Predicting the Public Health Impact of Different Adult Pneumococcal Vaccines in Japan Using a Dynamic Transmission Model

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Background

- *Streptococcus pneumoniae* is an important pathogen and leading cause of vaccine-preventable bacterial infections, including invasive pneumococcal disease (IPD). Infants, the elderly, and immunocompromised people are at increased risk of IPD
- In Japan, the 7-valent pneumococcal conjugate vaccine (PCV7) was recommended for children under 5 years of age in 2010 and was replaced in the national immunization program (NIP) by a 13-valent PCV (PCV13) in 2013.[2] A 15-valent PCV (PCV15) was recommended in 2023[1] and a 20-valent PCV (PCV20) was then recommended for the pediatric population[2]
- Pediatric IPD in vaccine type (VT) serotypes (ST) has greatly decreased since the first PCVs were recommended due to high vaccination coverage rates (VCR).[3,4] This led to a concomitant decrease in VT IPD in adults due to indirect protection, however a significant burden of non-vaccine type (NVT) IPD remains in adults
- The current pneumococcal vaccine recommendation for adults is a 23-valent polysaccharide pneumococcal vaccine (PPSV23), but a new 21-valent PCV, V116, that targets STs primarily circulating in adults (**Table 1**) has been filed for the regulatory approval for adult use in Japan

Methods

Model structure

- A compartmental model[5] was adapted to capture the carriage transmission of *Streptococcus pneumoniae* and the progression to disease (**Figure 1**)
- We incorporated the introduction of historical age- and ST-specific vaccines, which provided protection against both carriage acquisition and disease
- In the model, the population was divided into four age groups: 0-4, 5-14, 15-64, and 65+ year-olds

Model calibration and inputs

- The model was calibrated to age- and ST-specific IPD data from 2008-2019 (**Figure 2**). Data for all model age groups were available from surveillance reports from 2014-2019,[6,7] while data from Suga et al[8] was used to supplement pediatric IPD surveillance data from 2008-2013
- Estimated parameters include carriage acquisition rates, competition parameters between STs, vaccine efficacies against carriage, and case-to-carrier ratios
- The calibrated model was used to project IPD under five adult vaccination scenarios beginning in 2020. Specifically, we compared introducing two different adult vaccines in the 65+ year-old Japanese population: PCV20 or V116 relative to the status quo of PPSV23. We also considered two different adult vaccination coverage rate (VCR) assumptions for each PCV. All scenarios assumed PCV20 vaccination was used in the pediatric population
- We considered two different sets of assumptions regarding VCRs:
  - In the continued VCR scenario, we modeled VCRs to maintain the present coverage of ~12% in 65+ year-olds, which was the estimated overall population VCR when considering vaccination occurs in ~39% of 65+ year-olds[4]
  - In the increased VCR scenario, we modeled an expanded vaccination policy to 65+ year-olds, rather than just 65+ year-olds, in 2020 and assumed a VCR of ~39% in the entire 65+ year-old population

Results

- The calibrated model aligned with the historical data over all age groups and ST classes (**Figure 2**). We focused our results on the 65+ year-old population
- Given that PCV20 was introduced in the pediatric population at the same time as adult PCVs, the projected decreases in adult IPD incidence are a combination of direct protection and indirect protection from pediatric vaccination. These indirect effects were identical across all scenarios
- In the scenario where only 65-year-olds (continued VCR) were vaccinated, IPD incidence in the 65+ year-old population is projected to decrease by 27.8%, 29.9%, or 28.0% with PPSV23, V116, or PCV20 vaccination (**Table 2**). In the scenario where individuals aged 65+ year-old (increased VCR) were vaccinated, IPD incidence in the same population is projected to decrease by 39.2% or 32.7% with V116 or PCV20 vaccination (**Table 2**)
- In the scenario where individuals aged 65+ years-old were vaccinated and in STs present in V116 but not PCV20 (9N, 15A, 15C, 16F, 17F, 20A, 23A, 23B, 24F, 31, and 35B), projections predicted a decrease in incidence from V116 vaccination and an increase in incidence with PCV20 or PPSV23 vaccination (**Figure 3**, V116-non-PCV20)
- In STs present in PCV20 but not V116 (1, 4, 5, 6B, 9V, 14, 18C, 19F, and 23F), projections predicted a decrease in incidence under all three vaccines (**Figure 3**, PCV20-non-V116)

Figure 1. Model diagram

- Upon carriage acquisition, individuals moved to either the colonized, co-colonized, or triple-colonized classes, depending on whether one or two serotypes were acquired (denoted in blue). A small proportion of individuals from these colonized classes would develop a pneumococcal disease (denoted in red and orange). Recovery then moved individuals back to the non-colonized class (denoted in light green), sequentially clearing one serotype at a time. Vaccination (dark green border) reduced the risk of carriage acquisition and disease development for vaccine serotypes

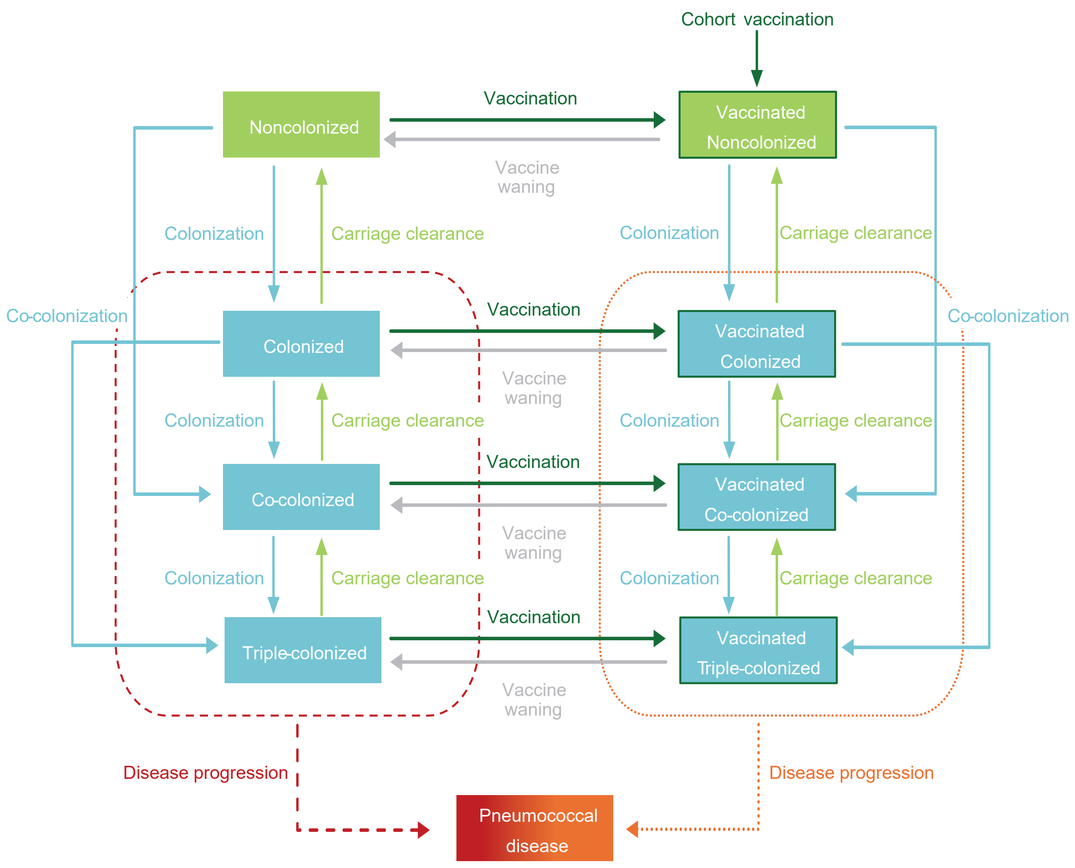


Table 1. Serotype classes (STCs) with respective serotypes included in each class

- Shading indicates inclusion in different adult vaccines. V116 contains deOAc15B pneumococcal polysaccharide which has a molecular structure similar to 15C (referred to as 15C hereafter). We include 6C as a vaccine type due to cross-protection from 6A[9]

Serotype class (STC)	Serotypes included in class	PCV20	V116	PPSV23
1	4, 6B, 9V, 14, 18C, 19F, 23F	–		–
2	1, 5	–		–
3	3	–	–	–
4	7F, 19A	–	–	–
5	6A, 6C	–	–	
6	22F, 33F	–	–	–
7	9N, 17F, 20 (20A)		–	–
8	8, 10A, 11A, 12F	–	–	–
9	15B	–	–	–
10	15A, 15C, 16F, 23A, 23B, 24F, 31, 35B		–	
11	Non-vaccine types (NVTs)			

Figure 2. Model calibration compared to data

- The correspondence between empirical IPD incidence (solid line) and modeled IPD incidence (dotted line) by vaccination group and age group. Note that data for 5-14, 15-64, and 65+ year-olds data spanned 2014-2019, while for 0- to 4-year-olds data spanned 2008-2019

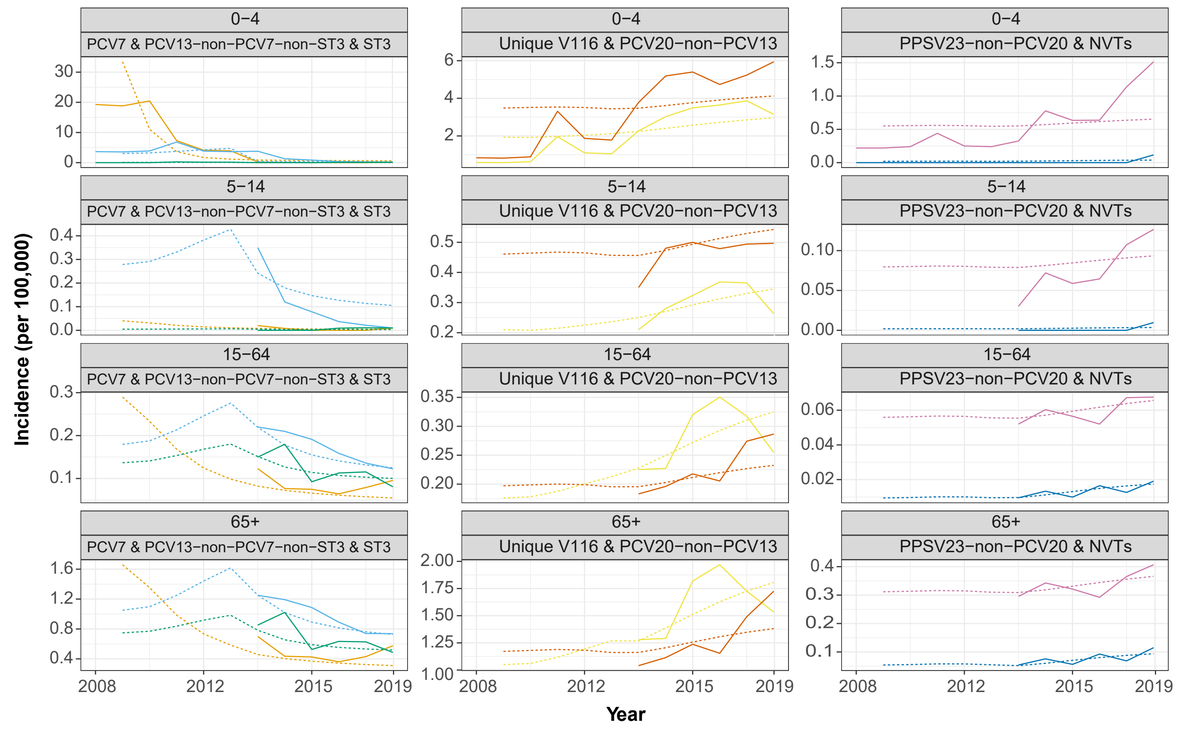
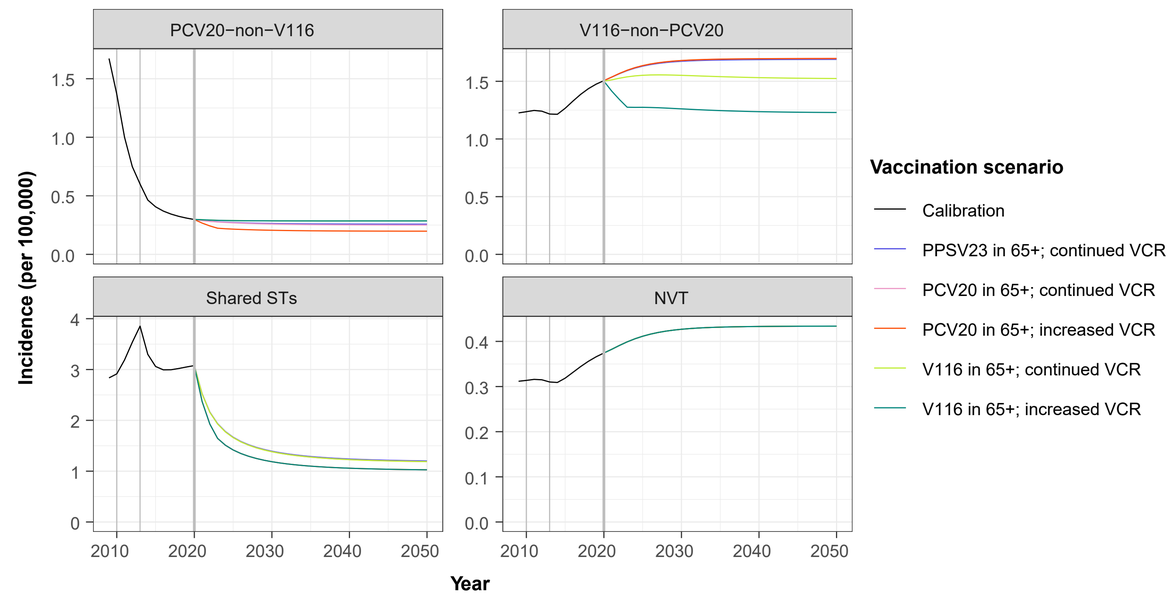


Figure 3. 30-year projections of IPD incidence for 65+ year-olds

- The five different adult vaccination scenarios for 65+ year-olds were grouped by whether the serotypes were included in PCV20 but not V116, V116 but not PCV20, both PCV20 and V116, or were non-vaccine types. Vertical grey lines indicate when different vaccines were introduced, PCV7 in 2010, PCV13 in 2013, and new vaccinations introduced in 2020. Note lines for different vaccination scenarios may be overlapping



Calibration and model projections for 65+ year–old population
In all projections the pediatric vaccination is PCV20

Table 2. Projected IPD incidence in 65+ year-olds

- IPD incidence at the start of the projection and 10 years after the continuation of the adult status quo (with the implementation of PCV20 in pediatrics) or after the introduction of adult and risk group vaccination with V116 or PCV20 under two different VCR scenarios

Scenario	Vaccination coverage rate in 65+ year-olds	Age group	IPD incidence at start of projection	10-year projections of IPD incidence (% change from projection start)
PPSV23	~12%	65+	5.20	3.76 (-27.8%)
V116	~12%	65+		3.65 (-29.9%)
PCV20	~12%	65+		3.75 (-28.0%)
V116	~39%	65+		3.16 (-39.2%)
PCV20	~39%	65+		3.50 (-32.7%)

Conclusions

- V116 led to greater reductions in IPD among the 65+ year-old population compared to PPSV23 or PCV20
- Expanding vaccination recommendations from 65-year-olds to all individuals aged 65+ year-old led to even greater projected reductions in IPD, with V116 averting the most disease. It is important to underscore the additional protection and reduction in disease offered to adults when expanding the age-based recommendation to all individuals aged 65+ year-old
- The differential in incidence between the V116 and PCV20 scenarios increased as the VCR increased
- With the V116 scenarios, the model did not predict any resurgence of STs previously included in pediatric vaccines (PCV13, PCV20) but not included in V116, likely due to the indirect protection offered from a robust pediatric vaccination program

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Disclosures

RJO, PMM, TMM, OS, and KMB are full-time employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA and may hold stock or stock options in Merck & Co., Inc., Rahway, NJ, USA. SW was a full-time contractor of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA. AT and TM are full-time employees of MSD K.K., Tokyo, Japan and may hold stock or stock options in Merck & Co., Inc., Rahway, NJ, USA.

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