TB: An old disease with new wrinkles

Updates from the GA TB program

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TB in the United States, 2016

- A total of 9,287 TB cases were reported in the U.S. in 2016 (preliminary data from CDC)
- Foreign-born individuals represented 68% of U.S. TB cases
- 13 million people in the U.S. are estimated to have Latent TB Infection.

Georgia's TB Rank

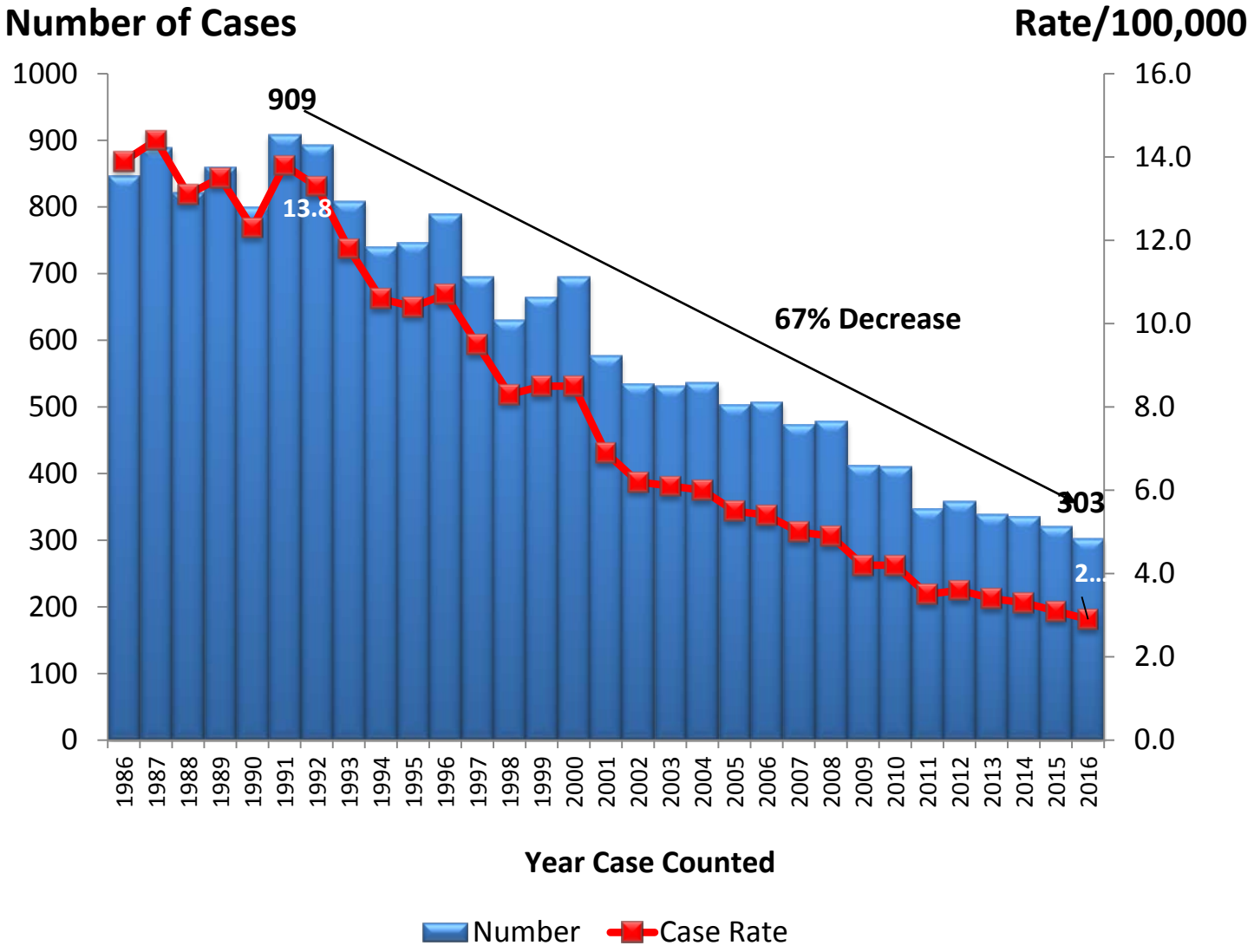
5th in TB incidence

State	Population	Cases 2014	Cases 2013
California	38,802,500	2,145	2,166
Texas	26,956,958	1,269	1,222
New York	19,746,227	787	865
Florida	19,893,297	595	651
Georgia	10,097,343	335	338
Illinois	12,880,580	320	327
New Jersey	8,938,175	308	320
North Carolina	9,943,964	195	216
Pennsylvania	12,787,209	209	214
Washington	7,061,530	195	209

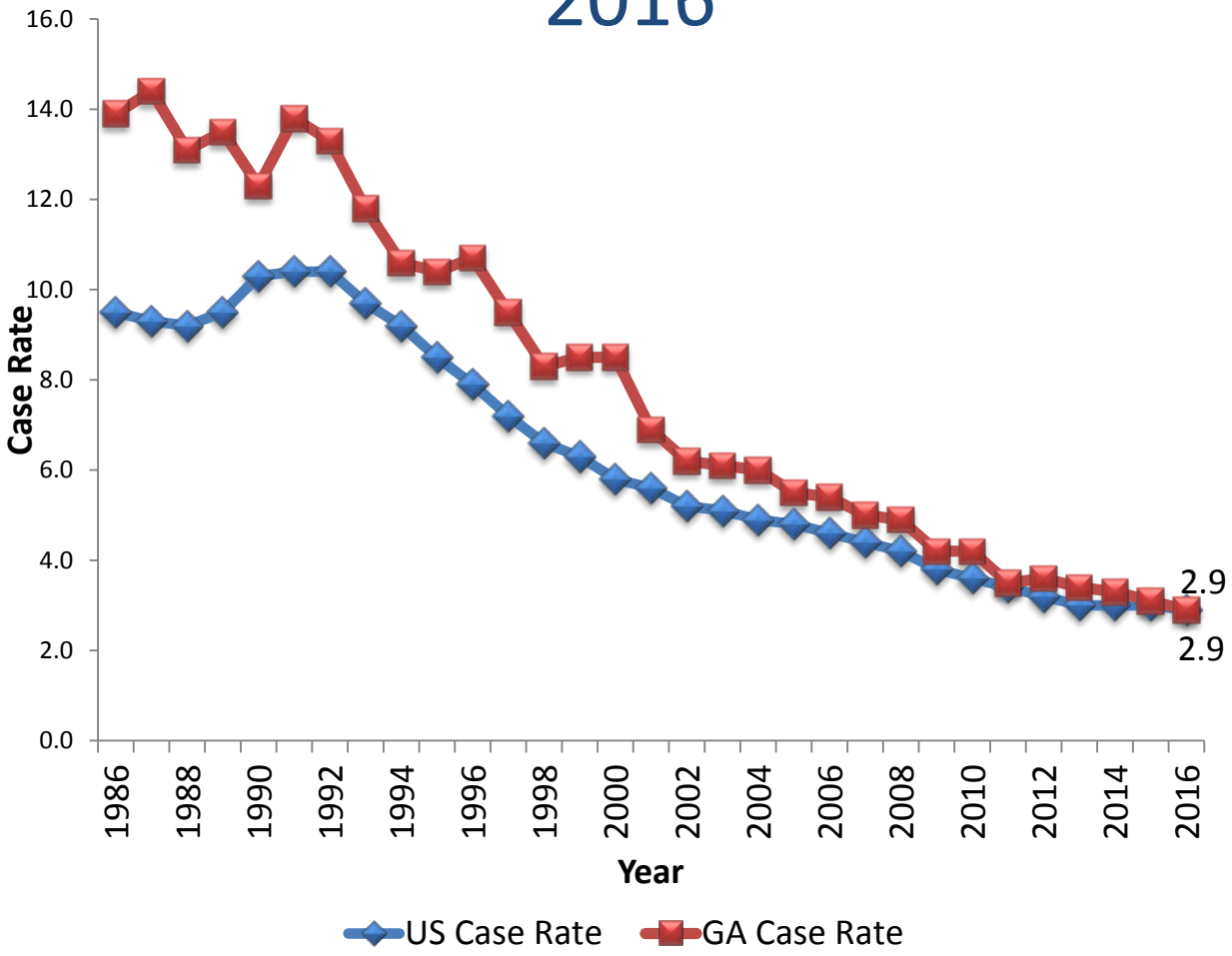
8th in TB case rates

State	Population	Cases 2014	Cases 2013	Case Rate 2014	Case Rate 2013
Hawaii	1,419,561	136	115	9.6	8.2
Alaska	736,732	62	71	8.4	9.6
California	38,802,500	2,145	2,166	5.5	5.6
District of Columbia	658,893	32	37	4.9	5.7
Texas	26,956,958	1,269	1,222	4.7	4.6
New York	19,746,227	787	865	4.0	4.4
New Jersey	8,938,175	308	320	3.4	3.6
Georgia	10,097,343	335	338	3.3	3.4
Maryland	5,976,407	198	175	3.3	2.9
Arkansas	2,966,369	93	72	3.1	2.4

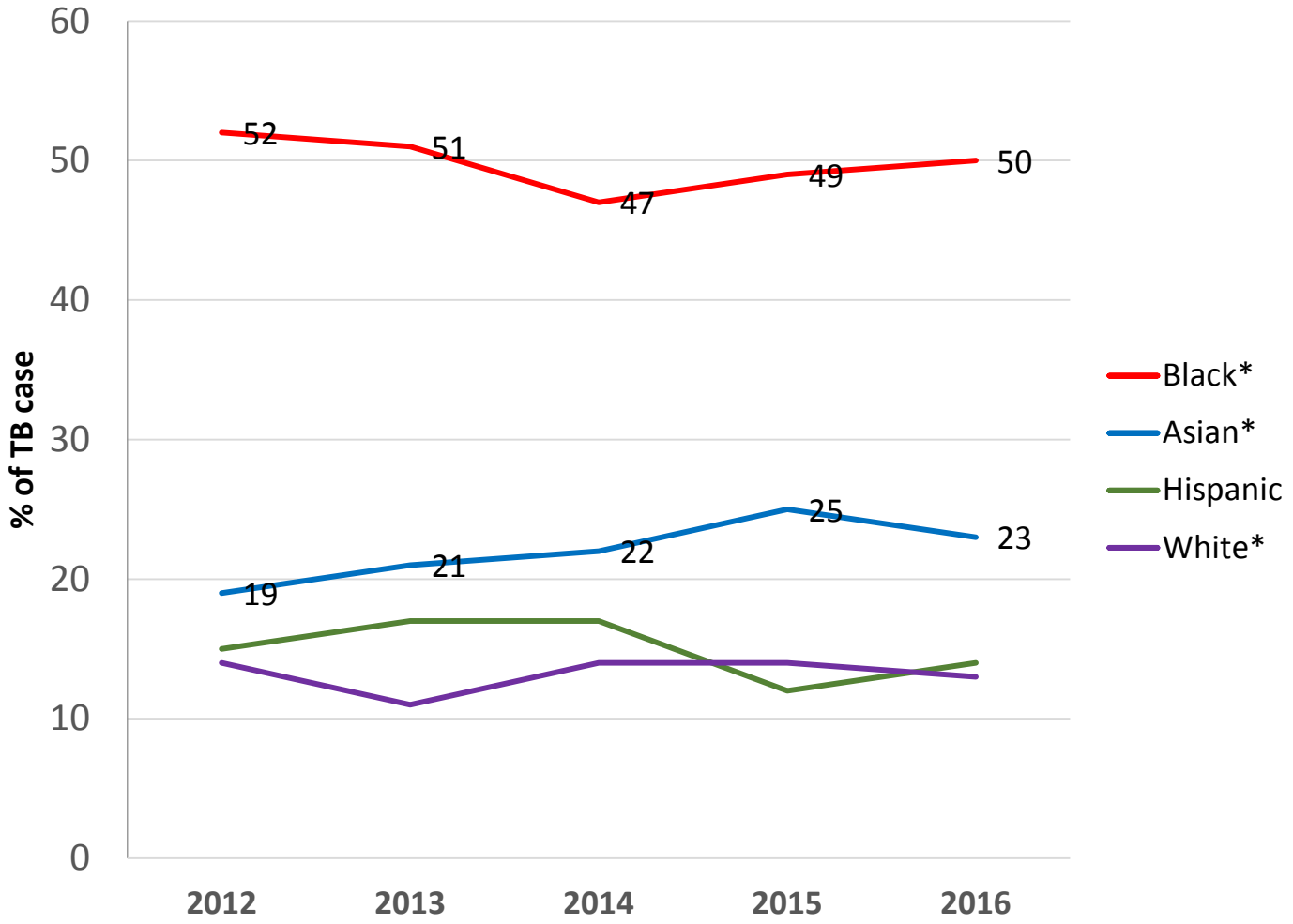
TB Cases and Case Rates Georgia,1986-2016



TB Case Rates Georgia and U.S., 1986-2016

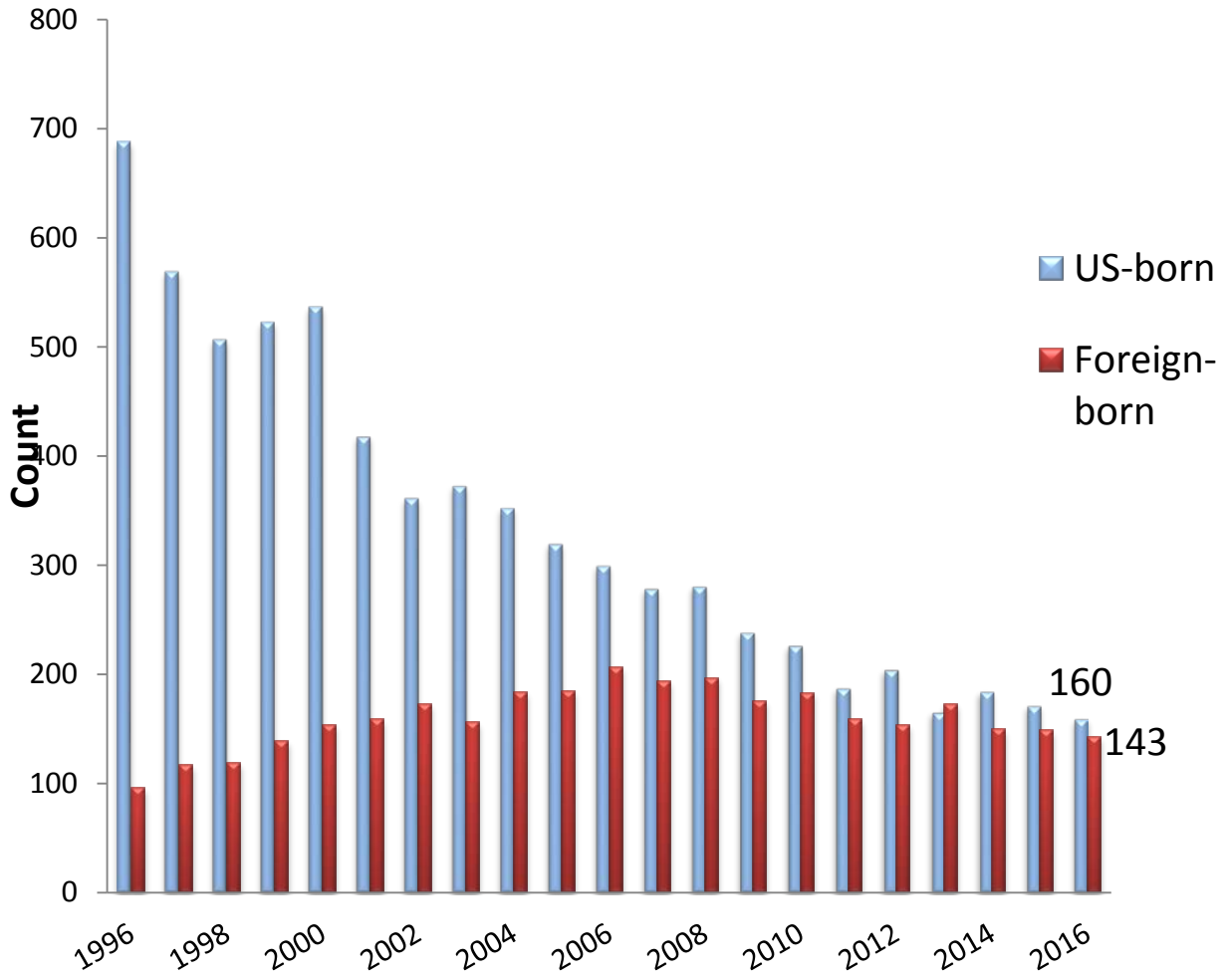


Percentage of TB cases by Race/Ethnicity Georgia, 2012-2016

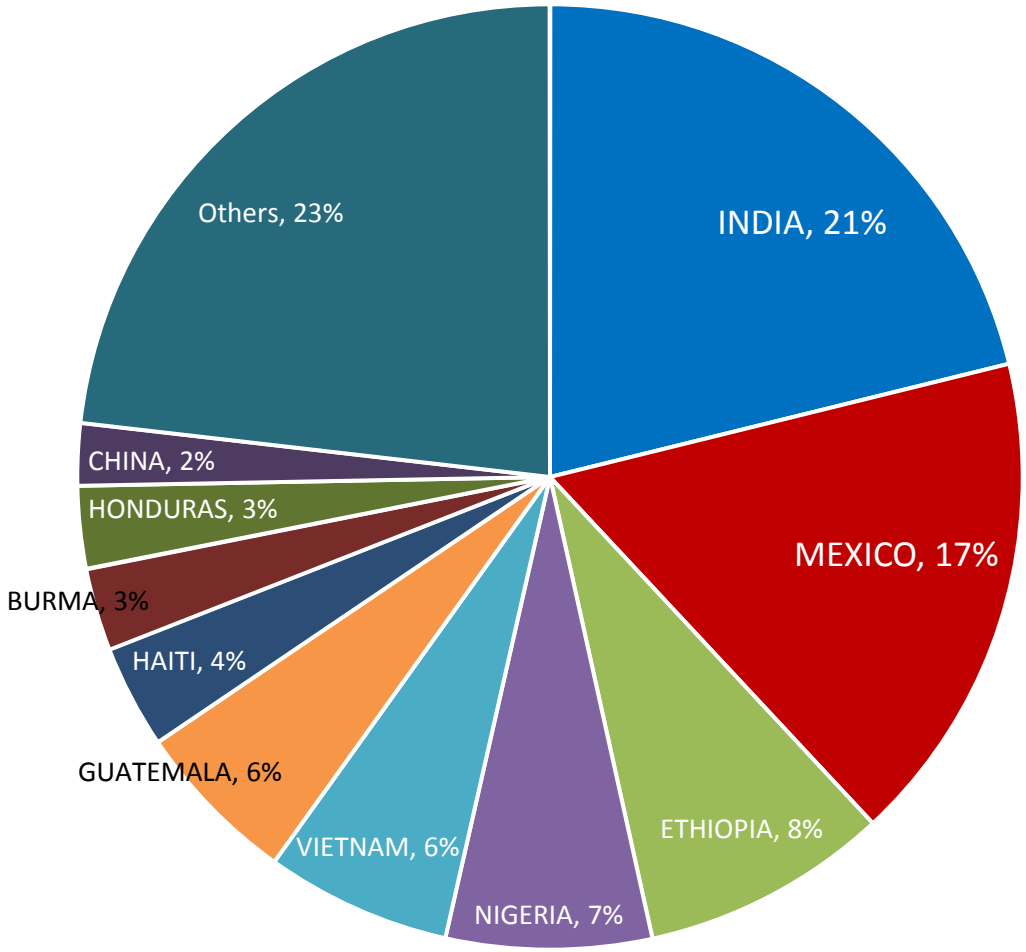


* non-hispanic

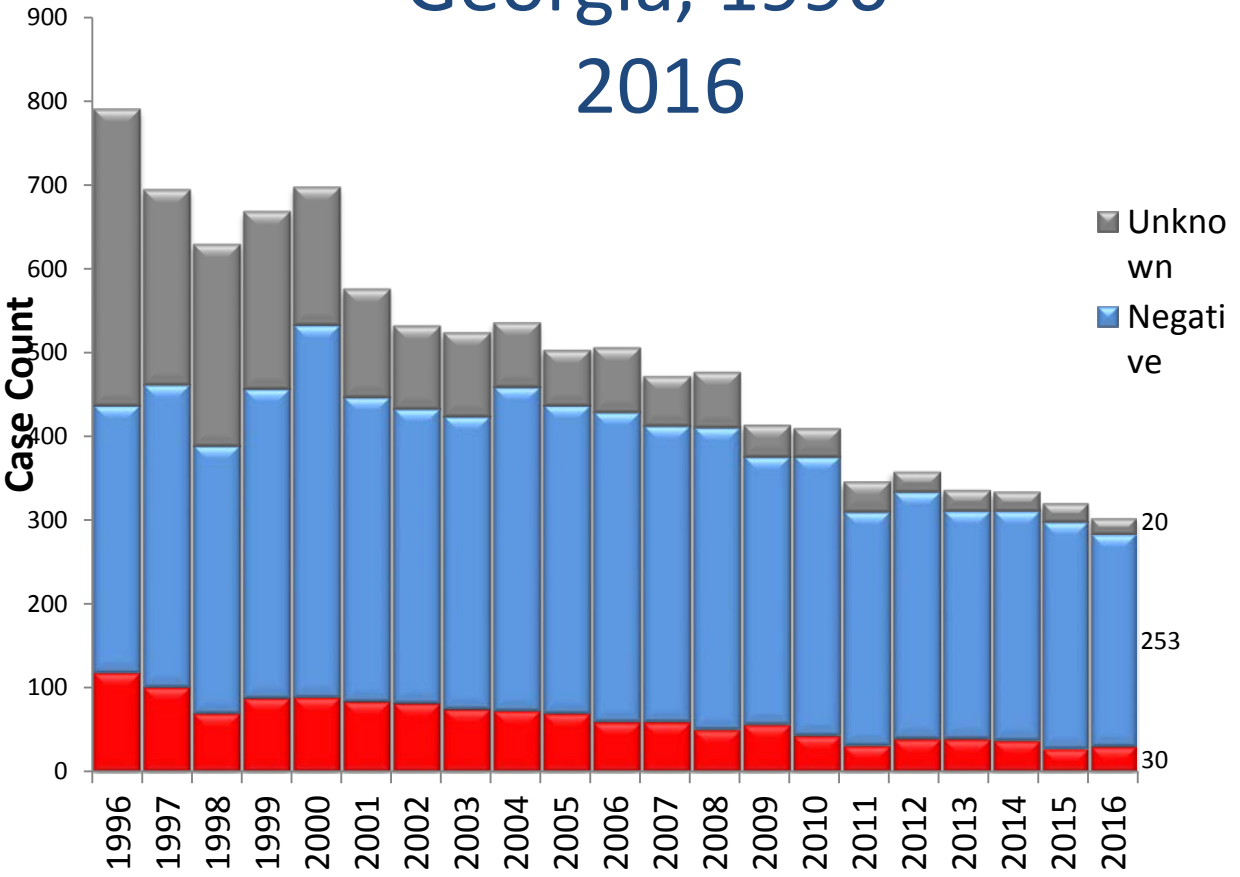
US-born and Foreign-born TB Cases Georgia,1996-2016



Percent of Foreign-born TB Cases (*n*=143) by Country of Origin, Georgia, 2016

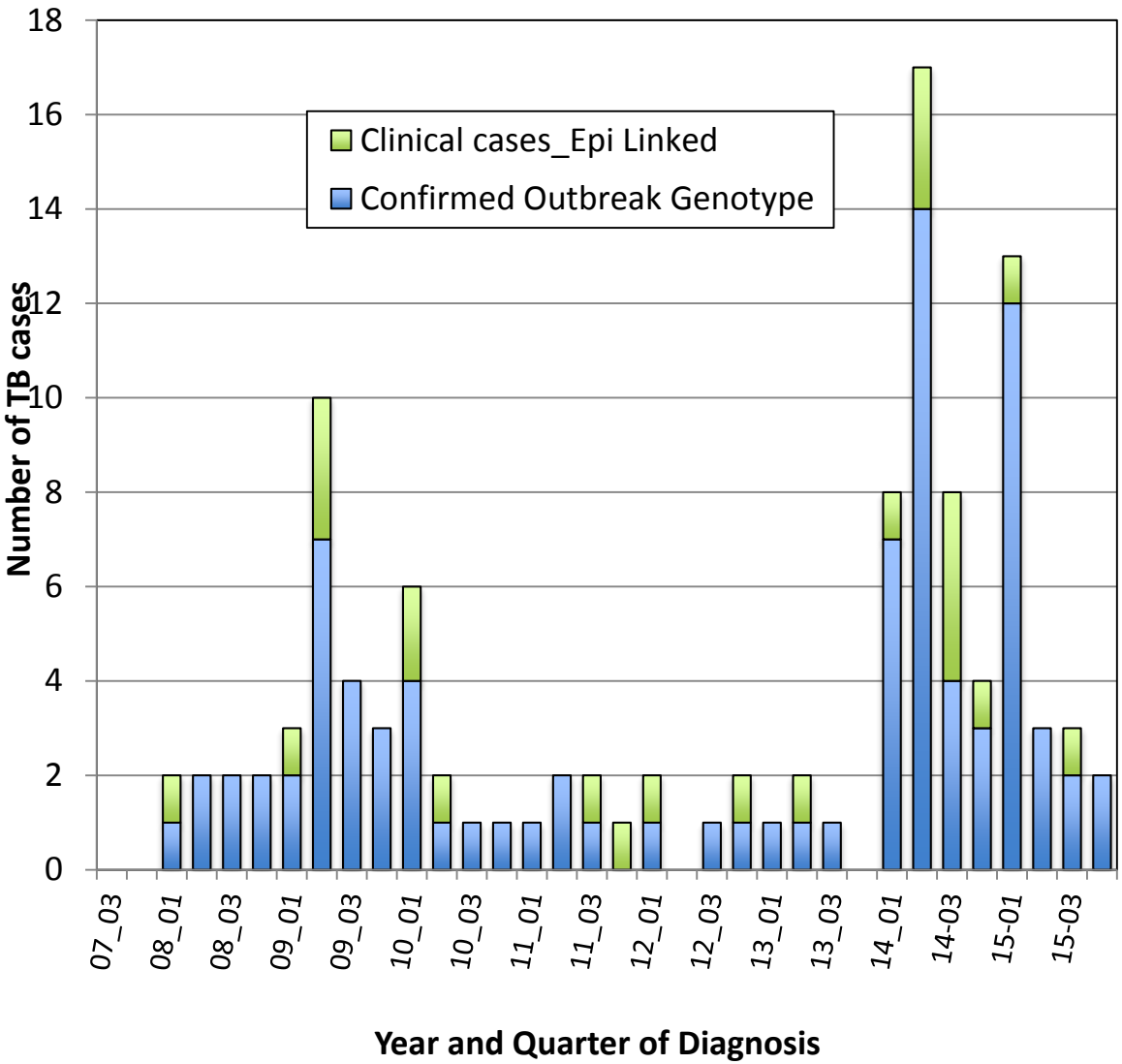


HIV Status of TB Cases Georgia, 1996-2016



World TB Day 2017

TB Homeless Outbreak Cases - Metro Atlanta, INHR strain Summary 12/31/2016



Since January 2008:

111 cases of active TB (in 107 people)

- 87 culture positive (79 pulm, 4 pleural/pulmonary, 1 pleural only, 1 lymph node, 2 meningitis)
- 24 clinical cases

Of pulmonary TB cases
- 55% smear positive
- 28% cavitary

- 37% HIV positive
- median CD4 110 cells/ul
- 93% knew HIV diagnosis prior to TB
- 78% were not on ART

- 98% male at birth
- 101 current or former shelter residents
- 3 shelter volunteers

12 deaths (11%)
9 deaths after treatment started
3 deaths before diagnosis known

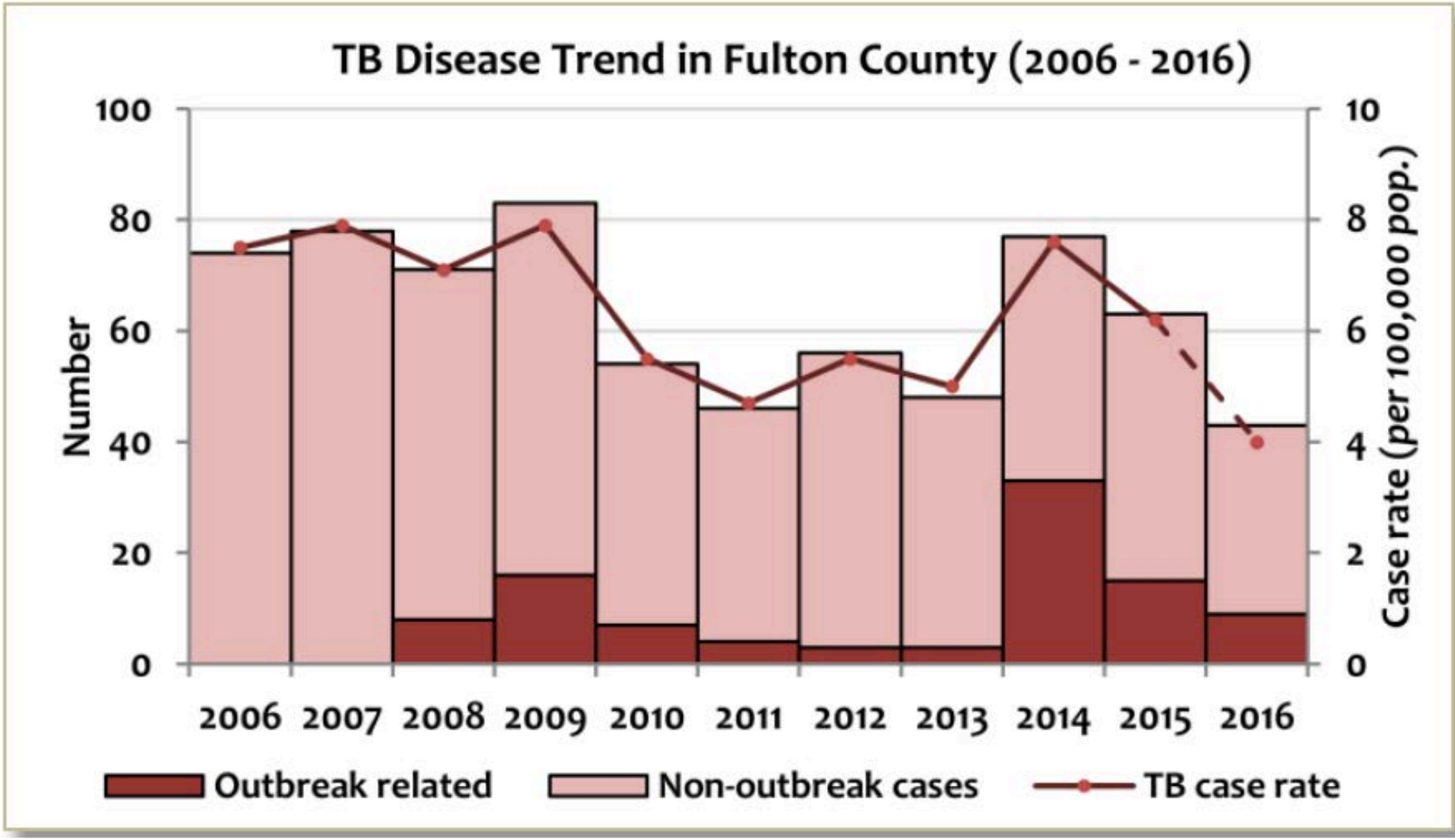
5 shelters involved:
- Atlanta Union Mission, Peachtree/Pine, Central Presbyterian Night Shelter (closes every summer), Salvation Army (Luckie Street), Atlanta Recovery Center

Identification and treatment of contacts continues.

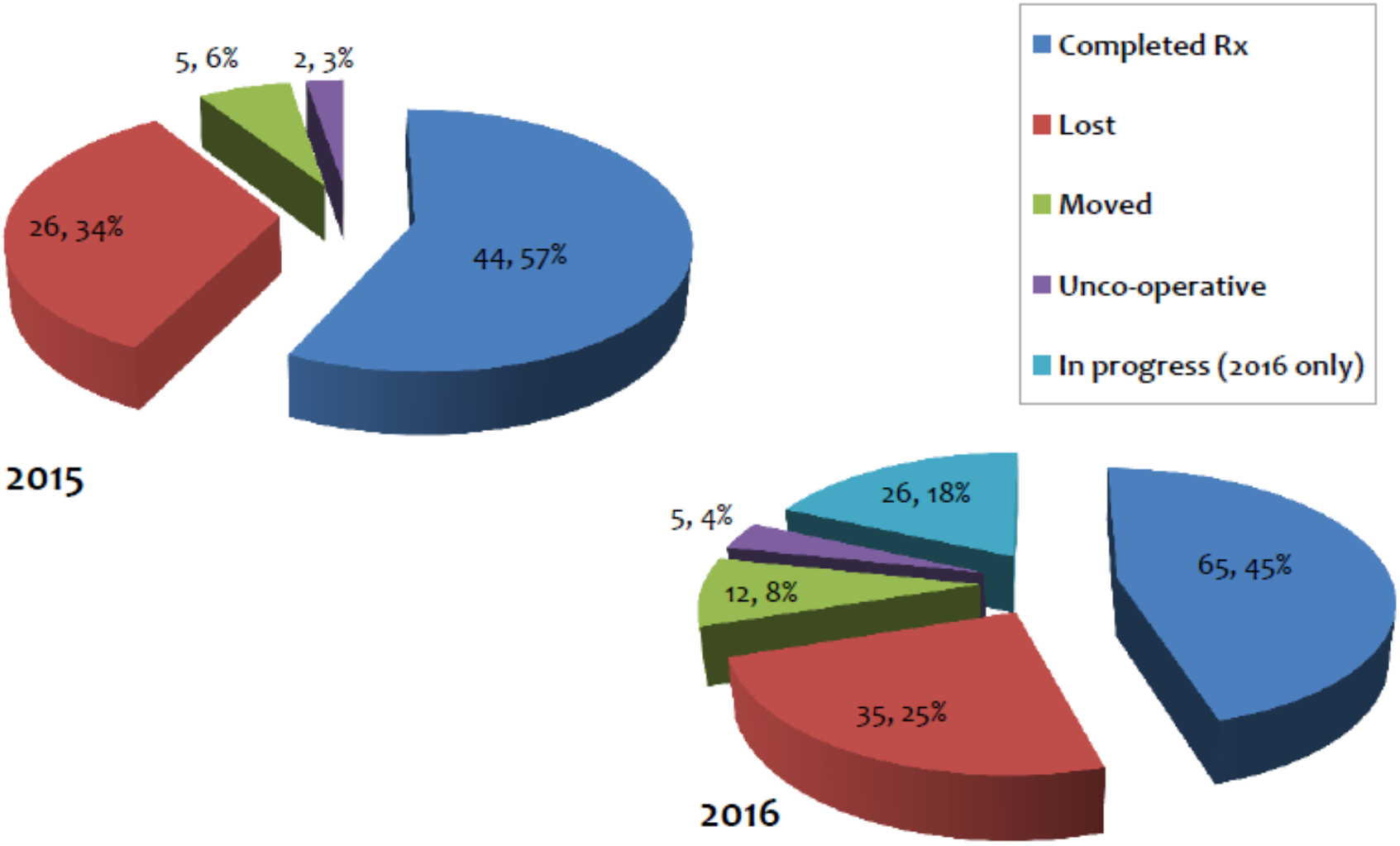
A coalition of homeless shelter providers and public health agencies have developed a TB control plan for homeless shelters.

Fulton County Success Story

- TB cases in Fulton County have declined by 77% over the last 16 years (from 2000 to 2016)
- TB cases from a TB outbreak in Atlanta homeless shelters declined from 44 cases in 2014 to 10 cases in 2016
- The decrease in cases of TB in Fulton County is attributable to the collaboration and dedicated work of clinicians, health care agencies, and community organizations, especially those serving at-risk populations, such as the TB Task Force

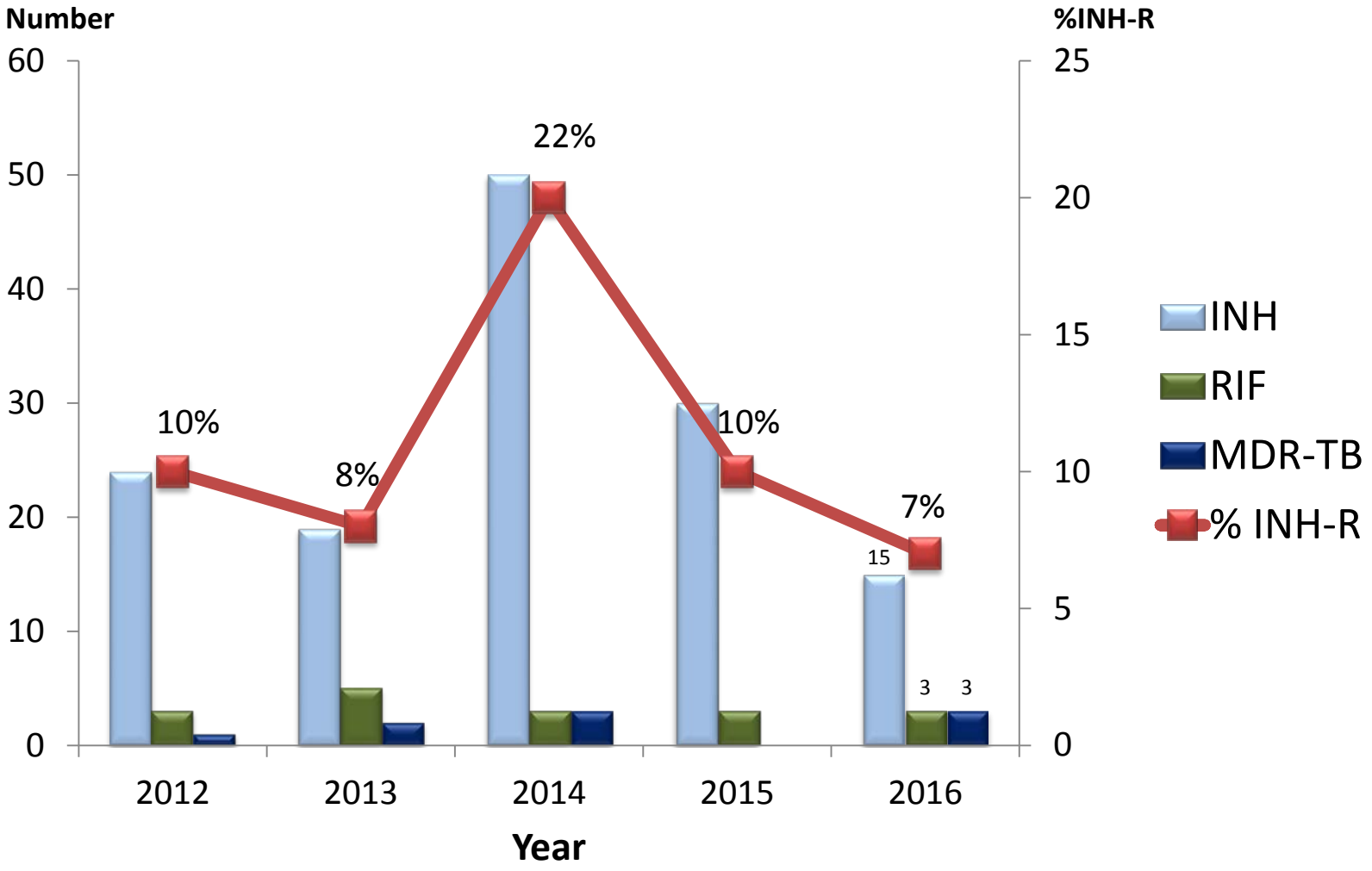

TB Disease Trend in Fulton County (2006 - 2016)
Number
Case rate (per 100,000 pop.)
100
80
60
40
20
0
10
8
6
4
2
0
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
Outbreak related
Non-outbreak cases
TB case rate

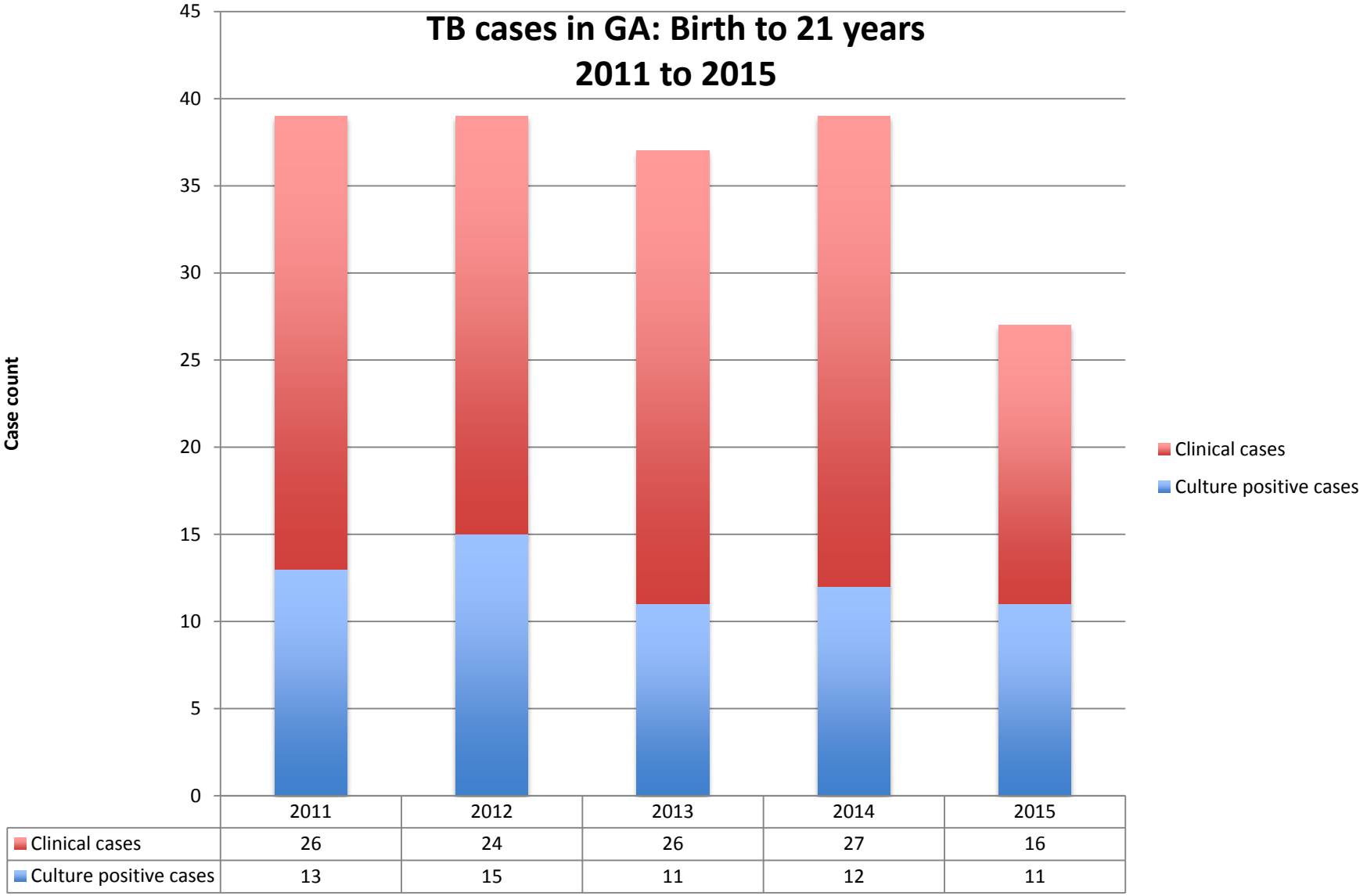
Fulton TB Program
Treatment completion for LTBI



UNITE TO END TB

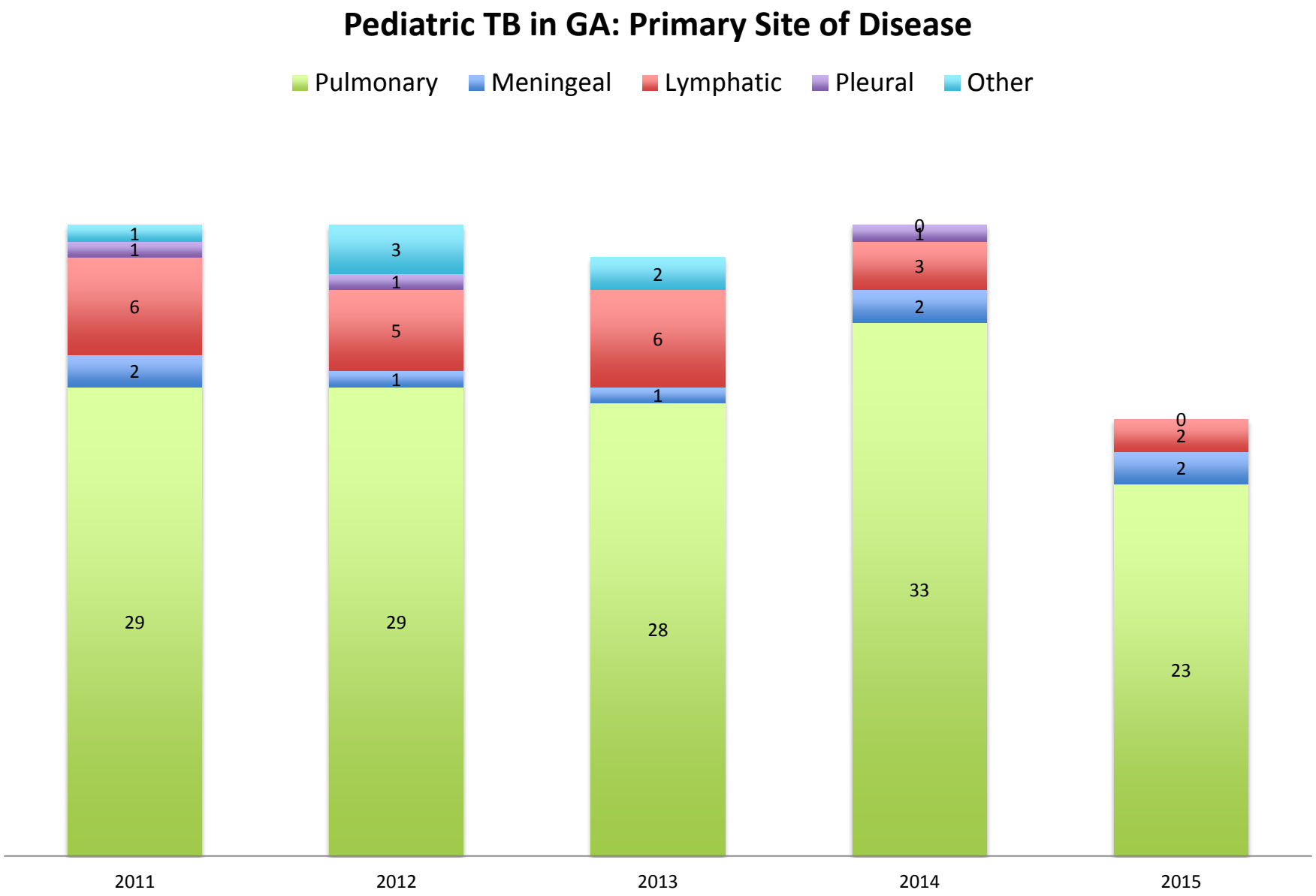
Primary Drug Resistance and MDR-TB Georgia, 2012-2016

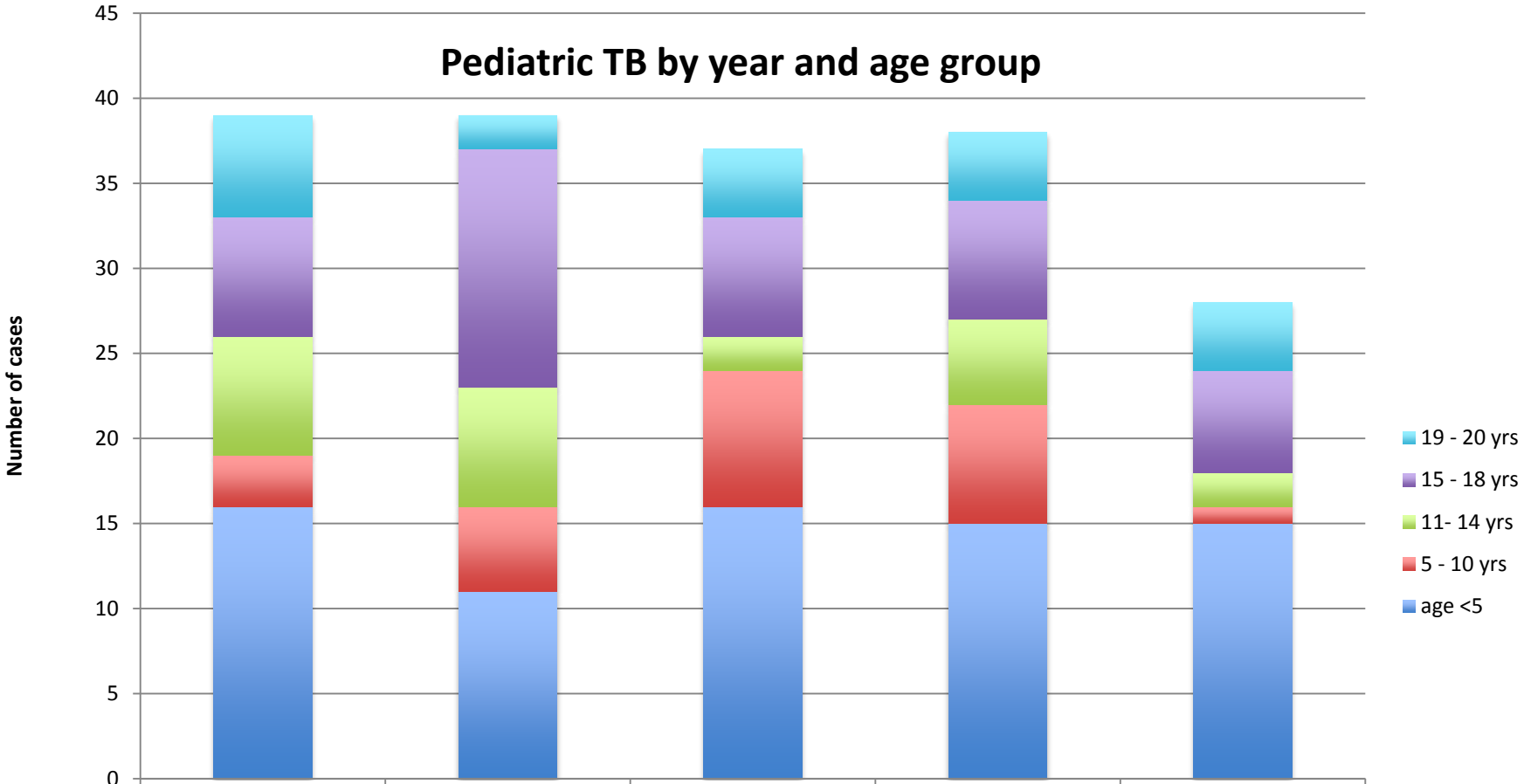




	2011	2012	2013	2014	2015
Clinical cases	26	24	26	27	16
Culture positive cases	13	15	11	12	11

Peds Cases	**39**	**39**	**37**	**39**	**27**
Total Cases		~336	~334	334	321


Pediatric TB in GA: Primary Site of Disease
Pulmonary
Meningeal
Lymphatic
Pleural
Other
1
1
6
2
29
3
1
5
1
29
2
6
1
28
0
1
3
2
33
0
2
2
23
2011
2012
2013
2014
2015



	2011	2012	2013	2014	2015
19 - 20 yrs	6	2	4	4	4
15 - 18 yrs	7	14	7	7	6
11- 14 yrs	7	7	2	5	2
5 - 10 yrs	3	5	8	7	1
age <5	16	11	16	15	15

Year

Contacts to cases

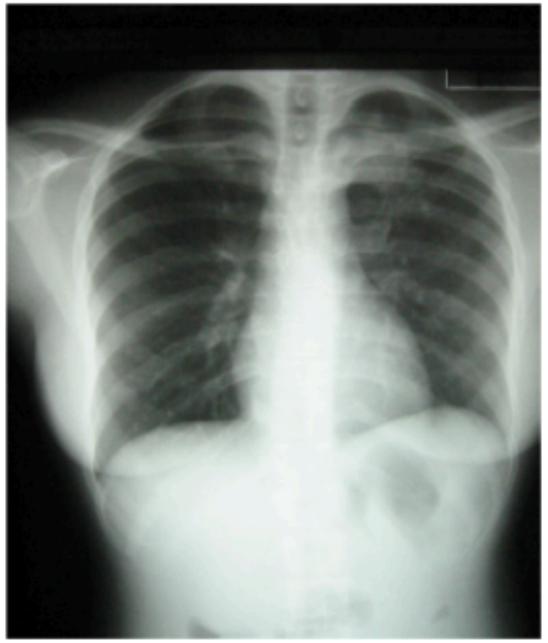
Preliminary Results of 2015 Contact Investigations		
Age of Contacts	N	%
All Ages (adult and pediatric)	3,903	
All Pediatric contacts (0-17 yrs old)	933	24%
Completely evaluated	630	68%
a. LTBI	86	14%
b. Active TB	6	1%
Pediatric contacts (0-4 yrs old)	131	
Completely evaluated	99	76%
a. LTBI	17	17%
b. Active TB	5	5%
Pediatric contacts (5-14 yrs old)	564	
Completely evaluated	370	65%
a. LTBI	51	14%
b. Active TB	1	0.3%
Pediatric contacts (15-17 yrs old)	238	
Completely evaluated	161	68%
a. LTBI	18	11%
b. Active TB	0	0%

New Wrinkles

- Diagnostics for active TB
  - Nucleic acid amplification tests
    - Organism confirmation (or exclusion)
    - Rifampin resistance
  - Gene sequencing
    - the whole shebang
- Latent TB
  - Diagnostics: New tests aren't necessarily better tests
  - Treating LTBI is KEY to decreasing TB cases in the U.S.

Patient 1

- 18 yo girl with hx of asthma presented to the ER with wheezing and pleuritic L chest pain x 2 weeks. She has occasional productive cough with clear sputum. Wants to get rx for inhalers. No fever, chills, night sweats, wt loss
- Moved to Atlanta from Indiana 2 wks ago tp attend a job training program. Multiple family members there were diagnosed with active TB. Her PPD was positive one month ago. She plans to start treatment for LTBI with the county health department here. She is living in a dormitory with other students from the job training program.
- PE is significant for T 38.2, scattered wheezes and 2 cm circle of induration on her L forearm.
- Her CXR is shown here:
- Sputum AFB smears x 3 are negative
- She feels much improved by hospital day 2 with beta agonist treatment and Doxycycline.
- Pulmonary consultant declined to pursue bronchcoscopy.



Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 62 / No. 41
October 18, 2013

Availability of an Assay for Detecting *Mycobacterium tuberculosis*, Including Rifampin-Resistant Strains, and Considerations for Its Use — United States, 2013

Xpert MTB/RIF assay Result	Interpretation
MTB detected, RIF resistance detected	MTB target is present in sample A mutation in rpoB gene is present. RMP resistance is possible. Further testing needed
MTB detected, RIF resistance not detected	MTB target is present in sample No mutations in rpoB gene were detected. Probably RMP susceptible
MTB not detected	MTB target is not detected.

Sensitivity for culture positive TB: 97% in smear positive

76% in smear negative

Combined Sputum Smear (SS) and NAA tests for Infection control and TB diagnostics

SS results (on ≥ 2 samples)	NAA results (on ≥ 1 sample)	Infection control implications	TB diagnostic implications
All neg	All neg	Supports discontinuing airborne infection isolation (AII)	Active TB not excluded. Use clinical judgement. Further testing and/or empiric treatment may be indicated.
≥1 pos	All neg	Supports discontinuing AII. Cannot exclude active TB.	Consistent with NTM. Cannot exclude active TB.
≥1 pos	≥1 pos for MTB and neg for RIFres	Continue AII until d/c criteria are met	Consistent with active pulmonary TB.
≥1 pos	≥1 pos for MTB and pos for RIFres	Continue AII. D/C criteria stricter usually.	Consistent with active pulmonary TB. Further testing require to confirm Rif resistance result (rapid sequencing at CDC and DST)
SS not done	≥1 pos for MTB and neg for RIFres	Supports continuing AII. Need SS to evaluate completely.	Consistent with active pulmonary TB.
All neg	≥1 pos for MTB and neg for RIFres	Continue AII and consult infection control for guidance.	Consistent with active pulmonary TB.
All neg	≥1 pos for MTB and pos for RIFres	Continue AII and consult infection control for guidance. D/C criteria stricter usually.	Consistent with active pulmonary TB. Further testing require to confirm Rif resistance result (rapid sequencing at CDC and DST)

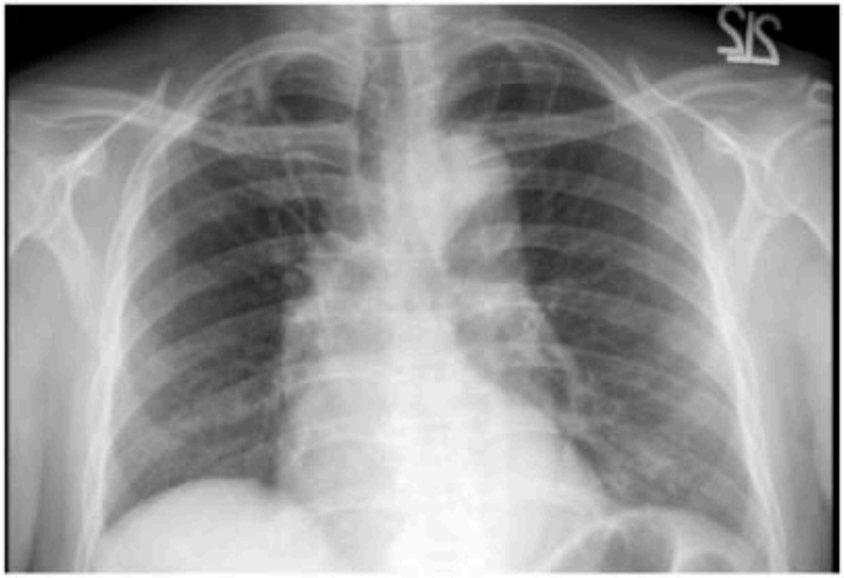
Patient 2

Abnormal CXR: Evaluate for nursing home admission

- M.M. is a 63 yo man from Ethiopia (30 yrs ago) who has multi-infarct dementia and abuses alcohol. His wife can no longer handle him at home. He is in the hospital awaiting placement in a nursing home. He does not speak English and refuses to talk with a translator.
- The patient would not allow PPD placement. His wife reports the patient has never been diagnosed with any form of TB and has never had pneumonia. She does not know anyone who has had TB.
- He is eating well and has no fever or observed cough over 4 days in the hospital. His weight now is the same as it was 4 years ago on a prior admission.

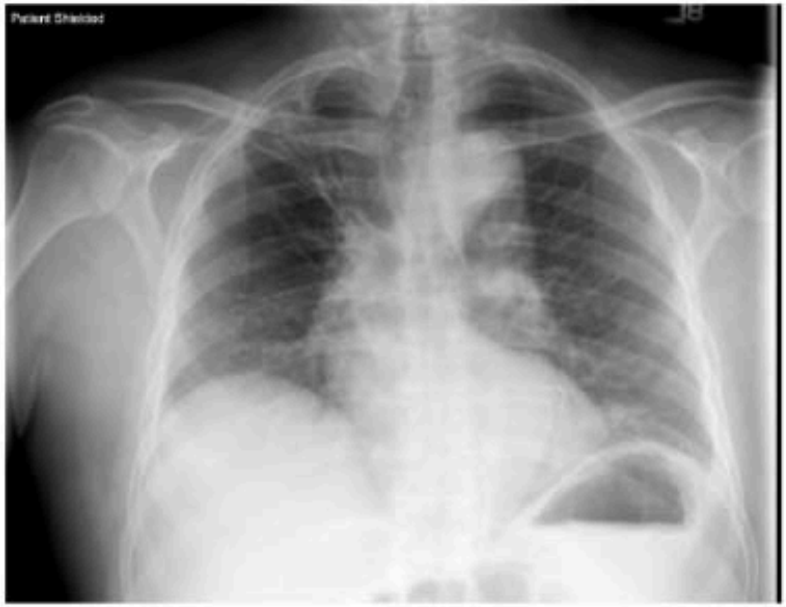
Patient 2: CXRs

2012



FINDINGS:
There is bronchiectasis and scarring in the right upper lung with retraction of the minor fissure. Globular high density structures projecting in the infrahilar regions, best seen on the lateral view, could represent calcified mediastinal/hilar lymph nodes. No additional focal consolidation or pneumothorax. No acute osseous abnormality. Included soft tissues are grossly within normal limits

10/10/16



FINDINGS:
LUNGS/PLEURA: Unchanged right upper lobe bronchiectasis with scarring, most notable in the right upper lobe. No pleural effusion or pneumothorax.
HEART AND MEDIASTINUM: The cardiac contour and mediastinum appear unchanged in comparison 2012. There are calcified hilar and mediastinal lymph nodes.
BONES AND SOFT TISSUES: No acute abnormality

For patient 2, choose the best answer below:

A. If an interferon-gamma-release-assay (IGRA) test is positive, this patient has latent TB.

B. If an interferon-gamma-release-assay (IGRA) is positive, this patient has active TB.

C. If an interferon-gamma-release assay (IGRA) is negative, this patient can be admitted to the nursing home without further investigation.

D. This patient has latent TB and should be treated with medication to prevent active TB. This treatment can be started after he is admitted to the nursing home.

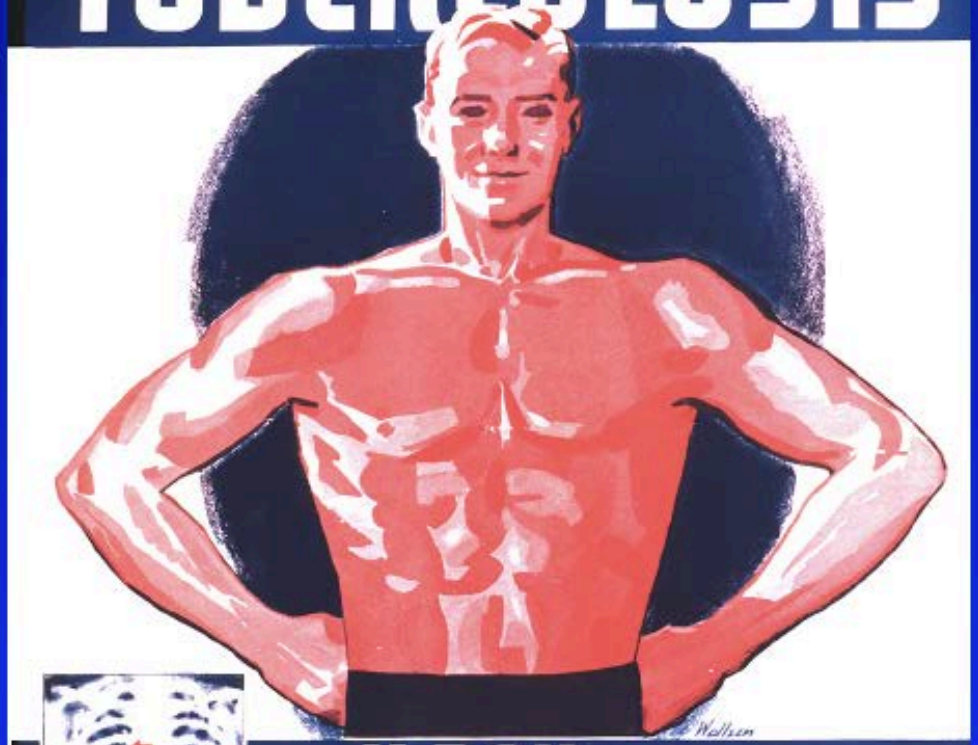
E. The patient has possible active TB.

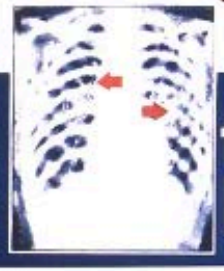
Purpose of Evaluation determines diagnostic testing approach

Purpose	Clinical/epidemiologic state	Diagnostic approach
Diagnose active TB	• Symptomatic	Chest imaging Other body site imaging Microbiology and fluid analyses
Exclude active TB	• Symptomatic or Asymptomatic • Concern about missing active TB because of personal or public health risks	Chest imaging Other body site imaging Microbiology and fluid analyses
Prevent future active TB	• Asymptomatic • Prior Exposure risk • Risk for disease progression • Risk of both prior exposure and disease progression	Tests for Latent TB infection If positive, must do CXR Even if LTBI tests are neg, CXR may be pursued.

Negative TST or IGRA tests do <u>not</u> EXCLUDE active TB.

"Healthy looks" can hide
TUBERCULOSIS

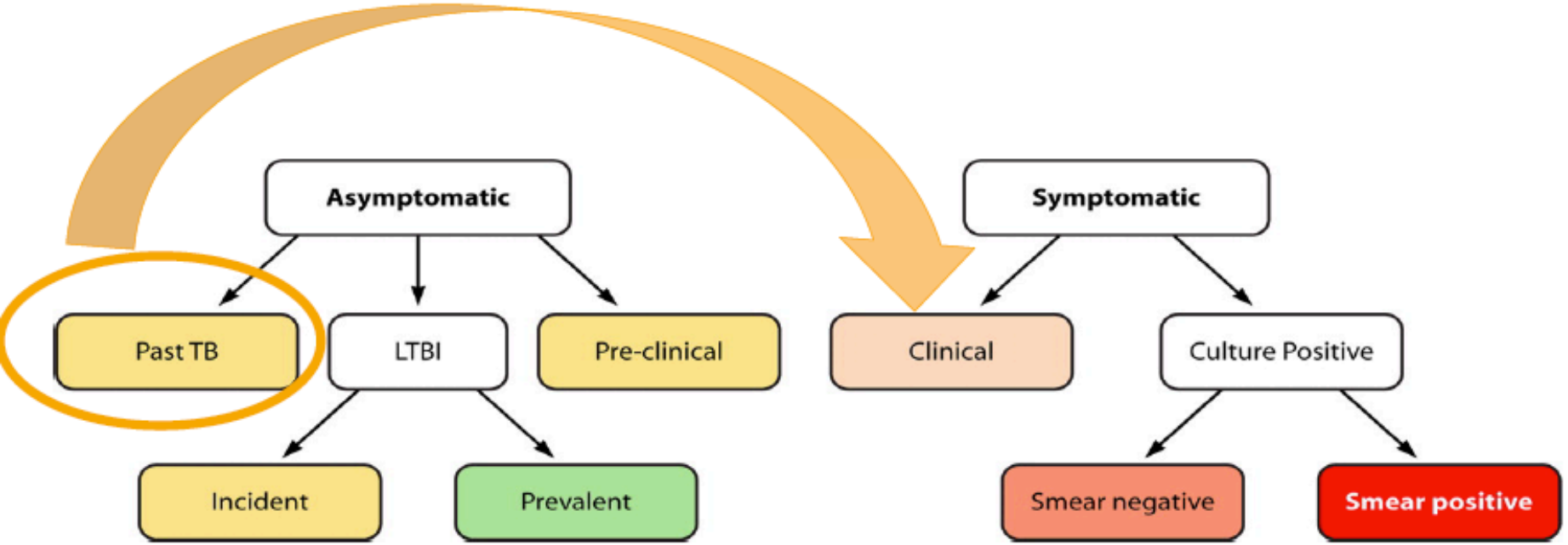




the X-RAY will show it
before *you* know it

Christmas Seals Fight Tuberculosis

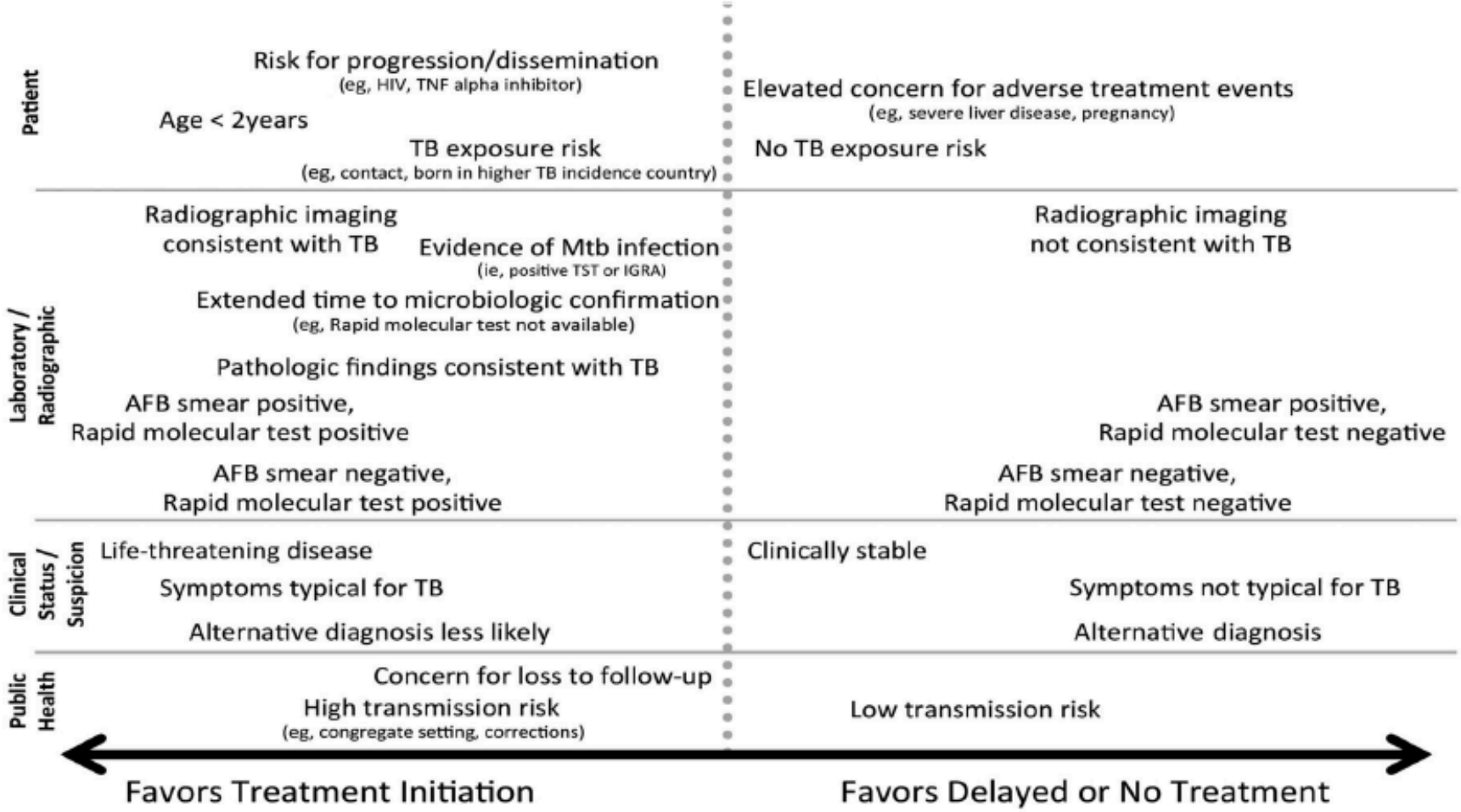
Clinical states of M. tuberculosis infection.



Shajo Kunnath-Velayudhan, and Maria Laura Gennaro Clin. Microbiol. Rev. 2011;24:792-805

Clinical Microbiology Reviews

Factors to be considered in deciding to initiate treatment empirically for active tuberculosis (TB) (prior to microbiologic confirmation).



Payam Nahid et al. Clin Infect Dis. 2016;63:e147-e195

Clinical Infectious Diseases

Patient 3

- 51 yo woman with hypertension presented with 3 weeks of night sweats, R pleuritic chest pain, and weight loss. Imaging studies reveal a large R pleural effusion and mediastinal adenopathy.
- She is not currently employed but has worked as a cook and uses alcohol to excess.
- PPD 25mm induration
- Pleural fluid studies: exudative with lymphocytic pleocytosis. AFB smears and gram stain negative. Cytology negative.
- Sputum studies: AFB smears negative x 3
- The patient is started on therapy for pleural TB with INH/B6, Rifampin, PZA, and Ethambutol and is discharged to the care of the county health department.
- After 8 weeks, the pleural fluid and sputum AFB culture are reported as no growth.

For patient 3
choose the best answer:

A. Stop TB medications. The patient has completed treatment for her positive PPD.
B. Continue TB treatment to complete 6 months of therapy for clinical TB.
C. Inquire about the clinical response to treatment. If the patient has gained weight, has no further fever or night sweats, then you can stop therapy.
D. Inquire about the clinical response to treatment. If the patient has gained weight, has no further fever or night sweats, or chest discomfort, then therapy should be continued for clinical TB.

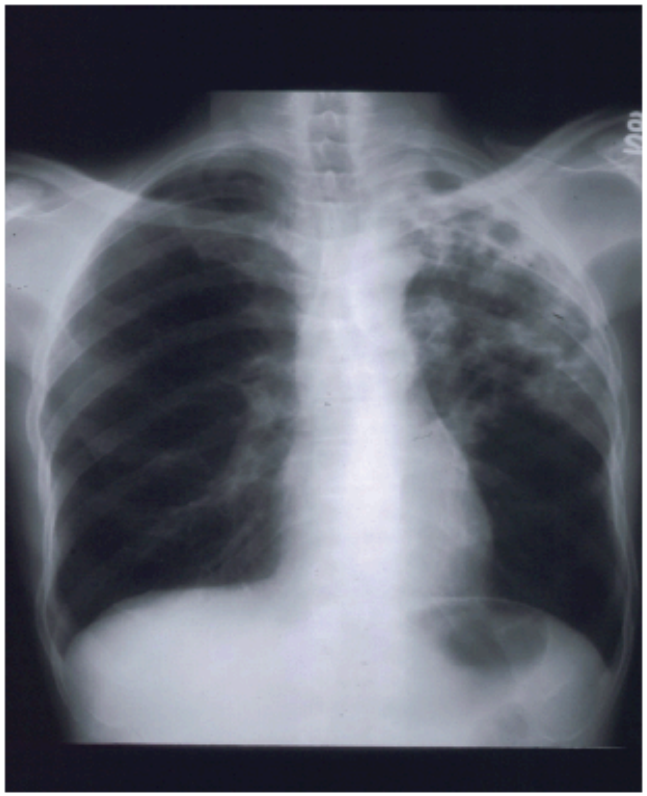
Clinical (i.e. not culture-proven) diagnosis of TB

- Alternate diagnoses excluded
- Response to therapy
  - Was therapy for another diagnosis given at the same time?
- Clinical diagnosis more common for:
  - TB meningitis
  - Pleural TB (pleural biopsy is highest yield for cx)
  - Lymph node TB (sent to path only- no micro)

Patient 4

- 45 yo man from Nigeria presents to the ER complaining of 2 weeks of cough, fever, and now headache. He arrived in the U.S. 4 years ago and is currently working as a parking deck attendant. He had a PPD placed last year and it was 25 mm. He was told he should not have any treatment for the positive PPD because he was "too old".
- No prior medical problems
- PE: T 39, appears ill, mild thrush, Neuro exam non-focal

- CBC: WBC 4.3K 90% N, 8% L, 2% M, H/H 10/31
- Sputum 3+ AFB, Mtb PCR positive
- CSF:
  - OP 17cm H2O
  - WBC 120 – 90% L
  - P 75 mg/dL
  - Glu 35 mg/dL (serum 125 mg/dL)
  - India Ink negative, Crypto Ag negative, gram stain negative, AFB smear negative
  - Mtb PCR test negative



For patient 4
Choose the best answer:

A. He should be started on therapy with INH/B6, Rifampin, PZA, and Ethambutol. He probably has HIV and some other OI is likely the cause of his meningitis.

B. He should be started on therapy with INH/B6, Rifampin, PZA and Ethambutol. Steroids are indicated for TB meningitis, but it is too dangerous to give steroids if you haven't proved that the meningitis is from TB.

C. He should be started on therapy with INH/B6, Rifampin, PZA, Ethambutol and steroids. If his HIV test is positive, he should be started on anti-retroviral therapy within 7 days.

D. He should be started on therapy with INH/B6, Rifampin, PZA, Ethambutol and steroids. If his HIV test is positive, anti-retroviral therapy should be given only after he has completed 8 weeks of TB therapy.

Xpert MTB/Rif for Extrapulmonary TB: Pooled Analysis*

Specimen type	Comparison	Sensitivity (95% CI)	Specificity (95% CI)
Lymph node tissue and aspirate	Culture (14 studies, 849 samples)	84.9 (72–92)	92.5 (80–97)
	Composite reference standard (5 studies, 1 unpublished)	83.7 (74–90)	99.2 (88–100)
Cerebrospinal fluid	Culture (16 studies, 709 samples)	79.5 (62–90)	98.6 (96–100)
	Composite reference standard (6 studies, 512 samples)	55.5 (51–81)	98.8 (95–100)
Pleural fluid	Culture (17 studies, 1385 samples)	43.7 (25–65)	98.1 (95–99)
	Composite reference standard (7 studies, 698 samples)	17.0 (8–34)	99.9 (94–100)
Gastric lavage and aspirate	Culture (12 studies, 1258 samples)	83.8 (66–93)	98.1 (92–100)
Other tissue samples	Culture (12 studies, 699 samples)	81.2 (68–90)	98.1 (87–100)

* *WHO. Updated Policy Guidance on Xpert MTB/RIF, 2013.*

CDC

TB Meningitis

- HIV is a risk factor for TB meningitis
- Short term morbidity and mortality are high
  - HIV coinfected patients have worse 9 month survival
- Empiric therapy indicated if the diagnosis is suspected
- Treatment:
  - INH, Rifampin, PZA, Ethambutol for 2 months,
  - INH/Rifampin for an additional 7 to 10 months
- Repeat lumbar puncture to monitor treatment response
- Adjunctive corticosteroids offer mortality benefit
  - Dexamethasone or Prednisolone tapered over 6 to 8 weeks

Q5

Choose the correct statement:

A. Single drug resistance to PZA is the most common form of drug resistance among Mtb isolates from U.S. patients.

B. Resistance to INH requires the addition of at least one additional medication to the treatment regimen.

C. The Genexpert test can detect MTb from direct specimens, but even if it detects Mtb, it is not sensitive to detect Rifampin resistance.

D. Rifabutin can substitute for Rifampin in any TB treatment regimen.

Treatment of INH-Resistant TB

- 4 drug regimen – Ethambutol was added because of the possibility of INH resistance
- Need for RCT to study regimens for INH-R TB

6 months of Rifampin, PZA and Ethambutol

or

9 months of therapy

- 2 months Rifampin, PZA, Ethambutol
- 7 months Rifampin, Ethambutol

"Some experts add a Fluoroquinolone for severe disease"

Patient 8

- 64 yo man with Crohn's disease and paranoid schizophrenia has been treated with infliximab for 6 years. He recently started a new round of infusions in the GI clinic. Screening labs were sent prior to the first dose for this round. An interferon-gamma-release-assay test was positive. His internist calls you concerned about this new result. The patient had a positive PPD 25 years ago and was treated with 6 months of medication by the health department.

For patient 8, choose the best answer:

A. The IGRA result suggests his treatment for latent TB was not effective. He should be treated again. He should not receive any more infliximab until latent TB treatment is completed.

B. The IGRA result is expected based on his history. No further action is needed.

C. The IGRA test suggests he could have been re-infected with TB. He should have a CXR immediately and the infliximab should be held.

D. Screening for symptoms of active TB is indicated (at each visit). Any symptoms of cough, fever, weight loss or night sweats, should prompt an evaluation beginning with a CXR.

TNF blocking agents and TB prevention

- Optimal screening method for LTBI not clear
  - 2-step TST plus IGRA, either positive
  - TST plus IGRA, either positive
  - Epi risk factors considered in addition to LTBI tests
- LTBI treatment and TNF blocker timing
  - Recs range from "after 3-4 weeks LTBI Rx" to "consider postponing until after LTBI Rx is complete"
- If active TB develops while on TNF blocker
  - Hold TNF blocker until TB disease is "under control"
  - IRIS can happen during this time

Patient 9

- 24 yo student from a local college presents for evaluation of a positive interferon-gamma-release-assay.
- She is starting coursework in Occupational Therapy. Her first clinical rotation is next month.
- She has no medical problems. Takes oral contraceptives for birth control.
- She has never had TB testing before. Does not know anyone with TB.
- Grew up in rural GA. Attended public high school. Has worked in retail and as a nanny prior to starting college.
- PE: normal
- CXR: normal

Q9

Choose the best answer:

A. The IGRA result is more likely to be false-positive than true-positive.

B. If she doesn't take treatment for latent TB infection, she should not be allowed to start her clinical rotations.

C. A PPD test is indicated. If this is negative, it will "trump" the IGRA result.

D. The IGRA test should be repeated every year while she is a healthcare worker because repeated test results can predict the risk of active TB.

Latent TB Infection (LTBI)

LTBI is the presence of *M. tuberculosis* organisms (tubercle bacilli) without symptoms or radiographic evidence of TB disease.

Expanding targeted testing and treatment of latent TB infection is key to eliminating TB disease in the United States

- Up to 13 million people in the U.S. are estimated to have latent tuberculosis (TB) infection.
- Latent TB infection is a condition in which a person is infected with the TB bacteria, but does not currently have active TB disease and cannot spread TB to others. However, if these bacteria become active and multiply, latent TB infection can turn into TB disease.
- Without treatment, on average 5-10% of people with latent TB infection will develop TB disease. For some people, that risk is much higher.
- CDC and the U.S. Preventive Services Task Force recommend testing populations that are at increased risk for TB infection.

Available diagnostic tests for LTBI

	PPD-based TST	IFN-γ release assays
Examples	Tubersol, Aplisol, PPD RT23	QuantiFERON-TB gold in tube, T-SPOT.*TB*
Testing format	Intra-dermal skin test	Ex vivo assay (ELISA or ELISPOT)
Antigens used	PPD	ESAT-6 and CFP-10
Intended use	Screening for LTBI	Screening for LTBI
Sensitivity in immunocompromised	High Reduced	Modest Reduced
Specificity impact of BCG	Modest High	High None
Ability to distinguish latent from active TB	Low	Low
Ability to predict progression to active TB	Modest	Modest
Reagent costs/ Laboratory Needed	Low / No	High / Yes

Adapted from Pai and Sotgui. Eur Resp J 2016;47:704

When to use IGRA tests

- IGRAs = TST (no preference)
  - in all situations in which TST is recommended for diagnosing *M. tuberculosis* infection
- **IGRAs are preferred for testing in:**
  - Persons who have received BCG
  - Persons from groups with poor rates of return for TST reading.
- **TST is preferred** for: children < 5 years.
- As with TST, IGRAs generally should not be used for testing persons with low risk of infection and low risk of disease due to *M. tuberculosis.*

With rare conditions, positive predictive value is driven by specificity. This figure shows PPV (vertical axis) by prevalence (horizontal) for increasing specificity values.

Source: Zenilman JM et al, Sexually Transmitted Infections 2003;79:94-97.

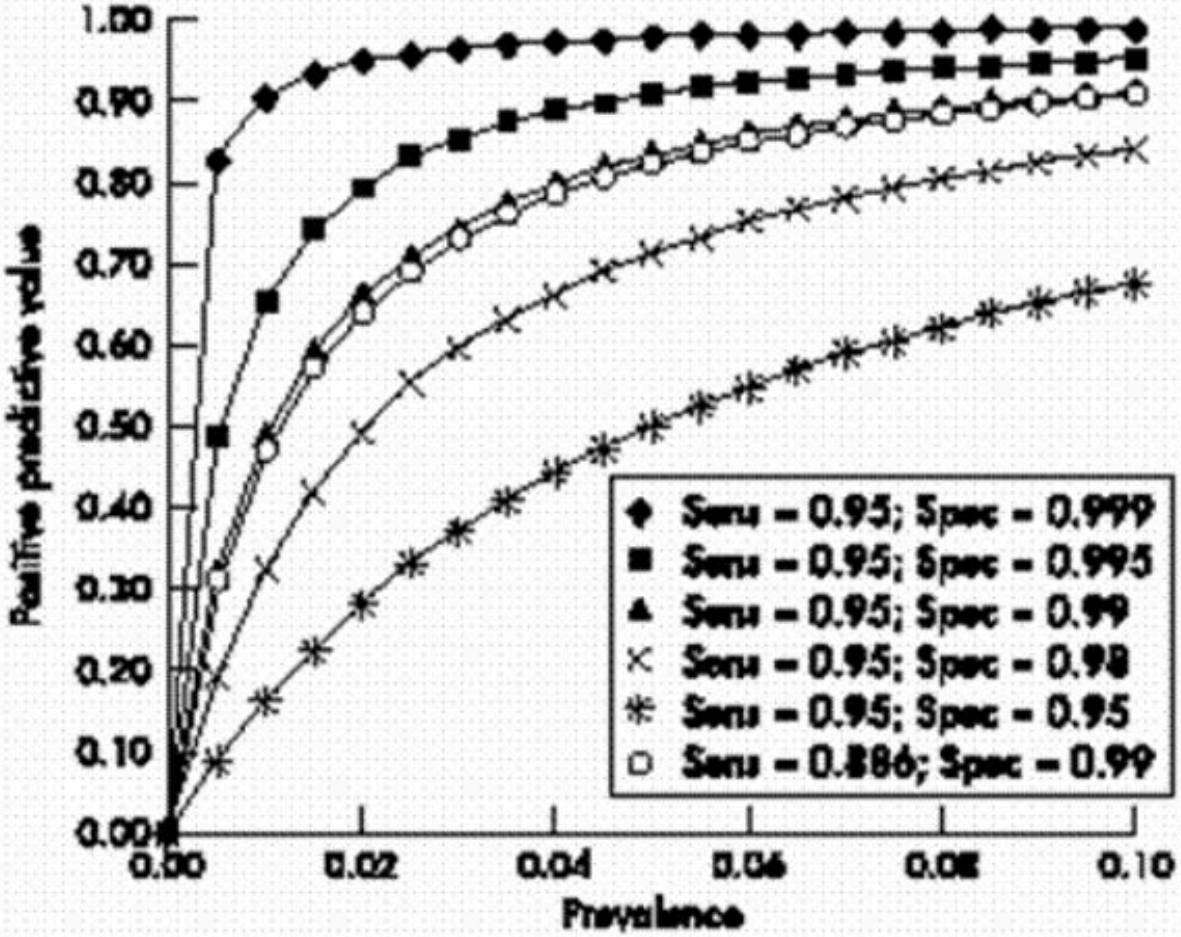


Figure 1 Calculated positive predictive values for a test with sensitivity of 88.6%–95% and specificity of 95%–99.9% in theoretical populations with disease prevalences of 0.0%–10.0%. Note steep decrease in PPV at lower prevalence levels.

Q9a

Indicate your next course of action:

A. Repeat interferon-gamma-release assay
B. Place a PPD
C. Recommend Rifampin 600 mg daily x 4 months
D. Recommend Levofloxacin 750 mg daily x 9 months
E. Recommend INH 300mg/B625mg daily x 9 months
F. Recommend INH 900mg/Rifapentine 900 mg once weekly by DOT x 12 doses

2011 CDC Recommendations
Treatment of Latent Tuberculosis Infection

Adults:

- 9-mo regimen of isoniazid (INH)
- 4 months Rifampin
- 12 doses weekly INH/Rifapentine by DOT

Clinical monitoring

- Monthly for signs/symptoms of possible adverse effects
- Routine baseline and follow-up labs not required except for
  - HIV-infected persons
  - Pregnant women or those in early postpartum period
  - Persons with chronic liver disease or who use alcohol regularly

Patient 10

- A 62 yo man is a close contact of a smear positive pulmonary TB case. He takes no regular medicines, smokes cigarettes and drinks 1 pint of vodka daily.
  - Baseline PPD 0mm induration
  - 8 week PPD 15 mm induration
  - CXR: flattened diaphragms, no infiltrates
  - Chem panel: AST 62, ALT 45, Alk phos 130, T Bili 1.5
  - HIV negative

For patient 10
choose the best answer

A. Treatment for Latent TB infection is contraindicated because of his active alcohol use
B. Rifampin 600 mg daily x 4 months is the best treatment for him because his active alcohol use makes INH too dangerous
C. He is an appropriate candidate for treatment with INH 900 mg and Rifapentine 900 mg weekly x 12 weeks by DOT
D. Public health law can be used to require him to follow your recommendations.

LTBI rx and Hepatotoxicity

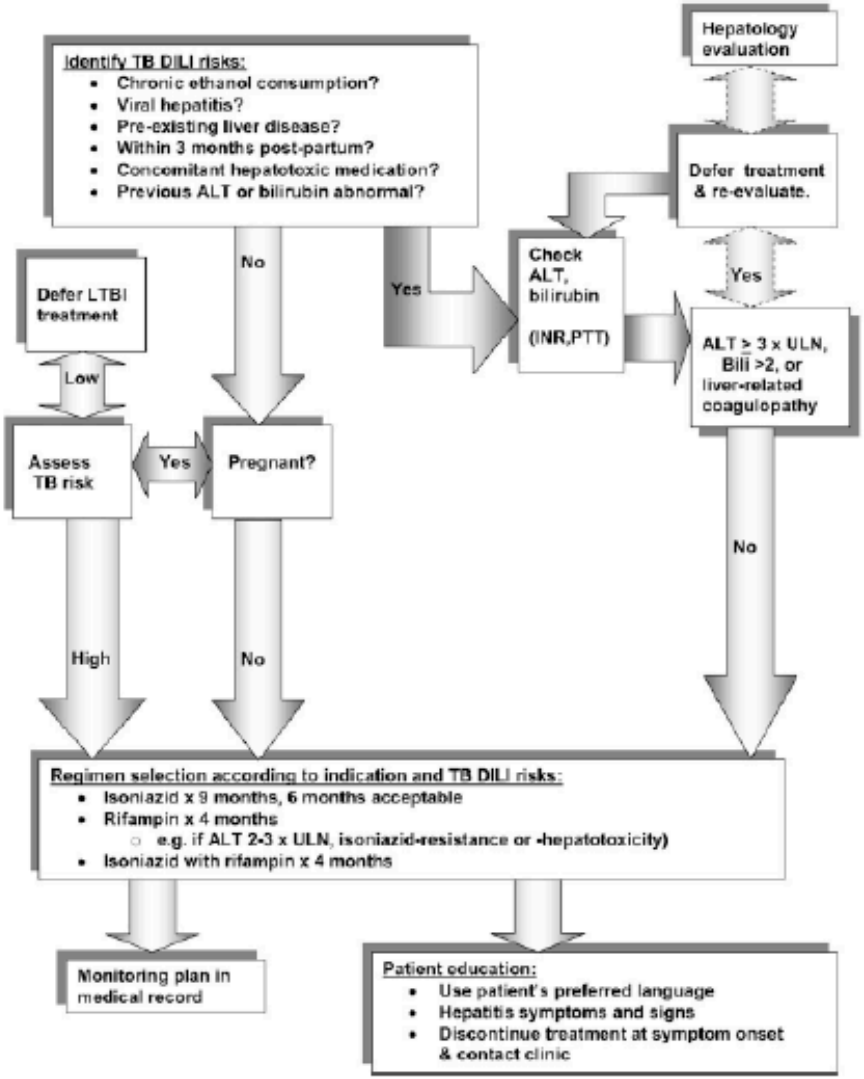
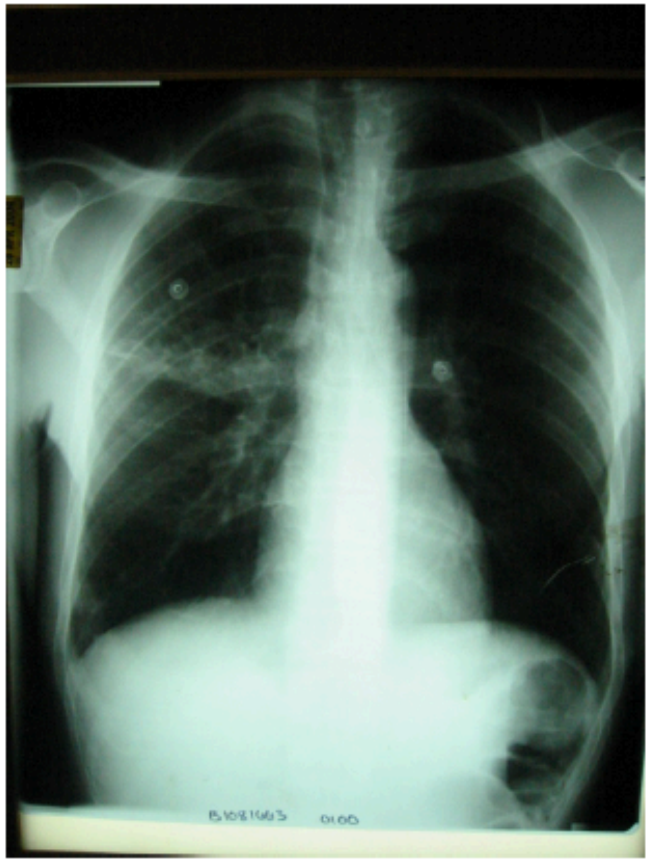


Figure 1. Latent tuberculosis infection (LTBI) pretreatment clinical evaluation and counseling. *Dotted lines* signify management according to physician's discretion. ALT = alanine aminotransferase; DILI = drug-induced liver injury; INR = international normalized ratio; PTT = partial thromboplastin time; ULN = upper limit of normal.

Am J Respir Crit Care Med Vol 174. pp 935–952, 2006

Patient 11

- 45 yo homeless man with AIDS (not on ART or any other medication) presents with 1 month of productive cough with associated fever, chills, and night sweats.
- Vital signs: T 38.2 R 18 P 106 BP 108/64
- PE significant for temporal wasting, oral thrush, poor dentition
- CXR as shown
- Sputum AFB smear: 4+
- Treatment with INH/B6, Rifampin, PZA and Ethambutol is started.
- The patient improves over the next 3 days.
- MTb PCR test on the smear positive sputum is reported as negative.



For patient 11,
choose the best answer:

A. The Mtb PCR test is not sensitive enough to exclude TB on a smear positive specimen.
B. The most likely diagnosis is pulmonary MAC.
C. The current 4 drug therapy should be continued.
D. It would be very dangerous to remove the patient from airborne precautions.

Mycobacterium kansasii

- Second most common cause of NTM in the U.S.
  - Most common in southern and central states
  - Cases more likely from urban than rural areas
  - Increased rates in areas with high HIV prevalence
- Environmental reservoirs:
  - tap water
  - No other water or soil source of M. kansasii found
  - Limited genetic diversity of strains by PFGE
- Infection via aerosol route

M. kansasii: Clinical presentation

- Pulmonary *M. kansasii* hard to distinguish from tuberculosis
  - Cavitary disease quite common
  - Early disease: nodular/bronchiectatic infiltrates
- M. kansasii in AIDS
  - Pulmonary disease alone
    - Cavities assoc. with high CD4
  - Pulmonary disease plus dissemination
    - Dissem. Assoc. with low CD4

M. kansasii: Treatment

- Susceptible to most anti-TB meds except PZA
  - rifampin, rifabutin, isoniazid (higher MICs), ethambutol, ethionamide, amikacin, streptomycin (higher MICs), clarithromycin
  - Also susceptible to: Sulfamethoxazole, quinolones
- Rifampin resistance associated with treatment failure
- Key to successful Rx is multidrug regimen including rifampin
- Rx length: 20 months or 12 months culture negative (whichever is longer)

Patient 7

- A colleague asks you to see his aunt in the office. Wants your advice on her TB treatment.

- 65 yo woman from India has been here in U.S. visiting her family for 2 months and has a plane ticket to return home to India in 2 days. She has been having low grade fever, night sweats and abdominal discomfort for the past week.
- Four months ago, she was diagnosed with abdominal TB at home in India. She was treated with daily self-administered medication (5 pills) and felt completely well within 2 weeks after starting therapy. She has continued the pills here in the U.S. but is concerned that her TB symptoms have returned. She does not have any medical records with her. From her description you gather the diagnosis was based on CT scans of her abdomen.
- She has no cough – never had a cough. Her weight is stable. She walks 2 miles every morning.
- PE: normal
- CXR today: normal

- She shows you her supply of pills. One bottle has large brownish pills with RHEZ printed on the side. She takes 4 of these daily. The other bottle has small white pills . She takes 1 of these daily.

For patient 7, what is the best management?

A. Call CDC quarantine office to ask them if it is OK for her to fly on a commercial airline in 2 days. Give her an Rx for Levofloxacin 750 mg to take along with her current medications.

B. Give her an Rx for Levofloxacin 750 mg (30 day supply) to take along with her current medications. Tell her to seek care in India if she does not feel better by the time she has completed the Levofloxacin.

C. Admit her to the hospital in airborne isolation and order CT scan of Chest/abdomen/pelvis, induced sputum for AFB smear and culture, AFB blood and urine cultures. Tell her to cancel her trip home. Start treatment with INH, Rifampin, PZA, Ethambutol, B6, IV Amikacin, and Levofloxacin.

D. Tell her you agree that it is possible she has return of TB symptoms and that she may have drug resistant disease. Encourage her family (your colleague) to pursue further evaluation once she is home in India. Emphasize the importance of obtaining body fluids for culture and getting drug susceptibility results to guide management.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta, GA 30329-3724

March 23, 2017

Dear Colleagues:

The purpose of this communication is to inform you of national planning for the introduction of universal whole-genome sequencing (WGS) and subsequent changes to the National TB Genotyping Service.

The Division of Tuberculosis Elimination, in collaboration with colleagues in the CDC Antimicrobial Resistance Coordination and Strategy Unit, will be supporting the use of WGS for all new isolates of *Mycobacterium tuberculosis* referred for genotyping beginning in spring 2018. All isolates will undergo both conventional genotyping as well as WGS for a period of 3 years. This period of overlap will allow for modification of information systems that will facilitate programmatic use of WGS data. During this overlap period, functionality of TB GIMS and cluster alerting based on conventional genotyping will be maintained. After this transition period, prospective WGS will become the standard method performed to identify TB clusters. Currently, plans are being made for capture of this information in TB GIMS; additional details regarding the timeframe and mechanism for access to these and other data (e.g., retrospective WGS analysis for clusters of concern) will be provided in the future. A presentation with additional details is scheduled during the 2017 National TB Conference in Atlanta, Georgia.

The use of WGS is an exciting advancement that enhances the discriminatory power for cluster identification and investigation, which should allow for a more focused investment of public health interventions. Additionally, WGS allows for the surveillance of molecular determinants associated with drug resistance. At this time, data will be captured for the purposes of surveillance only as the methodology will not be performed for diagnostic use in a regulatory environment. Molecular surveillance of drug resistance does not replace the CDC MDDR service which will continue to be available for rapid analysis of isolates and sediments.

To support the infrastructure required for universal WGS, up to two public health laboratories will be awarded funds to support this activity through competitive selection as described in the Epidemiology and Laboratory Capacity funding opportunity announcement (K3- Antimicrobial Resistance Regional Laboratory Network) that was recently released. The selected laboratories will operate as part of the Antimicrobial Resistance Laboratory Network. Additional details regarding requirements and eligibility can be found in the funding announcement.

We look forward to the roll out of universal WGS in support of our public health partners. Please contact Jamie Posey (404-639-1712 or hzp9@cdc.gov) with questions.

Sincerely,

Angela M. Starks
Chief, DTBE Laboratory Branch

Thomas R. Navin
Chief, DTBE Surveillance, Epidemiology,
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