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Persistence of immunity following a single dose of inactivated poliovirus vaccine: a phase 4, open label, non-randomised clinical trial

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Summary

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Contributors

All authors contributed equally to the study and the decision to submit for publication. All authors had access to the data. The underlying data were verified by AKS, CFE, LB, and VJ.

Declaration of interests

We declare no competing interests.

See **Online** for appendix 1

See **Online** for appendix 2

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Background—The polio eradication endgame required the withdrawal of Sabin type 2 from the oral poliovirus vaccine and introduction of one or more dose of inactivated poliovirus vaccine (IPV) into routine immunisation schedules. However, the duration of single-dose IPV immunity is unknown. We aimed to address this deficiency.

Methods—In this phase 4, open-label, non-randomised clinical trial, we assessed single-dose IPV immunity. Two groups of infants or children were screened: the first group had previously received IPV at 14 weeks of age or older (previous IPV group; age >2 years); the second had not previously received IPV (no previous IPV group; age 7–12 months). At enrolment, all participants received an IPV dose. Children in the no previous IPV group received a second IPV dose at day 30. Blood was collected three times in each group: on days 0, 7, and 30 in the previous IPV group and on days 0, 30, and 37 in the no previous IPV group. Poliovirus antibody was measured by microneutralisation assay. Immunity was defined as the presence of a detectable antibody or a rapid anamnestic response (ie, priming). We used the χ^2 to compare proportions and the Mann–Whitney U test to assess continuous variables. To assess safety, vaccinees were observed for 30 min, caregivers for each participating child reported adverse events after each follow-up visit and were questioned during each follow-up visit regarding any adverse events during the intervening period. Adverse events were recorded and graded according to the severity of clinical symptoms. The study is registered with ClinicalTrials.gov, NCT03723837.

Findings—From Nov 18, 2018, to July 31, 2019, 502 participants enrolled in the study, 458 (255 [65%] boys and 203 [44%] girls) were included in the per protocol analysis: 234 (93%) in the previous IPV group and 224 (90%) in the no previous IPV group. In the previous IPV group, 28 months after one IPV dose 233 (>99%) of 234 children had persistence of poliovirus type 2 immunity (100 [43%] of 234 children were seropositive; 133 [99%] of 134 were seronegative and primed). In the no previous IPV group, 30 days after one IPV dose all 224 (100%) children who were type 2 poliovirus naive had seroconverted (223 [>99%] children) or were primed (one [<1%]). No adverse events were deemed attributable to study interventions.

Interpretation—A single IPV dose administered at 14 weeks of age or older is highly immunogenic and induces nearly universal type 2 immunity (seroconversion and priming), with immunity persisting for at least 28 months. The polio eradication initiative should prioritise first IPV dose administration to mitigate the paralytic burden caused by poliovirus type 2.

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Introduction

In 1988, the World Health Assembly, the governing body of WHO, resolved to eradicate poliomyelitis by the year 2000.[1–4] Although substantial progress has been made, wild poliovirus type 1 continues to circulate in two countries (Afghanistan and Pakistan), with an exportation to southeast Africa in 2022. As of Sept 19, 2023, 30 wild poliovirus type 1 (WPV1) and 871 cases with circulating vaccine-derived poliovirus (cVDPVs) were reported globally for the year 2022. To date, seven WPV1 cases and 264 cVDPVs were reported to WHO in 2023.[5]

In 2000, an outbreak of circulating vaccine-derived poliovirus 1 highlighted that the Sabin-strain polioviruses in the oral poliovirus vaccine (OPV) could potentially revert and display

the neurovirulence and transmissibility characteristics of WPV.[6,7] Because the continued use of the live-attenuated Sabin-strain polioviruses is incompatible with eradication, the Strategic Advisory Group of Experts on Immunization (SAGE) recommended the cessation of OPV, starting with Sabin poliovirus type 2.[8]

In 2016, trivalent OPV was replaced by a bivalent (poliovirus types 1 and 3) OPV (bOPV) globally and inactivated poliovirus vaccine (IPV) was introduced into routine immunisation.[9] IPV is included to mitigate the potential consequences of the growing type 2 immunity gap following the switch from trivalent OPV to bOPV. An increasing number of type 2 circulating vaccine-derived polioviruses emerged following the withdrawal of trivalent OPV,[10] and the annual circulating vaccine-derived poliovirus 2 disease burden surpassed the WPV burden since 2017.[10,11]

In 2022, one patient with poliomyelitis with circulating vaccine-derived poliovirus 2 was reported in Rockland County, NY, USA. Closely related additional circulating vaccine-derived poliovirus 2 were detected in environmental samples in New York State, USA; London, UK; and Israel,[12] showing the potential of poliovirus finding populations with low immunity and spreading across borders and continents.

Multiple doses of IPV produce long-lasting humoral immunity against paralytic poliomyelitis.[13–15] Studies focusing on single-dose IPV have shown variable seroconversion rates, depending on age at first administration,[16–19] and a high proportion of infants who do not seroconvert responded with a priming immune response.[16–19] Although IPV does not induce mucosal intestinal immunity per se, it decreases the duration of excretion and titre of the virus excreted.[20]

The increased IPV demand in 2015–16 led to critical supply constraints, and the available vaccines were rationed to the highest-risk countries in Africa and Asia. Nepal and other countries that were judged to be at lower poliomyelitis risk faced multi-year stockouts.[21]

It is not known how long children who are seropositive or primed after a single dose of IPV stay seropositive or primed. However, waning immunity has been documented in animal models after a single dose.[22] It is not clear if priming directly protects against paralysis, following poliovirus infection, and the role of IPV in responding to type 2 circulating vaccine-derived poliovirus outbreak control remains under discussion.

We aimed to determine the persistence of immunity more than 2 years after a single dose of IPV was provided through routine immunisation of infants at 14 weeks of age.

Methods

Study design and participants

In this phase 4 open-label, non-randomised clinical trial we evaluated the persistence of humoral immunity to type 2 poliovirus more than 2 years after a single dose of IPV vaccine. Participants were recruited from Nov 18, 2018, to July 31, 2019, at three outpatient clinics in Kathmandu, Nepal: Tribhuvan University Teaching Hospital, Kanti Children’s Hospital, and Patan Hospital.

Children presenting to outpatient clinics for immunisation services or treatment for minor illnesses were potentially eligible for participation. Only children born after the global and national switch on April 30, 2016, from trivalent OPV to bOPV were considered for inclusion. Two separate non-overlapping groups of children were recruited. Children older than 2 years who had received one dose of IPV as part of routine immunisation (between 3 and 6 months of age) were enrolled into the previous IPV group, and infants aged 7–12 months with no previous IPV vaccination were enrolled in the no previous IPV group. We confirmed the vaccination status using vaccination cards or the study site immunisation register. We excluded children whose parents or caregivers were planning to leave the study area, those who had difficult access to the study sites, those with chronic illness (including severe malnutrition), recent acute illness requiring hospitalisation, suspected bleeding disorder or immunodeficiency, or known allergy to any component of IPV (appendix 1 pp 14–15).

Parents or caregivers of each participating child provided written informed consent. The study complied with the International Conference on Harmonisation Good Clinical Practice Guidelines, and the trial protocol was approved by the Ethical Review Committee, WHO, Geneva, and the Nepal Health Research Council, Kathmandu, Nepal. The protocol was shared with the US Centers for Disease Control and Prevention (CDC), which deferred to the WHO Ethical Review Committee.

Procedures

After providing informed consent, caregivers answered a medical history questionnaire. Each participating child had a physical examination, including anthropometry before a venipuncture and received a dose of IPV intramuscularly along with other vaccines due based on age. All participants in the previous IPV group attended two follow-up visits at 7 days (range 6–8) and 30 days (27–33); those in the no previous IPV groups attended follow-up visits on days 30 (27–33) and 37 (36–38). Caregivers reported any adverse events at each follow-up visit; during each visit caregivers were also questioned about adverse events. Following ascertainment of illness or poliovirus vaccination, venipuncture was completed. Participants in the no previous IPV group received a second dose of IPV at the first follow-up visit. No national or subnational mass polio immunisation campaign was done during the study period.

All participants received one IPV (0·5 mL) dose intramuscularly into their thigh. Imovax Polio (R Sanofi Pasteur, Lyon, France) in prefilled syringes contained the following vaccine strains and potencies: type 1 (Mahoney, 40 D antigen units), type 2 (MEF-1, 8 D antigen units), and type 3 (Saukett, 32 D antigen units). The study vaccines were shipped to and stored at study sites according to the manufacturer’s guidelines, with storage temperature monitored twice a day and recorded in temperature logs.

Trained staff obtained 1 mL venous blood from each participant at each visit and stored samples at 2–8°C until centrifugation, which occurred within 24 h after collection. After centrifugation, serum was aliquoted into cryovials for storage at −40°C until shipment to the Polio and Picornavirus Laboratory Branch, CDC, Atlanta, GA, USA.

Poliovirus antibodies were measured by microneutralisation assay.[23] Samples were tested in triple replicates along with multiple replicates of a reference antiserum pool, controls (cells only), and back titration plates. Poliovirus neutralisation titres were reported by the Spearman–Kärber method as the highest dilution of serum that protected 50% of the cell cultures. Antibody titre of less than 1:8 was considered non-detectable, the highest serial dilution was 1:1024, and the highest reported reciprocal titre was calculated as 1:1448 or more. Laboratory personnel were blinded to participants' information.

Participants were observed for 30 min after vaccination to record local and systemic adverse events. Participants' caregivers were asked to report any adverse event following immunisation between vaccination and the next follow-up visit and were asked to provide information on any adverse events at each follow-up visit. Any serious adverse event was notified to the Data and Safety Monitoring Board within 24 h of reporting.

Outcomes

We evaluated humoral immunity to all 3 types of polioviruses by measuring poliovirus neutralising antibody titres. A challenge dose of IPV was used to assess priming against poliovirus type 2 induced by the first IPV dose. Seroprevalence was defined as the presence of detectable neutralising antibody titre (≥1:8) against poliovirus. Seroconversion was defined as a change from the non-detectable neutralising antibody (<1:8) to a detectable antibody (≥1:8). Priming immune response was defined as a change from poliovirus non-detectable neutralising antibody titre at baseline to detectable neutralising antibody titre 7 days after a challenge IPV dose. Immunity was defined as seroprevalence and priming immune response in the previous IPV group, or seroconversion and priming immune response in the no previous IPV group against poliovirus. Boosting was defined as an increase in neutralising antibody titres by four times or more following an IPV dose in children with detectable neutralising antibody titres at baseline. Because of the maximum reported titre of 1:1448 or more, boosting could only be assessed in children with titres of 1:8 or more and 1:362 or less at baseline.

Statistical analysis

A sample size of 250 children per group (adjusted for 5% dropout rate) was estimated a priori to detect a 10% or more one-sided difference between the proportions of children who were immune (seropositive or primed) in each age group, with 90% power and 0·05 alpha. This was assuming that 90% of infants (>6 months of age) vaccinated at randomisation would have detectable immunity to type 2 poliovirus.

Statistical analysis was performed with R (version 4.2.2) and SAS (version 9.4). χ^2 tests or Fisher's exact tests were used to compared proportions, and the Mann–Whitney U test was used to assess continuous variables of participants with a detectable titre, and the bootstrap method determined 95% CI around the median titre. A p value of 0·05 or less was considered significant. The trial is registered with ClinicalTrials.gov, NCT03723837.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

From Nov 18, 2018, to July 31, 2019, 1579 children were screened for eligibility, of whom 502 (32%) participants were enrolled and 458 (91%) met all study requirements and were included in the per-protocol analysis: 234 (51%; median age 32 months [IQR 30–34]) in the previous IPV group, and 224 (49%; median age 9 months [9–10] in the no previous IPV group; figure 1). The results of the modified intention-to-treat analyses were almost identical to the per-protocol analysis (appendix 2 pp 5–6).

Participants' baseline characteristics and poliovirus seroprevalence are shown in table 1. Almost all participants received three doses of bOPV as part of routine immunisation. Baseline seroprevalence rates were high to poliovirus types 1 and 3 in both groups after receiving three doses of bOPV in routine immunisation and differed to poliovirus type 2 according to whether the child had previously received an IPV vaccine. The nutritional status of children and the educational status of mothers differed between the two groups (table 1).

In the previous IPV group, 28 months after receiving IPV 233 (>99%) of 234 children had persistent poliovirus type 2 immunity (100 [43%] of 234 children were seropositive; 133 [99%] of 134 children were primed). In the no previous IPV group, all 224 (100%) infants (median age at vaccination 9 months [IQR 9–10]) had seroconversion (223 [>99%] children) or were primed (1 [<1%] child) to poliovirus type 2 30 days after receiving a single dose of IPV.

Type 2 antibody titres were low at enrolment and increased substantially after vaccination with a second (previous IPV group) or a first IPV dose (no previous IPV group; table 2).

In the previous IPV group, the median reciprocal titre to poliovirus type 2 was less than 8 at enrolment (visit 1), but titres increased to 1448 or more (95% CI ≥1448 to ≥1448) on day 7 (visit 2) after the challenge IPV dose, and titres remained at 1448 or more (≥1448 to ≥1448) on day 30 (visit 3). In the no previous IPV group, the median reciprocal titre to poliovirus type 2 was also less than 8 at enrolment (visit 1), which increased to 576 (455 to 724) on day 30 day (visit 2), and remained relatively stable on day 37 (724 [576 to 910]; visit 3; table 2).

The assessment of boosting was restricted to participants in the previous IPV group with titres of 1:8 or more and less than 1:362 at baseline to document an increase by four-times. All 96 (100%) eligible children boosted their antibody titres following the challenge IPV dose.

We compared the proportion of children who were seropositive to types 1 and 3 polioviruses at enrolment. Almost all children had detectable antibodies for poliovirus types 1 and 3 (table 1). As expected, reciprocal antibody titres were significantly lower for both type 1 and type 3 polioviruses at baseline in the previous IPV group compared with more recently

bOPV-immunised children in the no previous IPV group. The poliovirus type 3 titres were significantly lower than those of poliovirus type 1 in both groups (table 3).

A single dose of IPV closed the immunity gap to type 2 poliovirus in most children even though they were not previously exposed to type 2 polioviruses (figure 2).

There were no adverse events during the 30 min observation period after IPV administration, and only one serious adverse event was reported afterward. A 9-month-old infant was admitted to the hospital 1 day after a second dose of IPV with severe pneumonia and recovered fully after treatment. 23 (10%) children in the previous IPV group and 41 (18%) children in the no previous IPV group had mild or moderate adverse events (appendix 3 p 1). The Data Safety and Monitoring Board concluded that all reported adverse events were unrelated to the study intervention.

Discussion

Our findings suggest that the immunity after a single IPV dose given at age 14 weeks or older persists for at least 28 months. It also reinforces the previous findings that a single dose of IPV induces almost universal immunity (seroconversion and priming) against poliomyelitis when administered after 14 weeks of age or older.

Poliovirus-neutralising antibodies decline over time and might fall below detectable levels. Before our study, only a study from Pakistan reported the 1-year persistence of neutralising antibodies after two doses of IPV.[24] More data are available on the persistence of immunity after multiple IPV doses.[14] In Sweden, the OPV was never introduced, and follow-up of antibodies induced by multiple IPV doses showed long-term persistence.[25,26] Older adults without detectable antibodies in the Netherlands showed a rapid anamnestic immune response after a challenge vaccine.[27] Therefore, the absence of detectable antibodies does not necessarily mean the absence of immunity.[14,16]

As the age of single-dose IPV administration increases, a growing proportion of infants seroconvert, and the remaining individuals are increasingly primed; therefore, the proportion of unsuccessful vaccinations decreases.[17–20] Whether a single IPV dose induces long-term protection remains a question to be answered. Few reports have shown poliomyelitis after a single dose of IPV.[28] Nevertheless, in 2020, SAGE recommended a two-dose IPV schedule in routine immunisation.[29] Experimental data in rhesus macaques suggest that two doses of IPV induce long-term immunity, whereas a single dose does not.[22] Our findings suggest that up to 28 months a single dose of IPV might perform similarly to the single dose hepatitis A vaccine, which induces long-term immunity and has been approved by SAGE for routine immunisation in children aged 1 year or older.[30]

The immunogenicity of IPV is well characterised and inversely associated with the concentrations of maternally derived type-specific poliovirus antibodies.[14,16,21,31] Immune system immaturity and tolerance can contribute to lower IPV responsiveness in early infancy.[14] Administering IPV at later ages in infancy can overcome interference from maternally derived antibodies,[17,32] as can IPV with higher potency.[33,34] Nevertheless, the almost universal immunity induced in Nepal after a single IPV dose reinforces data from

Bangladesh, which showed 94·2% seroconversion and 100% with priming immune response after a single IPV dose in infants (aged 9–13 months) who were naive to poliovirus type 2.[32]

To respond to IPV supply issues and high costs, some countries adopted a two-dose fractional IPV schedule, with doses given at 6 weeks and 14 weeks of age.[35] Seven years of experience from the Indian subcontinent suggests the high effectiveness of this approach. In countries using a single IPV dose in routine immunisation, pre-existing IPV humoral immunity could be boosted rapidly, and mucosal immunity induced with a live virus vaccine after epidemic transmission.[36,37]

Our study had limitations. First, we relied on vaccination records to verify that the participants received IPV in routine immunisation at age 14 weeks or older. Second, the study design did not allow for a randomised and masked allocation. Third, all children had received bOPV previously; therefore, cross-immunity to poliovirus type 2 in children exposed to poliovirus types 1 and 3 was possible, but heterotypic neutralising antibodies are generally transient. Moreover, a study in Cuba did not detect cross-immunity from bOPV in poliovirus type 2.[36] Fourth, we used a rapid anamnestic response following a second dose of IPV to indicate a priming immune response. Because we cannot classify the exact proportion of the participants as having not responded following the first dose, our results might lead to some misclassifications.

In conclusion, our data show an immunity persistence of 28 months or more after a single IPV dose and high immunogenicity of single-dose IPV when given at age 14 weeks or older. Additional studies are needed to determine whether a second IPV dose is required for lifelong protection. Our results from Nepal might have programmatic implications elsewhere. The polio eradication initiative should prioritise the administration of a first dose of IPV in children who are polio naive, especially in areas in which routine immunisation was compromised by the COVID-19 pandemic. These additional efforts could reduce the paralytic case burden from circulating vaccine-derived poliovirus 2 and might accelerate the interruption of all polioviruses.[38] Furthermore, our data might contribute to the discussion on whether single-dose IPV vaccinees should be targeted for catch-up immunisation, for example at school entry, with a second IPV dose to induce lifelong poliovirus type 2 immunity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Data sharing

The data collected for this trial, including individual de-identified participant data and the data dictionary, will be shared on request after publication. Furthermore, the study protocol, with statistical analysis plan will be provided on request by the corresponding author after publication.

References

1. World Health Assembly. Global eradication of poliomyelitis by the year 2000. Resolutions of 41st World Health Assembly. Geneva: World Health Organization, 1988.
2. Rachlin A, Patel JC, Burns CC, et al. Progress toward polio eradication—worldwide, January 2020–April 2022. MMWR Morb Mortal Wkly Rep 2022; 71: 650–55. [PubMed: 35552352]
3. Deblina Datta S, Tangermann RH, Reef S, William Schluter W, Adams A. National, regional and global certification bodies for polio eradication: a framework for verifying measles elimination. J Infect Dis 2017; 216 (suppl 1): S351–54. [PubMed: 28838172]
4. WHO. Report from the Twentieth meeting of the Global Commission for the Certification of Eradication of Poliomyelitis. 2019. https://polioeradication.org/wp-content/uploads/2016/07/20th-meeting-of-the-Global-Commission-for-the-Certification-of-Eradication-of-Poliomyelitis-17-18-October-2019.pdf (accessed May 17, 2022).
5. Lee SE, Greene SA, Burns CC, Tallis G, Wassilak SGF, Bolu O. Progress Toward Poliomyelitis Eradication—Worldwide, January 2021–March 2023. MMWR Morb Mortal Wkly Rep 2023; 72: 517–22. [PubMed: 37167156]
6. Kew O, Morris-Glasgow V, Landaverde M, et al. Outbreak of poliomyelitis in Hispaniola associated with circulating type 1 vaccine-derived poliovirus. Science 2002; 296: 356–59. [PubMed: 11896235]
7. Jenkins HE, Aylward RB, Gasasira A, et al. Implications of a circulating vaccine-derived poliovirus in Nigeria. N Engl J Med 2010; 362: 2360–69. [PubMed: 20573924]
8. Global Polio Eradication Initiative. Polio eradication & endgame strategic plan 2013–2018. Geneva: World Health Organization, 2013.
9. Global Polio Eradication Initiative. Polio endgame & legacy—implementation, best practices, and lessons learned. J Infect Dis 2017; 216 (suppl 1): S1–379. [PubMed: 28838196]
10. Macklin GR, O'Reilly KM, Grassly NC, et al. Evolving epidemiology of poliovirus serotype 2 following withdrawal of the serotype 2 oral poliovirus vaccine. Science 2020; 368: 401–05. [PubMed: 32193361]
11. Alleman MM, Jorba J, Henderson E, et al. Update on vaccine-derived poliovirus outbreaks—worldwide, January 2020–June 2021. MMWR Morb Mortal Wkly Rep 2021; 70: 1691–99. [PubMed: 34882653]
12. Link-Gelles R, Lutterloh E, Schnabel Ruppert P, et al. Public health response to a case of paralytic poliomyelitis in an unvaccinated person and detection of poliovirus in wastewater—New York, June–August 2022. MMWR Morb Mortal Wkly Rep 2022; 71: 1065–68. [PubMed: 35980868]
13. Vidor E. Poliovirus Vaccinated—Inactivated. In: Plotkin SA, Orenstein WA, Offit PA, Edwards KM, eds. Plotkin's Vaccines (7th edn). Philadelphia, PA: Elsevier, 2013: 841–65.
14. Robertson SE, Traverso HP, Drucker JA, et al. Clinical efficacy of a new, enhanced-potency, inactivated poliovirus vaccine. Lancet 1988; 1: 897–99. [PubMed: 2895828]
15. Grassly NC. Immunogenicity and effectiveness of routine immunization with 1 or 2 doses of inactivated poliovirus vaccine: systematic review and meta-analysis. J Infect Dis 2014; 210 (suppl 1): S439–46. [PubMed: 24634499]
16. Resik S, Tejeda A, Sutter RW, et al. Priming after a fractional dose of inactivated poliovirus vaccine. N Engl J Med 2013; 368: 416–24. [PubMed: 23363495]
17. Ahmad M, Verma H, Deshpande J, et al. Immunogenicity of fractional dose inactivated poliovirus vaccine in India. J Pediatric Infect Dis Soc 2022; 11: 60–68. [PubMed: 34791350]

18. Zaman K, Kovacs SD, Vanderende K, et al. Assessing the immunogenicity of three different inactivated polio vaccine schedules for use after oral polio vaccine cessation, an open label, phase IV, randomized controlled trial. Vaccine 2021; 39: 5814–21. [PubMed: 34481702]
19. Anand A, Zaman K, Estívariz CF, 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]
20. Cuba IPV Study Collaborative Group. Randomized, placebo-controlled trial of inactivated poliovirus vaccine in Cuba. N Engl J Med 2007; 356: 1536–44. [PubMed: 17429085]
21. Hampton LM, Farrell M, Ramirez-Gonzalez A, et al. Cessation of trivalent oral poliovirus vaccine and introduction of inactivated poliovirus vaccine—worldwide, 2016. MMWR Morb Mortal Wkly Rep 2016; 65: 934–38. [PubMed: 27606675]
22. Bhaumik SK, Kulkarni RR, Weldon WC, et al. Immune priming and long-term persistence of memory B cells after inactivated poliovirus vaccine in Macaque models: support for at least 2 doses. Clin Infect Dis 2018; 67 (suppl 1): S66–77. [PubMed: 30376091]
23. Weldon WC, Oberste MS, Pallansch MA. Standardized methods for detection of poliovirus antibodies. Methods Mol Biol 2016; 1387: 145–76. [PubMed: 26983734]
24. Saleem AF, Mach O, Yousafzai MT, et al. One-year decline of poliovirus antibodies following fractional-dose inactivated poliovirus vaccine. J Infect Dis 2021; 223: 1214–21. [PubMed: 32798224]
25. Böttiger M Polio immunity to killed vaccine: an 18-year follow-up. Vaccine 1990; 8: 443–45. [PubMed: 2251870]
26. Böttiger M A study of the sero-immunity that has protected the Swedish population against poliomyelitis for 25 years. Scand J Infect Dis 1987; 19: 595–601. [PubMed: 2831621]
27. Herremans TM, Reimerink JH, Buisman AM, Kimman TG, Koopmans MP. Induction of mucosal immunity by inactivated poliovirus vaccine is dependent on previous mucosal contact with live virus. J Immunol 1999; 162: 5011–18. [PubMed: 10202050]
28. Desai S, Diener T, Tan BK, et al. An unusual case of vaccineassociated paralytic poliomyelitis. Can J Infect Dis Med Microbiol 2014; 25: 227–28. [PubMed: 25285130]
29. WHO. Meeting of the Strategic Advisory Group of Experts on Immunization, October 2020—conclusions and recommendations. Wkly Epidemiol Rec 2020; 48: 585–608.
30. World Health Organization. SAGE April 2022 meeting highlights. 2022. https://www.who.int/news/item/11-04-2022-sage-april-2022-meeting-highlights (accessed May 31, 2022).
31. Dayan GH, Thorley M, Yamamura Y, et al. Serologic response to inactivated poliovirus vaccine: a randomized clinical trial comparing 2 vaccination schedules in Puerto Rico. J Infect Dis 2007; 195: 12–20. [PubMed: 17152004]
32. Aziz AB, Verma H, Jeyaseelan V, et al. One full or two fractional doses of inactivated poliovirus vaccine for catch-up vaccination in older infants: A randomised clinical trial in Bangladesh. J Infect Dis 2022; 226: 1319–26. [PubMed: 35575051]
33. Swartz TA, Handsher R, Stoeckel P, et al. Immunologic memory induced at birth by immunization with inactivated polio vaccine in a reduced schedule. Eur J Epidemiol 1989; 5: 143–45. [PubMed: 2767220]
34. Sáez-Llorens X, Clemens R, Leroux-Roels G, 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]
35. Anand A, Molodecky NA, Pallansch MA, Sutter RW. Immunogenicity to poliovirus type 2 following two doses of fractional intradermal inactivated poliovirus vaccine: a novel dose sparing immunization schedule. Vaccine 2017; 35: 2993–98. [PubMed: 28434691]
36. Resik S, Tejeda A, Mach O, et al. Does simultaneous administration of bivalent (Types 1 and 3) oral poliovirus vaccine and inactivated poliovirus vaccine induce mucosal cross-immunity to poliovirus type 2? Clin Infect Dis 2018; 67 (suppl 1): S51–56. [PubMed: 30376088]
37. Jafari H, Deshpande JM, Sutter RW, et al. Polio eradication. Efficacy of inactivated poliovirus vaccine in India. Science 2014; 345: 922–25. [PubMed: 25146288]

38. Modlin JF, Bandyopadhyay AS, Sutter R. Immunization against poliomyelitis and the challenges to worldwide poliomyelitis eradication. J Infect Dis 2021; 224 (suppl 2): S398–404. [PubMed: 34590135]

Research in context

Evidence before this study

Multiple doses of inactivated poliovirus vaccine (IPV) are required to immunise a high proportion of children, when starting the immunisation scheme at 6–8 weeks of age. Following a single dose of IPV three outcomes are possible: 1) seroconversion, 2) priming immune response, or 3) no immune response. Priming is the least well characterised, but several studies have reported the priming effect to last 6 months or more. However, studies assessing longer durations were judged unethical. We searched PubMed and Cochrane from the inception of each database to Dec 17, 2017, using the search term “persistence of poliovirus antibody”. The search returned 222 citations. We reviewed all abstracts (or titles where no abstract was available) and found three articles of potential interest. Subsequently, we monitored PubMed for relevant citations and found one article of interest published in 2021. After review of these articles, we found that no article that we uncovered provided information on the long-term persistence of single-dose IPV-induced immunity.

Added value of this study

The study provides conclusive evidence that the immunity induced after a single dose of IPV persists for more than 2 years. Immunity is composed of seroconversion leading to seropositivity and a priming immune response characterised by a rapid seroconversion from non-detectable to detectable antibodies within 7 days of a second dose IPV challenge. Furthermore, the study shows the immunogenicity of a single IPV dose when given later in infancy (ie, 9 months of age), resulting in almost 100% seroconversion.

Implications of all the available evidence

Our findings suggest that to reduce or eliminate the remaining polio disease burden and boost mucosal immunity in OPV-vaccinated children, the Global Polio Eradication Initiative should prioritise administration of IPV in infants aged 14 weeks or older in routine immunisation or campaigns.

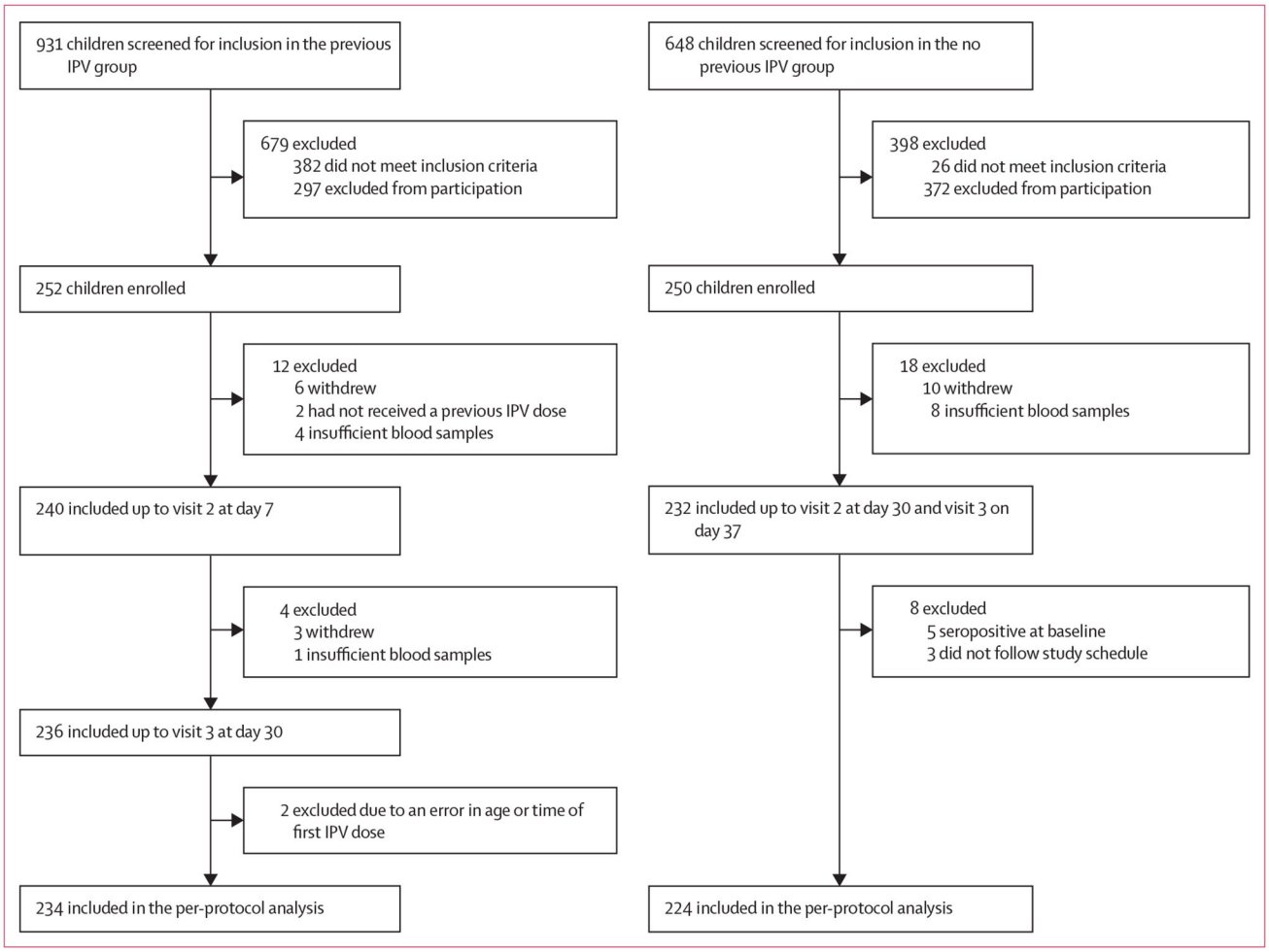

Figure 1:

Trial profile

IPV=inactivated poliovirus vaccine.

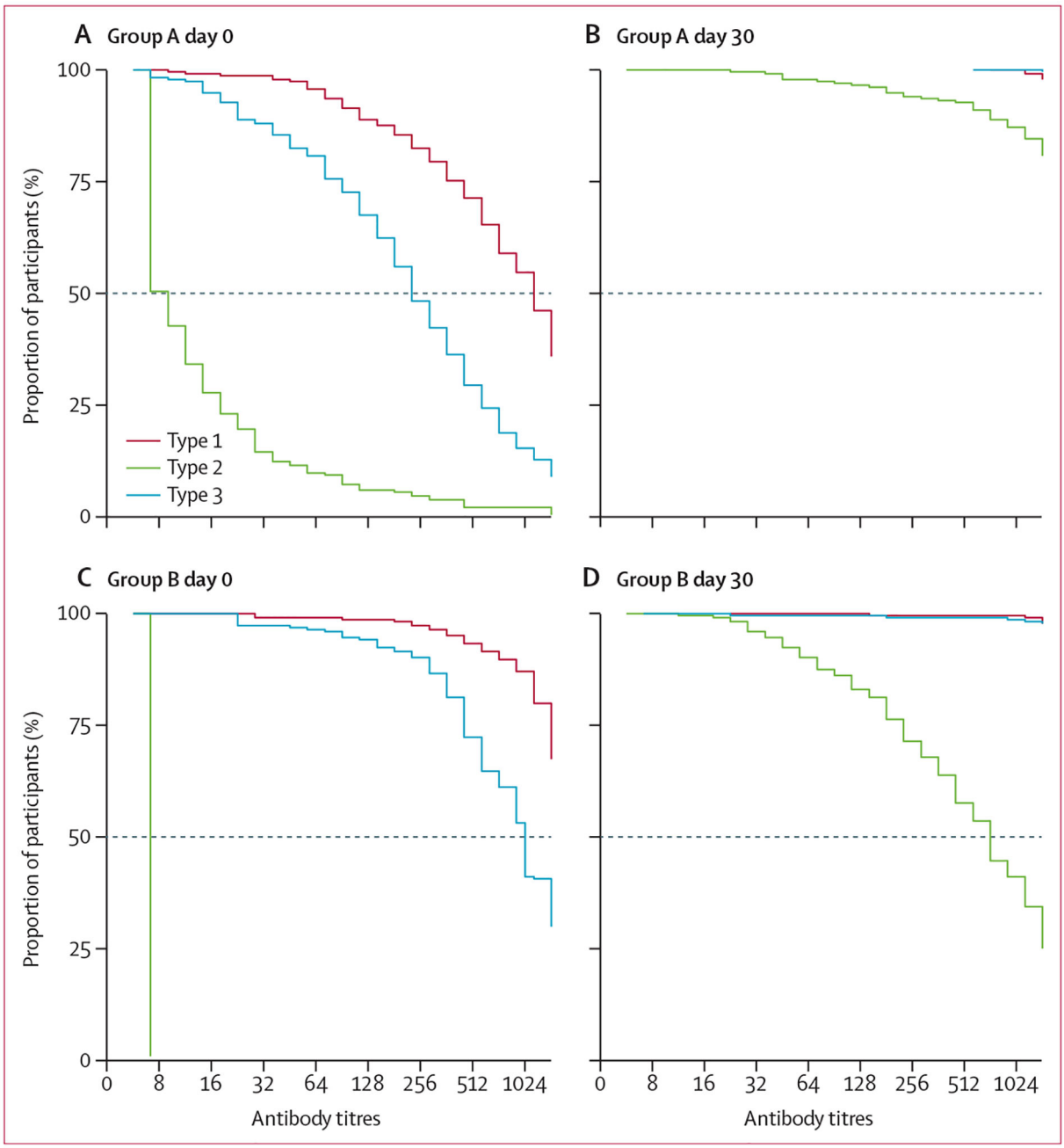

Figure 2:

Reverse cumulative antibody titres for poliovirus types 1, 2, and 3 at different study visits (A) Antibody titres at day 0 in the previous IPV group. (B) Antibody titres at day 30 in the previous IPV group after receiving a booster dose of IPV. (C) Antibody titres at day 0 in the no previous IPV group. (D) Antibody titres at day 30 in the no previous IPV group after receiving a first dose of IPV.

Table 1:

Baseline characteristics

	Previous IPV group (n=234)	No previous IPV group (n=224)	p value
Age at enrolment, months	32 (30–34)	9 (9–10)	<0·01
Age at initial IPV receipt, weeks	16 (15–17)	NA	..
Time since IPV receipt, months	28 (26–30)	NA	..
Sex			..
Male	136 (58%)	119 (53%)	0·28
Female	98 (42%)	105 (47%)	..
Vaccination history			..
Three OPV doses	234 (100%)	221 (99%)	0·13
Three pentavalent doses	234 (100%)	221 (99%)	0·13
One IPV dose before trial *	234 (100%)	0	..
Nutritional status			..
Wasting	2 (1%)	1 (1%)	1·00
Stunting	34 (15%)	8 (4%)	0·0010
Mother's education status			..
No formal education	21 (9%)	6 (3%)	0·0040
Primary school	41 (18%)	30 (13%)	0·14
Middle school	75 (32%)	69 (31%)	0·82
High school	39 (17%)	61 (27%)	0·010
University graduate	58 (25%)	58 (26%)	0·81
Baseline seroprevalence			..
Poliovirus type 1	233 (>99%)	222 (99%)	0·19
Poliovirus type 2	100 (43%)	0	NA
Poliovirus type 3	229 (98%)	218 (98%)	1·00

Data are n (%) or median (IQR). IPV=inactivated poliovirus vaccine. NA=not applicable.

* Inclusion criteria.

Table 2:

Immunity to poliovirus type 2 immunity 28 months following single-dose IPV or 30 days after a single dose of IPV

	Previous IPV group (n=234)	No previous IPV group (n=224)	p value
Enrolment (day 0 visit)			
Seroprevalence	100 (43%)	0	NA
Titre	<8 (<8 to <8)	<8 (<8 to <8)	1·00
Day 7 visit			
Priming immune response	133/134 (99%)	NV	NA
Titre	≥1448 (≥1448 to ≥1448)	NV	NA
Day 30 visit			
Seroconversion	0/1	223	NA
Titre	NA	576 (455 to 724)	NA
Day 37 visit			
Priming immune response	NV	1/1 (100%)	NA
Titre	NV	NA	NA
Immunity after one IPV dose [*]	233 (>99%) [†]	224 (100%) [‡]	1·00
Antibody titres after two IPV doses	≥1448 (≥1448 to ≥1448)	724 (576 to 910)	0·0006

Data are n (%), n/N (%), or median (95% CI). IPV=inactivated poliovirus vaccine. NA=not applicable. NV=no visit.

[*] In the previous IPV group, the challenge IPV dose was administered 28 months after first IPV dose (administered at median age of 4 months); in the no previous IPV group, the challenge IPV dose was administered 1 month after first IPV dose (administered at median age 9 months [IQR 9–10]); in both arms blood was collected 7 days after the challenge IPV dose to assess priming immune responses.

[†] Immune response was seroprevalence (reciprocal antibody titre 8 or more) and priming immune response.

[‡] Immunity was seroconversion and priming immune response.

Table 3:

Seroprevalence against poliovirus types 1 and 3 at day 0 (enrolment) and day 30

	Previous IPV group (n=234)*	No previous IPV group (n=224)†	p value
Day 0			
Poliovirus type 1			
Seroprevalence	233 (>99%)	222 (99%)	0·19
Titre	910 (724–1152)	≥1448 (≥1152 to ≥1448)	0·031
Poliovirus type 3			
Seroprevalence	229 (98%)	218 (97%)	0·49
Titre	181 (144–228)	910 (724–910)	0·026
Day 30			
Poliovirus type 1			
Seroprevalence	234 (100%)	224 (100%)	1·00
Titre	≥1448 (≥1448 to ≥1448)	≥1448 (≥1448 to ≥1448)	1·00
Poliovirus type 3			
Seroprevalence	234 (100%)	223 (>99%)	0·63
Titre	≥1448 (≥1448 to ≥1448)	≥1448 (≥1448 to ≥1448)	1·00

Data are n (%) or median (95% CI). IPV=inactivated poliovirus vaccine. bOPV=bivalent oral polio vaccine.

*At day 0 children had received three bOPV doses and one dose of IPV (given in infancy); at day 30 children had received one additional dose of IPV (given at study enrolment).

†At day 0 children had received three bOPV doses; at day 30 children had received one dose of IPV (given at study enrolment).