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Immunogenicity to poliovirus type 2 following two doses of fractional intradermal inactivated poliovirus vaccine: A novel dose sparing immunization schedule

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Abstract

Introduction: The polio eradication endgame strategic plan calls for the sequential removal of Sabin poliovirus serotypes from the trivalent oral poliovirus vaccine (tOPV), starting with type 2, and the introduction of ≥1 dose of inactivated poliovirus vaccine (IPV), to maintain an immunity base against poliovirus type 2. The global removal of oral poliovirus type 2 was successfully implemented in May 2016. However, IPV supply constraints has prevented introduction in 21 countries and led to complete stock-out in >20 countries.

Methods: We conducted a literature review and contacted corresponding authors of recent studies with fractional-dose IPV (fIPV), one-fifth of intramuscular dose administered intradermally, to conduct additional type 2 immunogenicity analyses of two fIPV doses compared with one full-dose IPV.

Results: Four studies were identified that assessed immunogenicity of two fIPV doses compared to one full-dose IPV. Two fractional doses are more immunogenic than 1 full-dose, with type 2 seroconversion rates improving between absolute 19–42% (median: 37%, $p < 0.001$) and relative increase of 53–125% (median: 82%), and antibody titer to type 2 increasing by 2–32-fold (median: 10-fold). Early age of administration and shorter intervals between doses were associated with lower immunogenicity.

Discussion: Overall, two fIPV doses are more immunogenic than a single full-dose, associated with significantly increased seroconversion rates and antibody titers. Two fIPV doses together use two-fifth of the vaccine compared to one full-dose IPV. In response to the current IPV shortage, a schedule of two fIPV doses at ages 6 and 14 weeks has been endorsed by technical oversight committees and has been introduced in some affected countries.

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Contributors

AA and RWS jointly prepared the first draft of the manuscript and all authors reviewed and approved the manuscript. NM led data analysis. All authors contributed to interpretation of results.

Conflict of interest

All authors declare that they have no conflict of interest.

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the U.S. Centers for Disease Control and Prevention.

Keywords

Fractional inactivated polio vaccine; Inactivated polio vaccine; Priming; Polio immunogenicity

1. Introduction

Indigenous wild poliovirus type 2 was last detected in Northern India in 1999, and declared as eradicated by the Global Certification Commission in September 2015 [1]. The Global Polio Eradication Initiative (GPEI) prepared a strategic action plan which called for the sequential removal of Sabin serotypes from the trivalent oral poliovirus vaccine (tOPV), and the introduction of inactivated poliovirus vaccine (IPV) [2]. By May 2016, Sabin type 2 was successfully withdrawn globally when tOPV was replaced with bivalent OPV (bOPV), containing poliovirus types 1 and 3. The switch was preceded by a phased introduction of one dose of IPV in the routine immunization schedule. Countries were prioritized for IPV introduction based on the historical risk profile of generating circulating vaccine-derived polioviruses.

The Strategic Advisory Group of Experts (SAGE) on Immunization has recommended introduction of at least one dose of intra-muscular IPV at age ≥14 weeks, with bOPV at ages 6,10 and 14 weeks, to provide an immunity base to type 2 poliovirus after cessation of Sabin type 2 [3]. The immunity base against type 2 should decrease the paralytic consequences of poliovirus type 2 exposure and improve immunological response to type 2 containing poliovirus vaccine administered in the event of a type 2 poliovirus outbreak. IPV introduction (in previously OPV-only using countries) has increased global IPV demand, stand-alone as well as that used in combination vaccines, from about 80 million doses in 2013 to about 200 million doses in 2016. The supply commitments by IPV manufacturers were expected to meet the increased demand through expanded production; however, the quantity of IPV promised by the manufacturers has repeatedly been reduced (currently <50% of initial commitments). These supply reductions have led to at least 49 countries either having to delay IPV introduction or experience a stock-out of IPV after introduction [4]. IPV supply constraints are expected to last until 2018–2019.

Fractional IPV (fIPV), in which one-fifth (0.1 ml) of the full dose of intramuscular IPV (0.5 ml) is administered intradermally, is a potential option to stretch limited supplies of IPV. Here we present a literature review and comparative analysis of poliovirus type 2 immunogenicity between two doses of fIPV and one full-dose IPV.

Based on promising preliminary evidence from the data presented in this review, in 2012, SAGE recommended that development of fIPV be prioritized [5]. Since then, in response to the IPV supply constraints, a new schedule of two fIPV doses at ages 6 and 14 weeks in addition to bOPV at ages 6, 10 and 14 weeks was developed and endorsed by advisory committees [6].

2. Methods

PubMed database was searched for studies published from January 01, 1959 onwards. Search terms used were: inactivated poliovirus vaccine; fractional inactivated poliovirus vaccine; and intradermal inactivated poliovirus vaccine. Assessment was limited to studies that assessed enhanced potency IPV (eIPV), hence-forth called IPV, and studies using original potency IPV were excluded from the review. Studies were selected for review if they assessed immunogenicity of fractional one-fifth intradermal IPV in infants who had received no prior poliovirus vaccine and did not administer type 2 OPV with IPV. Among studies selected for review, primary assessment was restricted to those that compared immunogenicity of one full-dose of intramuscular IPV to two doses of intradermal fIPV.

In terms of statistical methods, we compared the proportion with seroconversion in the 2-dose fIPV and single full-dose arms. In all of the studies, blood for serological assessment was collected 4 weeks after the fIPV/IPV dose, except in a study in Cuba in which blood was collected 4 months after the first full-dose IPV [7]. For the antibody titer distribution, we were able to obtain subject-specific titer values and compared the two study arms using the Wilcoxon rank-sum test. For median antibody titers, 95% confidence intervals were calculated using bootstrapping with 10,000 replications [8]. In addition, for each study arm we prepared the reverse cumulative antibody titer distribution curves. All statistical analyses were conducted in R (version 2.92) [9].

3. Results

Three studies comparing fIPV and full-dose IPV did not meet selection criteria and were therefore excluded [10–12]. Four studies were identified that compared two fIPV doses to one full-dose IPV. Two additional studies were identified that assessed immunogenicity of two fIPV doses though did not compare it to one full-dose IPV. Also three additional studies assessed immunogenicity of full-dose IPV at age 14 weeks, the standard recommended full-dose schedule.

Table 1 lists the nine studies that were identified. Studies were implemented from 1992 to 2015. In India two studies reported 70–89% type 2 seroconversion with two doses of fIPV at ages 6 and 14 weeks [13,14]. Fig. 1 displays, by study, the reverse cumulative antibody curves 4-weeks after one full-dose IPV compared with 4-weeks after two fIPV doses and demonstrates in all studies that two fIPV doses induce more robust antibody titers than a single full dose.

In Cuba, type 2 seroconversion with fIPV at age 6 and 10 weeks was 19% higher compared to IPV at age 6 weeks (55% vs 36%; $p < 0.001$), a relative increase of 53% [15]. Median titers were 2-fold higher with two fIPV doses compared to one IPV dose. In Bangladesh, type 2 seroconversion with fIPV at ages 6 and 14 weeks was 43% higher compared to IPV at age 6 weeks (81% vs 38%; $p < 0.001$), a relative increase of 113% [16]. Type 2 median antibody titers after two fIPV doses were 16-fold higher compared to one IPV dose. This study also assessed immunologic priming with IPV, a seroconversion response assessed one week after administration of a second dose of IPV/fIPV among those who did

not seroconvert after the first dose. Overall, after one fIPV dose, 78% of participants either seroconverted or were primed.

In Oman, type 2 seroconversion with fIPV at ages 2 and 4 months was 40% higher compared to IPV at age 2 months (72% vs 32%; $p < 0.001$), a relative increase of 125% [17]. The median antibody titer was 5-fold higher with two fIPV doses compared to one IPV dose. In a second study in Cuba, type 2 seroconversion with fIPV at ages 4 and 8 months was 35% higher compared to IPV at age 4 months (98% vs 63%; $p < 0.001$), a relative increase of 56% [7]. Type 2 median antibody titers were 32-fold higher after two fIPV doses compared to one IPV dose. After one fIPV dose at age 4 months 97% of participants had either seroconverted or were primed.

Overall, two doses of fIPV were more immunogenic with higher seroconversion (absolute increase median: 37%, range: 19–42%; relative increase median: 84%, range: 53–125%) and higher antibody titers (median: 10-fold; range: 2–32-fold) than one full-dose IPV given at the age of first fIPV dose.

Three studies from India and Latin America reported 69–80% type 2 seroconversion after one full-dose IPV at age 14 weeks with median titers of 18–36 [18–20].

4. Discussion

In April 2016, in light of global IPV shortage SAGE recommended that countries consider an IPV schedule of two fractional doses (0.1 ml each) at ages 6 and 14 weeks in lieu of one full-dose (0.5 ml) at age 14 weeks [21]. The WHO position paper on polio states that "*in the context of an IPV shortage, countries could consider instituting a 2-dose fractional dose schedule which could ensure that all eligible infants receive IPV, is dose-sparing and results in better immunogenicity than a single full dose of IPV*". The data presented here formed the basis of the advisory committee recommendation of two fIPV doses at ages 6 and 14 weeks as an alternative to one full-dose of IPV at age ≥14 weeks in addition to bOPV at ages 6, 10 and 14 weeks. Two fIPV doses, 4 weeks to 4 months apart are more immunogenic for type 2 poliovirus (and for types 1 and 3; data not shown) than one IPV dose administered at the age of first intradermal dose. The type 2 immunogenicity of two fIPV doses were related directly to the age at first administration and the interval between the doses, starting later and having a longer interval was more immunogenic, consistent with the "prime-boost" concept for inactivated vaccines.

Two fIPV doses use two-fifth of the amount of vaccine compared to one full-dose IPV. Therefore, each full-dose IPV, which would have been used to vaccinate one child can now be used to vaccinate at least two infants, stretching limited supplies of IPV. Fractional IPV does not require modification of existing IPV vaccine vial or its contents to make IPV compatible to draw the vaccine in devices for intradermal injection. Multi-dose IPV vial policy permits use of vials up to 28 days from the date of first use and this will minimize wastage particularly in immunization sessions, in which the number of vaccine recipients is less than the maximum number of fIPV doses that could be withdrawn from an IPV vial.

To prevent an IPV stock-out, two fIPV doses were introduced in routine immunization nationally in Sri Lanka (ages 2 and 4 months) and in April 2016 in 8 States and Territories of India (ages 6 and 14 weeks) [Fig. 2]. By the end of 2016, India expanded fIPV nationwide and this policy is targeting now the entire 26 million annual birth cohort of India, with two fIPV doses at ages 6 and 14 weeks.

In June 2016, India conducted a fIPV mass campaign to successfully administer an intradermal dose of fIPV in over 90% of recipients (target population: 291,305), demonstrating the programmatic feasibility of intradermal fIPV administration in a well-functioning immunization program [22]. The experience in fIPV campaign in India and other studies has demonstrated that training of vaccinators to successful administer fIPV intradermally is critical in achieving the full immunological potential of fIPV.

Though no study has compared two fIPV doses at ages 6 and 14 weeks to one full-dose IPV at age 14 weeks, three studies were identified that reported type 2 seroconversion of 70–89% with two fIPV doses at ages 6 and 14 weeks in India and Bangladesh. In a follow-up study in Bangladesh, by the same study investigators at the same site with specimens tested at the same laboratory, type 2 seroconversion with one full-dose IPV at age 14 weeks was 74% (68%-78%) with median titer of 45 (95% CI: 36–64) [Unpublished data]. This is in contrast to 81% (74%-86%) type 2 seroconversion with two fIPV doses at ages 6 and 14 weeks with median antibody titer of 455 (288–1448), 10-fold higher than that with one full-dose IPV at 14 weeks of age. Additionally, three more studies from India and Latin America reported type 2 seroconversion of 69–80% with one full-dose IPV at age 14 weeks with median titer of 18–36; type 2 seroconversion and antibody titers similar to that observed in Bangladesh with one full-dose IPV at age 14 weeks. Therefore, although limited, existing evidence suggests that two fIPV doses at ages 6 and 14 weeks is more immunogenic for type 2 poliovirus than one full-dose IPV at age 14 weeks. Ongoing randomized clinical trials will provide direct comparative evidence from the same study on type 2 immunogenicity of two fIPV doses at ages 6 and 14 weeks of age to full-dose IPV at age 14 weeks.

To mitigate the programmatic difficulties with administering fIPV, the program has been encouraging device manufacturers to develop needle adapters and needle-free jet injectors to facilitate the intradermal administration of fIPV. These devices are now becoming increasingly available to developing countries that are interested to use fIPV. The studies assessed in this review used different devices to inject intradermal IPV, including syringe-needle, microneedle device and needle-free jet injectors. This demonstrates consistency of immunological performance of fractional IPV across multiple devices and offers flexibility to immunization programs, considering introduction of fractional IPV, in selecting devices for administering fractional IPV.

In addition, compared to one full-dose IPV at 14 weeks, two fIPV doses at ages 6 and 14 weeks may aid in reaching more children with at least one IPV dose. Globally it is estimated that 7.2 million children receive first dose of diphtheria-tetanus and pertussis (DTP1) vaccine at age 6 weeks but never receive the third dose at age 14 weeks [23]. Using DTP coverage as a proxy for potential IPV coverage, administering fIPV at ages 6 and 14 weeks is likely to increase reach of IPV compared to administering only at 14 weeks of

age. Also administration of IPV with the first dose of OPV at age 6 weeks could potentially reduce the incidence of vaccine-associated paralytic poliomyelitis (VAPP).

Our review also identified limitations. There are limited data comparing the mucosal immunity induced by fIPV with full dose IPV. One published study evaluated the mucosal immunity after three fIPV doses, and found small differences with full-dose IPV [17]. A study in Bangladesh reported that after two full or fractional doses of IPV at ages 6 and 14 weeks, there were no statistically significant differences in shedding [16]. Another unpublished study in Cuba is evaluating the differences following fIPV, full-dose IPV, and a placebo control group. Data from this, and another study in Sri Lanka should be available by the end of 2016. In addition, the timing and extent of antibody decay probably needs further study. One published study from the Philippines suggest that fIPV and full-dose IPV-induced antibodies after a primary series have similar decay characteristics after a follow-up of about 12 months [10]. Seroconversions observed in all studies discussed in this review, except those in Cuba, are likely to be affected by community transmission of OPV as tOPV was used in routine immunization and campaigns during the duration of the study. This exposure is likely to have affected type 2 seroconversion in fIPV as well as that in full-dose IPV groups. In the Bangladesh study, only 14% type 2 seroconversion was observed in the bOPV arm by 18 weeks of age.

Furthermore, the SAGE is currently discussing an immunization schedule for the post-eradication period (i.e., after cessation of routine bOPV use). It is possible to design a two-dose fIPV schedule that seroconverts more than 90% of infants associated with high antibody titers: two-doses of fIPV at ages 4 and 8 months [7].

Because of the challenges with IPV supply constraints, the GPEI had a short timeline to find a dose-sparing schedule for IPV. Interestingly, the solution found of two fIPV doses offers a more immunogenic alternative to one full-dose of IPV. This alternative can stretch IPV supplies to reach at least twice the number of children, avoid IPV stock-out and fulfill the objective of the Polio End-game Strategic Plan to give every child an opportunity to receive at least one IPV dose. Countries are now challenged to ensure that all infants receive at least one dose of IPV to maintain an immunity base against poliovirus type 2.

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References

[1]. Adams A, Salisbury DM. Eradicating polio. Science (New York, NY) 2015;350:609.

[2]. The Global Polio Eradication Initiative. Polio eradication and endgame strategic plan 2013–2018. Geneva, Switzerland; 2013.

[3]. World Health Organization. Meeting of the strategic advisory group of experts on immunization, November 2013 – conclusions and recommendations. Wkly Epidemiol Rec 2014;89:1–20. [PubMed: 24466571]

[4]. Hampton LM, Farrell M, Ramirez-Gonzalez A, Menning L, Shendale S, Lewis I, et al. Cessation of trivalent oral poliovirus vaccine and introduction of inactivated poliovirus vaccine - worldwide, 2016. MMWR Morb Mortal Wkly Rep 2016;65:934–8. [PubMed: 27606675]

[5]. World Health Organization. Meeting of the strategic advisory group of experts on immunization, April 2012 - conclusions and recommendations. Wkly Epidemiol Rec. 2012:201–16. Geneva, Switzerland.

[6]. World Health Organization. Polio vaccines: WHO position paper – March 2016. Wkly Epidemiol Rec 2016;12:145–68.

[7]. Resik S, Tejeda A, Sutter RW, Diaz M, Sarmiento L, Alemani N, et al. Priming after a fractional dose of inactivated poliovirus vaccine. New England J Med 2013;368:416–24. [PubMed: 23363495]

[8]. Efron B, Tibshirani R. An introduction to the bootstrap. London: Chapman & Hall/CRC; 1993.

[9]. R Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2015., <https://www.R-project.org/>.

[10]. Cadorna-Carlos J, Vidor E, Bonnet MC. Randomized controlled study of fractional doses of inactivated poliovirus vaccine administered intradermally with a needle in the Philippines. Int J Inf Dis: IJID: Off Publ Int Soc Inf Dis 2012;16:e110–6.

[11]. Estivariz CF, Jafari H, Sutter RW, John TJ, Jain V, Agarwal A, et al. Immunogenicity of supplemental doses of poliovirus vaccine for children aged 6–9 months in Moradabad, India: a community-based, randomised controlled trial. Lancet Infect Dis 2012;12:128–35. [PubMed: 22071249]

[12]. Resik S, Tejeda A, Mach O, Fonseca M, Diaz M, Alemany N, et al. Immune responses after fractional doses of inactivated poliovirus vaccine using newly developed intradermal jet injectors: a randomized controlled trial in Cuba. Vaccine 2015;33:307–13. [PubMed: 25448109]

[13]. Samuel BU, Cherian T, Rajasingh J, Raghupathy P, John TJ. Immune response of infants to inactivated poliovirus vaccine injected intradermally. Vaccine 1992;10:135. [PubMed: 1311491]

[14]. Nirmal S, Cherian T, Samuel BU, Rajasingh J, Raghupathy P, John TJ. Immune response of infants to fractional doses of intradermally administered inactivated poliovirus vaccine. Vaccine 1998;16:928–31. [PubMed: 9682339]

[15]. Resik S, Tejeda A, Lago PM, Diaz M, Carmenates A, Sarmiento L, et al. Randomized controlled clinical trial of fractional doses of inactivated poliovirus vaccine administered intradermally by needle-free device in Cuba. J Infect Dis 2010;201:1344–52. [PubMed: 20350164]

[16]. Anand A, Zaman K, Estivariz CF, Yunus M, Gary HE, Weldon WC, et al. Early priming with inactivated poliovirus vaccine (IPV) and intradermal fractional dose IPV administered by a microneedle device: A randomized controlled trial. Vaccine 2015;33:6816–22. [PubMed: 26476367]

[17]. Mohammed AJ, AlAwaidy S, Bawikar S, Kurup PJ, Elamir E, Shaban MM, et al. Fractional doses of inactivated poliovirus vaccine in Oman. New England J Med 2010;362:2351–9. [PubMed: 20573923]

[18]. Sutter RW, Bahl S, Deshpande JM, Verma H, Ahmad M, Venugopal P, et al. Immunogenicity of a new routine vaccination schedule for global poliomyelitis prevention: an open-label, randomised controlled trial. Lancet 2015;386:2413–21. [PubMed: 26388534]

[19]. Asturias EJ, Bandyopadhyay AS, Self S, Rivera L, Saez-Llorens X, Lopez E, et al. Humoral and intestinal immunity induced by new schedules of bivalent oral poliovirus vaccine and one or two doses of inactivated poliovirus vaccine in Latin American infants: an open-label randomised controlled trial. Lancet 2016;388:158–69. [PubMed: 27212429]

[20]. Saez-Llorens X, Clemens R, Leroux-Roels G, Jimeno J, Clemens SA, Weldon WC, et al. Immunogenicity and safety of a novel monovalent high-dose inactivated poliovirus type 2 vaccine in infants: a comparative, observer-blind, randomised, controlled trial. Lancet Infect Dis 2016;16:321–30. [PubMed: 26719058]

[21]. World Health Organization. Summary of the April 2016 meeting of the strategic advisory group of experts on immunization (SAGE). Geneva, Switzerland; 2016. p. 1–4.

[22]. Bahl S, Verma H, Bhatnagar P, Haldar P, Satapathy A, Kumar KN, et al. Fractional-dose inactivated poliovirus vaccine immunization campaign – Telangana State, India, June 2016. MMWR Morb Mortal Wkly Rep 2016;65:859–63. [PubMed: 27559683]

[23]. Subaiya S, Dumolard L, Lydon P, Gacic-Dobo M, Eggers R, Conklin L. Global routine vaccination coverage, 2014. MMWR Morb Mortal Wkly Rep 2015;64:1252–5. [PubMed: 26562454]

Further reading

[24]. Resik S, Tejeda A, Mach O, Sein C, Molodecky N, Jarrahian C, et al. Needle-free jet injector intradermal delivery of fractional dose inactivated poliovirus vaccine: association between injection quality and immunogenicity. Vaccine 2015;33:5873–7. [PubMed: 26192350]

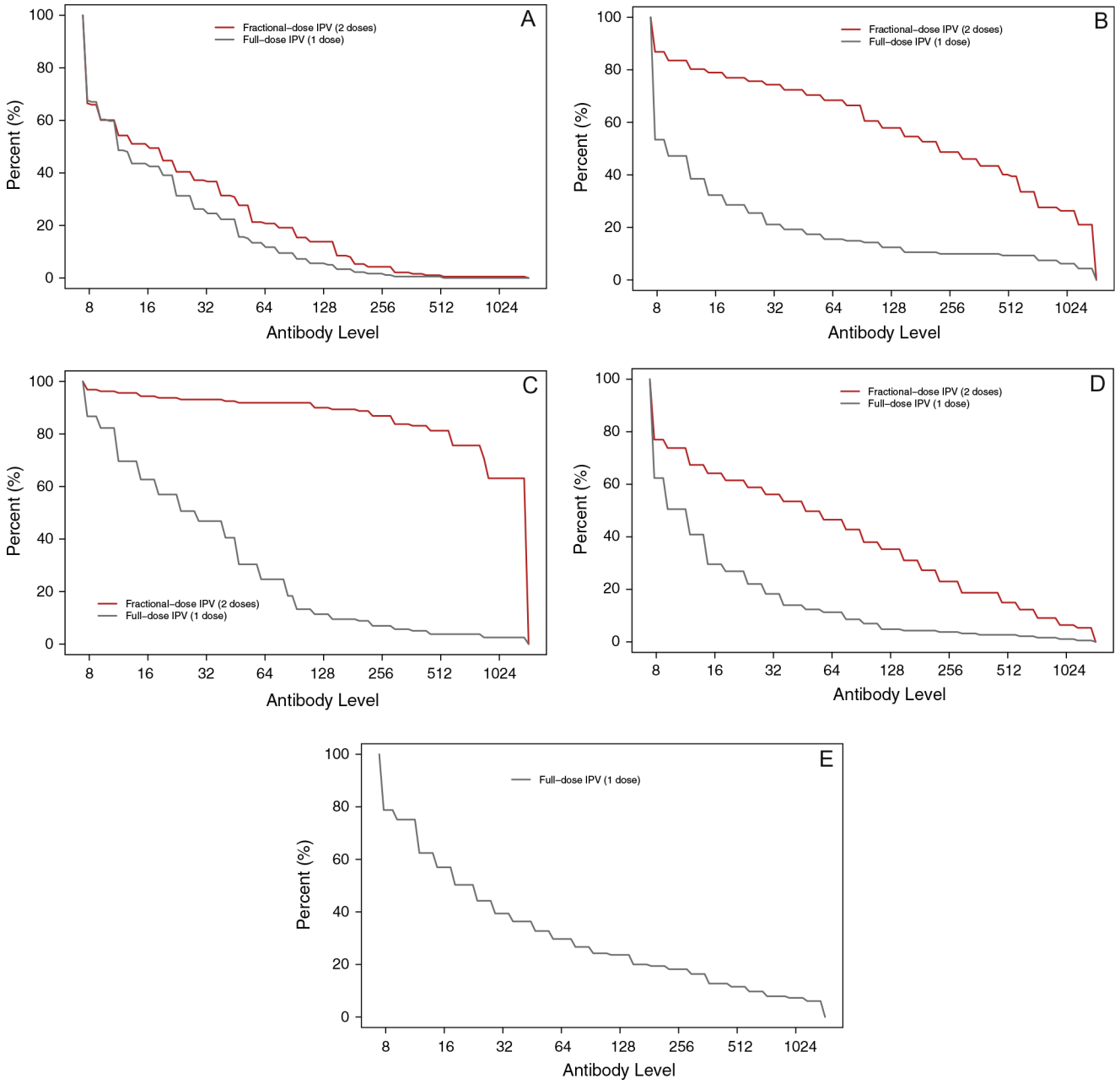

Fig. 1.

Reverse cumulative poliovirus antibody distribution curves for type 2 poliovirus. Footnote: Panel A: Cuba 1 [15]; Panel B: Oman [17], Panel C: Cuba 2 [7]; Panel D: Bangladesh [16]; and Panel E: India [18].

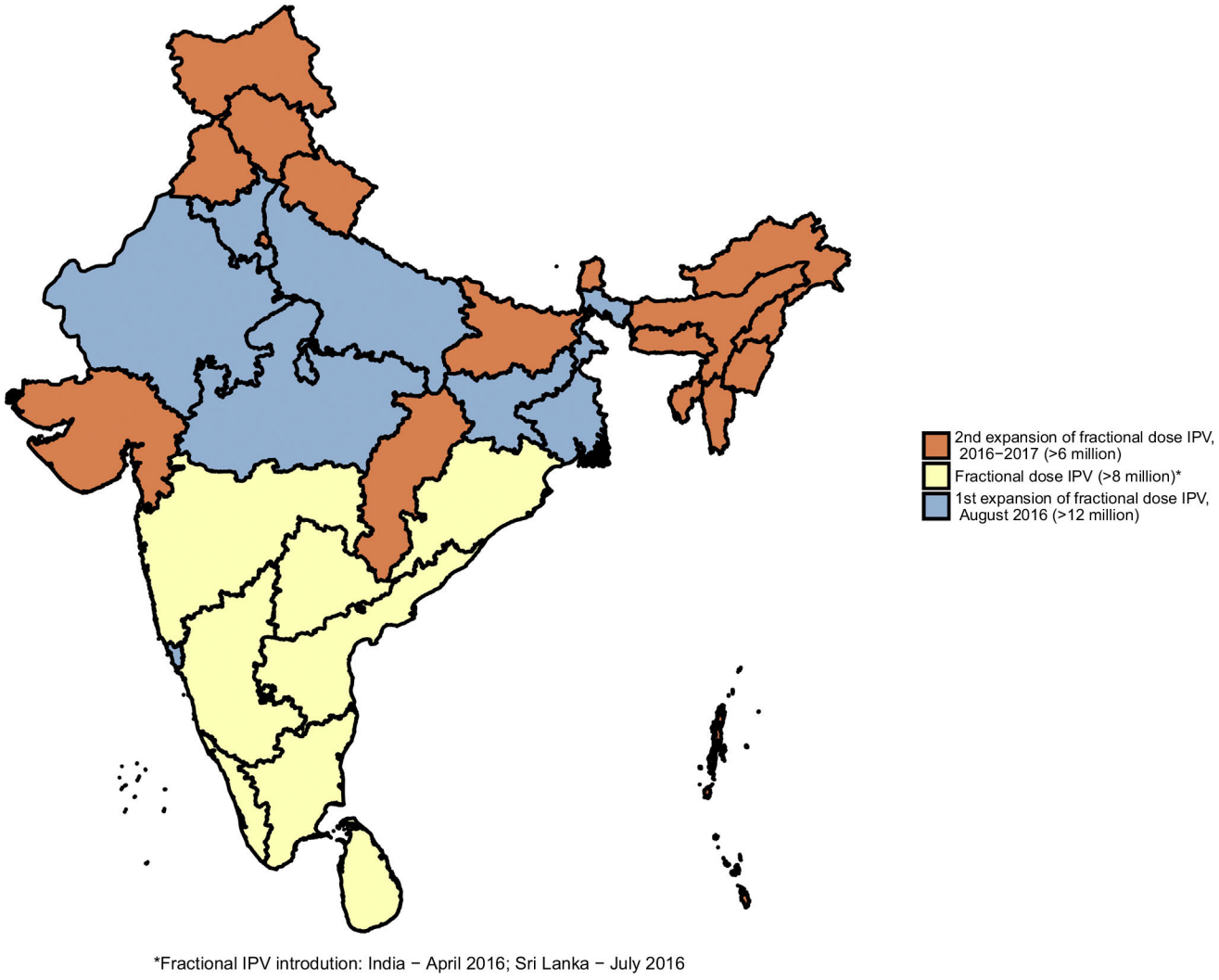

Fig. 2.

Sri Lanka and, States and Territories of India which have, or will introduce in 2016–2017 a two-dose fIPV routine immunization schedule for poliomyelitis prevention.

Table 1

Clinical trials comparing two fractional intradermal inactivated poliovirus vaccine (IPV) doses (0.1 ml) to one full intramuscular IPV dose (0.5 ml).

Country, field-work	IPV manufacturer	IPV type & schedule	Device for injection	Type 2 SC (95%CI)	Absolute increase in type 2 SC (ID vs IM)	Relative increase in type 2 SC (ID vs IM in%)	SC & priming$^{\mu}$ after first IPV dose	Median type 2 Ab titer, (95%CI)	Type 2 Ab fold increase (ID/IM)
Studies that compared ID fractional IPV to IM IPV									
Cuba [15], 2006–07	Statens Serum Institute	IM (6 wks)	Syringe-needle	36 (29–43)	19*	53	–	11 (11–13)	2
		ID (6,10 wks)	Disposable Syringe Jet Injector (DSJI): Biojector 2000	55 (48–62)			–	22 (13–35)	
Oman [15], 2007	GlaxoSmithKline	IM (2 mos)	Syringe-needle	32 (25–39)	40*	125	–	9(9–11)	5*
		ID (2, 4 mos)	DSJI: Biojector 2000	72 (66–78)			–	45 (28–72)	
Cuba [15], 2009–10	Netherlands Vaccine Institute$^{\beta}$	IM (4 mos)	Syringe-needle	63 (55–70)	35*	56	99	28 (18–36)	32*
		ID (4, 8 mos)	DSJI: Biojector 2000	98 (94–99)			97	898 (713–1448)	
Bangladesh [15], 2012–13	Netherlands Vaccine Institute$^{\beta}$	IM (6 wks)	Syringe-needle	38 (31–46)	43*	113	90	28 (18–51)	16*
		ID (6,14 wks)	NanoPass MJ600 microneedle	81 (74–86)			78	455 (288–5767)	
Relevant studies on ID fractional IPV									
India [15], 1991	Institut Merieux	ID (6,14 wks)	BCG needle and syringe	89 (56–98)	–		–	96 (15–512)	–
India [15], 1998	Institut Merieux	ID (6–8,14 wks)	BCG needle and syringe	70 (52–83)	–		–	223$^{\varnothing}$ (-)	–
Relevant studies on 14 week IM IPV									
India [15], 2013–14	Panacea Biotec	IM (14 wks)	Syringe-needle	69 (61–76)				18 (13–23)	
Latin America [15], 2013	Sanofi-Pasteur	IM (14 wks)	Syringe-needle	80 (74–85)				28 (23–37)	
Panama [15], 2014–15	Sanofi-Pasteur	IM (14 wks)	Syringe-needle	75 (66–82)				36(18–114) $^{\alpha}$	

IPV: Inactivated Poliovirus Vaccine; CI: Confidence Interval; SC: Seroconversion; Ab=Antibody; IM: Intramuscular; ID: Intradermal.

$^{\varnothing}$Geometric mean.

$^{\alpha}$Interquartile range.

[μ] Priming was defined as demonstration of a seroconversion response one week after receipt of an second dose of IPV among those who did not demonstrate a seroconversion response to the first dose.

[β] Netherlands Vaccine Institute is now part of Bilthoven Biologicals.

[*] Statistically significant with p<0.001. P-value calculated using fisher's exact test and Wilcoxon rank-sum tests for categorical and discrete data, respectively.