



Invasive Pneumococcal Disease Update

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INDIGENOUS HEALTH




Disclosures

- Research grants to my institution from Astra Zeneca, Merck, Pfizer



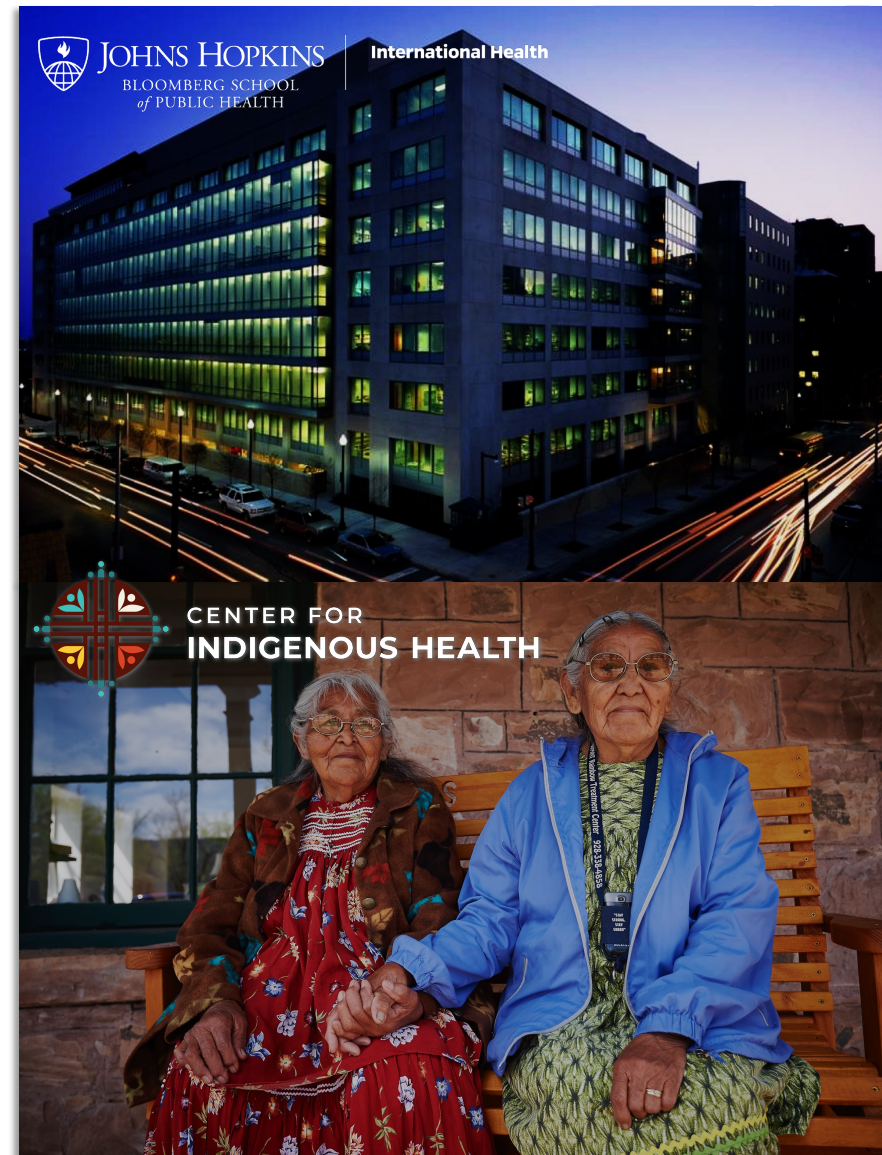


Overview

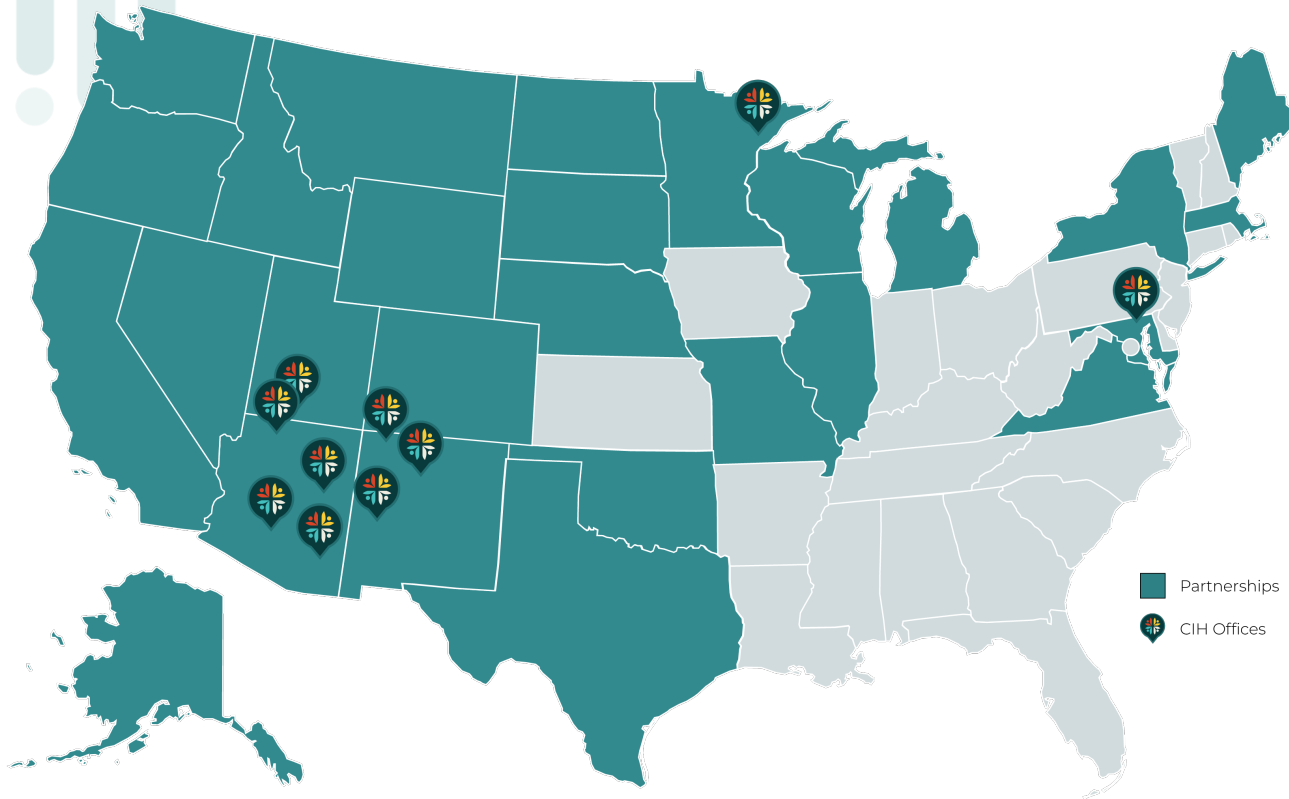
- Background
 - Active bacterial surveillance for invasive pneumococcal disease (IPD)
 - Serotype 4 IPD resurgence
 - Pneumococcal vaccine recommendations
- 

Johns Hopkins Center for Indigenous Health

- **Founded:** 1991 at Johns Hopkins Bloomberg School of Public Health in the Department of International Health
- **Mission:** We work in partnership with communities to advance Indigenous well-being and health leadership to the highest level.
- **Vision:** Thriving Indigenous communities worldwide



Our Center's Scope



Today, over **300** staff and faculty work at the CIH.

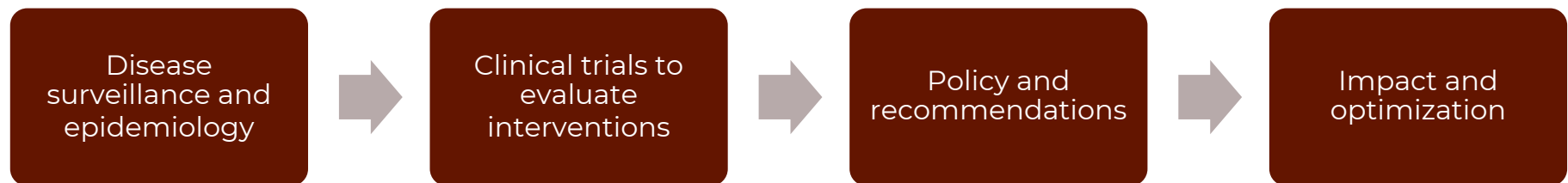
80% of CIH employees are Indigenous

Over **90%** of the CIH team is working on the frontlines of Indigenous communities

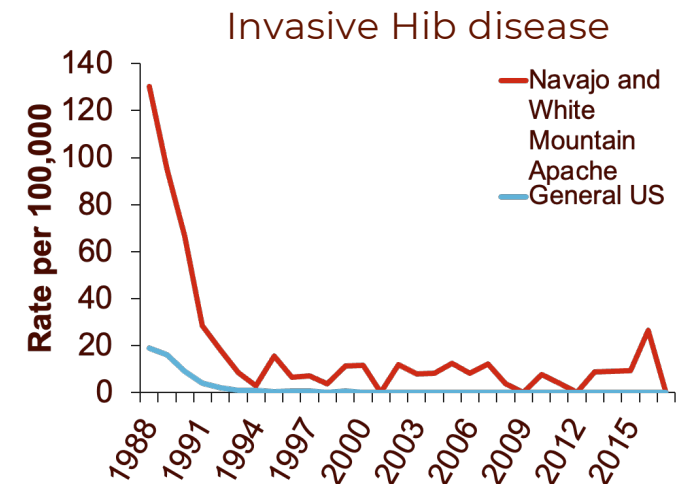
Working across **27** states and **165+** communities

Core Areas of Work: Training, Behavioral/Mental Health, Infectious Disease

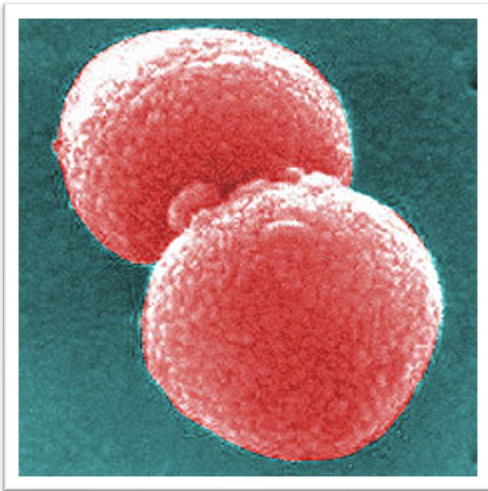
Infectious Disease Prevention



4 of 8 immunizations recommended in the first year of life in the US were proven efficacious by CIH

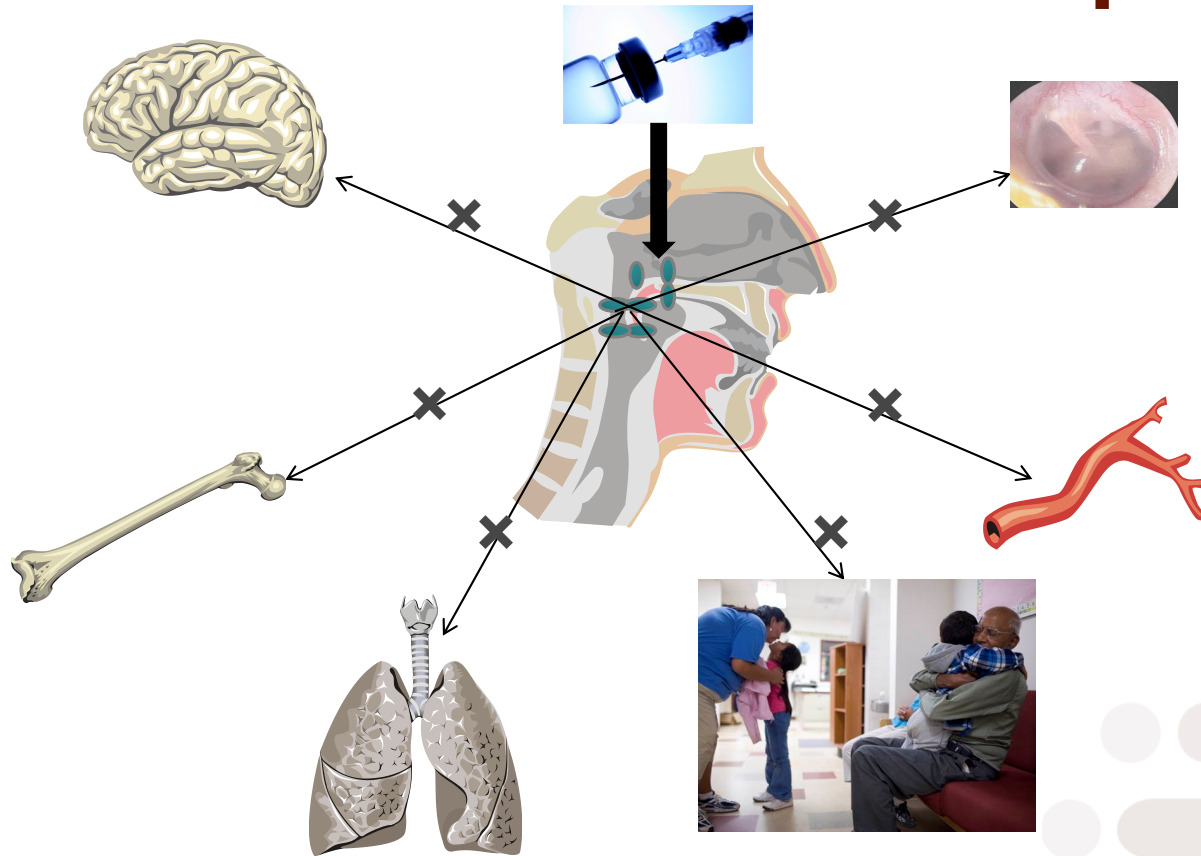


What is *Streptococcus pneumoniae*?



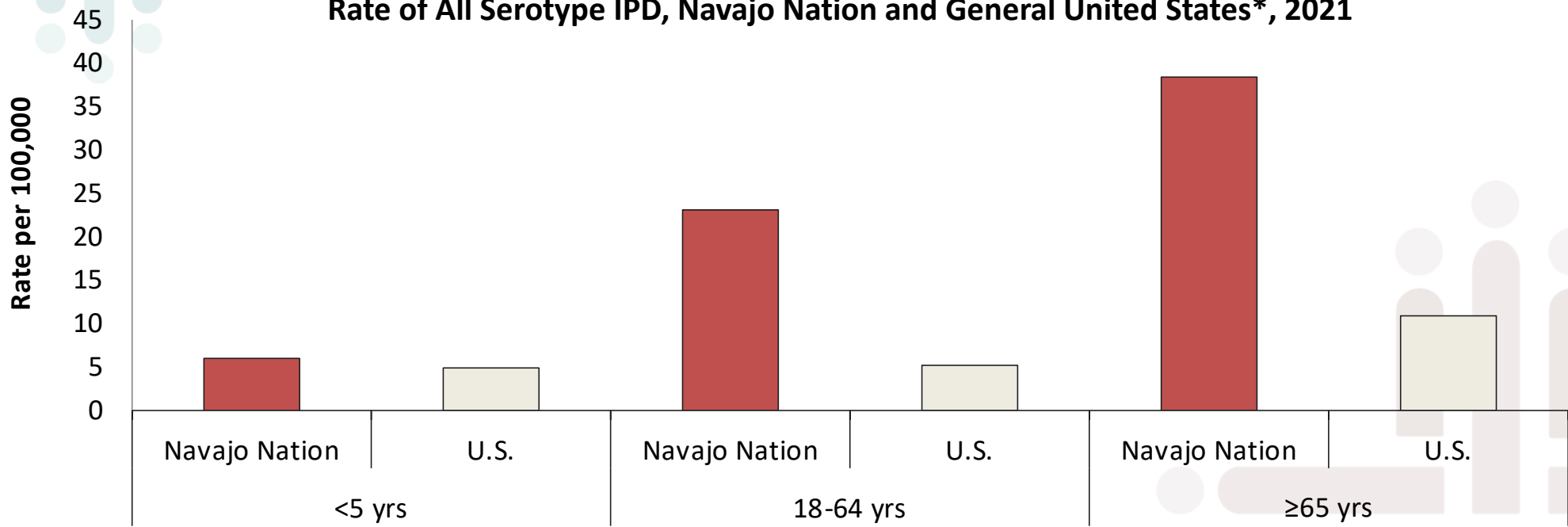
- A gram-positive bacteria
- Over 100 different serotypes
 - Serotypes differ by the polysaccharide capsule
- Can cause:
 - Invasive disease (pneumonia, meningitis, blood infection)
 - Otitis media (ear infection), sinusitis

Pneumococcus and the Nasopharynx



Invasive Pneumococcal Disease, Navajo Nation

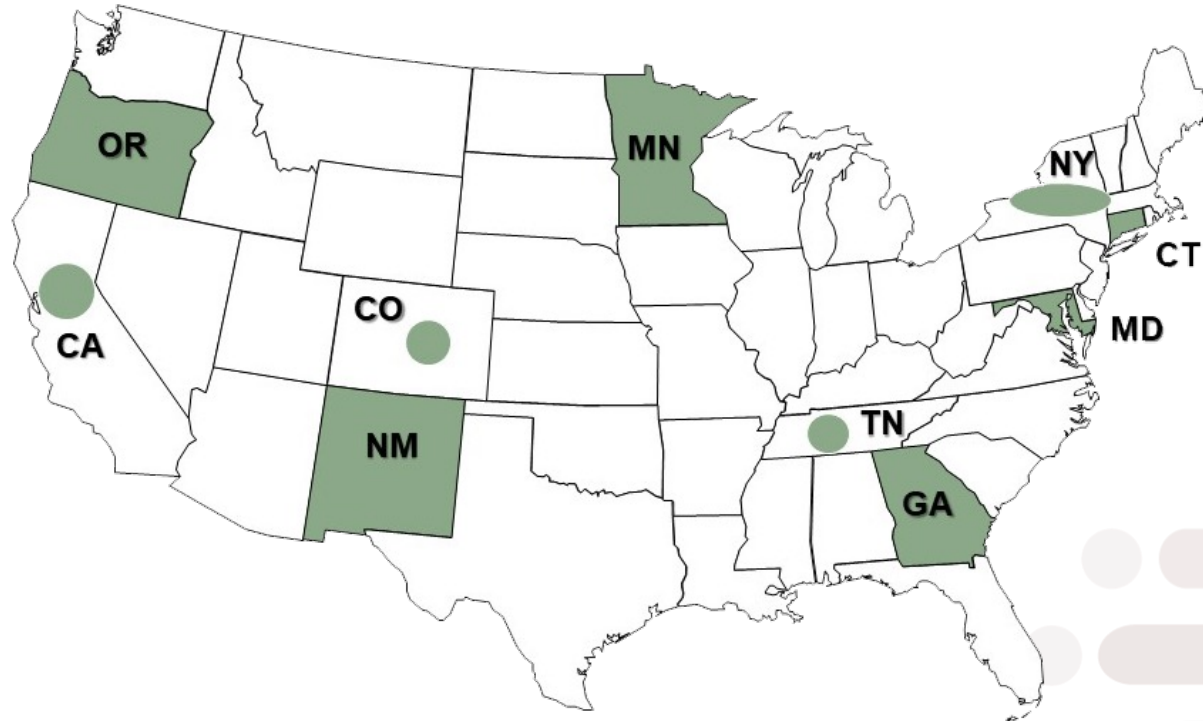
Rate of All Serotype IPD, Navajo Nation and General United States*, 2021



*<https://www.cdc.gov/abcs/bact-facts-interactive-dashboard.html>

US CDC Active Bacterial Core surveillance

Surveillance population: 45.5 million



Active Bacterial Surveillance (ABS)

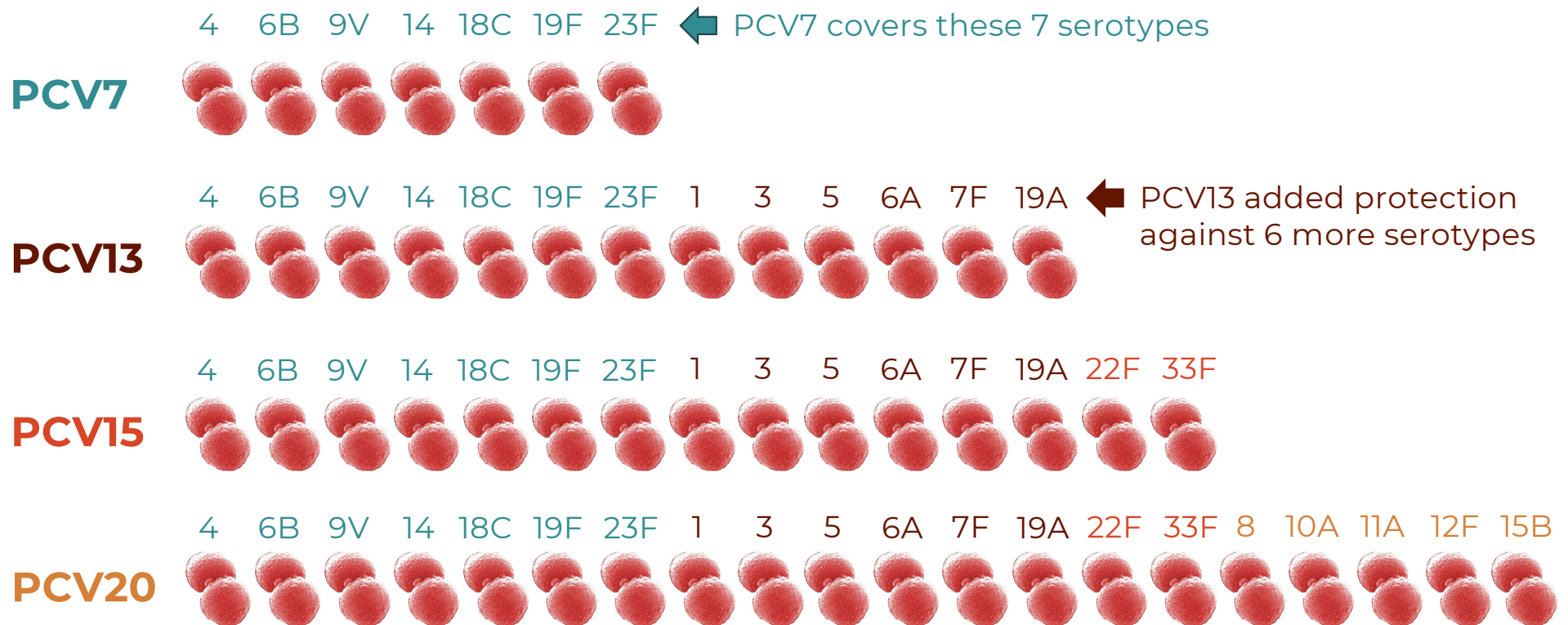
- Tribal/academic partnership with Johns Hopkins Center for Indigenous Health
 - Provides data for White Mountain Apache Tribe and Navajo Nation as a whole
 - >20 years of collaboration
- Active, laboratory-based surveillance
 - *Streptococcus pneumoniae*
 - *Haemophilus influenzae*
 - *Neisseria meningitidis*
 - *Staphylococcus aureus*
 - Group A *Streptococcus*



Key:

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

What do the pneumococcal conjugate vaccines (PCV) cover?



PCV use in Navajo Nation

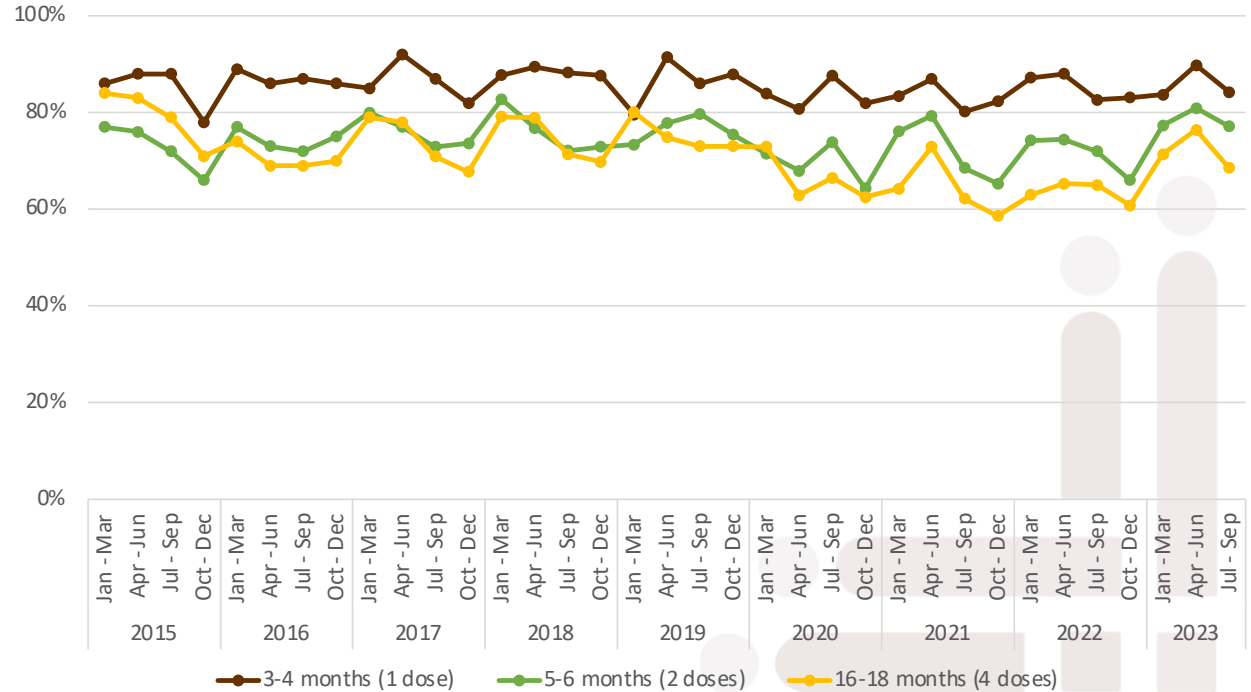
Children <5y

- **2000:** PCV7
- **2010:** PCV13
- **2023:** PCV15 and PCV20

Adults ≥65

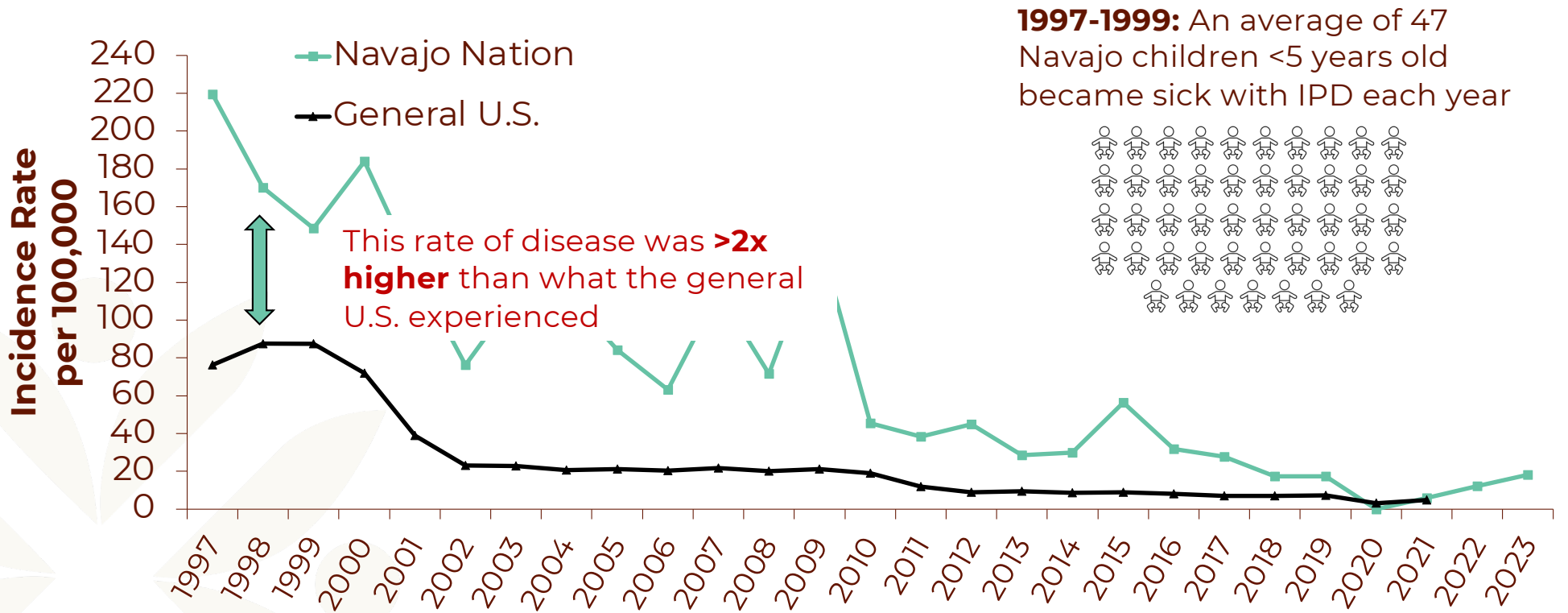
- **2014:** PCV13 introduced in series with PPSV23
- **2019:** PCV13 recommendation changed to shared clinical decision-making
- **2021:** PCV15 in series with PPSV23 or PCV20

IHS Quarterly Age-Appropriate PCV Coverage for Navajo Area*, Jan. 2015 – Sept. 2023

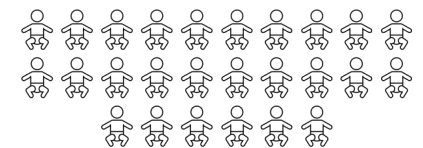
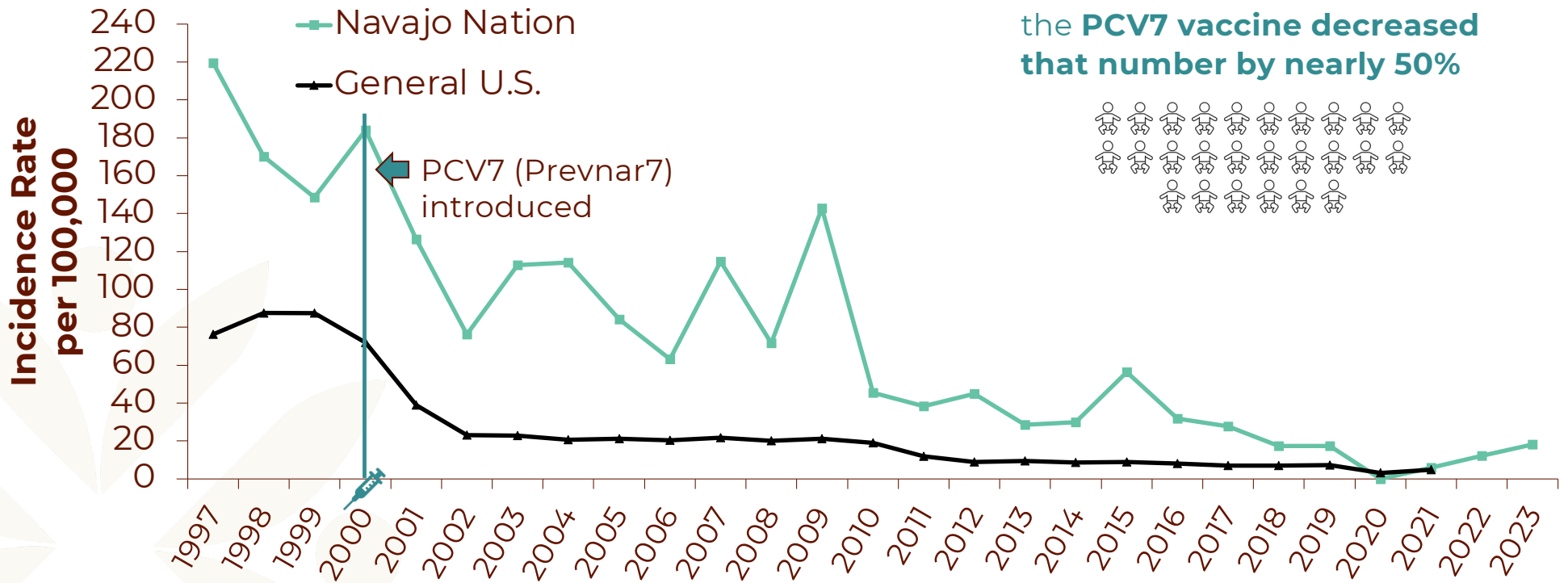


*<https://www.ihs.gov/NonMedicalPrograms/ihpes/immunizations/>

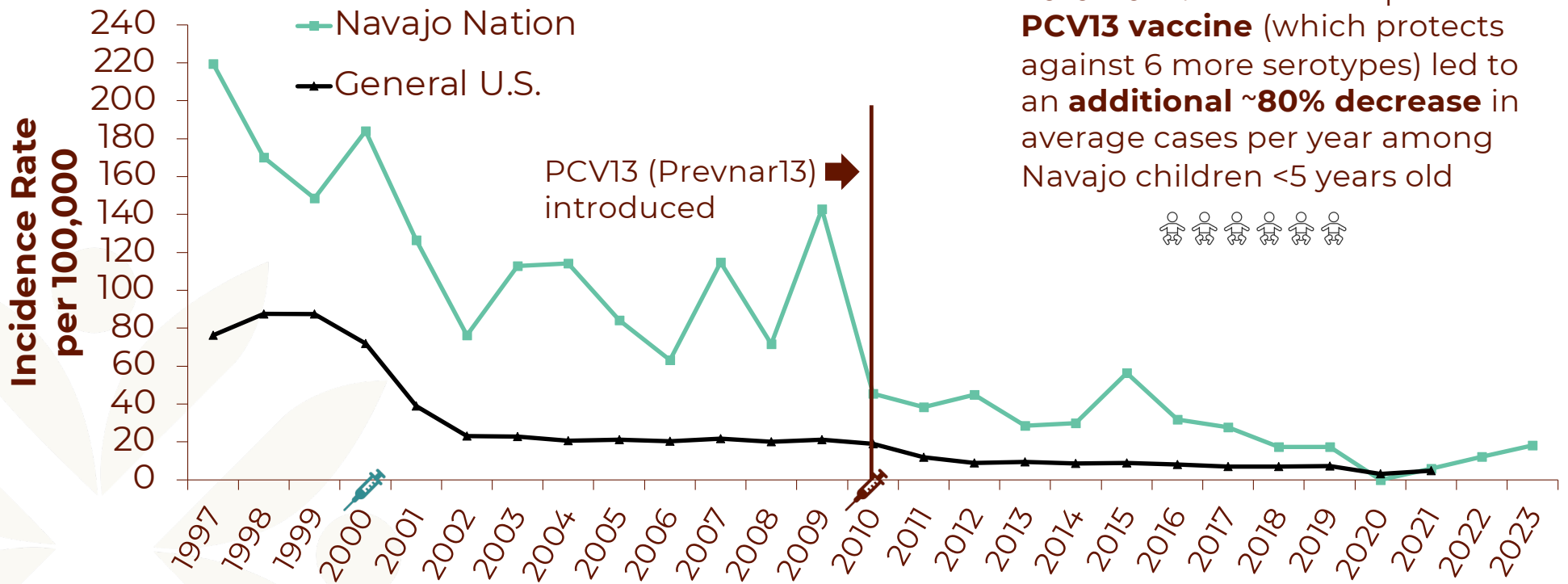
Rate of invasive pneumococcal disease (IPD) among Navajo children <5 years, 1997-2023



Rate of invasive pneumococcal disease (IPD) among Navajo children <5 years, 1997-2023



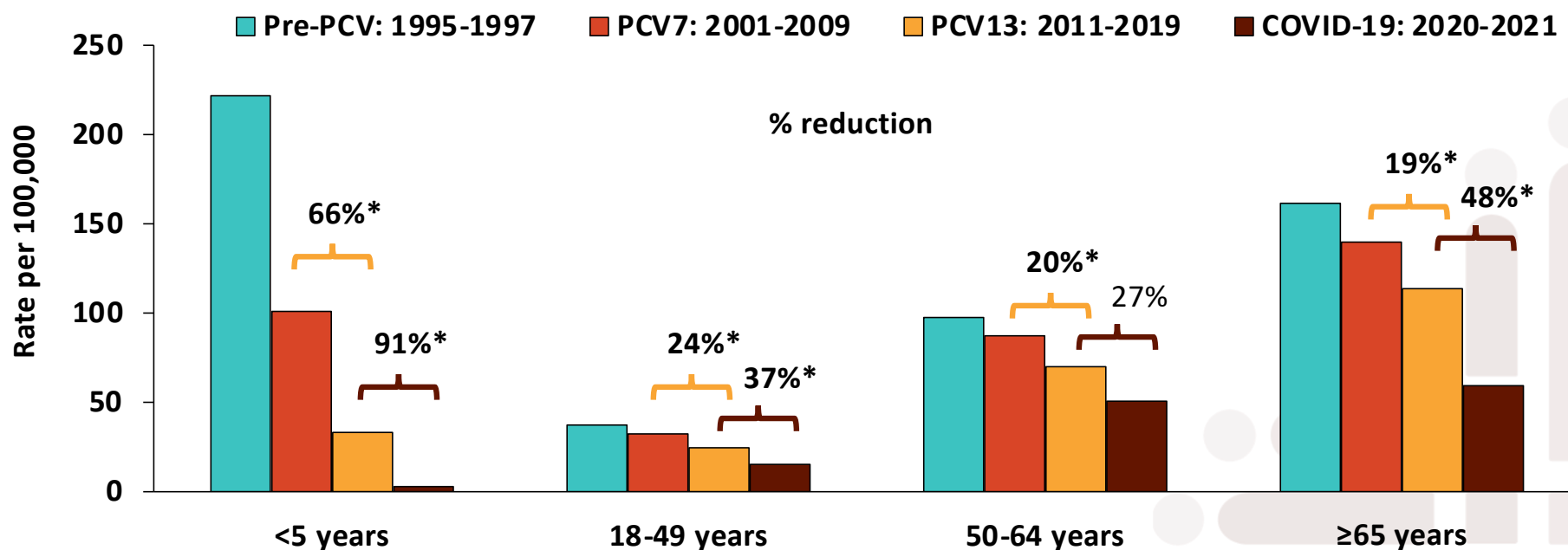
Rate of invasive pneumococcal disease (IPD) among Navajo children <5 years, 1997-2023



PCV impact across age groups

- PCVs have been very successful at decreasing the burden of IPD in Navajo Nation
- COVID-19 pandemic led to an unprecedented decline in IPD

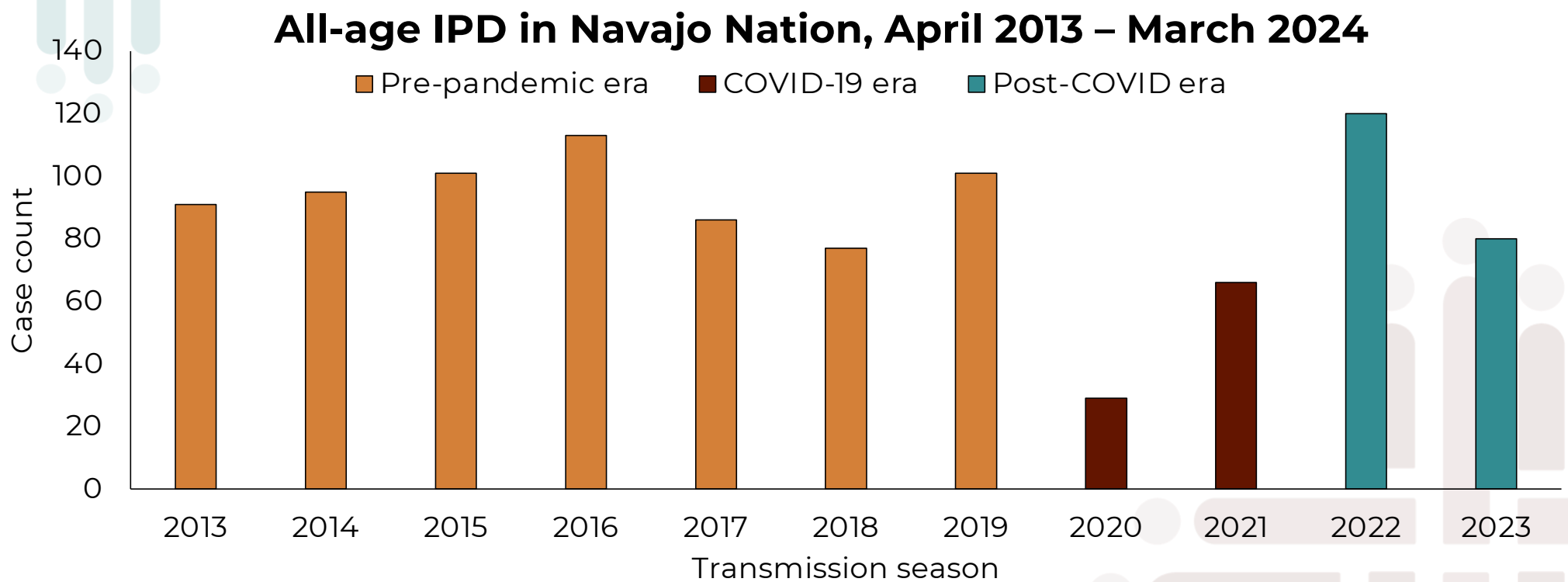
Overall IPD incidence by era, Navajo Nation



Littlepage et al., Impact of Pneumococcal Conjugate Vaccines (PCV) and the COVID-19 Pandemic on Invasive Pneumococcal Disease (IPD) Among Native Americans Living on the Navajo Nation, ISPPD 2022, Toronto, Canada

*p<0.05

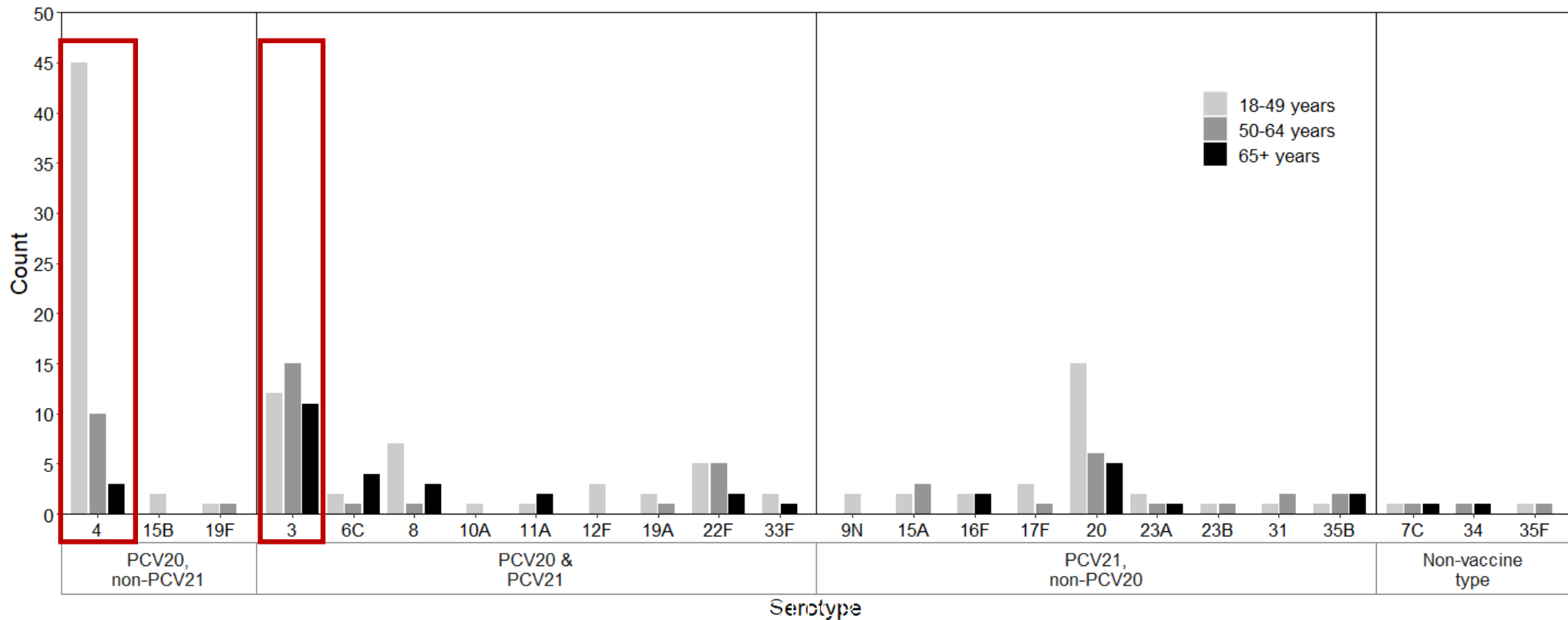
Post-pandemic IPD rebound



Transmission season = April of the year indicated - March of the following year

Sergent et al., Impact of pneumococcal conjugate vaccines and the COVID-19 pandemic on otitis media and invasive pneumococcal disease, Navajo Nation Human Research Review Board 2023 Conference, Flagstaff, Arizona

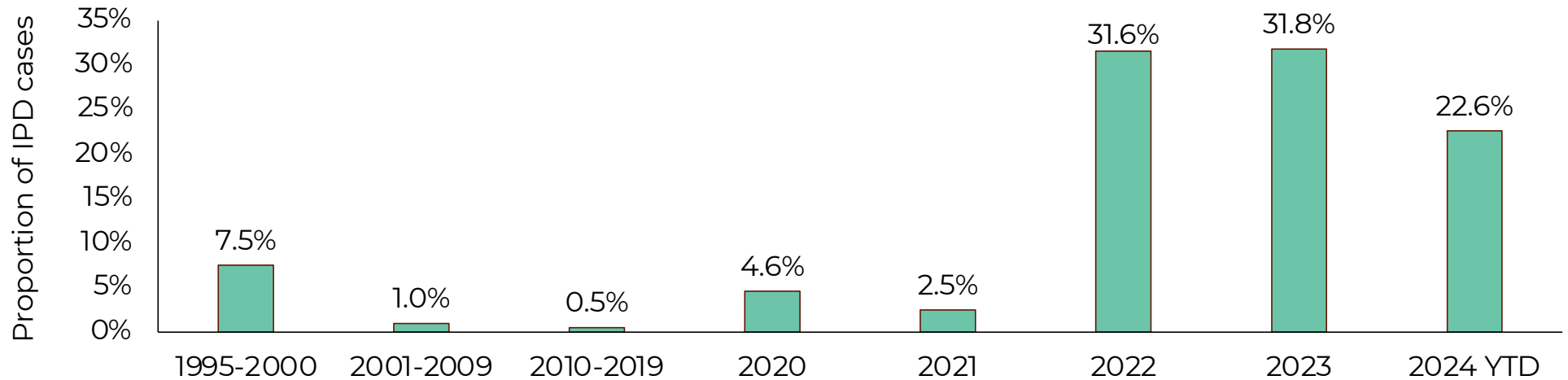
IPD serotype distribution by age group, NN & WMAT, Jan 2022 - Mar 2024



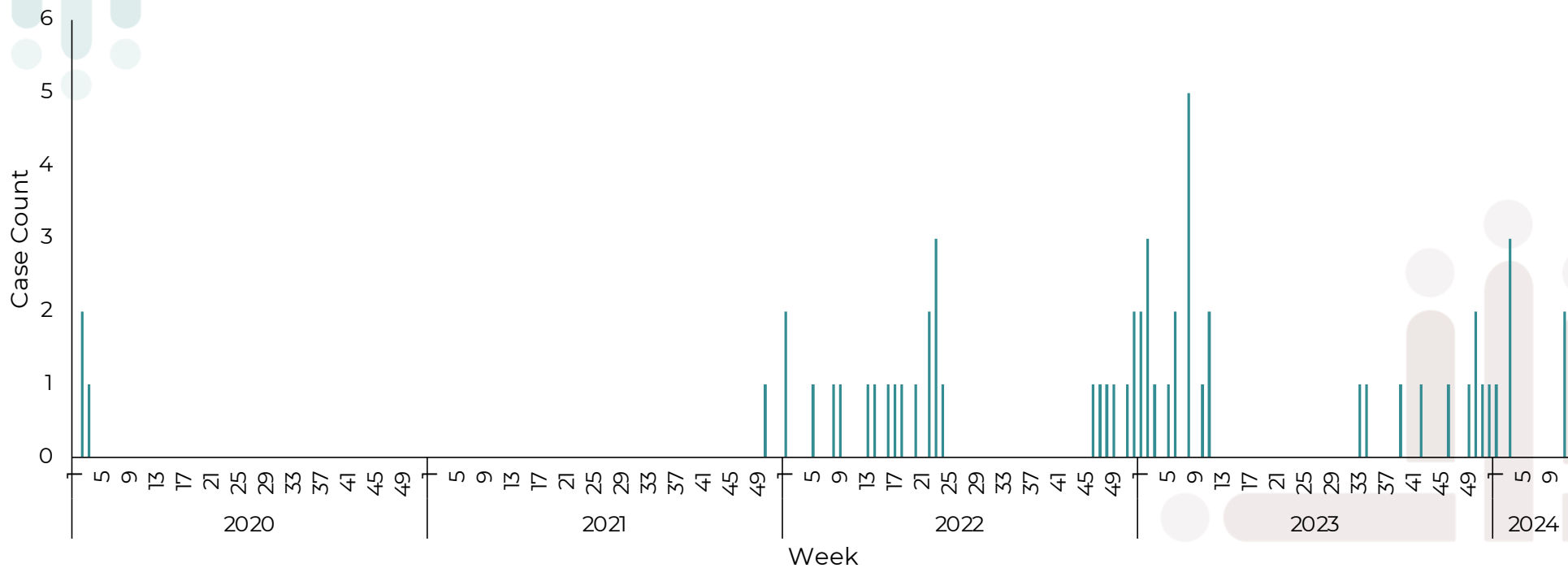
Resurgence of serotype 4 IPD among adults in Navajo Nation

- Serotype 4 has been included in every vaccine
 - Disease caused by this serotype was virtually eliminated after 2000
 - Now accounts for >25% of IPD cases

Proportion of IPD in Navajo Nation Caused by Serotype 4, Jan 1995 – Mar 2024



Serotype 4 IPD cases by week, Navajo Nation, Jan 2020 – Mar 2024



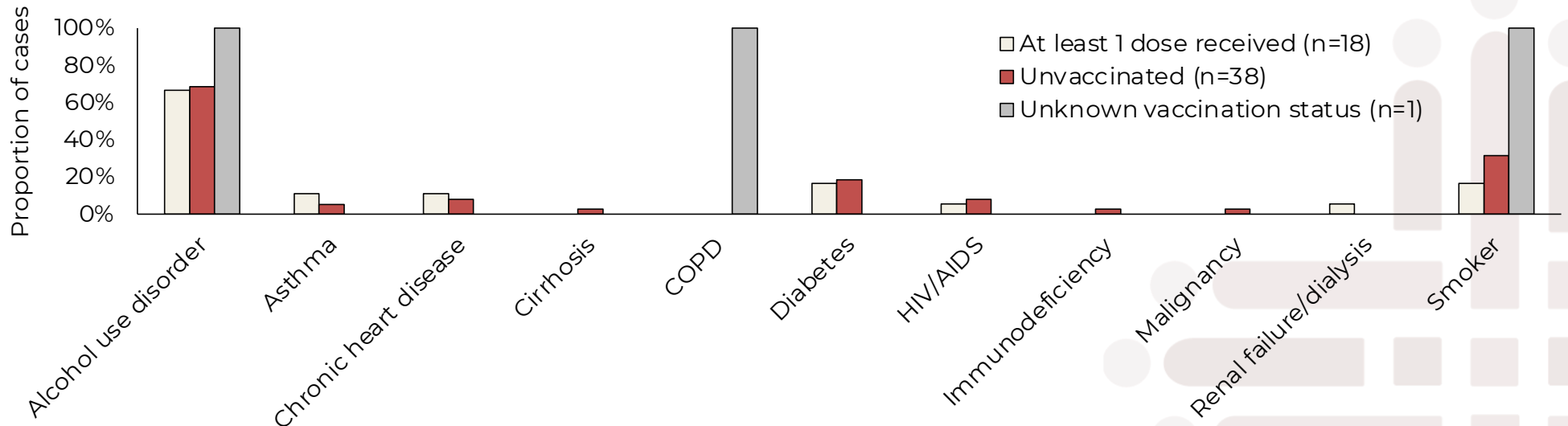
Serotype 4 IPD in Navajo Nation, Jan. 2022 – Mar. 2024

- All serotype 4 IPD cases (n=58) have occurred among **adults** (median age: 39 years; 70.7% male)
- **Pneumonia** is the most common clinical syndrome (present in 91% of cases)
- Most cases:
 - **Lived in a private residence** (84%)
 - Resided in a single service unit (59%)
 - Cases of serotype 4 IPD detected across Navajo Nation

Serotype 4 IPD in Navajo Nation, Jan. 2022 – Mar. 2024

- Mainly **unvaccinated adults with ≥ 1 indication for vaccination**
 - Most commonly alcohol misuse or smoking

Indications for Vaccination Among Serotype 4 IPD Cases*, Jan 2022 – Mar 2024



Vaccination history among serotype 4 IPD cases, Navajo Nation, Jan 2022 – Mar 2024

- 31% of individuals were vaccinated, most >10 years before their illness (median: 14.1 years since last dose)
 - PPSV23 only: n=11
 - PCV7: n=5 (all doses given as part of routine childhood immunizations)
 - PCV13 & PPSV23: n=2

The Journal of Infectious Diseases

MAJOR ARTICLE



Upsurge of Conjugate Vaccine Serotype 4 Invasive Pneumococcal Disease Clusters Among Adults Experiencing Homelessness in California, Colorado, and New Mexico

Bernard Beall,¹ Hollis Walker,² Theresa Tran,³ Zhongya Li,³ Jasmine Varghese,³ Lesley McGee,¹ Yuan Li,¹ Benjamin J. Metcalf,¹ Ryan Gierke,¹ Emily Mosites,¹ Sopi Chochua,^{1,20} and Tamara Pijishvili¹

¹Respiratory Disease Branch, National Center for Immunizations and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA, ²HRC Inc., Contractor to Respiratory Diseases Branch, Centers for Disease Control and Prevention, Atlanta, Georgia, USA, and ³ASRT Inc., Contractor to Respiratory Diseases Branch, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases

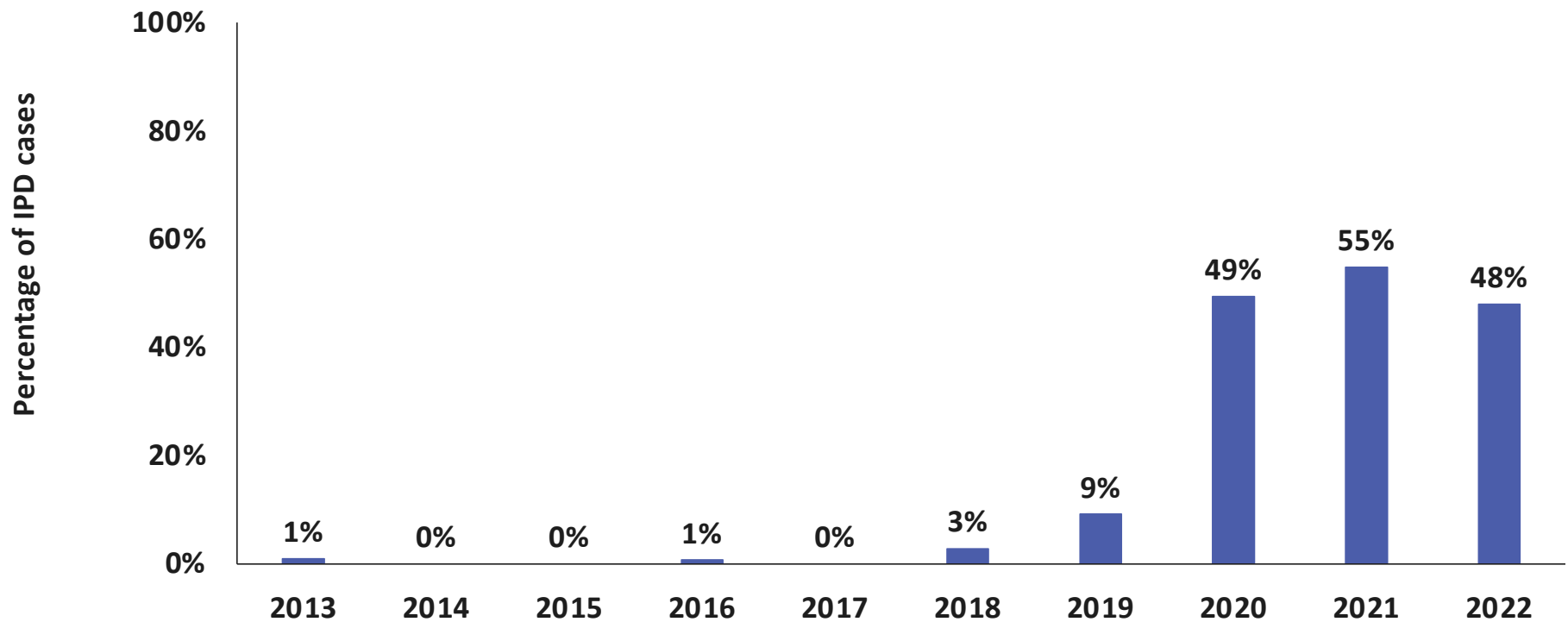


Increase in Invasive Pneumococcal Disease due to *Streptococcus pneumoniae* Serotype 4 — Alaska, 2013-2022

Laurie Orell, MPH CPH

Slide citation: Laurie Orell et al., Increase in Invasive Pneumococcal Disease due to *Streptococcus pneumoniae* Serotype 4 — Alaska, 2013-2022, ISPPD 2024, Cape Town, South Africa

Percentage of IPD cases in due to serotype 4 in Alaska, by year



Slide citation: Laurie Orell et al., Increase in Invasive Pneumococcal Disease due to *Streptococcus pneumoniae* Serotype 4 — Alaska, 2013-2022, ISPPD 2024, Cape Town, South Africa

IPD case characteristics, by serotype — Alaska, 2013-2022

	Serotype 4 [N=324]		Non-serotype 4* [N=1,058]		
	No.	(%)	No.	(%)	p value
Aged ≥18 years	321	(99)	944	(89)	<0.01
Male	213	(66)	627	(60)	<0.05
Alaska Native peoples	205	(63)	512	(48)	<0.01
Hospitalized	289	(89)	951	(90)	--
Died	36	(11)	127	(12)	--

*Excludes cases without serotype data

Call to Action

- The Alaska Division of Public Health and CDC's Arctic Investigations Program noted a similar increase in serotype 4 IPD in Alaska
- Together, Navajo Nation and Alaska data led Dr. Christensen to issue a **'Call to Action' to increase PCV20 vaccination rates among eligible adults**



April 2, 2024

IHS CMO Highlights Importance of PCV-20 Vaccination: Increase in Invasive Pneumococcal Disease from Serotype 4

On April 2, 2024, IHS Chief Medical Officer Dr. Loretta Christensen issued a call to action to increase 20-valent pneumococcal conjugate vaccine (PCV20) vaccination rates among American Indians and Alaska Natives to mitigate the risk of invasive pneumococcal disease (IPD) in tribal communities. Dr. Christensen is challenging all facilities to target 85% PCV20 vaccination rates for those impacted by the CDC [Advisory Committee on Immunization Practices \(ACIP\) recommendations](#) for this vaccine.

Serotype 4 Epidemiology:¹

Over the last decade, there has been a measurable rise in the proportion of cases of IPD due to serotype 4, especially in the [Navajo Area](#) and [Alaska Area](#) for which [data](#) is available. In the Navajo Area, since 2022 the median age of serotype 4 IPD (n = 44) is 39 years with higher prevalence among those with pre-existing risk factors, including smokers and those with alcohol use disorder. Adults in Alaska, especially Alaska Native adults, have experienced an [88-fold increase](#) in serotype 4 IPD from 2019-2020 compared to 2011-2018.

Recommendations:²

On October 20, 2021, the ACIP recommended 15-valent pneumococcal conjugate vaccine (PCV15) or 20-valent pneumococcal conjugate vaccine (PCV20) for PCV-naïve adults who are either aged ≥65 years or aged 19–64 years with certain underlying conditions. When PCV15 is used, it should be followed by a dose of pneumococcal polysaccharide vaccine (PPSV23), typically ≥1 year later.

**Underlying medical conditions include: cerebrospinal fluid leak; chronic heart disease; chronic kidney disease (excluding maintenance dialysis and nephrotic syndrome, which are included in immunocompromising conditions); chronic liver disease; chronic lung disease (including moderate persistent or severe persistent asthma); cochlear implant; diabetes mellitus; immunocompromising conditions (on maintenance dialysis or with nephrotic syndrome; congenital or acquired asplenia or splenic dysfunction; congenital or acquired immunodeficiencies; diseases and conditions treated with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, Hodgkin disease, and solid organ transplant; HIV infection; and sickle cell disease or other hemoglobinopathies). IHS also recommends targeting vaccination for persons experiencing homelessness, those suffering from alcohol use disorder, and recreational tobacco users.*

PCV recommendations

- Childhood immunization schedule
- Everyone ≥ 65 years
- Adults 19-64 years with:
 - Certain **underlying medical conditions** (e.g., diabetes, chronic heart, liver or lung disease, immunocompromising conditions) or other **risk factors** (including alcoholism and smoking)



Adults 19–64 years old with specified immunocompromising conditions Complete pneumococcal vaccine schedules

Prior vaccines	Option A	Option B
None*	PCV20	PCV15 → ≥ 8 weeks → PPSV23
PPSV23 only	≥ 1 year → PCV20	≥ 1 year → PCV15
PCV13 only	≥ 1 year → PCV20	≥ 8 weeks → PPSV23 → ≥ 5 years → PPSV23 Review pneumococcal vaccine recommendations again when your patient turns 65 years old.
PCV13 and 1 dose of PPSV23	≥ 5 years → PCV20	≥ 5 years [†] → PPSV23 Review pneumococcal vaccine recommendations again when your patient turns 65 years old.
PCV13 and 2 doses of PPSV23	≥ 5 years → PCV20	No vaccines recommended at this time. Review pneumococcal vaccine recommendations again when your patient turns 65 years old.
Immunocompromising conditions	<ul style="list-style-type: none"> Chronic renal failure Congenital or acquired asplenia Congenital or acquired immunodeficiency[§] Generalized malignancy 	<ul style="list-style-type: none"> HIV infection Hodgkin disease Iatrogenic immunosuppression[¶] Leukemia Lymphoma

* Also applies to people who received PCV7 at any age and no other pneumococcal vaccines

[†] The minimum interval for PPSV23 is ≥ 8 weeks since last PCV13 dose and ≥ 5 years since last PPSV23 dose

[§] Includes B- (humoral) or T-lymphocyte deficiency, complement deficiencies (particularly C1, C2, C3, and C4 deficiencies), and phagocytic disorders (excluding chronic granulomatous disease)

[¶] Includes diseases requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids and radiation therapy

Adults 19–64 years old with chronic health conditions Complete pneumococcal vaccine schedules

Prior vaccines	Option A	Option B
None*	PCV20	PCV15 → ≥1 year → PPSV23
PPSV23 only	≥1 year → PCV20	≥1 year → PCV15
PCV13 [†] only	≥1 year → PCV20	≥1 year → PPSV23 Review pneumococcal vaccine recommendations again when your patient turns 65 years old.
PCV13 [†] and PPSV23	<p>No vaccines are recommended at this time. Review pneumococcal vaccine recommendations again when your patient turns 65 years old.</p>	
Chronic health conditions	<ul style="list-style-type: none"> Alcoholism Chronic heart disease, including congestive heart failure and cardiomyopathies Chronic liver disease 	<ul style="list-style-type: none"> Chronic lung disease, including chronic obstructive pulmonary disease, emphysema, and asthma Cigarette smoking Diabetes mellitus

* Also applies to people who received PCV7 at any age and no other pneumococcal vaccines

[†] Adults with chronic medical conditions were previously not recommended to receive PCV13

PneumoRecs VaxAdvisor

Tool to help determine which pneumococcal vaccines children and adults need.



Enter a patient's age, pneumococcal vaccination history, and underlying medical conditions. Move through this tool to create customized pneumococcal vaccination recommendations.

<19 years

19 through 64 years

≥65 years

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Patient Characteristics

Has the patient ever received PCV15 or PCV20?

No

Yes

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Patient Characteristics

Age

19 through 64 years

PCV15 or PCV20

No prior doses

Does the patient have any of the following risk factors ?


Yes, one of these risk factors

Select

- Alcoholism
- Cerebrospinal fluid (CSF) leak
- Chronic heart¹, liver, or lung² disease
- Chronic renal failure
- Cigarette smoking
- Cochlear implant
- Congenital or acquired asplenia
- Congenital or acquired immunodeficiencies³

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Patient Characteristics

Age

19 through 64 years

PCV15 or PCV20

No prior doses

Risk Factors

Yes

PPSV23

Has received prior doses

PCV13


No prior doses

Recommendation

Give one dose of PCV15 or PCV20 at least 1 year after their last dose of PPSV23. Regardless of which vaccine is used (PCV15 or PCV20), their pneumococcal vaccinations are complete.

Got It!

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Pneumococcal Disease (PD)

Cases Are On the Rise

Stay safe and get vaccinated if you are 65+ or have conditions that increase your risk of PD.



PD can cause life threatening illnesses like meningitis and pneumonia. Vaccines are safe and highly effective against PD. Contact your healthcare provider today.



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Vaccination is recommended for elders 65+ or adults with the following conditions:

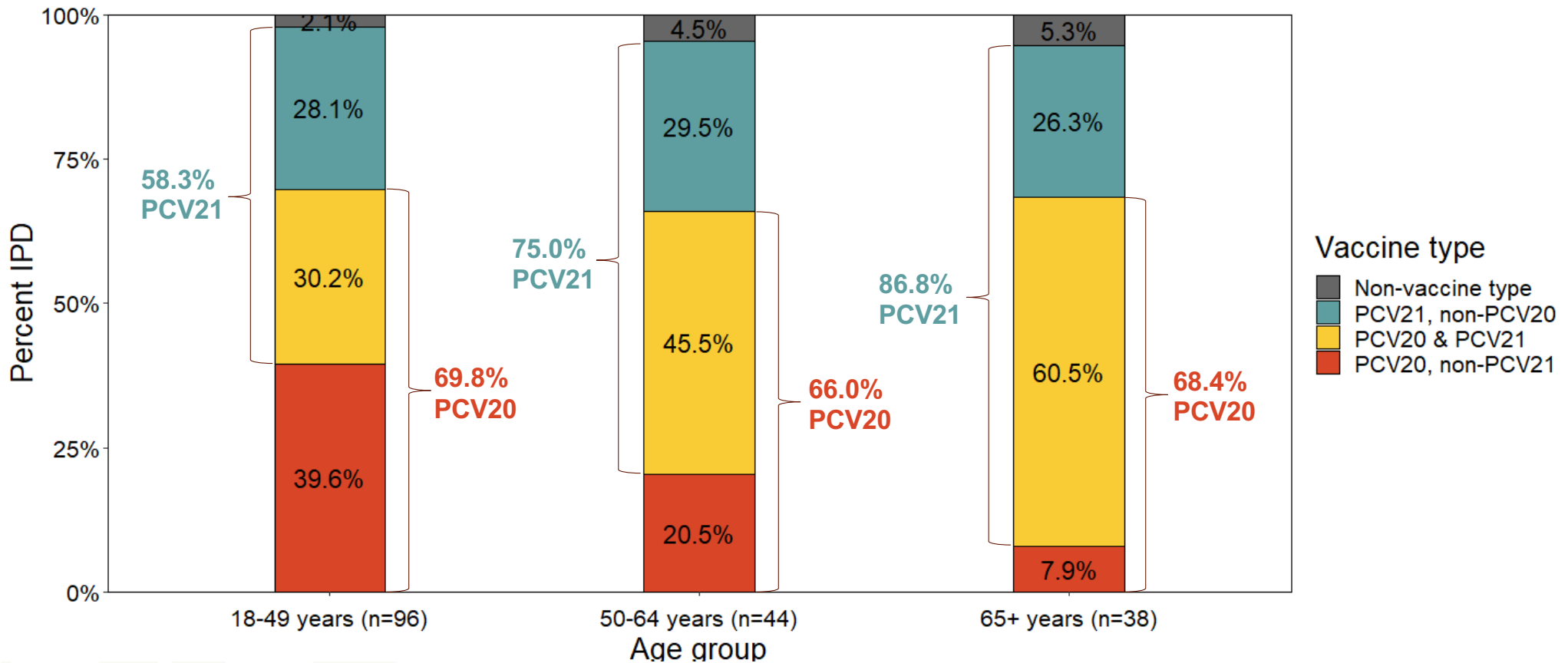
- Cigarette smoking
- Diabetes
- Cancer
- Chronic heart, liver, or lung disease
- Alcoholism
- Weak immune system

Adults with these conditions should contact their healthcare provider about the pneumococcal vaccine.



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IPD by vaccine category among adults with a pneumococcal vaccine indication, NN & WMAT, Jan 2022 - Mar 2024



Serotype 4 Carriage Prevalence, NN/WMAT

Year	Serotype 4 Carriage Prevalence	
	Adults	Children
1997-2000	(pending)	2.2% 15/681
2007	<1% 1/778	<1% 2/838
2010-2012	0% 0/2499	0% 0/2625
2015-2017	<1% 7/903	0% 0/600
2018-2019	6% 18/301	--
2022-2023	--	0% 0/500
2024	?	?

Molecular methods have been used for studies since 2015. Adult samples have included OP swabs since 2015.
 Millar et al *Pediatr Infect Dis J* 2009;28: 711-716; Grant et al, *Pediatr Infect Dis J* 2016;35:907-914; Hammitt et al, submitted, Sergent et al, submitted

Conclusions

- PCVs have been a powerful to prevent disease and reduce health disparities
- Serotype 4 has emerged as a substantial contributor to IPD in adults in Alaska and the Navajo Nation
 - Most cases occurred in people who had not received pneumococcal conjugate vaccine but who had a risk factor indication to be vaccinated
- PCV21 has great potential to prevent IPD in adults but does not include serotype 4

Serotype 4 IPD is a vaccine preventable disease

Acknowledgements

- Study participants
- Navajo Epidemiology Center
- IHS/Tribal clinical and laboratory partners
- CDC/AIP
- Azarian lab at UCF
- IRBs of the Navajo Nation, Phoenix Area IHS, and JHSPH
- CIH faculty and staff
- Funding: IPD surveillance in ABS and recent carriage studies supported in part by research grants from the Investigator-Initiated Studies Program of Merck Sharp & Dohme LLC



Thank you!

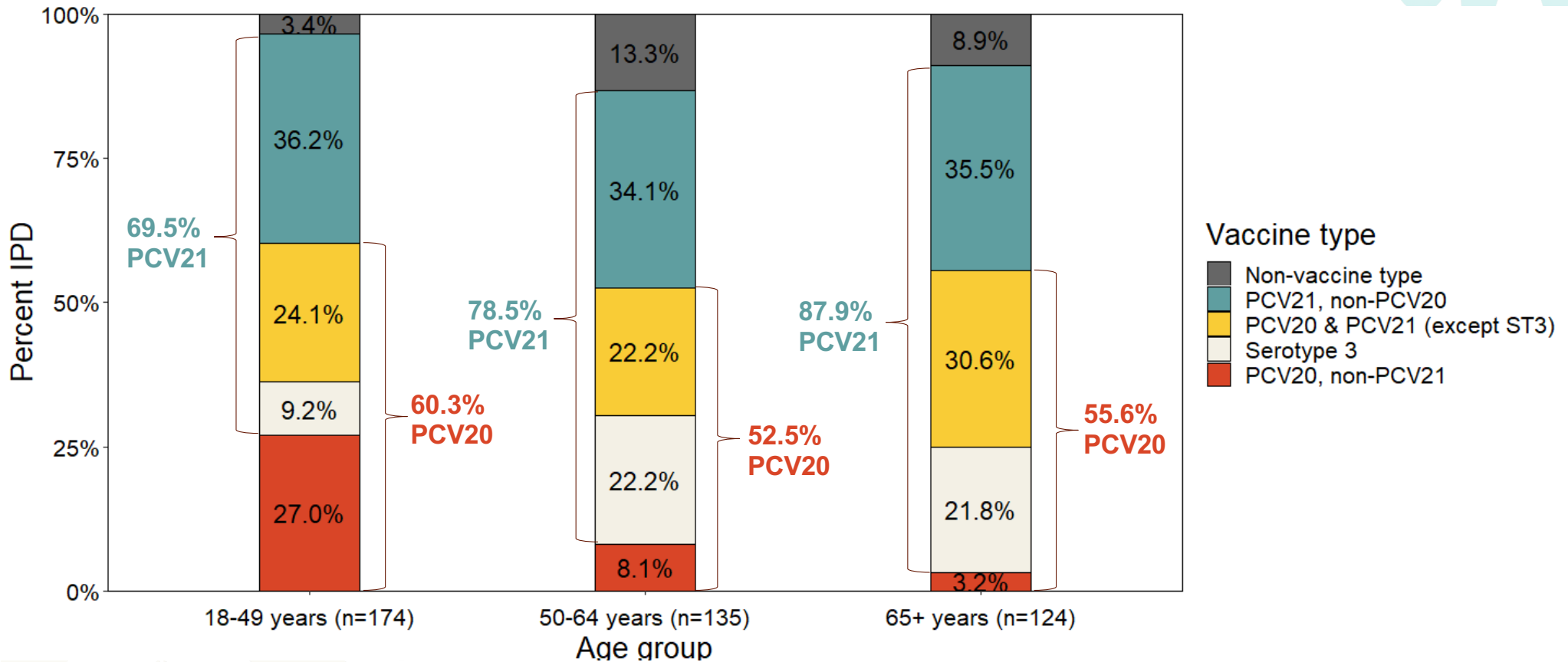
Any questions?



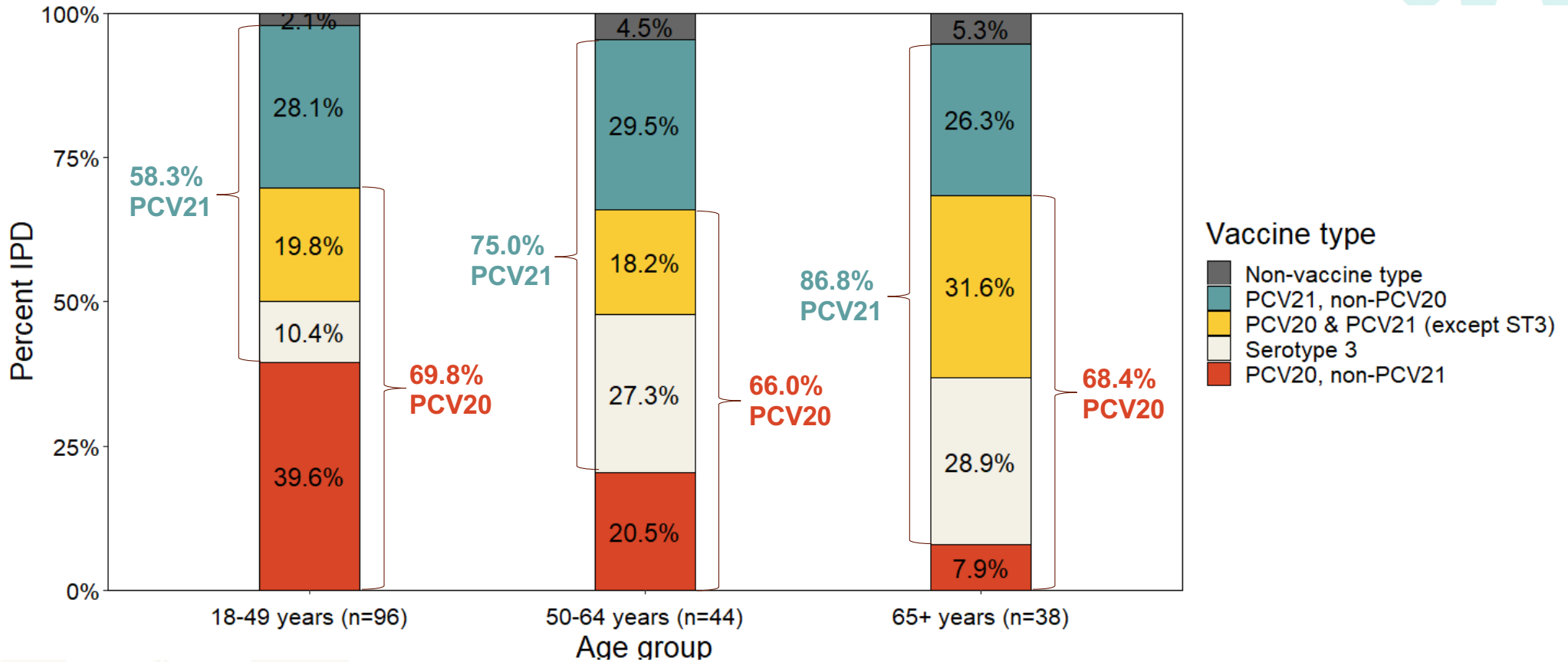
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IPD by vaccine category among adults with a pneumococcal vaccine indication, NN & WMAT, Jan 2018 - Mar 2024



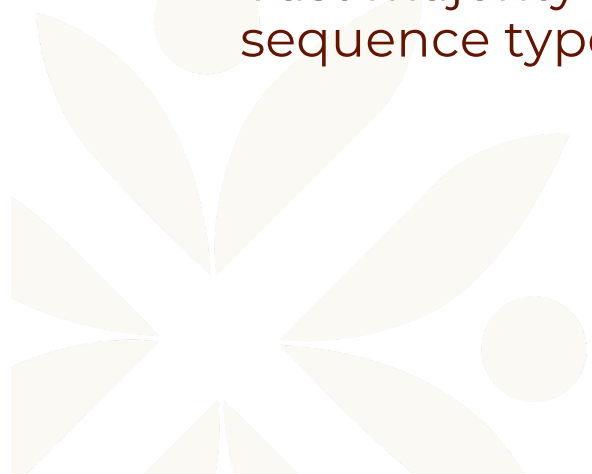
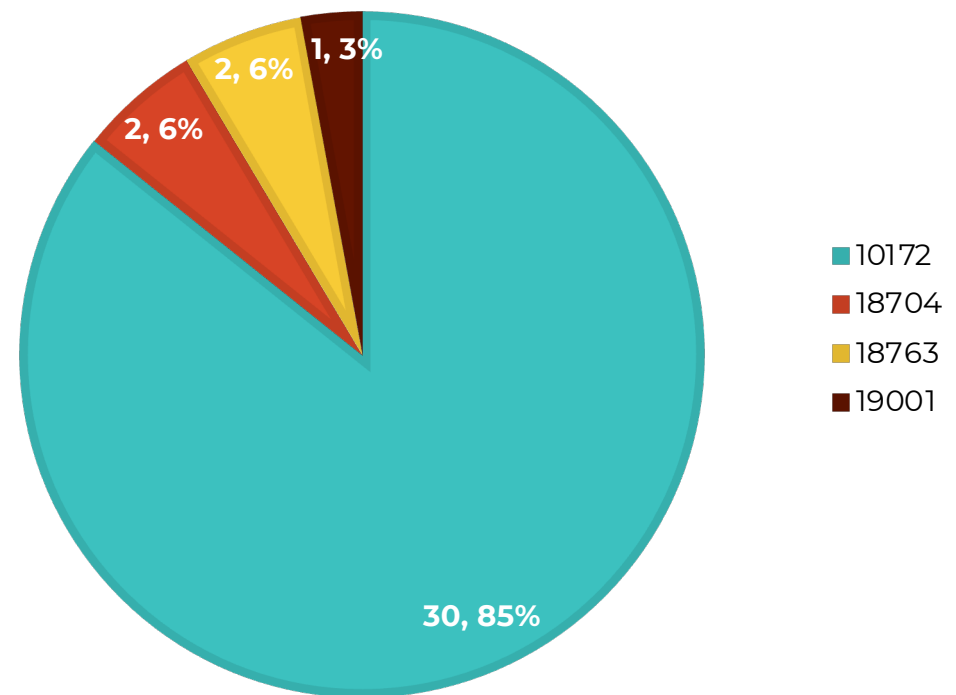
IPD by vaccine category among adults with a pneumococcal vaccine indication, NN & WMAT, Jan 2022 - Mar 2024



Serotype 4 sequence types, Navajo Nation, Jan 2023 – Mar 2024



- Whole genome sequencing data available starting Jan. 2023 (N=35)
- Vast majority are sequence type 10172



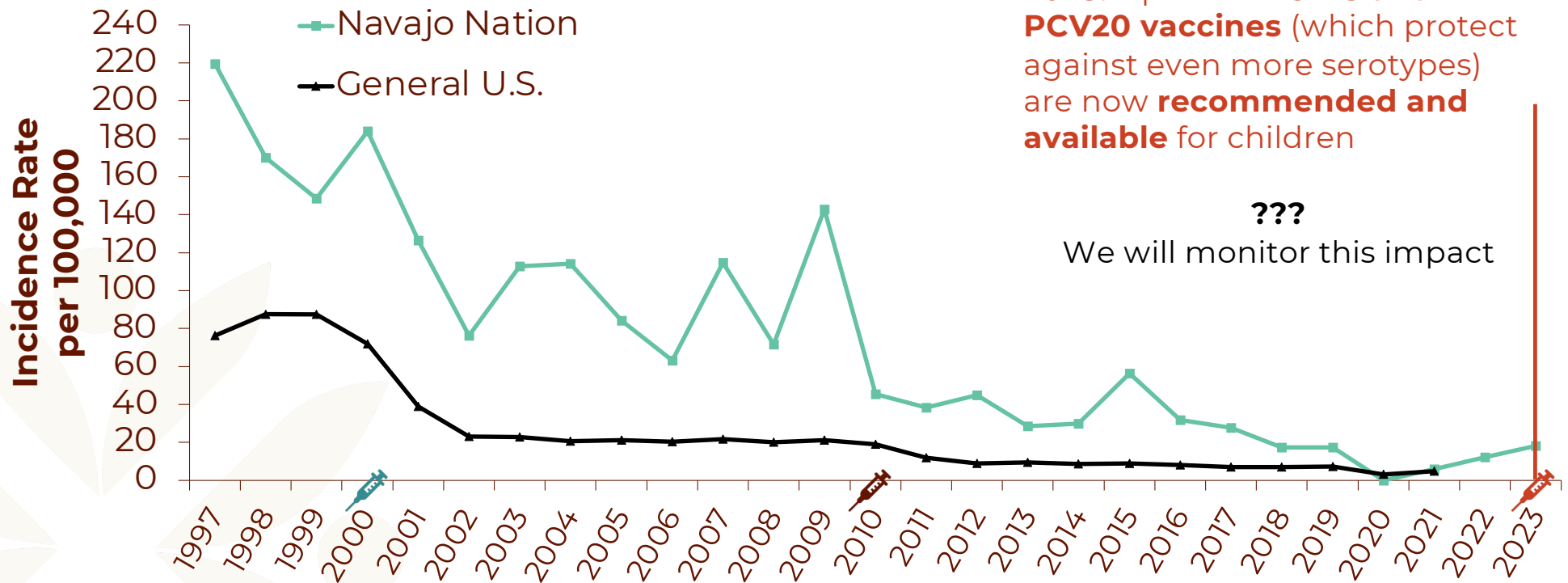
Serotypes Covered by Pneumococcal Conjugate Vaccines (PCV) and Polysaccharide Vaccine (PPV)

PRODUCT			SEROTYPE																																		
			4	6B	9V	14	18C	19F	23F	1	5	7F	3	6A	19A	6C	22F	33F	8	10A	11A	12F	15BC	2	9N	17F	20	15A	16F	23A	23B	24F	31	35B			
Discontinued	PCV-7	(Pfizer)	█	█	█	█	█	█					█																								
Licensed	PCV-10	(GSK)	█	█	█	█	█	█	█	█		█																									
Licensed	PCV-10	(SII)		█	█	█		█	█	█		█	█																								
Licensed	PCV-13	(Pfizer)	█	█	█	█	█	█	█	█	█	█	█	█	█																						
Licensed	PCV15	(Merck)	█	█	█	█	█	█	█	█	█	█	█	█		█	█																				
Licensed	PCV20	(Pfizer)	█	█	█	█	█	█	█	█	█	█	█	█		█	█	█	█	█	█	█	█														
Investigational	PCV24	(Merck)	█	█	█	█	█	█	█	█	█	█	█	█		█	█	█	█	█	█	█	█	█	█	█	█										
Investigational	PCV21	(Merck)										█	█	█		█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█		
Licensed	PPV-23	(Merck)	█	█	█	█	█	█	█	█	█	█		█		█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█		

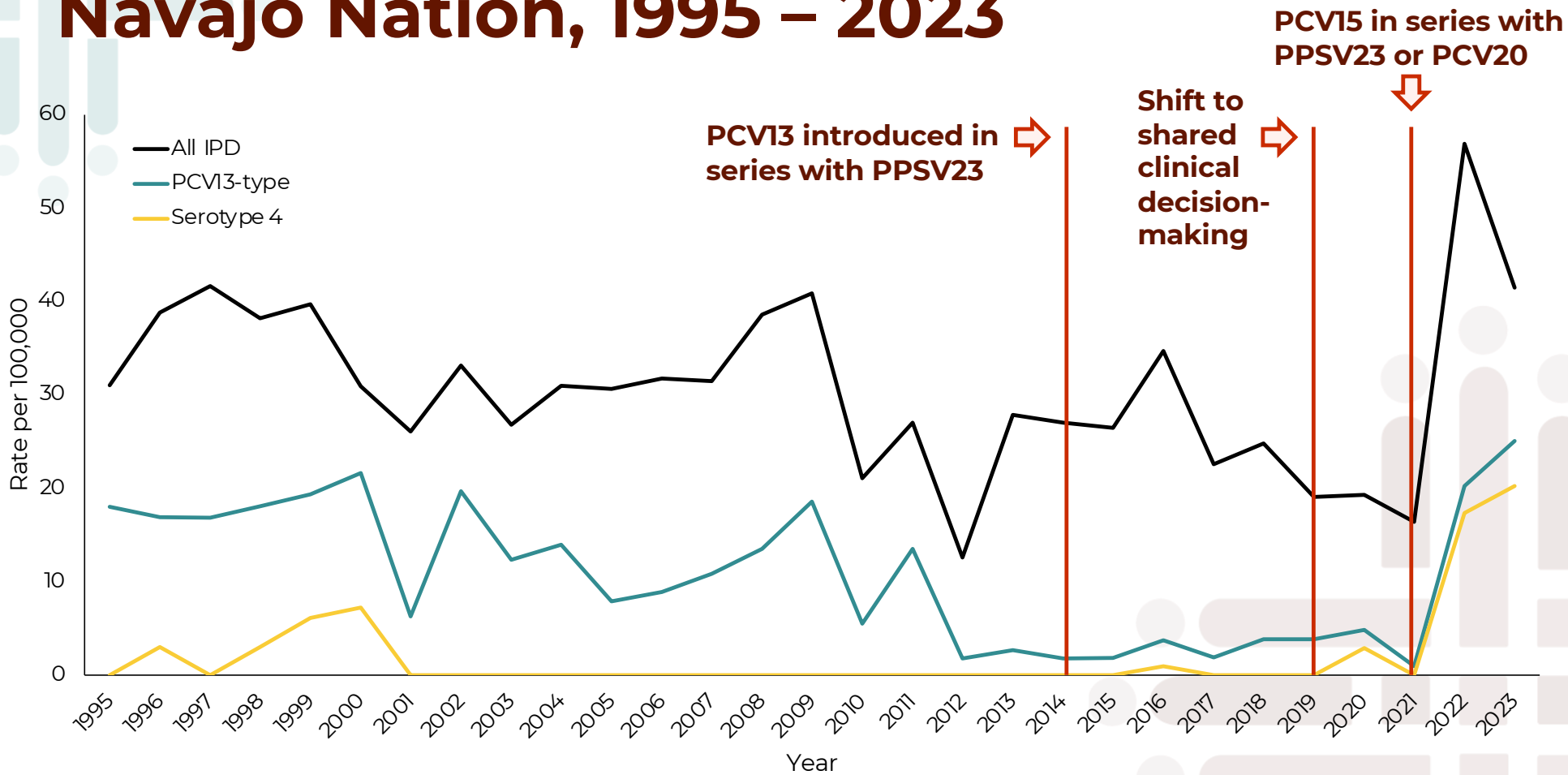
█ Demonstrated cross-protection from a related included serotype



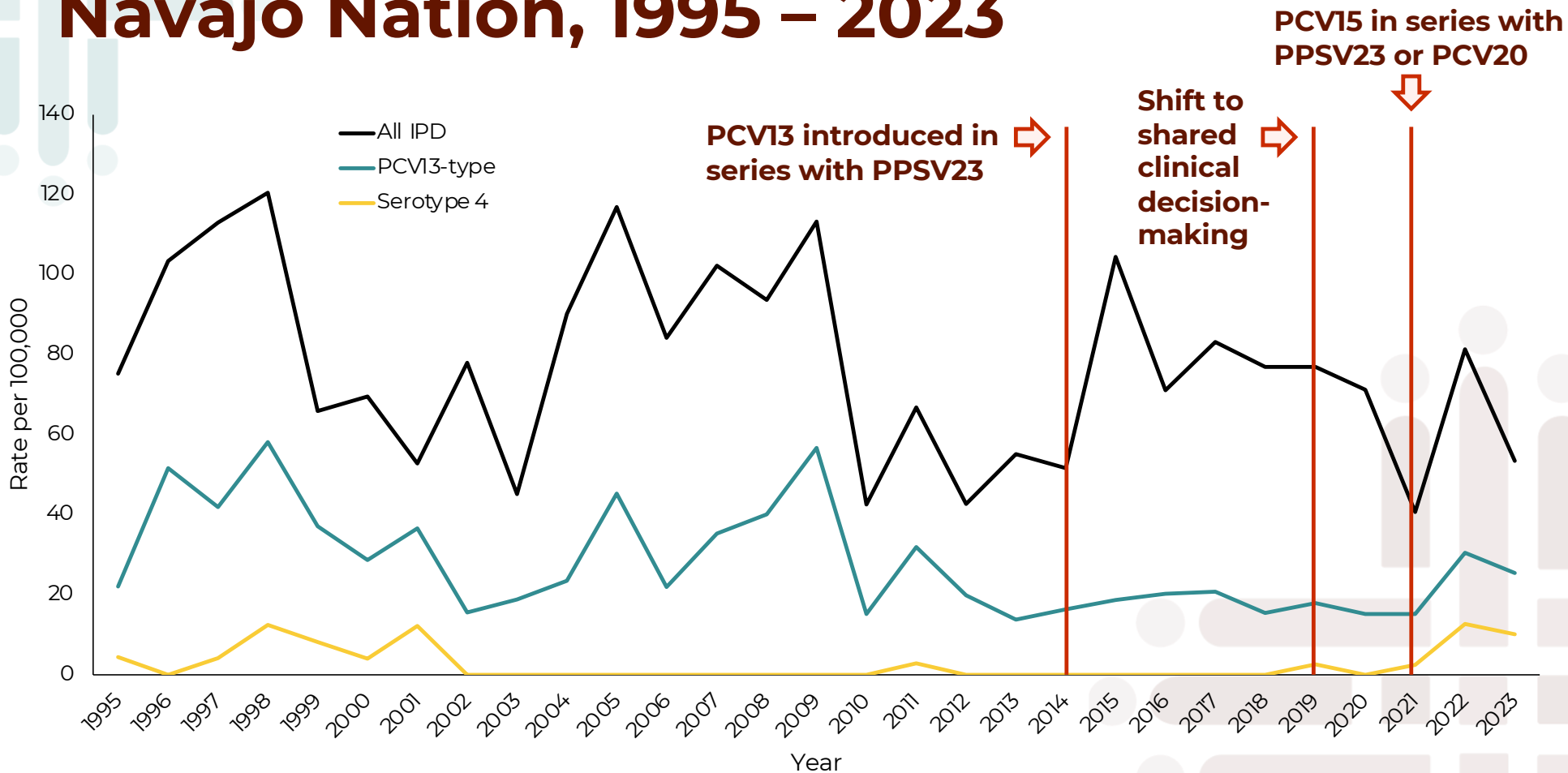
Rate of invasive pneumococcal disease (IPD) among Navajo children <5 years, 1997-2023



Rate of IPD among adults 18-49 years, Navajo Nation, 1995 – 2023



Rate of IPD among adults 50-64 years, Navajo Nation, 1995 – 2023



Rate of IPD among adults 65+ years, Navajo Nation, 1995 – 2023

