

1 Title: Assessing the efficiency of catch-up campaigns for introduction of
2 pneumococcal conjugate vaccine; a modelling study based on data from Kilifi,
3 Kenya

4 Short title: The efficiency of catch-up campaigns for PCV introduction

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19

20 Abstract:

21

22 *Background:* The World Health Organisation recommends the use of catch-up campaigns as
23 part of the introduction of pneumococcal conjugate vaccines (PCVs) to accelerate herd
24 protection and hence PCV impact. The value of a catch-up campaign is a trade-off between
25 the costs of vaccinating additional age groups and the benefit of additional direct and
26 indirect protection. There is a paucity of observational data, particularly from low-middle
27 income countries to quantify the optimal breadth of such catch-up campaigns.

28

29 *Methods:* In Kilifi, Kenya PCV10 was introduced in 2011 using the 3-dose EPI infant schedule
30 and a catch-up campaign in children <5 years old. We fitted a transmission dynamic model
31 to detailed local data including nasopharyngeal carriage and invasive pneumococcal disease
32 (IPD) to infer the marginal impact of the PCV catch-up campaign over hypothetical routine
33 cohort vaccination in that setting, and to estimate the likely impact of alternative campaigns
34 and their dose-efficiency.

35

36 *Results:* We estimated that, within 10 years of introduction, the catch-up campaign among
37 <5y olds prevents an additional 65 (48 to 84) IPD cases, compared to PCV cohort
38 introduction alone. Vaccination without any catch-up campaign prevented 155 (121 to 193)
39 IPD cases and used 1321 (1058 to 1698) PCV doses per IPD case prevented. In the years
40 after implementation, the PCV programme gradually accrues herd protection and hence its
41 dose-efficiency increases: 10 years after the start of cohort vaccination alone the
42 programme used 910 (732 to 1184) doses per IPD case averted. We estimated that a two-
43 dose catch-up among <1y olds uses an additional 910 (732 to 1184) doses per additional IPD
44 case averted. Furthermore, by extending a single dose catch-up campaign to children 1 to
45 <2y old and subsequently to 2 to <5y olds the campaign uses an additional 412 (296 to 606)
46 and 543 (403 to 763) doses per additional IPD case averted. These results were not sensitive
47 to vaccine coverage, serotype competition, the duration of vaccine protection or the
48 relative protection of infants.

49

50 *Conclusions:* We find that catch-up campaigns are a highly dose-efficient way to accelerate
51 population protection against pneumococcal disease.

52

53 Manuscript:

54

55 **Introduction**

56 With the aid of Gavi, the Vaccine Alliance (Gavi), many low income countries, in particular
57 across Africa, have introduced pneumococcal conjugate vaccines (PCVs) into their infant
58 immunisation programmes. However, there remain Gavi countries particularly in south Asia
59 and northern Africa, some with large infant populations, who are yet to follow [1]. Country
60 policy makers, along with global stakeholders, have high interest in achieving optimal health
61 impact from PCV as quickly as possible, however, approaches for achieving maximum and
62 rapid impact have to be weighed against relative cost. In situations where vaccine supply is
63 constrained, as was the case several years ago for PCV, issues of efficiency and equity in
64 vaccine use are also a consideration [2]. The World Health Organisation (WHO) recommends
65 that catch-up campaigns can be used as part of the introduction of PCVs to accelerate the
66 build-up of herd protection and hence PCV impact [3]. However, it is unclear if such catch-
67 up campaigns are an efficient way to use PCV or if the gains from such approach are less
68 than the relative increase in the number of doses required.

69

70 The value of a catch-up campaign is assessed by quantifying the trade-off between the costs
71 of vaccinating additional age groups and the benefit of additional direct and indirect
72 protection. However, there are few observational data on the impact of PCV campaigns,
73 particularly from low-and middle income countries (LMICs), to quantify the optimal
74 approach of catch-up campaigns. One of the few well-studied examples of a PCV
75 introduction catch-up campaign in a LMIC occurred in Kilifi, Kenya. The 10- valent
76 pneumococcal non typeable *Haemophilus influenzae* protein D-conjugate vaccine (PCV10)
77 was introduced into the Kenyan routine childhood vaccination programme in early January
78 2011 using the WHO Expanded Programme on immunization (EPI) schedule of 3 infant
79 doses at 6, 10 and 14 weeks. Additionally, in Kilifi County, at the introduction of the cohort
80 programme a 3 dose catch-up campaign was offered to all infants less than 12 months of
81 age and a 2 dose catch-up to children 12-59 months of age.

82

83 We fitted a transmission dynamic model of pneumococcal carriage (a precondition for
84 disease and the source of person to person community transmission) and disease to
85 detailed pre- and post PCV introduction data from Kilifi. We aimed to quantify the marginal
86 impact of the PCV catch-up campaign on carriage and disease in Kilifi over the hypothetical
87 impact of a routine cohort vaccination programme alone in that setting. The model also
88 allowed estimation of the likely impact and efficiency of alternative catch-up campaigns.

89

90 **Methods**

91 Data

92 *Study population and mixing patterns*

93 Kilifi County is a mainly rural area at the Indian Ocean coast of Kenya. The Kilifi Health and
94 Demographic Surveillance System (KHDSS) was established in 2000. Approximately 260,000
95 people reside in the KHDSS area and 60% are younger than 20 years of age [4]. Within the
96 KHDSS numerous studies regarding pneumococcus and it's health effects have been
97 conducted that informed this work (Table 1). The demographic structure of the model is
98 based on 2009 mid-year population census estimates and assumes no demographic changes

99 with time. To adjust for changes in the population age distribution we used respective
100 annual mid-year population estimates to calculate the invasive pneumococcal disease (IPD)
101 incidence rates. A cross sectional prospective diary-based contact survey was conducted in
102 the northern part of KHDSS in 2009 [5,6]. In total 623 randomly selected participants of all
103 ages produced 568 completed diaries in which they reported their contacts during 24 hours
104 and reported 27,395 physical (i.e. skin to skin) contacts with 10,042 unique individuals. This
105 information was used as a proxy for transmission of pneumococcal carriage [7,8]. Standard
106 methods were used to calculate the WAIFW (Who Acquires Infection From Whom) mixing
107 matrix for age groups <1y, 1-5y, 6-15y, 16-19y, 20-49y and older than 50 years for Kilifi HDSS
108 [5,8-10].

109

110 *Pneumococcal carriage and IPD*

111 The model was fitted to vaccine type and non-vaccine type carriage prevalence and IPD
112 incidence between 2009 and 2015. During that period annual cross sectional carriage
113 surveys were conducted in Kilifi HDSS [11]. In each study a nasopharyngeal swab was
114 collected from more than 500 randomly selected individuals of all ages. Surveillance with
115 passive case finding for IPD was introduced at Kilifi County Hospital in 1998 for children and
116 in 2007 for adults. Among the residents of Kilifi HDSS, 30 to 70 cases of IPD have been
117 reported annually [12]. Much of that variation is due to changes in disease caused by
118 serotype 1, which has been reported to be unstable in various settings before [13,14].

119

120 *Duration of carriage*

121 We used average age-specific pneumococcal colonization clearance rates estimated from a
122 longitudinal carriage survey in Kilifi HDSS [15] and reported for the age groups <22 months,
123 22-40 months and 41-59 months. Based on other studies [16], we assumed that clearance
124 rates in individuals older than 5 years of age were 60% higher than in children of age 2-4
125 years.

126

127 *Serotype competition*

128 As the competition parameter, which determines the proportion by which the likelihood of
129 acquisition is reduced by heterologous carriage, based on local data was only estimated
130 serotype specific [15] rather than for pooled vaccine type and non-vaccine type groups we
131 used a log-normal prior distribution with a median of 0.11 based on estimates from other
132 settings [17-19].

133

134 *Vaccine coverage*

135 As part of KHDSS, electronic individual-based records of the delivery of vaccines are
136 routinely collected at vaccine clinics [20]. We calculated weekly estimates of PCV coverage
137 for the two years after PCV introduction; each stratified by weekly age cohorts from
138 newborns up to 5 years of age. Two such coverage estimates were calculated: vaccine
139 coverage of at least two doses of PCV administered before the age of 1 year, which was
140 deemed “infant protection”, and vaccine coverage of at least one dose of PCV administered
141 after the age of 1 year, deemed “toddler protection”. The choice of at least 2 doses for
142 infants and at least one dose for toddlers was chosen on the basis of observed coverage
143 rates. For calculation of the number of doses used we assumed that vaccinated infants
144 within the routine program received 3 doses, infants vaccinated as part of the catch-up
145 received 2 doses and toddlers received 1 dose. Data for vaccination rates were available

146 only through late 2012; we extrapolated those rates forward in time by assuming the
147 coverage rates as of later 2012 to continue for the rest of the study period.

148

149 *Vaccine efficacy*

150 The efficacy against VT nasopharyngeal carriage of a single dose of PCV10 administered to
151 children 12-59 months old has been estimated in a randomised controlled trial in Kenya at
152 36% (95% CI:-1 to 60) [21]. We further assumed that vaccine efficacy against VT IPD of a
153 complete primary series was 80% based on a meta-analysis for PCVs for infants elsewhere
154 [22]. These two estimates of vaccine efficacy against VT carriage and VT IPD were used as
155 priors in the fitting process. Those who were vaccinated in infancy, i.e. before one year of
156 age, may have different vaccine efficacy against acquisition of colonisation, progression to
157 invasive disease and the duration of protection than vaccinated toddlers. Hence we allowed
158 for the model to estimate these parameters for infants as a common proportion of that of
159 toddlers, under the null-hypothesis that no difference exists.

160

161 *Duration of vaccine protection*

162 As estimates of the duration of protection from PCV were not available from studies within
163 the KHDSS we used estimates derived from external studies. Hence our prior on the
164 duration of protection against carriage and disease is centered around 6 years [16,23,24].

165

166 Model

167 We used a Susceptible, Infected & Infectious, Susceptible – type model of the transmission
168 of grouped vaccine and non-vaccine pneumococcal serotypes as described previously
169 [16,17]. The group of vaccine serotypes consisted of all pneumococcal serotypes targeted by
170 PCV10, i.e. serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Individuals were grouped into
171 compartments by their age (weekly age groups until 5 years of age and yearly age groups
172 thereafter), their infection status (either susceptible, infected with a vaccine serotype, a
173 non-vaccine serotype or both at the same time) and by their vaccination status
174 (unprotected, infant protection, toddler protection).

175

176 Adaptive Markov chain Monte Carlo methods were used to fit the model to the observed
177 data (Figure 1) [25]. A Poisson likelihood was used for IPD and a multinomial likelihood was
178 used for carriage prevalence. We used a Metropolis Hastings algorithm to create samples
179 from the posterior parameter distributions. Prior information was used according to their
180 availability as described earlier (Table 1 and Figure 1).

181

182 Vaccination scenarios

183 After fitting the model parameters to match the observed rates of pneumococcal carriage
184 and disease in Kilifi HDSS we created multiple hypothetical PCV introduction scenarios to
185 determine what would have happened if PCV10 had been introduced using different catch-
186 up strategies. For this we define 3 alternative vaccination scenarios which assume that
187 administration of vaccines followed exactly the vaccine uptake that was observed in Kilifi
188 except for the respectively excluded parts of the catch-up programmes. These scenarios
189 were:

190 1. U5 catch-up (observation and extrapolation) - Vaccination according to observed
191 vaccine coverage in Kilifi HDSS (i.e. all children under 5 years of age).

192 2. U2 catch-up (hypothetical) - Vaccination according to observed vaccine coverage in
193 Kilifi HDSS for all children under 2 years of age.
194 3. U1 catch-up (hypothetical) - Vaccination according to observed vaccine coverage in
195 Kilifi HDSS for all children under 1 year of age.
196 4. Cohort introduction (hypothetical) - Vaccination according to observed vaccine
197 coverage in Kilifi HDSS only for those children eligible for vaccination through cohort
198 introduction.

199

200 **Sensitivity analysis**

201 We studied how competition, the duration of protection, the relative protection of infants if
202 compared to toddlers and the vaccine efficacy against carriage and IPD within the range of
203 their posterior distribution impacted on our main outcome; i.e. the number of vaccine doses
204 needed to prevent a case of IPD (NVN) and the ratio of NVN's of the considered introduction
205 strategies. We used a multivariable linear regression model on the centred posterior
206 samples and report the 95% credible interval limits of the joint distribution of the respective
207 parameter posterior and the model coefficient as a measure of the sensitivity of the NVN
208 ratio to the considered parameters.

209 We separately assessed the sensitivity of our finding to variable coverage levels in a
210 univariate sensitivity analysis. Rather than the observed coverage levels in Kilifi, for this we
211 assumed that protection through routine immunization as well as the catch-up campaign
212 achieved either 80%, 60% or 40% coverage.

213

214 **Results**

215 The introduction of PCV10 together with a catch-up campaign in under 5 year old children
216 was predicted to prevent 220 (172 to 270) cases of IPD in Kilifi within the first 10 years after
217 the start of the vaccination programme. Once the full direct and indirect effects of the
218 programme are established the vaccination programme was predicted to avert 23 (17 to 28)
219 cases of IPD annually (Figure 2a); the majority of those among children (Figure 1).

220

221 The catch-up campaign among children up to 5 years of age was estimated to accelerate
222 direct and indirect effects of PCV. By doing so the Kilifi programme was estimated to
223 prevent an additional 65 (48 to 84) cases of IPD (Figure 2b) over 10 years in the overall
224 population, if compared to a cohort introduction without a catch-up campaign. A catch-up
225 programme confined to children less than 2 years or less than 1 year of age was estimated
226 to prevent 34 (26 to 43) or 18 (14 to 22) IPD cases, respectively, in comparison to cohort
227 introduction alone. The majority of cases averted by the catch-up campaigns would have
228 occurred within the first 6 to 8 years after the start of vaccination (Figure 2a).

229

230 Within the first 10 years of the PCV infant programme in Kilifi about 205,000 doses of
231 vaccine were predicted to be used as part of the routine immunisation schedule. The under
232 5 catch-up campaign required 17,000 additional doses of vaccine (Figure 3a). We estimated
233 that, in the 10 years following introduction of PCV10 in Kilifi, routine vaccination without
234 any catch-up campaigns would use 1321 (1058 to 1698) doses of PCV for each case of IPD
235 averted. As herd protection gradually develops this program gains efficiency in the first
236 years after introduction; that is, the annual number of cases prevented increases while the
237 number of vaccinated individuals remains similar (Figure 2a). By the 10th year after the start

238 of cohort vaccination without a catch-up campaign we estimated that routine vaccination
239 uses 910 (732 to 1184) doses of PCV per IPD case averted.

240

241 The number of vaccine doses needed to prevent a case of IPD under the four scenarios is
242 shown in Table 2. Extending catch-up PCV immunization to children in the second year of
243 life is the most efficient additional use of PCV but any catch-up campaigns is more efficient
244 than routine birth cohort immunization. The most efficient introduction strategy for PCV is
245 introduction alongside an under 5 year old catch-up.

246

247 Our results were not sensitive to variations in vaccine coverage (Figure S2 and Table S1) or
248 competition, the duration of protection, the relative protection of infants by PCV as
249 compared to toddlers and the vaccine efficacy against carriage and IPD (Figure S1).

250

251 **Discussion**

252 In many high-income countries PCVs have been introduced with the help of catch-up
253 campaigns to accelerate the direct and indirect protection that is offered to the community
254 [26–28]. We used extensive data from the Kilifi HDSS, a well-studied mix of rural and urban
255 Kenyan communities representing a typical low income setting, to estimate the incremental
256 effects that different catch-up campaigns are likely to have over routine vaccination and,
257 therefore, whether PCV catch-up campaigns are an efficient use of PCV supply. We found
258 that rapidly increasing the protection in the community via catch-up not only reduces cases
259 of IPD by direct protection of older children but also reduces the burden of IPD in the whole
260 childhood population by developing herd protection more rapidly. Any of the three catch-up
261 programs considered in the analysis were estimated to use fewer vaccine doses to prevent a
262 case of IPD than cohort introduction during the first 10 years; the catch-up schedules were
263 more efficient than routine cohort vaccination programme alone even after full herd effects
264 are in place, in the 10th year of the programme. While the catch-up doses given to one year
265 olds were estimated to be the most efficient ones, we find that cohort introduction
266 alongside a catch-up campaign in under 5 year old children was the most efficient
267 introduction strategy overall.

268

269 Data on the observed impact of PCV catch-up campaigns is sparse and mostly
270 circumstantial. Catch-up campaigns of different sizes have been used for introduction of
271 PCVs into countries including the UK, USA, Israel, Brazil and Kenya, however, a head to head
272 comparison with cohort introductions that would allow an evaluation of the additional
273 impact of the catch-up is challenging because of the dissimilarity of the underlying
274 population and other factors including vaccine coverage, intensity of pneumococcal
275 transmission, differences in demographic structure and population mixing, serotype
276 distribution and prevalence of epidemiological risk factors such as HIV infection.

277

278 As well as extending direct protection to vulnerable older children, catch-up campaigns also
279 rapidly increase the proportion of individuals in the transmitting population who are
280 protected against VT acquisition and hence onward transmission. This indirect effect is non-
281 linear, preventing a high number of infections for each increment in vaccine coverage when
282 that coverage is low but suffering from a saturation effect for higher coverage levels. As a
283 result, predictions of the optimal extent of catch-up campaigns need to account for these
284 non-linear effects; i.e. incorporate transmission dynamics.

285
286 Most of our posterior estimates that had an informative prior were similar to that prior,
287 showing that in most instances the model is able to match the data well using the pre-
288 specified parameter space. The notable exception was the vaccine efficacy against carriage
289 in toddlers. While the model was unable to replicate the observed steep decrease in VT
290 prevalence following vaccination using the mean prior estimate of 36% efficacy the
291 posterior suggests a mean efficacy of 55% which has been observed in other sites [23] and
292 falls well into the range of the prior estimate.
293
294 We have restricted our analyses to catch-up campaigns that targeted age groups under five
295 years of age as those were deemed feasible both from a programmatic and a supply point of
296 view. However, including older children may well be efficient in particular in settings where
297 older children contribute substantially to the transmission of pneumococci. Also, we have
298 not considered programmatic issues associated with implementation of catch-up
299 campaigns. Due to the immense additional burden on available staff catch-up campaigns
300 can disrupt routine immunization services. Furthermore, we have studied the most efficient
301 use of PCV supply but not the cost-effectiveness or affordability of catch-up campaigns for
302 PCV introduction. One of the major differences in a cost-effectiveness analysis is that it
303 takes into account the higher delivery costs of vaccine through a supplementary
304 immunization activity. Assuming that doses delivered as part of a PCV catch-up campaign
305 were up 75% more expensive than doses delivered through the routine epi schedule,
306 however, did not qualitatively change our findings on the superior efficiency of catch-up
307 programs.
308
309 We did not account for population growth in our model which may impact the transmission
310 dynamics in the post vaccination era and hence on our findings. However, modelling work
311 predicting the impact of PCV10 in Kilifi from pre-vaccination data has shown that accounting
312 for population growth in Kilifi is unlikely to qualitative change the prediction but only slightly
313 reduces the long term impact of vaccination on IPD [29]. As the impact of a catch-up
314 campaign is mostly visible within a few years after vaccination it is likely largely unaffected
315 by long term changes in demographics. Hence, accounting for population growth is likely to
316 further favor the use of catch-up campaigns for introduction of PCV. Other models have
317 taken into account more of the diversity of pneumococcal serotypes by either modelling
318 them individually or by using finer grouping [19,29–31]. Despite the considerable
319 heterogeneity of serotypes in regards to their ecology within both our VT and NVT group
320 our model captures the post-vaccination dynamics well. The impact of catch-up campaigns
321 largely concerns the acceleration of long term impact of the programme and hence nuances
322 in the dynamics of specific serotypes are unlikely to qualitatively change our findings.
323
324 The generalisability of our results beyond Kilifi HDSS is dependent on a number of factors.
325 We show in a sensitivity analysis the robustness of our findings to vaccine coverage, vaccine
326 efficacy against the carriage and IPD, the ratio of toddler to infant protection, the duration
327 of vaccine induced protection and the between-serotype group competition (see Appendix
328 Figure S1 and S2). However, other factors that could not be systematically assessed in this
329 analysis include transmission intensity and serotype distribution. In settings with higher
330 transmission intensity, birth cohort PCV introduction likely takes longer to establish full herd
331 effects. As a result, catch-up campaigns that accelerate the build-up of herd protection have

332 the potential to prevent more IPD cases and hence be even more efficient strategy for PCV
333 use. Furthermore, we did not account for potential cross-reactivity of PCV10 against
334 serotypes 6A and 19A which has been reported previously [32,33]. However, both 6A and
335 19A carriage prevalence increased in the post vaccination era in Kilifi [11].
336

337 We assumed that two PCV doses in infancy, given as part of the routine EPI schedule are
338 similarly efficacious at preventing VT carriage and disease as a single catch-up dose in
339 toddlers and young children. Fitting to the data from Kilifi our model did not reject this
340 hypothesis. While our results are robust to factors including this differences in relative
341 protection in infants and toddlers and variable vaccine coverage (proportion of protected
342 infants and toddlers) the number of doses that are administered to establish protection
343 could have a larger impact. Twelve months after the introduction of PCV in Kilifi 76% of
344 infants eligible for 3 doses of PCV aged less than one year had received at least two doses of
345 PCV and 62% of children 1 to 4 years old had received at least 1 dose. We have chosen the
346 dosing of catch-up campaigns to align with what was rolled out in Kilifi, however, other
347 dosing regimens have been used [34], notably South Africa with two doses in infancy
348 followed by a booster dose at 9 months of age [35]. In our analysis we assume for simplicity
349 that all children receive the exact number of doses that in this analysis was deemed
350 sufficient to induce protection. Drop-out rates in Kilifi are relatively low, e.g. more than 97%
351 of infants who received one dose go on to receive a second dose before one year of age, but
352 including drop-outs in the analysis would further decrease the efficiency of the cohort
353 introduction in comparison to the catch-up campaigns. To define protection in our model
354 we used 2 doses in infancy and 1 dose for catch-up campaigns as a protective schedule but
355 assumed that vaccinated children would eventually receive 3 doses as part of the routine
356 schedule or alternatively 2 or 1 dose if part of the catch-up campaign in <1 year old or older
357 children respectively. Assuming instead that the children protected through routine
358 immunization and catch-up campaigns had received 2 doses and 1 doses respectively did
359 not qualitatively change the results.
360

361 **Conclusion**

362 Pneumococcal conjugate vaccines are among the most expensive vaccines currently
363 available and make up more than 30% of the annual budget of Gavi. Proposed ways to use
364 PCVs more efficiently include a potential reduction in the number of infant doses if herd
365 effects have been established [36] or a dilution of the current formulation. We show here
366 that catch-up campaigns present an important, readily available tool, which can increase the
367 efficiency of PCVs impact on disease at introduction. For countries yet to introduce, or
368 potentially also for countries with lagging coverage, strategies that include catchup
369 campaigns warrant serious consideration.
370
371

372 **Declarations**

373
374 Availability of data and materials
375 The majority of datasets used and/or analysed during the current study are available from
376 the indicated published resources. The remaining data, including model code is available
377 from the corresponding author on reasonable request.

378 Competing interests

379 SF has received funding related to pneumococcal vaccine research from Bill and Melinda
380 Gates Foundation, the World Health Organisation and Gavi, the vaccine Alliance. KLOB has
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388

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395

396 Authors' contributions

397 JAS and WJE designed the study. SF conducted the analyses, interpreted the results and
398 wrote the first draft of the manuscript. JO, OLPW, MO, KLOB, MK, DJN, WJE and JAS advised
399 on methodology and / or data interpretation. All authors have contributed to the writing of
400 the manuscript. All authors have read and approved the final manuscript.

401

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516

Tables

Table 1: Overview of model parameters.

| Model parameters | contribution | # of parameters | Prior | | | Posterior | | | |
|-----------------------|-------------------------------------|-------------------|-----------------------------|------------|---------|------------|------------|------|---------------|
| | | | Distribution | mean | sd | source | median | CR | |
| Study population | Age group size | fixed | 6 age groups | | | KHDSS [4] | | | |
| | Contact patterns | fixed | 6x6 age groups | | | KHDSS [5] | | | |
| | Carriage prevalence | outcome | 2 types x 6 age groups | | | KHDSS [11] | | | |
| | IPD | outcome | 2 types x 6 age groups | | | KHDSS [12] | | | |
| | observed vaccine coverage | fixed | 27040 (weekly age and time) | | | KHDSS [4] | | | |
| Transmission dynamics | Clearance rates | fixed | 2 types x 4 age groups | | | KHDSS [15] | | | |
| | VE carriage (toddlers) | fitted - prior | 1 | normal | 0.36 | 0.15 | KHDSS [11] | 0.56 | 0.41 to 0.72 |
| | VE IPD (infants) | fitted - prior | 1 | normal | 0.80 | 0.1 | [22] | 0.86 | 0.67 to 0.99 |
| | duration of protection (toddlers) | fitted - prior | 1 | normal | 6 years | 3 | [23,24] | 5.50 | 2.05 to 11.01 |
| | relative level of infant protection | fitted - prior | 1 | normal | 1 | 0.1 | assumption | 0.97 | 0.78 to 1.17 |
| | competition parameter | fitted - prior | 1 | log normal | 0.15 | 0.15 | [17,18] | 0.19 | 0.07 to 0.44 |
| | susceptibility to infection | fitted - no prior | 2 types x 4 age groups | | | | | | |
| | invasiveness | fitted - no prior | 2 types x 4 age groups | | | | | | |

Table 2: The impact and efficiency of alternative introduction strategies. The number of vaccine doses needed to prevent a case of IPD (NNV) is used as a measure of efficiency. Incremental NNV refers to the additional number of doses needed to prevent one additional cases of IPD in respect to cohort introduction with the next smaller catch-up.

| Introduction of PCV via | IPD averted after 10 years | Doses administered | Incremental NNV | NNV |
|-------------------------|----------------------------|--------------------|---------------------|---------------------|
| Cohort only | 155 (121 to 193) | 204,671 | 1321 (1058 to 1698) | 1321 (1058 to 1698) |
| + U1 catch-up | 173 (134 to 216) | 218,089 | 757 (618 to 973) | 1263 (1012 to 1623) |
| + U2 catch-up | 189 (147 to 235) | 224,952 | 412 (296 to 606) | 1188 (958 to 1527) |
| + U5 catch-up | 220 (172 to 270) | 241,546 | 543 (403 to 763) | 1098 (894 to 1405) |

Figures

Figure 1: Model fit to carriage prevalence and IPD incidence (upper panel) and prior and posterior parameter estimates (lower panel). Points with 95% confidence bounds represents data and lines with ribbons represent median model estimates with 95% credible intervals. In the lower panel the grey line indicates the prior density distribution and the bars the posterior sample.

Figure 2: The predicted number of cases averted by PCV10 vaccination in Kilifi if introduced with a catch-up campaign in less than 5, 2 or 1 year olds and without catch-up campaign. Lines represent median estimates and ribbons 95% credible intervals.

Figure 3: The predicted number of IPD cases averted by PCV10 vaccination in Kilifi in respect to the number of doses administered. In the dose-efficacy plane (left panel) the aggregated dose-efficiency of the alternative introduction strategies within 10 years after the start of vaccination is shown. Coloured dots and lines represent medians and 95% credible intervals (the number of doses administered is fixed as taken from the health register). In the right panel the (incremental) number of doses needed to prevent one (additional) case of IPD. Figures for cohort vaccination alone and cohort vaccination in year 10 are presented as absolute values, the catch-up scenarios are presented as incremental values over the next smaller campaign.





