



Pneumococcal carriage and disease in Native Americans in the era of routine use of PCV13

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Disclosures

- Research grants from Merck, Pfizer, GSK

Overview

- Pneumococcal Carriage
 - Southwest US
 - Alaska Native (CDC/AIP)
- Invasive Pneumococcal Disease
 - Southwest US
 - Alaska Native (CDC/AIP)
- Adult Community Acquired Pneumonia
 - Southwest US

PCV13 coverage

- Children

- Indian Health Service (IHS) immunization registry
 - 3-4 mos (1 dose): ~85%
 - 7-15 mos (3 doses): ~80%
 - 24-27 mos (4 doses): ~85%

- Adults ≥ 65 years

- CAIH study participants: ~60-80% in 2015-2017
- Alaska VacTrAK: 13% in 2015, 24% in 2016



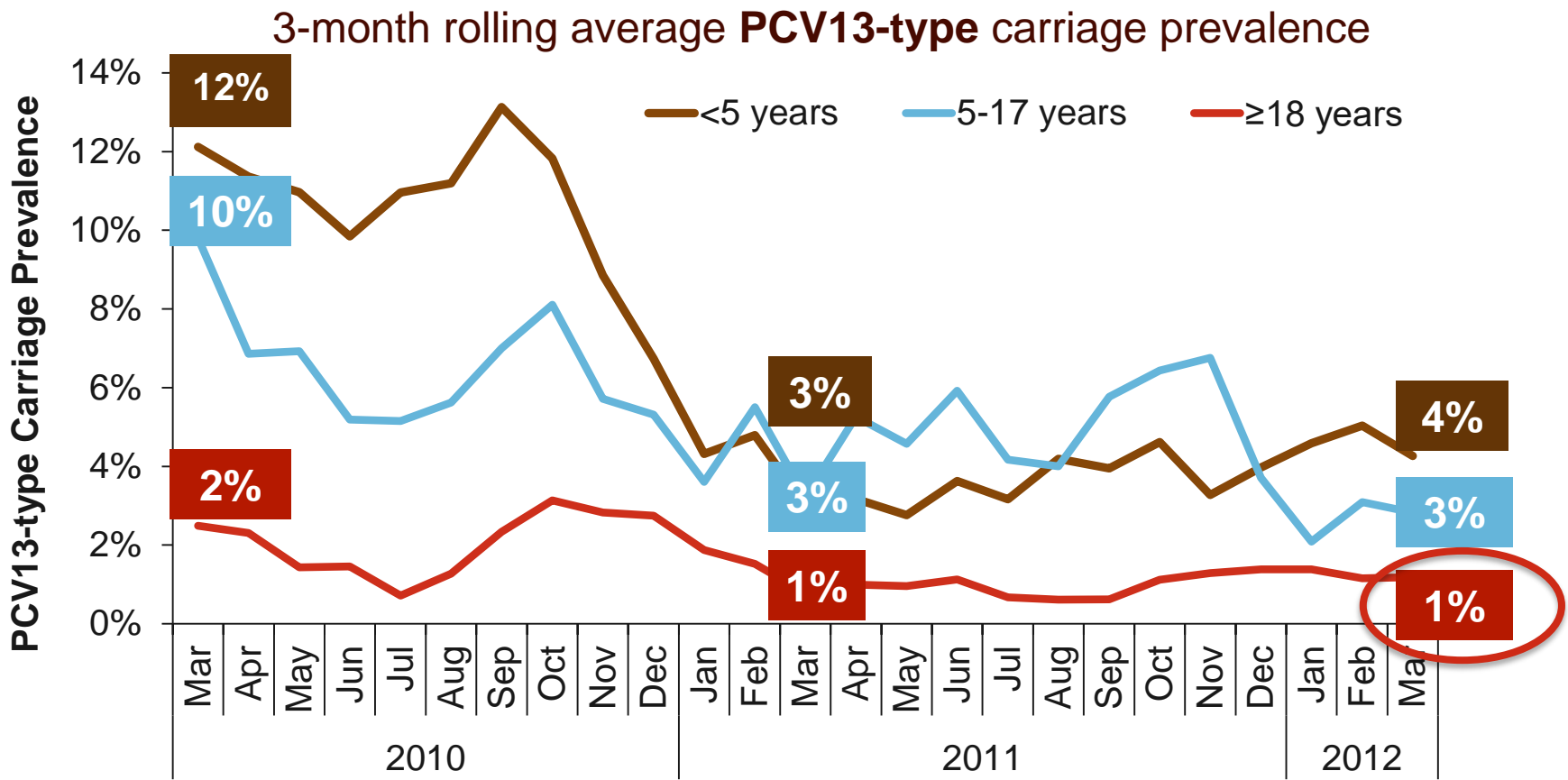
Pneumococcal Carriage

Funding for CAIH study: Clinical Research Collaboration with Pfizer, Inc.



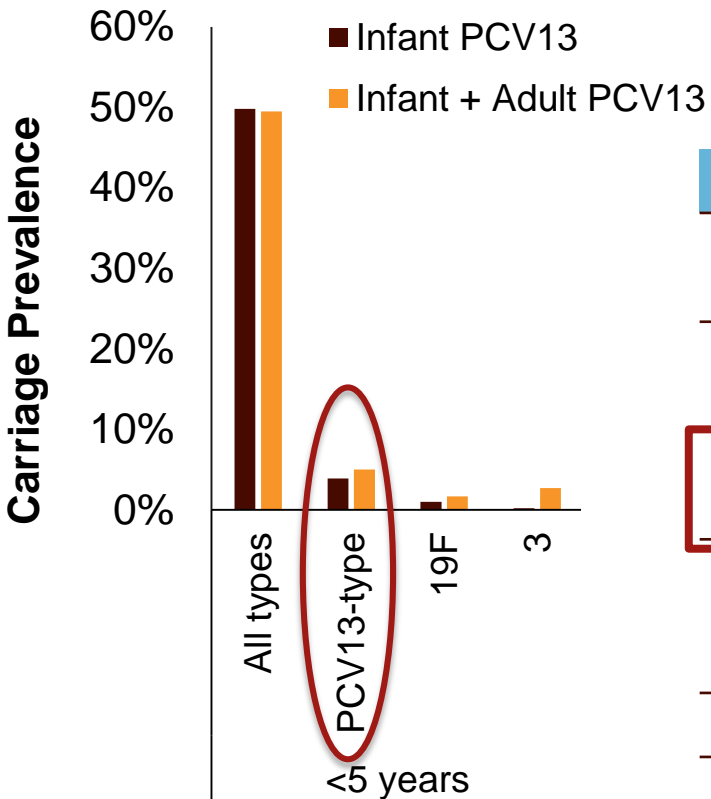
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Nasopharyngeal carriage: Early infant PCV13 era (2010-2012)



Convenience sample; household based
NP flocced swab with broth-enrichment culture
Serotyping by latex agglutination and Quellung

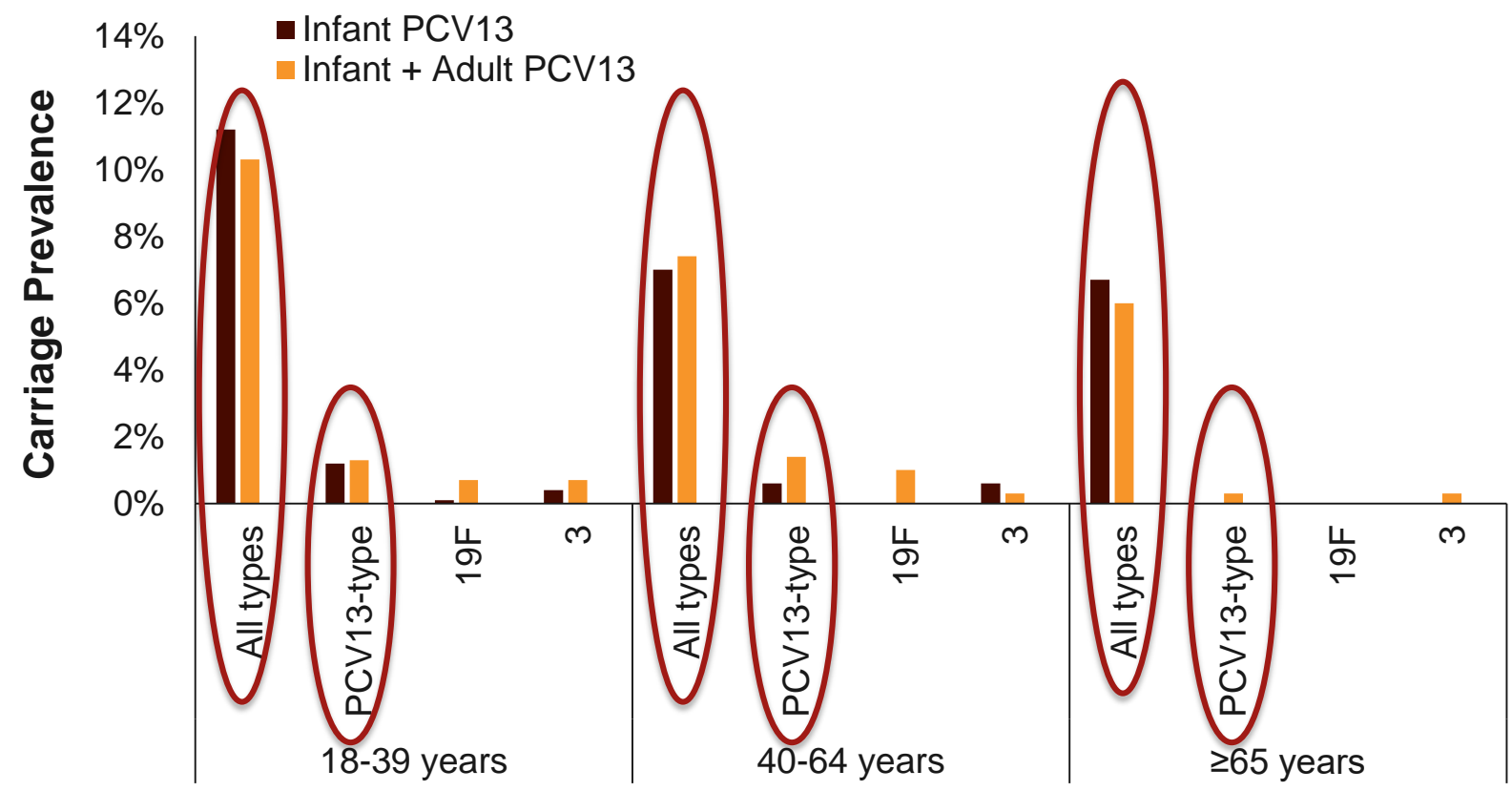
Nasopharyngeal carriage: Infant PCV13 (2011-2012) vs Infant + Adult PCV13 eras (2015-2017)



Infant PCV13	N=1365
Infant + Adult	N=600

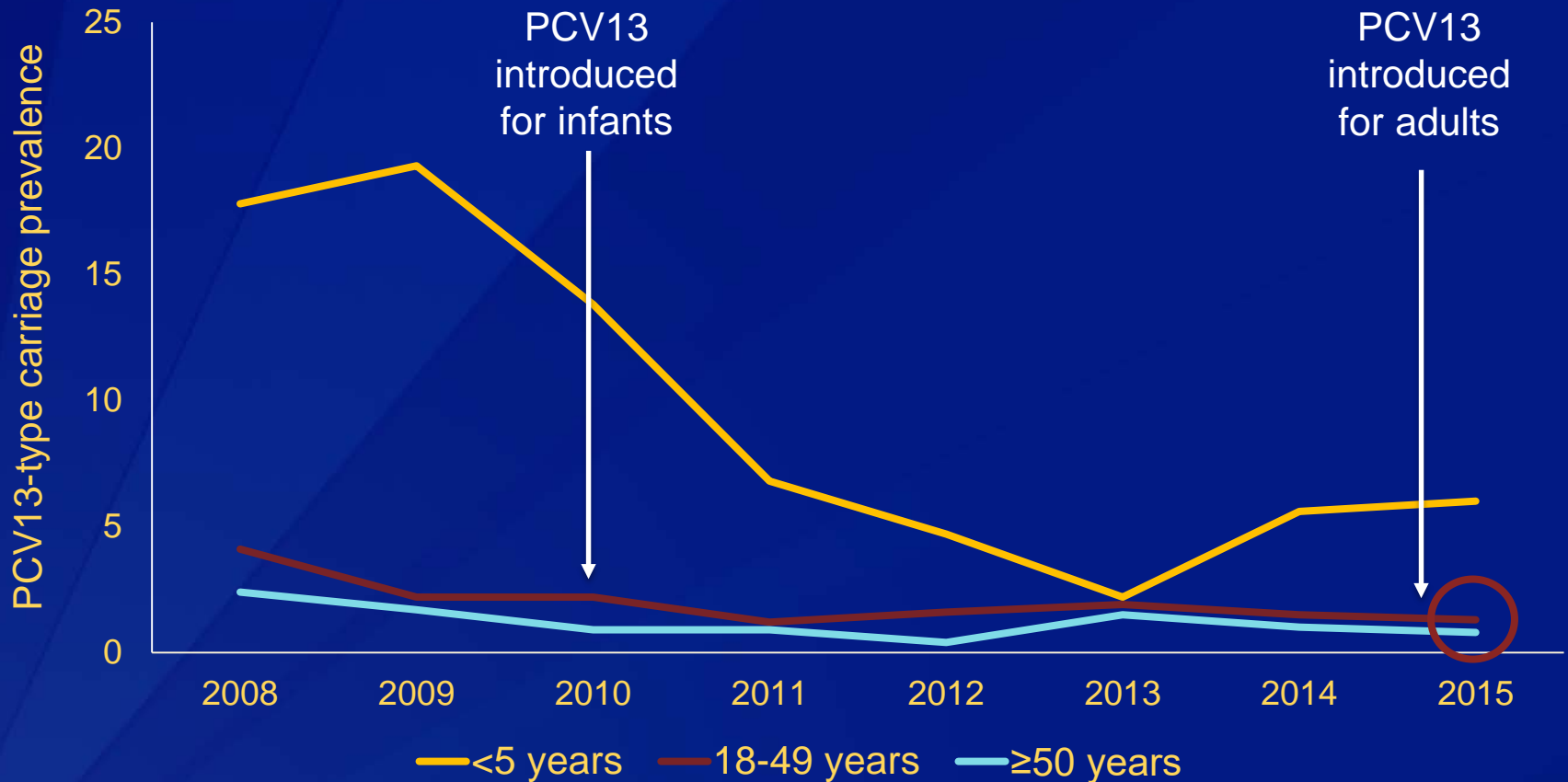
Characteristic	Infant PCV13	Infant+Adult PCV13
Design	Convenience, household based	Convenience
Population	Native American; all ages	Native American; <5yrs and adults
Median age (IQR), adults	27 years (22, 34)	53 years (33, 68)
Specimen	NP flocced swab stored in STGG	NP flocced swab stored in STGG; OP swab in adults
Culture	Broth enrichment	Broth enrichment
Serotyping	Quellung	Sequotyping

Nasopharyngeal carriage: Infant PCV13 (2011-2012) vs Infant+Adult PCV13 eras (2015-2017)



Infant PCV13	N=1020	N=157	N=45
Infant + Adult	N=301	N=296	N=300

PCV13-type Nasopharyngeal Carriage in Alaska Native People in Rural Alaska



Slide courtesy of Mike Bruce, CDC/Arctic Investigations Program

Conclusions

- PCV13-type pneumococcal carriage in adults was very low following infant PCV13 introduction and remains low



Invasive Pneumococcal Disease



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CAIH Active Bacterial Surveillance

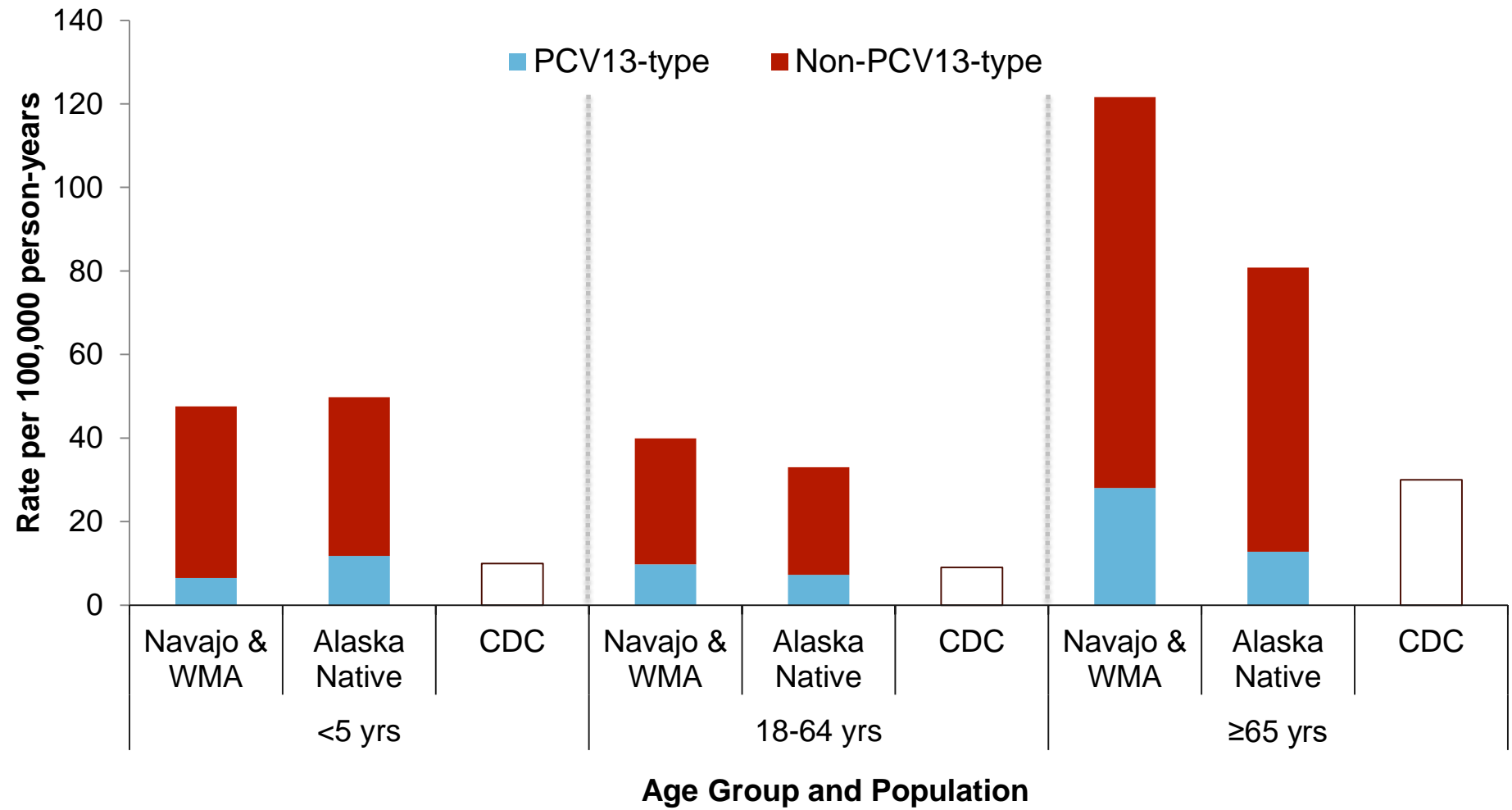


Key:

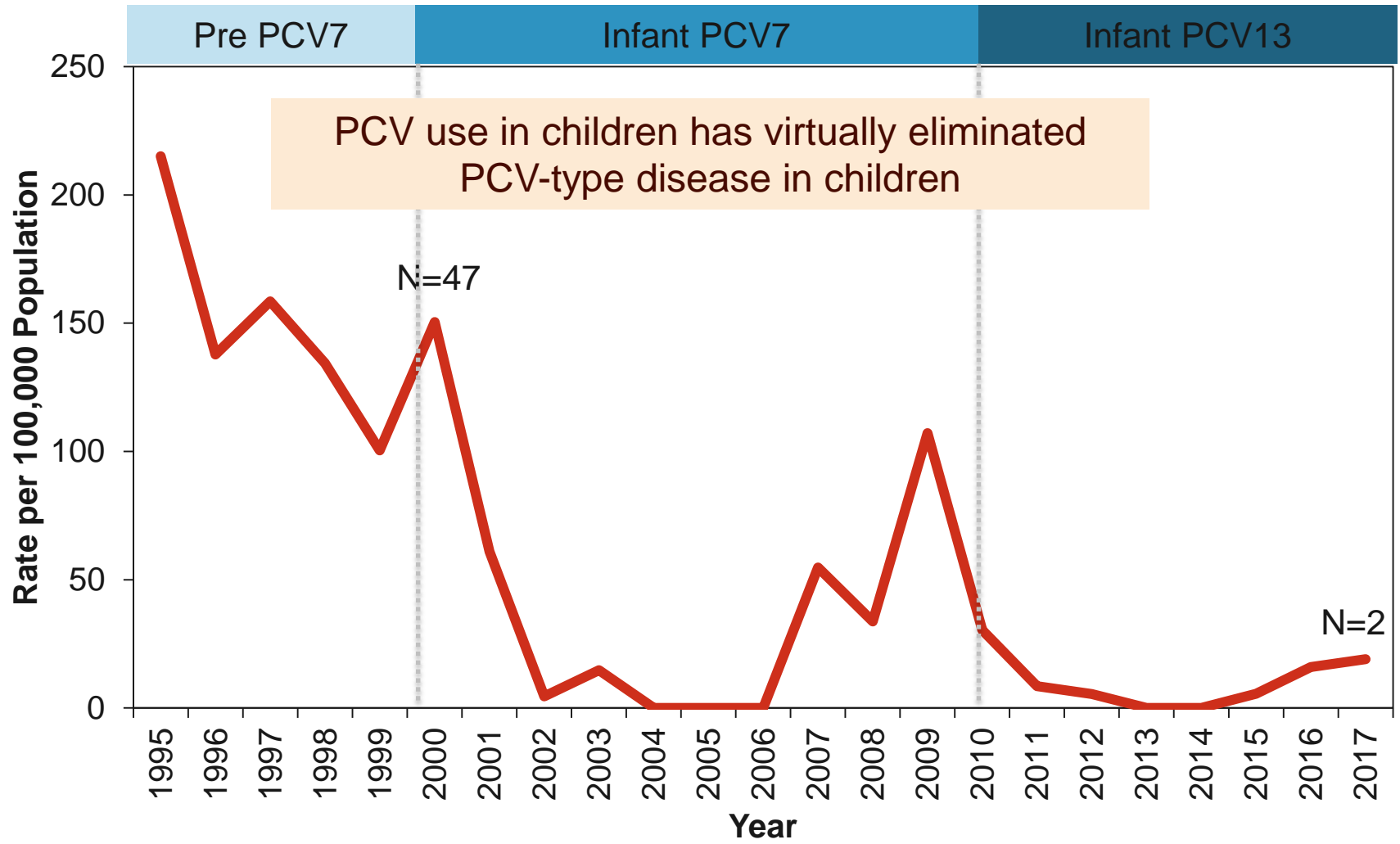
- Navajo Nation
- White Mountain Apache
- Hopi
- ▲ Surveillance Laboratory

- **Actively contact laboratory facilities**
 - Navajo – 21 labs
 - White Mountain Apache – 3 labs
- **Identify** pneumococcal isolates that meet inclusion criteria
 - Serotyped at CDC/Arctic Investigations Program
- **Conduct chart reviews**

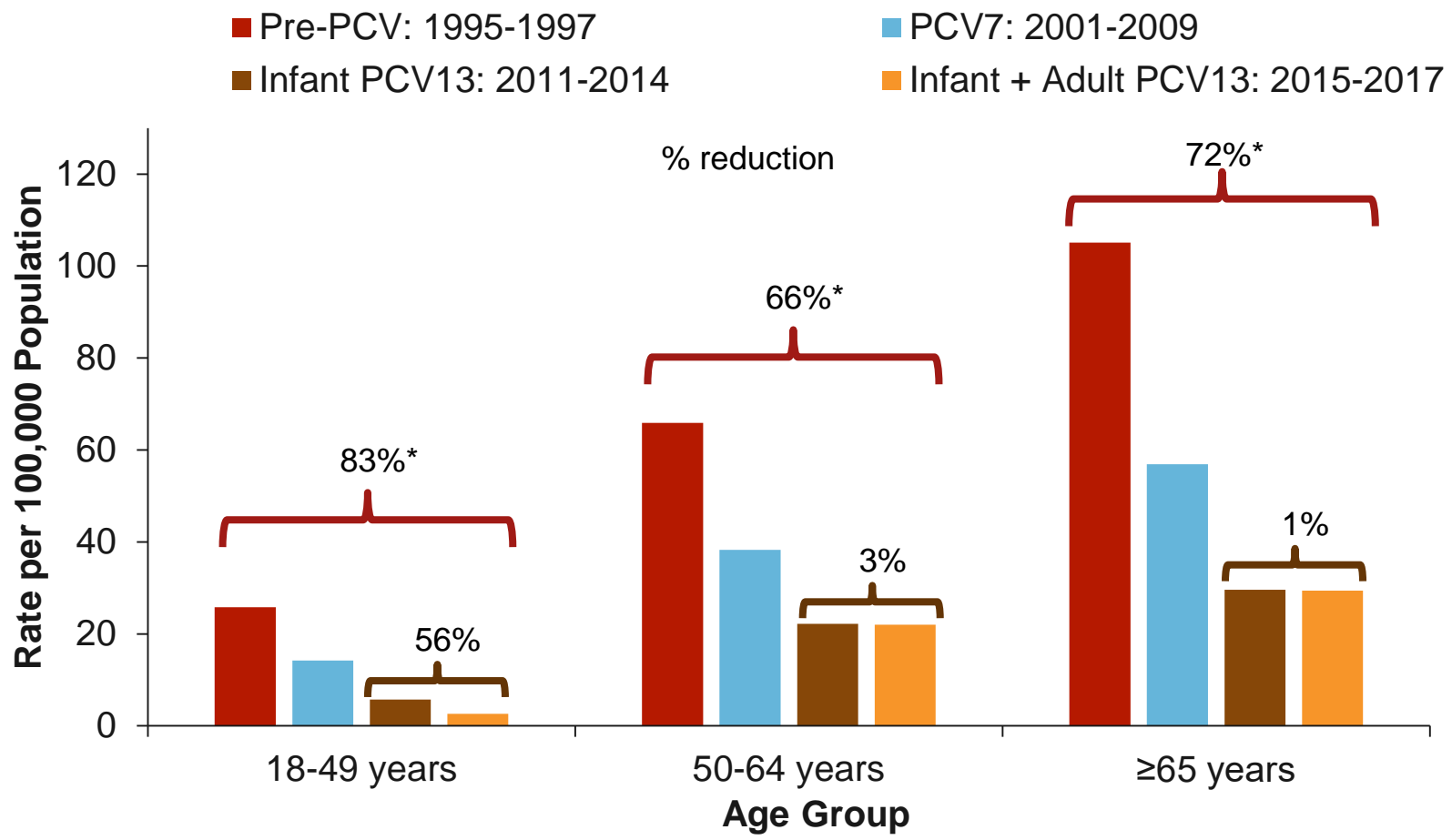
All Serotype IPD: Native Americans, Alaska Natives and General US, 2011-2015



PCV13-type IPD: Navajo children <5 years, 1995-2017

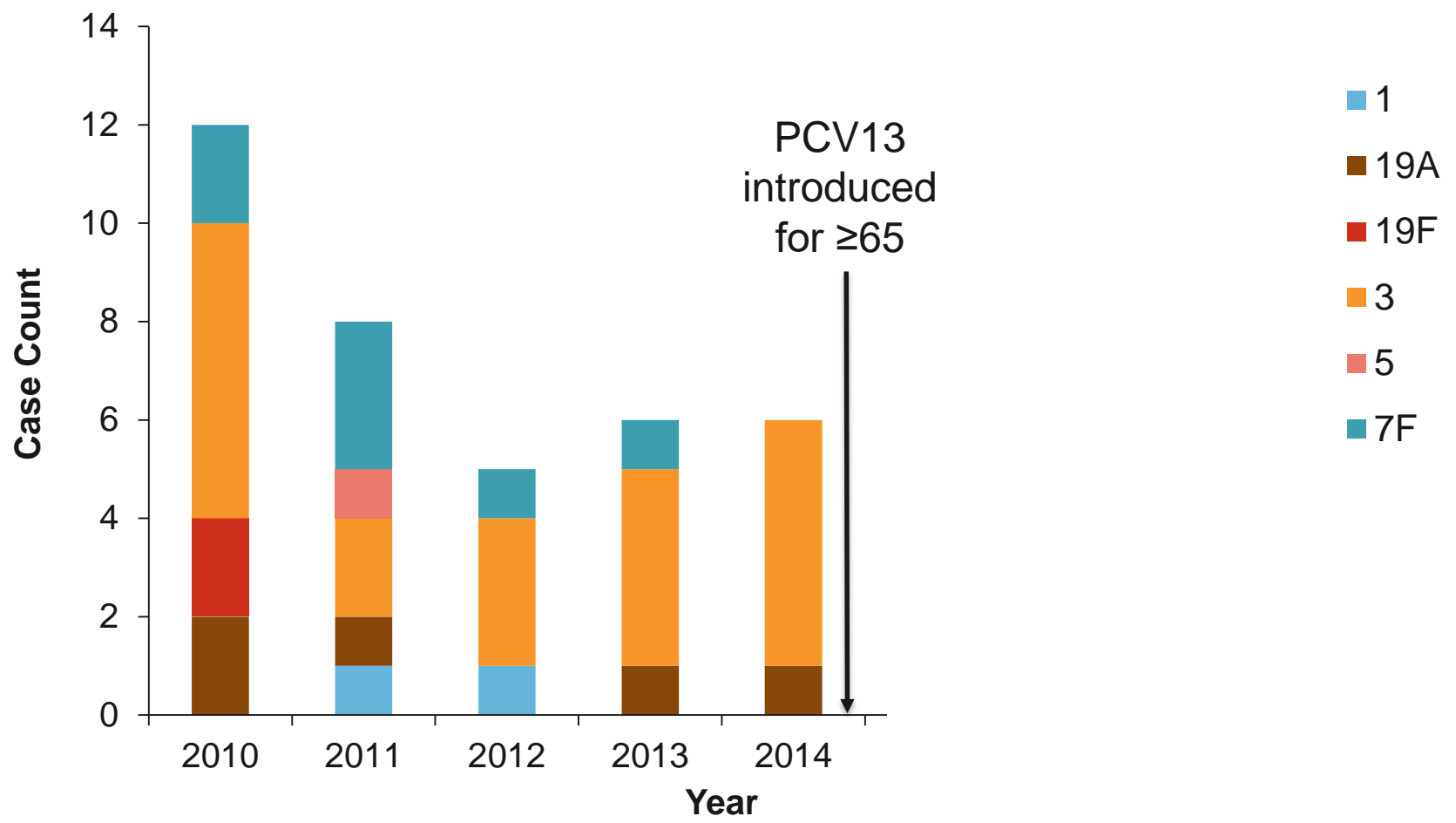


PCV13-type IPD incidence pre- vs. post-PCV, Navajo adults ≥ 18 years

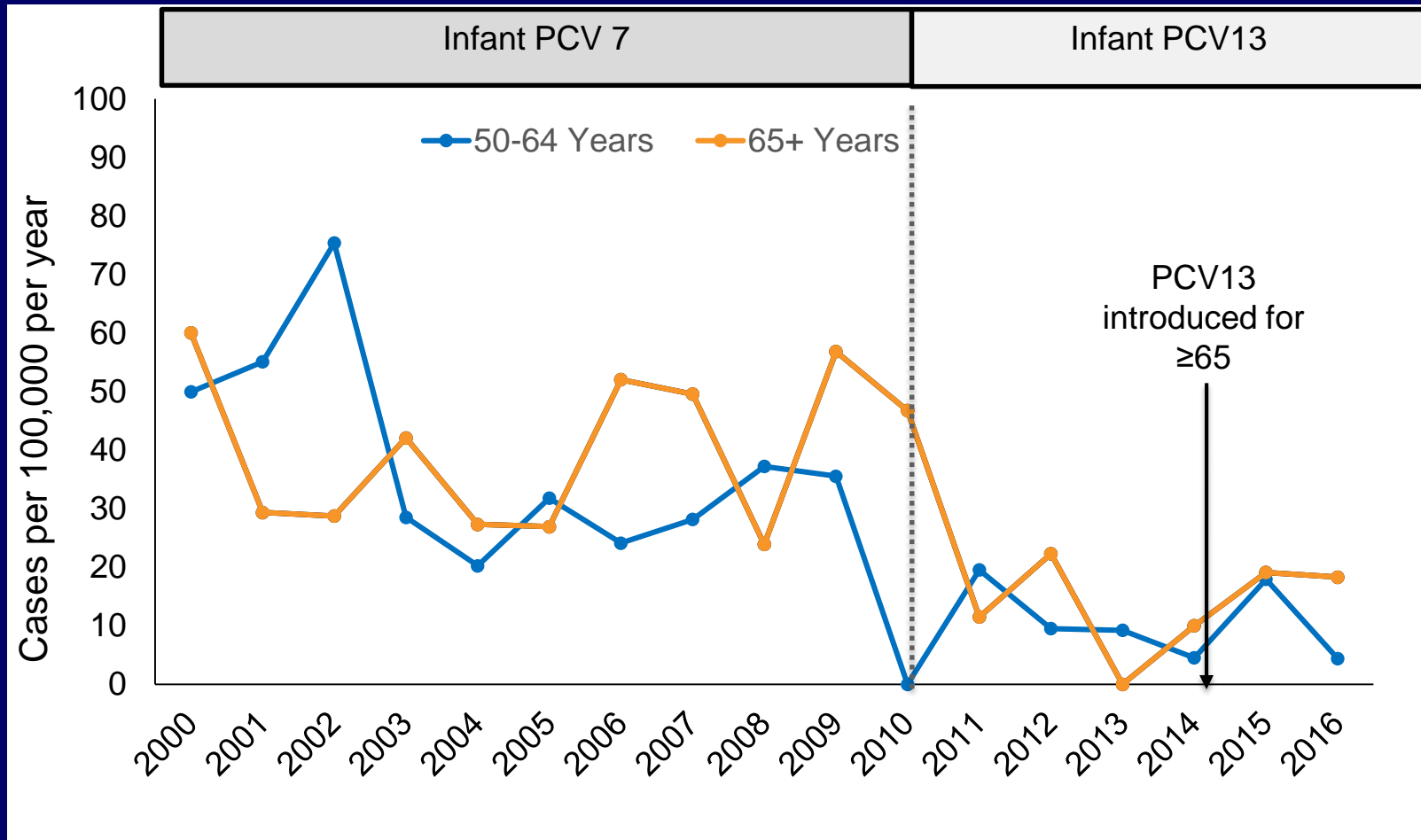


*Statistically significant

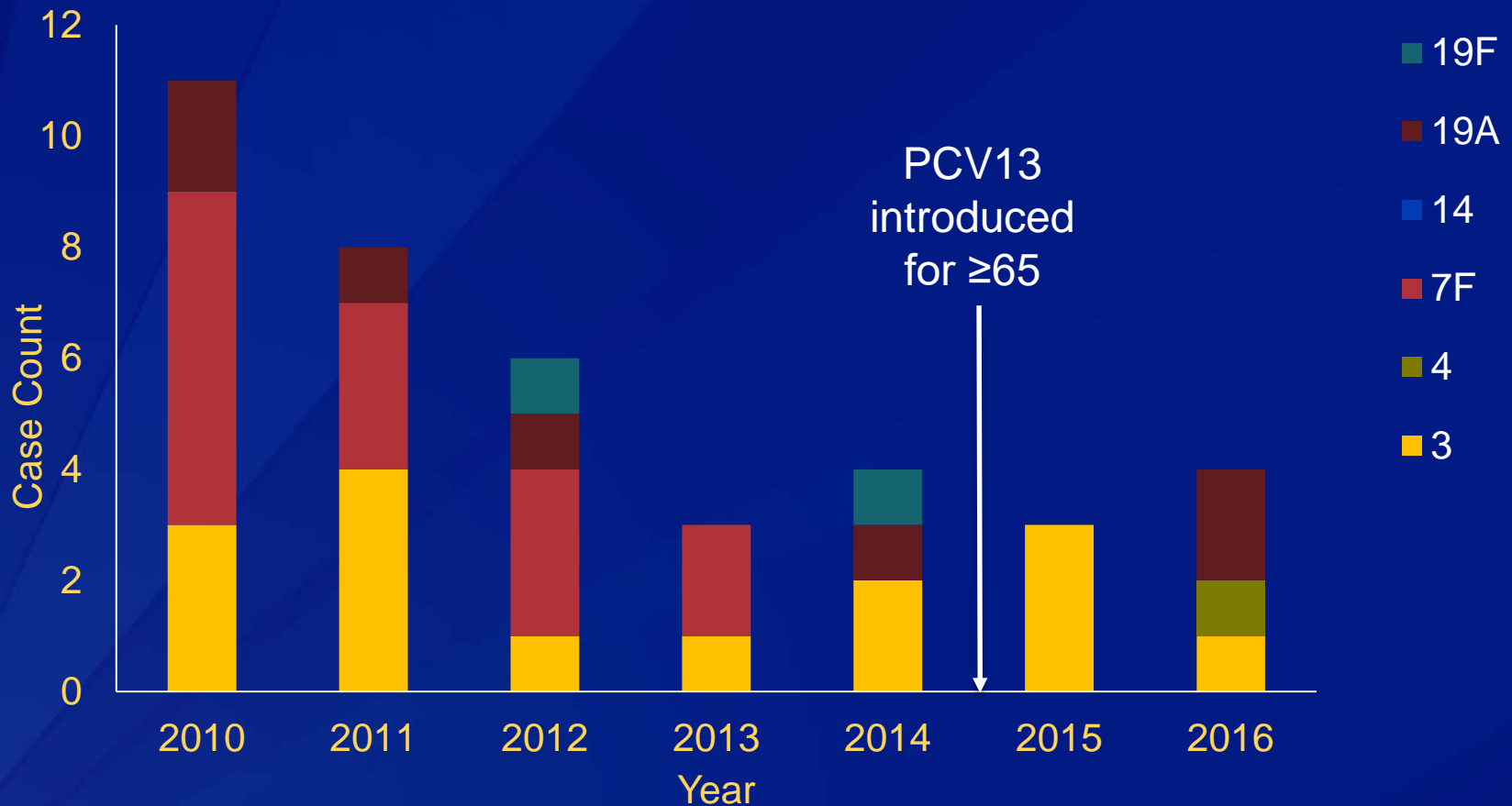
PCV13-type IPD serotype distribution: adults ≥ 65 years, Navajo, 2010-2017



PCV13-type IPD: Alaska Native adults ≥ 50 years, 2000-2016



PCV13-type IPD distribution: ≥ 65 years Alaska, 2010-2016



Conclusions

- PCV13-type NP carriage in adults was very low prior to use of PCV13 in older adults and remains low
- Substantial indirect effects had been achieved by 2014-2015, leaving little opportunity to assess impact of PCV13 in ≥ 65 year olds on carriage or IPD



Native American Adult Pneumonia Etiology Study, March 2016 – March 2018

Funding: Clinical Research Collaboration with Pfizer, Inc.



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Study activities

- Cases identified through surveillance at 5 IHS hospitals
 - Native American adult hospitalized with community acquired pneumonia (CAP)
 - Two or more clinical signs/symptoms at least one of which is respiratory
- Controls identified within 2 weeks of case
 - Age-matched, convenience sample
 - Without CAP or suspicion of CAP
 - 1 control for every 2 cases

- Obtain informed consent








- Collect specimens



- Administer questionnaire and perform chart review



Laboratory data

		Assay	Test performed by
	Blood	Culture, per clinical team Serum for biomarkers*	Indian Health Service To be determined
	Urine	SS-UAD for 24 serotypes* <i>S. pneumoniae</i> BinaxNOW*	Pfizer Pfizer
	NP/OP swab	Multiplex PCR* <i>lytA</i> PCR, serotype-specific PCR*	JHU/CDC (pending) Pfizer (pending)
	Sputum	Culture, per clinical team	Indian Health Service
	CXR	Radiography, per clinical team	Indian Health Service

*available for cases and controls

SSUAD

- **SSUAD 1**
 - PCV13 serotypes, clinically validated and FDA approved for research
- **SSUAD 2**
 - Serotypes 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F
 - Well-characterized; not clinically validated at start of study
- **Population-specific thresholds**
 - SSUAD results from 400 Native American adults in the study community used to inform established thresholds → reset the positivity cut-off for serotype 14

Demographic characteristics

Characteristic	CXR+ Cases N=355 n (%)	Controls N=269 n (%)	P-value	
Female	193 (54.4)	200 (74.4)	<0.001	
Median age, years (IQR)	66 (51, 79)	68 (54, 79)		
Age group (years)				
	18-49	78 (22.0)	54 (20.1)	0.93
	50-64	89 (25.1)	67 (24.9)	
	65-79	107 (30.1)	82 (30.5)	
	≥80	81 (22.8)	66 (24.5)	
Smoker resides in household	22 (6.2)	5 (1.9)	<0.01	
Primary fuel for cooking is wood	13 (2.8)	10 (3.7)	0.97	
Household has piped water ¹	289 (98.6)	234 (99.2)	0.58	
Household has flush toilet	292 (82.2)	236 (87.7)	0.10	

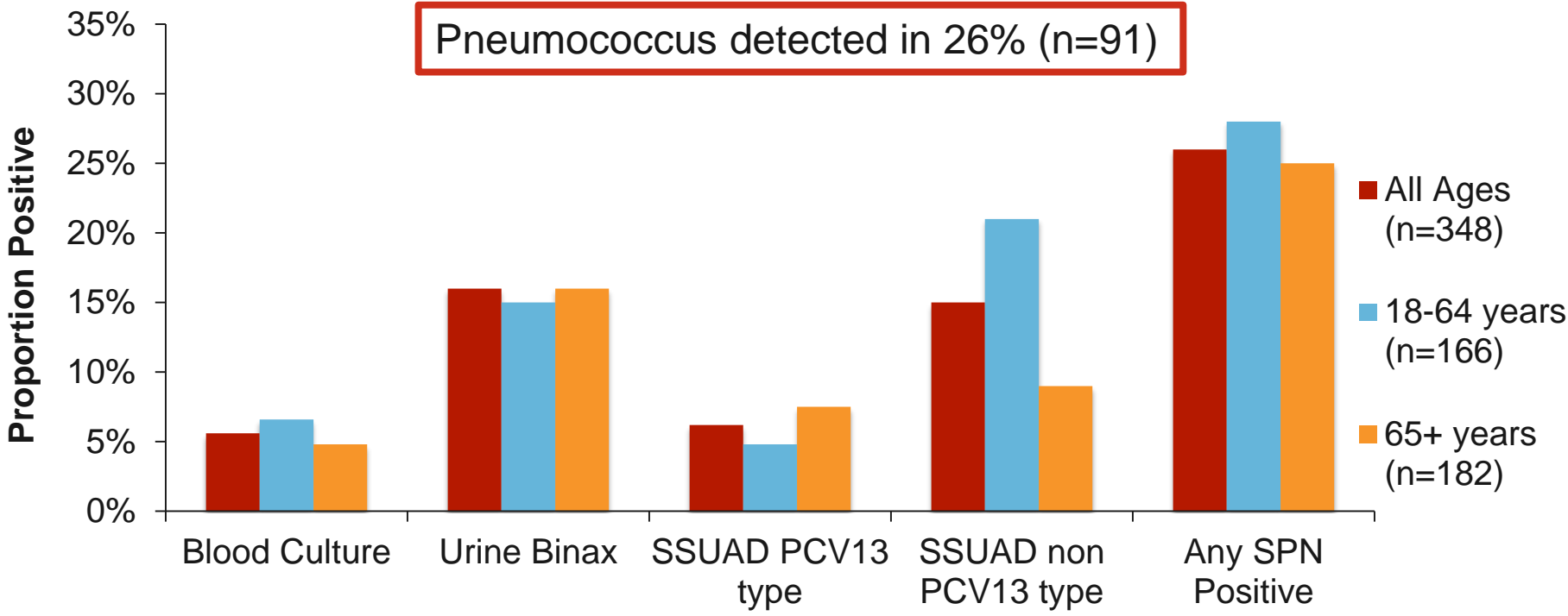
¹Denominator includes 293 cases and 236 controls with available data.

Clinical characteristics

Characteristic	CXR+ Cases N=355 n (%)	Controls N=269 n (%)	P-value
Duration of illness* - days median (IQR)	3 (2, 7)	n/a	
Any underlying condition	335 (94.4)	218 (81.0)	<0.001
Chronic lung disease	39 (11.0)	5 (1.9)	<0.001
Chronic heart disease	49 (13.8)	10 (3.7)	<0.001
Diabetes	161 (45.4)	97 (36.1)	0.04
Malignancy	45 (12.7)	12 (4.5)	<0.001
No. of chronic conditions – median (IQR)	1 (0, 4)	1 (0, 3)	0.31
Outcome, discharged alive – n (%)	349 (98.3)	n/a	
Immunization history			
<u><65 years</u>	<u>n (%)</u>	<u>n (%)</u>	
PPV23 ever	110 (65.9)	58 (47.9)	<0.01
PCV13 ever	13 (7.8)	4 (3.3)	0.11
<u>≥65 years</u>	<u>n (%)</u>	<u>n (%)</u>	
PPV23 ever	172 (91.5)	144 (97.3)	0.03
PCV13 ever	152 (80.8)	120 (81.1)	0.96

*from illness onset to hospital presentation

S. pneumoniae positivity by test CXR+ cases with any pneumococcal test (N=348)



SSUAD increased the detection of pneumococcal cases by 57%.

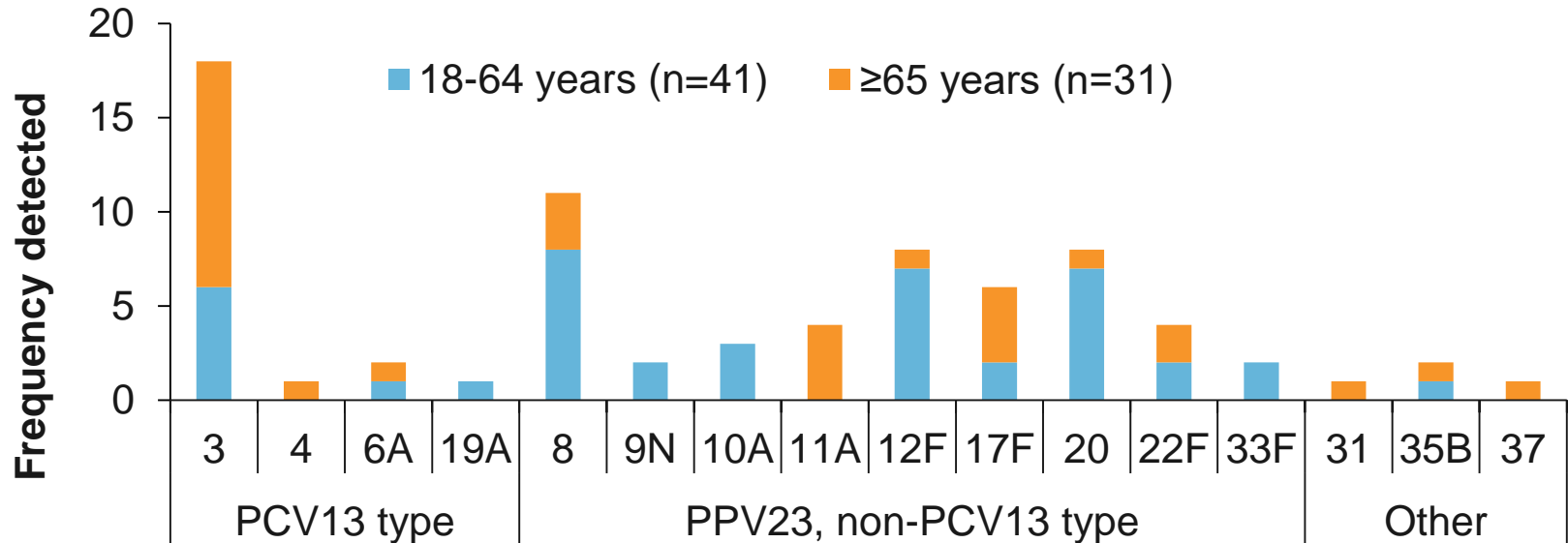
There was **100% serotype concordance** between SSUAD serotype and blood culture serotype.

Urine test results among CXR+ cases with any pneumococcal testing and community controls

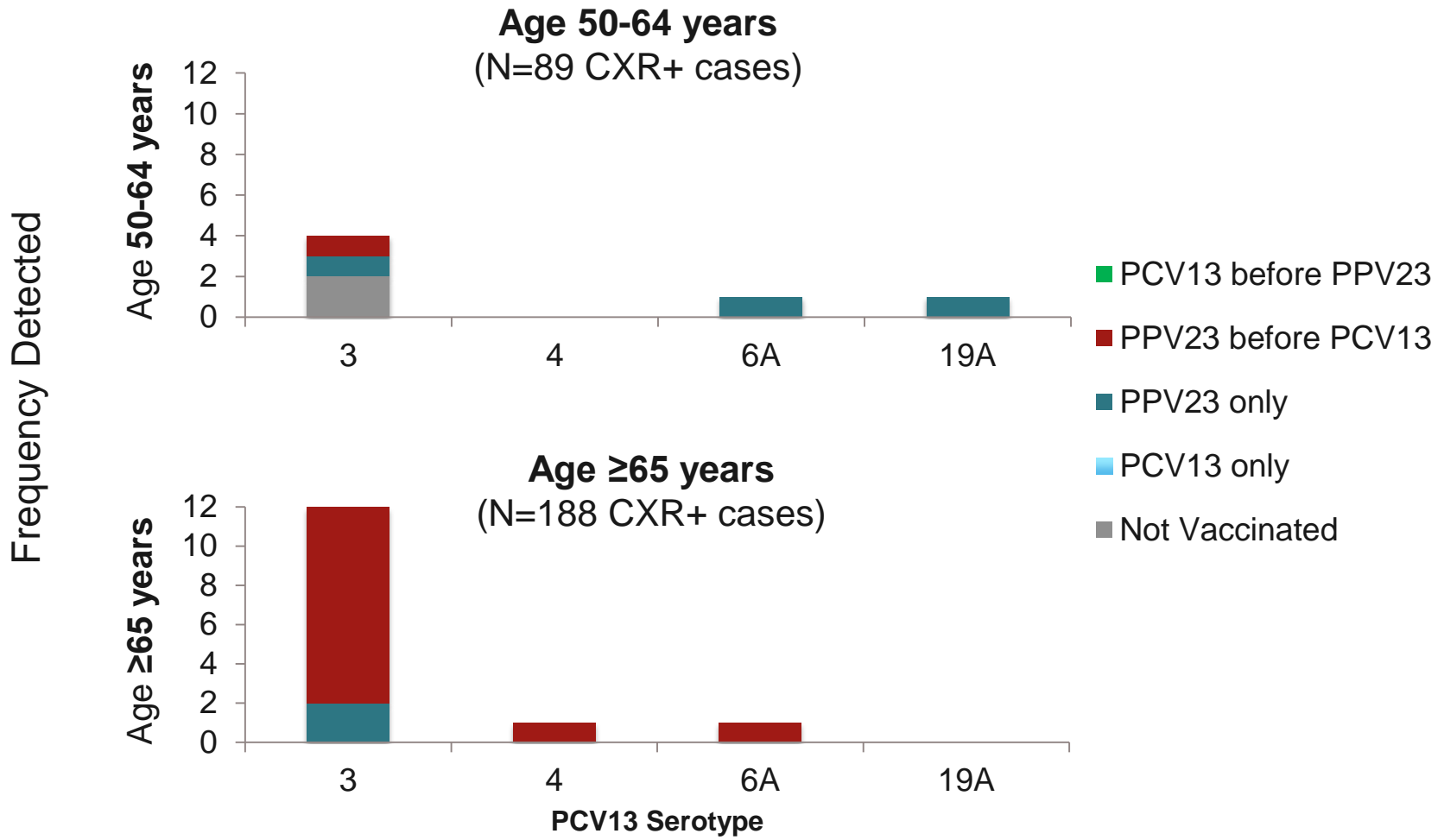
	Cases with ≥ 1 pneumococcal test			Controls		
	≥ 18 yrs N=348 n(%)	18-64 yrs N=166 n(%)	≥ 65 yrs N=182 n(%)	≥ 18 yrs N=249 n(%)	18-64 yrs N=116 n(%)	≥ 65 yrs N=133 n(%)
SSUAD+	68 (19.5)	40 (24.1)	28 (15.4)	7 (2.8)	5 (4.3)	2 (1.5)
BinaxNow+	54 (15.5)	25 (15.1)	29 (15.9)	8 (3.2)	2 (1.7)	6 (4.5)

Serotype results for CXR+ pneumococcal CAP

- Serotype data available in 72/91 (79%) pneumococcal cases
 - 22 (31%) were PCV13-type; excluding ST3, 4 (6%) were PCV13-type
 - 13 (62%) of 21 with vaccination status available had received PCV13 (all had received PPV23 first then PCV13)



PCV13 serotypes and vaccination status by age



Conclusions

- PCV13-type NP carriage in adults was very low prior to use of PCV13 in older adults and remains low
- Substantial indirect effects had been achieved by 2014-2015, leaving little opportunity to assess impact of PCV13 in ≥ 65 year olds on carriage or IPD
- **Pneumococcus remains an important cause of CXR+ CAP among Native American adults**
 - Non-PCV13 serotypes and serotype 3 predominated
 - SSUAD increased the detection of pneumococcal pneumonia over conventional methods but did not reveal an substantial burden of PCV13-type disease (except serotype 3) in the context of high PCV13 use in infants and ≥ 65 year olds

Acknowledgements

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