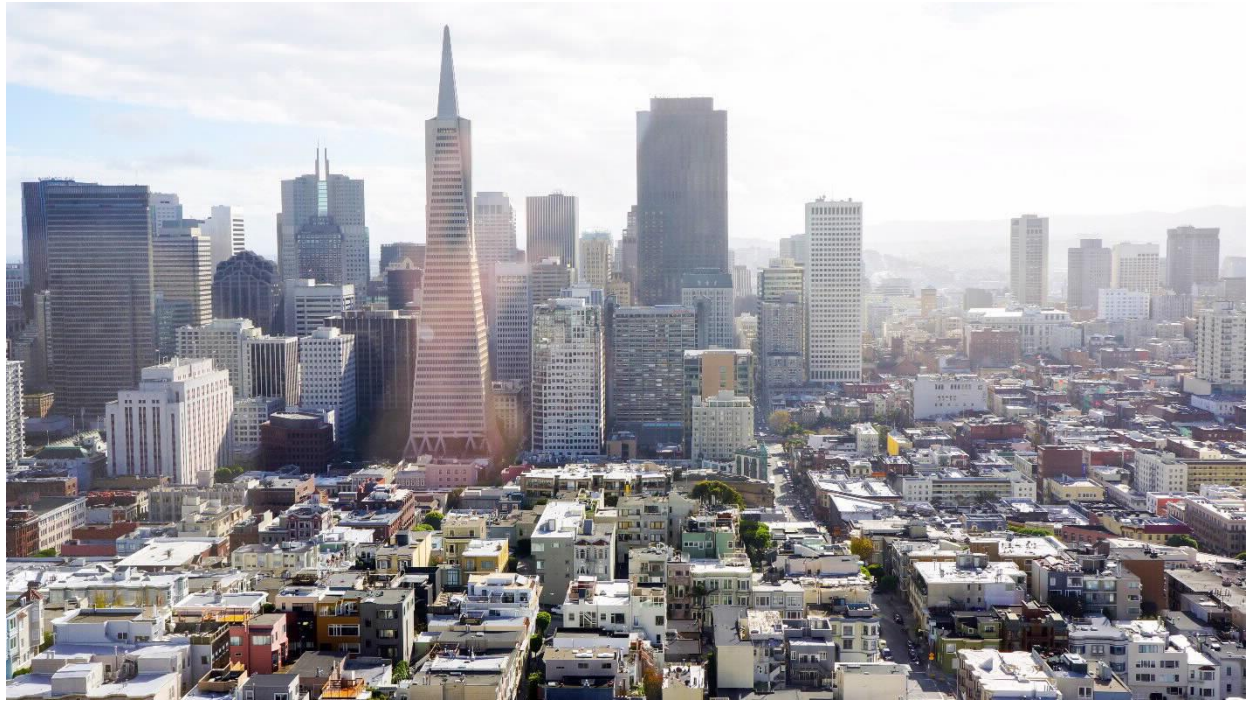

Nursing Case Management of the 4 month short course regimen for active TB

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TB Prevention and Control Section

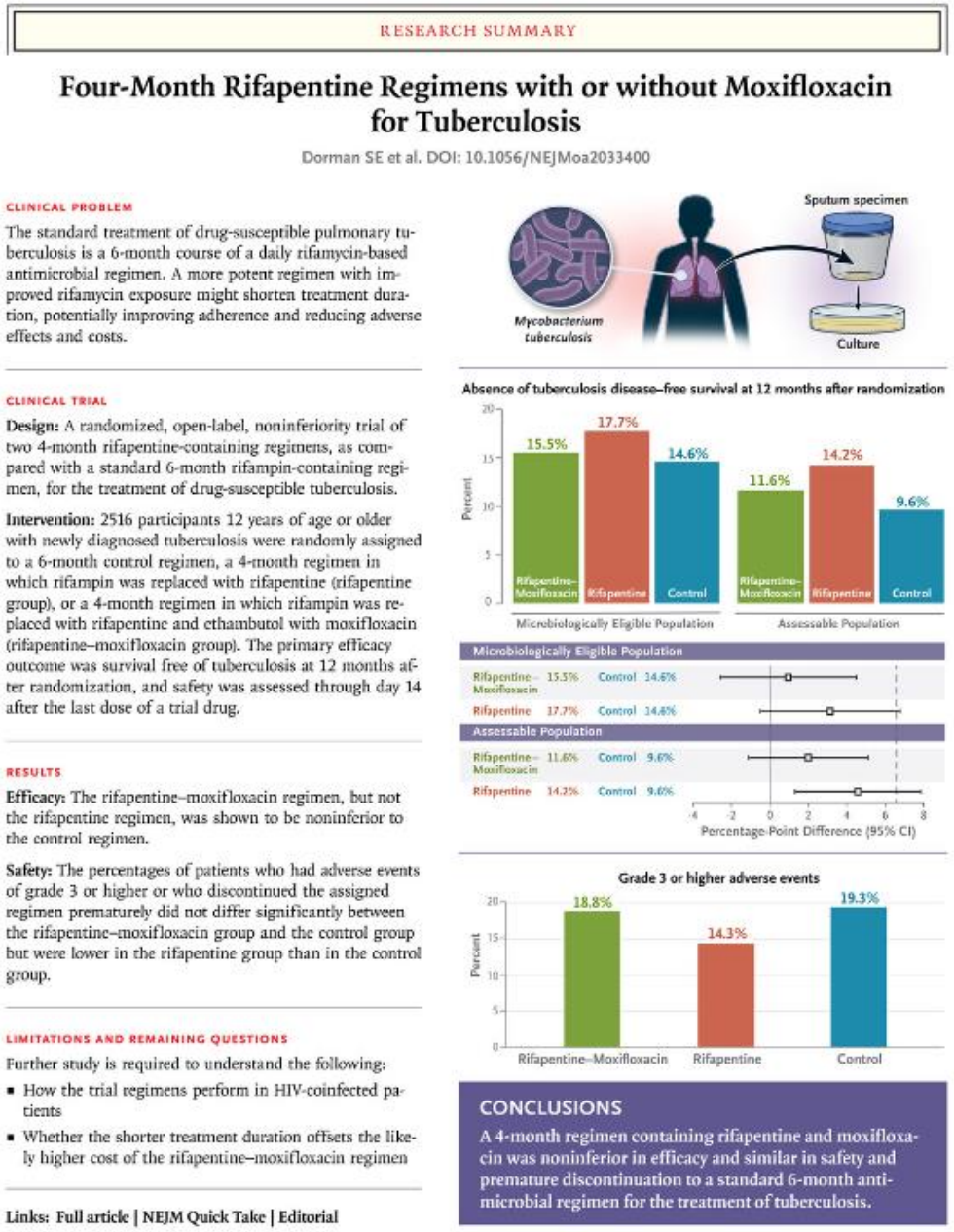
San Francisco Department of Public Health

POPULATION HEALTH DIVISION

SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH

Objectives

1. Describe the 4 month rifapentine- moxifloxacin short course regimen
2. Describe which patients may best benefit from the regimen
3. Identify common side effects associated with the regimen and how to mitigate and monitor



RESEARCH SUMMARY

Four-Month Rifapentine Regimens with or without Moxifloxacin for Tuberculosis

Dorman SE et al. DOI: 10.1056/NEJMoa2033400

CLINICAL PROBLEM

The standard treatment of drug-susceptible pulmonary tuberculosis is a 6-month course of a daily rifamycin-based antimicrobial regimen. A more potent regimen with improved rifamycin exposure might shorten treatment duration, potentially improving adherence and reducing adverse effects and costs.

CLINICAL TRIAL

Design: A randomized, open-label, noninferiority trial of two 4-month rifapentine-containing regimens, as compared with a standard 6-month rifampin-containing regimen, for the treatment of drug-susceptible tuberculosis.

Intervention: 2516 participants 12 years of age or older with newly diagnosed tuberculosis were randomly assigned to a 6-month control regimen, a 4-month regimen in which rifampin was replaced with rifapentine (rifapentine group), or a 4-month regimen in which rifampin was replaced with rifapentine and ethambutol with moxifloxacin (rifapentine–moxifloxacin group). The primary efficacy outcome was survival free of tuberculosis at 12 months after randomization, and safety was assessed through day 14 after the last dose of a trial drug.

RESULTS

Efficacy: The rifapentine–moxifloxacin regimen, but not the rifapentine regimen, was shown to be noninferior to the control regimen.

Safety: The percentages of patients who had adverse events of grade 3 or higher or who discontinued the assigned regimen prematurely did not differ significantly between the rifapentine–moxifloxacin group and the control group but were lower in the rifapentine group than in the control group.

LIMITATIONS AND REMAINING QUESTIONS

Further study is required to understand the following:

- How the trial regimens perform in HIV-coinfected patients
- Whether the shorter treatment duration offsets the likely higher cost of the rifapentine–moxifloxacin regimen

Links: Full article | NEJM Quick Take | Editorial

CONCLUSIONS

A 4-month regimen containing rifapentine and moxifloxacin was noninferior in efficacy and similar in safety and premature discontinuation to a standard 6-month antimicrobial regimen for the treatment of tuberculosis.

- Landmark trial (S31/A5349) that demonstrated that pan-susceptible pulmonary TB could be treated with duration of < 6 months- the first to do so in almost 40 years.
- Led by the U.S. Centers for Disease Control and Prevention's (CDC) Tuberculosis Trials Consortium (TBTC) with collaboration from the AIDS Clinical Trials Group (ACTG).
- Randomized, phase 3 controlled trial with more than 2,500 participants ages 12 and older enrolled at 34 clinical sites in 13 countries, including 214 people living with HIV.

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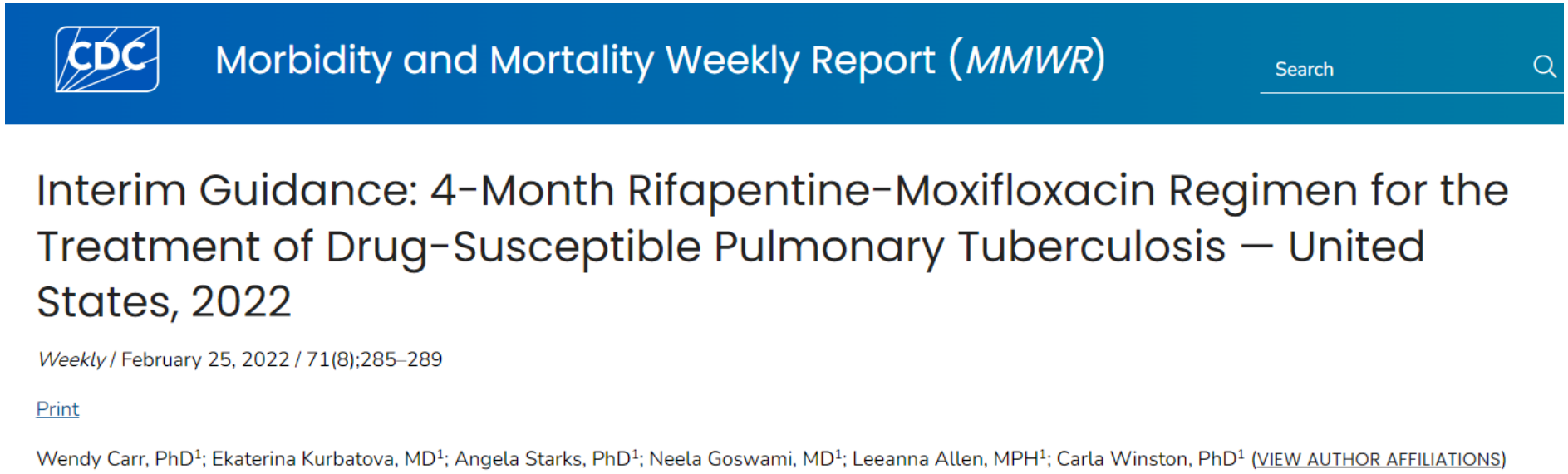
Dorman et al, Four month Rifapentine Regimens with or without Moxifloxacin for Tuberculosis. N Engl J Med 2021; 384:1705-1718. Slide courtesy of J Louie

Results of the trial

- Demonstrated that 4 months of INH, rifapentine, moxifloxacin, pyrazinamide are as effective as the standard HRZE regimen for pan-susceptible pulmonary TB
- Follow-up analysis confirmed that the 4-month regimen had noninferior efficacy at 18 months compared to the standard 6-month control regimen
- Recommended as a treatment option for pan-susceptible pulmonary TB by CDC



Four month RPT-MOX short course regimen

- For pan-susceptible pulmonary TB in age 12 years and older who weigh > than or equal to 40kg (88lbs)
- Intensive phase
  - 8 weeks/56 doses of daily treatment with rifapentine (RPT), isoniazid (INH), pyrazinamide (PZA), and moxifloxacin (MOX)

then

- Continuation phase
  - 9-weeks (63 doses) of daily treatment (continuation phase) with RPT, INH, and MOX

Total dose count 119

National Tuberculosis Coalition of America (NTCA) eligibility

- Age range >12* - ?
- Only pulmonary (may have cavity on chest X-ray)*
- No history of taking TB medications with the past 6 months*
- If HIV positive, CD4 >100 cells/mm3 (see anti-retroviral therapy caveats)
- Weight > 40 kg
- Creatinine <2.0
- Potassium ≥ 3.5 meq/L
- Hgb ≥ 7.0 g/dL
- Platelets ≥ 100,000/mm3
- LFTs ≤ 2X ULN
- Negative pregnancy test for women of childbearing age (12-55 years)/not breastfeeding
- Medication review with no significant drug-drug interactions
- Rapid molecular detection of drug resistance from initial specimen should be ordered

*TB Program specific

Regimen not recommended in...

- Suspected or documented extrapulmonary TB (e.g., CNS, bones, joints, pericardial, genito-urinary or miliary TB) or disseminated TB*
- Mono- or multi-drug resistance (either previously known or identified on PCR, tNGS, WGS or DST)
- Pregnant or breast feeding
- Receiving HIV medications that include protease inhibitors, integrase inhibitors, entry and fusion inhibitors, or non-nucleoside reverse transcriptase inhibitors other than efavirenz
- History of prolonged Qt syndrome, arrythmia, recent ischemic heart disease, arrhythmias or structural heart disease
- Concurrent use of Qt-prolonging medication (e.g., clarithromycin, quinidine, fluconazole, antipsychotics: haloperidol, chlorpromazine, anti-emetics: ondansetron and domperidone, etc.).

*TB Program specific

Continued

- The 4-month daily treatment regimen was not studied in the following and CDC recommends clinical consultation in patients who:
- There is concern for drug resistance to any drug in the regimen
- Person received >5 doses of prior TB treatment in the preceding 6 months whether for active TB or LTBI
- Person who received any drugs in the regimen in the prior 30 days (e.g. fluroquinolone for UTI)

Baseline studies at SF TB Clinic

- GeneXp (MTB PCR) and sputum x 3 for AFB smear and culture
- CXR (and in our clinic CT chest)
- Molecular tests to be sent if AFB smear or culture positive for susceptability to INH, rifamycin, and fluroquinolone
- CBC and CMP
- Therapeutic drug levels* (rifapentine trough and 5 hour peak)

*TB Program specific

Monitoring/Follow up

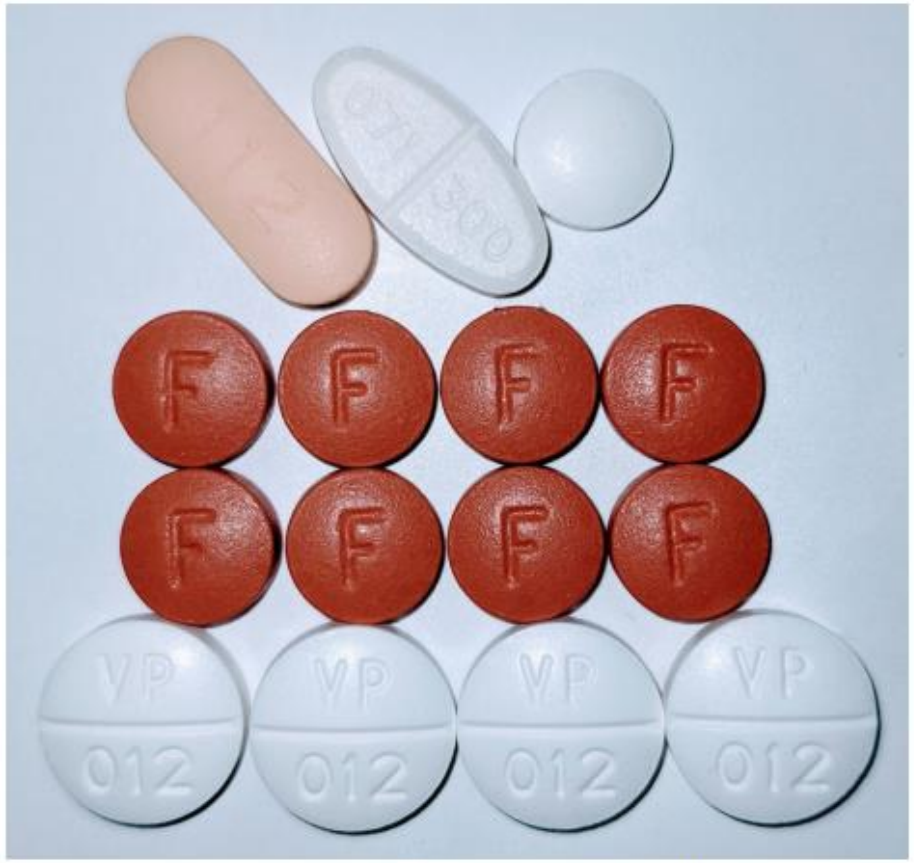
- F/u chest imaging at 2 and 4 months (end of treatment)
- Sputum- we collect at weeks 2, 4, 8, 17 (end of treatment)
- CBC, CMP, Magnesium at weeks 2, 4, 8, 12, 17

- Post end of treatment- CXR and sputa x 2 for AFB smear and culture at 3, 6, 12 months post end of treatment

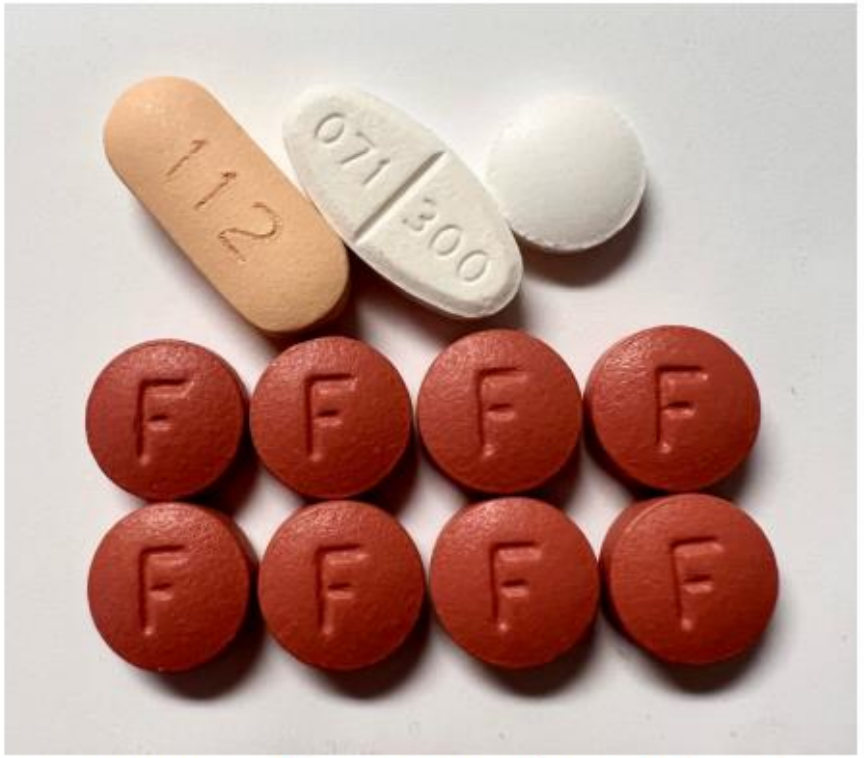
Case management

- ✓Make sure there is enough supply for an entire treatment regimen
- ✓Review pill burden, need for daily dosing, side effects
- ✓Medications should be taken 7 days per week, at least 5 via DOT
- ✓Monthly clinical visits
- ✓Sputum, labs, and EKG when indicated
- ✓Verify payment

Pill count: HPMZ 4-month regimen (>70 kg)

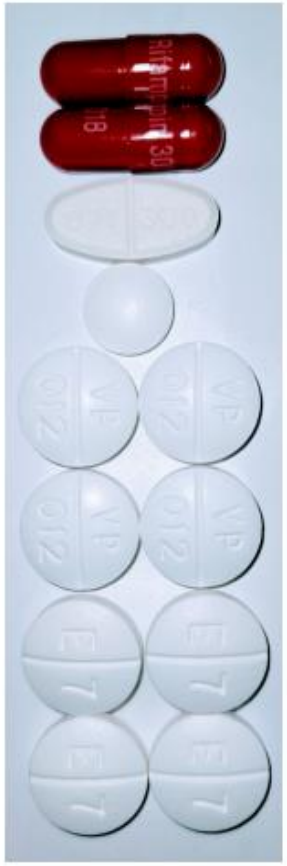


Initiation phase x 8 weeks; 15 pills daily



Continuation phase x 9 weeks: 11 pills daily

Pill count: Standard therapy with HRZE (>70 kg)



Initiation phase x 8 weeks: 12 pills daily

Continuation phase x 16-28 weeks: 4 pills daily

Dosing

Medication / Initial	Body weight	Dose/day
Isoniazid (INH, H)	>40kg (88lbs)	300mg
Rifapentine (RPT, P)	>40kg (88lbs)	1200mg
Moxifloxacin (MOX, M)	>40kg (88lbs)	400mg
Pyrazinamide (PZA, Z)	40-<55kg (88-121 pounds)	1000mg
	>55-75kg (121-165 pounds)	15000mg
	>75kg (>165 pounds)	2000mg

From NTCA provider guidance, 4 month HPMZ regimen https://www.tbcontrollers.org/docs/resources/4-Month-HPMZ-TB-Regimen_NTCA-Provider-Guidance.pdf

Medication considerations

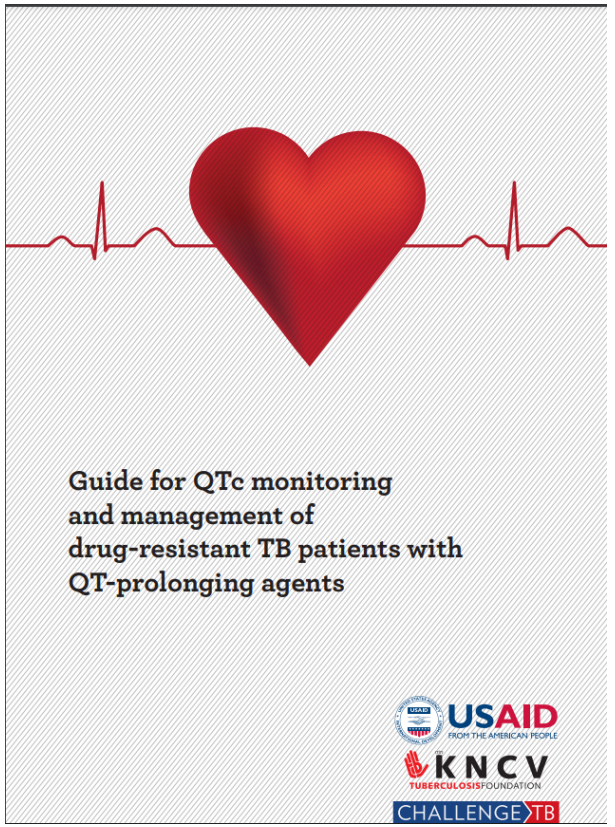
Fluroquinolones (FQs):Moxifloxacin, Levofloxacin

- Most common adverse effects: Nausea and diarrhea, headaches, dizziness, insomnia
- Other: Worsening myasthenia gravis, irreversible peripheral neuropathies, aortic dissection/rupture in pts with known risk factors (known aortic aneurysm, PVD, uncontrolled HTN)
- Rare: hepatotoxicity
- FDA Black Box warnings:
  - Joint or tendon pain, muscle weakness, "pins and needles" tingling or pricking sensation, numbness in arms or legs, confusion, hallucinations, and significantly low blood sugar levels
- Important administration: Do not administer within 2 hours of ingestion of milk-based products, antacids, or other medications containing divalent cations (iron, magnesium, calcium, zinc, vitamins, didanosine, sucralfate)

FDA Drug Safety Communiation: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-advises-restricting-fluoroquinolone-antibiotic-use-certain

FQs (continued)

- Potential for prolonged QTc
  - Moxifloxacin > Levofloxacin
  - Increased risk of arrythmia
    - Data varies on what is safe QTc to continue FQ if QTc is prolonged
    - USAID/KNCV/Challenge TB guide says to worry if QTc if prolonged by >/= 60 msec or if >500ms (Frederica correction)
  - Check patient medication list for other drugs that may be QT prolonging (commonly https://crediblemeds.org/healthcare-providers/clinical-overview-long-qttorsades)



EKG

- SF DPH TB Clinic practice
  - Patients are eligible if their baseline EKG is without Qtc prolongation. We monitor EKG monthly during treatment
  - Using Friderica correction Qtc < 450 ms (men) or < 470 ms (women)
  - For further guidance see https://www.challengetb.org/publications/tools/pmdt/Guidance_on_ECG_monitoring_in_NDR_v2.pdf
- NTCA- recommends EKG "if indicated"
- CDC- "Baseline ECG is not routinely recommended for all patients starting this 4-month rifapentine-moxifloxacin regimen. Patient co-morbidities and potential drug-drug interactions should be evaluated."

Rifapentine

Most common adverse effects (similar to rifampin):

- Red/orange body fluids
- GI upset
- Hepatotoxicity
- Rash
- Flu like syndrome (myalgias, fever)
- Hypersensitivity reaction (urticaria, flushing, hypotension, facial swelling, and bronchoconstriction)
- Dizziness, hypotension

Adverse Events During Treatment. CDC, 2016, https://www.cdc.gov/tb/topic/treatment/adverseevents.htm

Rifapentine continued

- Hepatoxicity
  - Less well defined than rifampin but likely similar
  - Usually effects transaminases (AST/ALT) but can see cholestatic picture (ele vated alk phos and total bilirubin)
- Reliability of oral or other systemic hormonal contraceptives may be affected; consider using alternative contraceptive measures (e.g. barrier)
- Many drug-drug interactions

https://www.currytbcenter.ucsf.edu/sites/default/files/2022-12/Rifamycin_2022.pdf

Isoniazid

- Mild elevation in liver transaminases
- Hepatitis/acute liver injury
- Peripheral neuropathy
- CNS changes, optic neuritis, drug-induced lupus, diarrhea, DRESS/hypersensitivity reaction

Pyrazinamide

- Gout (hyperuricemia) and arthralgias
- Hepatotoxicity
- GI upset
- Rash
- Photosensitivity

Nitrosamines

- FDA is investigating impurities in some medications (including the rifamycin class) called nitrosamines.
- Common in water and foods like cured or dried meats, dairy products and vegetables. All people are exposed to some level of impurities.
- Nitrosamine impurities may increase the risk of cancer if people are exposed to them above acceptable levels over long periods of time.
- FDA recommends that health care professional should continue to use these medications when appropriate even though they may have low levels of nitrosamines.
- TB treatment is a short period and so our clinic feels okay using. NTCA recommends discussing with patients.

What should I as the case manager be prepared for?

- Side effects
- Monthly clinical visits

NTCA Provider Guidance handout

NTCA PROVIDER GUIDANCE

A 4-Month Regimen to Treat Pulmonary Tuberculosis: Isoniazid, Rifapentine, Moxifloxacin, and Pyrazinamide (HPMZ)

What is the 4-month HPMZ Regimen for treatment of drug susceptible TB?

The HPMZ regimen consists of an **8-week intensive phase** of isoniazid (H), rifapentine (P), moxifloxacin (M), and pyrazinamide (Z) given daily, followed by a **9-week continuation phase** of isoniazid, rifapentine, and moxifloxacin given daily. The total duration of therapy is 17-weeks.

What is the medication dosage of the HPMZ regimen?

Medication	Body weight	Dose/day
Isoniazid (INH, H)	> 40 kg (88 pounds)	300 mg
Rifapentine (RPT, P)	> 40 kg (88 pounds)	1200 mg
Moxifloxacin (MOX, M)	> 40 kg (88 pounds)	400 mg
Pyrazinamide (PZA, Z)	40–<55 kg (88–121 pounds)	1000 mg
	>55–75 kg (121–165 pounds)	1500 mg
	> 75 kg (> 165 pounds)	2000 mg

The entire regimen should be administered once daily with food 7 days per week.

What are the advantages and disadvantages of the HPMZ Regimen?

Potential pros of the 4-month regimen

- A shorter duration of treatment for culture-positive pulmonary TB.
- Facilitates treatment completion in patients with barriers
  - planned geographic relocation, incarceration, or
  - residents in congregate or institutionalized settings
- Avoids potential for ocular toxicity with ethambutol (EMB)
- May reduce time to culture conversion

Potential cons of the 4-month regimen

- Higher pill burden
- Required to be taken with food to optimize drug absorption.
- Avoid drug-drug interactions with comedications (e.g., antacids)
- Potentially higher program cost for HPMZ regimen
- Limited long-term outcome data (12 months post-randomization)
- Potential side effects of fluoroquinolone (e.g., QT prolongation, tendonitis, effects on gut microbiota)
- Lack of data for treating extrapulmonary TB, including CNS disease and osteomyelitis

	Standard Regimen (HRZE) >75Kg	Short course regimen (HPMZ) >75Kg
Intensive Phase	8 weeks — Isoniazid, Rifampin, Pyrazinamide, Ethambutol, Vitamin B6	8 weeks — Isoniazid, Rifapentine, Moxifloxacin, Pyrazinamide, Vitamin B6
Continuation Phase	16-28 weeks — Isoniazid, Rifampin, Vitamin B6	9 weeks — Isoniazid, Rifapentine, Moxifloxacin, Vitamin B6

Photos courtesy of George Lee, RN

Treatment interruption:

- The 56 doses of initiation phase should be administered completely within 70 days.
- The 63 doses of the continuation phase should be administered within 84 days.
- If these targets are not met, the patient should be considered to have interrupted therapy and should be managed with clinical judgment and in consultation as described in TB treatment guidelines.

Are there drug-drug interactions?

There are common interactions for isoniazid, rifapentine, and moxifloxacin:

- Isoniazid increases blood levels of phenytoin and disulfiram
- Rifapentine, similar to rifampin, decreases blood levels of oral or implanted hormonal contraceptives, warfarin, sulfonylureas, methadone, suboxone, some anti-hypertensives and steroids.
- Some cardiac medications and certain antiretroviral drugs may have serious drug-drug interactions.
- Moxifloxacin interacts with other medications that are QTc prolonging. Please see additional information on use of moxifloxacin under Programmatic Consideration (Page 2).
- **Please check drug-drug interactions**

Possible adverse events (AEs) with HPMZ

Mild to moderate:
Continue to monitor, discontinue if needed

- Joint pain
- Tendonitis
- LFTs ≥ 3-5X ULN
- Rash
- Fever
- Pruritis
- Nausea
- Vomiting

Moderate to Severe:
Recommend discontinuing treatment

- Hypersensitivity
- Hypotension, mild to profound syncope/fainting
- Dizziness
- Life threatening syndromes (fever, chills HA, dizziness and musculoskeletal pain)
- Thrombocytopenia
- Shortness of breath, wheezing, acute bronchospasm
- Urticarial petechiae, purpura
- Conjunctivitis
- Angioedema and shock
- Chest pain/angina, palpitations, or cardiac arrhythmias
- Elevated liver function tests (LFTs) ≥ 5X ULN

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Patient checklist before starting HPMZ

- ✓ Age ≥ 12 years
- ✓ Weight > 40 kg
- ✓ If HIV-positive, CD4>100 cells/mm³, please see NTCA FAQ for additional HIV treatment recommendations.
- ✓ Negative pregnancy test if of childbearing age
- ✓ Not breastfeeding
- ✓ Baseline laboratory values: serum creatinine < 2.0, potassium ≥ 3.5 meq/L, Hgb ≥ 7.0 g/dL, platelets ≥ 100,000/mm³, LFTs ≤ 2X upper limit of normal
- ✓ No suspected or documented extrapulmonary TB
- ✓ No history of taking TB drugs within past 6 months
- ✓ Medication review with no drug–drug interactions with HPMZ
- ✓ Rapid molecular detection of drug resistance from initial specimen should be ordered if available
- ✓ Patient can be started on the HPMZ regimen while awaiting drug susceptibility test (DST) results, including for fluoroquinolones

Programmatic Considerations for HPMZ

Case management:

- Ensure drug supply available for full 17-week course
- Discuss pill burden and need for once-daily dosing
- Medications taken 7 days a week and DOT/eDOT at least 5 days a week
- Monthly clinical visits
- Sputum, laboratory, and EKG monitoring when indicated
- Verify reimbursement for HPMZ by program or third party

Moxifloxacin

- Educate about food and drug interactions: Avoid taking dairy products, sucralfate, antacids, multivitamins, iron, aluminum, magnesium, or calcium within 4 hrs. before or 8 hrs. after HPMZ
- Access EKG for patients with cardiac risks per practice standards for long term moxifloxacin administration.
- Review cardiac history: This regimen is contraindicated in patients with active ischemia and/or history of arrhythmias.
- CDC does not recommend use with other medications that prolong QTc; however, some experts may choose to prescribe this regimen in patients with h/o prolonged QTc or patients on other QT-prolonging drugs with careful and appropriate EKG monitoring.

Rifapentine

- Discuss FDA alert regarding nitrosamine with patient

Baseline and follow-up monitoring and evaluation for patients on HPMZ regimen

(**X** = recommended; **O** = optional)

Evaluation Types		Baseline	Intensive Phase (Total 56 doses) Week 1	2	3	4	5	6	7	8	Continuation Phase (Total 63 doses) 9	10	11	12	13	14	15	16	17
Clinical assessment and evaluation	Symptoms, medication, drug–drug interaction	X				X				X				X					X
	Weight	X				X				X				X					X
	EKG if indicated	O				O				O				O					O
Laboratory testing	CBC, Platelet, LFT, Creatinine, Potassium, Calcium, Magnesium	X				O				O				O					O
	HIV (if positive CD4 count and HIV RNA)	X																	
	Hepatitis B and C Diabetes screen	O																	
	Pregnancy test	X																	
Microbiology (Sputum)	AFB smear and culture	X	O	O	O	X				X				O					O
	Rapid molecular test	X																	
	Phenotypic drug susceptibility test	X								O									
Imaging	Chest radiograph	X								O									O
Administered medication	Isoniazid (INH, H)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Rifapentine (RPT, P)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
DOT/eDOT with food ≥ 5 days/ week	Moxifloxacin (MOX, M)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Pyrazinamide (PZA, Z)		X	X	X	X	X	X	X	X									
	Vitamin B6		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Consultation with TB clinical experts at either local or state level, or TB Center of Excellence (COE) recommended:

- For treatment of lymph node or pleural disease.
  - Avoid using this regimen for sites such as as with CNS or bone disease
- For concerns regarding slow or incomplete clinical response or treatment failure
- For interruption in therapy or changes in drug regimen

Please refer to the full NTCA FAQ for detailed discussion of the HPMZ regimen:
https://www.tbcontrollers.org/docs/resources/4-Month-HPMZ-TB-Regimen_NTCA-FAQ.pdf

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Management

Evaluations for patients treated with a 4-month rifapentine-moxifloxacin TB treatment regimen

			Intensive Phase[a,b] (Total doses: 56)								Continuation Phase[a,c] (Total doses: 63)								
		Base-line	WEEK 1	WEEK 2	WEEK 3	WEEK 4	WEEK 5	WEEK 6	WEEK 7	WEEK 8	WEEK 9	WEEK 10	WEEK 11	WEEK 12	WEEK 13	WEEK 14	WEEK 15	WEEK 16	WEEK 17
Collect sputum sample	Acid-fast bacilli smear microscopy and culture[d]	X				X				X				X[e]					X[e]
	Phenotypic drug-susceptibility test[f]	X								X[e]									
	Rapid molecular test[g]	X																	
Conduct chest radiograph	Chest radiograph[h]	X								X[e]									X[e]
Evaluate patient health	Assess weight[i], symptoms of TB disease[j], current medications, and any patient co-morbidities and potential drug-drug interactions	X				X				X				X					X
	Review patient's clinical history, social determinants of health, and adverse drug reactions[j]	X				X				X				X					X
Conduct laboratory testing	Alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, alkaline phosphate[k]	X				X[e]				X[e]				X[e]					X[e]
	Platelet count	X				X[e]				X[e]				X[e]					X[e]
	Creatinine	X				X[e]				X[e]				X[e]					X[e]
	Test blood levels of potassium, calcium, and magnesium[l]	X				X[e]				X[e]				X[e]					X[e]
	Pregnancy test[m]	X																	
	HIV test	X																	
	CD4 count, HIV viral load (if HIV-positive)[n]	X[e]																	
	Hepatitis B and C screen[o]	X[e]																	
	Diabetes screen[p]	X[e]																	
Administer medication[a,q]	Rifapentine (RPT)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Moxifloxacin (MOX)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Isoniazid (INH)[r]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Pyrazinamide (PZA)		X	X	X	X	X	X	X	X									

https://www.cdc.gov/tb/topic/treatment/tbdisease.htm

= Optional or contingent on other information (https://www.cdc.gov/mmwr/volumes/71/wr/mm7108a1.htm?s_cid=mm7108a1_w).

Managing common side effects to reduce barriers to treatment success

Case Study

- 50 yoM, pmhx of DM (A1C 8%), found to have smear positive, PCR positive (no RIF resistance detected) pulmonary TB. Started on 4 month short course regimen HPMZ 2 weeks ago.
- Calls you and tells you he is having nausea daily since starting the regimen and feels terrible
- What do you do???

Nausea and vomiting and GI Upset (oh my!)

- Discuss with provider
- Consider:
  - Checking LFTs
  - If LFTs are normal or <3x ULN, likely okay to continue HPMZ if patient willing

- Now what???
  - Take TB medications with food
  - Anti-emetics (i.e. ondansetron, etc)
  - Ginger candies
  - Distraction activities
  - Take before bed
  - What other strategies do you use ?

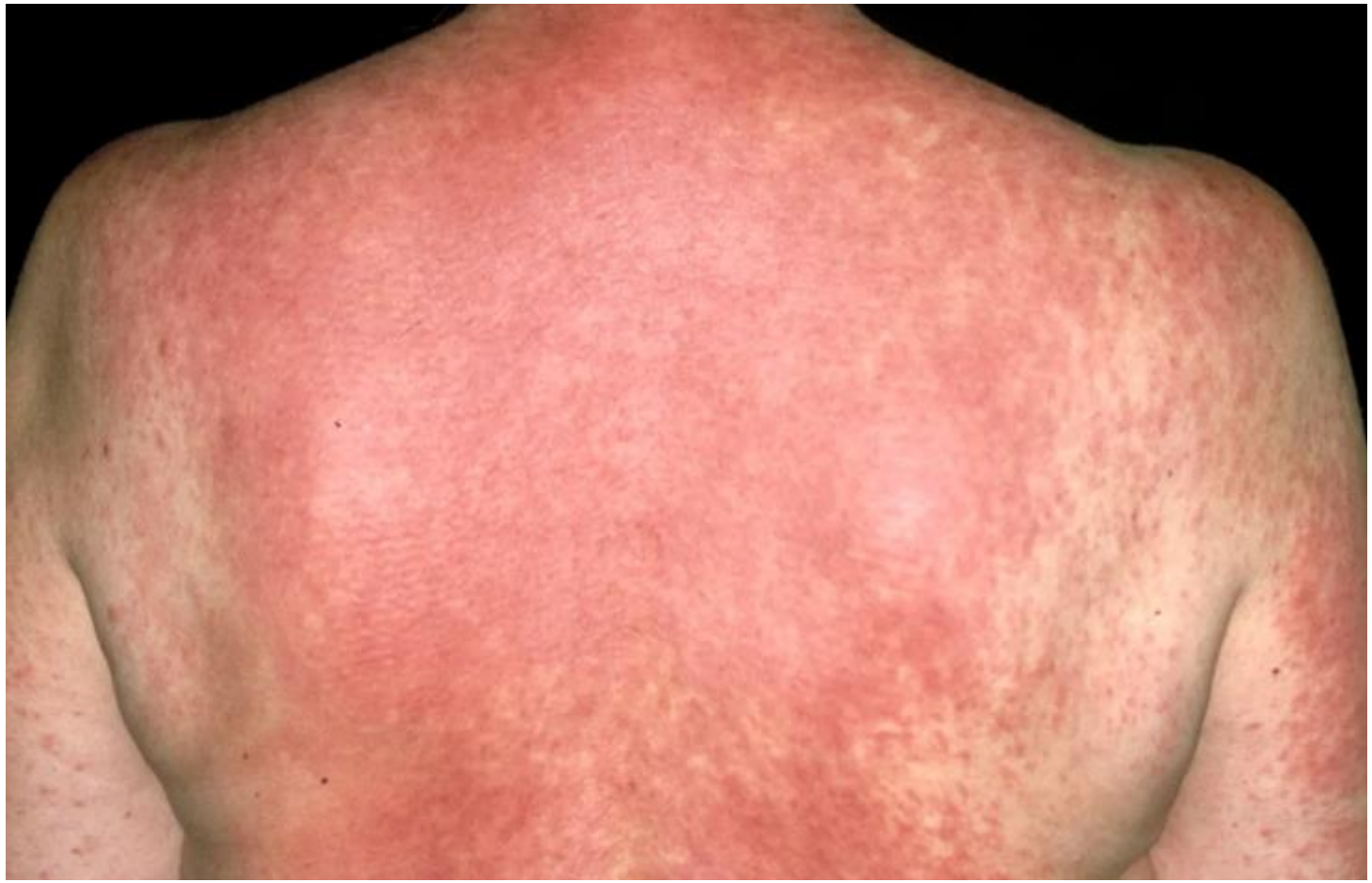
Elevated liver tests

- Common to see asymptomatic hyper-bilirubinemia (normal range 0.3-1.2 mg/dl)

- When to hold medications and discuss with provider:
  - AST/ALT >3x ULN and pt with symptoms of hepatotoxicity (nausea, vomiting, abdominal pain, anorexia, jaundice)
  - AST/ALT >5x ULN and pt without symptoms
  - Total bilirubin >3 ULN

Rash and pruritus

- Mild or severe
- If mild, consider anti-histamine (like cetirizine) or topical steroid, in conversation with provider
- If severe, hold meds, consider hospitalization



Other

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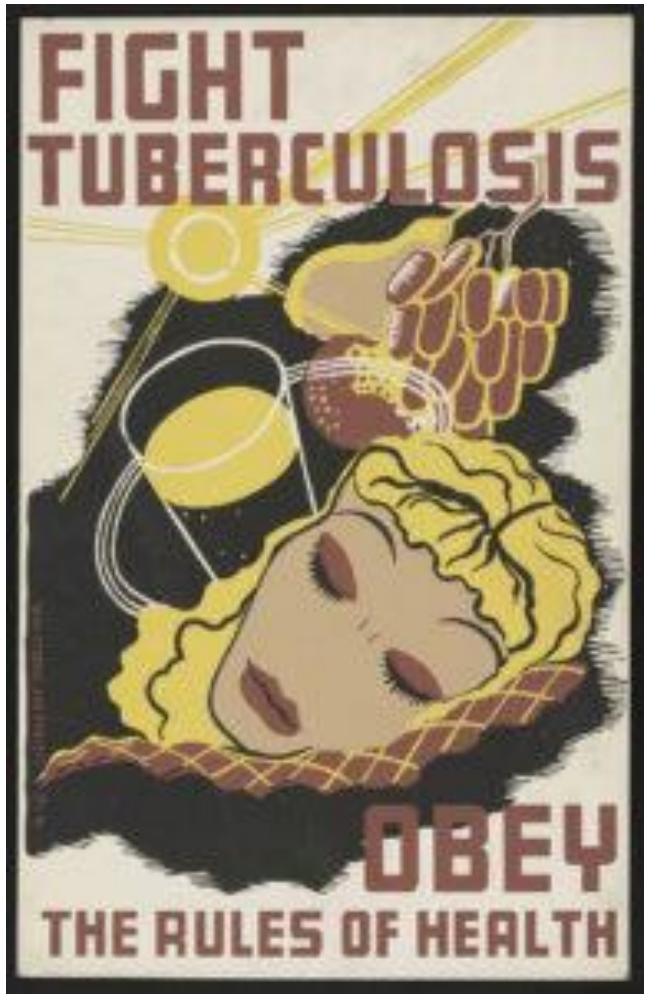
Therapeutic Drug monitoring

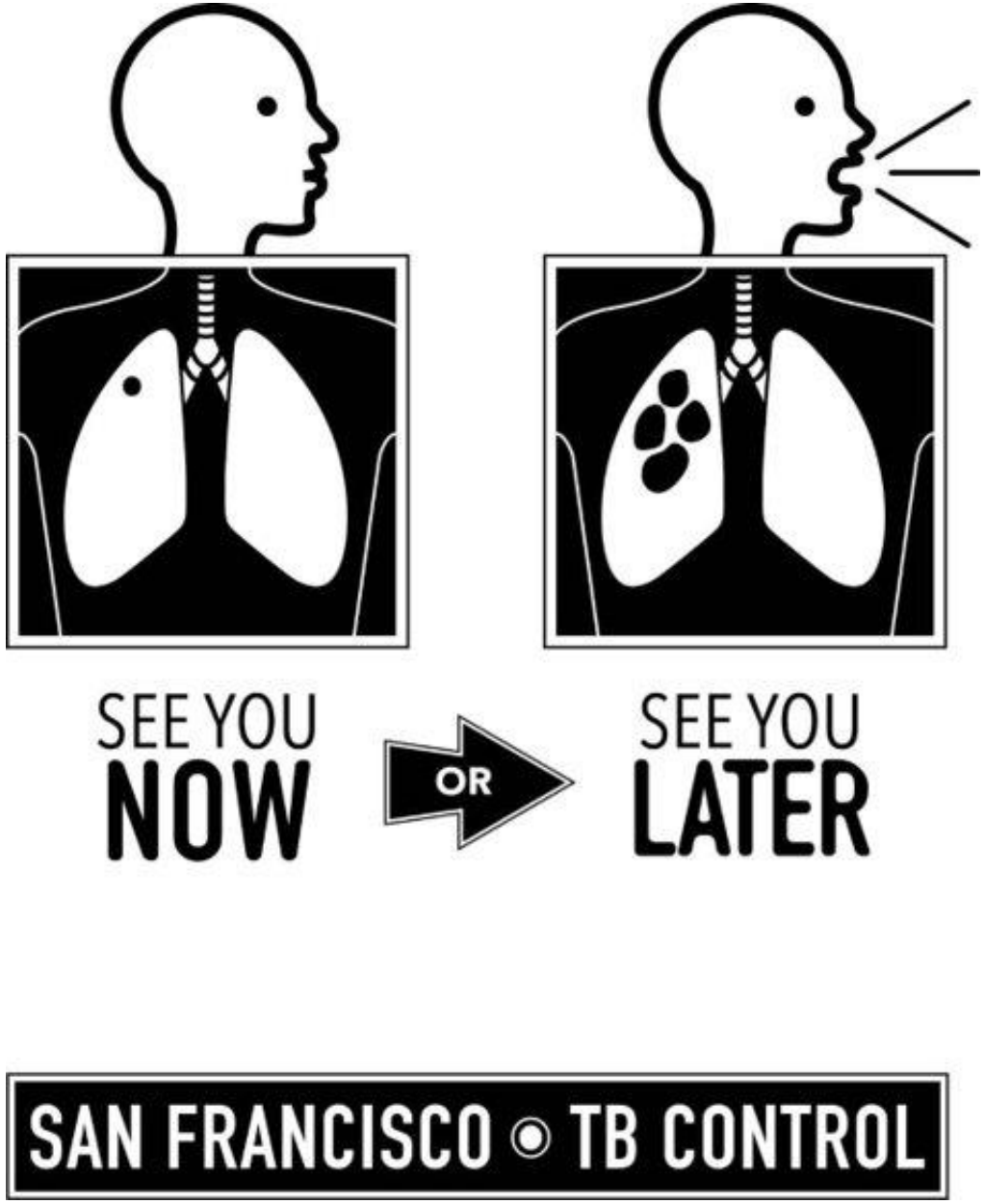
- CDC: no evidence to do so
- SF DPH TB Clinic: we check a rifapentine trough and 5 hour peak in all patients after at least one-two weeks on treatment



HPMZ management

- If patient wants to stop regimen, discuss with provider
- Consider stopping regimen and re-challenging with HRZE
- If concern for treatment failure (e.g., radiographic improvement is slow or smear and cultures do not show improvement by 8-12 weeks), consider extending HPMZ to 6 months (or longer if needed), or switch to standard HRZE in consultation with provider/clinical experts

SF DPH TB Clinic Experience with HPMZ



SF active TB Cases 2023

- Total active cases: 69
- N=63, incidence 8.8 per 100,000 (non- US born)
- N= 6, incidence of 1.3 per 100,000 (US born)
- Median age: 63.5 years (range 24-96), 1 pediatric case
- 47.8% of cases were ≥65 years of age
- Non-US Born:
  - Most common countries of origin: China (24.6%), Philippines (15.9%), Vietnam (10.1%), US (7.2%), Mexico (5.3%)
  - Other countries make up 37.7%: Burma, Cuba, El Salvador, France, Georgia, Guatemala, India, Indonesia, South Korea, Macau, Nepal, Nicaragua, Nigeria, Pakistan, Peru, Samoa, South Africa, Ukraine, United Kingdom

SF DPH TB Clinic experience

Started offering HPMZ to eligible patients in August 2021

- 8/1/2021 - 12/31/23: 160 patients were started on treatment for active TB
- 22 patients started on HPMZ out of 30 offered HPMZ (based on clinic inclusion/exclusion criteria)
- Median age 32.5 years (range 14-86)

<u>TB sites:</u>

Pulmonary (19), isolated pleural (1) and lymph node (2)

<u>Chest X-ray imaging for pulmonary TB cases:</u>

Cavitary disease -7 (36.8%)

More than one lobe involved- 9 (47.4%)

<u>Microbiology for pulmonary TB cases:</u>

AFB smear positive-12 (63.2%)

GeneXp positive – 13 (68.4%)

Culture positive – 15 (78.9%)

Findings in our clinic

- ~82% of patients experienced at least one adverse event while on HPMZ (18/22 patients)
- ~40% experienced mild symptoms:
  - nausea and/or vomiting (18.2%)
  - rash (9%)
  - myalgias (4.5%)
- 45.5% experienced moderate symptoms
  - nausea and/or vomiting (22.7%)
  - nausea and or vomiting with liver function test >3x upper limit of normal (9.1%)
  - dermatologic (9.1%)
  - dizziness, flushing, palpitations, anxiety (4.5%)
- One patient experienced a severe AE of syncope, anorexia, rash, and hypokalemia leading to a fall and hospitalization
- 11 patients prematurely discontinued HPMZ: 10 due to moderate AE(s), 1 due to severe AE
- 9 patients have completed treatment. No treatment failures to date

Conclusions of our review

- HPMZ was associated with significant side effects (11 people stopped treatment and switched to other regimens)
- All patients except for one over age 50 discontinued treatment due to side effects
- HPMZ tends to be better tolerated by younger patients
- Most commonly, patients experienced nausea/vomiting, rash, and elevated liver function tests >3x upper limit of normal with nausea/vomiting
- May be most beneficial to people with cavitary disease and shortened length of treatment (9 months to 4 months)

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Thank you!

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POPULATION HEALTH DIVISION
SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH