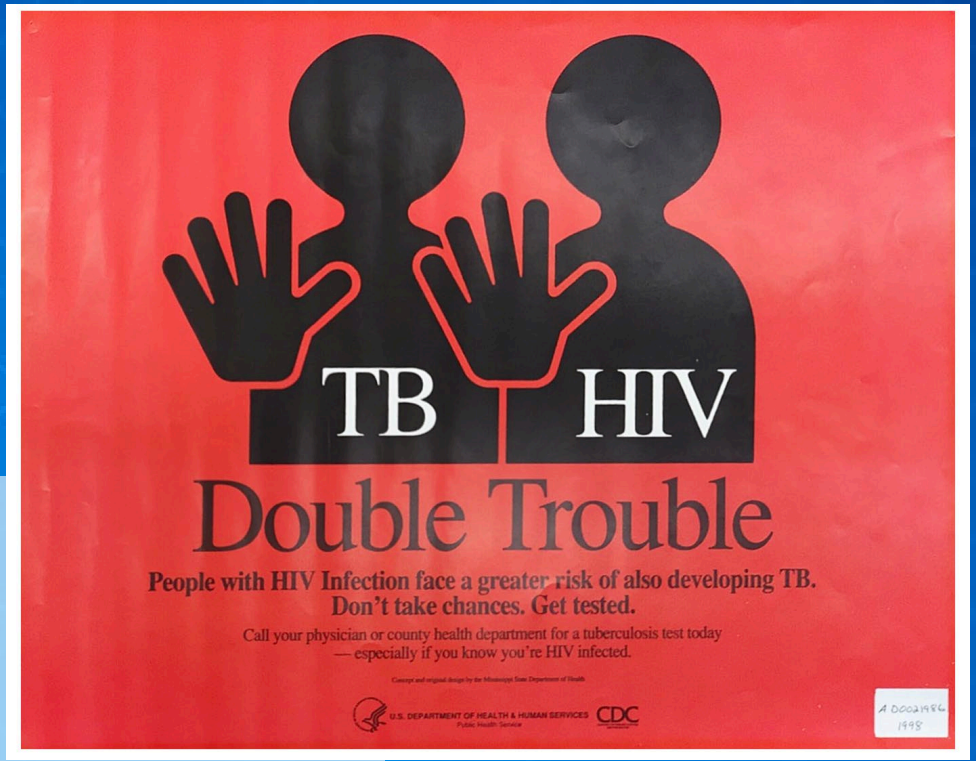
MAYO CLINIC

Center for Tuberculosis




# HIV and TB coinfection

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Mayo Clinic Center for Tuberculosis
Rochester, MN
October 2025

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**Accreditation Statement**
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A record of attendance will be provided to all registrants for requesting credits in accordance with state nursing boards, specialty societies or other professional associations.

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**Available Credit**
- 1.00 ACPE,
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- 1.00 ANCC
- 1.00 Attendance
- 1.00 IPCE

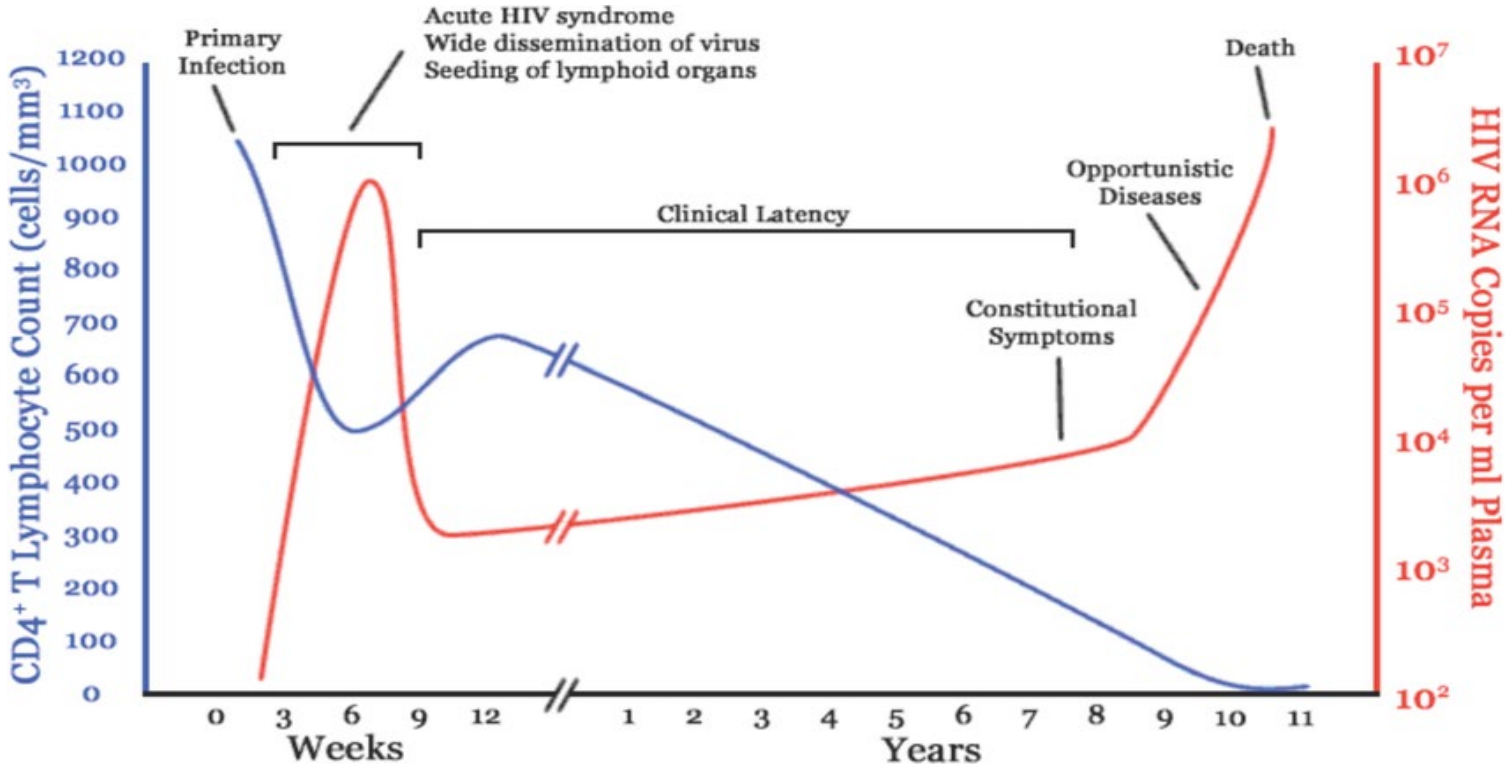
# Disclosure:

No relevant financial disclosures to report and no mention of off-label use of any medications or products

# LEARNING OBJECTIVE

- Evaluate current strategies in diagnosing TB-HIV co-infection.
- Evaluate current strategies in treating TB-HIV co-infection.
- Identify challenges in the management of TB-HIV co-infections.
- Analyze emerging research advancements in the management of TB-HIV co-infection.




Tuberculosis can occur at any stage during HIV infection

## HIV (Human Immunodeficiency Virus)

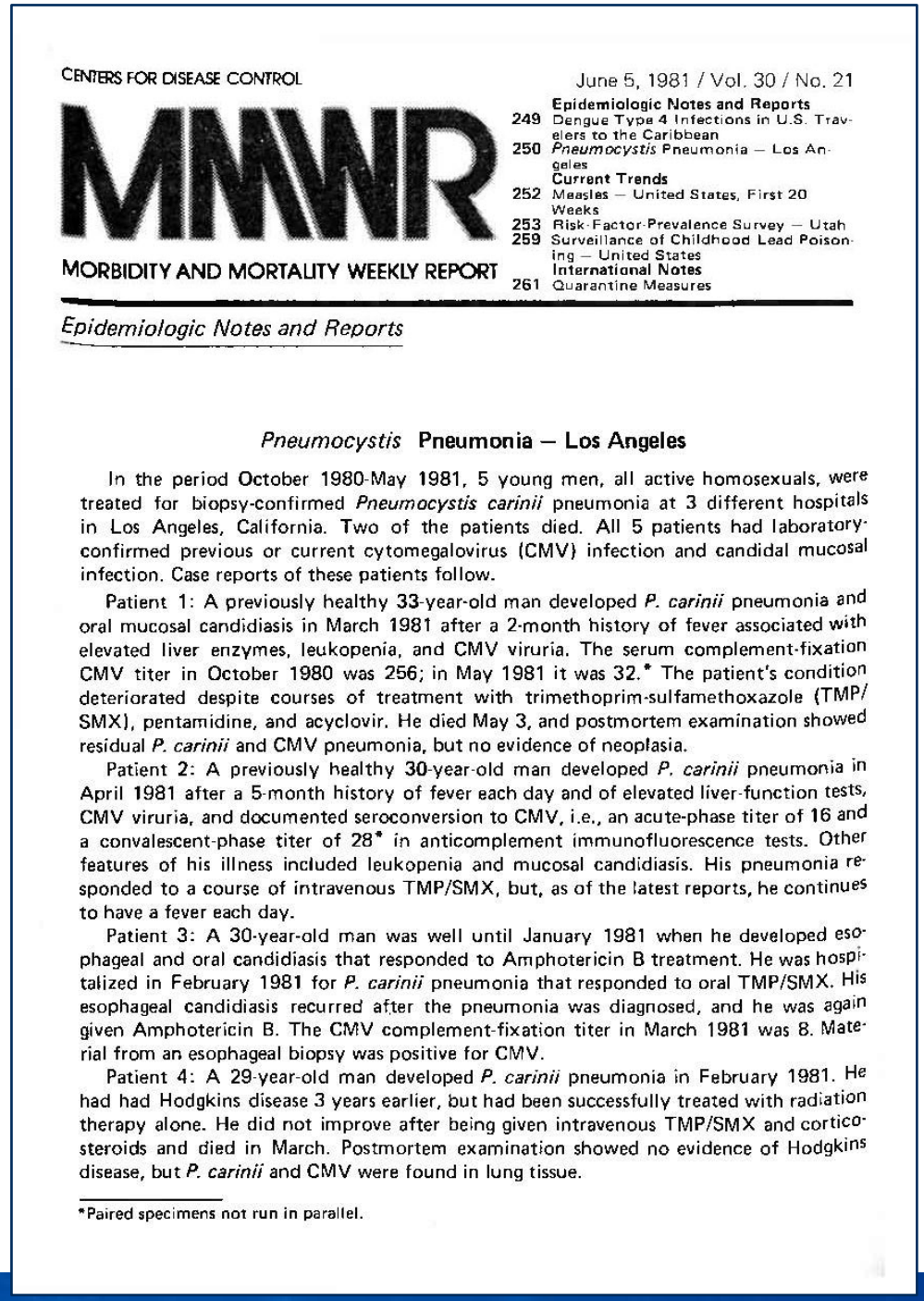
- Transmission: Blood, body fluids (sex), maternal-fetal, needle sharing
- Attacks immune cells (CD4+ T helper cells)
- Acute infection → dissemination to organs, lymph nodes, other tissues → latent state within cells

## AIDS (Acquired Immune Deficiency Syndrome)

- Late stage of HIV infection (advanced immune suppression)
- CD4 T cell count < 200 cells/mm3 or opportunistic infection/malignancy

# HIV in the United States

- 1981: First published reports of AIDS
- 1983: HIV identified as virus that causes AIDS
- 1985: First commercially available HIV test
- 1987: First ARV approved (zidovudine)
- 1995: Peak of HIV related mortality, over 40,000 deaths
- 1995: First protease inhibitor ARV approved
- 1996: First NNRTI ARV approved



CENTERS FOR DISEASE CONTROL

June 5, 1981 / Vol. 30 / No. 21

MMWR

MORBIDITY AND MORTALITY WEEKLY REPORT



*Epidemiologic Notes and Reports*

## *Pneumocystis* Pneumonia — Los Angeles

In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.

Patient 1: A previously healthy 33-year-old man developed *P. carinii* pneumonia and oral mucosal candidiasis in March 1981 after a 2-month history of fever associated with elevated liver enzymes, leukopenia, and CMV viruria. The serum complement-fixation CMV titer in October 1980 was 256; in May 1981 it was 32.* The patient's condition deteriorated despite courses of treatment with trimethoprim-sulfamethoxazole (TMP/SMX), pentamidine, and acyclovir. He died May 3, and postmortem examination showed residual *P. carinii* and CMV pneumonia, but no evidence of neoplasia.

Patient 2: A previously healthy 30-year-old man developed *P. carinii* pneumonia in April 1981 after a 5-month history of fever each day and of elevated liver-function tests, CMV viruria, and documented seroconversion to CMV, i.e., an acute-phase titer of 16 and a convalescent-phase titer of 28* in anticomplement immunofluorescence tests. Other features of his illness included leukopenia and mucosal candidiasis. His pneumonia responded to a course of intravenous TMP/SMX, but, as of the latest reports, he continues to have a fever each day.

Patient 3: A 30-year-old man was well until January 1981 when he developed esophageal and oral candidiasis that responded to Amphotericin B treatment. He was hospitalized in February 1981 for *P. carinii* pneumonia that responded to oral TMP/SMX. His esophageal candidiasis recurred after the pneumonia was diagnosed, and he was again given Amphotericin B. The CMV complement-fixation titer in March 1981 was 8. Material from an esophageal biopsy was positive for CMV.

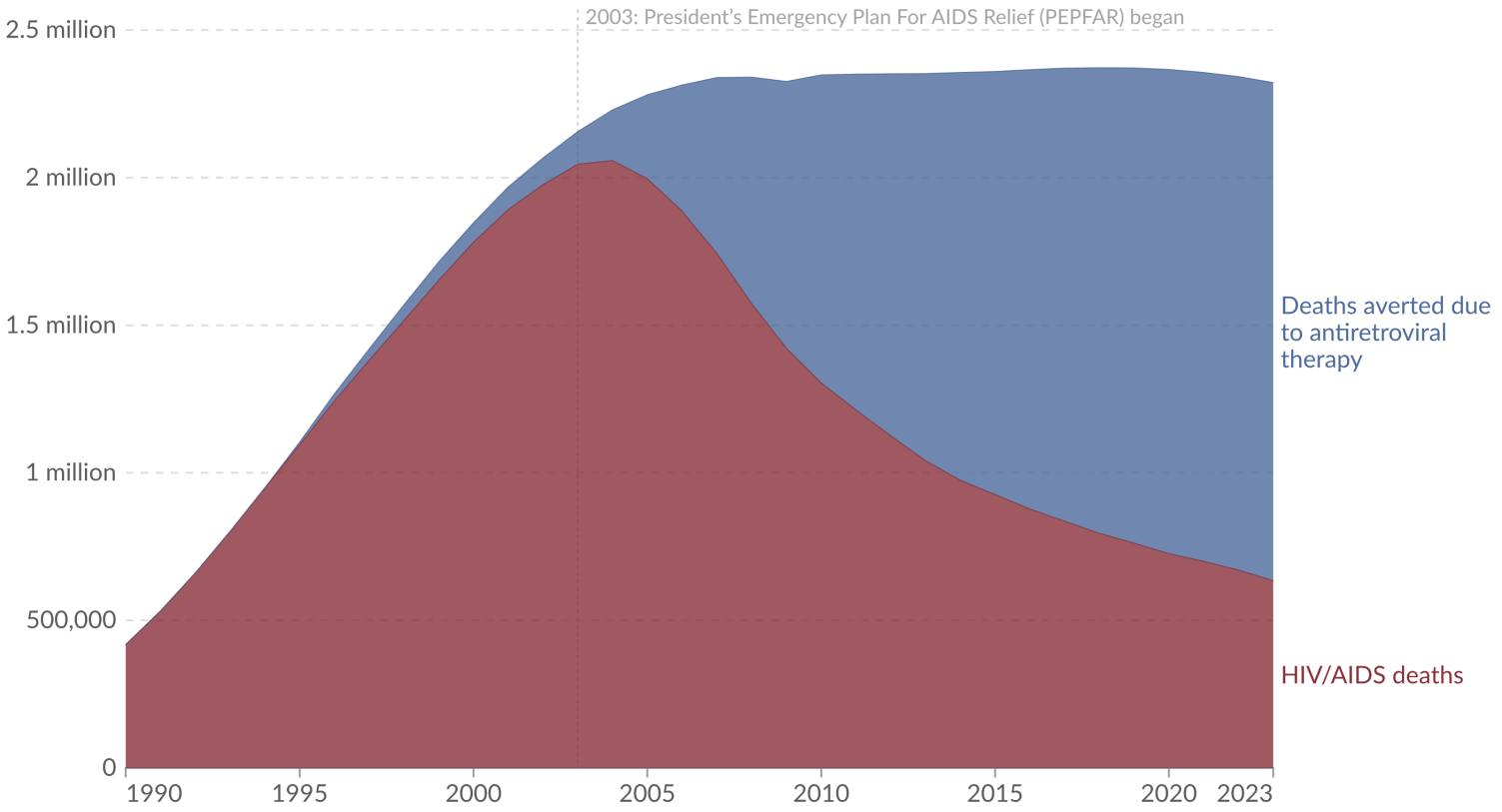
Patient 4: A 29-year-old man developed *P. carinii* pneumonia in February 1981. He had had Hodgkins disease 3 years earlier, but had been successfully treated with radiation therapy alone. He did not improve after being given intravenous TMP/SMX and corticosteroids and died in March. Postmortem examination showed no evidence of Hodgkins disease, but *P. carinii* and CMV were found in lung tissue.

*Paired specimens not run in parallel.

# HIV/AIDS deaths averted by antiretroviral therapy, World

Our World in Data

Estimated annual number of deaths from HIV/AIDS[1] and the estimated number of deaths averted by antiretroviral therapy[2] (ART). Estimates are based on treatment access, treatment efficacy, surveillance data, and epidemiological modeling.




**Data source:** Joint United Nations Programme on HIV/AIDS (2024)

OurWorldinData.org/hiv-aids | CC BY

**1. HIV/AIDS** Acquired immunodeficiency syndrome (AIDS) is a condition that describes the most advanced stages of HIV infection. It is defined by the occurrence of at least one of more than 20 life-threatening cancers or "opportunistic infections" that can take advantage of a weakened immune system.

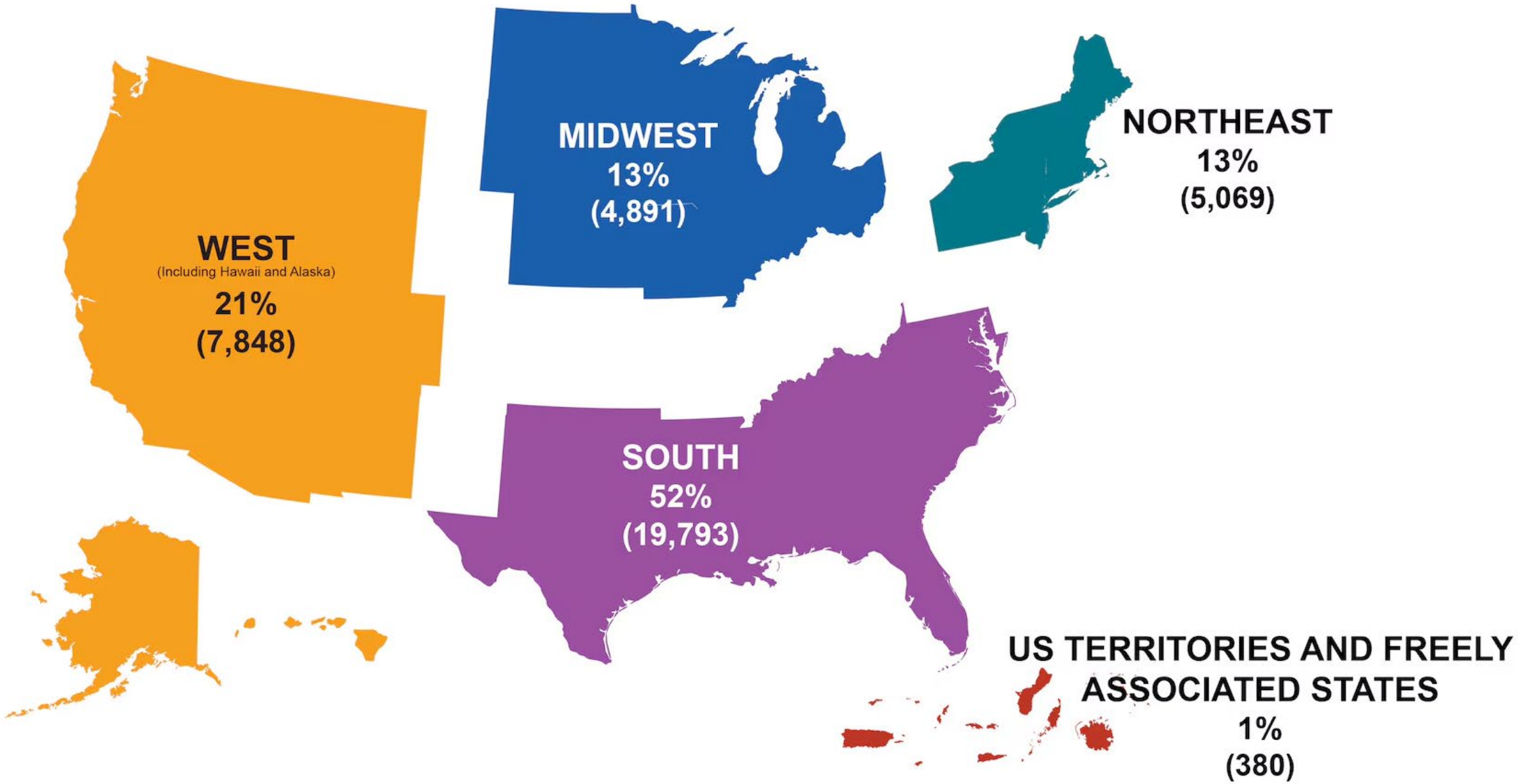
**2. Antiretroviral therapy** Antiretroviral therapy (ART) is a long-term medical treatment for HIV/AIDS. It works by suppressing the virus from multiplying in the body. This keeps the infection under control and helps to prevent the disease from progressing.

- Increasing availability of ARVs lead to decreasing deaths worldwide
- 2006: First single tablet HIV regimen introduced (three HIV medicines, combined into one pill taken once daily)

# HIV in the United States

- Currently 1.1 million adults and adolescents living with HIV
- Men 79%, women 18%, TGW 2%
- 38,000 new HIV diagnoses in 2022
- New HIV diagnoses have remained steady over past 10-15 years, despite HIV PrEP and other interventions

HIV Surveillance Report: Diagnoses, Deaths, and Prevalence of HIV in the United States and 6 Territories and Freely Associated States, 2022



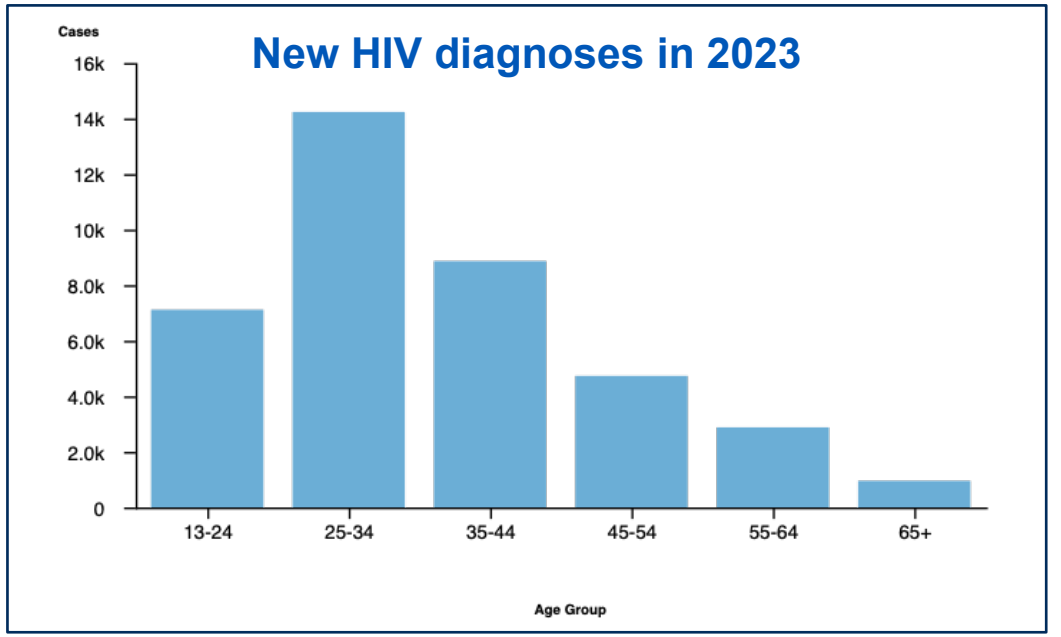

HIV Surveillance Report: Diagnoses, Deaths, and Prevalence of HIV in the United States and 6 Territories and Freely Associated States, 2022

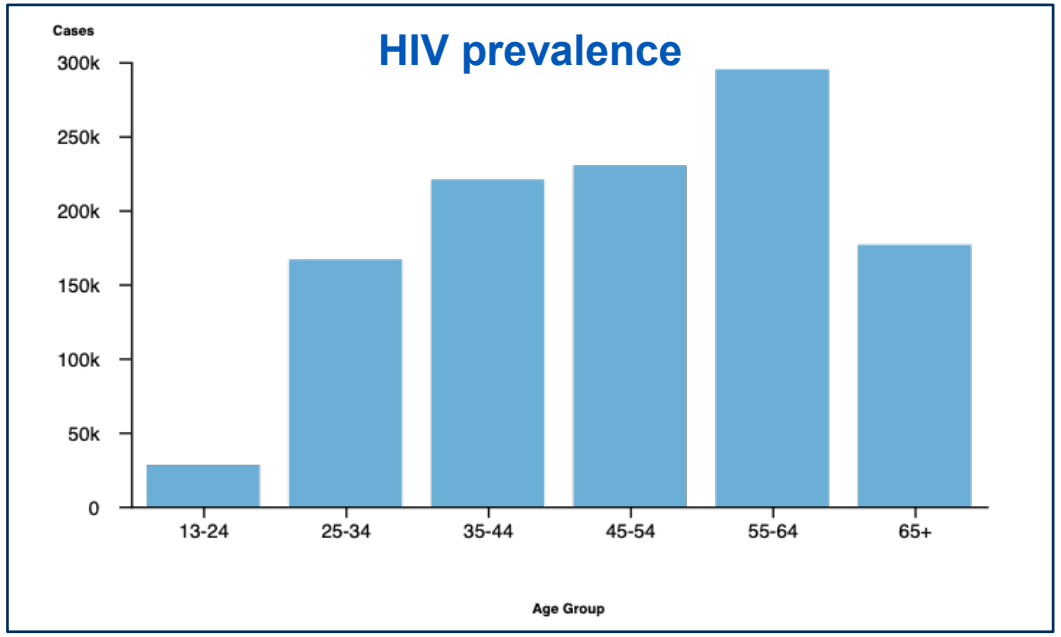
Most new HIV diagnoses are in younger age groups

- 25-34 years: 37%
- 35-44 years: 22%

People with HIV in the US are living longer on antiretroviral therapy

- > 55 years: 41%




Centers for Disease Control and Prevention. NCHHSTP AtlasPlus. https://www.cdc.gov/nchhstp/about/atlasplus.html.

| | New diagnoses in 2023, n (%) | New diagnoses in 2023, rate per 100,000 | HIV prevalence in 2023, n (%) |
|---|---|---|---|
| **American Indian/Alaska Native** | 202 (1%) | 9.8 | 3279 (<1%) |
| **Asian** | 815 (2%) | 4.6 | 18,026 (2%) |
| **Black/African American** | 14,747 (38%) | 41.9 | 438,422 (39%) |
| **Hispanic/Latino** | 13,025 (34%) | 25.2 | 286,599 (26%) |
| **White** | 8,904 (23%) | 5.2 | 307,068 (28%) |

Centers for Disease Control and Prevention. NCHHSTP AtlasPlus.https://www.cdc.gov/nchhstp/about/atlasplus.html

Centers for Disease Control and Prevention. NCHHSTP AtlasPlus.https://www.cdc.gov/nchhstp/about/atlasplus.html

# Social determinants of health

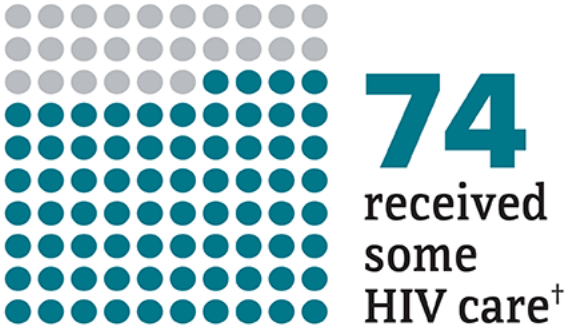
Factors associated with HIV diagnoses:

- Lack of medical insurance
- Medically underserved areas
- Overcrowded housing units
- Renter-occupied housing with rent at least 30% of household income

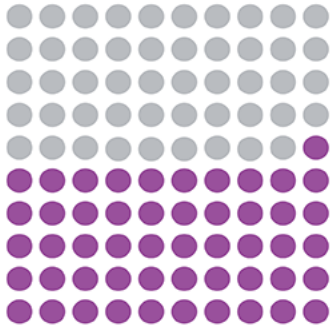
Centers for Disease Control and Prevention. NCHHSTP AtlasPlus.https://www.cdc.gov/nchhstp/about/atlasplus.html
Lockhart E et al. AIDS Behav. 2025 Sep 8:10.1007/s10461-025-04865-x

# Linkage to HIV care continuum

For every 100 people overall with diagnosed HIV:



**74** received some HIV care†



**51** were retained in care ‡

**65** were virally suppressed **

HIV Surveillance Report: Diagnoses, Deaths, and Prevalence of HIV in the United States and 6 Territories and Freely Associated States, 2022

# HIV antiretroviral treatment

- Antiretrovirals cannot eradicate or cure HIV infection
- Antiretrovirals do reduce HIV associated morbidity, prolong life, restore and preserve immunologic function
- Antiretrovirals also prevent HIV transmission
- Single tablet regimens (one pill, once a day) are the mainstay of treatment in the current era
- Life expectancy of PWH on ART with high CD4 counts is only a few years lower than the general population

Trickey A et al. Lancet HIV 2023: 10; e295–307

# HIV & TUBERCULOSIS

**Which one of the following statements is correct regarding TB and HIV?**

A. Patients with HIV and symptoms of TB disease should always be evaluated for TB, regardless of tuberculin skin test (TST) or TB-interferon gamma release assay (IGRA) results

B. A negative TST or TB-IGRA can rule out active TB disease

C. An unremarkable chest x-ray in a patient with symptoms of TB rules out TB disease

D. Obtaining three negative acid fast spontaneous sputum specimens rules out TB with 100% sensitivity

E. A positive acid fast smear on a sputum specimen confirms TB disease

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# Key points: TB and HIV co-infection

- HIV infection increases risk of developing active TB disease
- Manifestations of active TB depend on the degree of immunosuppression
- Increased risk of extrapulmonary TB
- Broader differential diagnosis of symptoms
  - HIV infection
  - Tuberculosis
  - Other opportunistic infections
- Everyone with HIV should be offered antiretroviral therapy

# Mycobacterium tuberculosis

- Any CD4 count
- Screen all people diagnosed with HIV for latent tuberculosis…repeat testing after CD4 > 200
- Annual risk of reactivation 3-16% (= lifetime risk for non-HIV)
- TST > 5 mm, positive TB-IGRA

# RISK OF ACTIVE TB DISEASE

| | |
|---|---|
| **No risk factors** | 5% in the first 2 years after infection<br>10% lifetime risk |
| **HIV** | 10-100 x relative risk |
| **Organ transplant** | 20-70 x relative risk |
| **TNF alpha inhibitors** | 1.6-25.1 x relative risk |
| **Diabetes mellitus** | 1.6-7.83 x relative risk |

Ai JW et al. Emerg Microbes Infect. 2016 Feb; 5(2): e10

# Early HIV infection (CD4 ≥ 200 cells/mm$^3$)

- Similar presentation to HIV uninfected
- Fever, cough, weight loss, anorexia, fatigue, weight loss, night sweats
- Upper lobe, cavitary pulmonary disease

# Advanced HIV infection (CD4 < 200 cells/$mm^3$)

- More variable pulmonary infiltrates, less typical distribution
- Extrapulmonary TB
- Disseminated TB
- May also be subclinical with no symptoms, normal CXR

# Subclinical TB

- Continuum of infection between latent and clinically active TB
- HIV weakens host immune responses, leading to increasing TB replication, host damage and development of clinical symptoms
- Radiology or microbiology testing may be positive prior to development of symptoms

Bajema et al. BMC Infectious Diseases (2019) 19:14

# Subclinical tuberculosis among adults with HIV: clinical features and outcomes in a South African cohort

Kristina L. Bajema[1*], Ingrid V. Bassett[2], Sharon M. Coleman[3], Douglas Ross[4], Kenneth A. Freedberg[2], Anna Wald[5] and Paul K. Drain[6,7]

- 654 adults with untreated HIV, median CD4 count 206
- At enrolment: TB symptom screening, single sputum specimen

| **Active TB** N=96 (15%) | **Subclinical TB** N=28 (4%) |
|---|---|
| AFB smear positive 14% | AFB smear positive 29% |
| Median CD4 count 68 | Median CD4 count 136 |
| Death, N=25 (26%) | Death, N=3 (11%) |

Bajema et al. BMC Infectious Diseases (2019) 19:14

42-year-old man presents with 2-3 months of fevers, sweats, abdominal pain, diarrhea and unintentional weight loss; both QuantiFERON TB and HIV screen are positive. CD4 T cell count is 38 cells/mcl. Chest x-ray noted bilateral ground glass opacities and mediastinal lymphadenopathy. CT abdomen noted diffuse adenopathy and small bowel wall thickening.

**Which of these is the next best step in evaluation for tuberculosis?**

A. Obtain sputum for acid fast smear, mycobacterial culture, MTB PCR
B. TB is unlikely, look for other opportunistic infections
C. Await CD4 count to determine risk of TB disease
D. Start empiric TB therapy, defer initiation of HIV antiretroviral therapy until TB treatment is completed

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# DIAGNOSIS OF TB DISEASE

# Approach to diagnosing TB disease in HIV

- Assess for symptoms and signs
- Test the site of symptoms or signs
- Obtain chest radiograph
- Obtain sputum testing x3
- Refer everyone with HIV regardless of symptoms or TB testing to an HIV provider and public health

# Microbiology

- Sputum, bronchial cultures
- Test extrapulmonary sites if concerning symptoms or signs
  - Urine – multiple specimens may increase yield
  - Ascitic fluid
  - Tissue (lymph node, GI, GU, peritoneum)
  - Cerebrospinal fluid
  - Stool

# Microbiology

- Send specimens for:
  - Acid fast smear, mycobacterial culture, TB NAAT
  - Histopathology
  - Rapid molecular resistance tests
  - Culture-based (phenotypic) drug susceptibility testing
- Testing for other opportunistic infections should be considered

# TB THERAPY

# TB therapy in people with HIV

- Same regimens as people without HIV for drug susceptible and drug-resistant TB
- 4-month moxifloxacin-rifapentine regimen may be an option
  - CD4 ≥ 100
  - On or starting ART
  - No clinically significant drug-drug interactions with HPMZ
  - Better outcomes if on antiretroviral therapy
  - **Review drug-drug interactions between HIV antiretrovirals**

# Drug susceptible TB

- Intensive phase: INH, rifampin or rifabutin, PZA, EMB for 8 weeks
- Continuation phase: INH, rifampin or rifabutin for 16 weeks

- **Total duration of therapy**
  - Pulmonary, drug susceptible uncomplicated: 6 months
  - Positive sputum culture after 2 months of treatment, severe cavitary disease, disseminated extrapulmonary disease: 9 months
  - EPTB with meningitis: 9-12 months
  - EPTB at other sites: 6 months

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Four-Month Rifapentine Regimens with or without Moxifloxacin for Tuberculosis

S.E. Dorman, P. Nahid, E.V. Kurbatova, P.P.J. Phillips, K. Bryant, K.E. Dooley, M. Engle, S.V. Goldberg, H.T.T. Phan, J. Hakim, J.L. Johnson, M. Lourens, N.A. Martinson, G. Muzanyi, K. Narunsky, S. Nerette, N.V. Nguyen, T.H. Pham, S. Pierre, A.E. Purfield, W. Samaneka, R.M. Savic, I. Sanne, N.A. Scott, J. Shenje, E. Sizemore, A. Vernon, Z. Waja, M. Weiner, S. Swindells, and R.E. Chaisson, for the AIDS Clinical Trials Group and the Tuberculosis Trials Consortium

**Feb 2022: CDC added 4-month HPMZ regimen as a treatment option for U.S. patients aged ≥12 years with drug-susceptible pulmonary TB**

Dorman SE et al. N Engl J Med 2021;384:1705–18

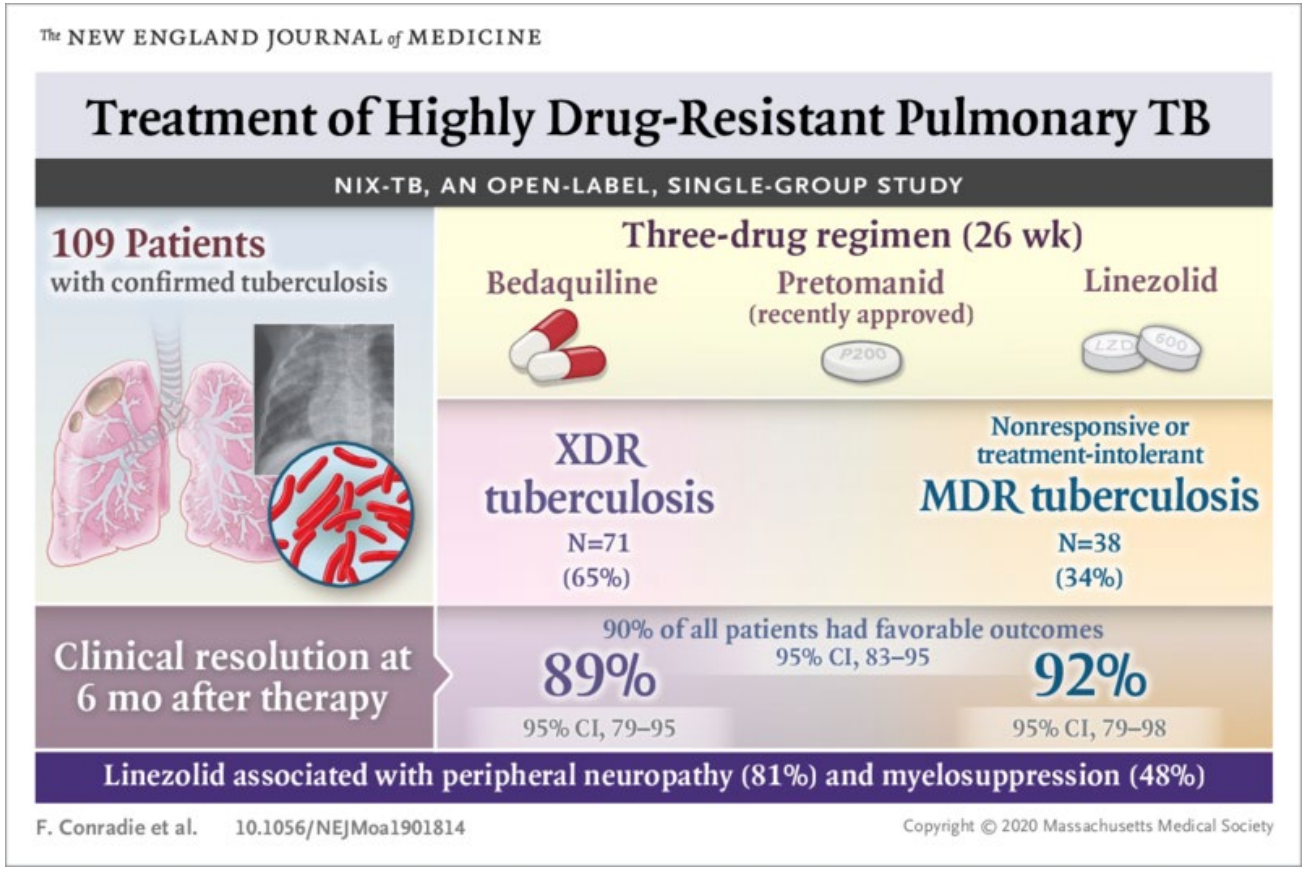
# HPMZ 4 MONTH REGIMEN

| MAY BE AN OPTION | NOT RECOMMENDED | NOT PREFERRED |
|---|---|---|
| • Drug susceptible pulmonary tuberculosis<br>• Age 12 years or older<br>• Weight > 40 kg<br>• **HIV with CD4 ≥ 100, on or starting ART without clinically significant drug-drug interactions with HPMZ**<br>• Negative sputum culture, reflecting likely paucibacillary or low mycobacterial burden disease | • Body weight <40 kg<br>• Age <12 years<br>• Pregnant or breastfeeding<br>• Most extrapulmonary TB infection<br>• History of prolonged QT syndrome or concurrent use of ≥ 1 QT-prolonging medications (in addition to MOX)<br>• Receiving medications with clinically relevant drug-drug interactions with RPT, MOX, INH, or PZA<br>• Drug resistant TB | • Received > 5 doses of treatment directed against active or latent TB in the preceding 6 months<br>• Received > 5 doses with 1 or more of these drugs (fluoroquinolone, INH, RIF, rifabutin, PZA) for any reason in the preceding 30 days<br>• ALT or AST > 3 x ULN, or total bilirubin > 2.5 x ULN<br>• Advanced liver or kidney disease |

MMWR Morb Mortal Wkly Rep 2022 Feb 25;71(8):285-289. https://www.cdc.gov/tb/topic/treatment/tbdisease.html

# BPaL

- NIX trial: BPaL for 26 weeks for MDR and XDR TB
- HIV with CD4 > 50 included
- 51% of participants were HIV positive (almost all on ART already)
- 90% had favorable outcome, regardless of HIV status
- Similar adverse effects, including LZD neuropathy




Conradie F et al. N Engl J Med 2020; 382:893-902

# Treatment Complexities Among Patients with Tuberculosis in a High HIV Prevalence Cohort in the United States

Destani J. Bizune,[1] Russell R. Kempker,[2] Michelle Kagei,[3] Aliya Yamin,[4] Omar Mohamed,[4] David P. Holland,[2,4] Alawode Oladele,[5] Yun F. Wang,[6,7] Paulina A. Rebolledo,[1,2] Henry M. Blumberg,[1,2] Susan M. Ray,[2] and Marcos C. Schechter[2]

- Retrospective cohort of 274 adults with culture confirmed TB, 2008-2015, Atlanta GA
- 96 (35%) patients with HIV, median CD4 count of 86, 81% on ART during TB treatment

| | **TB** N=178 (65%) | **HIV-TB** N=96 (35%) |
|---|---|---|
| Treatment interruption due to AEs | 15% | 34% |
| Hospital readmission | 21% | 50% |
| Median TB treatment | 8.8 months | 9.9 months |
| Cure | 85% | 75% |

Bizune DJ et al. AIDS Res Hum Retroviruses 2018 Dec 1; 34(12): 1050–1057

# ANTIRETROVIRAL THERAPY

**Which of the following is a contraindication to prompt initiation of HIV antiretroviral therapy in those with HIV-TB coinfection?**

A. CD4 count less than 50

B. CD4 count greater than 500

C. Drug resistant TB

D. TB meningitis

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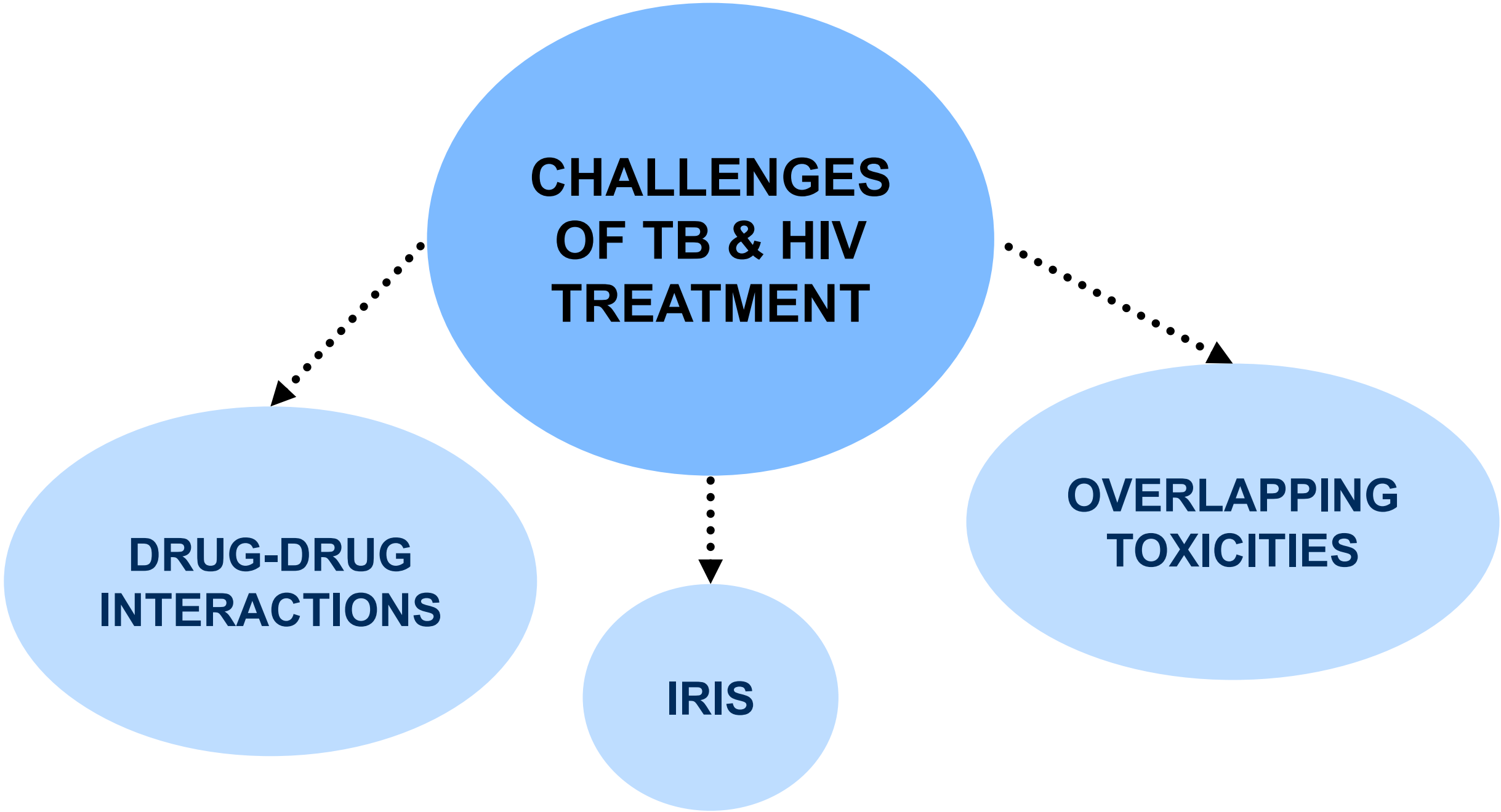
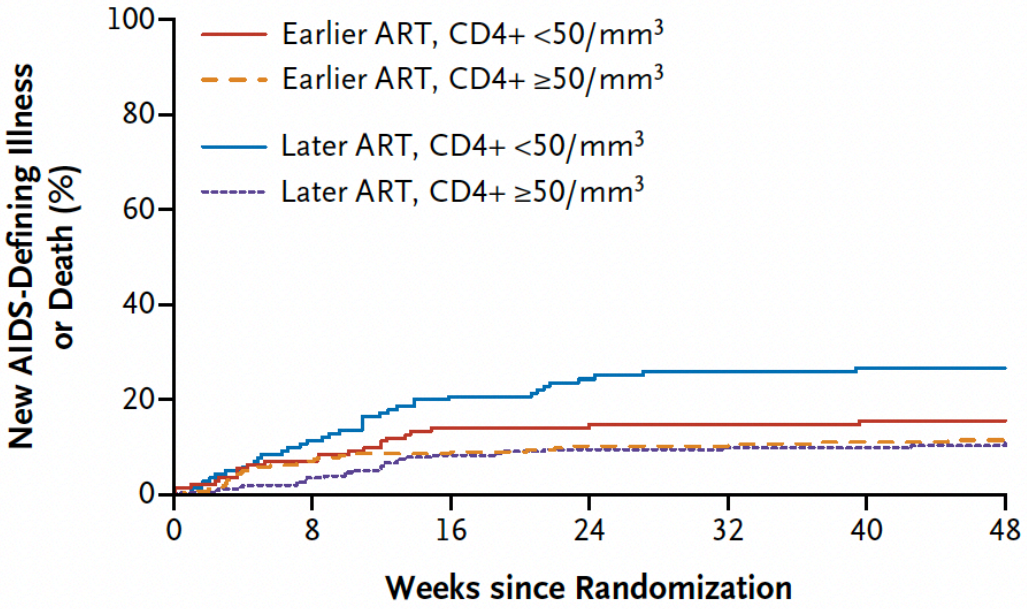

CHALLENGES OF TB & HIV TREATMENT
DRUG-DRUG INTERACTIONS
IRIS
OVERLAPPING TOXICITIES

# Initiation of antiretroviral therapy

- Historically initiation of ART was delayed until several months into or after completion of TB treatment
- Concerns for drug adverse effects, overlapping toxicities, adherence, pill burden, cost and risk of IRIS

Burke RM et al. J Int AIDS Soc 2021 Jul; 24(7): e25772

- Early ART is associated with significant benefits
  - Reduced mortality in those with CD4 count < 50 cells/mm$^3$
  - Reduced AIDS defining events
- Benefits of early ART are not outweighed by potential complications
  - Increased risk of IRIS
  - No difference in treatment limiting drug toxicities




**No. at Risk**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Earlier therapy | | | | | | | |
| CD4+ <50/mm³ | 144 | 132 | 121 | 121 | 118 | 114 | 74 |
| CD4+ ≥50/mm³ | 261 | 236 | 225 | 220 | 217 | 210 | 152 |
| Later therapy | | | | | | | |
| CD4+ <50/mm³ | 141 | 125 | 110 | 103 | 101 | 98 | 69 |
| CD4+ ≥50/mm³ | 260 | 246 | 232 | 226 | 224 | 220 | 149 |

Havlir DV et al. N Engl J Med 2011;365:1482-91

# When to start ART

**Current recommendations: Start ART as soon as possible**

- CD4 count < 50 cells/mm$^3$: Start ART as soon as possible, within 2 weeks of starting TB treatment
- CD4 count ≥ 50 cells/mm$^3$: Start ART within 8 weeks of starting TB treatment

**Exception: TB meningitis**

ART should not be initiated in the first 8 weeks of TB treatment

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. 2023

# Antiretroviral therapy dosing

| | |
|---|---|
| **RIFAMPIN** | Dolutegravir 50 mg twice daily |
| | Efavirenz 600 mg once daily |
| **RIFABUTIN** | Efavirenz 400 mg once daily<br>Rifabutin 450-600 mg daily |
| | Dolutegravir 50 mg once daily |

*Plus two other antiretrovirals (tenofovir, emtricitabine, lamivudine, abacavir etc.)

# Rifamycin drug-drug interactions

- Induction of metabolizing enzymes
  - CYP3A4 substrates: Protease inhibitors, rilpivirine, rifabutin
  - CYP2B6 substrates: Efavirenz
  - UGT1A1: InSTIs (dolutegravir)
- Induction of efflux transporters
  - P-glycoprotein: Protease inhibitors, tenofovir alafenamide
- Rifamycin enzyme induction is maximal at 2 weeks after starting and persists for up to 4 weeks after stopping rifamycin
- Potency of induction: Rifampin, rifapentine > rifabutin

| | PROTEASE INHIBITORS | InSTIs | NNRTIs | NRTIs |
|---|---|---|---|---|
| **RIFABUTIN** | • Rifabutin 150 mg daily<br>• Only with ritonavir boosting, not cobicistat | • No DTG dose change, rifabutin 300 mg daily<br>• No RAL dose change<br>• BIC, CAB IM, EVG/c not recommended | • Increase DOR to 100 mg bid<br>• EFV 450-600 mg/day<br>• Increase RPV 50 mg daily | • TAF not recommended<br>• No TDF dose change |
| **RIFAMPIN** | Coadministration not recommended | • DTG 50 mg bid<br>• RAL 800 mg bid<br>• BIC, CAB IM + PO, EVG/c not recommended | • EFV 600 mg daily<br>• Other NNRTIs not recommended | • TAF not recommended<br>• No TDF dose change |
| **RIFAPENTINE** | Coadministration not recommended | • Can use with DTG 50 mg daily, RAL 400 mg bid<br>• BIC, CAB IM + PO, EVG/c not recommended | • No EFV dose change<br>• Other NNRTIs not recommended | • TAF not recommended<br>• No TDF dose change |

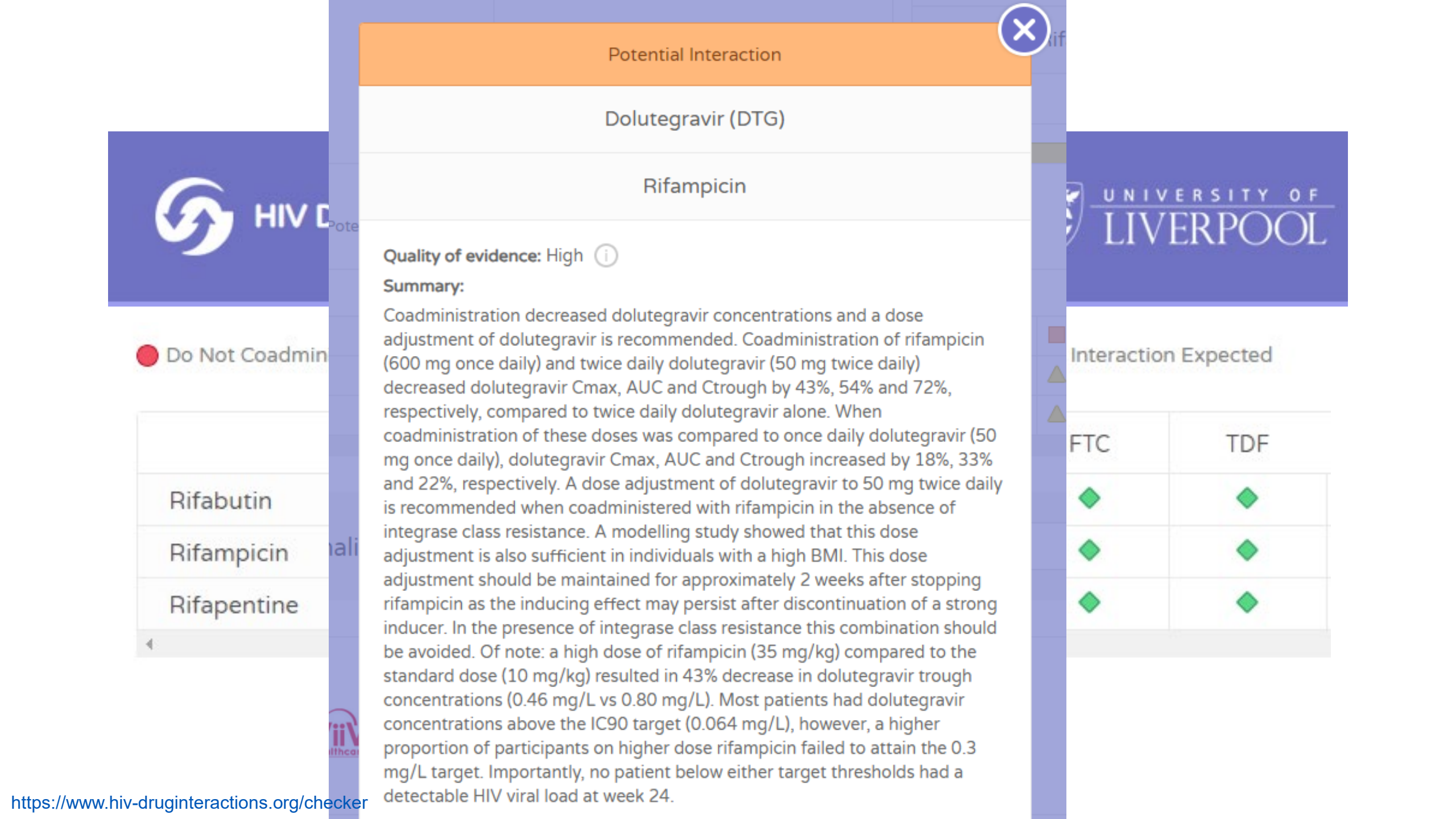
# HIV Drug Interactions

UNIVERSITY OF LIVERPOOL

Do Not Coadminister | Potential Interaction | Potential Weak Interaction | No Interaction Expected

| | DTG | EFV | FTC | TDF |
|---|---|---|---|---|
| Rifabutin | ◆ | ■ | ◆ | ◆ |
| Rifampicin | ■ | ▲ | ◆ | ◆ |
| Rifapentine | ■ | ▲ | ◆ | ◆ |

https://www.hiv-druginteractions.org/checker




https://www.hiv-druginteractions.org/checker

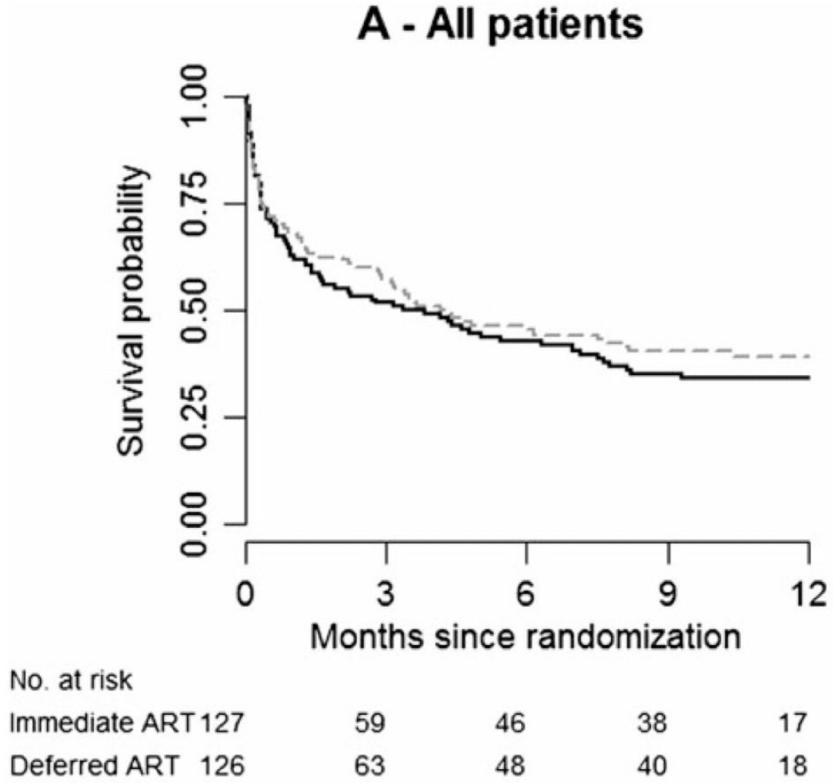
# TB MENINGITIS

# HIV and TB meningitis

- Very high mortality
- Worse outcomes with earlier initiation of ART
- Higher CSF concentrations of inflammatory cytokines and more intracerebral inflammation
- Adjunctive corticosteroids may reduce inflammation and improve outcomes…unclear benefit in HIV

# TB meningitis and ART initiation

- Randomized double-blind placebo control trial of 253 people with HIV and TB meningitis
- Immediate vs deferred (2 months) ART start
- TB therapy, adjunctive dexamethasone
- Death within 9 months
  - Immediate ART 76/127 people
  - Deferred ART 70/126
- High rates of adverse events 90% vs 89%



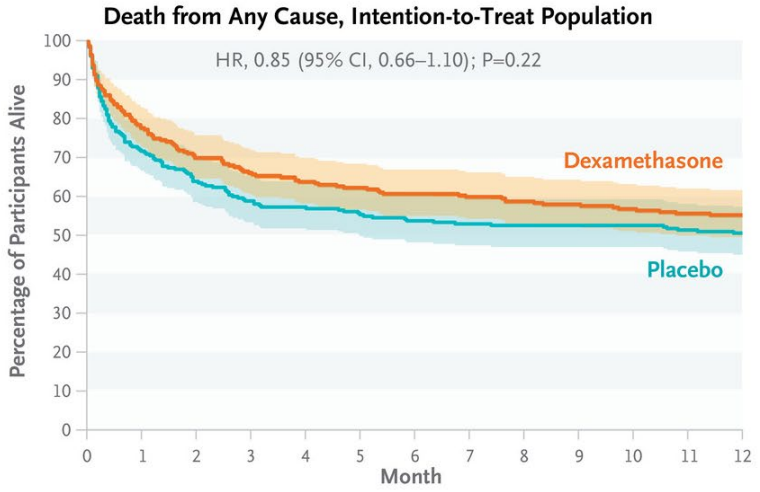

Torok ME et al. Clin Infect Dis 2011 Jun; 52(11): 1374–1383

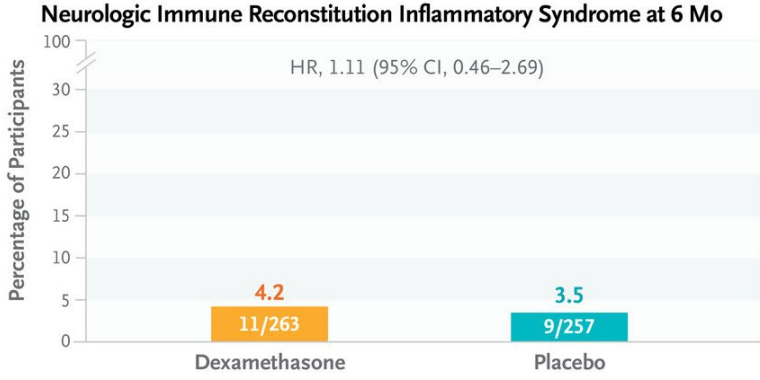
# Adjunctive corticosteroids

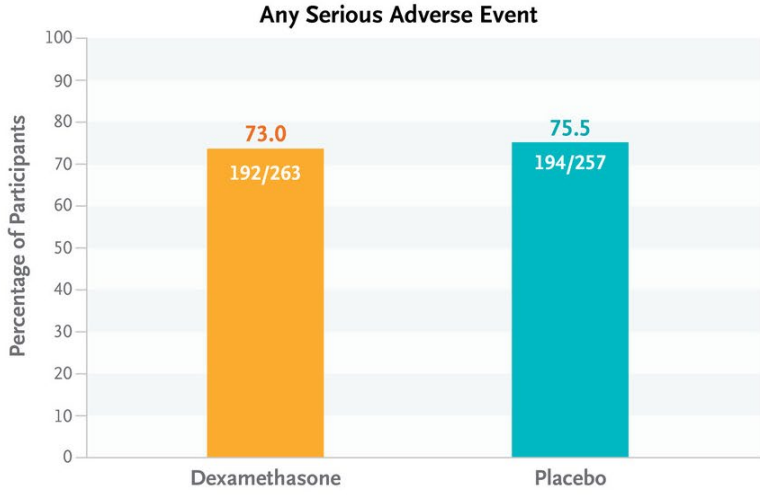
- Adjunctive corticosteroid therapy is recommended in CNS TB
- Dexamethasone 0.3–0.4 mg/kg/day for 2–4 weeks, then taper by 0.1 mg/kg per week until dose of 0.1 mg/kg, then 4 mg per day and taper by 1 mg/week for a total duration of 12 weeks
- Adjunctive corticosteroids increase overall survival in TB meningitis
  - Risk ratio 0.75
  - Little impact on long-term neurological complications
  - Limited data in HIV (included one trial, N=98)

Prasad K et al. Cochrane Database Syst Rev 2016 Apr 28;4(4):CD002244

- Double-blind, randomized, placebo-controlled trial of 520 adults with HIV and TB meningitis in Vietnam and Indonesia
- Adjunctive dexamethasone vs placebo
  - Grade II or III: 4 weeks IV + 4 weeks oral
  - Grade I: 3 weeks IV + 3 weeks oral
- No difference in overall mortality
  - 44.1% in dexamethasone, 49.0% in control
- Immunosuppressed: Half had CD4 <50
- Cerebral inflammation may be mediated through different mechanisms in HIV




Donovan J et al. N Engl J Med 2023 Oct 12;389(15):1357-1367

# IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS)

# Immune reconstitution inflammatory syndrome (IRIS)

- Advanced HIV being treated for TB are at significant risk of immune-mediated deterioration during the first weeks of starting or restarting ART, or switching to an effective regimen
- Rapid decrease in HIV viral load and early immune recovery on ART leads to an enhanced immune response to TB bacteria
- TB-IRIS occurs in around 18% after initiation of ART

# TB-IRIS

- Paradoxical IRIS
  - Known TB infection initially responding to TB therapy
  - Deteriorates after ART induced immune reconstitution

- Unmasking IRIS
  - Undiagnosed, subclinical TB infection
  - ART induced immune reconstitution leads to an inflammatory presentation of TB disease

# Manifestations

- Inflammation at site of TB disease with recurrent local symptoms
- Systemic inflammation symptoms (fevers, sweats, weight loss etc)
- Enlarged, suppurative lymphadenopathy
- Abscess formation
- Worsening infiltrates, effusions or other radiologic findings
- Granulomatous hepatitis

- Median onset: 14 days after starting ART
- Can be delayed up to 3 months

# Diagnosis of TB-IRIS

- Typical clinical features
  - Initial reliable TB diagnosis
  - Initial response to TB treatment
  - Deterioration with compatible symptoms, signs and imaging within 3 months of starting ART

- Exclusion of alternative diagnoses (eg. TB drug resistance)

# Other opportunistic infections

- More than one opportunistic infection is possible in immunologically advanced HIV infection
- May require treatment for multiple infections or malignancies
- Increases possibilities of drug adverse effects, toxicities and interactions
- Trimethoprim-sulfamethoxazole prophylaxis (Pneumocystis, Toxoplasma) may also be needed if CD4 count is less than 200

# Risk of IRIS

- Lower CD4 count (<50 cells/mm3)
- High HIV viral load
- Short interval between starting ATT and ART
- Extrapulmonary or disseminated TB (higher mycobacterial burden)

# Management of TB-IRIS

- Continue ART and TB therapy
- Evaluate for treatment failure, other infections or diseases
- Prednisone course
  - If no evidence of treatment failure or other opportunistic infection
  - Reduce TB IRIS morbidity

- Low mortality 1-2% (except TB meningitis)
- Significant morbidity

# Prednisone prophylaxis

- Randomized, double-blind, placebo-controlled trial of 240 people initiating HIV ART, had started TB treatment within 30 days before ART
- Prednisone 40 mg daily for 14 days, then 20 mg per day for 14 days
- Median CD4 49
- TB IRIS: 32% in prednisone vs 46% in placebo
- Deaths: 5 in prednisone vs 4 in placebo
- Severe infections: 11 in prednisone vs 18 in placebo
- **Consider pre-emptive prednisone in high risk** (starting ART within 30 days of starting ATT, CD4 ≤100/mm3) who are responding well to ATT and who do not have rifampin resistance, Kaposi sarcoma, or active hepatitis B

# LATENT TB INFECTION

# LTBI screening recommendations

- Screen all with HIV
- Retest those with advanced HIV (CD4 count <200) and negative initial screening tests once they start ART and reach CD4 count ≥200
- Annual testing for LTBI  if prior negative test and at high risk for repeated or ongoing exposure to persons (incarceration, travel to a high-TB incidence area, homelessness)

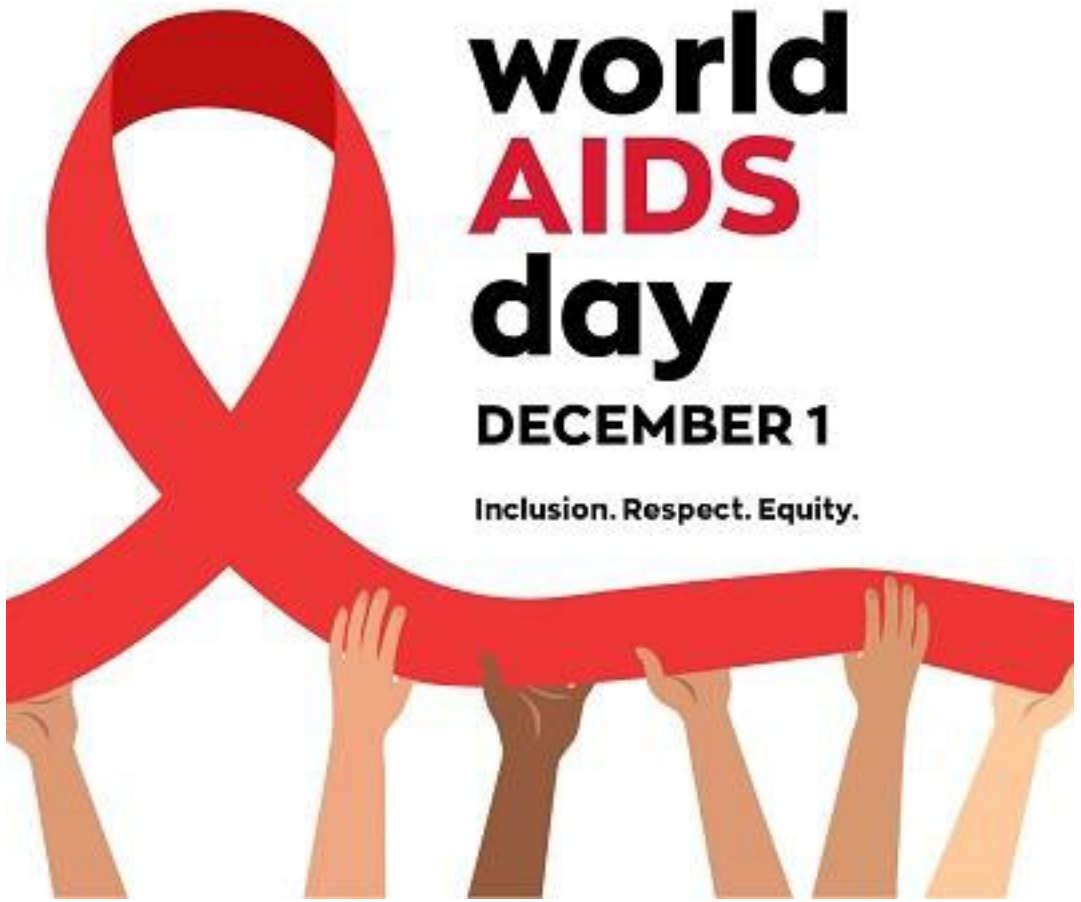
| PREFERRED LTBI REGIMENS | |
|---|---|
| **Once weekly isoniazid + rifapentine for 3 months (3HP)** | Only for virally-suppressed patients receiving an efavirenz-, raltegravir-, or once-daily dolutegravir-based ARV regimen<br><br>Review for drug-drug interactions with ART |
| **Daily isoniazid + rifampin for 3 months (3HR)** | Review for drug-drug interactions with ART |
| **ALTERNATIVE LTBI REGIMENS** | |
| **Daily isoniazid for 6-9 months** | Any antiretroviral regimen |
| **Once daily isoniazid + rifapentine for 1 month (1HP)** | Only for patients receiving an efavirenz-based ARV regimen<br><br>Review for drug-drug interactions with ART |
| **Daily rifampin for 4 months (4R)** | Review for drug-drug interactions with ART |

# Key points: TB and HIV co-infection

- HIV infection increases risk of developing active TB disease
- Manifestations of active TB depend on the degree of immunosuppression
- Increased risk of extrapulmonary TB
- Broader differential diagnosis of symptoms
  - HIV infection
  - Tuberculosis
  - Other opportunistic infections
- Everyone with HIV should be offered antiretroviral therapy

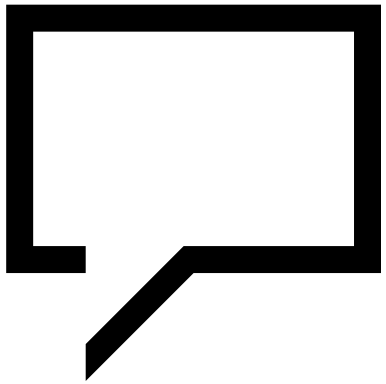
# Linkage to HIV care

- Refer everyone with HIV to the health department and an HIV clinic, regardless of symptoms or TB test results
- All persons with HIV infection should be linked to HIV care and offered antiretroviral therapy
- Treating HIV infection prevents complications for the individual and prevents HIV transmission in the community




https://www.hiv.gov/federal-response/policies-issues/hiv-aids-care-continuum

# QUESTIONS & ANSWERS




# Thank you