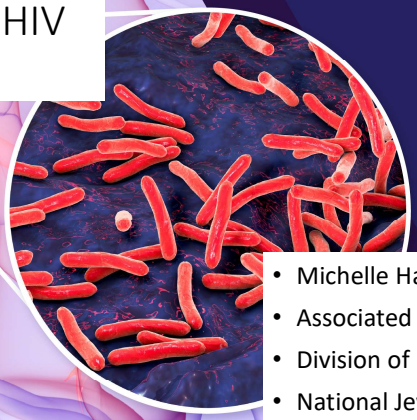
Updates in the management of TB infection and disease in people living with HIV



62ND ANNUAL

Denver TB Course (Hybrid Event)

MARCH 25-27, 2026

- Michelle Haas, MD
- Associated Professor of Medicine
- Division of Mycobacterial and Respiratory Infections
- National Jewish Health

Disclosures

- I have nothing to disclose

National Jewish Health

Objectives

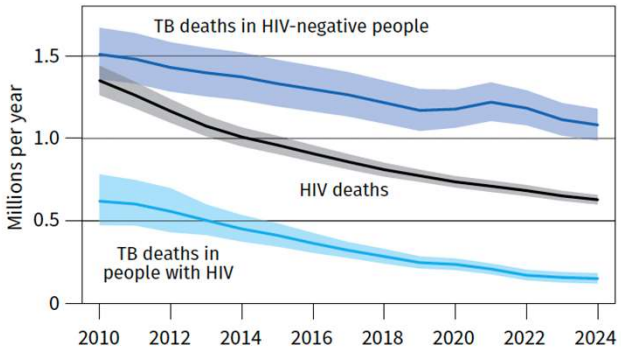
- Understand the epidemiology of TB-HIV
- Be able to discuss specific treatment considerations for TB disease in people living with HIV (PLHIV)
- Be able to discuss LTBI treatment options for PLHIV on ART
- Understand drug interaction considerations for PWHIV and TB who receive ART

Global TB Report 2025

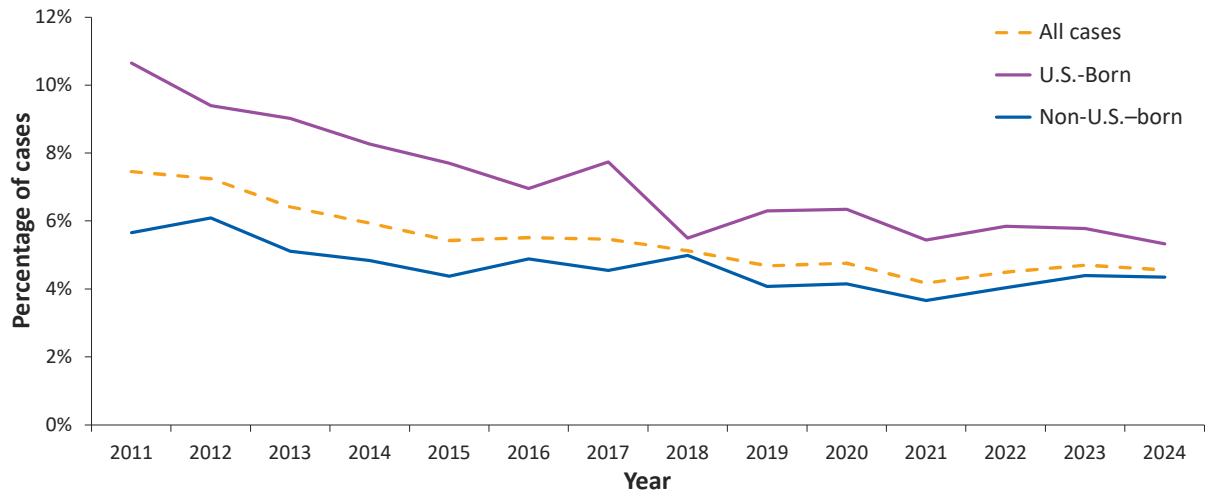
- In 2024, TB caused an estimated 1.23 million deaths (95% UI: 1.13–1.33 million),
- 1.08 million among HIV-negative people
  - (95% UI: 0.99–1.18 million)
- **150 000 among people with HIV**
  - (95% UI: 120 000–183 000)

Global trends in the estimated number of deaths caused by TB and HIV (in millions), 2010–2024[a,b]

Shaded areas represent 95% uncertainty intervals.



Percentage of HIV Coinfection* by Origin of Birth† Among Persons with TB, United States, 2011–2024



* Persons alive at diagnosis with HIV test results
† Persons born in the United States, certain U.S. territories, or elsewhere to at least one U.S. citizen parent are categorized as U.S.-born. All other persons are categorized as non-U.S.–born.

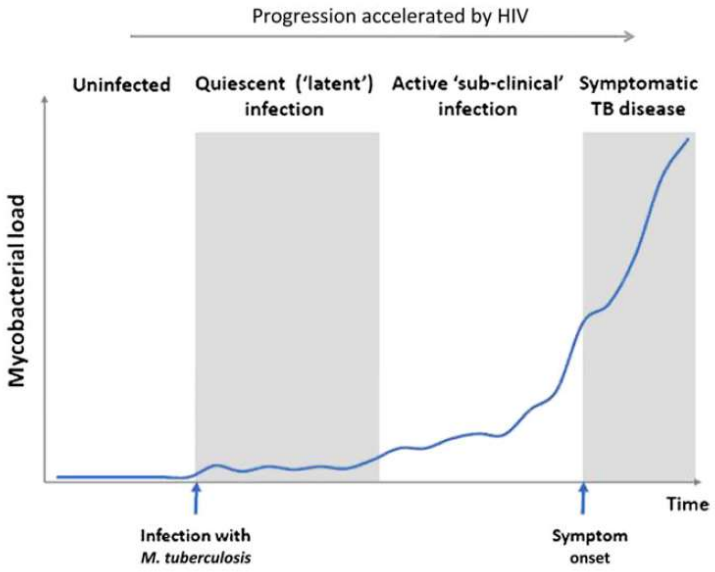
Cumulative number of deaths (in millions) averted by a) TB treatment as well as b) antiretroviral treatment for people diagnosed with TB who were also living with HIV, globally and by WHO region, 2010–2024

Indonesia is included in the WHO Western Pacific Region.

	HIV-NEGATIVE PEOPLE		PEOPLE LIVING WITH HIV[a]		TOTAL	
WHO REGION	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
African Region	6.6	5.4–7.7	5.2	4.4–6.0	12	10–13
Region of the Americas	1.5	1.4–1.6	0.27	0.24–0.29	1.8	1.6–1.9
South-East Asia Region	17	14–19	0.85	0.52–1.2	18	15–20
European Region	1.3	1.2–1.5	0.25	0.22–0.28	1.6	1.4–1.7
Eastern Mediterranean Region	4.2	3.6–4.7	0.056	0.024–0.088	4.2	3.7–4.8
Western Pacific Region	14	13–16	0.42	0.34–0.50	15	13–16
Global	**45**	**40–50**	**7**	**6.0–7.9**	**52**	**46–57**

[a] Deaths from TB among people with HIV are officially classified as deaths caused by HIV/AIDS (with TB as a contributory cause). This is the reason why the estimates make a clear distinction between people with and without HIV.

The Spectrum of TB Infection in people living with HIV-TB



Lawn, SD and Wood R, JID 2011

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 NOVEMBER 30, 2006 VOL. 355 NO. 22

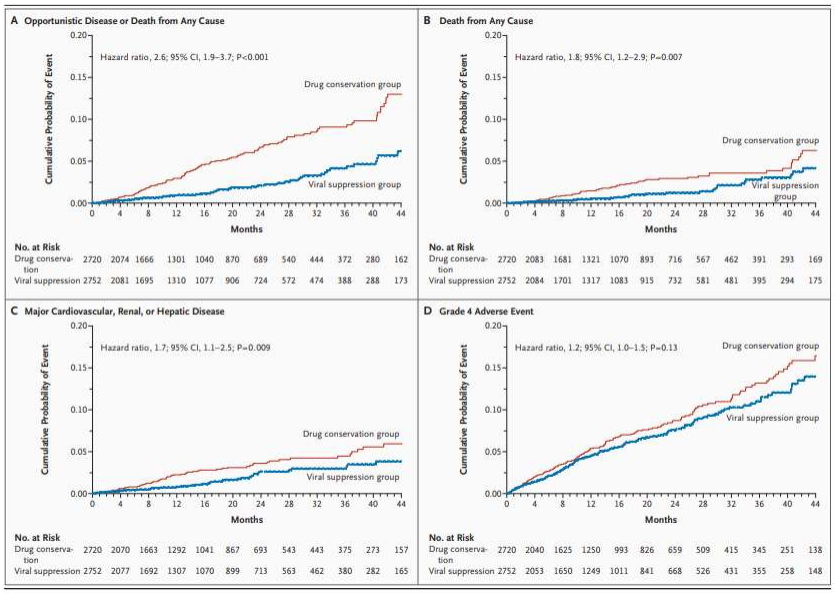
CD4+ Count–Guided Interruption of Antiretroviral Treatment

The Strategies for Management of Antiretroviral Therapy (SMART) Study Group*

- N=5472 participants, N=2720 (drug conservation), N= 2752 (viral suppression) followed for 16 months initially
- Drug conservation group after 16 months: defer/stop ART until CD4 is <250 cells/mm3, allow CD4 to increase to 350, then stop again
- Baseline:
  - median 597 cells/mm3; nadir CD4+ 250 cells/mm3,
  - 71.7% with HIV RNA levels of <=400 copies per mL

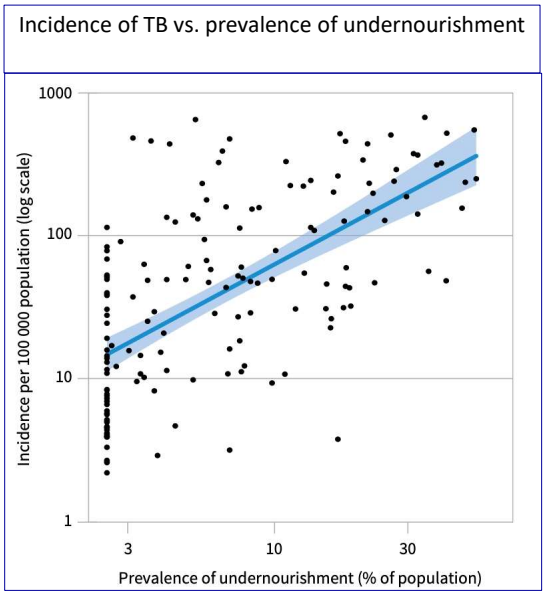
Even short ART treatment interruptions increase risk of death

- Drug conservation group within 2 months:
  - average CD4+ count decreased by 87 cells mm3 per month after randomization
  - increase in % with a detectable plasma HIV RNA level from 6% to 72%) after cessation of ART
  - Increased risk of death, cardiovascular disease, and opportunistic infections
    - Seen as early as 4-8 months after interruptions



Competing risk factors and need to treat the "whole patient"

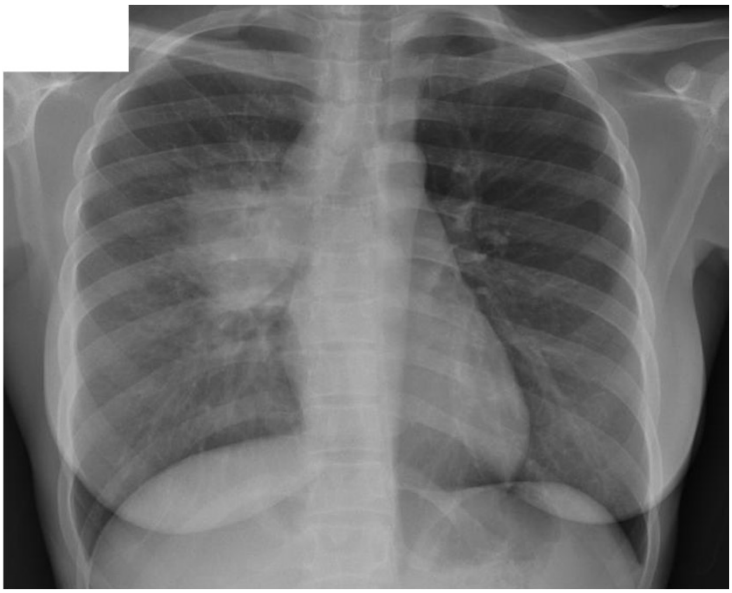
- What interfered with your ability to take your HIV medications?
  - Partner passed away
  - Lost my job
  - House burned down
  - Need to support children's nutritional needs
  - My HIV medications make me hungry



HPI

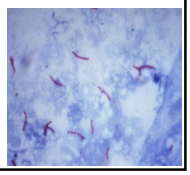
20 y/o woman with newly diagnosed HIV with cough, and lymphadenopathy.

- 15 weeks pregnant
  - Experiencing homelessness



Diagnostics for TB in the US in routine practice settings

US based setting	Time to final result	sensitivity/specificity for PTB	sensitivity for other sources	Cost	Ref
AFB smear	1-3 days	30-70%/varies	<50%	$4 (wide variation)	AJRCCM, 2018
Xpert MTB/Rif	90 min-1 day	60-90%/99%	CSF-70%; pleural fluid 49%; LN aspirate 82%	$100 (in the US); $14.00 outside US	Cochrane Rev, 2014 and 2021; CID 2016
Culture	6 weeks	10 cfu/ml	10 cfu/ml	$50 (wide variation)	

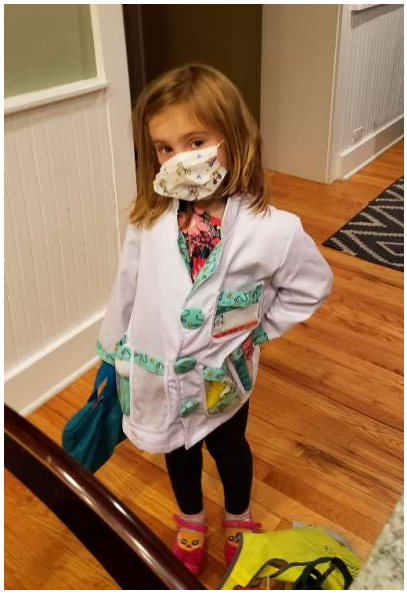


Diagnostics for TB Globally in routine practice settings in addition to what we have in the US

Outside of the US	Time to final result	sensitivity/specificity for PTB	sensitivity for other sources	Cost	Ref
Xpert ultra	2 hours	similar to liquid culture	CSF-90%; gastric aspirate 74%; pleural fluid 75%; LN aspirate 70%; stool 56%; nasopharyngeal aspirate 43%	$8	Cochrane Rev 2022, 2021; LancetMicrobe 2024; 5: e520–28
Xpert MTB/XDR	2 hours	90-94%	likely similar to Xpert MTB/RIF	$15.00	OFID 2024
urine-LAM	25 minutes	18-70%/96-98%	n/a; largely for use in PWHIV	$5	JCI 2020

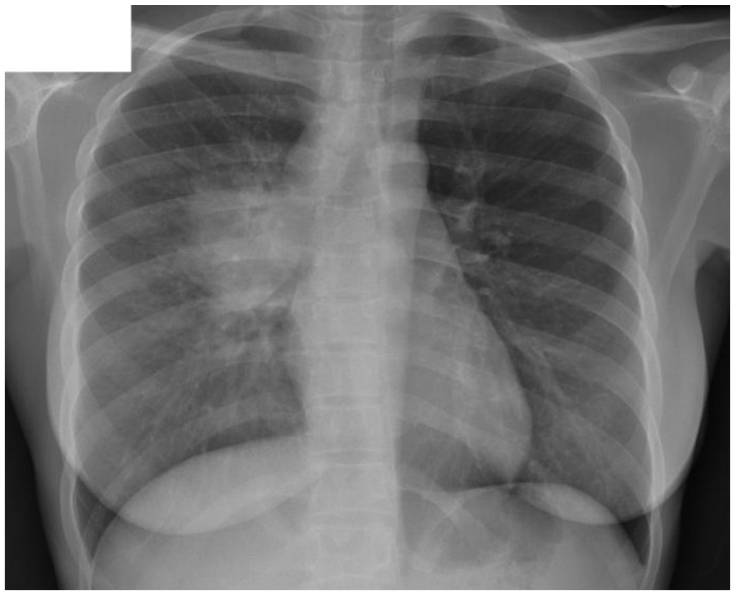
TB diagnostics: summary

- The best test is still culture in the US : unacceptable diagnostic delays
- Point of care testing is improving but there are still gaps…
- What to do?
  - Maintain high index of suspicion
  - Empiric treatment followed by assessing clinical response



HPI - continued

- Sputum – smear negative X 3
- Gene Xpert MTB/RIF negative
- IGRA positive
- CD4 count 500 cells/µL
- Lived in Kampala for most of her life prior to moving to the US



HPI

- Excisional cervical lymph node biopsy performed
  - Caseating granulomas throughout
  - Rare AFB
- Started on isoniazid, rifampin, ethambutol, pyrazinamide two weeks after initial presentation
- Sputum cultures grew *M. tuberculosis* after 13 days

HPI continued

- She returns to clinic in 2 weeks feeling well.
  - When should we offer antiretroviral therapy?
  - What options are available for antiretroviral therapy?
  - What is the role for trimethoprim-sulfamethoxaxole (TMP-SMX or co-trimoxazole) and when should this be offered?

Summary of the Evidence: IDSA/ATS TB treatment Guidelines

- Standard 6-month regimens for most with drug-susceptible pulmonary TB
- Extend therapy to 9 months:
  - positive cultures at 2 months and cavitary disease
  - ART is not administered or CD4 <100
  - WHO guidelines: no recommendations to extend treatment for drug-susceptible pulmonary TB

Nahid P, et al. Clin Infect Dis 2016; 63 (7): e147-e195.

4-month daily rifapentine-moxifloxacin regimen was non-inferior to standard 4-drug therapy for treatment of drug-susceptible TB in people with HIV

- International randomized open-label phase 3 noninferiority trial of the following:
  - 4-month daily regimen substituting rifapentine for rifampin and moxifloxacin
    - Isoniazid (H), moxifloxacin (M), pyrazinamide (Z), rifapentine (P) x 8 weeks followed by 9 weeks of HMP
    - H, E, Z, P x 8 weeks followed by 9 weeks of HP
    - Standard 6-month regimen.
  - N=194/2516 (7.8%), Median age 35
  - median CD4+ count was 344 cells/µL (interquartile range: 223–455)
  - All on efavirenz-based ART, starting within 8 weeks.
  - Noninferiority criteria were met if the upper bound of the 95% CI of the difference was <6.6% in both the microbiologically eligible and assessable analysis populations
- Fewer AEs in rifapentine-based regimens (15%) than the control regimen (21%).

Pettit A, et al. 2023;76(3):e580–e9

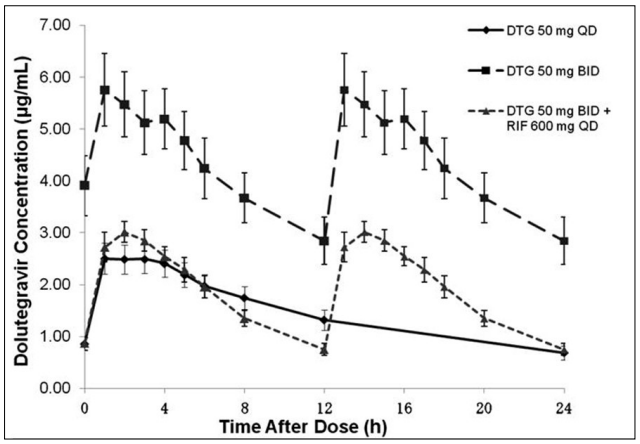
Co-treatment considerations

Trimethoprim-sulfamethoxazole therapy for Patients with TB and HIV

- US guidelines: CD4 count is less than 200 cells/µL, stop when the CD4 count >200 for 3 months
- WHO guidelines: initiate irrespective of CD4 count, continue while on TB treatment
  - Discontinue after TB treatment if:
    - clinically stable on ART, with evidence of immune recovery and viral suppression
  - However, continue if malaria and severe bacterial infections are highly prevalent, irrespective of CD4 count

Effect of rifampin on serum concentrations of dolutegravir (DTG) 50mg BID

- INSPIRING Phase 3b non-comparative open label RCT HIV-TB:
  - DTG 50mg BID + 2NRTIs during TB tx and 2 weeks post therapy vs. Efavirenz (EFV) + 2NRTIs
  - Week 24 of 52:
    - 69 received DTG, 44 EFV
    - Proportions with VL <50 c/mL:
      - DTG 56/69 (81%)
        - 5 discontinued due to protocol deviations/LTFU
      - EVF 39/44 (89%)
        - 2 discontinued due to adverse events



Dooley K et al. CID, 2020

Rifampin Effect on Tenofovir Alafenamide (TAF) Plasma/Intracellular Pharmacokinetics

- Healthy volunteers:
  - Plasma TAF Cmax and AUC decreased by 45% and 47% respectively
  - IC TFV-DP decreased by 40% *but still 82% higher than those achieved by standard dose of TDF*
- Case series of 6 individuals presented at ID week, 2022 was reassuring for maintaining viral load suppression
- PWHIV on TAF who received rifampin: higher intracellular TFV-DP than TDF

Mohzari Y, et al. Abstract # 1281, ID Week 2022
Cerrone, M et al. JAC 2019
Mpofu R et al. Abstract # 0646 CROI 2026

Rifapentine and Dolutegravir are safe, some dose adjustments may be needed

Dooley, KE et al. Lancet HIV 2020 Jun;7(6):e401-e409

AT Podany et al. CID 2024;79(4):983–9

- DOLPHIN trial:
  - Phase ½ single arm trial (total of 50 individuals)
  - 50 mg of daily dolutegravir in place of efavirenz for 8 weeks, then 12 doses once weekly INH-rifapentine
  - Followed 4 weeks after completion of treatment. HIV viral loads were measured at baseline and at weeks 11 and 24.
  - Viral loads less than 40 copies/mL at weeks 11 and 24.
- AIDS Clinical Trials Group A5372: Dolutegravir 50mg BID with daily isoniazid and rifapentine
  - N=331 had VL <50 copies/ML; 1 had VL 160 which was undetectable again on day 42
  - median (Q1, Q3) dolutegravir trough concentration
    - Day 0: 1751 ng/mL (1195, 2542)
    - Day 28: 1987 ng/mL
  - No serious adverse events were reported.

Fixed-dose combination bictegravir–emtricitabine–tenofovir alafenamide twice-daily for treatment of HIV during rifampicin-based tuberculosis treatment (INSIGHT Study): a phase 2b, open-label, randomised non-comparative trial

*Anushka Naidoo, Kogieleum Naidoo, Marothi P Letsoalo, Roeland E Wasmann, Gillian Dorse, Rubeshan Perumal, Mahomed-Yunus S Moosa, Emmanuella C Osuala, Resha Boodhram, Benjamin Chimukangara, Lubbe Wiesner, Dennis Israelski, Paolo Denti, James F Rooney, Kelly E Dooley, on behalf of the INSIGHT Study Team**

Lancet HIV 2026; 13: e9–20

- primary outcome: proportion in the bictegravir with HIV-RNA <50 copies per mL at week 24
- N=80 in the bictegravir group; N=42 in the dolutegravir group
- HIV-1-RNA in the bictegravir and dolutegravir groups were <50 copies per mL in 75/80 (94%, 95% CI 86–98) of bictegravir and 40/42 (95%, 84–99) of dolutegravir @ week 24
- Grade ≥3 adverse events: 36/80 (45%) bictegravir group; 23/42 (55%) dolutegravir group.
  - None related to study treatment

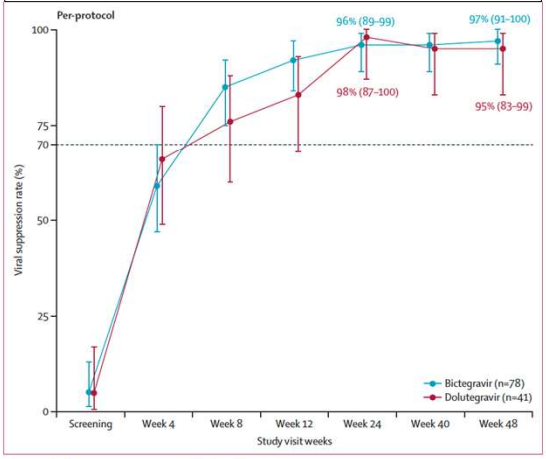


Figure 2: **Viral suppression rates over time by study group**
The dashed line represents the pre-defined response rate of at least 70%. Viral suppression rates are reported with two-sided 95% CI.

Summary of drug-drug interactions

TB Drug	ARV Drug	Dose adjustment
Rifampin	NNRTIs (use TAF with caution*)	No
	Efavirenz 600mg	
	Dolutegravir 50mg BID	yes
	Raltegravir 800mg BID	yes
	ibalizumab	No
	Doravirine	do not use
	Etravirine	do not use
	Bictegravir*, elvitegravir	do not use
	cabotegravir/rilpivirine	do not use
	protease inhibitors	do not use
	lenacapavir	do not use
	fostemsavir	do not use

TB Drug	ARV Drug	Dose adjustment
rifapentine weekly	NNRTIs (use TAF with caution)	No
	Efavirenz 600mg	No
	Dolutegravir	No
	Raltegravir	No
	ibalizumab	No

TB Drug	ARV Drug	Dose adjustment
Rifapentine daily	NNRTIs (use TAF with caution)	No
	Efavirenz 600mg	No
	Dolutegravir bid	Yes

TB Drug	ARV Drug	Dose adjustment
Rifabutin	NNRTIs (use TAF with caution)	No
	ETR without boosted PIs	No
	doravirine 100mg bid	Yes
	rilpivirine 50mg daily	Yes
	Dolutegravir 50mg daily	No
	Raltegravir 400mg bid	No
	ibalizumab	No
	Protease inhibitor -- dose adjust rifabutin to 150mg	yes-rifabutin

*may change?

HIV-TB treatment guidelines

Summary recommendations for co-treatment of HIV-TB

- Dolutegravir (DTG) + 2 nucleosides or Raltegravir (RAL)
  - Dolutegravir of 50mg BID with rifampin
  - Raltegravir to 800mg BID with rifampin
- Do not use elvitegravir, cabotegravir (IM or PO) or bictegravir-containing regimens
  - Stay tuned for possible updated recommendations with respect to bictegravir
- 2nd line: Efavirenz + 2 nucleosides
- Rifabutin-based TB treatment
  - Alternative when PI class needed
  - Can be used with DTG or RAL with no dose adjustment
  - Could use oral rilpivirine if dose is increased to 50mg daily
- Rifapentine
  - efavirenz, raltegravir, or once-daily dolutegravir-based ARV regimen (weekly)
  - For daily rifapentine—probably BID dolutegravir*

*guidelines have not been updated yet

Timing of ART in patients with TB (who have started TB treatment)

- CAMELIA-NEJM 2011
- STRIDE-NEJM 2011
- SAPiT-NEJM 2010, 2011
- TB-HAART, Lancet-ID 2014

- Always treat TB before initiating ART whenever possible
- CD4 count cut points are at the time of diagnosis of TB
- Advanced AIDS (CD4 < 50): immediate ART (within 2 weeks) improves survival
  - Markedly increased risk of IRIS, including fatal IRIS events
  - Overall survival benefit despite IRIS
- CD4 > 50: early ART (~ 2 months) provides good balance of competing risks of death/AIDS vs. IRIS
- Caveats
  - CNS involvement – no benefit to immediate therapy, and there may be increased risk

Adverse events in treatment of HIV and TB

- GI intolerance, rash, hepatotoxicity
- IRIS
  - Paradoxical worsening after clinical improvement
  - Unmasking of another opportunistic infection
- Addition of TB treatment to ART may not be associated with increased risk of adverse events
  - Data comparing adverse events from TB-HAART and other trials (CAMELA, SAPiT, STRIDE)
    - similar rates of adverse events during anti-TB therapy with and without concomitant ART
    - Suggests that adding in ART does not increase risk of adverse events

Mycobacterium tuberculosis Infection and Disease | NIH (hiv.gov)

Types of immune reconstitution inflammatory syndrome (IRIS) events in HIV-TB

- Fevers
- New or worsening adenitis
- New or worsening pulmonary infiltrates
- New or worsening pleuritis, pericarditis, or ascites
- Intracranial tuberculomas, worsening meningitis
- Disseminated skin lesions
- Epididymitis, hepatosplenomegaly, soft tissue abscesses

Initiation of ART+ prednisone reduces IRIS risk in HIV-TB for people with CD4 counts <100

RCT, N=240, CD4 <100

Prednisone 40mg x 14 days, then 20mg x 14 days vs. placebo

Primary endpoint was TB-IRIS in 12 weeks

Results:

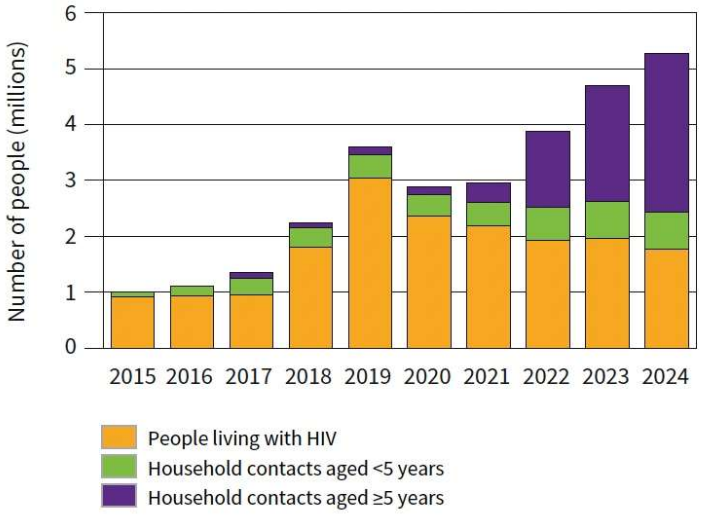
- Median CD4 was 49
- TB-IRIS in 32.5% of prednisone group, 47% placebo (RR 0.7, 95% CI 0.51-0.96, p=0.03).
- No difference in deaths

Meintjes, G. et al. N Engl J Med 2018; 379:1915-1925

HIV-TB treatment guidelines

Treatment of LTBI

Global number of people provided with TPT, 2015–2024



Global TB Report, 2025

Recommended LTBI regimens for people Living with HIV

LTBI treatment	Regimen	Notes
first line	INH + rifapentine once weekly for 12 doses	efavirenz, dolutegravir, raltegravir based regimens
second line	INH + rifampin daily x 3 months	check drug-interactions with rifampin
Alternative #1	rifampin daily x 4 months	check drug-interactions with rifampin
Alternative #2	INH daily + B6 for 9 months	WHO recommends 6 months of INH
Not recommended by CDC or NTCA	INH+ rifapentine daily x 4 weeks	efavirenz based regimens only.
drug resistant LTBI	consult with public health/other experts	

DHHS Opportunistic Infection Guidelines, accessed 3.2026

Isoniazid and Rifapentine (3HP) both once weekly for 12 doses

Evidence for use of 3 months of daily isoniazid with rifampin (3HR) in PWHIV

- No difference in the incidence of TB disease comparing 3HR to 6-9 months of daily INH
- Hepatotoxicity less frequent with 3HR
- Other adverse effects were more common with 3HR compared to daily INH and could lead to treatment discontinuation
- Monitoring similar to 3HP
- Weight based dosing similar to active TB treatment

Whalen CC, et al. NEJM 1997 Sep 18;337(12):801-8.
Rivero A et al. Inferm Infecc Microbiol Clin. 2007 May;25(5):305-10.
Johnson JL et al. AIDS 2001 Nov 9;15(16):2137-47

ONE MONTH OF RIFAPENTINE/ISONIAZID TO PREVENT TB IN PEOPLE WITH HIV: BRIEF-TB/A5279

- Phase 3 RCT, open-label, 10 countries participating, n=3,000
  - >13 years, living in high TB-burden areas OR who were TST/IGRA positive
  - ART with efavirenz or nevirapine; followed for 3 years
  - Randomized to 1HP* or 9H*
  - Primary endpoint: incidence rates of active TB, TB death or death from an unknown cause

- Results:
  - **634 (21%) had positive TST or IGRA**
  - Primary endpoint:
    - N=34 1HP arm; 35 9H arm, for incidence rates of 0.69/100 PY for 1HP and 0.72/100 PY for 9H (IR difference = -0.025, upper 95% CI: 0.31, Table).
    - TB incidence rates were higher among those with +TST/IGRA but not different between the two arms
  - Treatment completion was 97% with 1 HP vs. 90% in the 9H arm, p<0.01

*1HP=isoniazid/rifapentine daily x 4 weeks; 9H=isoniazid daily x 9 months

Swindells, S. et al. N Engl J Med 2019; 380:1001-1011

Summary – treatment of HIV-related TB: LTBI

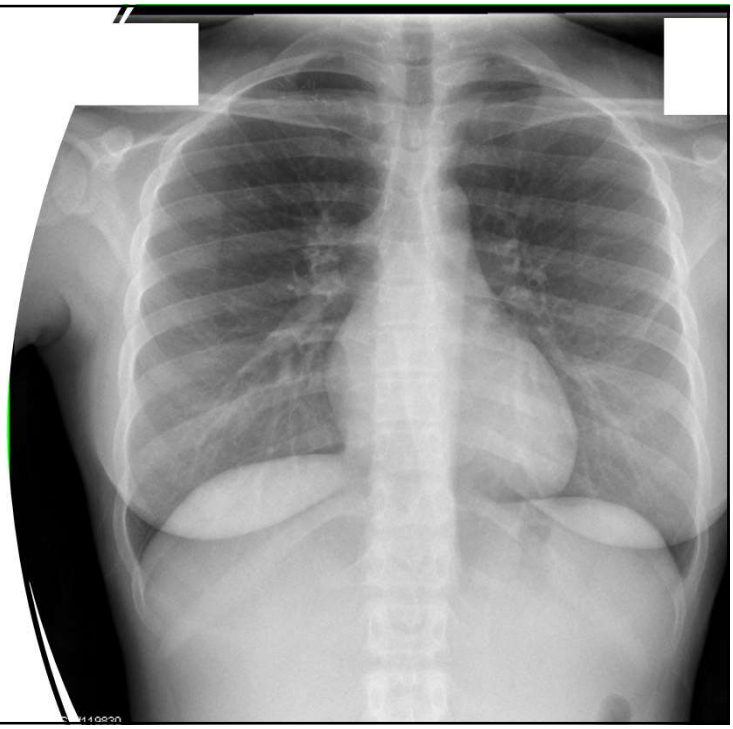
- All people with HIV should be screened for TB infection and offered treatment for LTBI
- Short course rifamycin-based regimens are preferred for people with HIV who need LTBI treatment
  - Shorter course regimens are better tolerated and are easier to complete
  - Most of the data are in INH-rifamycin combination regimens

Summary – treatment of HIV-related TB: issues with antiretroviral therapy

- HIV treatment initiated with consideration of the data that maximize benefit and lower risk of IRIS:
  - Less than 2 weeks if CD4 count is less than 50, then okay to wait and start within 2 months after starting active TB treatment if >50
    - Exceptions:
      - Considerations during pregnancy, transmission to partners
  - Preferred: dolutegravir or raltegravir-based with TDF+FTC
    - Still some limited role for PI/rifabutin combinations and efavirenz
    - Growing experience with offering TAF but guidelines still don't fully endorse

Patient follow-up

- emtricitabine/tenofovir/ efavirenz initiated
- TB treatment completed at 6 months
- Delivered a healthy baby who is HIV free



Questions?

Thank you!