EMORY UNIVERSITY SCHOOL OF MEDICINE | Department of Medicine

TB Treatment and Prevention – 2025 brief update

Marcos C. Schechter, MD

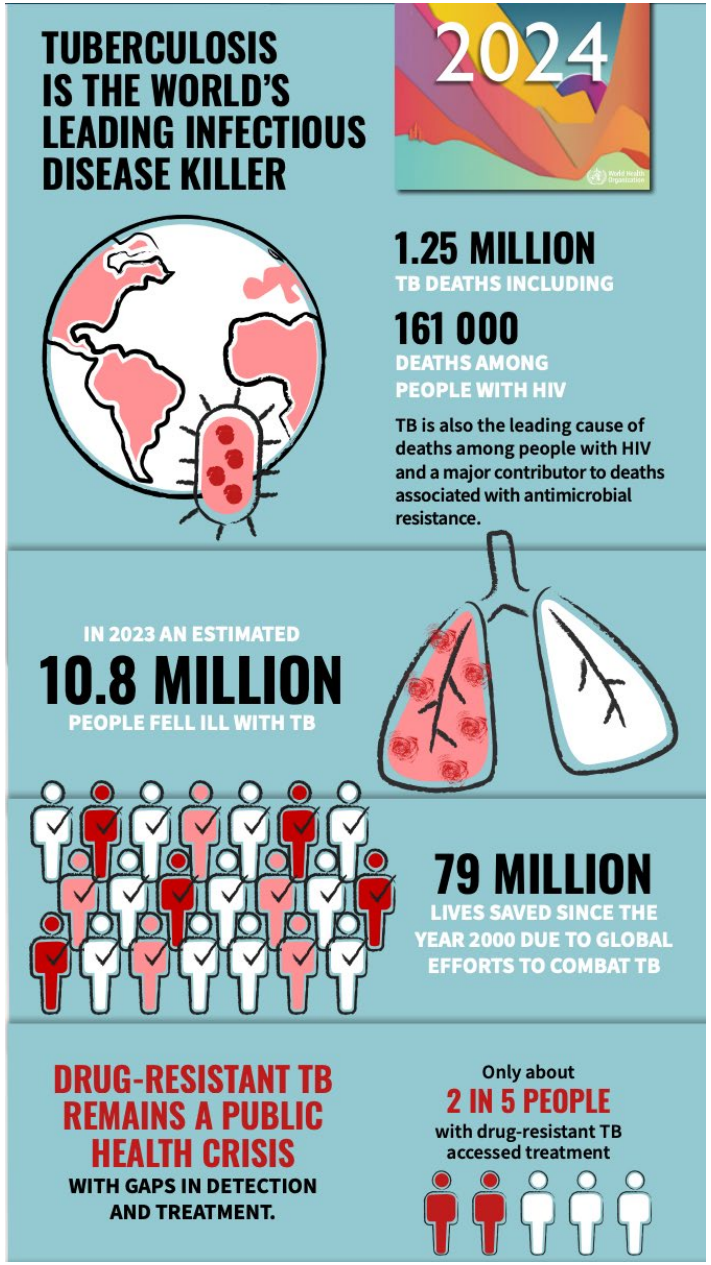
Emory University School of Medicine, Division of Infectious Diseases
Grady Memorial Hospital, Atlanta, GA
Associate Medical Consultant for the Georgia Department of Public Health TB Program

Grady

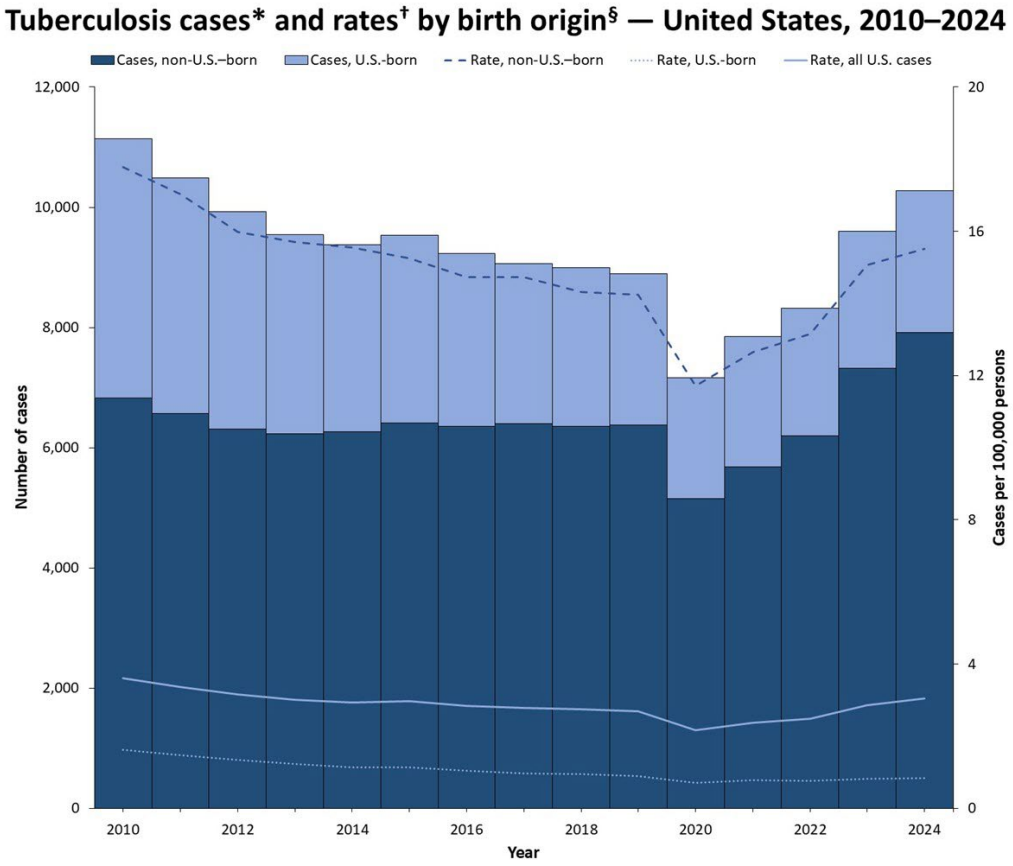
EMORY UNIVERSITY SCHOOL OF MEDICINE
Department of Medicine

The updates

- Epidemiology
- Diagnostic tests
- US-approved regimens for rifampin and isoniazid-susceptible TB
- US-approved regimens for rifampin-resistant TB
- Regimens for TB latent TB infection



WHO TB Report, 2024



*Case counts are based on data reported to the National Tuberculosis Surveillance System as of March 4, 2025.
†Annual tuberculosis rates were calculated as cases per 100,000 persons. Rates for all U.S. cases were calculated using midyear population estimates from the U.S. Census Bureau's 2010-2020 National Intercensal Population Totals and Vintage 2024 data; rates by birth origin were calculated using midyear estimates from the Current Population Survey.
§Persons born in the United States or 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. Case counts for persons without a known origin of birth are not represented in the figure.

CDC TB Provisional Data, 2024

- 10,000 cases
- 0.8 per 100K US born
- 15.5 per 100K non-US born
- ~100 MDR cases (2023)

Diagnostic tests currently used in the US

CXR and pulmonary TB

- **Active pulmonary TB Grady 2008-2015:**

Normal CXR: 7% HIV-negative vs 22% HIV-positive

- **CXR and HIV**

CD4 < 200 associated with atypical findings

- **Cavitary lesions and HIV:**

CD4 < 200 → ~20% with cavities

CD4 ≥ 200 → ~55% with cavities

Schechter MC *et al* CID 2017
Kwan CK *et al* Clin Micro Review 2011

CXR and pulmonary TB

Bottom line: a normal CXR does NOT rule out pulmonary TB, particularly among people living with HIV

Sputum-based tests

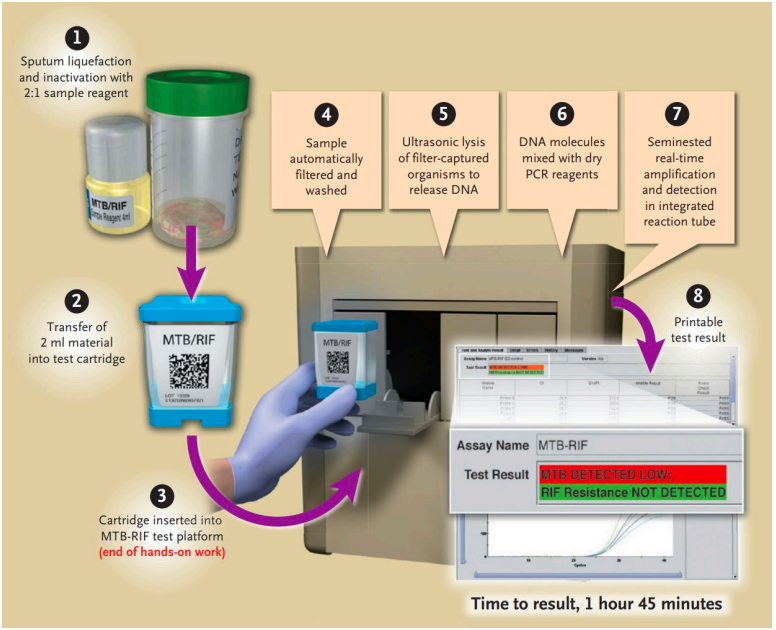
Test	Threshold	Turn around time	Comments
AFB smear	10K bacilli/ml	Lab dependent	↑ Sensitivity with 2-3 sputa ↑ Sensitivity with AM sputa
AFB culture	10 bacilli/ml	Up to 8 weeks	Required for phenotypic DST
Gene Xpert MTB/Rif	? 131 cfu's/ml	Lab dependent	Genotypic rifampin DST

The Gene Xpert MTB/Rif

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 9, 2010 VOL. 363 NO. 11

Rapid Molecular Detection of Tuberculosis and Rifampin Resistance



- **Sensitivity 1 Xpert**

98.2% smear-positive culture-positive

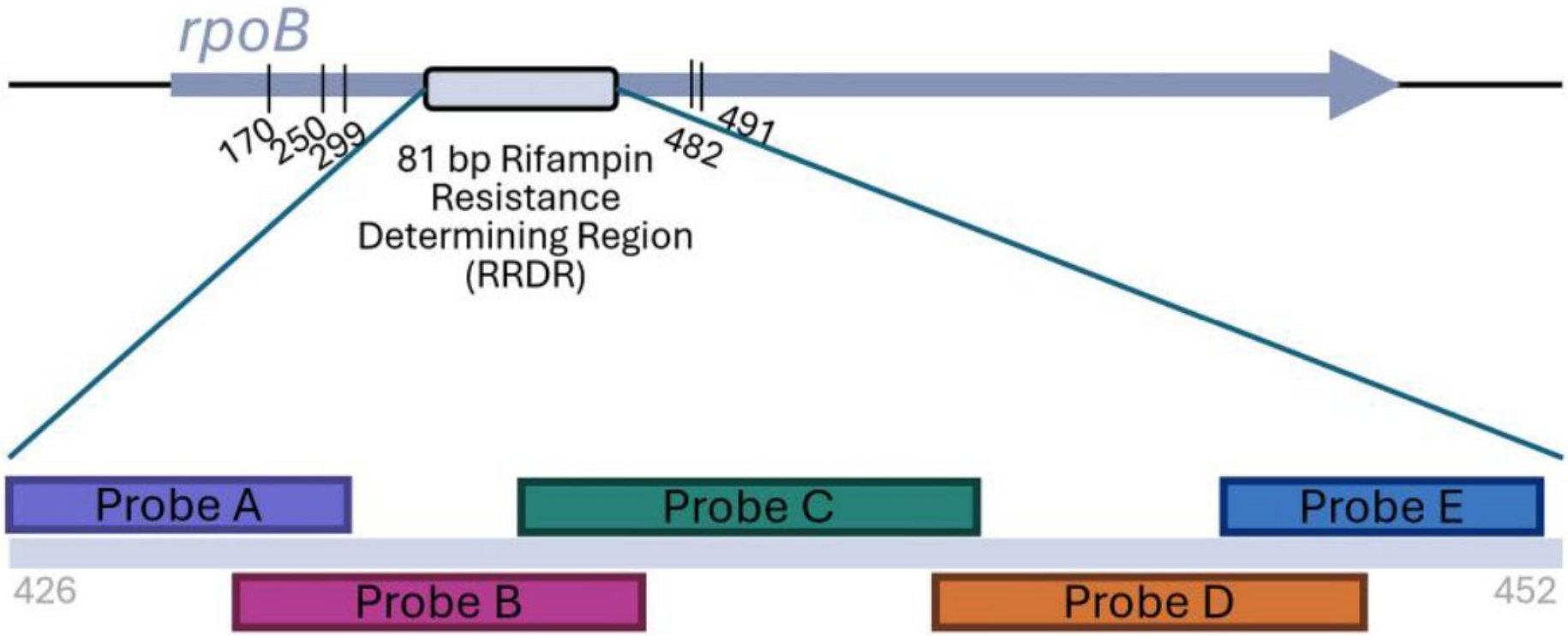
72.5% smear-negative culture-positive

- **99.2% specific for culture-confirmed TB**

Xpert vs smear

Xpert result for MTB	Smear result	Interpretation
Positive	Positive	TB!
Positive	Negative	Very likely TB
Negative	Negative	Cannot rule out TB
Negative	Positive	Probably an NTM

How does this work?



Haas AL *et al* OFID 2025

Discordance between molecular and phenotypic tests

TABLE 1 Outcome of rifampicin-throughout treatment by resistance level and type of *rpoB* mutation

	Relapse-free success n	Clinically adverse[#]		OR	95% CI	Bacteriologically adverse[¶]		OR	95% CI
		n	%			n	%		
***rpoB* mutation group**[§]	75	184	71			163	68.5		
High-level	56	140	71.4	1		125	69.1	1	
Borderline (any)	19	44	69.8	0.93	0.50–1.72	38	66.7	0.90	0.48–1.69
Individual borderline mutations[§]									
Leu430Pro	5	13	72.2	0.99	0.35–2.79	11	68.8	0.94	0.32–2.73
Asp435Tyr	2	5	71.4	0.88	0.19–4.07	5	71.4	0.99	0.21–4.56
His445Asn	3	3	50	0.4	0.09–1.83	3	50	0.45	0.10–2.05
His445Leu	1	8	88.9	2.28	0.39–13.29	6	85.7	1.95	0.32–11.84
Leu452Pro	5	13	72.2	0.99	0.35–2.79	11	68.8	0.94	0.32–2.73
Ile491Phe	3	2	40	0.29	0.06–1.50	2	40	0.32	0.06–1.68

Van Deun *et al* ERS 2021

The CDC MDDR (tNGS)

Rifampin (RIF)	**Result**	**Interpretation**
RIF interpretation		RIF resistant
rpoB*	Ser450Leu	

Comments and Disclaimers

* DTBE Reference Laboratory has transitioned from the E. coli to the M. tuberculosis numbering system for reporting rpoB gene mutations.

Isoniazid (INH)	**Result**	**Interpretation**
INH interpretation		INH resistant
inhA	T-8C	
fabG1	No mutation	
katG	Ser315Thr	

Ethambutol (EMB)	**Result**	**Interpretation**
EMB interpretation		EMB resistant
embB	Met306Val	

Pyrazinamide (PZA)	**Result**	**Interpretation**
PZA interpretation		No result. Cannot rule out PZA resistance.
pncA	No MTBC amplification detected	

Fluoroquinolones (FQ)	**Result**	**Interpretation**
FQ interpretation		FQ resistant
gyrA	Asp94Gly	
gyrB	No mutation	

Consult your local TB program and/or your CDC COE for any case of known or suspected rifampin resistance or if you cannot use a rifamycin (“virtual resistance”)

Interferon-γ Release Assays and Tuberculin Skin Testing for Diagnosis of Latent Tuberculosis Infection in Healthcare Workers in the United States

Susan E. Dorman[1], Robert Belknap[2,3], Edward A. Graviss[4], Randall Reves[2,3], Neil Schluger[5], Paul Weinfurter[6], Yaping Wang[1], Wendy Cronin[7], Yael Hirsch-Moverman[5], Larry D. Teeter[4], Matthew Parker[2,3], Denise O. Garrett[8], and Charles L. Daley[9,10]; for the Tuberculosis Epidemiologic Studies Consortium

	Serial testing Q6 months for 2 years (n≅2,500)		
	TST	QFT-GIT	T.SPOT
Conversion [1]	0.9%	6.1%[2]	8.3%
Reversion at 6 mo	91.7%	76.4%	77.1%

[1] No simultaneous conversion in all 3 tests

TB treatment in the US - 2025

AMERICAN THORACIC SOCIETY DOCUMENTS

Updates on the Treatment of Drug-Susceptible and Drug-Resistant Tuberculosis

An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline

Jussi J. Saukkonen*, Raquel Duarte*, Sonal S. Munsiff*, Carla A. Winston*, Manoj J. Mammen, Ibrahim Abubakar, Carlos Acuña-Villaorduña, Pennan M. Barry, Mayara L. Bastos, Wendy Carr, Hassan Chami, Lisa L. Chen, Terence Chorba, Charles L. Daley, Anthony J. Garcia-Prats, Kelly Holland, Ioannis Konstantinidis, Marc Lipman, Giovanni Battista Migliori, Farah M. Parvez, Adrienne E. Shapiro, Giovanni Sotgiu, Jeffrey R. Starke, Angela M. Starks, Sanket Thakore, Shu-Hua Wang, Jonathan M. Wortham, and Payam Nahid; on behalf of the American Thoracic Society, U.S. Centers for Disease Control and Prevention, European Respiratory Society, and Infectious Diseases Society of America

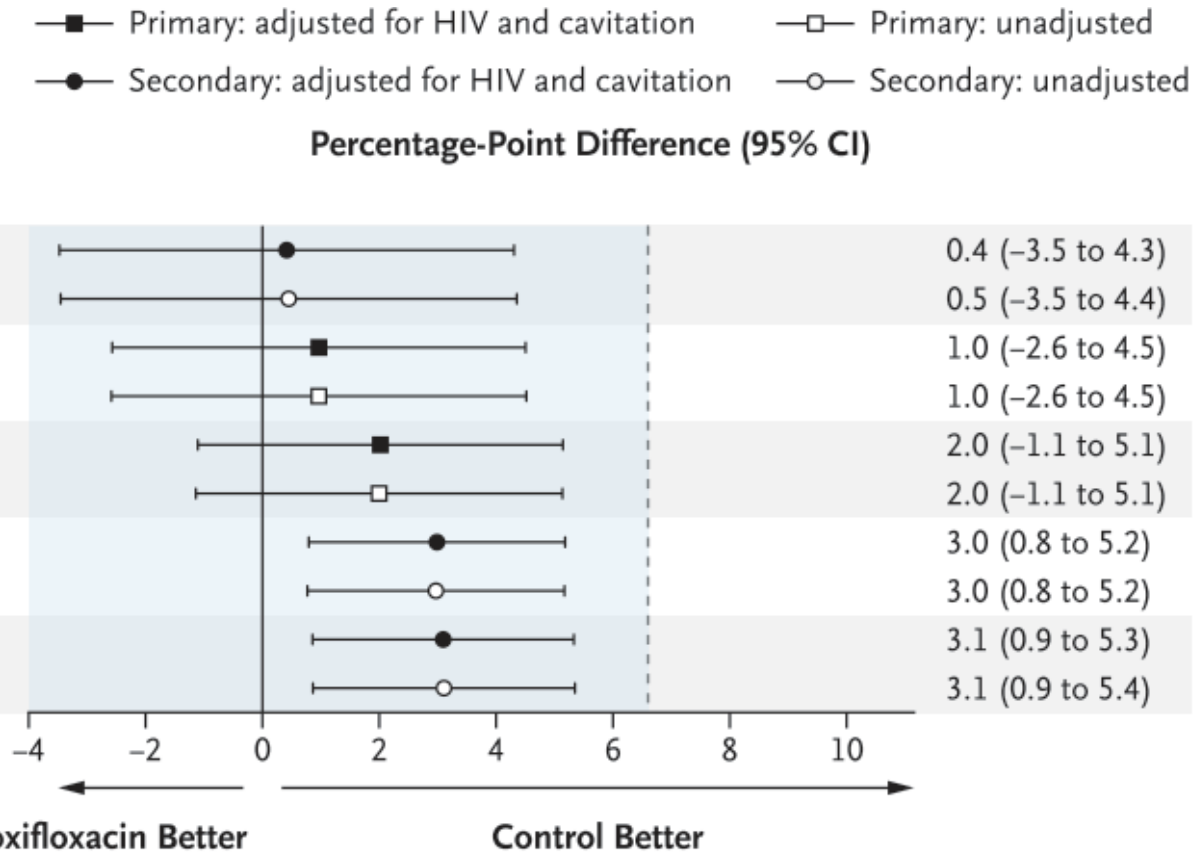
This official clinical practice guideline was approved by the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) September 2024, was cleared by the U.S. Centers for Disease Control and Prevention (CDC) September 2024, and was approved by the European Respiratory Society (ERS) October 2024

RIF/INH/FQ susceptible TB among those age ≥ 12

ORIGINAL ARTICLE

Four-Month Rifapentine Regimens with or without Moxifloxacin for Tuberculosis

4 mo rifapentine + INH + Moxi + 2 mo PZA



Analysis Population	Rifapentine–Moxifloxacin	Control
	% (no. with unfavorable outcome/total no.)	
Intention to treat	21.3 (181/849)	20.9 (173/829)
Microbiologically eligible	15.5 (123/791)	14.6 (112/768)
Assessable	11.6 (88/756)	9.6 (70/726)
Per-protocol 75%	6.1 (43/706)	3.1 (21/673)
Per-protocol 95%	5.8 (37/641)	2.7 (15/563)

Caution

Open Forum Infectious Diseases

MAJOR ARTICLE

Experience With Four-Month Rifapentine and Moxifloxacin–Based Tuberculosis Treatment in San Francisco

Janice K. Louie,[1,2] Rocio Agraz-Lara,[1] Gustavo E. Velásquez,[3] Allison Phillips,[1] and John D. Szumowski[3]

[1]Tuberculosis Prevention and Control Program, San Francisco Department of Public Health, San Francisco, California, USA, [2]Division of Infectious Diseases, Department of Medicine, University of California, San Francisco, San Francisco, California, USA, and [3]Division of HIV, Infectious Diseases, and Global Medicine, Department of Medicine, University of California, San Francisco, San Francisco, California, USA

81% had an AE

50% stopped due to AEs

FQ-DST not routinely available

Cost

Children 3 mo to <16 years

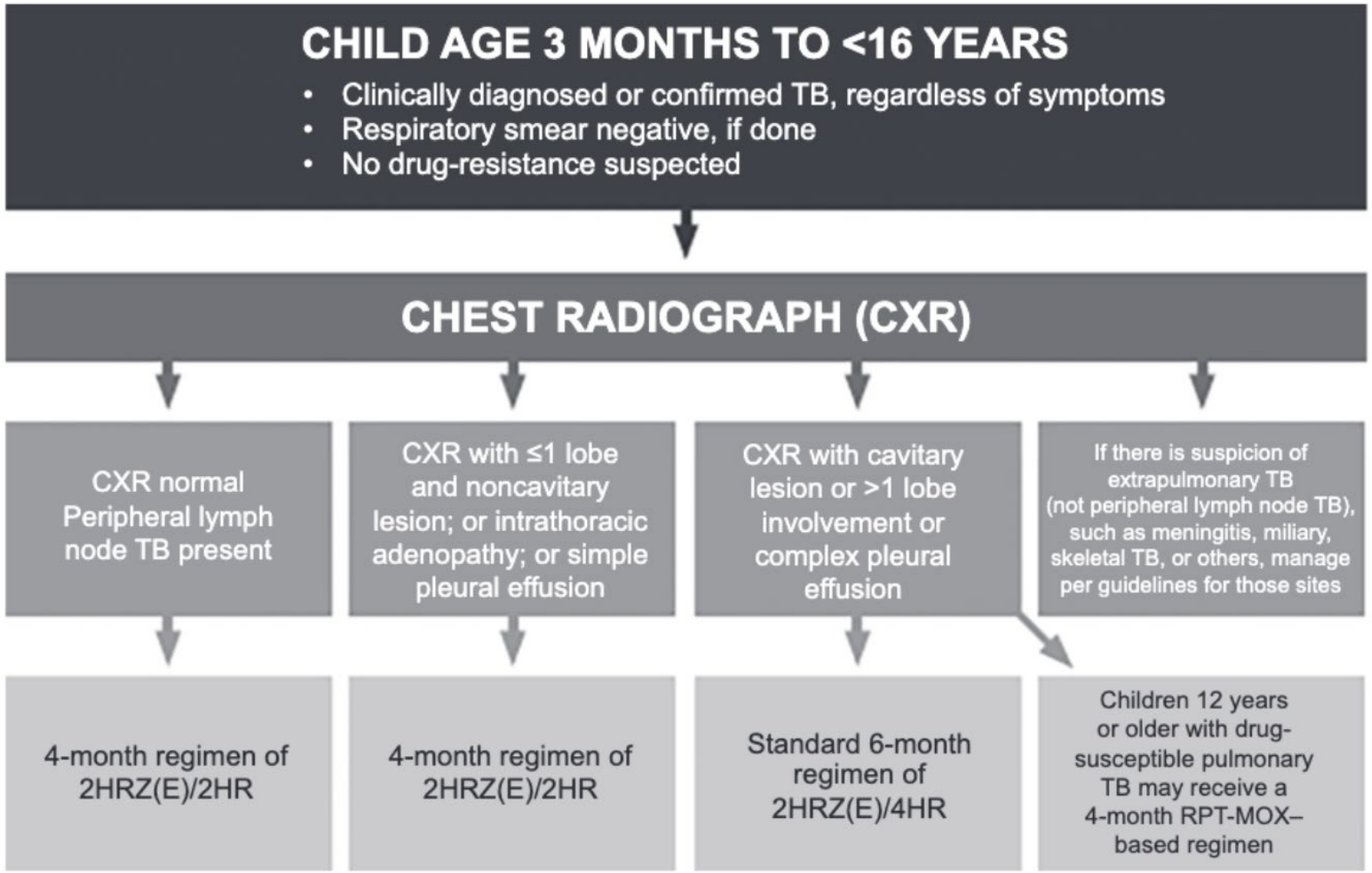
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 10, 2022 VOL. 386 NO. 10

Shorter Treatment for Nonsevere Tuberculosis in African and Indian Children

A. Turkova, G.H. Wills, E. Wobudeya, C. Chabala, M. Palmer, A. Kinikar, S. Hissar, L. Choo, P. Musoke, V. Mulenga, V. Mave, B. Joseph, K. LeBeau, M.J. Thomason, R.B. Mboizi, M. Kapasa, M.M. van der Zalm, P. Raichur, P.K. Bhavani, H. McIlleron, A.-M. Demers, R. Aarnoutse, J. Love-Koh, J.A. Seddon, S.B. Welch, S.M. Graham, A.C. Hesseling, D.M. Gibb, and A.M. Crook, for the SHINE Trial Team*

Children 3 mo to <16 years



Saukkonen JJ *et al* Am Journal of Crit Care Medicine 2025

Rifampin-R TB ≥14 yo

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 5, 2020 VOL. 382 NO. 10

Treatment of Highly Drug-Resistant Pulmonary Tuberculosis

Francesca Conradie, M.B., B.Ch., Andreas H. Diacon, M.D., Nosipho Ngubane, M.B., B.Ch., Pauline Howell, M.B., B.Ch., Daniel Everitt, M.D., Angela M. Crook, Ph.D., Carl M. Mendel, M.D., Erica Egizi, M.P.H., Joanna Moreira, B.Sc., Juliano Timm, Ph.D., Timothy D. McHugh, Ph.D., Genevieve H. Wills, M.Sc., Anna Bateson, Ph.D., Robert Hunt, B.Sc., Christo Van Niekerk, M.D., Mengchun Li, M.D., Morounfolu Olugbosi, M.D., and Melvin Spigelman, M.D., for the Nix-TB Trial Team*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Bedaquiline–Pretomanid–Linezolid Regimens for Drug-Resistant Tuberculosis

F. Conradie, T.R. Bagdasaryan, S. Borisov, P. Howell, L. Mikiashvili, N. Ngubane, A. Samoilova, S. Skornykova, E. Tudor, E. Variava, P. Yablonskiy, D. Everitt, G.H. Wills, E. Sun, M. Olugbosi, E. Egizi, M. Li, A. Holsta, J. Timm, A. Bateson, A.M. Crook, S.M. Fabiane, R. Hunt, T.D. McHugh, C.D. Tweed, S. Foraida, C.M. Mendel, and M. Spigelman, for the ZeNix Trial Team*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A 24-Week, All-Oral Regimen for Rifampin-Resistant Tuberculosis

Bern-Thomas Nyang'wa, M.B., B.S., Catherine Berry, B.Med., Emil Kazounis, M.Med.Sci., Ilaria Motta, Ph.D., Nargiza Parpieva, Sc.D., Zinaida Tigay, M.D., Varvara Solodovnikova, M.D., Irina Liverko, Sc.D., Ronelle Moodliar, M.B., B.S., Matthew Dodd, M.Sc., Nosipho Ngubane, M.B., B.Ch., Mohammed Rassool, M.B., B.Ch., Timothy D. McHugh, Ph.D., Melvin Spigelman, M.D., David A.J. Moore, M.D., Koert Ritmeijer, Ph.D., Philipp du Cros, M.B., B.S., and Katherine Fielding, Ph.D., for the TB-PRACTECAL Study Collaborators*

BPaL/M for RIF-R/FQ-S

BPaL for RIF-R/FQ-R

Consult your local TB program and/or your CDC COE for any case of known or suspected rifampin resistance or if you cannot use a rifamycin (“virtual resistance”)

Latent TB treatment

Recommendations and Reports

Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020

Timothy R. Sterling, MD[1]; Gibril Njie, MPH[2]; Dominik Zenner, MD[3]; David L. Cohn, MD[4]; Randall Reves, MD[4]; Amina Ahmed, MD[5]; Dick Menzies, MD[6]; C. Robert Horsburgh, Jr., MD[7]; Charles M. Crane, MD[8]; Marcos Burgos, MD[8,9]; Philip LoBue, MD[2]; Carla A. Winston, PhD[2]; Robert Belknap, MD[4,8]

[1]Vanderbilt University Medical Center, Nashville, Tennessee; [2]National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Division of Tuberculosis Elimination, CDC, Atlanta, Georgia; [3]Institute for Global Health, University College London, London, England; [4]Denver Health and Hospital Authority, Denver, Colorado; [5]Levine Children's Hospital, Charlotte, North Carolina; [6]Montreal Chest Institute and McGill International TB Centre, Montreal, Canada; [7]Boston University Schools of Public Health and Medicine, Boston, Massachusetts; [8]National Tuberculosis Controllers Association, Smyrna, Georgia; [9]University of New Mexico Health Science Center and New Mexico Department of Health, Albuquerque, New Mexico

MMWR 2020

LTBI regimens

TABLE 3. Recommendations for regimens to treat latent tuberculosis infection

Priority rank*	Regimen	Recommendation (strong or conditional)	Evidence (high, moderate, low, or very low)
Preferred	3 mos isoniazid plus rifapentine given once weekly	Strong	Moderate
Preferred	4 mos rifampin given daily	Strong	Moderate (HIV negative)†
Preferred	3 mos isoniazid plus rifampin given daily	Conditional	Very low (HIV negative)
		Conditional	Low (HIV positive)
Alternative	6 mos isoniazid given daily	Strong§	Moderate (HIV negative)
		Conditional	Moderate (HIV positive)
Alternative	9 mos isoniazid given daily	Conditional	Moderate

Abbreviation: HIV = human immunodeficiency virus.

* *Preferred:* excellent tolerability and efficacy, shorter treatment duration, higher completion rates than longer regimens and therefore higher effectiveness; *alternative:* excellent efficacy but concerns regarding longer treatment duration, lower completion rates, and therefore lower effectiveness.

† No evidence reported in HIV-positive persons.

§ Strong recommendation for those persons unable to take a preferred regimen (e.g., due to drug intolerability or drug-drug interactions).

Shorter, rifamycin-based regimens preferred:

↑ completion, ↓ liver toxicity, ~ efficacy

6 months of INH is an alternative regimen

MMWR 2020

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 14, 2019 VOL. 380 NO. 11

One Month of Rifapentine plus Isoniazid to Prevent HIV-Related Tuberculosis

S. Swindells, R. Ramchandani, A. Gupta, C.A. Benson, J. Leon-Cruz, N. Mwelase, M.A. Jean Juste, J.R. Lama, J. Valencia, A. Omoz-Oarhe, K. Supparatpinyo, G. Masheto, L. Mohapi, R.O. da Silva Escada, S. Mawlana, P. Banda, P. Severe, J. Hakim, C. Kanyama, D. Langat, L. Moran, J. Andersen, C.V. Fletcher, E. Nuermberger, and R.E. Chaisson, for the BRIEF TB/A5279 Study Team*

- **1 month of daily rifapentine+INH vs 9H for PLHIV**
- **68% of the trial population had a negative TST and/or IGRA**
- **Median CD4 473, 76% had an UD VL**

DHHS recommends… but I am not sure

MDR contacts

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Levofloxacin for the Prevention of Multidrug-Resistant Tuberculosis in Vietnam

Greg J. Fox, Ph.D., Nguyen Viet Nhung, Ph.D., Nguyen Cam Binh, Ph.D., Nguyen Binh Hoa, Ph.D., Frances L. Garden, Ph.D., Andrea Benedetti, Ph.D., Pham Ngoc Yen, M.Sc., Nguyen Kim Cuong, Ph.D., Emily L. MacLean, Ph.D., H. Manisha Yapa, Ph.D., David W. Dowdy, Ph.D., Nguyen Huu Lan, M.D., Elyse Guevara-Rattray, M.I.P.H., Pham Duc Cuong, B.A., Ori Solomon, Ph.D., Marcel A. Behr, M.D., Ben J. Marais, Ph.D., Steven M. Graham, Ph.D., Dick Menzies, M.D., Nguyen Thu Anh, Ph.D., and Guy B. Marks, Ph.D.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Levofloxacin Preventive Treatment in Children Exposed to MDR Tuberculosis

A.C. Hesseling, S.E. Purchase, N.A. Martinson, L. Fairlie, H.S. Schaaf, J. Brigden, S. Staples, D.M. Gibb, A. Garcia-Prats, F. Conradie, C. McGowan, C. Layton, E. Batist, A.-M. Demers, S. Nyamathe, L. Frigati, R. Turner, T. Duong, and J.A. Seddon

NEJM Evidence

Published December 18, 2024
NEJM Evid 2025;4(1)
DOI: 10.1056/EVIDoa2400190

ORIGINAL ARTICLE

A Meta-Analysis of Levofloxacin for Contacts of Multidrug-Resistant Tuberculosis

Trinh Duong, M.Sc.,[1] Joanna Brigden, M.Sc.,[1] H. Simon Schaaf, M.D., Ph.D., Paeds,[2] Frances Garden, Ph.D.,[3] Ben J. Marais, M.D., Ph.D.,[4] Thu Anh Nguyen, M.D., Ph.D.,[4,5,6] Ian R. White, Ph.D.,[1] Diana M. Gibb, M.D., M.Sc.,[1] Nguyen Viet Nhung, M.D., Ph.D.,[7] Neil A. Martinson, M.B.B.Ch.,[8,9] Lee Fairlie, F.C.Paeds,[10] Leonardo Martinez, Ph.D., M.P.H.,[11] Charlotte Layton, M.Sc.,[1] Andrea Benedetti, Ph.D.,[12,13] Guy B. Marks, M.B.B.S., Ph.D.,[3,5] Rebecca M. Turner, Ph.D.,[1] James A. Seddon, M.B.B.S., Ph.D.,[2,14] Anneke C. Hesseling, M.D., Ph.D.,[2] and Greg J. Fox, M.B.B.S., Ph.D.[4,5,15] for the TB-CHAMP and VQUIN MDR-TB trial teams*

Relative difference in cumulative incidence: 0.41 (95%CI 0.18 to 0.92)

All of TB in 15 min! We did it ☺

Grady

EMORY UNIVERSITY SCHOOL OF MEDICINE

Department of Medicine