Vaccination Recommendations for Travellers from Polio-infected Countries: Report of the SAGE Polio Working Group

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Overview

- Context for the SAGE WG meeting 5-6 Feb 2014
- Key questions to the WG
  - Infected countries
  - Target population
  - Vaccine
  - Timing of supplementary vaccination
- Other considerations
- WG recommendations

Context of the SAGE Polio WG Discussions

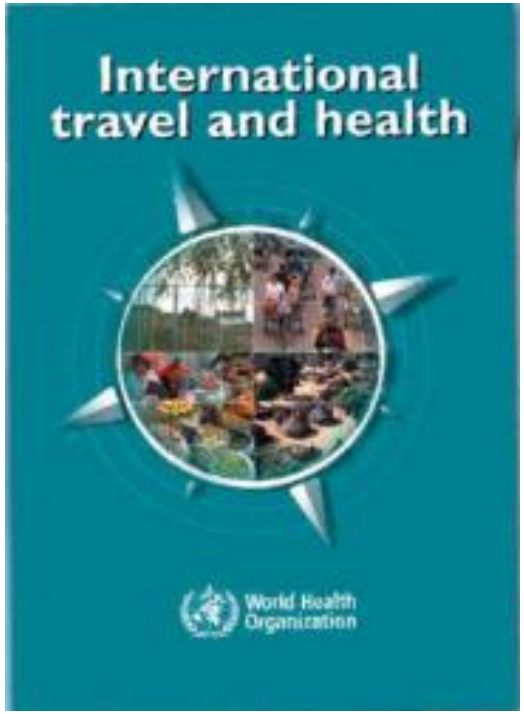
Background

- WHO Member States are increasingly concerned about the international spread of poliovirus (e.g. the recent WHO Executive Board (EB) discussions, EMRO RCM resolution, India's vaccination requirements for travellers)
- The recent scientific evidence (e.g. role of adults in international spread, duration of intestinal immunity, role of IPV to boost intestinal immunity) may require a review of the WHO's existing guidance.
- Member states have asked WHO for clarification on multiple aspects of its recommendations for travellers

Request to the Polio WG

- WHO requested that SAGE review the recent scientific evidence regarding the vaccination of travellers and provide updates to the WHO recommendation in light of recent scientific evidence

WHO Recommendations for Travellers: International Travel and Health (ITH) 2013



- Travellers to polio-infected areas should have completed the age-appropriate polio vaccine series, and also receive another dose of polio vaccine before departure
- Travellers from polio infected areas should have completed a full course of vaccination against polio, preferably with OPV, and also receive an additional dose of OPV at least 6 weeks before each international journey.
- All travellers are advised to carry an official vaccination record (patient-retained record), preferably using the IHR 2005 International Certificate of Vaccination or Prophylaxis.

Key Questions Considered by the WG

Infected countries

- What is the definition of "polio-infected" countries?

Target population

- What is the recommended population for vaccination (e.g. age considerations, residents vs. all travellers)?

Vaccine

- What vaccine(s) are acceptable for vaccination of travellers from polio-infected countries (e.g. OPV/IPV)?

Timing of vaccination

- What is the minimal and maximum interval for vaccination prior to travel?

Infected countries

- What is the definition of "polio-infected" countries?

Target population

- What is the recommended population for vaccination (e.g. age considerations, residents vs. all travellers)?

Vaccine

- What is the acceptable vaccination for travellers (e.g. OPV/IPV)?

Timing of vaccination

- What is the optimum frequency for booster dose?
- What is the optimal/minimal interval for vaccination?

Definition of 'Polio-infected Countries'

The WG reaffirmed the following definitions used by WHO to identify countries with active poliovirus transmission:

- **Endemic wild poliovirus transmission**:
  - Continued transmission of an indigenous WPV which by definition has never been interrupted.
  - Endemic WPV transmission is considered to be interrupted, when all indigenous WPVs have not been detected for > 12 months from any source (e.g. AFP cases, their contacts, environmental samples, stool surveys)
- **Re-established wild poliovirus transmission**:
  - Persistence of WPV of non-indigenous origin for > 12 months in a previously polio-free country.
  - Re-established WPV transmission is considered to be interrupted, when the imported strain of WPV has not been detected for > 12 months from any source (e.g. AFP, contacts, environmental samples, stool surveys)

Definition of 'Polio-infected Countries' (2)

- **Re-infection with wild poliovirus** :
  - a) at least one AFP case with isolation of WPV in a person who has not travelled outside the country during the two months prior to onset of paralysis *or* b) detection of 2 or more genetically related WPVs in environmental samples and/or other non-AFP sources (e.g. stool surveys).
  - Re-infection with WPV is considered to be interrupted, when there is no detection of the imported strain of WPV for > 6 months from any source (e.g. AFP cases, their contacts, environmental samples, stool surveys)

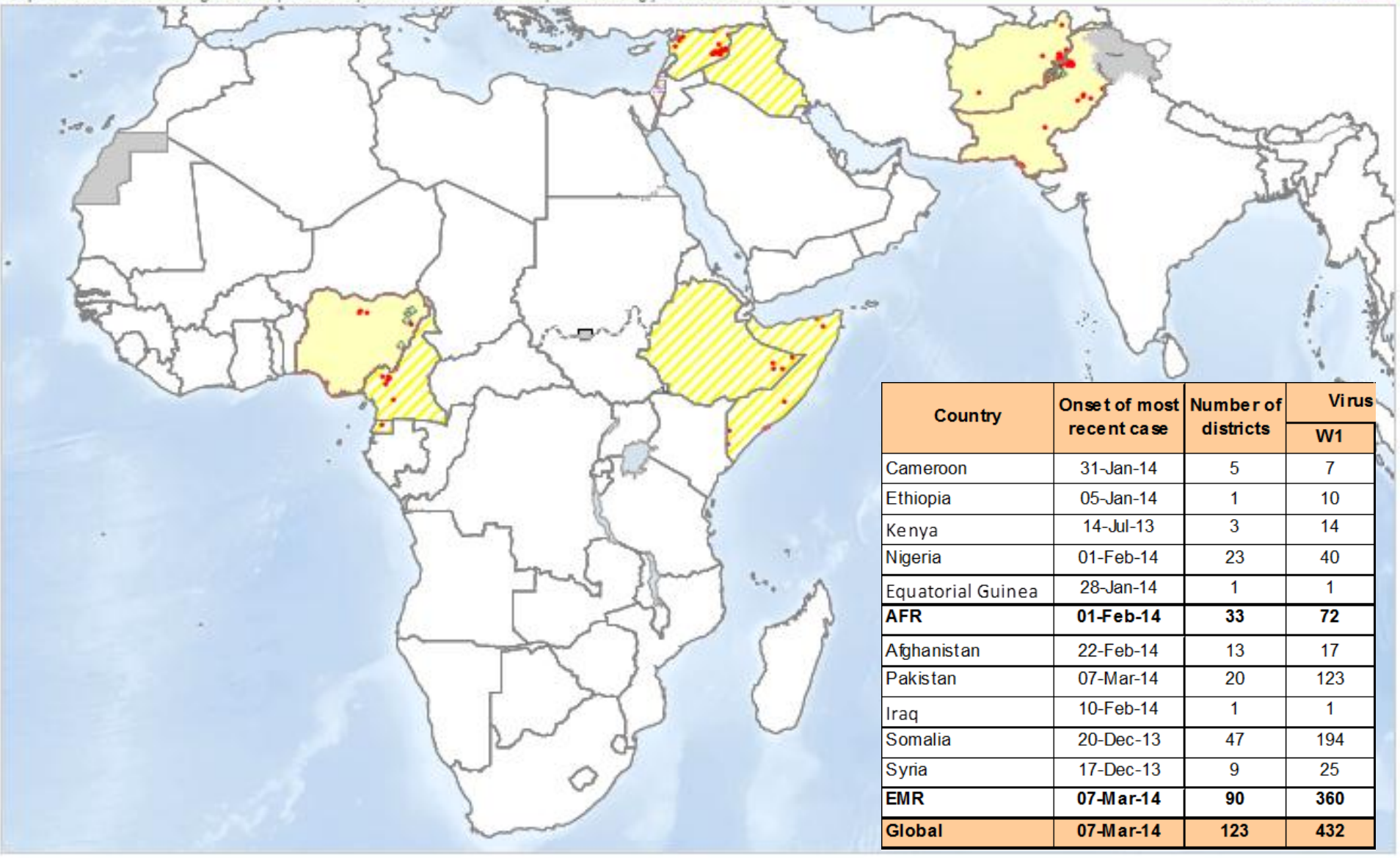
- **Re-infection with a cVDPV**:
  - Detection of a genetically related cVDPV in 2 or more AFP cases in a country, or detection of a genetically related cVDPV in 2 or more environmental samples or samples from other sources.
  - Re-infection with cVDPV is considered to be interrupted when there has been no detection of the cVDPV for > 6 months

GLOBAL WILD POLIO CASES, cVDPVs & ENVIRONMENTAL POSITIVE - R6M*

World Health Organization

Map shows the incidents of global wild polio cases, cVDPVs & environmental positive during previous six months

MAP DATE: 26 March 2014, Version 1.0



Country	Onset of most recent case	Number of districts	Virus
			W1
Cameroon	31-Jan-14	5	7
Ethiopia	05-Jan-14	1	10
Kenya	14-Jul-13	3	14
Nigeria	01-Feb-14	23	40
Equatorial Guinea	28-Jan-14	1	1
AFR	**01-Feb-14**	**33**	**72**
Afghanistan	22-Feb-14	13	17
Pakistan	07-Mar-14	20	123
Iraq	10-Feb-14	1	1
Somalia	20-Dec-13	47	194
Syria	17-Dec-13	9	25
EMR	**07-Mar-14**	**90**	**360**
Global	**07-Mar-14**	**123**	**432**

Country with positive WPV in environmental sampling sites within previous 6 months

Wild Polio Virus Type 1

cVDPV2

Endemic countries

Country with WPV case in previous 6 months

Infected countries

Target population

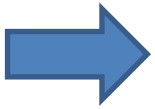
Vaccine

Timing of vaccination

- What is the recommended population for vaccination (e.g. age considerations, residents vs. all travellers)?

Age Consideration: Role of Adults in International Spread of Poliovirus

- Several lines of evidence suggest older individuals play an important role in international spread of poliovirus
  - Multiple studies (e.g. India and Israel) found that individuals of all ages can become infected and excrete poliovirus if challenged with an OPV virus or if in contact with children who excrete poliovirus
  - Out of 179 importation events in 2004-13, 27 (15%) were associated with long-distance travel (i.e., transmission between non-contiguous countries or across oceans) where adult travellers were more likely to be involved
  - Several documented cases of adult travellers who were excreting wild poliovirus (e.g. three cases from Mexico, Nepal, and Zaire to the U.S. between 1980 and 1989, one case from Pakistan to Australia in 2007, and three cases from Xinxiang to Beijing in 2011)



The recommendation for travellers from polio-infected countries should apply to all residents and long-term visitors (i.e. non-residents who spend more than 4 weeks in the country) of all ages

Infected countries

Target population

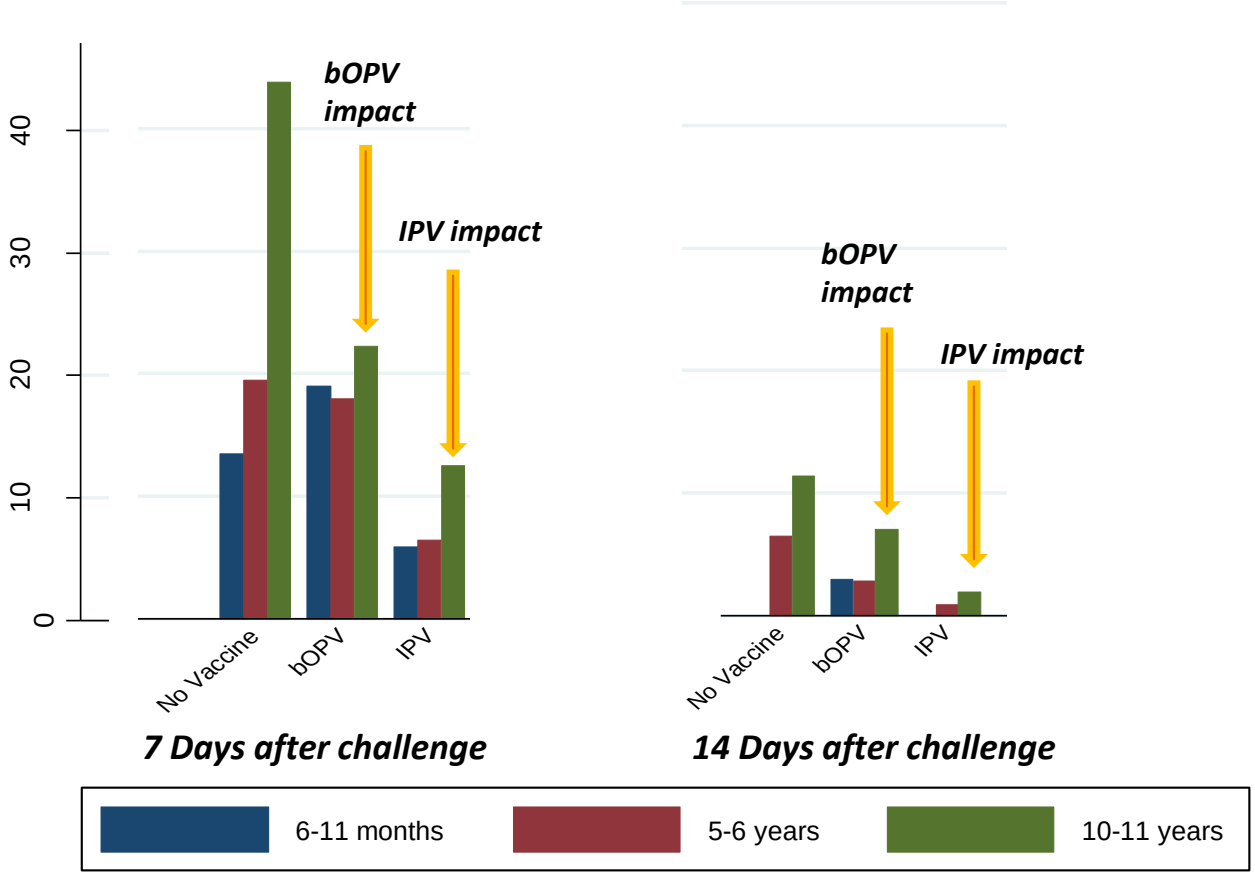
Vaccine

Timing of vaccination

- What vaccine(s) are acceptable for vaccination of travellers from polio-infected countries (e.g. OPV/IPV)?

New Evidence for the Impact of IPV on Boosting Intestinal Immunity

% of subjects excreting type 1 PV after receiving IPV, bOPV or no vaccine with a challenge OPV dose at day 28 (India, 2011)



- In previously OPV-vaccinated individuals, one dose of bOPV or IPV can reduce the excretion of poliovirus significantly (by 50% with bOPV and by 75% with IPV)
- Another recent study in South India (2014) confirmed this finding

Thus, either OPV or IPV can be used as a booster dose for travellers

Source: Jafari H et al. Unpublished data

Infected countries

Target population

Vaccine

Timing of vaccination

- What is the minimal and maximum interval for vaccination prior to travel?

Rationale to Determine Minimum Interval Before Travel

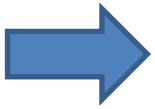
- **Rapidity of antibody response to OPV and IPV:** In naive population, early studies with seronegative children demonstrated that an immune response could be observed as early as 7-10 days after vaccination, reaching maximum titers within 4 weeks

- **Duration of poliovirus excretion**: A review of cross-sectional and longitudinal studies of wild or Sabin poliovirus excretion concluded that live polioviruses are excreted by unvaccinated population for 3-4 weeks following the onset of paralysis

Rapidity of Antibody Response in Naive Populations

- A series of early studies* with seronegative children demonstrated that an immune response (rising antibody titers) could be observed as early as 7-10 days after vaccination, reaching maximum titers usually within 4 weeks

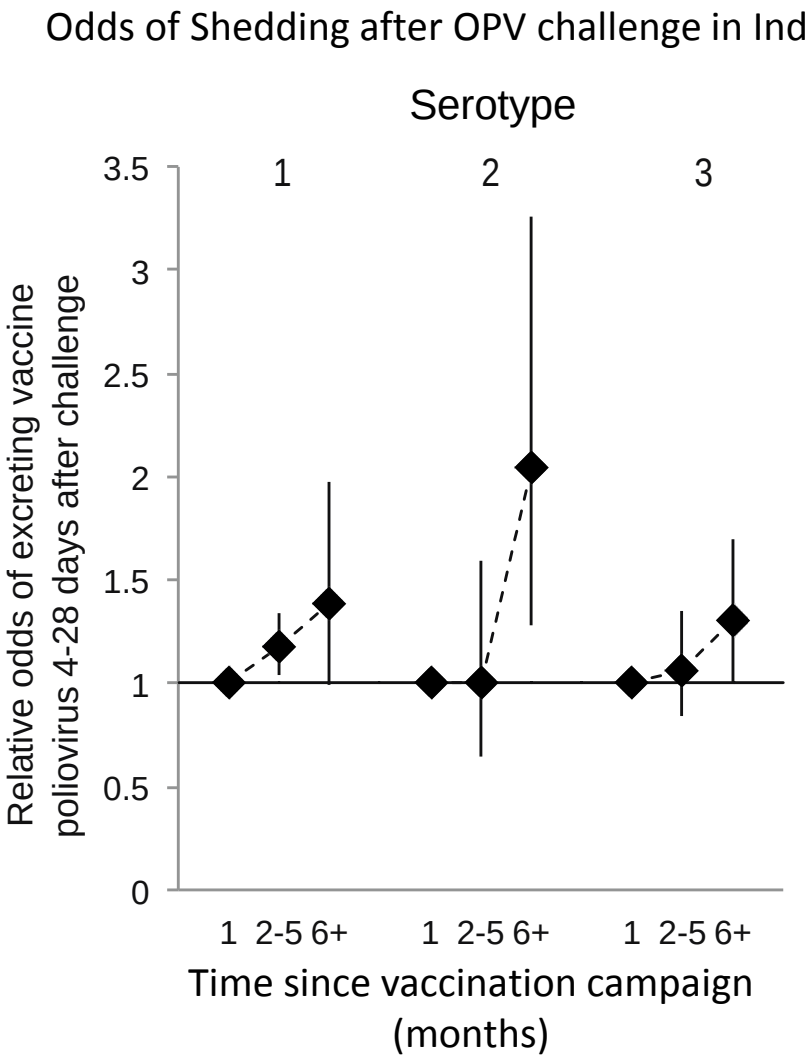
- Based on this evidence, the WHO Technical Report Series (TRS 910 for IPV, 2004) recommends that immune response should be measured at approximately 4 weeks following the immunization



Thus, in those responding to vaccination, high antibody titers would be expected within 4 weeks of administration of OPV or IPV

* Including a) Koprowski H et al. Am J Hyg, vol. 55, 1952, p.108-126, b) Sabin AB et al. Am. J. Med. Sc. 1955, 230, 1, c) Horstmann DM et al. J. Exp. Med., Jul 1957; 106: 159 - 177. and d) Smorodintsev AA et al. Bull World Health Organ. 1959;20:1053-74. Ogra PL et al. N Engl J Med 1968; 279:893-900

Duration of Intestinal Immunity



- An analysis of AFP surveillance data in India showed the intestinal immunity is short-lived (less than 12 months)
- Two studies in India support this finding (intestinal immunity wanes rapidly after the last OPV dose)

With rapidly declining intestinal immunity, travellers of all ages from polio-infected counties should receive a booster dose within 12 months prior to each travel

Source: Grassly N et al. J Infect Dis 205: 1554-1561

Summary: Proposed Updates to WHO Recommendations for Travellers from Polio-infected Countries

Infected countries	• The recommendations should apply to all polio-infected countries (i.e. wild or cVDPV, whether detected in clinical cases, environmental samples or other sources); within 6 months (re-infected countries) or 12 months (endemic countries)
Target population	• The recommendations should apply to all residents and long-term visitors (i.e. non-residents who spend more than 4 weeks in the country) - transit and short stay visitors do not need a booster dose.
Vaccine	• OPV or IPV can be used to boost previously vaccinated individuals
Timing of vaccination	• Resident travellers* of all ages should have received a booster dose between 4 weeks and 12 months prior to each travel

** Include all residents and long-term visitors in all polio-infected countries*

Other Considerations

- **Small infants**: all children travelling from polio-infected countries should have completed their age-appropriate primary series for polio vaccination according to the national immunization schedule

- **Urgent Travel**: Travellers from polio-infected countries embarking on last minute/urgent (i.e. less than 2 weeks) should receive one dose of OPV or IPV before departure if they have not received a dose of polio vaccine within 12 months before the date of travel

- **Travellers <u>to</u> polio infected countries**: the WG recommended keeping the current ITH recommendations (2013) that recommends a one-time polio vaccine booster for travellers from polio-free countries who have completed a primary series

Questions to the SAGE

Does SAGE endorse the proposed revisions to the WHO recommendations for the vaccination of travellers from polio-infected countries?

- Vaccination recommendations for travellers from polio-infected countries should apply to all residents and long-term visitors (i.e. non-residents who spend more than 4 weeks in the country) of all ages;
- All such travellers from polio-infected countries should have received one additional dose of OPV or IPV between 4 weeks and 12 months prior to each travel;
- Such travellers from polio-infected countries embarking on last minute/urgent (i.e. less than 2 weeks) travel that cannot be postponed should receive one dose of OPV or IPV before departure if they have not received a dose of polio vaccine within 12 months.

Backup

Key Operational Considerations

The WG also discussed a number of operational issues related to the implementation of vaccination recommendations:

- **Documentation**: each polio-infected country would need to ensure its travellers have access to a standardized certificate (e.g., WHO "Yellow Booklet")

- **Acceptable vaccines**: WHO pre-qualified polio vaccines or other nationally- licensed polio vaccine is acceptable

- **Administrative and Financial issues**: Departure and arrival countries should assess and secure the financial and human resources necessary to implement polio vaccination recommendations

- **Communication** : Polio-infected (departure) and arrival countries should develop appropriate communication strategies

Key Operational Considerations (Continued)

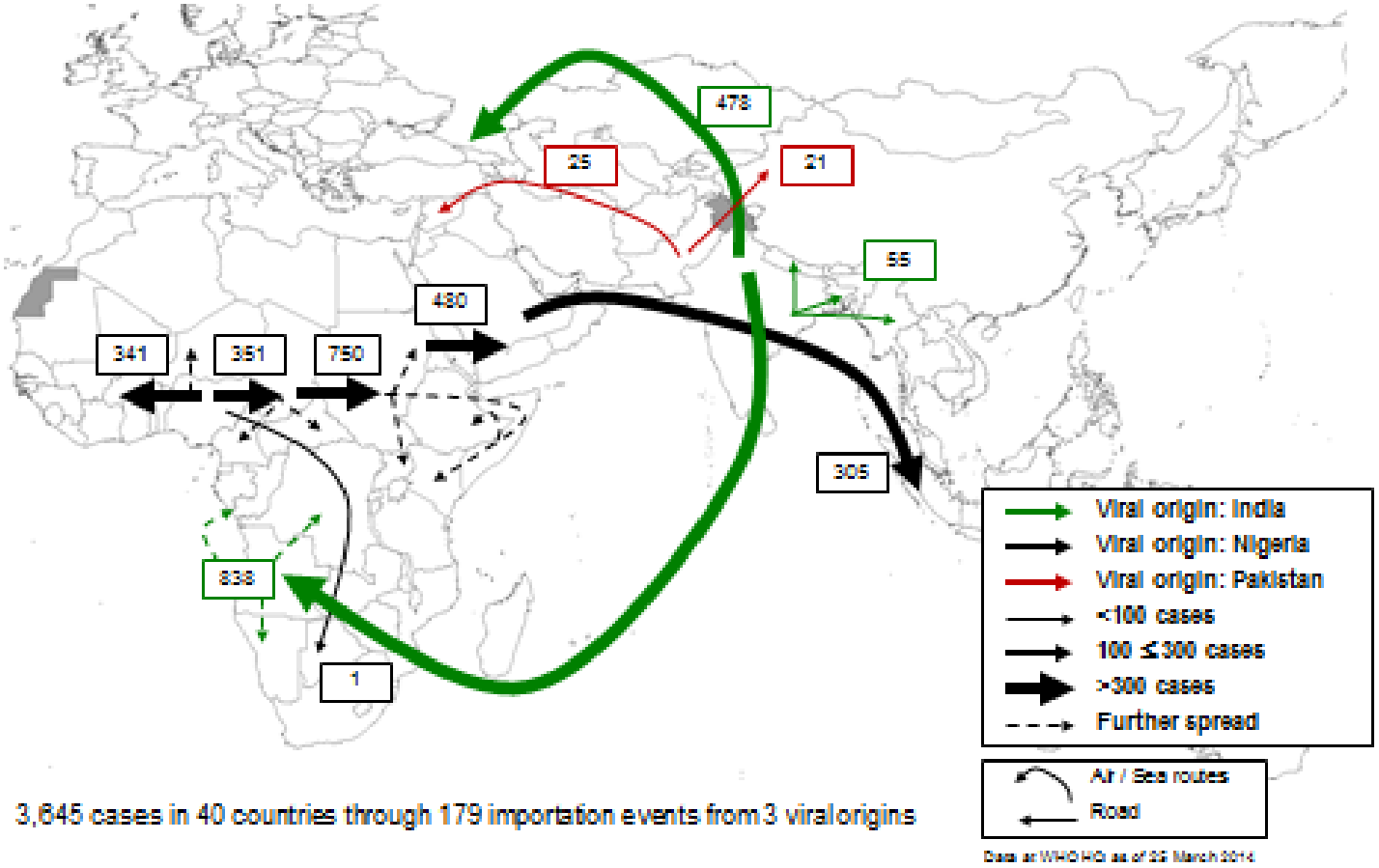
Role of countries of departure (polio-infected countries)

- May consider special measures to boost population immunity near ground-crossing points with a high volume of travellers (e.g. expanded age group campaigns or vaccination at the border)

Role of countries of arrival

- Establish options for managing arriving travellers from polio-infected countries who are not able to produce a valid certification of vaccination
- Explore the potential value of linking proof of polio vaccination to the issuance of entry visas for travellers from polio-infected countries

Background: Historical Impact of Poliovirus Importation (2004-13)

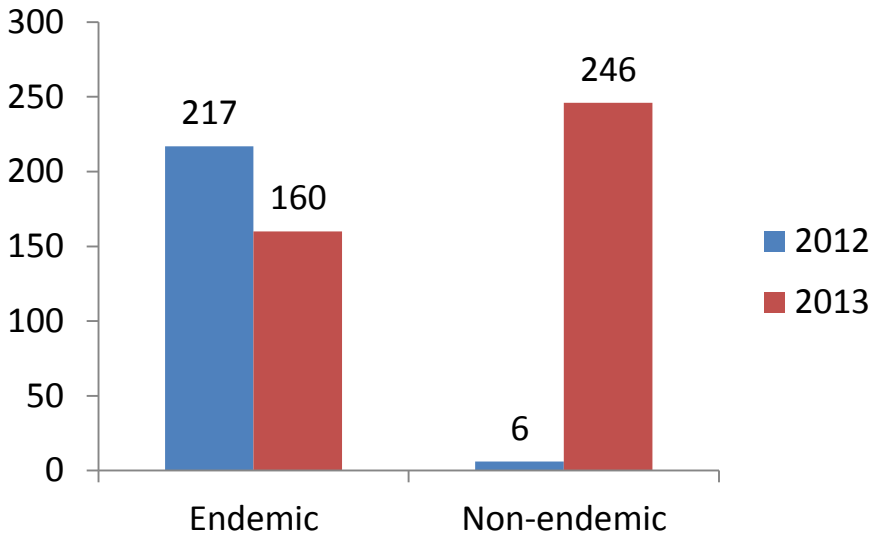


- Between 2004 and 2013, 179 importation events into previously polio-free countries
- These events resulted in more than 3,500 paralytic cases and cost $1.1 billion in international funds for control

Poliovirus Importation Events in 2013

Overview of Polio cases in 2013

# of polio cases in 2012-13



- In 2013, there were new importation events in the Middle-East, Horn of Africa and Cameroon.
- It caused 246 paralytic cases and cost $86 million to the program in 2013

- The relative importance of importation events has further increased because of the progress made towards eradication
- These events gravely divert attention and scarce resources from the eradication goal

Rapidity of Antibody Response to Boosting Dose

Table 2. Rates of Seroconversion and Priming Immune Response after One or Two Doses of Inactivated Poliovirus Vaccine for Poliovirus Types 1, 2, and 3.*

Immune Response	Fractional IPV Dose (N=157)	Full IPV Dose (N=153)	P Value	Between-Group Difference (95% CI)
	no./total no. (%)			*percentage points*
Poliovirus type 1				
Seroconversion after first dose	26/157 (16.6)	71/153 (46.4)	<0.001	29.8 (19.2 to 39.6)
Priming response	119/131 (90.8)	80/82 (97.6)	0.1	6.8 (–1.3 to 13.7)
Seroconversion between visits 3 and 4	2/12 (16.7)	2/2 (100)	0.13	83.3 (–3.2 to 97.1)
Seroconversion after second dose	121/131 (92.4)	82/82 (100)	0.01	7.6 (0.9 to 14.0)
Cumulative seroconversion	147/157 (93.6)	153/153 (100)	0.002	6.4 (2.0 to 11.7)
Poliovirus type 2				
Seroconversion after first dose	74/157 (47.1)	96/153 (62.7)	0.008	15.7 (4.1 to 26.6)
Priming response	78/83 (94.0)	56/57 (98.2)	0.42	4.3 (–5.4 to 12.5)
Seroconversion between visits 3 and 4	2/5 (40.0)	1/1 (100)	>0.99	60.0 (NP)
Seroconversion after second dose	80/83 (96.4)	57/57 (100)	0.41	3.6 (–4.7 to 10.9)
Cumulative seroconversion	154/157 (98.1)	153/153 (100)	0.26	1.9 (–1.5 to 5.9)
Poliovirus type 3				
Seroconversion after first dose	23/157 (14.6)	49/153 (32.0)	<0.001	17.3 (7.5 to 26.9)
Priming response	120/134 (89.6)	102/104 (98.1)	0.01	8.5 (1.5 to 15.5)
Seroconversion between visits 3 and 4	3/14 (21.4)	1/2 (50.0)	0.90	28.6 (NP)
Seroconversion after second dose	123/134 (91.8)	103/104 (99.0)	0.018	7.2 (0.9 to 13.7)
Cumulative seroconversion	146/157 (93.0)	152/153 (99.3)	0.006	6.4 (1.6 to 11.9)

* Seroconversion was defined as an increase in the antibody titer that was four times as high as the expected decline in maternally derived antibodies. Cumulative seroconversion reflects the sum of the seroconversions occurri… first and the second dose. P values were calculated with the use of chi-square tests (with the Yates-correct… with Fisher's exact test if the number of participants in a cell was 5 or fewer). NP denotes not presented (i… bers of participants in the cells were too small to calculate meaningful 95% confidence intervals).

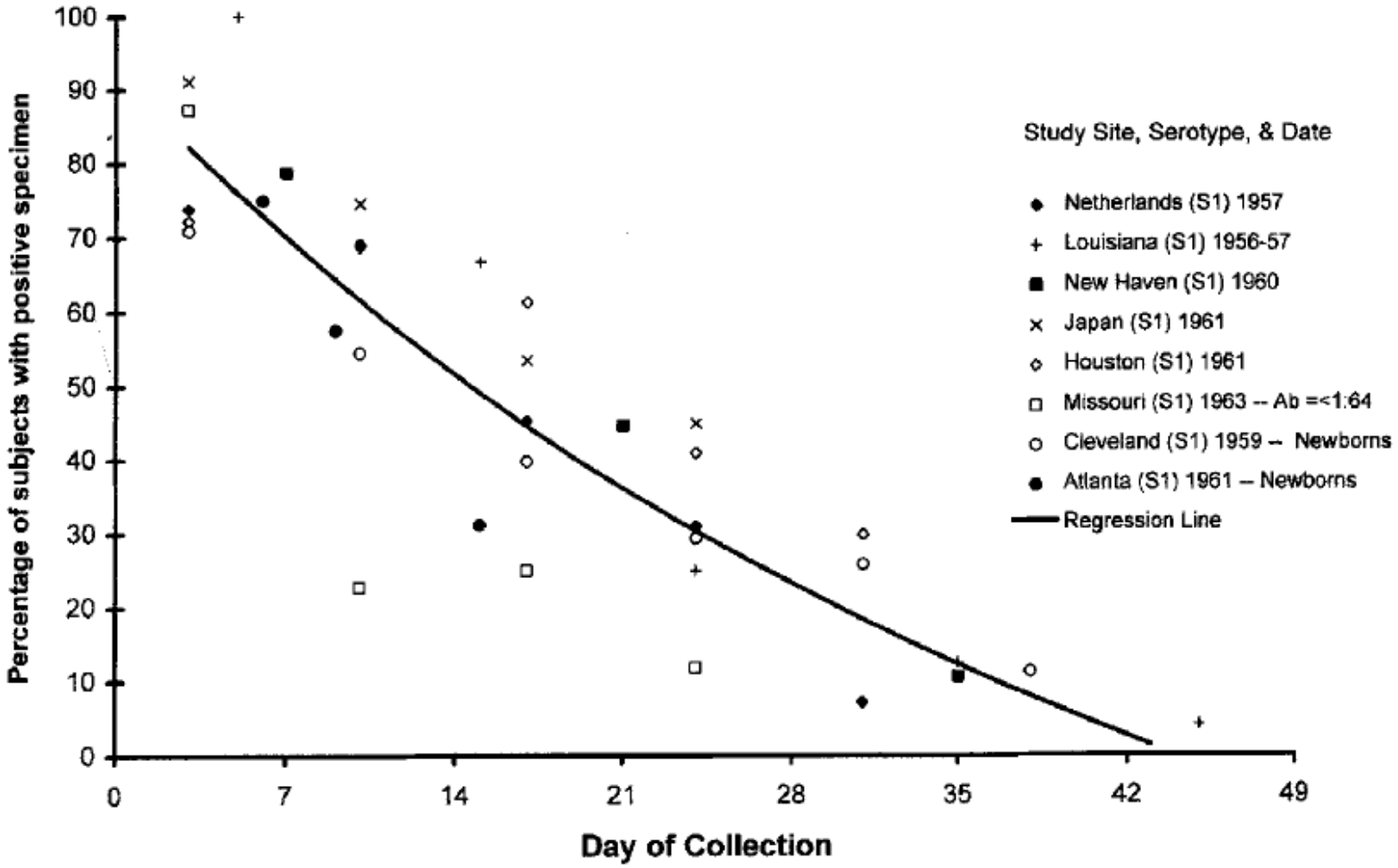
Several studies (Oman 2000,Cuba 2014) demonstrate that the anamnestic response occurs within 7 days (maximum antibody response)

Serotype	7-days response	Median Ab titer at 7 days
1	97.6%	≥1448
2	98.2%	≥1448
3	98.1%	≥1448

Resik S et al. N Engl J Med 2013;368:416-24.

Duration of poliovirus excretion After Infection

Duration of faecal excretion of Sabin type 1 virus by OPV recipients



Source: Alexander et al. JID 1997; 175 (suppl 1)