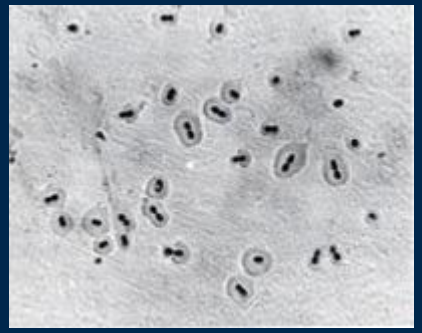
Streptococcus pneumoniae disease in the conjugate vaccine era.

Suzy Dawid MD, PhD

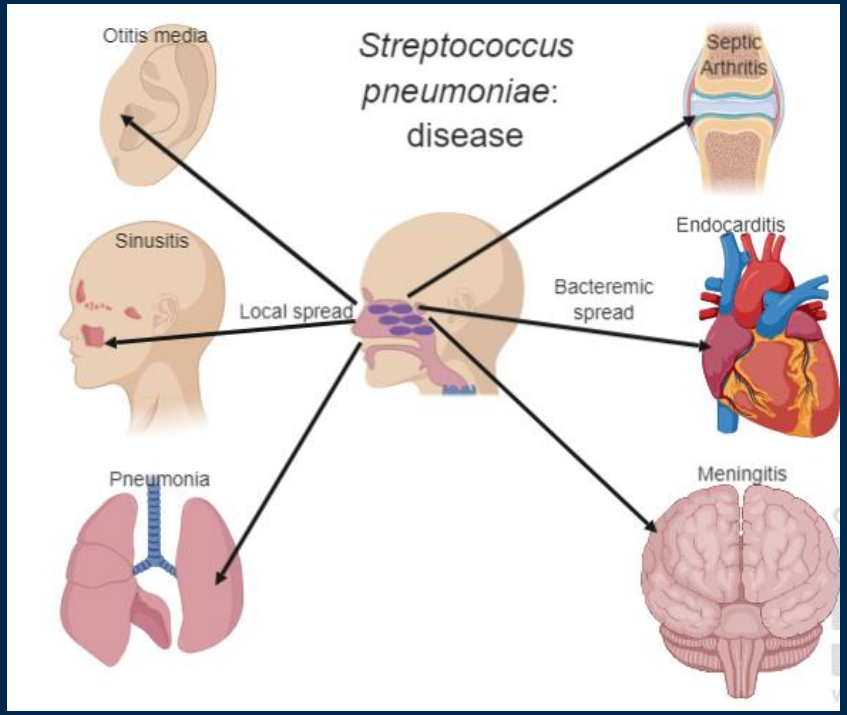
UNIVERSITY OF MICHIGAN HEALTH
MICHIGAN MEDICINE

Streptococcus pneumoniae



- Gram positive, alpha hemolytic diplococcus
- Facultative anaerobe
- Major virulence factors:
  - Polysaccharide capsule
    - Over 100 distinct capsule types
  - Pneumolysin toxin
  - Natural competence/ horizontal gene transfer

Streptococcus pneumoniae



- Colonizes the nasopharynx of up to 60% of children <2, adults 10-15%
- Colonization is asymptomatic but colonized children serve as a reservoir for disease in older populations.
- Disease:
  - Otitis media – 24-31% of isolates are Sp
  - Sinusitis
  - Conjunctivitis
  - Pneumonia –
  - Bacteremia -
  - Meningitis – leading bacterial cause in children

Colonization dynamics

- Children are colonized with a changing sequence of strains, duration of colonization weeks-months.
- New acquisition is the biggest risk for disease development.
- Children serve as the reservoir for infection in adults/elderly
- Different capsule serotypes tend to affect children v adults

High risk groups

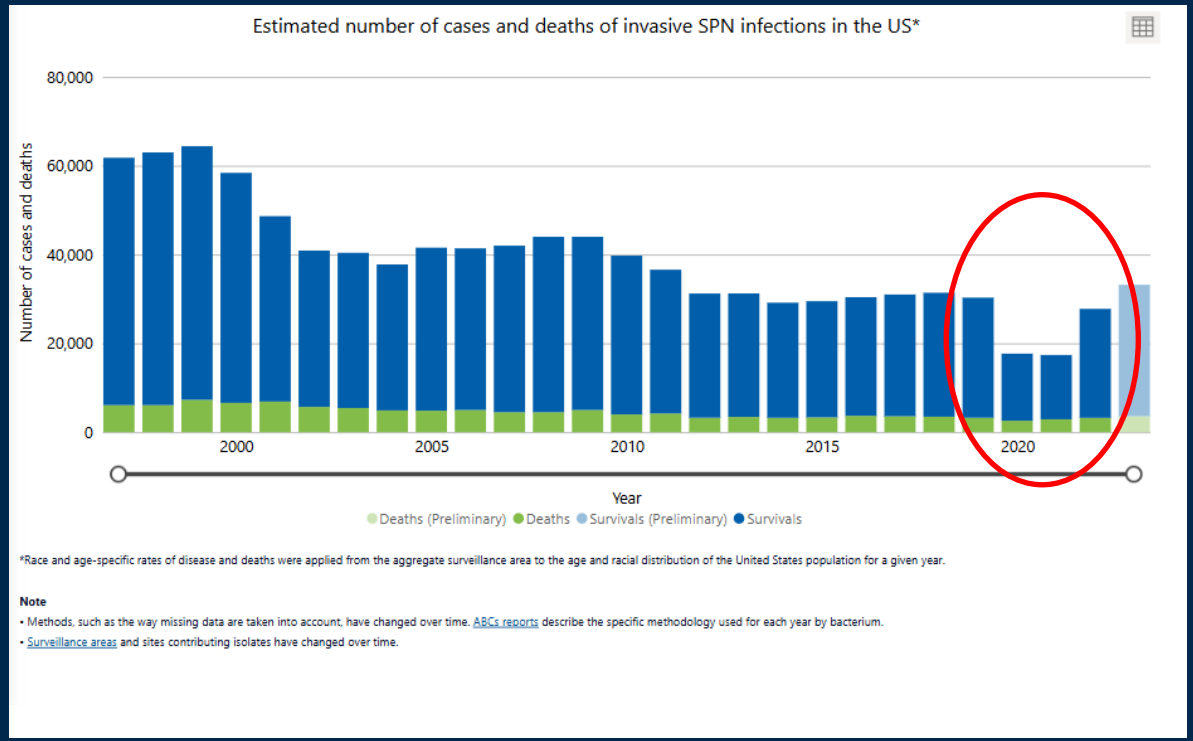
- Asplenia and HgbSS (bacteremia)
- HIV or other immunodeficiency
- Cochlear implant, CSF leak
- Chronic conditions
- Alaska Natives and certain American Indian groups have high rates of disease.

Viral co-infection promotes invasive disease

- Decreases in invasive pneumococcal disease was seen during the Covid19 pandemic period of 2021-2022.
- Israeli study showed no significant change in % colonized or duration/density of colonization.
- Incidence of community acquired pneumonia and bacteremic pneumonia were strongly reduced
- Temporally associated with drops in RSV, influenza and hMPV.

Dana Danino, Decline in Pneumococcal Disease in Young Children During the Coronavirus Disease 2019 (COVID-19) Pandemic in Israel Associated With Suppression of Seasonal Respiratory Viruses, Despite Persistent Pneumococcal Carriage: A Prospective Cohort Study, *Clinical Infectious Diseases*, Volume 75, Issue 1, 1 July 2022, Pages e1154–e1164,

Decrease in S pneumoniae invasive disease during the Covid pandemic.

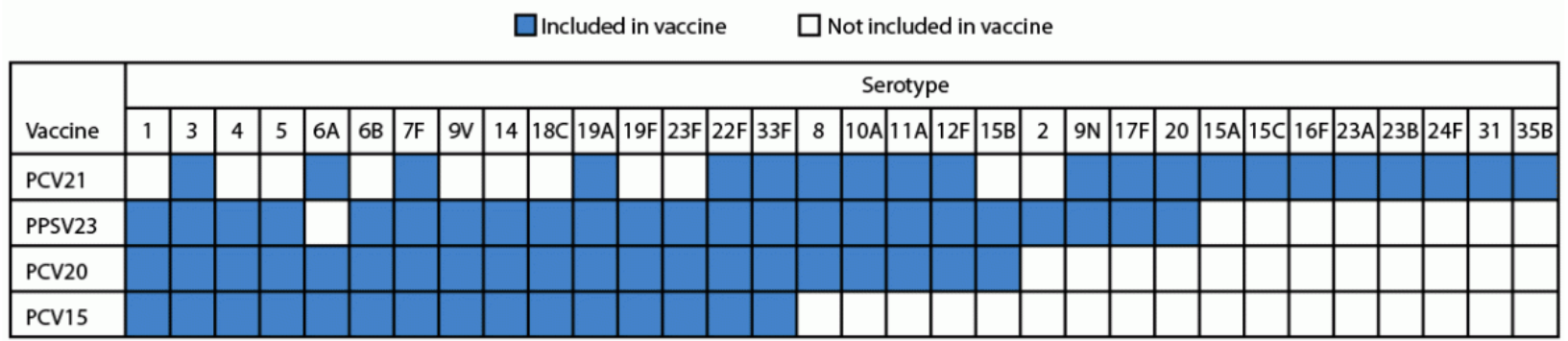


Pneumococcal vaccines

- PPSV23 (1983) does not provide protection in children <2 and immunity is short lived.
- PCV7 was released in 2001, PCV 13 in 2011 and PCV 15/20 in 2024.
- PCV20 and PCV21 are now available for adults.
    - PCV21 replaces some of the original vaccine components with 8 adult prominent serotypes

Serotype	PCV 7	PCV 13	PCV 20	PPSV 23
1		x	x	x
2				x
3		x	x	x
4	x	x	x	x
5		x	x	x
6A		x	x	
6B	x	x	x	x
7F		x	x	x
8			x	x
9N				x
9V	x	x	x	x
10A			x	x
11A			x	x
12F			x	x
14	x	x	x	x
15B			x	x
17F				x
18C	x	x	x	x
19A		x	x	x
19F	x	x	x	x
20				x
22F				x
23F	x	x	x	
33F				x

FIGURE. Serotypes*,† included in pneumococcal vaccines currently recommended for adults — United States, 2024



Vaccine	Serotype																												
	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F	22F	33F	8	10A	11A	12F	15B	2	9N	17F	20	15A	15C	16F	23A	23B	24F	31	35B
PCV21		■			■		■				■			■	■	■	■	■	■			■	■	■	■	■	■	■	■	■	■	■
PPSV23	■	■	■	■		■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■								
PCV20	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■												
PCV15	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■																	

Abbreviations: PCV = pneumococcal conjugate vaccine; PCV15 = 15-valent PCV; PCV20 = 20-valent PCV; PCV21 = 21-valent PCV; PPSV23 = 23-valent pneumococcal polysaccharide vaccine.

Vaccine guidelines

- Children receive PCV15/20 at 2,4,6 and 15 months
- High risk groups who have not received PCV receive one or two PCV20
- Adults over age **50** receive one PCV15/20/21 (even if they have already received PPSV23)

Streptococcus pneumoniae surveillance. Active Bacterial Core Surveillance (ABCs)

- Began in 1997
- All invasive infections (isolated from a normally sterile site)
- No information on pneumonia or otitis media
- Can be used to understand herd immunity and new serotypes

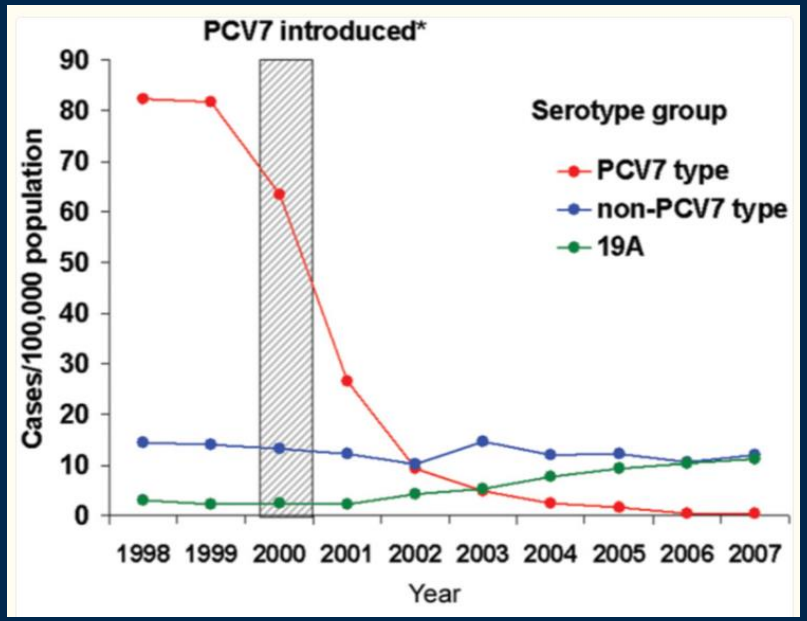
Before PCV7

- 17,000 cases of invasive disease per year in children <5
  - 13,000 bacteremia
  - 700 meningitis
  - ~200 deaths/ year
  - ~5 million cases of otitis media

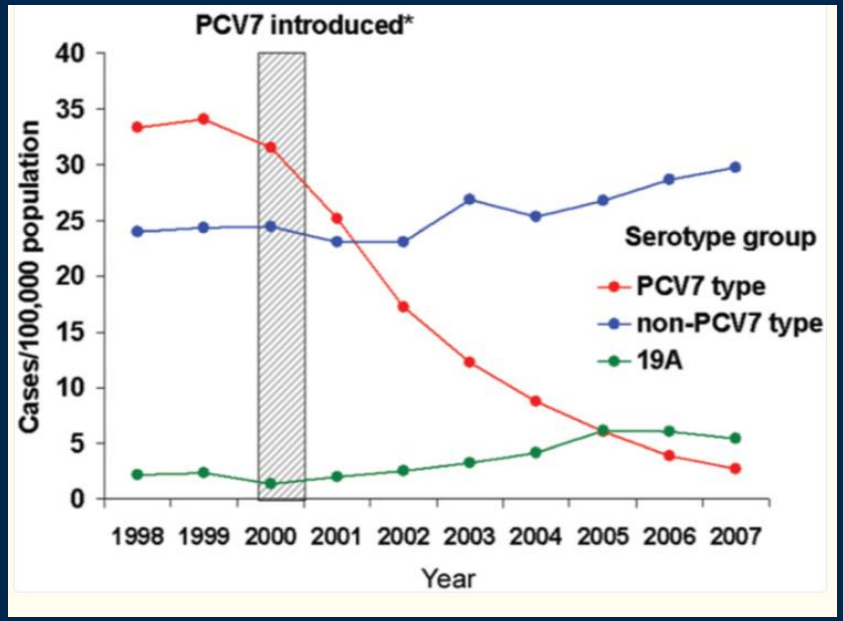
PCV7/13 era

- Following introduction in 2000, dramatic drop in rates of invasive disease in children.
- Levels started to rise due to serotype replacement.
- Due to increase in serotype 19A, antibiotic resistance increased.
- Impact on colonization resulted in herd immunity in adults.

Emergence of non PCV7 serotypes after introduction of PCV7 in adults and children



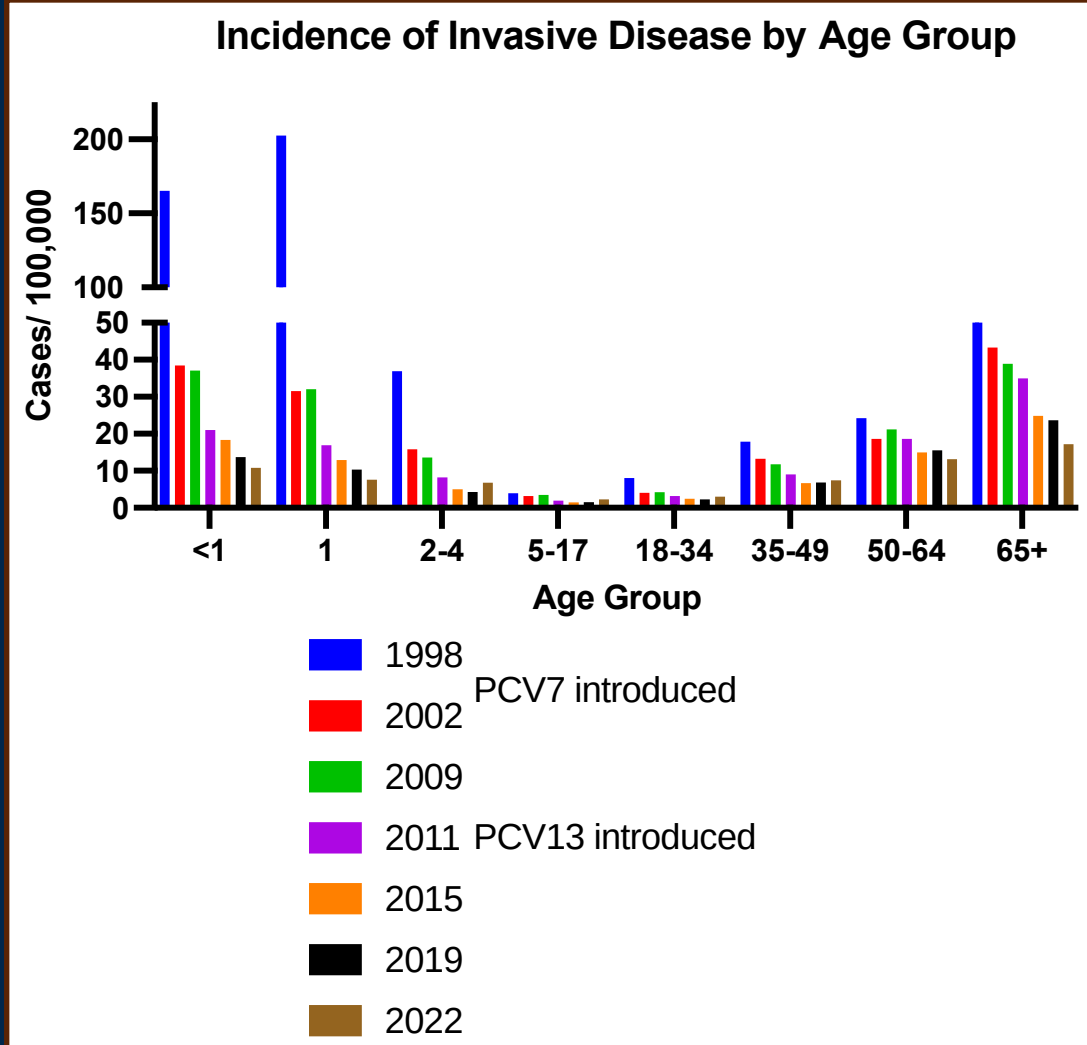
Children <5



Adults >65

Musher DM, Anderson R, Feldman C. The remarkable history of pneumococcal vaccination: an ongoing challenge. Pneumonia (Nathan). 2022 Sep 25;14(1):5.

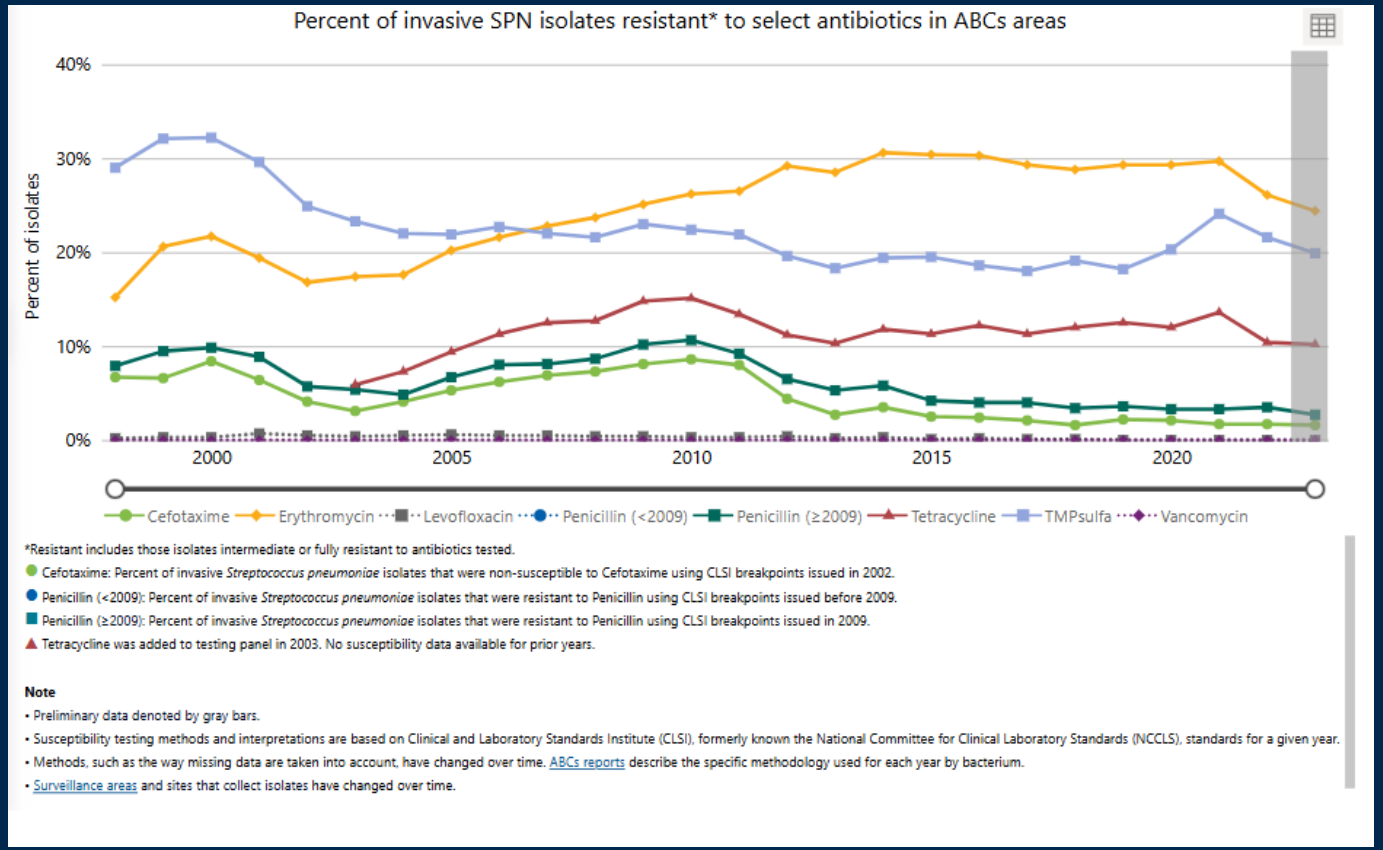
All age groups benefited from conjugate vaccine use



Post PCV13

- Invasive disease decreased 90% in children
- No rise in incidence of disease rates overall
- Remaining invasive isolates are non PCV13
- Rates of antibiotic resistance have fallen
- Vaccination of adults >65 with PCV13 followed by PPSV 23 recommended in 2014

PCV13 use correlates with sustained drops in penicillin and cephalosporin resistance



macrolides

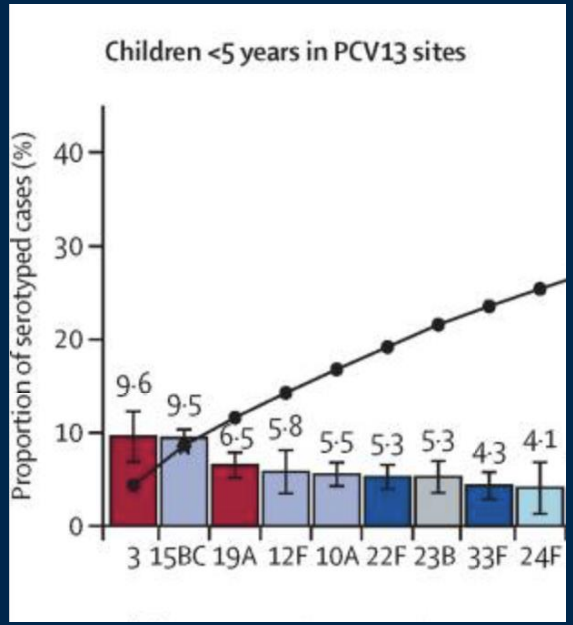
TMP sulfa

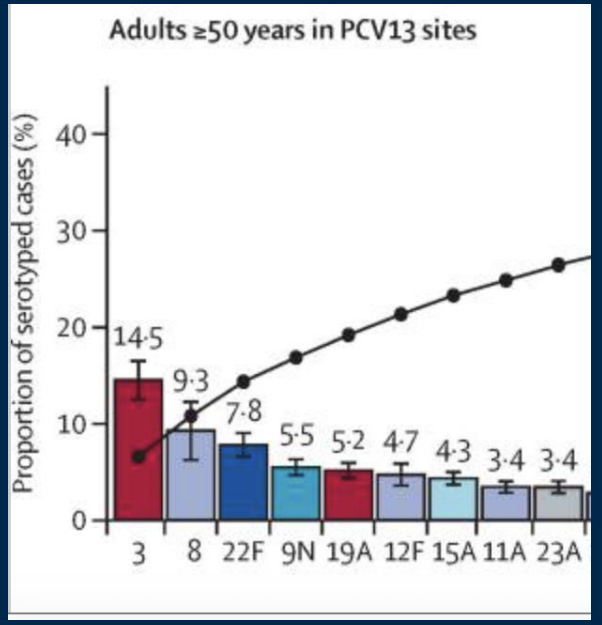
Penicillin

Cefotaxime

WHO-commissioned Pneumococcal Serotype Replacement and Distribution Estimation (PSERENADE) project

- Surveyed invasive disease-causing serotypes in >40 sites in 40 countries
- Used PCV13 for >5 years
- At least 70% vaccine uptake

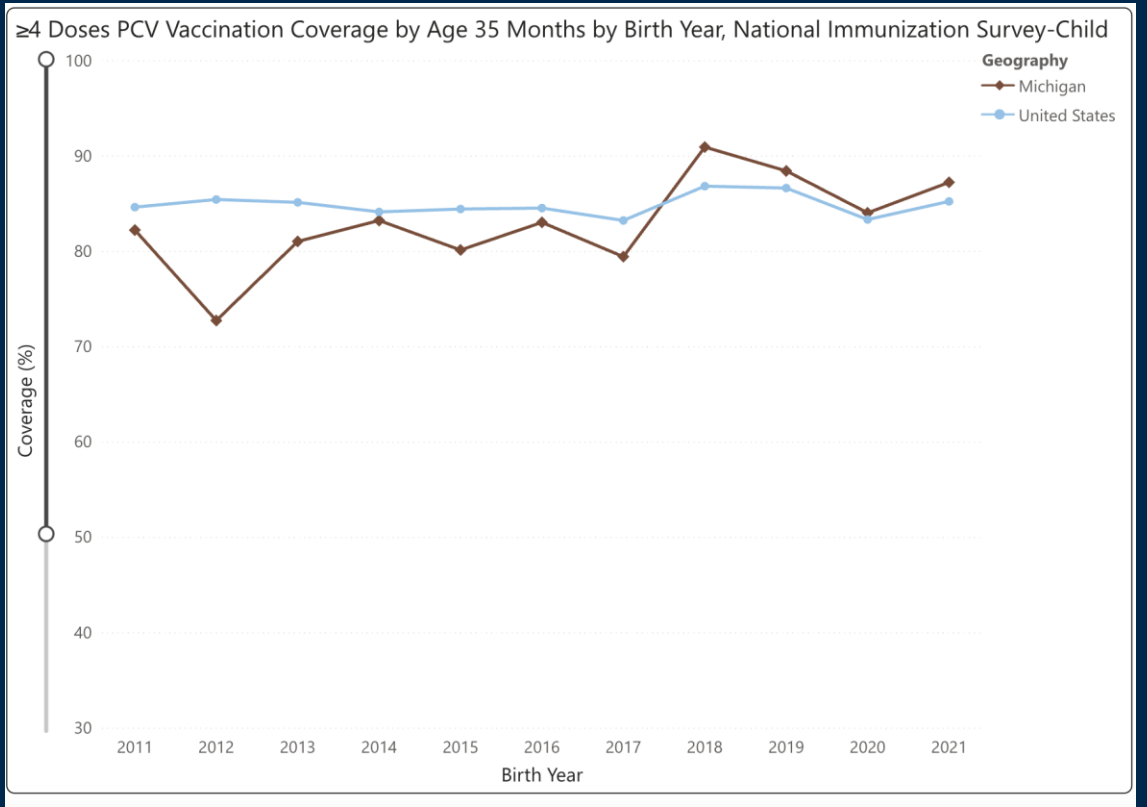




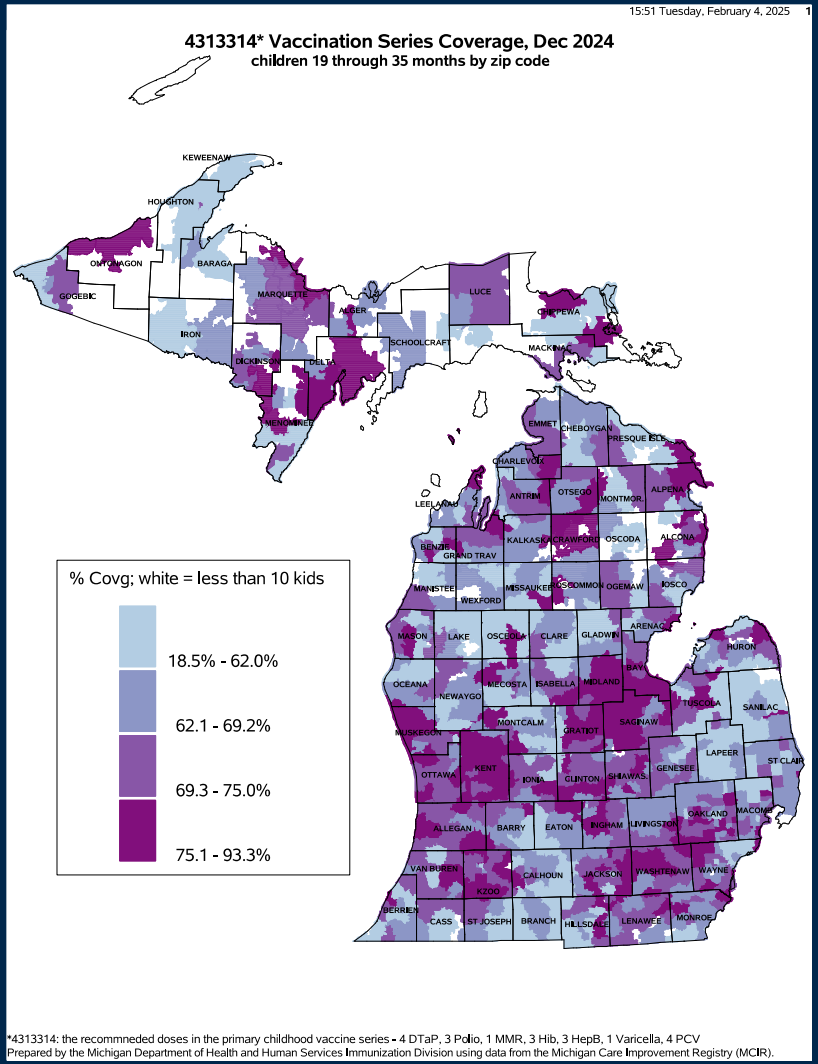
PSERENADE Team. Serotype distribution of remaining invasive pneumococcal disease after extensive use of ten-valent and 13-valent pneumococcal conjugate vaccines (the PSERENADE project): a global surveillance analysis. Lancet Infect Dis. 2025 Apr;25(4):445-456.

Vaccination rates in Michigan

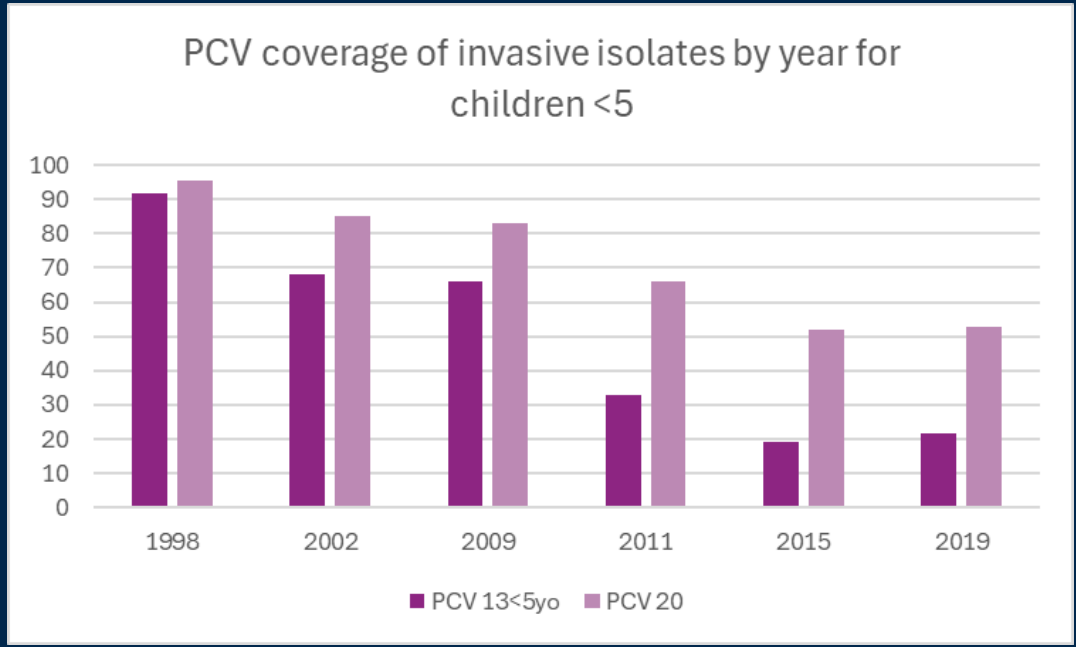
- Most recent MI report card (2023):
- 74.4% have completed PCV



Current vaccine coverage in MI



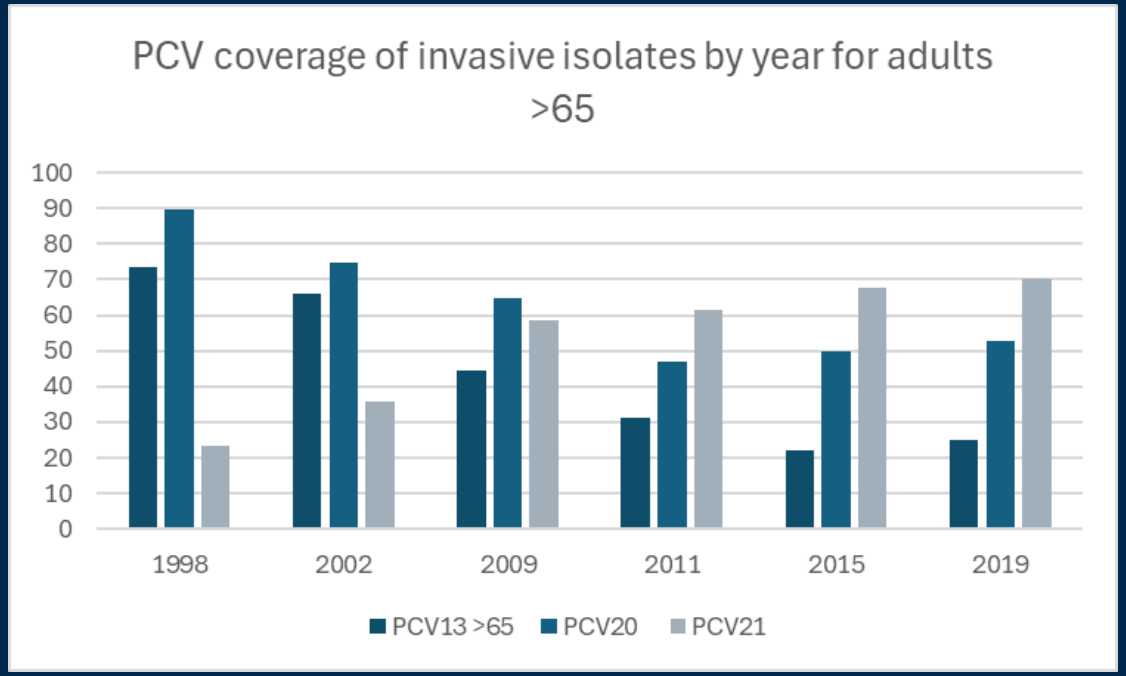
Vaccine coverage of invasive serotypes by year



Adult vaccine coverage (US): PPSV23 largely replaced by PCV15/20/21 by 2024

- PCV13 recommended in 2014 (with PPSV23), PCV20 alone recommended in 2023
- In 2022 (US):
  - 23% of 19-64 yo with high risk conditions were vaccinated
  - 64% of adults over 65 were vaccinated.
- In MI 2023
  - 49% >65 vaccinated

Vaccine coverage in adults by vaccine type

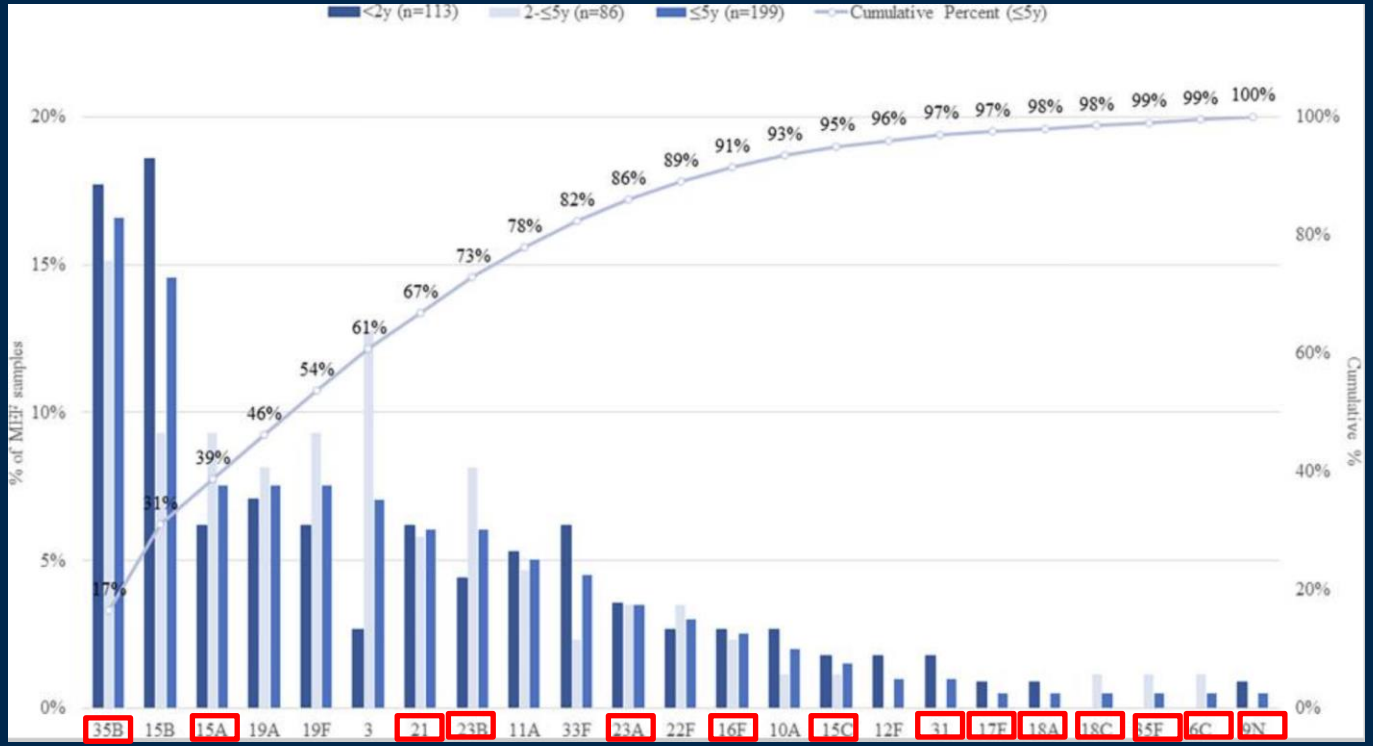


Certain groups who are at high risk for disease due to Serotype 4 should not get PCV21 (currently Navaho Nations and areas in the Western US).

What about rates of otitis media?

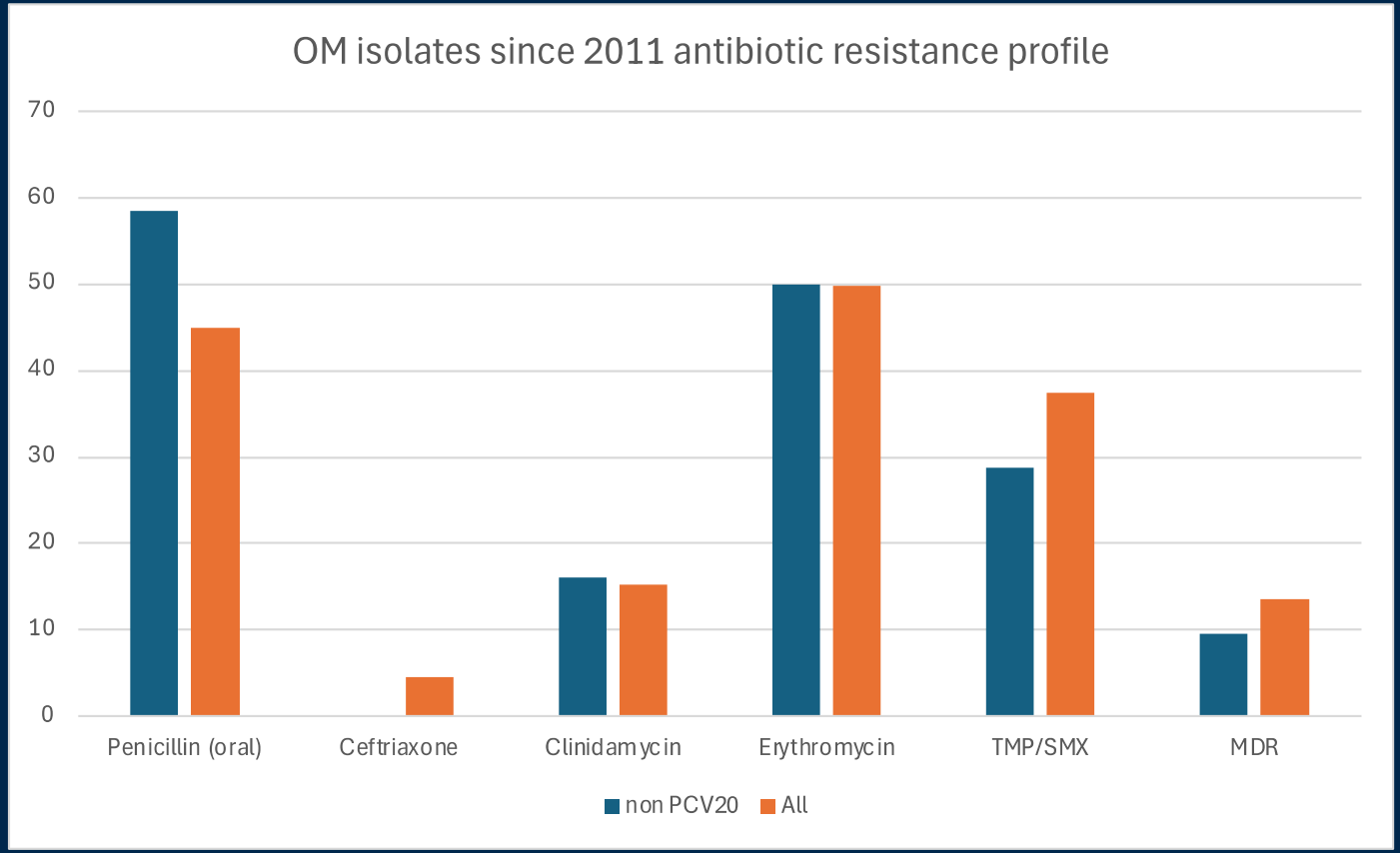
- Less impact compared with invasive disease
- Serotype distribution is different

Serotypes associated with OM since 2011



Non PCV20

Grant LR, Apodaca K, Deshpande L, Kimbrough JH, Hayford K, Yan Q, Mendes R, Cané A, Gessner BD, Arguedas A. Characterization of *Streptococcus pneumoniae* isolates obtained from the middle ear fluid of US children, 2011-2021. Front Pediatr. 2024


OM isolates since 2011 antibiotic resistance profile
70
60
50
40
30
20
10
0
Penicillin (oral)
Ceftriaxone
Clinidamycin
Erythromycin
TMP/SMX
MDR
non PCV20
All

Take home points

- Immunization has decreased rates of invasive disease in all age groups
- Invasive disease still occurs, usually with non vaccine serotypes
- Expansion to PCV20 will help to some extent, around 50% of strains will not be covered in all age groups.
- Older individuals benefit from infant immunization, after the wide-spread uptake of PCV20, it may be more beneficial to use PCV21 in adults to cover the remaining serotypes.
- Some concern that increased valency vaccines may decrease immunogenicity against individual serotypes.

Vaccination recommendations are fluid, check the PneumoRecs VaxAdvisior on the CDC web site for patient specific recommendations.

THANK YOU

Questions?