

Immuno-persistence after the 4th and 5th dose of inactivated polio vaccines in school-aged children

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Brief Communication

Keywords:

Posted Date: January 30th, 2024

DOI: <https://doi.org/10.21203/rs.3.rs-3890516/v1>

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Additional Declarations: There is **NO** Competing Interest.

Immuno-persistence after the 4th and 5th dose of inactivated polio vaccines in school-aged children

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Abstract

Despite decades of research, questions remain about the persistence of neutralising antibodies (nAb) and serological correlates of polio vaccine efficacy. In a cross-sectional study among 299 children in Hong Kong, we estimated that the mean nAb titres against polioviruses type 1, 2 and 3 (PV1, PV2 and PV3) one month after receiving the 4th dose of inactivated polio vaccine (IPV) at 19 months of age were 2,068 (95% credible interval: 1,517 – 2,864), 4,705 (3,439 – 6,436) and 2,758 (1,894 – 4,086), but declined substantially in 4 years to 268 (222 – 325), 751 (630 – 900), and 411 (323 – 521), respectively. Administration of the 5th dose of IPV restored nAb titres among children aged 6-7 years, and the decline in nAb titres was slightly slower with the estimated mean titres of 355 (272 – 462), 538 (427 – 681), and 548 (378 – 786) against PV1, PV2, and PV3 at 4 years post the 5th dose. We estimated that the proportion of children who were seroprotected against PV1, PV2 and PV3 would drop below 90% at: (i) 8.2, 10.8, 8.7 years after the 4th dose; and (ii) 11.6, 11.2, 11.0 years after the 5th dose, highlighting the importance of maintaining populational immune persistence at high nAb levels.

The Global Polio Eradication Initiative (GPEI) has made steady progress over the past decade [1]. Following the eradication of wild poliovirus type 2 (WPV2) in 2015, GPEI's Polio Eradication and Endgame Strategic Plan 2013-18 called for globally synchronised and sequential removal of Sabin virus strains contained in oral polio vaccines (OPVs), starting with poliovirus type 2 [2]. However, the implementation of endgame strategies was set back by the COVID-19 pandemic that began in 2020: the delays in introducing inactivated polio vaccine (IPV) into essential immunisation in all regions led to decreasing immunity against type 2 poliovirus; the routine childhood immunisation was interrupted in many countries and the World Health Organization (WHO) estimated that the number of under-vaccinated children increased from 18.4 million in 2019 to 20.5-24.5 million in 2020-2022 [3].

Consequently, outbreaks of circulating vaccine-derived poliovirus type 2 (cVDPV2) have become as great a public health threat as WPV, with more cases of cVDPV2 than WPV since 2017. Outbreaks of cVDPVs continued to be detected globally, including in China, with one positive environmental sample from Xinjiang Uygur Autonomous Region in 2018 and one case of paralysis reported in Sichuan Province in 2019 [4]. Recently, cases of paralytic polio caused by cVDPVs were reported in the US and Israel, and cVDPVs were detected in environmental samples in Canada, Israel, UK, and US [5-7]. The resurgence of polioviruses in middle- and high-income settings signals the potential for cVDPVs to spread globally, putting under-vaccinated populations at high risk of contracting the paralytic disease.

Following the global coordination of type-2 OPV cessation from routine immunization to prevent the emergence of cVDPV2, middle- and high-income jurisdictions in the WHO Western Pacific Region have adopted full IPV vaccinations of four or more doses (**Table S1**) [8]. For example, four doses of IPV are given in Malaysia, Japan and South Korea, five in Singapore and Taiwan and six in Hong Kong and Macau [8]. Hong Kong has applied full IPV schedule since February 2007, with six IPV vaccines (containing wild strains) given at the age of 2 months, 4 months, 6 months, 18 months, 6-7 years and 11-12 years [9]. In May 2016, mainland China replaced trivalent OPV (tOPV) from its childhood immunisation with a new schedule, which involved administering one dose of attenuated Sabin strain IPV (sIPV) at 2 months of age, followed by three doses of a bivalent OPV (bOPV) at 3 months, 4 months, and 4 years of age [10, 11]. In 2020, mainland China further revised its polio vaccination schedule, which included sIPV doses at 2 months and 3 months of age, and bOPV doses at 4

months and 4 years of age [12]. Additionally, some eastern coastal provinces, such as Jiangsu, Shanghai, and Zhejiang have already switched to exclusive use of four doses of sIPV at 2, 3, 4, and 18 months of age [13-15].

Although various IPV schedules have been adopted across jurisdictions, consensus regarding the immuno-persistence of IPV remains elusive. Previous clinical trials on IPV reported a high seroconversion rate 14-28 days after vaccination [16, 17]. However, the trajectory of waning neutralising antibody (nAb) titres several years after vaccination and potential implications on long-term protection against polio remains poorly understood. This is particularly relevant for countries such as China that are situated near Afghanistan and Pakistan, where wild poliovirus (WPV) is still endemic [1]. Here, we assessed the persistence of nAb titres against polioviruses by conducting a cross-sectional serological study among Hong Kong children after the 4th and 5th dose of IPV. The unique data generated from this study can inform the design and adjustment of polio vaccination strategies.

Persistence of neutralising antibodies against polioviruses

Between November 2021 and January 2023, we recruited 299 children aged 19 months to 10.5 years, including 156 and 143 children who were 1-48 months post the 4th dose and 5th dose, respectively (**Table S2**). We collected 2 mL of serum from each child to measure nAb titres against WPV strains Mahoney, MEF-1 and Saukett, corresponding to poliovirus type 1, 2, and 3 (PV1, PV2, and PV3) [18].

The nAb titres against PV1, PV2 and PV3 were above 8, which is generally regarded as the threshold for seroprotection, among all participating children (**Figure 1**). We estimated that the mean nAb titres against PV1, PV2 and PV3 one month after receiving the 4th dose (i.e., at 19 months of age) were 2,068 (95% credible interval: 1,517 – 2,864), 4,705 (3,439 – 6,436) and 2,758 (1,894 – 4,086), respectively. These nAb titres declined substantially over time, with the estimated mean titres decreased by 7-8 folds in 4 years to 268 (222 – 325), 751 (630 – 900), and 411 (323 – 521), respectively.

Administration of the 5th dose of IPV restored nAb titres among children aged 6-7 years (**Figure 1**). We estimated that the mean nAb titres against PV1, PV2 and PV3 increased to 1,183 (994 – 1,422), 2,780 (2,364 – 3,297) and 1,956 (1,510 – 2,524), respectively, one

month after receiving the 5th dose. The decline in nAb titres after the 5th dose was slightly slower compared with that after the 4th dose, with estimated mean titres of 355 (272 – 462), 538 (427 – 681), and 548 (378 – 786) against PV1, PV2, and PV3, respectively, at 4 years post the 5th dose.

Estimates of seroprotection rates

We also estimated the proportion of children with nAb titres greater than the threshold of 8, i.e., seroprotection rate, against PV1, PV2 and PV3 as a function of the time elapsed since receiving the 4th or 5th dose of IPV (**Figure 1**). Assuming exponential waning of the nAb titres, we estimated that the seroprotection rates 4 years after receiving the 4th IPV dose were 99.9% (99.4 – 100), 100% (100 – 100), and 99.8% (99.2 – 100) against PV1, PV2 and PV3, respectively. In the absence of additional doses following the 4th dose, we estimated seroprotection rates would remain high at 97.2% (92.0 – 99.6), 100% (99.8 – 100) and 98.0% (94.6 – 99.6) at 8 years post the 4th dose but are uncertain by 12 years after the 4th dose with a wide range of credible interval: the seroprotection rates were estimated to be 13.8% (0 – 75.6), 89.1% (27.2 – 100) and 50.1% (0 – 95.0). We estimated that seroprotection rates would decline more slowly after administration of the 5th dose: 100% (99.8 – 100), 100% (100 – 100), and 99.9% (99.4 – 100) against PV1, PV2 and PV3 at 8 years; and 97.8% (79.4 – 100), 94.0% (44.0 – 100), and 95.9% (67.4 – 100) at 12 years post the 5th dose despite the wide 95% credible intervals.

The large variance in the empirical nAb titres led to the high uncertainty in our estimates of waning rates and seroprotection durations. As such, we used the lower limits of the 95% credible intervals as conservative estimates of the seroprotection durations (**Figure 1**).

Under this approach, we estimated that the proportion of children who were seroprotected against PV1, PV2 and PV3 would drop below 90% at: (i) 8.2, 10.8, 8.7 years after the 4th dose; and (ii) 11.6, 11.2, 11.0 years after the 5th dose, respectively.

Discussion

Our study showed that nAb titres induced by the 4th dose of IPV against PV1, PV2 and PV3 remained seroprotective for at least 7 years in more than 90% of children. Since more than 90% of polio cases occur among children under 5 years [19], our estimated seroprotection

duration after the 4th IPV dose is consistent with the existing IPV schedules in most high- and middle-income jurisdictions, which administer at least four doses of IPV with the 4th dose given by 18 months of age [8]. These findings significantly contribute to the currently limited and sometimes inconsistent data on long-term persistence of immunity induced by IPV [8]. Germany has switched to exclusive use of wild-type IPV (wIPV) in 1998, with three doses given at the age of 2, 4, 11 months and a booster dose at the age of 9-16 years, but a polio seroprevalence study on 11,410 samples collected from children aged <18 in 2005-2020 reported that 4.1%, 1.7% and 13.4% of them were exclusively seronegative against PV1, PV2, and PV3, respectively [20]. Similarly, another seroprevalence study on 219 samples from Italian college students in 2010 also reported that 30.6%, 8.7% and 21.5% of them were exclusively seronegative against PV1, PV2, and PV3 [21], confirming that the nAbs against polioviruses drop over time after vaccinations [22-27]. However, a more recent study by Ma et al studied nAb from recipients of wIPVs and sIPVs in mainland China, reporting 97.1-100% seroprotection rates against all polio types 10 years after the 4th dose of both wIPV and sIPV [28]. Nonetheless, Ma et al reported substantial nAb waning 2-6 years after the 4th dose for PV1 and more rapid waning within the first 2-3 years for PV2 and PV3, whereas our study estimated that rapid waning of nAb against all three polioviruses would not begin until 6-9 years after the 4th dose of IPV [28].

Our study is the first to show that the waning of polio nAb was slightly slower following the 5th dose of IPV compared to the 4th dose (**Figure 1**). However, due to the high variability of nAb distributions, the differences in estimated waning rates were not statistically significant. According to the childhood vaccination schedule in Hong Kong, our participants received the 4th, 5th, and 6th dose of IPV at ages 18 months, 6-7 years, and 11-12 years, meaning that there were only 4 years of follow-up data post the 4th or 5th dose of IPV. Assuming that our subjects are representative of the general population, artificially quadrupling the sample size (to 1196 children by using four replicas of our subjects as the data for parameter inference) would slightly narrow the 95% CrI of the estimated seroprotection rates, which increased the estimated seroprotection duration by half to one year for both of the 4th and 5th doses (**Figure S1**). The larger variance in nAb might also be due to the cross-sectional design of our study, and ideally, longitudinal serological data from the same group of vaccinated children should be collected for the assessment of immuno-persistence. In the sensitivity analysis, we

estimated lower nAb titres against all three PV types among female participants after the 4th dose, but slightly lower nAb titres among male participants after the 5th dose in our study (**Table S3**). As such, a substantially larger sample size and a longer longitudinal follow-up of vaccinated children would be needed to robustly characterize the waning of nAb and seroprotection against polioviruses for longer time horizons.

In Hong Kong, the last local wild-type polio case was notified in 1983, the last imported WPV cases from Pakistan were reported in 2011 and the last probable vaccine-associated paralytic poliomyelitis due to OPV vaccination in mainland China was hospitalised in 2014 [29]. Since 2014, no circulation of PVs was reported in Hong Kong. Given that nearly all the immunity detected in Hong Kong residents were induced by IPVs, questions remain about the serological correlates of polio vaccine efficacy, specifically whether the vaccines are equally protective against antigenically distinct strains of the same types. In 2010, a poliomyelitis outbreak was caused by a wild PV1 in Congo with a unique and consequential mutation signature (PV1-RC2010), resulting in 445 deaths with 47% mortality [30]. Later serological studies reported that 15-29% of individuals vaccinated with IPVs in Germany and 15-50% of individuals vaccinated with OPVs and/or IPVs in Russia were seronegative against this PV1-RC2010 strain, though 100% of them in Germany and 92-96% of them in Russia were seropositive against Sabin or wild PV1 vaccine strains [31, 32]. Further, a smaller scale serological study in the US tested a panel of wild and vaccine-derived PV1 against 26 sera from vaccine-immunized healthy individuals: despite a significant reduction in nAb against PV1 strains that were immunologically different from the vaccine strain, especially with only 54% seropositive rate against PV1-RC2010, administration of a booster dose of IPV restored nAb against all strains [33]. Similarly, if a higher nAb titre cutoff for seropositivity were applied to our data, the estimated seroprotection duration of both 4th and 5th dose would reduce by 1.5 - 2.1 years for the threshold of 16 and 3.1 - 4.2 years for the threshold of 32 (**Figure S2**). Phylogenetic analysis also indicated that circulating polioviruses in unimmunized populations serve as a reservoir that seeds outbreaks in sub-optimally vaccinated populations [34], suggesting the importance of maintaining populational immune persistence at high nAb levels in reducing the emergence of immune escapes.

Our estimates of nAb persistence and seroprotection rates support the inclusion of 4-5 doses of IPV in the polio immunisation schedules after the complete substitution of OPV in

most middle- and high-income countries. However, there is no consensus on the number of IPV required during the transition period when both bOPV and IPV are used. Currently, most low- and middle-income countries are giving only 1-2 doses of IPV in their childhood immunisation programme, including many provinces in mainland China, Cambodia, Laos, Mongolia and the Philippines (**Table S1**) [8]. Recent clinical trials of sIPV in China suggested that seroprotection against PV2 might not be sufficient for vaccine schedules combining 2 doses of sIPV and 1-2 doses of bOPV, with GMT of nAb against PV2 ranging 32 to 224 and seropositivity rate of 93-96% within 28-60 days after vaccination [35, 36]. A third dose of IPV might be required to sustain high nAb against polioviruses, particularly for PV2.

Central to the efforts for polio eradication is also to induce intestinal mucosal immunity able to limit virus replication in the intestine to interrupt transmission. Unlike immunisation schedules combining both OPV and IPV, IPV-only series is not sufficient to induce significant levels of enteric immunity [7, 37, 38]. There are observations of an age-related decline in intestinal mucosal immunity and virus neutralising ability among children immunised with either IPV-only schedules or schedules combining with OPV and IPV, which raise important attention to the critical role of mucosal immunity in limiting the magnitude and duration of virus shedding [38]. Promising new data is emerging on the safety and immunogenicity of novel OPV2 with improved genetic stability after intestinal passage [39], allowing new possibility in the design of vaccination strategies towards the goal of global polio eradication.

In conclusion, it is critical to maintain high immune persistence against polioviruses of all types for eradicating poliomyelitis, particularly in developing countries where the routine childhood immunisations have been interrupted and delayed during and after the COVID-19 pandemic.

Word count: 2,396

Methods

Participant recruitment

Between November 2021 and January 2023, we recruited 299 children aged 19 months to 10.5 years who are residents of Hong Kong. Eligible participants should have received their first four doses of polio vaccine as an IPV, either standalone or as a combination vaccination with DTaP of any wild strain derived IPV; and those who have also received the fifth dose of polio vaccines should have the fifth dose as an IPV, either standalone or as a combination vaccination with DTaP [9]. The exclusion criteria included: (1) being immunosuppressed either due to primary or secondary causes at the time of vaccination or during previous vaccinations; (2) having received any OPV vaccine; (3) residing in areas with active use of OPV vaccines; (4) the vaccination records were not retrieved or confirmed; (5) being vaccinated in a private hospital. We only allowed one of the identical twins to participate in the study due to the similarity of genetics and immunity. Eligible participants were arranged clinic visits for a self-administered questionnaire and blood collection, with details included in **Table S2**.

Serological tests

Serum samples were collected and used to measure anti-poliovirus antibody titres per serotype by neutralisation test. Serial dilutions of sera were mixed with challenge polioviruses (i.e., Mahoney, MEF-1, or Saukett) and incubated with cultured Vero cells. Specific neutralizing antibodies contained in the sera should bind to and neutralize the challenge poliovirus which does not affect cellular viability resulting in changing the color of the medium. The serum titre was determined using a spectrophotometric method and expressed as the reciprocal dilution (i.e., titres).

Estimating the persistence of neutralising antibody titres against polioviruses

We first used the Shapiro–Wilk test with Bonferroni correction to test the normality of the log-transformed nAb titres by poliovirus type, number of doses and time since vaccination (**Table S2**). Except for the subgroup of participants 1-3 months after the 5th dose against PV3, the null hypothesis that the log-transformed nAb titres are normally distributed was

not rejected for other groups at the alpha level of 0.05. Given the small sample size in each of the subgroups, we assumed that the log-transformed nAb titres were normally distributed hereafter.

We denoted the poliovirus type as s , the number of doses received as j , and the time elapsed since receiving the j -th dose of IPV as t . We applied \log_2 transformation to the nAb titre data and assumed that the log-transformed nAb titres followed a normal distribution with mean $\mu_{j,s}(t)$ and standard deviation $\sigma_{j,s}(t)$. Given poliovirus type s and IPV dose j , we assumed exponential waning of nAb titres (i.e. linear waning of their log-transformed counterparts). We modelled $\mu_{j,s}(t)$ and $\sigma_{j,s}(t)$ using three parameters, namely the mean of log-transformed nAb titre immediately after the j th dose of IPV ($\mu_{0,j,s}$), waning rate of the mean of log-transformed nAb titre ($\kappa_{j,s}$) and coefficient of variation of the log-transformed nAb titre ($CV_{j,s}$) which was assumed to be time-invariant:

$$\begin{aligned}\mu_{j,s}(t) &= \mu_{0,j,s} - \kappa_{j,s}t \\ \sigma_{j,s}(t) &= CV_{j,s}\mu_{j,s}(t) .\end{aligned}$$

Let $x_{j,s,i}$ be the log-transformed nAb titre against poliovirus type s for subject i who received the j th dose t_i time units ago. The likelihood function was:

$$L(\mu_{0,j,s}, \kappa_{j,s}, CV_{j,s}) = \prod_i N\left(\frac{x_{j,s,i} - \mu_{j,s}(t_i)}{\sigma_{j,s}(t_i)}\right)$$

where N is the standard normal pdf. The statistical inference was performed in a Bayesian framework with noninformative (flat) priors using Markov Chain Monte Carlo with Gibbs sampling.

As a sensitivity analysis, we further investigated the sex difference in the log-transformed nAb titres. We denoted the mean of log-transformed nAb titres immediately after the j th dose of IPV for males as $\mu_{0,j,s,male}$ and the difference in the mean of log-transformed nAb titres immediately after the j th dose of IPV between males and females as $\mu_{0,j,s,sex}$. We modelled $\mu_{j,s}(t)$ for males and females respectively:

$$\begin{aligned}\mu_{j,s}(t) &= (\mu_{0,j,s,male} + \mu_{0,j,s,sex} \times 1_{female}) - \kappa_{j,s} \times t \\ \sigma_{j,s}(t) &= CV_{j,s}\mu_{j,s}(t),\end{aligned}$$

Where 1_{female} is an indicator function:

$$1_{female} := \begin{cases} 1, & \text{if the subject is a female} \\ 0, & \text{if the subject is a male} \end{cases}$$

The statistical inference was then performed similarly to the original model without gender differences.

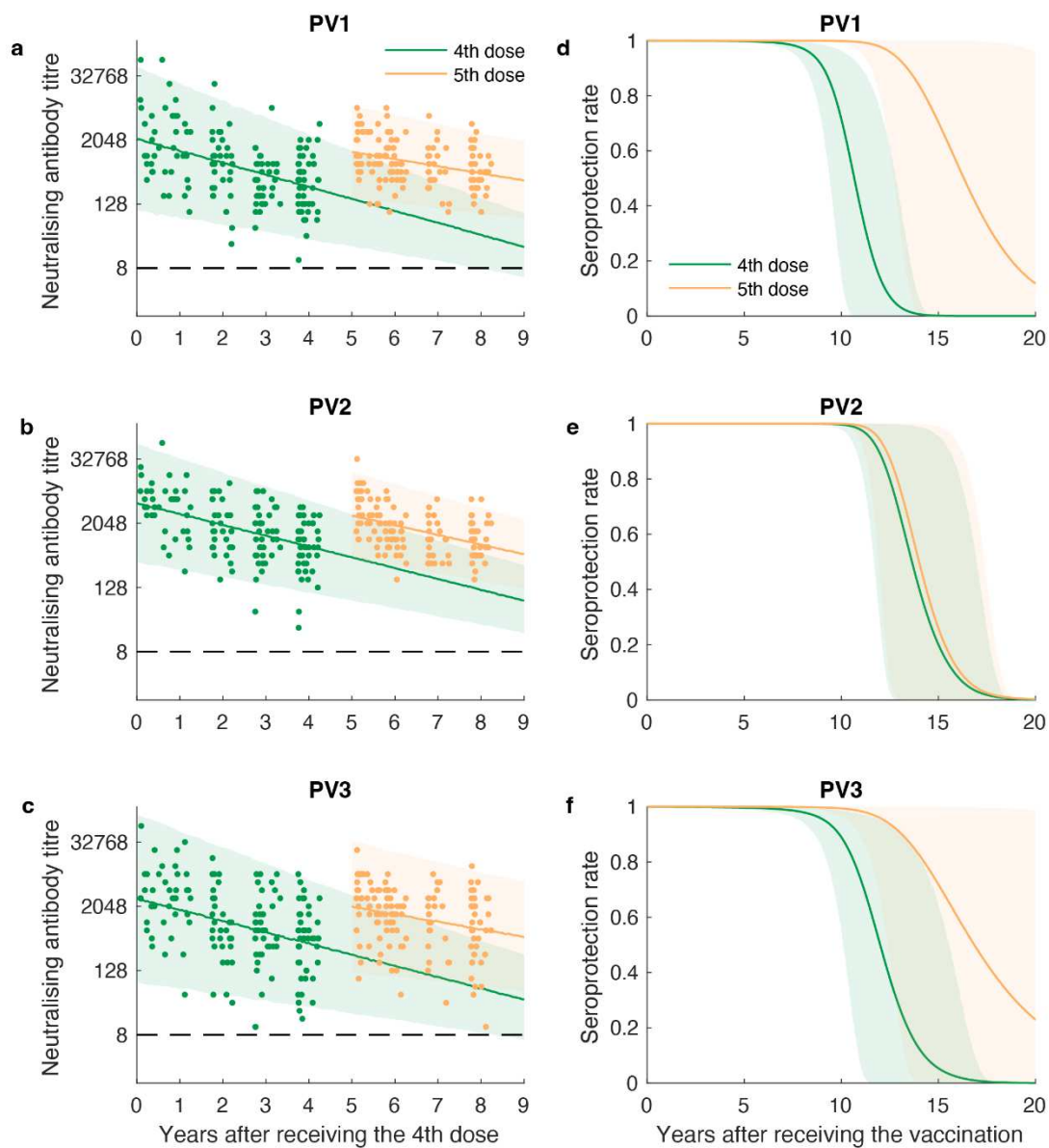


Figure 1. Neutralising antibody titres and estimated seroprotection rates after receiving the 4th and 5th dose of IPV among school-aged children in Hong Kong. (a-c) The empirical data and posterior distribution of neutralising antibody titres against poliovirus type 1, 2 and 3 (PV1, PV2 and PV3) after receiving the 4th and 5th dose of IPV. Most children in Hong Kong receive the 4th dose at the age of 18 months and the 5th dose at the age of 6-7 years which corresponds to Primary School Grade 1 (i.e. most children receive the 5th dose 4-5 years after receiving the 4th dose). The x-axis shows the number of years after receiving the 4th dose. Each dot represents the observed neutralising antibody titre from each subject. Solid lines and shades represent the posterior mean and 95% highest density region (HDR) of the distribution of neutralising antibody titres. The dashed line indicates the threshold of 8. (d-f) The proportion of children with neutralising antibody titres greater than 8 (i.e.,

seroprotection rates) against PV1, PV2 and PV3 as a function of time since receiving the 4th or 5th dose of vaccination. Solid lines and shades represent the posterior mean and 95% CrI of the estimates.

Ethics declarations

The study protocol and related materials have been approved by the HKU/HA HKW Institutional Review Board (reference no.: UW21-196) and were conducted in accordance with the Declaration of Helsinki. Informed consent had been sought from the parents or legal guardians of the participants.

Conflict of interest

KL, CWKP, THKL, TTYL, EHYL and JTW declare that there was no conflict of interest. JCVZ and CP are employees of Sanofi.

Acknowledgement

We sincerely thank all staff and participants of this study. This research was supported by Sanofi (including funding from Sanofi via a collaborative study PER00098), Health and Medical Research Fund (reference no.: CID-HKU2, COVID19F05, 21200122), Health and Medical Research Fund Research Fellowship Scheme (reference no.: 06200097) and the AIR@InnoHK administered by Innovation and Technology Commission of The Government of the Hong Kong Special Administrative Region. We thank Dr Corey Peak from Bill & Melinda Gates Foundation for valuable comments and suggestions, and his institutional affiliation is provided for identification purpose only which does not constitute institutional endorsement. Health and Medical Research Fund and AIR@InnoHK had no role in study design, data collection, data analysis, data interpretation or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Data availability

All data included in the analyses are available in the main text or supplementary materials.

Code availability

All codes are available at <https://github.com/kathyleung> after the manuscript is accepted for publication.

Supplementary Information

Table S1. Vaccination schedule by countries or regions in the Western Pacific Region

Country/region	Number of doses	Vaccination time	IPV vaccines used
Cambodia [40]	1 IPV + 3 bOPV	bOPV: 6 weeks, 10 weeks, 14 weeks IPV: 14 weeks	Unknown
Hong Kong [41, 42]	6 IPV	2 months, 4 months, 6 months, 18 months, 6-7 years, 11-12 years	wIPVs
Japan [43, 44]	4 IPV	3 between 2-12 months; 1 between 12-18 months	Both wIPVs and sIPVs
Laos [45, 46]	1 IPV + 3 bOPV	bOPV: 6 weeks, 10 weeks, 14 weeks IPV: 14 weeks	wIPVs
Macau [47, 48]	5 IPV	2 months, 4 months, 6 months, 18 months, 5-6 years	wIPVs
Mainland China (except Shanghai, Jiangsu and Zhejiang) [49, 50]	2 IPV + 2 bOPV	IPV: 2 months, 3 months bOPV: 4 months, 4 years	sIPVs
Mainland China (Shanghai, Jiangsu, Zhejiang) [13-15, 50]	4 IPV	2 months, 3 months, 4 months, 18 months	sIPVs
Malaysia [51]	4 IPV	2 months, 3 months, 5 months, 18 months	wIPVs
Mongolia [52, 53]	1 IPV + 4 bOPV	bOPV: birth, 2 months, 3 months, 4 months IPV: 5 months	wIPVs
The Philippines [54, 55]	2 IPV + 3 bOPV	bOPV: 6 weeks, 10 weeks, 14 weeks IPV: 14 weeks, 9 months	wIPVs
South Korea [56, 57]	4 IPV	2 months, 4 months, 6-18 months, 4-6 years	wIPVs
Taiwan [58, 59]	5 IPV	2 months, 4 months, 6 months, 18 months, 5 years	wIPVs
Vietnam [60, 61]	2 IPV + 3 bOPV	bOPV: 2 months, 3 months, 4 months IPV: 5 months, 9 months	wIPVs

Table S2. Participating children by the time after receiving the 4th or 5th dose of IPV

Classification	Number of Participants (%)
1-3 months after the 4 th dose	8 (2.7%)
6 months after the 4 th dose	12 (4.0%)
12 months after the 4 th dose	20 (6.7%)
24 months after the 4 th dose	31 (10.3%)
36 months after the 4 th dose	39 (13.0%)
48 months after the 4 th dose	46 (15.3%)
1-3 months after the 5 th dose	22 (7.3%)
6 months after the 5 th dose	21 (7.0%)
12 months after the 5 th dose	35 (11.7%)
24 months after the 5 th dose	27 (9.0%)
36 months after the 5 th dose	38 (12.7%)

Table S3. Estimated mean nAb titres one month after receiving the 4th and 5th dose of IPV

IPV dose	PV type	Male	Female
4	PV1	2,317 (1,390 – 3,862)	1,772 (1,098 – 2,918)
4	PV2	4,762 (3,146 – 7,490)	4,553 (2,972 – 7,132)
4	PV3	2,813 (1,653 – 4,914)	2,797 (1,604 – 4,970)
5	PV1	1,023 (739 – 1,424)	1,270 (941 – 1,721)
5	PV2	2,684 (1,965 – 3,720)	2,870 (2,197 – 3,761)
5	PV3	1,689 (1,086 – 2,617)	2,160 (1,449 – 3,257)

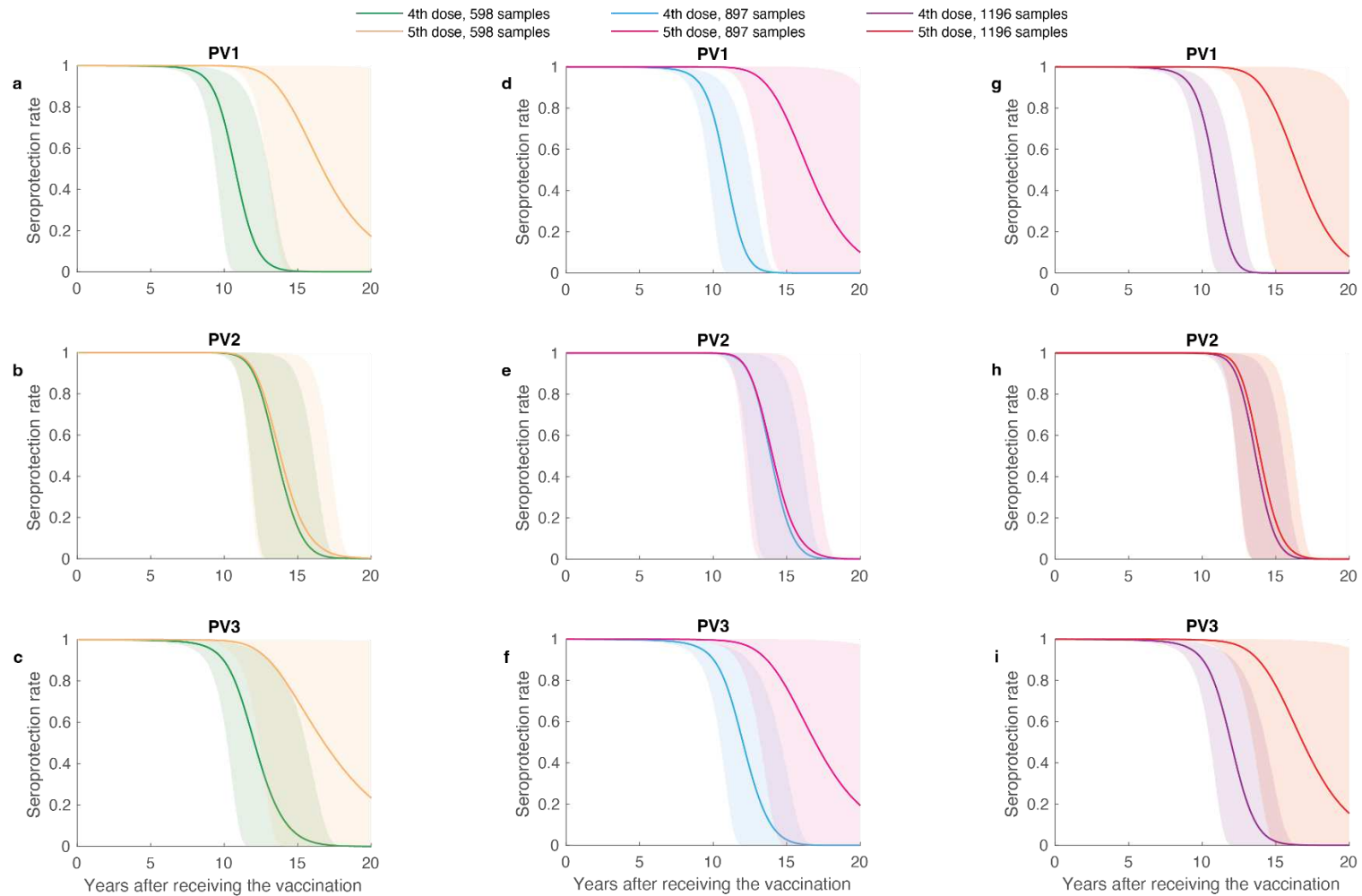


Figure S1. Comparison of estimated seroprotection rates after receiving the 4th and 5th dose of IPV with increased sample sizes. The seroprotection rates against PV1, PV2 and PV3 as a function of time since receiving the 4th or 5th dose of vaccination assuming there were (a-c) 598 samples; (d-f) 897 samples; and (g-i) 1196 samples. Solid lines and shades represent the posterior mean and 95% CrI of the estimates from data from increased sample size by replicating the original samples by (a-c) twice, (d-f) three times and (g-i) four times.

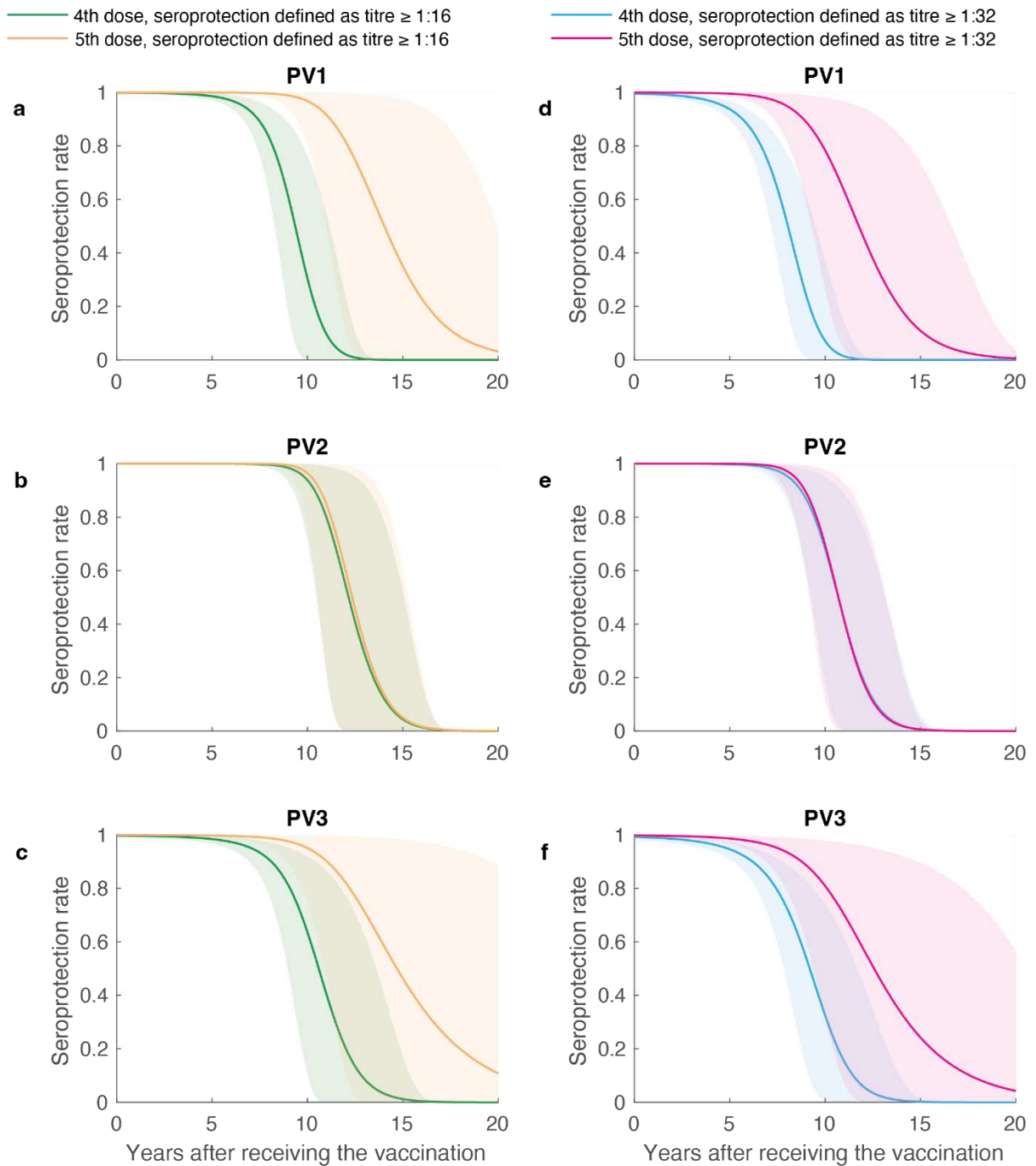


Figure S2. Comparison of estimated seroprotection rates after receiving the 4th and 5th dose of IPV with different thresholds. The seroprotection rates against PV1, PV2 and PV3 as a function of time after receiving the 4th or 5th dose of vaccination under the nAb titre threshold (a-c) ≥ 16 ; (d-f) ≥ 32 . Solid lines and shades represent the posterior mean and 95% CrI of the estimates under various pre-set threshold.

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