TBCB Tuberculosis Control Branch

PEDIATRIC TB INFECTION

KRISTEN WENDORF, MD, MS

CDPH California Department of PublicHealth

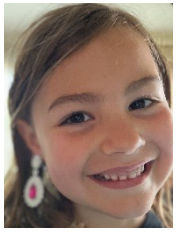
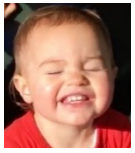
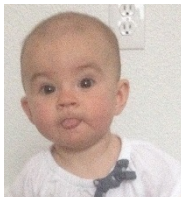
TAKE HOME LESSONS:

I HAVE NO FINANCIAL DISCLOSURES

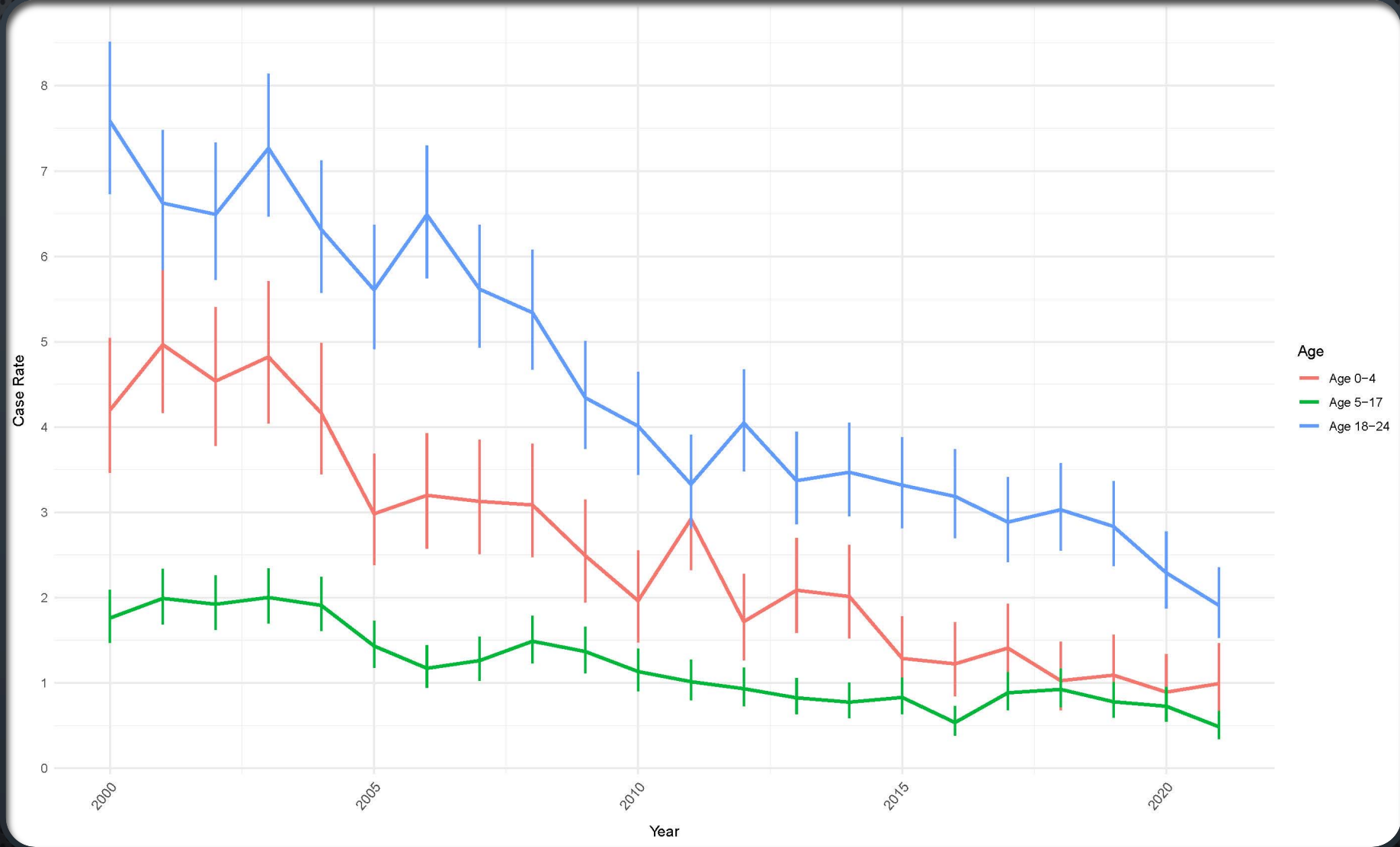
- **PERFORM TB TESTING ONLY** AMONG CHILDREN:
  - WITH ELEVATED RISK OF TB **EXPOSURE**
  - WITH ELEVATED RISK OF TB **PROGRESSION**
- **USE IGRAS FOR TB TESTING** AMONG NON-US–BORN CHILDREN 2 YEARS AND OLDER
- **USE SHORTEST EFFECTIVE TREATMENT** REGIMEN FOR TB INFECTION
  - RIFAMPIN
  - 3HP

CALIFORNIA PEDIATRIC ACTIVE TUBERCULOSIS DISEASE EPIDEMIOLOGY

2 CASES PER WEEK IN CA KIDS (<18 YRS)

1	2		4		6	7
8		10		12	13	14
15	16		18	19		21
	22	23	24	25	26	
28		30				

TRENDS IN AVERAGE ANNUAL TB INCIDENCE RATES BY AGE GROUP, 2000 - 2021



DEMOGRAPHIC CHARACTERISTICS

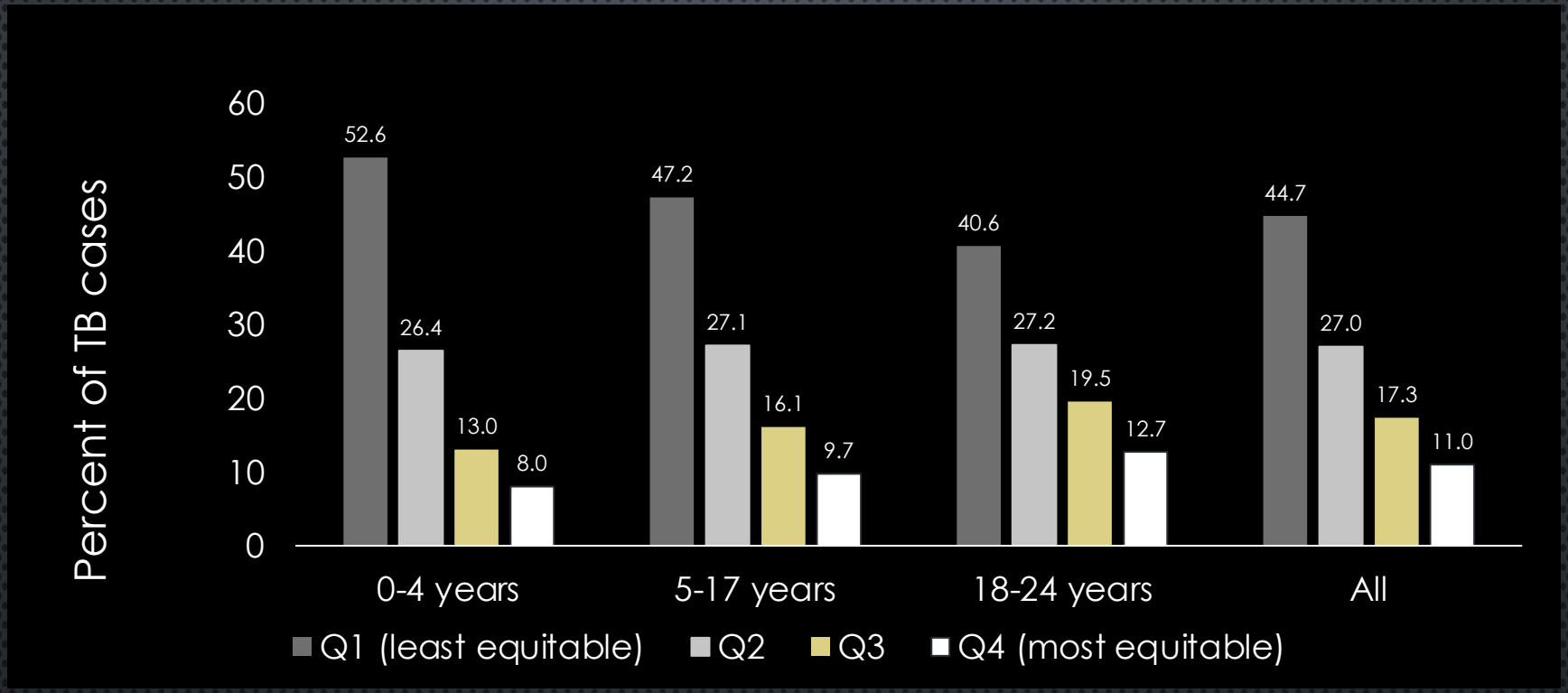
	Age 0-4 (N=1566)	Age 5-17 (N=1986)	Age 18-24 (N=4279)	Total: All < 25 (N=7831)
Sex				
Male	807 (51.5%)	975 (49.1%)	2427 (56.7%)	4209 (53.7%)
Female	759 (48.5%)	1010 (50.9%)	1852 (43.3%)	3621 (46.2%)
Race/Ethnicity				
White	73 (4.7%)	85 (4.3%)	185 (4.3%)	343 (4.4%)
Black	92 (5.9%)	127 (6.4%)	295 (6.9%)	514 (6.6%)
Hispanic/Latine	1084 (69.2%)	1240 (62.4%)	2242 (52.4%)	4566 (58.3%)
Asian	295 (18.8%)	504 (25.4%)	1529 (35.7%)	2328 (29.7%)
American Indian or Alaskan Native	2 (0.1%)	1 (0.1%)	3 (0.1%)	6 (0.1%)
Native Hawaiian or Pacific Islander	12 (0.8%)	18 (0.9%)	16 (0.4%)	46 (0.6%)
Multiple Races	3 (0.2%)	5 (0.3%)	4 (0.1%)	12 (0.2%)
Origin				
U.S. Born	1317 (84.1%)	1061 (53.4%)	1191 (27.8%)	3569 (45.6%)
Non-U.S. Born	248 (15.8%)	921 (46.4%)	3083 (72.0%)	4252 (54.3%)

Distribution of known risk factors, 2010-2021

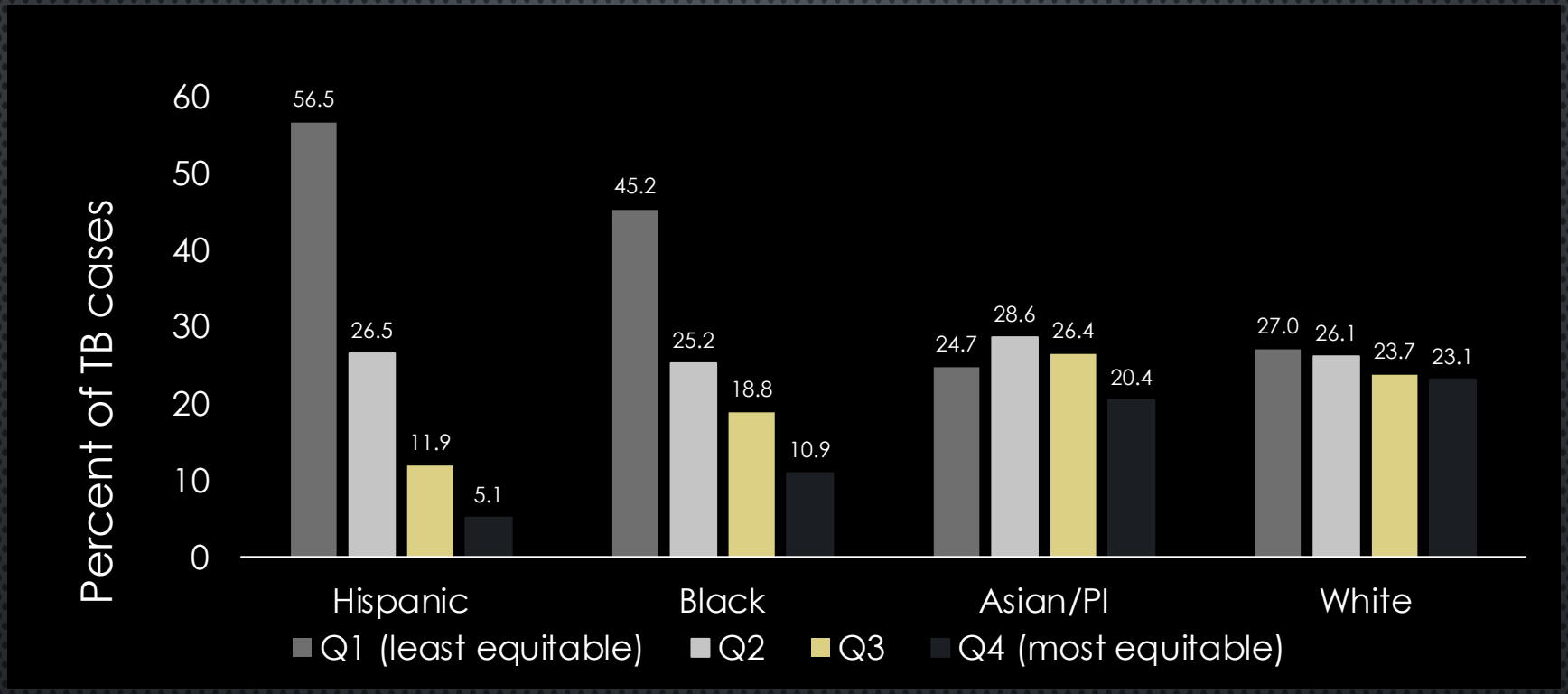
	Age 0-4 (N=512)	Age 5-17 (N=736)	Age 18-24 (N=1733)	Total: All <25 (N=2981)
Previous TB				
Yes	3 (0.6%)	18 (2.4%)	33 (1.9%)	54 (1.8%)
No	509 (99.4%)	718 (97.6%)	1700 (98.1%)	2927 (98.2%)
Contact of Infectious TB Patient				
Yes	270 (52.7%)	151 (20.5%)	178 (10.3%)	599 (20.1%)
No	242 (47.3%)	585 (79.5%)	1555 (89.7%)	2382 (79.9%)

	Age 0-4 (N=457)	Age 5-17 (N=651)	Age 18-24 (N=1556)	All <25 (N=2664)
Immune Compromised (2011 - 2021)				
Yes	6 (1.3%)	21 (3.2%)	93 (6.0%)	120 (4.5%)
No	451 (98.7%)	629 (96.6%)	1461 (93.9%)	2541 (95.4%)
Missing	0 (0%)	1 (0.2%)	2 (0.1%)	3 (0.1%)

**Note that this information is only available for cases <15 years and ages are grouped 0-4 and 5-14

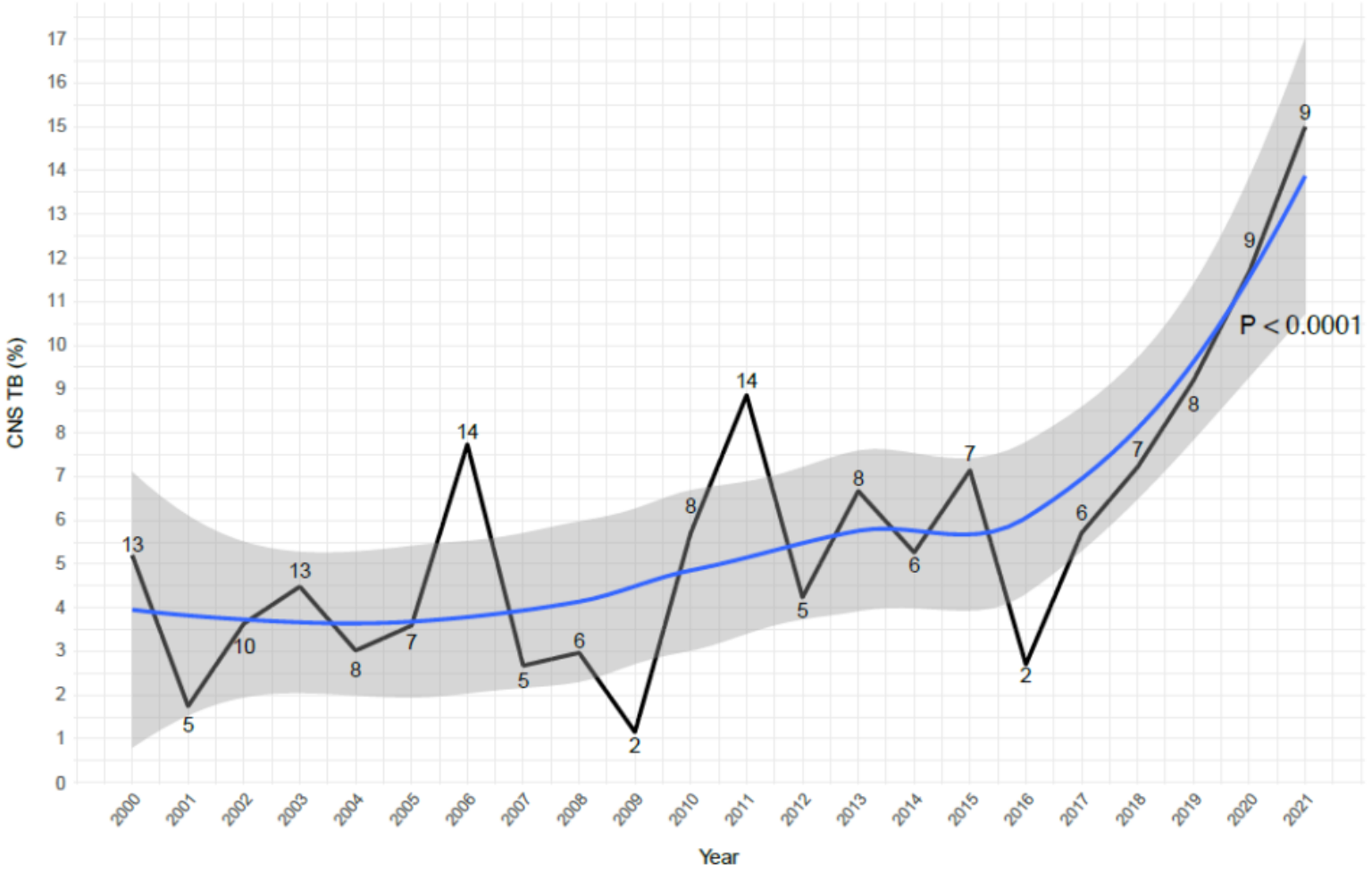


HEALTHY PLACES INDEX BY AGE GROUP



HEALTHY PLACES INDEX BY RACIAL/ETHNIC GROUP

Percent of annual pediatric and young adult TB cases < 18 years old in CA that have CNS TB



Numeric labels along line indicate the number of cases < 18 years old with CNS TB each year. Smoothed trend line produced using Loess Regression and trend significance assessed using two sided Cochran-Armitage trend test.

FINDING AND TREATING LTBI

STEP 1: DO A TB RISK ASSESSMENT
CDPH PEDIATRIC RISK ASSESSMENT

LTBI testing is recommended if any of the 3 boxes below are checked.

☐ **Birth, travel, or residence** in a country with an elevated TB rate for at least 1 month

- Includes any country other than the United States, Canada, Australia, New Zealand, or a country in western or northern Europe
- Interferon Gamma Release Assay is preferred over Tuberculin Skin Test for foreign-born persons ≥2 years old

☐ **Immunosuppression,** current or planned

HIV infection, organ transplant recipient, treated with TNF-alpha antagonist (e.g., infliximab, etanercept, others), steroids (equivalent of prednisone ≥2 mg/kg/day, or ≥15 mg/day for ≥2 weeks) or other immunosuppressive medication

☐ **Close contact** to someone with infectious TB disease during lifetime

Treat for LTBI if LTBI test result is positive and active TB disease is ruled out.

HOW OFTEN DO I DO A RISK ASSESSMENT?

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN®

Recommendations for Preventive Pediatric Health Care

Bright Futures/American Academy of Pediatrics

Bright Futures
prevention and health promotion for infants, children, adolescents, and their families

Each child and family is unique; therefore, these Recommendations for Preventive Pediatric Health Care are designed for the care of children who are receiving competent parenting, have no manifestations of any important health problems, and are growing and developing in a satisfactory fashion. Developmental, psychosocial, and chronic disease issues for children and adolescents may require frequent counseling and treatment visits separate from preventive care visits. Additional visits also may become necessary if circumstances suggest variations from normal.

These recommendations represent a consensus by the American Academy of Pediatrics (AAP) and Bright Futures. The AAP continues to emphasize the great importance of continuity of care in comprehensive health supervision and the need to avoid fragmentation of care.

Refer to the specific guidance by age as listed in the *Bright Futures Guidelines* (Hagan JF, Shaw JS, Duncan PM, eds. *Bright Futures: Guidelines for Health Supervision of Infants, Children, and Adolescents*. 4th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2017).

The recommendations in this statement do not indicate an exclusive course of treatment or standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

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	INFANCY								EARLY CHILDHOOD							MIDDLE CHILDHOOD						ADOLESCENCE										
AGE[1]	Prenatal[2]	Newborn[3]	3-5 d[4]	By 1 mo	2 mo	4 mo	6 mo	9 mo	12 mo	15 mo	18 mo	24 mo	30 mo	3 y	4 y	5 y	6 y	7 y	8 y	9 y	10 y	11 y	12 y	13 y	14 y	15 y	16 y	17 y	18 y	19 y	20 y	21 y
HISTORY Initial/Interval	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
MEASUREMENTS																																
Length/Height and Weight		•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
Head Circumference		•	•	•	•	•	•	•	•	•	•	•																				
Weight for Length		•	•	•	•	•	•	•	•	•	•																					
Body Mass Index[5]												•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
Blood Pressure[6]		★	★	★	★	★	★	★	★	★	★	★	★	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
SENSORY SCREENING																																
Vision[7]		★	★	★	★	★	★	★	★	★	★	★	★	•	•	•	•	★	•	★	•	★	•	•	•	•	•	•	★	★	★	★
Hearing		•[8]	•[9] →	→	★	★	★	★	★	★	★	★	★	★	•	•	•	★	•	★	•	←							←		•	→
DEVELOPMENTAL/BEHAVIORAL HEALTH																																
Developmental Screening[11]								•			•		•																			
Autism Spectrum Disorder Screening[12]											•	•																				
Developmental Surveillance		•	•	•	•	•	•		•	•		•		•	•	•	•	•	•	•	•	•	•						•	•	•
Psychosocial/Behavioral Assessment[13]		•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•						•	•	•	•
Tobacco, Alcohol, or Drug Use Assessment[14]																						★	★	★	★	★	★	★	★	★	★	★
Depression Screening[15]																							•	•	•	•	•	•	•	•	•	•
Maternal Depression Screening[16]				•	•	•	•																									
PHYSICAL EXAMINATION[17]		•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
PROCEDURES[18]																																
Newborn Blood		•[19]	•[20] →	→																												
Newborn Bilirubin[21]		•																														
Critical Congenital Heart Defect[22]		•																														
Immunization[23]		•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
Anemia[24]						★			•	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★
Lead[25]							★	★	• or ★[26]		★	• or ★[26]		★	★	★	★															
Tuberculosis[27]				★			★		★			★		★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★
Dyslipidemia[28]												★			•		★		★	←	• →	•	•	•	•	•	•	←			•	→
Sexually Transmitted Infections[29]																						★	★	★	★	★	★	★	★	★	★	★
HIV[30]																						★	★	★	★	←	• →		★	★	★	
Cervical Dysplasia[31]																																•
ORAL HEALTH[32]							•[33]	•[33]	★		★	★	★	★	★	★	★															
Fluoride Varnish[34]							←				•					→																
Fluoride Supplementation[35]							★	★	★		★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★						
ANTICIPATORY GUIDANCE	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•

1 month
6 months
12 months
Annually

STEP 2: PLACE A TB TEST IF THE RISK ASSESSMENT IS POSITIVE

LTBI testing is recommended if any of the 3 boxes below are checked.

☐ **Birth, travel, or residence** in a country with an elevated TB rate for at least 1 month

- Includes any country other than the United States, Canada, Australia, New Zealand, or a country in western or northern Europe
- Interferon Gamma Release Assay is preferred over Tuberculin Skin Test for foreign-born persons ≥2 years old

☐ **Immunosuppression**, current or planned

HIV infection, organ transplant recipient, treated with TNF-alpha antagonist (e.g., infliximab, etanercept, others), steroids (equivalent of prednisone ≥2 mg/kg/day, or ≥15 mg/day for ≥2 weeks) or other immunosuppressive medication

☐ **Close contact** to someone with infectious TB disease during lifetime

Treat for LTBI if LTBI test result is positive and active TB disease is ruled out.

STEP 3: EVALUATE FOR TB DISEASE

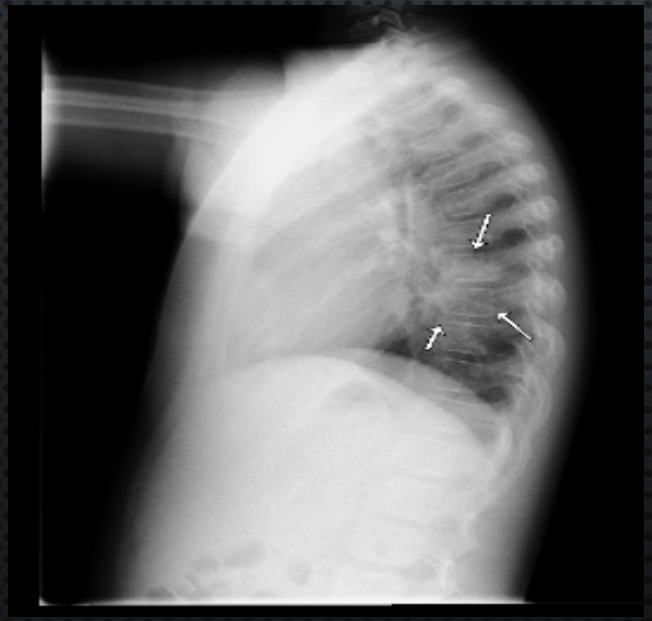
Child with positive risk assessment and positive TB test – what's next?

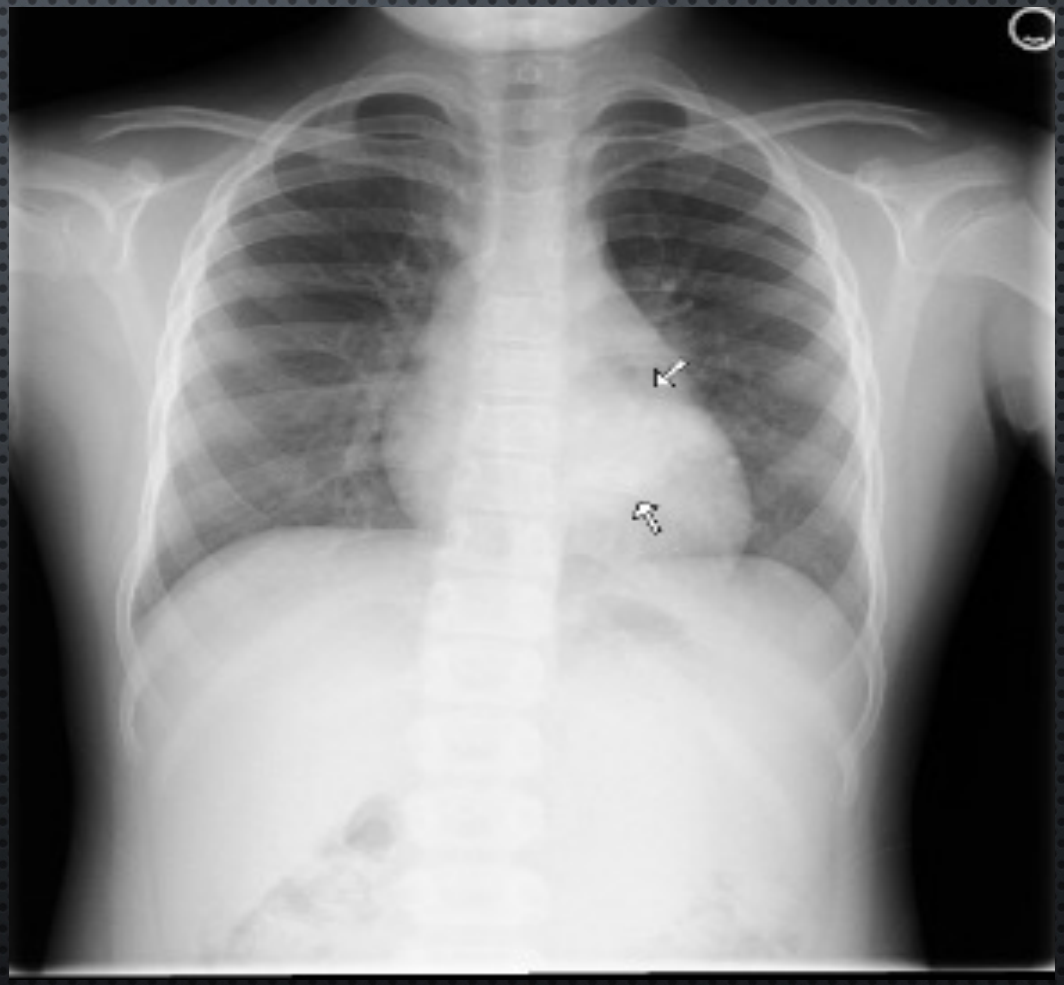
- Evaluate for active TB
  - Symptom screen
  - Physical exam
  - Growth Chart
  - Chest x-ray (PA and lateral)

- If no evidence of active TB, treat for LTBI

6 YEAR OLD TB CONTACT

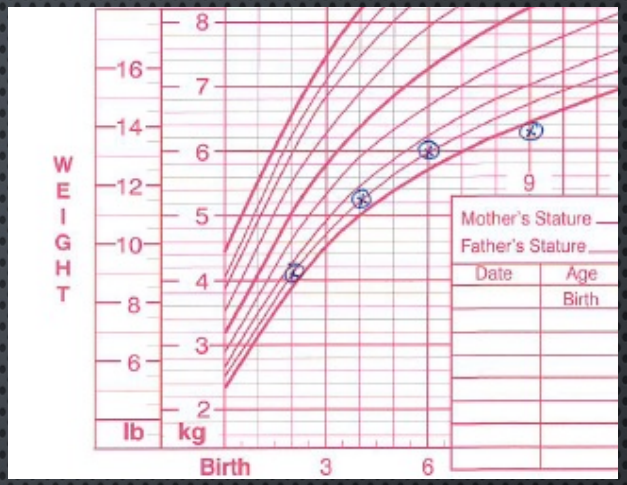
- No symptoms
- No past medical history
- Child tracking on growth curve (25%ile)
- Physical exam normal
- TST 15mm (US-born)

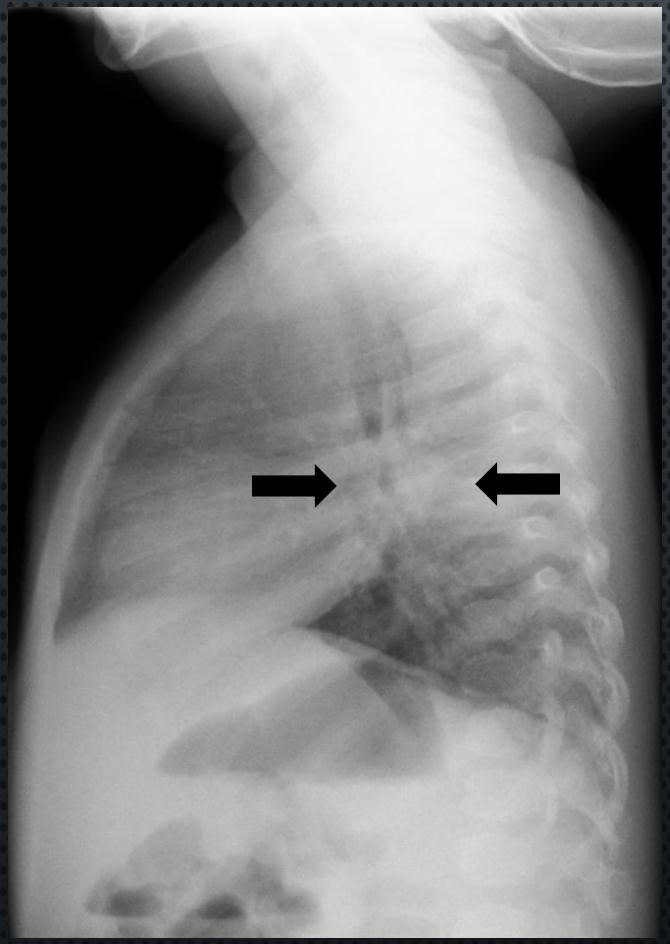


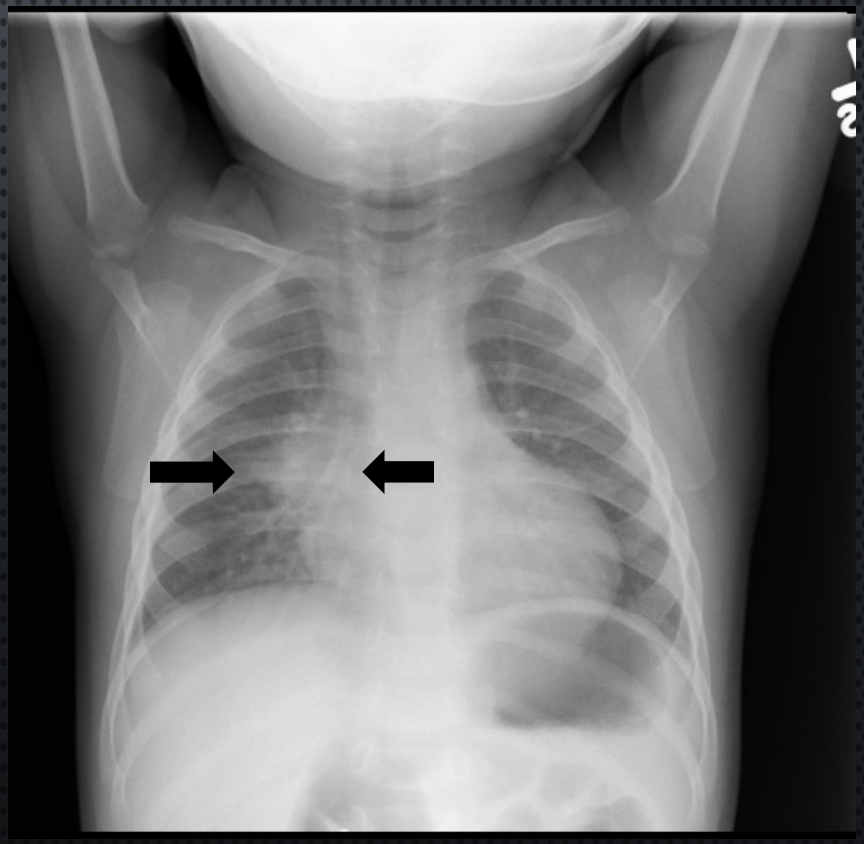


9 MONTH TB CONTACT

- No symptoms
- No past medical history
- **Poor growth**
- Physical exam normal
- TST **20 mm** (US-born)





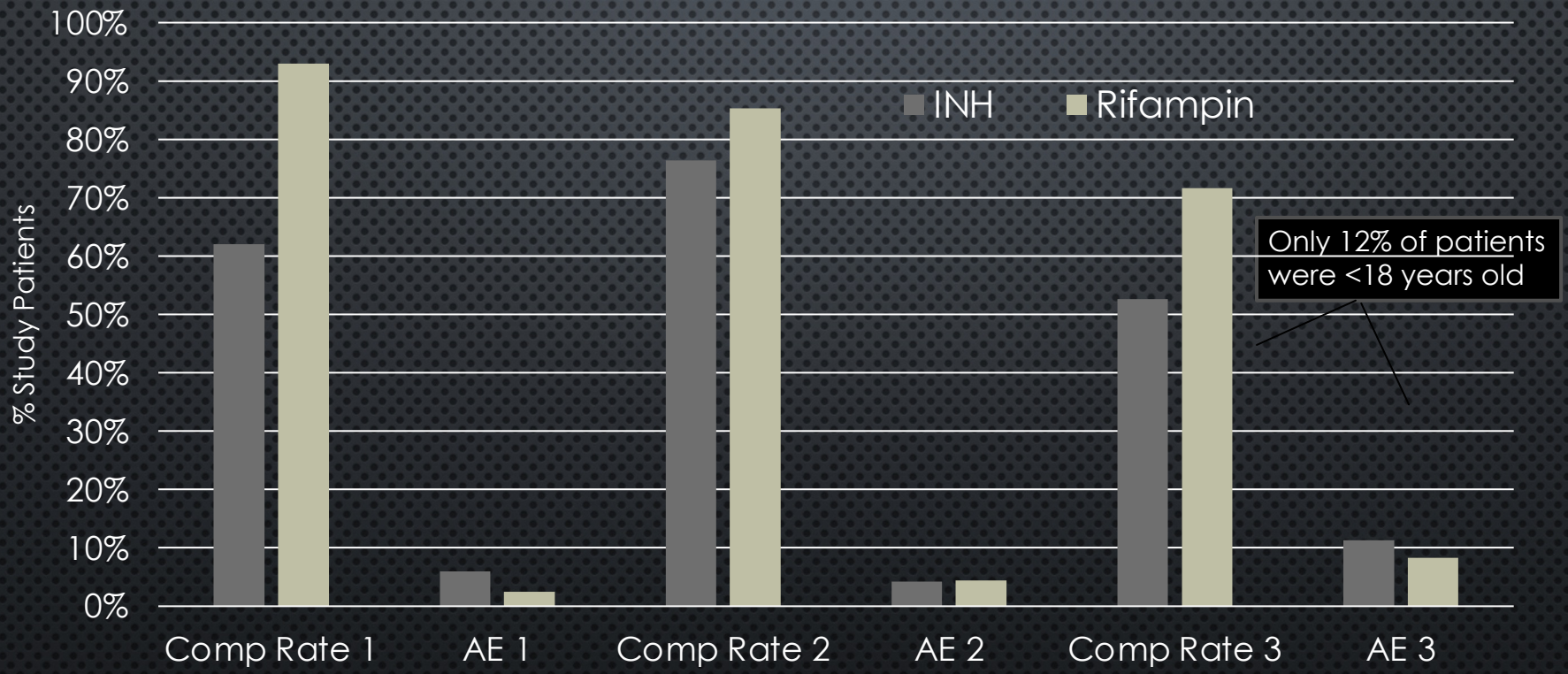


STEP 4: TREAT FOR LTBI WITH SHORT-COURSE REGIMENS

TB INFECTION TREATMENT OPTIONS

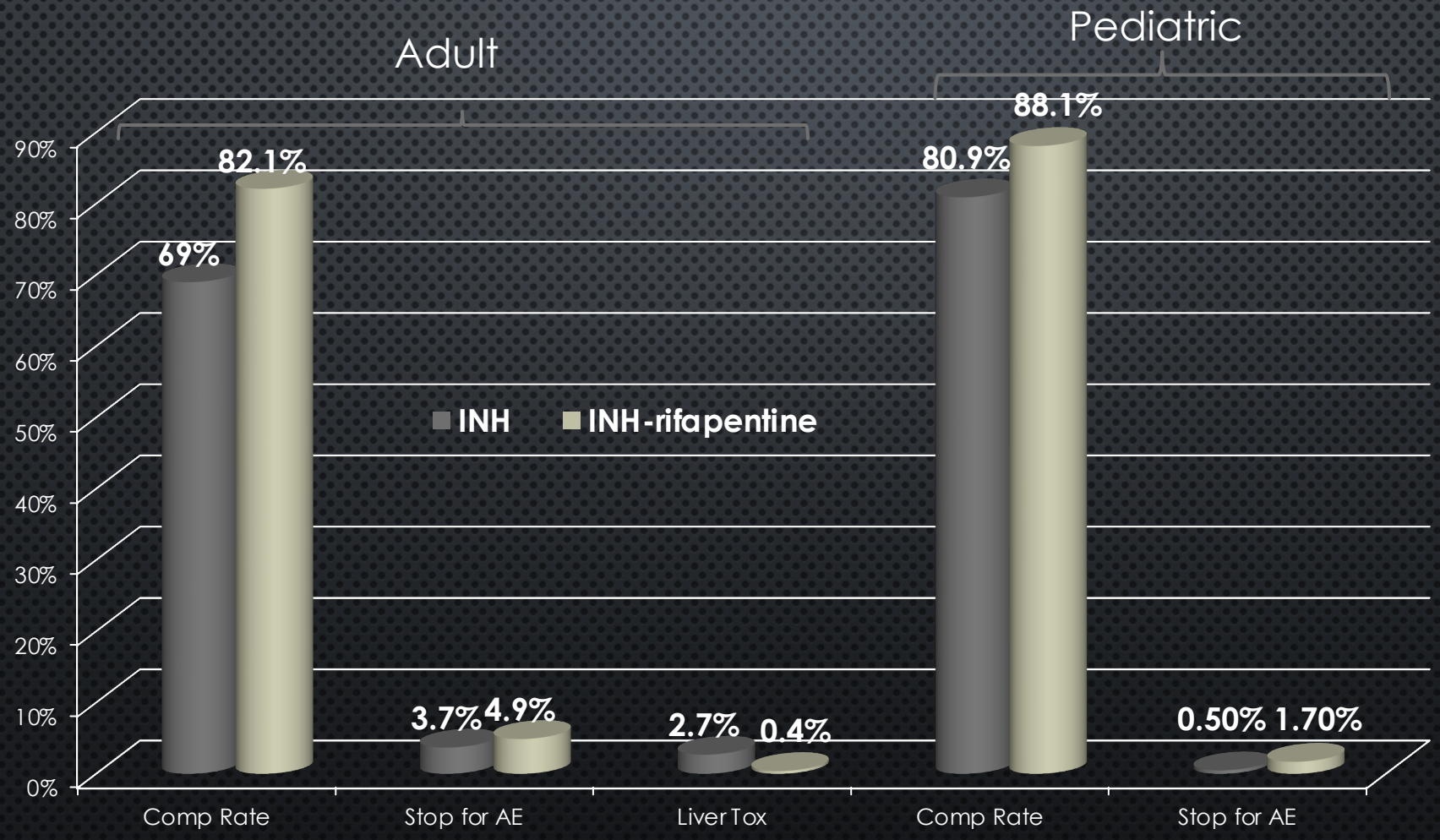
	Drug	Dose	Duration	Notes
Historical:	**Isoniazid**	10-15mg/kg daily	9 months	Great for infants on window tx
New:	**Rifampin**	20 mg/kg daily	**4 months**	Great for all ages
New:	**Isoniazid & Rifapentine (3HP)**	**Weekly** Dose varies by age	**12 weeks**	Great for kids who can swallow pills

RIFAMPIN (4MO) VS ISONIAZID (9MO)



Cruz AT, Starke JR. *Int J Tuberc Lung Dis* 2014;18:1057-61
Diallo T, Menzies. *N Engl J Med* 2018;379:454-63
Page, KR et al. *Arch Intern Med* 2006;166:1863-70.

3HP WEEKLY (12 WEEKS) VS INH (9MO)



Sterling TR et al. NEJM 2011;365:2155-66.
Villarino ME et al. *JAMA Ped* 2015;169:247-55.

ISONIAZID + RIFAPENTINE (3HP)

GOOGLE: "CDPH 3HP"

What are the doses?

Drug	Dosage	Maximum dose
INH	15 mg/kg rounded to nearest 50/100 mg in patients ≥ 12 years	900 mg
	25 mg/kg rounded to the nearest 50/100 mg in patients 2-11 years	
Rifapentine	10.0 – 14.0 kg = 300 mg	900 mg
	14.1 – 25.0 kg = 450 mg	
	25.1 – 32.0 kg = 600 mg	
	32.1 – 49.9 kg = 750 mg	
Rifapentine tablets can be crushed and administered with semi-solid food for children unable to swallow pills		

LTBI TREATMENT MONITORING

- Monthly monitoring
  - Weight
  - Compliance
  - Signs/symptoms of TB or medication toxicity
- Ensure therapy completion
  - 3HP = 11 doses within 16 weeks
  - Rifampin = 120 doses within 6 months
  - Isoniazid = 270 doses within 12 months
- Provide documentation of LTBI treatment completion

WINDOW TREATMENT

TB RISK AMONG INFECTED CHILDREN

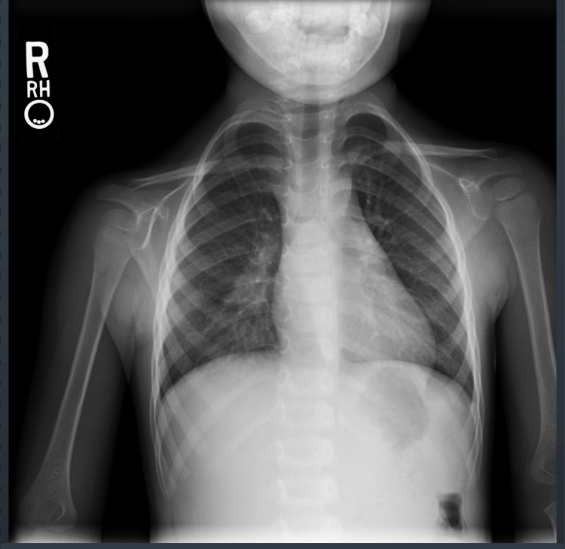
Age at primary infection	Any TB disease	Pulmonary disease	TB meningitis or miliary disease
<1 year	**50%**	30-40%	**10-20%**
1-2 years	**20-30%**	10-20%	**2-5%**
2-5 years	**5%**	5%	**0.5%**
5-10 years	2%	2%	<0.5%
>10	10-20%	10-20%	<0.5%

Adapted from Marais BJ et al. The natural history of childhood intra-thoracic tuberculosis – a critical review of the pre-chemotherapy literature. Int J Tuberc Lung Dis. 2004;8:392-402.

WINDOW TREATMENT FOR KIDS <5 RECENTLY EXPOSED TO TB

- Kids <5 yrs and recent TB exposure (previous 3 months) have high risk for TB progression, but also risk for **falsely negative TB test**

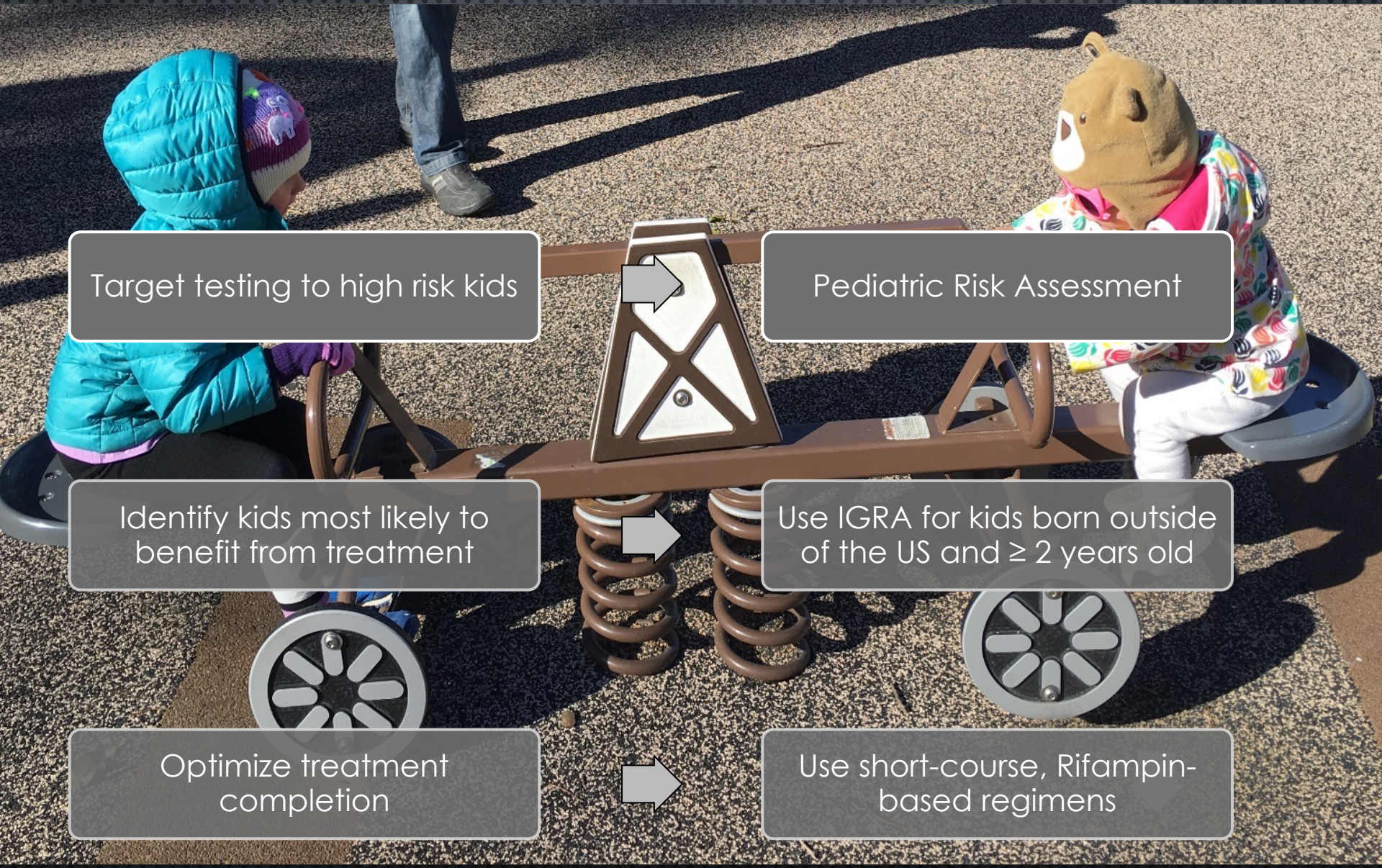
- STEP 1: Screen – known exposure
- STEP 2: Test – do a TB test
  - **Evaluate fully for TB disease even if test is negative**
- STEP 3: Treat
  - If evidence of active TB – **treat for TB disease**
  - If no evidence of active TB and POSITIVE test – **treat for LTBI**
  - If no evidence of active TB and NEGATIVE test – **treat for LTBI** until you can trust a negative TB test (i.e. at least 8 weeks after exposure and 6 months of age). This is called WINDOW treatment



CASE EXAMPLE

- 9 YO HOUSEHOLD CONTACT OF KNOWN CASE
  - BORN IN MEXICO
- INITIAL EVALUATION WITHIN 1 WEEK OF LAST EXPOSURE:
  - ASYMPTOMATIC
  - NORMAL PE
  - NORMAL CXR
  - NEGATIVE QFT
  - NO TREATMENT GIVEN AGE >5 YEARS, IF THIS WAS A KID <5 YOU WOULD START LTBI TREATMENT
- 2-3 WEEKS OF COUGH ATTRIBUTED TO ASTHMA, VISITED PCP
  - CXR BY PCP WITH CONSOLIDATION TREATED WITH ANTIBIOTICS AND PREDNISOLONE
  - TB STAFF NOT NOTIFIED!
- FOLLOW-UP QFT +, SPUTUM GREW MTB

CONCLUSION



Target testing to high risk kids → Pediatric Risk Assessment

Identify kids most likely to benefit from treatment → Use IGRA for kids born outside of the US and ≥ 2 years old

Optimize treatment completion → Use short-course, Rifampin-based regimens