

# Preventing and Identifying Pediatric TB; Focus Contact Investigations



No disclosures



# Learning Objectives

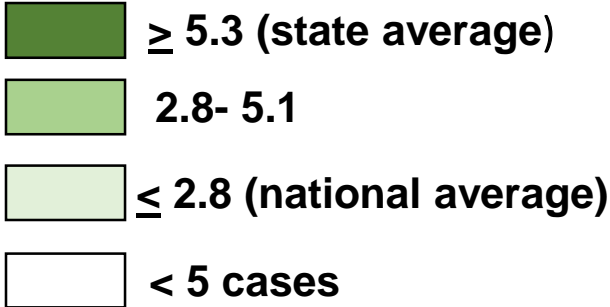
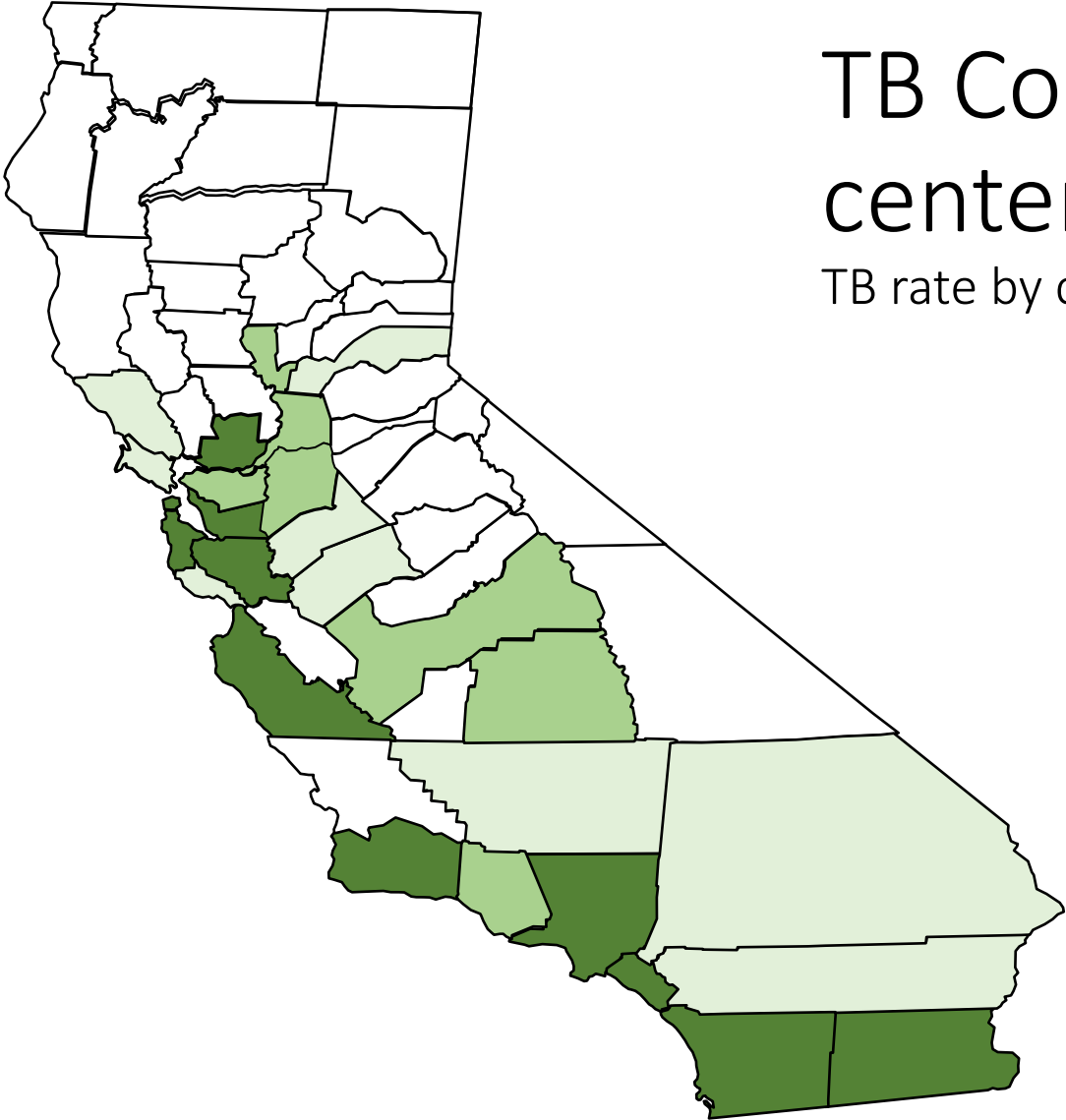
- Understand epidemiology of active pediatric TB in California
- Quickly identify young children at risk of TB exposure during contact investigations
- Ensure thorough medical evaluations are performed on pediatric contacts
- TB disease in children is a clinical diagnosis: use all available information!
- Use short-course regimens to treat pediatric contacts with LTBI to avoid active disease

# Pediatric TB Epidemiology in California

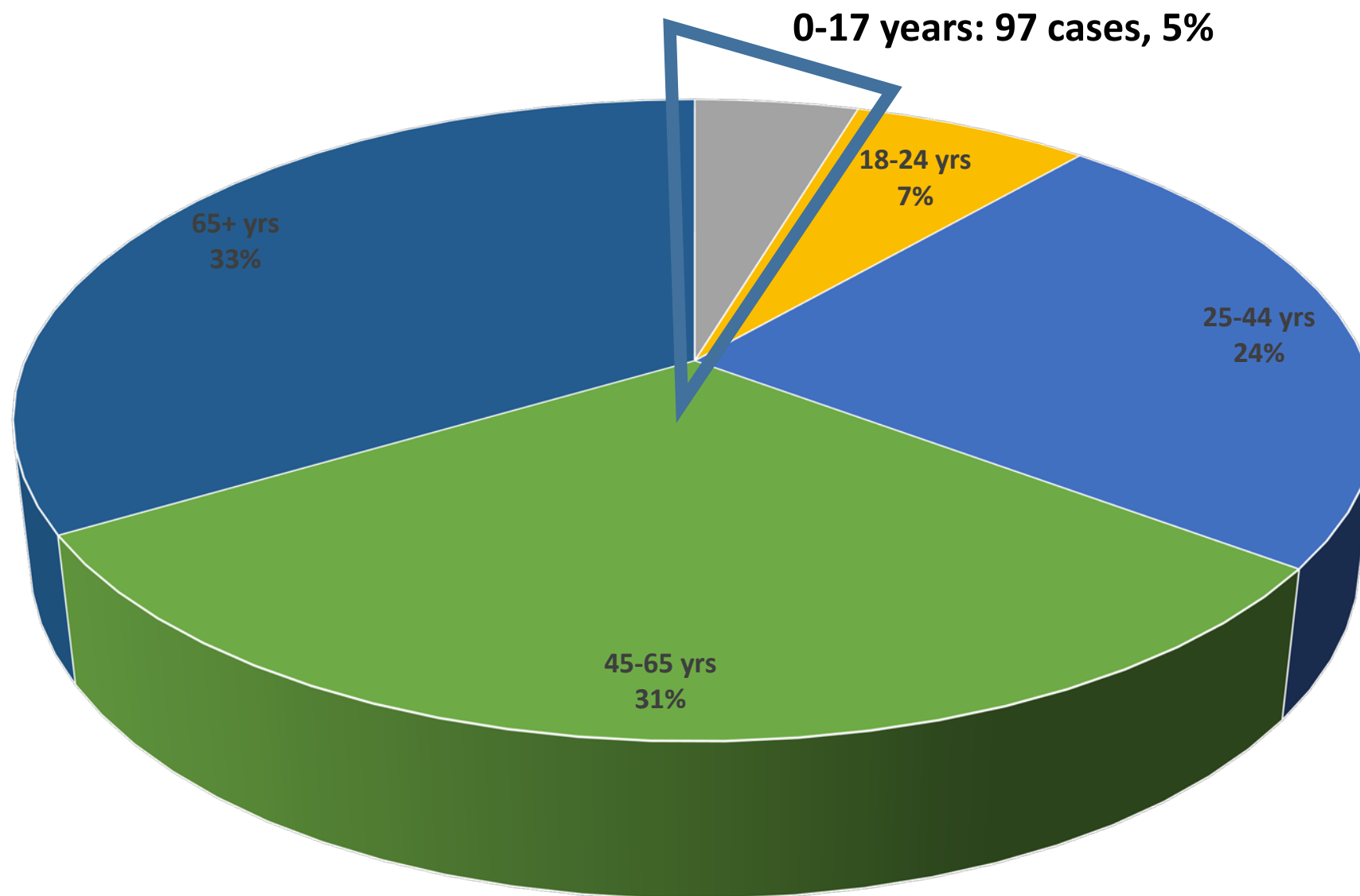


# TB Concentrated in population centers

TB rate by county 2018



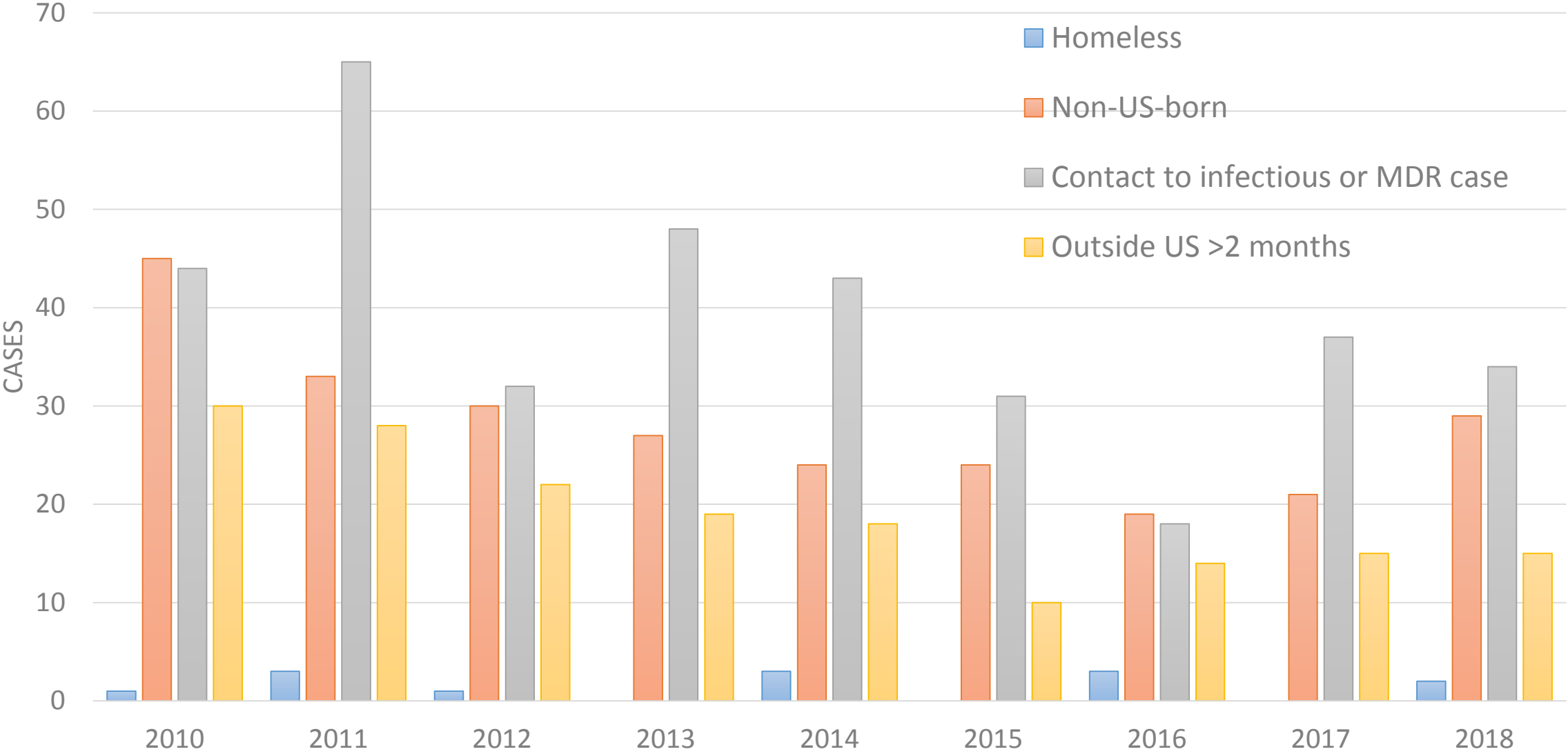
# Age at TB Diagnosis, California, 2018



# 2 Cases Per Week in CA Kids (<18 yrs)

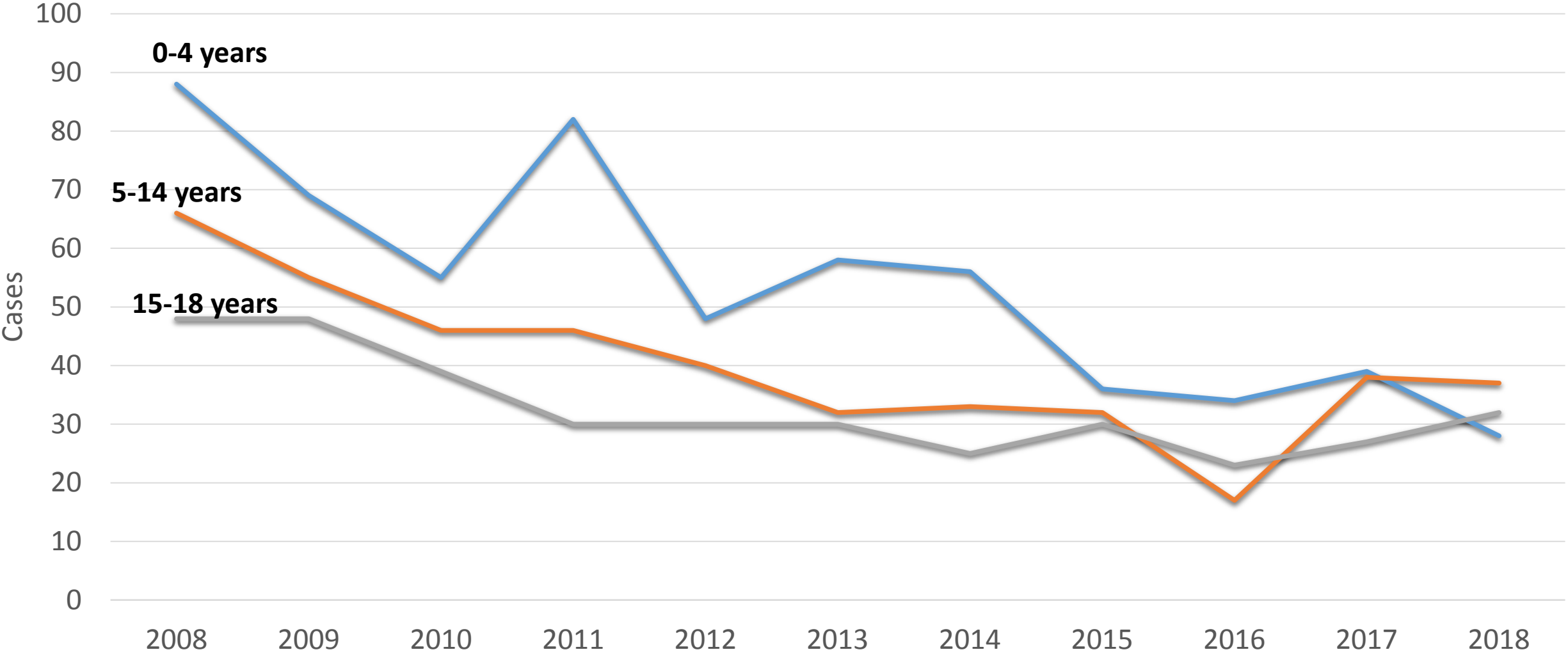
1		3	4		6	7
	9	10	11	12		14
15	16			19	20	21
21	22	23	24		26	
		30	31			

# California Pediatric Cases by Risk Factors, 2010-2018

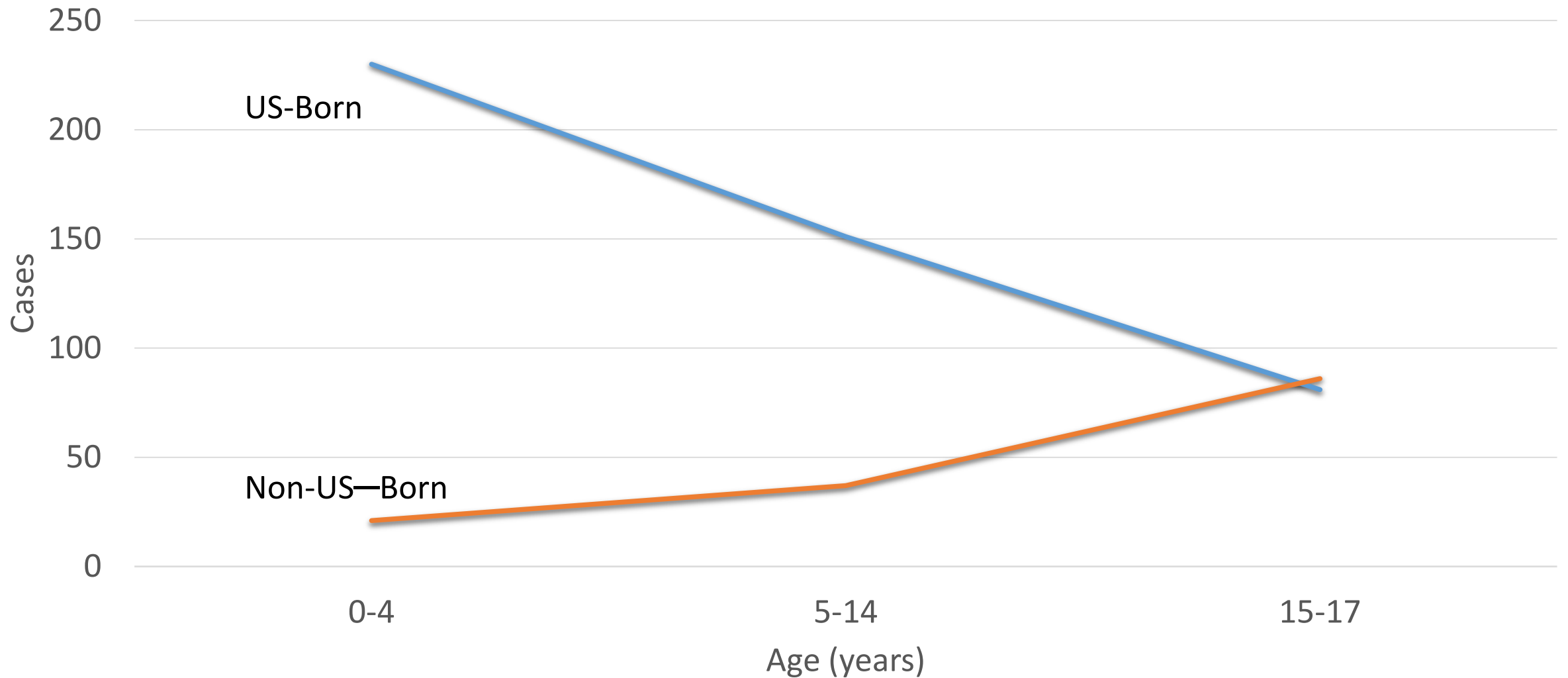




# Pediatric Tuberculosis Cases (Age <18 years): California, 2008-2018



# Pediatric Cases 2013-2018 (N=606)



# TB risk among infected children

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

# Contact Investigations: Why the Focus on Children <5 years old?



# Prevalence of active TB among contacts in high-income countries\*

	Included studies	Contacts with active TB	Contacts Screened	Proportion (%)	95% CI
<b>All ages</b>	*Fox GJ et al. <i>Eur Respir J</i> 2013; 41: 140-156				
All	87	5058	308048	1.4	1.1-1.8
Index smear +	27	1704	72936	3.3	2.2-4.8
Index XDR/MDR	2	0	554	0.0	
Household contact	29	2047	56221	3.0	2.0-4.4
All close contacts	45	3053	127699	1.9	1.3-2.7
Casual contacts	9	73	15607	0.4	0.2-0.6
HIV+ contacts	2	15	133	11.4	7.0-18.0
<b>≤ 5 years</b>	<b>10</b>	<b>212</b>	<b>4057</b>	<b>4.7</b>	<b>3.4-6.4</b>
<b>5-14 years</b>	9	253	5665	2.9	1.7-5.1
<b>15 years +</b>	9	507	17867	2.3	1.1-4.8

# Prevalence of LTBI among contacts in high-income countries\*

	Included studies	Contacts with latent TB	Contacts Screened	Proportion (%)	95% CI
<b>All ages</b>					
All	92	79511	284505	28.1	24.2-32.4
Index smear +	34	25910	78784	34.8	27.6-42.7
Index XDR/MDR	2	287	554	52.6	49.5-55.7
Household contact	33	20960	67175	30.0	21.3-40.5
All close contacts	29	20213	68738	28.0	18.9-39.4
Casual contacts	7	5779	27383	18.7	11.8-28.5
HIV+ contacts	3	28	151	25.0	11.4-46.4
<b>≤ 5 years</b>	<b>17</b>	<b>2093</b>	<b>6900</b>	<b>16.3</b>	<b>9.2-27.0</b>
<b>5-14 years</b>	10	1407	4871	<b>18.4</b>	11.8-27.5
<b>15 years +</b>	8	6221	12633	<b>41.9</b>	30.5-54.2

# Prevalence of LTBI among foreign and locally born contact in high-income countries

	Included studies	Contacts with LTBI	Contacts Screened	Proportion %	95% CI	OR 95% CI	P-value
Locally-born	6	1536	7576	<b>17.0</b>	11.8-24.0	1.0	
Foreign-born	6	1849	4298	<b>39.2</b>	30.0-49.3	<b>3.39</b> (3.1-3.71)	<0.0001



# Pediatric TB Contact Investigations:

## What You Need to Know





# Pediatric Case Finding

- IGRA/TST and CXR have a much higher positive predictive value among pediatric contacts recently exposed to TB
- Goals of CI:
  - Identify additional infectious cases
  - Identify those exposed (especially those high risk)
  - Ensure access to medical evaluation and treatment
  - Identify environmental factors contributing to transmission
  - Link a child with active TB to known case of culture-confirmed TB for presumed drug susceptibility
  - Identify LTBI and treat to prevent disease



# Evaluate the index case

- Features associated with contagiousness
- Environment and extent of exposure
- Known/suspected resistance patterns



# Features indicative of potentially contagious TB

Category	Feature
Clinical	Presence of cough Productive cough Laryngeal involvement Draining skin/soft tissue Inappropriate treatment or early in treatment Unknown drug resistance
Radiographic	Cavitary lesion Apical lung segment involvement
Microbiological	Acid-fast sputum smear positive
Environmental	Indoor spaces with poor ventilation Recirculating air with droplet nuclei Inadequate cleaning of contaminated equipment or specimens Airway instrumentation

# Evaluate the child

- Verify exposure(s)
- Broad symptom screen
- Child's medical history including growth parameters
- Complete physical exam
- TB test
  - **TST or IGRA if US-born**
  - **IGRA if born outside of US (and  $\geq 2$  years old)**
- 2-view CXR



# Contact Investigation #1: Next Steps?

- Both children with infiltrates (despite NO symptoms), one with new positive TST
- Collect specimens
  - Induced sputum if cooperative
  - Often effort dependent
  - **Bronchodilators + hypertonic saline**
- Treat for active TB



# Contact Investigation #1: Pearls

- Consolidation on CXR of an asymptomatic child is concerning for TB!
- TB test can be negative early on despite evidence of TB disease
- Collecting good specimens really helps
  - ~50% of pediatric TB cases are culture negative
- Decision to treat is decision to treat



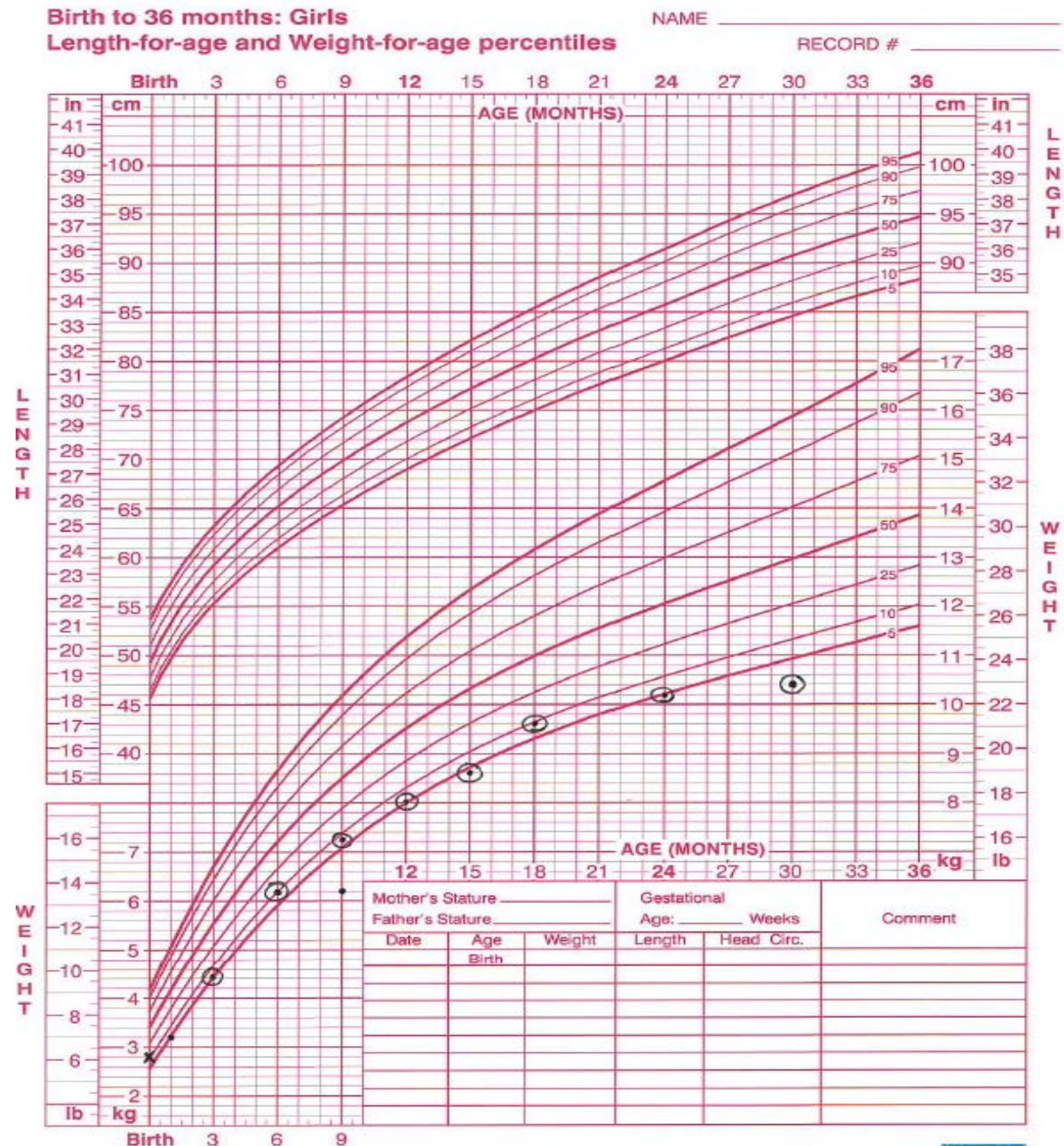
# Contact Investigation #2: Next Steps

- Collected gastric aspirates
- Started treatment for INH- resistant TB



# Growth Curves

- CDC and WHO curves
- Choose by gender and age





# Pediatric TB isn't just adult TB in little people...

- Most common form of TB is intrathoracic
- Often only enlarged nodes on CXR
- Children typically asymptomatic
- Only ~30% culture positive
- Often symptoms are generalized and not specific for TB



# Contact Investigation #2: Pearls

- Medical history and growth charts inform decision-making
- Decision to treat = decision to treat



# Window Treatment and LTBI: Using Short-Course Regimens



# Pediatric Contacts without evidence of TB disease

## **<5 years and +TST/IGRA**

- Treat for LTBI based on index case susceptibilities

## **<5 years and –TST/IGRA**

- Window treatment with LTBI therapy
  
- Repeat TST/IGRA 8-12 weeks after last exposure to TB



# Contact Investigation #3: Next Steps?

- TB exposure history
  - Exposure was limited to previous 1 week, would be fast for development of adenopathy
- Historical information and imaging
  - Previous films from admission infant worse than current film
- Repeat evaluation
  - Repeat exams, CXRs one week later were normal
- Treatment
  - Children on levofloxacin for window

# Contact Investigation #3: Pearls

- Be sure to include plausibility and patient history in your decision making
- **If the picture is unclear and children are well appearing, consider re-evaluating**
- Treatment for LTBI and TB disease should be based on source case's presumed susceptibility pattern

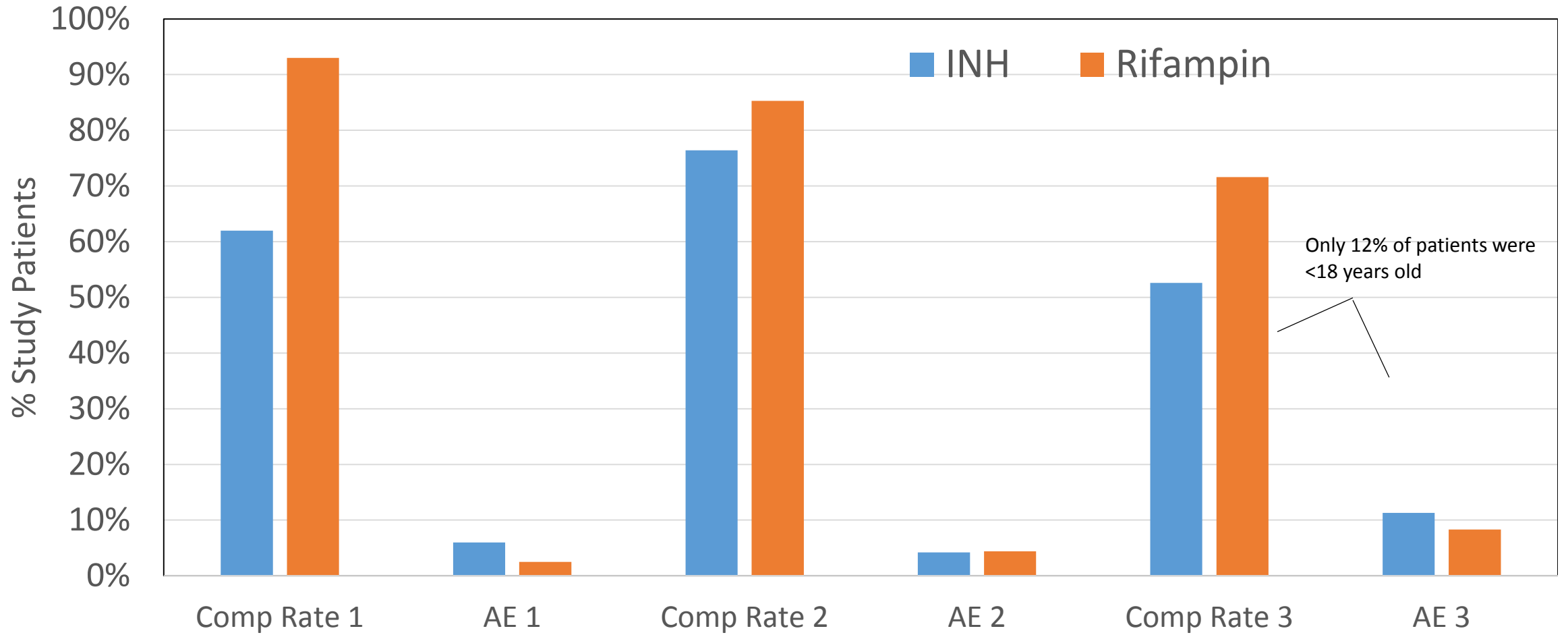


# TB Infection Treatment Options

	Drug	Dose	Duration	Notes
Historical:	<b>Isoniazid</b>	10-15mg/kg daily	9 months	Poor adherence!
New:	<b>Rifampin</b>	15-30 mg/kg daily	<b>4 months</b>	
New:	<b>Isoniazid &amp; Rifapentine</b>	<b>Weekly</b> Dose varies by age	<b>12 weeks</b>	Age 2 years and older
New:	<b>Levofloxacin</b>	15-20 mg/kg daily	<b>9 months</b>	MDR contacts



# Rifampin (4mo) vs Isoniazid (9mo)





# Rifampin (4mo) Efficacy

- No cases of TB during 562 person-years of follow-up (RIF)
- 2 cases of TB during 542 person-years of follow-up (INH)



# Rifampin Dosing

- Typical dosing:
  - 15-20 mg/kg daily
- Dosing for infants/toddlers:
  - **20-30 mg/kg daily**
- Dosing for CNS or severe TB:
  - **20-30 mg/kg daily (consider IV)**



# Rifampin Treatment of TB Infection

## Pros

- Shorter duration
- Better completion
- Fewer side effects
- Less hepatotoxicity

## Cons

- Orange body fluids
- Drug interactions
  - **Hormonal Contraceptives**
  - Warfarin
  - Prednisone
  - HIV Antiretrovirals



# Isoniazid-Rifapentine (3HP) Weekly (12 weeks)

## New England Journal

**Ages  $\geq 12$  years (n=7731)**

- RCT compared 12 weeks 3HP to 9 months INH
- Followed for 33 months
- Conclusion: Safe and non-inferior to INH

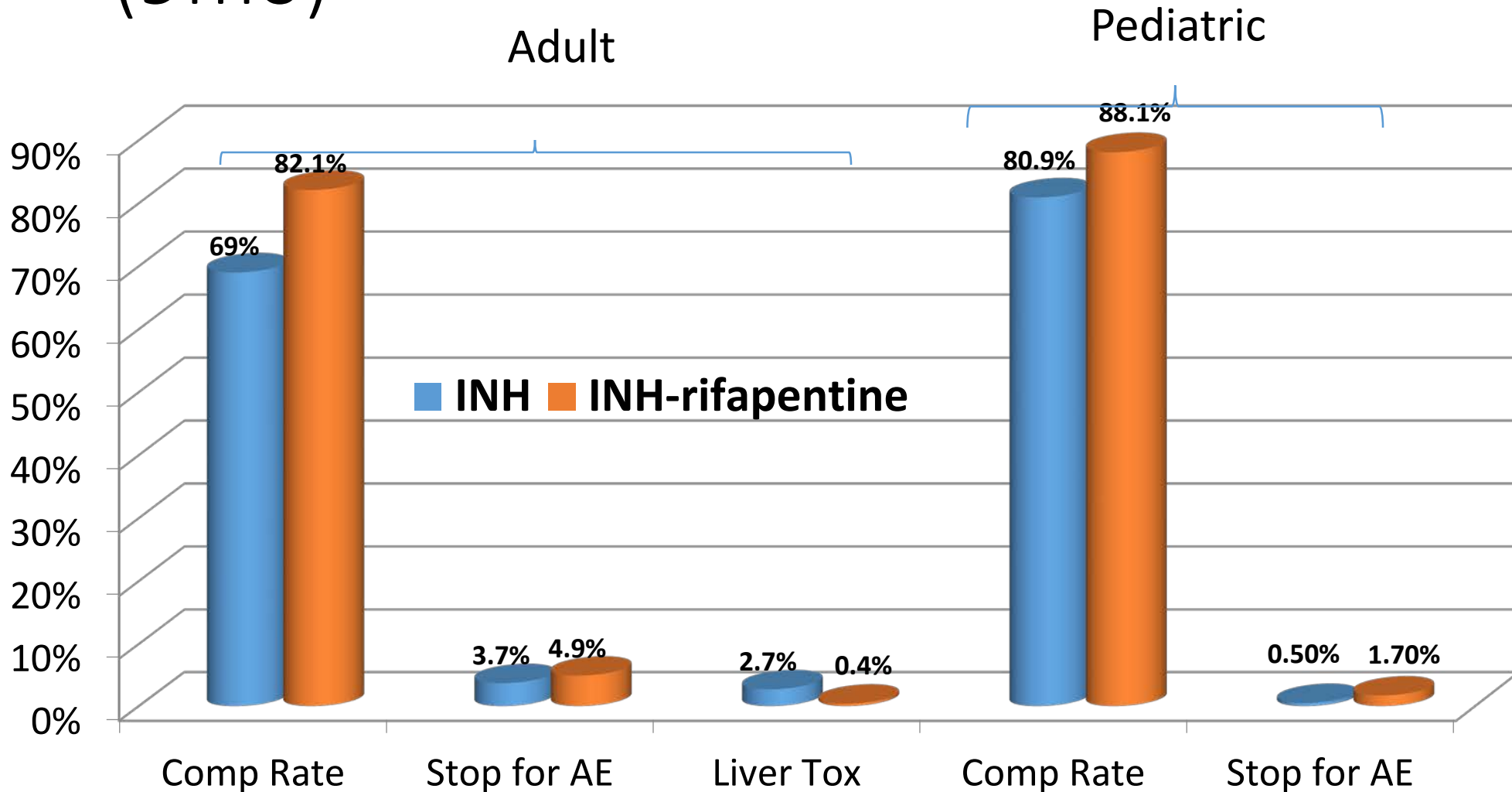
## JAMA Pediatrics

**Ages 2-17 years (n=905)**

- RCT compared 12 weeks 3HP (DOT) to 9 months INH (SAT)
- Followed for 33 months
- Conclusion: Safe and non-inferior to INH



# 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

## What are the doses?

<b>Drug</b>	<b>Dosage</b>	<b>Maximum dose</b>
INH	15 mg/kg rounded to nearest 50/100 mg in patients $\geq 12$ 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		

# 3HP Treatment of TB Infection

## Pros

- Shortest length of therapy
- Better completion
- Less hepatotoxicity

## Cons

- Drug Interactions
- Can't use in kids <2
- Many pills taken at once; no pediatric formulation
- Really need to make sure no missed doses



# LTBI 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





# Contact Investigation #4: Pearls

- Ensure follow-up testing after 10-12 weeks for kids exposed to TB cases
- Remind parents to report ANY possible TB symptoms to public health
- 2-view CXR can provide more diagnostic information



# Source Case Investigation: Pearls

- If a young child is identified as a TB case, this is a sentinel event  
-> must look for the source case!
- Be sensitive to “blame” for exposing a child to TB during source case investigation



# Conclusion

- Know your index case
- Do thorough evaluations of contacts
  - Ask about prior medical history and growth
  - Use IGRAs for kids born outside the US and  $\geq 2$  years old
  - Order 2-view CXR on all contacts  $<5$  years old
- Review all your information for decision making, and repeat your evaluation or CXR if needed
- Treatment
  - A decision to treat is a decision to treat
  - Use short-course LTBI regimens





Questions?

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