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Polio vaccination coverage and seroprevalence of poliovirus antibodies after the introduction of inactivated poliovirus vaccines for routine immunization in Japan

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ABSTRACT

In Japan, the oral poliovirus vaccine (OPV) was changed to 2 types of inactivated poliovirus vaccine (IPV), the standalone conventional IPV (cIPV) and the Sabin-derived IPV combined with diphtheria-tetanus-acellular pertussis vaccine (DTaP-sIPV), for routine immunization in 2012. We evaluated polio vaccination coverage and the seroprevalence of poliovirus antibodies using data from the National Epidemiological Surveillance of Vaccine-Preventable Diseases (NESVPD) from 2011 to 2015. Several years before the introduction of IPV in 2012, OPV administration for children was refused by some parents because of concerns about the risk of vaccine-associated paralytic poliomyelitis. Consequently, in children aged <1 years who were surveyed in 2011–2012, polio vaccination coverage (45.0–48.8%) and seropositivity rates for poliovirus (type 1: 51.7–65.9%, type 2: 48.3–53.7%, and type 3: 15.0–29.3%) were decreased compared to those surveyed in 2009. However, after IPV introduction, the vaccination coverage (95.5–100%) and seropositivity rates (type 1: 93.2–96.6%, type 2: 93.1–100%, and type 3: 88.6–93.9%) increased among children aged <1 years in 2013–2015. In particular, seropositivity rates and geometric mean titers (GMTs) for poliovirus type 3 in <5-year-old children who received 4 doses of IPV (98.5% and 247.4, respectively) were significantly higher than in those who received 2 doses of OPV (72.5% and 22.9, respectively). Furthermore, in <5-year-old children who received 4 doses of either DTaP-sIPV or cIPV, the seropositivity rates and the GMTs for all 3 types of poliovirus were similarly high (96.5–100% and 170.3–368.8, respectively). Our findings from the NESVPD demonstrate that both the vaccination coverage and seropositivity rates for polio remained high in children after IPV introduction.

Abbreviations: IPV, inactivated poliovirus vaccine; sIPV, Sabin-derived inactivated poliovirus vaccine; cIPV, conventional inactivated poliovirus vaccine; DTaP-sIPV, Sabin-derived inactivated poliovirus vaccine combined with diphtheria-tetanus-acellular pertussis vaccine; DTaP-cIPV, conventional inactivated poliovirus vaccine combined with diphtheria-tetanus-acellular pertussis vaccine; OPV, oral poliovirus vaccine; NESVPD, National Epidemiological Surveillance of Vaccine-Preventable Diseases; GMTs, geometric mean titers; CIs, confidence intervals; AFP, acute flaccid paralysis; VAPP, vaccine-associated paralytic poliomyelitis.

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1. Introduction

In Japan, the trivalent oral poliovirus vaccine (OPV) was introduced to the national immunization program in 1964 and was used for approximately 50 years until August 2012. During this period, 2 doses of OPV were used to establish a polio-free status with high vaccination coverage. According to the virological characterization of poliovirus isolates, type 1 non-Sabin-like poliovirus was identified following isolation from a patient with acute flaccid paralysis (AFP) in 1980; this was the last polio case resulting from wild poliovirus in Japan [1,2]. However, the risk of vaccine-associated paralytic poliomyelitis (VAPP) persisted, and the occurrence of patients due to vaccine-related poliovirus among susceptible persons raised serious concern. To reduce the potential risks associated with OPV, the World Health Organization (WHO) recommends the introduction of the inactivated poliovirus vaccine (IPV) into routine immunization schedules (after a thorough review of local epidemiology, including risk of importation of wild polioviruses) [3].

In Japan, the polio vaccine used for routine immunization was replaced with the standalone Salk IPV, derived from wild poliovirus strains (conventional IPV; cIPV) on September 1, 2012. Consequently, standard polio vaccination schedules were revised as follows: (a) 4 IPV doses (3 primary doses in an interval of 3–8 weeks and 1 booster dose at 12–18 months after the 3 primary doses) for children aged 3–12 months old who have not received OPV, (b) 3 IPV doses (2 doses in an interval of 3–8 weeks and 1 dose at 12–18 months after the 2 doses) for children who have received 1 OPV dose, and (c) no additional IPV administration for children who have received 2 OPV doses [4]. On November 1, 2012, Japan became the first country in the world to introduce the Sabin-derived IPV (sIPV); tetracomponent antigens vaccine (sIPV combined with diphtheria-tetanus-acellular pertussis vaccine; DTaP-sIPV) into its routine immunization program. In December 2015, the cIPV-containing tetracomponent antigens vaccine (cIPV combined with diphtheria-tetanus-acellular pertussis vaccine; DTaP-cIPV) also became available for routine immunization in Japan. Details of each IPV-containing vaccine are summarized in Supplementary Table 1.

The purpose of this study is to evaluate polio vaccination coverage and the seroprevalence of antibodies against polioviruses among children aged <5 years according to the transition from OPV to IPV for routine immunization in Japan.

2. Materials and methods

2.1. Data source

Data about the polio vaccination history and seroprevalence of antibodies to polioviruses were extracted from the National Epidemiological Surveillance of Vaccine-Preventable Diseases (NESVPD) database in Japan. The NESVPD is a cross-sectional survey of vaccine-preventable diseases and is mainly used for monitoring the current immune status of the population regarding 11 selected diseases (poliomyelitis, influenza, Japanese encephalitis, rubella, measles, pertussis, diphtheria, tetanus, human papillomavirus infection, varicella, and hepatitis B) by the Ministry of Health, Labour and Welfare, in collaboration with the National Institute of Infectious Diseases, prefectural governments, and prefectural public health laboratories. The survey is conducted annually, mainly from July to September, and collects serum samples and vaccination history from randomly sampled healthy individuals across all age groups with their informed consent [5].

2.2. Data for this study

Serum neutralization antibody titers against type 1, 2, and 3 polioviruses were measured in 9 prefectural public health laboratories in Hokkaido, Yamagata, Gunma, Chiba, Tokyo, Toyama, Aichi, Yamaguchi, and Ehime Prefecture in Japan using a standard microneutralization test, according to the procedure for the NESVPD [6]. Briefly, serum samples were serially diluted twofold from 1:4 to 1:2048, and mixed with 100 cell culture infectious dose 50% of poliovirus (Sabin 1, 2, or 3 strain). The results of the serological test and vaccination status were entered into the database of NESVPD via a closed network system.

We analyzed data about antibody titers against polioviruses and polio vaccination status of children aged <5 years from Hokkaido, Yamagata, Gunma, Chiba (2013–2015), Tokyo, Toyama, Aichi, Yamaguchi (2011, 2013), and Ehime prefectures. The number of participants was 427 in 2011, 376 in 2012, 416 in 2013, 397 in 2014, and 369 in 2015 (Table 1). Neutralizing antibody titers $\geq$8 were considered positive protective levels. Calculation of the geometric mean titers (GMTs) included antibody negatives (titers <4 and 4), and titers of <4 were considered as 2.

Ethical approval was not required for this study because the NESVPD is conducted for public health on the basis of the Immunization Law in Japan, and data extracted from the database of the NESVPD did not include personally identifiable information.

2.3. Statistical analyses

To evaluate the seroprevalence of antibodies against poliovirus among children with different vaccination histories, Fisher's exact test was used to compare seropositivity rates with 95% confidence intervals (CIs), and Wilcoxon rank-sum test was used to compare GMTs with 95% CIs. Statistical analyses were performed using JMP software version 12.2.0 (SAS Institute Japan Ltd., Tokyo, Japan). The level of statistical significance was set at $p < 0.05$ after Bonferroni correction.

3. Results

3.1. Characteristics of participants

The survey period was mainly from July to September each year. Serum samples and vaccination history were collected from most participants during this period [87.6% (374/427) in 2011, 87.5% (329/376) in 2012, 92.5% (385/416) in 2013, 92.2% (366/397) in 2014, and 84.0% (310/369) in 2015] (Table 1). There were no significant differences in the median age ($p = 0.58$) and sex ($p = 0.84$) of the participants between the different survey years.

3.2. Polio vaccination coverage

Data on polio vaccination status in children according to age from 2011 to 2015 are shown in Table 1 and Fig. 1. The number of children with an unknown vaccination status was 55 (12.9%) in 2011, 61 (16.2%) in 2012, 95 (22.8%) in 2013, 58 (14.6%) in 2014, and 38 (10.3%) in 2015. In this study, the coverage of $\geq$1 dose of polio-containing vaccines was estimated after exclusion of the children with unknown vaccination status. The coverage of $\geq$1 dose of polio-containing vaccines in 2011 and 2012 was particularly low in children aged <1 year (45.0% and 48.8%, respectively) and those aged 1 year (89.1% and 78.0%, respectively). However, this coverage increased in 2013–2015 both children aged <1 year (96.6% in 2013, 95.5% in 2014, and 100% in 2015) and those aged 1 year (97.2% in 2013, 100% in 2014 and 2015) (Table 1).

Table 1
Number of children aged <5 years according to the polio vaccination status in Japan (NESVPD 2011–2015).

Survey year	Age (years)	Total	Vaccination status			≥1 Dose % (95% CIs) [b]
			≥1 Dose [a]	None	Unknown	
2011	**Total**	**427**	**325**	**47**	**55**	**87.4 (83.6–90.4)**
	0	67	27	33	7	45.0 (33.1–57.5)
	1	128	98	12	18	89.1 (81.9–93.6)
	2	86	73	2	11	97.3 (90.8–99.3)
	3	89	77	0	12	100 (95.2–100)
	4	57	50	0	7	100 (92.9–100)
2012	**Total**	**376**	**272**	**43**	**61**	**86.3 (82.1–89.7)**
	0	52	20	21	11	48.8 (34.3–63.5)
	1	110	71	20	19	78.0 (68.5–85.3)
	2	84	68	1	15	98.6 (92.2–99.7)
	3	79	67	0	12	100 (94.6–100)
	4	51	46	1	4	97.9 (88.9–99.6)
2013	**Total**	**416**	**316**	**5**	**95**	**98.4 (96.4–99.3)**
	0	49	28	1	20	96.6 (82.8–99.4)
	1	133	105	3	25	97.2 (92.1–99.1)
	2	83	67	0	16	100 (94.6–100)
	3	88	69	1	18	98.6 (92.3–99.7)
	4	63	47	0	16	100 (92.4–100)
2014	**Total**	**397**	**336**	**3**	**58**	**99.1 (97.4–99.7)**
	0	55	42	2	11	95.5 (84.9–98.7)
	1	130	115	0	15	100 (96.8–100)
	2	88	75	0	13	100 (95.1–100)
	3	77	67	0	10	100 (94.6–100)
	4	47	37	1	9	97.4 (86.5–99.5)
2015	**Total**	**369**	**331**	**0**	**38**	**100 (98.9–100)**
	0	45	33	0	12	100 (89.6–100)
	1	126	115	0	11	100 (96.8–100)
	2	72	63	0	9	100 (94.3–100)
	3	89	87	0	2	100 (95.8–100)
	4	37	33	0	4	100 (89.6–100)

[a] Number of children who receive ≥1 dose of polio-containing vaccines.
[b] Estimated after exclusion of children with unknown vaccination status. CIs: confidence intervals; NESVPD: National Epidemiological Surveillance of Vaccine-Preventable Diseases.

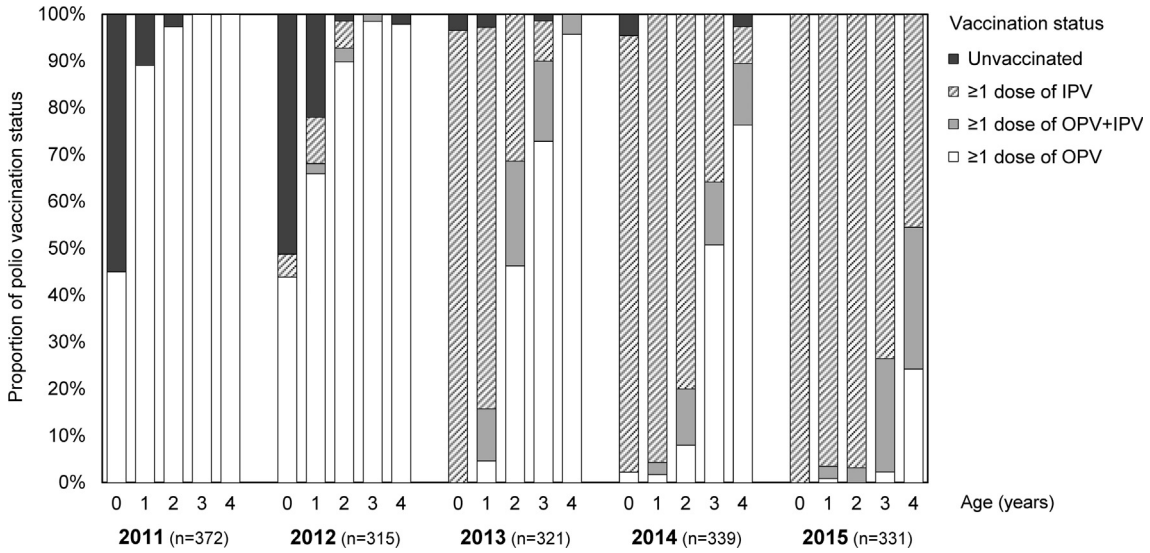

Fig. 1. Age distribution of polio vaccination status according to the type of polio-containing vaccines in children aged <5 years in Japan (NESVPD 2011–2015). Data on children with available polio vaccination status (excluding unknown vaccination status) are presented. IPV: inactivated poliovirus vaccine (including cIPV: conventional IPV, DTaP-sIPV: Sabin-derived IPV combined with diphtheria-tetanus-acellular pertussis vaccine, and DTaP-cIPV: cIPV combined with diphtheria-tetanus-acellular pertussis vaccine); OPV: oral poliovirus vaccine; NESVPD: National Epidemiological Surveillance of Vaccine-Preventable Diseases.

Polio vaccination status based on the type of polio-containing vaccines changed from 2011 to 2015 (Fig. 1). In the 2011 survey, which was conducted before the introduction of IPV for the routine immunization program in Japan, all children aged <5 years were vaccinated with OPV only. In 2012, most of the participants were surveyed from July to September, just before the introduction of IPV. The 2012 survey showed that children aged 3–4 years were mostly vaccinated with OPV, and a small population of children aged 0–2 years were vaccinated with IPV. However, most children aged 0–1 years surveyed in 2013 were vaccinated with IPV and those aged 2–3 years had a heterogeneous (OPV and/or IPV) vaccination history. The proportion of children aged <5 years who received IPV only increased to 70.2% in 2014 and to 85.8% in 2015. Moreover, among children aged <5 years who received IPV (excluding children vaccinated with unknown IPV type and unknown dose information), the proportion of children who

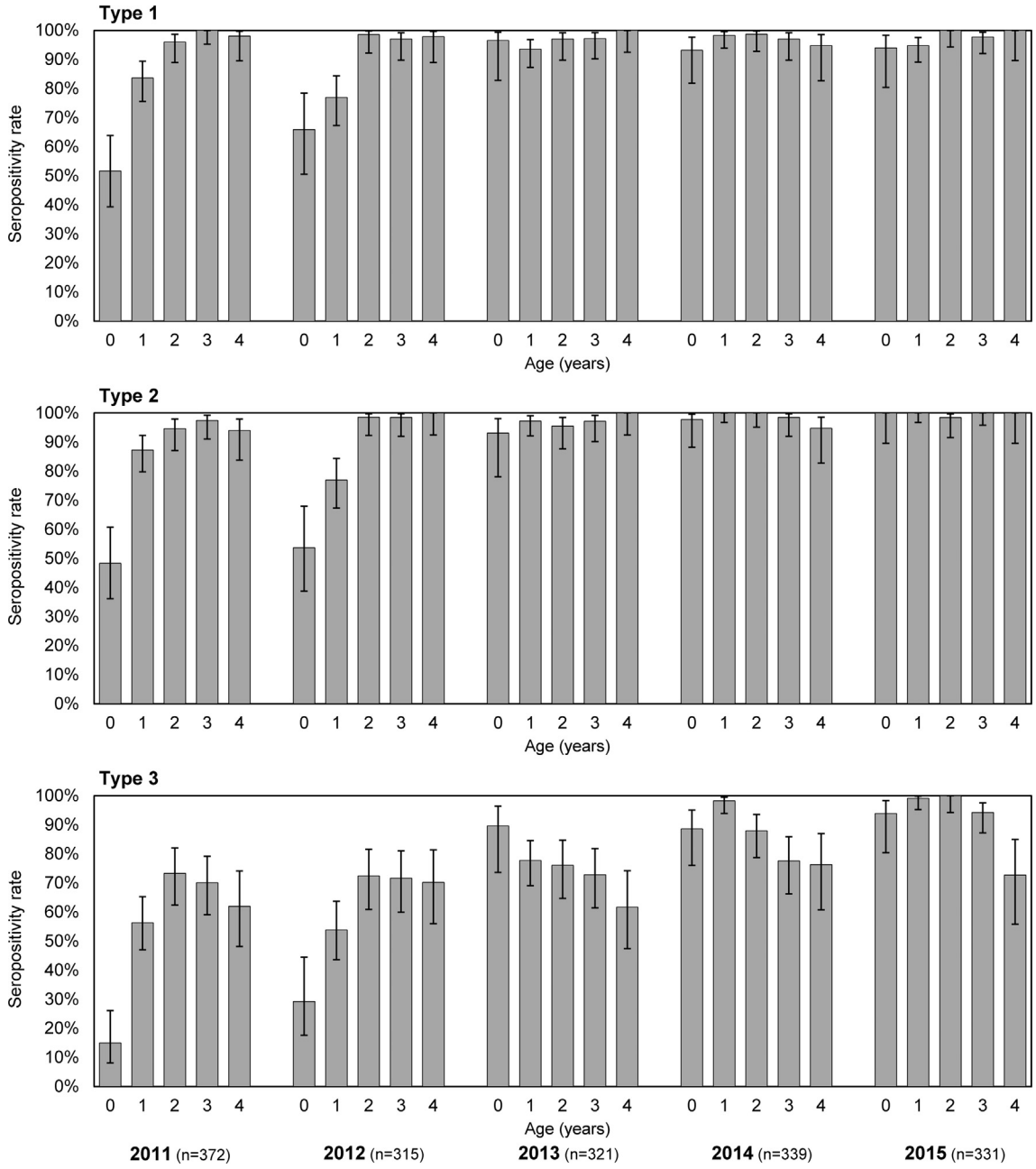

Fig. 2. Seroprevalence of antibodies to types 1, 2, and 3 poliovirus in children aged <5 years in Japan (NESVPD 2011–2015). Data of antibody titers on children with available polio vaccination status (excluding unknown vaccination status) are presented. The error bars represent the 95% confidence intervals. NESVPD: National Epidemiological Surveillance of Vaccine-Preventable Diseases.

received 4 doses of IPV increased [6.7% in 2013, 39.5% in 2014, and 56.0% in 2015 (data not shown in Fig. 1)].

3.3. Seroprevalence of antibodies to poliovirus

The age distribution of polio-neutralizing antibody positives in children aged <5 years with an available polio vaccination status is shown in Fig. 2. In the 2011–2012 surveys, low seropositivity rates for poliovirus type 1 (51.7–65.9%), type 2 (48.3–53.7%), and type 3 (15.0–29.3%) were observed in children aged <1 years. Furthermore, the seropositivity rates in children aged 1 year were <90% for poliovirus type 1 (76.9–83.6%) and type 2 (76.9–87.3%), and were <60% for poliovirus type 3 (53.8–56.4%). However, in the 2013–2015 surveys, the seropositivity rates for all 3 types of poliovirus increased in children aged <1 year (type 1: 93.2–96.6%, type 2: 93.1–100%, and type 3: 88.6–93.9%) and 1 year (type 1: 93.5–98.3%, type 2: 97.2–100%, and type 3: 77.8–99.1%). The seropositivity rates for poliovirus type 3 were low among children with a high OPV vaccination rate; however, they were as high as those for poliovirus types 1 and 2 among children with a high IPV vaccination rate (Figs. 1 and 2).

3.4. Comparison of seroprevalence for poliovirus according to the vaccination status

A comparison of seropositivity rates and GMTs among children aged <5 years who had completed the polio vaccination (2 doses of OPV: OPV2, 1 dose of OPV followed by 3 doses of IPV: OPV+IPV3, and 4 doses of IPV: IPV4) is shown in Fig. 3 and Supplementary Fig. 1. In children who received OPV2, the seropositivity rates

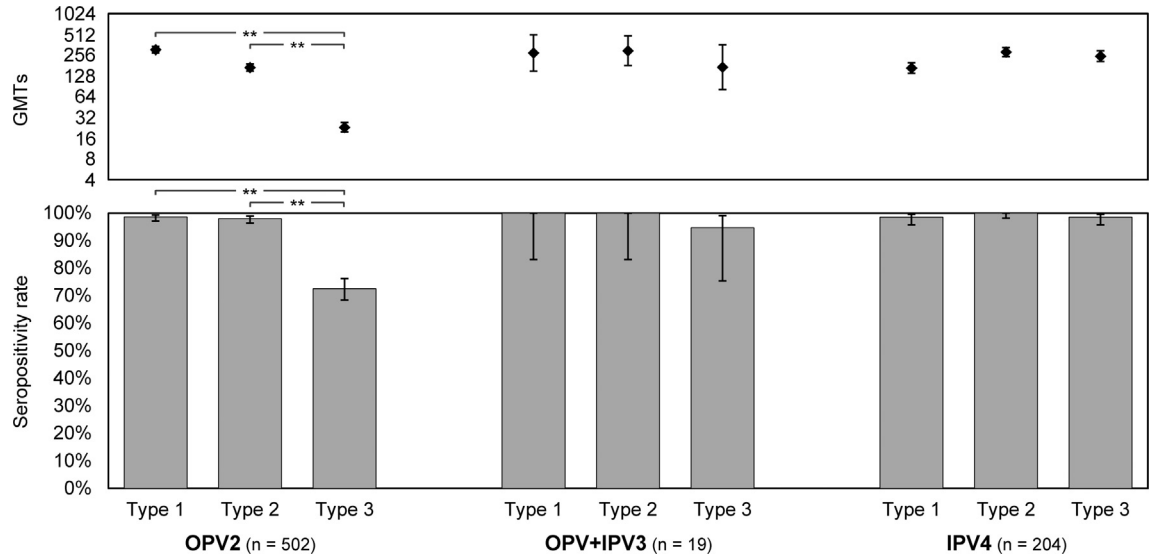

Fig. 3. Comparison of seroprevalence for poliovirus in children aged <5 years according to the polio vaccination status in Japan (NESVPD 2011–2015). Data of antibody titers on children who completed polio vaccination are presented. The error bars represent the 95% confidence intervals. **p < 0.01. OPV2: 2 doses of OPV; OPV+IPV3: 1dose of OPV followed by 3 doses of IPV; IPV4: 4 doses of IPV; OPV: oral poliovirus vaccine; IPV: inactivated poliovirus vaccine (including cIPV: conventional IPV, DTaP-sIPV: Sabin-derived IPV combined with diphtheria-tetanus-acellular pertussis vaccine, and DTaP-cIPV: cIPV combined with diphtheria-tetanus-acellular pertussis vaccine); GMTs: geometric mean titers; NESVPD: National Epidemiological Surveillance of Vaccine-Preventable Diseases.

and the GMTs (with the corresponding 95% CIs) for poliovirus type 3 were 72.5% (68.4–76.2%) and 22.9 (19.5–26.9), respectively. These results were significantly lower when compared to poliovirus types 1 and 2 ($p < 0.01$). In children who received IPV (OPV+IPV3 and IPV4), both the seropositivity rate and the GMTs for poliovirus type 3 were high [OPV+IPV3: 94.7% (75.4–99.1%) and 171.4 (81.0–362.7), IPV4: 98.5% (95.8–99.5%) and 247.4 (206.6–296.4)]. The median titers for poliovirus in each vaccination status were similar to those of GMT. (Supplementary Table 2). No significant differences in seropositivity rates among children who received IPV were found between the different types of poliovirus (Fig. 3). In the reverse cumulative polio-neutralizing antibody distribution in children aged <5 years, the distribution of antibody titers to poliovirus types 1 and 2 were similar according to the vaccination status. However, the proportion of children in each antibody titer to poliovirus type 3 who received OPV2 was low, compared to those who received OPV+IPV3 and IPV4 (Supplementary Fig. 1).

3.5. Comparison of seroprevalence for poliovirus according to the IPV dose

The comparison of seroprevalence according to the dose of vaccination with IPV-containing vaccines (DTaP-sIPV or cIPV) is shown in Fig. 4 and Supplementary Fig. 2.

In children aged <5 years who received DTaP-sIPV (Fig. 4a), the seropositivity rates (with corresponding 95% CIs) for poliovirus type 3 in those who received 3 doses [96.4% (92.7–98.2%)] or 4 doses [100% (96.7–100%)] were significantly higher than those who received ≤2 doses [73.3% (48.0–89.1%)] ($p < 0.05$ for 3 doses vs. ≤2 doses, $p < 0.01$ for 4 doses vs. ≤2 doses). Moreover, the GMTs (with corresponding 95% CIs) for poliovirus types 1, 2, and 3 in children who received 4 doses [type 1: 172.3 (132.1–224.7), type 2: 368.8 (299.9–453.6), and type 3: 332.0 (268.4–410.7)] were significantly higher than those who received ≤2 doses and 3 doses ($p < 0.05$ for 4 doses vs. 3 doses in type 1, $p < 0.01$ for others). Similar results were observed in median titers (Supplementary Table 2). In the reverse cumulative distribution of antibody titers to all 3 types of poliovirus, the proportion of children aged <5 years who received 4 doses of DTaP-sIPV was high in each antibody titer, compared to those who received ≤2 doses and 3 doses of DTaP-sIPV (Supplementary Fig. 2a, c, e).

In children aged <5 years who received cIPV (Fig. 4b), there were significant differences in the seropositivity rates for poliovirus types 1 and 3 according to the number of vaccination doses ($p < 0.01$). GMTs (with corresponding 95% CIs) for poliovirus types 1, 2, and 3 were significantly higher in children who received 4 doses [type 1: 170.3 (136.6–212.3), type 2: 197.2 (159.0–244.5), and type 3: 173.1 (127.8–234.3)] than in those who received ≤2 doses and 3 doses ($p < 0.01$), which is similar to the findings in children who received DTaP-sIPV. In the reverse cumulative distribution of antibody titers in children aged <5 years who received cIPV, the proportion of children who received 4 doses was higher than those who received ≤2 doses and 3 doses (Supplementary Fig. 2b, d, f).

A comparison between the DTaP-sIPV and cIPV groups showed that the seropositivity rates for poliovirus types 1, 2, and 3 were high (96.5–100%) among children who received 4 doses of either vaccine (Fig. 4). There were no significant differences in the seropositivity rates between DTaP-sIPV and cIPV groups.

4. Discussion

In September 2012, standalone cIPV was introduced to the routine immunization program in Japan and OPV was removed from the list of routine immunization. Subsequently, sIPV-containing vaccines were introduced to the routine immunization in November 2012. In the period from 2011 to 2015, a change in the proportion of children aged <5 years who had mainly 3 patterns of vaccination history (OPV, OPV+cIPV, and DTaP-sIPV) should be considered. The introduction of the sIPV products to the routine immunization program in Japan was the first of its kind in the world. Therefore, this study provides valuable information on the status of population immunity after the introduction of sIPV-containing vaccines for routine immunization.

In Japan, high coverage of 2 doses of OPV was maintained after the establishment of a polio-free status, and OPV coverage for the first and second dose was >90% in 2001–2010 [7]. However, vaccine-related polioviruses have been isolated from some cases with AFP [8–10], and 21 VAPP cases (15 cases who received OPV

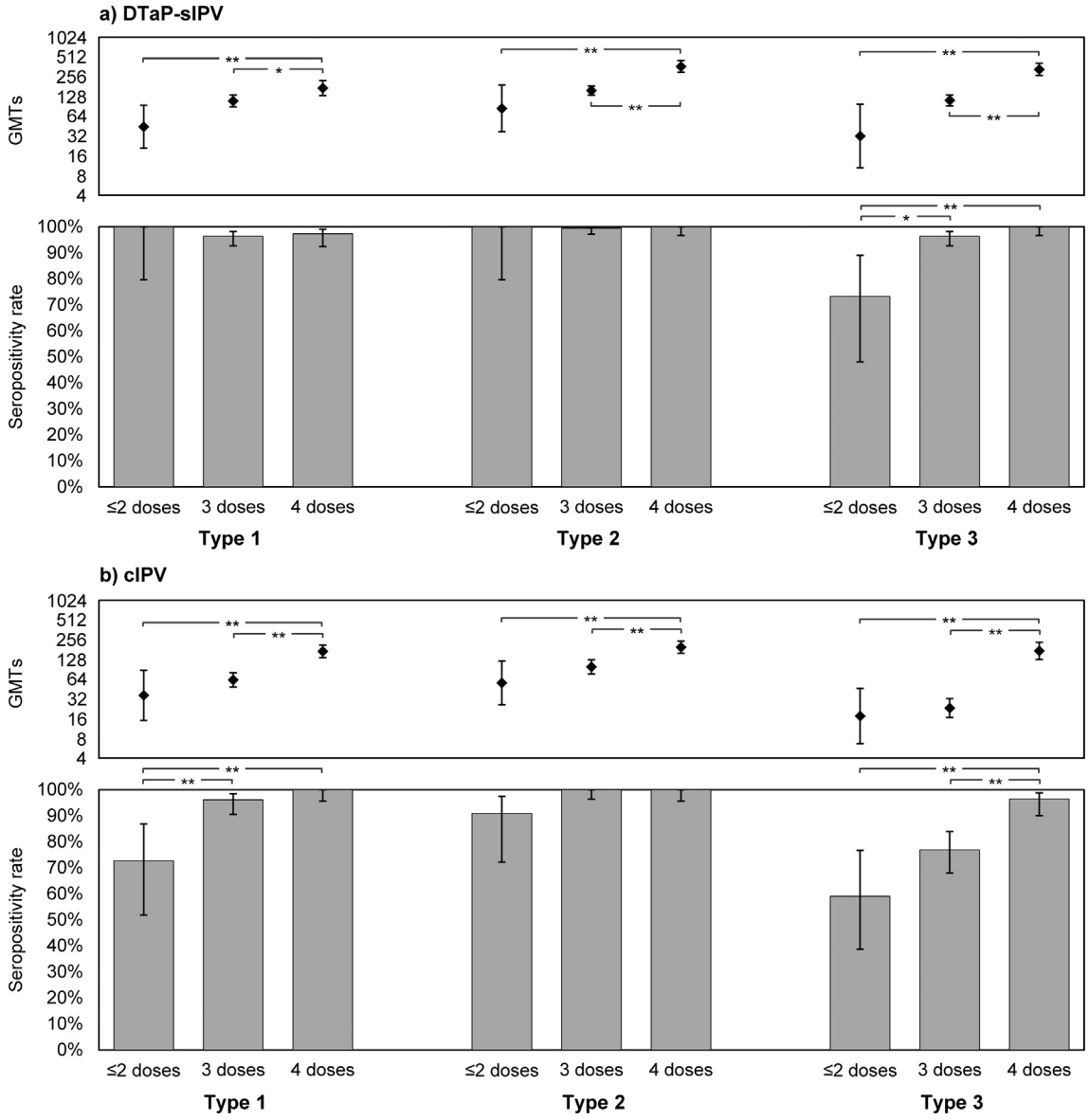

Fig. 4. Comparison of seroprevalence for poliovirus in children aged <5 years according to the dose of IPV-containing vaccine in Japan (NESVPD 2011–2015). Data of antibody titers on children with available polio vaccination status (type of IPV and dose information) are presented. The error bars represent the 95% confidence intervals. a) Children vaccinated with DTaP-sIPV [≤2 doses: n = 15, 3 doses: n = 193, 4 doses: n = 112]. b) Children vaccinated with cIPV [≤2 doses: n = 22, 3 doses: n = 104, 4 doses: n = 85]. *p < 0.05, **p < 0.01. IPV: inactivated poliovirus vaccine; DTaP-sIPV: Sabin-derived IPV combined with diphtheria-tetanus-acellular pertussis vaccine; cIPV: conventional IPV; GMTs: geometric mean titers; NESVPD: National Epidemiological Surveillance of Vaccine-Preventable Diseases.

and 6 cases who had contact with vaccinee of OPV) were reported by a national relief system for adverse events under the Immunization Law between 2001 and 2010 [11]. Several years before the introduction of IPV, OPV administration for children was refused in some parents because of growing public concern about the risk of VAPP. Consequently, OPV coverage declined to <85% in 2011–2012 [7,12]. In our study, low coverage of OPV in children aged 0–1 years in 2011–2012 was observed. However, after the introduction of IPV to the routine immunization, the coverage of ≥1 dose of polio-containing vaccines was high (≥95%) in children aged <5 years who were surveyed in 2013–2015. After the IPV introduction in September 2012, some of the remaining unimmunized children could have been immunized with cIPV or DTaP-sIPV.

Our study showed that seropositivity rates for poliovirus types 1 and 2 corresponded with the coverage of ≥1 dose of polio-containing vaccines; high seropositivity rates were observed in the age groups with high vaccination coverage. However, in the age groups that mainly received OPV, seropositivity rates were lower for poliovirus type 3 than those for types 1 and 2. Even in children who completed polio vaccination with 2 doses of OPV, the seropositivity rates and GMTs for poliovirus type 3 were significantly lower than those for types 1 and 2. Low seropositivity rates for poliovirus type 3 after receiving OPV have also been reported in developing countries [13,14]. Similar results were shown in other studies in the United States and the Republic of Korea; formerly, immunization for OPV was recommended in 3 or 4 doses to infants. Seropositivity rates for poliovirus type 3 in age groups recommended to receive OPV were lower than those in age groups recommended to receive IPV [15–17].

In the age groups that mainly received IPV, high seropositivity rates for all 3 types of poliovirus were observed in our study. These results suggested that the level of antibody titers to type 3 poliovirus induced by IPV immunization was higher than those induced by OPV immunization. Interestingly, although the proportion of

children receiving IPV was high in those aged 1 year in 2013 and those aged 2 years in 2014, seropositivity rates for poliovirus type 3 were lower than those for poliovirus types 1 and 2. These results may be because of the relatively high proportion of children receiving OPV+IPV in these age groups. However, the number of participants receiving OPV+IPV was not sufficient for analysis. Further investigation is necessary.

We observed high seropositivity rates (≥95%) for all 3 types of poliovirus in children who received 4 doses of sIPV, and the GMTs in the 4-dose group were higher than those in the 3-dose group. According to phase II and III clinical studies of sIPV-containing tetracomponent vaccine, the seropositivity rates against all 3 types of the Sabin strain were high (100.0%) after booster immunization, and the GMTs were higher in the booster immunization group than those in the primary immunization group [18]. Two sIPV-containing vaccines produced by different manufacturers were introduced into the routine immunization in Japan (as of November 2018) (Supplementary Table 1), and the immunogenicity profiles were similar between the two vaccine products [19]. These results indicated the importance of completing 4 doses of IPV to obtain a high level of immunity.

In the comparison between the sIPV and cIPV groups, although both groups showed high seropositivity rates, the GMTs were lower in the cIPV group than in the sIPV group. The results of GMTs may be explained by the differences in the neutralizing reactivity between homologous and heterologous poliovirus strains. However, the GMTs in children who received 4 doses of either vaccine were above the protective level; thus, they are probably not clinically significant. Furthermore, recent data from a study in China indicated that the antibodies induced by sIPV neutralized multiple wild poliovirus strains [20]. These results suggest that children immunized with sIPV are also protected against currently circulating wild polioviruses those as with OPV.

There are several limitations in this study. First, a small number of participants were randomly collected from 9 of 47 prefectures, which are located in the different geographical areas of Japan, and participants with an unknown vaccination status were excluded from the analysis of vaccination coverage and seropositivity rates. Therefore, our results are possibly overestimated, and the data may not entirely represent the population of interest. Second, the period after vaccination was not considered for the analysis of seropositivity rates and GMTs. Third, for measurement of neutralizing antibody titers against poliovirus, no currently circulating wild poliovirus strain was used. Fourth, as the participants were randomly collected in each year, the same individuals were not followed in each study year.

WHO encourages global IPV introduction to minimize the risk of polio outbreaks caused by type 2 vaccine-derived polioviruses and VAPP as the final stage of global polio eradication [21]. However, serious shortages in the global cIPV supply have become apparent from 2016 to 2017, and a sustainable IPV supply is critical for future polio immunization strategies. From the viewpoint of safer vaccine production, sIPV development is being studied in middle- and low-income countries as a more realistic and feasible IPV option than cIPV. In China, standalone sIPV developed by a domestic vaccine manufacturer was licensed in 2015 and introduced onto the market, and several other manufacturers are also developing sIPV products [22]. In addition, clinical development of sIPV is ongoing in many countries.

In this regard, our results are valuable as the first follow-up study on the mid-term immunogenicity of sIPV-containing vaccines after their introduction to routine nationwide immunization program. This study should be continued to monitor the long-term immunogenicity of sIPV-containing vaccines in order to evaluate whether the 5th booster IPV dose is required for preschool children or young adults in Japan.

5. Conclusions

In conclusion, our findings demonstrate that both the polio vaccination coverage and seropositivity rates for all 3 types of poliovirus remained high in children after the introduction of IPV in the routine immunization in Japan. These results indicate that the transition from OPV to IPV for routine immunization was successful.

Conflict of interest

None.

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Author contributions

Conception and design of the study: HS, KT, HS, KO. Test and data collection: AG, ST, TN, CH, TO, MI, MI, RO, YY. Data analysis: HS, SA, HO, SM. Writing the paper and revising important content: HS, KT, HS, KO.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2019.02.034.

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