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Supplementary appendix 1

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Supplementary Appendix

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1 Serotype groupings

Fig S1 shows that serotype 1 (ST1) declined post-PCV7 and continued to decline post-PCV13. Given the secular trends unrelated to vaccination and the very low incidence post-PCV13 ST1 was excluded from the models. As in other PCV13-using settings, ST3 increased post-PCV13 and, following the COVID 19 lockdowns in England, has rapidly increased again– behaviour similar to other NVTs. ST3 was therefore treated as a NVT in the base case for both models and included in VT3 for PCV15 in a sensitivity analysis as it induces higher post-booster responses to ST3 than PCV13.

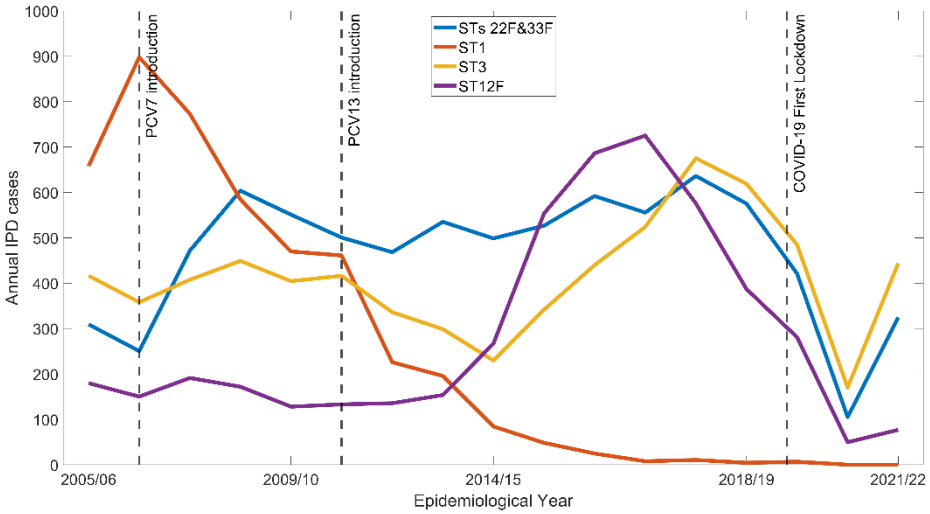


Figure S1. Annual number of Invasive Pneumococcal Disease (IPD) cases in England caused by serotypes 1 and 3 by epidemiological year July to June adjusted for changes in surveillance sensitivity up to 2009/10. Numbers for 2005/6 are the annual average from 2000/1 to 2005/6. Also shown are serotypes 22F and 33F which showed an increase followed by a decrease post-PCV7, and serotype 12F which showed an increase followed by a decrease post-PCV13. (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate Vaccine)

Six model scenarios were developed to investigate the potential impact of replacing the current 13-valent pneumococcal conjugate vaccine (PCV13) with PCV15 or PCV20 among infants in England to accommodate different assumptions about ST3 and the degree of competition between VT3 and NVT.

The competition between VT3 (a serotype grouping for the unique serotypes included in PCV15 or PCV20) and NVT (C8 in Fig S7) will determine the magnitude of the replacement of VT3 with NVT. According to previous experience with PCV7 and PCV13 in England, the value of this competition parameter is likely to be close to 1 (full competition leading to the maximum serotype replacement). In sensitivity analyses partial carriage replacement was assumed (C8=0.5) For PCV15 model scenarios in which ST3 was included in VT3 (Fig S2) it was assumed that the efficacy against carriage of ST3 by PCV15 was 25% of the efficacy against carriage of that assumed for the other VT3 serotypes. Since ST3 currently comprises about half of the IPD cases due to STs 22F and 33F under this scenario the overall VEc for VT3 is 0.625 of the value assumed under the base case for VT3. The base case scenarios for the PCV15 and PCV20 models are S1 and S2 respectively.

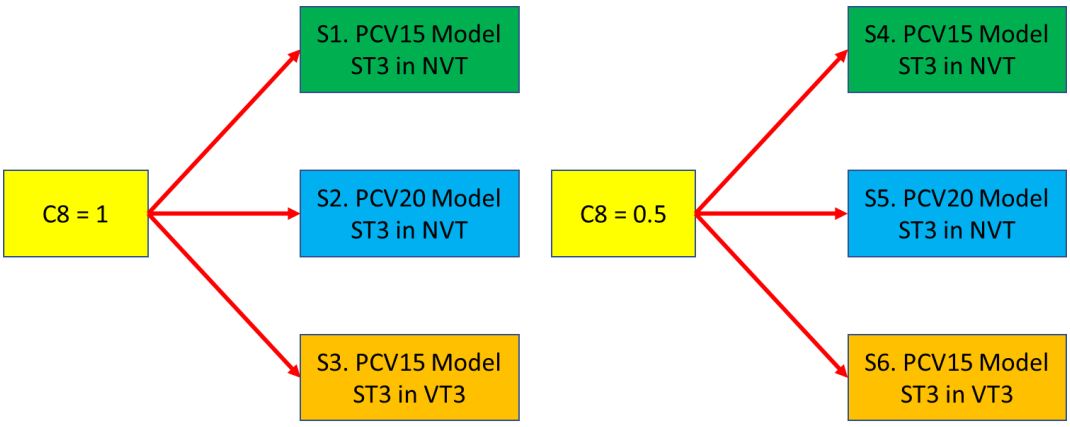


Figure S2. Tree diagrams of 6 model scenarios of PCV15 and PCV20 models according to allocating ST3 and C8 values (competition parameter between VT3 and NVT). The baseline

scenarios for the PCV15 and PCV20 model are S1&2 respectively. (PCV: Pneumococcal Conjugate Vaccine)

Table S1. Model scenarios used for the base case and sensitivity analyses for the PCV15 and PCV20 models. (PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype)

Scenario No	Scenario	Model	ST3	Competition parameter between VT3 and NVT (C8 in Fig S7)
1	Base case	PCV15	In NVT	1
2	Base case	PCV20	In NVT	1
3	Sensitivity analysis 1	PCV15	In VT3	1
4	Sensitivity analysis 2	PCV15	In NVT	0.5
5	Sensitivity analysis 3	PCV20	In NVT	0.5
6	Sensitivity analysis 4	PCV15	In VT3	0.5

All the carriage prevalence and IPD data are stratified according to serotype groupings in these model scenario assumptions.

2 Data

Model parameters related to pneumococcal transmission and competition between serotype groupings were estimated through a fitting procedure which utilised pre-PCV7 carriage data and IPD cases spanning the pre-PCV7 and post-PCV13 periods. It took into account demographic changes in the English population over this time, contact patterns between different age groups, and age-specific PCV7 and PCV13 coverage data.

2.1 Carriage and IPD data

The pre-PCV7 carriage data were derived from a longitudinal family study conducted between 2001 and 2002 in England in which a total of 3,869 nasopharyngeal swabs were collected from 489 individuals (1). These carriage data were categorized into seven age groups (under 1, 1-2, 3-4, 5-9, 10-19, 20-39, and 40+ years) and allocated to the serotype groupings used in the different model scenarios that implement decisions regarding ST3 (Fig S2). Due to the fine stratifications of the carriage data with four serotype groupings and seven age groups, some strata had zero positive swabs and we assumed a value of 0.5 to enable calculation of CCRs.

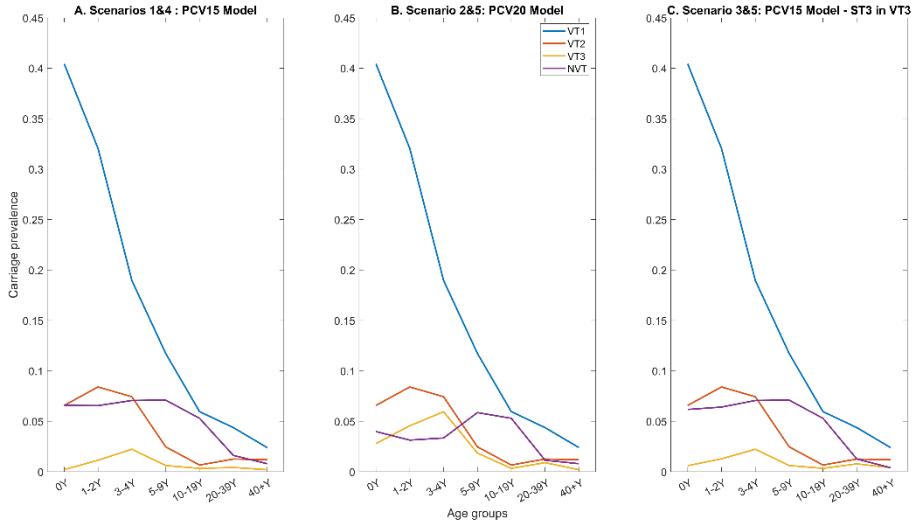


Figure S3. Pneumococcal carriage prevalence by age groups and serotype groupings (VT1, VT2, VT3 and NVT) according to PCV7, 13, 15&20 in the pre-PCV7 era from the longitudinal carriage swab data in 2000/01 in England (1), VT1: PCV7, VT2: PCV13 – PCV7 – ST1&3. A: PCV15 model scenarios 1&4 assuming VT3: PCV15 – PCV13 and NVT: non-PCV15 + ST3; B: PCV20 model scenarios 2&5 assuming VT3: PCV20 – PCV13 and NVT: non-PCV20 + ST3; C: PCV15 model scenarios 3&6 assuming VT3: PCV15 – PCV13 + ST3 and NVT: non-PCV15. IPD incidence. (PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype)

Table S2. Case : Carrier ratios (CCRs) by eleven age groups and four serotype groupings according to PCV15 and PCV20 model base-case scenarios. The same values for VT1 and VT2 as they share the same serotypes. VT3 and NVT for PCV15 and PCV20 are separated due to different additional serotypes included PCV15/20. (PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type serotype groupings, and NVT: Non Vaccine Type serotype groupings)

SG	Model	0Y	1-2Y	3-4Y	5-9Y	10-14Y	15-24Y	25-44Y	45-64Y	65-74Y	75-84Y	85+Y
VT1	Common	0.00014986	0.000121	9.43E-05	2.13E-05	1.09E-05	1.62E-05	5.3E-05	0.000152	0.000236	0.000408	0.000848
VT2		0.0001095	4.34E-05	2.78E-05	1.83E-05	2.87E-05	3.45E-05	4.21E-05	7.04E-05	0.000102	0.000153	0.000382
VT3	PCV15	0.00056822	2.85E-05	2.13E-05	2.97E-05	2.57E-05	1.64E-05	4.26E-05	0.000179	0.000297	0.000513	0.000904
	PCV20	0.0001326	2.44E-05	1.62E-05	2.48E-05	7.21E-05	6.92E-05	0.000154	0.000891	0.001106	0.001496	0.00229
NVT	PCV15	0.00009582	3.38E-05	3.14E-05	9.48E-06	7.17E-06	1.55E-05	0.000107	0.000347	0.000469	0.000644	0.001186
	PCV20	0.00009201	4.55E-05	5.05E-05	6.84E-06	4.32E-06	5.22E-06	5.25E-05	0.000169	0.000269	0.000402	0.000844

The UKHSA compiles a national enhanced surveillance dataset of serotyped IPD cases organised by epidemiological years (July to June) spanning 2000/01 to 2021/22. As previously described, the annual number of IPD cases was adjusted for those with missing serotype or age , and the upward trend in all reported IPD resulting from improved surveillance sensitivity prior to 2009/2010 (2). The adjusted annual average number of IPD cases from 2000/01 to 2005/06 was used for the pre-PCV7 baseline (Fig S4). Unlike previous iterations (3), the current model is fitted to IPD data restricted to England as inclusion of cases from Wales ended in 2017.

We used the IPD cases in 2018/19 (Fig S5) as the baseline (VacYear 0) with transition from PCV13 to PCV15 or PCV20 occurring in VacYear 1, assuming that at the time of transition pneumococcal transmission dynamics perturbed by social distancing and other measures during the COVID-19 pandemic (4) will have returned to pre-pandemic levels in VacYear 0.

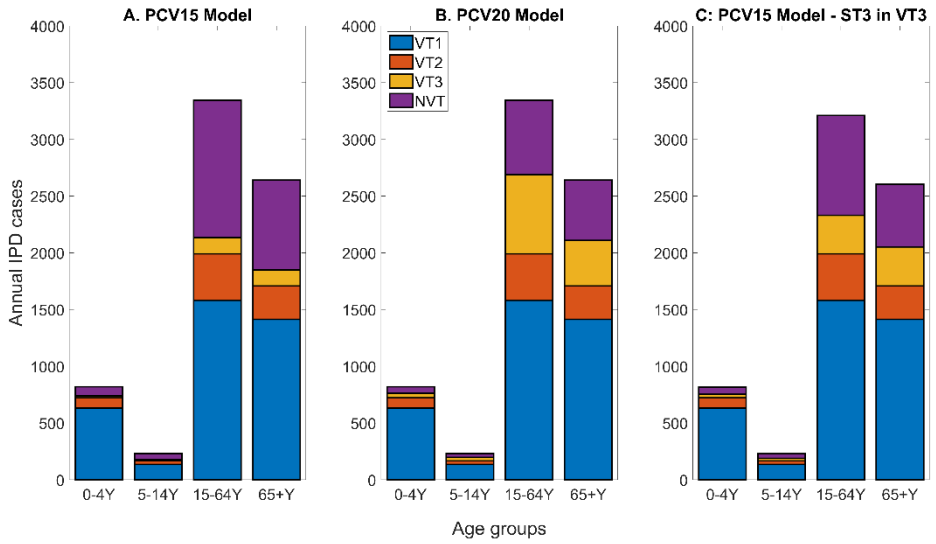


Figure S4. Bar charts of the IPD cases in the pre-PCV7 era as 2005/06 by age groups and serotype groupings in England. (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype)

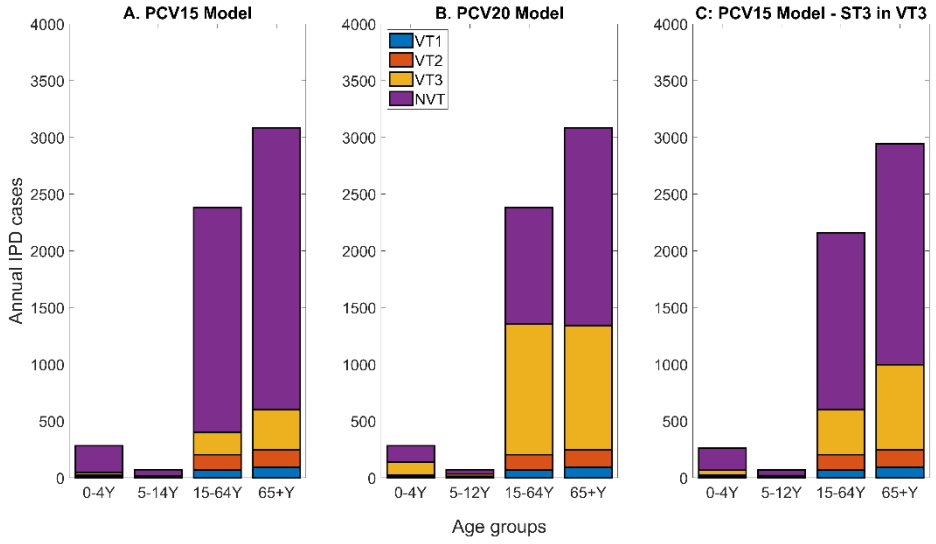


Figure S5. Bar charts of the IPD cases in the post-PCV13 era in 2018/19 by age groups and serotype groupings in England. (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype)

2.2 Population structure

Population data, including yearly age breakdowns, were obtained from census data spanning the pre-PCV7 to the post-PCV13 period. Additionally, we incorporated estimated

demographic changes extending to 2045, which were sourced from the Office of National Statistics (5). Not only is the number of individuals over 65 years of age expected to increase but so is the mean age of those in this age group which will result in an increase in the IPD incidence in 65 year olds without any change in schedule or PCV used. The model is stratified into 100 yearly age bands and outputs are generated for each yearly age band so future demographic changes (i.e increasing mean age of 65+ year olds) are accommodated in the model. For presentational purposes however we group the individual year of age outputs into broader age- bands, eg 65+ years

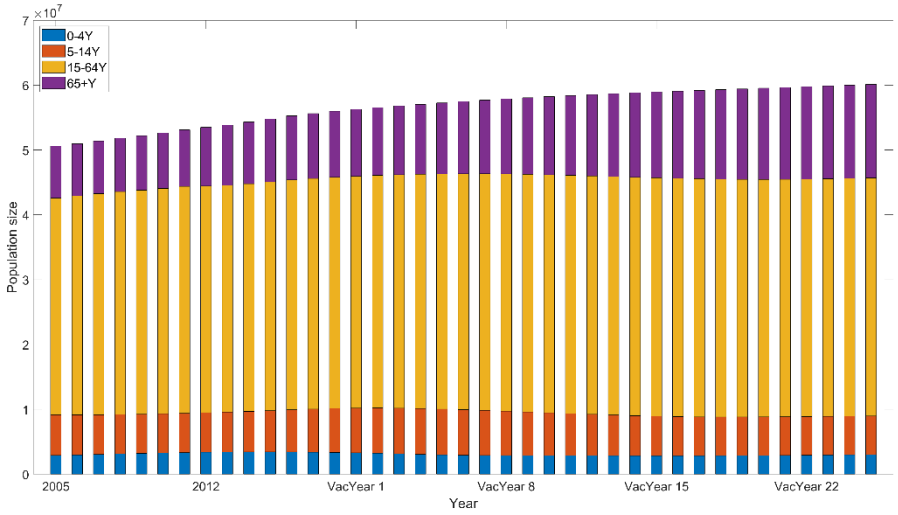


Figure S6. Population size by four age groups in England between 2005 and 2044 (VacYear 25). VacYear 1 (2024) is the first year of replacing PCV13 with new PCV and changing the 2+1 schedule to 1+1. (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype, VacYear: Epidemiological year since the change of PCV13 with new PCV)

2.3 Contact patterns between age group

As previously described (3), the contact patterns between age groups were obtained from the POLYMOD survey conducted in England in 2006 (6) supplemented by an additional contact survey of infants under one year of age (7). The combined contact matrix was

adjusted using the size of the age groups in the English population in each year between 2005 and 2044.

2.4 PCV coverage data

The monthly PCV coverage by dose in each monthly birth cohort up to the age of two year old during the first two years of the PCV7 introduction including a catch-up and the routine 2+1 PCV7 programme was obtained from the General Practice Research database as previously described (8). Annual PCV coverage data for the second priming dose and the booster dose were obtained from UKHSA reports (9). As previously described 5, in the absence of first dose coverage data we assumed 95% coverage and the timing as observed for PCV7 during the first two years of the PCV7 programme. We obtained the timing of the second and booster doses from the vaccination dates of children with non-PCV type IPD in England and Wales (10). For the 1+1 schedule, which we start from VacYear 1, we assumed that the coverage for the first and booster doses onwards is the same as in 2018/19.

3 Model structure

The models are realistic-age-structured with the population divided into 100 annual age cohorts (0, 1, 2, 3, …, 99). Each annual age-cohort is divided into 48 equal-sized age-cohorts each of which is 365/48 (7.6) days long to simplify vaccinating monthly as coverage data are available by calendar month. This generates 4,800 age-cohorts representing the total population in England. For model outputs the age-cohorts are amalgamated into demographically typical groups eg ≥65 years.

3.1 Transition between model compartments

All individuals are assumed to be born susceptible (Sus) to pneumococcal carriage infection and become infected after acquiring carriage with VT1, VT2, VT3 and NVT as determined by the serogroup specific force of infection (FOI) denoted as $\lambda 1$, $\lambda 2$, $\lambda 3$ and $\lambda 4$. If an individual is already carrying a serotype from one serotype grouping, the FOI for acquisition of a serotype

from another serotype grouping is reduced when there is competition between serotype groupings in carriage (1-Ci) as depicted in Fig S7. This parameter determines the degree of serotype replacement when VT carriage is reduced by vaccination.

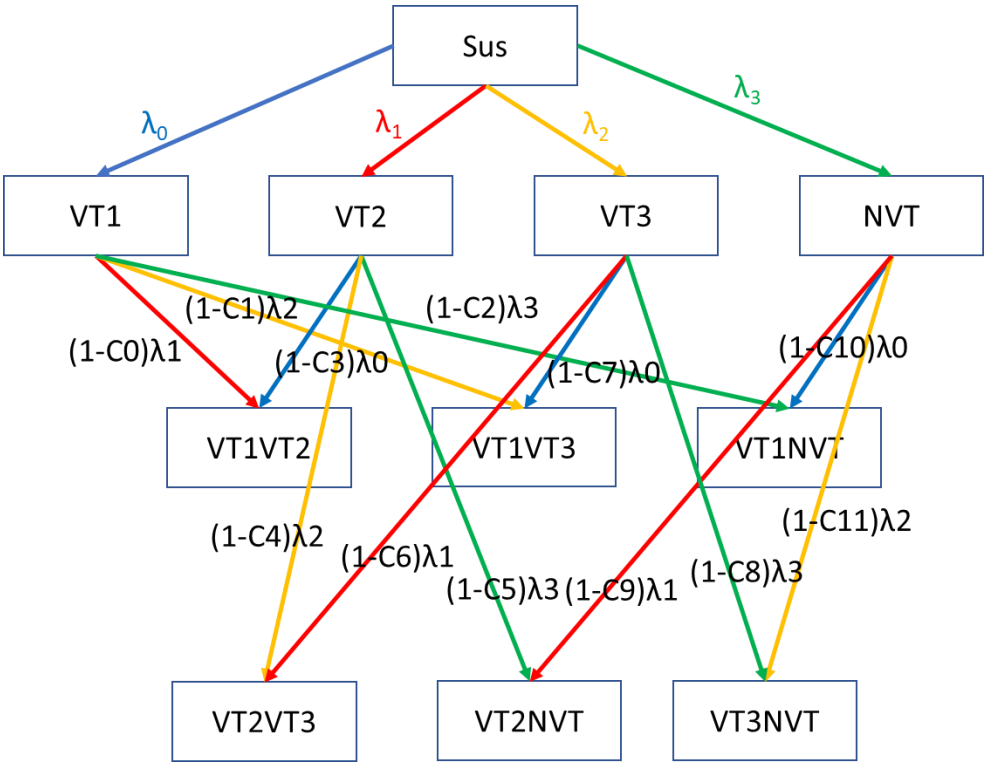


Figure S7. A flowchart of the compartment transitions in the pneumococcal transmission dynamics. Competition parameters (Ci) between compartments reduce the forces of infection (λ0: Blue for VT1, λ1: red for VT2, λ2: yellow for VT3, and λ3: green for NVT). The directions of the arrows indicate acquiring carriage infection and moving to other compartments. Clearing of carriage infection occurs in the opposite directions. (PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type)

The model allows individuals to carry two serotype groupings at the same time. The previous PCV13 model (3) allowed three co-infections but the microarray study on the longitudinal study samples indicated a very small chance (4 out of 317 swabs serotyped) of having three or more co-infections with different serotype groupings (Fig 7 in (3)). Therefore, the model has 11 compartments consisting of one susceptible, four single serotype groupings, and 6

double serotype grouping compartments. Following clearance of a carriage infection an individual moves back to the preceding compartment. The model does not assume any innate or serotype-specific immunity generated as a result of a carriage infection. As in our previous modes, IPD is assumed to develop at the time of carriage acquisition (incident infection), while transmission can occur at any time during the carriage episode.

Individuals already carrying a serotype from one of the four serotype groupings will have some degree of protection against infections from another serotype grouping, according to the level of competition (Ci) between the groupings. The effect of competition is to reduce the FOIs between single and double serotype grouping compartments by 1 - Ci. As shown in Fig S3, there are 11 separate parameters (C0 to C11) reflecting competitions between infectious compartments. Reduction by vaccination of the prevalence in carriage of serotypes in the VT1, VT2 and VT3 compartments will reduce competition with NVTs and generate serotype replacement. When the Ci value is 1, the magnitude of the replacement is a maximum while when Ci value is 0 the replacement will be minimal.

3.2 Vaccination

We assume that the first dose of the PCV provides vaccinated individuals with partial protection, while the second dose or the first dose given to those aged 1 year old during the 2006 catch-up provides full protection. Specifically, the vaccine efficacy against acquiring carriage infection (VEc) for partial protection is assumed to be half of the VEc for full protection, as described in (3). We assume that both partial protection and full protection decline exponentially with an average duration of 5 years, with full protection transitioning to partial protection (3). However, when individuals in compartments with waned or partial protection receive an additional dose, their protection is boosted back to the full protection level.

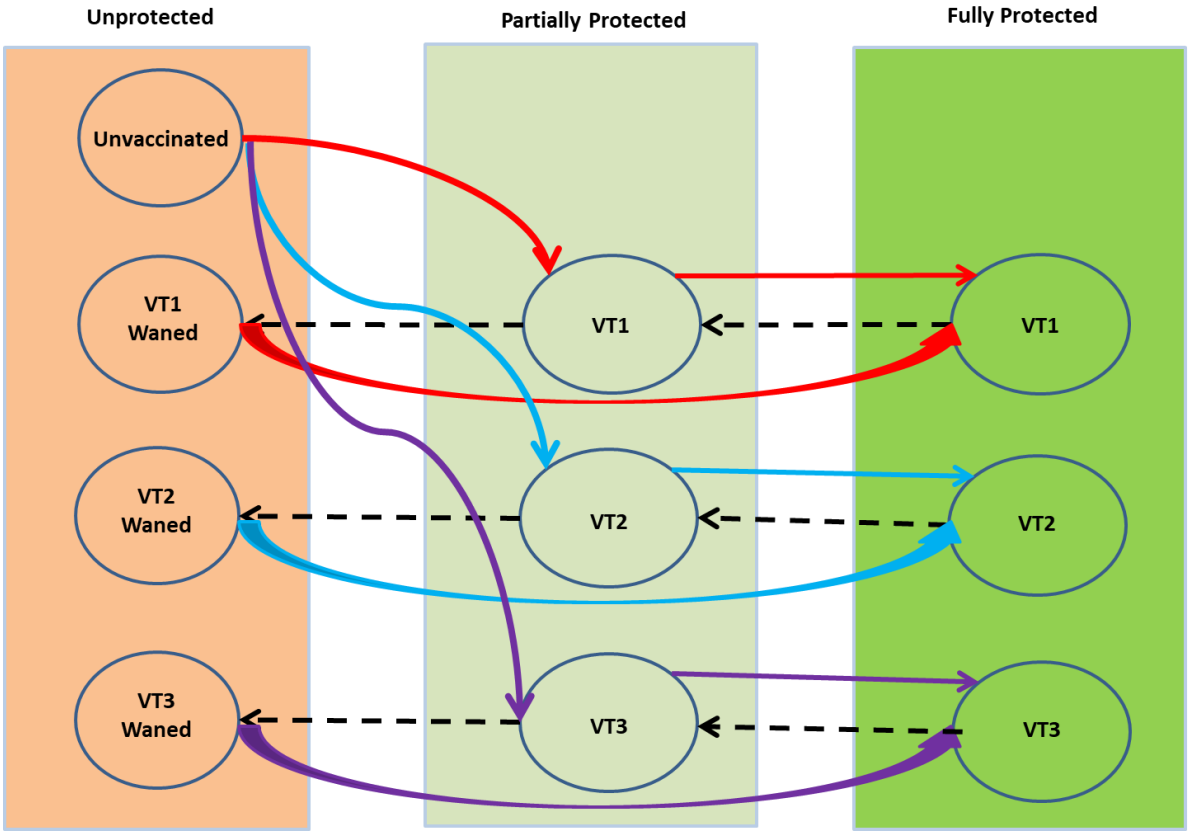


Figure S8. A flowchart describing changes of the PCV protection status according to PCV doses (solid lines) and waning (dashed lines) with PCV7 (VT1), PCV13 (VT2) and new PCV (VT3, PCV15 or PCV20) (red arrows for VT1, blue arrows for VT2 vaccination and purple arrows for VT3). (PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type)

Individuals with partial or full protection are assumed to have 100% protection against developing IPD which then wanes with the same exponential decay function as VEc (3). VEc of VT3 is assumed to be the same value as VEcVT1 or VEcVT2 when included in PCV15 or PCV20 (Table 1). The vaccination with new PCVs runs for 25 years as the long-term simulation.

4 Fitting results

4.1 Forces of infection

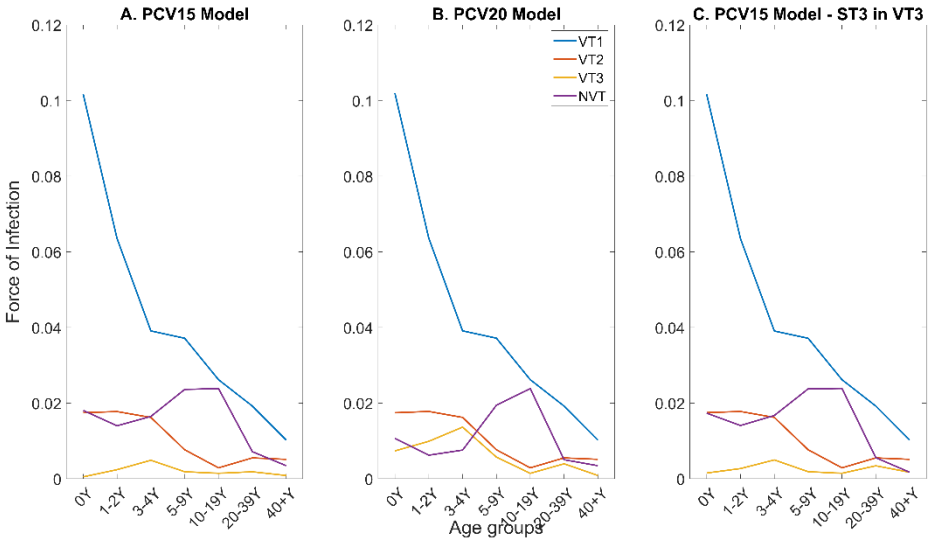


Figure S9. Forces of infection by age groups and serotype grouping according to scenarios of PCV15 and PCV20 models estimated using the carriage prevalence and invasive pneumococcal disease data in the pre-PCV era in England (1) (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype, VEc: Vaccine Efficacy against acquiring carriage, VacYear: Epidemiological year since the change of PCV13 with new PCV)

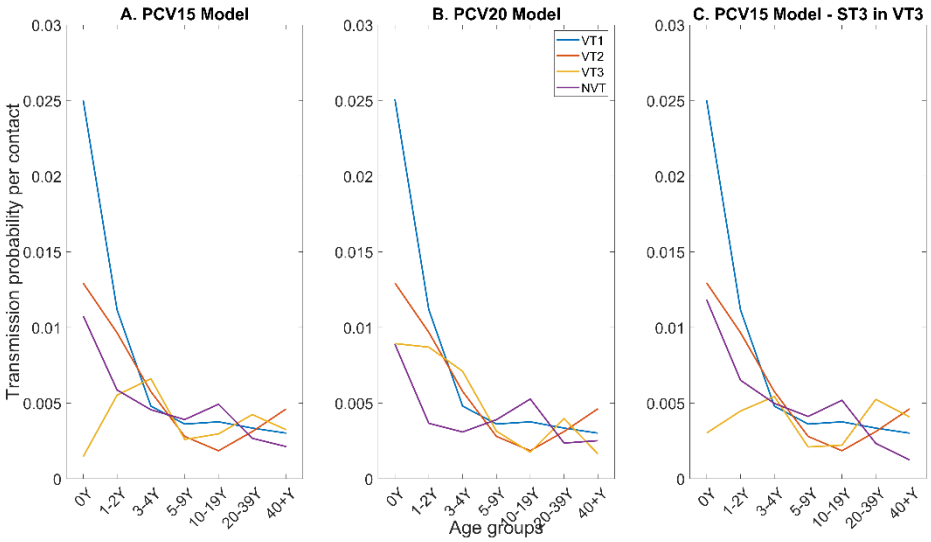


Figure S10. Transmission probabilities per contact by age groups and serotype groupings according to scenarios of PCV15 and PCV20 models estimated using the carriage prevalence and invasive pneumococcal disease data in the pre-PCV era in England (1) (PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type)

4.2 Case carrier ratios

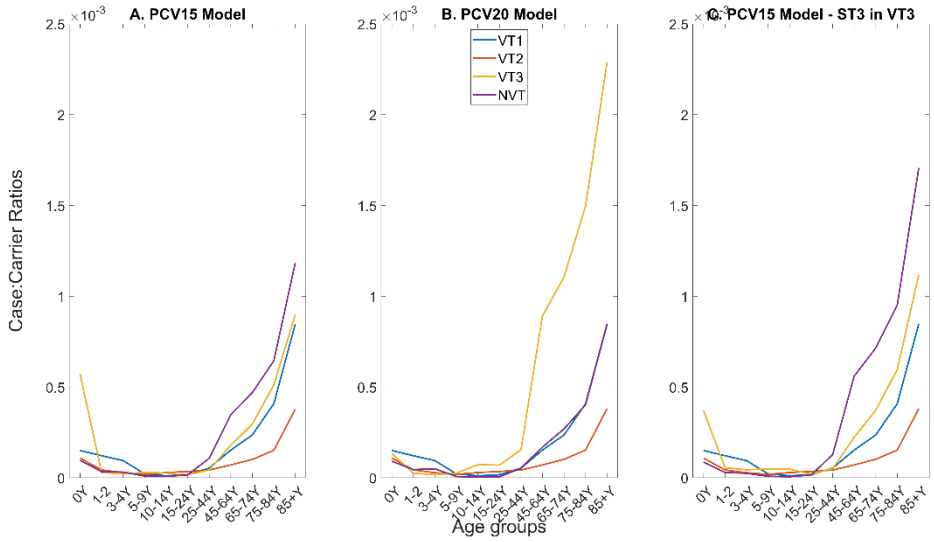


Figure S11. Case:Carrier ratios (CCRs) by 11 age groups and four serotype groupings according to the PCV15 and PCV20 model scenarios in Figure S2 and Table 1 using the number of newly infected individuals and the IPD cases during the pre-PCV7 year from the pre-PCV static model in England (1) (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype)

4.3 Parameter estimates from fitting the dynamic models for the six model scenarios

Table S3. Medians and Uncertainty Intervals (in brackets) of the 100 parameter sets of the estimated competition parameters by age group (units indicate the degree of competition between 1 and 0, 0 = no competition and no serotype replacement), VEc (Vaccine Efficacy against acquiring carriage infection) of VT1 and VT2 with PCV7 and PCV13, and proportional increase in CCR of the NVT group from 2014/15 until 2017/18 by comparing the model outputs to the IPD cases by four pneumococcal serotype groupings and age groups in England between 2005/06 and 2018/19 according to 6 model scenarios of PCV715 and PCV20 models in Figure S2. Assumed values of VEcVT1, VEcVT2 and VEcVT3 with new PCV are also presented (VEcVT3 is assumed to be the same value of VEcVT1 or VEcVT2). (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype, VEc: Vaccine Efficacy against acquiring carriage, VacYear: Epidemiological year since the change of PCV13 with new PCV)

Parameters	Age group	PCV15 Model, C8=1	PCV20 Model, C8=1	PCV15 Model, ST3 in VT3, C8=1	PCV15 Model, C8=0.5	PCV20 Model, C8=0.5	PCV15 Model, ST3 in VT3, C8=0.5
C0	<5Y	0.311 (0.269 ,0.338)	0.324 (0.298 ,0.342)	0.313 (0.298 ,0.330)	0.324 (0.301 ,0.343)	0.321 (0.306 ,0.338)	0.305 (0.293 ,0.321)
	5-64Y	0.048 (0.005 ,0.065)	0.045 (0.012 ,0.059)	0.064 (0.054 ,0.077)	0.089 (0.081 ,0.094)	0.119 (0.113 ,0.129)	0.043 (0.006 ,0.052)
	65+Y	0.122 (0.109 ,0.131)	0.135 (0.122 ,0.151)	0.190 (0.181 ,0.200)	0.105 (0.069 ,0.123)	0.113 (0.098 ,0.122)	0.107 (0.096 ,0.118)
C1	<5Y	0.014 (0.000 ,0.071)	0.358 (0.084 ,0.447)	0.471 (0.277 ,0.561)	0.545 (0.485 ,0.598)	0.660 (0.614 ,0.705)	0.001 (0.000 ,0.015)
	5-64Y	0.657 (0.558 ,0.756)	0.405 (0.286 ,0.529)	0.787 (0.754 ,0.819)	0.006 (0.000 ,0.058)	0.006 (0.000 ,0.062)	0.473 (0.436 ,0.500)
	65+Y	0.009 (0.000 ,0.341)	0.005 (0.000 ,0.064)	0.003 (0.000 ,0.018)	0.002 (0.000 ,0.160)	0.005 (0.000 ,0.040)	0.002 (0.000 ,0.017)
C2	<5Y	0.044 (0.000 ,0.279)	0.004 (0.000 ,0.097)	0.003 (0.000 ,0.027)	0.001 (0.000 ,0.015)	0.001 (0.000 ,0.028)	0.008 (0.000 ,0.195)
	5-64Y	0.002 (0.000 ,0.017)	0.003 (0.000 ,0.026)	0.001 (0.000 ,0.007)	0.002 (0.000 ,0.132)	0.002 (0.000 ,0.040)	0.001 (0.000 ,0.011)
	65+Y	0.170 (0.006 ,0.643)	0.155 (0.000 ,0.999)	0.320 (0.049 ,1.000)	0.432 (0.009 ,1.000)	0.497 (0.020 ,1.000)	0.048 (0.001 ,0.231)
C4	<5Y	0.998 (0.714 ,1.000)	1.000 (0.872 ,1.000)	1.000 (1.000 ,1.000)	0.513 (0.032 ,1.000)	1.000 (0.536 ,1.000)	1.000 (1.000 ,1.000)
	5-64Y	0.409 (0.020 ,0.999)	0.537 (0.002 ,1.000)	0.818 (0.146 ,1.000)	0.443 (0.008 ,1.000)	0.805 (0.177 ,1.000)	1.000 (0.468 ,1.000)
	65+Y	0.979 (0.211 ,1.000)	0.998 (0.641 ,1.000)	1.000 (1.000 ,1.000)	1.000 (0.989 ,1.000)	1.000 (1.000 ,1.000)	1.000 (1.000 ,1.000)
C5	<5Y	0.999 (0.898 ,1.000)	1.000 (0.997 ,1.000)	1.000 (1.000 ,1.000)	1.000 (0.532 ,1.000)	1.000 (1.000 ,1.000)	1.000 (1.000 ,1.000)
	5-64Y	0.361 (0.000 ,0.927)	0.374 (0.000 ,1.000)	0.492 (0.081 ,1.000)	0.448 (0.019 ,1.000)	1.000 (0.192 ,1.000)	0.471 (0.056 ,1.000)
	65+Y	0.280 (0.003 ,0.763)	0.281 (0.002 ,1.000)	0.240 (0.014 ,1.000)	0.225 (0.000 ,0.979)	0.191 (0.013 ,1.000)	0.199 (0.008 ,1.000)
VEc	VT1_7	0.462 (0.459 ,0.468)	0.458 (0.454 ,0.462)	0.461 (0.451 ,0.466)	0.458 (0.455 ,0.470)	0.458 (0.448 ,0.461)	0.461 (0.451 ,0.472)
	VT1_13	0.364 (0.363 ,0.367)	0.365 (0.363 ,0.370)	0.362 (0.361 ,0.368)	0.364 (0.361 ,0.370)	0.363 (0.361 ,0.365)	0.367 (0.362 ,0.372)
	VT2_13	0.185 (0.178 ,0.192)	0.190 (0.179 ,0.199)	0.183 (0.180 ,0.189)	0.188 (0.184 ,0.192)	0.187 (0.183 ,0.191)	0.189 (0.184 ,0.194)
VT1_7/VT1_13		0.788 (0.779 ,0.797)	0.796 (0.790 ,0.806)	0.785 (0.778 ,0.802)	0.796 (0.774 ,0.809)	0.791 (0.785 ,0.810)	0.796 (0.778 ,0.813)
CCR Increase	<5Y	0.102 (0.090 ,0.119)	0.112 (0.098 ,0.138)	0.108 (0.100 ,0.116)	0.066 (0.056 ,0.078)	0.067 (0.054 ,0.083)	0.095 (0.084 ,0.106)
	65+Y	0.224 (0.213 ,0.237)	0.281 (0.265 ,0.295)	0.248 (0.242 ,0.261)	0.283 (0.267 ,0.299)	0.281 (0.267 ,0.293)	0.239 (0.230 ,0.253)
VEc	VT1_New	0.287 (0.283 ,0.292)	0.291 (0.287 ,0.298)	0.284 (0.281 ,0.295)	0.290 (0.280 ,0.299)	0.287 (0.284 ,0.296)	0.292 (0.282 ,0.303)
	VT2_New	0.146 (0.139 ,0.153)	0.152 (0.142 ,0.160)	0.143 (0.140 ,0.152)	0.150 (0.142 ,0.155)	0.148 (0.144 ,0.155)	0.150 (0.143 ,0.158)
	VT3_New	0.287 (0.283 ,0.292)	0.291 (0.287 ,0.298)	0.284 (0.281 ,0.295)	0.290 (0.280 ,0.299)	0.287 (0.284 ,0.296)	0.292 (0.282 ,0.303)
	VT3_New	0.146 (0.139 ,0.153)	0.152 (0.142 ,0.160)	0.143 (0.140 ,0.152)	0.150 (0.142 ,0.155)	0.148 (0.144 ,0.155)	0.150 (0.143 ,0.158)

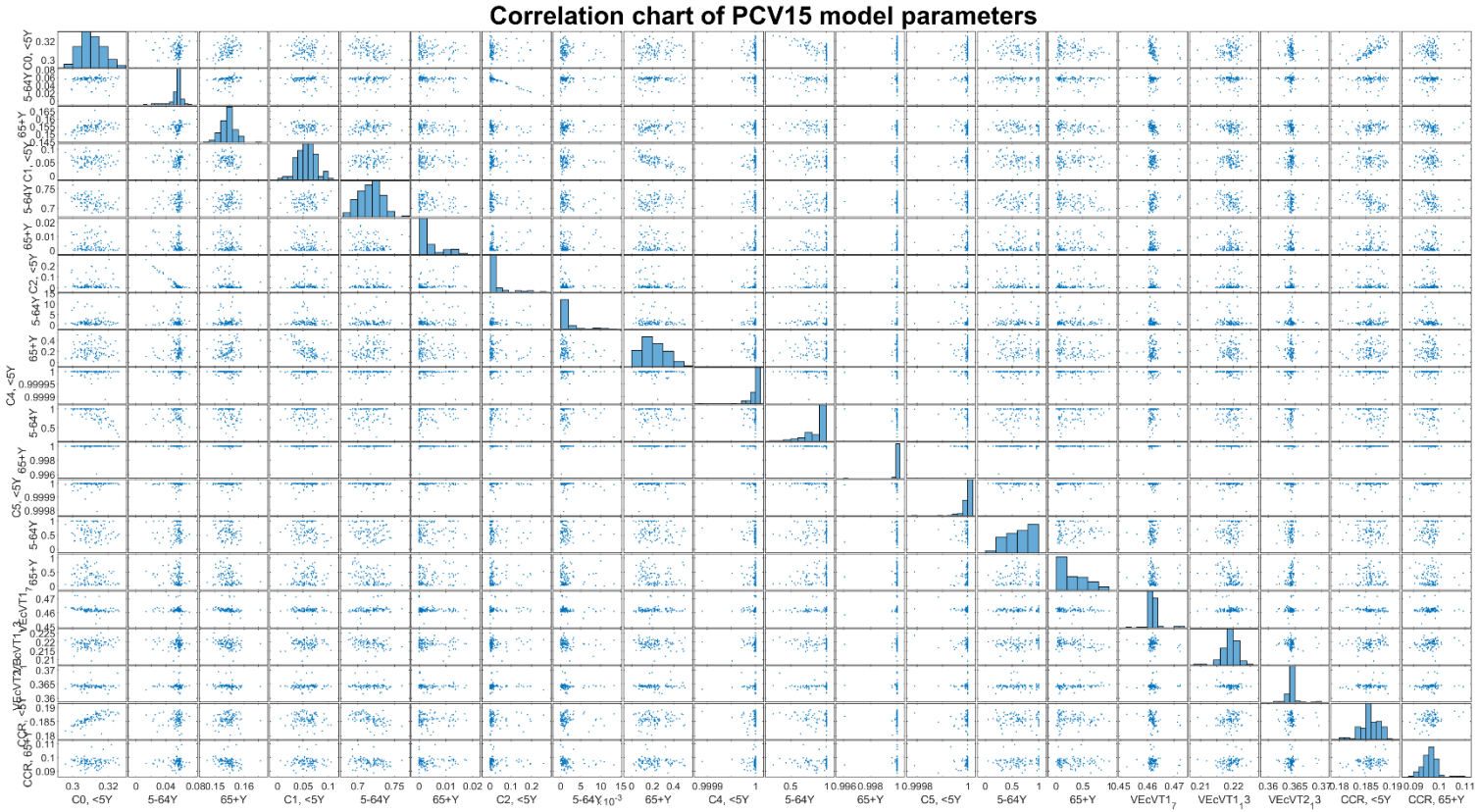


Figure S12. Correlation charts of 100 parameter sets of PCV15 model fitted to the carriage data obtained in 2001/02 in England (1) and historical IPD data between 2005/06 and 2018/19 (11) in England by four serotype groupings and age groups. (C values: Competition parameters, VEc: Vaccine Efficacy against acquiring carriage, PCV: Pneumococcal Conjugate Vaccine, IPD: Invasive Pneumococcal Disease)

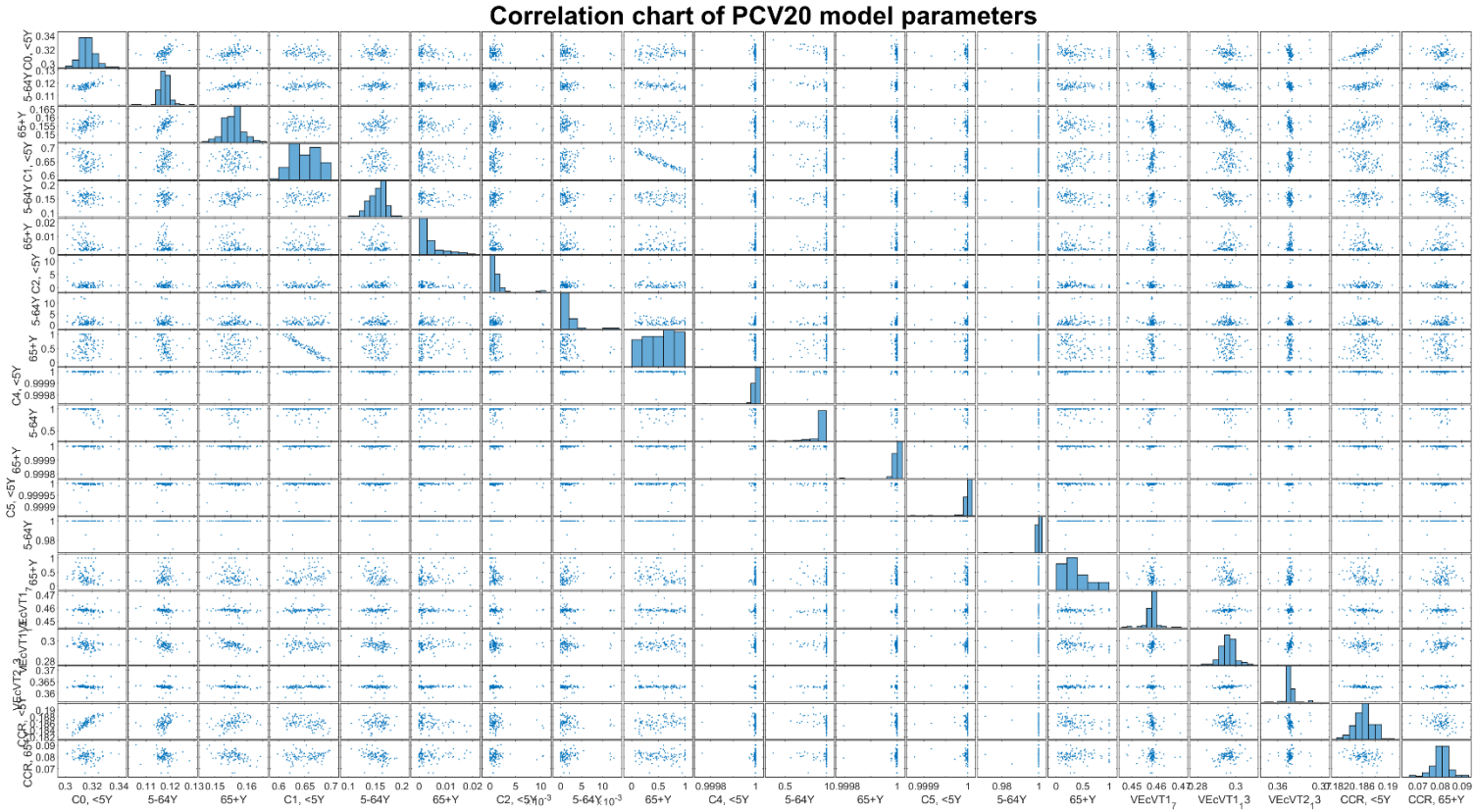
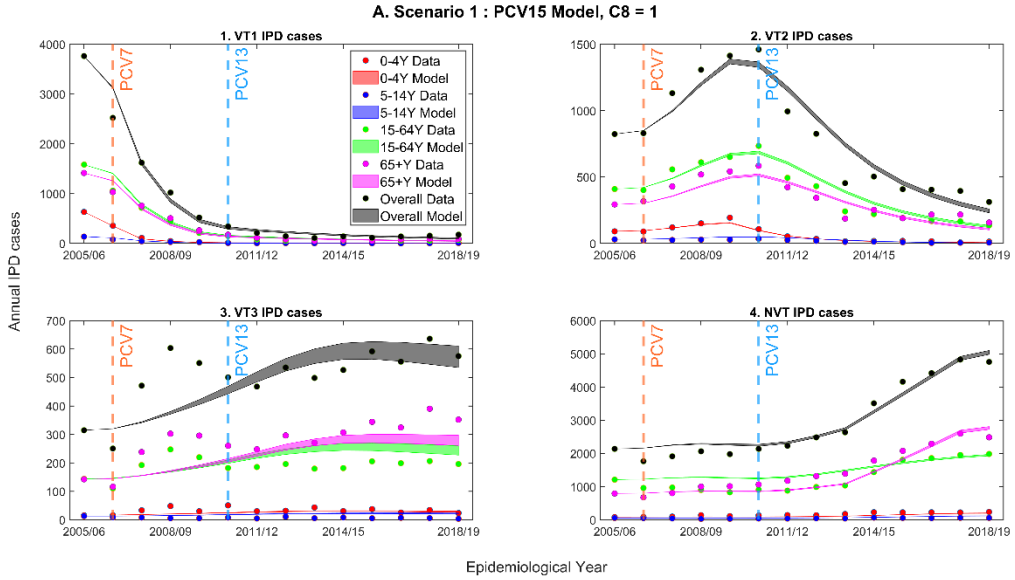
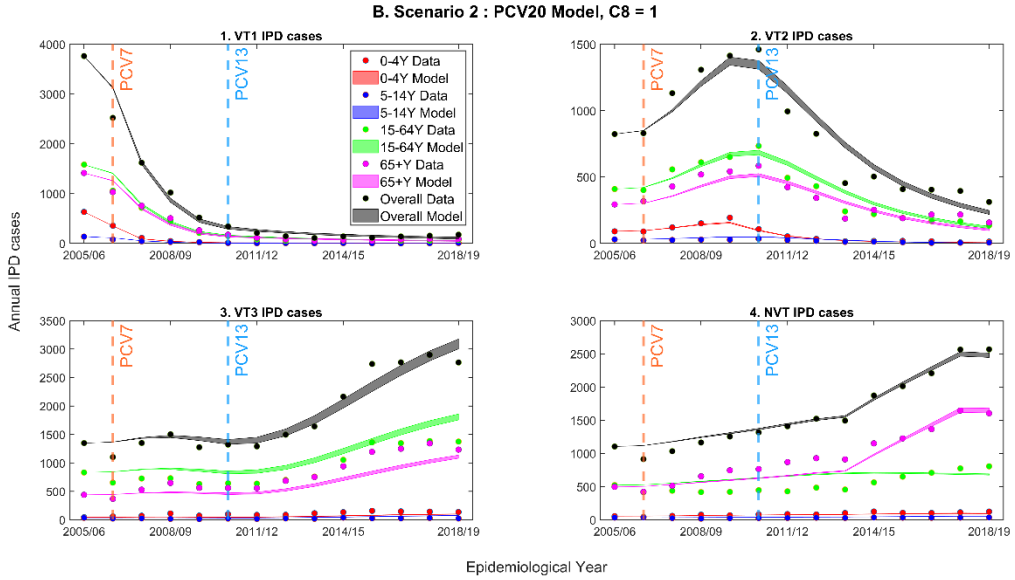
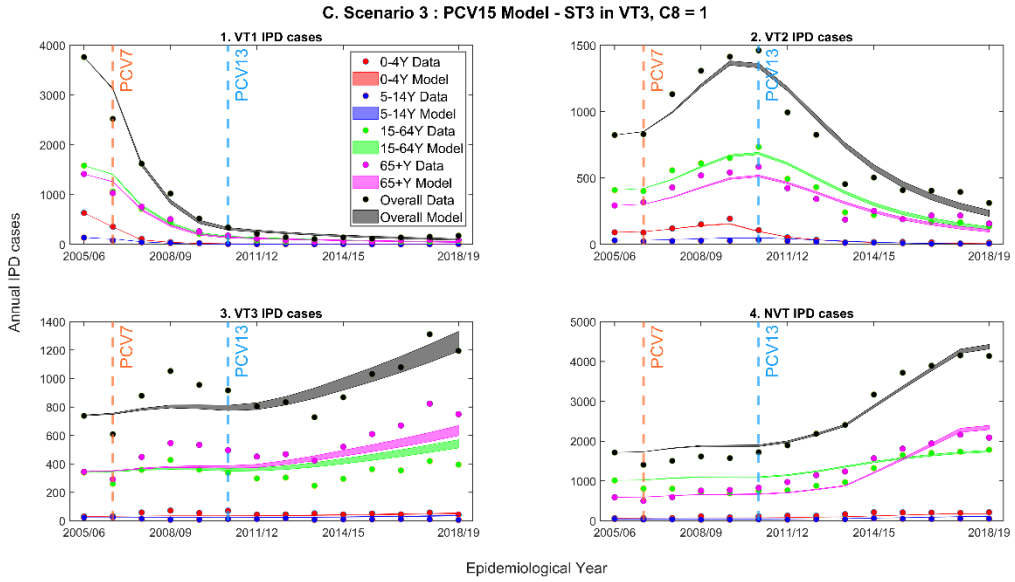


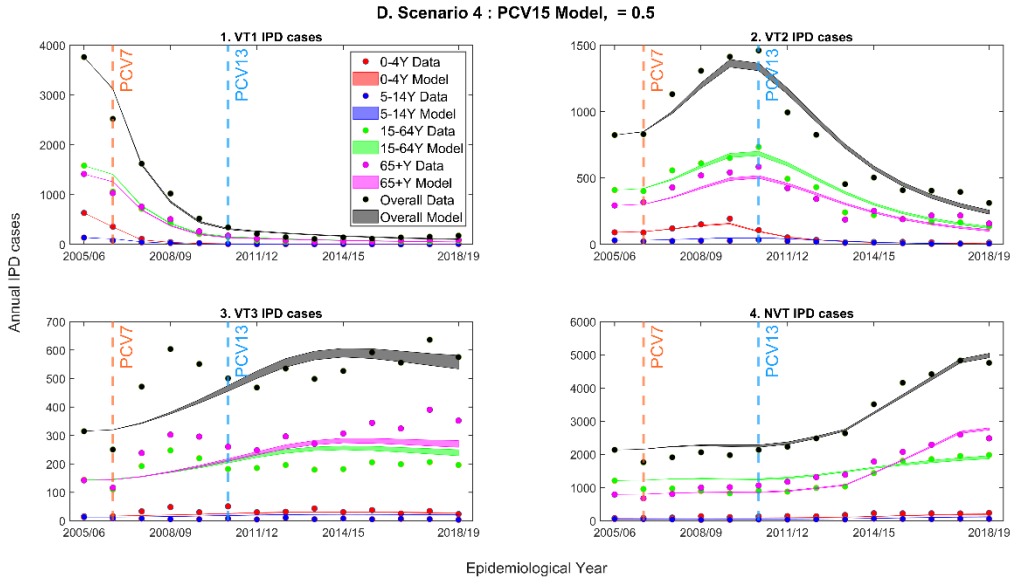
Figure S13. Correlation charts of 100 parameter sets of PCV20 model fitted to the carriage data obtained in 2001/02 in England (1) and historical IPD data between 2005/06 and 2018/19 (11) in England by four serotype groupings and age groups. (C values: Competition parameters, VEc: Vaccine Efficacy against acquiring carriage, PCV: Pneumococcal Conjugate Vaccine, IPD: Invasive Pneumococcal Disease)

4.4 Fitting results for the six model scenarios






C. Scenario 3 : PCV15 Model - ST3 in VT3, C8 = 1
1. VT1 IPD cases
2. VT2 IPD cases
3. VT3 IPD cases
4. NVT IPD cases
PCV7
PCV13
0-4Y Data
0-4Y Model
5-14Y Data
5-14Y Model
15-64Y Data
15-64Y Model
65+Y Data
65+Y Model
Overall Data
Overall Model
Annual IPD cases
Epidemiological Year
2005/06
2008/09
2011/12
2014/15
2018/19


D. Scenario 4 : PCV15 Model, = 0.5
1. VT1 IPD cases
2. VT2 IPD cases
3. VT3 IPD cases
4. NVT IPD cases
PCV7
PCV13
0-4Y Data
0-4Y Model
5-14Y Data
5-14Y Model
15-64Y Data
15-64Y Model
65+Y Data
65+Y Model
Overall Data
Overall Model
Annual IPD cases
Epidemiological Year
2005/06
2008/09
2011/12
2014/15
2018/19

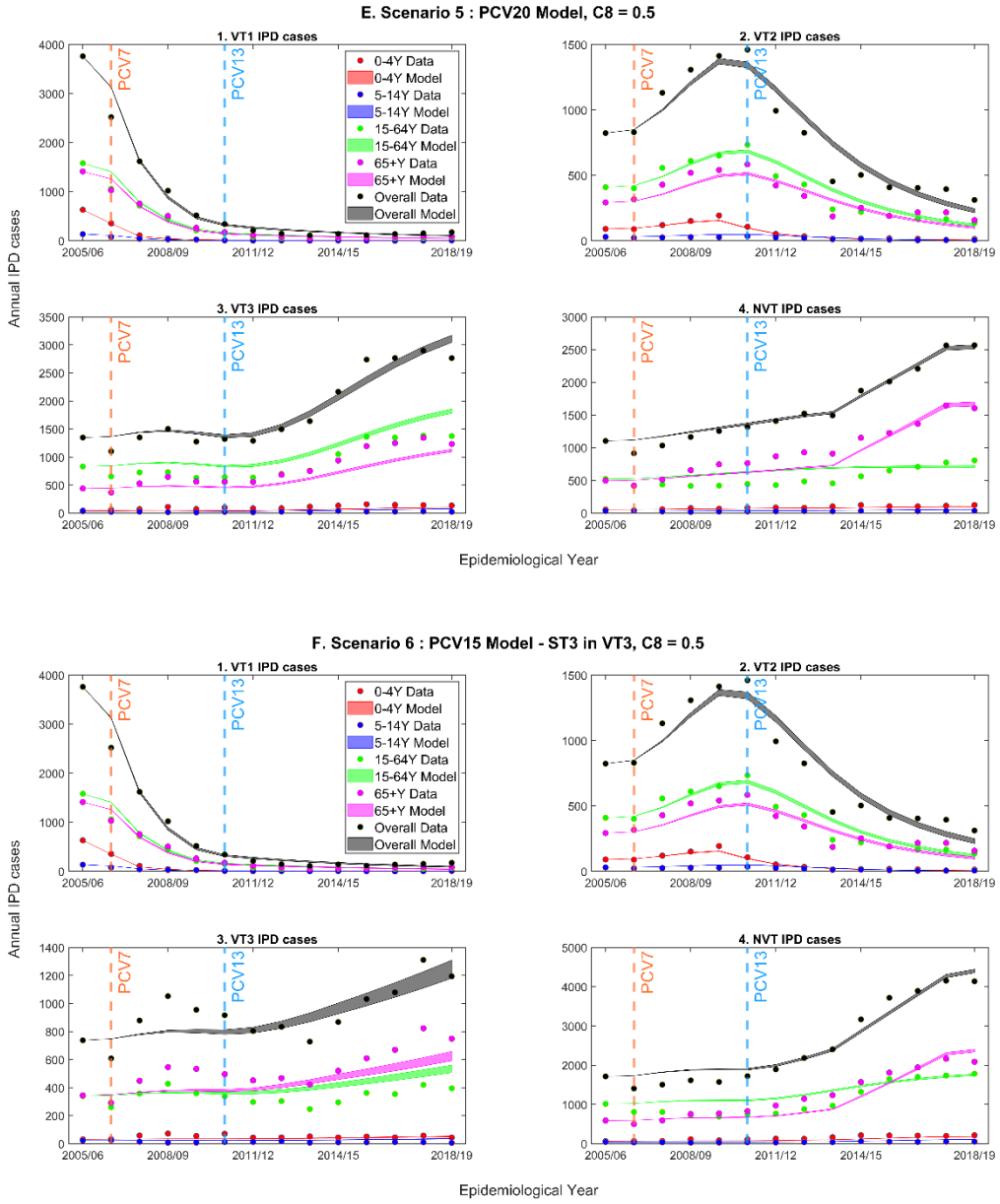
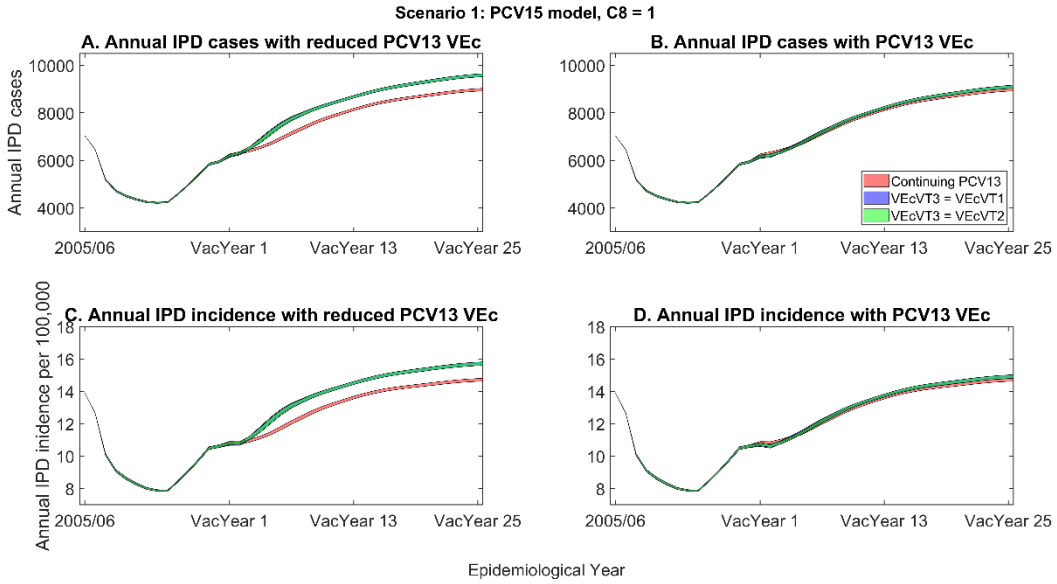
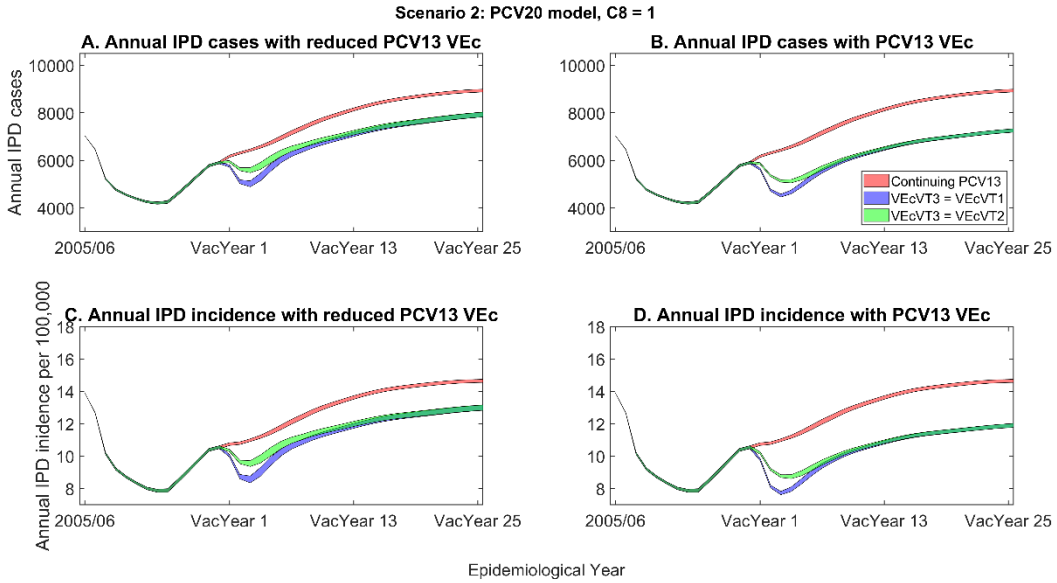


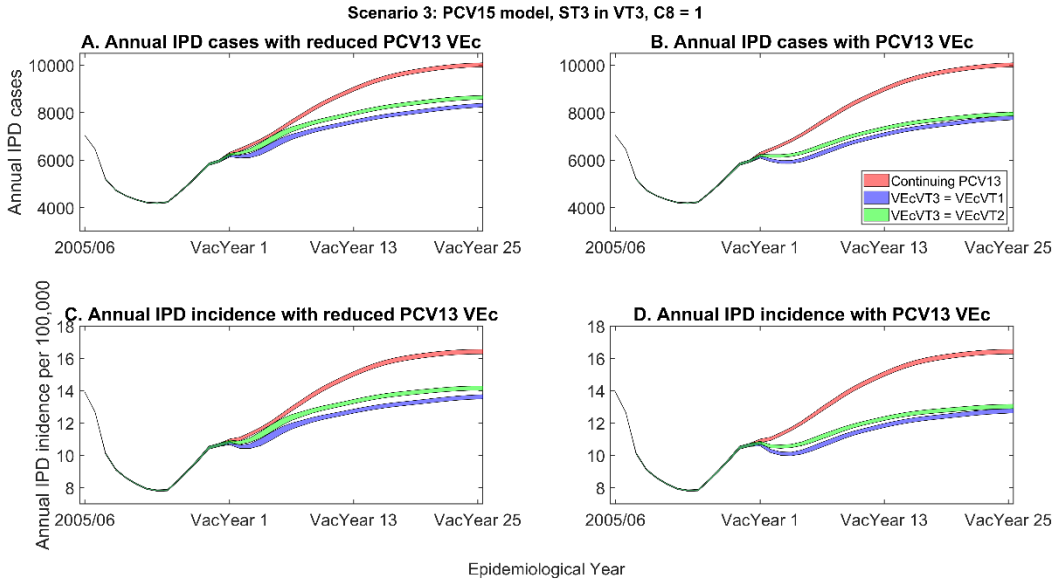
Figure S14. Comparison of the annual IPD cases and the fitted model outputs from 100 parameter sets by four serotype groupings and age groups for the six PCV15 and PCV20 model scenarios in Figure S2 to the IPD data between 2005/06 and 2018/19 in England. Note: Y axis changes between graphs (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype)

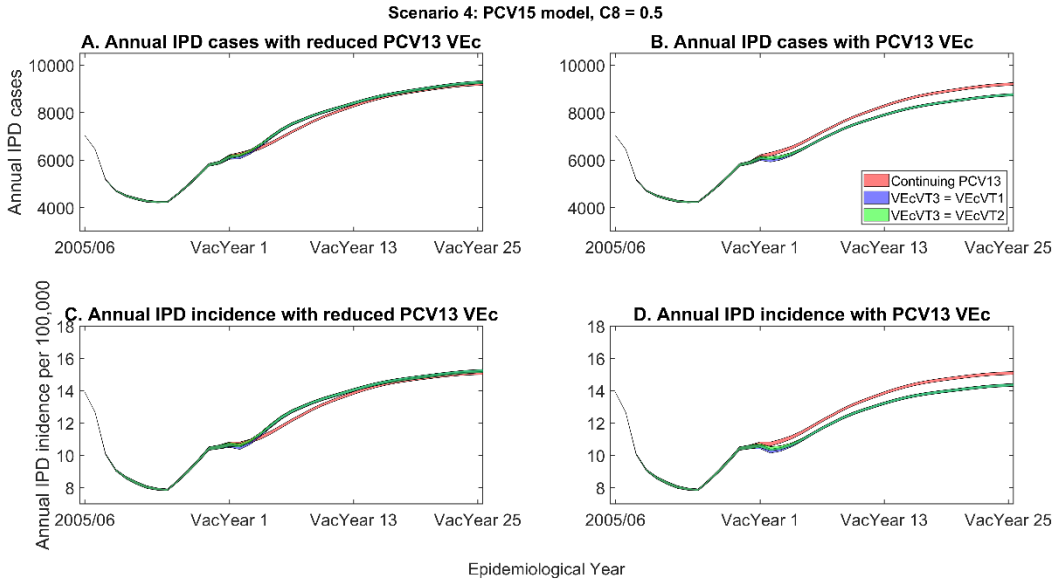
5 Long-term simulations

5.1 Model predictions for the six model scenarios: IPD cases and incidence per 100,000






Scenario 3: PCV15 model, ST3 in VT3, C8 = 1
A. Annual IPD cases with reduced PCV13 VEc
B. Annual IPD cases with PCV13 VEc
C. Annual IPD incidence with reduced PCV13 VEc
D. Annual IPD incidence with PCV13 VEc
Annual IPD cases
Annual IPD inidence per 100,000
10000
8000
6000
4000
18
16
14
12
10
8
2005/06
VacYear 1
VacYear 13
VacYear 25
Continuing PCV13
VEcVT3 = VEcVT1
VEcVT3 = VEcVT2
Epidemiological Year


Scenario 4: PCV15 model, C8 = 0.5
A. Annual IPD cases with reduced PCV13 VEc
B. Annual IPD cases with PCV13 VEc
C. Annual IPD incidence with reduced PCV13 VEc
D. Annual IPD incidence with PCV13 VEc
Annual IPD cases
Annual IPD inidence per 100,000
10000
8000
6000
4000
18
16
14
12
10
8
2005/06
VacYear 1
VacYear 13
VacYear 25
Continuing PCV13
VEcVT3 = VEcVT1
VEcVT3 = VEcVT2
Epidemiological Year

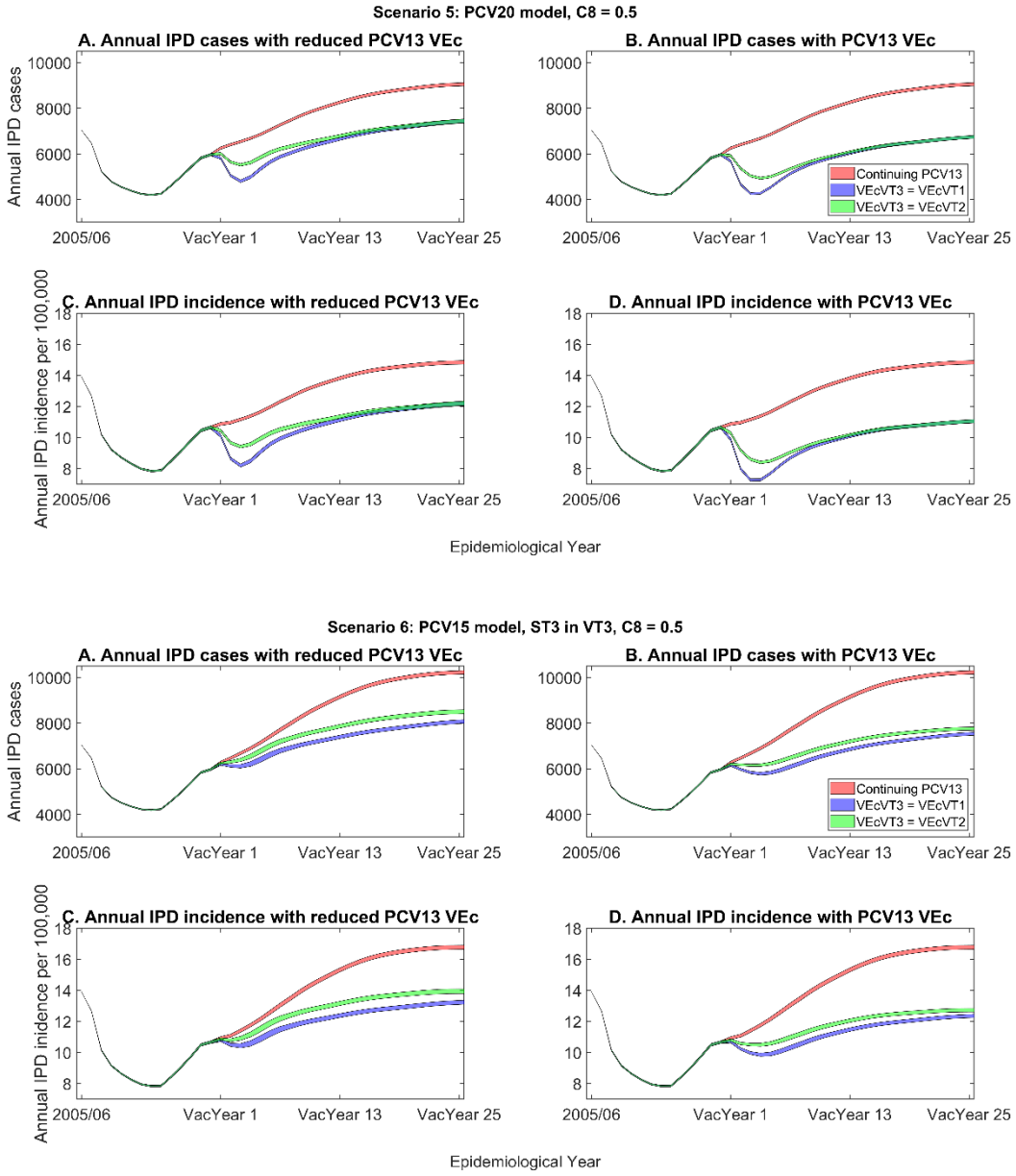
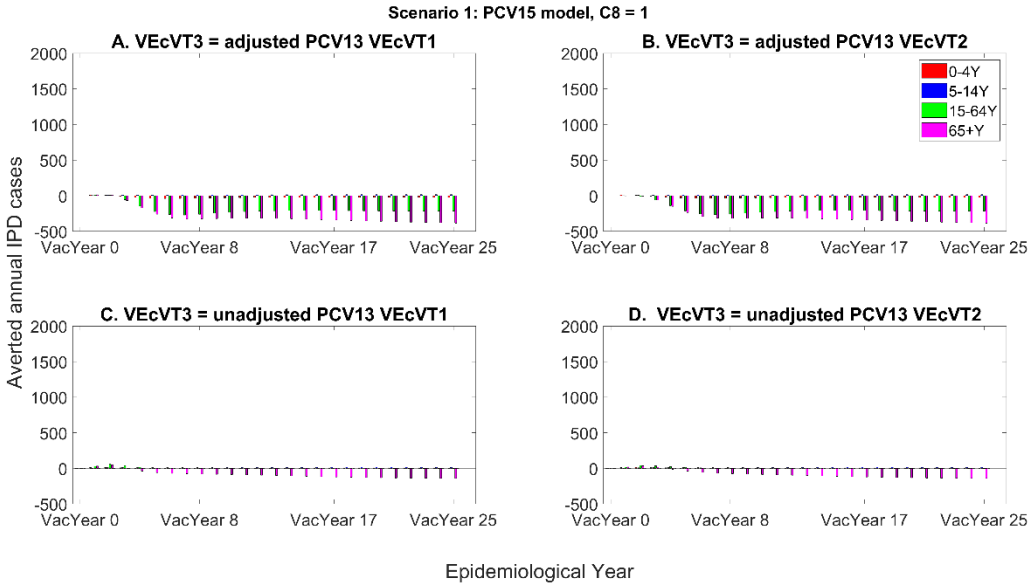
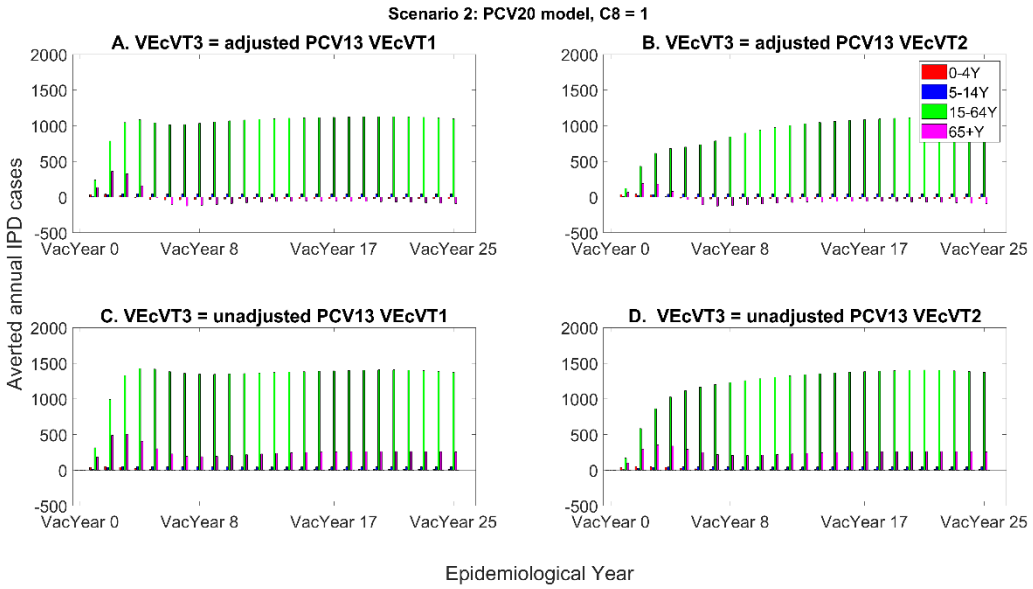
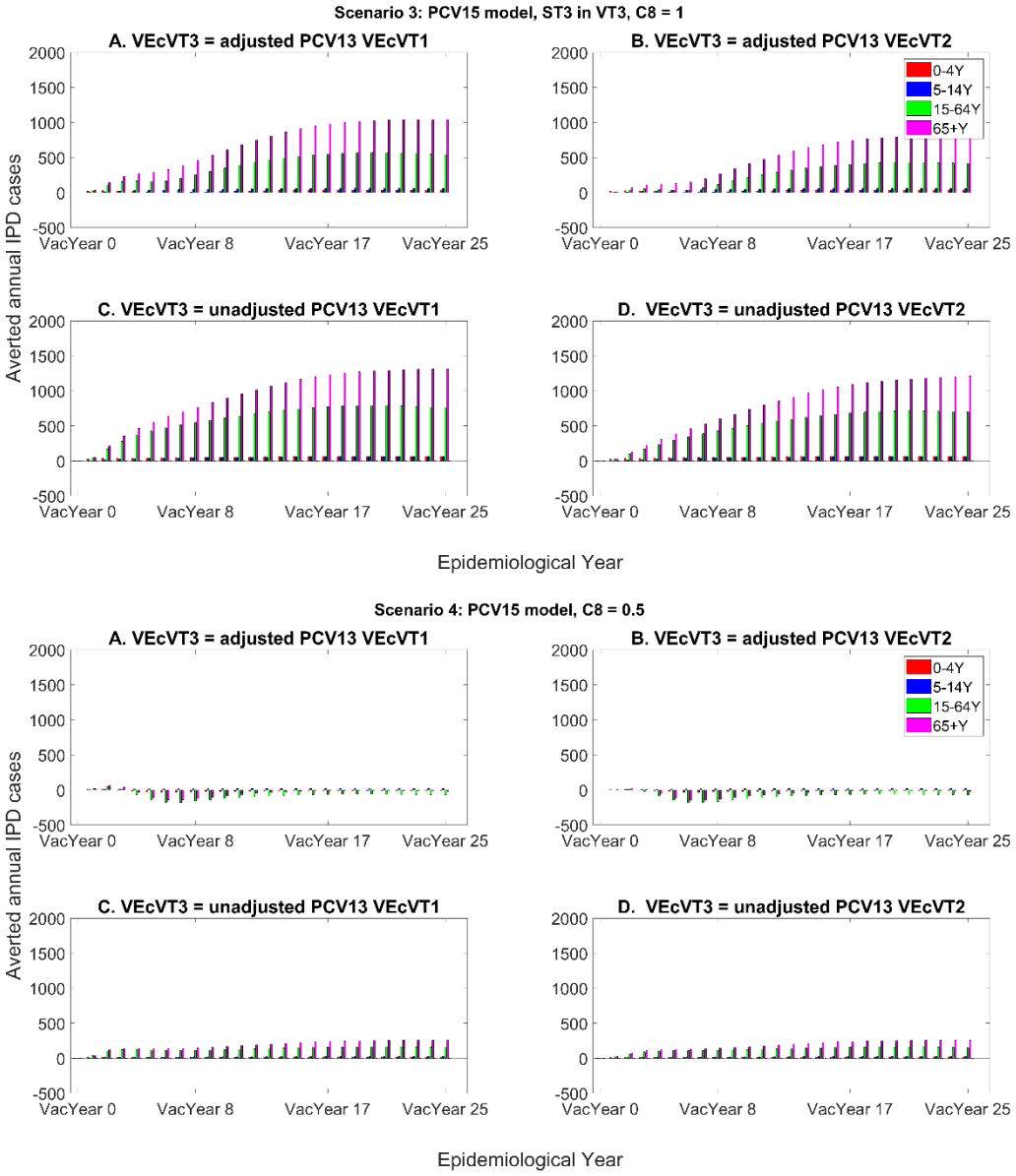


Figure S15. The annual IPD cases and incidences per 100,000 (median and uncertainty intervals in shaded area) from the six model scenarios in Figure S2 for all ages combined. Blue for scenarios assuming VEcVT3 as VecVT1; green for scenarios assuming VecVT3 as VEcVT2; red continuing with PCV13. VacYear 0 is assumed to be 2018/19 and VacYear 1 is the first year when PCV13 changes to a new PCV and the 1+1 schedule from the 2+1 in England. VEcVT1 and VEcVT2 are assumed to be the values presented in Table 2. (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype, VEc: Vaccine Efficacy against acquiring carriage, VacYear: Epidemiological year since the change of PCV13 with new PCV)

5.2 IPD cases prevented (averted) by year and age groups for the six model scenarios






Scenario 3: PCV15 model, ST3 in VT3, C8 = 1
A. VEcVT3 = adjusted PCV13 VEcVT1
B. VEcVT3 = adjusted PCV13 VEcVT2
C. VEcVT3 = unadjusted PCV13 VEcVT1
D. VEcVT3 = unadjusted PCV13 VEcVT2
0-4Y
5-14Y
15-64Y
65+Y
Averted annual IPD cases
2000
1500
1000
500
0
-500
VacYear 0
VacYear 8
VacYear 17
VacYear 25
Epidemiological Year
Scenario 4: PCV15 model, C8 = 0.5
A. VEcVT3 = adjusted PCV13 VEcVT1
B. VEcVT3 = adjusted PCV13 VEcVT2
C. VEcVT3 = unadjusted PCV13 VEcVT1
D. VEcVT3 = unadjusted PCV13 VEcVT2
0-4Y
5-14Y
15-64Y
65+Y
Averted annual IPD cases
2000
1500
1000
500
0
-500
VacYear 0
VacYear 8
VacYear 17
VacYear 25
Epidemiological Year

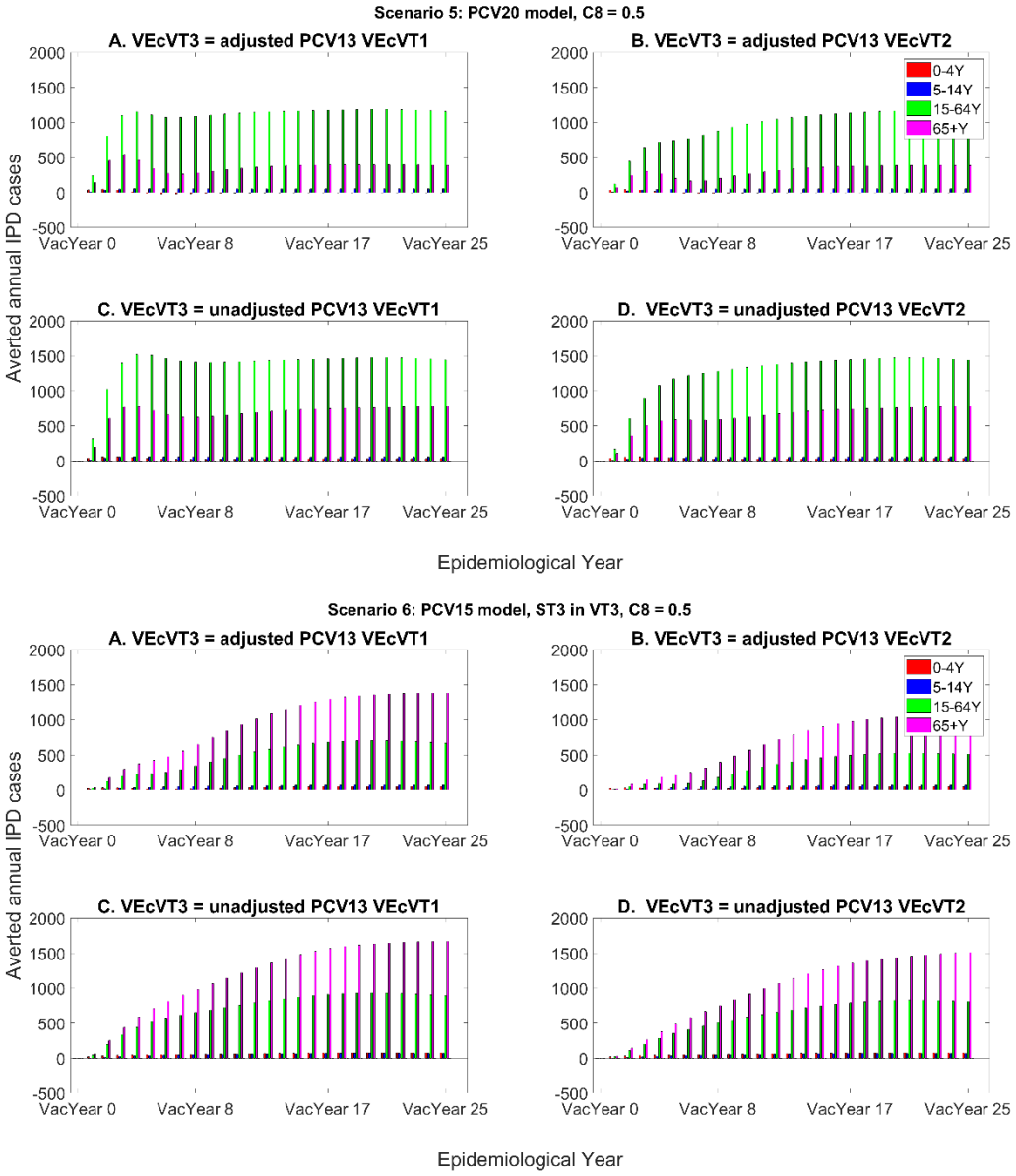
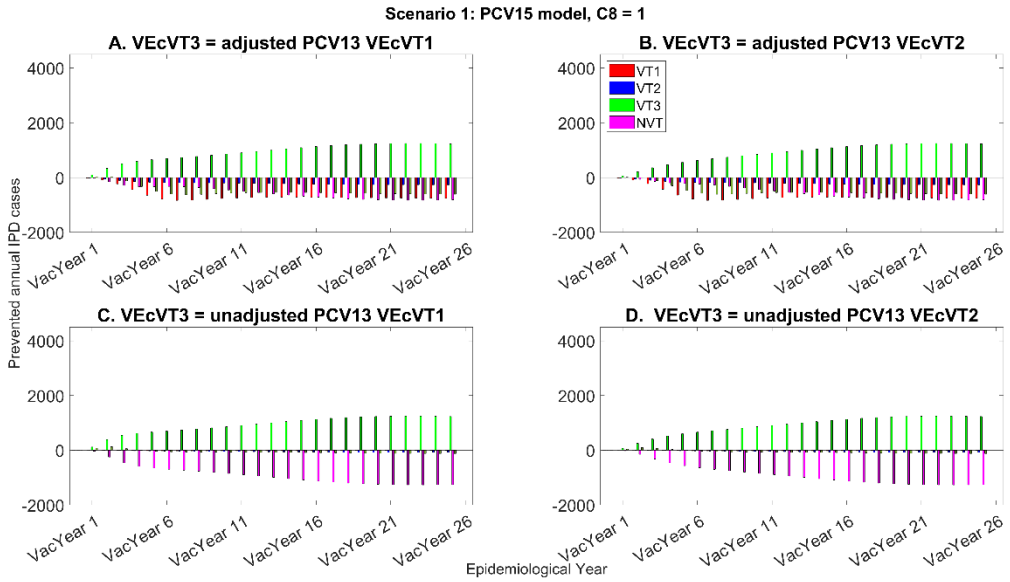
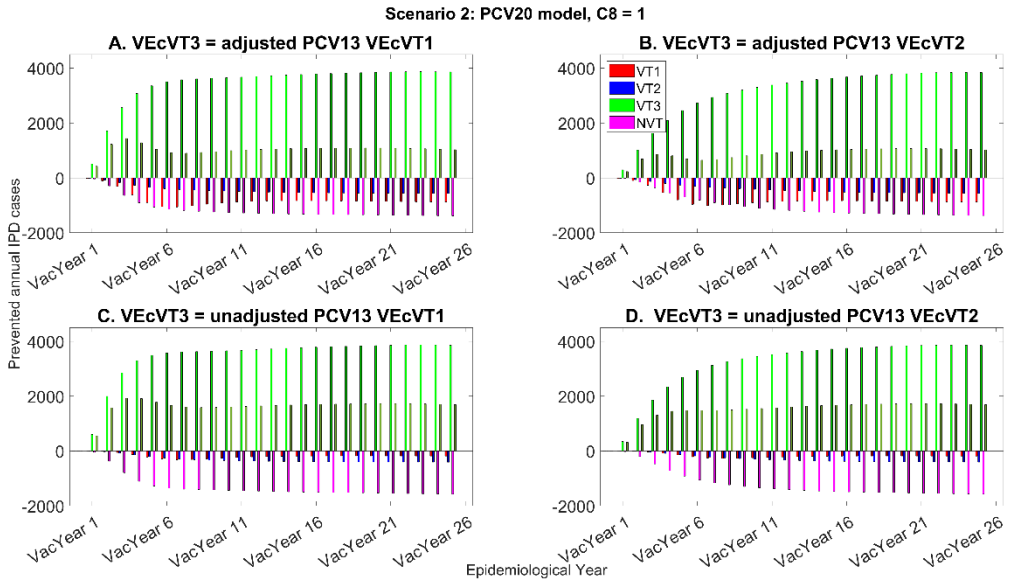
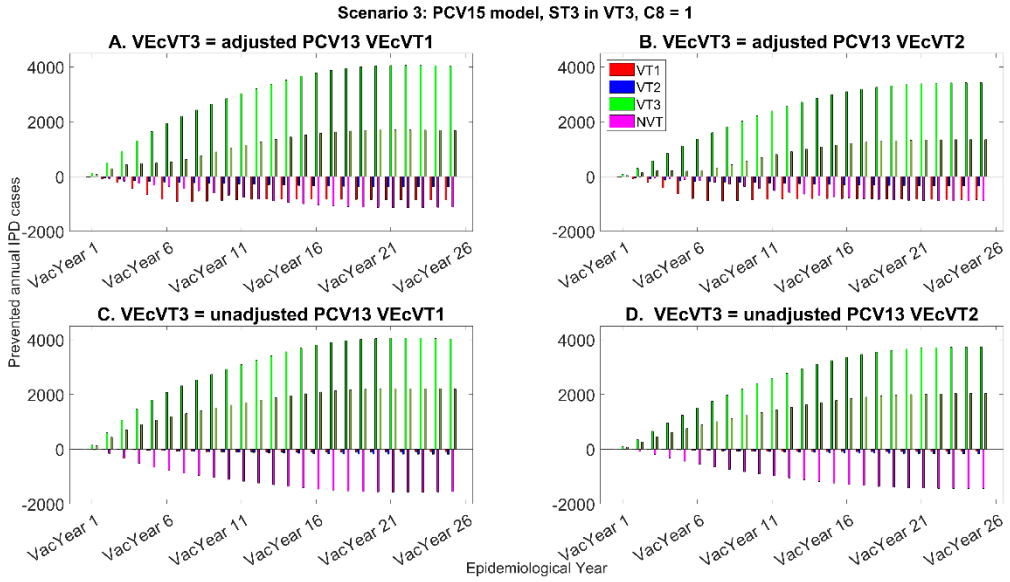


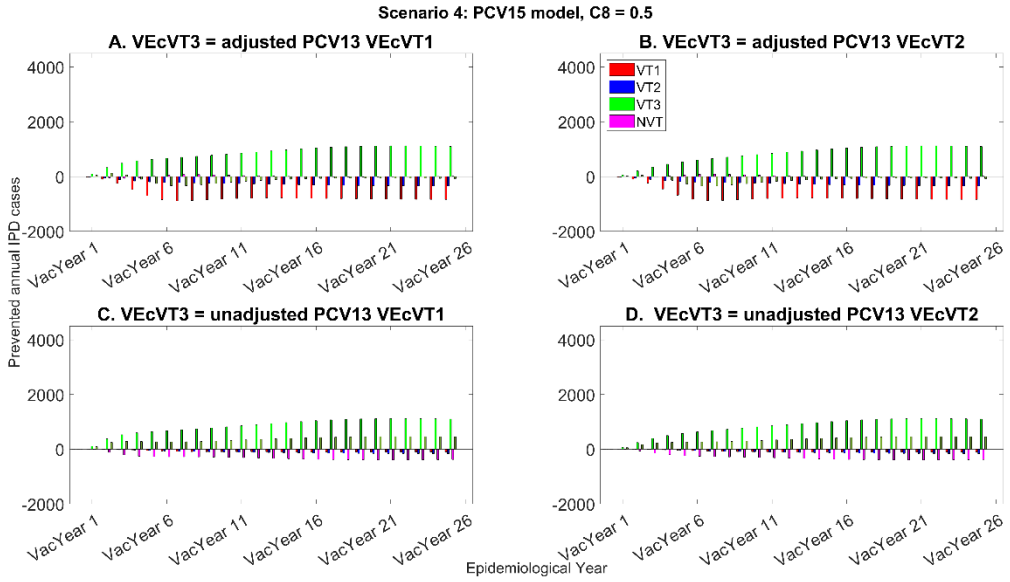
Figure S16. Averted annual IPD cases (uncertainty intervals in shaded area) by age groups for the six PCV15 and PCV20 model scenarios in Figure S2. VacYear 0 is assumed to be 2018/19 and VacYear 1 is the first year when PCV13 changes to a new PCV and the 2+1 schedule changes to the 1+1 schedule in England. VEcVT3 is assumed to be VEcVT1 or VEcVT2 as in Table 2. (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype, VEc: Vaccine Efficacy against acquiring carriage, VacYear: Epidemiological year since the change of PCV13 with new PCV)

5.3 IPD cases prevented (averted) by year and serotype groupings for the six model scenarios






Scenario 3: PCV15 model, ST3 in VT3, C8 = 1
A. VEcVT3 = adjusted PCV13 VEcVT1
B. VEcVT3 = adjusted PCV13 VEcVT2
C. VEcVT3 = unadjusted PCV13 VEcVT1
D. VEcVT3 = unadjusted PCV13 VEcVT2
VT1
VT2
VT3
NVT
Prevented annual IPD cases
Epidemiological Year
4000
2000
0
-2000
VacYear 1
VacYear 6
VacYear 11
VacYear 16
VacYear 21
VacYear 26


Scenario 4: PCV15 model, C8 = 0.5
A. VEcVT3 = adjusted PCV13 VEcVT1
B. VEcVT3 = adjusted PCV13 VEcVT2
C. VEcVT3 = unadjusted PCV13 VEcVT1
D. VEcVT3 = unadjusted PCV13 VEcVT2
VT1
VT2
VT3
NVT
Prevented annual IPD cases
Epidemiological Year
4000
2000
0
-2000
VacYear 1
VacYear 6
VacYear 11
VacYear 16
VacYear 21
VacYear 26

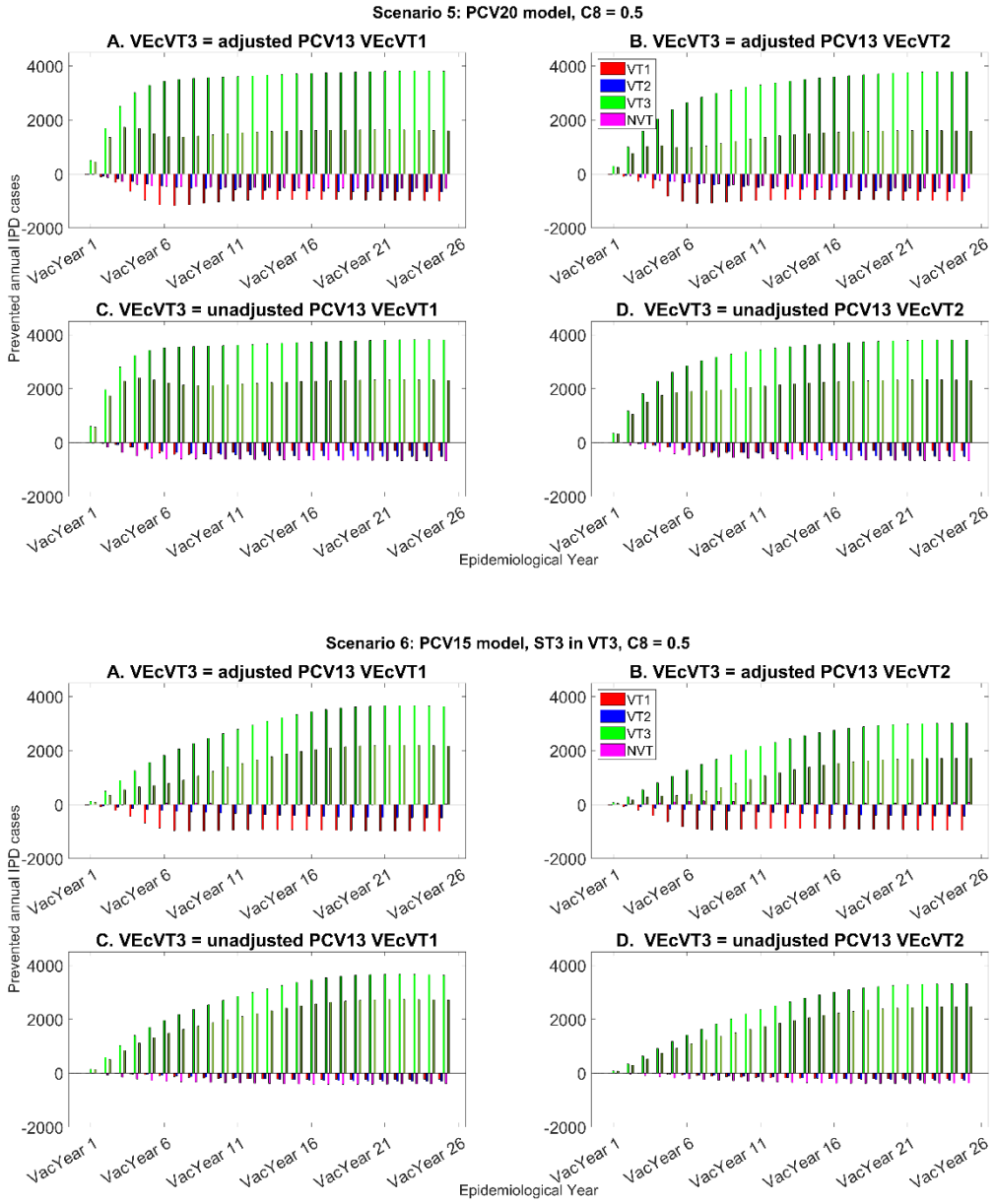


Figure S17. Medians of prevented (averted) annual IPD cases by four serotype groupings according to the six model scenarios in Fig S2. VacYear 0 is assumed to be 2018/19 and VacYear 1 is the first year when PCV13 changes to a new PCV and the 2+1 schedule changes to the 1+1 schedule in England. VEcVT3 is assumed to be VEcVT1 or VEcVT2 as in Table 2. (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype, VEc: Vaccine Efficacy against acquiring carriage, VacYear: Epidemiological year since the change of PCV13 with new PCV) (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate

Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype, VEc: Vaccine Efficacy against acquiring carriage, VacYear: Epidemiological year since the change of PCV13 with new PCV)

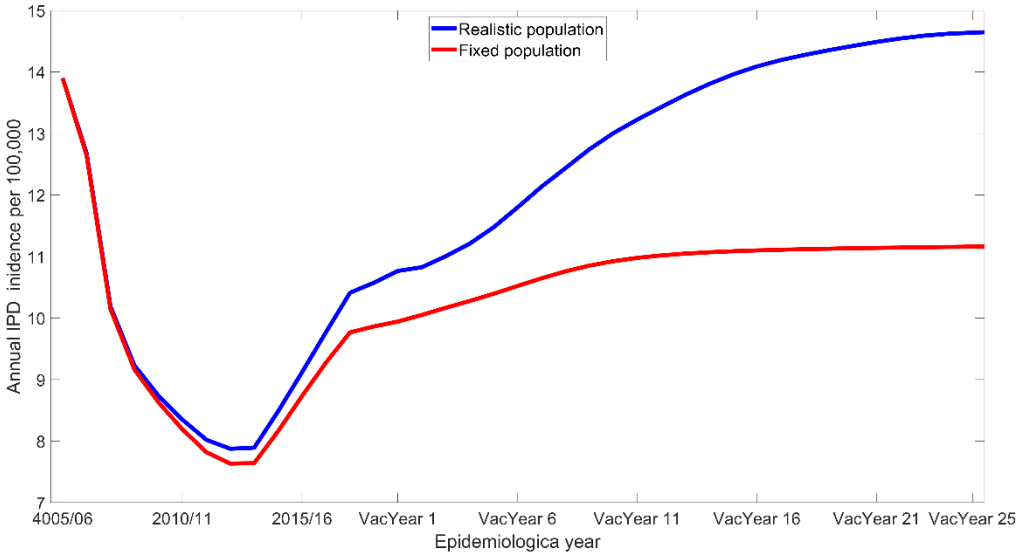


Figure S18. Annual overall IPD incidences per 100,000 from the long-term simulation model with continuing PCV13 in England with the 2+1 schedule change to 1+1 from VacYear 1. Blue line denotes the model results with the realistic population (blue) size using the population projections obtained from ONS (5), and Red line with the fixed population at 2005/06 (red). (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate Vaccine, VacYear: Epidemiological year since the change of PCV13 with new PCV)

5.4 Cumulative numbers of cases averted for the six model scenarios over 5 and 25 years

Table S4. Median (Uncertainty Intervals in brackets) of accumulated averted numbers of the IPD cases among 0-4 year olds for the first five and twenty five years according to the six PCV15 and PCV20 model scenarios since the change of PCV13 to PCV15 or PCV20 from VacYear1 in England (C8 is the competition parameter between VT3 and NVT). VEcVT3 is assumed to be one of four values of

adjusted or unadjusted VEcVT1 or VEcVT2 in Table 1. (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype, VEc: Vaccine Efficacy against acquiring carriage, VacYear: Epidemiological year since the change of PCV13 with new PCV)

		C8 = 1		C8 = 0.5	
Model	VEcVT3 value	5 years	25 years	5 years	25 years
PCV15	Adjusted VEcVT1	-53(-61, -38)	-609(-663, -542)	-29(-35, -19)	-367(-397, -328)
	Adjusted VEcVT2	-41(-51, -27)	-593(-646, -526)	-26(-32, -16)	-362(-392, -324)
	Unadjusted VEcVT1	35(32, 39)	125(99, 143)	69(64, 73)	394(366, 424)
	Unadjusted VEcVT2	45(42, 50)	138(111, 157)	71(66, 75)	398(370, 427)
PCV20	Adjusted VEcVT1	60(41, 79)	-457(-534, -382)	124(117, 139)	-4(-34, 94)
	Adjusted VEcVT2	97(78, 114)	-353(-426, -279)	136(129, 150)	49(20, 143)
	Unadjusted VEcVT1	170(160, 179)	332(277, 390)	249(243, 256)	828(788, 860)
	Unadjusted VEcVT2	204(195, 210)	419(364, 472)	253(249, 260)	872(835, 903)
PCV15, ST3 in VT3	Adjusted VEcVT1	92(76, 116)	615(555, 709)	112(102, 129)	843(787, 907)
	Adjusted VEcVT2	96(79, 119)	662(599, 753)	106(96, 122)	810(756, 873)
	Unadjusted VEcVT1	179(168, 202)	1,353(1,302, 1,459)	204(195, 216)	1,598(1,549, 1,651)
	Unadjusted VEcVT2	182(171, 205)	1,391(1,337, 1,495)	196(187, 207)	1,576(1,529, 1,627)

Table S5. Median (Uncertainty Intervals in brackets) of accumulated averted numbers of overall IPD cases for the first five and twenty five years according to the six PCV15 and PCV20 model scenarios since the change of PCV13 to PCV15 or PCV20 from VacYear1 in England (C8 is the competition parameter between VT3 and NVT). VEcVT3 is assumed to have the value of VEcVT1 or VEcVT2 in Table 1. (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype, VEc: Vaccine Efficacy against acquiring carriage, VacYear: Epidemiological year since the change of PCV13 with new PCV)

		C8 = 1		C8 = 0.5	
Model	VEcVT3 value	5 years	25 years	5 years	25 years
PCV15	Adjusted VEcVT1	-899(-1,019, -699)	-12,493(-13,400, -11,683)	-126(-238, 10)	-2,793(-3,662, -1,684)
	Adjusted VEcVT2	-886(-1,002, -687)	-12,403(-13,299, -11,597)	-354(-453, -235)	-3,096(-3,939, -2,026)
	Unadjusted VEcVT1	206(175, 242)	-1,654(-1,873, -1,326)	1,181(1,112, 1,262)	9,041(8,545, 9,853)
	Unadjusted VEcVT2	229(203, 259)	-1,589(-1,801, -1,270)	967(913, 1,032)	8,801(8,326, 9,587)
PCV20	Adjusted VEcVT1	5,407(5,041, 5,745)	26,048(24,081, 27,650)	6,701(6,535, 6,925)	37,911(36,836, 39,336)
	Adjusted VEcVT2	3,275(2,975, 3,586)	22,380(20,300, 23,960)	4,072(3,930, 4,247)	32,883(31,838, 34,283)
	Unadjusted VEcVT1	7,741(7,530, 7,920)	41,225(39,956, 42,375)	9,320(9,209, 9,532)	54,306(53,441, 55,523)
	Unadjusted VEcVT2	5,514(5,369, 5,628)	38,279(37,145, 39,309)	6,499(6,368, 6,616)	50,254(49,384, 51,233)
PCV15, ST3 in VT3	Adjusted VEcVT1	1,767(1,506, 2,068)	29,050(27,771, 30,974)	2,332(2,168, 2,608)	38,045(36,414, 39,507)
	Adjusted VEcVT2	798(575, 1,068)	21,064(19,724, 22,767)	1,141(1,040, 1,382)	27,355(26,457, 28,938)
	Unadjusted VEcVT1	3,221(3,081, 3,448)	41,451(40,559, 43,289)	3,921(3,741, 4,097)	51,116(49,529, 52,520)
	Unadjusted VEcVT2	2,152(2,086, 2,344)	35,631(34,813, 37,058)	2,573(2,471, 2,697)	43,082(42,271, 44,098)

6 Equations

6.1 Pre-PCV static model

This is a static model of the pneumococcal compartments built to estimate the force of infections (FOI) by four serotype groupings (VT1, VT2, VT3 and NVT) and age groups (0 Y, 1-2 Y, 3-4 Y, 5-9 Y, 10-19 Y, 20-39 Y, and 40Y+) at the pre-vaccination equilibrium given competition parameters between infectious compartments.

6.1.1 Equations S1.

$$S_i(t) = \left(1 - \lambda_{0,i-1}(t) - \lambda_{1,i-1}(t) - \lambda_{2,i-1}(t) - \lambda_{3,i-1}(t)\right) S_{i-1}(t-1) + \rho_{i-1}\left(VT1_{i-1}(t-1) + VT2_{i-1}(t-1) + VT3_{i-1}(t-1) + NVT_{i-1}(t-1)\right),$$

$$VT1_i(t) = \left(1 - \rho_{i-1} - P_{0,i-1}\lambda_{1,i-1}(t) - P_{1,i-1}\lambda_{2,i-1}(t) - P_{2,i}\lambda_{3,i-1}(t)\right) VT1_{i-1}(t-1) + \rho_{i-1}\left(VT1VT2_{i-1}(t-1) + VT1VT3_{i-1}(t-1) + VT1NVT_{i-1}(t-1)\right),$$

$$VT2_i(t) = \left(1 - \rho_{i-1} - P_{3,i-1}\lambda_{0,i-1}(t) - P_{4,i-1}\lambda_{2,i-1}(t) - P_{5,i-1}\lambda_{3,i-1}(t)\right) VT2_{i-1}(t-1) + \rho_{i-1}\left(VT1VT2_{i-1}(t-1) + VT2VT3_{i-1}(t-1) + VT2NVT_{i-1}(t-1)\right),$$

$$VT3_i(t) = \left(1 - \rho_{i-1} - P_{6,i-1}\lambda_{0,i-1}(t) - P_{7,i-1}\lambda_{1,i-1}(t) - P_{8,i-1}\lambda_{3,i-1}(t)\right) VT3_{i-1}(t-1) + \rho_{i-1}\left(VT1VT3_{i-1}(t-1) + VT2VT3_{i-1}(t-1) + VT2NVT_{i-1}(t-1)\right),$$

$$NVT_i(t) = \left(1 - \rho_{i-1} - P_{9,i-1}\lambda_{0,i-1}(t) - P_{0,i-1}\lambda_{1,i-1}(t) - P_{11,i-1}\lambda_{2,i-1}(t)\right) NVT_{i-1}(t-1) + \rho_{i-1}\left(VT1NVT_{i-1}(t-1) + VT2NVT_{i-1}(t-1) + VT3NVT_{i-1}(t-1)\right),$$

$$VT1VT2_i(t) = (1 - 2\rho_{i-1})VT1VT2_{i-1}(t-1) + P_{0,i-1}\lambda_{1,i-1}(t)VT1_{i-1}(t-1) + P_{3,i-1}\lambda_{0,i-1}(t)VT2_{i-1}(t-1),$$

$$VT1VT3_i(t) = (1 - 2\rho_{i-1})VT1VT3_{i-1}(t-1) + P_{1,i-1}\lambda_{2,i-1}(t)VT1_{i-1}(t-1) + P_{7,i-1}\lambda_{0,i-1}(t)VT2_{i-1}(t-1),$$

$$VT1NVT_i(t) = (1 - 2\rho_{i-1})VT1NVT_{i-1}(t-1) + P_{2,i-1}\lambda_{3,i-1}(t)VT1_{i-1}(t-1) + P_{10,i-1}\lambda_{0,i-1}(t)NVT_{i-1}(t-1),$$

$$VT2VT3_i(t) = (1 - 2\rho_{i-1})VT2VT3_{i-1}(t-1) + P_{4,i-1}\lambda_{2,i-1}(t)VT2_{i-1}(t-1) + P_{6,i-1}\lambda_{1,i-1}(t)VT3_{i-1}(t-1),$$

$$VT2NVT_i(t) = (1 - 2\rho_{i-1})VT2NVT_{i-1}(t-1) + P_{5,i-1}\lambda_{3,i-1}(t)VT1_{i-1}(t-1) + P_{9,i-1}\lambda_{1,i-1}(t)NVT_{i-1}(t-1),$$

$$VT3NVT_i(t) = (1 - 2\rho_{i-1})VT3NVT_{i-1}(t-1) + P_{8,i}\lambda_{3,i}(t)VT1_{i-1}(t-1) + P_{11,i}\lambda_{2,i}(t)NVT_{i-1}(t-1),$$

for $i = 2, \ldots, 4800$, weekly age cohorts (48 cohorts for each annual age cohort comprising 100 year cohorts between 0y and 99y) , where for $S_1 = 1, VT1_1 = VT2_1 = VT3_1 = NVT_1 = VT1VT2_1 = VT1VT3_1 = VT1NVT_1 = VT2VT3_1 = VT2NVT_1 = VT3NVT_1 = 0$, $\lambda_{0,i}(t)$, $\lambda_{1,i}(t)$, $\lambda_{2,i}(t)$, and $\lambda_{3,i}(t)$ are the force of carriage infection at time *t* for VT1, VT2, VT3 and NVT, respectively, $P_{n,i}$ (1 – $C_{n,AG}$, competition parameter Cn at age group (AG) of age *i* in Fig S7), is a reduction parameter on the force of carriage infection, and ρ_i is a clearance rate of carriage infection at age *i*.

The prevalence by serogroups and age groups (AG) are calculated as follows:

$$\text{Prevalence}_{VT1,AG} = \frac{\sum_{i \in AG}(VT1_i + VT1VT2_i + VT1VT3_i + VT1NVT_i)\, Population(Age)}{48 * Population(AG)},$$

$$\text{Prevalence}_{VT2,AG} = \frac{\sum_{i \in AG}(VT2_i + VT2VT3_i + VT2NVT_i)\, Population(Age)}{48 * Population(AG)},$$

$$\text{Prevalence}_{VT3,AG} = \frac{\sum_{i \in AG}(VT3_i + VT3NVT_i)\, Population(Age)}{48 * Population(AG)},$$

$$\text{Prevalence}_{NVT,AG} = \frac{\sum_{i \in AG}(NVT_i)\, Population(Age)}{48 * Population(AG)},$$

where assuming the detection rate using the quelling method(12) for serotyping for VT1 among VT1VT2, VT1VT3 and VT1NVT is assumed to be 100%, 100% for VT2 among VT2VT3 and VT2NVT, and

100% for VT3 among VT3NVT. This assumption could be changed if a more sensitive serotyping method than the quelling method is used to detect multiple infections in carriage samples.

The Nelder-Mead (Downhill Simplex) method (13) finds the best fitting model parameters for prevalence by maximising the following Poisson likelihood:

$$\text{LogLikelihood}(\text{Model}|\text{data}) =$$

$$\sum_{SG=1}^{4}\sum_{AG=1}^{7}\left(CarriageData_{SG,Age\ group} \times \log(\text{Prevalence}_{SG,Age\ group} * CarriageData_{all,Age\ group}) - \text{Prevalence}_{SG,Age\ group} * CarriageData_{all,Age\ group}\right),$$

where *SG* is for four serotype groupings and $CarriageData_{SG,Age\ group}$ consists of positive swabs in total swabs tested in seven age group ($CarriageData_{all,Age\ group}$).

When the static model is fitted to the pre-vaccination prevalence, the transmission probabilities per contact by four serotype groupings and seven age groups are calculated using these FOIs and Contact matrix combined POLYMOD survey (6) and infant contact survey (7), and population sizes of the seven age groups. The number of newly infected individuals in this static model as a denominator and IPD cases in 11 age groups (0Y, 1-2Y, 3-4Y, 5-9 Y, 10-14 Y, 15-24 Y, 25-44 Y, 45-64 Y, 65-74 Y, 75-84 Y, and 85+Y) as a numerator are used to calculate the Case:Carrier Ratios (CCRs) by four serotype groupings and eleven age groups. This method assumes that developing IPD occurs at the timing of the carriage acquisition. There is another assumption of the timing of the IPD occurrence throughout the duration of carriage infection, but we chose the former assumption as we found both methods provide very similar model outputs. The equilibrium of the static model is used as the initial values for the unvaccinated compartments in the dynamic transmission model to minimise the computing time of the fitting and long-term simulation procedures without running the model for the burn-in periods since it is the equilibrium of the pre-PCV era.

Transmission probability calculation:

$$NoInfectious_{VT1,AG} = \sum_{Week\epsilon AG} (Comp_{VT1} + Comp_{VT1VT2} + Comp_{VT1VT3} + Comp_{VT1NVT})Pop_{age}/48,$$
$$NoInfectious_{VT2,AG} = \sum_{Week\epsilon AG} (Comp_{VT2} + Comp_{VT1VT2} + Comp_{VT2VT3} + Comp_{VT2NVT})Pop_{age}/48,$$
$$NoInfectious_{VT3,AG} = \sum_{Week\epsilon AG} (Comp_{VT3} + Comp_{VT1VT3} + Comp_{VT2VT3} + Comp_{VT3NVT})Pop_{age}/48,$$
$$NoInfectious_{NVT,AG} = \sum_{Week\epsilon AG} (Comp_{NVT} + Comp_{VT1NVT} + Comp_{VT2NVT} + Comp_{VT3NVT})Pop_{age}/48,$$

where "NoInfectious" denotes the sum of infectious individuals in each age group (AG) with the carriage of VT1, VT2, VT3 or NVT according to the proportion of the infectious compartments multiplied by the weekly population size in England.

$$NewlyInfected_{SG,AG_i} = \sum_{AG_j=0}^{6} \left(NoInfectious_{SG,AG_j} \times POLYMOD_{AG_i,AG_j}\right),$$

Where "NewlyInfected" values are the sum of newly infected individuals, SG is one of four serotype groupings of VT1, VT2, VT3 or NVT, and POLYMOD is a mixing matrix between 7 age groups.

$$Q_{SG,AG_i} = {FOI_{SG,AG_j}}/{NewlyInfected_{AG_i,AG_j}},$$

where "Q" values are the transmission probabilities per contact, FOIs are estimated forces of infection obtained from the fitting the static model to the pre-PCV7 carriage data stratified by four serotype groupings (SG) and 7 age groups (AG), and the "NewlyInfected" is the sum of the newly infected individuals by four serotype groupings (SG) and 7 age groups (AG).

Case:Carrier ratio calculation:

$$NewInfections_{VT1,AG} = \sum_{Week\epsilon AG} \left(FOI_{0,AG}(Comp_{Sus} + C_3 Comp_{VT2} + C_7 Comp_{VT3} + C_{10} Comp_{NVT})\right) Pop_{age}/48,$$
$$NewInfections_{VT2,AG} = \sum_{Week\epsilon AG} \left(FOI_{1,AG}(Comp_{Sus} + C_0 Comp_{VT1} + C_6 Comp_{VT3} + C_9 Comp_{NVT})\right) Pop_{age}/48,$$
$$NewInfections_{VT3,AG} = \sum_{Week\epsilon AG} \left(FOI_{2,AG}(Comp_{Sus} + C_1 Comp_{VT1} + C_4 Comp_{VT2} + C_{11} Comp_{NVT})\right) Pop_{age}/48,$$

$$NewInfections_{NVT,AG} = \sum_{Week \epsilon AG} \left(FOI_{3,AG}(Comp_{Sus} + C_2 Comp_{VT1} + C_5 Comp_{VT2} + C_8 Comp_{VT3})\right) Pop_{age}/48,$$

where "NewInfectiouns" denotes the sum of new infected individuals in each age group (11 AGs, the eleven age groups is different to seven FOI age groups) with the estimated FOI0, FOI1, FOI2 and FOI3 of VT1, VT2, VT3 or NVT respectively. Comp denotes the proportion of Sus (susceptible), VT1, VT2, VT3 and NVT in each weekly age cohort.

$$CCR_{SG,AG_i} = \text{IPD\_Cases}_{SG,AG_j} \Big/ NewInfections_{SG,AG},$$

Where CCR_{SG,AG_i} denotes the case:carrier ratio of one of four serotype groupings (SG) of VT1, VT2, VT3 or NVT, and 11 age groups (AG), and $\text{IPD\_Cases}_{SG,AG_j}$ is the number of IPD cases in 2005/06 corresponding to the SG and AG.

6.2 Dynamic transmission model

Upon the estimated model parameters from the static model, the dynamic model can run from 2005/06 until 2018/19 with additional two VEc values for PCV7 and PCV13, and two proportional increases in NVT CCR in U4Y and 65+Y age groups between 2014/15 and 2017/18. The reason to choose only NVT grouping and two age groups for the CCR increase assumption was that these proportional CCR increase were very close to zero in 5-64Y age group according to the previous study (3) and not noticeable in VT3 groups for additional serotypes in both PCV15 and PCV20 (Fig 1).

6.2.1 Discrete difference equations S2.

In the dynamic model, there are two procedures to run for each weekly time step: one for transmission procedures to move individuals between compartments according to infection status, and another for vaccination procedures to vaccinate individuals according to vaccine coverage data and wane vaccine protection. Here are the discrete difference equations for the dynamic model.

6.2.1.1 Transmission procedure:

$$S_{i,Vac}(t) = \left(1 - \lambda_{0,i-1}(t-1) - \lambda_{1,i-1}(t-1) - \lambda_{2,i-1}(t-1) - \lambda_{3,i-1}(t-1)\right) S_{i-1,Vac}(t-1) + \rho_{i-1}\left(VT1_{i-1,Vac}(t-1) + VT2_{i-1,Vac}(t-1) + VT3_{i-1,Vac}(t-1) + NVT_{i-1,Vac}(t-1)\right),$$

$$VT1_{i,Vac}(t) = \left(1 - \rho_{i-1} - P_{0,i-1}\lambda_{1,i-1}(t-1) - P_{1,i-1}\lambda_{2,i-1}(t-1) - P_{2,i-1}\lambda_{3,i-1}(t-1)\right) VT1_{i-1,Vac}(t-1) + \lambda_{0,i-1}(t-1)S_{i-1,Vac}(t-1) + \rho_{i-1}\left(VT1VT2_{i-1,Vac}(t-1) + VT1VT3_{i-1,Vac}(t-1) + VT1NVT_{i-1,Vac}(t-1)\right),$$

$$VT2_{i,Vac}(t) = \left(1 - \rho_{i-1} - P_{3,i-1}\lambda_{0,i-1}(t-1) - P_{4,i-1}\lambda_{2,i-1}(t-1) - P_{5,i-1}\lambda_{3,i-1}(t-1)\right) VT2_{i-1,Vac}(t-1) + \lambda_{1,i-1}(t-1)S_{i-1,Vac}(t-1) + \rho_{i-1}\left(VT1VT2_{i-1,Vac}(t-1) + VT2VT3_{i-1,Vac}(t-1) + VT2NVT_{i-1,Vac}(t-1)\right),$$

$$VT3_{i,Vac}(t) = \left(1 - \rho_{i-1} - P_{7,i-1}\lambda_{0,i-1}(t-1) - P_{6,i-1}\lambda_{1,i-1}(t-1) - P_{8,i-1}\lambda_{3,i-1}(t-1)\right) VT3_{i-1,Vac}(t-1) + \lambda_{2,i-1}(t-1)S_{i-1,Vac}(t-1) + \rho_{i-1}\left(VT1VT3_{i-1,Vac}(t-1) + VT2VT3_{i-1,Vac}(t-1) + VT3NVT_{i-1,Vac}(t-1)\right),$$

$$NVT_{i,Vac}(t) = \left(1 - \rho_{i-1} - P_{9,i-1}\lambda_{1,i-1}(t-1) - P_{10,i-1}\lambda_{0,i-1}(t-1) - P_{11,i-1}\lambda_{2,i-1}(t-1)\right) NVT_{i-1,Vac}(t-1) + \lambda_{3,i-1}(t-1)S_{i-1,Vac}(t-1) + \rho_{i-1}\left(VT1NVT_{i-1,Vac}(t-1) + VT2NVT_{i-1,Vac}(t-1) + VT3NVT_{i-1,Vac}(t-1)\right),$$

$$VT1VT2_{i,Vac}(t) = (1 - 2\rho_{i-1})VT1VT2_{i-1,Vac}(t-1) + P_{0,i-1}\lambda_{1,i-1}VT1_{i-1,Vac}(t-1) + P_{3,i-1}\lambda_{0,i-1}VT2_{i-1,Vac}(t-1),$$

$$VT1VT3_{i,Vac}(t)$$

$$= (1 - 2\rho_{i-1})VT1VT3_{i-1,Vac}(t-1) + P_{1,i-1}\lambda_{2,i-1}VT1_{i-1,Vac}(t-1)$$

$$+ P_{7,i-1}\lambda_{0,i-1}VT3_{i-1,Vac}(t-1),$$

$$VT1NVT_{i,Vac}(t)$$

$$= (1 - 2\rho_{i-1})VT1NVT_{i-1,Vac}(t-1) + P_{2,i-1}\lambda_{3,i-1}VT1_{i-1,Vac}(t-1)$$

$$+ P_{10,i-1}\lambda_{0,i-1}NVT_{i-1,Vac}(t-1),$$

$$VT2VT3_{i,Vac}(t)$$

$$= (1 - 2\rho_{i-1})VT2VT3_{i-1,Vac}(t-1) + P_{4,i-1}\lambda_{2,i-1}VT2_{i-1,Vac}(t-1)$$

$$+ P_{6,i-1}\lambda_{1,i-1}VT3_{i-1,Vac}(t-1),$$

$$VT2NVT_{i,Vac}(t)$$

$$= (1 - 2\rho_{i-1})VT2NVT_{i-1,Vac}(t-1) + P_{5,i-1}\lambda_{3,i-1}VT2_{i-1,Vac}(t-1)$$

$$+ P_{9,i-1}\lambda_{1,i-1}NVT_{i-1,Vac}(t-1),$$

$$VT3NVT_{i,Vac}(t)$$

$$= (1 - 2\rho_{i-1})VT3NVT_{i-1,Vac}(t-1) + P_{8,i-1}\lambda_{3,i-1}VT3_{i-1,Vac}(t-1)$$

$$+ P_{11,i-1}\lambda_{2,i-1}NVT_{i-1,Vac}(t-1),$$

for *i = 0 to 4799*, of all weekly age cohorts (48 weekly cohorts for each annual age cohort comprising 100 year cohorts between 0y and 99y), ρ_i is the recovery rate by age of the *i*-the weekly cohort, $P_{n,i} = \left(1 - C_{n,i}\right), for\ n = 0\ to 11$ is the *n*-th competition parameter for the age group of the *i*-th weekly cohort.

6.2.1.2 Vaccination procedure

After running the transmission routine, the individuals in the model population change their vaccination status according to the vaccine coverage and duration of vaccine protection (waning) of PCV7, PCV13 and new PCV (PCV15 or PCV20). Since the move between vaccination compartments are different in the periods of PCV7, PCV13 and new PCV vaccination, we split the vaccination routines in these different periods.

To describe the equations in simple terms, we represent the compartments in the vaccination routines as *X = S, VT1, VT2, VT3, NVT, VT1VT2, VT1, VT3, VT1NVT, VT2VT3, VT2NVT, or VT3NVT*,

6.2.1.2.1 PCV7 period:

Unvaccinated:

$$X_{i,1}(t) = \Big(1 - \varphi_{1,i}(t-1) - \varphi_{2,i}(t-1) - \varphi_{3,i}(t-1)\Big) X_{i-1,1}(t-1),$$

Partially protected with PCV7, j=2:

$$X_{i,2}(t) = \big(1 - \varphi_{2,i}(t-1) - \varphi_{3,i}(t-1) - \omega\big)X_{i-1,2}(t-1) + \varphi_{1,i(if\ age<1)}(t-1)X_{i-1,1}(t-1) + \omega X_{i-1,3}(t-1),$$

Fully protected with PCV7:

$$X_{i,3}(t) = (1-\omega)X_{i-1,2}(t-1) + \varphi_{1,i(if\ age\geq 1)}(t-1)X_{i-1,1}(t-1) + \Big(\varphi_{1,i(if\ age<1)}(t-1) + \varphi_{2,i}(t-1) + \varphi_{3,i}(t-1)\Big) X_{i-1,1}(t-1) + \Big(\varphi_{2,i}(t-1) + \varphi_{3,i}(t-1)\Big)\Big(X_{i-1,2}(t-1) + X_{i-1,4}(t-1)\Big),$$

Vaccine protection waned with PCV7:

$$X_{i,4}(t) = \Big(1 - \varphi_{2,i}(t-1) - \varphi_{3,i}(t-1)\Big) X_{i-1,4}(t-1) + \omega X_{i-1,2}(t-1),$$

6.2.1.2.2 PCV13 period:

Unvaccinated:

$$X_{i,1}(t) = \Big(1 - \varphi_{1,i}(t-1) - \varphi_{2,i}(t-1) - \varphi_{3,i}(t-1)\Big) X_{i-1,1}(t-1),$$

Partially protected with PCV7, j=2:

$$X_{i,2}(t) = \big(1 - \varphi_{2,i}(t-1) - \varphi_{3,i}(t-1) - \omega\big)X_{i-1,2}(t-1) + \omega X_{i-1,3}(t-1),$$

Fully protected with PCV7:

$$X_{i,3}(t) = (1-\omega)X_{i-1,2}(t-1),$$

Vaccine protection waned with PCV7:

$$X_{i,4}(t) = \big(1-\varphi_{2,i}(t-1)-\varphi_{3,i}(t-1)-\omega\big)X_{i-1,4}(t-1)+\omega X_{i-1,2}(t-1),$$

Partially protected with PCV13:

$$X_{i,5}(t) = \big(1-\varphi_{2,i}(t-1)-\varphi_{3,i}(t-1)-\omega\big)X_{i-1,5}(t-1)$$
$$+\Big(\varphi_{1,i}(t-1)+\varphi_{2,i}(t-1)\Big)X_{i-1,1}(t-1)+\omega X_{i-1,6}(t-1),$$

Fully protected with PCV13:

$$X_{i,6}(t) = (1-\omega)X_{i-1,6}(t-1)+\varphi_{3,i}(t-1)X_{i-1,1}(t-1)$$
$$+\Big(\varphi_{2,i}(t-1)+\varphi_{3,i}(t-1)\Big)\Big(X_{i-1,2}(t-1)+X_{i-1,4}(t-1)+X_{i-1,5}(t-1)$$
$$+X_{i-1,7}(t-1)\Big),$$

Vaccine protection waned with PCV13:

$$X_{i,7}(t) = \Big(1-\varphi_{2,i}(t-1)-\varphi_{3,i}(t-1)\Big)X_{i-1,7}(t-1)+\omega X_{i-1,5}(t-1),$$

6.2.1.2.3 New PCV period:

Unvaccinated:

$$X_{i,1}(t) = \Big(1-\varphi_{1,i}(t-1)-\varphi_{2,i}(t-1)-\varphi_{3,i}(t-1)\Big)X_{i-1,1}(t-1),$$

Partially protected with PCV7, j=2:

$$X_{i,2}(t) = \big(1-\varphi_{2,i}(t-1)-\varphi_{3,i}(t-1)-\omega\big)X_{i-1,2}(t-1)+\omega X_{i-1,3}(t-1),$$

Fully protected with PCV7:

$$X_{i,3}(t) = (1-\omega)X_{i-1,2}(t-1),$$

Vaccine protection waned with PCV7:

$$X_{i,4}(t) = \big(1 - \varphi_{2,i}(t-1) - \varphi_{3,i}(t-1) - \omega\big)X_{i-1,4}(t-1) + \omega X_{i-1,2}(t-1),$$

Partially protected with PCV13:

$$X_{i,5}(t) = \big(1 - \varphi_{2,i}(t-1) - \varphi_{3,i}(t-1) - \omega\big)X_{i-1,5}(t-1) + \omega X_{i-1,6}(t-1),$$

Fully protected with PCV13:

$$X_{i,6}(t) = (1-\omega)X_{i-1,6}(t-1),$$

Vaccine protection waned with PCV13:

$$X_{i,7}(t) = \Big(1 - \varphi_{2,i}(t-1) - \varphi_{3,i}(t-1)\Big)X_{i-1,7}(t-1) + \omega X_{i-1,5}(t-1),$$

Partially protected with new PCV:

$$X_{i,8}(t) = \big(1 - \varphi_{2,i}(t-1) - \varphi_{3,i}(t-1) - \omega\big)X_{i-1,8}(t-1) + \Big(\varphi_{1,i}(t-1) + \varphi_{2,i}(t-1)\Big)X_{i-1,1}(t-1) + \omega X_{i-1,9}(t-1),$$

Fully protected with new PCV:

$$X_{i,9}(t) = (1-\omega)X_{i-1,9}(t-1) + \varphi_{3,i}(t-1)X_{i-1,1}(t-1) + \Big(\varphi_{2,i}(t-1) + \varphi_{3,i}(t-1)\Big)\Big(X_{i-1,2}(t-1) + X_{i-1,4}(t-1) + X_{i-1,5}(t-1) + X_{i-1,7}(t-1) + X_{i-1,8}(t-1) + X_{i-1,10}(t-1)\Big),$$

Vaccine protection waned with new PCV:

$$X_{i,10}(t) = \Big(1 - \varphi_{2,i}(t-1) - \varphi_{3,i}(t-1)\Big)X_{i-1,10}(t-1) + \omega X_{i-1,8}(t-1),$$

for $i = 0\ to\ 4799$, of all weekly age cohorts (48 cohorts for each annual age cohort comprising 100 year old cohorts between 0Y and 99Y). To run all weekly cohorts in each time step in the model, there are 11 equations for the transmission routine and a maximum of 110 equations for the vaccination routine, and in total 580,080 (121 * 4,800) equations. The movement between vaccine

protected groups depends on the monthly vaccine uptake and vaccine protection waning according to the duration of vaccine protection. π is a reduction parameter on the FOI, λ, which is 1-Competition parameter between serotype groupings, φs are monthly vaccination rates for each dose (two primary and booster doses), $VEcVT1$, $VEcVT2$, and $VEcVT3$ reduce FOIs due to VEc of PCV7, PCV13 and new PCV against acquiring carriage of VT1, VT2 and VT3, ω is a waning parameter (1/duration of vaccine protection), and ρ is a clearance rate, 1/ duration of colonisation (fixed at 5 years).

6.2.1.3 Transmission routine (with vaccination):

$$S_{i,Vac}(t) = \Big(1 - (1 - VEcVT1)\lambda_{0,i-1}(t-1) - (1 - VEcVT2)\lambda_{1,i-1}(t-1) - (1 - VEcVT3)\lambda_{2,i-1}(t-1) - \lambda_{3,i-1}(t-1)\Big) S_{i-1,Vac}(t-1) + \rho_{i-1}\Big(VT1_{i-1,Vac}(t-1) + VT2_{i-1,Vac}(t-1) + VT3_{i-1,Vac}(t-1) + NVT_{i-1,Vac}(t-1)\Big),$$

$$VT1_{i,Vac}(t) = \Big(1 - \rho_{i-1} - P_{0,i-1}(1 - VEcVT2)\lambda_{1,i-1}(t-1) - P_{1,i-1}(1 - VEcVT3)\lambda_{2,i-1}(t-1) - P_{2,i-1}\lambda_{3,i-1}(t-1)\Big) VT1_{i-1,Vac}(t-1) + (1 - VEcVT1)\lambda_{0,i-1}(t-1)S_{i-1,Vac}(t-1) + \rho_{i-1}\Big(VT1VT2_{i-1,Vac}(t-1) + VT1VT3_{i-1,Vac}(t-1) + VT1NVT_{i-1,Vac}(t-1)\Big),$$

$$VT2_{i,Vac}(t) = \Big(1 - \rho_{i-1} - P_{3,i-1}(1 - VEcVT1)\lambda_{0,i-1}(t-1) - P_{4,i-1}(1 - VEcVT3)\lambda_{2,i-1}(t-1) - P_{5,i-1}\lambda_{3,i-1}(t-1)\Big) VT2_{i-1,Vac}(t-1) + (1 - VEcVT2)\lambda_{1,i-1}(t-1)S_{i-1,Vac}(t-1) + \rho_{i-1}\Big(VT1VT2_{i-1,Vac}(t-1) + VT2VT3_{i-1,Vac}(t-1) + VT2NVT_{i-1,Vac}(t-1)\Big),$$

$$VT3_{i,Vac}(t) = \Big(1 - \rho_{i-1} - P_{7,i-1}(1 - VEcVT1)\lambda_{0,i-1}(t-1) - P_{6,i-1}(1 - VEcVT2)\lambda_{1,i-1}(t-1)$$
$$- P_{8,i-1}\lambda_{3,i-1}(t-1)\Big) VT3_{i-1,Vac}(t-1)$$
$$+ (1 - VEcVT3)\lambda_{2,i-1}(t-1)S_{i-1,Vac}(t-1)$$
$$+ \rho_{i-1}\Big(VT1VT3_{i-1,Vac}(t-1) + VT2VT3_{i-1,Vac}(t-1) + VT3NVT_{i-1,Vac}(t-1)\Big),$$

$$NVT_{i,Vac}(t) = \Big(1 - \rho_{i-1} - P_{9,i-1}(1 - VEcVT2)\lambda_{1,i-1}(t-1) - P_{10,i-1}(1 - VEcVT1)\lambda_{0,i-1}(t-1)$$
$$- P_{11,i-1}(1 - VEcVT3)\lambda_{2,i-1}(t-1)\Big) NVT_{i-1,Vac}(t-1)$$
$$+ \lambda_{3,i-1}(t-1)S_{i-1,Vac}(t-1)$$
$$+ \rho_{i-1}\Big(VT1NVT_{i-1,Vac}(t-1) + VT2NVT_{i-1,Vac}(t-1)$$
$$+ VT3NVT_{i-1,Vac}(t-1)\Big),$$

$$VT1VT2_{i,Vac}(t)$$
$$= (1 - 2\rho_{i-1})VT1VT2_{i-1,Vac}(t-1)$$
$$+ P_{0,i-1}(1 - VEcVT2)\lambda_{1,i-1}VT1_{i-1,Vac}(t-1)$$
$$+ P_{3,i-1}(1 - VEcVT1)\lambda_{0,i-1}VT2_{i-1,Vac}(t-1),$$

$$VT1VT3_{i,Vac}(t)$$
$$= (1 - 2\rho_{i-1})VT1VT3_{i-1,Vac}(t-1)$$
$$+ P_{1,i-1}(1 - VEcVT3)\lambda_{2,i-1}VT1_{i-1,Vac}(t-1)$$
$$+ P_{7,i-1}(1 - VEcVT1)\lambda_{0,i-1}VT3_{i-1,Vac}(t-1),$$

$$VT1NVT_{i,Vac}(t)$$
$$= (1 - 2\rho_{i-1})VT1NVT_{i-1,Vac}(t-1) + P_{2,i-1}\lambda_{3,i-1}VT1_{i-1,Vac}(t-1)$$
$$+ P_{10,i-1}(1 - VEcVT1)\lambda_{0,i-1}NVT_{i-1,Vac}(t-1),$$

$$VT2VT3_{i,Vac}(t)$$

$$= (1 - 2\rho_{i-1})VT2VT3_{i-1,Vac}(t-1)$$

$$+ P_{4,i-1}(1 - VEcVT3)\lambda_{2,i-1}VT2_{i-1,Vac}(t-1)$$

$$+ P_{6,i-1}(1 - VEcVT2)\lambda_{1,i-1}VT3_{i-1,Vac}(t-1),$$

$$VT2NVT_{i,Vac}(t)$$

$$= (1 - 2\rho_{i-1})VT2NVT_{i-1,Vac}(t-1) + P_{5,i-1}\lambda_{3,i-1}VT2_{i-1,Vac}(t-1)$$

$$+ P_{9,i-1}(1 - VEcVT2)\lambda_{1,i-1}NVT_{i-1,Vac}(t-1),$$

$$VT3NVT_{i,Vac}(t)$$

$$= (1 - 2\rho_{i-1})VT3NVT_{i-1,Vac}(t-1) + P_{8,i-1}\lambda_{3,i-1}VT3_{i-1,Vac}(t-1)$$

$$+ P_{11,i-1}(1 - VEcVT3)\lambda_{2,i-1}NVT_{i-1,Vac}(t-1),$$

for *i = 0 to 4799*, of all weekly age cohorts (48 weekly cohorts for each annual age cohort comprising 100 year cohorts between 0y and 99y), ρ_i is the recovery rate by age of the *i*-the weekly cohort, $P_{n,i} = \left(1 - C_{n,i}\right), for\ n = 0\ to 11$ is the *n*-th competition parameter for the age group of the *i*-th weekly cohort, and Vac = 0 to 9, for vaccine protection status (0: unvaccinated, 1: partially protected with PCV7, 2: fully protected with PCV7, 3: Vaccine protection waned with PCV7, 4: partially protected with PCV13, 5: fully protected with PCV13, 6: Vaccine protection waned with PCV13, 7: partially protected with new PCV, 8: fully protected with new PCV, and 9: Vaccine protection waned with new PCV), and the reductions ($VEcVT1, VEcVT2,$ and $VEcVT3$) on the FOIs are given according to the status of the PCV vaccine protection:

0: Susceptible, $VEcVT1$ = 0, $VEcVT2$ = 0, $VEcVT3$ = 0,

1: Partial protected with PCV7, $VEcVT1$= 0.5* $VEcVT1$ of PCV7, $VEcVT2$ = 0, VEcVT3 = 0,

2: Fully protected with PCV7, $VEcVT1$= $VEcVT1$ of PCV7, $VEcVT2$= 0, VEcVT3 = 0,

3: PCV7 protection waned, $VEcVT1$ = 0, $VEcVT2$= 0, VEcVT3 = 0,

4: Partial protected with PCV13, $VEcVT1$ = 0.5* $VEcVT1$ of PCV13, $VEcVT2$= 0.5* $VEcVT2$ of PCV13, VEcVT3 = 0,

5: Fully protected with PCV13, $VEcVT1$ = $VEcVT1$ of PCV13, $VEcVT2$= $VEcVT2$ of PCV13, VEcVT3 = 0,

6: PCV13 protection waned, $VEcVT1$ = 0, $VEcVT2$= 0, VEcVT3 = 0,

7: Partial protected with new PCV, $VEcVT1$ = 0.5* $VEcVT1$ of new PCV, $VEcVT2$= 0.5* $VEcVT2$ of new PCV, VEcVT3 = 0.5 * $VEcVT3$ of new PCV,

8: Fully protected with new PCV, $VEcVT1$ = $VEcVT1$ of new PCV, $VEcVT2$= $VEcVT2$ of new PCV, VEcVT3 = $VEcVT3$ of new PCV,

9: New PCV protection waned, $VEcVT1$ = 0, $VEcVT2$= 0, VEcVT3 = 0,

VEcVT3: VEc of new PCV against additional serotypes according to model scenarios considered.

6.2.1.3.1 Forces of infection (FOI)

$$FOI_{k_{SG},AG_i} = QValue_{k_{SG},AG_i} \times InfSum_{k_{SG},AG_i},$$

where $InfSum_{k_{SG},AG_i} = \sum_{AG_j=1}^{7} Infected_{k_{SG},AG_j} \times POLYMOD_{Year,AG_i,AG_j} \times {}^{365}/_{48}$,

and

$$Infected_{VT1,AG_j} = \sum_{i \in AG_j} \sum_{Vac=0}^{9} \left(VT1_{i,Vac} + VT1VT2_{i,Vac} + VT1VT3_{i,Vac} + VT1NVT_{i,Vac}\right) \times {}^{PopSize_{Year}(Age(i))}/_{48},$$

$$Infected_{VT2,AG_j}$$

$$= \sum_{i \in AG_j} \sum_{Vac=0}^{9} \left(VT2_{i,Vac} + VT1VT2_{i,Vac} + VT2VT3_{i,Vac} + VT2NVT_{i,Vac}\right)$$

$$\times PopSize_{Year}\left(Age(i)\right) \Big/ 48,$$

$$Infected_{VT3,AG_j}$$

$$= \sum_{i \in AG_j} \sum_{Vac=0}^{9} \left(VT3_{i,Vac} + VT1VT3_{i,Vac} + VT2VT3_{i,Vac} + VT3NVT_{i,Vac}\right)$$

$$\times PopSize_{Year}\left(Age(i)\right) \Big/ 48,$$

$$Infected_{NVT,AG_j}$$

$$= \sum_{i \in AG_j} \sum_{Vac=0}^{9} \left(NVT_{i,Vac} + VT1NVT_{i,Vac} + VT2NVT_{i,Vac} + VT3NVT_{i,Vac}\right)$$

$$\times PopSize_{Year}\left(Age(i)\right) \Big/ 48,$$

i is a weekly age index from 0 to 4,799, AG_j is the *j-th* age group among seven age groups (under 1, 1-2, 3-4, 5-9, 10-19, 20-39, and 40+ years), Vac indicates the status of the vaccine protection (0: unvaccinated, 1: partially protected with PCV7, 2: fully protected with PCV7, 3: Vaccine protection waned with PCV7, 4: partially protected with PCV13, 5: fully protected with PCV13, 6: Vaccine protection waned with PCV13, 7: partially protected with new PCV, 8: fully protected with new PCV, and 9: Vaccine protection waned with new PCV), $PopSize_{Year}\left(Age(i)\right)$ for the size of the age group that the week index, i, belong to in each Year, and $i \in AG_j$ for those week indices belong to the age group of AG_j.

6.2.1.3.2 IPD cases calculation

The numbers of IPD cases by serotype groupings and age groups in each Year are calculated according to the following equations:

$$IPD\_Cases_{VT1,Year,AG} = \sum_{i \in AG} \sum_{Vac}^{0,3,6,9} \left(CCR_{VT1,AG(i)} \times \lambda_{1,i-1} \times \left(S_{i-1,Vac} + P_{3,i-1} \times VT2_{i-1,Vac} + P_{7,i} \times VT3_{i-1,Vac} + P_{10,i} \times NVT_{i-1,Vac} \right) \right) \times {}^{PopSize_{Year,age(i-1)}}/_{48},$$

$$IPD\_Cases_{VT2,Year,AG} = \sum_{w \in AG} \sum_{Vac}^{0,1,2,3,6,9} \left(CCR_{VT2,AG(i-1)} \times \lambda_{2,i-1} \times \left(S_{i-1,Vac} + P_{0,i-1} \times VT1_{i-1,Vac} + P_{6,i} \times VT3_{i-1,Vac} + P_{9,i-1} \times NVT_{i-1,Vac} \right) \right) \times {}^{PopSize_{Year,age(i-1)}}/_{48},$$

$$IPD\_Cases_{VT3,Year,AG} = \sum_{i \in AG} \sum_{Vac}^{0,1,2,3,4,5,6,9} \left(CCR_{VT3,AG(i-1)} \times \lambda_{3,i-1} \times \left(S_{i-1,Vac} + P_{1,i-1} \times VT1_{i-1,Vac} + P_{3,i-1} \times VT2_{i-1,Vac} + P_{3,i-1} \times NVT_{i-1,Vac} \right) \right) \times {}^{PopSize_{Year,age(i-1)}}/_{48},$$ and

$$IPD\_Cases_{NVT,Year,AG} = \sum_{i \in AG} \sum_{Vac=0}^{9} \left(CCR_{NVT,AG(i-1)} \times \lambda_{4,i} \times \left(S_{w,Vac} + P_{2,i-1} \times VT1_{i-1,Vac} + P_{5,i-1} \times VT2_{i-1,Vac} + P_{8,i-1} \times VT3_{i-1,Vac} \right) \right) \times {}^{PopSize_{Year,age(i-1)}}/_{48},$$

where $CCR_{NVT,AG(i)}$ is the case:carrier ratio for NVT serotype grouping and age group of the *i*-th weekly cohort, $P_{n,i}\ for\ n = 0\ to 11$ is (1 - $C_{n,i}$, the n-th competition parameter for the age group of the i-th weekly cohort), Vac is for the vaccination status.

The Nelder-Mead method finds the set of model parameters that maximize the Poisson likelihood with the following formula:

$$LogLikelihood\ (Model|data) = \sum_{Y=2005/06}^{2018/19} \sum_{SG=1}^{4} \sum_{AG=1}^{6} \left(IPDModel_{Y,SG,AG} \times log\left({}^{IPDModel_{Y,SG,AG}}/_{IPDData_{Y,SG,AG}} \right) - \left(IPDModel_{Y,SG,AG} - IPDData_{Y,SG,AG} \right) \right)$$

for four serotype groupings (SG) and six age groups (AG) in each year (Y) from 2005/06 to 2018/19.

7 Parameter derivation summary

Table S6. Summary of key model parameter derivations and those that were varied in the fitting and

sensitivity analysis (IPD: Invasive Pneumococcal Disease, PCV: Pneumococcal Conjugate Vaccine, VT: Vaccine Type, NVT: Non Vaccine Type, ST: Serotype, VEc: Vaccine Efficacy against acquiring carriage, VacYear: Epidemiological year since the change of PCV13 with new PCV)

Parameter	**How derived**	**Comment**
Duration of a carriage episode by age, $\frac{1}{\rho_i}$	Fitting a Markov Chain model to household transmission data in pre-PCV7 longitudinal carriage study	Calibrated to be the same for VT1, VT2 or NVT groups as described in references (0-1Y: 72 days, 2-4Y: 28 days, 5-17Y: 18 days, and 18+Y: 17 days) (14, 15)
Force of carriage infection (FOI) at age *i* and time *t*: $\lambda_{0,i}(t), \lambda_{1,i}(t), \lambda_{2,i}(t)$ and $\lambda_{3,i}(t)$	Calculated from the pre-PCV static model using the given 15 competition parameters	Directly solving the static model equations using the observed pre-PCV carriage prevalence by seven age groups and four serotype groupings using the Nelder-Mead method (13) (Fig S9).
Transmission probabilities per contact by age groups and serotype groupings	Calculated using four forces of infections and the contact matrix between seven age groups	Direct calculation (Fig S10)
Case : Carrier ratio (CCR) by four serotype groupings and eleven age groups (<2 m, 2-3 m, 4-5 m, 6-11 m, 1Y, 2Y, 3Y, 4Y, 5-9Y, 10-14Y, 15-24Y, 25-44Y, 45-64Y, 65-74Y, 75-84Y, and 85+Y)	Calculated using the number of new carriage episodes from the static model and IPD cases in the pre-PCV year	Assuming the timing of developing IPD at the carriage acquisition (Fig S11).

Incidence of new carriage episodes by VT1, VT2, VT3 or NVT serotype groupings and age groups	Fitting a pneumococcal static model to the pre-PCV7 longitudinal carriage dataset (1)	By four serotype groupings and eleven age groups
Duration of vaccine protection against carriage acquisition of VT1 and, VT2 and VT3 serotype groupings, $\frac{1}{\omega}$	Fixed at 5 years for both partial and full protections. When waned from full protection, they acquire another 5 years of partial protection.	In the model fitting, duration is inversely related to degree of protection so cannot be estimated independently. Duration was therefore fixed at 5 years (3, 16).
Degree of full vaccine protection against carriage of VT1 and VT2 (two fitted parameters VEcVT1 and VEcVT2), (d_7 = VEcVT1 and d_{13} = VEcVT2 in equations)	Fitting a dynamic transmission model to changes in the pre- and post- PCV7 and PCV13 IPD data	For those who have waned to the partial protection category, the degree of protection was assumed to be half that of the full protection (Table 1).
Degree of full vaccine protection against carriage of VT3, d_{new}	Assumed to be the same value of VEcVT1 or VEcVT2	This value cannot be estimated until the IPD dataset of post VT3 PCV become available (assumed in Table 1).
Eleven Competition parameters in three age groups (0-14Y, 15-64Y and 65+Y): C0, C1, C2, C3, C4, and C5 (15 fitted parameters)	Fitting a dynamic transmission model to changes in the pre- and post- PCV7 and PCV13 IPD data	The magnitude of the increase in NVT IPD cases is determined by these competition parameters. The higher the level of competition the greater the increase in NVT IPD cases (Table S3).
C3, C5, C6, C7, C10 and C11	Assumed to be 0.5	These parameters are insensitive due to the carriage reduction of VT groups

C8	Assumed to be 1 as a baseline and 0.5 for the sensitivity analysis	The competition between VT3 and NVT is not estimable as the VT3 vaccine has not been introduced yet. Drawing from past experiences, where replacement occurred at a maximum level, we assumed complete replacement (Competition = 1) and conducted a sensitivity analysis with a lower value.
Duration of vaccine protection against IPD	Fixed at 5 years for partial and full protections.	An exponential decay function was used as a waning parameter. Waning the full protection moved individuals to have a partial protection for another five years of protection (3, 16).
Degree of vaccine protection against IPD (VEd) given carriage acquisition	Fixed at 100% while fully or partially protected	The fitting resulted in about 100% so this parameter was fixed at 100%. Despite seeming high, given waning the overall protection against IPD as a function of time since vaccination appears realistic (3, 16).
Proportional increase CCR of NVTs from 2014/15 in two age groups (2 fitted parameters)	Fitting a dynamic transmission model to changes in the post- PCV13 IPD data from 2014/15 to 2018/19	One-time proportionate increase is assumed to continue out to 2030/31 (Table S3) (3, 16)

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