Four Month Treatment Regimen (HPMZ)

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November 6, 2025

TB Nurse Expert Meeting · November 6-7, 2025 · San Antonio, Texas

Four Month Treatment Regimen (HPMZ)

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TB Nurse Expert Meeting
San Antonio, TX
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Financial Disclosure

Consultant for Oak Therapeutics NIH SBIR grant

Treatment shortening regimen – Drug Sensitive TB

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Four-Month Rifapentine Regimens with or without Moxifloxacin for Tuberculosis

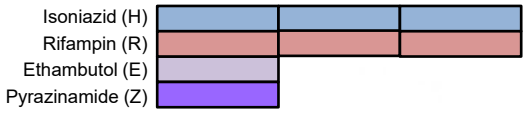
S.E. Dorman, P. Nahid, E.V. Kurbatova, P.P.J. Phillips, K. Bryant, K.E. Dooley, M. Engle, S.V. Goldberg, H.T.T. Phan, J. Hakim, J.L. Johnson, M. Lourens, N.A. Martinson, G. Muzanyi, K. Narunsky, S. Nerette, N.V. Nguyen, T.H. Pham, S. Pierre, A.E. Purfield, W. Samaneka, R.M. Savic, I. Sanne, N.A. Scott, 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

2234 participants (194 PLHIV, 1703 with cavity on CXR)
Randomized 1:1:1 to 3 arms
Noninferiority study

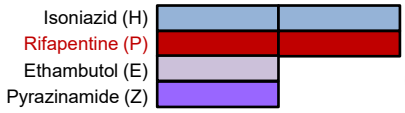
N Engl J Med 2021;384:1705-18.

Study 31/A5349

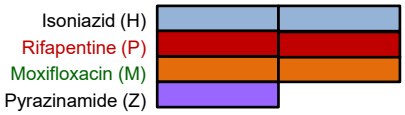
Control (2HRZE/4HR)



RPT (2HPZE/2HP)

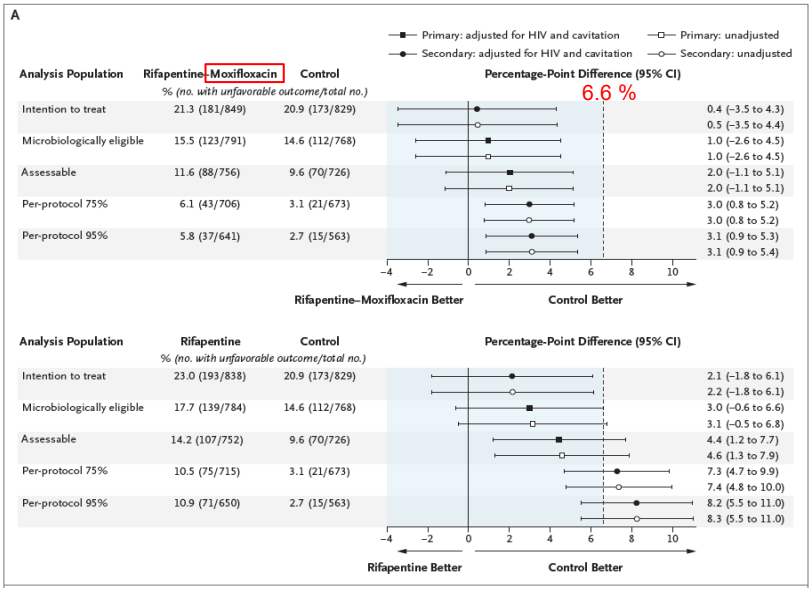


RPT/Moxi (2HPZM/4HPM)



Notes:
- HRZE dosed at standard doses
- Dosed daily, 7 days/week, observed 5 days/week
- Rifapentine 1200 mg (8 tablets)
- Moxifloxacin 400 mg

Study 31 - Results



N Engl J Med

Safety and Efficacy Study 31/A5349

TABLE 1. EFFICACY AND SAFETY OUTCOMES IN S31/A5349

	EFFICACY		SAFETY	
Regimen	**Favorable outcomes**	**Unfavorable outcomes**	**Grade 3 or higher AEs**	**All-cause mortality**
Control (2HRZE/4HR)	90.4% (656/726)	9.6% (70/726)	19.3% (159/825)	0.8% (7/825)
RPT-MOX (2HPZM/2HPM)	88.4% (668/756)	11.6% (88/756)	18.8% (159/846)	0.4% (3/846)

TABLE 2. EFFICACY AND SAFETY OUTCOMES IN S31/A5349 AMONG PLHIV

	EFFICACY				SAFETY			
Regimen	**Favorable outcomes**		**Unfavorable outcomes**		**Grade 3 or higher AEs**		**All-cause mortality**	
	HIV+	HIV-	HIV+	HIV-	HIV+	HIV-	HIV+	HIV-
Control (2HRZE/4HR)	84.7% (50/59)	90.8% (605/666)	15.3% (9/59)	9.2% (61/666)	21.4% (15/70)	19.1% (144/755)	2.9% (2/70)	0.7% (5/755)
RPT-MOX (2HPZM/2HPM)	91.4% (53/58)	88.1% (615/698)	8.6% (5/58)	11.9% (83/698)	13.9% (10/72)	19.3% (149/774)	0% (0/72)	0.4% (3/774)

https://www.treatmentactiongroup.org/publication/an-activists-guide-to-shorter-treatment-for-drug-sensitive-tuberculosis/

Groups That May Not Benefit

- Patients< 12 years old and ≥75 years old
- Pregnant women – no studies
- Patients with severe liver disease – Not likely to tolerate INH and PZA
- Patients with severe renal disease – No guidance on renal dosing

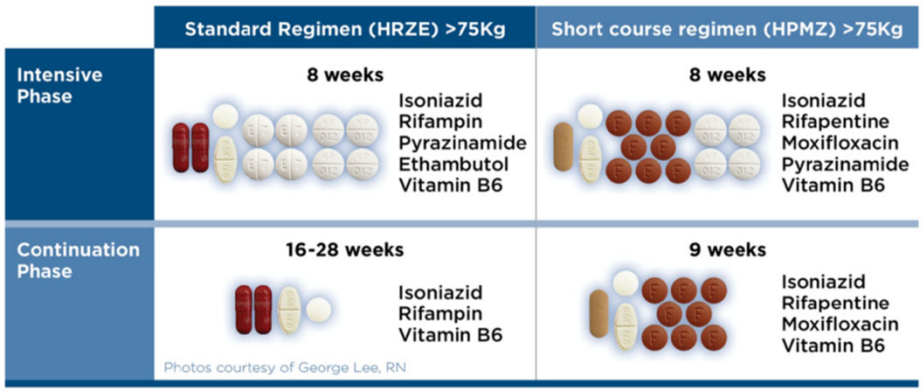
Groups That May Not Benefit

- Patients with multiple medication interactions – Rifapentine works like rifampin regarding drug interactions
- The study specifically excluded patients with central nervous system (CNS), bone, miliary, and pericardial TB. Patients with extensive disease, even pulmonary, that would require 9 or more months of standard treatment – Not for bone, CNS, miliary or pericardial disease
- Tiny patients (< 88 lb.) – must weigh at least 40 kg
- Patients with long QTc syndrome – moxifloxacin can prolong QTc

Potential Challenges

- Pill burden
  - 1 INH, 8 rifapentine, 1 moxifloxacin, 1 pyridoxine (everybody gets these) + PZA for weight
- Tolerability (versus safety, efficacy)
- Familiarity with the regimen
  - Substitutions?
    - There is no guidance on substituting any of the drugs
  - EOT and they need more treatment?
    - There is no real guidance on how long to extend treatment
- Drug shortages!

Pill Burden



4-Month-HPMZ-TB-Regimen_NTCA-FAQ

4 Month Rifapentine Regimen in Actuality

NY experience
- 46% of patients with TB were eligible
- 36% completed the regimen
- 42% discontinued due to adverse events

SF experience
- 18.8% of patients with TB were eligible
- 41% completed treatment
- 81% had adverse events

Int J Tuberc Lung Dis 2025. 29(7):318–324
Open Forum Infectious Diseases, Volume 11, Issue 4, April 2024, ofae178

Questions?

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Four Month Rifapentine/Moxifloxacin Short Course TB Regimen Pilot Project

Rachel Munoz, RN
Elizabeth Foy, MSN, RN
Texas Department of State Health Services
Tuberculous and Hansen's Disease Unit

Presented for the Heartland National TB Center, Nurse Expert Meeting
San Antonio, Texas, November 6 -7, 2025

DSHS Approach to New TB Guidelines

- **Consider Implementation with a Texas Lens:**
  - Does this fit our population?
  - What infrastructure is needed to implement?
  - What questions can we anticipate?
  - What education is needed before adopting?
- **Considerations for These Guidelines:**
  - Do we have the medications to support four months of isoniazid, rifapentine, moxifloxacin, and pyrazinamide (HPMZ)?
  - Is there value in piloting this first before putting paper into practice?

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Decision: Pilot the Regimen First

Goal
- Enroll 20–25 patients

14 Month Plan
- Enroll from April to November 2025
- Closure in June 2026

Participant Tracking
- Enrollment or declination reported to TB Unit

Ongoing Assessment
- Monthly case reviews
- Decisions on treatment

Medical Consultation
- Pilot oversight
- Consultation
- Standing Delegation Orders (SDOs)

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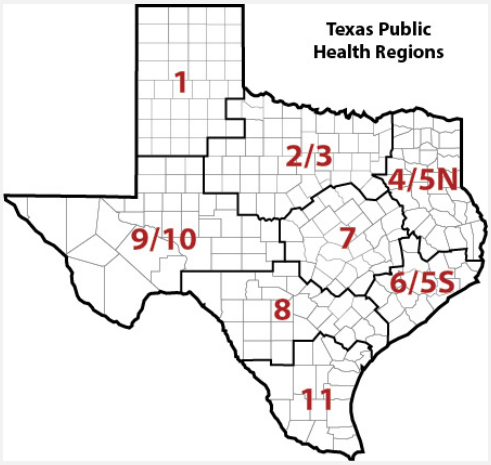
Pilot Site Selection

1. Public Health Region (PHR 1)
2. PHR 8
3. PHR 11
4. City of El Paso Department of Public Health
5. Harris County Public Health
6. Austin Public Health
7. Williamson County and Cities Health District
8. San Antonio Metropolitan Health District



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Pilot Timeline

- April 10, 2025: Kick-off meeting; enrollment start date
- April 24, 2025: Dr. Armitige's 4 HMPZ webinar
- April - November 2025: Enroll patients
- May – December 2025: Monthly case reviews
- June 10, 2026: Last date of therapy
- July 15, 2026: Finalize Data and Develop Final Report
- September 1, 2026: Include in FY27 SDOs

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Overview of Enrolled Patients

Age Ranges	• 19–68 years
Disease Site	• 16 pulmonary • 2 pulmonary/extrapulmonary (pleural) • 2 extrapulmonary (pleural, cervical lymph)
Initial Radiology	• 13 patients had cavitation on initial radiology
Dosing 7 Days/Week	• All eligible patients transitioned to VDOT

Total Active: 15
Disenrolled: 3
Completed: 2
Total Enrolled: 20

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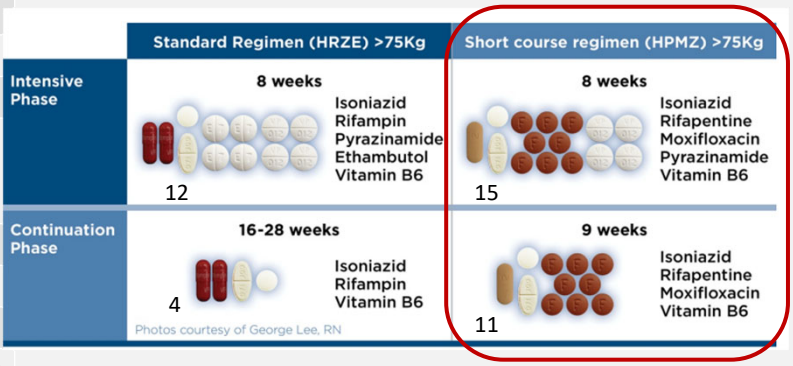
Eligible Patients Who Did Not Start HPMZ*

#	Reason Declined
1	Pill burden
2	Pill burden
3	Pill burden
4	Uncontrolled diabetic, concern for non-adherence and possible tendonitis
5	Pill burden
6	Moving out of jurisdiction
7	Pill burden
8	Started RIPE in hospital, doing well
9	Pill burden
10	Baseline nausea; pill burden



https://www.tbcontrollers.org/docs/resources/4-Month-HPMZ-TB-Regimen_NTCA-FAQ.pdf

*Data as of October 15, 2025

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Preliminary Findings During Therapy

- **Nausea** – Six patients; either self-resolved or supported with antiemetics
- **Joint pain** – One patient; resolved when PZA stopped
- **Muscle pain** – One patient; "Charlie horse," self-resolved
- **Itching** – One patient; resolved with Benadryl
- **GI/Other**: Two patients; increase in bowel movements (1), elevated LFTs (1)

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Reasons for Stopping HPMZ

1 Patient, Drug Susceptibility Results

- INH mono-resistance, identified about eight weeks into HPMZ
- Patient transitioned to an INH-mono resistant TB regimen (*credit given* for the 49 doses of HMPZ received)

1 Patient, Culture Results

- Cultured out M. bovis (naturally PZA resistant); identified about one month into HPMZ
- Patient *restarted* TB therapy with INH/RIF/B6 x nine months

1 Patient, Side Effects

- Patient had a baseline history of GERD, gastroparesis, colitis
- Elevated liver enzymes after seven days on HPMZ
- Re-started with a liver-friendly regimen

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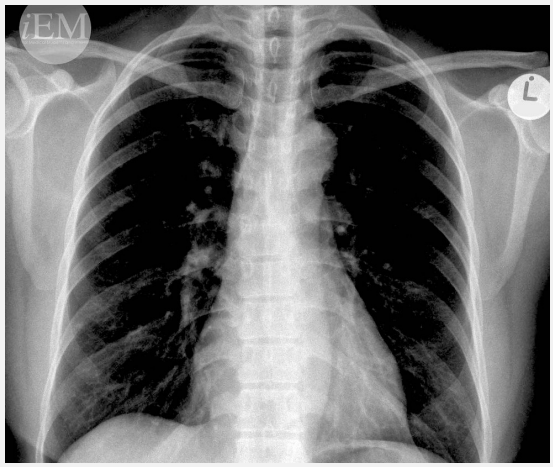
Extending Therapy Past Four Months

- One patient with cavitation on initial radiology extended to six months of therapy based on final CXR results
  - 26-year-old non-U.S. born
  - Initial sputum smear positive >10
  - Culture conversion at about seven weeks
  - Baseline weight 131 lbs; gained 18 lbs by month four
  - Past history of marijuana use



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Considerations

- Patient's comorbidities, baseline weight, extent of disease may impact a four-month regimen tolerability
- Patient education and support
  - Be clear about the number of pills
  - Describe as a four to six-month regimen
  - Address side effects, especially nausea
- Importance of assessing risk factors for PZA intolerability (as well as other drugs in the regimen)
- Availability of fluoroquinolone susceptibilities
- Consider messaging to hospitals, providers who may start patients on standard four-drug therapy

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Resources

- **Standing Delegation Orders (SDOs)** – updated with new Fiscal Year 2026 dates (no content changes) for pilot sites only.
- **Webinar** – The Assembly on Pulmonary Infectious and Tuberculosis (PI-TB) Early Career Professionals Working Group, "Pulmonary Infection Network of Experts" – "New TB Treatment Guidelines: A Clinician's Guide to the ATS/CDC/ERS/IDSA 2025 Update". https://site.thoracic.org/assemblies/pitb/pine
- **Article** - Galvis ME, Gao GE, Salerno MM, Whitehead M, Juste D, Buchanan C, Chuck C, Iskhakova F, Macaraig M, Dworkin F, Burzynski J, Nilsen D. Challenges to initiate and complete a 4-month rifapentine-moxifloxacin TB treatment regimen. Int J Tuberc Lung Dis. 2025 Jun 27;29(7):318-324. doi: 10.5588/ijtld.24.0616. PMID: 40579760; PMCID: PMC12233099. https://pmc.ncbi.nlm.nih.gov/articles/PMC12233099/
- **Article** - Janice K Louie, Rocio Agraz-Lara, Gustavo E Velásquez, Allison Phillips, John D Szumowski, Experience With Four-Month Rifapentine and Moxifloxacin–Based Tuberculosis Treatment in San Francisco, Open Forum Infectious Diseases, Volume 11, Issue 4, April 2024, ofae178. https://doi.org/10.1093/ofid/

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Thank you!

HPMZ Pilot Project

Case Study for Client on HPMZ

November 7, 2025

Lori Eitelbach, BSN, RN
TB Program Manager, Williamson County and Cities Health District

Objectives

- Familiarization of new regimen
- Overcoming challenges
- Points for discussion

Case History

Background:

- 68-year-old male originally from Nepal
- Arrived in U.S. 2 months prior to TB diagnosis on tourist visa
- Planned to stay 6 months visiting family
- Began permanent resident application via Civil Surgeon

Social & Family:

- Married with 3 grown children
- Lives with wife, son, daughter-in-law, and 2 grandchildren (ages 2 & 4)
- Retired farmer (previously worked in agriculture in Nepal)

Case History, continued

Medical History:

- Comorbidities: Diabetes, Asthma
- HIV: Negative
- Prior smoker and drinker all his adult life, but quit 14 years ago
- Denies TB exposure

Clinical Findings:

- Positive QFT and abnormal CXR during Civil Surgeon exam
- Cough: “For a long time,” attributed to asthma
- Weight: 114.6 lbs — appeared thin and frail
- Denies: Fever, night sweats, lymphadenopathy
- Didn’t note weight loss but mentioned pants are looser fitting

Initial Diagnostic Results

- Baseline CXR - right greater than left upper lobe reticulonodular opacities.
- Positive QFT
- Initial sputum smears negative x 3
- NAAT positive, Rif sensitive
- Diagnosed w/ pulmonary TB and offered HPMZ regimen
- Client accepted HPMZ because his VISA would expire in 4 mos.
- Start date 8/1/25

Challenge #1

Familiarizing treating team and client with new regimen

- Does client meet inclusion criteria?
- Are there any exclusions to consider?
- What are the treating team's concerns?
  - Tolerance to meds (s/e)
  - How to immediately DOT 7-days/week
- What are the client's concerns?
  - High pill burden
  - Completing tx before VISA expires

Inclusions:

- Diagnosed with known or suspected drug susceptible pulmonary TB.
- Aged 12 years and older through age 75 years, with a body weight of ≥40 kgs.
- If HIV positive, have a CD4 count above 100 and are taking antiretroviral therapy (ART) compatible with rifapentine.
- Have no additional drug interactions or contraindications to the drugs used in the regimen.
- Tolerant of pill burden (at most 15 pills/day, 7 days/week, 17 weeks in total).

Exclusions:

- Pregnant or breastfeeding.
- Younger than age 12, older than age 75 years.
- Body weight below 40 kgs.
- Known or possible resistance to isoniazid, pyrazinamide, rifamycins, or fluoroquinolones.
- Drug-drug interactions with regimen medications, including certain anti-retroviral (ARV) medications for HIV.

Overcoming Challenge #1

- **Treating team**
  - Familiarizing ourselves with new SDO requirements:
    - Mag included in labs
    - Lab draws every month even if asymptomatic
    - Peripheral neuropathy checks
    - New Pilot program documents
    - Counting 7-day week doses
    - Putting client on VDOT asap
  - Touching base with each team member - confident/comfortable using regimen?
  - Monthly HPMZ calls with Pilot Program participants and Dr. Armitige - crucial for comfort/confidence in managing side effects and determining progress
- **Client**
  - Supporting adjustment to daily, observed dosing
  - Reassurance that side effects can be managed

Challenge #2

Nausea, Constipation and Weight Loss

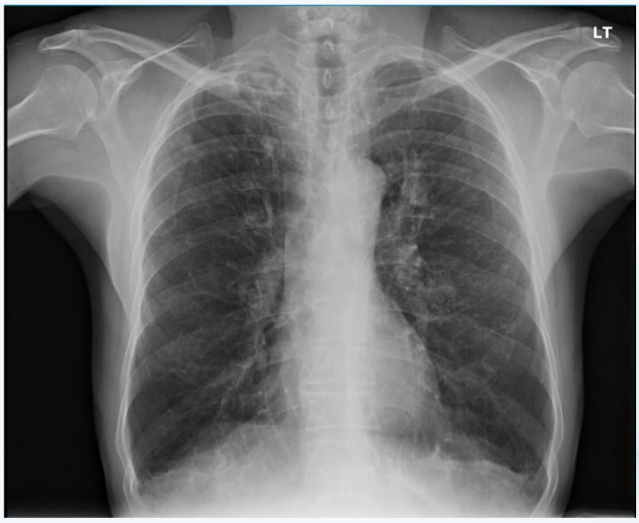
- From 1st dose he experienced nausea
- Occasional vomiting and constipation
- Quick weight loss of 4 lbs to 110 lbs from already low baseline weight of 114 lbs.
- Sits outside in hot sun all day – feels too cold in air conditioning
- No routine BS checks – HgBA1C = 9.2

Overcoming Challenge #2

- After some trial and error over 3-4 weeks:
  - Zofran 8mg BID
  - Dulcolax daily
  - Increase fluids to 8 oz every 3-4 hours
  - Drink Glucerna for protein
- Added Prilosec 20mg daily for upset stomach
- Encouraged establishing care with PCP for diabetes management

Update on Client Status at 2 months

- Labs stable. LFTs remained normal
- Cough fully resolved after only 2 weeks on meds
- Slow weight gain of 3lbs
- Pansensitive
- Stopped taking Prilosec and is taking Zofran prn now
- 1st set of sputums from August were all culture positive
- 2nd set of sputums from September were all culture negative
- PZA dc'ed after 56 DOT doses (7 day/week DOT) on 8/11/25
- 2-month CXR - Hyperinflation with increased scarring and perihilar prominence. Emphysematous change and scarring



7/22/25:
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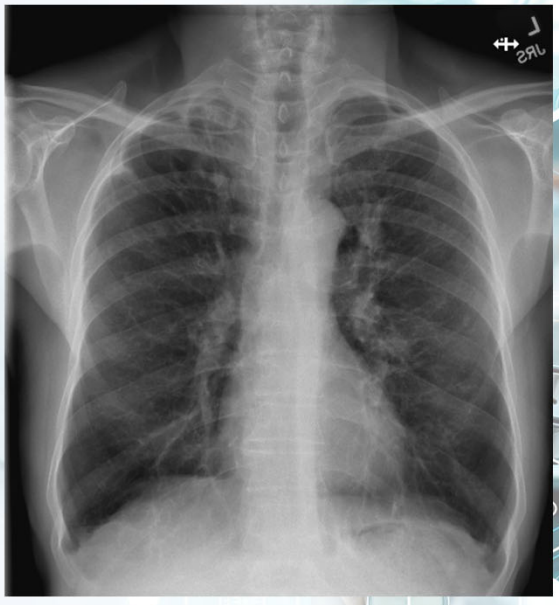

10/16/25: Hyperinflation with increased scarring and perihilar prominence. Emphysematous change and scarring.

Comparison of 2 WCCHD Clients on HPMZ

	Client #1	Client #2
Age	68	24
Country of Birth	Nepal	Nicaragua
Profession	Farmer (heavy labor)	Roofer (heavy labor)
Normal weight	Unknown	130 lbs
Weight at tx start	114 lbs	110 lbs
Comorbids	Diabetes, Asthma	Seizure Disorder
Imaging	No cavity	Cavitary
Initial smears	Negative	Positive
Culture Conversion	2 months	2 months
Side effects of tx	Nausea, weight loss	none
Weight gain at 2 months of tx	3 lbs	15 lbs
Estimated end of tx	4 months	4 months

Wrap up Information

- Contact Investigation
  - 5 family contacts; all negative on 2nd round except son diagnosed w/ LTBI on 1st round
  - Client will complete HPMZ at same time as son will complete Rifampin x 4 months!
- Client would most likely have completed tx before his VISA expired, however he was able to get 6-month extension

Teaching Points/Points for Discussion

- Don't be afraid of HPMZ ☺
- Clients tolerate the pill burden and do well with that number of meds x 4 months
- Side effects are manageable – we CAN make our clients comfortable!
- 4 months goes by so quickly – it's crazy and amazing to think we can treat an active pulmonary TB client successfully in 4 months!


THANK YOU