National introduction of fractional-dose inactivated polio vaccine in Sri Lanka following the global “switch”

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Abstract
As part of the Polio eradication and endgame strategic plan 2013–2018 to achieve and sustain a polio-free world, the use of oral polio vaccine (OPV) must eventually be stopped. This process started in April 2016, with the worldwide, planned synchronized “switch”, whereby use of OPV containing poliovirus type 2 ceased. Prior to the switch, in line with international guidance on risk mitigation, Sri Lanka had introduced a single full dose (0.5 mL intramuscularly) of inactivated polio vaccine (IPV) into routine immunization. However, the two global suppliers of World Health Organization (WHO)-prequalified IPV had significant challenges in scaling up production to meet the new demand, resulting in a global shortage in April 2016. The WHO Strategic Advisory Group of Experts on Immunization recommended that countries should consider a two-dose schedule of intradermal fractional IPV (fIPV). After rapid consideration of the programmatic cost and logistic implications, Sri Lanka was the first country to roll out this dose-sparing schedule nationwide. The country ensured smooth implementation of fIPV use, reaching out to all eligible infants, maintaining equity and sustaining the IPV vaccination. With expedited refresher training in intradermal vaccination, confident, well-trained and dedicated health-care staff, from the field up to provincial levels, worked together as a dedicated team. Health authorities at all levels reported that public acceptance of the additional injections of the new schedule was high. A post-introduction evaluation and an assessment of population-level immunity are under way.

Keywords fractional-dose inactivated poliovirus, national immunization programme, oral polio vaccine, poliovirus, poliovirus type 2

Background
In May 2012, the 65th World Health Assembly declared the completion of poliovirus eradication to be “a programmatic emergency of global proportions for public health”. The goal of the subsequent Polio eradication and endgame strategic plan 2013–2018 was to end poliomyelitis (polio) disease resulting from both wild poliovirus and circulating vaccine-derived poliovirus (cVDPV), to achieve and sustain a polio-free world. Part of the plan’s strategy called for strengthening of routine immunization and globally synchronized withdrawal of oral polio vaccine (OPV), beginning with cessation of the use of OPV type 2 by mid-2016. Globally, the last wild poliovirus type 2 (WPV2) was reported in 1999 but cVDPV has been reported, owing to suboptimal population-level immunization coverage of trivalent OPV (tOPV: containing polio vaccine viruses types 1, 2 and 3). In September 2015, the Global Commission for the Certification of Poliomyelitis Eradication declared the worldwide eradication of WPV2, and recommended that the synchronized global “switch” from the use of tOPV to bivalent OPV (bOPV: containing polio vaccine viruses types 1 and 3) should occur during April 2016.

Prior to the “switch”, the 155 countries and territories using tOPV in their routine immunization programmes were recommended to introduce injectable inactivated polio vaccine (IPV) before the end of 2015. This strategy was intended to mitigate the potential consequences should any re-emergence of poliovirus type 2 occur following the switch in April 2016. In line with the global recommendations, the World Health Organization (WHO) Regional Office for South-East Asia worked with its 11 Member States to monitor country situations and ensure introduction of IPV and continuation through the switch from tOPV to bOPV by April 2016.

Sri Lanka is an island in the Indian Ocean, with a total land area of 65 610 km² and a population of 20 277 597 at the last census in 2012. For 2016, the estimated population was 21 203 000 and the number of annual live births was 331 073. Sri Lanka is administratively divided into nine provinces and 25 districts. For health service provision, 342 divisions function as basic operational units under the provincial and regional directors of health services. Each health administrative division is named as a medical officer of health (MOH) area. The MOH of the area, together with other categories of public health staff, is responsible for the provision of integrated primary public health care services.

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health services to the community. In addition to the provision at community clinics, immunization services are provided in curative health-care institutions/hospitals and are under the supervision of the regional epidemiologist and MOH. The vaccine storage facilities at district-level stores or MOH offices receiving vaccine stocks for divisional vaccine stores are responsible for providing stocks of vaccines to curative health-care institutions/hospitals and also responsible for cold-chain management at the institution and data handling in providing information on vaccinations. The regional epidemiologist at the district level is responsible for overall immunization and vaccine-preventable disease programmes in the districts, and accountable for all immunization service provisions at MOH areas and at curative health-care institutions/hospitals.

Sri Lanka has been a Gavi (The Vaccine Alliance)-graduate country since 2015 and thus is not eligible for financial support for vaccination programmes. However, special support was extended by Gavi for IPV introduction, through a commitment to support the supply of IPV vaccine from 2015 to 2018, through the United Nations Children’s Fund (UNICEF), under the Global Polio Eradication Initiative. In compliance with the regional guidance, by July 2015 Sri Lanka had successfully introduced a full-dose 0.5 mL IPV single intramuscular vaccination to all infants at 4 months of age. This was the first time the IPV vaccine was introduced through the national immunization programme and all infants had been receiving only tOPV up to July 2015. Since the country planned to change over from tOPV to bOPV on 30 April 2016 as the “switch” date, it introduced trivalent IPV for all infants aged 4 months into the national schedule from the preceding July, in order to maintain immunity to poliovirus type 2.

A subsequent IPV consignment was expected in mid-2016. However, in April 2016, the country received a verbal communication from WHO informing them of a worldwide supply shortage of IPV. The two global suppliers of WHO-prequalified IPV had significant challenges in scaling up production to meet the new demand. Categorized as a low-risk country for polio (a tier-4 country in the risk-categorization scale of high to low from 1 to 4), Sri Lanka was at the lowest priority to receive scarce IPV supplies. A joint deputation from UNICEF and WHO formally informed the Ministry of Health of the short supply of IPV in May 2016 and that the subsequent consignment of IPV to Sri Lanka would be delayed to beyond September 2017, owing to the global scarcity.

The Central Epidemiology Unit, the implementing authority of the national immunization programme for the Ministry of Health, Sri Lanka, was stunned by this unexpected information and the deferment of the subsequent IPV consignment. Discussions were held with relevant global and regional authorities, to comprehend the reasons for the IPV scarcity and explore the options for forward planning to receive the required supplies of IPV in the country. However, efforts to receive vaccines ahead of the postponed rescheduled timeline were not successful.

Devising a country strategy in the face of the global shortage of inactivated polio vaccine

In the context of the IPV shortage, WHO advised countries to consider using fractional doses (one fifth of the full IPV dose) via the intradermal route, as an alternative to the intramuscular injection of a full dose of IPV, depending on the programmatic cost and logistic implications. Countries were advised to consider instituting a two-dose schedule of intradermal fractional IPV (fIPV) of 0.1 mL per dose administered to infants at 6 and 14 weeks, separated by a minimum interval of 4 weeks.

To devise a strategy to maintain population immunity for poliovirus type 2 in the face of the IPV stock-out, in early June 2016, the National Advisory Committee on Communicable Diseases (ACCD) in Sri Lanka, which is equivalent to the national immunization technical advisory group, deliberated on the evidence compiled by national officers, with assistance from the WHO Regional Office for South-East Asia. In addition, the experience in India, as the first country to introduce fIPV into their immunization schedule at subnational levels, was sought via personal communication. The key points listed next were considered by ACCD in their decision-making.

- Study findings considered in the decision-making by the WHO Strategic Advisory Group of Experts on Immunization, and in the WHO position paper on polio vaccines, were reviewed. The evidence for non-inferior seroconversion rates for the fIPV two-dose schedule compared with the single full-dose IPV schedule was an important factor in decision-making.
- The reduction in required stocks associated with changing over to a fractional dose (estimated 70,000 2.5 mL vials per year, reduced to 28,000 2.5 mL vials), which was a 60% reduction of the initial stock requirement, would permit the country to use existing vaccine stocks for an extended period, to sustain IPV vaccination until mid-2017.
- There would also be a reduction of the vaccine cost per child, from US$ 1.90 per dose per child for a single 0.5 mL IPV dose, to US$ 0.76 per child for two fIPV doses. This is a 60% cost reduction for an “IPV fully immunized child” to develop the expected immunity to poliovirus type 2.
- The fIPV schedule could be continued even if an adequate supply of IPV were to become available in the future, until the global recommendations for the schedule change for full withdrawal of OPV are put in place.
- Implementation feasibility was also considered:
  - rapid refresher training could be provided for midwives, as they would all have already received hands-on skill training in intradermal vaccination during their basic training;
  - refresher training in intradermal vaccination could be easily provided for nursing officers alongside BCG nursing officers;
  - 0.1 mL auto-disable syringes could be used until Gavi supplies become available;
  - it would be feasible to co-administer the first fIPV dose with pentavalent (diphtheria–tetanus–whole cell pertussis, hepatitis B and Haemophilus influenzae type b) vaccine and bOPV at 2 months, and the second dose at 4 months, within the existing vaccination schedule;
  - full-dose IPV at 4 months of age could be continued for a further 2 months, in parallel with the fIPV schedule starting at 2 months of age, until infants who received the fractional dose at 2 months reach the age of 4 months.
- Manufacturer positions considered were:
  - manufacturer licensing was only for intramuscular use and not for intradermal use at the time of the decision;
Thus, the ACCD committee decision was based on the recommendations of the WHO position paper; 11
- the manufacturer recommendation that a higher number of punctures should not be made on the vaccine vial stopper of 10-dose vials was not relevant, since Sri Lanka only had 5-dose vials;
- the manufacturer had neither opposed nor specifically endorsed fIPV implementation by countries.

Based on this information, the ACCD recommendation to introduce fIPV into the national immunization schedule on an “off-label” basis was endorsed by the National Medicinal Drug Evaluation Committee of the National Medicinal Drug Regulatory Authority. All experts in ACCD acknowledged that the decision taken by ACCD was crucial, as Sri Lanka was the first country to take the decision to change over to fIPV nationwide, to mitigate imminent stock-out of IPV in a rational manner and sustain the immunization programme.

Planning and implementation of the strategy

Planning of the schedule change for IPV into a fractional two-dose schedule implemented within the routine immunization programmes was examined systematically, in order to provide the best available services in an appropriate, affordable and cost-effective manner. 12 Regional epidemiologists were advised to organize immediate district-level refresher training on intradermal administration of the vaccine, for public health midwives and immunization nurses in curative health-care institutions/hospitals. National-level training-of-trainer programmes were conducted for the regional epidemiologists on how to administer fIPV, using the 5-dose vials of IPV that were available. The doses, route and site of administration were explained for the two doses to be given at the age of 2 months and 4 months, together with the other two recommended vaccines (OPV and pentavalent vaccine), and to be administered intradermally to the left upper arm. The WHO multidose vial policy continued to be used for IPV, whereby vials opened in a fixed clinic could be used at more than one immunization session, provided that: (i) the expiry date had not passed; and (ii) the vaccine was stored under appropriate cold-chain conditions. Guidelines on the changes to the vaccination schedule and stock balancing were circulated.

Immediate training of public-health-care workers was started at district level as refresher training (as all public health midwives have had initial hands-on skill training during the basic midwifery training), with one full day of training providing relevant information on the importance of IPV vaccination, the schedule change and video clips on the technique. The hands-on skill training included a half-day training of vaccination of volunteers drawn from adult health staff colleagues during the training, with a subsequent 1–2 days spent undertaking intradermal vaccination of BCG vaccine to neonates alongside BCG vaccination nursing officers at health-care institutions. Nursing officers involved in vaccination, at immunization clinics in curative care institutions/hospitals were also given the refresher training on intradermal vaccination, together with BCG nurses.

Given the urgency of the training schedule, the initial expenditure required for training (US$ 750–1000) was mobilized from the existing central-level Ministry of Health budget for the national-level training. Subsequently, considering the country priority, it was decided to implement the programme with minimum additional expenditure, by integrating it into existing programmes for training health-care staff. Provincial and district health authorities took responsibility for providing training from provincial health budgets, bearing the minimum cost of around US$ 250–500 for refreshments and travel for each programme at district and divisional levels. Health-care staff volunteered as resource persons for training, without expecting additional fees.

An intensive mass-media campaign was not conducted; as it had already been done during the introduction of IPV vaccine, this was deemed to be only a schedule change. However, print media were used to ensure general public awareness. Awareness among parents was raised by public health midwives during their home visits for routine services, and at health educational sessions in maternal and child health-care clinics. The public health midwives were assisted to be confident in answering questions from the public by the use of role-plays during their training sessions.

Other essentials for programmatic readiness to change the schedule for the IPV vaccination, such as stock management, were conducted with close monitoring of existing IPV stocks at each level. A decision was taken to move extra vaccine stocks from divisional levels (which is the lowest level of vaccine stores) to district-level walk-in cold rooms (as a result of IPV-dose sparing in the schedule change), to optimize cold-chain monitoring as a precautionary measure to minimize vaccine wastage.

Discussion

Sri Lanka is the first country to have implemented the use of fIPV in their national immunization programme. The Central Epidemiology Unit of the Ministry of Health, Sri Lanka, as the centrally accountable authority for both the national immunization programme and the vaccine-preventable disease surveillance programme, took the leadership for fIPV implementation in the country, as part of an incorporated, coordinated system of communicable disease surveillance. The Central Epidemiology Unit has the capacity to make policy decisions on immunization, and to coordinate the planning and implementation of such decisions throughout the country. The stock management of vaccines and other supplies, cold-chain monitoring, and implementation of the immunization programme is centrally coordinated, monitored and supervised by the Central Epidemiology Unit.

Sri Lanka rapidly evaluated the required elements of the schedule change from a full intramuscular dose to the alternative intradermal fIPV, considering the programmatic cost and logistic implications of this option in the context of an IPV shortage. The country also ensured smooth implementation of fIPV immunization for all eligible infants, sustaining the sequential IPV vaccination programme as recommended by the Global Polio Eradication Initiative, 2 to maintain population-level immunity to poliovirus type 2.
The recommendation of early and appropriately timed protection, provided by scheduling fractional intradermal doses, administered at 6 and 14 weeks (separated by a minimum interval of 4 weeks), was met by providing fIPV within the regular immunization programme schedule at 8 and 16 weeks. The country opted to take the initiative of off-label use of the vaccine at the time of decision-making, and relevant strategic decisions were successfully implemented.

Confident, well-trained and dedicated health-care staff working at grass-roots level in the field; medical officers of health, including medical officers, public health nursing sisters, public health midwives and public health inspectors and staff of the hospital-level immunization clinics; district health authorities; and provincial health authorities worked as a dedicated team. Their monumental efforts ensured smooth and successful implementation of fIPV immunization as a national programme. Each immunization clinic is conducted by a qualified medical officer and this has facilitated the provision of quality immunization services for intradermal fIPV administration at immunization clinics. All relevant health professionals receive high-quality, comprehensive basic public health training at their initial recruitment, which gave national authorities the confidence that refresher training on administration of intradermal vaccine was sufficient to make implementation a success. Health authorities at all levels reported high levels of public acceptance of the additional injections resulting from the change in schedule.

Health authorities identified the challenge of accurate documentation of the vaccinations and vaccine stock balance over the initial period of implementation while the two schedules (full dose and fractional dose) overlapped for a period of 2 months, until all those receiving the fractional dose at 2 months had reached the age of 4 months. Further, the authorities identified the challenge of stock management at divisional level, which is the lowest level of vaccine storage and is expected to store only 1 month of buffer stock in addition to stock for the current month. This challenge has been addressed through arrangements to re-collect additional vaccine stocks resulting from the change from 5-dose vials to 25-dose vials. Relevant changes in the dose schedule for IPV were incorporated into the web-based immunization information system, and related training of health-care professionals was successfully carried out to implement the flow of information to the central level.

The country has shown that the additional funding required for training and implementation was not a constraint on implementation of the emergency decision taken by the national immunization programme, since the government considered it a priority and health-care staff and existing integrated maternal and child health-care services committed to the programme without expecting any additional expenses.

The national immunization programme is currently conducting a post-introduction evaluation of the fIPV programme, to identify any implementation challenges. In addition, the country plans to assess the population-level immunity for poliovirus type 2, comparing children who have received full-dose IPV with those receiving fIPV, to ensure adequate development of immunity from the fractional dose.

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References


13. Resik S, Tejeda A, Lago PM, Diaz M, Carmenes A, Sarmiento L et al. Randomized controlled clinical trial of fractional doses of...
inactivated poliovirus vaccine administered intradermally by
doi:10.1086/651611.

Shaban MM et al. Fractional doses of inactivated poliovirus
NEJMoa0909383.

Priming after a fractional dose of inactivated poliovirus vaccine. N 

et al. Early priming with inactivated poliovirus vaccine (IPV) and
intradermal fractional dose IPV administered by a microneedle

17. Principles and considerations for adding a vaccine to a national
immunization programme: from decision to implementation and
who.int/immunization/programmes_systems/policies_strategies/