Evidence to Recommendations Framework (Preliminary): Use of 20-valent Pneumococcal Conjugate Vaccine in U.S. Children

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Advisory Committee on Immunization Practices
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Evidence to Recommendations (EtR) framework

EtR Domain	Question
Public Health Problem	• Is the problem of public health importance?
Benefits and Harms	• How substantial are the desirable anticipated effects? • How substantial are the undesirable anticipated effects? • Do the desirable effects outweigh the undesirable effects? • What is the overall certainty of this evidence for the critical outcomes?
Values	• Does the target population feel the desirable effects are large relative to the undesirable effects? • Is there important variability in how patients value the outcomes?
Acceptability	• Is the intervention acceptable to key stakeholders?
Feasibility	• Is the intervention feasible to implement?
Resource Use	• Is the intervention a reasonable and efficient allocation of resources?
Equity	• What would be the impact of the intervention on health equity?

Evidence to Recommendations (EtR) framework

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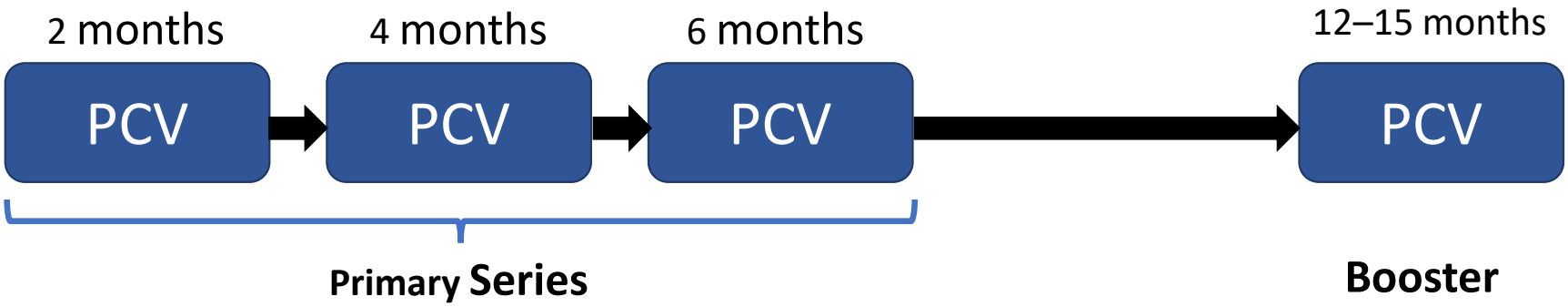
Benefits and Harms	• How substantial are the desirable anticipated effects? • How substantial are the undesirable anticipated effects? • Do the desirable effects outweigh the undesirable effects? • What is the overall certainty of this evidence for the critical outcomes?
Equity	• What would be the impact of the intervention on health equity?

All children under age 2 years have the same pneumococcal vaccine recommendations

- **3 primary series and a booster="3+1" schedule**



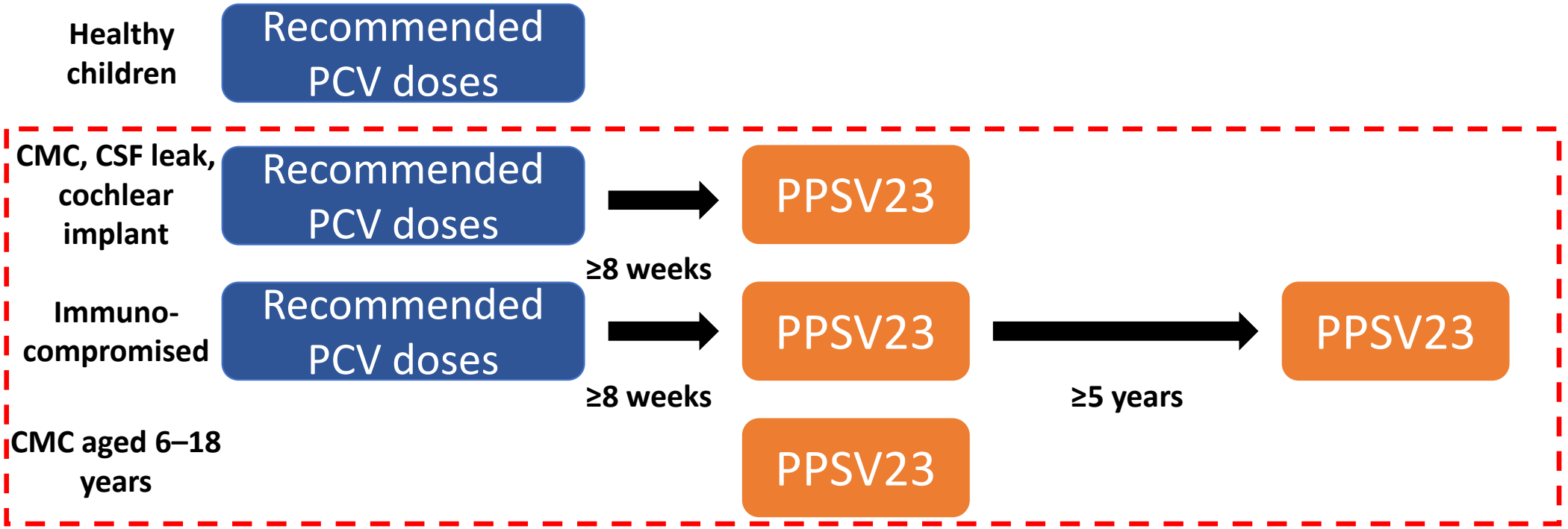
Either **PCV13** or **PCV15** can be used for U.S. children.

All children under age 2 years have the same pneumococcal vaccine recommendations

- **3 primary series and a booster="3+1" schedule**

Should PCV20 be recommended as an option for pneumococcal conjugate vaccination according to currently recommended dosing and schedules, for U.S. children aged <2 years?

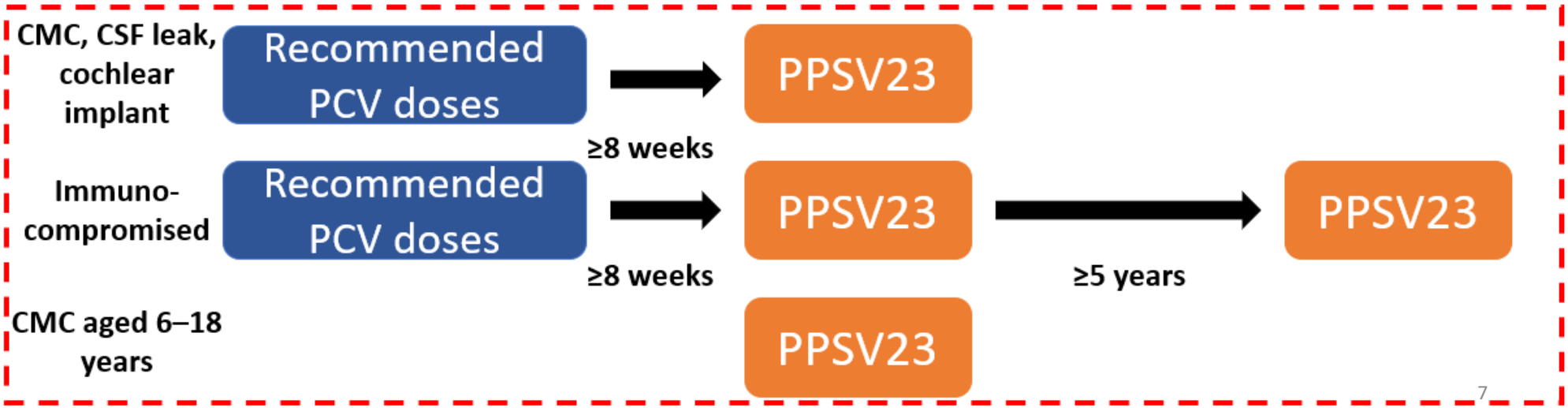
Children age ≥2 years with certain underlying conditions recommended to receive PPSV23 in addition



Note: Excludes catch-up vaccination schedules.
CMC=chronic medical conditions, including chronic heart disease, chronic lung disease, diabetes mellitus
CSF=cerebrospinal fluid

Use of 15-Valent Pneumococcal Conjugate Vaccine Among U.S. Children: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2022 | MMWR (cdc.gov)

Should PCV20 without PPSV23 be recommended as an option for pneumococcal vaccination for U.S. children aged 2–18 years with underlying medical conditions that increase the risk of pneumococcal disease?



PICO Question	Should PCV20 be recommended as an option for pneumococcal vaccination for U.S. children?	
Population	**All U.S. children aged <2 years**	**U.S. children aged 2–18 years with underlying medical conditions**
Intervention	**PCV20 according to currently recommended dosing and schedules**	**PCV20 (without PPSV23)**
Comparison	PCV13 or PCV15 according to currently recommended dosing and schedules	
Outcomes	VT-IPD, VT- pneumonia, VT- AOM, VT- pneumococcal deaths, serious adverse events following vaccination	

VT: vaccine-type, IPD: invasive pneumococcal disease, AOM: acute otitis media

EtR Domain: Public Health Problem

Summary of pneumococcal disease epidemiology in children

- **Use of PCVs (PCV7, PCV13) significantly decreased the incidence of pneumococcal disease in U.S. children.**
- **Outpatient ARIs caused by pneumococcus, such as AOM, sinusitis, and pneumonia, are common causes of outpatient visits and antibiotic prescribing.**
- **Risk of disease remains high in children with underlying conditions that increase the risk of pneumococcal disease.**
- **In 2018–2019, the proportion of IPD caused by vaccine serotypes was:**
  - PCV20, non-PCV13: ~30% of IPD
  - PCV15, non-PCV13: ~15% of IPD

Gierke. February 2023 ACIP meeting presentation
King. February 2023 ACIP meeting presentation

Public Health Problem

Is pneumococcal disease of public health importance in U.S. children?

- □ No
- □ Probably no
- □ Probably yes
- □ Yes
- □ Varies
- □ Don't know

Public Health Problem

Is pneumococcal disease of public health importance in U.S. children?

- □ No
- □ Probably no
- □ Probably yes
- □ Yes
- □ Varies
- □ Don't know

- Variability in Work Group members' interpretations for children aged <2 years due to significant reductions in pneumococcal disease.
- Most agreed that pneumococcal disease continues to be of public health importance due to the remaining disease burden.

EtR Domain: Benefits and Harms

Outcomes (Benefits)

Outcome	Importance	Description
VT- IPD	**Critical**	Studies assessing PCV20 against these clinical outcomes are currently not available → PCV20 immunogenicity studies for GRADE → PCV13/PPSV23 clinical outcome studies for background
VT- non-bacteremic pneumococcal pneumonia	**Critical**	
VT- acute otitis media	**Critical**	
VT- pneumococcal deaths	**Critical**	

AOM=acute otitis media, IPD=invasive pneumococcal disease, VT=vaccine-type

Outcomes (Harms)

Outcome	Importance	Description
Serious adverse events	**Critical**	Safety data for PCV20 are available

Background

PCV13 effectiveness (3+1) in children, VT-IPD

Study	Population	Dosing schedule (Year of introduction)	Method	Outcome	Vaccine Effectiveness	(95% CI)
Savulescu, 2022	Children 2m – 59m; Spidnet (12 European sites, 2012-2018	2+1 or 3+1 (variable)	Indirect cohort	3 + 1 doses, ≥12 months	**89.7% (adjusted*)**	**(82, 94)**
Van der Linden, 2016*	Children <2 years; Germany (GNRCS)	3+1 (December 2009)	Indirect cohort	PCV13-type; post-booster	**91%**	**(61, 99)**
Weinberger, 2016	Children 2.5 – 56m; Germany (ESPED)	3+1 (December 2009)	Indirect cohort	PCV13-type +6C; ≥2 dose before 12 months or one dose on/after 12 months	**85% (adjusted)**	**(64, 94)**
Dominguez, 2017	Children 7m - 59m; Spain (Catalonia)	3+1 (public, July 2016)	Matched case-control	PCV13-type; 7-59m; ≥2 doses before 12 months or one dose after 12 months	**78.9%**	**(52.8, 90.5)**
Moore, 2016	Children 2-59m; US	3+1 (2010)	Matched case-control	PCV13-type; ≥1 dose	**86.0% (unadjusted)**	**(75.5, 92.3)**

* Adjusted by site, age, year of notification and at least one underlying disease

Post-licensure vaccine effectiveness studies have shown that PCV13 is highly effective against VT-IPD

PCV13 effectiveness, VT-pneumococcal pneumonia

Study	Population	Dosing schedule (Year of introduction)	Method	Outcome	VE	(95% CI)
Zhang, 2021	Children born December 2016 – November 2018, China	3+1 (2017)	Indirect cohort; VT-CAP defined as hospital discharge diagnosis code of pneumonia + deep upper respiratory aspirate with PCV13 serotypes.	VT-CAP; ≥3 doses	**62.1% (adjusted)**	**(26.3, 80.5)**
Lewnard, 2021*	Children 4 to 59 months, Israel	2+1 (2010)	Nested case-control; Used: • PCV-conferred protection against VT pneumococcal carriage • Protection against progression from carriage to pneumonia	CAP attributed to PCV13, 12-59 months; 2+1 doses	**77.0 % (adjusted)**	**(-16.0, 100.0)**

CAP=community acquired pneumonia

*funded by Pfizer

Limited data on PCV13 effectiveness against VT-pneumococcal pneumonia in children. PCV13 likely protective.

PCV13 effectiveness, VT-AOM

Study	Population	Dosing schedule (Year of introduction)	Method	Outcome	VE	(95% CI)
Pichichero, 2018*	Children ≤36 months, United States	3+1 (2010)	Prospective longitudinal cohort (PCV13 v PCV7 period)	PCV13-non-PCV7 serotypes; PCV13 full primary series (regardless of booster status) vs. PCV7 for middle-ear fluid samples at onset of AOM	**86% (adjusted)**	**(61, 94)**
				Serotype 3; PCV13 full primary series (regardless of booster status) vs. PCV7 for middle-ear fluid samples at onset of AOM	**5% (adjusted)**	**(–181, 68)**
Ochoa-Gondar, 2015	≤14 years; Spain (Catalonia region)	3+1 (2016, publicly available)	Indirect cohort	PCV13-type; ≥1 dose	**62% (unadjusted)**	**(-141, 95)**
Dagan, 2021*	Children 5 to 35 months, Israel	2+1 (2010)	Nested case-control	PCV13-type; ≥2 doses vs. 0 doses	**77.4% (adjusted)**	**(35.3, 92.1)**
				Serotype 3; ≥2 doses vs. 0 doses	**89.0% (adjusted)**	**(23.9, 98.4)**

Limited data on PCV13 effectiveness against VT-pneumococcal AOM in children. PCV13 likely protective.

*funded by Pfizer

PPSV23 effectiveness, VT-IPD (Pre-PCV U.S. data)

Table. Estimates of pneumococcal polysaccharide vaccine effectiveness among 173 children 2 through 5 years of age, using the indirect cohort method

Group	Vaccine serotype/total(%) Vaccinated children[a]	Unvaccinated children[a]	Effectiveness (95% CI)[b]
All children	35/48 (73)	110/125 (88)	63% (8% to 85%)
Children with SCD	27/33 (82)	12/13 (92)	62% (-294% to 98%)
Children without SCD	8/15 (53)	98/112 (88)	84% (40% to 96%)
Nonconjugate vaccine serotype[c]	1/14 (7)	18/33 (55)	93% (45% to 100%)

[a]23-valent pneumococcal polysaccharide vaccine.
[b]Effectiveness (95% confidence interval) estimated as (1- odds ratio or 95% confidence bound) x 100%.
[c]Children infected with a serotype not in proposed conjugate vaccine (15) (excludes children infected with serotypes 4, 6B, 9V, 14, 18C, 19F, 23F).
SCD, sickle-cell disease.

Pre-PCV era data showed that PPSV23 is protective against VT-IPD among children with underlying medical conditions.

Fiore et al. EID 1999

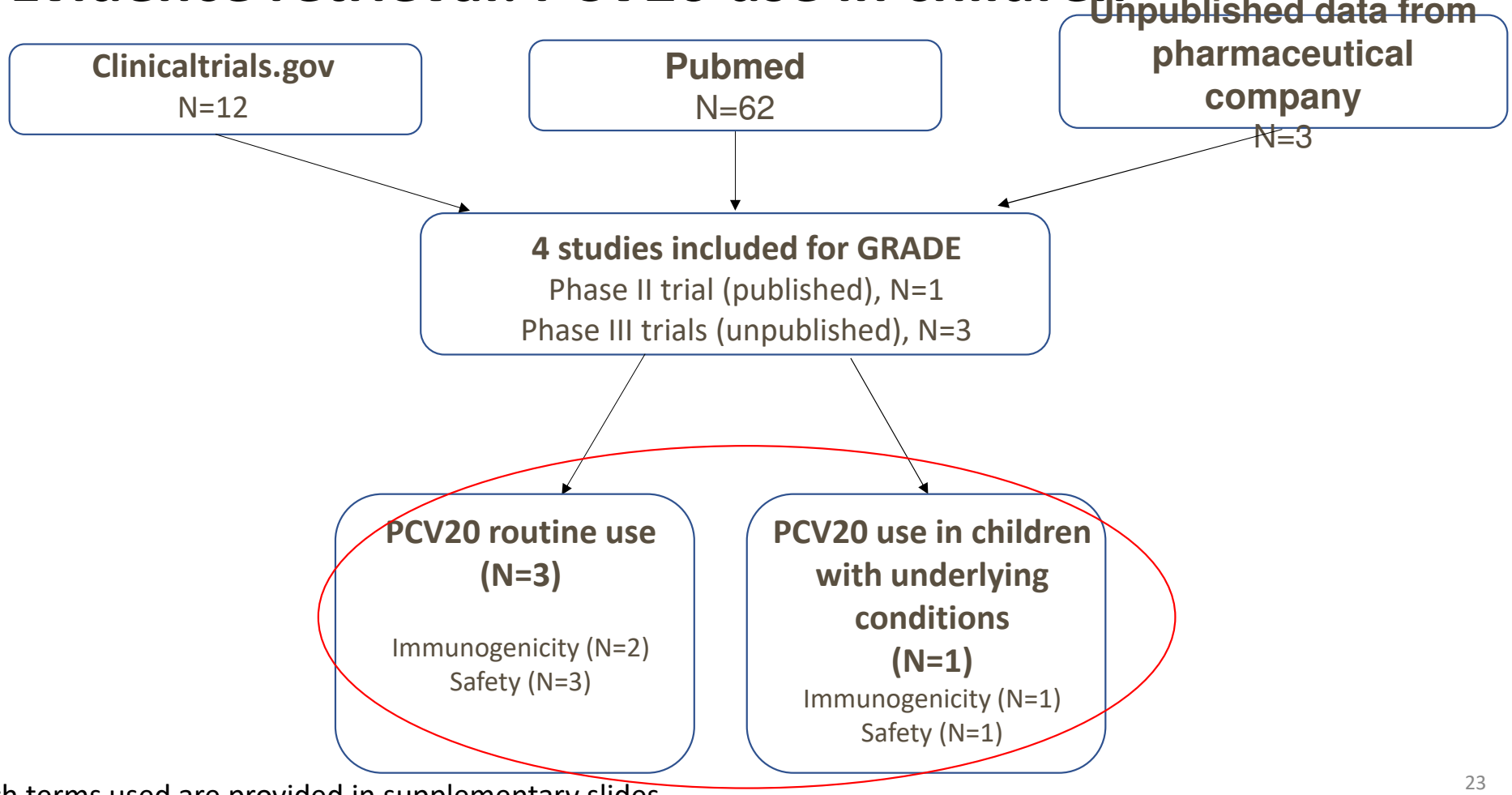
PPSV23 effectiveness, non-invasive pneumococcal disease

- **No study on PPSV23 VE against AOM identified in a recent systematic review[1]**
- **Two randomized-controlled trials (RCTs)[2,3] evaluated PCV7-PPSV23 in series against AOM**
  - No efficacy in the PCV7-PPSV23 groups

1. Marra et al. Value Health 2022
2. Veenhoven et al. Lancet 2003
3. Van Kempen et al. Int J Pediatr Otorhinolaryngol 2006

GRADE: PCV20 use in children

Evidence retrieval: PCV20 use in children



Search terms used are provided in supplementary slides

Summary of evidence:
Benefits, children <2 years

- **Informed by 2 randomized controlled trials (Phase II and III)[1,2]**
  - Healthy children randomized to either PCV13 or PCV20
  - PCVs given using 3+1 schedule
- **Summary of findings**
  - PCV20 had numerically **lower** immune responses* vs. PCV13 for most of the 13 shared serotypes
  - **Post dose 3**:
    - PCV20 did **not** meet noninferiority criteria vs. PCV13 for some serotypes
  - **Post dose 4**:
    - PCV20 **noninferior** to PCV13 for all 13 shared serotypes
    - PCV20 **noninferior** to PCV13** for all 7 additional serotypes

*measured as IgG GMCs and GMRs

**Compared with the serotype with lowest immune response among PCV13 serotypes except for serotype 3

1. Senders et al. PIDJ 2021
2. Pfizer unpublished data from B7471011

Summary of evidence:
Harms, children <2 years

- **Serious adverse events (SAEs) across 3 studies (dose 1 through 6 months after dose 4):**
  - PCV20: 4.5% (n=1,567) vs PCV13: 3.7% (n=1,376)
- **None were considered to be vaccine-related**

1. Senders et al. PIDJ 2021
2. Pfizer B7471011, unpublished data
3. Pfizer B7471013, unpublished data, limited to US and Puerto Rico sites

Should PCV20 be recommended as an option for pneumococcal conjugate vaccination according to currently recommended dosing and schedules, for U.S. children aged <2 years?

Type	Outcome	Importance	Included in evidence profile	Certainty for healthy individuals
Benefits	VT- IPD	Critical	Yes	Moderate
	VT-pneumonia	Critical	Yes	Moderate
	VT- AOM	Critical	Yes	Moderate
	VT- pneumococcal deaths	Critical	Yes	Moderate
Harms	SAEs following vaccination	Critical	Yes	Moderate

AOM=acute otitis media, IPD=invasive pneumococcal disease, SAE=serious adverse events, VT=vaccine-type

Benefits and Harms

How substantial are the desirable anticipated effects?

- **Routine PCV20 use for children aged <2 years**

□ Minimal
□ Small
□ Moderate
□ Large
□ Varies
□ Don't know

- PCV20 provides the broadest serotype coverage among available PCVs.
- Unknown how substantial the protection conferred from PCV20 will be based on available data.

Benefits and Harms

How substantial are the undesirable anticipated effects?

- **Routine PCV20 use for children aged <2 years**

□ Minimal
□ Small
□ Moderate
□ Large
□ Varies
□ Don't know

Benefits and Harms

Do the desirable effects outweigh the undesirable effects?

- **Routine PCV20 use for children aged <2 years**

□ Favors intervention*
□ Favors current recommendation
□ Favors both
□ Favors neither
□ Varies
□ Don't know

***Intervention:** PCV20 use
Comparison: PCV13 or PCV15 use

Benefits and Harms

Do the desirable effects outweigh the undesirable effects?

- **Routine PCV20 use for children aged <2 years**

Favors Intervention (PCV20):

- PCV20 is expected to prevent more disease compared with current PCVs (PCV13, PCV15)

Favors Both (PCV20 or PCV13/PCV15):

- Clinical implications of the **lower** immunogenicity PCV20 compared with PCV13 unknown
- Clinical implications of **improved** immunogenicity of PCV15 against serotype 3* unknown

*Banniettis. February 24, 2022 ACIP meeting presentation

Summary of evidence:

Benefits, children 2–18 years with underlying conditions

- **No studies conducted among children with underlying medical conditions**
- **Informed by 1 non-randomized trial (Phase III), no comparator**
  - Healthy children aged 15 months to 17 years received a dose of PCV20
    - Children aged <5 years received ≥3 doses of PCV13
- **Summary of findings**
  - PCV20 was immunogenic* for all 20 vaccine serotypes 1 month after vaccination vs. pre-vaccination.

*Measured as IgG GMCs and GMFR and OPA GMFRs
Pfizer unpublished data from B7471014

Summary of evidence:
Harms, children 2–18 years with underlying conditions

- **Serious adverse events (SAEs) :**
  - PCV20: 0.6% (n=831)
- **None were considered to be vaccine-related**

Pfizer unpublished data from B7471014

Should PCV20 without PPSV23 be recommended as an option for pneumococcal vaccination for U.S. children aged 2–18 years with underlying medical conditions that increase the risk of pneumococcal disease?

Type	Outcome	Importance	Included in evidence profile	Certainty for children with underlying conditions
Benefits	VT-IPD	Critical	Yes	Very Low
	VT-pneumonia	Critical	Yes	Very Low
	VT-AOM	Critical	Yes	Very Low
	VT-pneumococcal deaths	Critical	Yes	Very Low
Harms	SAEs following vaccination	Critical	Yes	Very Low

AOM=acute otitis media, IPD=invasive pneumococcal disease, SAE=serious adverse events, VT=vaccine-type

Benefits and Harms

How substantial are the desirable anticipated effects?

- **PCV20 use for children aged 2–18 years with underlying medical conditions**

□ Minimal
□ Small
□ Moderate
□ Large
□ Varies
□ Don't know

- PCV20 provides the broadest serotype coverage among available PCVs.
- Unknown how substantial the protection conferred from PCV20 will be based on available data.
- No data from this population.

Benefits and Harms

How substantial are the undesirable anticipated effects?

- PCV20 use for children aged 2–18 years with underlying medical conditions

□ Minimal
□ Small
□ Moderate
□ Large
□ Varies
□ Don’t know

Benefits and Harms

Do the desirable effects outweigh the undesirable effects?

- **PCV20 use for children aged 2–18 years with underlying medical conditions**

□ Favors intervention*
□ Favors current recommendation
□ Favors both
□ Favors neither
□ Varies
□ Don't know

***Intervention:** PCV20 use
Comparison: PPSV23 use after currently recommended PCV (PCV13 or PCV15) doses

Benefits and Harms

Do the desirable effects outweigh the undesirable effects?

- **PCV20 use for children aged 2–18 years with underlying medical conditions**

Favors Intervention (PCV20):

- PCV20 is expected to prevent more disease compared with current recommendations (PPSV23 after recommended PCV13/15 doses)

Favors Both (PCV20 or PPSV23 after recommended PCV13/PCV15 doses):

- No data on PCV20 use in this population
- Clinical implications of **improved** immunogenicity of PCV15 against serotype 3* unknown

*Banniettis. February 24, 2022 ACIP meeting presentation

EtR Domain: Equity

Compared with coverage among children with private insurance only, children who were uninsured, and those insured by Medicaid and other insurance was lower

	≥3 PCV doses (%)	≥4 PCV doses (%)
Private insurance only (Ref) (N=16,629)	96.2	90.0
Any Medicaid (N=10,200)	91.3*	78.8*
Other insurance (N=2,168)	91.1*	80.6*
Uninsured (N=608)	83.9*	62.3*

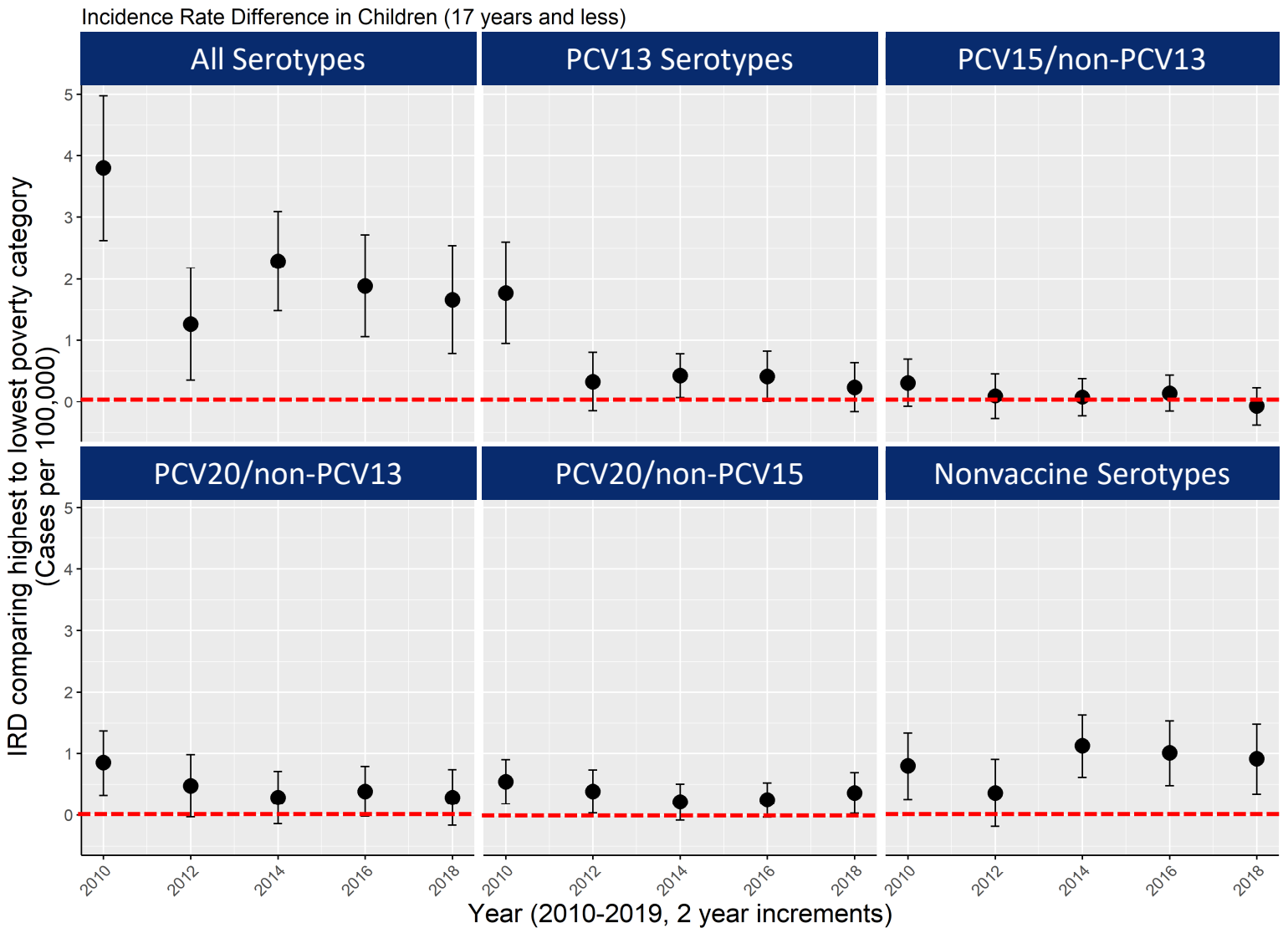
PCV=pneumococcal conjugate vaccine
*statistically significant difference compared with Ref.
Hill et al. MMWR 2023

Nationally representative PPSV23 vaccine coverage data among children with indications are limited

- **Vaccine coverage among children with sickle cell anemia, Michigan Medicaid program[1]**
  - 4PCV + 1 PPSV23 at age 5 years: **64%**
  - 4PCV + 2 PPSV23 at age 10 years: **53%**
- **Self-administered survey of parents/guardians of children aged <18 years with nephrotic syndrome[2]**
  - PPSV23 receipt: **43%**
- **Data from single-center quality improvement studies among children seen in specialty care clinics reported 20–30% PPSV23 coverage at baseline[3,4]**

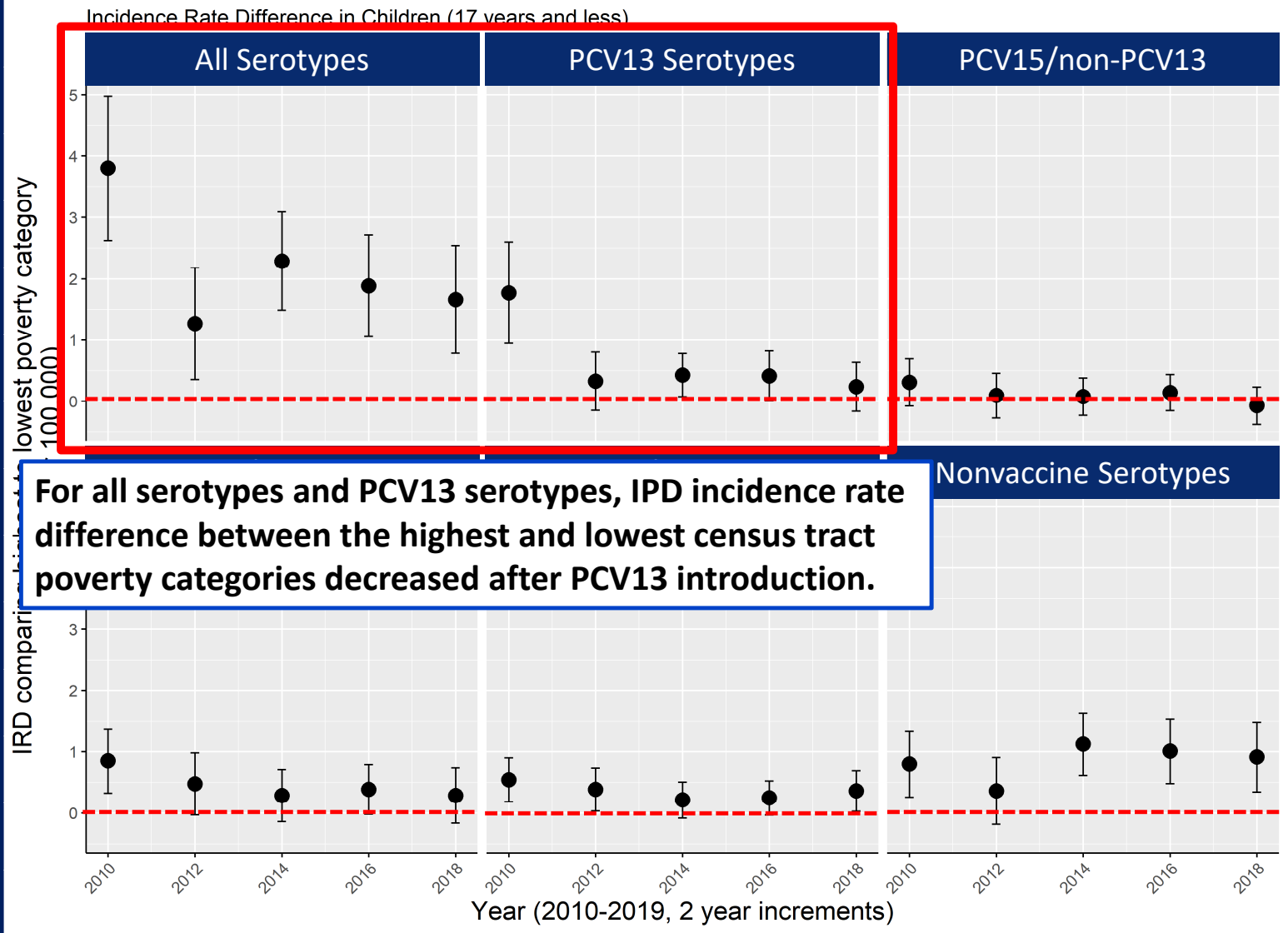
1. Reeves et al. Pediatric Blood & Cancer, 2018
2. Tran et al. Frontiers in Pediatrics, 2021
3. Mirza et al. The Ochsner Journal, 2022
4. Harris et al. Pediatrics, 2022

IPD incidence rate difference in children aged ≤17 years by census tract poverty, ABCs 2010–2019



CDC ABCs, unpublished data

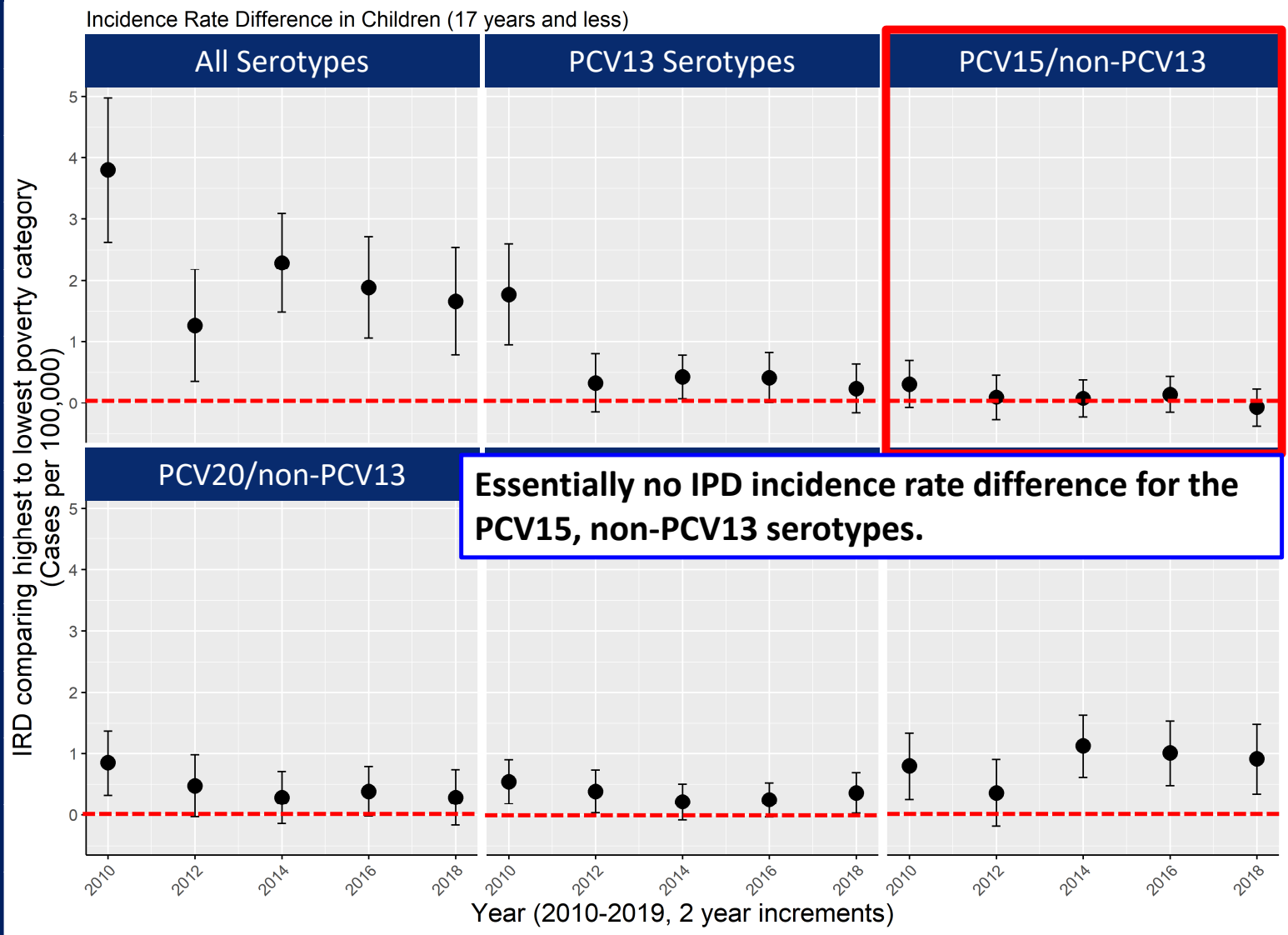
IPD incidence rate difference in children aged ≤17 years by census tract poverty, ABCs 2010–2019



For all serotypes and PCV13 serotypes, IPD incidence rate difference between the highest and lowest census tract poverty categories decreased after PCV13 introduction.

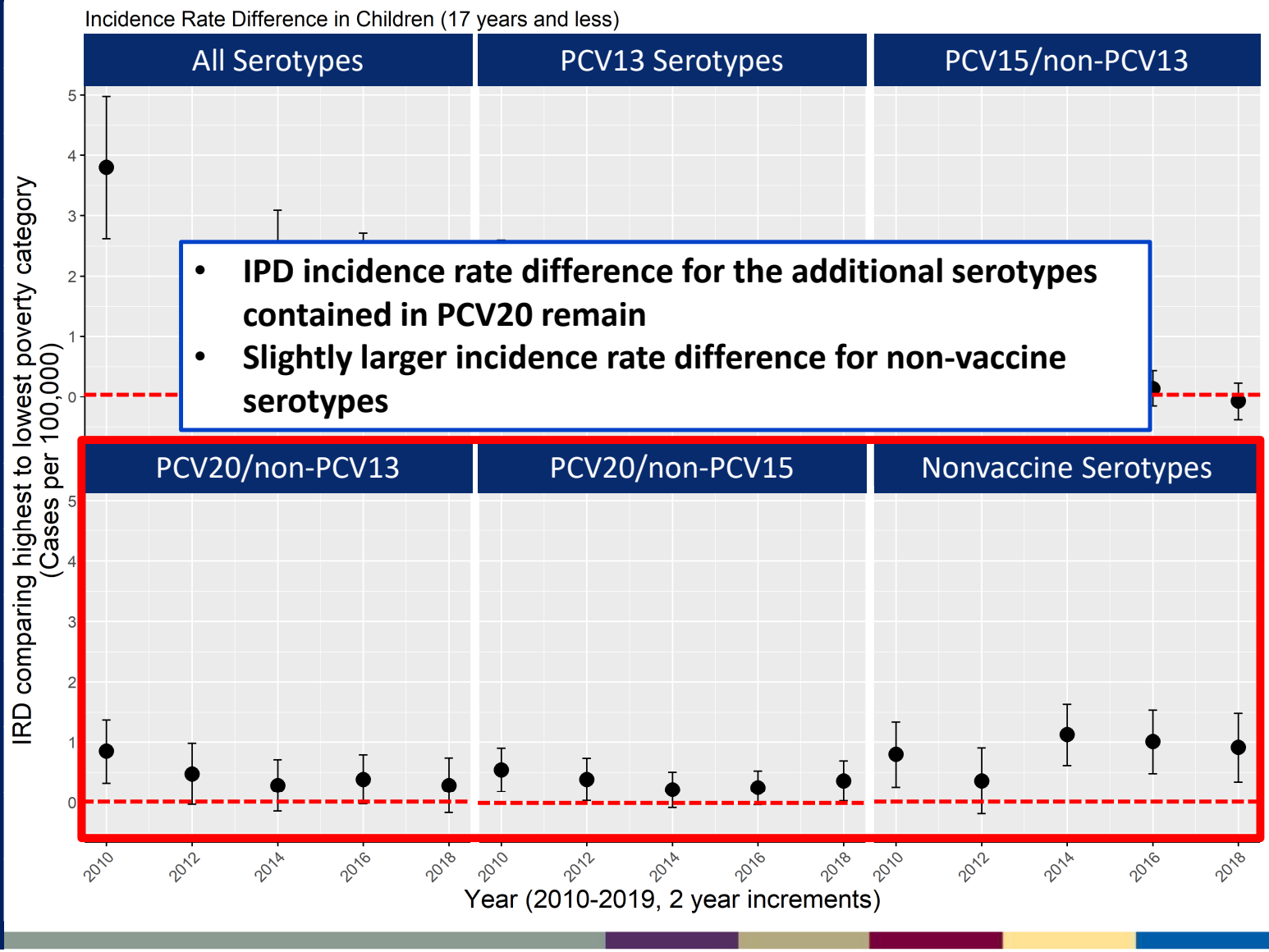
CDC ABCs, unpublished data

IPD incidence rate difference in children aged ≤17 years by census tract poverty, ABCs 2010–2019



CDC ABCs, unpublished data

IPD incidence rate difference in children aged ≤17 years by census tract poverty, ABCs 2010–2019



CDC ABCs, unpublished data

Equity

What would be the impact of recommending PCV20 for U.S. children on health equity?

- □ Reduced
- □ Probably reduced
- □ Probably no impact
- □ Probably increased
- □ Increased
- □ Varies
- □ Don’t know

Equity

What would be the impact of recommending PCV20 for U.S. children aged <2 years on health equity?

Probably reduced:

- New interventions are likely to be accessible to wealthy communities, first

→VFC program mitigates inequities in access to recommended vaccines

Probably no impact:

- Remaining disparities in vaccine-type disease seem to be minimal

Probably increased:

- Post-PCV13 data showed that PCV13 reduced disparities in vaccine-type disease

VFC=Vaccines for Children

Equity

What would be the impact of recommending PCV20 for U.S. children aged 2–18 years with underlying medical conditions on health equity?

Probably no impact:

- Risk-based recommendation is less likely to be equitable compared with routine vaccine recommendations.

Probably increased:

- PCV20 use could simplify the pneumococcal vaccine recommendations and improve vaccine coverage.

Summary of Work Group Interpretation of the EtR Domains (Preliminary)

EtR Domains	PCV20, <2 years (routine)	PCV20, 2–18 years old
Public Health Problem	Yes	
Benefits and Harms		
a. Benefits	Moderate	
b. Harms	Minimal	
c. Benefit>Harm?	Favors intervention/Favors both (split)	
d. Overall certainty: effectiveness	2 (moderate)	4 (very low)
e. Overall certainty: safety	2 (moderate)	4 (very low)
Equity	Probably increased (different opinions)	

Acknowledgements

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Supplementary Slides

GRADE Summary of Evidence

Search strategy: PCV20 use in children

Database	Strategy	No. identified	Included in GRADE

Clinicaltrials.gov	Inclusion: Relevant Phase 2, or 3 randomized controlled trials of PCV20
	• Involved human subjects
	• Reported primary data
	• Included infants and children (age ≤18 years)
	• Included data relevant to the efficacy or effectiveness or immunogenicity and safety outcomes being measured
	• Included data for the dosage and timing being recommended:
	  ○ 3+1 series for infants starting the vaccine series as currently recommended
	  ○ Catch-up vaccine schedule for older infants and children who did not start the 3+1 series in time
	  ○ Use of PCV20 to complete the PCV13 series
	  ○ Use of PCV20 in series with PPSV23 in older children with underlying conditions in series with PPSV23
		12	3*

Pubmed Medline	"PCV20" or "20-valent pneumococcal conjugate vaccine" Included studies using the criteria listed above	62	1
Additional resources	Unpublished and other relevant data by consulting with the vaccine manufacturer	2	3*

*Same trials. Unpublished data from these trials were obtained from pharmaceutical companies.

Included Studies: Routine PCV20 Use in Children Aged <2 years

Author, year	Study design	Intervention	Country	Age	Total population	N Intervention	N comparison	Outcomes	Funding source
Senders, 2021	Phase II RCT in healthy full-term infants	PCV20 @ 2, 4, 6, and 12 months of age	US	42–98 days of age at consent	460	232	228	Immuno-genicity and safety	Pfizer
B7471011	Phase III RCT in healthy full-term infants	PCV20 @ 2, 4, 6, and 12 – 15 months of age	US, Puerto Rico	42–98 days of age at consent	1998	1001	997	Immuno-genicity and safety	Pfizer
B7471013	Phase III RCT in healthy infants	PCV20 @ 2, 4, 6, and 12 – 15 months of age	US, Puerto Rico, Canada, Chile, Argentina, EU	42–98 days of age at consent	1511	1000	551	Safety	Pfizer

RCT=Randomized Controlled Trial

GRADE Summary of Findings: Routine PCV20 use in Children Aged <2 Years

Certainty assessment							№ of patients		Results		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	comparison	Relative (95% CI)	Absolute (95% CI)		
Vaccine effectiveness												
2[1-2]	RCT	Not serious	Not serious	Serious[a]	Not serious	Not serious	921-1022	910-989	• PCV20 had numerically lower immune responses compared with PCV13 for most of the 13 shared serotypes. • PCV20 did not meet noninferiority criteria for some serotypes after dose 3. • PCV20 noninferior to PCV13 for all 13 shared serotypes after dose 4. • PCV20 noninferior to PCV13[b] for all 7 additional serotypes after dose 4.		Moderate	Critical

a. These are all immunogenicity studies and there are no correlates of protection for most outcomes.
b. Compared with serotype with lowest immune response among PCV13 serotypes except for serotype 3

References
1. Senders S, Klein NP, Lamberth E, Thompson A, Drozd J, Trammel J, Peng Y, Giardina PC, Jansen KU, Gruber WC, Scott DA, Watson W. Safety and Immunogenicity of a 20-valent Pneumococcal Conjugate Vaccine in Healthy Infants in the United States. Pediatr Infect Dis J. 2021 Oct 1;40(10):944-951. doi: 10.1097/INF.0000000000003277.
2.B7471011. A Phase 3, Randomized, double-blind trial to evaluate the safety and immunogenicity of a 20-valent pneumococcal conjugate vaccine in healthy infants

GRADE Summary of Findings: Routine PCV20 use in Children Aged <2 Years

Certainty assessment							№ of patients		Results		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Comparison	Relative (95% CI)	Absolute (95% CI)		
Serious Adverse Events (SAEs) following vaccination												
2[1-3]	RCT	Not serious	Not serious	Not serious	Serious[a]	Not serious	4.5% (n=1567)	3.7% (n=1376)	No vaccine-related serious adverse events reported		Moderate	Critical

a. No vaccine-related serious adverse events reported

References
1.Senders S, Klein NP, Lamberth E, Thompson A, Drozd J, Trammel J, Peng Y, Giardina PC, Jansen KU, Gruber WC, Scott DA, Watson W. Safety and Immunogenicity of a 20-valent Pneumococcal Conjugate Vaccine in Healthy Infants in the United States. Pediatr Infect Dis J. 2021 Oct 1;40(10):944-951. doi: 10.1097/INF.0000000000003277.
2.B7471011. A Phase 3, Randomized, double-blind trial to evaluate the safety and immunogenicity of a 20-valent pneumococcal conjugate vaccine in healthy infants
3.B7471013. A Phase 3, Randomized, double-blind trial to evaluate the safety of a 20-valent pneumococcal conjugate vaccine in healthy infants. Data limited to U.S. and Puerto Rico sites.

Included Study: PCV20 Use in Children Aged 2–18 Years with Underlying Medical Conditions

Author, year	Study design	Intervention	Country	Age	Total population	N Intervention	N comparison	Outcomes	Funding source
B7471014	Phase III Clinical Trial in healthy children, some previously vaccinated	Single dose PCV20 @ 15m to <24m; **previous vaccination ≥3 doses of PCV13**	US	15m to <24m	209	209	N/A	Immuno-genicity and safety	Pfizer
		Single dose PCV20 @ 2y to <5y; **previous vaccination ≥3 doses of PCV13**		2y to <5y	216	216	N/A		
		Single dose PCV20 @ 5y to <10y		5y to <10y	201	201	N/A		
		Single dose PCV20 @ 10 to <18y		10y to <18y	205	205	N/A		

GRADE Summary of Findings: PCV20 Use in Children Aged 2–18 Years with Underlying Medical Conditions

Certainty assessment							№ of patients		Results		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	comparison	Relative (95% CI)	Absolute (95% CI)		
Vaccine effectiveness												
1[1]	Non-RCT	Very Serious[a]	Not applicable	Very Serious[b,c]	Not serious	Not serious	752-757	None	IgG GMCs were higher 1-month post-PCV20 dose compared to before vaccination for 13/13 shared serotypes and 7/7 additional serotypes, for all age groups		Very Low	Critical

a. Study design is an open label non-randomized controlled trial with no comparator group. Downgraded for lack of randomization, lack of blinding, and lack of a comparison group.
b. Study population did not include children with underlying conditions
c. This is an immunogenicity study and there are no correlates of protection for some critical outcomes considered

References
B7471014. Safety and Immunogenicity Study of 20vPnC in Healthy Children 15 Months Through 17 Years of Age

GRADE Summary of Findings: PCV20 use in Children Aged 2–18 Years With Underlying Medical Conditions

Certainty assessment							№ of patients	Results		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PCV20 Intervention	Relative (95% CI)	Absolute (95% CI)		
Serious Adverse Events (SAEs) following vaccination											
1[1]	Non-randomized trial	Serious[a]	Not applicable	Serious[b]	Serious[c]	Not serious	0.6% (n=831)	No vaccine-related SAEs reported		Very Low	Critical

a. Study design is an open label non-randomized controlled trial with no comparator group
b. Study population did not include children with underlying conditions
c. No vaccine-related serious adverse events reported; relative risk crossing 1

Reference

B7471014. Safety and Immunogenicity Study of 20vPnC in Healthy Children 15 Months Through 17 Years of Age