

Ecological evidence of Pneumococcal Conjugate Vaccine impact on suspected pneumococcal pneumonia in the Pneumonia Etiology for Child Health (PERCH) study

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INTRODUCTION



The introduction of pneumococcal conjugate vaccine (PCV) reduces the incidence of pneumonia with chest X-ray alveolar consolidation (CXR-AC) [1] and vaccine-type nasopharyngeal (NP) carriage [2], a precondition for pneumococcal pneumonia. The latter has been documented at the community level. However measuring vaccine impact on pneumococcal pneumonia using these tests is limited because they have imperfect sensitivity and specificity for vaccine-type (VT) pneumococcal pneumonia. As the case definition increases in specificity the relative reduction in cases should increase, but with a loss of absolute impact. We assessed the effect of PCV coverage on VT colonized cases using four case definitions for suspected pneumococcal pneumonia.

METHODS

- **PERCH study** collected data between 2011 and 2014 [3]:
 - Cases aged 1-59 months hospitalized with WHO-defined severe or very severe pneumonia
 - Community controls aged 1-59 months
 - Sites in seven African and Asian countries
- **PCV community biologic coverage:** The age-standardized proportion of controls aged ≥ 2 months who received ≥ 3 doses, or ≥ 2 doses if both given ≥ 12 months of age, or ≥ 1 dose if given ≥ 24 months of age (Table 1)
- **Pneumococcal PCR positive:** Either pneumococcal PCR density in the nasopharynx/oropharynx (NP/OP) $\geq 6.9 \log_{10}$ copies/mL (or $\geq 4.4 \log_{10}$ copies/mL for those with prior antibiotic treatment) or $> 2.2 \log_{10}$ copies/mL in whole blood (WB)
- **Case definitions for suspected pneumococcal pneumonia:**
 - CXR-AC
 - CXR-AC and CRP > 40 mg/L
 - CXR-AC and pneumococcal PCR positive
 - CXR-AC and CRP > 40 mg/L and pneumococcal PCR positive
- **Analysis:** Ratios of 7-valent-type to non-7-valent-type NP colonization among each case definition compared between sites

RESULTS

Suspected pneumococcal pneumonia case definitions:

- 967/4232 (23%) cases had CXR-AC. Of these 857/967 (89%) had results available for CRP and pneumococcal PCR (Figure 1)

Vaccine-type NP growth:

- 849/857 (99%) cases had an NP culture performed (Figure 1)
- The proportion of NP pneumococcus that was 7-valent-type was:
 - 149/419 (36%) for CXR-AC
 - 86/230 (37%) for CXR-AC and CRP ≥ 40 mg/L
 - 113/180 (39%) for CXR-AC and pneumococcal PCR positive
 - 66/156 (42%) for CXR-AC and CRP > 40 mg/L and pneumococcal PCR positive
- The odds of vaccine-type colonization was lower among sites with PCV compared to sites without PCV (Table 2)
- The point estimate for relative reduction in odds of pneumococcal pneumonia decreased for more specific case definitions in Kenya and Gambia, where PCV coverage was estimated to be highest

TABLE 1: PCV community biologic coverage status

SITE	ENROLMENT START DATE	VACCINE	DATE INTRODUCED ^a	CONTROLS (N)	VACCINATED (%) ^b
Kenya	Aug 2011	PCV10	Feb 2011	853	73%
Gambia	Nov 2011	PCV13	Aug 2009	646	61%
South Africa	Aug 2011	PCV13	Apr 2009	774	44%
Mali	Jan 2012	PCV13	Mar 2011	678	33%
Zambia	Oct 2011	PCV13	Jul 2013	574	0%
Bangladesh	Jan 2012	None	Not routine	769	0%
Thailand	Jan 2012	None	Not routine	651	0%

^a Zambia introduced PCV during the study period; South Africa and The Gambia both began with PCV7 and switched to PCV13 in May 2011; ^b Age-standardized proportion

FIGURE 1: Flow diagram of specimen results

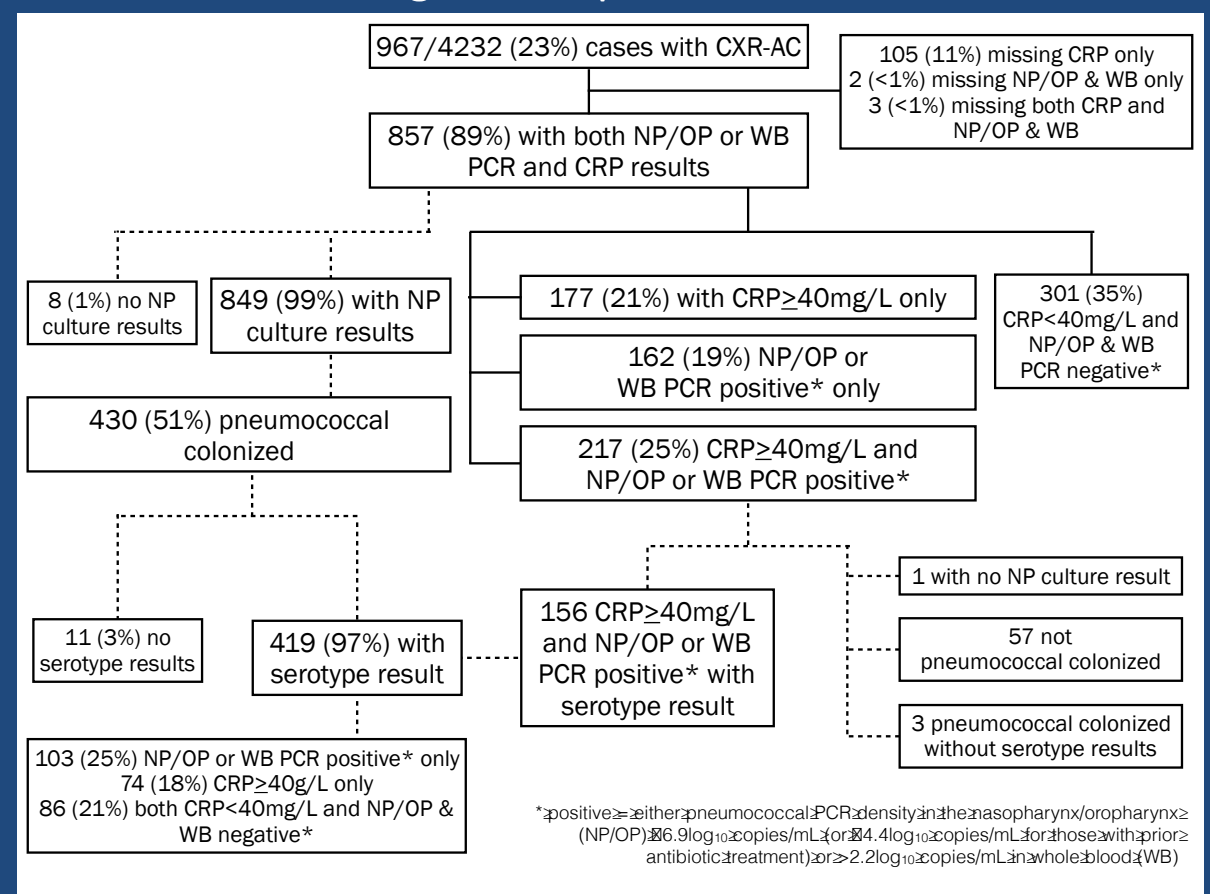


TABLE 2: Odds ratios of vaccine-type NP colonization for differing case definitions of pneumococcal pneumonia

SITE	CXR-AC	CXR-AC & CRP ≥ 40	CXR-AC & PCR+	CXR-AC & CRP ≥ 40 & PCR+
No PCV	Ref	Ref	Ref	Ref
Kenya	0.45 (0.23,0.89)	0.32 (0.11,0.92)	0.45 (0.18,1.13)	0.26 (0.06,1.05)
Gambia	0.19 (0.09,0.39)	0.18 (0.06,0.50)	0.14 (0.05,0.39)	0.11 (0.02,0.43)
South Africa	0.36 (0.21,0.62)	0.34 (0.15,0.74)	0.40 (0.20,0.78)	0.34 (0.13,0.86)
Mali	0.44 (0.23,0.85)	0.32 (0.12,0.81)	0.43 (0.18,1.01)	0.31 (0.09,1.00)

Data presented as odds ratios (95% confidence interval); No PCV=Bangladesh, Thailand, and Zambia; CRP = C-reactive protein; PCR+ = either pneumococcal PCR density in NP/OP $\geq 6.9 \log_{10}$ copies/mL (or $\geq 4.4 \log_{10}$ copies/mL for those with prior antibiotic treatment) or $> 2.2 \log_{10}$ copies/mL in whole blood

CONCLUSIONS

- In sites with PCV compared to those without, the odds of vaccine-type pneumococcal colonization was lower for all case definitions of pneumococcal pneumonia, which suggests evidence of PCV impact on pneumonia
- Compared to CXR-AC alone, the addition of CRP plus high pneumococcal PCR density in nasopharynx/oropharynx and whole blood shows a further increase in the point estimate for vaccine effect. This provides limited evidence to suggest this case definition may be more specific for vaccine-type pneumococcus
- Our findings are limited by low case numbers in many strata
- This case definition may be useful to assign suspected pneumococcal etiology for cases with evidence of radiographic pneumonia but further validation is required

References

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Funding

PERCH was supported by grant 48968 from The Bill & Melinda Gates Foundation to the International Vaccine Access Center, Department of International Health, Johns Hopkins Bloomberg School of Public Health.

