



*Syndemic Infectious Disease Provider Conference*

# Treatment Advances for Tuberculosis

**Kathy Ritger, MD, MPH**

**Medical Director, Tuberculosis Program**

**Chicago Department of Public Health**

**May 2, 2023**



*I have no financial interest to disclose.*

*This continuing education activity is managed by The St. Louis STI/HIV Prevention Training Center and accredited by Missouri State Medical Association (MSMA) in cooperation with the Chicago Department of Public Health.*

# ★ *“Tuberculosis? We still have that here?”*

- TB is curable

**YET,**

- An estimated 10.6 million people developed TB and 1.6 million died from TB worldwide in 2021
- Why?
  - Lack of healthcare access
  - Stigma
  - Lack of implementation of better diagnostics and treatments
  - Lack of an effective vaccine

## Fig. 2.1.2 Estimated TB incidence in 2021, for countries with at least 100 000 incident cases

The eight countries that rank first to eighth in terms of numbers of cases, and that accounted for two thirds of global cases in 2021, are labelled.

***“Until the COVID-19 pandemic, TB was the leading cause of death from a single infectious agent, ranking above HIV/AIDS.”***

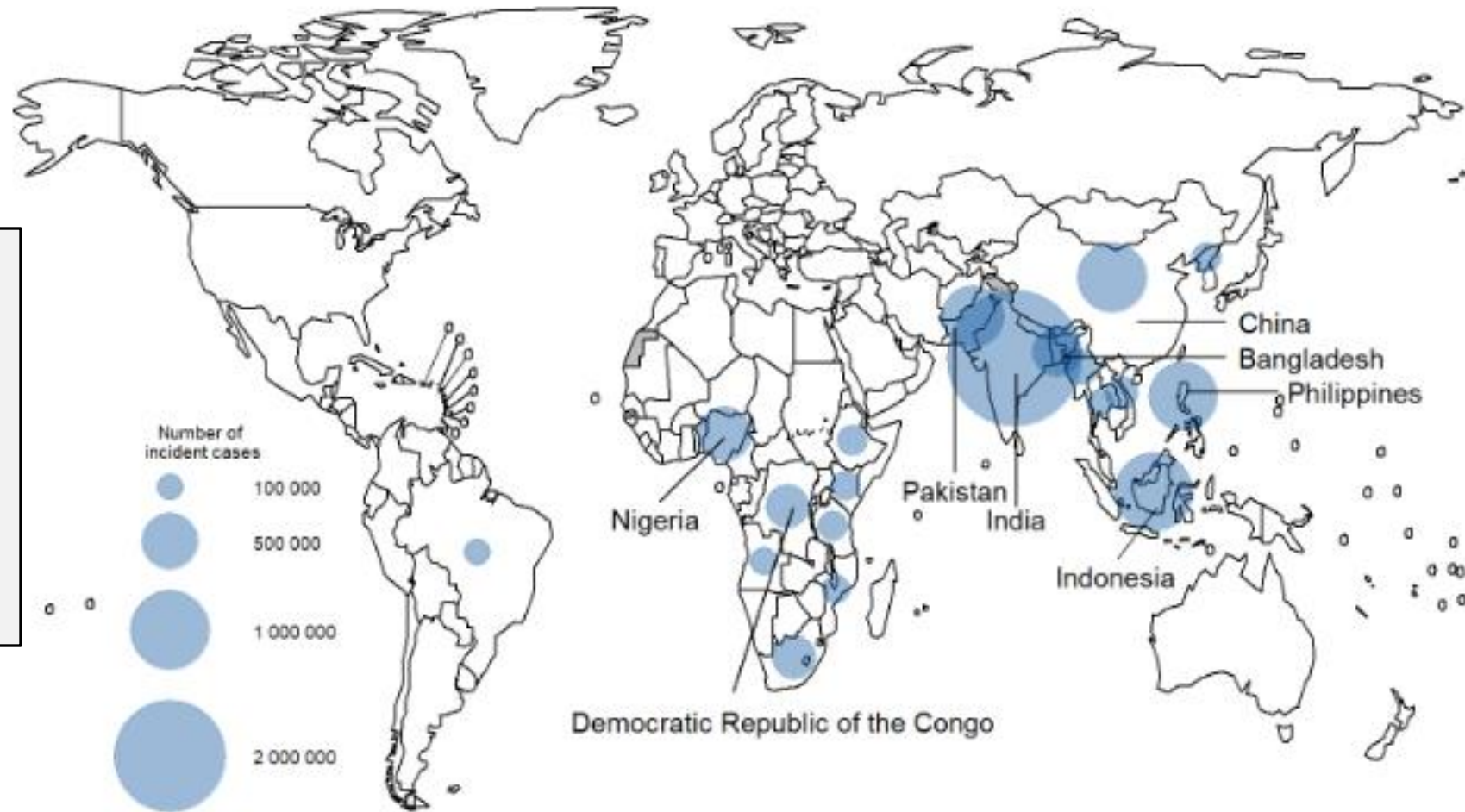
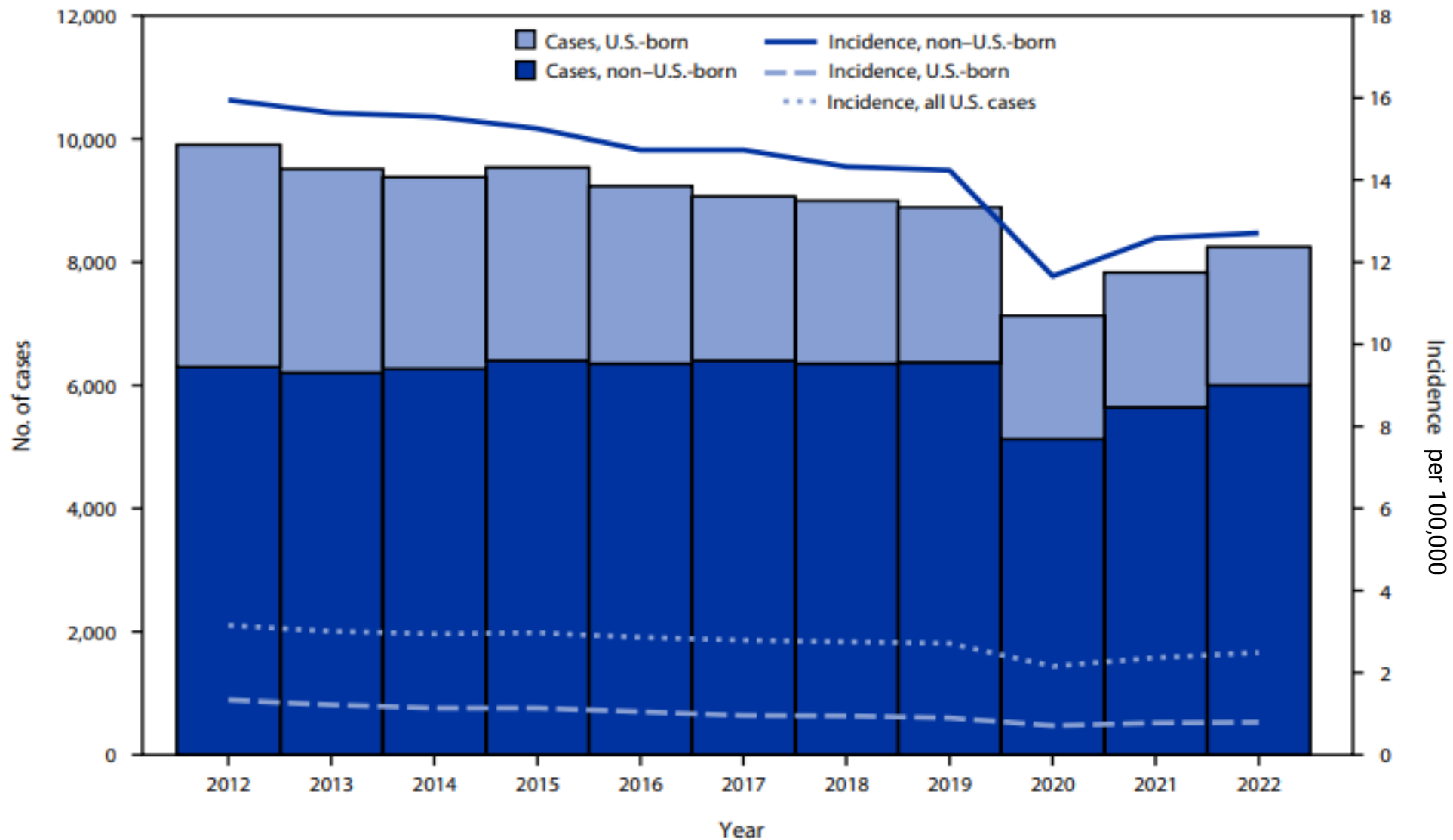
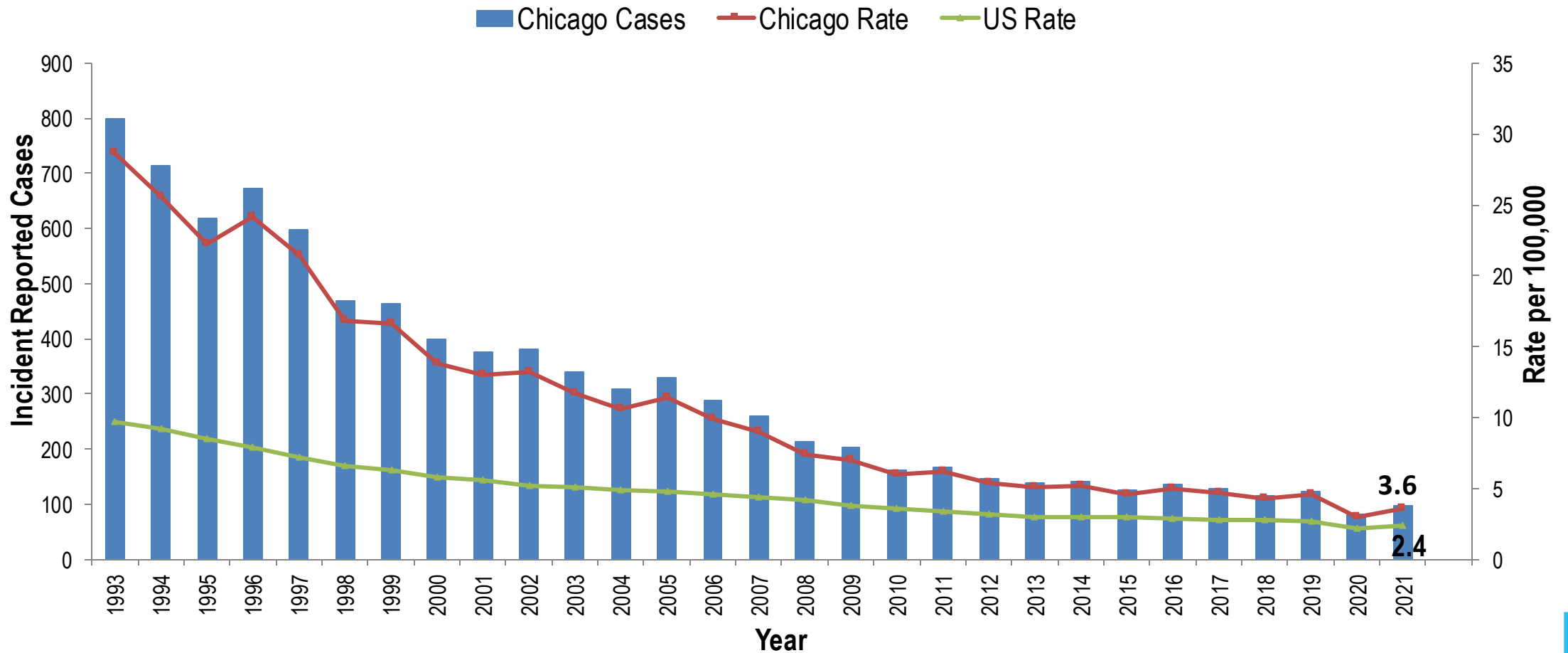


FIGURE. Tuberculosis disease cases\* and incidence,† by patient U.S. birth origin status<sup>§,¶</sup> — National Tuberculosis Surveillance System, United States, 2012–2022



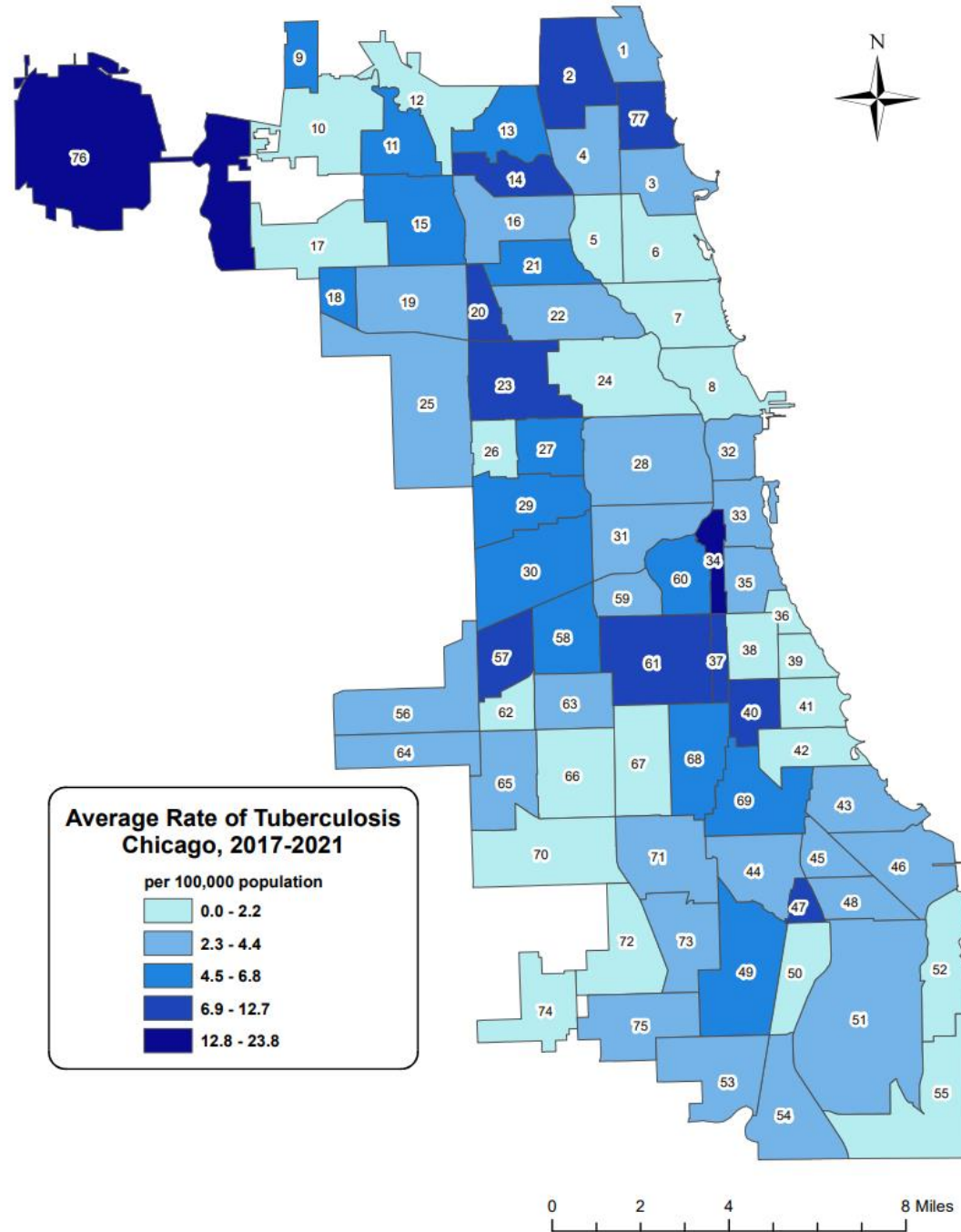


# Trend in TB Case Count and Rate, United States and Chicago, 1993-2021






# TB Case Rate by Chicago Community Area, 2017-2021





# Recent TB Treatment Advances



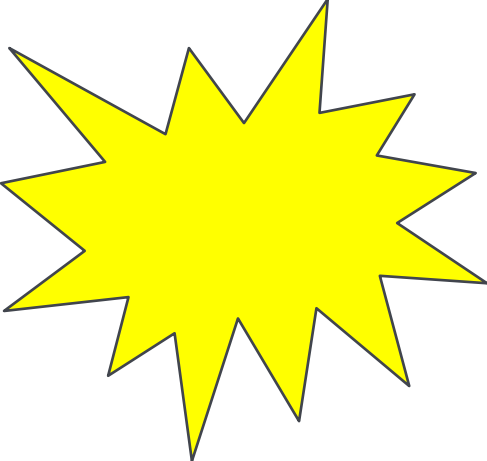

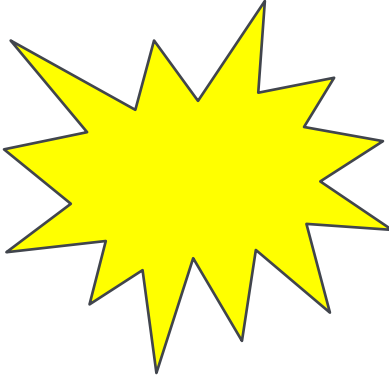

1. Shorter duration for drug-susceptible TB
  2. Shorter duration all-oral regimen for drug-resistant (or drug-intolerant) TB
- 
- 
- 
- 





# Recent TB Treatment Advances



- 1. Shorter duration for drug-susceptible TB**
  2. Shorter duration all-oral regimen for drug-resistant (or drug-intolerant) TB
- 
- 
- 
- 

# ★ Standard Treatment for Drug-Susceptible TB

Drug Name	Casual/ U.S. Abbreviations	WHO Abbreviations
Rifampin	R	R
Isoniazid	I	H
Pyrazinamide	P	Z
Ethambutol	E	E

Duration: 6 months

2-month intensive phase all four drugs

+

4-month continuation phase of R and I

= **2HRZE/4HR**



# 4-Month Regimen for Pulmonary TB with rifapentine and moxifloxacin



Drug Name	WHO Abbreviation
Isoniazid	H
Rifapentine	P
Moxifloxacin	M
Pyrazinamide	Z

- TB Trial Consortium Study 31 results published May 2021\*
  - Noninferior to standard treatment
- CDC endorsed February 2022
  - Approved for pulmonary TB
  - Age  $\geq 12$  yrs; weight  $> 40$ kg
  - Okay for HIV+ with  $CD4 > 100$
- Regimen consists of
  - 8-week intensive phase of HPMZ
  - +
  - 9-week continuation phase of HPM

**= 2HPMZ/2HPM**

\*Available at: <https://www.nejm.org/doi/full/10.1056/NEJMoa2033400>

# ★ 4-Month Regimen Pros & Cons





## ADVANTAGES

- Shorter duration!
- Facilitates treatment completion for patients planning to relocate or those in congregate or institutional settings
- Avoids potential ocular toxicity from ethambutol
- May reduce time to culture conversion

## DISADVANTAGES





- Greater number of daily pills
- Potentially higher drug cost
- Potential side effects of moxifloxacin
  - QTc prolongation
  - Tendonitis
- Limited long-term outcome data
- Lack of data for extrapulmonary TB
- Most susceptibility panels do not include fluoroquinolones

# ★ Comparison of Standard and Short Course Regimens

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

Photos courtesy of George Lee, RN

# ★ Comparison of Standard and Short Course Regimens

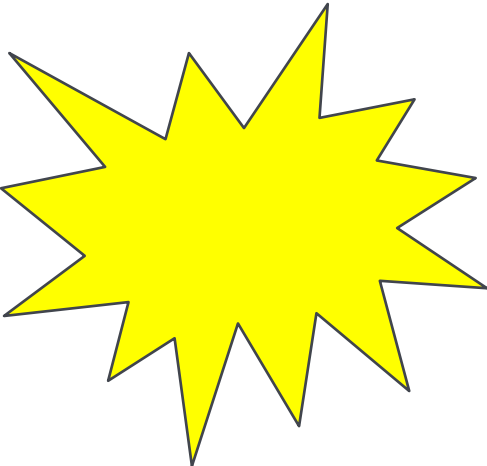
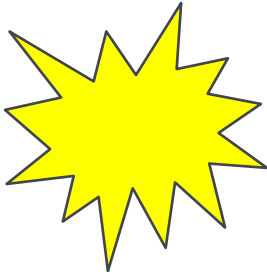
	Standard Regimen (HRZE) >75Kg	Short course regimen (HPMZ) >75Kg
Intensive Phase	<p>8 weeks</p>  <p>Isoniazid Rifampin Pyrazinamide Ethambutol Vitamin B6</p> <p><b>12</b></p>	<p>8 weeks</p>  <p>Isoniazid Rifapentine Moxifloxacin Pyrazinamide Vitamin B6</p> <p><b>15</b></p>
Continuation Phase	<p>16-28 weeks</p>  <p>Isoniazid Rifampin Vitamin B6</p> <p><b>4</b></p>	<p>9 weeks</p>  <p>Isoniazid Rifapentine Moxifloxacin Vitamin B6</p> <p><b>11</b></p>

Photos courtesy of George Lee, RN



# Recent TB Treatment Advances



1. Shorter duration for drug-susceptible TB
  2. Shorter duration all-oral regimen for drug-resistant (or drug-intolerant) TB
- 
- 
- 
- 



# Standard Treatment for Multi-Drug Resistant (MDR) TB

- 5-7 agents with activity against the organism
- Oral and injectable drugs (“2<sup>nd</sup> & 3<sup>rd</sup> line”)
- Many side effects
  - Aminoglycoside (e.g., amikacin) IM injections for 2-6 months
    - Renal and otic toxicity
  - Clofazamine: depression, skin discoloration, QTc prolongation
  - Cycloserine: psychiatric issues
- Duration: 18-24 months





# 6-Month All-Oral Regimen for Drug-Resistant TB



- August 2019: FDA approved pretomanid in combination with bedaquiline and linezolid based on the NIX-TB Trial\*
- NIX-TB found that this combination was 90% effective for highly-resistant TB and treatment-intolerant MDR-TB

Drug Name	Abbreviation
Bedaquiline	B
Pretomanid	Pa
Linezolid	L

**BPaL**

\*Available at: <https://www.nejm.org/doi/full/10.1056/NEJMoa1901814>



# BPaL

- 26-week duration
- 4 tablets daily for first 2 weeks, then 2-4 tablets daily for remainder
- Generally well-tolerated, almost all patients complete treatment
- Adverse effects mainly result from linezolid
  - Peripheral neuropathy
  - Hematologic abnormalities
- Upcoming publication of observational study of 70 U.S. patients
  - Includes patients w/ pulmonary and extrapulmonary disease
  - Includes patients with rifampin mono-resistance, rifampin-intolerant, and MDR-TB
- Procurement and cost of bedaquiline is big issue (\$28,000/course)

# Beyond BPaL

- Dec 2022: TB-PRACTECAL Trial\* published in NEJM
- 24-week, all-oral regimens
- BPaLM = BPaL + moxifloxacin
- BPaLC = BPaL + clofazamine
  
- BPaLM was noninferior to the accepted standard-care treatment and it had a better safety profile

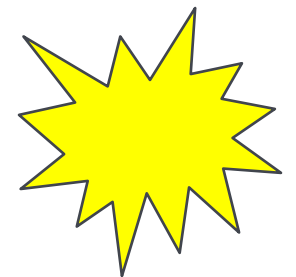
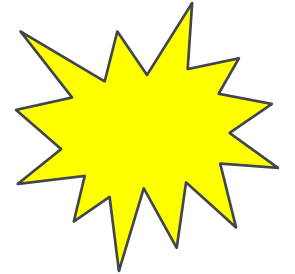
Drug Name	Abbreviation
Bedaquiline	B
Pretomanid	Pa
Linezolid	L
Moxifloxacin	M
Clofazamine	C

\*Pragmatic Clinical Trial for a More Effective, Concise and Less Toxic Regimen  
Available at: <https://www.nejm.org/doi/full/10.1056/NEJMoa2117166>



# Other Recent Advances in TB (headline version)

- Video directly observed therapy (vDOT)
- Shorter treatment regimen for TB infection
- Increased availability of molecular tests for detection of drug resistance
- Whole genome sequencing of all U.S. TB isolates
- Multiple vaccine trials!



Information regarding tuberculosis reporting, surveillance, and treatment is available on the Chicago Health Alert Network (HAN) website at:

<https://www.chicagohan.org/diseases-and-conditions/tuberculosis>

My email address: [kathleen.ritger@cityofchicago.org](mailto:kathleen.ritger@cityofchicago.org)



[Chicago.gov/Health](https://www.chicago.gov/Health)



[HealthyChicago@cityofchicago.org](mailto:HealthyChicago@cityofchicago.org)



[@ChicagoPublicHealth](https://www.facebook.com/ChicagoPublicHealth)



[@ChiPublicHealth](https://twitter.com/ChiPublicHealth)