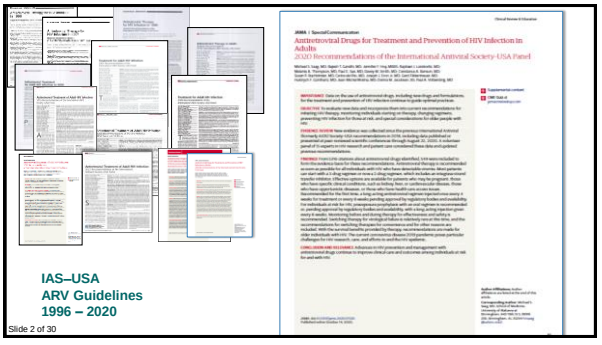
Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults 2020 Recommendations of the International Antiviral Society–USA Panel

Michael S. Saag, MD; Rajesh T. Gandhi, MD; Jennifer F. Hoy, MBBS; Raphael J. Landovitz, MD; Melanie A. Thompson, MD; Paul E. Sax, MD; Davey M. Smith, MD; Constance A. Benson, MD; Susan P. Buchbinder, MD; Carlos del Rio, MD; Joseph J. Eron, Jr, MD; Gerd Fätkenheuer, MD; Huldrych F. Günthard, MD; Jean-Michel Molina, MD; Donna M. Jacobsen, BS; Paul A. Volberding, MD

Saag, Gandhi, Hoy et al, *JAMA*, 2020.

IAS–USA



IAS–USA
ARV Guidelines
1996 – 2020

Clinical Review & Education

JAMA | Special Communication

Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults
2020 Recommendations of the International Antiviral Society-USA Panel

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IMPORTANCE Data on the use of antiretroviral drugs, including new drugs and formulations, for the treatment and prevention of HIV infection continue to guide optimal practices.

Supplemental content
CME Quiz at jamacmelookup.com

Saag MS, Gandhi RT, Hoy JF, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2020 recommendations of the International Antiviral Society-USA Panel. *JAMA.* 2020;E1-19. [Published online Oct 14, 2020]

Find the 2020 IAS-USA ARV Guidelines Article Online:

https://jamanetwork.com/journals/jama/fullarticle/2771873

- *Free to read in browser (paste the URL into your browser) until mid-November 2020*
- *Log in to JAMA to download a PDF*

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

2020 IAS–USA Antiretroviral Guidelines: Key Updates

- New recommendations on what regimens to start, including a role for a 2-drug regimen; new recommendations for switching and monitoring
- Updated approaches to prescribing pre-exposure prophylaxis (PrEP), including the use of a new long-acting injectable agent
  - When and how to use these medications
  - How to manage breakthrough infections
- New recommendations on management of aging among people with HIV
- Overview of the impact of COVID-19 disease on HIV

Slide 5 of 34

Saag, Gandhi, Hoy et al., *JAMA*, 2020.

2020 IAS–USA Antiretroviral Guidelines Process Overview

- Added aging and HIV and impact of COVID-19
- Developed by an international panel of 15 volunteer experts in HIV research and patient care appointed by the IAS–USA
  - Members receive no compensation and do not participate in industry promotional activities while on the panel
- Primarily for clinicians in highly resourced settings; however, principles are universally applicable
- Reviewed data published or presented from January 2018 through August 22, 2020
- Rated on strength of recommendation and quality of evidence

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

2020 IAS–USA Antiretroviral Guidelines Content

- When to start antiretroviral therapy (ART)
- Recommended initial regimens
- When and how to switch
- Laboratory monitoring
- Prevention
- Aging and HIV
- Cost
- Ending the HIV epidemic
- New directions and emerging trends

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Methods

- Literature searches in PubMed and EMBASE
- Hand searches for newly published reports, scientific abstracts, and safety reports relevant to adults in highly resourced areas
- Antiretroviral (ARV) manufacturers submitted lists of relevant scientific publications or abstracts presented at peer-reviewed conferences
- Data not published or presented in a peer-reviewed setting were not considered
- Drugs, formulations, combinations considered
  - Approved by regulatory agencies (eg, FDA, EMEA)
  - Submitted for regulatory approval (ie, in late development stages)

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Strength of Recommendation and Quality of Evidence Rating Scale

Rating	Definition
Strength of recommendation	
A	Strong support
B	Moderate support
C	Limited or weak panel support
Quality of evidence	
Ia	Evidence from ≥1 randomized clinical trials (RCTs) published in the peer-reviewed literature
Ib	Evidence from ≥ RCTs presented in abstract form at peer-reviewed scientific meetings
IIa	Evidence from cohort or case-control studies published in the peer-reviewed literature
IIb	Evidence from cohort or case-control studies presented in abstract from at peer-reviewed scientific meetings
III	Based on the panel's analysis of the available evidence

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Adapted in part from Canadian Task Force on Periodic Health Examination, *Can Med Assoc J*, 1979

Antiretroviral Therapy: When and What to Start

Moderated by:
Rajesh T. Gandhi, MD
Professor of Medicine
Harvard University
Boston, Massachusetts

Key Recommendations for When to Start Antiretroviral Therapy

- Initiate as soon as possible after diagnosis, including immediately (rapid or same-day start) if the patient is ready AIa
- Remove any structural barriers that delay ART AIa
- In setting of starting OI treatment, begin ART within 2 weeks for most OIs AIa
- *Exceptions are:*
  - Tuberculosis: within 2-8 weeks
    - Within 2-weeks for those with >50 CD4 cells/µL*
    - Within 2-8 weeks for those with higher CD4 cells counts
  - Cryptococcal meningitis: 4-6 weeks
- For individuals with cancer, immediate ART initiation with close attention to drug-drug interactions and monitoring for early ART adverse events

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Saag, Gandhi, Hoy et al, *JAMA*, 2020.

Recommended Initial ART for Most People With HIV

- Bictegravir/tenofovir alafenamide/emtricitabine
- Dolutegravir plus TAF/FTC or TDF/FTC or TDF/3TC
- Dolutegravir/lamivudine with caveats*

*Not recommended for:
1) rapid start (before results of hepatitis B and HIV genotypic testing are available)
2) patients with chronic hepatitis B
3) patients with HIV RNA level >500,000 copies/mL, or perhaps with CD4 cell count <200/µL
4) patients being treated for an active opportunistic infection
Monitor for adherence and virological response closely.

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Saag, Gandhi, Hoy et al, *JAMA*, 2020.

Other Recommended Initial ART Regimens

- Darunavir/cobicistat/TAF/FTC or + TDF/3TC
- Dolutegravir/abacavir/3TC
- Doravirine/TDF/3TC or + TAF/FTC or + TDF/3TC
- Efavirenz (400 mg or 600 mg) + TDF/3TC or + TDF/FTC
- Raltegravir + TAF/FTC or + TDF/FTC or + TDF/3TC
- Rilpivirine/TAF/FTC or /TDF/3TC

* See advantages and disadvantages in the article

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Recommendations for Starting ARV in the Setting of OIs

- Active TB; on rifamycin
  - Dolutegravir 50 mg bid
  - Efavirenz 600 mg qd
  - Raltegravir 800 mg bid

  } plus 2 nRTIs
- Bictegravir with rifampin is not recommended
- Boosted PIs:
  - Only if an InSTI or efavirenz is not available
  - If possible, rifabutin not rifampin should be used with PIs

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Recommended Initial ART During Pregnancy

- Atazanavir/ritonavir
- Darunavir/ritonavir
- Dolutegravir
- Efavirenz
- Raltegravir
- Rilpivirine*

} plus TDF/FTC or TDF/3TC

- Dolutegravir plus TAF/FTC

*Data and experience more limited

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

When and How to Switch ART Regimens

Paul E. Sax, MD
Professor of Medicine
Brigham And Women's Hospital
Boston, Massachusetts

Key Recommendations for When and How to Switch ART Regimens

- Thorough review of treatment history required – regimen tolerability, co-medications, food requirements, costs, and results from prior resistance tests
- Follow-up HIV viral load in 1 month after *any* switch
- Switching after viral suppression
  - If HBSAg positive, include TAF or TDF whenever possible
  - If NRTI resistance in the past, do not switch from boosted PI to low genetic barrier drug (e.g., NNRTI or RAL)
  - Simplification to certain 2-drug regimens (DTG/3TC, DTG/RPV, boosted PI/3TC, eventually CAB/RPV) may be appropriate to manage toxicity or in response to patient preference, provided *both* drugs are active

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Saag, Gandhi, Hoy et al, *JAMA*, 2020.

Key Recommendations for When and How to Switch ART Regimens

- Adjusting regimens in those with concomitant disease
  - Kidney disease
  - Liver disease
  - Cardiovascular disease
  - Bone disease
  - Weight gain
  - Cancer and autoimmune disease

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Saag, Gandhi, Hoy et al, *JAMA*, 2020.

Key Recommendations for When and How to Switch ART Regimens (cont)

- Switching for virologic failure
  - Definition: HIV RNA >200 c/mL on 2 consecutive tests
  - Obtain resistance genotype, preferably while on or within 4 weeks of stopping failing treatment
- Failure of an initial NNRTI regimen → Active NRTIs plus DTG
- Failure of an initial PI or DTG/BIC regimen → usually no resistance
- Failure of an initial RAL or EVG regimen with INSTI resistance – if INSTI is used, twice-daily DTG
- Failure in those with a complex treatment history – at least 2 fully active drugs, with consideration of fostemsavir and/or ibalizumab

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Discussion Questions on Switching

- Should all patient on a "boosted" regimen switch to an unboosted regimen if possible?
- When cab/rpv is approved, should I be giving it every 4 weeks or every 8 weeks?
- Is it possible to use DTG/3TC in patients with impaired renal function? If so, down to what estimated GFR?
- If someone has failed NNRTI-based regimens in the past, but has no documented NNRTI resistance, are they still a candidate for DTG/RPV or CAB/RPV?
- Should we switch regimens in people with low-level viremia (between 50-200)?
- Do you recommend medications switches for people who have gained weight on TAF plus INSTI-based regimens?
- Under what circumstances should we use fostemsavir and/or ibalizumab?

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Laboratory Monitoring in Individuals With HIV

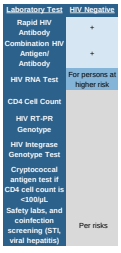
Moderated by:
Davey M. Smith, MD
Professor of Medicine
University of California San Diego
San Diego, California

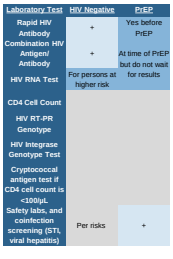
Recommended Laboratory Monitoring

- At HIV diagnosis
- During ART
- At virologic failure
- Before and during PrEP
  - Oral regimen
  - Injectable regimen
- Routine vaccinations

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

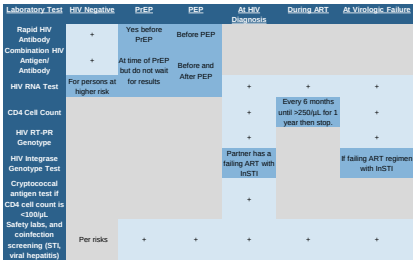




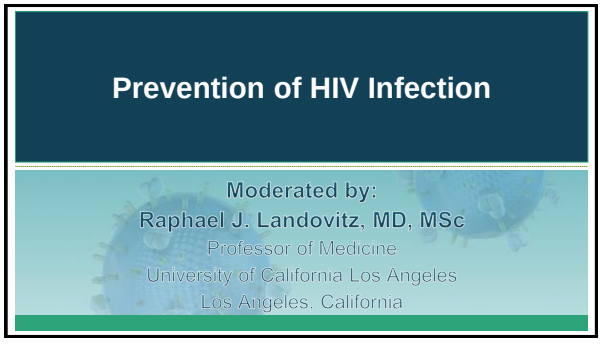
Laboratory Test	HIV Negative	PrEP	PEP
Rapid HIV Antibody	+	Yes before PrEP	Before PEP
Combination HIV Antigen/ Antibody	+	At time of PrEP but do not wait for results	Before and After PEP
HIV RNA Test	For persons at higher risk		
CD4 Cell Count			
HIV RT-PR Genotype			
HIV Integrase Genotype Test			
Cryptococcal antigen test if CD4 cell count is <100/µL			
Safety labs, and coinfection screening (STI, viral hepatitis)	Per risks	+	+

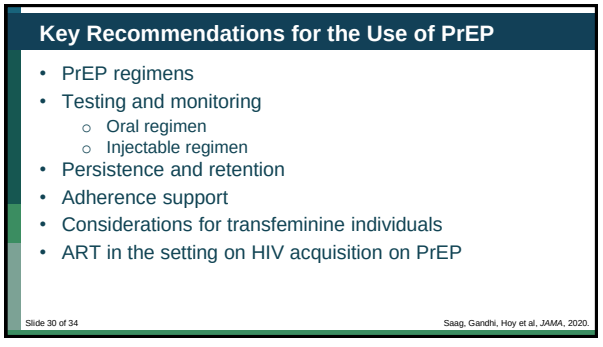
Laboratory Test	HIV Negative	PrEP	PEP	At HIV Diagnosis
Rapid HIV Antibody	+	Yes before PrEP	Before PEP	
Combination HIV Antigen/ Antibody	+	At time of PrEP but do not wait for results	Before and After PEP	
HIV RNA Test	For persons at higher risk			+
CD4 Cell Count				+
HIV RT-PR Genotype				+
HIV Integrase Genotype Test				Partner has a failing ART with InSTI
Cryptococcal antigen test if CD4 cell count is <100/µL				+
Safety labs, and coinfection screening (STI, viral hepatitis)	Per risks	+	+	+

Laboratory Test	HIV Negative	PrEP	PEP	At HIV Diagnosis	During ART
Rapid HIV Antibody	+	Yes before PrEP	Before PEP		
Combination HIV Antigen/ Antibody	+	At time of PrEP but do not wait for results	Before and After PEP		
HIV RNA Test	For persons at higher risk			+	+
CD4 Cell Count				+	Every 6 months until >250/µL for 1 year then stop.
HIV RT-PR Genotype				+	
HIV Integrase Genotype Test				Partner has a failing ART with InSTI	
Cryptococcal antigen test if CD4 cell count is <100/µL				+	
Safety labs, and coinfection screening (STI, viral hepatitis)	Per risks	+	+	+	+



Laboratory Test	HIV Negative	PrEP	PEP	At HIV Diagnosis	During ART	At Virologic Failure
Rapid HIV Antibody	+	Yes before PrEP	Before PEP			
Combination HIV Antigen/ Antibody	+	At time of PrEP but do not wait for results	Before and After PEP			
HIV RNA Test	For persons at higher risk			+	+	+
CD4 Cell Count				+	Every 6 months until >250/µL for 1 year then stop.	+
HIV RT-PR Genotype				+		+
HIV Integrase Genotype Test				Partner has a failing ART with InSTI		If failing ART regimen with InSTI
Cryptococcal antigen test if CD4 cell count is <100/µL				+		
Safety labs, and coinfection screening (STI, viral hepatitis)	Per risks	+	+	+	+	+





Poll Question #1
What do you prescribe as your first-line agent for PrEP?

1. I don't prescribe PrEP
2. TDF/FTC (on demand or daily)
3. TAF/FTC (daily)
4. Something else

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Poll Question #2
Do you prescribe 2-1-1 (on demand) PrEP dosing for MSM?

1. Yes, when a patient requests it
2. Yes, I offer it to patients for whom it would be a good option
3. No, I am not comfortable with this dosing regimen
4. No, no one wants to take it
5. Some other answer

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Aging and HIV: Polypharmacy, Frailty, and Neurocognition

Moderated by:
Jennifer F. Hoy, MBBS
Professor of Medicine
Monash University
Melbourne, Australia

Key Recommendations for the Aging and HIV

- Polypharmacy
- Frailty
- Neurocognitive impairment, mental health, and stigma

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Recommendations for Polypharmacy, Frailty, and Cognitive Function Screening for Older People with HIV

- Attention to polypharmacy is recommended in the management of older people with HIV. Assessment of mobility and frailty is recommended for patients ≥ 50 years using a frailty assessment that is validated in all persons with HIV
- Frequency of frailty assessment is guided by the baseline assessment: more frequent (every 1-2 years) in patients who are or are becoming frail and less frequent (up to 5 yearly) in patients who are robust
- In patients who are frail or prefrail, management of polypharmacy, geriatric assessment, exercise and physical therapy, and nutrition advice is recommended
- Routine assessment of cognitive function every other year using a validated instrument is recommended for people with HIV who are older than 60 years

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Recommendations for Polypharmacy, Frailty, and Cognitive Function Screening for Older People with HIV

- Assessment of mobility and frailty is recommended for patients aged 50 years or older using a frailty assessment that is validated in persons with HIV (evidence rating: BIa)
- The frequency of frailty assessment is guided by the baseline assessment and should be more frequent (every 1-2 years) in patients who are frail and less frequent (up to 5 yearly) in patients who are robust

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Recommendations for Polypharmacy, Frailty, and Cognitive Function Screening for Older People with HIV

- In patients who are frail or prefrail, management of polypharmacy, referral for complete geriatric assessment, exercise and physical therapy, and nutrition advice is recommended
- Routine assessment of cognitive function every other year using a validated instrument is recommended for people with HIV who are older than 60 years

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Frailty Phenotype

- Unintentional weight loss of >10 lbs (>4.5kg) or >5% of body mass in last year
- Weakness (assessment based on the handgrip strength)
- Exhaustion
- Slow gait (walking time over a distance of 15 feet)
- Low physical activity (energy expenditure weekly rate)
- Scored based on gender and age norms –



Robust

Pre-frail

Frail

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Poll Question 1

How frequently are you performing frailty assessments in your clinical practice?

1. Not at all
2. Only when you suspect a patient may be frail
3. At regular intervals in older people with HIV (routine assessment)

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Frailty Measurement Tools reported in People with HIV

- Fried's Frailty Phenotype
- Rockwood's Frailty Index
- Edmonton Frail Scale
- Short Physical Performance Battery

- Electronic Frailty Index (using EMR)

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Frailty Index

- The Frailty Index is composed of thirty plus age-related health variables.
- The number of deficits acquired by the individual is divided by the number of health variables assessed, to produce a Frailty Index score ranging from 0 - 1
- Scores <0.08 are defined as "robust", 0.08–0.24 defined as "pre-frail", and ≥0.25 defined as "frail".
- Deficits can be scored as "physical", "psychological" and "social/functional".

Development of Electronic Frailty Index (using EMR) being used in Primary Care

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Short Physical Performance Battery

Consists of 3 assessments of time to complete a task or ability to complete a task:

1. Repeated chair stands (From sitting position, stand then sit 5 times);
2. Balance tests (stand with feet side-by-side for 10 seconds, if able to do side by side move to stand with feet semi-tandem (one foot in front of the other foot, with big toe touching heel of the other foot) and then tandem (one foot directly behind other foot with all toes touching heel of the other foot) for 10 seconds
3. A 4 meter (ten foot) walk test.

A final summary performance score out of 12 is calculated

In order to classify people as frail, pre-frail and non-frail, the following cut-offs are used: SPPB 0-6 (frail), SPPB 7-9 (pre-frail), SPPB 10-12 (non-frail).

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

Edmonton Frail Scale

Includes a number of domains

Cognition: Place numbers in correct position on pre-drawn circle (clock face), then indicate time of "ten past eleven"
General Health status: In the past year, how many times admitted to hospital? How would you describe your health?
Functional independence: How many of the following activities do you require help?
Social Support: When you need help, can you count on someone who is willing/able to?
Medication Use: Use 5 or more different prescription medications? forget to take your medications?
Nutrition: Recently lost weight such that your clothing has become looser?
Mood: Do you often feel sad or depressed?
Continence: Do you have a problem losing control of urine when you don't want to?
Functional Performance: Timed Up and Go test Sit on this chair and when I say GO, please stand up and walk to the mark on the floor (3 metres) at a safe and comfortable pace, then return to the chair and sit down.

Slide

Poll Question 2

How frequently are you performing neurocognitive screening in your clinical practice?

1. Not at all
2. Only when you suspect a patient may have symptoms of neurocognitive impairment
3. At regular intervals in older people with HIV (routine assessment)

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Saag, Gandhi, Hoy et al, *JAMA*, 2020.

Neurocognitive Impairment Screening

- International HIV Dementia Scale
- HIV Dementia Scale
- Mini Mental State Examination
- Montreal Cognitive Assessment
- EACS NCI screening questions

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Saag, Gandhi, Hoy et al, *JAMA*, 2020.

Ending the HIV Epidemic

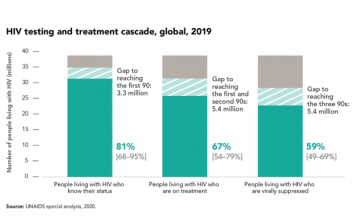
Moderated by:
Carlos del Rio, MD
Distinguished Professor for Emory Clinical and Academic Affairs at Grady
Emory University School of Medicine
Atlanta, Georgia

Ending the HIV Epidemic

- Status of the UNAIDS 90-90-90 initiative in 2020
- What is 95-95-95?
- What are the goals of Ending the HIV Epidemic in the US?
- What can clinicians do to help End the HIV Epidemic?

Saag, Gandhi, Hoy et al, *JAMA*, 2020.

Status of UNAIDS 90-90-90

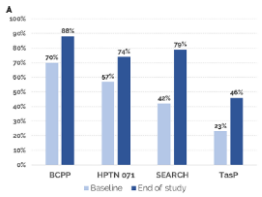


73% was the goal

Increase in 18 percentage points between 2015 and 2019 in viral suppressior

Saag, Gandhi, Hoy et al, *JAMA*, 2020.

What do the UTT trials tell us about the path to HIV epidemic control? Havlir D. et al. JIAS 2020



HIV incidence effect (~20-30% reduction) observed when UTT compared to a control *without* universal testing (BCPP & HPTN 071)

HIV incidence reduced (~30%) in *both arms* when control arm had universal testing (SEARCH)

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Saag, Gandhi, Hoy et al, *JAMA*, 2020.

Targets for ending the AIDS Epidemic

by 2020

90-90-90
Treatment

500 000
New infections among adults

ZERO
Discrimination

by 2030

95-95-95
Treatment

200 000
New infections among adults

ZERO
Discrimination

Incorporates PrEP

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Saag, Gandhi, Hoy et al, *JAMA*, 2020.

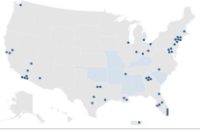
GOAL:

75%
reduction in new HIV infections in 5 years

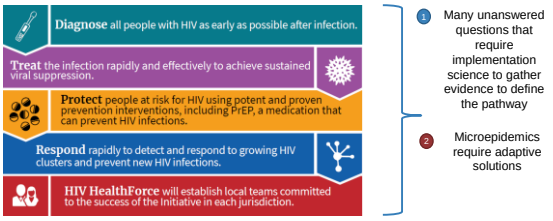
and at least
90%
reduction in 10 years.

FOCUSED EFFORT

- 48 Counties, DC, and San Juan account for 50% of new infections
- 7 States with substantial rural HIV burden



CDC NIH HRSA Health Resources & Services Administration INDIAN HEALTH SERVICE



What can clinicians do to help End the HIV Epidemic?

- Routinely testing for HIV in clinical settings
- Rapidly linking persons with HIV to care and prevention services
- Supporting patients in engagement to care and ART
- Prescribing PrEP to those who need it

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Saag, Gandhi, Hoy et al, *JAMA*, 2020.

New Directions and Emerging Trends

IAS–USA Recommendations 2020

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New ARV Classes and Mechanisms Being Investigated

- NRTTI
- Capsid inhibitor
- CCR5- binding mAb blocking HIV entry
- CD4-binding mAb blocking HIV entry
- Broadly HIV neutralizing antibodies

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

HIV and SARS-COV-2

- Impact on care and provision of medication
- Impact of COVID-19 in people with HIV on: Acquisition risk? Disease severity?
- Comorbidities in COVID-19, similar in HIV
- ARV drug changes in people with HIV and COVID-19?

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.

IAS-USA

These guidelines were organized and sponsored by the International Antiviral Society-USA (not IAS)

www.iasusa.org

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Saag, Gandhi, Hoy et al., *JAMA*, 2020.