



Clinical Updates: What's New in the TB Literature

Paul Saleeb, MD, MSPH

Prevention and Health Promotion Administration

Center for Tuberculosis Control and Prevention

October 1, 2026

Mission and Vision

MISSION

The mission of the Prevention and Health Promotion Administration is to protect, promote and improve the health and well-being of all Marylanders and their families through provision of public health leadership and through community-based public health efforts in partnership with local health departments, providers, community-based organizations, and public and private sector agencies, giving special attention to at-risk and vulnerable populations.

VISION

The Prevention and Health Promotion Administration envisions a future in which all Marylanders and their families enjoy optimal health and well-being.

Outline

- Risk of transmission in healthcare facilities
- Burden of asymptomatic TB
- High-dose rifampin
- Stratification for short-course regimens
- TB meningitis
- Treatment of MDR-TB
- Live vaccines and testing for latent TB infection

Clinical Infectious Diseases

MAJOR ARTICLE



Mycobacterium tuberculosis Transmission in Healthcare Settings: A Systematic Review of Frequency, Risk Factors, and Exposure Conditions

Fizza Manzoor,^{1,2,●} Chanu Rhee,^{1,2,●} Meghan A. Baker,^{1,2,●} and Michael Klompas^{1,2,●}

MTB Transmission in Healthcare Settings

- Contact investigations for TB transmission in U.S. HCF cost \$9.9 million per year.
- Actual rate of transmission is low (< 1% per year).
- Routinely use broad and conservative definitions for exposure in HCF
- Systematic review of MTB exposures in HCF

MTB Transmission in Healthcare Settings

- 86 studies included: 1083 index pts; 35,698 exposed; 2517 secondary cases
 - 7.1% overall transmission risk
- Secondary cases (2517):
 - 92% latent TB; 8% active TB
 - Exposed patients ~8x more likely to develop active TB than exposed HCW
- CDC Guidelines to Prevent Transmission in HCF published in 2005
 - 15.2% transmission risk before 2005; 3.8% after 2005

MTB Transmission in Healthcare Settings

- Median duration of exposure to pts and HCW: 24 hours
 - 93% of transmissions had exposures > 8 hours
- Proximity of exposure:
 - Face-to-face direct contact greatest risk for HCW
 - Shared room greatest risk for pts
- No infections in HCW wearing N95
 - Surgical masks probably ~ 50% protective
- < 2 air changes/hour was 3.4 times more likely to result in infection than > 2 air changes/hour

MTB Transmission in Healthcare Settings

Authors' Conclusions:

- Suggest definition of exposure in health care facilities as: individuals with > 8 hours cumulative exposure without wearing a respirator

Clinical Infectious Diseases

SUPPLEMENT ARTICLE



Asymptomatic Tuberculosis Across the Disease Spectrum: A Scoping Review of Epidemiology, Diagnosis, and Public Health Implications

Beatriz Barreto Duarte,^{1,2,3,●} Jerrold Ellner,⁴ Alicia D. Wright,⁵ Mark Hatherill,^{4,●} Amita Gupta,^{6,7,●} Timothy R. Sterling,⁵ Rajita Bhavaraju,⁸
and Bruno B. Andrade^{1,2,3,6,7}

The Burden of Asymptomatic TB

- Accumulating evidence attributing large proportion of TB burden to asymptomatic transmission
- Implication: reliance on traditional symptom screening strategy is unlikely to be sufficient to reduce TB incidence rates
- Asymptomatic TB: presence of confirmed pulmonary TB in absence of TB symptoms, regardless of radiographic findings
- Scoping review of epidemiology, diagnosis, public health implications

The Burden of Asymptomatic TB

- ~30% of asymptomatic TB progress in 2 years; ~30% regress; ~30% stable
- ~50% of bacteriologically confirmed TB cases may be asymptomatic at time of diagnosis
- Radiologic and molecular evidence of lung pathology and immune activation in asymptomatic TB
- Strategies for detection: active case finding; mobile, digital radiography; sputum biomarkers

Clinical Infectious Diseases

MAJOR ARTICLE



Safety of Triple-Dose Rifampin in Tuberculosis Treatment: A Systematic Review and Meta-Analysis

Omri A. Arbiv,^{1,2,3,●} Thomas Holmes,⁴ Marie JeongMin Kim,⁵ Marie Yan,^{5,6} Kamila Romanowski,^{6,●} Sarah K. Brode,^{1,7,●} William J. Burman,^{8,●} Dick Menzies,^{9,10,11,●} and James C. Johnston^{5,6,9,●}

High-Dose Rifampin

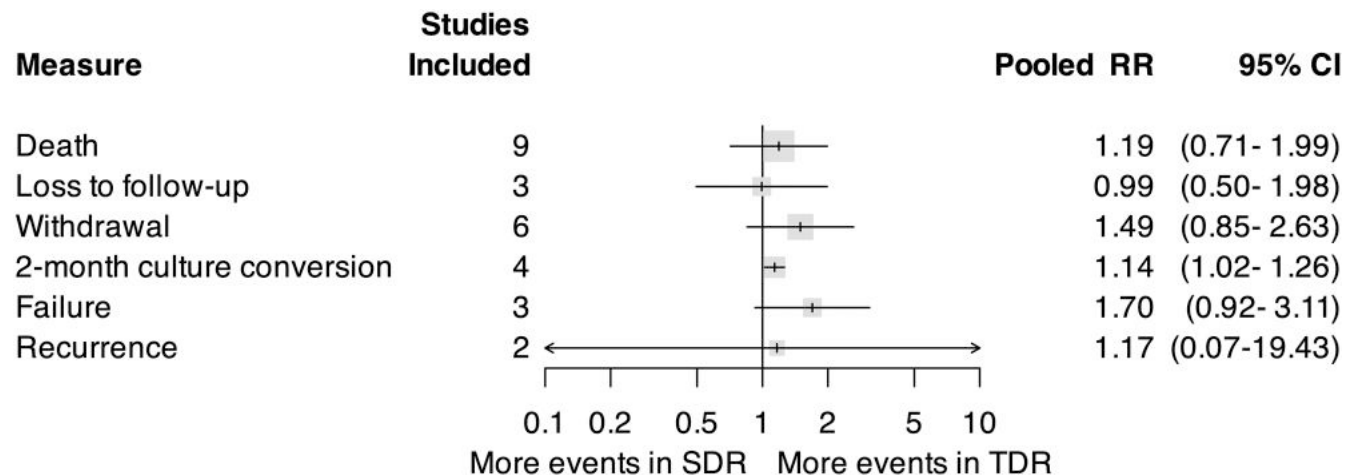
- RIF initially dosed at 600 mg (~ 10 mg/kg) once daily due to concerns for side effects and its high cost.
- Evidence over past several years of decreased time to sputum culture conversion, increased mycobacterial killing with high-dose RIF
 - No ceiling for highest dose and sputum culture conversion
- Recent studies have included doses up to 35 mg/kg.

High-Dose Rifampin

- Systematic review and meta-analysis of RCTs comparing standard-dose with double-dose and triple-dose RIF
- Primary outcome: pooled IRR of severe adverse events between standard-dose vs TDR
- 17 articles included:
 - 2313 individuals treated with SDR: 10-14 mg/kg/day
 - 2238 treated with DDR: 15-29 mg/kg/day
 - 1199 treated with TDR: ≥ 30 mg/kg/day

High-Dose Rifampin

- IRR for SAEs with triple-dose RIF vs standard-dose RIF: 1.48 (1.12-1.96)
 - Mostly hepatotoxicity
- No difference in death or other secondary outcomes



Arbiv et al. *Clin Infect Dis*. 2025;81(1):119-128.

High-Dose Rifampin

- No significant difference between standard-dose and double-dose RIF
- Conclusions: Double-dose RIF (1200 mg daily) is probably the maximum safe dose.

ORIGINAL ARTICLE

Trial of High-Dose Oral Rifampin in Adults with Tuberculous Meningitis

D.B. Meya,^{1,2} F.V. Cresswell,^{1,3,4} B. Dai,⁵ N. Engen,⁵ K. Naidoo,^{6,7} A.R. Ganiem,^{8,9}
D. Imran,¹⁰ M. Kabahubya,¹ R.J. Lessells,^{6,11} V. Yunivita,^{9,12} R. Estiasari,¹⁰
L. Tugume,¹ B. Hlabisa,⁶ M.Y. Kurniawati,^{13,14} N. Sagita,¹⁵ E. Kagimu,¹
K. Maharani,¹⁰ J. Gakuru,¹ M.N. Gaharu,¹⁶ T. Mugabi,¹ S. Kimuda,¹
S. Namombwe,¹ L. te Brake,¹⁷ R. Aarnoutse,¹⁷ E.M. Svensson,^{17,18}
A.S. Bangdiwala,⁵ S. Namanda,¹ N.C Bahr,⁵ A.K. Musubire,¹ M.Y.S. Moosa,¹⁹
R.L. Hamers,^{20,21} S. Marais,^{22,23} D.R. Boulware,² R. van Crevel,^{21,24,25}
and R. Ruslami,^{9,12} for the HARVEST Trial Team*

High-Dose Rifampin for TB Meningitis

- Only about 5% of RIF crosses into the CSF from the bloodstream.
- Mixed evidence for improved clinical outcomes with high-dose RIF for TBM
- HARVEST Trial: would RIF 35mg/kg/day in the intensive phase results in improved survival?

High-Dose Rifampin for TB Meningitis

- 499 individuals with TBM in Indonesia, South Africa, Uganda
 - Included PWHIV (61%)
- Primary outcome: survival at 6 months
 - Secondary outcomes: survival at 12 months; neurocognitive status
- RIF 35 mg/kg in the intensive phase vs 10 mg/kg
- Corticosteroids administered per national guidelines

High-Dose Rifampin for TB Meningitis

- Mortality at six months: 44.6% in high-dose RIF vs 40.7% in SOC (NS)
 - No difference in secondary outcomes
- Higher risk of death:
 - HIV on ART receiving high-dose RIF: hazard ratio 2.01
 - CSF WBC < 5: hazard ratio 2.01
- Higher rate of DILI with high-dose RIF: 8.0% vs 4.4%; no deaths

High-Dose Rifampin for TB Meningitis

Possible explanations for negative findings:

- High-dose RIF may have led to decreased exposure to glucocorticoids.
- More robust inflammation with high-dose RIF led to poor outcomes
 - Potentially why PWHIV on ART fared worse in this study

Clinical Infectious Diseases

MAJOR ARTICLE



Xpert MTB/RIF Cycle Threshold as a Marker of Tuberculosis (TB) Disease Severity: Implications for TB Treatment Stratification

Daniel J. Grint,^{1,●} Jasvir Dhillon,² Philip D. Butcher,² Jack Adams,² Tulika Munshi,² Adam A. Witney,² Katherine Gould,² Kenneth Laing,^{2,●} Christopher Cousins,² Sean Wasserman,^{2,3,●} Katherine Fielding,^{1,●} Tom Harrison,² and Amina Jindani²; on behalf of the RIFASHORT Study Team

Stratification for Short-Course Regimens

- Short-course regimens (4 months of treatment) are adequate for most individuals with active TB disease
 - Subset of those requiring longer therapy led to negative findings in some trials evaluating short-course regimens
- Authors aimed to stratify those requiring longer vs shorter courses of treatment for active TB.
- Analyzed data from RIFASHORT trial
 - RCT of 6 months RIPE vs 4 months RIF 1200 mg vs 4 months RIF 1800 mg
 - 4-month regimens did not meet noninferiority criteria
 - Composite of treatment failure and relapse
 - High proportion of favorable outcomes in all arms
 - 93% RIPE, 90% 4 months RIF 1200, 87% 4 months RIF 1800

Stratification for Short-Course Regimens

- Examined data on Xpert cycle threshold, sputum smear grade, sputum culture grade, CXR
- Strongest differentiation between relapse and non-relapse when combining disease burden on CXR and semiquantitative bacterial burden on Xpert
 - CXR: $\geq 50\%$ involvement, bilateral disease, cavities
 - Xpert: high semiquantitative burden: cycle threshold < 16
- Using this combination, the 4-month 1200 mg RIF regimen met noninferiority in mITT and PP analyses

The Journal of Infectious Diseases

MAJOR ARTICLE



Beyond Rifampin: Evaluating Rifapentine and Rifabutin as Alternative Treatments for Tuberculous Meningitis

Xueyi Chen,^{1,2,●} Carlos E. Ruiz-Gonzalez,^{3,4,a} Yuderleys Masias-Leon,^{3,4,a,●} Medha Singh,^{3,4,a,●} Oscar J. Nino-Meza,^{3,4,a,●} Charles A. Peloquin,^{5,●} Dmitri Artemov,^{6,●} and Sanjay K. Jain^{1,2,3,4,a,●}

TB Meningitis: Rifamycins

- Poor CNS penetration of RIF across blood-brain barrier into CSF: as low as 5%
- Mixed results from studies utilizing high-dose RIF for TBM
- Other rifamycins:
 - Rifabutin: improved CSF penetration
 - Rifapentine: long half-life
- Mouse model comparing human equivalent doses of RIF 10 mg/kg, RFB 300 mg, RFP 1200 mg (with Mfx)

TB Meningitis: Rifamycins

- Assessed CNS bactericidal activity, rifamycin tissue concentrations, brain inflammation, neuronal injury
- Bactericidal activity: Rifapentine regimen >> rifampin or rifabutin
 - Mfx did not improve CNS bactericidal activity of RFP
- Brain tissue concentrations > CSF concentrations for all rifamycins
- Rifapentine regimen caused least brain inflammation
 - Rifabutin caused less inflammation than rifampin
- Rifapentine regimen caused least neuronal injury

Open Forum Infectious Diseases

MAJOR ARTICLE



Cerebrospinal Fluid Concentrations of Bedaquiline, Pretomanid, and Linezolid During Curative Treatment of Fluoroquinolone-Resistant Pre-Extensively Drug-Resistant Tuberculous Meningitis

Adrian Robert Tramontana,^{1,●} Andrew Burke,² Maria Globan,^{3,●} Brett McWhinney,⁴ Aaron E. Bloch,^{1,●} Benjamin J. Smith,^{1,●} Justin T. Denholm,⁵ Connor James Wright,¹ and James S. Molton^{1,●}

TB Meningitis: BPaL Concentrations in the CNS

- Limited data on BPaL for MDR-TB meningitis
- Often combined with clofazimine, cycloserine to ensure adequate CNS penetration
- Case report: 35 y/o woman with miliary and CNS pre-XDR TB
 - Resistant to fluoroquinolones
 - Treated with BPaL, clofazimine, cycloserine
 - Required bilateral VP shunting, corticosteroids, thalidomide
 - Treated for 43 weeks

TB Meningitis: BPaL Concentrations in the CNS

- MTB isolate was susceptible to bedaquiline (MIC 0.5), pretomanid (0.5), linezolid (0.5)
- Measured CSF concentrations of pretomanid, bedaquiline, linezolid
- Pretomanid and linezolid levels were above their critical concentrations throughout the dosing intervals
 - After accounting for protein binding, Pto levels higher in CSF than plasma
 - BDQ level in CSF was 15-35% of plasma after single dose, but greater than plasma concentrations after 21 weeks

Clinical Infectious Diseases

BRIEF REPORT

Role of Low-Dose Infliximab for
Inflammatory Complications of
Central Nervous System Tuberculosis:
A Retrospective Cohort Study

Selwyn Selva Kumar D,¹ Nishi Somarkutty,^{1,●} Jayavelu Hariram Prasad D,²
Priyanka Gautam,¹ Veerasamy Nagaraj,^{1,●} Rajiv Karthik,^{1,●}
Harshad Arvind Vanjare,^{2,●} Prabhakar Thirumal Appaswamy,^{3,●}
Joy Sarojini Michael,⁴ George M. Varghese,^{1,●} and Abi Manesh¹

TB Meningitis: Host-Directed Therapy

- CNS inflammation responsible for morbidity, mortality due to TB meningitis
- Previously presented data on infliximab 10 mg/kg for TBM in India
 - Matched retrospective cohort study: 48% decrease in disability, 31% decrease in mortality
- Authors investigated lower dose of infliximab in the same clinical context.

TB Meningitis: Host-Directed Therapy

- Retrospective cohort study in South India: March 2023 – September 2024
 - 20 individuals with TBM and severe neurologic deficits despite corticosteroids
- Infliximab 5 mg/kg
- Outcome: reduction of ≥ 2 points in modified Rankin Scale score
- Results:
 - 60% disability free (mRS ≤ 2)
 - 75% clinical improvement
 - One case of dermatomal herpes zoster
 - Early improvement after first dose was highly predictive of long-term improvement.

The Journal of Infectious Diseases

MAJOR ARTICLE



Cerebrospinal Fluid Hypo-inflammation Drives Mortality in HIV-Associated Tuberculous Meningitis

Anna L. Wilt,^{1,2,●} David B. Meya,^{1,3,●} Fiona V. Cresswell,^{3,4,5,●} Abduljewad Wele,⁶ Mable Kabahubya,^{3,●} Enock Kagimu,^{3,●} Jane Gakuru,^{3,●} Timothy Mugabi,^{3,●} Sarah Kimuda,^{3,●} Suzan Namombwe,^{3,●} Asmus Tukundane,^{3,●} Elizabeth C. Okafor,^{1,●} Samuel Okurut,^{3,●} James E. Scriven,^{7,●} Biyue Dai,^{6,●} Nicole Engen,^{6,●} Nathan C. Bahr,^{1,●} David R. Boulware,^{1,●} and Tyler D. Bold^{1,2,●}

TB Meningitis: Immune Response in HIV

- Corticosteroids (CS) beneficial for TBM in people without HIV; no evidence of benefit in PWHIV
- Evidence of benefit of CS in patients with TBM and *LTA4HTT* genotype
 - Leukotriene A4 hydrolase: produces leukotriene as a chemoattractant for inflammatory cells
 - TT genotype: associated with CSF hyperinflammation
- Authors analyzed immune profile for individuals with both TBM and HIV, comparing survivors with non-survivors
 - This included the cohort in the HARVEST trial evaluating high-dose RIF in TBM

TB Meningitis: Immune Response in HIV

- 36% (54/149) died:
 - More severe disease at presentation: higher GCS, MRC scores
 - Lower baseline CD4 counts (but no difference in antiretroviral status)
 - Lower CSF immune markers: IFN- γ , TNF- α , and other Th1 cytokines
 - Lower baseline CD4 was directly associated with Th1 immunity in CSF.
- Corticosteroids:
 - Not shown to be beneficial in TBM with HIV infection in ACT HIV trial
 - Potential benefit in TBM with HIV infection if have higher CSF expression of Th1 cytokines (IFN- γ)
 - Need POC biomarkers for risk stratification

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Pragmatic Trial of a 6-Month Strategy for Rifampicin-Resistant Tuberculosis

Francesca Conradie, M.B., B.Ch.,¹ Tasnim Badat, M.B., B.Ch.,¹
Asanda Poswa, M.B., B.Ch.,¹ Shakira Rajaram, M.B., B.Ch.,²
Shaneen Kooverjee, M.B., B.Ch.,² Gary Maartens, Ph.D.,³
Graeme Meintjes, Ph.D.,^{4,5} Jennifer Hughes, M.B., B.Ch.,⁶
H. Simon Schaaf, M.Med.Paed.,⁶ Pauline Howell, M.B., B.Ch.,²
Norbert Ndjeka, Ph.D.,⁷ and Patrick P.J. Phillips, Ph.D.⁸

Treatment of MDR-TB: BEAT TB Trial

- Marked advancement in treatment of MDR-TB in the past 10 years with advent of BPaL/M
 - Nix-TB, ZeNix, TB-PRACTECAL studies
- Lack of data for regimens in young children, pregnancy, breast feeding
 - Pretomanid not recommended in these populations
- BEAT trial: efficacy and safety of 6-month regimens for children $\geq$ 6, pregnancy, breast feeding, fluoroquinolone resistance

Treatment of MDR-TB: BEAT TB Trial

- Phase 3 randomized, controlled, noninferiority trial in South Africa
 - RIF-resistant TB with or without resistance to INH, FQ
 - PWHIV included
- Treatment regimens:
 - BDQ, LZD, DEL, Lfx and/or CFZ for 6 months
 - Lfx discontinued if DST results demonstrated FQ resistance
 - CFZ discontinued if DST results demonstrated FQ susceptibility
 - SOC for 9 months: BDQ, LZD, Lfx, EMB, high-dose INH, PZA, CFZ
 - 18 months of treatment if FQ resistance detected

Treatment of MDR-TB: BEAT TB Trial

- Primary efficacy end point: cure or treatment completion at end of treatment and at 76 weeks
- Primary safety end point: adverse event $\geq$ grade 3
- 403 participants; 50.9% PWHIV

Drug resistance profile — no. (%)			
Susceptible to fluoroquinolones, no susceptibility testing for bedaquiline performed	123 (60.6)	123 (61.5)	246 (61.0)
Resistant to fluoroquinolones, no susceptibility testing for bedaquiline performed	7 (3.4)	15 (7.5)	22 (5.5)
Resistant to fluoroquinolones and susceptible to bedaquiline	35 (17.2)	24 (12.0)	59 (14.6)
Resistant to fluoroquinolones and bedaquiline	0	4 (2.0)	4 (1.0)
No susceptibility testing for fluoroquinolones or bedaquiline performed	38 (18.7)	34 (17.0)	72 (17.9)
Susceptible to linezolid	35 (17.2)	28 (14.0)	63 (15.6)

Treatment of MDR-TB: BEAT TB Trial

Table 2. Primary Efficacy Analysis (Intention-to-Treat Population).^{‡*}

Variable	Trial Strategy (N=202)	Control Strategy (N=200)	Total (N=402)
	number (percent)		
Primary end point: successful outcome at end of treatment and at end of follow-up	174 (86.1)	172 (86.0)	346 (86.1)
Cure at end of treatment and at end of follow-up	160 (79.2)	162 (81.0)	322 (80.1)
Cure at end of treatment and negative culture at last visit	14 (6.9)	10 (5.0)	24 (6.0)
Unsuccessful outcome at end of treatment	14 (6.9)	22 (11.0)	36 (9.0)
Treatment failure	7 (3.5)	10 (5.0)	17 (4.2)
Lost to follow-up during treatment	2 (1.0)	4 (2.0)	6 (1.5)
Died during treatment	4 (2.0)	7 (3.5)	11 (2.7)
Not evaluated because of withdrawn consent	1 (0.5)	1 (0.5)	2 (0.5)
Unsuccessful outcome at end of follow-up	14 (6.9)	6 (3.0)	20 (5.0)
Recurrence after cure at end of treatment	10 (5.0)	4 (2.0)	14 (3.5)
Died after cure at end of treatment	4 (2.0)	2 (1.0)	6 (1.5)

No difference with regards to sex, HIV infection, smear status, cavitory disease, FQ resistance

Treatment of MDR-TB: BEAT TB Trial

- Safety: 10 participants in each group died
- Grade ≥ 3 event: 34% in trial strategy cohort; 38% in control cohort
 - No differences with regards to peripheral neuropathy, optic neuropathy, QTc prolongation, treatment-related SAEs between groups.
- 10 pregnancies, 4 in study arm: all resulted in live births; one premature
 - 2 SAEs during pregnancy not related to treatment
- Conclusion: 6-month regimen of BDQ, LZD, DEL, Lfz/CFZ non-inferior to SOC, including in pregnancy, breastfeeding, ≥ 6 yrs old

Clinical Infectious Diseases

MAJOR ARTICLE



The Effect of Live-Virus Vaccines on Tests for Tuberculosis Infection During the US Immigration Medical Examination: Are Vaccines Causing False-Negative Results?

Joanna J. Regan,[●] Zanju Wang, and Christina R. Phares

Division of Global Migration Health, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Live Vaccines and Testing for Latent TB Infection

- Live-virus vaccines (MMR) associated with false-negative TST result
 - Based on very limited studies with few participants, older versions of TST
- Recommendation to delay TST and IGRA for at least four weeks after live-virus vaccination
- Potential for delays in immigration processing, necessary vaccinations
- Retrospective analysis conducted by CDC Division of Global Migration Health

Live Vaccines and Testing for Latent TB Infection

- Reviewed data from 2014 - 2022 for children ages 2 – 14:
 - Receipt of MMR, oral polio, and/or varicella vaccines
 - Receipt of TST or IGRA before vaccination, during 4-week period, or afterwards
- Data for 158,484 children reviewed:
 - 79% IGRA; 22% 2-4 y/o; 51% male
 - Baseline active TB rate 30/100000
- ~11,000 children received IGRA during critical interval (median 7 days after vaccination)
- ~330 received TST during critical interval (median 7 days)

Live Vaccines and Testing for Latent TB Infection

- Proportion with positive IGRA result by testing interval:
 - Before vaccination: 3.3%
 - During critical interval: 4.6%
 - After critical interval: 3.5%
- Proportion with positive TST result by testing interval:
 - Before vaccination: 6.6%
 - During critical interval: 15.7%
 - After critical interval: 7.2%
- Conclusion: increase in positivity was seen during critical interval; delay in LTBI testing after vaccination with live-virus vaccines is unnecessary

Questions/Discussion



Prevention and Health Promotion Administration

<https://phpa.health.Maryland.gov>