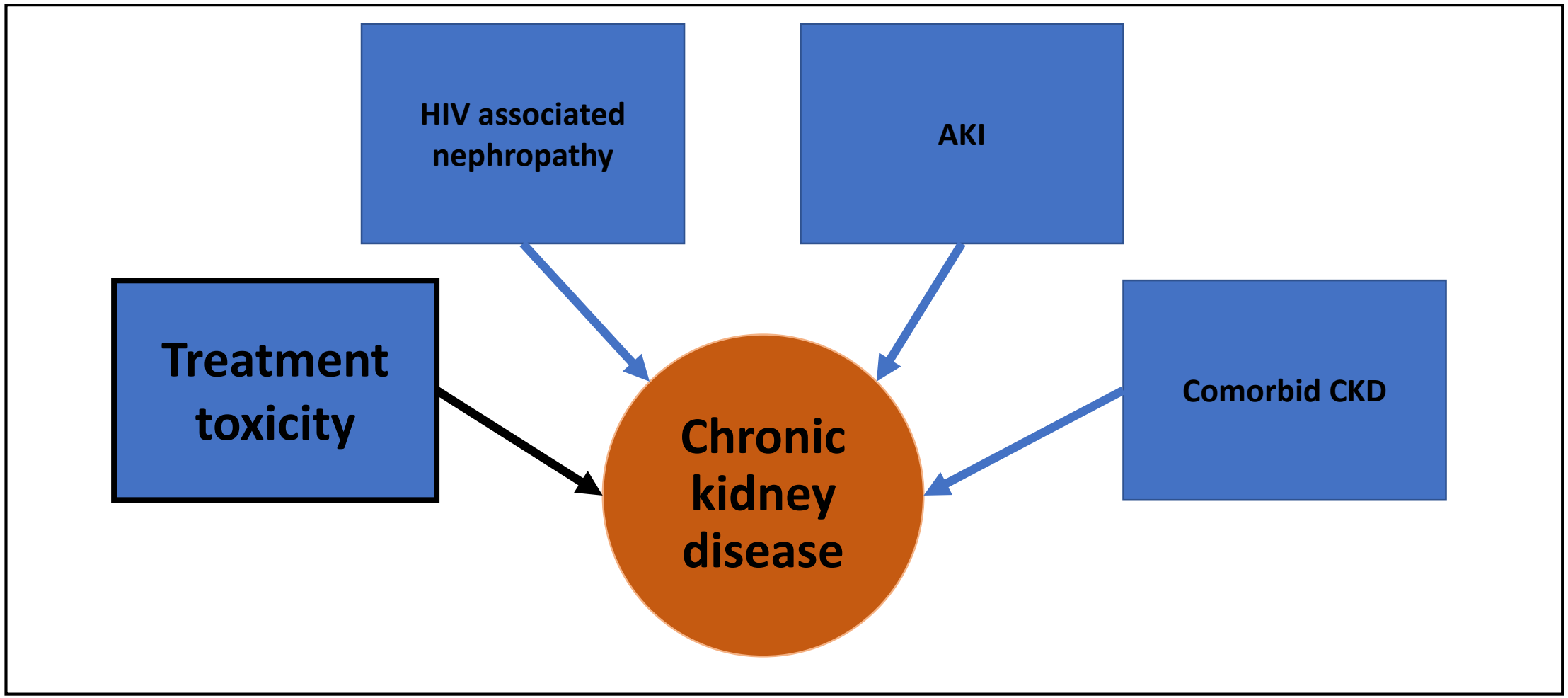
Aberg, J, et al, Primary Care Guidelines for the Management of Persons Infected With HIV: 2013 Update by the HIV Medicine Association of the Infectious Diseases Society of America, *Clinical Infectious Diseases*, Volume 58, Issue 1, 1 January 2014, Pages e1–e34, https://doi.org/10.1093/cid/cit665

NIH Ongoing Renal Monitoring Recommendations

	Monitoring Frequency					
Laboratory Test	**Entry into care**	**ART initiation or modification**	**2-8 weeks after initiation or modification**	**Every 3-6 months**	**Every 6 months**	**Every 12 months**
Basic Chemistry	X	X			X	
Urinalysis	X	X			X (If on TDF)	X

https://clinicalinfo.hiv.gov/en/guidelines

Kidney Disease in HIV



Renal AEs Vary by ART Class

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
Renal Effects/ Urolithiasis	**TDF:** ↑ SCr, proteinuria, hypophosphatemia, urinary phosphate wasting, glycosuria, hypokalemia, and non-anion gap metabolic acidosis. Concurrent use of TDF with COBI- or RTV-containing regimens appears to increase risk. **TAF:** Less impact on renal biomarkers and lower rates of proteinuria than TDF.	**RPV:** Inhibits Cr secretion without reducing renal glomerular function.	**ATV and LPV/r:** Associated with increased risk of chronic kidney disease in a large cohort study. **ATV:** Stone or crystal formation. Adequate hydration may reduce risk. **COBI (as a Boosting Agent for DRV or ATV):** Inhibits Cr secretion without reducing renal glomerular function.	**DTG, COBI (as a Boosting Agent for EVG), and BIC:** Inhibits Cr secretion without reducing renal glomerular function	**IBA:** SCr abnormalities ≥Grade 3 reported in 10% of trial participants.

https://clinicalinfo.hiv.gov/en/guidelines

Treatment toxicity

- Tenofovir based regimen considerations (see next slides)
- Common in combination with drugs that inhibit tubular creatinine secretion (i.e. **cobicistat, dolutegravir)**
  - Elevations in serum creatinine are typically in the range of 0.1-0.2mg/dL then plateau, **bictegravir** – less than dolutegravir, **raltegravir**)
- Combination with anti-HCV drugs increases tenofovir levels (e.g. valpatasvir)
- Protease inhibitors – indinavir, lopinavir and atazanavir have all been associated with renal stone formation
  - Atazanavir tubulo-interstitial nephritis

Milburn J, Jones R, Levy JB. Renal effects of novel antiretroviral drugs. *Nephrol Dial Transplant*. 2017;32(3):434-439. doi:10.1093/ndt/gfw064

Tenofovir Toxicity

Tenofovir Disoproxil Fumarate (TDF)

- TDF is an antiretroviral used in HIV treatment and as pre-exposure prophylaxis (PrEP) in Truvada
- Can cause gradual decline in GFR, phosphorous wasting
  - Can present with new proteinuria
- Although rare, proximal tubular dysfunction can progress to Fanconi syndrome, a complete tubulopathy that includes metabolic acidosis and bone disorders
- TDF is not recommended for use in persons who have a Crcl <60 mL/min
- Risk factors for TDF nephrotoxicity = low CD4 count, HCV coinfection, DM, Black, male gender, older age, and baseline hepatic or renal dysfunction
- Markers specific for tubular dysfunction:
  - Glycosuria with normal serum glucose
  - Urinary phosphorus wasting with low serum phosphorus

https://www.hiv.uw.edu/go/antiretroviral-therapy/adverse-effects/core-concept/all
Lucas, Gregory M et al. “Clinical practice guideline for the management of chronic kidney disease in patients infected with HIV: 2014 update by the HIV Medicine Association of the Infectious Diseases Society of America.” vol. 59,9 (2014): e96-138. doi:10.1093/cid/ciu617

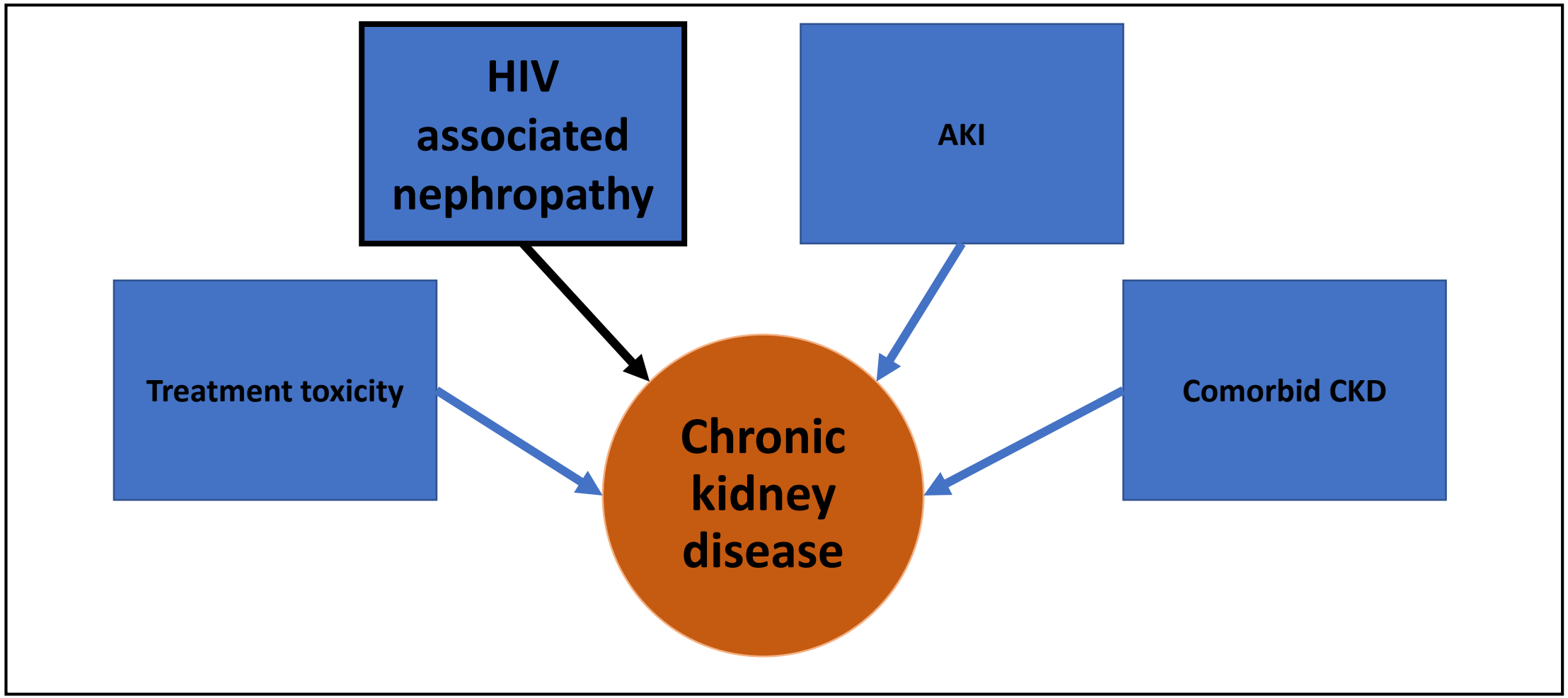
Tenofovir Toxicity, cont.

Tenofovir Alafenamide (TAF)

- TAF is a medication used in HIV treatment and as pre-exposure prophylaxis (PrEP) in Descovy
- 25 mg dose of TAF has 90% lower circulating plasma tenofovir levels when compared with a 300 mg dose of tenofovir disoproxil fumarate
- Improved GFR, glomerular and tubular proteinuria, and bone mineral density
- May see increase in certain lipid parameters (total cholesterol and HDL) but not others (total cholesterol/HDL ratio, triglycerides)
- Improved renal and bone safety profile but association with weight gain, especially when in combo with INSTI → research ongoing

https://www.hiv.uw.edu/go/antiretroviral-therapy/adverse-effects/core-concept/all

Kidney Disease in HIV



HIV-Associated Disease

May present with either AKI or CKD

- HIV associated nephropathy (HIVAN)
- Immune complex kidney disease (HIVICK)

HIVAN: Background

- First identified in 1984 in patients with advanced AIDS
- Almost exclusively found in African Americans (90%) or Latino populations (10%)
- Third leading cause of ESRD in African Americans ages 20-64

JE Locke (2019). Renal Disease and Kidney Transplant. Ryan White HIV/AIDS Clinical Conference.

HIVAN: Presentation + Treatment

- Rapidly progressive renal failure
- Definitive diagnosis via biopsy: Collapsing form of focal segmental glomerular sclerosis (FSGS)
- Direct HIV infection of renal epithelial cells
- Podocyte proliferation is hallmark (but less common in ART treated)
- Moderate-nephrotic range proteinuria without hematuria or RBC casts
- Enlarged, echogenic kidneys on renal US
- Progression to ESRD and/or death nearly universal
- Much less common now as people start ARTs upon diagnosis of HIV
- **Treatment mainstay is ART**, can also use ACEI and prednisone

HIVICK

- Diverse group of immune-mediated disease
  - Immune complex glomerulonephritis
  - Immunoglobulin A nephropathy
  - Lupus-like glomerulonephritis
- Antibody bound to HIV antigens are deposited on capillary loops and in the mesangium
- Complement activation may result in a lupus-like pathology
- Renal cell proliferation with immune complex disease predominately affects mesangial cells, distinguishing HIVICK from HIVAN
- **Presentation**: Proteinuria which may be nephrotic, hematuria, reduced GFR, and low levels of complement are common. May present at any age
- Prognosis appears better than for HIVAN

HIVICK, HIVAN citations

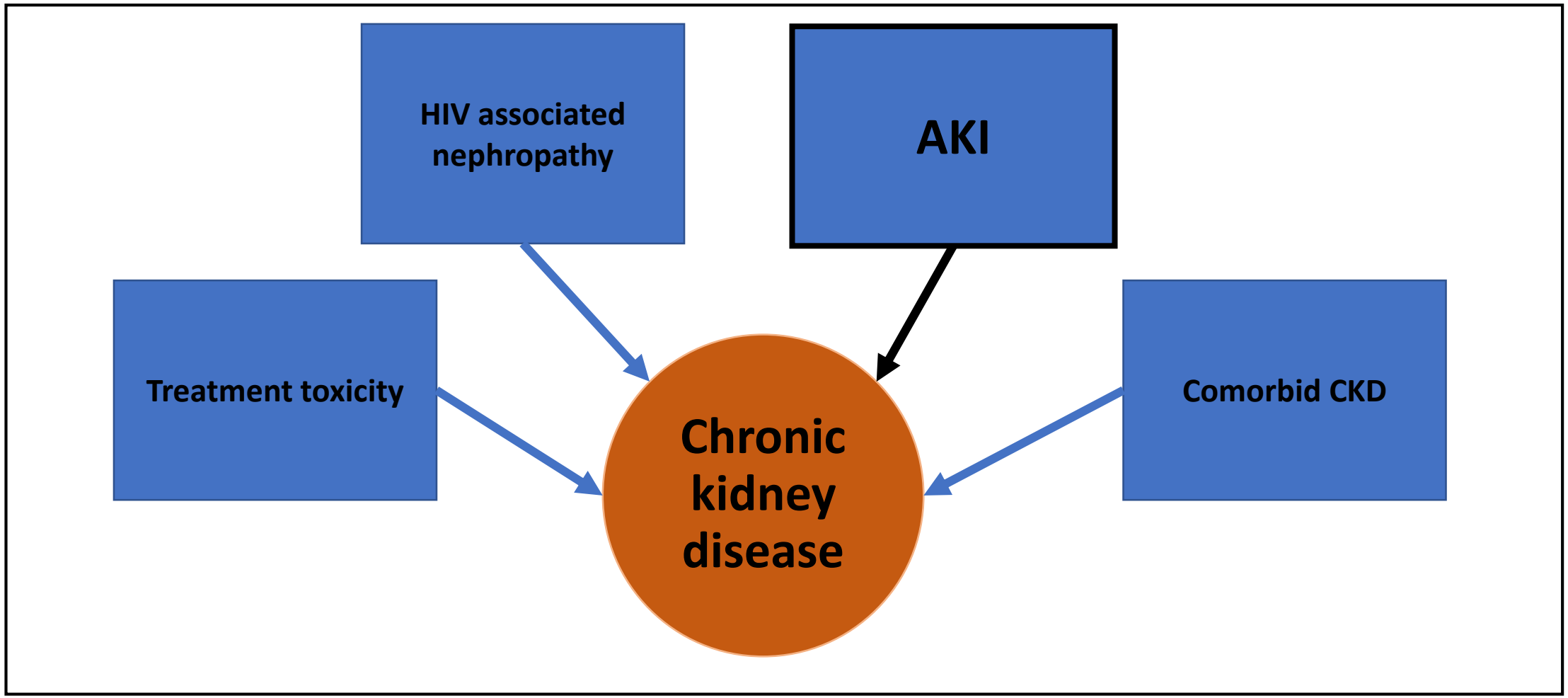
- Fogo AB, Lusco MA, Najafian B, Alpers CE. AJKD Atlas of Renal Pathology: HIV-Associated Immune Complex Kidney Disease (HIVICK). Am J Kidney Dis. 2016 Aug;68(2):e9-e10. doi: 10.1053/j.ajkd.2016.06.003. PMID: 27477364.

- Locke, Jayme E., “Renal Disease and Kidney Transplant” at New Orleans, LA, December 4-9, 2019, Ryan White HIV/AIDS Program Clinical Conference, IAS-USA

- Lucas GM, Ross MJ, Stock PG, et al. Clinical practice guideline for the management of chronic kidney disease in patients infected with HIV: 2014 update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis*. 2014;59(9):e96-e138. doi:10.1093/cid/ciu617

- Wyatt CM, Klotman PE, D'Agati VD. HIV-associated nephropathy: clinical presentation, pathology, and epidemiology in the era of antiretroviral therapy. *Semin Nephrol*. 2008;28(6):513-522. doi:10.1016/j.semnephrol.2008.08.005

Kidney Disease in HIV



Acute Kidney Injury in HIV

- More common in PWH than general population
- Risk factors for AKI:
  - Male sex
  - CD4 <200, VL >10,000
  - HCV co-infection
  - Older ART drugs
  - Plus traditional risk factors: Older age, Black, DM, CKD
- Associated with adverse outcomes

JE Locke (2019). Renal Disease and Kidney Transplant. Ryan White HIV/AIDS Clinical Conference.
Wyatt, Christina et al, Acute renal failure in hospitalized patients with HIV: risk factors and impact on in-hospital mortality, AIDS: Feb 28, 2006 - V 20 - Is 4 - p 561-565 doi: 10.1097/01.aids.0000210610.52836.07

Causes of AKI in HIV

Prerenal

- Even with ART, volume depletion, sepsis and liver disease (cirrhosis) risks remain

Intrarenal

- Acute tubular necrosis (nephrotoxic meds – more common vs. ischemic)
- Parenchymal infection (TB → granulomas, fungal infection)
- Interstitial nephritis – CMV, EBV
- Glomerular disease (HIVAN, HIVICK, HCV co-infection)

Postrenal

- Urinary obstruction-induced AKI relatively rare

JE Locke (2019). Renal Disease and Kidney Transplant. Ryan White HIV/AIDS Clinical Conference.
Campos P, Ortiz A, Soto K. HIV and kidney diseases: 35 years of history and consequences. *Clin Kidney J*. 2016;9(6):772-781. doi:10.1093/ckj/sfw104

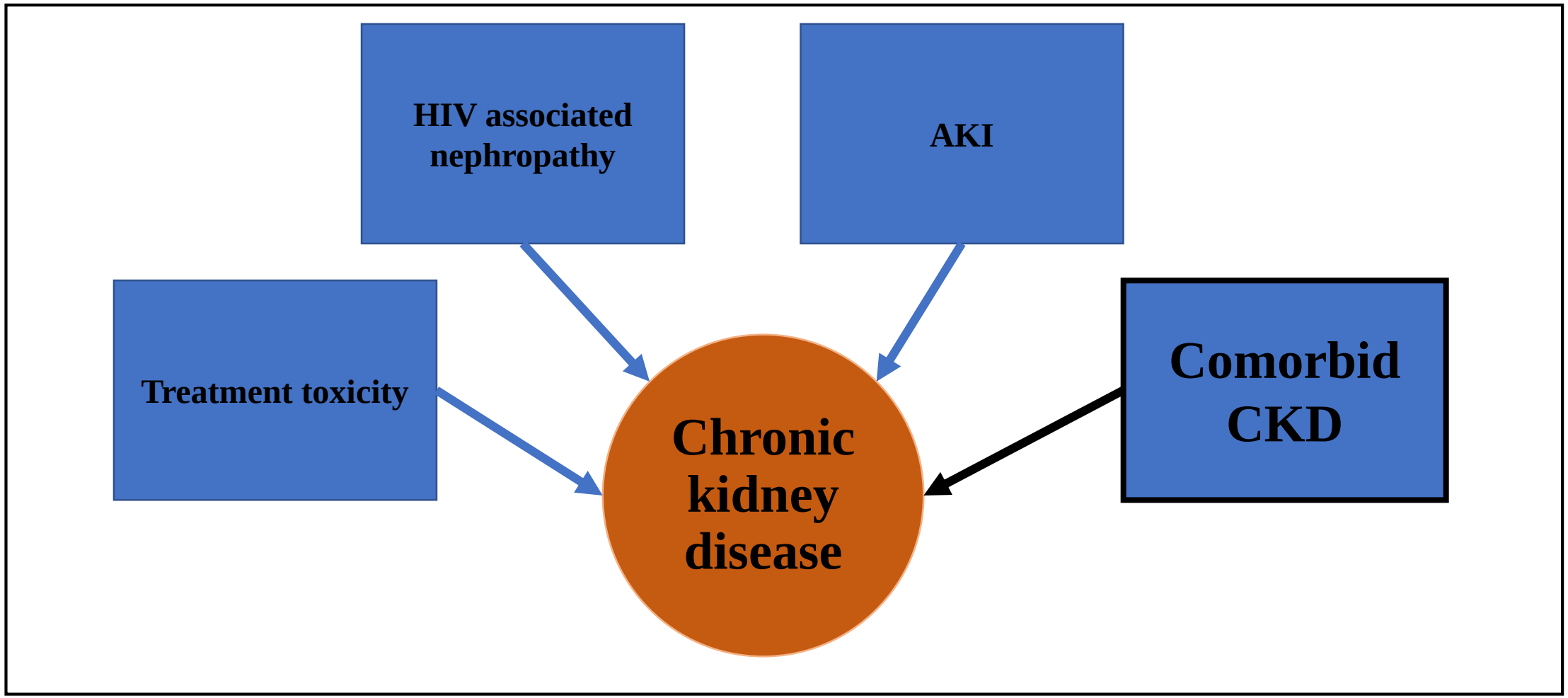
Acute Kidney Injury in HIV

Wyatt et al. AIDS 2006

- Acute renal failure was reported significantly more often during hospitalizations for PWH than for HIV-negative patients even after the introduction of ART
- Hospitalizations of patients with HIV complicated by ARF had much higher in-hospital mortality (27%) compared to admissions of patients with HIV without acute renal failure (4.5%)
- HIV infection associated with an increased risk of acute renal failure, even after adjustment for demographic and comorbid conditions

Wyatt, Christina et al, Acute renal failure in hospitalized patients with HIV: risk factors and impact on in-hospital mortality, AIDS: Feb 2006 - Vol 20 - Issue 4 - p 561-565 doi: 10.1097/01.aids.0000210610.52836.07

Kidney Disease in HIV

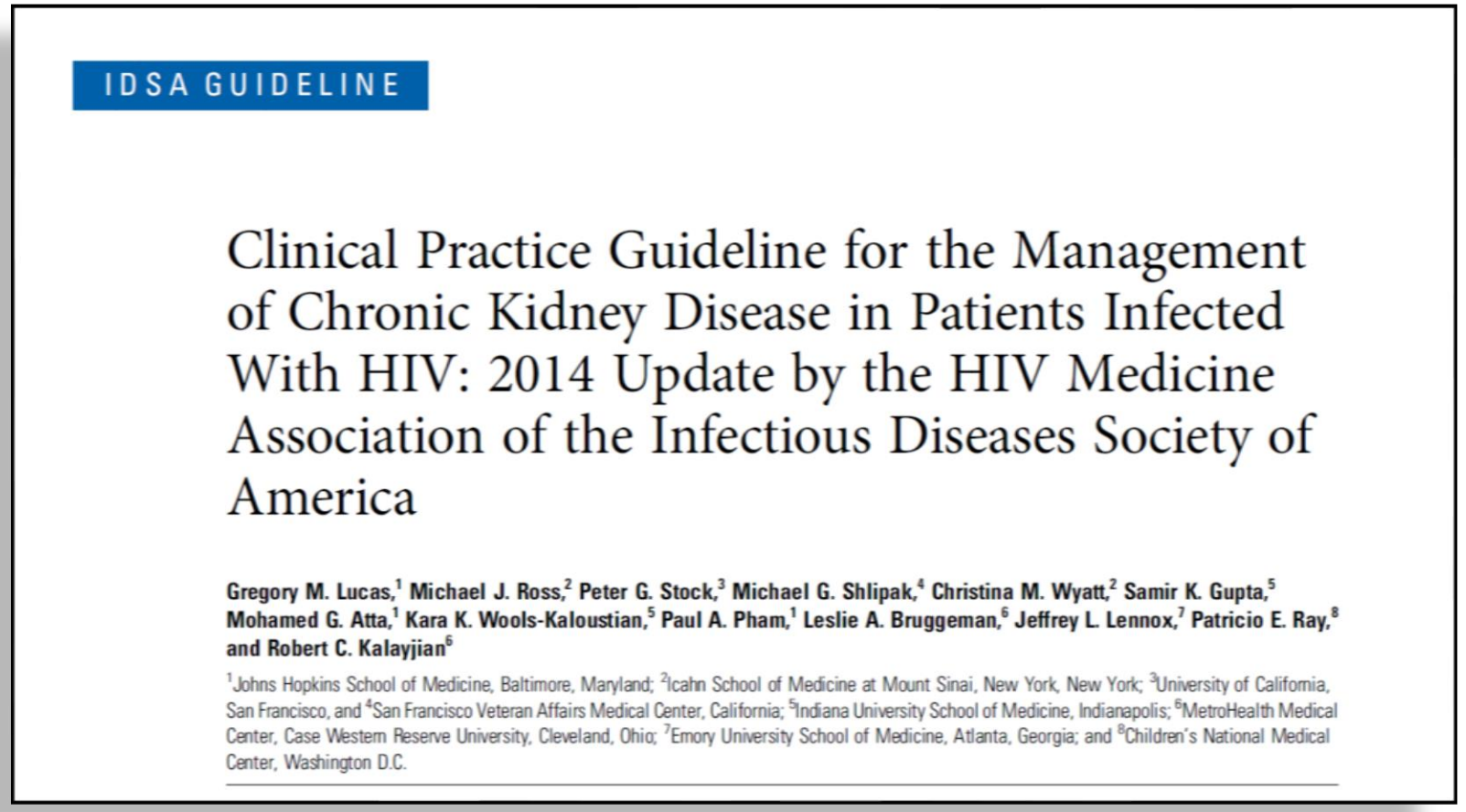


Renal Considerations in Selecting ART

Presence of Other Conditions	Chronic kidney disease (defined as CrCl <60 mL/min)	**In general, avoid TDF.** ABC may be used if patient is HLA-B*5701 negative. If HIV RNA is >100,000 copies/mL, do not use ABC/3TC plus (EFV or ATV/r). TAF may be used if CrCl >30 mL/min or if patient is on chronic hemodialysis (only studied with EVG/c/TAF/FTC). Consider avoiding ATV. **ART Options When ABC, TAF, or TDF Cannot be Used:** • DTG/3TC (if HIV RNA <500,000 copies/mL and without HBV coinfection) • DRV/r plus 3TC • DRV/r plus RAL (if CD4 count >200 cells/mm^3 and HIV RNA <100,000 copies/mL)	TDF has been associated with proximal renal tubulopathy. Higher rates of renal dysfunction have been reported in patients using TDF in conjunction with RTV-containing regimens. An adjusted dose of TDF can be used in patients with ESRD or in those who are on hemodialysis. Refer to Appendix B, Table 10 for specific dosing recommendations. TAF has less impact on renal function and lower rates of proteinuria than TDF. ATV has been associated with chronic kidney disease in some observational studies. ABC has not been associated with renal dysfunction.

https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/initiation-antiretroviral-therapy?view=full

Comorbid CKD



IDSA GUIDELINE

Clinical Practice Guideline for the Management of Chronic Kidney Disease in Patients Infected With HIV: 2014 Update by the HIV Medicine Association of the Infectious Diseases Society of America

Gregory M. Lucas,[1] Michael J. Ross,[2] Peter G. Stock,[3] Michael G. Shlipak,[4] Christina M. Wyatt,[2] Samir K. Gupta,[5] Mohamed G. Atta,[1] Kara K. Wools-Kaloustian,[5] Paul A. Pham,[1] Leslie A. Bruggeman,[6] Jeffrey L. Lennox,[7] Patricio E. Ray,[8] and Robert C. Kalayjian[6]

[1]Johns Hopkins School of Medicine, Baltimore, Maryland; [2]Icahn School of Medicine at Mount Sinai, New York, New York; [3]University of California, San Francisco, and [4]San Francisco Veteran Affairs Medical Center, California; [5]Indiana University School of Medicine, Indianapolis; [6]MetroHealth Medical Center, Case Western Reserve University, Cleveland, Ohio; [7]Emory University School of Medicine, Atlanta, Georgia; and [8]Children's National Medical Center, Washington D.C.

Comorbid CKD

- CKD is an important complication of HIV infection and treatment
- Prevalence of CKD among PWH in North America and Europe ranges from approx. 4.7 to 9.7%
- Patients living longer and HIV spreading among populations at high risk of renal disease → number of patients with HIV-related ESRD will rise
- ART decreased HIVAN-related ESRD, but can be nephrotoxic and can cause CV and metabolic dysfunction → worsening kidney disease

Comorbid CKD

- Risk factors for progression to ESRD:
  - HIV-associated nephropathy (HIVAN) diagnosis
  - African American lineage
  - Family history of ESRD
  - Magnitude of proteinuria
  - Advanced immunosuppression

Lucas GM, Ross MJ, Stock PG, et al. Clinical practice guideline for the management of chronic kidney disease in patients infected with HIV: 2014 update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis*. 2014;59(9):e96-e138. doi:10.1093/cid/ciu617

Comorbid CKD

- **Factors associated with an increased risk of CKD:**
  - Older age
  - Female sex
  - DM
  - Hypertension
  - Injection drug use
  - Lower CD4 cell count
  - History of acute kidney injury
  - Higher HIV RNA levels

Lucas GM, Ross MJ, Stock PG, et al. Clinical practice guideline for the management of chronic kidney disease in patients infected with HIV: 2014 update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis*. 2014;59(9):e96-e138. doi:10.1093/cid/ciu617

Creatinine Clearance Thresholds for Some ARTs

Generic Name (Abbreviations) *Trade Name*	Usual Daily Dose[a]	Dosing in Persons with Renal Insufficiency	Dosing in Persons with Hepatic Impairment

Some FDC products are not recommended in persons with different degrees of renal insufficiency. The recommendations for individual FDCs based on CrCl level are outlined below.

- *CrCl <70 mL/min:* **Initiation of Stribild is not recommended.**
- *CrCl <50 mL/min:* **FDCs not recommended:** Atripla, Combivir, Complera, Delstrigo, Dovato, Epzicom, Triumeq, or Trizivir.
- *CrCl <30 mL/min:* **FDCs not recommended:** Biktarvy and Truvada.
- *CrCl <30 mL/min* ***and*** *not on HD:* **FDCs not recommended:** Descovy, Genvoya, Odefsey, Symtuza.

The component drugs in some of the FDC products listed above may be prescribed as individual formulations with dose adjustment based on CrCl level as indicated below in this table.

https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/antiretroviral-dosing-recommendations-patients-renal-or-hepatic?view=full

ART Single Tablet Regimen (STR) in HD

Generic Name	Brand Name	Standard dosing	Dosing category	Other considerations
Single Tablet Regimen examples				
Elvitegravir/ Cobicistat/ Tenofovir Alafenamide/ Emtricitabine	Genvoya (single tablet regimen)	1 tablet 1x/daily	One tablet once daily. On HD days, administer after dialysis.	**Not recommended** in patients with CrCl <30 mL/min who are not receiving chronic HD.
Rilpivirine/Tenofovir Alafenamide/Emtricitabine	Odefsey (single tablet regimen)	1 tablet 1x/daily	One tablet once daily. On HD days, administer after dialysis.	**Not recommended** in patients with CrCl <30 mL/min who are not receiving chronic HD.
Darunavir/Cobicistat/Tenofovir Alafenamide/Emtricitabine	Symtuza (single tablet regimen)	1 tablet 1x/daily	In patients on Chronic HD: One tablet once daily. On HD days, administer after dialysis.	**Not recommended** in patients with CrCl <30 mL/min who are not receiving chronic HD.
Dolutegravir/ Abacavir/ Lamivudine**	Triumeq (single tablet regimen)	1 tablet 1x/daily		**Not recommended** if CrCl <50 mL/min. Instead, use the individual component drugs and adjust 3TC dose according to CrCl.
Dolutegravir/Rilpivirine	Juluca	1 tablet 1x/daily	No dose adjustment necessary. In patients with CrCl <30 mL/min, monitor closely for adverse effects.	

****Recommended first line agents**

https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/antiretroviral-dosing-recommendations-patients-renal-or-hepatic?view=full

First-line STR Evaluated for Safety in HD

- Ongoing studies of safety of first line STR bictegravir/emtricitabine/TAF
  - Eron et al., 2020: Daily regimen of B/FTC/TAF maintained virologic suppression in PWH on chronic HD
  - B/FTC/TAF may be an effective, safe and convenient once daily STR and ameliorate the need for dose adjustment in appropriate PWH who require chronic HD
  - Biktarvy package insert: *No dosage adjustment is recommended in patients with eCrCl greater than or equal to 30 mL per minute, or in virologically-suppressed adults with ESRD (eCrCl below 15 mL/min) who are receiving chronic hemodialysis. On days of hemodialysis, administer the daily dose of BIKTARVY after completion of hemodialysis treatment*
  - <u>Not yet in NIH HIV guidelines for use in HD</u>

Eron JJ, Wilkin A, Ramgopal M, et al. 1002. A Daily Single Tablet Regimen (STR) of Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) in Virologically-Suppressed Adults Living with HIV and End Stage Renal Disease on Chronic Hemodialysis. *Open Forum Infect Dis*. 2020;7(Suppl 1):S529-S530. Published 2020 Dec 31. doi:10.1093/ofid/ofaa439.1188

ART non-STR example of dosing for HD

Generic Name	Brand Name	Class	Standard dosing	Hemodialysis dosing
Medications that would need to be combined – Not full regimens				
Raltegravir	Isentress	INSTI	RAL 400 mg twice daily (using Isentress formulation) *or* RAL 1,200 mg once daily (using Isentress HD formulation only)	No dose adjustment necessary
Lamivudine	Epivir	NRTI	3TC 300 mg PO once daily *or* 3TC 150 mg PO twice daily	1 x 50 mg, then 25 mg every 24 hours
Tenofovir Disoproxil Fumarate	Viread	NRTI	300mg once daily	300mg every 7 days

https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/antiretroviral-dosing-recommendations-patients-renal-or-hepatic?view=full

ESRD without HD

- More limited data for patients not on hemodialysis with creatinine clearance between 15-29mL/min
- Some options without need for dose adjustment:
    - Abacavir
    - Dolutegravir (caution if INSTI experienced), Raltegravir, Elvitegravir
    - Darunavir
- Emtricitabine (FTC)
    - CrCl 15 to 29 mL/minute: Capsule: 200 mg every 72 hours.
    - CrCl <15 mL/minute: Capsule: 200 mg every 96 hours.

Kidney Transplants in PWH – IDSA Recommendations

- Recommend that HIV providers assess patients with HIV and ESRD or imminent ESRD for the possibility of kidney transplantation, considering history of opportunistic conditions, comorbidities, current immune status, and virologic control of HIV with ART *(strong, moderate)*.
- Recommend dose adjustment and pharmacologic monitoring of immunosuppressant drugs in patients with HIV after kidney transplantation to account for pharmacologic interactions with antiretroviral drugs. When feasible, ART should be selected that minimizes interactions with immunosuppressant drugs *(strong, moderate)*.

Clinical Infectious Diseases, Volume 59, Issue 9, 1 November 2014, Pages e96–e138, https://doi.org/10.1093/cid/ciu617

For more information…

https://www.hiv.uw.edu/go/antiretroviral-therapy

AETC Resources

- **Clinical Consultation Center**
  http://nccc.ucsf.edu
  - HIV Management
  - Perinatal HIV
  - HIV PrEP
  - HIV PEP line
  - HCV Management
  - Substance Abuse Management
- **AETC National Curriculum**
  http://aidsetc.org/nhc
- **AETC National HIV-HCV Curriculum**
  http://aidsetc.org/hivhcv
- **Hepatitis C Online**
  https://www.hepatitisc.uw.edu
- **AETC National Coordinating Resource Center**
  http://aidsetc.org
- **Additional Training for Midwest AIDS Training and Education Center (MATEC)**
  https://matec.info

AETC
Midwest

Questions?

Thank you!

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