HEARTLAND
NATIONAL TB CENTER
A PARTNERSHIP OF UT HEALTH NORTHEAST AND TCID

Evaluation and Management of Close Contacts those with MDR

MDR Skills Immersion
San Antonio, TX

Barbara J. Seaworth, M.D.
S

Contact Investigation of Persons with MDR TB

- Persons with MDR TB are as infectious as those with drug susceptible disease

- Transmission to household contacts similar to drug susceptible TB

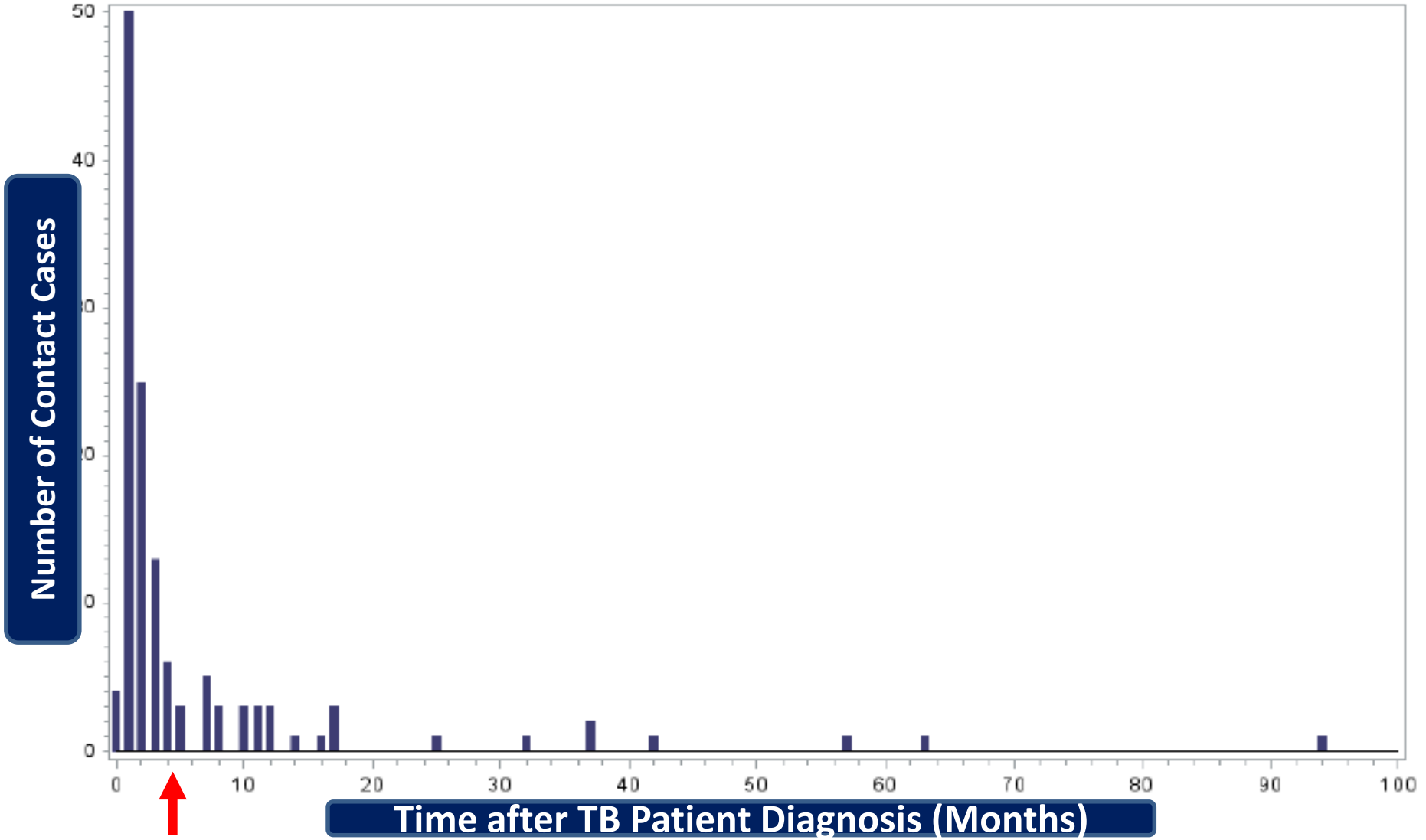
- **Active TB disease** noted in:
  - 3.6% in South Africa (all MDR or XDR)
  - Mortality 14% if MDR, 52% if XDR

    Vella, Int J Tuberc Lung Dis 2011

  - 5% in Peru (80% MDR)
    - Constant rate per year over three years

    Grandjean, 2011 Int J Tuberc Lung Dis

Timing of TB Diagnosis among 131 Contact DX after the Index Case Diagnosis



JID
June 2018

Persons at Risk of Progression from Latent TB Infection to Active TB Disease

- HIV infection
- Chronic kidney disease
- Silicosis
- **Recent exposure**
- Diabetes
- Chest x-ray abnormality c/w previous inadequately treated TB
- Intravenous drug use
- Smoking – active and passive
- Underweight by >10% (*Maybe*)

ATS-CDC. Am J Respir Crit Care Med 2000;161:S221

Persons at Risk of Progression from Latent TB Infection to Active TB Disease

- Immunosuppression
  - Pregnancy and first three months post partum
  - Organ transplant recipients
  - Hematologic cancers and head and neck cancers
  - Medications
    - TNFα inhibitors
    - Prednisone >15 mg, > 4 weeks
    - Chemotherapy
    - Other immunosuppressive drugs

Evaluation of **Contacts** of Active TB

< 5 or Significant Immunosuppression

- TB Testing
- Medical Assessment
  - Symptom Screen
  - Exam if < 5
- CXR

Children < 5
HIV positive
Chemo RX, TNF blockers

Without Significant Immunosuppression

- TB Testing
- Medical Assessment
  - Symptom Screen
- Exam & CXR only if TB testing positive and/or symptoms

ATS/IDSA/CDC

Clinical Practice Guidelines: Diagnosis of TB in Adults and Children

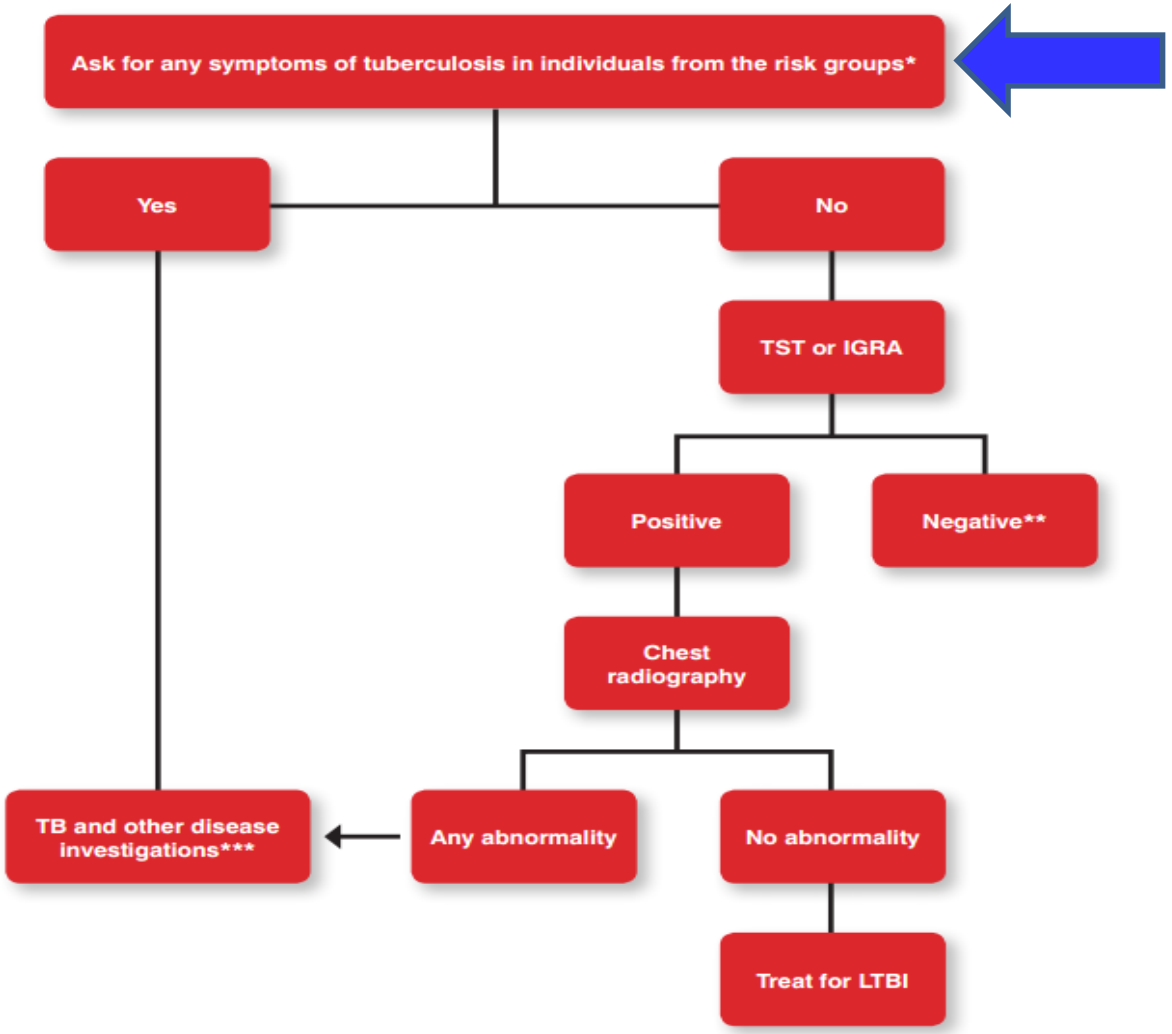
- We ***suggest*** **performing a TST rather than an IGRA** in healthy children under ~~5~~:
  - 1) for whom it has been decided testing is warranted
    - ***(conditional recommendation, very low-quality evidence)***

Clinical Infectious Disease 2016

2018 Pediatric Red Book recommends IGRA down to age 2

Remember that the TST or IGRA may be negative in those with active TB!

Figure 1. Algorithm for targeted diagnosis and treatment of LTBI in individuals from risk groups

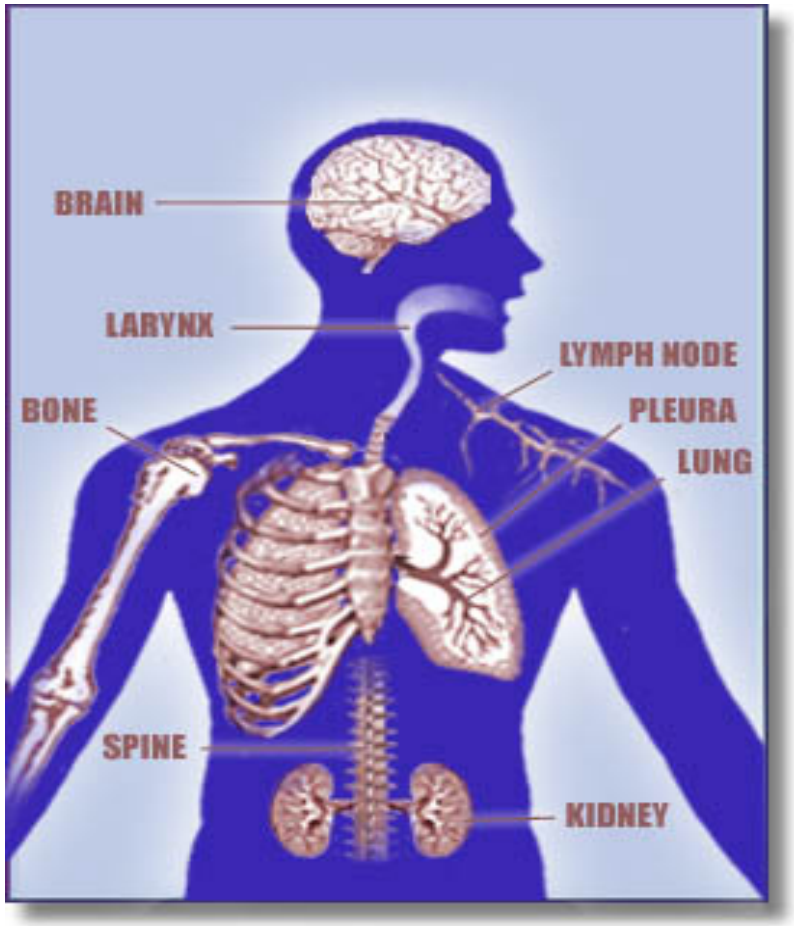


* Any symptoms of TB include any one of: cough, haemoptysis, fever, night sweats, weight loss, chest pain,

WHO Guidelines on the management of latent tuberculosis infection 2015

TB Exam – Focus on Possible Sites of TB Disease

- Lungs – Pulmonary
- Extrapulmonary
  - Larynx
  - **Lymph nodes** (cervical inguinal, supraclavicular, mediastinal, abdominal
  - Pleural effusion
  - Genitourinary
  - Bones & joints
  - Miliary (disseminated)
- Weight/growth curve/BMI



Radiologic Exam

- **WHO? –**
  - All TST or IGRA positive
  - All with symptoms of TB even if testing negative
  - All children < 5, HIV positive or with significant immunosuppression

- CXR must be done **before treatment of TB Infection**
  - Must be read as normal

    Or
  - IF abnormal:
    - Not consistent with Active TB
    - Stable abnormality confirmed over a 3 month period

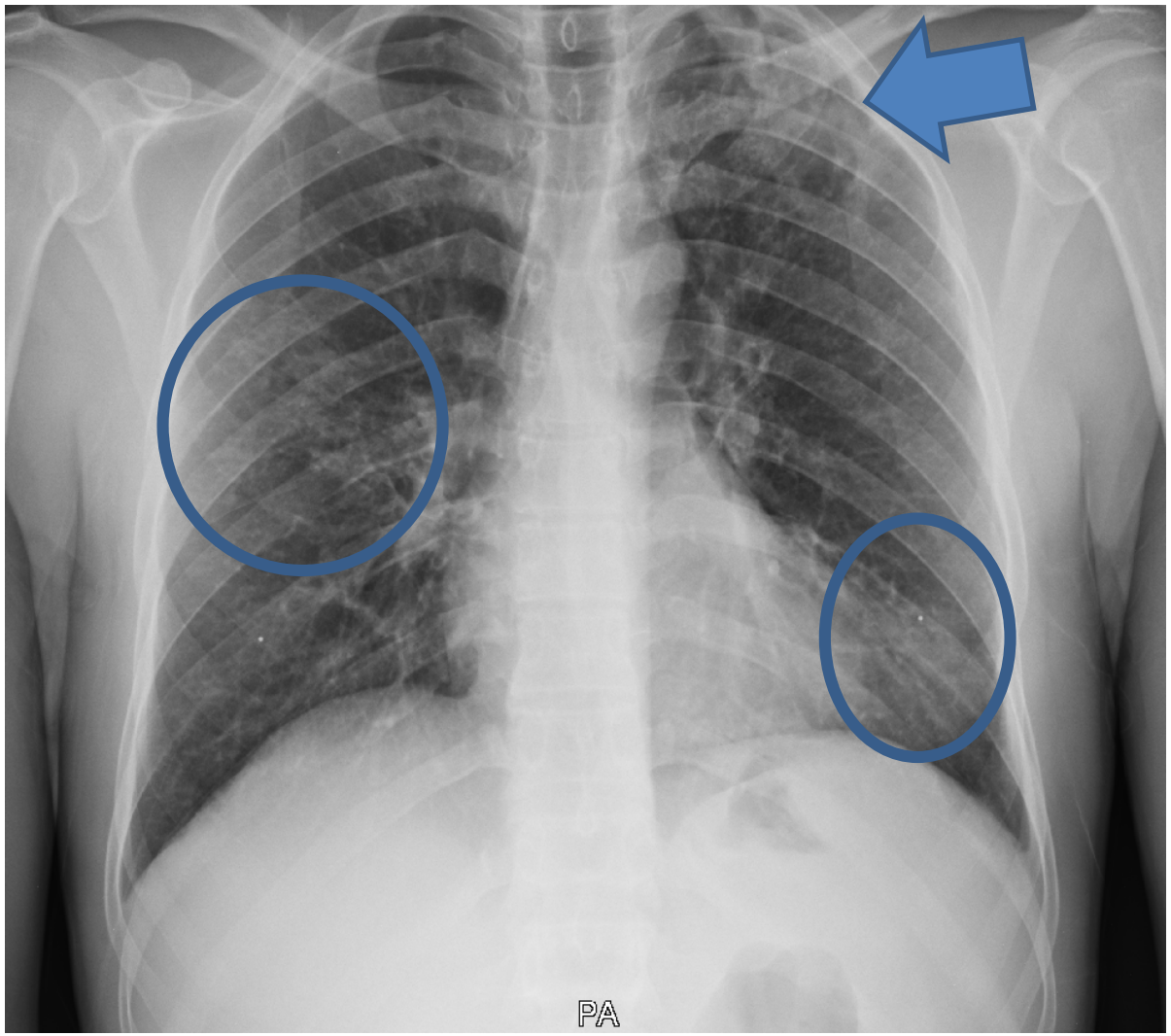
Bacteriologic and Histologic Examinations

When patient has symptoms and/or the CXR is abnormal

Every patient with extrapulmonary TB (TB adenopathy)

- **3** sputum specimens for
  AFB smear and culture
  Ask for a pcr (GeneXpert) on initial specimen if you suspect TB disease

- Collected 8-24 hours apart
  with at least 1 early morning specimen
  one induced specimen
  one observed specimen



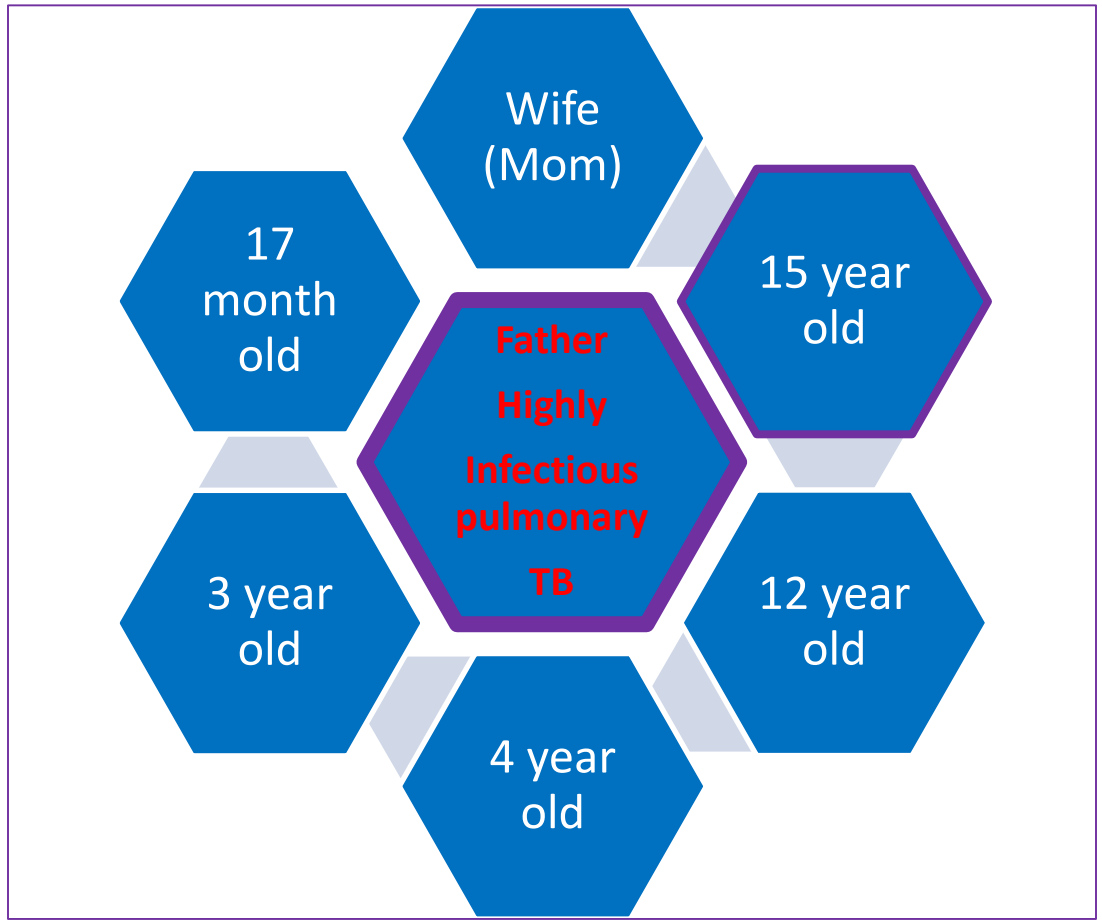
May 2019

37 year old African man
4 months of cough, weight loss, and poor energy
6 weeks after starting TB treatment remains strongly AFB smear positive

AFB – Acid Fast Bacilli

ACTIVE TB DISEASE

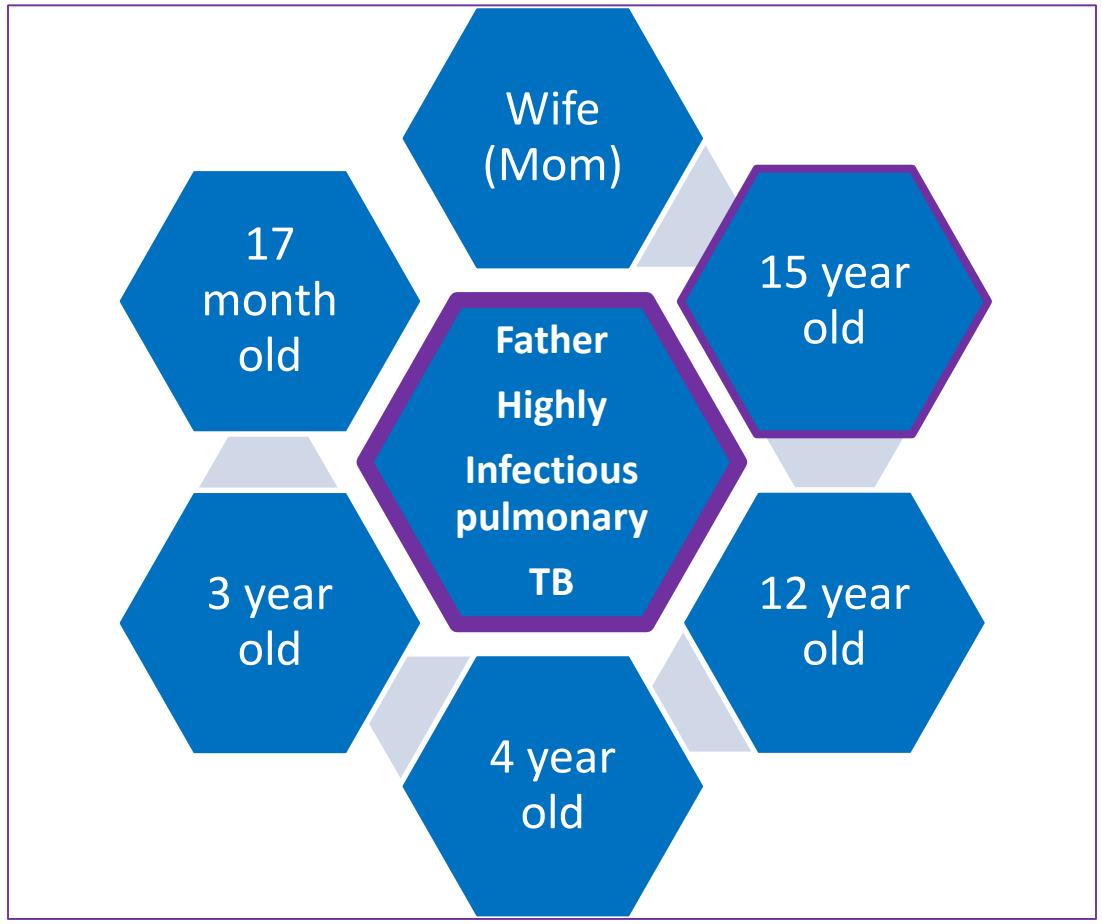
Family of Newly Diagnosed Patient Comes to Clinic – What Now?



- 1
- 2
- 3
- 4
- 5

Public Health's responsibility is to:
Find and treat disease if it is there
Find and treat LTBI if it is there
Protect the vulnerable contacts even if all tests are negative

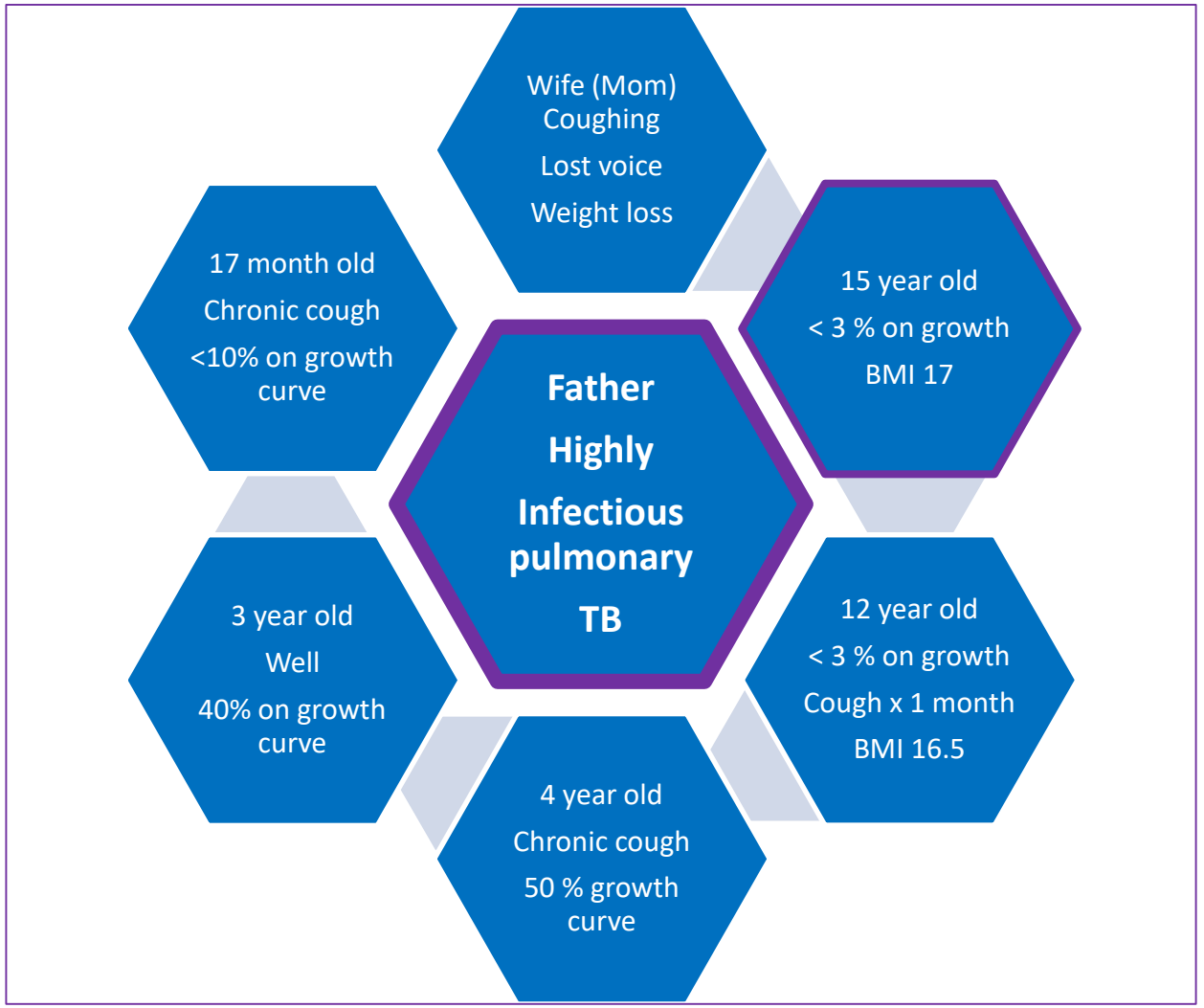
Family of Newly Diagnosed Patient Comes to Clinic – What Now?

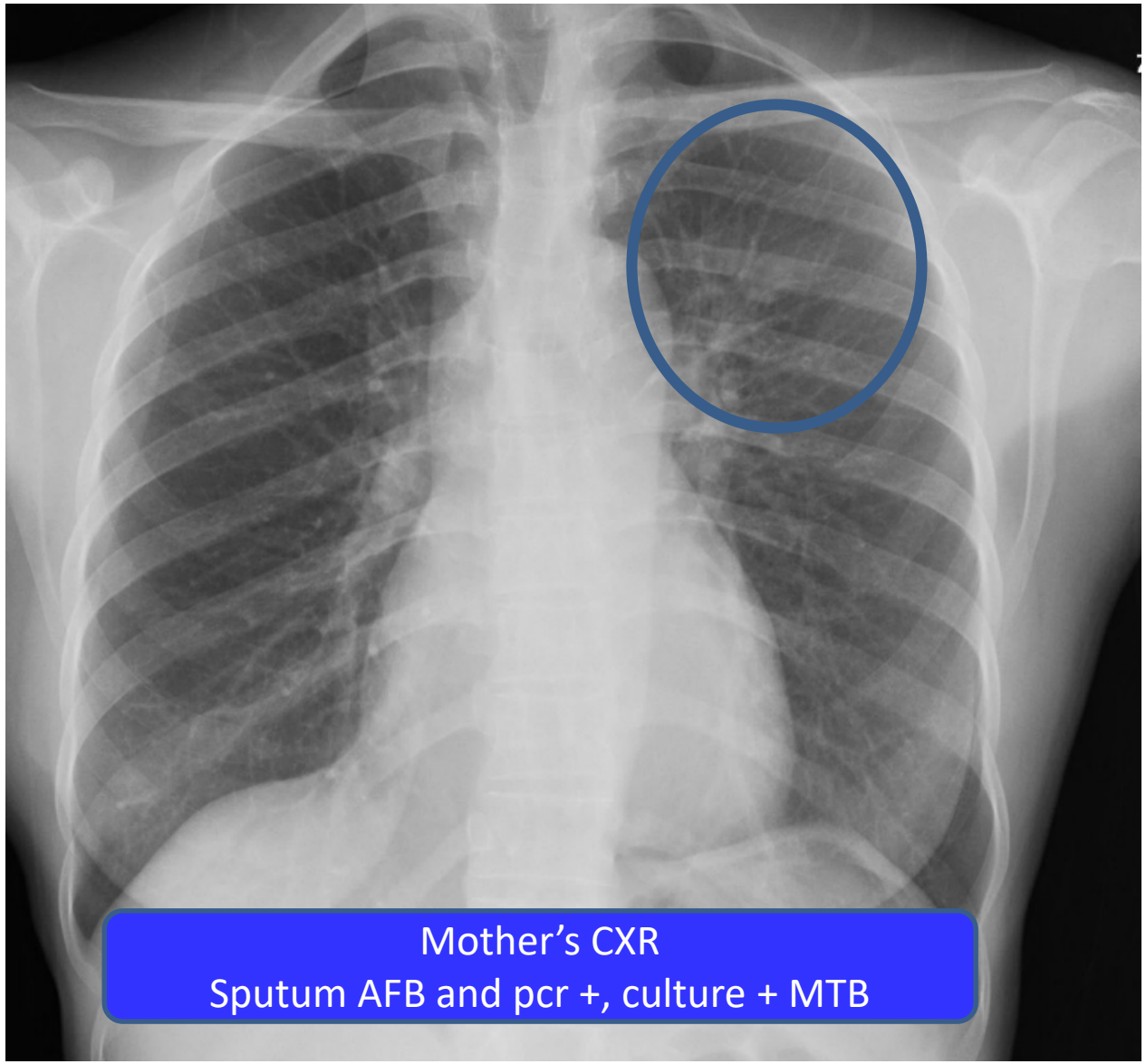


- IGRA – except 17 month old
  - BCG vaccinated
  - TST for children < 2
- Evaluate for symptoms of TB; generally do they look well? Kids playful?
- Medical Assessment
  - Weight, BMI, Growth scale for kids
  - Targeted exam – lungs, lymph nodes
- CXR
- Sputum if coughing

2019 Contact Investigation in Family

Epidemiology is Critical Information



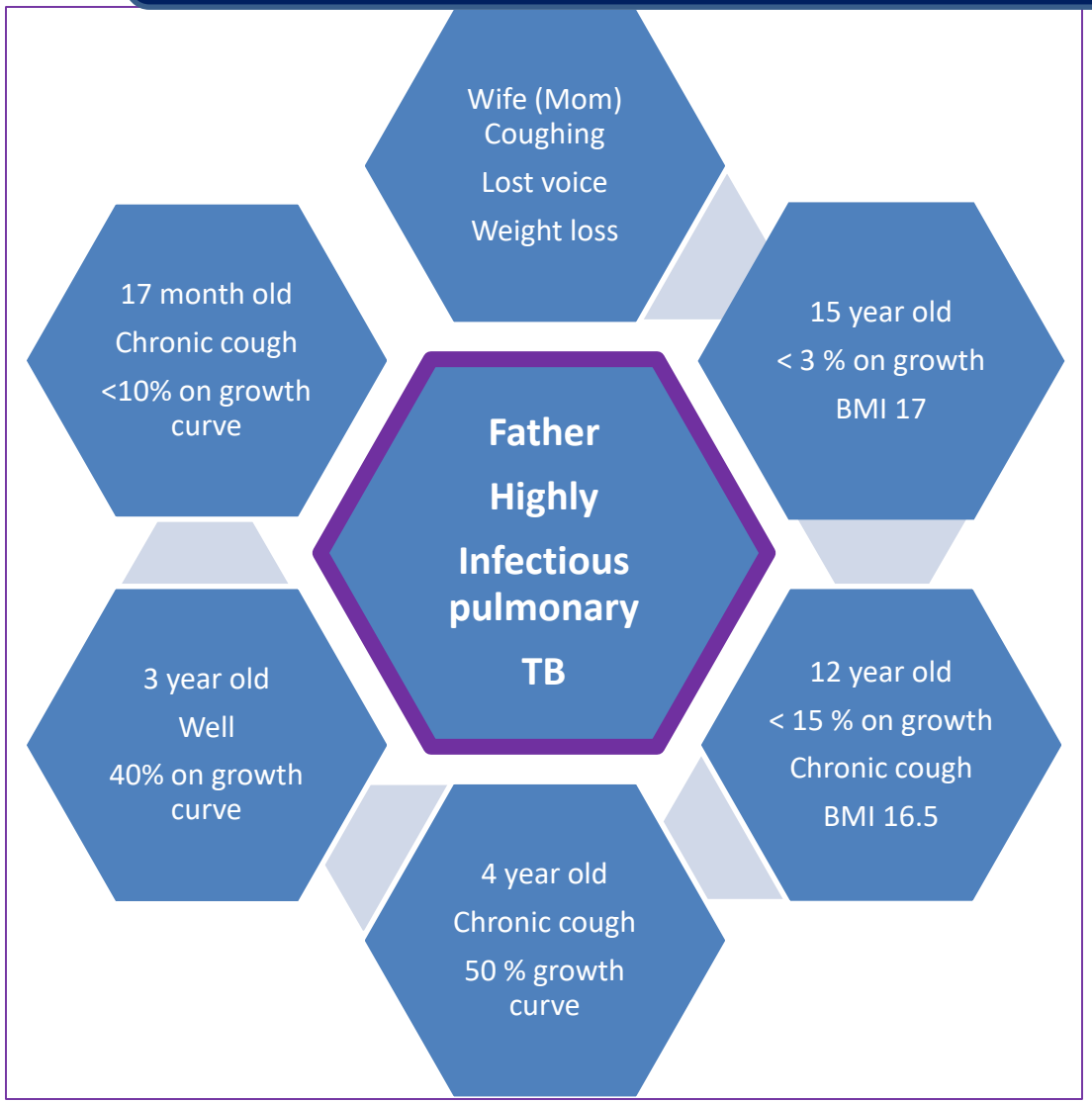


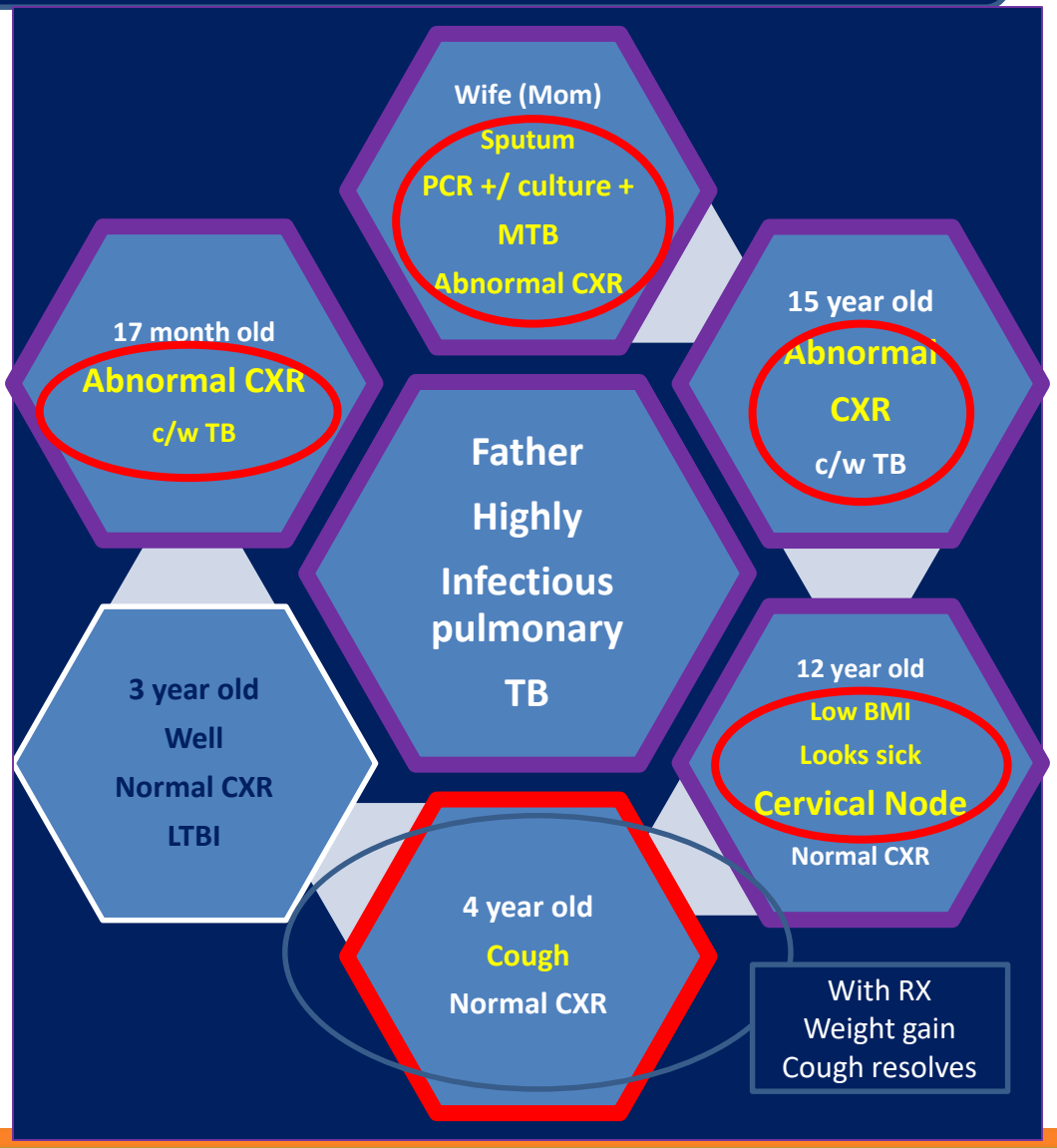
Mother's CXR
Sputum AFB and pcr +, culture + MTB

CXR read as normal

CXR can be normal -
Make sure your patient's really is.

2019 Contact Investigation in Family
All IGRA positive except 17 month old - 20 mm blistering TST





Management of Contacts of MDR TB

- **Evaluate possibility that source was MDR**
- CDC recommends clinical and radiographic follow up for 24 months whether individuals with LTBI presumed due to an MDR/XDR isolate are treated or not
- Discuss possible treatment with patient
  - 2 drugs to which source is susceptible for 6 – 12 months
    - Some experts use fluoroquinolone alone for 9 – 12 months
    - Levofloxacin or moxifloxacin and PZA or ethambutol and PZA
    - Some experts use any two of the above that will work

- CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000;49(No. RR-6):1–51.

WHO Programmatic Guidelines for MDR Contacts 2014

- Routine treatment of Contacts not yet recommended
- Contact investigation should be done to find active TB
  - MDR patients often sick longer; contacts more likely to have disease
- Children < 5 and people of all ages living with HIV
  - **Should receive a clinical evaluation every six months x 2 years after their last MDR-TB exposure.**

Int J Tuberc Lung Dis. 2014 August ; 18(8): 912–918. doi:10.5588/ijtld.13.0028.

Treatment for LTBI in contacts of MDR-TB patients, Federated States of Micronesia, 2009–2012

S. Bamrah[*], **R. Brostrom**[*,†], **F. Dorina**[‡], **L. Setik**[‡], **R. Song**[*,§], **L. M. Kawamura**[¶], **A. Heetderks**[*], and **S. Mase**[*]

[*]Division of TB Elimination, Centers for Disease Control and Prevention, Atlanta, Georgia

- Prospective, observational study of 119 MDR contacts in Micronesia (Chuuk islands)
- 104 contacts took LTBI treatment
  - 12 mo daily FQ or FQ+EMB
  - None developed TB disease with 36 mo follow-up
- 3 of 15 who declined LTBI rx later developed TB disease

EDITOR'S CHOICE

Systematic Review, Meta-analysis, and Cost-effectiveness of Treatment of Latent Tuberculosis to Reduce Progression to Multidrug-Resistant Tuberculosis

Suzanne M Marks ✉, Sundari R Mase, Sapna Bamrah Morris

Clinical Infectious Diseases, Volume 64, Issue 12, 15 June 2017, Pages 1670–1677,
https://doi.org/10.1093/cid/cix208

Published: 14 March 2017 **Article history ▾**

Selected studies that compared treatment vs nontreatment outcomes and performed a meta-analysis to estimate the relative risk of TB incidence and its 95% confidence interval

Results

We abstracted data from 21 articles that met inclusion criteria. Six articles presented outcomes for contacts who were treated compared with those not treated for MDR-LTBI; 10 presented outcomes only for treated contacts, and 5 presented outcomes only for untreated contacts. The estimated MDR-TB incidence reduction was 90% (9%–99%) using data from 5 comparison studies. We also found high treatment discontinuation rates due to adverse effects in persons taking pyrazinamide-containing regimens. Cost-effectiveness was greatest using a fluoroquinolone/ethambutol combination regimen.

Conclusions

Few studies met inclusion criteria, therefore results should be cautiously interpreted. We found a reduced risk of TB incidence with treatment for MDR-LTBI, suggesting effectiveness in prevention of progression to MDR-TB, and confirmed cost-effectiveness. However, we found that pyrazinamide-containing MDR-LTBI regimens often resulted in treatment discontinuation due to adverse effects.

Regimen-specific Data from 11 Studies, Outcome=Adverse Effects by Regimen

Total 11 studies	n	AE	AE stop	% AE	% AE stop
PZA/INH	1	0	0	0%	0%
PZA/INH/ETA	22	0	0	0%	0%
PZA/EMB	14	9	7	64%	50%
PZA/EMB/RIF	1	0	0	0%	0%
PZA/EMB/INH	9	0	0	0%	0%
PZA/EMB/INH/ETA	2	0	0	0%	0%
PZA/EMB/ETA	2	0	0	0%	0%
PZA/FQ	123	105	82	85%	67%
PZA/FQ/INH	6	4	4	67%	67%
PZA/CIP	1	1	0	100%	0%
Any PZA regimen	**181**	**119**	**93**	**66%**	**51%**
FQ	53	43	4	81%	8%
FQ/EMB	43	7	0	16%	0%
FQ/EMB/INH	210	48	2	23%	1%
FQ/ETA	12	7	0	58%	0%
Any FQ regimen	**318**	**105**	**6**	**33%**	**2%**
ETA/EMB	2	0	0	0%	0%
ETA/EMB/INH	4	0	0	0%	0%
CIP	2	2	2	100%	100%
All regimens	**507**	**226**	**101**	**45%**	**20%**

Pending ATS/CDC/ERS/IDSA Drug Resistant TB Guidelines

- Will answer whether treatment is better than observation
  - Based on systematic review by Marks et al
  - Will not provide definitive answer for contacts of MDR who have high level FQN resistance

MDR-TB Preventive Therapy Trials

- V-QUIN: LFX versus Placebo
- TB-CHAMP: LFX versus Placebo
- PHOENIX trial of DLM versus INH (US NIH, SA MRC)

Think TB

TREATMENT IS PREVENTION – WE DO NOT HAVE AN EFFECTIVE VACCINE – YET

TREATMENT STOPS TRANSMISSION