# Changes in Pneumococcal Meningitis Incidence Following Introduction of PCV10 and PCV13: Results from the Global PSERENADE Project

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## INTRODUCTION

The introduction of pneumococcal conjugate vaccines (PCV10 and PCV13) into national infant immunization programs worldwide has reduced invasive pneumococcal disease (IPD).

Pneumococcal meningitis is a small subset of pneumococcal disease but a major cause of severe childhood morbidity and mortality globally [1].

Because PCV impact may differ by syndrome, we assessed the change in pneumococcal meningitis incidence globally after PCV10/PCV13 introduction for children <5 years and adults ≥18 years, by PCV product.

## MATERIALS & METHODS

**Meningitis** = detection of *S. pneumoniae* in cerebrospinal fluid (CSF)

**Eligibility criteria for inclusion in primary analysis:**

- Site had CSF-positive meningitis incidence data [2]
- No bias over time detecting cases or affecting incidence rates
- At least 50% of isolates serotyped for serotype-specific analyses
- PCV10 or PCV13 used in national infant immunization program
- At least 50% vaccine uptake in birth cohort

**Statistical Analysis**

- Estimated site-specific meningitis incidence rate ratios (IRRs) for each year post-PCV10/13 relative to pre-PCV incidence using Bayesian multi-level, mixed effects Poisson regression
- Sites were grouped according to product (PCV10 vs. PCV13) & prior PCV7 impact (none, moderate or substantial)
- Weighted average IRRs were estimated for each product/PCV7 use group using linear mixed-effects regressions using data from sites with both pre- and post-PCV data only, but data from all sites (incl. post-only) contributed to shape of curve

**References:**

1. Wahl B, O'Brien KL, Greenbaum A, et al.. Global, regional, and national burden of *Streptococcus pneumoniae* and *Haemophilus influenzae* type b in children in the era of conjugate vaccines: updated estimates from 2000-2015. *Lancet Global Health* 2018; 6: e744–e757.
2. Deloria Knoll, M.; Bennett, J.C.; et al. Global Landscape Review of Serotype-Specific Invasive Pneumococcal Disease Surveillance among Countries Using PCV10/13: The Pneumococcal Serotype Replacement and Distribution Estimation (PSERENADE) Project. *Microorganisms* 2021, 9, 742. https://doi.org/10.3390/microorganisms9040742

**Figure 1: Availability of meningitis surveillance data in children <5y and adults ≥18y countries with PCV in the national infant immunization program†**

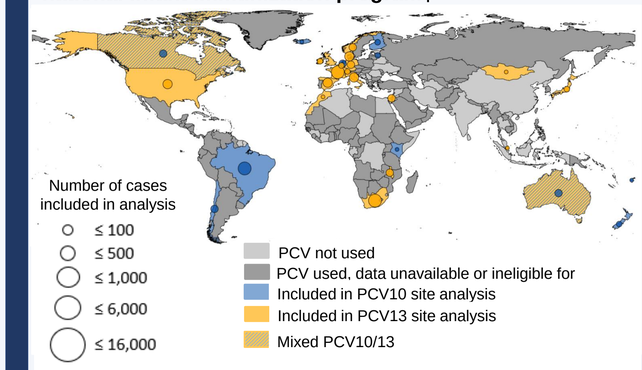



**Table: Summary of data by product and prior PCV7 impact**

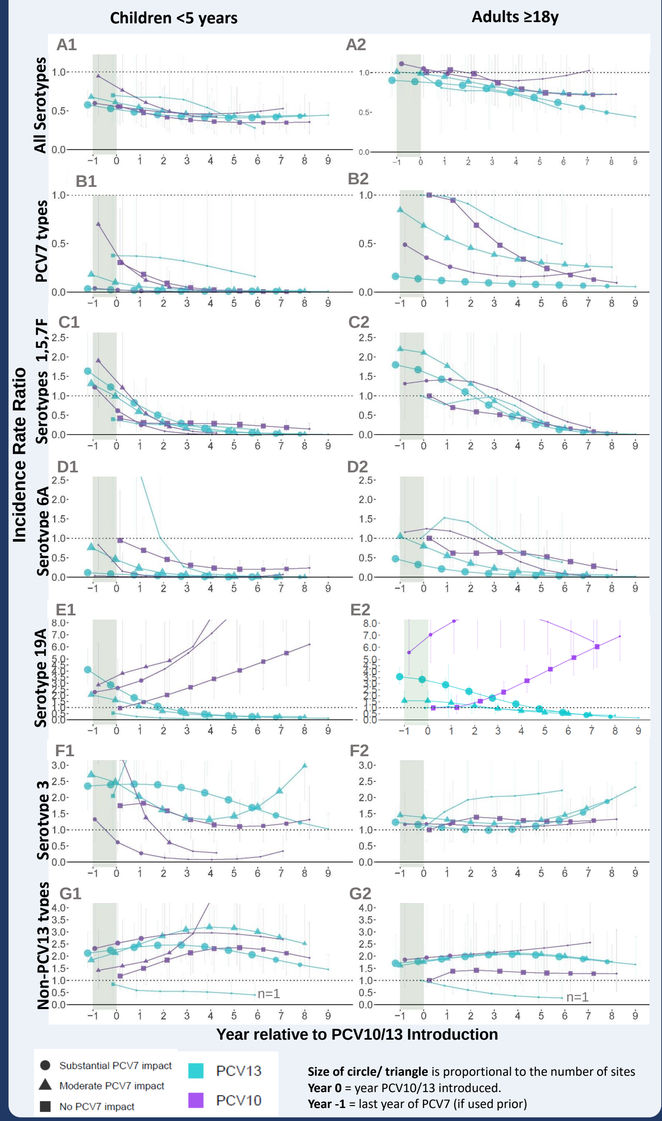
| Infant PCV used[a] | Impact of prior PCV7 use | High income, N sites (%) | Adult PCV/PPV rec., N(%)[b] | Sites, N any data (w/pre&post)[c] <5 years | Sites, N any data (w/pre&post)[c] ≥18 years | Cases, N any data (w/pre&post) <5 years | Cases, N any data (w/pre&post) ≥18 years |
|---|---|---|---|---|---|---|---|
| PCV13 | No use | 0(0%) | 0(0%) | 3(3) | 2(1) | 338(338) | 543(489) |
| | Moderate | 12(92%) | 12(92%) | 13(6) | 13(8) | 6822(6531) | 22328(19956) |
| | Substantial | 15(100%) | 11(92%) | 15(10) | 12(11) | 3292(2838) | 7926(7753) |
| | **Total** | **27(87%)** | **23(88%)** | **31(19)** | **27(20)** | **10452(9707)** | **30797(28207)** |
| PCV10 | No use | 3(50%) | 3(60%) | 6(4) | 5(4) | 2395(2346) | 4675(4191) |
| | Moderate | 3(100%) | 1(50%) | 2(2) | 2(2) | 198(198) | 172(72) |
| | Substantial | 5(100%) | 3(75%) | 5(5) | 4(4) | 364(364) | 928(928) |
| | **Total** | **11(79%)** | **7(64%)** | **13(11)** | **11(10)** | **2957(2908)** | **5775(5191)** |
| **Total** | | **36(82%)** | **28(78%)** | **42(28)** | **36(28)** | **13391(12444)** | **36322(33148)** |

[a]Product widely used in infant immunization program
[b]Adult pneumococcal vaccination is recommended (PPV23 with or without PCV10/13) among sites contributing to adult analysis.
[c]N with any post-PCV10/13 data; in parentheses with both pre-any PCV and post PCV10/13. For children, pre period excludes year of intro.; for adults, pre period includes year of intro.

## RESULTS

- Analyses included 44 surveillance sites (28 with both pre- and post-PCV data, 2 sites contributed data to both) in 33 countries
- Most sites used PCV13 (70%), used PCV7 prior (78%), were primarily high-income (82%), and had an older adult pneumococcal vaccine program (78% of those in adult analysis) (**Figure 1, Table**)

**Figure 2: Impact of PCV on pneumococcal meningitis in children <5y and adults ≥18y by PCV10/13 product and prior PCV7 impact**




## RESULTS: Figure 2

- Extensive PCV7 use in children substantially (~45%) reduced their CSF-positive pneumococcal meningitis prior to switch to PCV10/13, while indirect effects in adults was lower (~10%) (**A1-2, Year -1**)
- After PCV10/13 introduction, most declines in children <5y maximized by year 3-5, then stabilized (**A1-E1**)
- Reduction in all CSF-positive pneumococcal meningitis by year 5 was >50% in children <5y for both products, and ~30% in adults for most sites (**A1-2**)
- Vaccine-containing types (**PCV10: B-C; PCV13: B-E**) were virtually eliminated by year 5 for <5y, and took longer for ≥18y, with exception of serotype 3 for PCV13 which did not decline (**F1-2**)
- Serotype 19A was almost eliminated by PCV13 in both age groups but increased at PCV10 sites (**E1-2**)
- Serotype 3 was dynamic over the time period with no clear vaccine impact for either product (**F1-2**)
- Non-PCV13 serotypes (those not covered by either vaccine) increased in both age groups and both products, and peaked by year 5 (except one strata that declined, which had a single high HIV-prevalence site with concurrent non-vaccine interventions, including ART) (**G1-2**)
- **Limitations:** Data from low-income, high-burden, and meningitis-belt regions were sparse; direct comparisons between PCV10 and PCV13 were constrained due to few PCV10 sites; estimates may not reflect an individual site's experience.

## CONCLUSION

- PCVs reduced CSF-positive pneumococcal meningitis by over 50% after substantial use in children <5 years of age, driven by substantial declines in vaccine-type disease, which were partially offset by increases in non-vaccine-type disease
- Impact among adults showed overall net declines in most sites, but lower than for <5 years
- Pneumococcal meningitis was further reduced after switch from PCV7 to PCV10/13 at most sites
- Despite this study being global and the largest ever, nuanced comparisons of rate of decline between products are limited

*The **PSERENADE Team** includes the Hopkins Core Team & investigators in over 50 surveillance sites and at the WHO.

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