Conclusions from the PSERENADE Project: Implications for Pneumococcal Vaccine Policy and What is Happening Next

Presented by Maria Deloria Knoll, PhD

on behalf of the PSERENADE Team

Meningitis Research Foundation

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Conflicts of Interest

Dr. Maria Knoll reports grants from Merck, personal fees from Merck, and grants from Pfizer, outside the submitted work.

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The funders had no role in the design of the study or in the collection, analyses, or interpretation of data.

Background

- Pneumococcal conjugate vaccines (PCVs) have been widely introduced into infant immunization programs over the last 20 years
  - 10 years of PCV10 (GSK) and PCV13 (Pfizer) use
- Invasive pneumococcal disease (IPD) caused by serotypes targeted by the vaccines has been reduced
- But questions remain regarding the net overall impact after long term use on pneumococcal disease, in both children and adults
- Countries want to understand differences between PCV10 and PCV13 in the overall impact on all pneumococcal disease
- The amount of disease prevented in older children and adults through indirect herd protection has varied by country

Pneumococcal **Se**rotype **Re**placement a**n**d **D**istribution Estimation (**PSERENADE**) Project

The **PSERENADE Project** was conducted to use all available data **globally** to answer these questions.

Aim: to assess the impact of PCVs introduced into infant immunization programs on invasive pneumococcal disease (IPD), including meningitis.

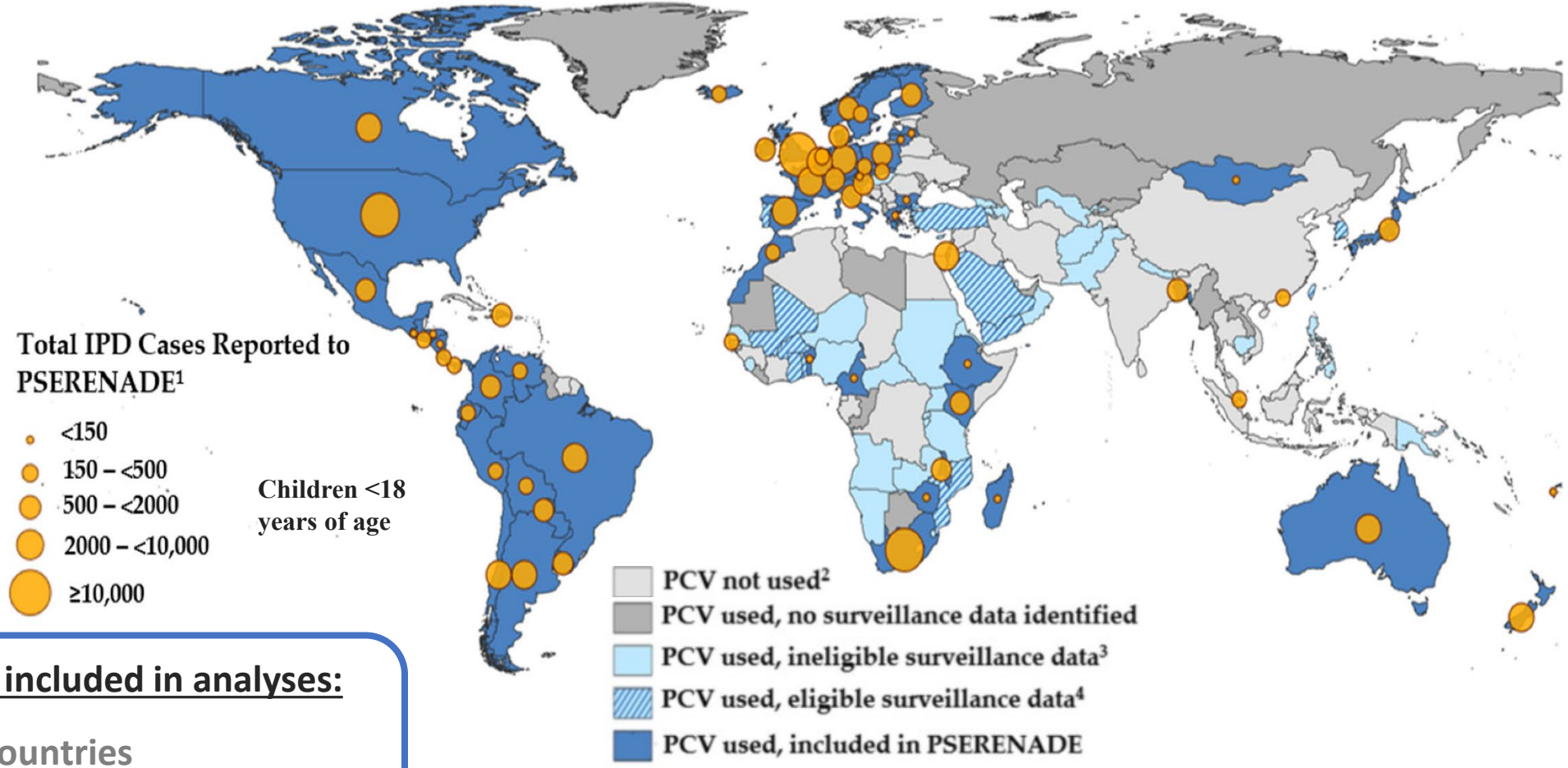
The following questions will be addressed in this presentation:

1. What were the direct effects of PCV10/13 vaccination in children <5 years old on all IPD?
2. Were there differences between countries that used PCV10 vs PCV13?
3. Was impact the same for meningitis?
4. What were the indirect effects on older children and adults?
5. What were the effects on Serotype 1 outbreaks?
6. Did vaccine schedule affect vaccine impact? Is a booster dose needed?
7. What pneumococcal serotypes remain?
8. What proportion of remaining disease is caused by serotypes covered by higher valency products?

Overview of Sites with invasive pneumococcal disease (IPD) data

Eligibility Criteria

- PCV universally recommended in the infant immunization schedule
- At least 50% uptake of PCV
- ≥1 complete post PCV year of invasive pneumococcal disease (IPD)*
- At least 50% of cases serotyped
- Stable surveillance system



Reference: Deloria Knoll et al. *Microorganisms*. 2021

Number of eligible sites included in analyses:

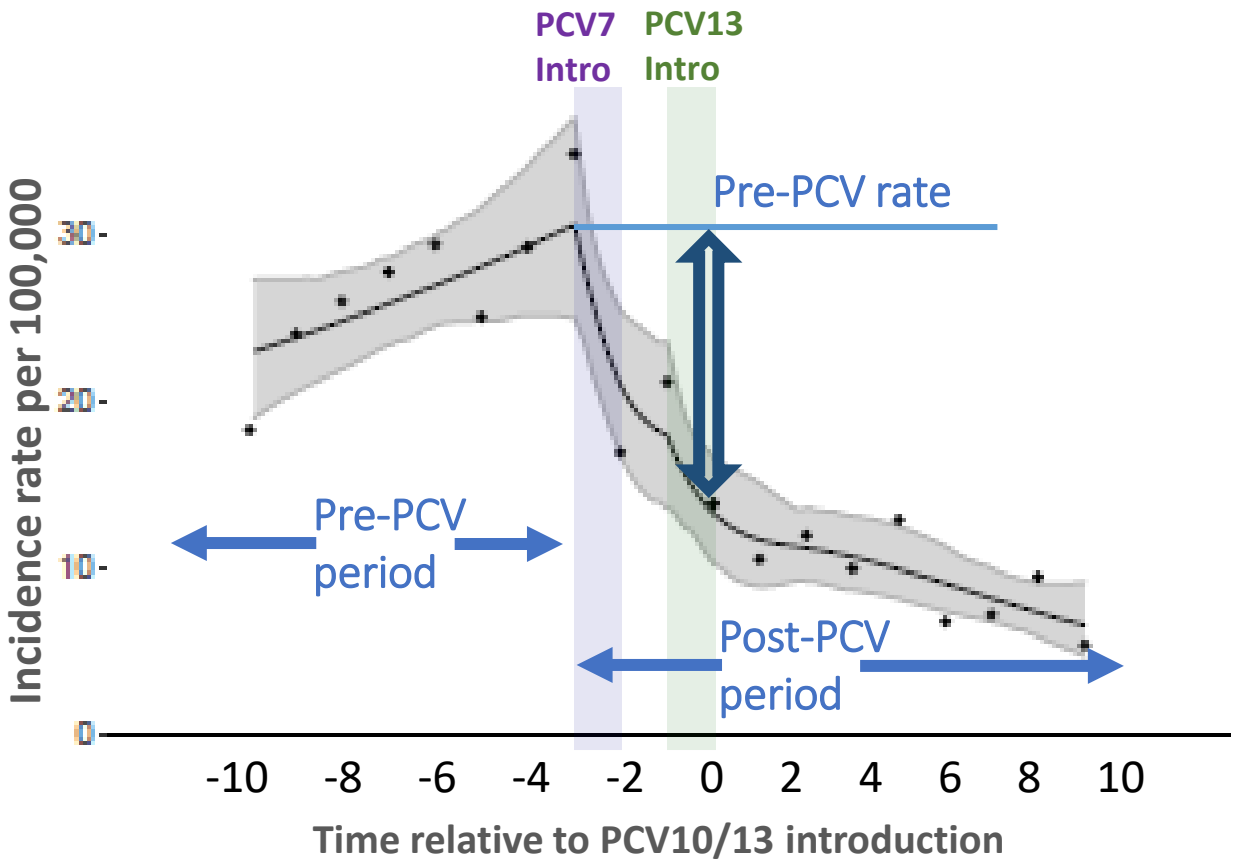
Incidence: 47 sites in 33 countries

Serotype Distribution: 54 sites in 41 countries

*IPD = predominantly pneumonia, meningitis and sepsis cases with pneumococcus detected in blood or cerebral spinal fluid (CSF)

Methods: estimating change in incidence over time relative to pre-PCV period (incidence rate ratios)

Step 1: estimate IPD Incidence over time for each site



*Time 0 = year of PCV7 introduction and year +4 = 5th year of PCV use

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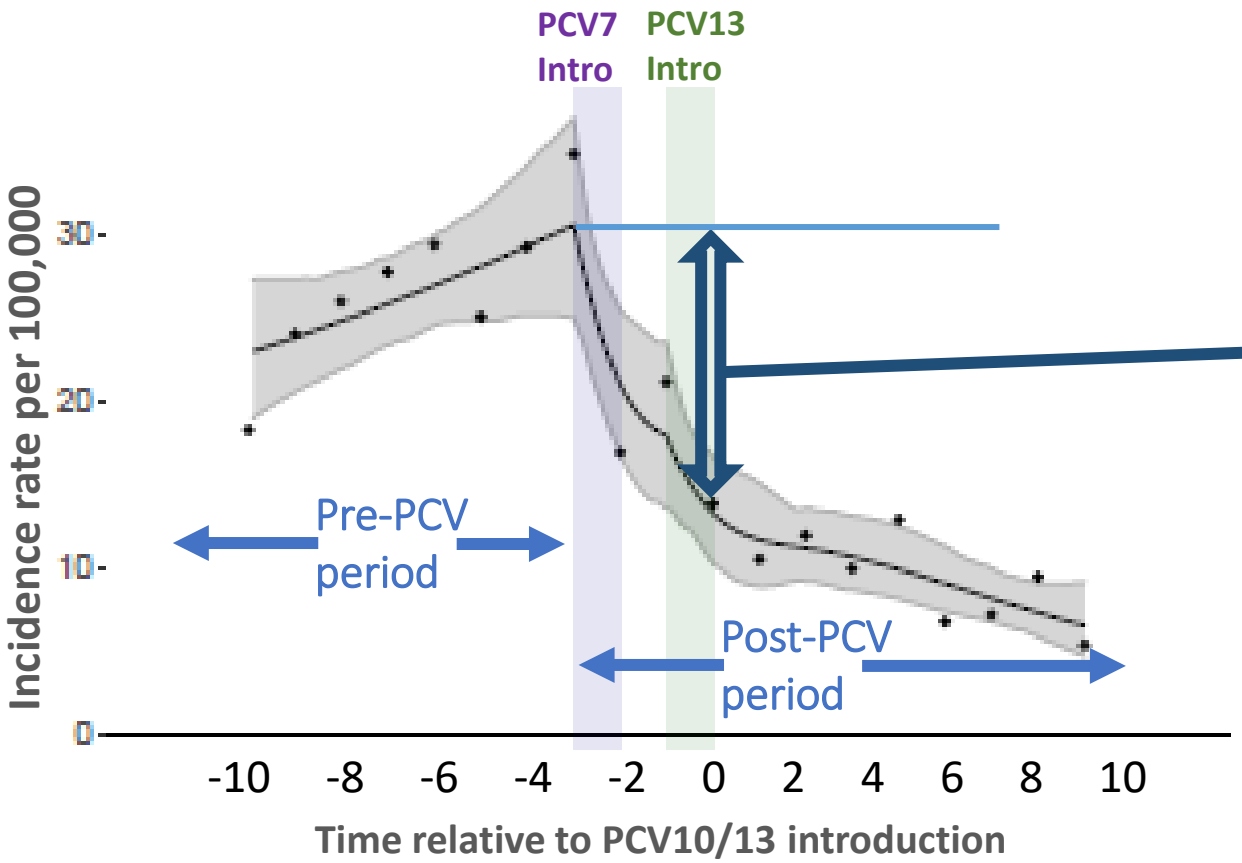
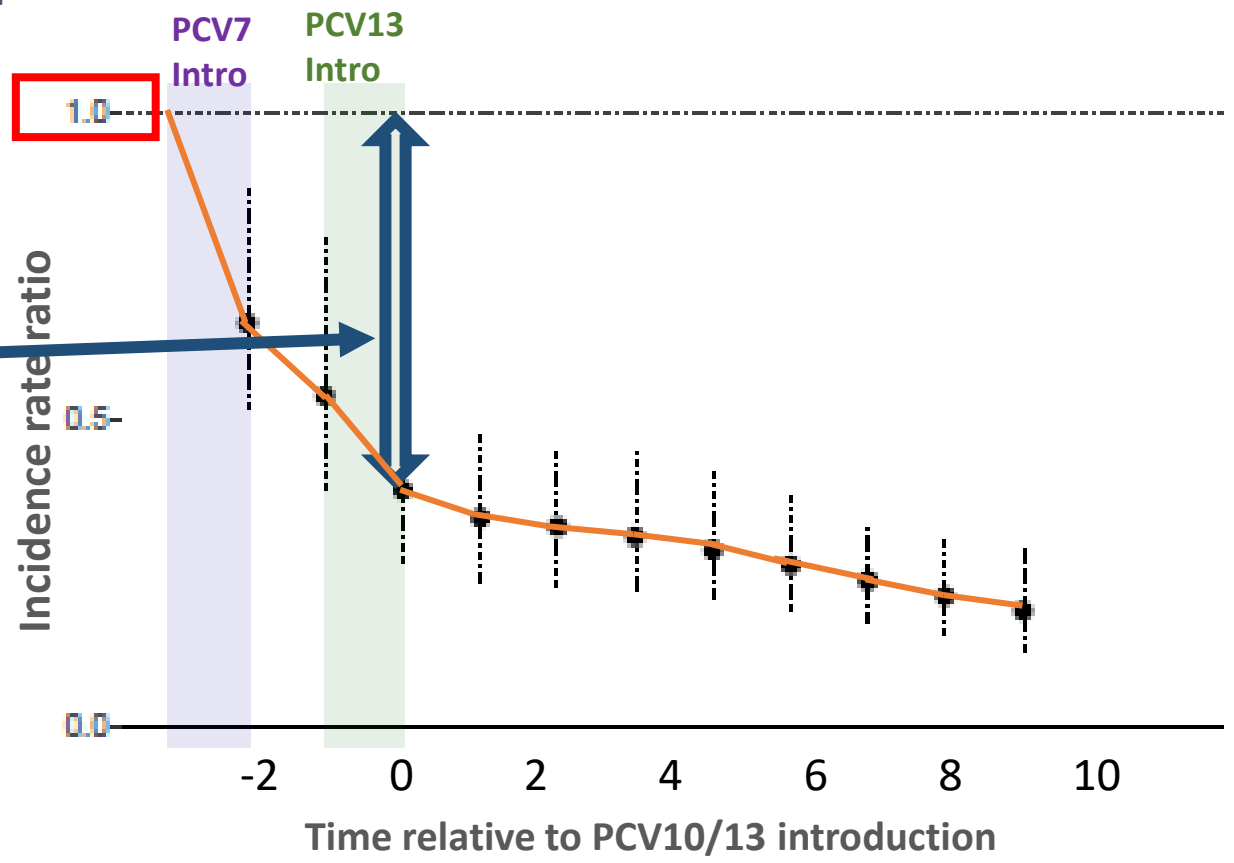


Observed IR (data from site)

Site-specific modeled IR & surrounding 95% CIs

Step 2: Calculate Incidence Rate Ratio relative to pre-PCV period



IRR and surrounding 95% CIs

*Time 0 = year of PCV7 introduction and year +4 = 5th year of PCV use

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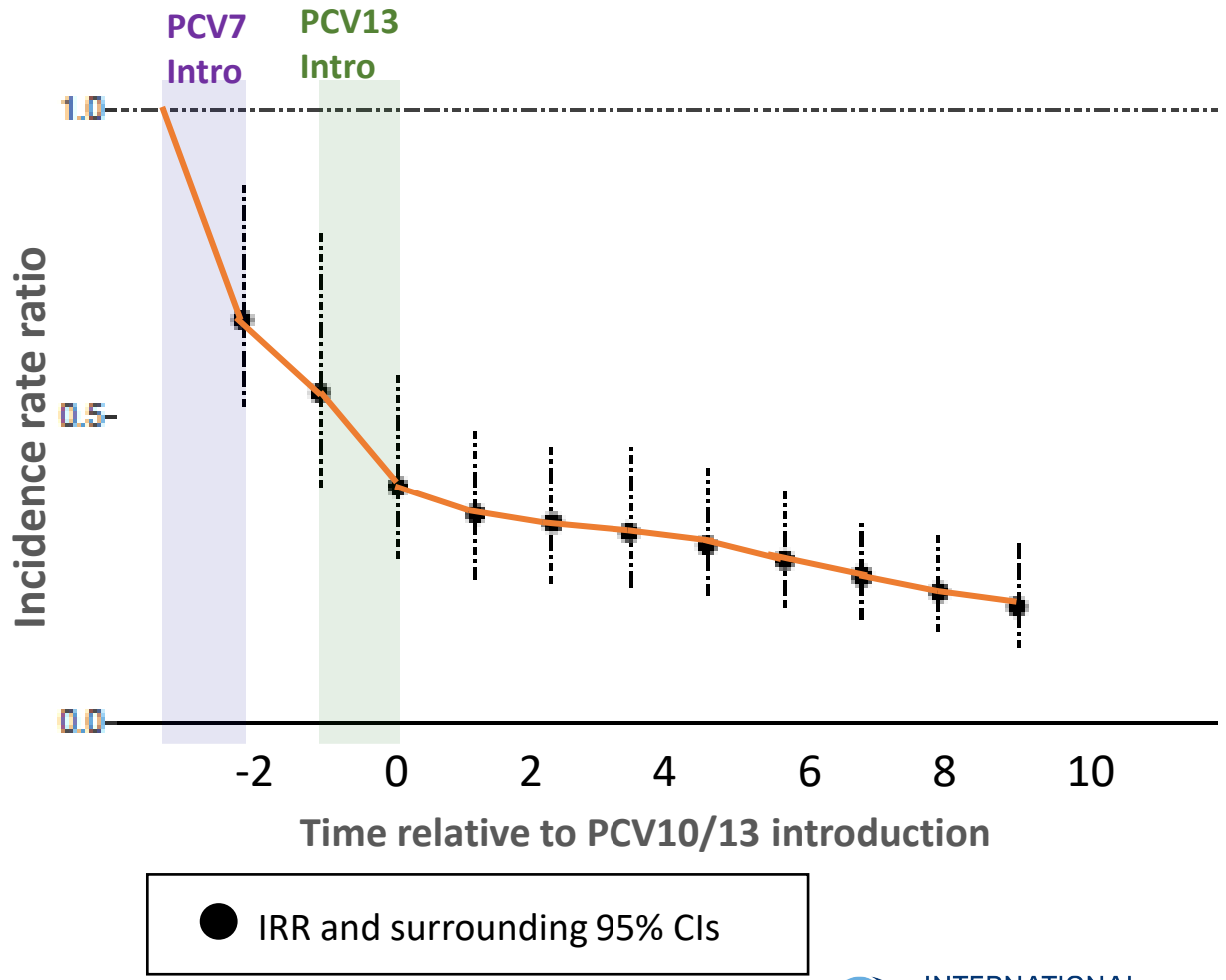

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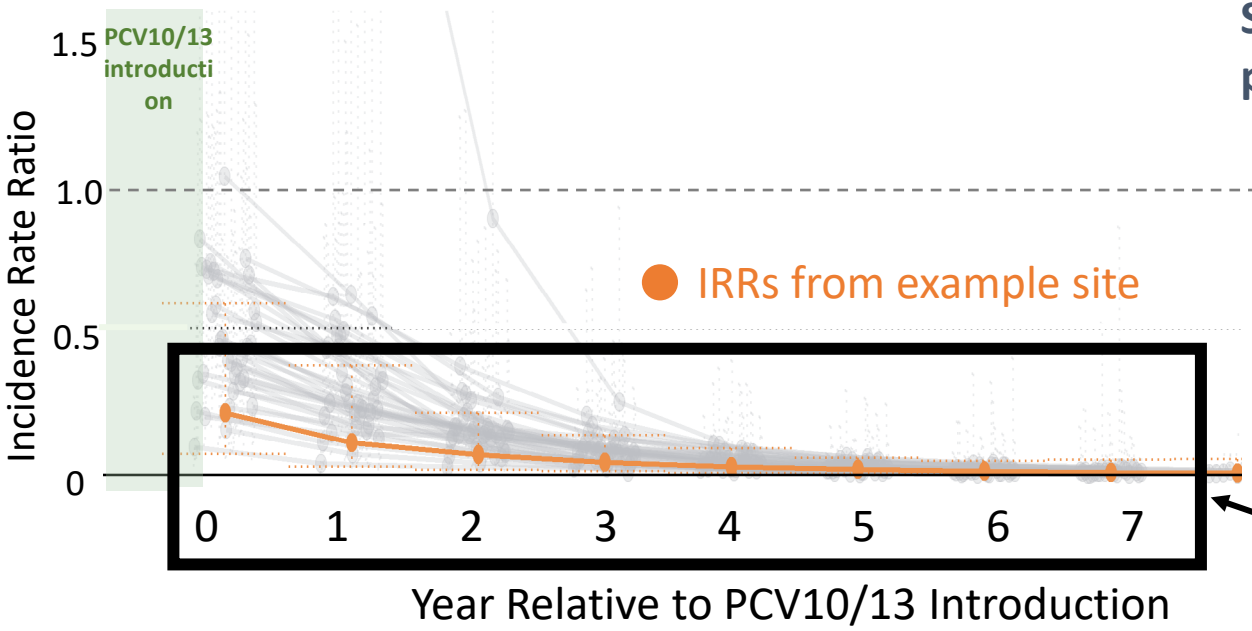
Methods: meta-averaged change in incidence across sites



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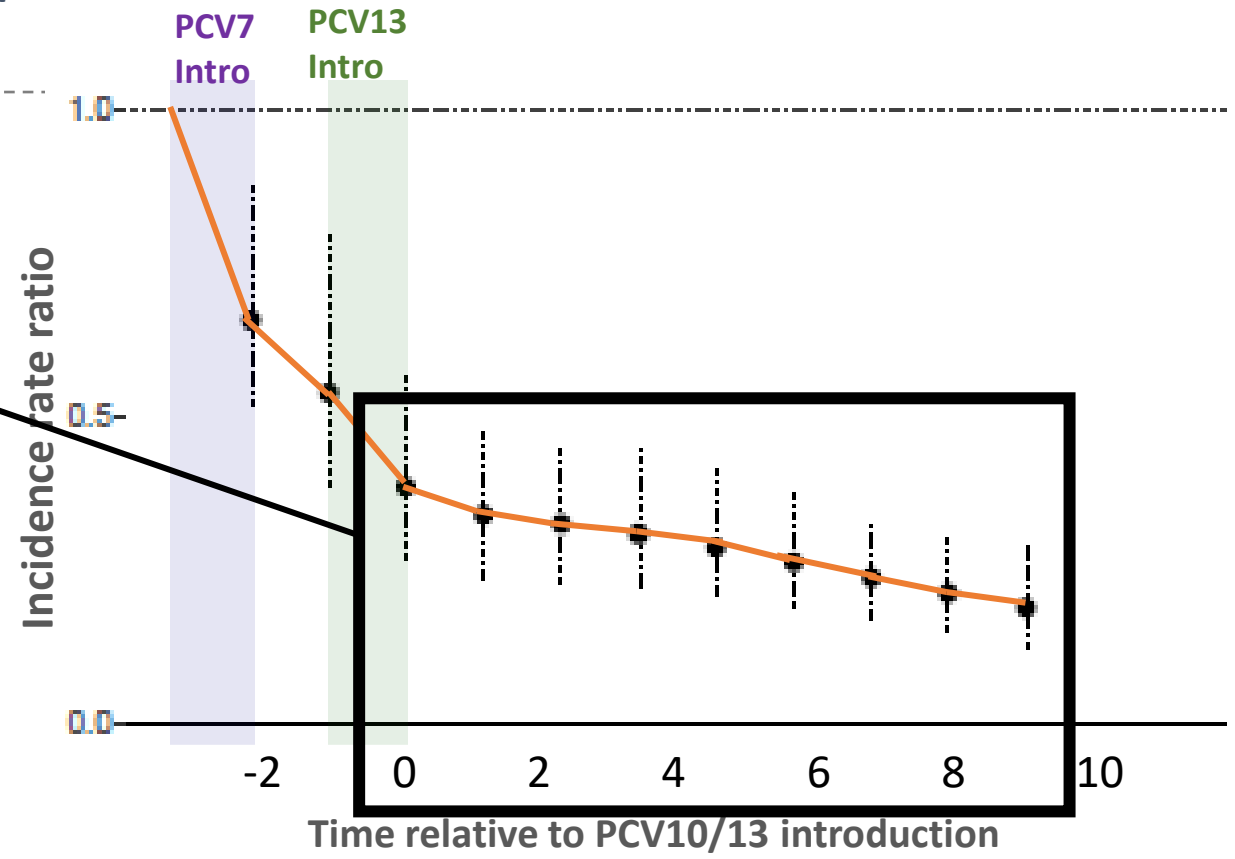
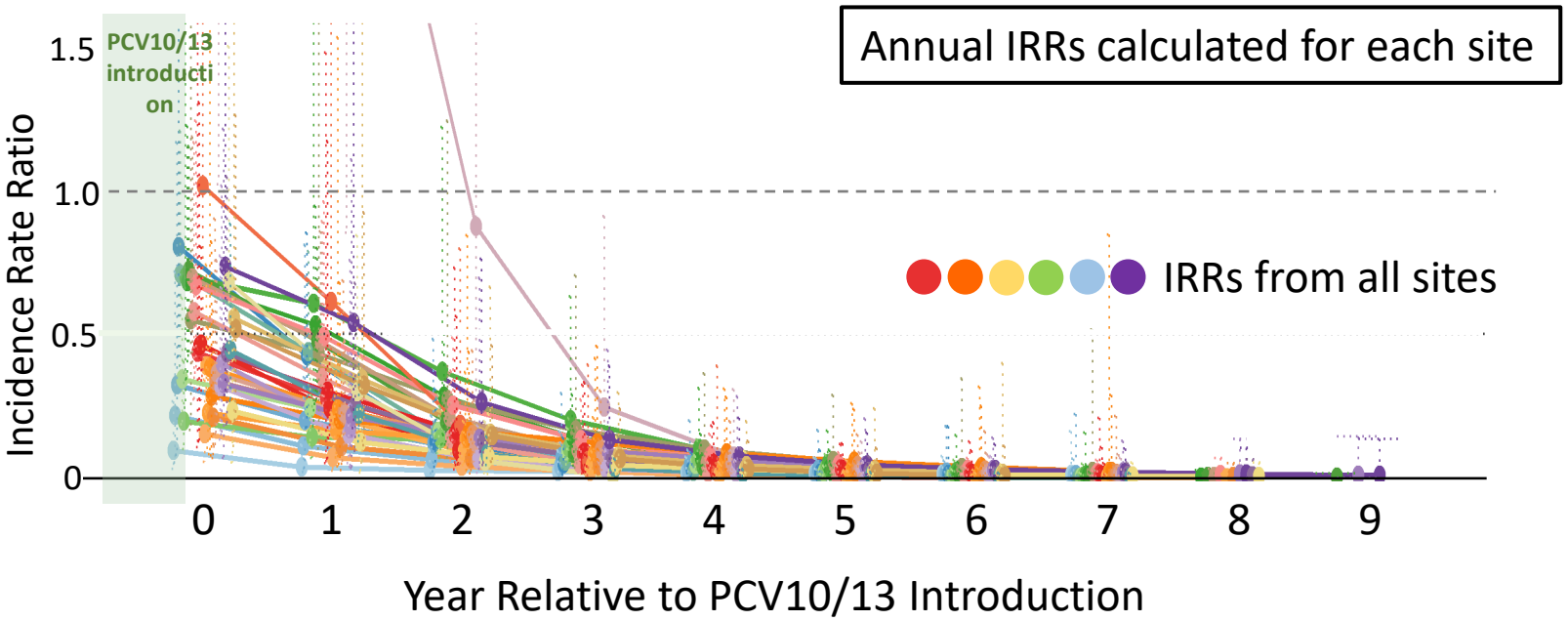
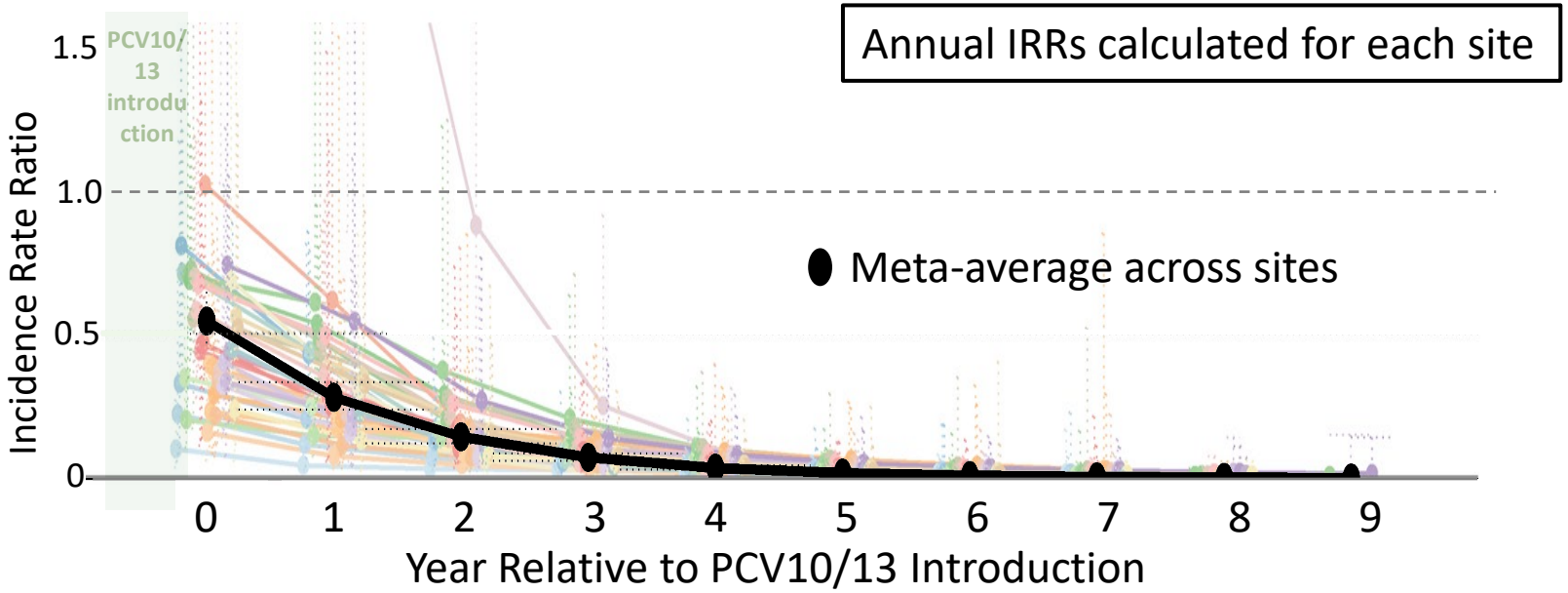


Methods: meta-averaged change in incidence across sites



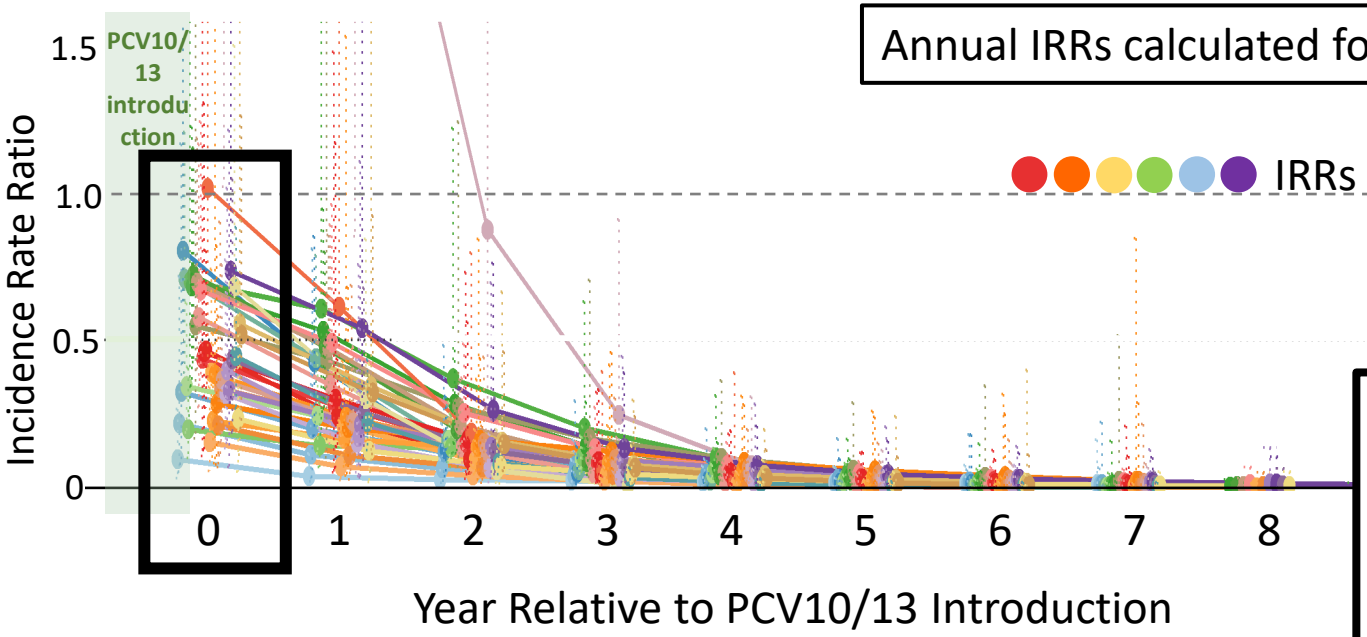
Methods: meta-averaged change in incidence across sites

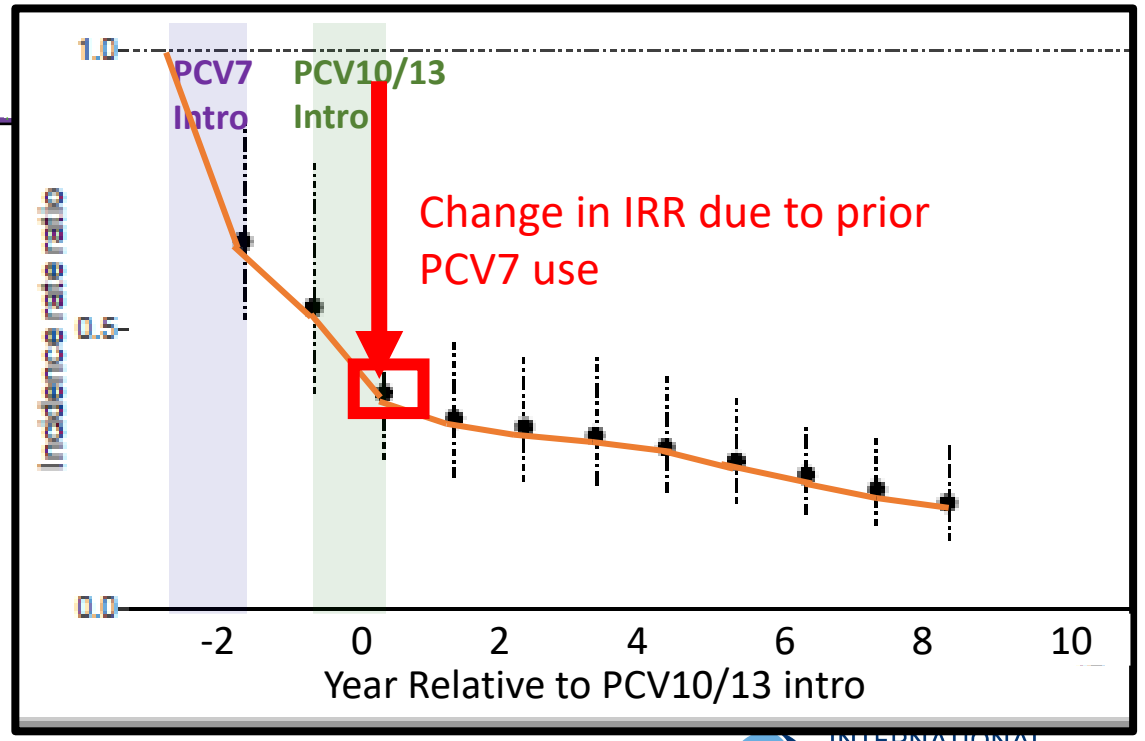
Annual IRRs calculated for each site



Why do IRRs at year 0 vary across the sites?

Annual IRRs calculated for each site





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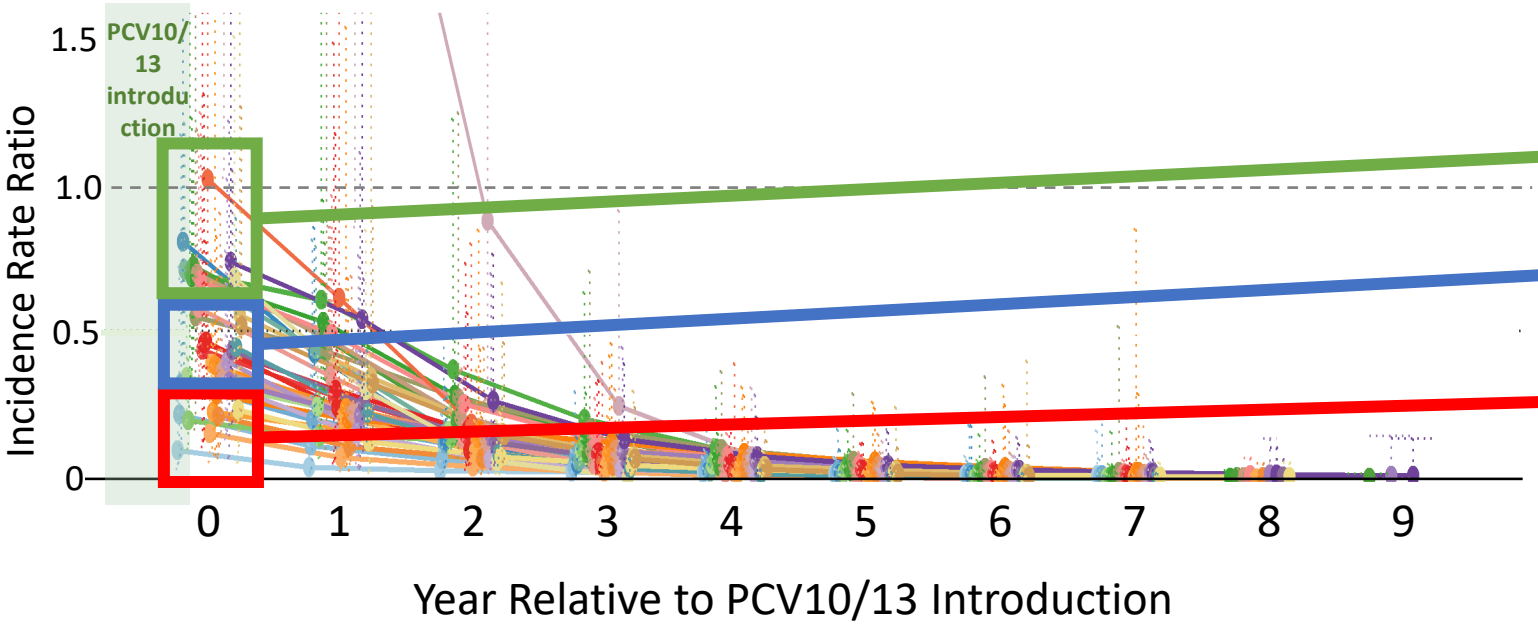
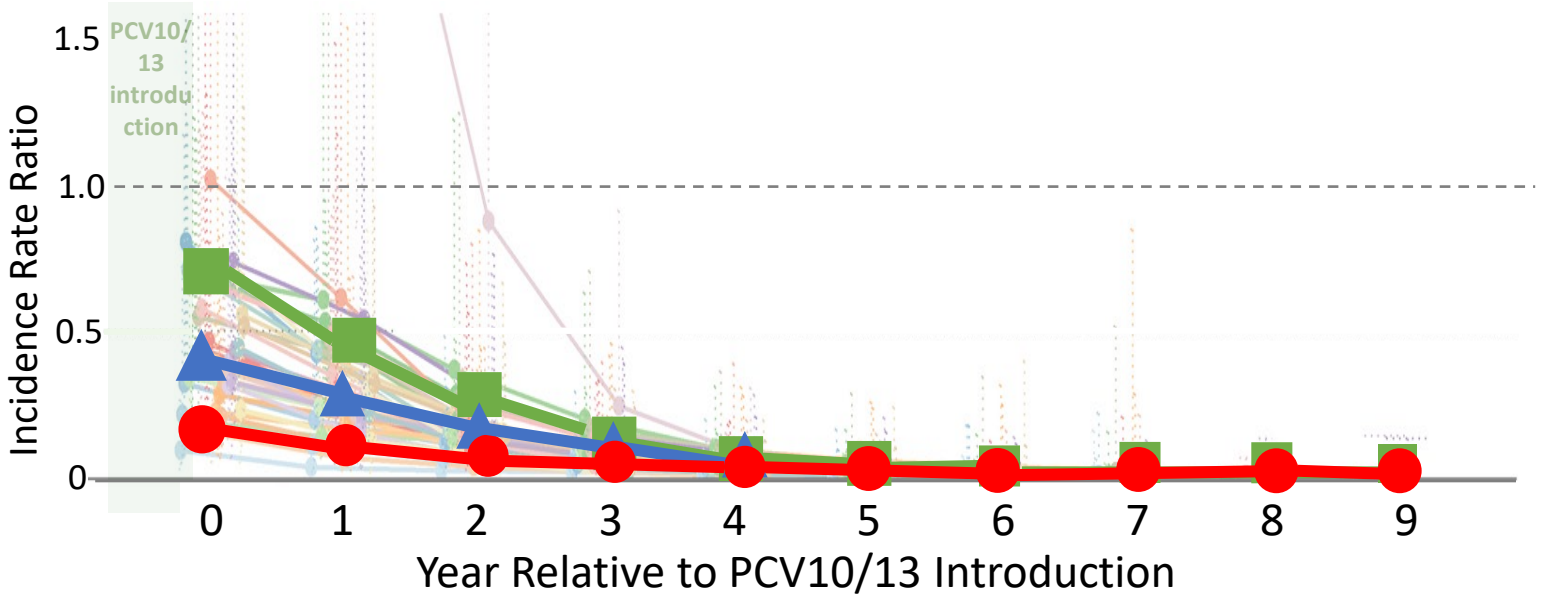


Stratification by prior PCV7 use

No PCV7 use
Moderate PCV7 impact
Substantial PCV7 impact

Methods: meta-averaged change in incidence across sites

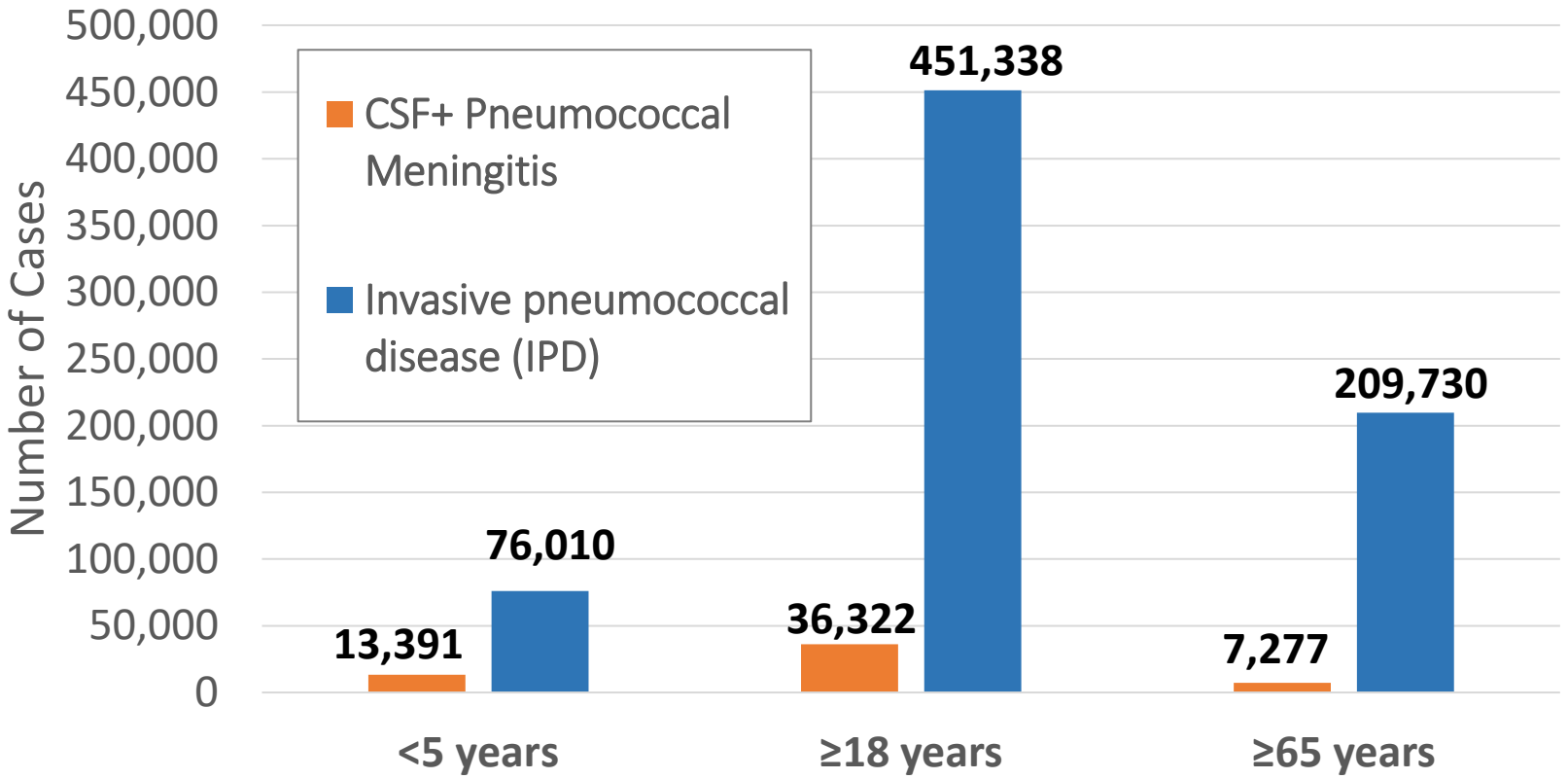


Stratification by prior PCV7 use

■	No PCV7 use
▲	Moderate PCV7 impact
●	Substantial PCV7 impact

Results:

Number of cases of pneumococcal meningitis and IPD



33 countries with eligible data

Over 500,000 IPD cases
- <5 years: ~76,000 cases
- 18+ years ~450,000 cases
- 65+ years ~210,000 cases

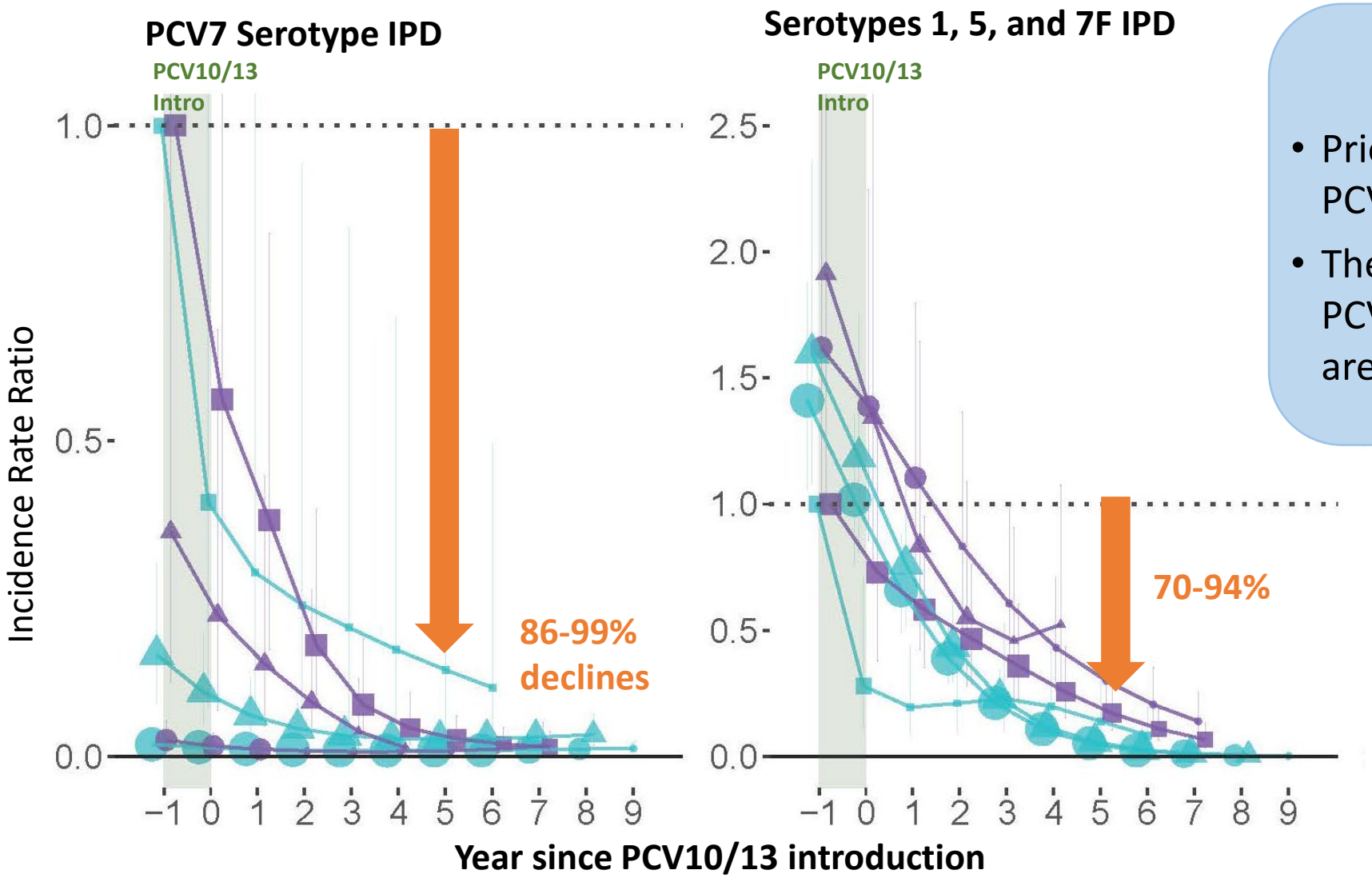
Proportion of IPD that was meningitis:
- <5 years: ~15%
- 18+ years: ~7%

Larger IPD sample size enables more sub-analyses

1. What were the direct effects of PCV10/13 vaccination in children <5 years old on all IPD?

2. Were there differences between countries that used PCV10 vs PCV13?

Change in IPD in children <5 years: PCV10 Types



Key messages

- Prior PCV7 use greatly impacted PCV7 type IPD
- The new serotypes covered by PCV10/13 declined substantially and are expected to continue declining

PCV13

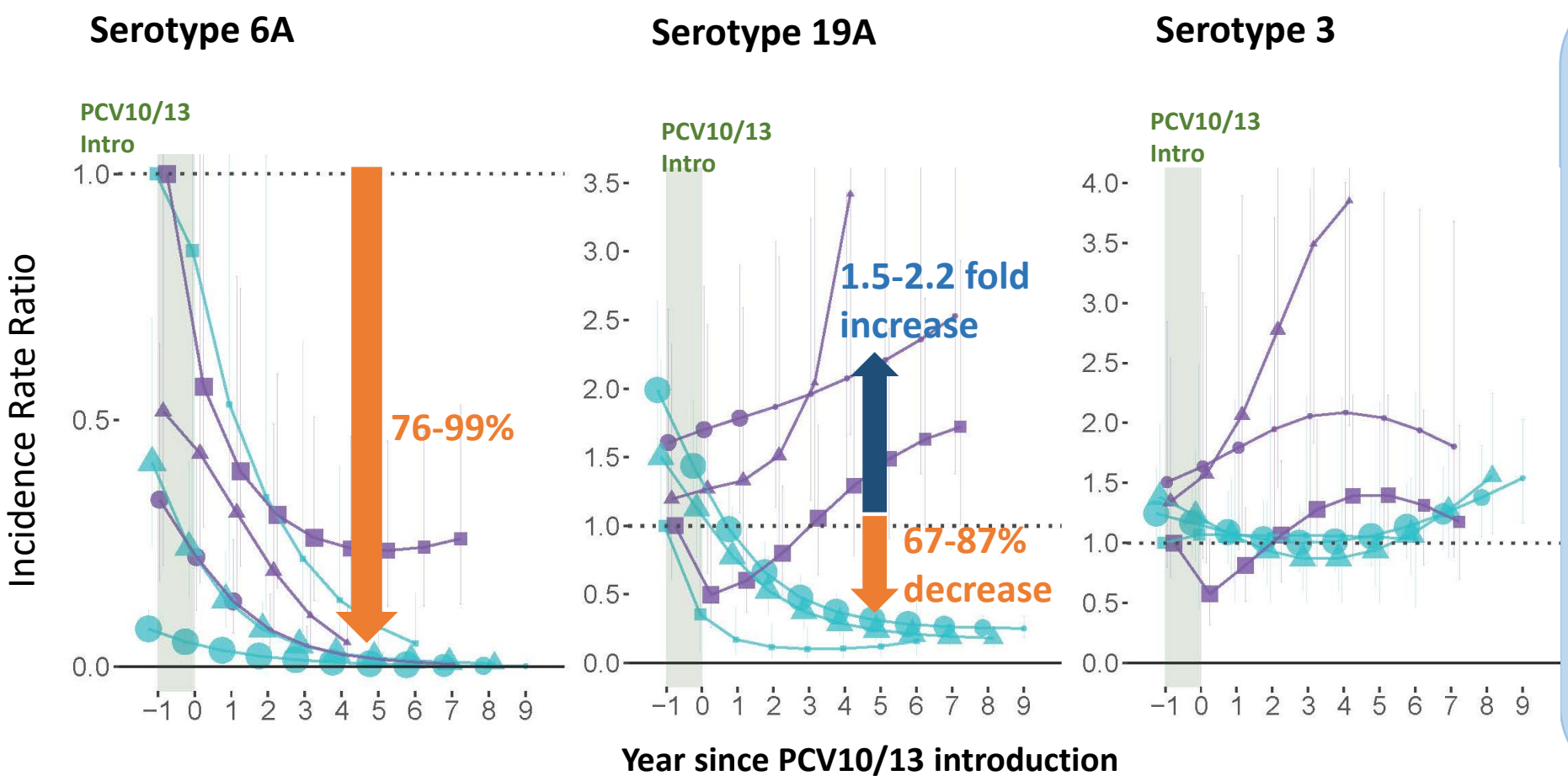
PCV10

PCV7 Impact

- Substantial
- Moderate
- No use

INTERNATIONAL VACCINE ACCESS CENTER

Change in IPD in children <5 years: PCV13 (non-PCV10) Types

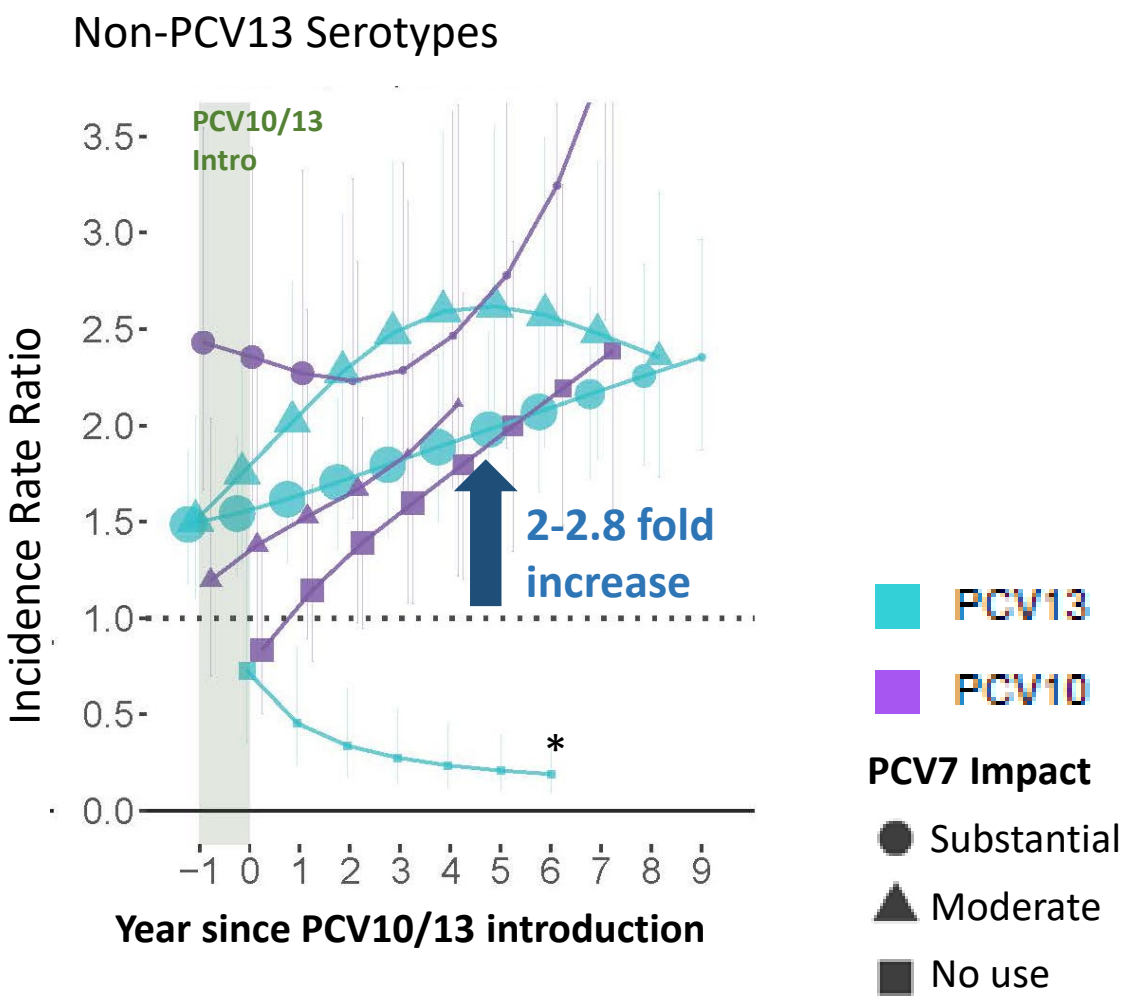


Key messages

- Evidence of cross protection against 6A for PCV10
- 19A was reduced at PCV13 sites, butnot eliminated; it increased at PCV10 sites
- No clear trends in Serotype 3 for either product

INTERNATIONAL VACCINE ACCESS CENTER

Change in IPD in children <5 years: Non-PCV13 Types



Key messages

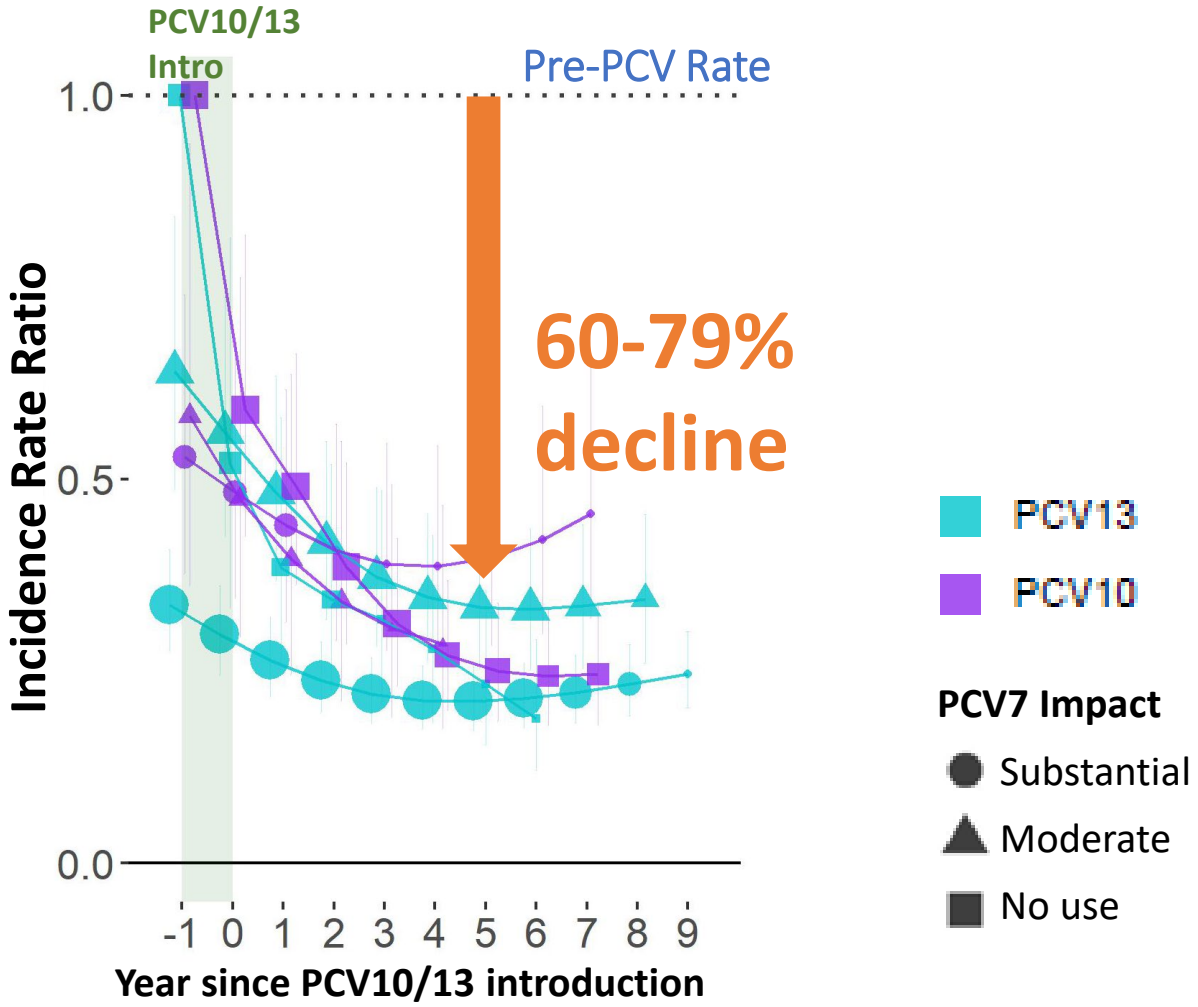
Non-vaccine serotypes increased 2-2.8 fold by year 5

Has not stabilized

Similar for both PCV10 & PCV13

*High HIV prevalence site that had other concurrent interventions besides PCV13, including ART therapy

Change in all IPD in children <5 years



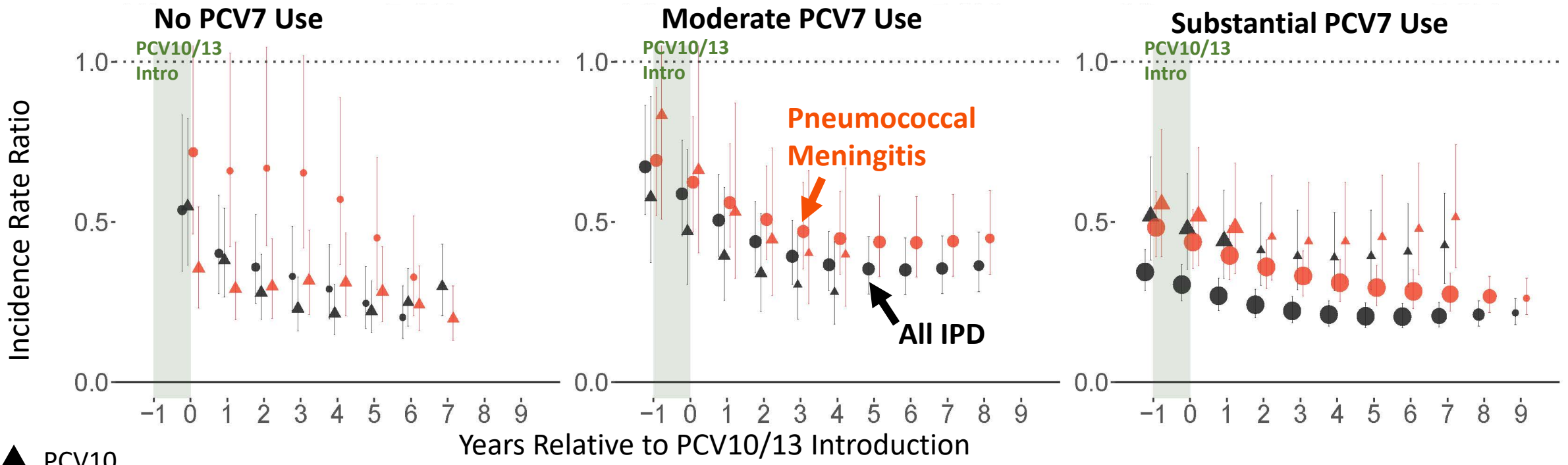
Key messages

- Overall, all IPD declined 60-79% (IRRs 0.21-0.40) by 5 years after PCV10/13 introduction across strata
- No meaningful differences between PCV10 and PCV13

3. Was impact the same for meningitis?

Impact of PCV on Pneumococcal Meningitis vs All IPD: Children <5y

by PCV10/13 product and years of prior PCV7 impact



PCV10

PCV13

Meningitis

All IPD

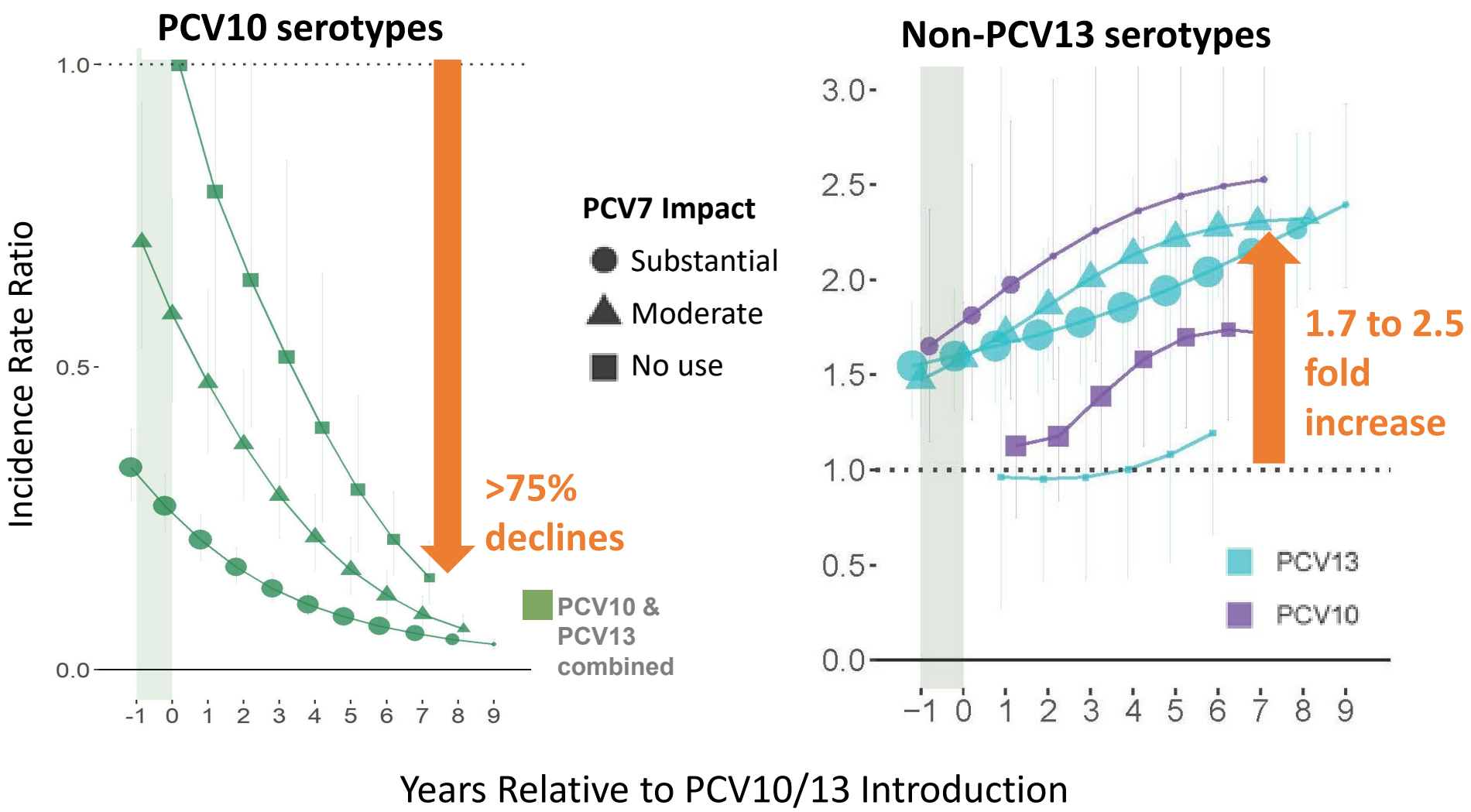
Key messages: children <5y

- Reduction in pneumococcal meningitis was >50% in all strata for both products
- PCV impact on pneumococcal meningitis was ~5% less than for all IPD

See poster: Changes in Pneumococcal Meningitis Incidence Following Introduction of PCV10 and PCV13: Results from the Global PSERENADE Project (J. Yang)

4. What were the indirect effects in adults?

Herd Effects of Infant PCV program on IPD in Adults >65 years



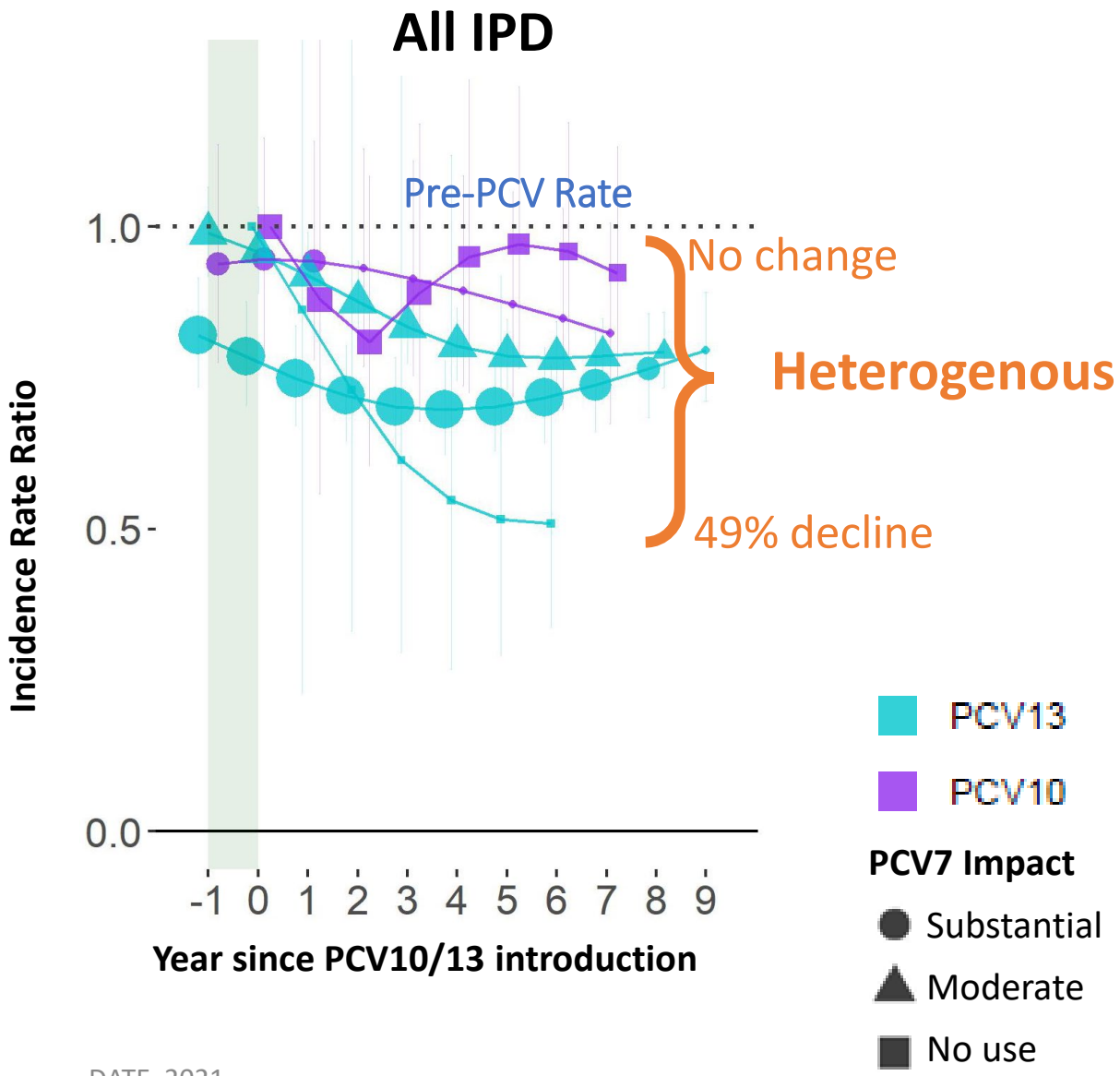
Key messages:

Vaccine type IPD decreased substantially (>75%) in adults >65y

- Took 2-3 years longer for the full effect than for children <5y

Non-vaccine type increased ~>2 fold

Herd Effects of Infant PCV program on all IPD in Adults ≥65 years



Key messages:

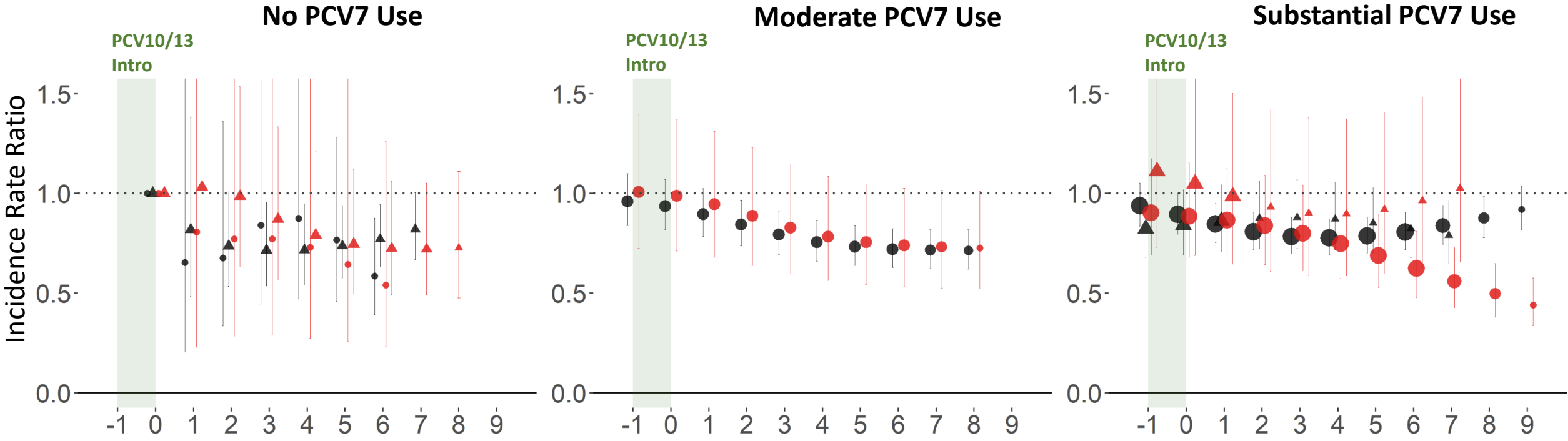
Net effect of VT declines and non-VT increases: Heterogenous

Total IPD incidence had sustained declines in some sites but others returned to baseline

3. Was impact the same for meningitis? (Adults)

Impact of PCV on Pneumococcal Meningitis vs all IPD: Adults ≥18y

by PCV10/13 product and years of prior PCV7 impact



Meningitis

All IPD

PCV10

PCV13

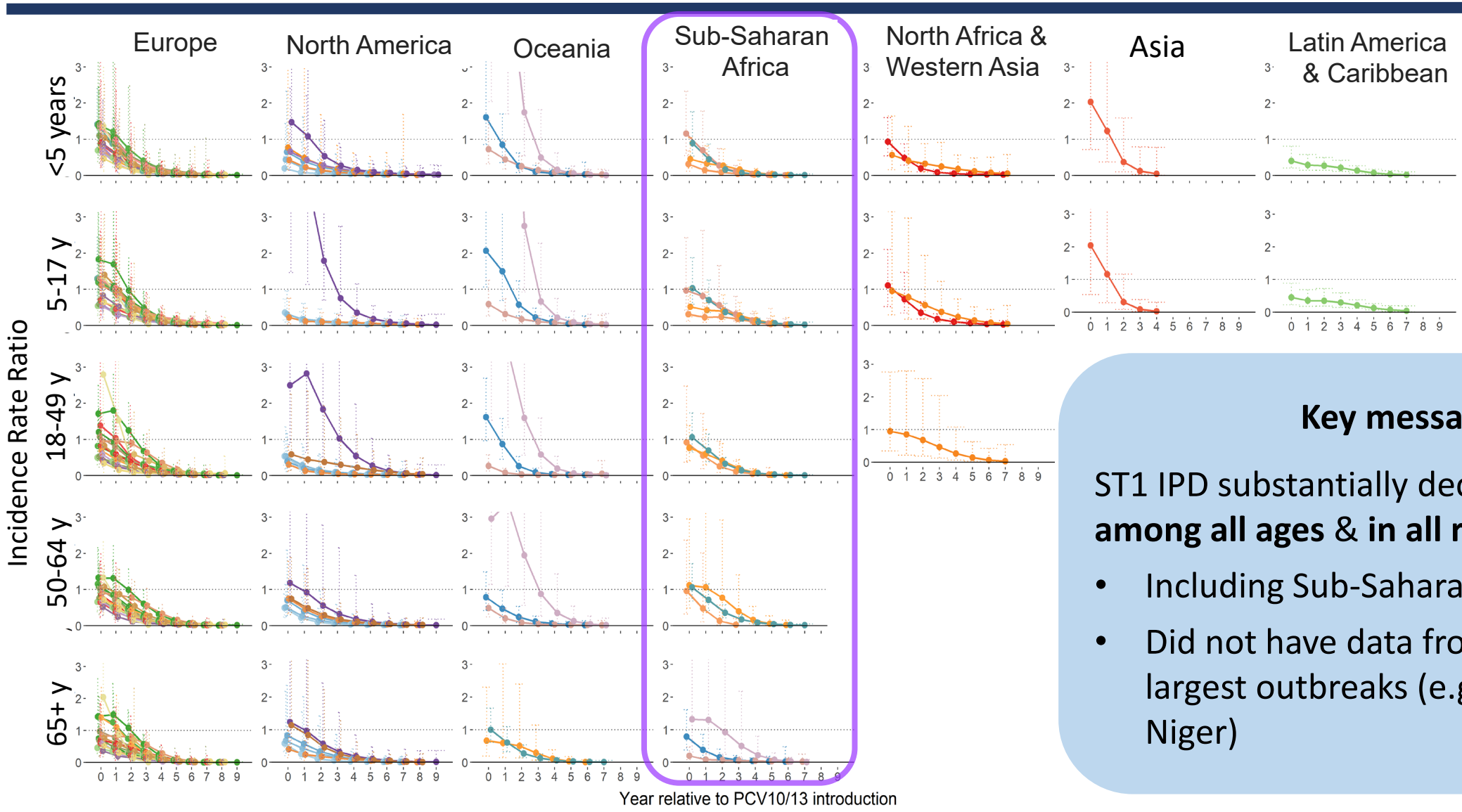
Key messages: Adults ≥18y

- Results for meningitis were generally similar to all IPD
- Heterogeneous by site, ranging from no net change to ~50% decline

See poster: Changes in Pneumococcal Meningitis Incidence Following Introduction of PCV10 and PCV13: Results from the Global PSERENADE Project (J. Yang)

5. What were effects of PCV10/13 on Serotype 1 outbreaks?

ST1 IPD IRRs, by region and age group



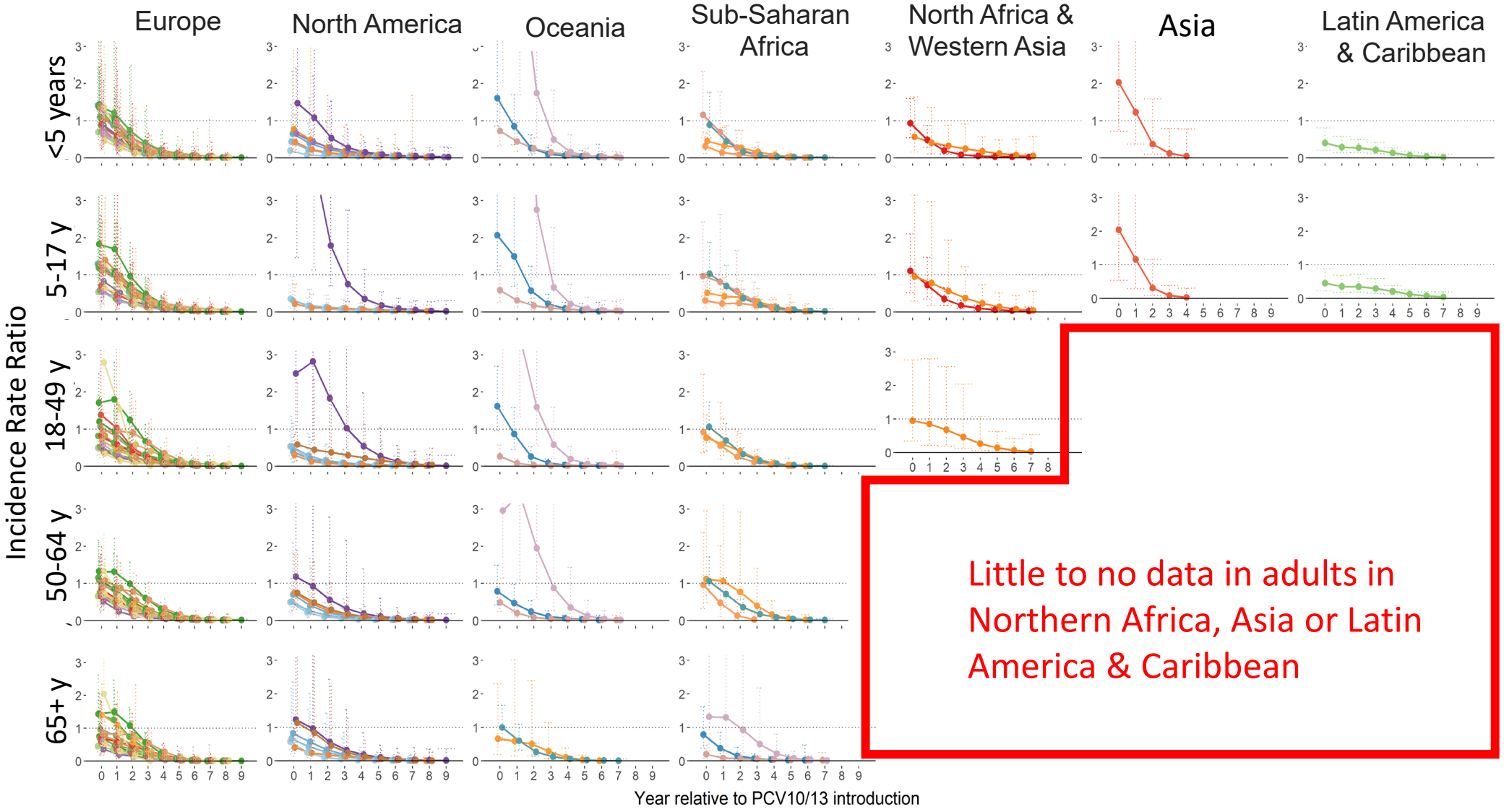
Key messages:

ST1 IPD substantially declined in all sites **among all ages** & **in all regions**

- Including Sub-Saharan Africa, but…
- Did not have data from countries with largest outbreaks (e.g., Burkina Faso, Niger)

Ref: Bennett JC et al. *Microorganisms*. 2021

ST1 IPD IRRs, by region and age group

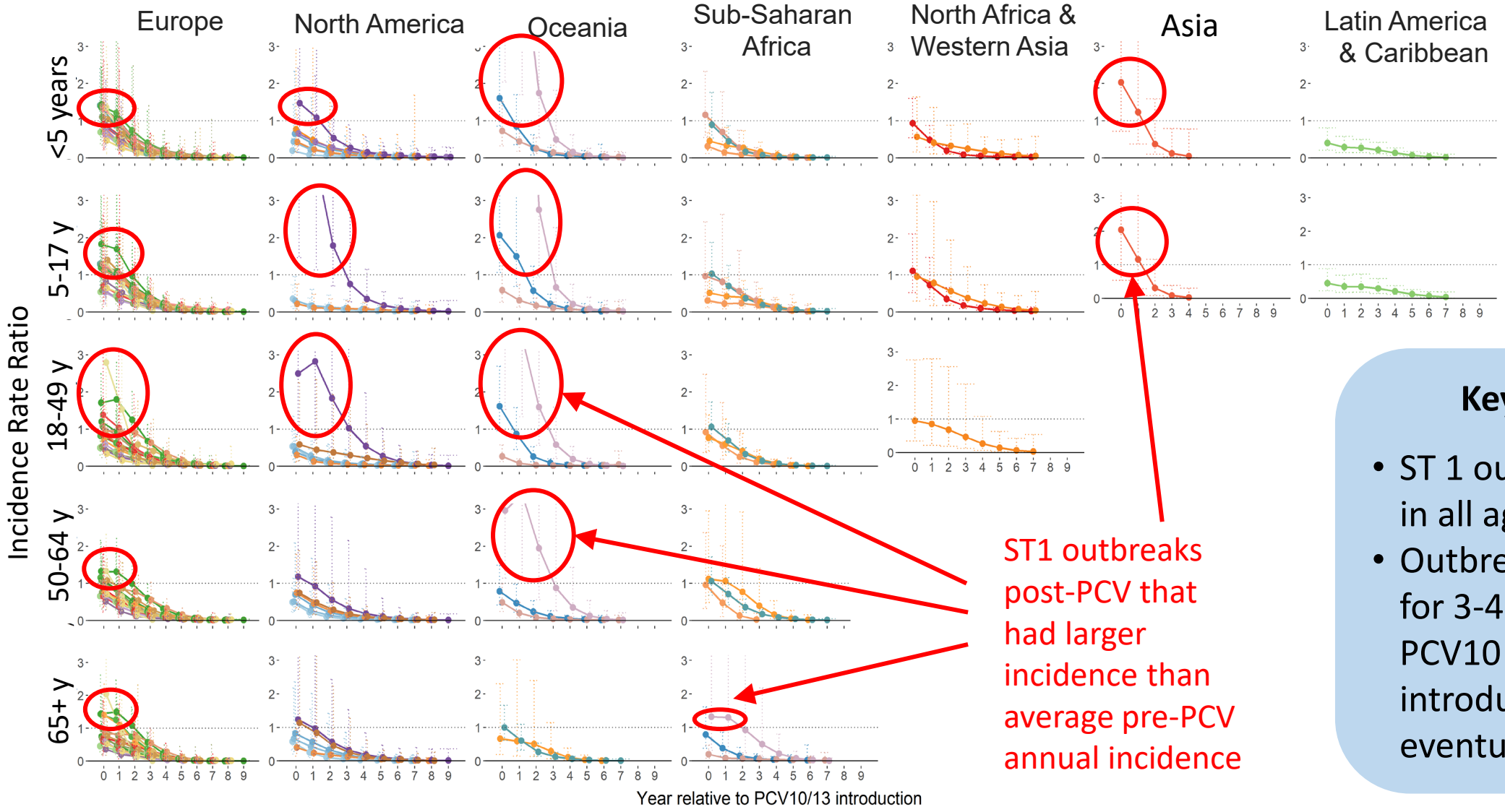


Little to no data in adults in Northern Africa, Asia or Latin America & Caribbean

Also do not have adult data in all regions

Ref: Bennett JC et al. *Microorganisms*. 2021

ST1 IPD IRRs, by region and age group



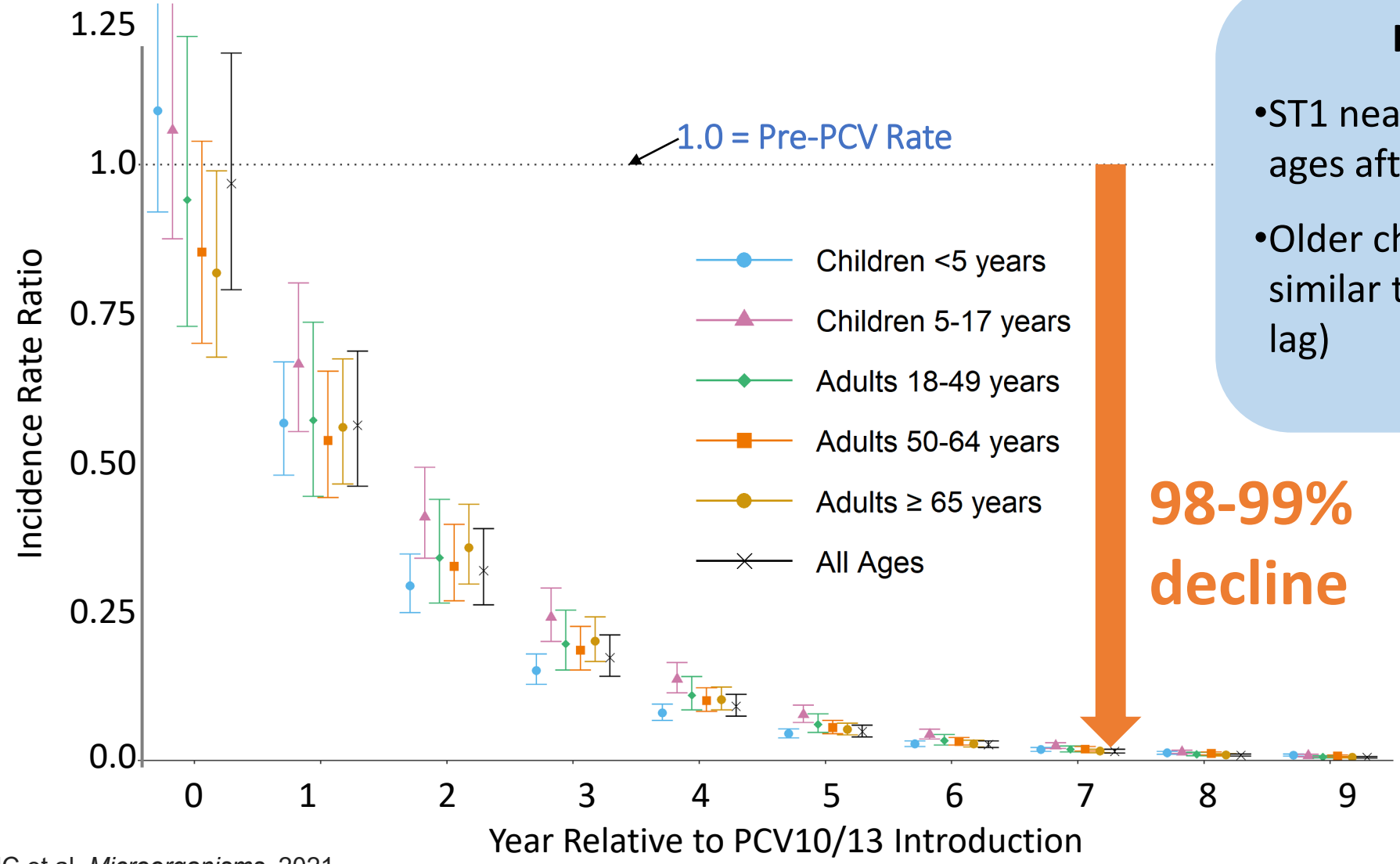
ST1 outbreaks post-PCV that had larger incidence than average pre-PCV annual incidence

Key messages:

- ST 1 outbreaks occurred in all age groups
- Outbreaks continued for 3-4 years after PCV10 and 13 introduction, but eventually stopped

Ref: Bennett JC et al. *Microorganisms*. 2021

Global weighted average IRRs for serotype 1 IPD: All age groups



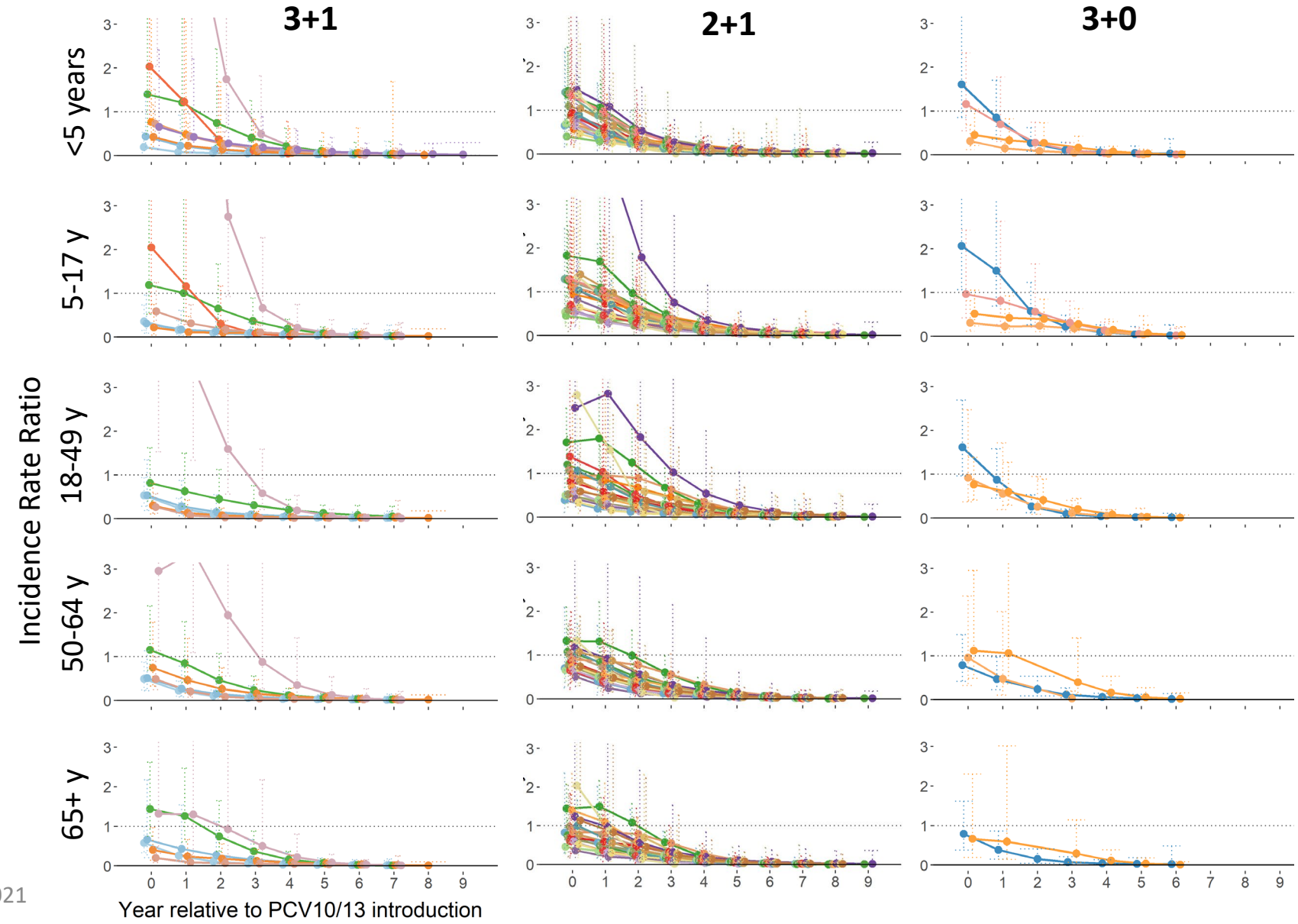
Key messages:

- ST1 nearly eliminated in all ages after 6 years
- Older children and adults similar to children <5y (small lag)

Bennett JC et al. *Microorganisms*. 2021

6. Did dosing schedule affect vaccine impact?
Is a booster dose needed?

Impact of Vaccine Schedule on Serotype 1 IRR



Key messages:

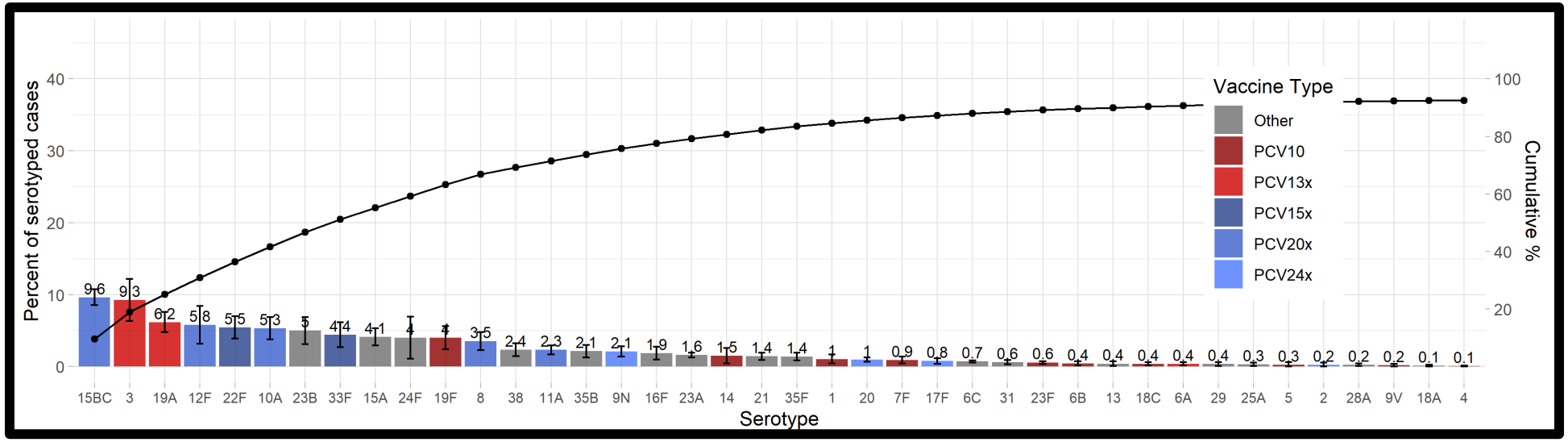
ST1 IRR decreased in all age groups similarly by vaccination schedule

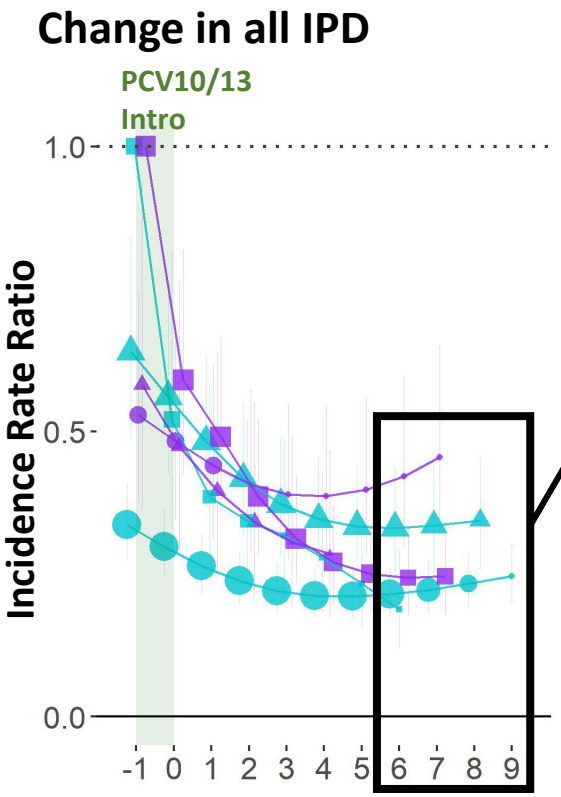
Reference: Bennett JC et al. *Microorganisms*. 2021

7. What pneumococcal serotypes remain?

8. What proportion of remaining disease is caused by serotypes covered by future higher-valency PCV products?

Serotype distribution after extensive PCV10/13 use



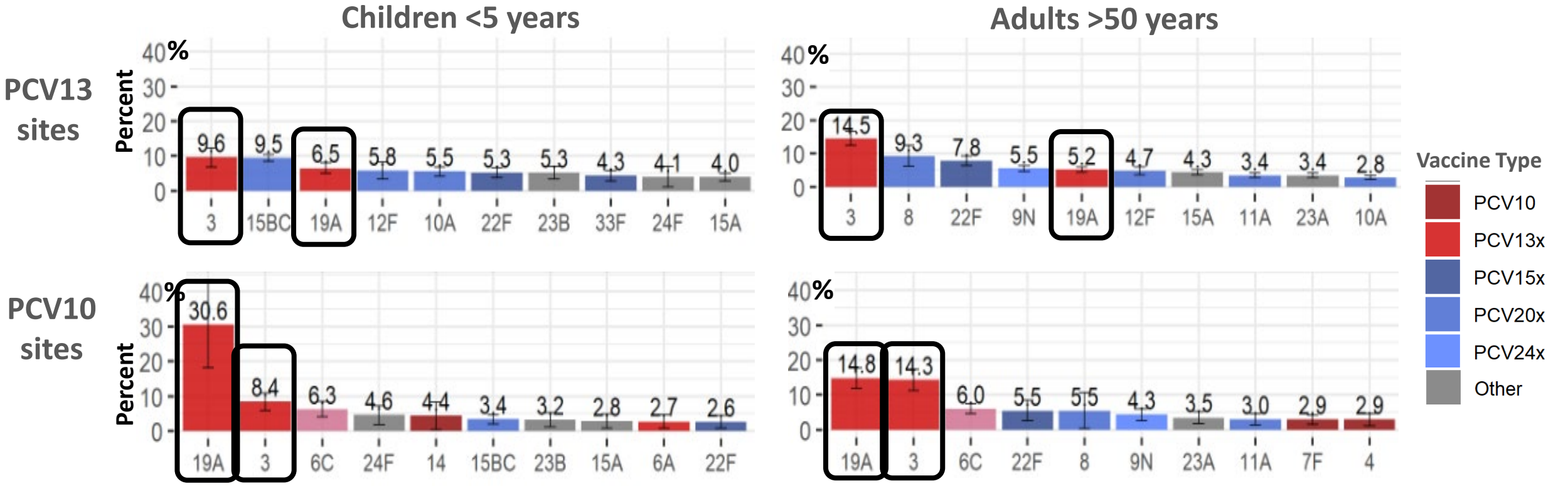


When did serotype distribution stabilize:

Children <5 years: after ~5 years of PCV10/13 use

Adults: after ~7 years of use

Serotype distribution after extensive PCV10/13 use (after 5-7 years use)

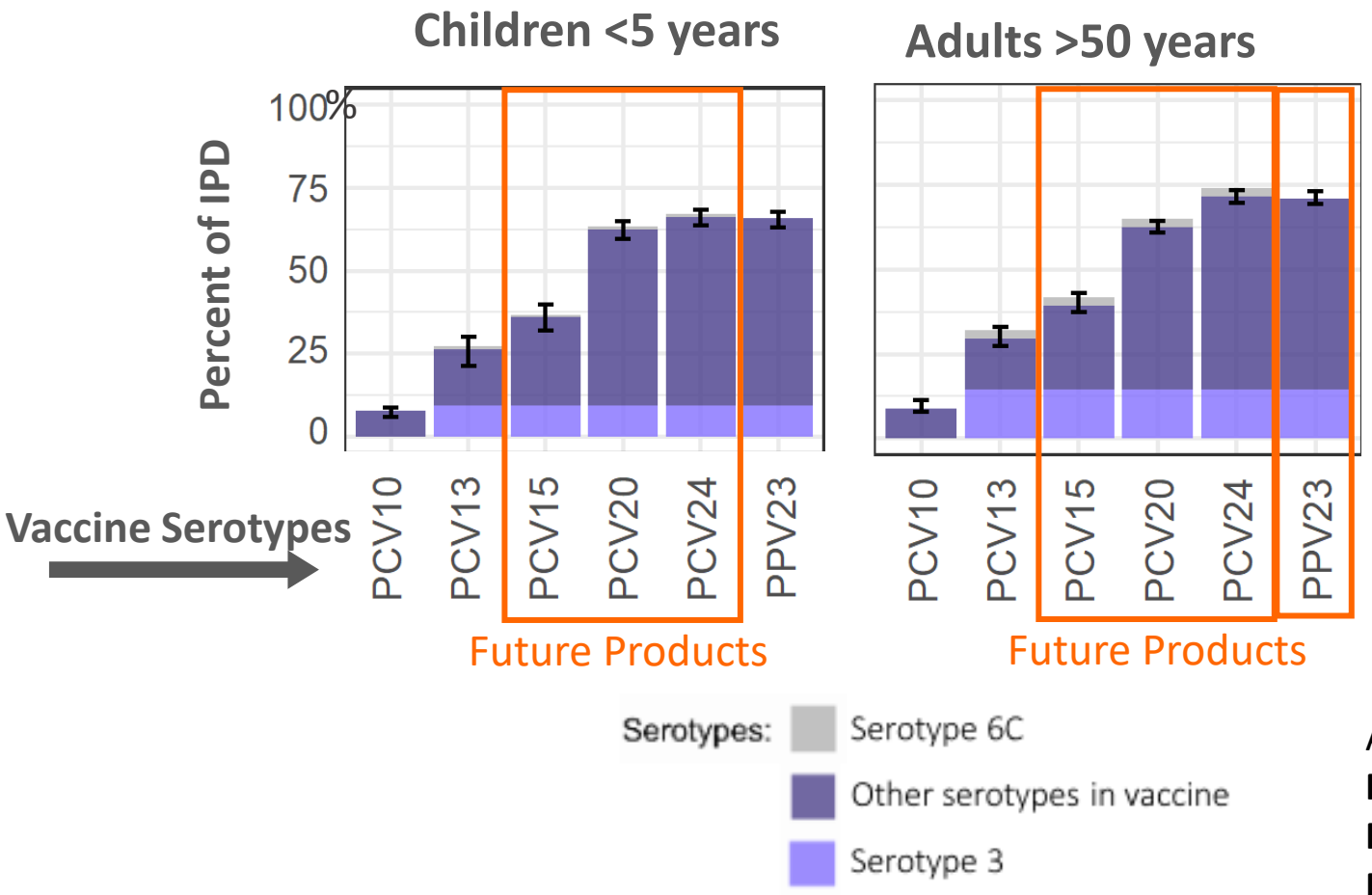


Key messages:

- ST 3 was dominant and at both PCV10 and PCV13 sites, and in both children and adults
- STs 19A was the leading serotypes at PCV10 sites and still observed at PCV13 sites

Percent of remaining IPD due to serotypes included in future vaccines

PCV13 Sites



Key messages:

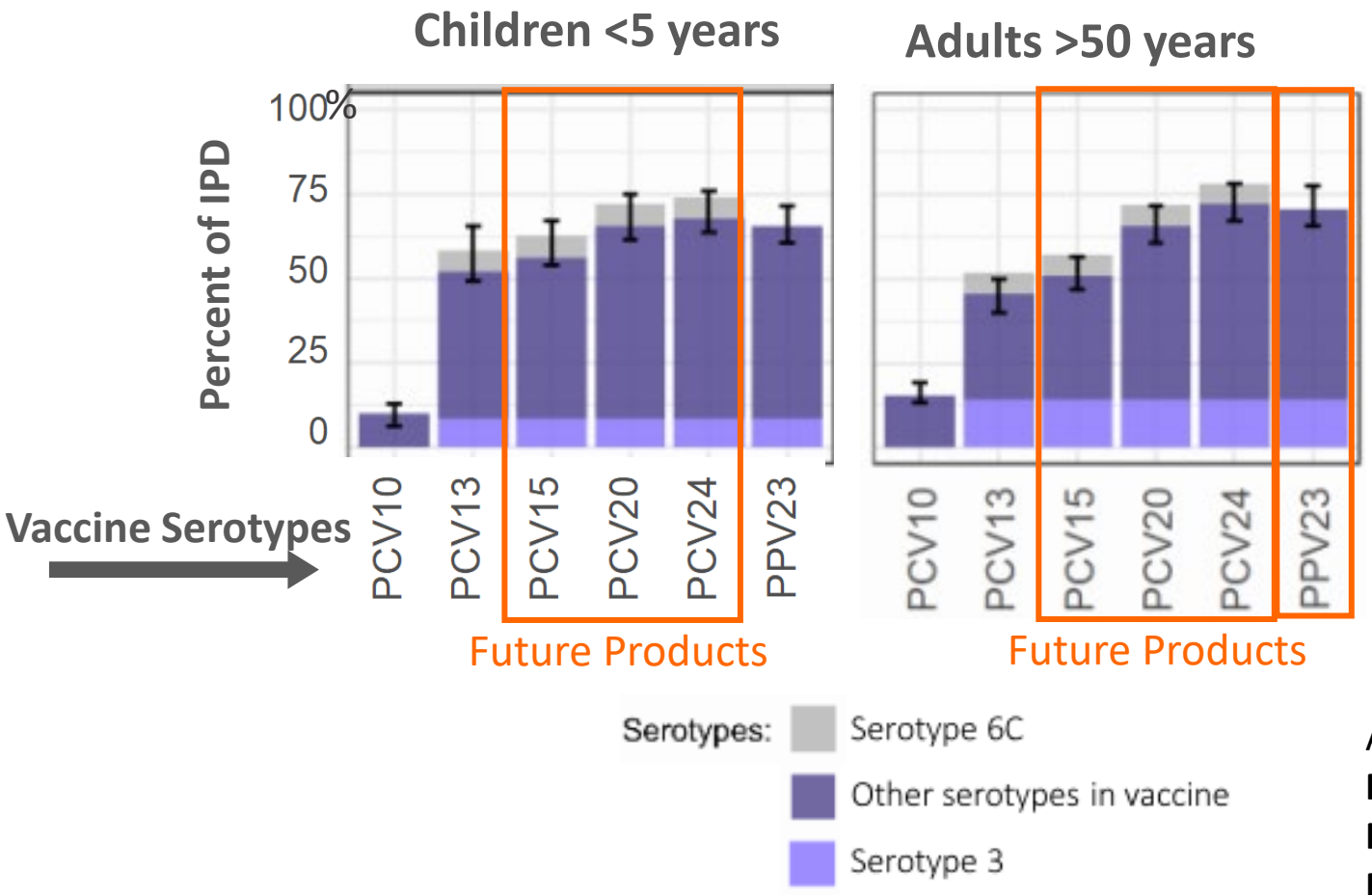
Future PCVs (PCV20 & PCV24) cover 50-60% of remaining cases (after excluding ST3)

Polysaccharide 23-valent (PPV23) covers ~60% of IPD in adults (after excluding ST3)

Additional Serotypes Covered by:
PCV15: 22F, 33F
PCV20: 22F, 33F, 8, 10A, 11A, 12F, 15BC
PCV24: 22F, 33F, 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20

Percent of remaining IPD due to serotypes included in future vaccines

PCV10 Sites



Key messages:

Results were similar for PCV10 sites

Additional Serotypes Covered by:
PCV15: 22F, 33F
PCV20: 22F, 33F, 8, 10A, 11A, 12F, 15BC
PCV24: 22F, 33F, 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20

Summary of PCV10 & PCV13 Impact

- All IPD in children <5 years declined 60-79%
  - Similar for PCV10 & PCV13
- All IPD declined on average ~20% in adults but was heterogeneous among sites
- Vaccine serotypes declined substantially in all age groups
- Non-vaccine serotypes increased in all age groups
- Impact on meningitis generally similar to all IPD
- Serotype 1 outbreaks declined substantially – across all age groups, vaccination schedules and regions
- Over half of remaining IPD in children is due to serotypes covered by possible future PCV20 & PCV24
- 75% of remaining adult IPD is due to serotypes covered by PPV23

What is Happening Next

For PSERENADE:

1. Heterogeneity among sites in herd effects in adults
2. Pneumonia cases
3. Determine if some non-VT serotypes emerging faster than others
4. Does a booster schedule matter for some serotypes?

   Ex. Breakthrough 19F cases seen with 3+0 schedule

Globally:

1. Results from Burkina Faso & Ghana anticipated (impact on ST1 in adults)
2. Higher valency PCV products (PCV15, PCV20, PCV24) anticipated
3. Policy/guidance about switching products must be determined
4. Push for data support and well characterized surveillance of older age groups in LMICs (especially in meningitis belt)

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Thank you!

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Publications & Presentations

Meningitis Research Foundation Oral Poster Presentation:

Changes in Pneumococcal Meningitis Incidence Following Introduction of PCV10 and PCV13: Results from the Global PSERENADE Project (J. Yang)

***Microorganisms* 2021: Special Issue on Epidemiology and Vaccination of Bacterial Meningitis**

Changes in Invasive Pneumococcal Disease Caused by Streptococcus pneumoniae Serotype 1 following Introduction of PCV10 and PCV13: Findings from the PSERENADE Project (Bennett, et al.)

Serotype Distribution of Remaining Pneumococcal Meningitis in the Mature PCV10/13 Period: Findings from the PSERENADE Project (Garcia Quesada, et al.)

Global Landscape Review of Serotype-Specific Invasive Pneumococcal Disease among Countries Using PCV10/13: The Pneumococcal Serotype Replacement and Distribution Estimation (PSERENADE) Project (Deloria Knoll, et al.)

WHO SAGE yellow book 2020

Changes in serotype-specific incidence and serotype distribution in older adults following the use of PCV in childhood immunization schedules, Session 9, page 13-16 (Hayford, et al.)

IDWeek 2021 Poster Presentations

Changes in Invasive Pneumococcal Disease Incidence Following Introduction of PCV10 and PCV13 Among Children <5 Years: The PSERENADE Project (J. Bennett)

Serotype Distribution by Age of Remaining Invasive Pneumococcal Disease After Long-Term PCV10/13 Use: The PSERENADE Project (M. Garcia Quesada)

Comparing Changes in Pneumococcal Meningitis Incidence to all Invasive Pneumococcal Disease Following Introduction of PCV10 and PCV13: The PSERENADE Project (Y. Yang)