POLIO ERADICATION
IN WHO SOUTH-EAST ASIA REGION

ROLE OF RESEARCH
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IN WHO SOUTH-EAST ASIA REGION

ROLE OF RESEARCH
## CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOREWORD</td>
<td>VI</td>
</tr>
<tr>
<td>EXECUTIVE SUMMARY</td>
<td>1</td>
</tr>
<tr>
<td>CONTEXT</td>
<td>2</td>
</tr>
<tr>
<td>EFFORTS TOWARDS POLIO ERADICATION</td>
<td>3</td>
</tr>
<tr>
<td>RESEARCH FOR POLIO ERADICATION IN SOUTH-EAST ASIA REGION</td>
<td>3</td>
</tr>
<tr>
<td>1 SUPPORT FOR LICENSURE OF NEW VACCINES</td>
<td>4</td>
</tr>
<tr>
<td>2 STRATEGY DEVELOPMENT/ADJUSTMENTS TO OVERCOME BARRIERS</td>
<td>4</td>
</tr>
<tr>
<td>- Identification of risk factors for wild poliovirus transmission</td>
<td>4</td>
</tr>
<tr>
<td>- Introduction of monovalent oral polio vaccines</td>
<td>4</td>
</tr>
<tr>
<td>- Clinical trials on monovalent OPV type 1 (mOPV1)</td>
<td>4</td>
</tr>
<tr>
<td>- Immunogenicity of supplemental dose of poliovirus vaccines</td>
<td>5</td>
</tr>
<tr>
<td>- Epidemiological analysis of VDPV outbreak in Indonesia</td>
<td>5</td>
</tr>
<tr>
<td>- Inactivated poliovirus vaccine (IPV) clinical trials and introduction</td>
<td>5</td>
</tr>
<tr>
<td>- Intestinal mucosal immunity against polioviruses</td>
<td>5</td>
</tr>
<tr>
<td>3 PROGRAMME EVALUATIONS THROUGH SEROPREVALENCE STUDIES</td>
<td>6</td>
</tr>
<tr>
<td>4 POLIO ENDGAME PLANNING AND VALIDATION</td>
<td>6</td>
</tr>
<tr>
<td>5 LESSONS LEARNT AND WAY FORWARD</td>
<td>7</td>
</tr>
<tr>
<td>ANNEXURE</td>
<td>8</td>
</tr>
<tr>
<td>1. CLINICAL TRIAL FOR LICENSURE OF VACCINES</td>
<td>8</td>
</tr>
<tr>
<td>2. STUDIES ON STRATEGY DEVELOPMENT/ADJUSTMENTS TO OVERCOME BARRIERS</td>
<td>9</td>
</tr>
<tr>
<td>3. SEROLOGICAL SURVEYS</td>
<td>12</td>
</tr>
<tr>
<td>4. STUDIES ON POLIO ENDGAME PLANNING AND VALIDATION</td>
<td>14</td>
</tr>
</tbody>
</table>
FOREWORD

The polio eradication programme in the WHO South-East Asia Region achieved a historic milestone when the Region was certified polio-free in March 2014. With this achievement, 80% of the world’s population now lives in certified polio-free areas.

Strategic innovations and tactical interventions were implemented in the Region to overcome the various challenges during the journey towards polio eradication. These strategies were driven by data generated through surveillance and monitoring systems and guided by multiple research studies conducted in the Region. Research conducted by way of clinical trials on polio vaccines, serological surveys and analytical studies led to policy changes and fine-tuning of strategies that ultimately led to a polio-free Region. Even the most complex research studies were completed successfully and reliable evidence generated to guide policy decisions.

I am aware that organizing and conducting research in the Region posed numerous challenges, but these were overcome successfully to achieve the desired outcome due to the sheer perseverance and commitment of those involved. I look forward to the lessons learnt from polio research being applied to research in other areas of public health.

I convey my gratitude to the staff of WHO and Member States who led these research studies and acknowledge the contribution of the scientists and research specialists who participated in the polio research studies in the Region.

Dr Poonam Khetrapal Singh
Regional Director
WHO South-East Asia Region
EXECUTIVE SUMMARY

WHO South-East Asia Region was certified polio-free in March 2014, three years after the last polio case due to wild poliovirus was reported in the Region. Of the 11 Member States in the Region, India proved to be the most difficult to interrupt the circulation of wild poliovirus due to a number of factors that facilitated the circulation of wild poliovirus and compromised the efficacy of the oral polio vaccine. Multiple innovative strategies were used in India to overcome the challenges. Research, coordinated by WHO, played a major role in polio eradication in India and the Region by supporting clinical trials that contributed to licensure and use of new polio vaccines in the Region as well as globally. New strategies were developed and adjusted based on a number of analytical research studies and clinical trials that led to a better understanding of the risk factors for poliovirus transmission and immunogenicity of available polio vaccines. Independent programme evaluations were conducted through periodic seroprevalence surveys that also contributed to optimization of the use of different polio vaccines. Research studies also contributed to the development of the polio endgame strategy through vaccine trials and epidemiological analysis. This publication summarizes the contribution of research in polio eradication in the WHO South-East Asia Region.
CONTEXT

Polio eradication, achieved after a hard-fought battle over two decades, is one of the truly monumental achievements of the WHO South-East Asia Region. The last case due to the wild poliovirus was reported from India in January 2011. The Region, with a quarter of the world’s population, was certified polio-free on 27 March 2014, following three years of no case of polio due to the wild poliovirus. This historic development in the journey towards global eradication of polio made WHO South-East Asia Region the fourth WHO Region, out of the six, to be certified as polio-free and ensured that 80% of the world’s population now lives in certified polio-free areas. The Region has demonstrated to the remaining polio-endemic regions of the world that polio eradication is a feasible target.

The journey of polio eradication in WHO South-East Asia Region was tough and challenging. An estimated 250 000 polio cases were occurring annually in the Region prior to 1988, when the Forty-first World Health Assembly adopted a resolution to eradicate polio from the world. The 11 Member States of the Region (Bangladesh, Bhutan, Democratic People’s Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand and Timor-Leste) committed to achieving polio-free status and intensified their polio eradication efforts. By 1999, all 11 Member States had interrupted transmission of wild poliovirus type 2 – one of the three serotypes of polioviruses. Ten of the 11 Member States of the Region had interrupted transmission of indigenous wild polioviruses of all three serotypes by 2000. Only India remained polio-endemic and was considered an ‘epicentre’ of polio with the highest burden of polio in the Region and the world and a major exporter of poliovirus to countries within and outside of the Region.

Furthermore, four Member States of the Region—Bangladesh, Indonesia, Myanmar and Nepal were re-infected with wild polioviruses following importations from polio-endemic countries between 2000 and 2010. Indonesia reported co-outbreaks of wild poliovirus (WPV) and circulating vaccine-derived poliovirus (cVDPV) in 2005. India and Myanmar also reported cVDPV outbreaks between 2005 and 2010. Aggressive outbreak control measures, requiring substantial resources, had to be undertaken to interrupt the wild poliovirus circulation and cVDPV outbreaks in these countries.
EFFORTS TOWARDS POLIO ERADICATION

Of the 11 Member States of the WHO South-East Asia Region, India proved to be the most challenging Member State to break the chains of poliovirus transmission. India’s large population size and density, high birth rate, difficult terrain, periodic natural calamities in polio reservoir areas of Bihar, socioeconomic condition, cultural diversity and social taboos especially in western Uttar Pradesh (UP), in- and out-bound migration rate and sub-optimal health systems made the eradication job even more difficult. Therefore, the polio eradication programme of India initiated large-scale mass polio vaccination campaigns using trivalent oral polio vaccine (tOPV) in 1995, along with routine oral polio vaccine programme and these campaigns were further intensified in 1999. Each nationwide campaign involves vaccinating nearly 170 million children under 5 years of age through the involvement of 2.3 million vaccinators and 150,000 supervisors. Eight nationwide polio vaccination campaigns and six subnational campaigns were conducted in India between 1999 and 2001. The frequency and scope of the supplementary polio vaccination campaigns were further augmented over the years and multiple innovative strategies were applied to address the operational and technical challenges, especially in the polio high-risk areas and populations.

Despite these focused interventions, the wild poliovirus circulation continued unabated in selected high-risk areas of Northern India and periodic outbreaks continued to occur, resulting in repeated importations and outbreaks in polio-free states of the country. The difficulty in interrupting the last chains of poliovirus transmission in India often questioned the effectiveness of global eradication strategies and the feasibility of global polio eradication.

Research, coordinated, led and supported by WHO, played a pivotal role in identifying and overcoming the barriers by licensing more immunogenic polio vaccines, supporting programmatic evaluations and guiding programmatic actions and fine-tuning strategies that led to polio eradication in India and in the WHO South-East Asia Region.

RESEARCH FOR POLIO ERADICATION IN SOUTH-EAST ASIA REGION

Research studies conducted in the WHO South-East Asia Region have contributed to polio eradication in four strategic areas:

1. Support for licensure of new vaccines
2. Strategy development/adjustments to overcome barriers
3. Programme evaluations through serological surveys
4. Polio Endgame planning and validation
1 SUPPORT FOR LICENSURE OF NEW VACCINES

The introduction of bivalent OPV in the immunization programme is considered a major milestone for polio eradication in India and the Region. A clinical trial conducted in India in 2008-2009, to assess the immunogenicity of a bivalent oral polio vaccine (bOPV) containing type 1 and 3 polioviruses, demonstrated the superiority of bOPV compared with trivalent OPV (tOPV), and the non-inferiority of bOPV compared with monovalent OPV type 1 (mOPV1) and monovalent OPV type 3 (mOPV3). The findings of this study allowed the licensure of bOPV not only by manufacturers in India but also in other countries such as Belgium (Glaxo Smith Kline), France (Sanofi Pasteur) and Italy (Novartis) and paved the way for the introduction and use of bOPV for the first time ever in Afghanistan in December 2009 followed by India and the other polio-endemic and infected countries in 2010. The use of bOPV ensured that immunity against poliovirus type 1 was maintained at high levels while simultaneously improving against poliovirus type 3 in northern India leading to the interruption both poliovirus types by January 2011.

2 STRATEGY DEVELOPMENT/ADJUSTMENTS TO OVERCOME BARRIERS

IDENTIFICATION OF RISK FACTORS FOR WILD POLIOVIRUS TRANSMISSION

The occurrence of polio cases due to the wild poliovirus in northern India despite multiple campaigns with trivalent OPV (tOPV) prior to 2005 triggered research for the identification of risk factors in these areas. Analytical research revealed that the high population density, high birth rates, low routine immunization coverage and poor sanitation were a major contributor to ongoing polio outbreaks and transmission in northern India. These risk factors not only created an environment favourable for transmission of wild poliovirus, but also reduced the uptake and efficacy of the oral polio vaccine.

INTRODUCTION OF MONOVALENT ORAL POLIO VACCINES

India introduced the monovalent oral polio vaccines (mOPV) in 2005 to overcome the challenges of suboptimal performance of the tOPV due to various risk factors. Analytical research demonstrated that in conditions where the efficacy of live-attenuated oral poliovirus vaccines is compromised by a high prevalence of diarrhoea and other infections, a dose of mOPV1 is almost three times more effective against type 1 poliovirus than tOPV. The polio eradication programme in India, keeping its priority to eliminate wild poliovirus type 1, ensured frequent immunization campaigns with mOPV1 in the traditional reservoir states of Uttar Pradesh (UP) and Bihar.

CLINICAL TRIALS ON MONOVALENT OPV TYPE 1 (mOPV1)

Two randomized double-blind controlled clinical trials conducted in India confirmed the immunogenic superiority of mOPV1 compared to tOPV (for Sabin type 1) and provided strong support for the ongoing large-scale use of mOPV1 to eliminate the remaining chains of WPV type 1 transmission in India and also in other countries with endemic or re-introduced transmission of wild poliovirus type 1.
IMMUNOGENICITY OF SUPPLEMENTAL DOSE OF POLIOVIRUS VACCINES

A community-based randomized clinical trial conducted in western UP demonstrated that high seroprevalence against poliovirus type 1 can be achieved with numerous doses of mOPV1. The study demonstrated that a single dose on inactivated poliovirus vaccine (IPV) closed the humoral immunity gap against type 2 and 3 polioviruses in children that had received multiple doses of OPV in the past. The findings from this study had important implications for the polio eradication efforts in northern India and for risk management post-eradication in India and worldwide.

EPIDEMIOLOGICAL ANALYSIS OF VDPV OUTBREAK IN INDONESIA

An investigation of outbreak of laboratory-confirmed type 1 vaccine-derived poliovirus (VDPV) cases on Madura Island in Indonesia in 2005 demonstrated that clinical and epidemiological features of both wild poliovirus (WPV) and VDPV cases were similar. Attack rates for VDPV were as high as those for WPV. Low population immunity due to low routine OPV coverage in rural areas and the absence of WPV circulation for more than a decade were major predisposing factors for the emergence of VDPV. Suboptimal surveillance and a limited initial immunization response may have contributed to widespread circulation. Sensitive surveillance and prompt high-quality immunization responses are recommended to prevent the spread of VDPVs.

INACTIVATED POLIOVIRUS VACCINE (IPV) CLINICAL TRIALS AND INTRODUCTION

Vaccine trials conducted recently in India to compare the immunogenicity of inactivated polio vaccine (IPV) with OPV have demonstrated that the humoral and mucosal immunity induced by a single dose of IPV is superior to that induced by a single dose of bOPV in children that have received multiple doses of OPV in the past. The comparatively significant impact of IPV on both mucosal and humoral immunity as demonstrated in the study has effectively contributed to the global policy of the introduction of one dose of IPV in the routine immunization schedules of all OPV-using countries as a part of the global Polio Eradication and Endgame Strategic Plan 2013-2018. It has also contributed to the change in the position of the World Health Organization that now recommends that all OPV-using countries should introduce at least one dose of IPV into routine vaccine schedules.

INTESTINAL MUCOSAL IMMUNITY AGAINST POLIOVIRUSES

Research studies in India confirmed that significant protective gut mucosal immunity develops after vaccination with OPV. However, in children vaccinated with multiple doses of OPV, additional doses of OPV have limited ability to further boost mucosal immunity in children. The study also observed that the efficacy of tOPV to produce mucosal immunity was significantly lower in UP and Bihar than in the rest of India.

Research analysis also demonstrated that there was a waning of the mucosal immunity against polio following OPV administration with the passage of time. These findings necessitated further vaccine trials and research studies to search for best ways to improve both humoral and mucosal immunity in the populations, especially in northern India.
3 PROGRAMME EVALUATIONS THROUGH SEROPREVALENCE STUDIES

Periodic serological surveys conducted in India between 2007 and 2014, helped to more accurately determine population immunity and proved particularly valuable to document programme quality, assess progress and adjust and optimize vaccination plans.

The first serological survey in India, conducted in 2007 in a high-risk district in UP demonstrated immunity gaps against polio in children 6 to 12 months of age, despite repeated good coverage with OPV during vaccination campaigns, highlighting again the low immunogenicity of tOPV in northern India.

Serological assessments conducted in India during 2008-09 proved that high level of population immunity against poliovirus type 1 was successfully achieved in young infants following the extensive use of mOPV1 leading to a rapid decline in polio cases due to wild poliovirus type 1. However, this resulted in large outbreaks of wild poliovirus type 3 in UP and Bihar due to reduction in population immunity against type 3 poliovirus, confirmed by the serological surveys conducted during this period.

Periodic serological surveys conducted 2010 onwards in India have confirmed that replacing mOPV1 with bOPV in campaigns was successful in maintaining very high population immunity to type 1 poliovirus and substantially decreasing the immunity gap to type 3 poliovirus.

Similar serosurveys have been conducted in other countries in the Region, although less frequently than in India, as a part of risk assessment. The recent serosurveys in Myanmar and Sri Lanka have observed high levels of immunity against poliovirus type 2, which is expected to reduce the risk of emergence of cVDPV2 after tOPV-bOPV switch.

4 POLIO ENDGAME PLANNING AND VALIDATION

A clinical trial conducted in The Gambia, Oman and Thailand in 1997 to assess an immunization schedule combining OPV and IPV demonstrated that a combined schedule of OPV and IPV (OPV at birth followed by both OPV and IPV at 6, 10 and 14 weeks of age) resulted in high seroprevalence against type 1 (95-99%), type 2 (99-100%) and type 3 (97-100%). The combined schedule also provided mucosal immunity equivalent to that produced by OPV alone.

An IPV introduction project was operationalized, in Yogyakarta, Indonesia, to generate information on the possible emergence of vaccine-derived polioviruses (VDPVs) in an IPV-only environment. An assessment of routine immunization coverage, seroprevalence and poliovirus detection in sewage samples, before and after a switch from OPV to IPV in 2007, demonstrated that under almost ideal conditions (good hygiene, maintenance of universally high IPV coverage, and corresponding high immunity against polioviruses), no emergence and circulation of VDPV could be detected in a tropical developing country setting after IPV was introduced. Vaccination coverage remained unchanged after the switch suggesting that programmatically there was no significant problem with the introduction of IPV into routine immunization schedule. The seroprevalence of poliovirus neutralizing antibodies after 3 doses of IPV reached 100% and a fourth dose, although increased the titer was considered unnecessary and therefore, removed from the immunization schedule as of 2013. This study also provides useful information on the possible dynamics of type 2 Sabin virus in all Member States that will switch from tOPV to bOPV in 2016.
The immunogenicity of the proposed routine vaccination schedule (OPV plus IPV) as recommended under the polio endgame strategy was assessed in India in 2014. The new schedule of bOPV and IPV demonstrated excellent immunogenicity against poliovirus types 1 and 3. A dose of IPV induced an immunity base against poliovirus type 2 (seroconversion and priming), and the second IPV dose boosted antibody titers. The study results are encouraging and strongly support the newly-recommended routine schedule for polio endgame strategy.

5 LESSONS LEARNT AND WAY FORWARD

Research studies conducted in the WHO South-East Asia Region have played a critical role to help overcome the barriers associated with the continued circulation of wild polioviruses and achieve polio-free status in the Region. During recent years, the studies have guided newer strategies targeted towards optimization and a greater effectiveness of the available polio vaccines.

Research studies conducted in the Region have contributed towards building capacity for designing and operationalizing clinical trials with vaccines as well as conducting complex field studies. Polio research studies conducted in the Region required a high degree of coordination, collaboration and cooperation among various stakeholders. This was successfully accomplished by liaising with various government bodies and international agencies and partnering with medical institutions and laboratories. Strong mechanisms for supervision and monitoring of the study procedures that were a part of the study protocol ensured high retention of study subjects, safety of the subjects and contributed to generation of reliable data that could be used by the national, regional and global advisory bodies on immunization policy with confidence. The capacity and infrastructure that has been created while conducting the polio studies as well as the experiences and the lessons learnt from conducting these studies will not only contribute to future research studies for polio but also for other vaccines and other health initiatives.

Research studies to fill major information gaps will have to continue as the world gets closer to global polio eradication and withdraws polio vaccines. Information on the levels and duration of immunity of the different polio vaccines that are currently in use as well as new polio vaccines that are on the horizon will be critical during the endgame implementation. The phased withdrawal of OPVs and the increasing use of IPV are likely to pose epidemiological challenges not previously encountered by the programme and research studies will continue to play a critical role during the endgame implementation.
### 1. CLINICAL TRIAL FOR LICENSURE OF VACCINES

**Immunogenicity of bivalent types 1 and 3 oral poliovirus vaccine: a randomized, double-blind, controlled trial**


*Lancet* 2010; 376: 1682–88

Cumulative two-dose seroconversion to poliovirus type 1 was 90% for mOPV1 and 86% for bOPV compared with 63% for tOPV (*p*<0.0001) and seroconversion to poliovirus type 3 was 84% for mOPV3 and 74% for bOPV compared with 52% for tOPV (*p*<0.0001). The findings showed the superiority of bOPV compared with tOPV, and the non-inferiority of bOPV compared with mOPV1 and mOPV3.

Poliovirus types 1 and 3 co-circulated in poliomyelitis-endemic countries. The polio programme, considering its priority to eliminate type 1 WPV, used mOPV1 with better efficacy against type 1 compared to tOPV. Frequent immunization campaigns with mOPV1 in the traditional reservoir states of Uttar Pradesh and Bihar successfully achieved high levels of population immunity to type-1 in young infants. However, this resulted in large outbreaks of type 3 polio in UP and Bihar during 2007-2009 due to reduction in population immunity to type-3 poliovirus. The polio programme needed a vaccine which could protect populations simultaneously against poliovirus type 1 and 3. The findings of this study led to the introduction of bOPV in India and globally.
2. STUDIES ON STRATEGY DEVELOPMENT/ADJUSTMENTS TO OVERCOME BARRIERS

a. New strategies for the elimination of polio from India

Nicholas C. Grassly, Christophe Fraser, Jay Wenger, Jagadish M. Deshpande, Roland W. Sutter, David L. Heymann, R. Bruce Aylward

Science 314, 1150 (2006)

There was a significant association between continued reporting of laboratory-confirmed polio cases by districts and (i) population density, (ii) the prevalence of diarrhoea, and (iii) low routine coverage with three doses of trivalent oral polio vaccine (tOPV). Relative odds of infection with paralytic polio declined with increasing number of doses of tOPV. However, the probability of protection per dose was unexpectedly low in Uttar Pradesh (UP). The estimated protective efficacy of tOPV against type 1 poliovirus was just 9% per dose in UP, significantly lower than the estimated 21% per dose in the rest of India. Similar results are obtained for type 3 poliovirus, although confidence intervals are wider, reflecting the lower number of reported cases.

High population densities and poor sanitation facilitate the transmission of polioviruses and possibly of other enteroviruses and diarrhoea, which interfere with the live attenuated oral polio vaccine. The global elimination of polio cases due to type 2 wild poliovirus, and the elimination of type 3 polio cases from all of India except a cluster of districts in western Uttar Pradesh, has motivated the introduction of monovalent vaccine, effective only against type 1 poliovirus, during immunization days in selected states of India in April 2005. Monovalent vaccine has potentially higher efficacy than the trivalent vaccine because of the absence of interference with the two other poliovirus types. However, exclusive use of monovalent vaccine during immunization days can put the population at risk of outbreaks of type 3 poliovirus. With new vaccine strategies based on careful use of monovalent vaccine targeted at districts with high population densities and poor sanitation, the analyses suggested that wild poliovirus could be eliminated from India.

b. Protective efficacy of a monovalent oral type 1 poliovirus vaccine: a case-control study

Nicholas C Grassly, Jay Wenger, Sunita Durrani, Sunil Bahl, Jagadish M Deshpande, Roland W Sutter, David L Heymann, R Bruce Aylward

Lancet April 12, 2007 DOI:10.1016/S0140-6736(07)60531-5

In areas of persistent poliovirus transmission in Uttar Pradesh, the protective efficacy of mOPV1 was estimated to be 30% (95% CI 19–41) per dose against type 1 paralytic disease, compared with 11% (7–14) for the trivalent oral vaccine. A total of 76–82% children (0–23 months) were estimated to be protected by vaccination against type 1 poliovirus at the end of 2006, compared with 59% at the end of 2004, before mOPV1 introduction.

Under conditions where the efficacy of live-attenuated oral poliovirus vaccines is compromised by a high prevalence of diarrhoea and other infections, a dose of mOPV1 is almost three times more effective against type 1 poliovirus than trivalent vaccine.
c. **Monovalent type 1 oral poliovirus vaccine among infants in India: report of two randomized double-blind controlled clinical trials**


Confirmed the immunogenic superiority of mOPV1 compared to tOPV (for Sabin type 1) in India when administered at birth and 30 days of age. Provided strong support for the ongoing large-scale use of mOPV1 to eliminate the remaining chains of WPV type 1 transmission in India and also in other countries with endemic or re-introduced transmission of wild poliovirus type 1.

d. **Immunogenicity of supplemental doses of poliovirus vaccine for children aged 6-9 months in Moradabad, India: a community-based, randomized controlled trial**


High seroprevalence of antibodies for type-1 poliovirus can be achieved in western Uttar Pradesh with numerous doses of mOPV1. The study demonstrated that a single dose of IPV closed the humoral immunity gap against type 2 and type 3 polioviruses in children who had received multiple OPV doses in the past. The findings from this study had important implications for the continued effort to eradicate polio in northern India and for risk management after eradication in India and worldwide.

e. **A large vaccine-derived poliovirus outbreak on Madura Island--Indonesia, 2005**


Between June and October 2005, 45 laboratory-confirmed type 1 vaccine-derived poliovirus (VDPV) cases were identified on Madura Island in Indonesia. Genetic sequencing data on VDPV isolates were consistent with replication and circulation for up to approximately two years. Concurrent circulation with type 1 wild poliovirus (WPV) enabled comparisons of VDPV and WPV cases and found that clinical and epidemiological features of both were similar. Attack rates for VDPV were as high as those for WPV. Of 41 VDPV case patients with known vaccination status, 25 (61%) had received zero oral polio vaccine (OPV) doses. Low population immunity due to low routine OPV coverage in rural areas and the absence of WPV circulation for more than a decade were major predisposing factors for the emergence of VDPV. Suboptimal surveillance and a limited initial immunization response may have contributed to widespread circulation. Sensitive surveillance and prompt high-quality immunization responses are recommended to prevent the spread of VDPVs.
f. Efficacy of inactivated poliovirus vaccine in India

Hamid Jafari, Jagadish M. Deshpande, Roland W. Sutter, Sunil Bahl, Harish Verma, Mohammad Ahmad, Abhishek Kunwar, Rakesh Vishwakarma, Ashutosh Agarwal, Shilpi Jain, Concepcion Estivariz, Raman Sethi, Natalie A. Molodecky, Nicholas C. Grassly, Mark A. Pallansch, Arani Chatterjee, R. Bruce Aylward

Science 345, 922 (2014)

IPV reduced excretion for poliovirus types 1 and 3 in children that had received multiple doses of OPV, demonstrating development of mucosal immunity. The study showed that mucosal immunity induced by a single dose of IPV was superior to that induced by a single dose of bOPV. The study also demonstrated that higher humoral antibody titers are associated with decreased excretion of the challenge virus.

The comparatively significant impact of IPV on both mucosal and humoral immunity as demonstrated in the study opened doors for the use of IPV in eradicating remaining reservoirs of infection in endemic countries, in mitigating the risks of cVDPVs after the tOPV-bOPV switch and as a potential response vaccine against outbreaks in future. The study demonstrated that both vaccines – IPV and OPV should be used. As a result, the World Health Organization no longer recommends an all-OPV schedule; rather, it recommends that all OPV-using countries introduce at least one dose of IPV into routine vaccine schedules.

g. Mucosal immunity after vaccination with monovalent and trivalent oral poliovirus vaccine in India

Nicholas C. Grassly, Hamid Jafari, Sunil Bahl, Sunita Durrani, Jay Wenger, Roland W. Sutter, R. Bruce Aylward

JID 2009; 200:794–80

This study demonstrated that significant protective gut mucosal immunity develops after vaccination with OPV in India. However, additional doses of OPV have limited ability to further boost mucosal immunity in children with multiple reported doses of mOPV. The study also observed that the efficacy of tOPV against excretion of serotypes 1 and 2 was significantly lower in UP and Bihar than in the rest of India. These findings necessitated further vaccine trials and research studies to search for best tools to boost both humoral and mucosal immunity in the populations, especially in northern India.

h. Waning intestinal immunity after vaccination with oral poliovirus vaccines in India

Nicholas C Grassly, Hamid Jafari, Sunil Bahl, Raman Sethi, Jagadish M Deshpande, Chris Wolff, Roland W Sutter, R Bruce Aylward

JID 2012; 205:1554–61

Previous vaccination with OPV was protective against excretion of vaccine poliovirus after challenge, but the odds of excretion increased significantly with the time since the child was last exposed to an immunization activity. Infection with OPV (vaccine “take”) is highly seasonal in India and results in intestinal mucosal immunity that appears to wane significantly within a year of vaccination. Also, findings suggest that strategies to more effectively induce and boost mucosal immunity will considerably facilitate the interruption of wild-type poliovirus transmission in remaining infected areas.
3. **SEROLOGICAL SURVEYS**

a. **Assessing population immunity in a persistently high-risk area for wild poliovirus transmission in India: a serological study in Moradabad, western Uttar Pradesh (2007)**


Poliovirus type 1, 2, and 3 seroprevalence were 88%, 70%, and 75% respectively, among 467 children in the 6-11-month age group, compared with 100%, 97%, and 93%, respectively, among 447 children in the 36 to 59-month age group (P < .001 for all serotypes).

This first-ever large-scale seroprevalence study in India conducted in 2007 provided extremely useful information that guided immunization policies, such as optimizing the use of different OPV formulations in vaccination campaigns and strengthening routine immunization services.

b. **An acute flaccid paralysis surveillance–based serosurvey of poliovirus antibodies in western Uttar Pradesh, India (2008-09)**

*Sunil Bahl, Howard E. Gary Jr, Hamid Jafari, Bidyut K. Sarkar, Surendra K. Pathyarch, Raman Sethi, Jagadish Deshpande*


The estimated seroprevalence for type 1 in 2008-2009 was high in children from each of the three age groups: 6–11 months, 12–24 months, and 25–69 months; the lowest estimate being 96.4% in the 6-11 month-old age group. The seroprevalence for poliovirus types 2 and 3 increased with age (6-11 months to 25–69 months); from 36.7% to 73.4% for type 2 and from 39.0% to 74.1% for type 3. In addition to the number of type-specific vaccine doses, father’s level of education, being from a Muslim family, height for age, and female sex were other demographic and socioeconomic risk factors associated with seronegativity to poliovirus. The seroprevalence and risk factors identified in this study were consistent with the epidemiology of polio, and the findings were instrumental in optimizing vaccination strategy in western Uttar Pradesh with respect to the choice of OPV types, the frequency of supplementary immunization campaigns, and the urgency to improve routine immunization services.

c. **Cross-sectional serologic assessment of immunity to poliovirus infection in high-risk areas of northern India (2010)**


Seroprevalence rates of antibodies to poliovirus types 1, 2, and 3 were 98%, 66% and 77% respectively, among 1280 infants from Bihar and Uttar Pradesh. Infants had received a median of 3 bOPV doses and 2 monovalent type 1 OPV (mOPV1) doses through campaigns and 3 trivalent OPV (tOPV) doses through routine immunization. In multivariable analysis, malnutrition was associated with a lower seroprevalence of type 3 antibodies. This study confirmed that replacing mOPV1 with bOPV in campaigns was successful in maintaining very high population immunity to type 1 poliovirus and substantially decreasing the immunity gap to type 3 poliovirus.
d. **Cross-sectional assessment of humoral immunity to poliovirus in high-risk communities of western Uttar Pradesh and Bihar, India: 2011**

*Unpublished*

Seroprevalence for poliovirus types 1, 2 and 3 were 98.5%, 85.0% and 88.2% respectively in UP and Bihar. The proportion seropositive for type-1 poliovirus among 6-7 months, 8-9 months and 10-11 months was 98.6%, 98.3% and 98.5% respectively. The corresponding figures for type-2 was 78.6%, 88.1% and 88.1%, and for type-3 it was 85.6%, 87.8% and 91.2%. The study confirmed that introduction of bOPV in 2010 in the high-risk states of Uttar Pradesh and Bihar successfully sustained high levels of population immunity against type-1 during 2011, while significantly improving the immunity to type-3 poliovirus. Continued use of tOPV in routine immunization and during the two nationwide polio vaccination campaigns has helped to attain high seroprevalence against type-2 poliovirus in the highest-risk areas of India during 2011.

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e. **Cross-sectional assessment of humoral immunity to poliovirus in high-risk communities of western Uttar Pradesh and Bihar, India: 2012**

*Unpublished*

High seroprevalence for types 1, 2 and 3 poliovirus in the high-risk blocks of UP and Bihar was maintained at high levels during 2012 (P1: 98.4%; P2: 90.1% and P3: 87.9%). High seroprevalence was also achieved and maintained in the adjoining non-high-risk blocks of UP and Bihar (P1: 96.2%; P2: 87.3% and P3:88.5%) (P value non-significant). High vaccination coverage during NIDs and SNIDs as well as continued use of tOPV in routine immunization helped to attain high seroprevalence for type 1 & 3 and increase in type 2 seroprevalence. The study justified the continued use of bOPV in the polio programme and indicated that strengthened routine coverage is important for improving seroprevalence against type 2. This seroprevalence study also confirmed that high population immunity for polio existed in both high-risk and adjoining non-high-risk blocks.

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f. **Achieving high seroprevalence against polioviruses in Sri Lanka—results from a serological survey, 2014**

*Deepa Gamage, Paba Palihawadana, Ondrej Mach, William C. Weldon, Steven M. Oberste, Roland W. Sutter*


A cross-sectional community-based survey covering 400 children in three districts of Sri Lanka (Colombo, Badulla, and Killinochi) in four age groups (9–11 months, 3–4 years, 7–9 years, and 15 years) demonstrated >95% seroprevalence for poliovirus type 1 and type 2. Seroprevalence for poliovirus type 3 was 95%, 90%, 77%, and 75% in the age groups 9–11 months, 3–4 years, 7–9 years, and 15 years respectively. Useful baseline data has been provided prior to the addition of inactivated poliovirus vaccine (IPV) and the switch from trivalent OPV (tOPV) to bivalent OPV (bOPV) in Sri Lanka.
g. Cross-sectional serologic assessment of immunity to poliovirus in differential risk areas of India: 2014

*Unpublished*

Overall seroprevalence for Bihar, Madhya Pradesh and Mumbai were 97.3%, 97.9% and 86.9% for poliovirus types 1, 2 and 3 respectively. The seroprevalence for poliovirus types 1, 2 & 3 for Bihar was 99.0%, 99.0% & 92.0%, for Madhya Pradesh 98.0%, 99.0% & 88.0% and for Mumbai 98.0%, 97.0% & 94.0% respectively. The study confirmed the high population immunity for all serotypes in all the different risk areas of India. The traditionally high-risk areas for polio in India have sustained high seroprevalence during 2014 for all poliovirus types. Areas with low routine immunization coverage and urban migratory clusters have also achieved high levels of population immunity against all 3 poliovirus types. The number of polio campaigns planned for 2015 (2 NIDs+3 SNIDs) in India is enough to sustain required immunity levels. Continued use of tOPV in routine immunization schedule and NIDs has helped to attain the highest seroprevalence against type-2 poliovirus during 2014, which is a good sign for the switch from tOPV to bOPV as a part of the polio endgame plan.

h. Serosurvey in Myanmar, 2013

*Unpublished*

The cross-sectional study on 1260 children, 1-14 years of age in three states (Yangon, Chin and Kayin) found a significant immunity gap to type 1 poliovirus among children 1-4 years of age in Chin with better immunity in older age groups in Chin and in other states. Low immunity to type 3 was observed in the three states, which was more marked among the older age group. A higher immunity to type 3 was observed among children aged 1-4 years in Chin; raising a question if it could have been due to undetected circulation of type 3 WPV/VDPV. The high level of immunity to type 2 in all age groups will help to reduce the risk of VDPV 2 emergence after the proposed tOPV-bOPV switch.

4. STUDIES ON POLIO ENDGAME PLANNING AND VALIDATION

a. Combined immunization of infants with oral and inactivated poliovirus vaccines: results of a randomized trial in The Gambia, Oman, and Thailand

*WHO Collaborative Study Group on Oral and Inactivated Poliovirus Vaccines*

*The Journal of Infectious Diseases 1997; 175 (Suppl):S215-27*

Of the 1685 infants enrolled for the study, 550 subjects were recruited from infants born at Phramongkutklao Hospital, Bangkok, Thailand. Children were randomized to receive OPV at birth and at 6, 10, and 14 weeks of age; or OPV at birth followed by both OPV and IPV at 6, 10, and 14 weeks of age; or placebo at birth followed by IPV at 6, 10, and 14 weeks of age. Serum specimens were available at 24 weeks for 1291 (77%) of 1685 enrolled infants. In the combined- OPV/ IPV schedule group, the proportion of children seropositive at 24 weeks was 95%-99% for type 1, 99%-100% for type 2, and 97%-100% for type 3. In The Gambia and Oman, the combined schedule performed significantly better than OPV for type 1 (95%-97% vs. 88%-90%) and type 3 (97%-99% vs. 72%-73%). Across the study sites, IPV given at 6, 10, and 14 weeks of age provided inadequate protection against poliovirus. The combined schedule provided the highest levels of serum antibody response, with mucosal immunity equivalent to that produced by OPV alone.
b. **Switch from oral to inactivated poliovirus vaccine in Yogyakarta province, Indonesia: summary of coverage, immunity, and environmental surveillance**

Gendro Wahjuhono, Revolusiana, Dyah Widhiastuti, Julitasari Sundoro, Tri Mardani, Woro Umi Ratih, Retno Sutomo, Ida Safitri, Ondri Dwi Sampurno, Bardan Rana, Merja Roivainen, Anna-Lea Kahn, Ondrej Mach, Mark A. Pallansch, Roland W. Sutter


The coverage, immunity and VDPV surveillance results following the IPV introduction project in Yogyakarta demonstrated that vaccination coverage (>95%) and immunity (approximately 100%) did not change substantially before and after the IPV switch. No VDPVs were detected. Before the switch, 58% of environmental samples contained Sabin poliovirus; starting six weeks after the switch, Sabin polioviruses were rarely isolated, and if they were, genetic sequencing suggested recent introductions. This project demonstrated that under almost ideal conditions (good hygiene, maintenance of universally high IPV coverage, and corresponding high immunity against polioviruses), no emergence and circulation of VDPV could be detected in a tropical developing country setting. This study also gives very useful information on the possible dynamics of type 2 Sabin virus in all countries which will switch from tOPV to bOPV.

c. **Immunogenicity of a new routine vaccination schedule for global poliomyelitis prevention: An open-label, superiority, randomized, controlled clinical trial**


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This randomized vaccine trial in India demonstrated that seroconversion against poliovirus type 1 was 98-99% while it was >90% against poliovirus type 3 after 4 doses, given to newborn children in the routine schedule at birth, 6, 10 and 14 weeks, of tOPV or bOPV + 1 dose of IPV (at week 14). Seroconversion against poliovirus type 2 was variable (depending on schedule), 96% after 4 doses of tOPV, 100% after 4 doses of tOPV + 1 dose of IPV, 19% after 4 doses of bOPV, and between 69-78% after 4 doses of bOPV + 1 dose of IPV. A second dose of IPV closed the remaining type 2 gaps. The study also confirmed the findings of earlier studies that IPV-vaccinated infants excrete poliovirus for shorter periods. The new routine immunization schedule of bOPV and IPV demonstrated excellent immunogenicity against poliovirus types 1 and 3. A dose of IPV induced an immunity base against poliovirus type 2 (seroconversion and priming). The study results are encouraging and strongly support the newly-recommended routine schedule for polio endgame strategy.
The WHO South-East Asia Region was certified polio-free in March 2014, after a hard-fought battle that lasted over two decades. A number of strategic innovations and interventions, guided by research studies, were implemented in the Region to overcome the various technical challenges faced by the programme during the journey towards polio eradication.

This publication provides a summary of WHO coordinated research studies conducted in the WHO South-East Asia Region and their contribution to the regional as well as global polio eradication initiative.