RWD174

Predicting Effectiveness For the 20-Valent Pneumococcal Conjugate Vaccine Against IPD in Children For 3+1 and 2+1 Dosing Regimens From Immunogenicity Data - A Modelling Study Based On Serotype-Specific Correlates of Protection

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INTRODUCTION

- Clinical trials of pneumococcal conjugate vaccines (PCVs) in infants use a single protective concentration (Cp) against invasive pneumococcal disease (IPD) for all serotypes in new formulations.
- However, Cp likely varies by serotype. Previous modeling studies have aimed to estimate Cps and predict vaccine effectiveness (VE) for serotypes in higher-valent PCVs using post-primary series endpoints from clinical trials.
- This study refined this approach by estimating serotype-specific Cp and predictive VE for PCV20 in 2+1 and 3+1 dosing schedules.

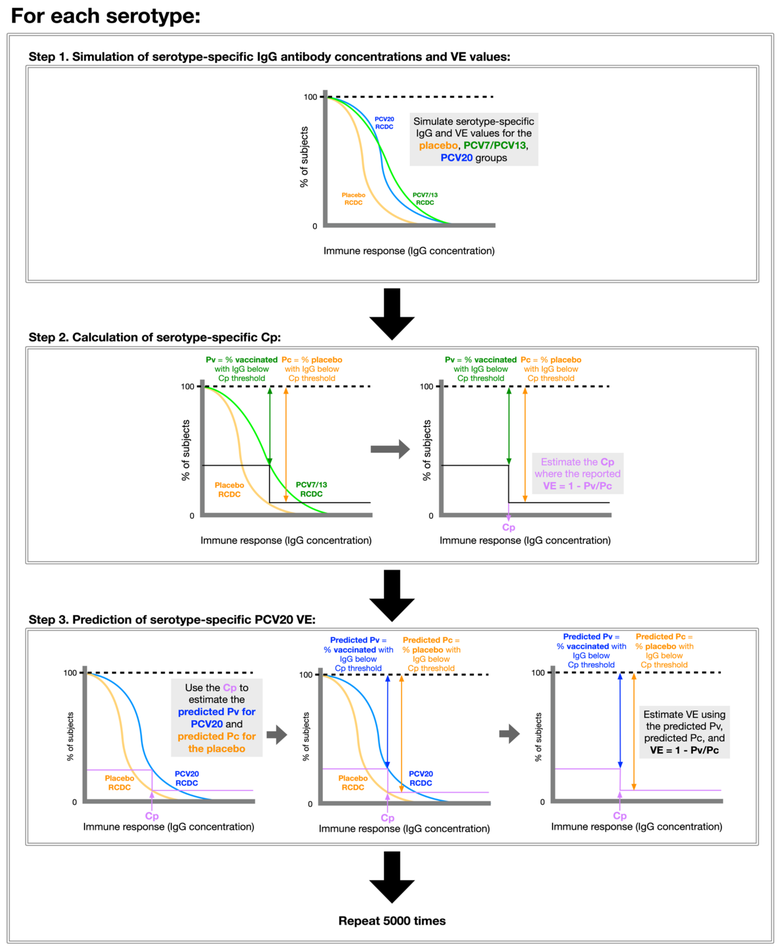
OBJECTIVE

The current study sought to estimate serotype-specific Cp and predictive VE using post-primary series and post-toddler dose summary-level IgG concentrations for PCV20 in 2+1 and 3+1 schedules and assess the reliability of the methodology via sensitivity analyses.

METHODS

- We computed serotype-specific Cps utilizing real-world effectiveness (RWE) data, and then used the newly derived Cps to predict VE of PCV20 in a serotype-specific manner using summary-level clinical trial data.
- The simulation process was executed by applying Siber et al. methodology used in previous work (1-4).
- We evaluated the method using:
  1. different sources of RWE to compute Cps
  2. immunogenicity to predict VE
- Finally, we report the variability in predicted serotype-specific VE of PCV20 for both 2+1 and 3+1 schedules.
- Data sources for the base case and sensitivity analyses can be found in the supplemental file.

Figure 1. Schematic of the RCDC modelling method to calculate serotype-specific Cp and predict PCV20 VE values



RESULTS

Table 1. Predicted serotype-specific Cp and PCV20 VE for 2+1 and 3+1 dosing schedules after the booster dose

Serotype	Predicted protective antibody concentration median (95% CI) µg/mL		Observed PCV7/13 VE median % (95% CI)		Predicted PCV20 VE median % (95% CI)	
	PCV20 post dose 4 in 3+1 dosing schedule	PCV20 post dose 3 in 2+1 dosing schedule	3+1 dosing schedule[5,6] (greater than 1 dose**)	2+1 dosing schedule[7] (completion of schedule**)	Post dose 4 in 3+1 dosing schedule	Post dose 3 in 2+1 dosing schedule
4	0.90 (0.43, 2.76)	0.83 (0.55, 1.19)	93 (65, 99)	96.1 (92, 98)*	91 (57, 98)	93 (87, 97)
6B	0.95 (0.48, 2.54)	0.39 (0.13, 2.21)	94 (77, 98)	95.9 (72, 99)	90 (68, 97)	94 (60, 99)
9V	0.29 (0.13, 1.50)	0.99 (0.50, 2.81)	100 (88, 100)	97.4 (77, 100)	100 (82, 100)	94 (65, 99)
14	1.20 (0.67, 2.52)	0.51 (0.22, 1.04)	94 (81, 98)	97.6 (92, 99)	92 (78, 97)	96 (88, 99)
18C	0.63 (0.31, 1.50)	0.68 (0.47, 0.95)	97 (85, 99)	96.1 (92, 98)*	96 (79, 99)	93 (87, 97)
19F	1.74 (0.94, 4.09)	1.91 (1.07, 4.18)	87 (65, 95)	92.3 (76, 98)	87 (61, 96)	88 (68, 96)
23F	0.46 (0.14, 2.14)	0.46 (0.27, 0.74)	98 (80, 100)	96.1 (92, 98)*	95 (68, 99)	93 (86, 97)
1	0.73 (0.51, 1.09)	0.93 (0.54, 1.99)	87 (77, 93)*	85.4 (63, 94)	78 (65, 86)	77 (47, 91)
3	0.44 (0.24, 1.42)	0.79 (0.50, 1.70)	80 (30, 95)	65.5 (34, 82)	60 (20, 80)	46 (21, 63)
5	0.76 (0.52, 1.18)	0.84 (0.59, 1.27)	87 (77, 93)*	83.4 (74, 90)*	82 (69, 89)	77 (64, 85)
6A	4.14 (2.94, 6.17)	1.55 (0.63, 6.42)	86 (76, 93)*	95.9 (72, 99)	81 (68, 88)	93 (61, 99)
7F	1.15 (0.67, 2.45)	0.50 (0.20, 1.83)	97 (83, 100)	94.1 (76, 99)	94 (73, 99)	100 (84, 100)
19A	1.35 (0.83, 2.44)	1.55 (1.03, 2.42)	86 (71, 94)	89.1 (80, 94)	85 (67, 94)	85 (74, 91)

**Aggregate observed VE data for PCV7/PCV13 is used for certain serotypes where serotype-specific observed VE data are not available.*
*** The same observed VE for PCV7/13 is applied to both the pre-booster and post-booster doses in the 3+1 or 2+1 dosing schedules analyses.*
Note: Serotype-specific Cp values were derived from simulated placebo GMC, PCV7/13 GMC, and observed PCV7/13 vaccine effectiveness using the RCDC curve; Absolute differences in Cp values were calculated before and after the booster dose for the same dosing schedule. Serotype-specific VE values were derived from simulated placebo GMC, PCV20 GMC, and serotype-specific Cp value using the RCDC curve; The same serotype-specific observed PCV7/13 VE values were used for the same dosing schedule before and after the booster dose in the model.
Abbreviations: *GMC: geometric mean concentration; VE: vaccine effectiveness; Cp: protective antibody concentration; CI: confidence interval; RCDC: reverse cumulative distribution curves; PCV: pneumococcal conjugate vaccine*
[5]Source: Whitney et al. (2006). Effectiveness of seven-valent pneumococcal conjugate vaccine against invasive pneumococcal disease: a matched case-control study.
[6]Source: Moore et al. (2016). Effectiveness of 13-valent pneumococcal conjugate vaccine for prevention of invasive pneumococcal disease in children in the USA: a matched case-control study.
[7]Source: Savulescu et al. (2022). Effectiveness of 10 and 13-valent pneumococcal conjugate vaccines against invasive pneumococcal disease in European children: SpIDnet observational multicentre study.

Figure 2. Predicted mean PCV20 VE vs. observed mean PCV13 VE for post-dose 4 in 3+1 base case

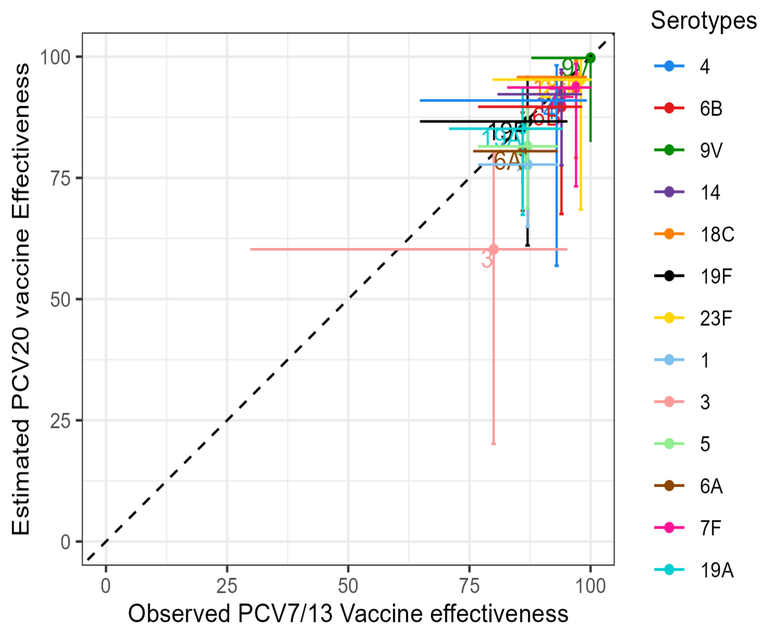
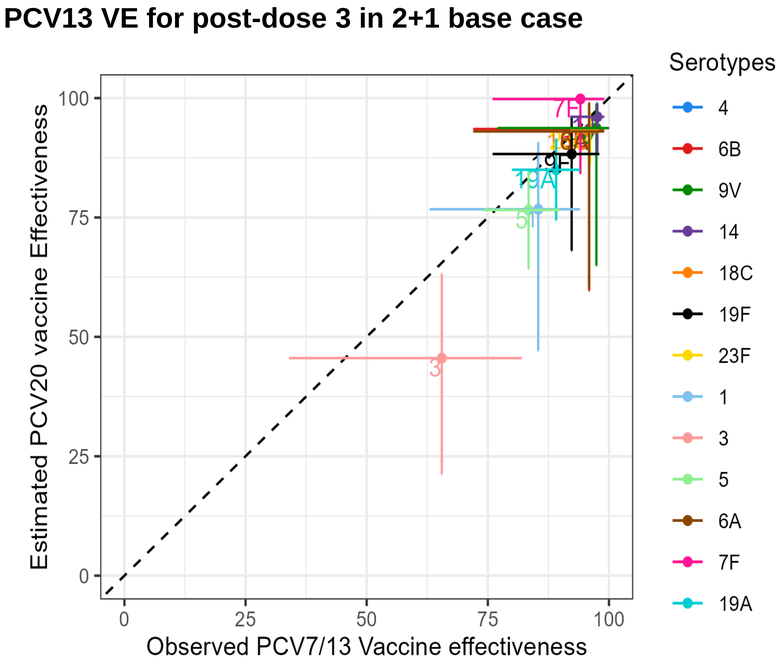


Figure 3. Predicted mean PCV20 VE vs. observed mean PCV13 VE for post-dose 3 in 2+1 base case



- Predicted VEs for PCV20 serotypes are relatively high and largely similar to that observed for PCV7/13 in the 3+1 schedule (Figure 2), as well as in the 2+1 schedule (Figure 3).
- Within serotype comparisons for 3+1 versus 2+1 schedules, there were very minor point estimate differences in predicted VE.
- The predicted VE for serotype 3 had the widest confidence intervals versus other serotypes (Table 1) for both schedules.
- Variations in estimated Cp and predicted VE were observed across serotypes, dosing schedules, and post-booster vs post-primary endpoints (supplemental material).

CONCLUSIONS

- **This is the first study to generate serotype-specific Cp and predictive VE against IPD using the post-booster endpoint.**
- **The estimated Cps from our evaluation suggest relatively high serotype specific VE for PCV20 similar to that observed for PCV7/13 in both the 3+1 and 2+1 analyses.**
- **Evaluating higher-valent PCVs VE with this method remains in its infancy given variability in estimates demonstrated in sensitivity analyses.**
- **These modeled data will need to be confirmed by results from post-licensure RWE studies.**

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Disclosure

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