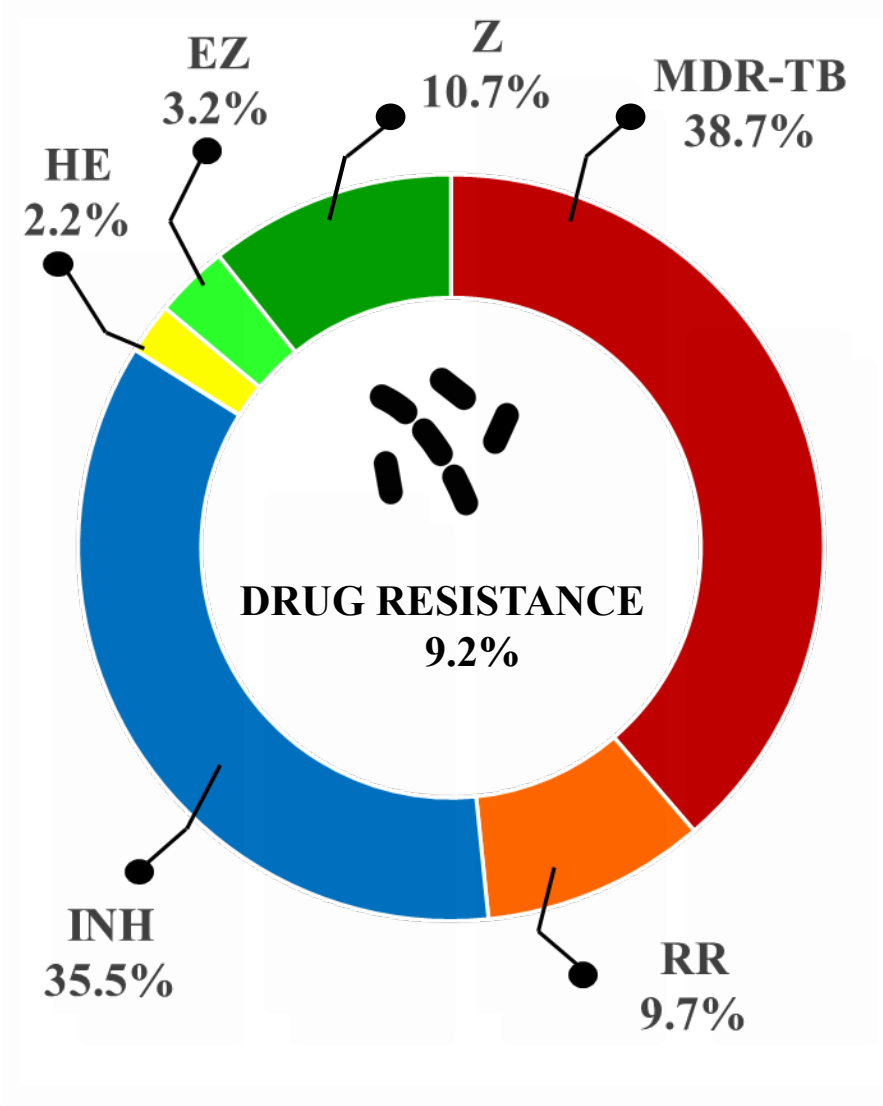
Drug Resistant TB in Wisconsin and in the Hmong: 2005-2021

Philip Wegner RN, MPH
TB Nurse Consultant
Wisconsin TB Program

Drug Resistant TB Wisconsin 2005-2021

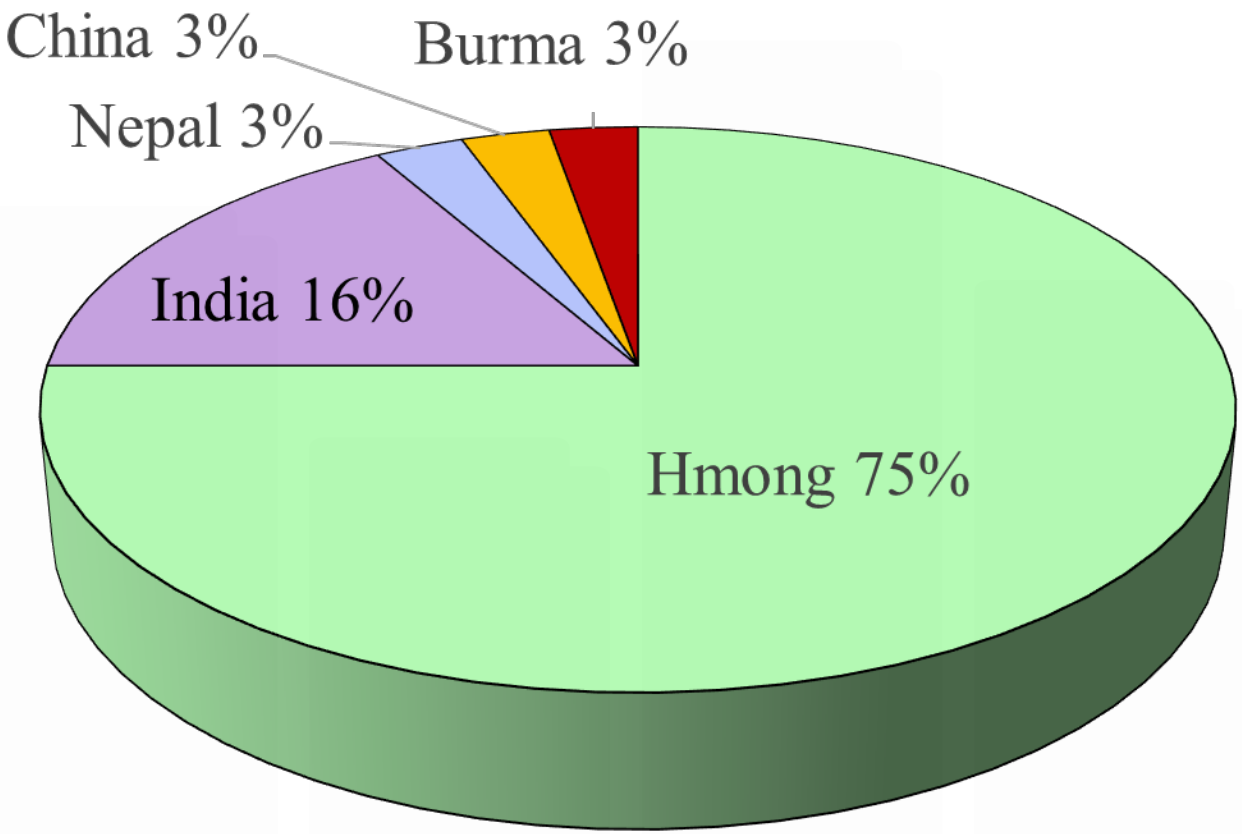


93 Drug Resistant TB cases

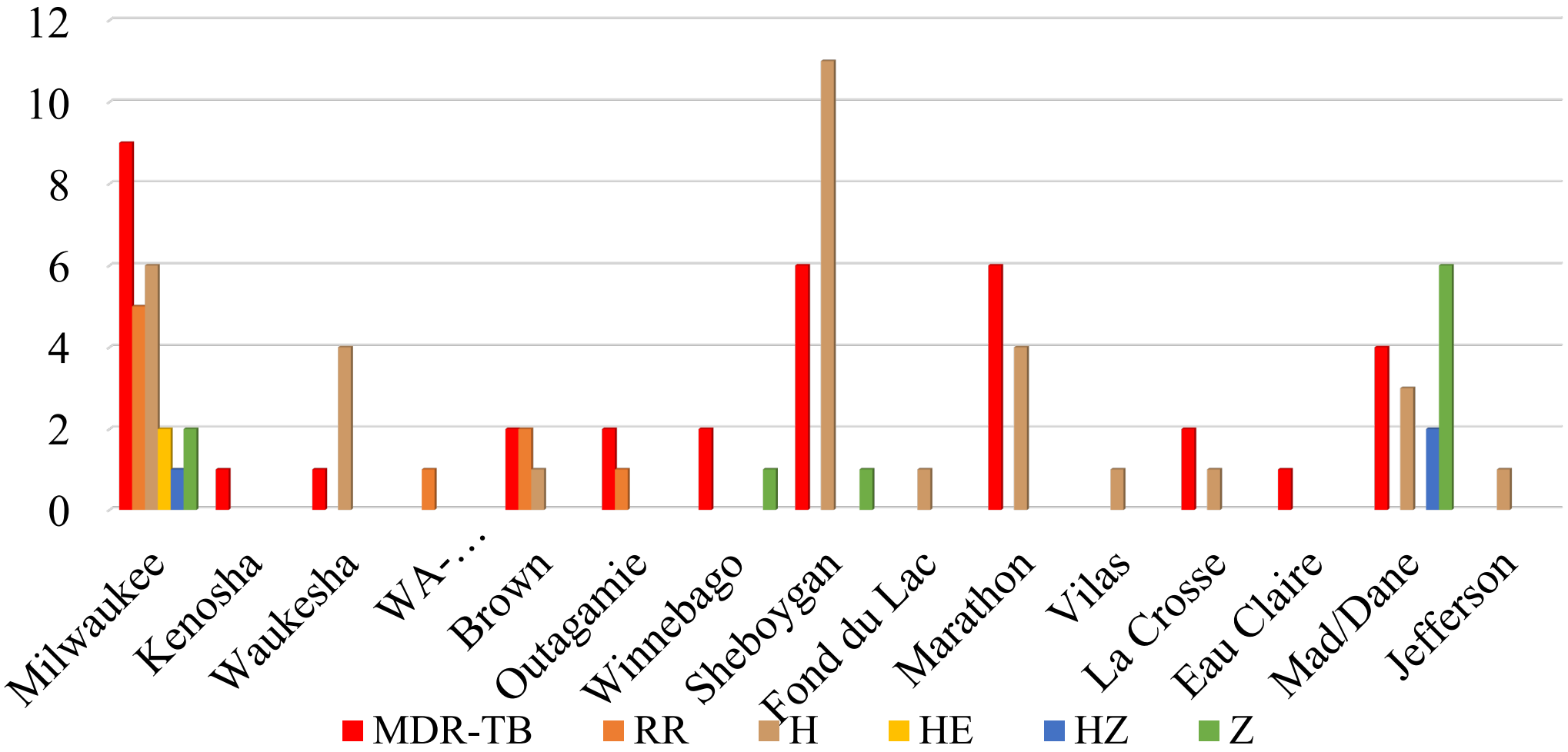
- 9.2% of all TB cases
- Close to 70% in two regions of the state
- 72% in Asian Population
- 12% Hispanic (Mexican)
- 15% U.S. –Born
- 1% African
- 14% related to Sheboygan Outbreak

MDR-TB = Multidrug Resistant Tuberculosis
RR= Rifampin Resistance
INH = Isoniazid Resistance
HE = INH and Ethambutol Resistance
EZ = EMB and Pyrazinamide (PZA) Resistance
Z= PZA Resistance

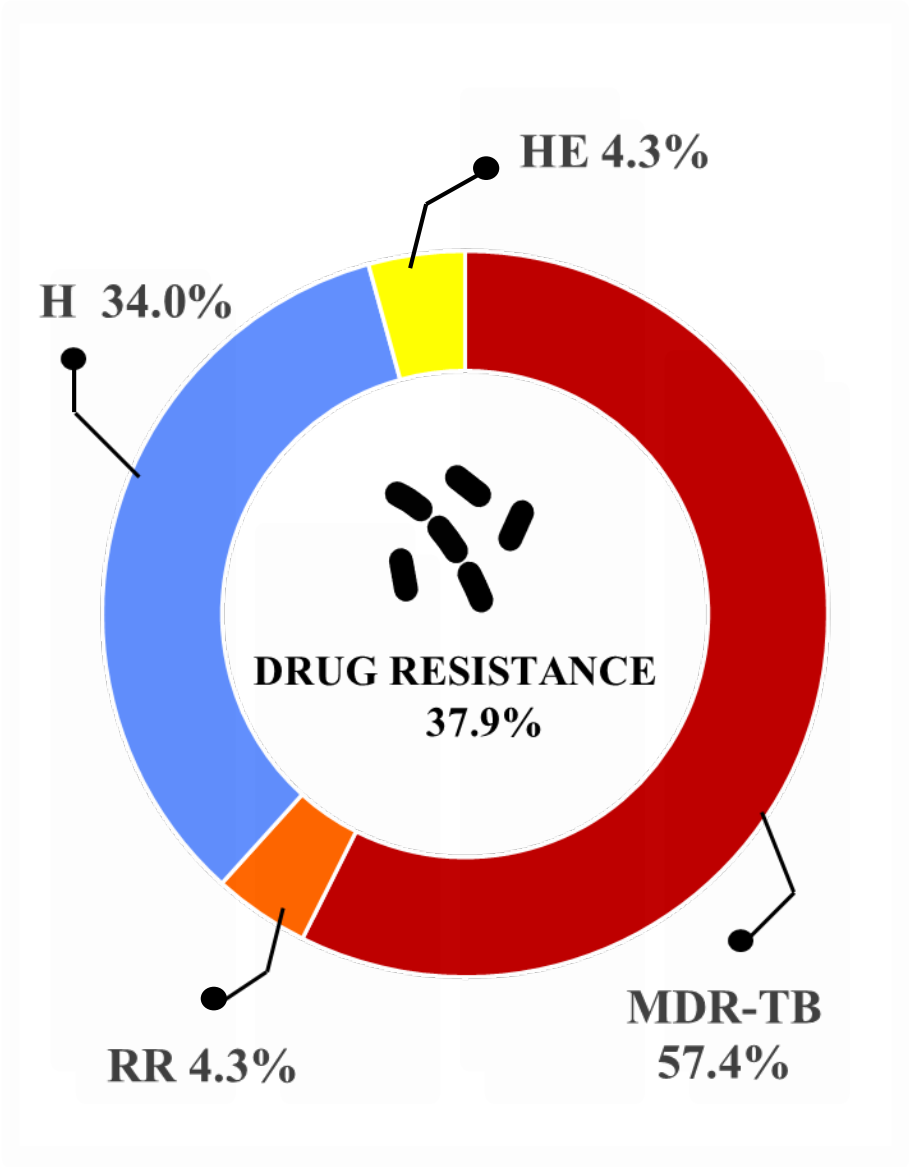
MDR-TB in Wisconsin 2005-2021



Drug Resistant-TB in Wisconsin 2005-2021



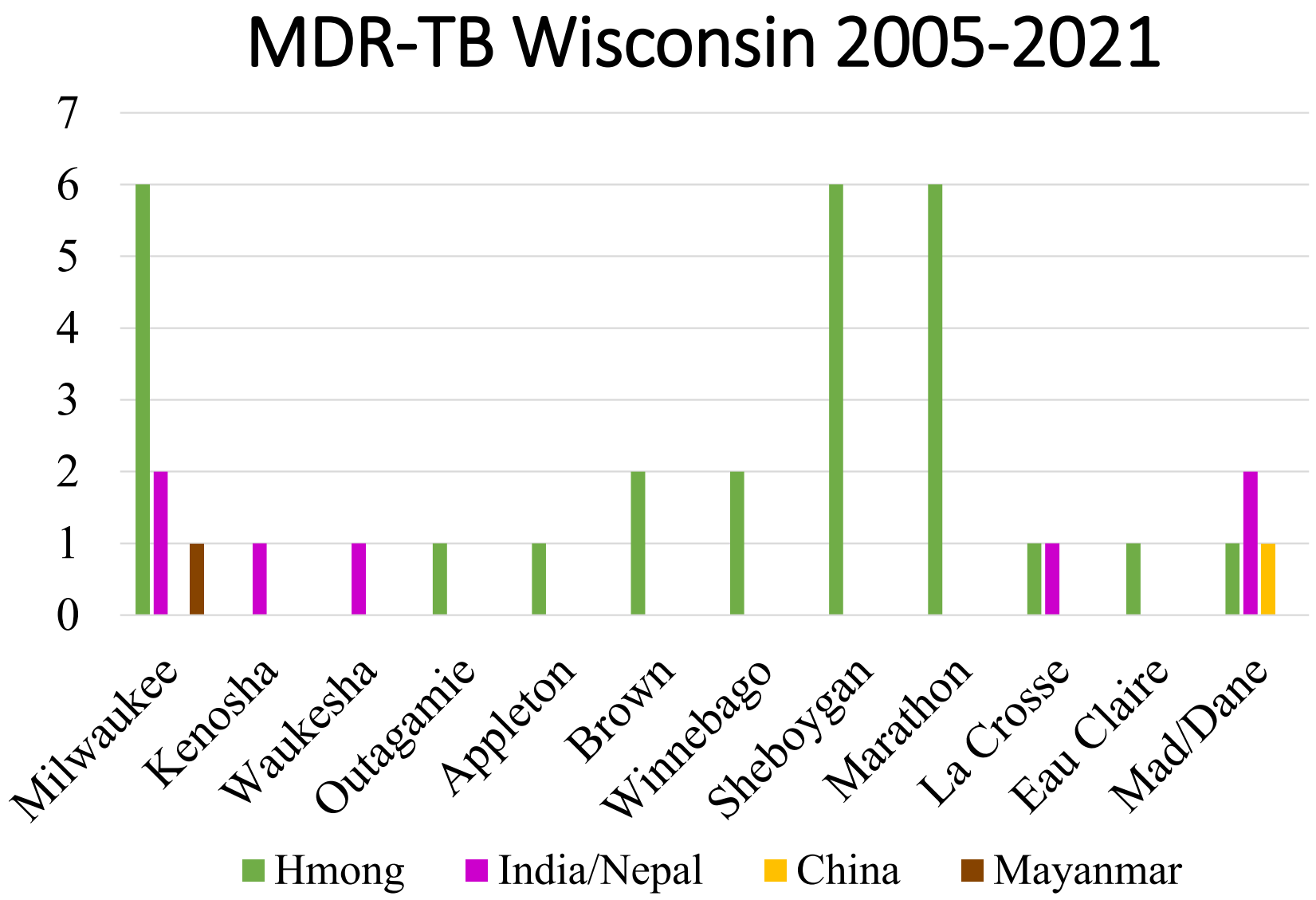
Drug Resistant TB in Wisconsin Hmong Population 2005-2021



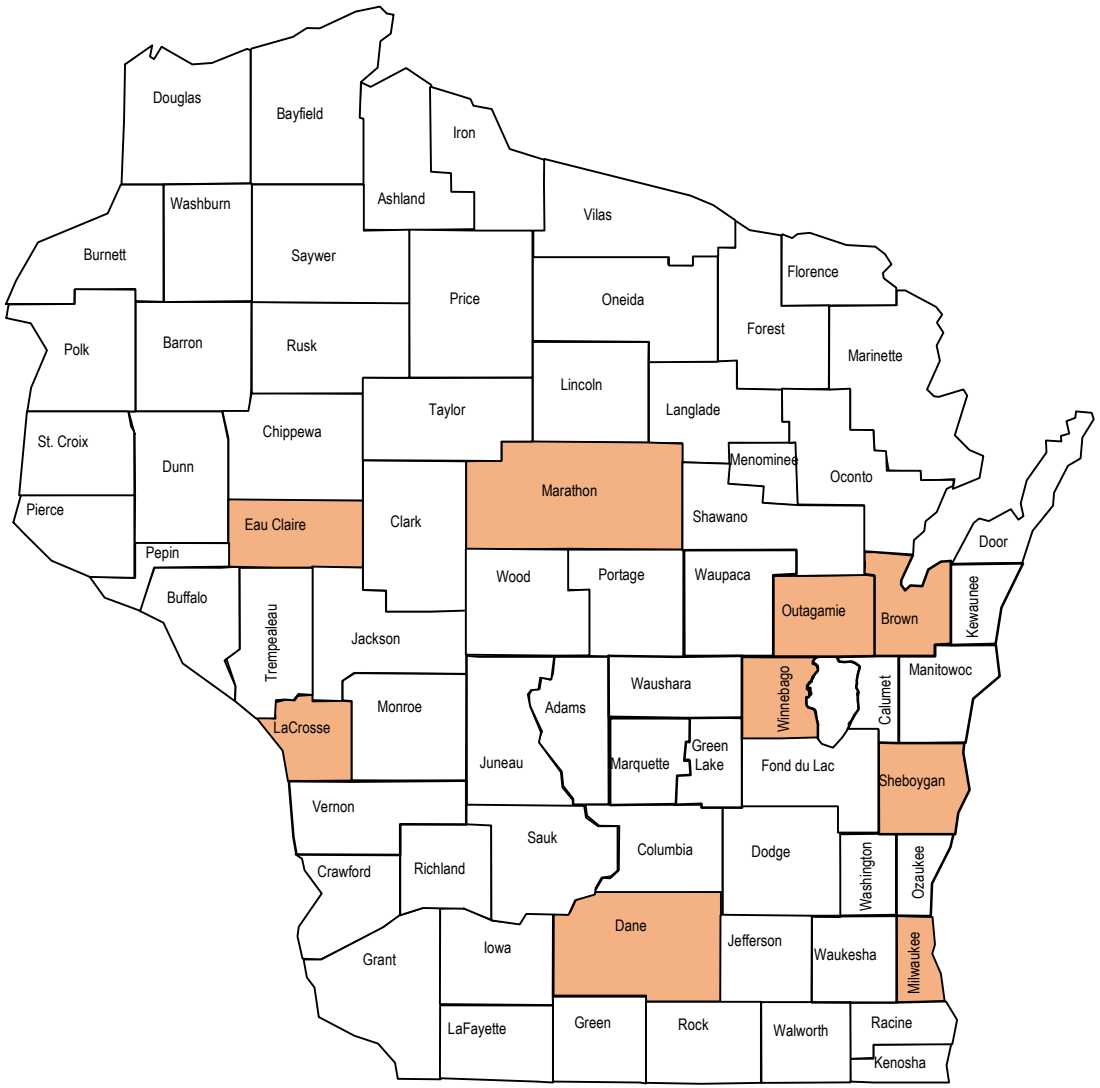
50% of Drug Resistant TB in Wisconsin

- Average Age (Foreign-Born) = 59
- Length of time in U.S. = 17 years
- 57% MDR-TB –Average Age = 66
- Average Age of U.S.-Born = 16
- 67% of MDR-TB in three counties [Milwaukee, Sheboygan, Marathon]
- 32% related to Sheboygan outbreak and genotype match

MDR-TB = Multidrug Resistant Tuberculosis
RR= Rifampin Resistance
INH = Isoniazid Resistance
HE = INH and Ethambutol Resistance


MDR-TB Wisconsin 2005-2021
7
6
5
4
3
2
1
0
Milwaukee
Kenosha
Waukesha
Outagamie
Appleton
Brown
Winnebago
Sheboygan
Marathon
La Crosse
Eau Claire
Mad/Dane
Hmong
India/Nepal
China
Mayanmar

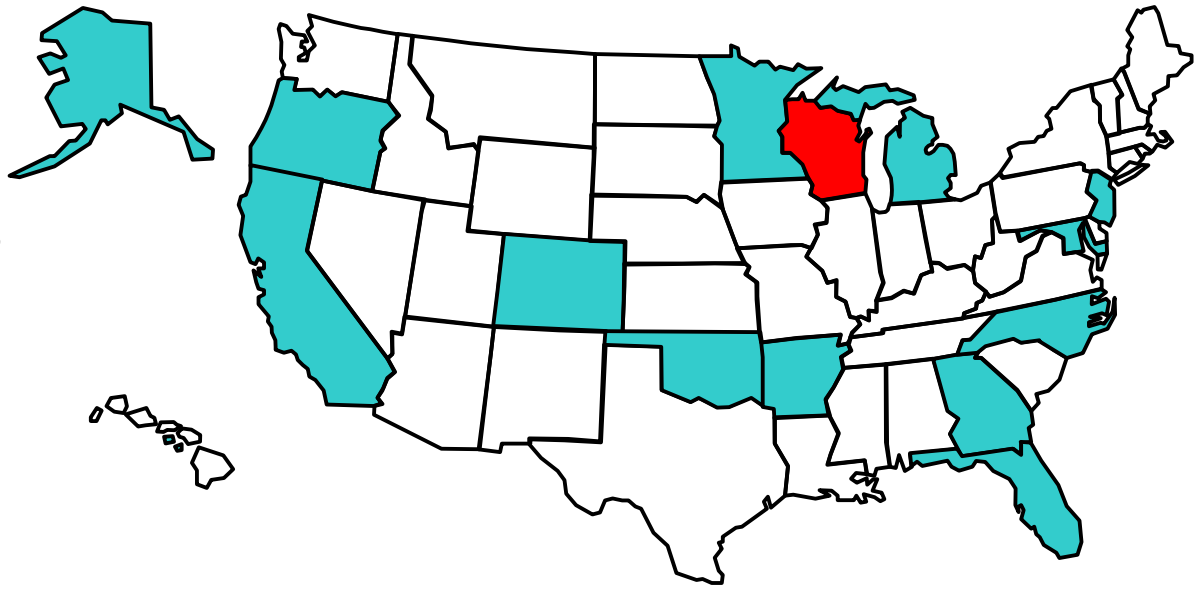
MDR-TB Wisconsin 2005-2021: Hmong



327,000 Hmong estimated in the US (2020 Census)

Top 10 Hmong Populations by State

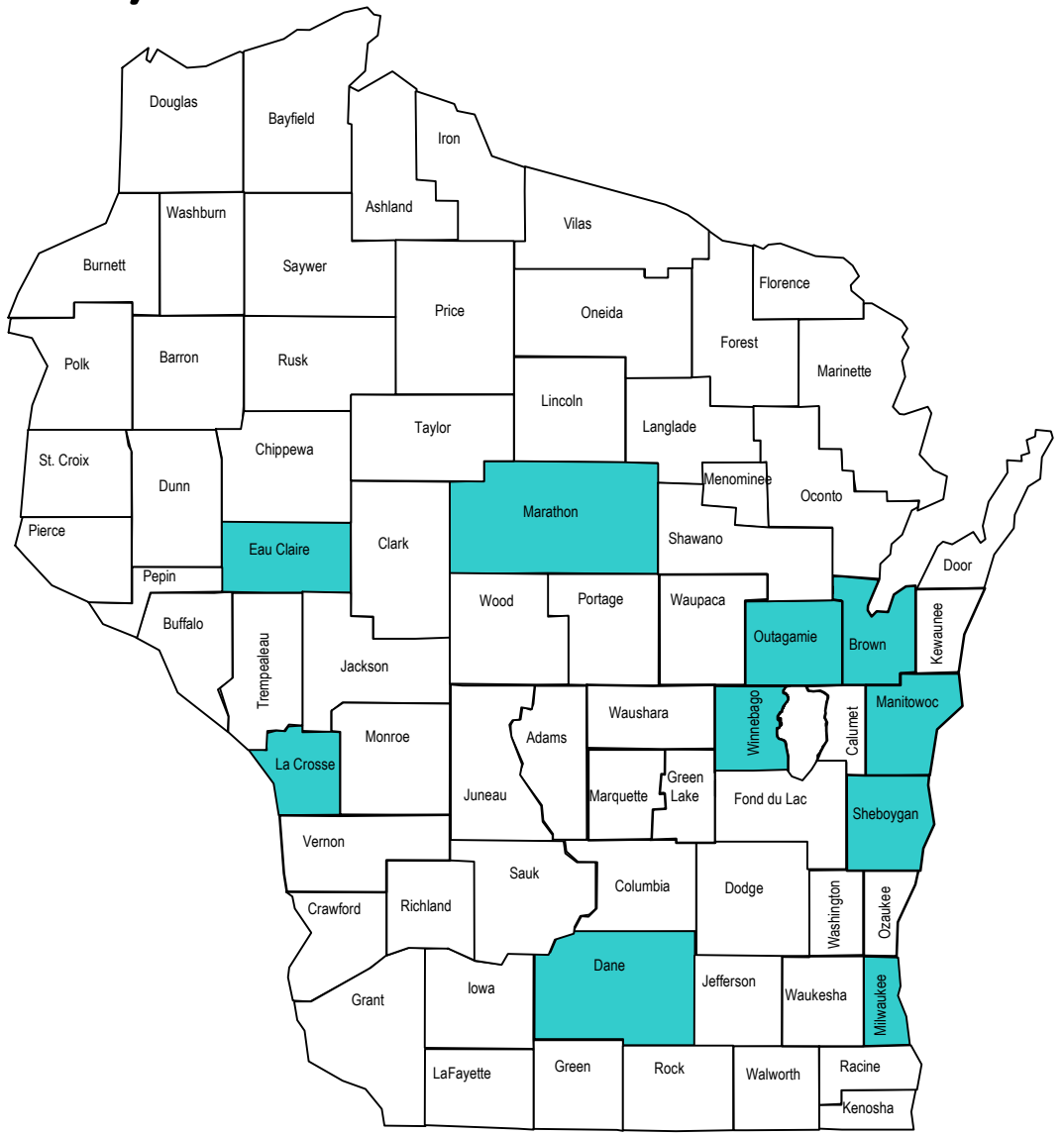
1. California – 96,255
2. Minnesota – 71,762
3. Wisconsin – 54,641
4. N. Carolina – 11,315
5. Michigan – 5,336
6. Colorado – 4,311
7. Alaska – 4,285
8. Georgia – 4,175
9. Oklahoma – 3,908
10. Oregon – 2,490



54,641 Hmong estimated in Wisconsin (2020 Census)

Top 10 Hmong Population by County

1. Milwaukee – 13,529
2. Marathon – 6,238
3. Sheboygan – 4,993
4. Dane – 6,626
5. Brown – 4,354
6. Outagamie – 3,604
7. La Crosse – 3,454
8. Winnebago – 2,748
9. Eau Claire – 2,209
10. Manitowoc – 1,810



BPaL: A Novel 6 month Treatment Regimen for Drug Resistant and Treatment Intolerant TB

Connie A. Haley, MD MPH

Southeast National TB Center, University of Florida, Division of Infectious Diseases and Global Medicine

Connie.haley@medicine.ufl.edu (615) 598-6411

CDC Surveillance Definitions, Jan. 18, 2022

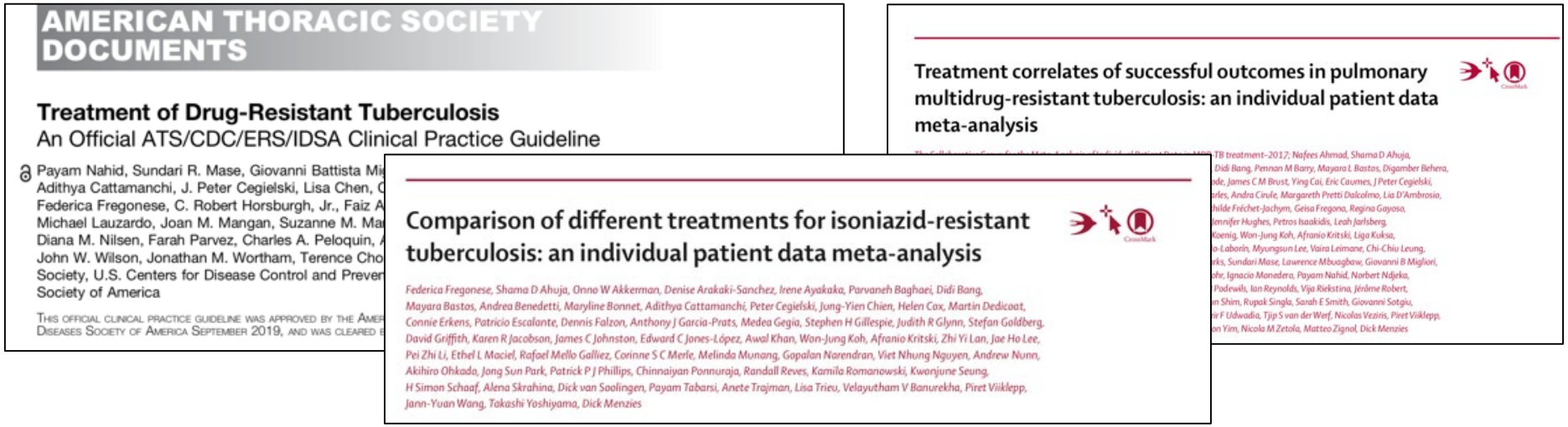
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service
Centers for Disease Control
and Prevention (CDC)

Memorandum

	Drug Classes				
Resistance Classification	Isoniazid & Rifampin	Fluoroquinolone (at least one)	Second-Line Injectable (at least one)	Bedaquiline	Linezolid
MDR TB	X				
Pre-XDR* TB	X		X		
	X	X			
XDR* TB	X	X	X		
	X	X		X	
	X	X			X

*Each row indicates one combination of drug resistance that meets the respective definition of pre-XDR or XDR TB.



- 2019 US guidelines based on meta-analyses of individual patient data in MDR-TB treatment
- Require at least 4-5 drugs
- Long duration of 18-24 months
- Many pills
- Hard to tolerate and potentially toxic
- Cure rates and mortality still inadequate

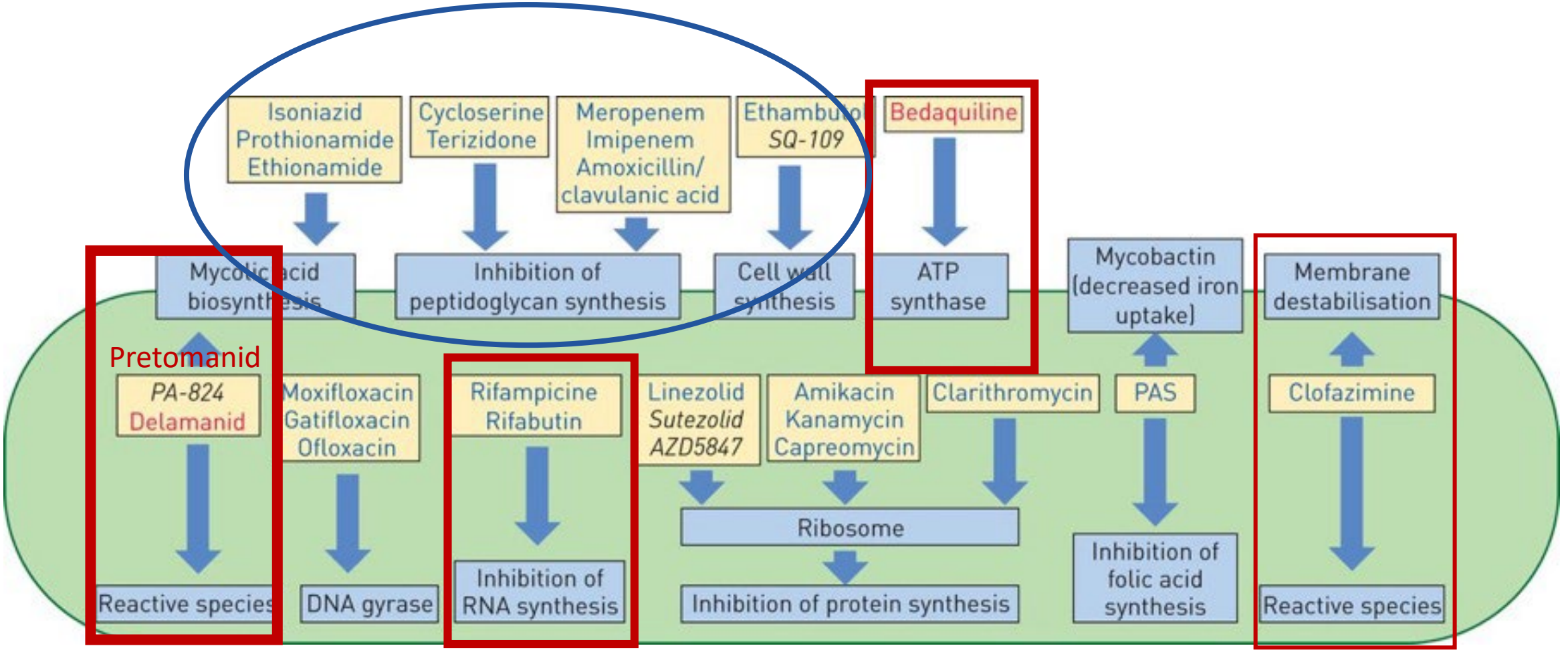
Nahid et al, AJRCCM 2019; Fregonese, et al., Lancet Resp, 2018; Ahmad, et al., Lancet, 2018
https://www.atsjournals.org/doi/pdf/10.1164/rccm.201909-1874ST

New MDR TB cases reported in the United States and U.S.-affiliated areas, 2014–2018

- 446 TB cases with at least resistance to INH and RIF
- 69 with additional resistance to a quinolone or an injectable (pre-XDR)
- 9 with additional resistance to both a quinolone and injectable (XDR TB)
- 6% (31/524) died within 12 months of initiating TB treatment
- 62% (326/524) completed treatment within the recommended 18–24 months.

N. Goswami, personal communication

Mechanisms of action of anti-tuberculosis drugs

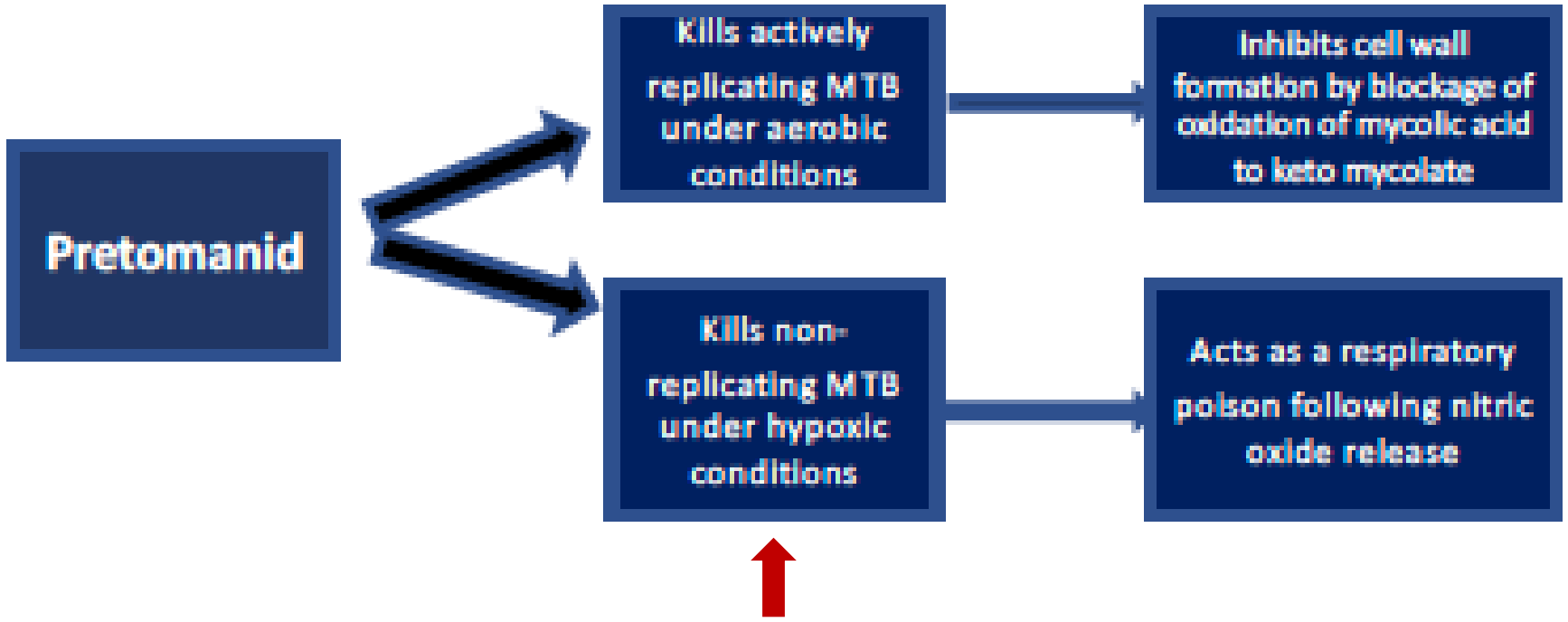


Ioana Diana Olaru et al. Eur Respir J 2015;45:1119-1131

Note: Red boxes indicate drugs that kill “persisters”

Pretomanid Mechanism of Action

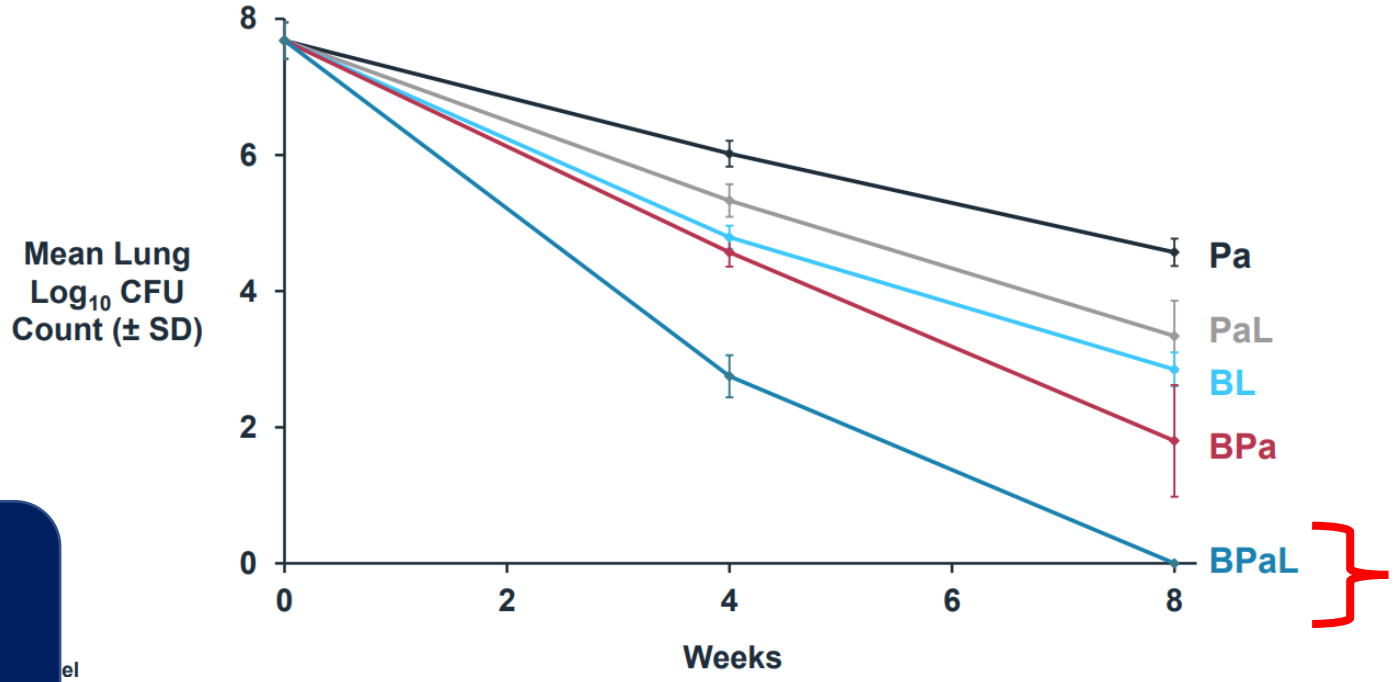
- Complex Mode of Action
  Requires Metabolism Inside MTB to Convert Drug to Active Form



Adapted from slide by B. Seaworth

Activity of BPaL: The Nix-TB Trial

Potent Bactericidal Activity with Pretomanid Alone,
Greatest with Full BPaL Regimen!



TB Alliance 2000: Goal is to Identify a "Universal Treatment Regimen" Regimen should be Short, Safe, Effective, and Affordable

el

TB Alliance

Activity of BPaL

Lung colony-forming unit counts assessed during treatment and relapse rates assessed after treatment of murine TB with regimens including pretomanid, bedaquiline, and linezolid.

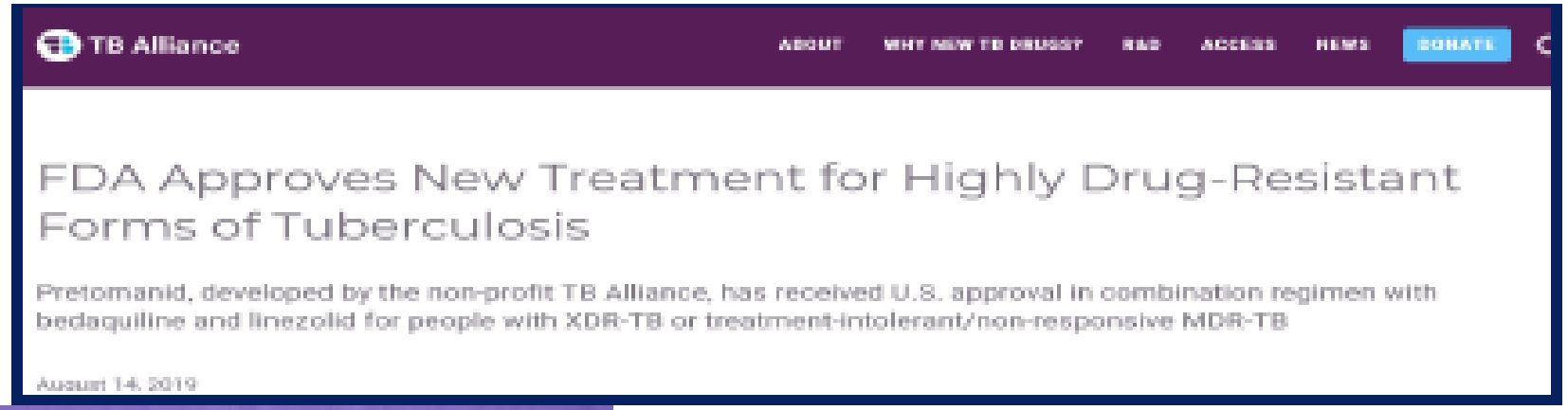
Only BPaL had no relapses

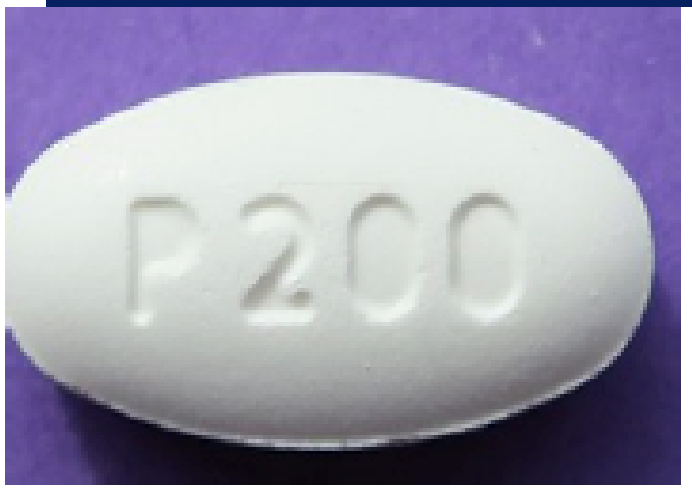
Regimen	Mean (±SD) Lung Log_{10} CFU Count at:			Proportion (%) Relapsing after Treatment for:		
	Month 1	Month 2	Month 3	2 Months	3 Months	4 Months
Untreated	6.47±0.06	*	*	-	--	
2 months RHZ/4 months RH	3.47±0.37	1.59±0.25	0.50±0.51	-	13/15 (87)	1/20 (5)
B	3.24±0.25					
Pa	4.57±0.22					
L	4.97±0.26					
Su	3.85±0.37					
BPa	4.21±0.40	1.62±0.19	0.52±0.36	15/15 (100)	10/15 (60)	**2/20 (10)**
BL	2.82±0.15	1.91±0.66				
BSu	2.88±0.07	0.65±0.50				
PaL	3.23±0.41	1.48±0.12				
PaSu	1.65±0.33	0.23±0.40				
BPaL	3.28±0.65	0.34±0.41	0.00±0.00	12/15 (80)	**0/14 (0)**	**0/20 (0)**
BPaSu	0.94±0.14	0.00±0.00	-	14/20 (70)	1/14(7)	

B=bedaquiline; CFU=colony-forming unit; H=isoniazid; L=linezolid; Pa=Pretomanid; R=rifampicin; Su=sutezolid; Z=pyrazinamide
Untreated mean lung log_{10} CFU counts Day -13 = 2.69±0.13; Day 0 untreated mean lung log_{10} CFU counts = 6.17±0.27
*no mice remained in the untreated control group at the 2- and 3-month time points; Day -13, CFU count in lungs 1 day post-infection; Day 0, CFU counts in lungs on first day of therapy. **Source: Adapted from Tasneen et al., 2016**

Slide courtesy of
B. Seaworth

As of 8/14/2019 …. **“BPaL” Regimen**





Pretomanid Approved by the US FDA

August 14, 2019

(Limited Population Pathway for Antibacterial and Antifungal Drugs)

INDICATIONS AND USAGE

Limited Population: Pretomanid Tablet is an antimycobacterial indicated, as part of a combination regimen with bedaquiline and linezolid for the treatment of adults with pulmonary extensively drug resistant (XDR), treatment-intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis (TB). Approval of this indication is based on limited clinical safety and efficacy data. This drug is indicated for use in a limited specific population of patients.

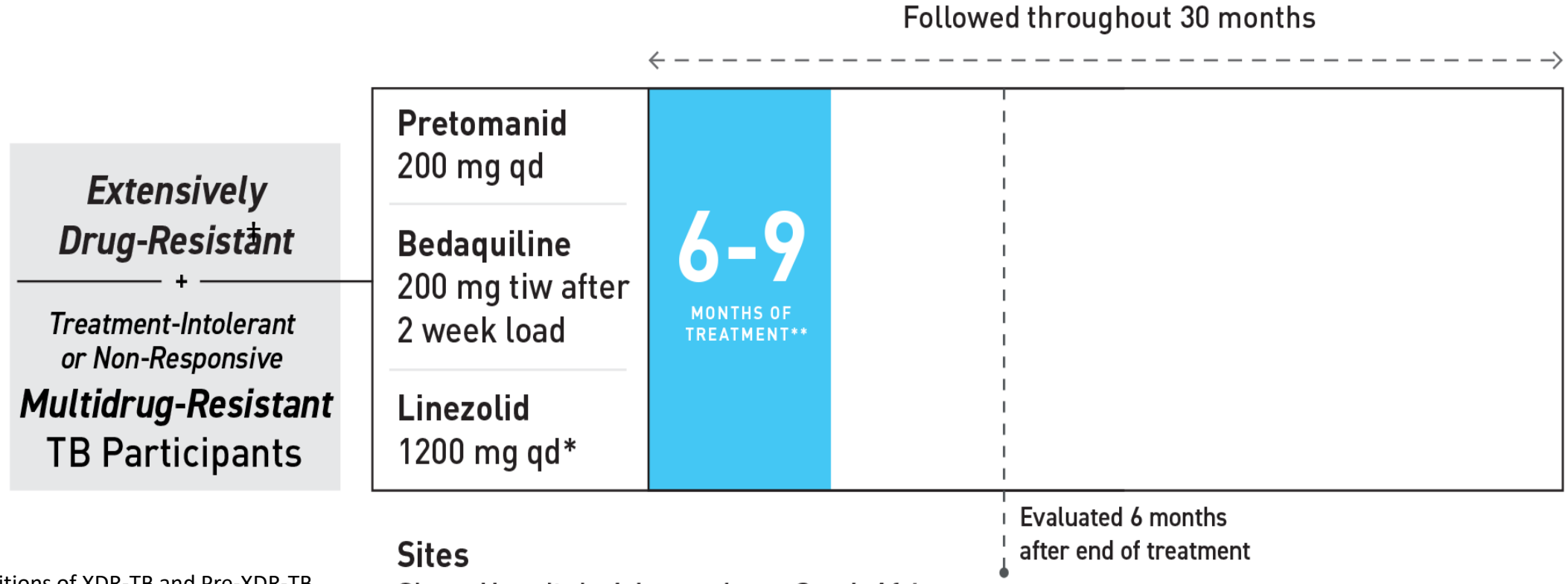
Please see full prescribing information:

https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/212860Orig1s000lbl.pdf

Courtesy of B. Seaworth

Nix-TB Phase 3 Trial in XDR-TB

109 Patients with XDR-TB or who have failed or are intolerant to MDR-TB Treatment



Sites
Sizwe Hospital, *Johannesburg, South Africa*
Brooklyn Chest Hospital, *Cape Town, South Africa*
King Dinuzulu Hospital, *Durban, South Africa*

**Amended from 600 mg bid strategy*
***If sputum culture is positive at 4 months, patients received an additional 3 months of treatment*
Primary endpoint is measured at six months of post-treatment follow up

† Pre-2021 WHO Definitions of XDR-TB and Pre-XDR-TB

- No comparison group
- Pulmonary not Extrapulmonary TB
- Only 2 extended to 9 mo.

Linezolid Dosing Flexibility

Trial was designed to start at the full approved dose of 1200 mg daily*

- Protocol-guided flexibility to modify the dose after the first month as needed:
  - Linezolid dose reductions, interruptions or discontinuation
- Bedaquiline and Pretomanid could not be changed

*1200mg is dose used for bacterial infections, which have higher MICs

Nix-TB Adverse Events of Special Interest

Key Safety Information

Key Concerns for Monitoring:

- Neuropathy
  - *Monitor visual function*
- Myelosuppression, especially anemia
  - *Monitor Complete Blood Counts*
- Hepatic enzyme elevations
  - *Monitor symptoms and signs and liver-related laboratory tests*

Nix-TB Primary Efficacy Analysis

- Primary endpoint – clinical and bacteriologic status 6 months after end of treatment
- Patient outcome categorized as either:
  - **Unfavorable outcome**
    - Clinical or bacteriologic failure during treatment
    - Bacterial relapse post-treatment
    - Patients requiring alternative treatment at any point, withdrawal, or any death in ITT analysis

    OR

  - **Favorable outcome, cured**

Nix-TB Results: Characteristics of Participants

- Patients had significant TB disease and poor health at baseline
  - Undernourished - mean BMI 20.6
  - 51% had HIV/AIDS
  - 65% XDR-TB
  - 85% had cavitary disease
  - Most had TB for >12 months before BPaL

Conradie et al. 2020

Nix-TB Results

- *New England Journal of Medicine*, March 2020

PARTICIPANT STATS

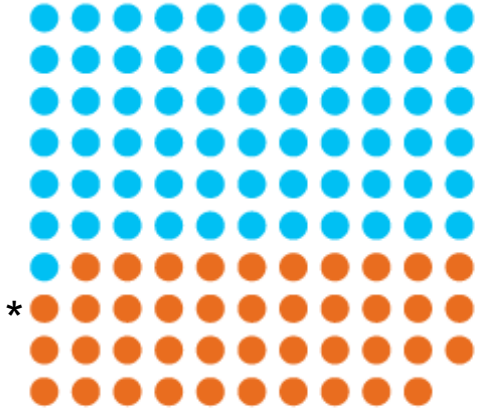
109 participants with **confirmed TB**

71 with **XDR TB**

65%

38 with **MDR TB**

34%



THE RESULTS

Favourable outcomes

with **XDR TB**

89%

79-95 (95% CI)

with **MDR TB***

92%

79-98 (95% CI)

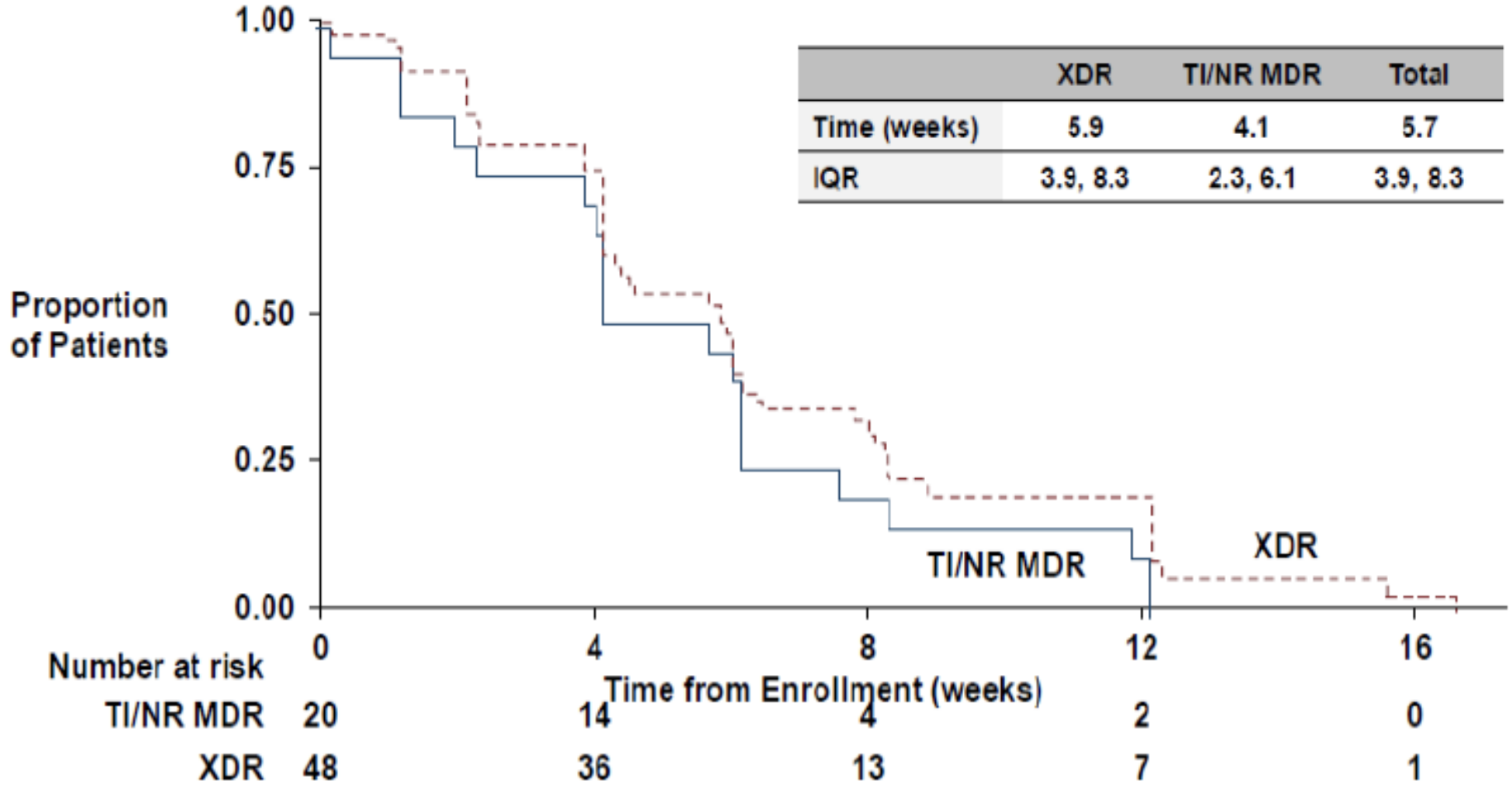
90% of all participants had **favourable outcomes**

95% CI (83-95)

Clinical resolution
6 months after therapy

*Treatment intolerant or non-responsive MDR-TB

Secondary Endpoint: Median Time to Sputum Culture Conversion ~ 6 Weeks



	XDR	TI/NR MDR	Total
Time (weeks)	5.9	4.1	5.7
IQR	3.9, 8.3	2.3, 6.1	3.9, 8.3

Conradie et al. 2020

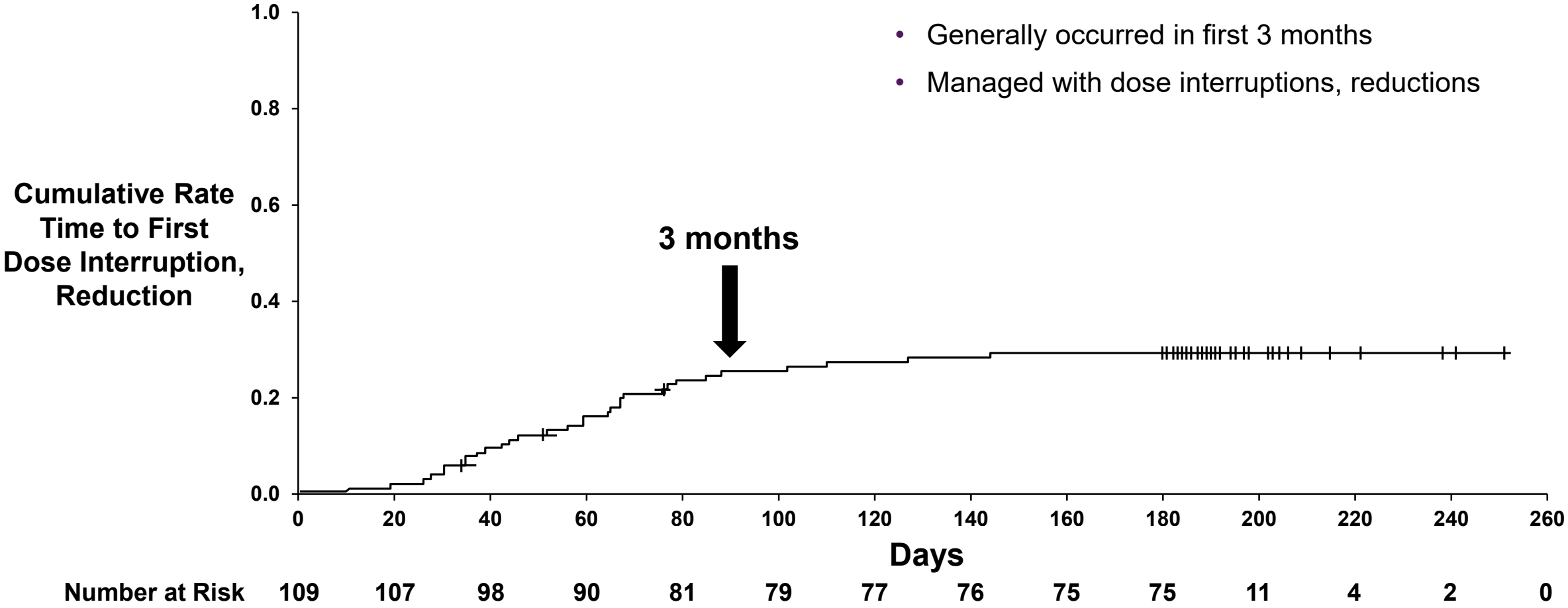
Nix-TB Results: Linezolid likely responsible for most adverse events and all dose modifications

- Peripheral neuropathy occurred in 81% of all patients
- Almost half (48%) had hematologic toxicity
- 50 pts interrupted LZD, resumed at same or lower dose
- 33 permanently discontinued LZD, with 27 surviving patients completing BDQ and Pa
- *Only 34 patients had no LZD dose interruptions*

FDA Briefing Document: "Adverse events (AEs) were as expected with this regimen. AEs were generally manageable through dose modifications, and the majority of patients were able to complete therapy."

Nix-TB Results: Myelosuppression - Early Onset, Managed with Dose Modifications

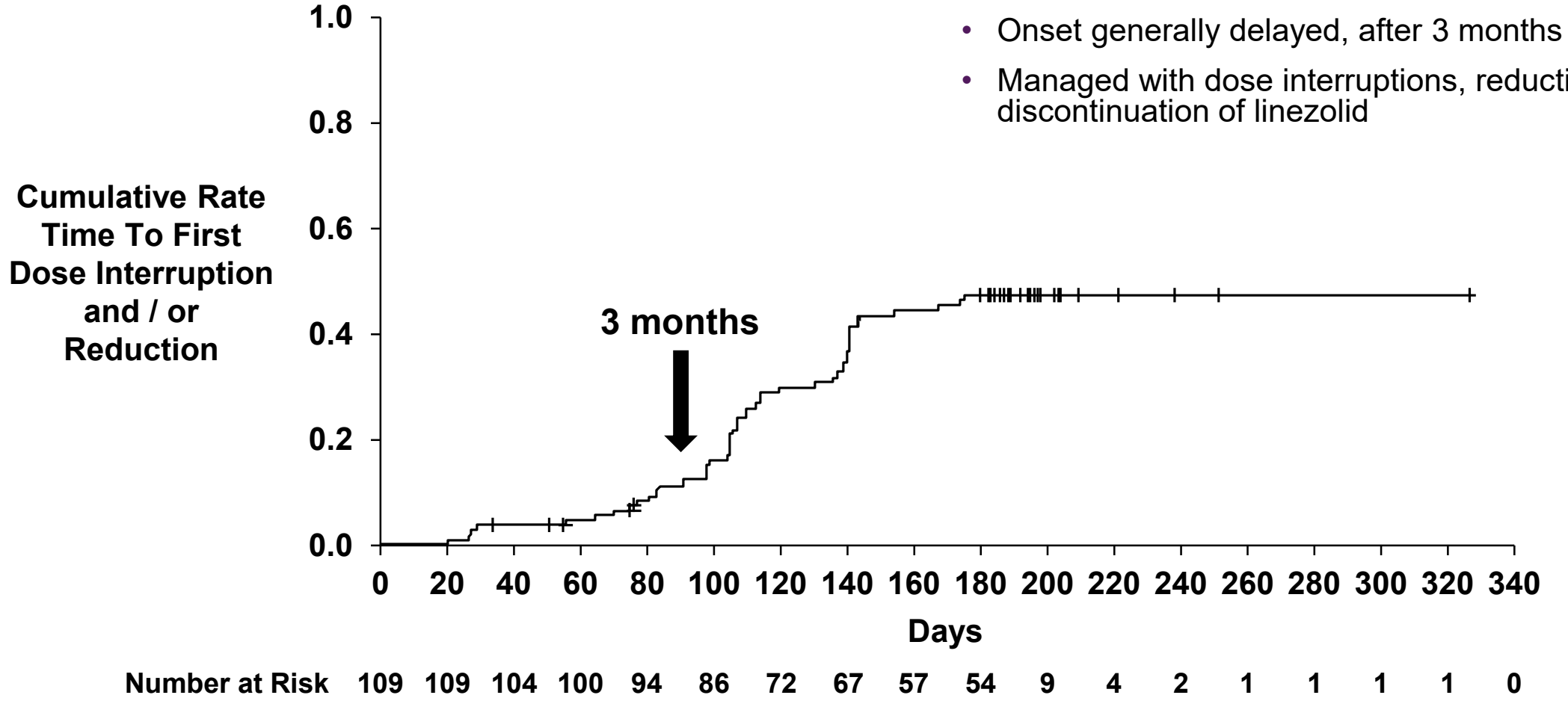
- Generally occurred in first 3 months
- Managed with dose interruptions, reductions



Data on File. Pretomanid- sponsor briefing document. TB Alliance. April 28, 2019

Nix-TB Results: Peripheral Neuropathy - Delayed Onset, Managed with Dose Modifications

- Onset generally delayed, after 3 months
- Managed with dose interruptions, reductions, discontinuation of linezolid



24 Months Post-treatment Follow-up Supports Long-Term Success

Presented at CROI, March 6-10, 2021

- Patients have been followed for a full 24 months after treatment:

  After two years of follow up, the results of the Nix trial have held firm:
  - **90% of patients with highly drug resistant TB survived and remained healthy long after completing treatment.**

- Deaths
  - 8 total deaths reported
  - 6 due to SAEs during study treatment
  - 2 due to SAEs during follow-up after completion
  - Only 2 of the fatal SAEs possibly related to study treatment

24-Month Nix-TB Results: Peripheral Neuropathy

Presented at CROI, March 6-10, 2021

- Patients in Nix-TB were administered detailed questionnaires focused on PN symptoms during the treatment phase and 2-year follow-up
- Most patients in Nix-TB experienced PN symptoms
- At 2 years follow-up, most patients who developed PN symptoms had completely resolved
- A few had mild-moderate residual symptoms, and 1 pt had severe symptoms
- Long-term follow up showed that neuropathy from the use of linezolid resolves for most patients.

SNTC: Minimizing linezolid toxicity

- LZD trough levels, NOT dosage, correlated with development of toxicity
- MIC of LZD<1 for *M. tuberculosis*
- Start with initial dose of Linezolid 600mg daily
- Obtain serum drug levels at 2-4 wks to prevent LZD mitochondrial toxicity
  - Keep LZD trough < 2mcg/mL (*Song, Brown*)
  - Achieve peak LZD 12-26mcg/mL
  - Ensure LZD serum levels are 4-16x over the organism's MIC
  - Adjust the dose or the dosing interval
- Clinical and lab monitoring throughout therapy

Peloquin, Microbiol Spectr. 2017;5(1). Brown et al. mBio. 2015;6(6):e01741-15.
Song, et al. EBioMedicine. 2015;2(11):1627-33.

ZeNIX Study

IAS 2021 18 – 21 July

ZeNix

Rationale

- Though 90% efficacy to cure XDR and TI MDR TB, high rate of adverse events was driven by linezolid at 1200mg/d
- Study needed to optimize linezolid dosing and improve safety

Study Design

- A Phase 3, multi-center, partially-blinded, randomized clinical trial in four parallel treatment groups
  - Males and Females, ages 14y and older
  - Compared Linezolid dosing strategies
  - BDQ given 200mg/d x8weeks then 100mg QD
  - PTM still 200mg/d
  - Favorable and unfavorable outcomes as in NIX-TB trial

ZeNIX Study Design

Extensively Drug-Resistant, Pre-Extensively Drug-Resistant

+

Treatment-Intolerant or Non-responsive Multidrug-Resistant TB Participants

randomized

B-Pa-L *L=1200 mg/d x 6 mos*	6 MONTHS OF TREATMENT*	
B-Pa-L *L=1200 mg/d x 2 mos*	6 MONTHS OF TREATMENT*	
B-Pa-L *L=600 mg/d x 6 mos*	6 MONTHS OF TREATMENT*	
B-Pa-L *L=600 mg/d x 2 mos*	6 MONTHS OF TREATMENT*	

Results			
Success Rate	**Neuropathy**	**Myelosuppression/ Anemia**	**LZD Dose modification**
93%	38%*	22%	51%
89%	24%	17%	30%
91%	24%	2%	18%
84%	13%	7%	18%

Allowed ages 14 years or older
20% HIV+
90% Pre-XDR or XDR

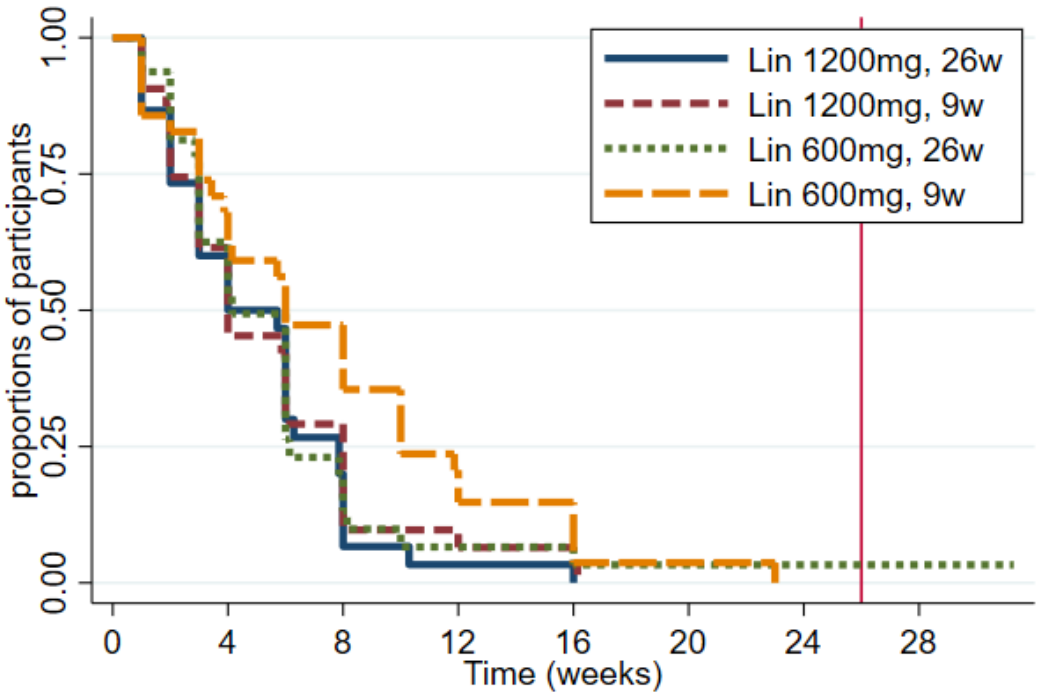
*Additional 3 months if sputum culture positive between week 16 and week 26 treatment visits

Pa pretomanid dose = 200 mg daily
B bedaquiline dose = 200 mg x 8 weeks, then 100 mg x 18 weeks

Pre-2021 WHO Definitions of XDR-TB and Pre-XDR-TB

*4 had optic neuropathy that reversed

Time to Culture Negative Status (MITT)

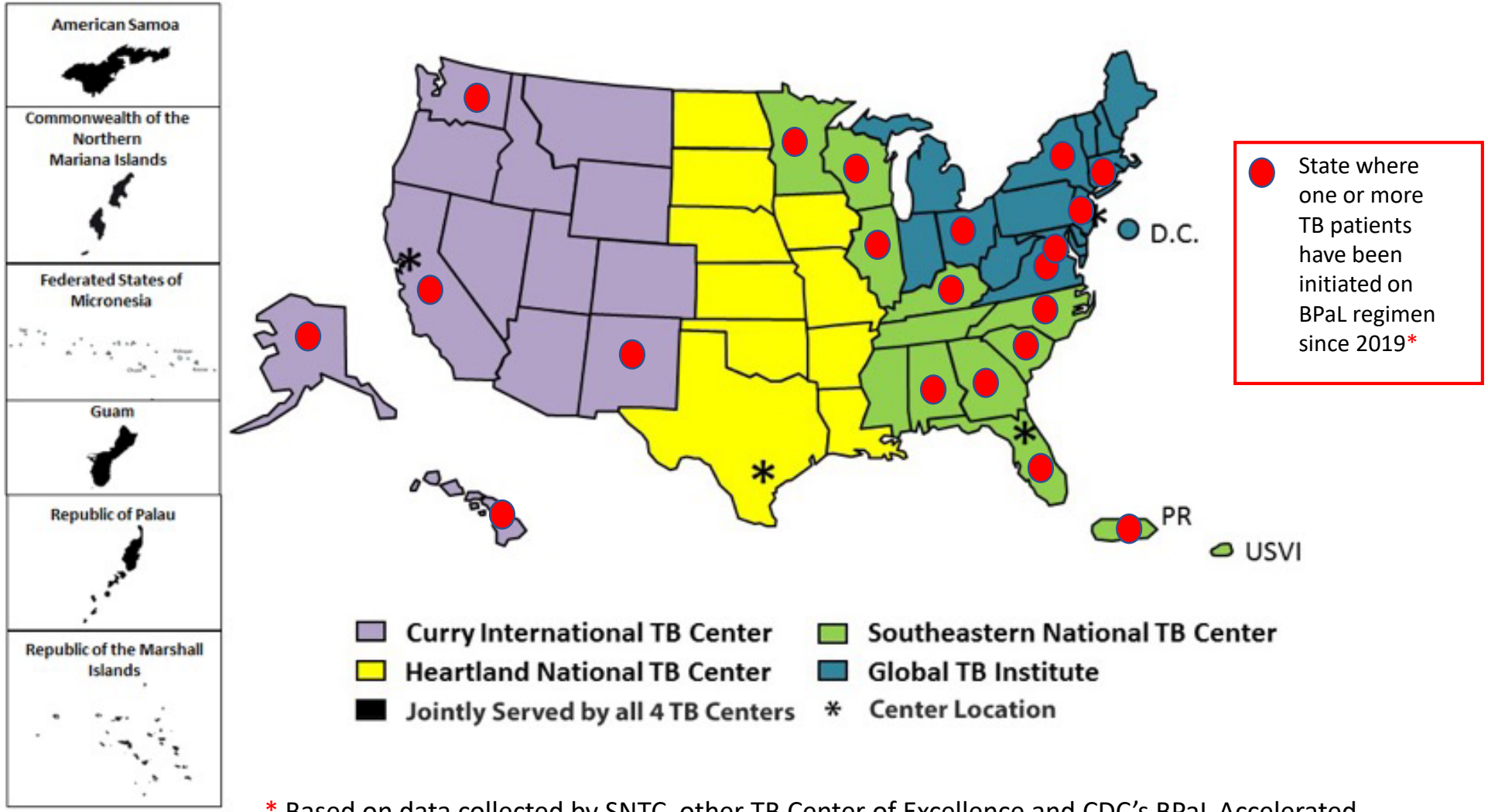


Number at risk								
Lin 1200mg, 26w	30	18	6	1	1	0	0	0
Lin 1200mg, 9w	32	19	9	3	2	0	0	0
Lin 600mg, 26w	32	19	6	2	2	1	1	1
Lin 600mg, 9w	35	23	16	7	4	1	0	0

TB-PRACTECAL Study

- Phase II/III clinical trial sponsored by Médecins Sans Frontières (MSF)
- 6-month **BPaL+moxifloxacin (BPaL+M)** vs. local standard of care
- 7 trial sites across Belarus, S. Africa, and Uzbekistan
- Age >=15
- NOT including: TB of the CNS, bone or joints
- Linezolid: 600mg QD for 16 weeks, then 300mg QD (or 600mg x3/wk) for remaining 8 weeks (or earlier when moderately tolerated)
- At the time of interim analysis, 242 patients had been enrolled
- Independent data safety and monitoring board stopped the study because BPaL+Moxi is superior to current care (longer regimens), and more patient data was extremely unlikely to change the trial's outcome.

BPaL Implementation in the US



* Based on data collected by SNTC, other TB Center of Excellence and CDC's BPaL Accelerated Monitoring (BAM) Project. **May not include all cases.**

BPaL in the United States and Wisconsin

- Used as treatment for ~ 120 TB clients so far in the United States
- BPaL Patients with rifampin-monoresistance, MDR, Pre-XDR, XDR and even some with significant Rifampin intolerance without resistance
- 7 TB clients have been treated with BPaL in Wisconsin
- Efficacy so far: no known treatment failures in the US

Reasons Rifamycins were not tolerated and BPaL considered

- Severe allergy to rifampin LTBI therapy
- Intolerant of Rifamycins and FQ
- Cytopenias on Rifamycins
- Severe gout/pancreatitis on RIPE
- Culture neg presumed MDR (INH resistant TB inadvertently given RIF monotherapy)
- Cancer patient with severe drug interactions with chemo requiring treatment prior to BMT

PRELIMINARY DATA!!!

Potential Adverse Events

- **Hepatotoxtic**
  - Unusual tiredness
  - Dark (tea-colored) urine
  - Loss of appetite
  - Tenderness in the upper right side of your stomach-area (abdomen)
  - Nausea/vomiting
  - Yellowing of your skin or the whites of your eyes
- **Low blood cell counts**
  - *Anemia* Low red blood cell counts
  - *Leukopenia* low white blood cell counts
  - *Thrombocytopenia* low blood platelet counts
  - *Pancytopenia* a combination of low red and white blood cell counts and low blood platelet counts
- **Mental Health concerns**
  - Anxiety/panic attacks
  - Depression

Potential Adverse Events

- **Peripheral neuropathy**
  - Symptoms of nerve problems in arms, hands, legs, feet, or other area including:
  - Numbness, tremors, burning, problems with balance, a feeling of “pins and needles”, weakness
- **Vision problems**
  - Optic neuropathy
- **QT prolongation** Stop if QTc> 500
  - Change in heartbeat (a fast or irregular heart beat)
  - Feel dizzy or faint
- **Male fertility**
  - It is not known if pretomanid can cause fertility problems in males
- **Lactic acidosis**
  - Nausea and vomiting that keep coming back

Other Considerations for BPaL

- Patients should tell their doctor if they are pregnant or plan to become pregnant.
  - It is not known whether pretomanid will harm an unborn baby. However, having TB during pregnancy may cause serious complications in both the mother and the baby. The benefit of treating TB may outweigh any risks to the baby.
- It may not be safe to breastfeed while using pretomanid. Ask the doctor about any risk.
- Pretomanid not studied for use in <14 years old.
- “Longer” MDR TB regimens also has substantial risk of toxicity that must be discussed with the patient

Case Study of a BPaL Regimen
Sheboygan County
Division of Public Health

Presenter: Miva Yang, RN & Case Manager

TB Team: Miva Yang RN, Amy Betke RN, Debra Schmidt RN
Amanda Strojinc RN-Clinical Supervisor

Case Background

- 65 year old South East Asian/Hmong refugee
  - Came to Sheboygan 1992
- Father of 8 children
  - Family spiritual leader
  - Hobbies: soccer, raising honey bees, gardening, repairing cars, woodworking
- Employed at a local company
  - Retired 2 year prior to his illness
- Language: Hmong and English sufficiency
- Father died December, 2019—family gathering to plan for funeral

Health History & Risk

- Generally healthy and physically active
  - Self sufficient, takes charge of his own health care
- Hypertension (on treatment)
- Hypokalemia
- Benign prostatic hyperplasia (on treatment)
- Non smoker, no drug/alcohol used
- Refugee camp pharmacy-technician

TB History

- Refugee screening 1992
- TST: 3/23/92 Results: 5mm, 3/30/92-6mm
- 2014-Contact of an Active TB case in Sheboygan
  - Tx-with RIPE
- T-Spot: positive
- CXR: Normal
- Treated: INH for 9 months
  - Self administered and completed

Active TB Diagnosis

- Symptoms started 12/3/2019
  - Fever on/off, night sweats, non-productive cough
- Treated by PCP with antibiotics for pneumonia but symptoms continued
- ED visit with inpatient admission on 1/12/20
- Abnormal CT chest obtained 1/13/20
- Sputum collection initiated at the hospital
- Referred to DPH on 1/13/20 with a suspicion for active TB
- Patient was discharged from hospital on 1/27/2020
  - Instructed to isolate at home until ruled out for active TB
  - Signed Voluntary Isolation agreement and “STOP” sign poster on door

Polling Question #1

Which of the following tests would be MOST helpful for diagnosis in this Hmong Patient?

1. QuantiFERON-plus
2. AFB smear
3. Mycobacterial culture
4. NAAT (nucleic acid amplification test)
5. GeneXpert

Table 2. Essential Laboratory Tests for the Detection of Mycobacterium tuberculosis

Test	Time Required
I. Nucleic acid amplification test, detection (NAAT-TB)	1 d
II. Nucleic acid amplification test, resistance markers (NAAT-R)	1–2 d
III. Acid-fast bacilli microscopy	1 d
IV. Growth detection Liquid Solid	Up to 6–8 wk (average 10–14 d) (average 3–4 wk)
V. Identification of Mycobacterium tuberculosis complex by DNA probe or HPLC	1 d[a]
VI. First-line drug susceptibility testing (liquid medium)	1 to 2 wk[a]
VII. Second-line and novel compound drug susceptibility testing	
i. Liquid (broth-based) medium	1 to 2 wk[a]
ii. Solid (agar- or egg-based) medium	3 to 4 wk[a]

Abbreviation: HPLC, high-performance liquid chromatography.[a]After detection of growth.

Official ATS/IDSA/CDC Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children
https://academic.oup.com/cid/article/64/2/111/2811357

AFB Smear, Culture, and Molecular Tests

Initial Testing (diagnosis)

If symptoms and radiology are consistent with TB,

- Positive NAAT/PCR or a Positive culture for MTBc == TB

But..

- Positive AFB *smear* is not enough…get PCR/NAAT too
  - If + PCR/NAAT==TB
  - If – PCR/NAAT, NOT likely TB (may be non-TB mycobacteria)

- Negative AFB smear does NOT rule out TB disease
  - Get PCR/NAAT for rapid diagnosis if TB suspected
- Negative AFB culture does NOT rule out TB disease
  - Can still have culture-neg TB (Consider risk, symptoms, radiology, response to therapy)

AFB Smear, Culture, and Molecular Tests

Follow up Testing (response to treatment)

- ❖AFB cultures indicate live TB organisms
- ❖NAAT/PCR remain positive long after the organisms are dead-not used to assess treatment response

Molecular Detection of Drug Resistance (MDDR) (Genotypic DST)

- ❖Specific mutations known to predict resistance to specific drugs; used to tailor appropriate initial therapy
- ❖If patient not responding/worsens despite TB therapy, repeat MDDR may identify new mutations to indicate acquired drug resistance

Molecular Detection of Drug Resistance (MDDR) (Genotypic DST)

❖Specific mutations known to predict resistance to specific drugs; used to tailor appropriate initial TB therapy

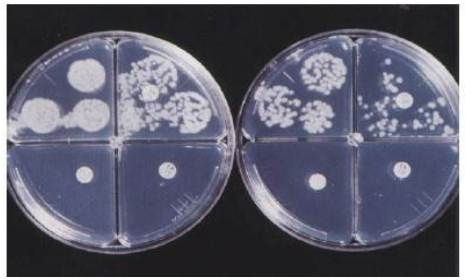
- rpoB (rifamycins)
- inhA and katG (INH)
- (also EMB, PZA, quinolones, linezolid, bedaquiline and injectables)

❖If patient not responding/worsens despite TB therapy, repeat MDDR may identify new mutations to indicate acquired drug resistance

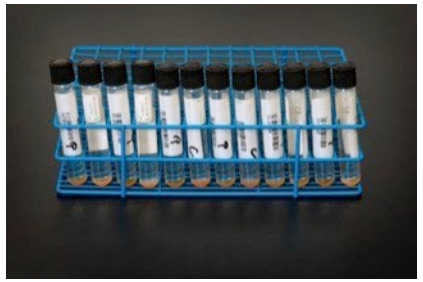
- **Must also obtain growth-based DST!!**

Growth-based (Phenotypic) Drug Susceptibility Testing

- Determines which drugs kill TB bacilli
  - Susceptible= TB Bacilli don't grow in presence of that drug
  - Resistant= TB bacilli do grow in presence of drug
- Time to results:
  - Solid medium: 7 - 14 days
  - Liquid medium: up to 21d



DST on solid media



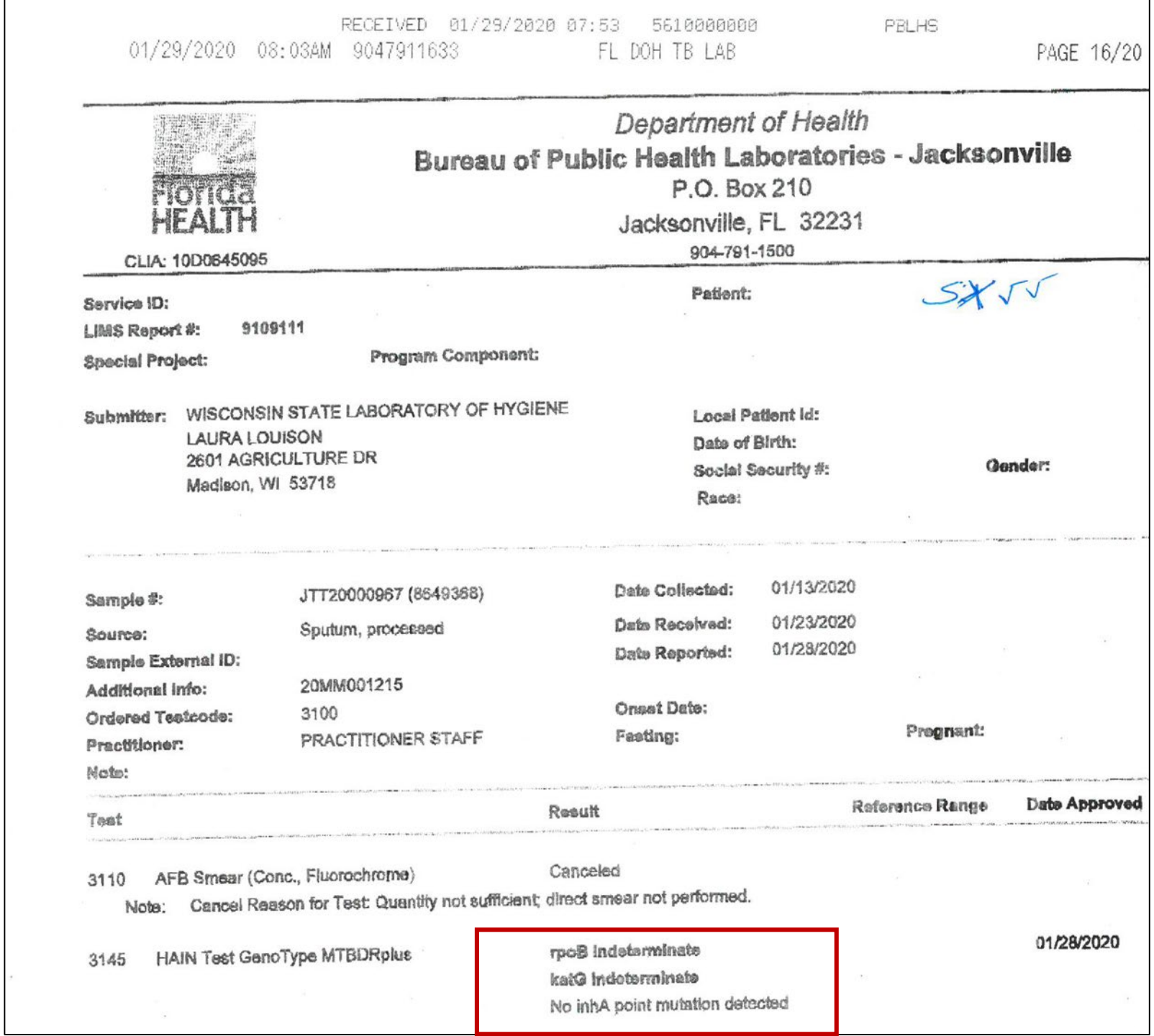
DST on liquid media

Back to our patient…

- AFB Smear +
- GeneXpert + *rpoB* mut (RIF resistant)

- Sample sent to FL Lab:
- HAIN MTBDRplus:
  - Resistance to RIF and INH
- HAIN MTBDRsl
  - Resistance to quinolones and injectables

- *FL PH lab will test any clinical sample OR a culture isolate*



RECEIVED 01/29/2020 07:53 5610000000 PBLHS
01/29/2020 08:03AM 9047911633 FL DOH TB LAB PAGE 16/20

Florida HEALTH

Department of Health
Bureau of Public Health Laboratories - Jacksonville
P.O. Box 210
Jacksonville, FL 32231
904-791-1500

CLIA: 10D0645095

Service ID:
LIMS Report #: 9109111
Special Project: Program Component:

Patient: SX √√

Submitter: WISCONSIN STATE LABORATORY OF HYGIENE
LAURA LOUISON
2601 AGRICULTURE DR
Madison, WI 53718

Local Patient Id:
Date of Birth:
Social Security #: Gender:
Race:

Sample #: JTT20000967 (8649368)
Source: Sputum, processed
Sample External ID:
Additional Info: 20MM001215
Ordered Testcode: 3100
Practitioner: PRACTITIONER STAFF
Note:

Date Collected: 01/13/2020
Date Received: 01/23/2020
Date Reported: 01/28/2020
Onset Date:
Fasting: Pregnant:

Test	Result	Reference Range	Date Approved
3110 AFB Smear (Conc., Fluorochrome)	Canceled		
Note: Cancel Reason for Test: Quantity not sufficient; direct smear not performed.			
3145 HAIN Test GenoType MTBDRplus	rpoB Indeterminate katG Indeterminate No inhA point mutation detected		01/28/2020

Full MDDR Results

- MDDR: Molecular Detection of Drug Resistance
- Sequencing and HAIN
  - RIF
  - INH
  - EMB
  - Quinolones
  - Injectables
  - Linezolid
  - Bedaquiline
- ***This patient has MDR-TB***
  - ***R to INH/RIF/EMB***

JTS20000033, specimen. DOC:01/13/2020, DOR: 02/11/2020 MTBDRplus:01/29/2020, DNA seq: 02/13/2020, MTBDRsl: 1/29/2020,			
Target	mutation	Detected by	Predicted (02/13/2020)
rpoB (RRDR)	His526Asp (CAC/GAC)	MTBDRplus , DNA Seq.	RIF- R
katG (ORF, aa 225-345)	Ser315Thr (AGC/ACC)	MTBDRplus , DNA seq	High level INH- R
mabA-inha promoter	No mutations	MTBDRplus , DNA seq.	
embB (ORF, aa 288-509)	Asp354Ala (GAC/GCC)	DNA seq.	Possibly/likely EMB- R
gyrA/gyrB (QRDR, aa 1-132)	No mutations	MTBDRsl DNA seq.	*Possibly FQ-S
rrs (1400 region)	No mutations	MTBDRsl	*Likely S to injectable drugs (kan, ami, vio)
eis (promoter)	No mutations	MTBDRsl	*Likely S to injectable drugs (kan)
atpE (ORF)	No mutations	DNA seq.	*Based on these results and due to potential contributory mutations at other loci, resistance to bedaquiline is not predicted but cannot be ruled out.
rplC (ORF, aa 84-217)	No mutations	DNA seq.	*Based on these results and due to potential contributory mutations at other loci, resistance to linezolid is not predicted but cannot be ruled out.
*Determination of MTBC Drug susceptibilities by culture growth (phenotypic) methods is the gold standard			

Culture-based Drug Susceptibility Testing

- or “phenotypic” DST
  - RIF
  - INH
  - EMB
  - Quinolones
  - Injectables
  - Linezolid
  - Bedaquiline

Florida HEALTH

Department of Health
Bureau of Public Health Laboratories - Jacksonville
P.O. Box 210
Jacksonville, FL 32231
CLIA: 10D0645095 904-791-1500

Service ID: **Patient**
LIMS Report #: 9209600
Special Project: **Program Component:**

Submitter: WISCONSIN STATE LABORATORY OF HYGIENE
LAURA LOUISON
2601 AGRICULTURE DR
Madison, WI 53718

Local Patient Id:
Date of Birth:
Social Security #: **Gender:**
Race:

Sample #:	JTS20000033 (8678751)	**Date Collected:**	01/13/2020
Source:	Sputum	**Date Received:**	02/11/2020
Sample External ID:		**Date Reported:**	03/12/2020
Ordered Testcode:	3315	**Onset Date:**	
Practitioner:	PRACTITIONER STAFF	**Fasting:**	**Pregnant:**

Note: Specimen identified as *M. tuberculosis* complex by WI State Lab of Hygiene and submitted for susceptibilities studies.

Test		Result	Reference Range	Date Approved
3315	Streptomycin MIC	32 µg/mL		03/12/2020
	Streptomycin Interpretation	Resistant	Susceptible: <2.0 Intermediate: 2.0-4.0 Resistant: ≥8	
	Isoniazid MIC	2 µg/mL		
	Isoniazid Interpretation	Resistant	Susceptible: <0.25 Intermediate:0.25-1. 0 Resistant: ≥2	
	Rifampin MIC	16 µg/mL		
	Rifampin Interpretation	Resistant	Susceptible:≤1 Resistant: ≥2	
	Ethambutol MIC	8 µg/mL		
	Ethambutol Interpretation	Resistant	Susceptible: ≤2 Intermediate: 4.0 Resistant:≥ 8	
	Kanamycin Interpretation	Not Tested	Susceptible: ≤2.5 Resistant: ≥5	
	Rifebutin MIC	2 µg/mL		
	Rifabutin Interpretation	Resistant	Susceptible: ≤0.25 Resistant: ≥0.5	

CLIA: 10D0645085

Jacksonville, FL 32231
904-791-1500

ce ID:
Report #: 9209600
al Project: Program Component:

Patient:

itter: WISCONSIN STATE LABORATORY OF HYGIENE
LAURA LOUISON
2601 AGRICULTURE DR
Madison, WI 53718

Local Patient Id:
Date of Birth:
Social Security #:
Race:

e #: JTS20000033 (8678751)
): Sputum
e External ID:
d Testcode: 3315
loner: PRACTITIONER STAFF

Date Collected: 01/13/2020
Date Received: 02/11/2020
Date Reported: 03/12/2020
Onset Date:
Fasting: Pregnant:

	Result	Reference Range
Capreomycin Interpretation	Susceptible	Susceptible: ≤5 Resistant: Breakpoint not established
Levofloxacin MIC Levofloxacin Interpretation	0.5 µg/mL Susceptible	Susceptible: ≤0.5 Resistant: Breakpoint not established
Linezolid MIC Linezolid Interpretation	0.25 µg/mL Susceptible	Susceptible: ≤1.0; Resistant: Breakpoint not established.
Ofloxacin Interpretation	Not Tested	Susceptible: ≤1 Resistant: ≥2
Ethionamide Interpretation	Not Tested	Susceptible: ≤1.2 Resistant: ≥2.5
Amikacin MIC Amikacin Interpretation	0.25 µg/mL Susceptible	Susceptible: ≤2 Resistant: Breakpoint not established
Moxifloxacin MIC Moxifloxacin Interpretation	0.25 µg/mL No Interpretation	Susceptible: ≤0.12 Resistant: Breakpoint not established
Para-Aminosalicylic Acid MIC Para-Aminosalicylic Acid Interpretation	<0.5 µg/mL Susceptible	Susceptible: ≤0.5 Resistant:Breakpoint not established
Cycloserine MIC Cycloserine Interpretation	8 µg/mL Susceptible	Susceptible: ≤8.0 Resistant: Breakpoint not established
Capreomycin MIC Capreomycin Interpretation	1.2 µg/mL Susceptible	Susceptible: ≤5 Resistant: Breakpoint not established
Levofloxacin MIC Levofloxacin Interpretation	0.5 µg/mL Susceptible	Susceptible: ≤0.5 Resistant: Breakpoint not established
Linezolid MIC Linezolid Interpretation	0.25 µg/mL Susceptible	Susceptible: ≤1.0; Resistant: Breakpoint not established.

PZA Susceptibility Testing

- Growth-based can be unreliable
- Florida Lab performs molecular testing only

904-791-1630. To consult with a TB Physician, call: 1-800-4TB-INFO.

3332	Pyrazinamide Molecular Susceptibility Interpretation	No pncA mutation detected Absence of a pncA mutation indicates PZA susceptibility, but cannot rule out resistance.	02/19/2020

Note: pncA DNA sequencing is an in-house developed and validated test for the detection of mutations associated with Pyrazinamide resistance.

Consultation

- Multiple case conferences starting on 1/31/2020
  - DPH, infectious disease, State TB program leads, SNTC
- Treatment with BPaL suggested
  - First case in Wisconsin recommended for this treatment
  - MD informed patient of treatment choices
- Baseline recommendations for assessments related to BPaL regimen were given: Full BPal Care Plan
  - Visual acuity, labs, EKG

For SNTC Consults: 1-4-TB-INFO

BPaL TB CARE PLAN

Baseline	Initiation of Treatment	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 9
CXR/PA & Lateral views Compare to others	Consider CT/ Other tests			CXR			CXR, Consider CT	
Request and review new or old records	Physician assessment	Physician assessment every 1-2 weeks	Physician assessment every 1-2 weeks	Physician assessment every month	→	→	→	→
Vision screen (acuity)		→	→	→	→	→	→	→
Review prior labs: CBC, BUN, Cr, Na, Cl, Ca, Mg, K, A1c or glucose, TSH		CBC weekly x 4 then monthly Electrolytes repeat if QTc prolongation on any EKG	→	→	→	→	→	→
Liver enzymes (LFTs): ALT, AST, Alkaline Phosphatase Total Bilirubin		LFTs weekly x 4 then monthly	→	→	→	→	→	→
Baseline EKG*		Every 2 weeks x 2 then monthly	→	→	→	→	→	→
Review prior sputum. Repeat sputum	Sputum in morning x 3 days for smear & culture	Sputum 1 weekly until SS– then 2 more until SS conversion. SCx3 until SC conversion			Extend 3 months if sputum culture positive after 4 months	→	→	→
Review drug susceptibility (DST)					Repeat DST if culture+ after 4 months			
Infection Control Isolation	Continue until culture negative x 3	→	→	→				
Therapeutic Drug Monitoring (TDM)	bedaquiline (BDQ) Pretomanid (Pa)	Peak/trough 1wk after TIW (BDQ) 2wks into Tx (Pa) 6hr & 24hr post dose (BDQ & Pa)	Peak/trough drug levels	Stop when levels WNL or continue PRN as needed	→	→	→	→
TDM	Linezolid (LZD)	Peak/trough 2wks after on Tx 2 hr and 6hr	Peak/trough drug levels	Stop when levels WNL or continue PRN as needed	→	→	→	→
Directly Observed Therapy (DOT)		DOT initiated/ patient education	→	→	→	→	→	→
Amylase & lipase if abdominal pain		→	→	→	→	→	→	→
Baseline weight & height	Calculate BMI/LBW	Weigh weekly x2 then monthly	→	→	→	→	→	→
Assess for peripheral neuropathy	→	→	→	→	→	→	→	→
Nutritional assessment →								
Assess overall health needs mental, emotional →								

Case Management Preparation

- Literature review
  - SNTC guide on BPaL treatment regimen
  - Nursing guide for managing side effects to Drug-resistant TB Treatment
- Modification of current Active TB monitoring forms to reflect the BPaL plan
- Handbook on Anti-Tuberculosis Agents (Pretomanid)
- Communication with state TB consultant and SNTC

Hospital Readmission

- 2/13/20: Home visit made for pretreatment baseline assessment
  - Visual acuity
  - TB Sx continued
  - little/no relief with Tylenol
  - Treatment Agreement (reviewed and signed)
- 2/15/20: Hospital readmission related to ongoing TB symptoms (fever/chills)
- In consultation with SNTC: MD started treatment on 2/18/2020
  - Amikacin, Moxifloxacin, Pyrazinamide and Linezolid
- BPaL treatment arrived at DPH
  - The regimen was started at the hospital on 2/21/2020
  - Client was discharged to continue home treatment with PHN case management

Polling Question #2

True or False:

Patients should be hospitalized to start treatment with BPaL.

1. True
2. False

Treatment-Case Management

- **BPaL:**
  Bedaquiline 400mg/daily/2weeks—>200mg M-W-F
  Linezolid 600mg/daily—->900mg (after drug level done)
  Pretomanid 200mg/daily (missed 5 days in May due to supplier issue)
- Daily DOT transitioned to VDOT on Weekends (after he is out of Isolation)
  - Daily and weekly assessments
- He is knowledgeable in taking temp, BP, weigh, taking his own prescribed medication on a daily basis
  - DPH monitored compliance of all medications
- Induced sputums, EKGs, labs (all coordinated with hospital/clinic)
- Drug level: Linezolid only

Wisconsin BPaL Nursing Assessment Form

Weekly Assessment Form for BPaL-Active TB

DAILY (D) *Additional daily assessment form: Peripheral Neuropathy Evaluation. WEEKLY (W). Not Assess (NA)

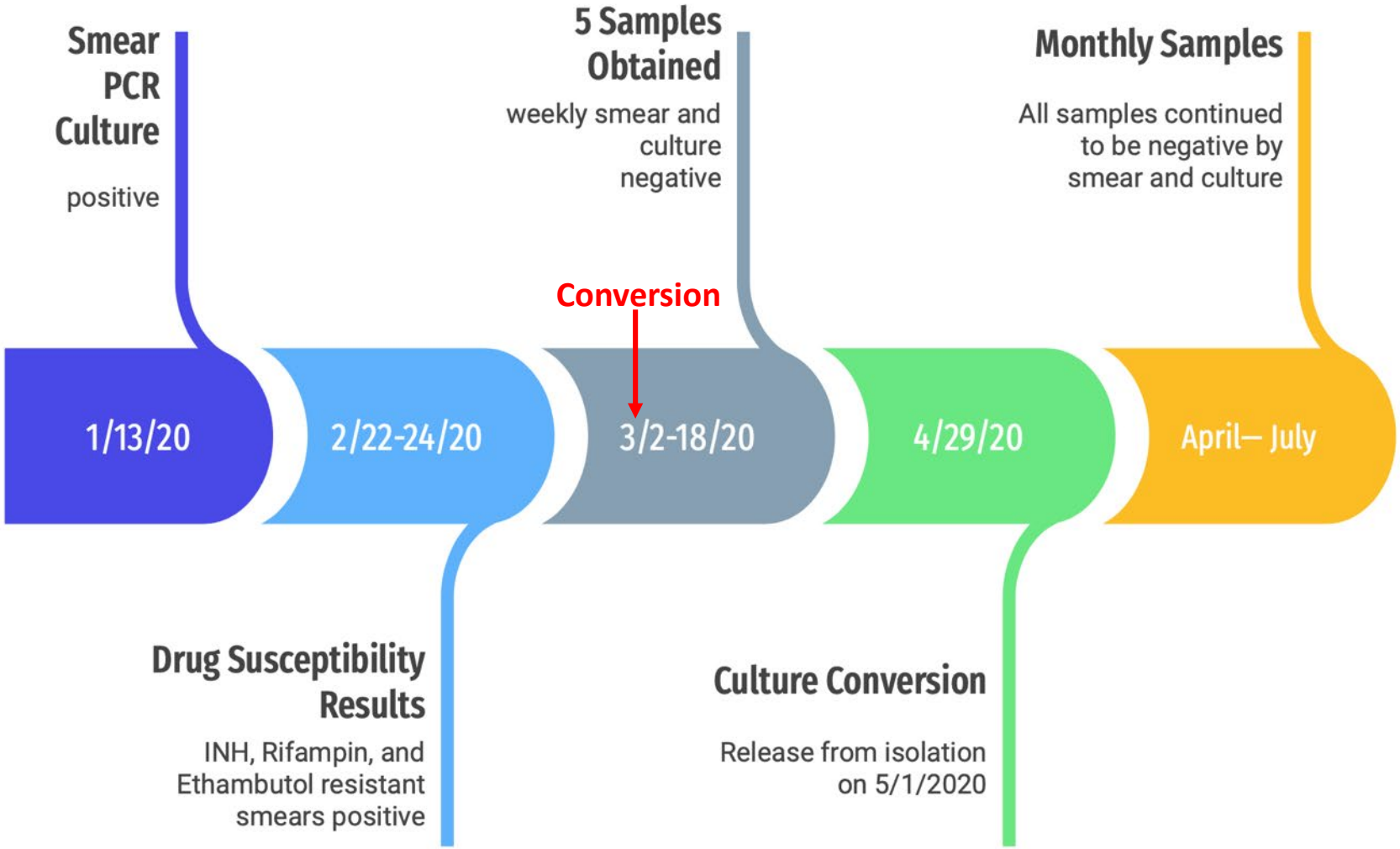
Circle all reported symptoms- make note in WEDSS under TB Clinical Tab.

Date:	Date:	Date:	Date:
Weight:______Temp:______	Weight:______Temp:______	Weight:______Temp:______	Weight:______Temp:______
Vitals:BP_______HR_______	Vitals::BP______HR______	Vitals:BP_______HR_______	Vitals:BP_______HR______
CNS / ENDO (D) Behavior Changes Anxiety / Irritable Vision Changes Photosensitivity Eye Pain with eye movement Headache Dizziness Confusion Numbness / Tingling* Changes in Sleep Loss of taste	CNS / ENDO (D) Behavior Changes Anxiety / Irritable Vision Changes Photosensitivity Eye Pain with eye movement Headache Dizziness Confusion Numbness / Tingling* Changes in Sleep Loss of taste	CNS / ENDO (D) Behavior Changes Anxiety / Irritable Vision Changes Photosensitivity Eye Pain with eye movement Headache Dizziness Confusion Numbness / Tingling* Changes in Sleep Loss of taste	CNS / ENDO (D) Behavior Changes Anxiety / Irritable Vision Changes Photosensitivity Eye Pain with eye movement Headache Dizziness Confusion Numbness / Tingling* Changes in Sleep Loss of taste
GI / GU / HEP (D) Nausea / Vomiting Diarrhea / Constipation Stool Color/Consistency Blood or mucus in stool Abdominal cramping Abdominal Pain (RUQ) Urine Color / ↓Output Jaundice Loss of Appetite heartburn	GI / GU / HEP (D) Nausea / Vomiting Diarrhea / Constipation Stool Color/Consistency Blood or mucus in stool Abdominal cramping Abdominal Pain (RUQ) Urine Color / ↓Output Jaundice Loss of Appetite heartburn	GI / GU / HEP (D) Nausea / Vomiting Diarrhea / Constipation Stool Color/Consistency Blood or mucus in stool Abdominal cramping Abdominal Pain (RUQ) Urine Color / ↓Output Jaundice Loss of Appetite heartburn	GI / GU / HEP (D) Nausea / Vomiting Diarrhea / Constipation Stool Color/Consistency Blood or mucus in stool Abdominal cramping Abdominal Pain (RUQ) Urine Color / ↓Output Jaundice Loss of Appetite heartburn
Cardiac - QTc Prolongation (D) Change in heartbeat Dizziness, chest pain Fainting, SOB Palpitations	Cardiac - QTc Prolongation (D) Change in heartbeat Dizziness, chest pain Fainting,SOB Palpitations	Cardiac - QTc Prolongation (D) Change in heartbeat Dizziness,chest pain Fainting, SOB Palpitations	Cardiac - QTc Prolongation (D) Change in heartbeat Dizziness,chest pain Fainting, SOB Palpitations
Skin / MS (W) Rash.itching Muscle or Joint Pain.gait Easy bruising Nose bleeds	Skin / MS (W) Rash, itching Muscle or Joint Pain Easy bruising Nose bleeds	Skin / MS (W) Rash,itching Muscle or Joint Pain Easy bruising Nose bleeds	Skin / MS (W) Rash,itching Muscle or Joint Pain Easy bruising Nose bleeds
TB Symptoms (W) Cough Fever Night Sweats Weight Loss Hemoptysis(LZD)	TB Symptoms(W) Cough Fever Night Sweats Weight Loss Hemoptysis (LZD)	TB Symptoms(W) Cough Fever Night Sweats Weight Loss Hemoptysis (LZD)	TB Symptoms(W) Cough Fever Night Sweats Weight Loss Hemoptysis (LZD)
Fatigue (W) Feeling of tiredness/lack of energy Unusual thirst Hunger	Fatigue(W) Feeling of tiredness/lack of energy Unusual thirst Hunger	Fatigue(W) Feeling of tiredness/lack of energy Unusual thirst Hunger	Fatigue(W) Feeling of tiredness/lack of energy Unusual thirst Hunger
Hypersensitivity / Anaphylaxis (W) Rapid onset of rash Swelling or airway Hypotension GI symptoms	Hypersensitivity / Anaphylaxis (W) Rapid onset of rash Swelling or airway Hypotension GI symptoms	Hypersensitivity / Anaphylaxis (W) Rapid onset of rash Swelling or airway Hypotension GI symptoms	Hypersensitivity / Anaphylaxis (W) Rapid onset of rash Swelling or airway Hypotension GI symptoms
PHN Initials:	PHN Initials:	PHN Initials:	PHN Initials:

WI BPaL Nursing Assessment Form (Detail)

CNS/ ENDO (D)	**GI / GU / HEP (D)**	**Cardiac - QTc Prolongation (D)**	**Skin / MS (W)**	**TB Symptoms (W)**	**Fatigue (W)**	**Hypersensitivity / Anaphylaxis (W)**
• Behavior Changes Anxiety / Irritable • Vision Changes Photosensitivity • Eye pain with eye movement • Headache • Dizziness • Confusion • Numbness / Tingling* • Changes in Sleep • Loss of taste	• Nausea / Vomiting • Diarrhea Constipation • Stool Color/Consistency • Blood or mucus in stool • Abdominal cramping • Abdominal Pain (RUQ) • Urine Color / ↓Output • Jaundice • Loss of Appetite • Heartburn	• Change in heartbeat • Dizziness • Chest pain • Fainting • SOB • Palpitations	• Rash • itching • Muscle or Joint Pain. • Gait • Easy bruising • Nose bleeds	• Cough • Fever • Night Sweats • Weight Loss • Hemoptysis (LZD)	• Feeling of tiredness/ • Lack of energy • Unusual thirst • Hunger	• Rapid onset of rash • Swelling or airway • Hypotension • GI symptoms

Bacteriology Summary



Radiological Studies

3/5/20

Improvement

Improvement noted in the right lung infiltrates. Left lung clear.

4/24/20

Stable

Stable study noted.

8/17/20

Stable

Stable study noted.

8/20/20

Treatment Complete

BPaL treatment is completed. Post treatment chest x ray series begins.

Post Tx

Clear

Lung volumes are upper normal with no effusions, consolidations or focal consolidations noted. Pulmonary vasculature is normal.

Laboratory and Assessment Findings

- Various weekly, biweekly and monthly labs were draw and all remained within normal limits
- Visual acuity was assessed throughout treatment and remained normal to baseline
- EKG and QTc were assessed at regular intervals and remained normal
- Drug levels were drawn for Linezolid; with a drug adjustment based on the peak & trough values
  - Initial dose was 600 mg
    - Lab value peaked at 9.99 (low)
  - Dose increased to 900 mg
    - Lab value peaked at 16.8
      - Normal range 12-26

MONITORING TOOL: LAB FLOW SHEET

	DATE																							
HEME	WBC																							
	Hgb																							
	Hct																							
	Platelets																							
	ESR																							
CHEMISTRY	Na+																							
	K+																							
	Ca++																							
	Cl-																							
	Mg++																							
	Total Bili																							
	Glucose																							
	CO2																							
	BUN																							
	Creatinine																							
	Uric Acid																							
	Alk Phos																							
	AST (SGOT)																							
	ALT (SGPT)																							
	T. Protein																							
	Albumin																							
	Cholesterol																							
USER DEFINED	Lipase																							
	Amylase																							
	ECG																							
	QTc																							
	TSH																							
OTHER	Weight (LBW)																							
	Vision-acuity																							
	Vision-color																							
DRUG LEVELS	Bedaquiline																							
	6h																							
	24h																							
	Pretomanid																							
	6h																							
	24h																							
	Linezolid	trough																						
	2h																							
	6h																							

Polling Question #3

What is the BEST way to treat a contact exposed to MDR-TB?

1. 3HP (3 months of INH rifapentine)
2. 2RZ (2 months of rifampin and PZA)
3. 6 months of PZA and EMB
4. 6-12 months of Levaquin or Moxifloxacin
5. Close monitoring without treatment for 2 years

CONTACT INVESTIGATION

- Large family and extended family members
  - Father's death gathering to plan for funeral and family gathering during the holiday
- Total contacts: 75
  - 17 contacts lived out of Sheboygan County jurisdiction
  - 45 contacts had a negative QFT x2
  - 7 contacts had QFT x1
  - 2 contacts had a TST reading of 0 mm x2
  - 2 contacts declined
- 2 conversions treated with Moxifloxacin/Levofloxacin

Challenges

Patient and Family

- Multigenerational family home
  - Family to temporarily move out
- Clients father died in December, 2019.
  - The client was not able to attend his funeral or burial out of state
  - Traditionally he would have been expected to manage and lead the family through this period
- Continued isolation after isolation from TB ended related to COVID-19

Public Health

- COVID 19 pandemic hit Wisconsin
- First BPaL regimen in the state
  - Medical appointments for the client were limited related to COVID restrictions
- Setting up VDOT for the first time
- Treatment costs were astronomical
  - Worked with TOBI admins and in house accounting department to ensure medications were paid for and available for the client

Success

- VDOT implementation
  - Eased stress related to COVID isolations and used less staff time
  - Implemented within our department as a whole
- Good working relationship with the client, hospital, infectious disease specialist, and the clients family
- We were able to share our modified assessment form R/T BPaL with other counties.
- Client was compliant and tolerated the regimen well with little to no side effects
- Post-treatment follow up to be completed in August, 2022
  - Symptom review and chest x-ray at 3 months (X2), 6 months and 12 months
  - If a chest xray would be abnormal, sputum would follow

Lessons learned

- Case management approach: role and responsibility of DPH
  - A lot of new items to track and stay on top of
- Payment Processing for this regimen was a new process
  - SCDPH paid for medications then sought reimbursement from the TB Dispensary program
- Utilized a different pharmacy with monthly ordering and payments
  - Metro Medical

Hearing from the client

- DPH received a thank you card, a plant and $100 gift card from the children of the client in thanks
  - The gift card was given to the Salvation Army

Intermission

Let’s take a 10 minute break!!

More Cases from the Field Marathon County Experience

Jessica Linzmeier, RN, BSN
PHN, Marathon County Health Department
Wausau, WI
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MCHD BPaL Client #1

- Hmong male in his 70s who moved to the United States in the 1990s as a refugee from Laos
- 14 mm TST at time of arrival—no LTBI treatment
- Spring ‘21, hospitalized for radiating chest pain and fatigue x 1-2 days and “throat clearing” x 1 week
- Chest CT: 2 RUL cavitary lesions; 2 other nodules in RLL
- HIV-negative

MCHD BPaL Client #1 (con't)

- Given his abnormal radiology findings and positive TST, thought to have pulmonary TB
- Client was initially started on RIPE
- GeneXpert in WI identified *rpoB* mutation (RIF-Resistant)
- RIPE treatment was stopped

Polling Question #4

Initial molecular testing for drug resistance is recommended for which of the following?

1. Patients from countries with high TB incidence
2. Patients previously treated for TB disease with recurrent disease
3. Patients with HIV infection
4. Patients who initially responded to TB treatment, then began to get worse
5. All of the above

Florida HEALTH

Bureau of Public Health Laboratories - Jacksonville

P.O. Box 210

Jacksonville, FL 32231

CLIA: 10D0645095

Patient: [redacted] **Date of Birth:** [redacted] **Sample #:** JTT21005681 (9988068)

Test	Result	Reference Range	Date Approved

Note: The *Mycobacterium tuberculosis complex* real-time PCR test is a laboratory developed test and is not an FDA approved method.

A "Negative" real-time PCR result does not mean that *Mycobacterium tuberculosis complex* (MTBc) is not present as false negative real-time PCR results can occur when the MTBc strain does not contain the DNA target (*IS6110* element).

A "Positive" real-time PCR result indicates the presence of MTBc DNA but does not confirm active disease. A "Positive" real time PCR result can occur when non-viable organisms or residual DNA is present.

3145	HAIN Test GenoType MTBDRplus	**rpoB point mutation detected** **katG point mutation detected** No inhA point mutation detected	RIF-R INH-R	06/10/2021

Note: –The HAIN test is investigational. Not intended for diagnostic purposes.
– The clinical application of the HAIN results should be determined by the responsible treating care provider; for assistance with the interpretation of results of this test, please contact the TB Physicians' Consultation Network at 800-4TB-INFO (800-482-4636).
–All control bands present (conjugate, amplification, TB complex, *rpoB*, *katG*, and *inhA*)
–As with any DNA-based assay, this test only screens the nucleic acid sequence and not the amino acid sequence. Therefore, it is possible that mutations that do not cause an amino acid exchange (silent mutations) will still produce the absence of one of the wild type probes.
The **GenoType MTBDRplus** test only indicates those resistances of the *M. tuberculosis* complex that have their origins in the *rpoB*, *katG* and *inhA* regions examined here. Resistances originating from mutations of other genes or gene regions as well as other rifampin and isoniazid resistance mechanisms will not be detected by this test.
The presence of multiple bacterial species in the sample to be analyzed might hamper the interpretation of the test.
Theoretically, a resistance can exist in spite of a wild type pattern. If, at investigation, the sample contains a strain that has developed only a partial resistance that is not covered by the mutation probes, the wild type pattern will appear. If the sample contains more than one *M. tuberculosis* strain (due to mixed culture or contamination) and one of these harbors a mutation that is not covered by the mutation probes, the wild type pattern will appear. As with other diagnostic assays, the results of this test may only be interpreted in combination with additional laboratory and clinical data available to the responsible treating care provider.

3146	HAIN Test GenoType MTBDRsl	No gyrA/gyrB point mutation detected No rrs and No eis point mutation detected	FQ-S INJ-S	06/10/2021

Client #1: MDDR from Florida Lab

JTT21005681, specimen. DOC: *5/31/2021*, DOR: 6/8/2021
MTBDR*plus*: *6/10/2021* DNA seq: 6/14/2021, MTBDR*sl*: *6/10/2021*,

Target	mutation	Detected by	Predicted (*6/15/2021*)	DST, MIC
katG (ORF, aa 225-345)	**Mut 1 present**	**MTBDR*plus***	**High level INH-R**	**INH=1.0 (R)**
rpoB (RRDR)	**Ser531Leu (TCG/TTG)**	MTBDR*plus*, DNA Seq.	**RIF-R, RFB-R**	**RIF=16 (R)**
mabA-inha promoter	No mutations	MTBDR*plus*		
gyrA/gyrB (QRDR, aa 1-132)	No mutations	MTBDR*sl* DNA seq.	*Possibly FQ-S	Levo=0.5 (S) Moxi=0.5 (S)
rrs (1400 region)	No mutations	MTBDR*sl*	*Likely S to injectable drugs (kan, ami, vio)	AK=0.25 (S)
eis (promoter)	No mutations	MTBDR*sl*	*Likely S to injectable drugs (kan)	
rplC (ORF, aa 84-217)	No mutations	DNA seq.	*Based on these results and due to potential contributory mutations at other loci, resistance to linezolid is not predicted but cannot be ruled out.	LZD=0.25 (S)

*Determination of MTBC Drug susceptibilities by culture growth (phenotypic) methods is the gold standard

Client #1 (cont'd)

- **Client's TB was MDR**—resistant to INH and RIF
- Medical co-morbidity: Insulin-dependent diabetes, hypertension, chronic kidney disease (stage 3), gout
- Medications: insulin (long and short acting), amlodipine, Lisinopril, pravastatin, sodium bicarb, cholecalciferol, folic acid, tramadol

- BPaL recommended (if patient and provider in agreement)

- Patient counseling/education conducted

Client #1: Challenge: Polypharmacy before BPaL

- Client initially had bottles of medications lined up every day; it was unclear if he was taking his medications as prescribed; Hba1c = 11.8
- Case manager brought a medication planner and set up client's medications to ensure client was receiving medications as prescribed; client's son was not receptive to learning how to set up medications
- FHCD Director contacted client's sons and explained that they needed to set up the medication planner themselves; it worked well overall but was challenging when sons were not available to fill planner on time, there was a new prescription, etc.

TB Alliance

Pill Burden for Drug-resistant TB Treatment

Client #1 Challenge: Getting Started with BPaL

- Finding a provider for MDR client
- Insurance authorization required for out of network provider
- Complex medical needs
- Multiple medical providers: ID, resident PCP, endocrinology, nephrology

Polling Question #5

Which of the following providers can treat a patient taking BPaL?

1. Infectious Diseases or Pulmonology specialists
2. Primary Care Physician
3. Nurse Practitioner
4. Medical 2nd year Resident
5. Any of the above

Client #1 Challenge: BPaL Procurement

- Prior authorization required by insurance for BDQ and PTM
  - Different “Patient Assistance Programs” for each
- BDQ very expensive - if client has any insurance they do not qualify for patient assistance program and state TB program will need to cover the difference
- Discussed using a traditional regimen, but BDQ would still be included

- BDQ only available from one pharmacy distributer nationwide
- PTM & LZD can be filled by any distributer
  - Aurora Pharmacy in Milwaukee

Polling Question #6

Should a different MDR-TB regimen be started while waiting for BPaL procurement?

1. Yes
2. No
3. It depends…

Client #1 Challenge: Delayed Initiation of BPaL

- Because of provider and insurance challenges, client did not start BPaL until 7 weeks after initial TB diagnosis
- Challenge building trust with client and family and explaining why client was not receiving TB medications for so long
- Client potentially becoming more infectious while waiting for medication and prolongation of isolation period
- Concerns about client and family members not adhering to voluntary isolation agreement (and involvement of FHCD Director, client relocating to county-sponsored housing)

BPaL Medication Storage

- BDQ must be kept in a dry, light-resistant container and cannot be stored in the same bottle/packaging with other medications
- PTM should not be removed from its original bottle for typical use
- LZD has no storage restrictions

BPaL Medication Administration

- Per Wisconsin TB Program, BPaL must be administered via DOT seven days per week throughout treatment
- Patients remain in isolation until cultures convert to negative
- After clients are released from isolation, video DOT may be an option in some situations

- BDQ dose is higher the first 14 days of treatment and is given daily, then dose is reduced and given only M, W, F
  - “Loading dose” because drug is widely distributed in the body

Polling Question #7

Which monitoring is NOT required in BPaL Clients?

1. Laboratory
2. Radiology
3. Vision
4. Hearing
5. ECG

BPaL Treatment Monitoring

Clinical monitoring for side effects

- Daily monitoring

  See worksheet O:\HEALTH\Communicable Disease\Tuberculosis\TB Forms\BPaL Daily Assessment Form Updated 2021-11-18.docx

- Weekly monitoring completed by case manager: O:\HEALTH\Communicable Disease\Tuberculosis\TB Forms\BPaL Weekly Assessment Form Updated 2021-11-18.docx

MCHD BPaL Daily Assessment Form

- SWITS start: SWITS end:
- DOT:
- Client Name: _____ Client DOB: _____
- Completed by: _____ Date Completed: _____
- Vitals: HR: RR: BP:
- Pain:
- BG readings: Noon: PM: HS: AM:
- Daily Symptom Check: Vision Changes, Photosensitivity, Pain with Eye Movement, Numbness/Tingling, Loss of taste
- Notes:

MCHD BPaL Weekly Assessment Form

- Weight, and *Same Items as daily assessment, plus:*
- TB-Related: Cough/Coughing up Blood, Fever, Night Sweats, Weight Loss without trying, Fatigue, Chest Pain, Shortness of Breath. (Notes:)
- Hypersensitivity/Anaphylaxis: Rapid onset of rash; Swelling or Airway Constriction; Hypotension. (Notes:)
- CNS/ENDO: Behavior Changes, Anxiety/Irritability, Vision Changes, Photosensitivity, Pain with eye movement, Headache, Dizziness, Confusion, Numbness/Tingling, Sleep changes, Loss of taste, Unusual thirst (Notes:)
- GI/GU/HEP: Nausea/Vomiting/Loss of appetite, Diarrhea/Constipation/Stool Color/Consistency, Blood or Mucus in Stool, Abdominal Cramping, RUQ Pain, Cola-Colored Urine or Stool, Decreased urine output, Jaundice, Heartburn (Notes:)
- Skin/MS: Rash/Itching, Muscle or Joint Pain; Gait Changes; Easy bruising, Nose bleeds
- Cardiac: Change in heartbeat, Palpitations, Dizziness, Fainting, Significant Hypertension (Notes:)

BPaL Treatment Monitoring (Cont'd)

Sputum collection

- Start 1.5 - 3 weeks after treatment initiation, depending on level of infectiousness/disease progression prior to treatment

- Collect sputum at least weekly or 2 - 3 samples every other week until **culture conversion**

- After culture conversion, collect sputum at least monthly throughout treatment and every 3-6 months for 24 months after treatment completion

Additional Monitoring during BPaL

ECG monitoring: BDQ can prolong QT interval

- Importance of EKG 2 weeks after treatment initiation and per protocol

*Providers of MCHD's client's have completed EKG testing at least monthly for the first few months of treatment

- Mobile devices can be used to obtain QTc (e.g., Kardia or smart phone)

Therapeutic Drug Monitoring (TDM): Serum levels of each drug collected at different time points to measure peak levels and clearance over time

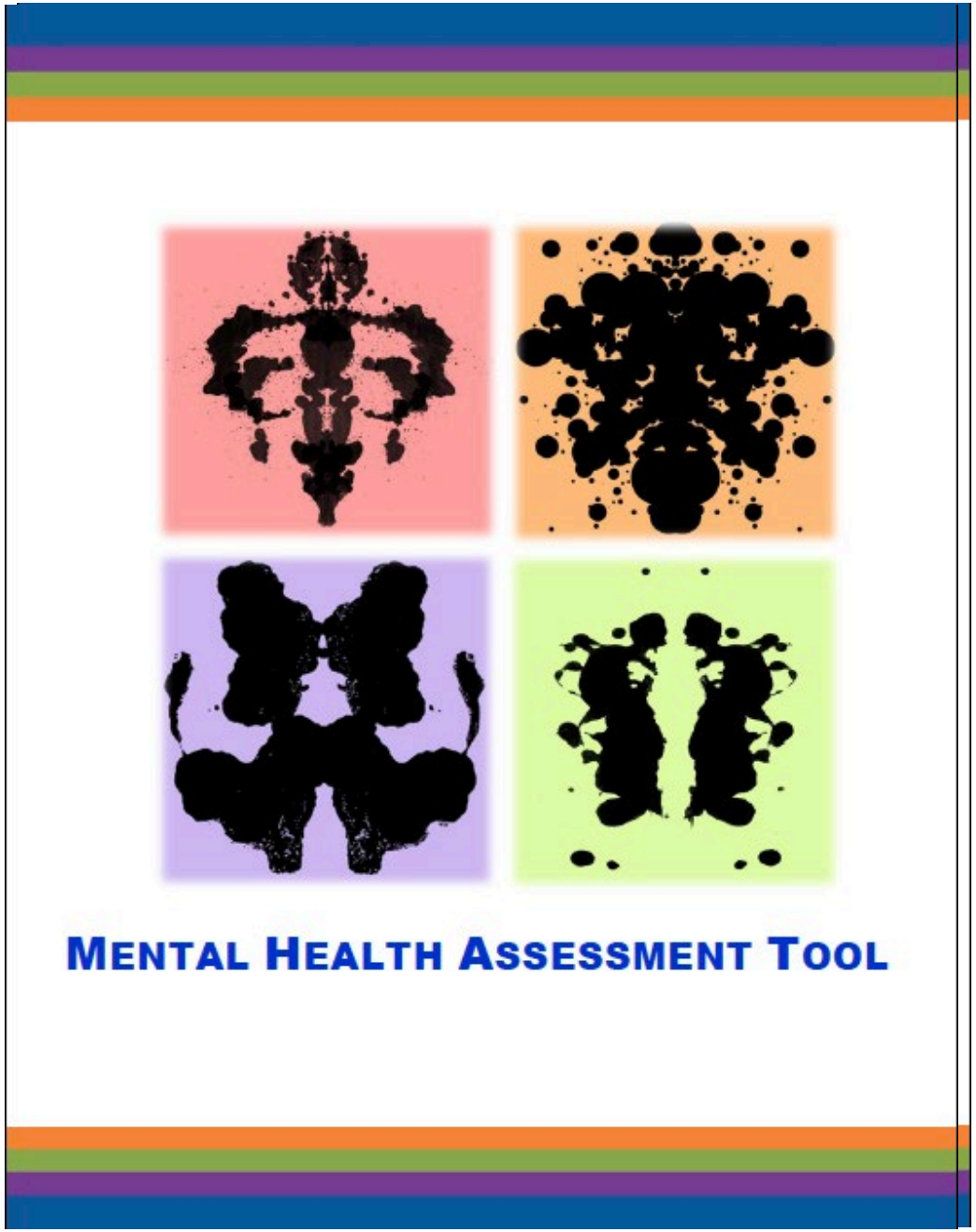
- Trough level before dose given (Keep low to minimize toxicity)
- Levels collected 2 and 6h after dose given to measure peak
- *LZD dosing frequency may be adjusted based on results

TDM: Serum Drug Levels of Client #1

	Trough (<2 ug/mL)	2h Peak (12-26ug/mL)	6h Peak (12-26 ug/mL)	Comment
Linezolid 600mg QD	9.3 (24h)	20.68	19.6	Trough far above 2. Hold 3 days and restart with longer dosing interval
Meds held	1.38 (48h)			
Meds held	0.22 (96h)			
Interval increased				
Linezolid 600mg MWF	Trace (48h)	13.7	8.7	Nl trough with intermittent dosing; Nl Peak

Client #1: Adverse Event During BPaL

- A few weeks later, new onset of chest pressure described as over entire chest, worse when sitting still, better when up and moving, radiating to his back, moderate to severe intensity.
- No shortness of breath, nausea/vomiting, diaphoresis, abdominal pain, numbness, weakness, tingling, trauma.
- Client went to the ER
- Chemistries, troponin, EKG were unremarkable; QTc unchanged
- CXR had improved since start of BPaL
- Given Toradol and prescription for albuterol inhaler and sent home



https://www.heartlandntbc.org/wp-content/uploads/2021/12/mental_health_screening_tool.pdf

Client #1: Other Challenges

- Total time from suspicion to TB to end of isolation: 4 months and three weeks
- Client was a difficult blood draw; he had a series of 4 blood draws two weeks into treatment and 2 blood draws 3 weeks into treatment
- Client’s BDQ script was only written for 24 weeks per instructions of national pharmacy; Additional delay waiting for PA for 2 remaining weeks of therapy

Special Considerations

- Extended isolation period for MDR and XDR clients
- Psychosocial considerations, more difficulty complying with isolation, postponed or canceled appointments for other health issues if phone or video visits are not available/not appropriate
- PHN case management scope versus role
- Hospitals' lack of access to BDQ and PTM for inpatients
- Potentially lengthy contact investigations and LTBI treatment of newly infected/newly identified contacts with LTBI

MCHD Client #2

- Hmong woman in her 80s (may be younger than stated age) who moved to US as a refugee in the 1990s
- TST upon US arrival was 16 mm; not treated for LTBI
- Comorbidities: diabetes, hypothyroidism, hyperlipidemia, congestive heart failure, pulmonary hypertension, B12 deficiency

- Developed worsening cough, shortness of breath, lower-grade fever, chills, night sweats and fatigue x 4-5 months
- HIV negative

Client #2 (cont'd)

- QFT: TB1-nil and TB2-nil values were both <1.
- CXR: bilateral non-enlarged axillary lymph nodes; Bulky, partially calcified mediastinal and bilateral hilar and paratracheal nodes
- CT: multifocal tree-in-bud opacities in both upper lobes, mediastinal and hilar lymph nodes
- Sputum: AFB smear +; PCR + for MTB; *rpoB* mutation on GeneXpert
- Molecular DST: mutations in *rpoB* (RIF), *katG* (INH) → **MDR TB**

Client #2 (cont'd)

- Earlier diagnosis of drug resistance led to earlier use of appropriate treatment
- Shorter waiting period to locate treating MD, address prior authorization forms for insurance coverage of BDQ and PTM
- BPaL started 1 month from day of admission to hospital and 19 days after molecular resistance results reported by CDC

Client #2 Challenge: Prolonged Conversion to Culture Negative

- First negative sputum culture was followed by another positive culture; all subsequent cultures have been negative
  - Requirement of 2 consecutive negative cultures prior to removal from isolation)
- If sputum culture grows non-TB mycobacterium, new culture must be started and grow for another 6 weeks before it can be reported out as negative for M. tb.

- Total time from suspicion of TB to end of isolation: 4 months and 2.5 weeks

Polling Question #8

Despite 2 months of BPaL treatment, your patient remains culture positive. Which is NOT a next step?

1. Check patient's adherence to treatment, even if taking DOT
2. Obtain serum levels for TB medications
3. Repeat drug-resistance testing
4. Change TB medications to something new

Therapeutic Drug Levels of Client #2

	Trough (<2 ug/mL)	2h Peak (12-26ug/mL)	6h Peak (12-26 ug/mL)	Comment
Linezolid 600mg QD	1.13 (24h)	17.66	11.54	Nl LZD trough; peaks indicate good absorption

Client #2: Increasing Neuropathy

- After 10 weeks of BPaL with LZD 600mg daily, she reported:
  - Her arms were hurting
  - Decreased sensation/increasing numbness in her fingers
  - Her right upper arm had pain/tightness
  - Her legs felt like they kept “falling asleep”
  - Legs felt weak and "trembling”
- She has underlying DM, hypothyroid and takes B12 injections
- No neuropathy reported at baseline
- Linezolid trough value was <2

Polling Question #9

What is the NEXT step for managing her increasing neuropathy?

1. Check her hemoglobin A1C and a serum glucose
2. Hold linezolid even though serum trough was low
3. Add B6 to her regimen
4. Ask the provider to increase B12 injections
5. Order nerve conduction studies

2nd BPaL Client: Increasing Neuropathy

- SNTC suggested holding Linezolid until symptoms resolved to let her mitochondria recover, then change to a TIW interval (M-W-F)
- Meds held over a weekend then restarted with Linezolid 600mg TIW
- Symptoms waxed and waned on meds for 4 TIW doses, then LZD permanently stopped by MD 12 weeks after BPaL started
  - BDQ and PTM continued after linezolid stoppex
- Numbness and tingling improved over ~2 months, “trembling” in legs persisted
- Client’s vision was also affected and improved after cessation of LZD
- Completed 6 months BPaL (BDQ and PTM) this week!

2nd BPaL Client: Vision/Neurologic Monitoring

Date	Tx start	5w	9w	10w	12w	13w	16w	19w	22w
L. eye	20/63	20/32	20/32	20/50	20/40	20/50	20/50	20/40	20/40
R. eye	20/80	20/50	20/50	20/63	20/63	20/63	20/63	20/50	20/50
Both	20/63	20/32	20/32	20/50	20/40	20/50	20/40	20/32	20/32
Color	ok	ok	ok	“so/so”	“guessing”			Great	
Neuro symptoms	Denies		Minimum sx	RUE>LUE hand falling asleep, pain 7-8, improved with Tylenol	Much improved, still in arms and legs	Still improving but present bilateral UE and LE	Numbness/tingling has “calmed down a bit”	Still “trembling” in legs; Numbness/ tingling gone	

Client #3

- 75yo Hmong (Laos) F wife of Client 1
- TST 0 mm upon arrival to United States in 1990s
- PMH: insulin-dependent DM, HTN, chronic kidney disease, neuropathy
- Spring ‘21, patient evaluated in ED for “leg swelling”
  - Complained of fatigue and cough since her covid vaccine the prior month
  - Ankle edema on exam
  - CXR: Patchy R lower lobe opacity, could reflect atelectasis or pneumonitis, no consolidation, effusion or pneumothorax. Follow up recommended.
- ED discharge dx – “pneumonia”, leg edema, gout, chronic renal failure
- Treated with Ceftin and Prednisone

Polling Question #10

If this patient has TB, the prednisone might make her symptoms….

1. Worse
2. Better
3. Both
4. Neither

Client #3

- 2 months later, she returned to ED c/o worsening weakness for several months; paresthesia on plantar surface of both feet; difficulty walking - uses assistant device. No other focal weakness, pain or fever.
- CXR: chronic opacities at lung bases unchanged from prior visit
- Meds: Insulin, lasix, prednisone, flexeral, tramadol, tylenol, losartan, simvastatin
- ER disposition- fatigue, malaise and anxiety about husband's illness
- A few weeks later, she was evaluated in husband's CI
  - Initial T Spot: Panel A=1 & Panel B= 3 spots (Negative, valid controls);
  - Reported coughing x1 month

Polling Question #11

Does the negative T-spot rule out TB disease in this patient?

1. Yes
2. No
3. I don’t know…

Client #3

- 7wk later, repeat T-spot “positive”: Panel A=19 & Panel B=34
- Now denies symptoms except fatigue
- CTA chest, abd and pelvis: Multiple lung nodules
- 3 Sputum collected - all were AFB smear negative; NAAT not done
- CT - guided biopsy of RLL lung nodule performed, AFB smear neg
- Two of three sputum were culture positive for M. tb after 6 weeks
- GeneXpert on culture growth was positive for TB and + for *rpoB* (rifampin resistant)

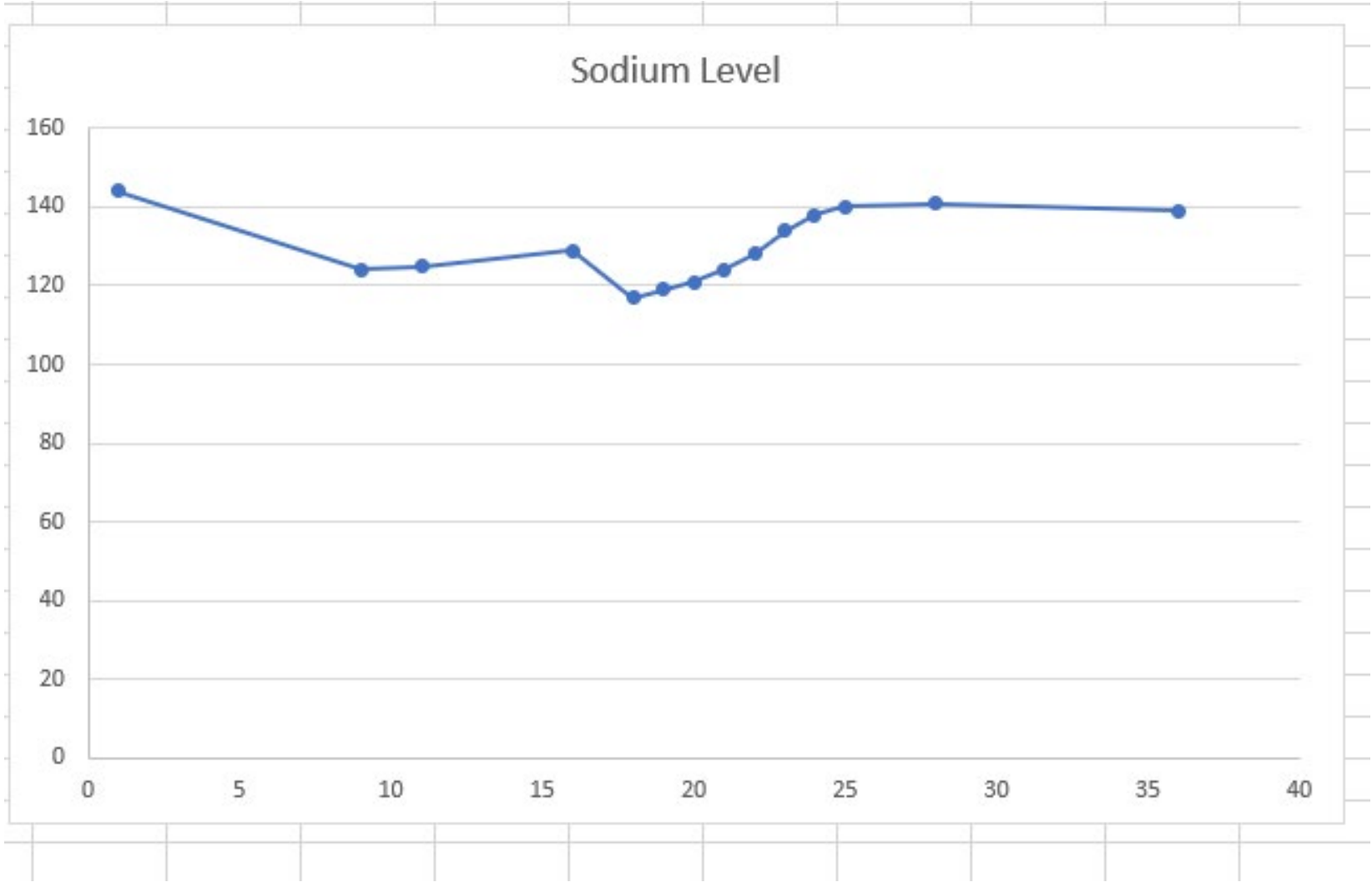
Client #3

- Client's PCP agreed to order BPaL and manage client's TB
- HIV Negative
- BPaL could not be prescribed until full molecular sensitivities were completed
- CDC reported INH and RIF, confirmed in Florida PH lab
- Client started BPaL 3 weeks after TB diagnosis via positive sputum cultures
- Total time from TB diagnosis to end of isolation: 3 months, 1 week

Client #3: Hospitalization during BPaL

- Less than 2 weeks into treatment, client developed hyponatremia and hypomagnesemia
- On day 16 client was hospitalized with NA 117 and Mag 1.7, accompanied by nausea, vomiting, dehydration and weakness
- Cardiac CCU, QT interval not prolonged
- BPaL held until nausea and vomiting improved, electrolytes replaced
- Client found to have TB-associated adrenal insufficiency and steroids were replaced

Client #3: Sodium Levels by Day



MDR Contact Investigations and LTBI Treatment

- CI can take months if there are household contacts or caregivers who initially test negative for TB infection (related to ongoing exposure and extended client isolation)
- If contacts are newly infected, must know susceptibilities of index case(s) to determine appropriate treatment
- If susceptible, Moxifloxacin and levofloxacin are used for MDR LTBI treatment for adults; for children less than age 15, levofloxacin is preferred
- If newly infected contacts are not treated for MDR LTBI, monitoring should occur every six months for at least 2 years

SNTC Final Comments

Prior to Starting	**Week 1-2**	**Week3-4**	**Month 2**	**Month 3**	**Month 4**	**Month 5**	**Month 6**	**End of TX**
Assess for symptoms and signs of liver disease (such as fatigue, anorexia, nausea, jaundice, dark urine, liver tenderness, and hepatomegaly)	X	X	X	X	X	X	X	Post-treatment follow up for relapse 1,2,3,6,9,12,15,18 and 24 months
Monitor for side effects: *See below:*	X	X	X	X	X	X	X	
Laboratory tests: ALT, AST Alkaline phosphatase Bilirubin CBC Serum Potassium Calcium Magnesium	Week 2	Week 4	X	X	X	X	X	
HIV CD4 if positive for HIV Pregnancy females								
Request MIC levels for Linezolid								
Linezolid Serum levels Peak 2 hrs. after meds are ingested Trough 24 hours after last dose before next dose	Week 2							
Prior to Starting	Week 1-2	Week3-4	Month 2	Month 3	Month 4	Month 5	Month 6	End of TX
Sputum If patient is unable to produce document attempt	X	X **Check for sputum conversion**	X	X	X	X	X	X
Vision Acuity/color discrimination	X	X	X	X	X	X	X	X

Serum Linezolid level at 6h helpful for delayed absorption
Mental health screening at baseline, as indicated
Neurologic screening
QTc screening

Take Home Points

- Rapid molecular diagnostics and new safer treatment regimens are HERE
- Shorter all oral BPaL for MDR or TI TB treatment appears safe and effective
- Seek expert consultation for TB complex patients
- TB nurses and programs are the key to successful treatment and cure
- Sharing experiences builds capacity and informs practice
- *This is only the beginning of a new era in TB!*

Acknowledgements

- Wisconsin State and Local TB Program Staff and lab
- Wisconsin Virtual TB Summit Planning Committee
- Dave Ashkin, SNTC
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- Heidi Hammond-Epstein, SNTC
- SNTC Team
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- Chuck Peloquin, UFL ID Pharmacokinetics lab
- Neela Goswami, CDC DTBE
- Sister TB COEs (GTBI, HNTC, CITC)
- VA TB Foundation
- Global TB Alliance

Therapeutic Drug Monitoring

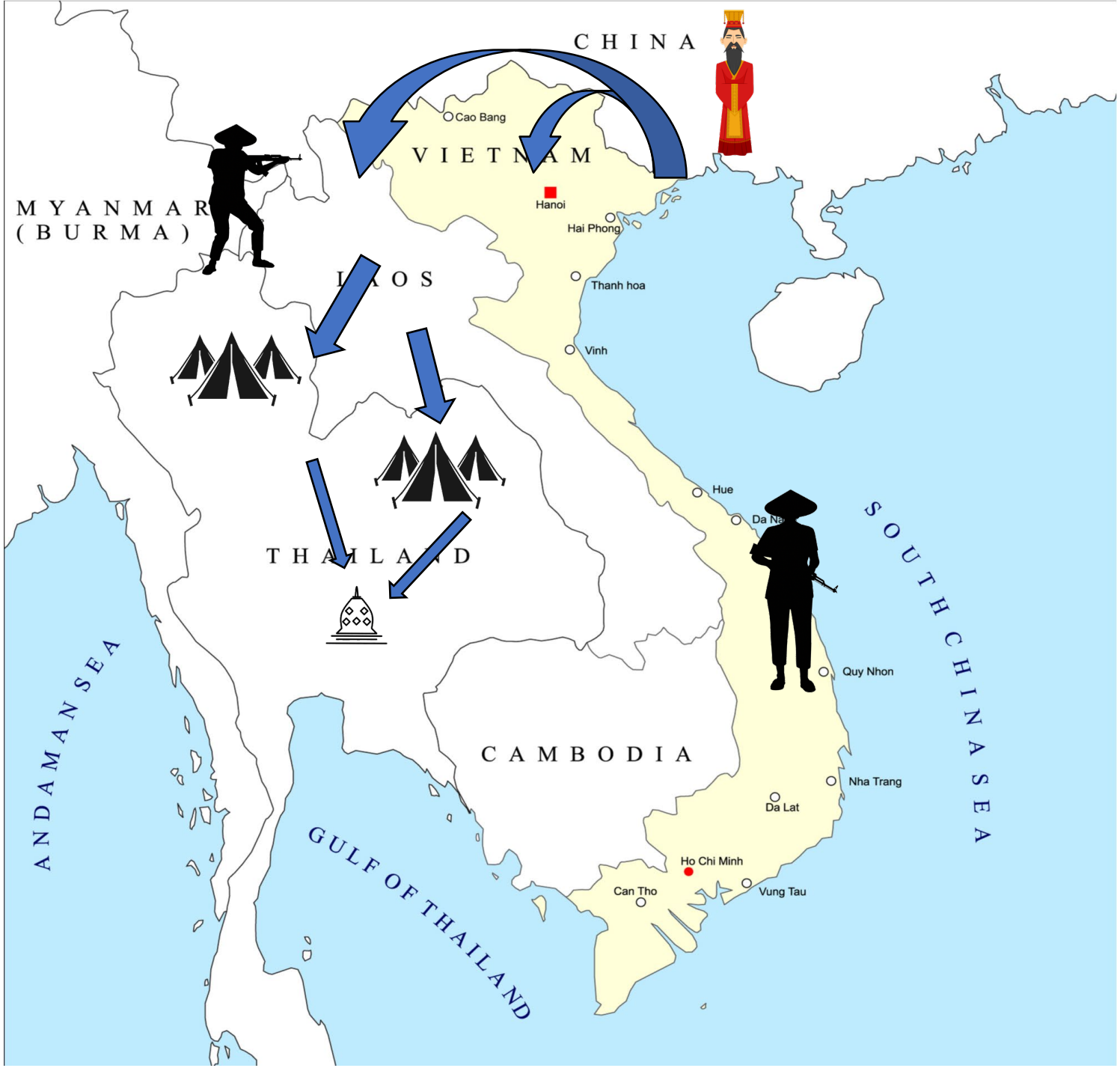
- University of Florida Infectious Diseases Pharmacokinetic Laboratory https://idpl.pharmacy.ufl.edu/formsand-catalog/
- National Jewish Medical Center https://www.nationaljewish.org/for-professionals/diagnostic-testing/adx/our-laboratories/therapeutic-drug-monitoring

SNTC Consult Team: 1 800 4 TB INFO

Hmong Population in Wisconsin

Philip Wegner RN, MPH
TB Nurse Consultant
Wisconsin TB Program


Hmong Community
of Sheboygan


CHINA
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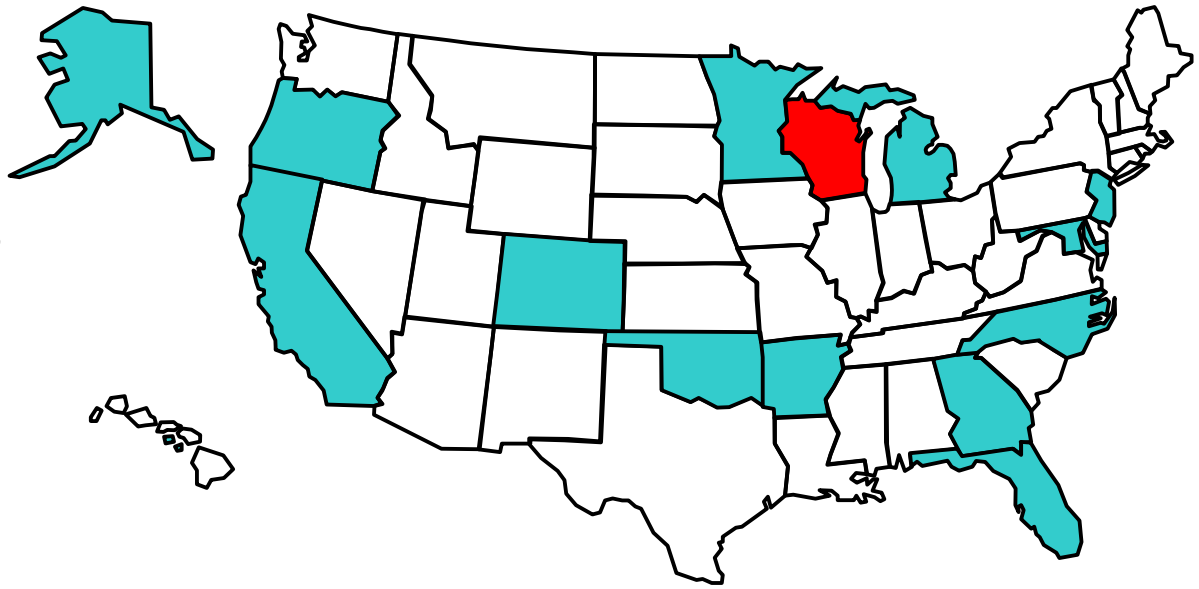
MYANMAR
(BURMA)
LAOS
Thanh hoa
Vinh
Hue
Da Nang
THAILAND
SOUTH CHINA SEA
ANDAMAN SEA
Quy Nhon
CAMBODIA
Nha Trang
Da Lat
GULF OF THAILAND
Ho Chi Minh
Can Tho
Vung Tau

327,000 Hmong estimated in the US (2020 Census)

Top 10 Hmong Populations by State

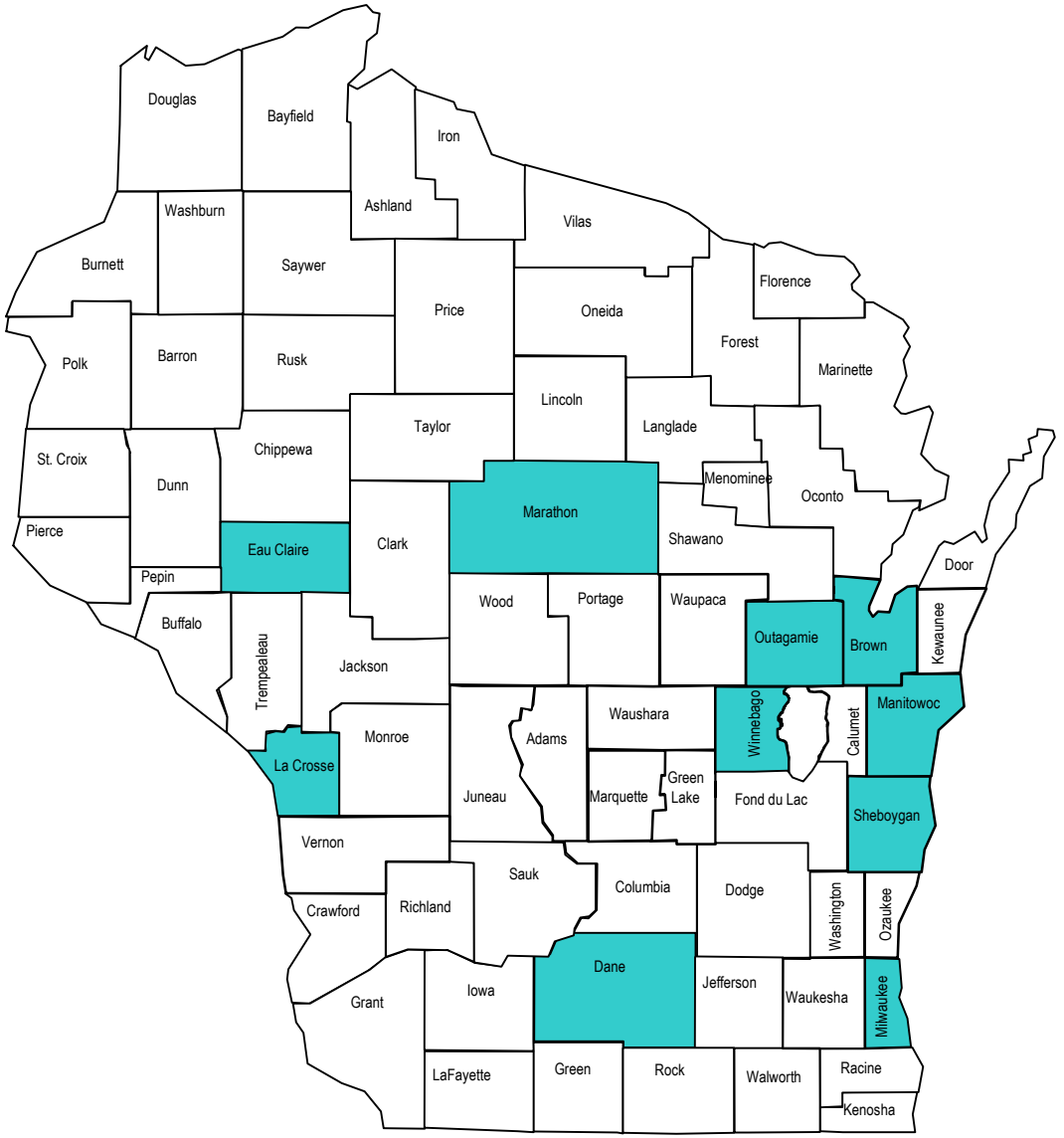
1. California – 96,255
2. Minnesota – 71,762
3. Wisconsin – 54,641
4. N. Carolina – 11,315
5. Michigan – 5,336
6. Colorado – 4,311
7. Alaska – 4,285
8. Georgia – 4,175
9. Oklahoma – 3,908
10. Oregon – 2,490



54,641 Hmong estimated in Wisconsin (2020 Census)

Top 10 Hmong Population by County

1. Milwaukee – 13,529
2. Marathon – 6,238
3. Sheboygan – 4,993
4. Dane – 6,626
5. Brown – 4,354
6. Outagamie – 3,604
7. La Crosse – 3,454
8. Winnebago – 2,748
9. Eau Claire – 2,209
10. Manitowoc – 1,810



Family

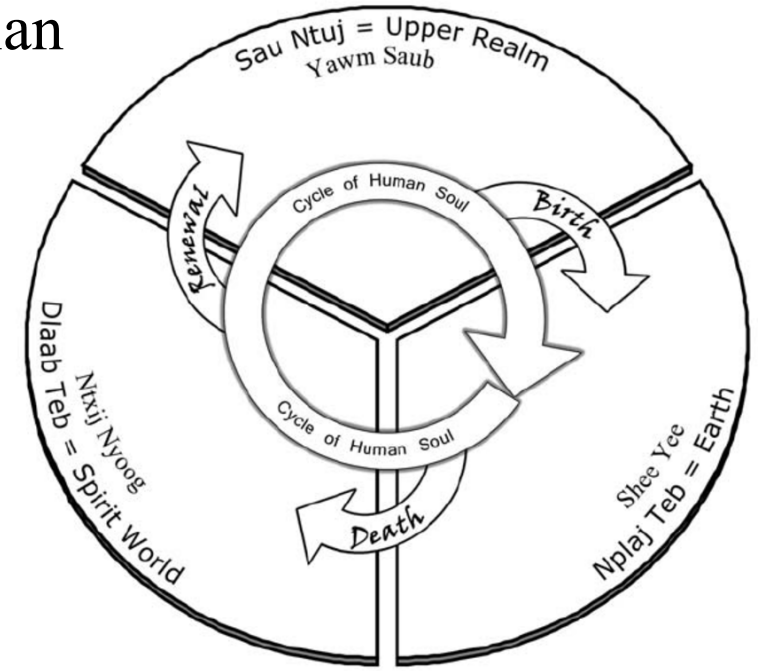
Patriarchal and Patralinial
Clan is everyone with that last name
Clan exogamy –marry from different clan

Illness

Separation of body and souls
(more than one in each body)
Caused by suffering ancestral spirits
Shaman is a contact between worlds
Western medicine not the best treatment

Religion

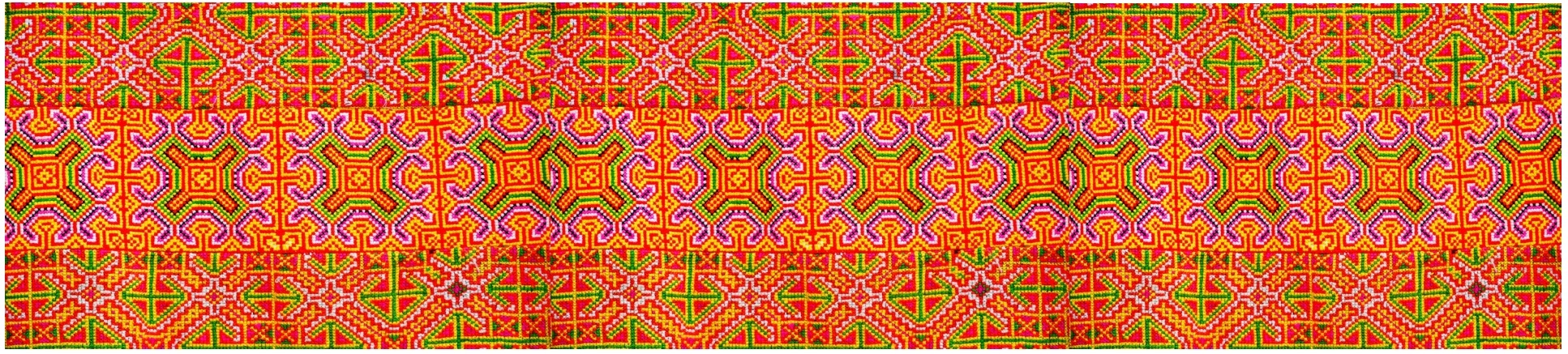
Animistic (65%)



Christian
(35%)

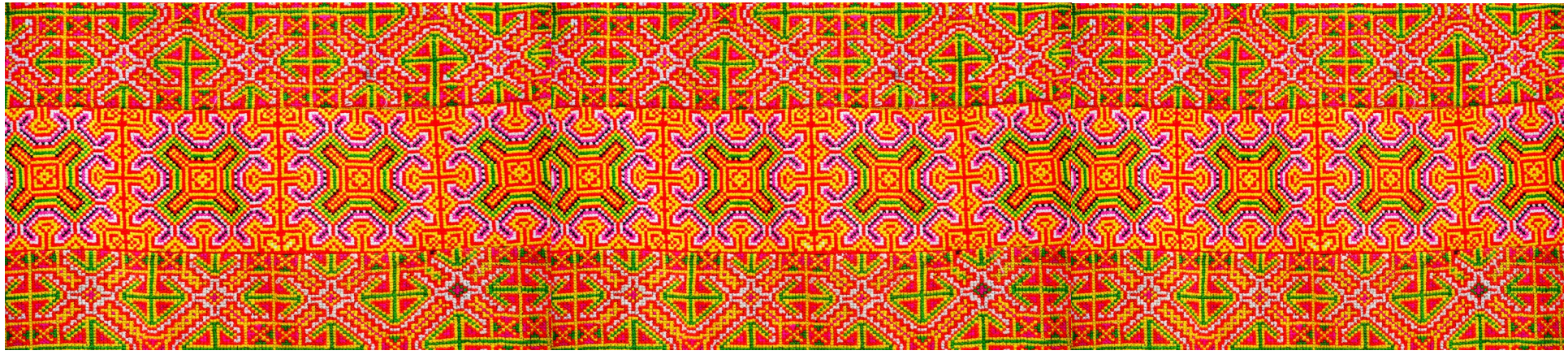
Recommendations/Tips

- Show respect for individuals and culture
- Be humble and explain everything
- Build trust which takes time
- Careful not to have them Lose Face
- Eye Contact, Body Language/Tone is important
- Hmong Time
- Caution with touch (especially of the head)



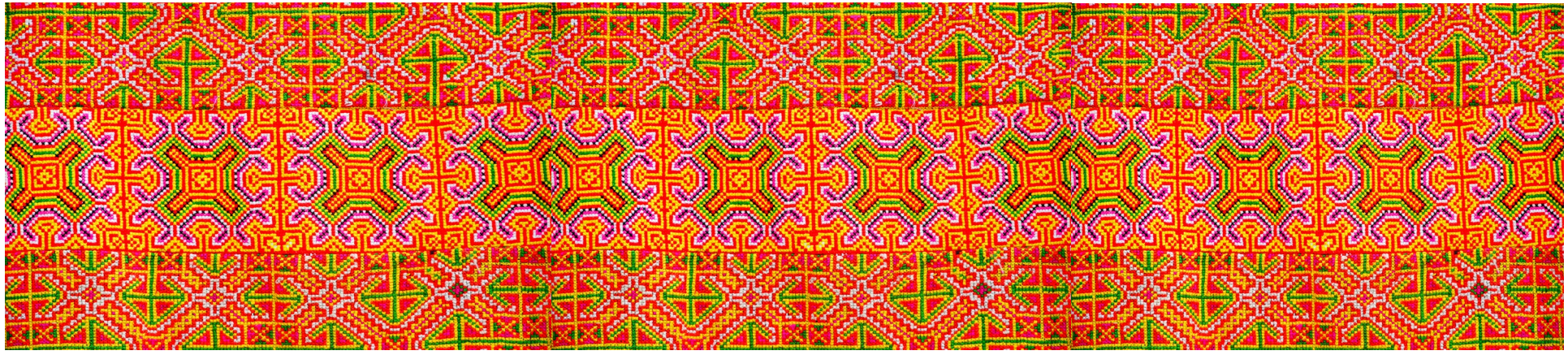
Examples

Most traditional Hmong families do not enjoy hearing direct comments about their children, especially infants and babies. A comment such as "your child is cute" is **not** looked upon favorably. Many Hmong believe that if a bad spirit hears such comments, it might come and take the child's soul away



Examples

When talking to a Hmong person, he or she may not look directly at you or give eye contact. The person you are speaking to may look down or away from you. Traditionally looking directly into the face of a Hmong person or making direct eye contact is considered to be rude and inappropriate.



Hmong patient education resources

Yam Uas Koj Yuav Tsum Tau Paub Txog Ntawm Koj Cov Tshuaj Kho Tus Kab Mob Sib Kis Vas Nab Lauj (TB)

Tshuaj RIFAMPIN

Koj tau txais cov tshuaj los mus kho koj tus kab mob sib kis Vas Nab Lauj (TB) lawm. Koj tsis muaj tus kab mob Vas Nab Lauj (TB) thiab tsis tau kis tus kab mob Vas Nab Lauj (TB) rau ib leej tib neeg twg. Cov tshuaj no yuav pab kom koj **ZAM DHAU** kev kis tau tus kab mob Vas Nab Lauj (TB).

Nyob rau lub sij hawm uas noj Cov Tshuaj no:

- Qhia rau koj tus kws kho mob los sis tus nawj yog hais tias koj muaj lus nug los sis nyhav siab txog ntawm cov tshuaj.
- Mus ntsib koj lub tsev kho mob raws li daim phiaj xwm.

Yam Uas Koj Yuav Tsum Tau Paub Txog Ntawm Koj Cov Tshuaj Kho Tus Kab Mob Sib Kis Vas Nab Lauj (TB)

Tshuaj ISONIAZID

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Yam Uas Koj Yuav Tsu Tau Paub Txog Ntawm Koj Cov Tshuaj Kho Tus Kab Mob Sib Kis Vas Nab Lauj (TB)

Tshuaj ISONIAZID thiab RIFAPENTINE

Koj tau txais cov tshuaj los mus kho koj tus kab mob sib sis Vas Nab Lauj (TB). Koj tsis muaj tus kab mob Vas Nab Lauj (TB) thiab tsis tau kis tus kab mob Vas Nab Lauj (TB) rau ib leej tib neeg twg. Cov tshuaj no yuav pab kom koj **ZAM DHAU** kev kis tau tus kab mob Vas Nab Lauj (TB).

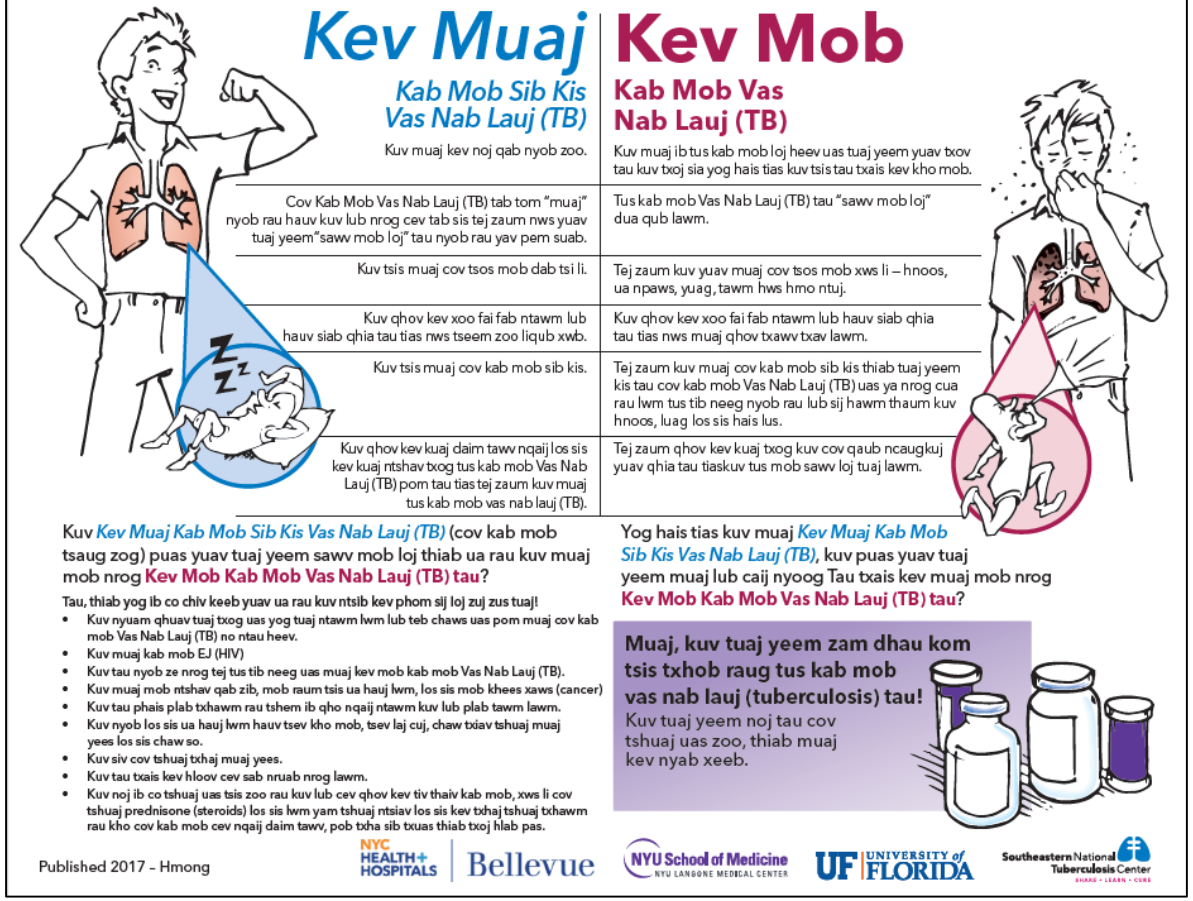
Nco Qab Ntsoov Tuaj Cuag Peb Nyob Rau Txhua Lub Lim piam:

Koj yuav tau ntsib tus neeg ua hauj lwm ntawm lub chaw saib xyuas kev nyab xeeb los mus muab cov ntshuaj rau koj. Cov phiaj xwm no raug hu ua kev kho mob los ntawm kev kho mob tsom kwm ncaj nraim (directly observed therapy (DOT)).

DOT tuaj yeem muab kev pab rau koj tau ntau txoj hau kev.

- Tus neeg ua hauj lwm ntawm lub chaw saib xyuas kev nyab xeeb yuav pab cim tseg los mus

Saib txog Cov Teeb Meem Tuaj Yeem Tshwm Sim Tau ntawm no:



Kev Muaj

Kab Mob Sib Kis Vas Nab Lauj (TB)

Kuv muaj kev noj qab nyob zoo.

Cov Kab Mob Vas Nab Lauj (TB) tab tom "muaj" nyob rau hauv kuv lub nrog cev tab sis tej zaum nws yuav tuaj yeem "saww mob loj" tau nyob rau yav pem suab.

Kuv tsis muaj cov tsos mob dab tsi li.

Kuv qhov kev xoo fai fab ntawm lub hauv siab qhia tau tias nws tseem zoo liqub xwb.

Kuv tsis muaj cov kab mob sib kis.

Kuv qhov kev kuaj daim taww nqaij los sis kev kuaj ntshav txog tus kab mob Vas Nab Lauj (TB) pom tau tias tej zaum kuv muaj tus kab mob vas nab lauj (TB).

Kev Mob

Kab Mob Vas Nab Lauj (TB)

Kuv muaj ib tus kab mob loj heev uas tuaj yeem yuav txov tau kuv txoj sia yog hais tias kuv tsis tau txais kev kho mob.

Tus kab mob Vas Nab Lauj (TB) tau "saww mob loj" dua qub lawm.

Tej zaum kuv yuav muaj cov tsos mob xws li – hnoos, ua npaws, yuag, tawm hws hmo ntuj.

Kuv qhov kev xoo fai fab ntawm lub hauv siab qhia tau tias nws muaj qhov txaww txav lawm.

Tej zaum kuv muaj cov kab mob sib kis thiab tuaj yeem kis tau cov kab mob Vas Nab Lauj (TB) uas ya nrog cua rau lwm tus tib neeg nyob rau lub sij hawm thaum kuv hnoos, luag los sis hais lus.

Tej zaum qhov kev kuaj txog kuv cov qaub ncaugkuj yuav qhia tau tiaskuv tus mob sawv loj tuaj lawm.

Kuv *Kev Muaj Kab Mob Sib Kis Vas Nab Lauj (TB)* (cov kab mob tsaug zog) puas yuav tuaj yeem sawv mob loj thiab ua rau kuv muaj mob nrog Kev Mob Kab Mob Vas Nab Lauj (TB) tau?

Tau, thiab yog ib co chiv keeb yuav ua rau kuv ntsib kev phom sij loj zuj zus tuaj!

- Kuv nyuam qhuav tuaj txog uas yog tuaj ntawm lwm lub teb chaws uas pom muaj cov kab mob Vas Nab Lauj (TB) no ntau heev.
- Kuv muaj kab mob EJ (HIV)
- Kuv tau nyob ze nrog tej tus tib neeg uas muaj kev mob kab mob Vas Nab Lauj (TB).
- Kuv muaj mob ntshav qab zib, mob raum tsis ua hauj lwm, los sis mob khees xaws (cancer)
- Kuv tau phais plab txhawm rau tshem ib qho nqaij ntawm kuv lub plab tawm lawm.
- Kuv nyob los sis ua hauj lwm hauv tsev kho mob, tsev laj cuj, chaw txiav tshuaj muaj yees los sis chaw so.
- Kuv siv cov tshuaj txhaj muaj yees.
- Kuv tau txais kev hloov cev sab nruab nrog lawm.
- Kuv noj ib co tshuaj uas tsis zoo rau kuv lub cev qhov kev tiv thaiv kab mob, xws li cov tshuaj prednisone (steroids) los sis lwm yam tshuaj ntsiav los sis kev txhaj tshuaj txhawm rau kho cov kab mob cev nqaij daim tawv, pob txha sib txuas thiab txoj hlab pas.

Yog hais tias kuv muaj *Kev Muaj Kab Mob Sib Kis Vas Nab Lauj (TB)*, kuv puas yuav tuaj yeem muaj lub caij nyoog Tau txais kev muaj mob nrog Kev Mob Kab Mob Vas Nab Lauj (TB) tau?

Muaj, kuv tuaj yeem zam dhau kom tsis txhob raug tus kab mob vas nab lauj (tuberculosis) tau!

Kuv tuaj yeem noj tau cov tshuaj uas zoo, thiab muaj kev nyab xeeb.

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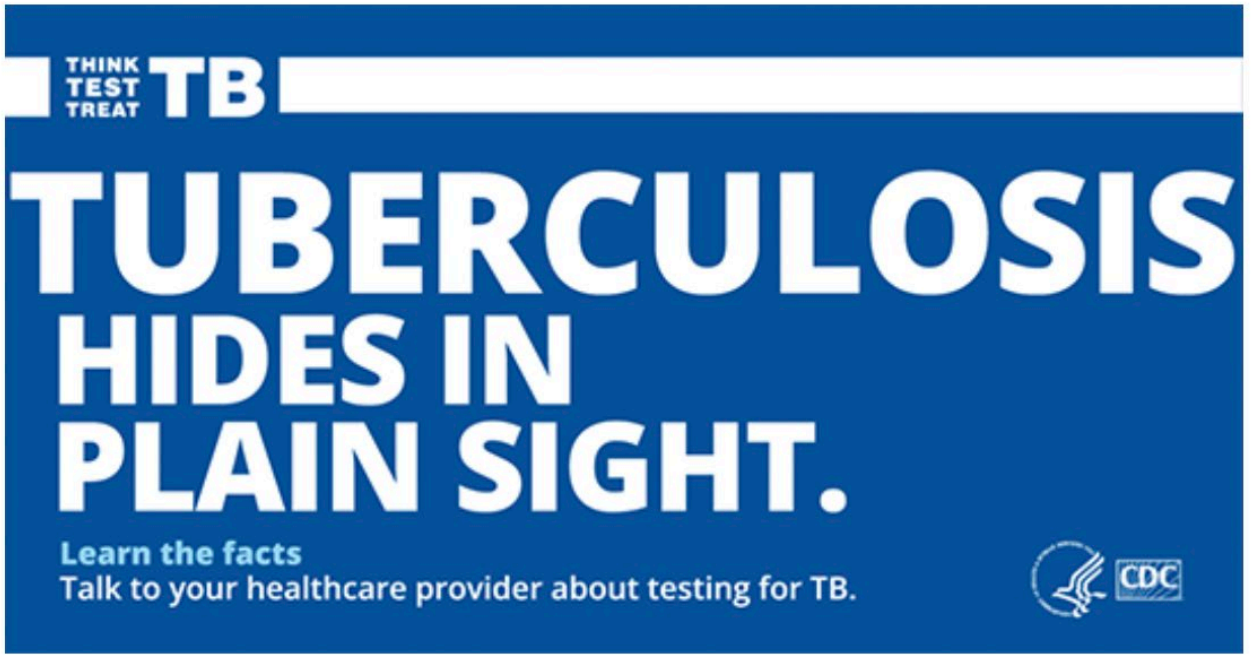
NYU School of Medicine NYU LANGONE MEDICAL CENTER

UF UNIVERSITY of FLORIDA

Southeastern National Tuberculosis Center

CDC Launches Think. Test. Treat TB Campaign in U.S.



CDC has launched *Think. Test. Treat TB*, the first national communications campaign to increase testing and treatment for latent tuberculosis (TB) infection in the United States. Eliminating TB in the United States requires expanding testing and treatment of latent TB infection. **READ MORE** →

Thank You Wisconsin TB Family!