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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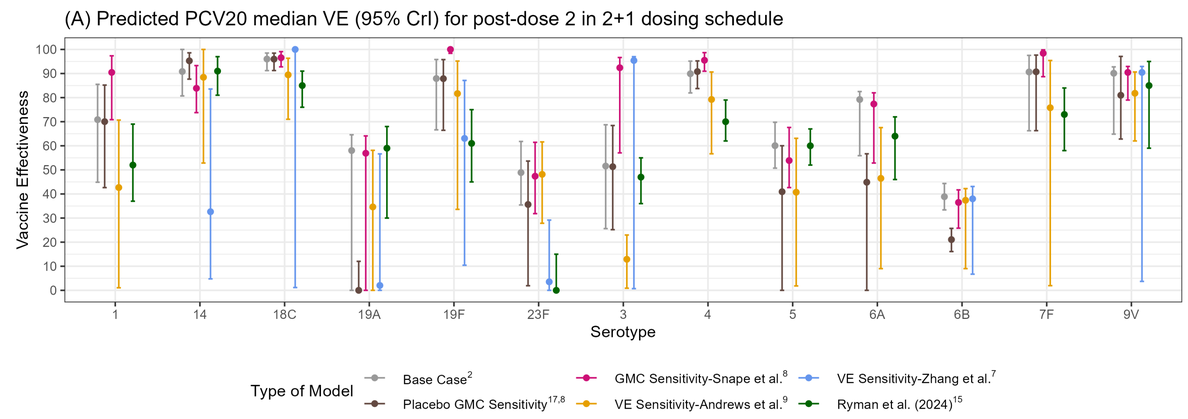
Table S1. Summary-level base case input data and sources for observed geometric mean anti-body level concentrations for 2+1 and 3+1 dosing schedule

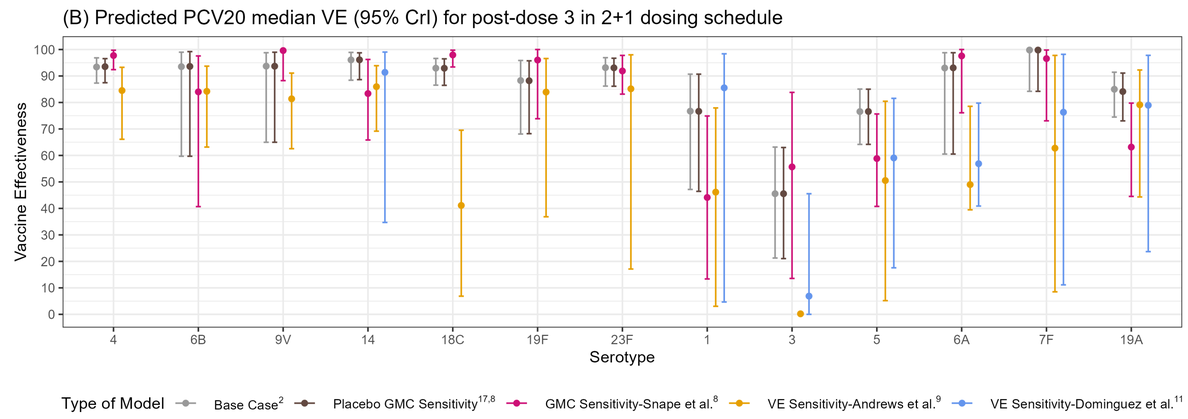
	Observed geometric mean serotype-specific antibody concentration (µg/mL)				
Serotype	Placebo (95% CI)[1]	PCV13 post dose 3 (95 % CI)[2]	PCV20 post dose 3 (95% CI)[3]	PCV13 post dose 4 (95 % CI)[3]	PCV20 post dose 4 (95% CI)[3]
4	0.03 (0.03, 0.04)	5.36 (4.91, 5.85)	4.11 (3.77, 4.48)	4.84 (4.5, 5.22)	3.77 (3.52, 4.04)
6B	0.08 (0.07, 0.08)	4.63 (4.09, 5.25)	2.64 (2.36, 2.95)	5.74 (5.27, 6.24)	4.01 (3.7, 4.35)
9V	0.06 (0.05, 0.06)	5.04 (4.67, 5.43)	3.68 (3.42, 3.97)	4.3 (4.02, 4.59)	3.44 (3.23, 3.67)
14	0.22 (0.20, 0.24)	5.66 (5.12, 6.26)	4.52 (4.08, 5.00)	6.34 (5.88, 6.83)	5.68 (5.27, 6.12)
18C	0.06 (0.06, 0.07)	3.61 (3.33, 3.91)	2.71 (2.52, 2.93)	4.69 (4.34, 5.05)	3.46 (3.24, 3.7)
19F	0.14 (0.13, 0.15)	8.08 (7.40, 8.83)	6.19 (5.68, 6.75)	5.79 (5.36, 6.25)	5.01 (4.68, 5.36)
23F	0.08 (0.08, 0.09)	4.4 (3.95, 4.90)	2.64 (2.40, 2.91)	6.18 (5.66, 6.75)	3.95 (3.63, 4.31)
1	0.05 (0.04, 0.05)	2.53 (2.33, 2.75)	1.71 (1.58, 1.84)	2.12 (1.97, 2.27)	1.47 (1.37, 1.57)
3	0.06 (0.06, 0.06)	1.09 (1.01, 1.17)	0.72 (0.67, 0.78)	0.85 (0.8, 0.9)	0.56 (0.53, 0.6)
5	0.12 (0.11, 0.13)	2.41 (2.21, 2.64)	1.74 (1.60, 1.89)	2.51 (2.33, 2.7)	1.87 (1.74, 2)
6A	0.08 (0.08, 0.08)	11.82 (10.66, 13.11)	7.75 (7.04, 8.53)	11.69 (10.91, 12.53)	9.01 (8.45, 9.61)
7F	0.09 (0.08, 0.09)	4.63 (4.09, 5.25)	3.61 (3.40, 3.84)	5.18 (4.88, 5.49)	3.91 (3.7, 4.14)
19A	0.25 (0.23, 0.26)	5.49 (5.02, 6.01)	4.51 (4.11, 4.94)	4.13 (3.84, 4.45)	3.53 (3.3, 3.77)

**Aggregate observed VE data for PCV7/PCV13 is used for certain serotypes where serotype-specific observed VE data is not available.*
[1]Source: Ryman et al. (2022)
[2]Source: Korbal et al. (2024)
[3]Source: Senders et al. (2024)

Figure S1. Serotype-specific predicted PCV20 median VE (95% CI) across base case and sensitivity analyses



[2]Source: Korbal et al. (2024). Phase 3 Safety and Immunogenicity Study of a Three-Dose Series of Twenty-Valent Pneumococcal Conjugate Vaccine in Healthy Infants and Toddlers.
[7]Source: Zhang et al. (2021). Effectiveness of 13-Valent Pneumococcal Conjugate Vaccine against Community Acquired Pneumonia among Children in China, an Observational Cohort Study.
[8]Source: Snape et al. (2010). Immunogenicity and Reactogenicity of a 13-Valent-Pneumococcal Conjugate Vaccine Administered at 2, 4, and 12 Months of Age: A Double-Blind Randomized Active-Controlled Trial.
[9]Source: Andrews et al. (2019). Effectiveness of the Seven-Valent and Thirteen-Valent Pneumococcal Conjugate Vaccines in England: The Indirect Cohort Design, 2006-2018.
[15]Source: Ryman et al. (2024). Potential serotype-specific effectiveness against IPD of pneumococcal conjugate vaccines V114 and PCV20 in children given a 2+1 dosing regimen.
[17]Source: Siber et al. (2007). Estimating the protective concentration of anti-pneumococcal capsular polysaccharide antibodies.

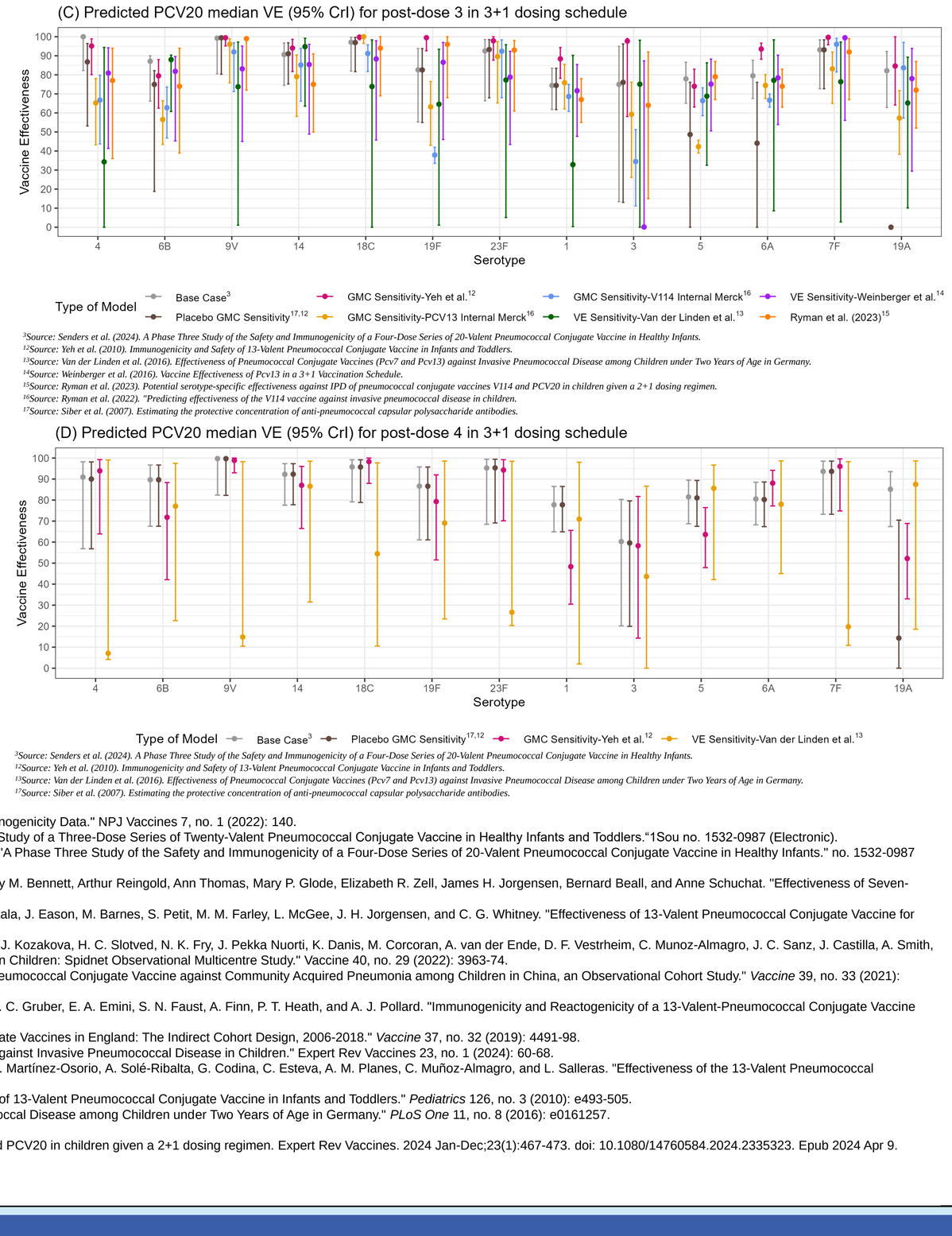


[2]Source: Korbal et al. (2024). Phase 3 Safety and Immunogenicity Study of a Three-Dose Series of Twenty-Valent Pneumococcal Conjugate Vaccine in Healthy Infants and Toddlers.
[8]Source: Snape et al. (2010). Immunogenicity and Reactogenicity of a 13-Valent-Pneumococcal Conjugate Vaccine Administered at 2, 4, and 12 Months of Age: A Double-Blind Randomized Active-Controlled Trial.
[9]Source: Andrews et al. (2019). Effectiveness of the Seven-Valent and Thirteen-Valent Pneumococcal Conjugate Vaccines in England: The Indirect Cohort Design, 2006-2018.
[11]Source: Dominguez et al. (2017). Effectiveness of the 13-Valent Pneumococcal Conjugate Vaccine in Preventing Invasive Pneumococcal Disease in Children Aged 7-59 Months. A Matched Case-Control Study.
[17]Source: Siber et al. (2007). Estimating the protective concentration of anti-pneumococcal capsular polysaccharide antibodies.

Table S2. Predicted serotype-specific protective antibody concentration (Cp), Observed PCV7/13 vaccine effectiveness (VE), and Predicted PCV20 VE for 2+1 and 3+1 dosing schedule before and after booster dose (full table)

	Predicted protective antibody concentration median (95% CI) µg/mL				Observed PCV7/13 VE median % (95% CI)		Predicted PCV20 VE median % (95% CI)			
Serotype	PCV20 post dose 3 in 3+1 dosing schedule	PCV20 post dose 4 in 3+1 dosing schedule	PCV20 post dose 2 in 2+1 dosing schedule	PCV20 post dose 3 in 2+1 dosing schedule	3+1 dosing schedule[4,5] greater than one dose**	2 +1 dosing schedule[6] completion of schedule**	Post dose 3 in 3+1 dosing schedule	Post dose 4 in 3+1 dosing schedule	Post dose 2 in 2+1 dosing schedule	Post dose 3 in 2+1 dosing schedule
4	0.01 (0.01, 0.17)	0.90 (0.43, 2.76)	0.08 (0.05, 0.12)	0.83 (0.55, 1.19)	93 (65, 99)	96.1 (92, 98)*	100 (82, 100)	91 (57, 98)	90 (82, 95)	93 (87, 97)
6B	0.08 (0.08, 0.33)	0.95 (0.48, 2.54)	0.08 (0.08, 0.08)	0.39 (0.13, 2.21)	94 (77, 98)	95.9 (72, 99)	87 (66, 90)	90 (68, 97)	39 (33, 44)	94 (60, 99)
9V	0.07 (0.06, 0.36)	0.29 (0.13, 1.50)	0.06 (0.06, 0.28)	0.99 (0.50, 2.81)	100 (88, 100)	97.4 (77, 100)	99 (81, 100)	100 (82, 100)	90 (65, 93)	94 (65, 99)
14	0.34 (0.16, 0.83)	1.20 (0.67, 2.52)	0.03 (0.01, 0.09)	0.51 (0.22, 1.04)	94 (81, 98)	97.6 (92, 99)	91 (74, 97)	92 (78, 97)	91 (81, 100)	96 (88, 99)
18C	0.20 (0.09, 0.49)	0.63 (0.31, 1.50)	0.04 (0.02, 0.08)	0.68 (0.47, 0.95)	97 (85, 99)	96.1 (92, 98)*	97 (82, 100)	96 (79, 99)	96 (91, 99)	93 (87, 97)
19F	0.75 (0.46, 1.48)	1.74 (0.94, 4.09)	0.65 (0.34, 1.49)	1.91 (1.07, 4.18)	87 (65, 95)	92.3 (76, 98)	83 (55, 94)	87 (61, 96)	88 (67, 96)	88 (68, 96)
23F	0.05 (0.01, 0.32)	0.46 (0.14, 2.14)	0.01 (0.01, 0.01)	0.46 (0.27, 0.74)	98 (80, 100)	96.1 (92, 98)*	93 (66, 99)	95 (68, 99)	49 (35, 62)	93 (86, 97)
1	0.38 (0.27, 0.57)	0.73 (0.51, 1.09)	0.33 (0.19, 0.72)	0.93 (0.54, 1.99)	87 (77, 93)*	85.4 (63, 94)	74 (62, 83)	78 (65, 86)	71 (45, 86)	77 (47, 91)
3	0.20 (0.09, 1.01)	0.44 (0.24, 1.42)	0.39 (0.22, 1.00)	0.79 (0.50, 1.70)	80 (30, 95)	65.5 (34, 82)	75 (13, 95)	60 (20, 80)	52 (26, 69)	46 (21, 63)
5	0.20 (0.12, 0.34)	0.76 (0.52, 1.18)	0.09 (0.04, 0.16)	0.84 (0.59, 1.27)	87 (77, 93)*	83.4 (74, 90)*	78 (65, 87)	82 (69, 89)	60 (51, 70)	77 (64, 85)
6A	0.75 (0.50, 1.22)	4.14 (2.94, 6.17)	0.08 (0.08, 0.38)	1.55 (0.63, 6.42)	86 (76, 93)*	95.9 (72, 99)	80 (68, 88)	81 (68, 88)	79 (56, 83)	93 (61, 99)
7F	0.46 (0.26, 1.02)	1.15 (0.67, 2.45)	0.30 (0.16, 0.73)	0.50 (0.20, 1.83)	97 (83, 100)	94.1 (76, 99)	93 (73, 98)	94 (73, 99)	91 (66, 98)	100 (84, 100)
19A	0.19 (0.06, 0.50)	1.35 (0.83, 2.44)	0.24 (0.04, 0.36)	1.55 (1.03, 2.42)	86 (71, 94)	89.1 (80, 94)	82 (63, 92)	85 (67, 94)	58 (0.00, 65)	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*
[4]Source: Whitney et al. (2006). Effectiveness of seven-valent pneumococcal conjugate vaccine against invasive pneumococcal disease: a matched case-control study.
[5]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.
[6]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.



[3]Source: Senders et al. (2024). A Phase Three Study of the Safety and Immunogenicity of a Four-Dose Series of 20-Valent Pneumococcal Conjugate Vaccine in Healthy Infants.
[12]Source: Yeh et al. (2010). Immunogenicity and Safety of 13-Valent Pneumococcal Conjugate Vaccine in Infants and Toddlers.
[13]Source: Van der Linden et al. (2016). Effectiveness of Pneumococcal Conjugate Vaccines (Pcv7 and Pcv13) against Invasive Pneumococcal Disease among Children under Two Years of Age in Germany.
[14]Source: Weinberger et al. (2016). Vaccine Effectiveness of Pcv13 in a 3+1 Vaccination Schedule.
[15]Source: Ryman et al. (2023). Potential serotype-specific effectiveness against IPD of pneumococcal conjugate vaccines V114 and PCV20 in children given a 2+1 dosing regimen.
[16]Source: Ryman et al. (2022). "Predicting effectiveness of the V114 vaccine against invasive pneumococcal disease in children.
[17]Source: Siber et al. (2007). Estimating the protective concentration of anti-pneumococcal capsular polysaccharide antibodies.

[3]Source: Senders et al. (2024). A Phase Three Study of the Safety and Immunogenicity of a Four-Dose Series of 20-Valent Pneumococcal Conjugate Vaccine in Healthy Infants.
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[13]Source: Van der Linden et al. (2016). Effectiveness of Pneumococcal Conjugate Vaccines (Pcv7 and Pcv13) against Invasive Pneumococcal Disease among Children under Two Years of Age in Germany.
[17]Source: Siber et al. (2007). Estimating the protective concentration of anti-pneumococcal capsular polysaccharide antibodies.

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