

PUBLIC HEALTH GRAND ROUNDS

Office of the Director

January 21, 2010



PUBLIC HEALTH GRAND ROUNDS



The screenshot shows the CDC Connects website interface. At the top left is the CDC logo and the word "Connects". To the right, the date "Tuesday, November 17, 2009" is displayed. Below this is a dark red banner with the text "Office of The Director" and icons for home and email. A breadcrumb trail reads "CDC Connects > Office of The Director > The Director > Archives". The main content area features a blue header with the words "PUBLIC HEALTH GRAND ROUNDS" in white, above a collage of images including a person in a lab coat, a stethoscope, and hands being washed. Below the images is the section title "Grand Rounds" followed by a paragraph of text describing the series and its focus on public health issues. At the bottom of the text block, it mentions the typical schedule (third Thursday of every month) and provides a link to "CDC IPTV".

Office of The Director

Tuesday, November 17, 2009

CDC Connects > Office of The Director > The Director > Archives

PUBLIC HEALTH GRAND ROUNDS

Grand Rounds

The Public Health Grand Rounds is a monthly series created to further strengthen CDC's common scientific culture and foster discussion and debate on major public health issues. Each session of the Public Health Grand Rounds will focus on key issues and challenges related to a specific health topic, including cutting-edge scientific evidence and potential impact of different interventions. The sessions will also highlight how CDC is already addressing these challenges and discuss the recommendations for future research and practice.

Grand Rounds sessions are typically held on the third Thursday of every month at Roybal's Global Communications Center, Auditorium A, between 9-10 a.m. For those unable to attend, the sessions will be available on [CDC IPTV](#).

Available on [IPTV](http://intra-apps.cdc.gov/itso/iptv/iptvschedule.asp) : <http://intra-apps.cdc.gov/itso/iptv/iptvschedule.asp>

IPTV link also available on Grand Rounds [intranet](#) site:

<http://intranet.cdc.gov/od/odweb/about/directorGrandRounds.htm>



PUBLIC HEALTH GRAND ROUNDS

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PUBLIC HEALTH GRAND ROUNDS



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For those outside of CDC, a broadband link is available at:
<http://www.cdc.gov/about/grand-rounds> (Grand Rounds **internet** site)



Continuing Education Credits



**Starting today, January 21, 2010
Credit Hours will be available for:**

- Physicians (CME)
- Non-Physicians (CME)
- Nurses (CNE)
- Certified Health
Education Specialists (CECH)
- Pharmacist (CPE)
- Other Professionals (CEU)

ALL Continuing Education credits/contact hours for PHGR are issued online through the CDC/ATSDR Training & Continuing Education Online system,

<http://www2a.cdc.gov/TCEOnline>



Knowledge to Action Science Clips

Selection of Polio-related Articles: Dr. Steve Wassilak (NCIRD)



Public Health Library & Information Center

CDC Knowledge to Action Science Clips: January 11 - January 15, 2010
Vol. 2, Issue: 3

This week's featured scientific articles include:

Communicable Diseases – Polio

[Gender inequity and age-appropriate immunization coverage in India from 1992 to 2006.](#)

Corsi DJ, Diego BG, Kumar R, Awasthi S, Jotkar R, Kaur N, Jha P.
BMC Int Health Hum Rights. 2009;9 Suppl 1:S3.

[Public health response to imported case of poliomyelitis, Australia, 2007.](#)

Carnie JA, Lester R, Moran R, Brown L, Meagher J, Roberts JA, Thorley BR.
Emerg Infect Dis. 2009 Nov;15(11):1733-7.

[Deconstructing social resistance to pulse polio campaign in two North Indian districts.](#)

Chaturvedi S, Dasgupta R, Adhish V, Ganguly KK, Rai S, Sushant L, Srabasti S, et al.
Indian Pediatr. 2009 Nov;46(11):963-74.

[Polio: measuring the protection that matters most.](#)

Fine PE.
J Infect Dis. 2009 Sep 1;200(5):673-5.

<http://intranet.cdc.gov/scienceclips>



We Welcome Any Feedback!

The Public Health Grand Rounds email address:

grandrounds@cdc.gov

For information about the Grand Rounds or to suggest future topics, please contact Dr. Tanja Popovic at tpopovic@cdc.gov.

If you have specific questions about the broadband link and other connectivity issues, or if interested in receiving future CDC Public Health Grand Rounds announcements, please contact Mr. Shane Joiner at sjoiner@cdc.gov.



CDC Public Health Grand Rounds Partner Evaluation Survey

**Foodborne Diseases: Better Information with Better Public Health Information
December 17, 2009; 9:00 a.m.–10:15 a.m. (EST)**

		Strongly Disagree	Disagree	Agree	Strongly Agree
1.	The Grand Rounds session was engaging.		20%	80%	
2.	The session was appropriate in length.		20%	40%	40%
3.	I was able to easily access the session through the broadband link.			20%	80%
4.	The session helped me to understand more about foodborne disease.		20%	40%	20%
5.	The session helped me to think about how my organization can further collaborate with CDC.		20%	80%	
6.	I would attend another Grand Rounds session.			20%	80%
7.	I encouraged and invited other colleagues to participate in Grand Rounds.		20%	40%	40%



Stay Tuned: Spring 2010



- Feb 18 Neural Tube Defects and Folic Acid Fortification
- Mar 18 Radiological and Nuclear Preparedness
- Apr 15 Preventing Health Effects from Nanotechnology
- May 20 Chlamydia Prevention and Control





Polio Vaccination Effectiveness in India – Implications for Polio Eradication



**Global Immunization Division and Division of Viral Diseases,
National Center for Immunization and Respiratory Diseases
NCIRD**



Outline

- ❑ **Stephen L. Cochi, MD, MPH, GID/NCIRD**
 - *The Global Picture of Polio*
- ❑ **Hamid Jafari, MD, GID/NCIRD detailed to World Health Organization, India**
 - *Defining the Challenges in India and Refining the Strategies and Tools to Achieve Polio Eradication*
- ❑ **Mark A. Pallansch, PhD, DVD/NCIRD**
 - *Research Needed to Accelerate Polio Eradication in India*
- ❑ **Walter R. Dowdle, PhD, Task Force for Global Health**
 - *Polio Eradication in Perspective*



THE GLOBAL PICTURE OF POLIO



Stephen L. Cochi, MD, MPH
Senior Advisor

**Global Immunization Division,
National Center for Immunization and Respiratory Diseases**





THE GLOBAL PICTURE OF POLIO

- ❑ **Background**
- ❑ **Progress since 1988**
- ❑ **Addressing the Remaining Challenges**
- ❑ **Global Importance of India**





THE GLOBAL PICTURE OF POLIO

Background

Progress since 1988

Addressing the Remaining Challenges

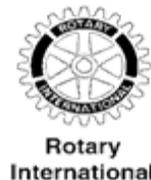
Global Importance of India





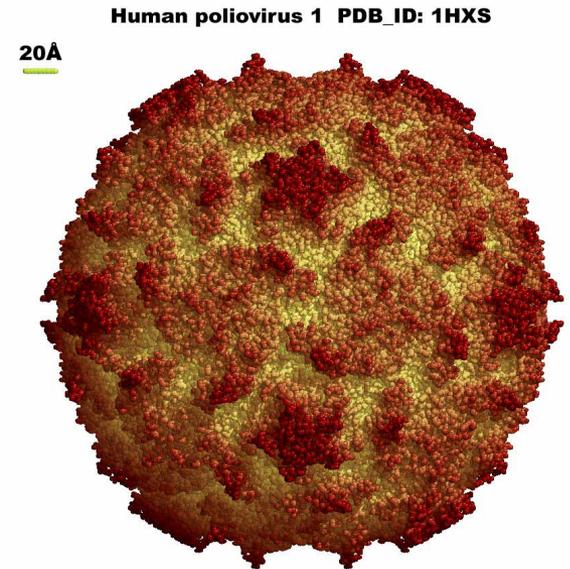
The Global Polio Eradication Initiative (GPEI)

- ❑ **World Health Assembly Polio Eradication Resolution in 1988**
- ❑ **GPEI is a Public-Private Partnership led by**
 - World Health Organization (WHO)
 - Rotary International
 - Centers for Disease Control & Prevention
 - United Nations Children's Fund (UNICEF)



Polio – The Viruses and the Disease

- ❑ Human infection by one of 3 poliovirus serotypes (RNA viruses - *Enterovirus* genus)
- ❑ Transmitted person-to-person, by fecal-oral route
- ❑ Highly infectious, ubiquitous infection in absence of immunization
- ❑ Paralysis is a rare outcome (<1%)



CTV 8th Report - Images by Jean-Yves Sgro ©2004
images at virology.wisc.edu/virusworld

Coordinates from: PDB: www.rcsb.org/pdb/ VIPER: mmtsb.scripps.edu/viper/



Polio Vaccines

	OPV	IPV
Route	Oral	Injection
Current cost per dose	\$0.15	\$2-3
Live virus excretion	Yes	No
Contact immunization	Yes	No
Intestinal mucosal immunity	Yes	Limited
Systemic immunity in tropical countries	Reduced	High
Risk of vaccine-associated paralytic polio	Yes	No

OPV, Oral Polio Vaccine
IPV, Inactivated Polio Vaccine



The Global Polio Eradication Initiative: the Four Key Strategies

Strengthening Routine Childhood Immunization



Conducting Surveillance for Wild Poliovirus



Conducting Supplementary Immunization Activities (SIAs)

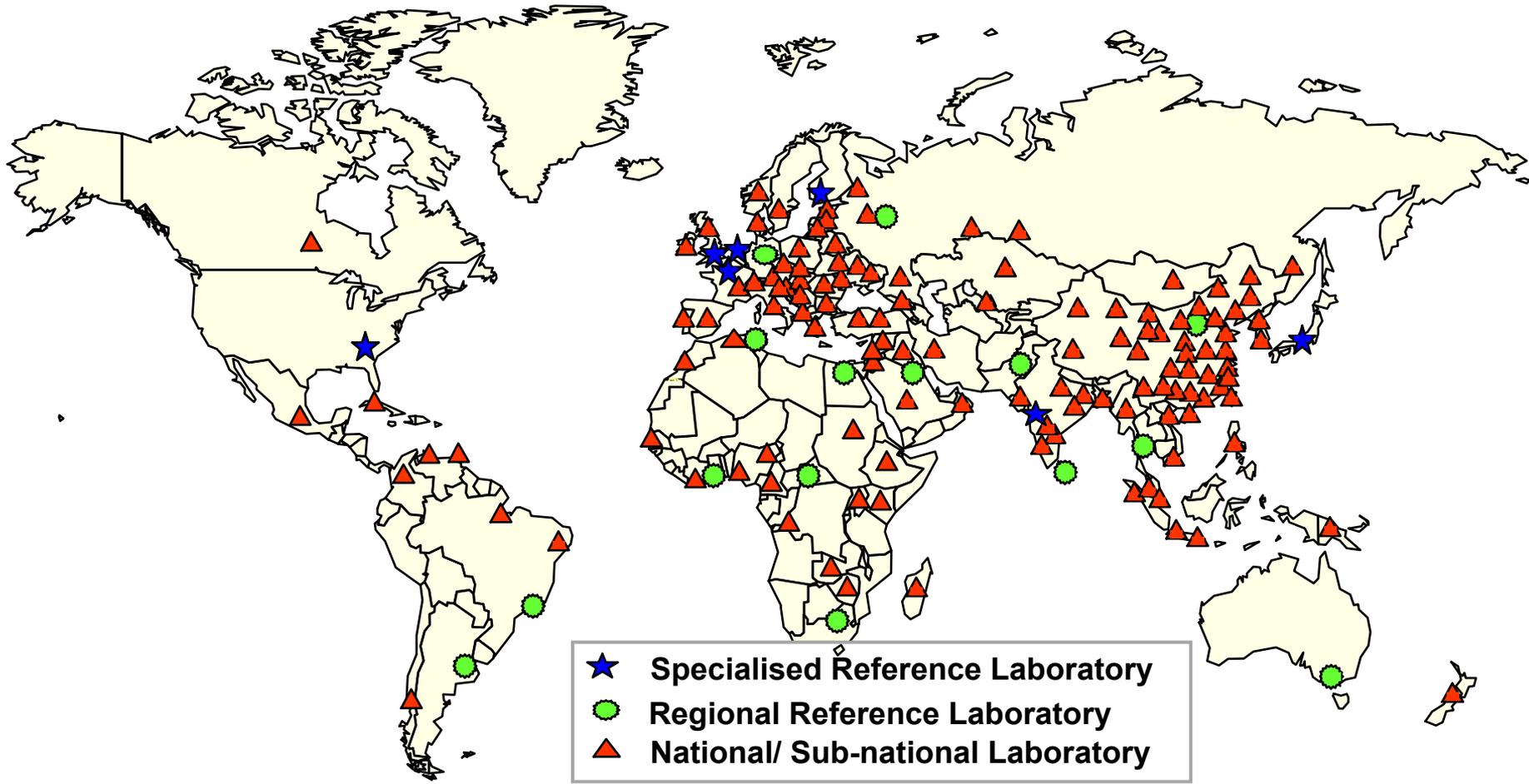


Conducting Intensive House-to-House Targeted "Mop-up" Campaigns



Polio Laboratory Network Structure, 2010

N=145

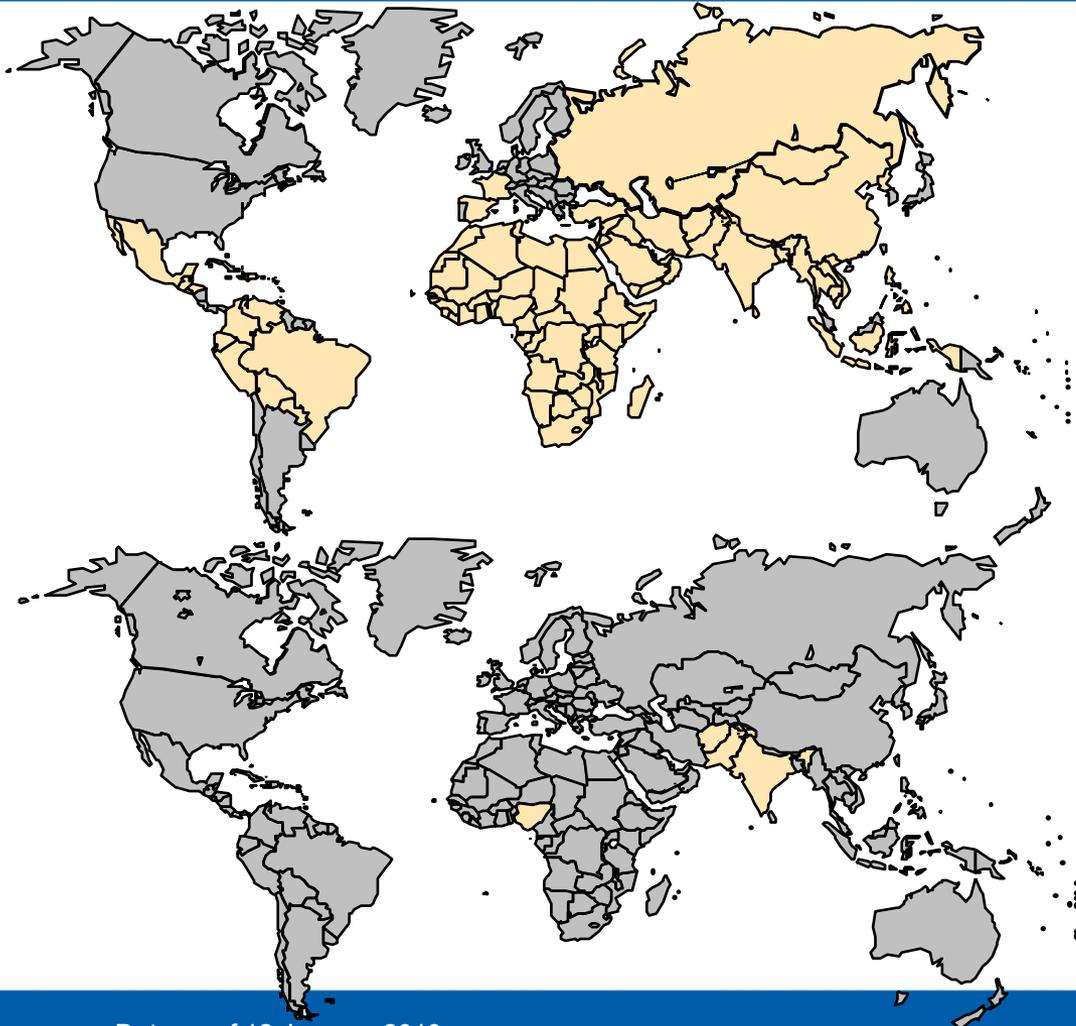


THE GLOBAL PICTURE OF POLIO

- Background
- **Progress since 1988**
- Addressing the Remaining Challenges
- Global Importance of India



Global Progress from 1988 to 2009: Polio Endemic Countries and Cases



1988
350,000 Cases, 35,000 Deaths
in 125 Countries

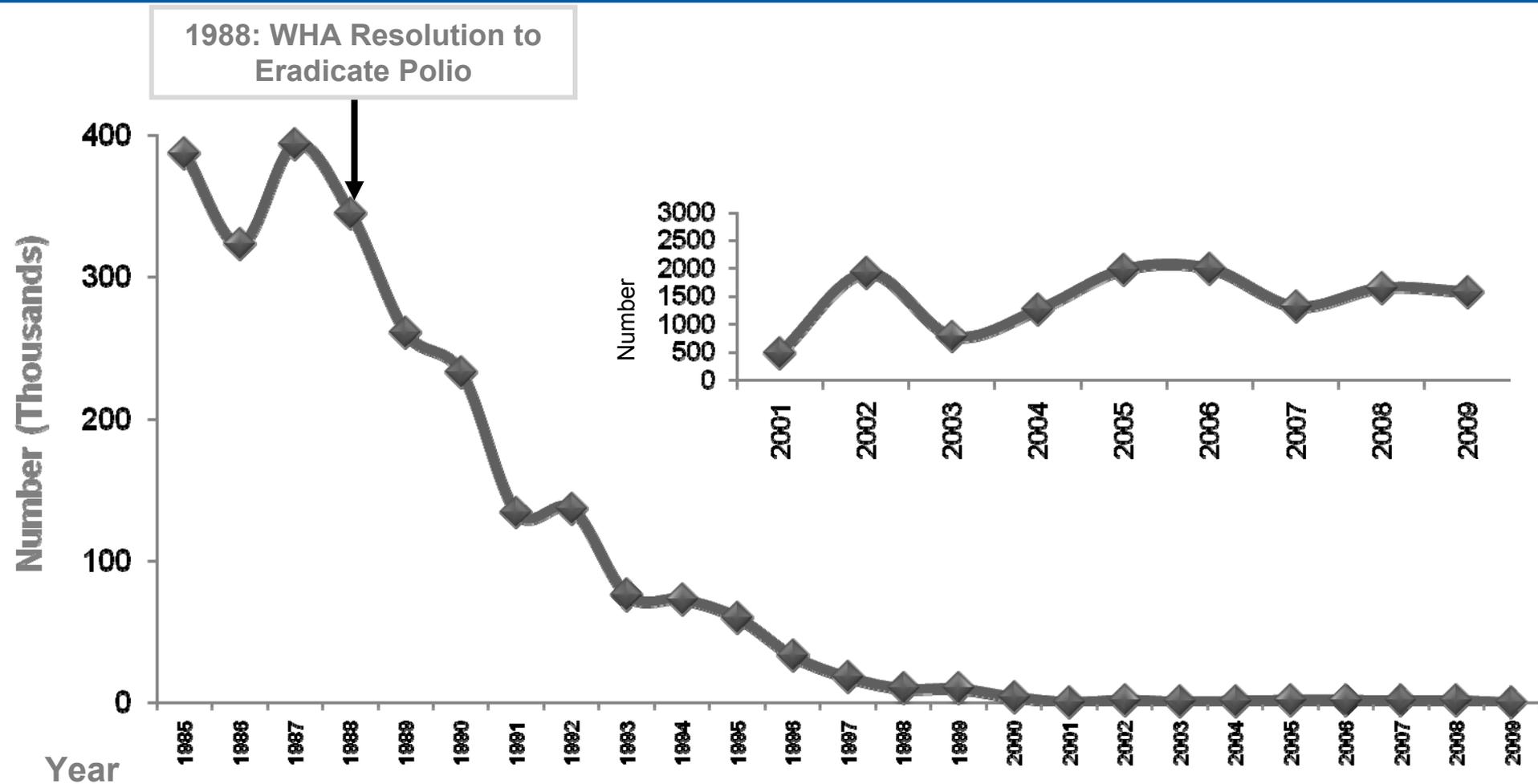
2009
1,579 Cases, 158 Deaths
in 23 Countries
4 Endemic Countries

Data as of 12 January 2010

Endemic, as used by WHO, indicates countries that have never interrupted WPV transmission



Global Progress since 1988: Polio Cases, 1985-2009

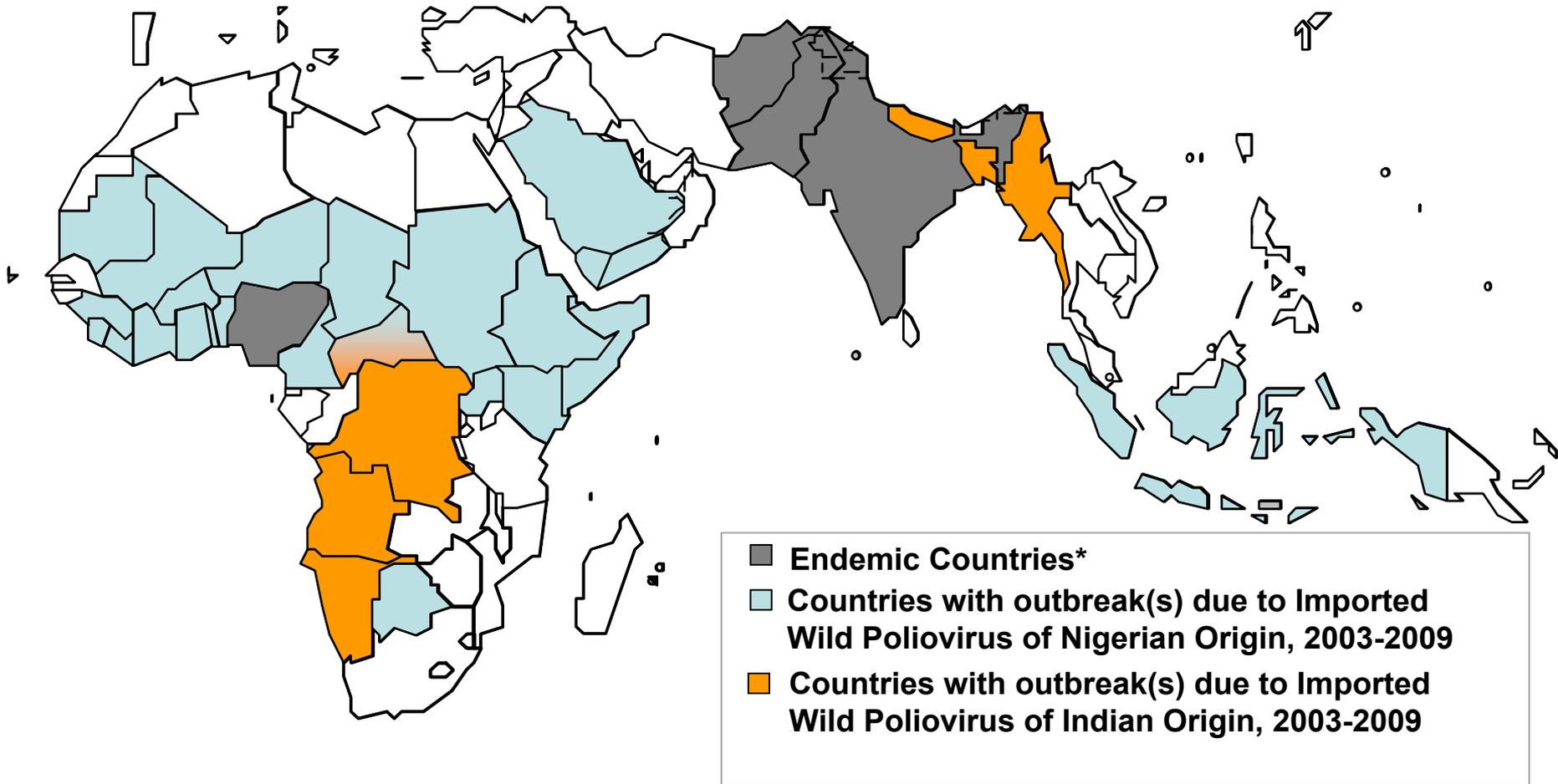


Source: WHO/Polio database 193 WHO Member States



Pattern of Poliovirus Importation/Spread, 2003-2009

Special Importance of India and Nigeria

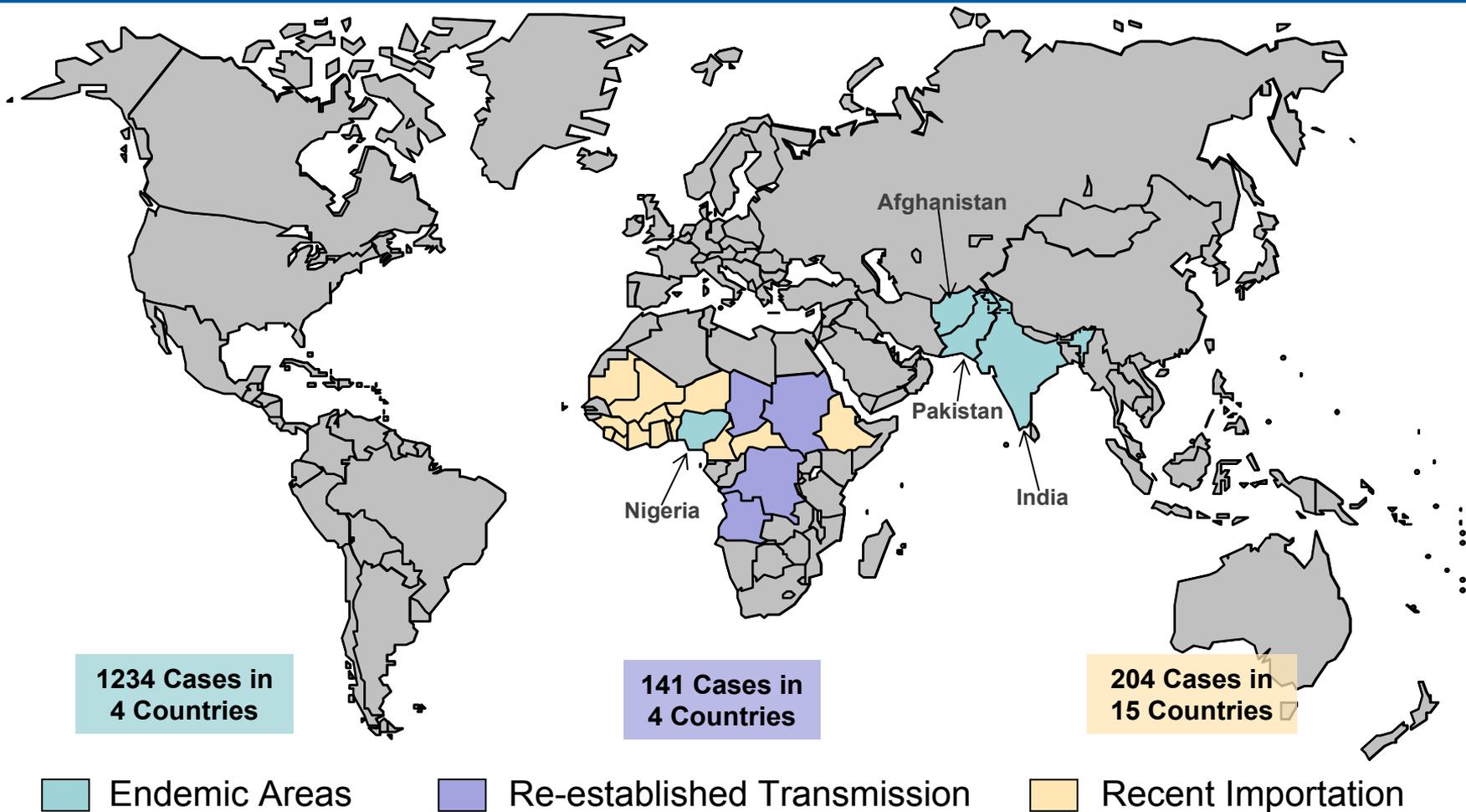


*Never interrupted transmission



Poliovirus Transmission, 2009

Definitions and Geographic Focus



THE GLOBAL PICTURE OF POLIO

- ❑ Background

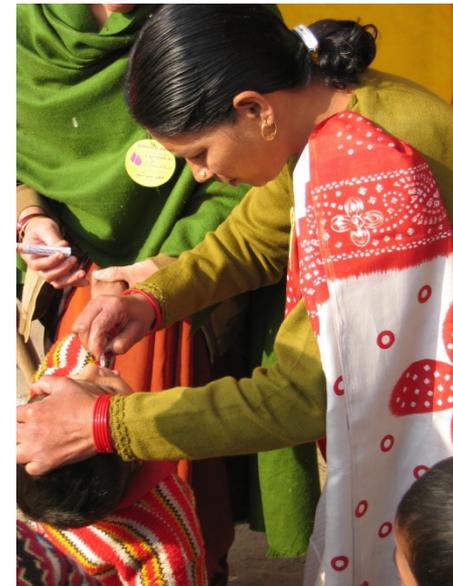
- ❑ Progress since 1988

- ❑ **Addressing the Remaining Challenges**

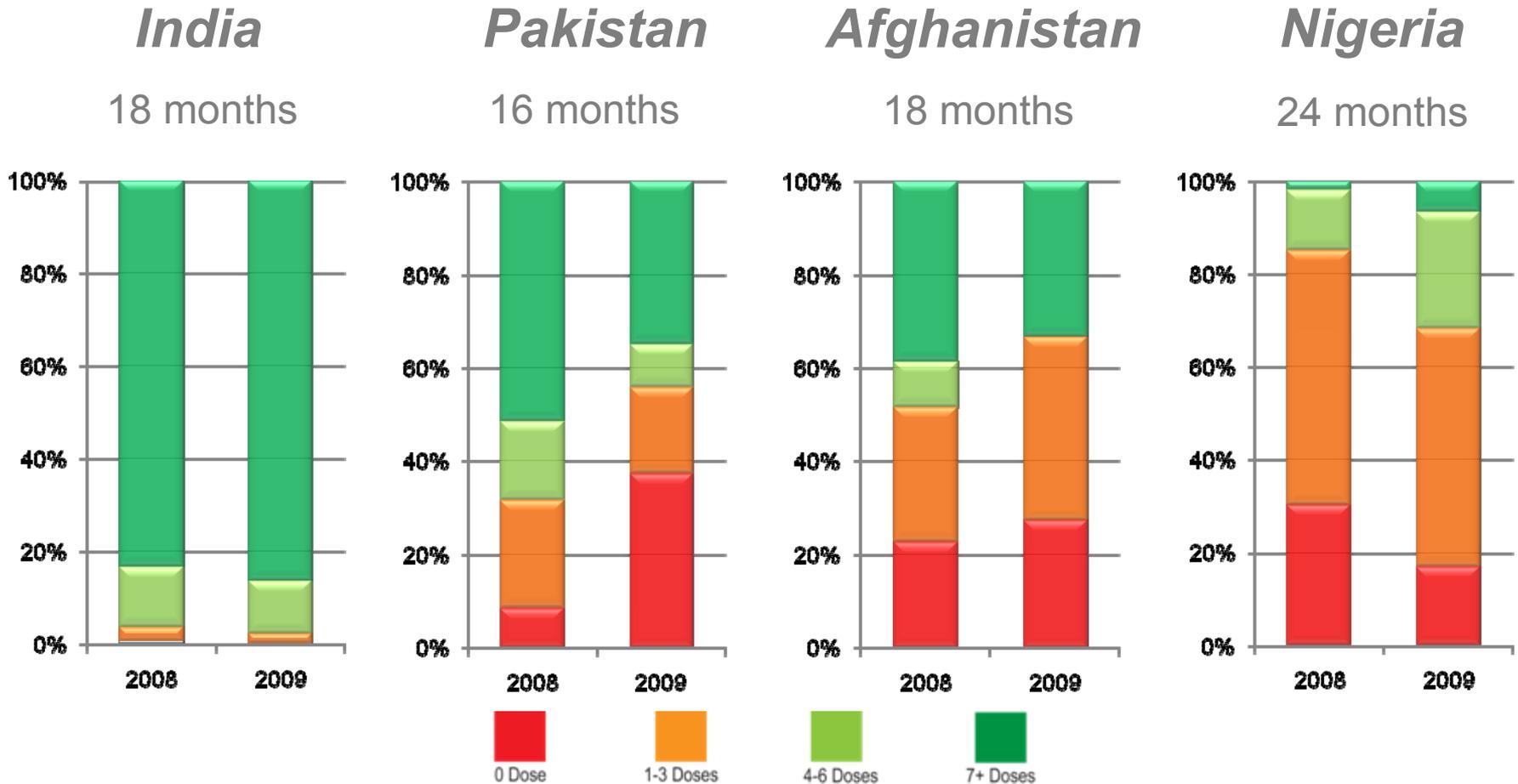
- Failure to vaccinate

- Vaccine failure

- ❑ **Global Importance of India**



Median Age and OPV Status of Polio Cases, 'Endemic' Countries, 2008 and 2009



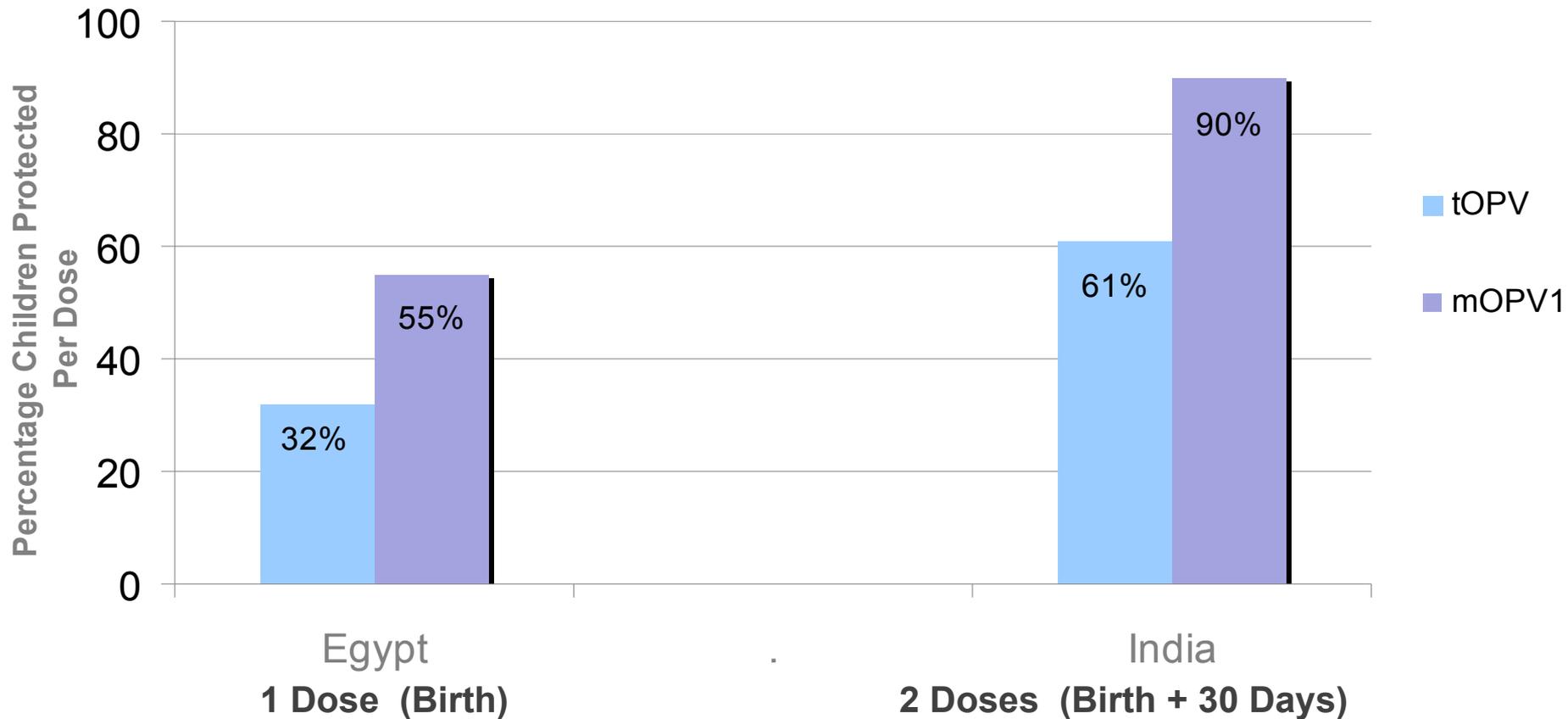
As of 05 January 2010, WHO data

OPV, Oral Polio Vaccine



Immunogenicity of Monovalent OPV1 vs. Trivalent OPV

Randomized Clinical Trials



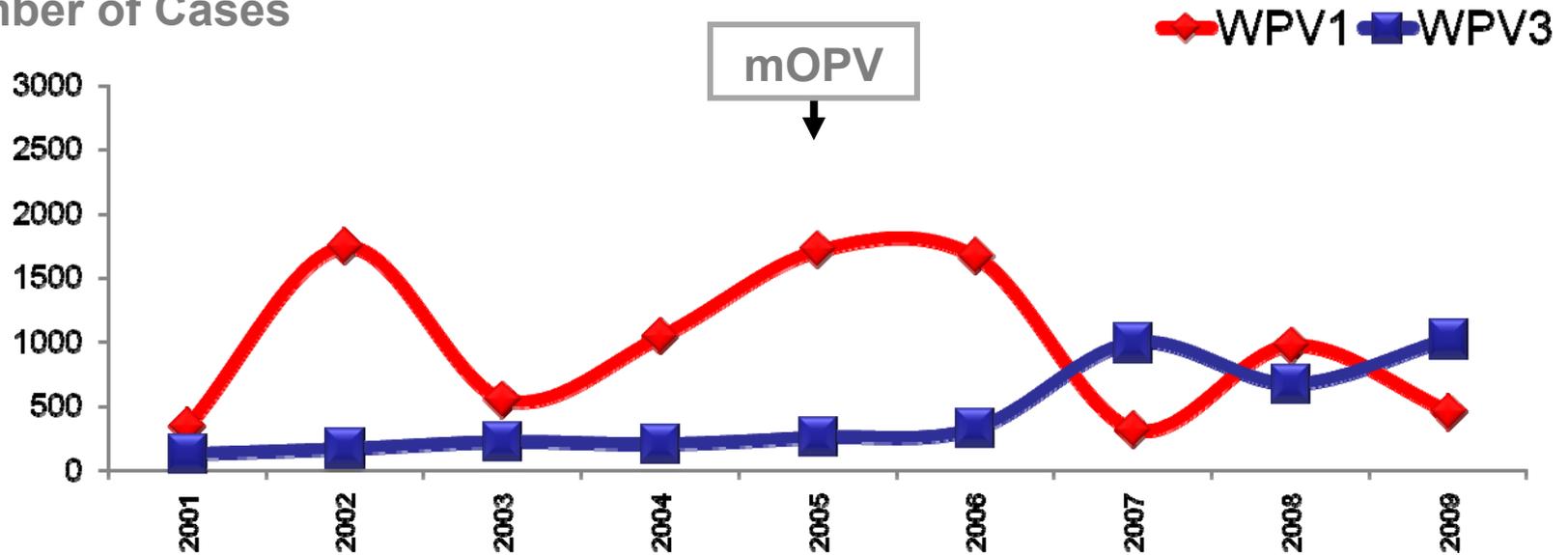
OPV, Oral Polio Vaccine





Global Polio Cases by Serotype, 2001-2009

Number of Cases



Source: WHO/Polio database 193 WHO Member States

mOPV, Monovalent Oral Polio Vaccine





THE GLOBAL PICTURE OF POLIO

- ❑ Background
- ❑ Progress since 1988
- ❑ Assessing the Remaining Obstacles
- ❑ **Global Importance of India**





Importance of India to Achieving Global Polio Eradication

**Historically, epicenter of polio in the world,
#1 in current polio burden**

Major exporter of poliovirus today



DEFINING THE CHALLENGES IN INDIA AND REFINING THE STRATEGIES AND TOOLS TO ACHIEVE POLIO ERADICATION



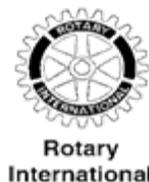
Hamid Jafari, MD
Medical Epidemiologist
Global Immunization Division,
National Center for Immunization and Respiratory Diseases

Project Manager
National Polio Surveillance Project:
World Health Organization, New Delhi, India
and Government of India



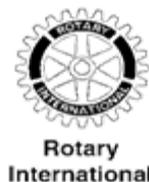
DEFINING THE CHALLENGES IN INDIA AND REFINING THE STRATEGIES AND TOOLS TO ACHIEVE POLIO ERADICATION

- ❑ Recent History of Polio in India
- ❑ Current Status of Polio in India
- ❑ Challenges
- ❑ Strategy Adjustments in 2010 to Achieve Polio Eradication in India



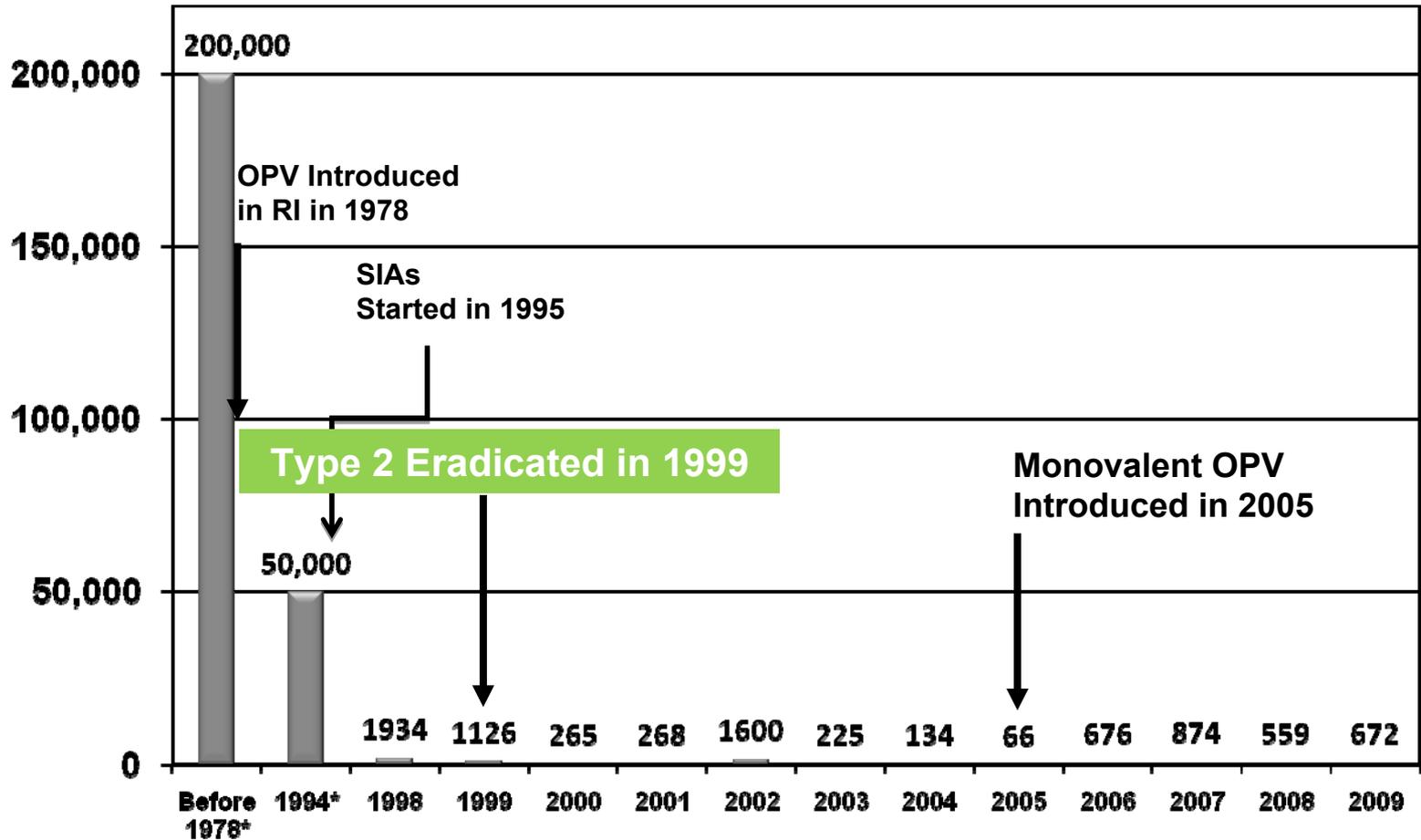
DEFINING THE CHALLENGES IN INDIA AND REFINING THE STRATEGIES AND TOOLS TO ACHIEVE POLIO ERADICATION

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Recent History of Polio in India

Number of Cases

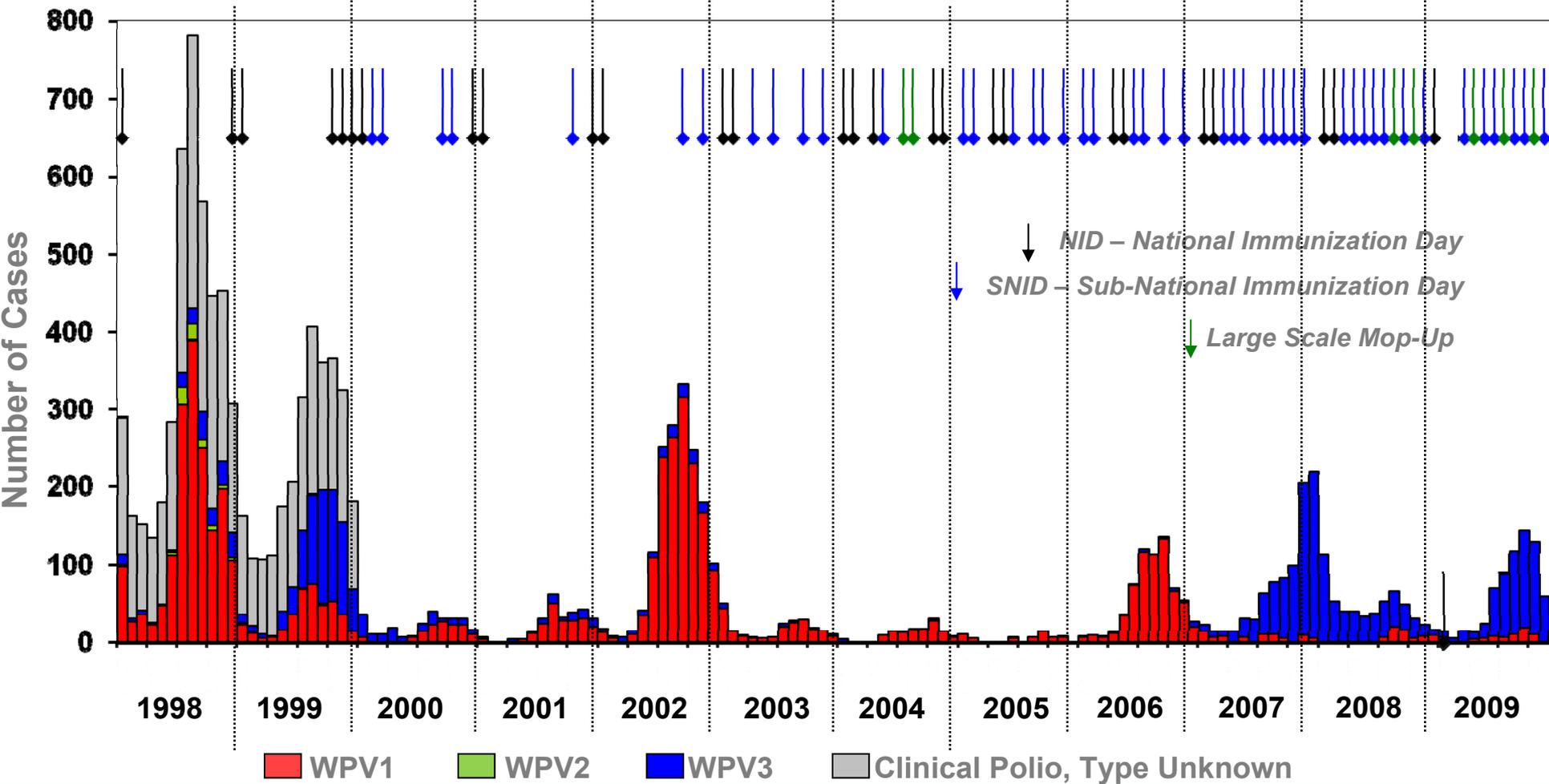


Based on estimates by Indian Academy of Pediatrics and World Health Organization

OPV, Oral Polio Vaccine
 RI, Routine Immunization
 SIAs, Supplementary Immunization Activities



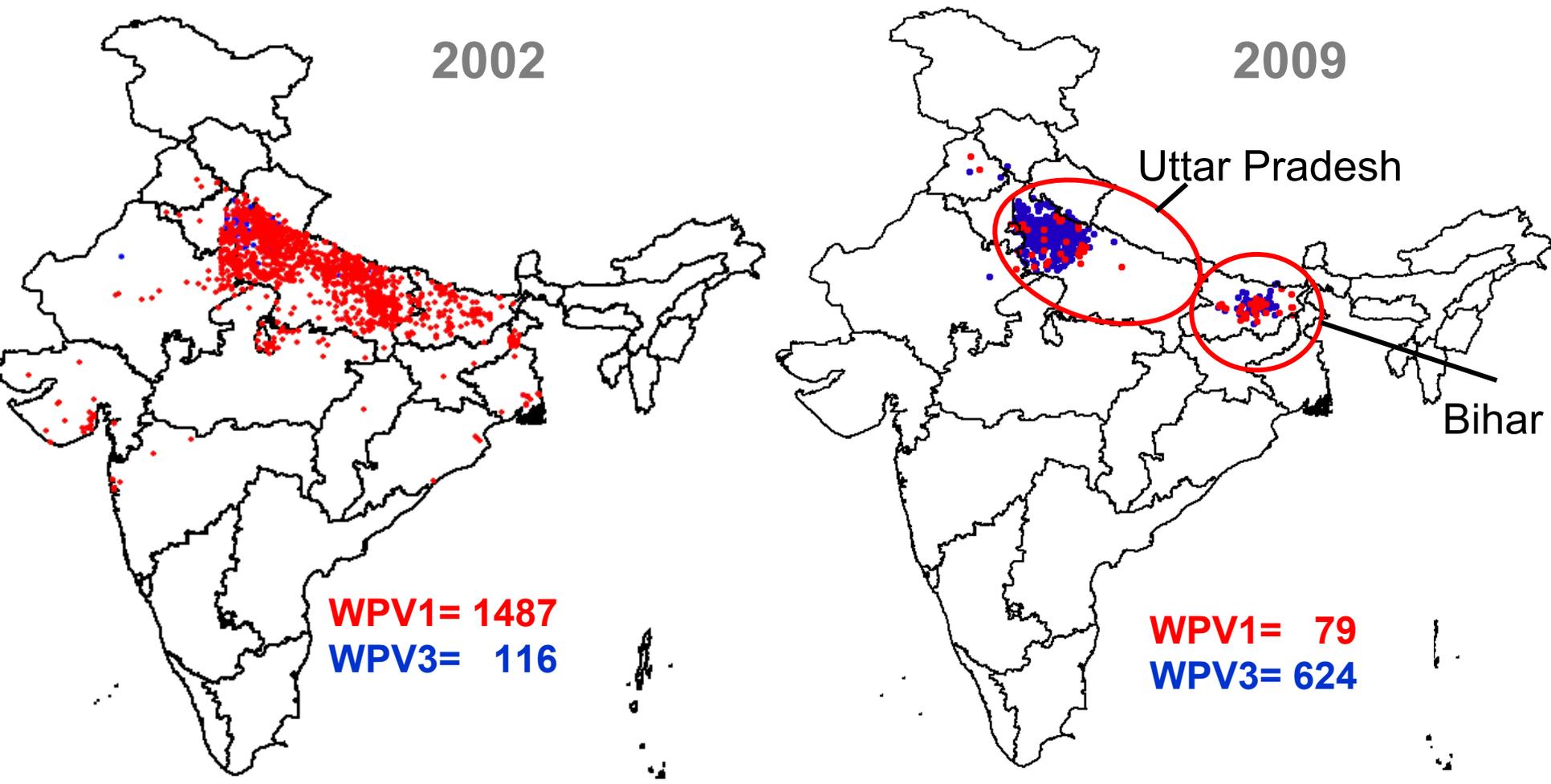
Monthly Incidence of Polio by Serotype India, January 1998 – December 2009



Data as of 9 January 2010, National Polio Surveillance Project (NPSP)



Location of Wild Poliovirus Cases by Serotype India, 2002 and 2009



Data as of 05 Jan 2010, National polio Surveillance Project

WPV1, Wild polio virus type 1
WPV3, Wild polio virus type 3



Importance of Uttar Pradesh and Bihar in Polio Eradication

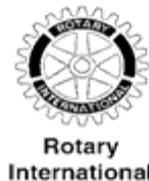
- ❑ **Since 2002, western Uttar Pradesh (UP) and Bihar have been the only endemic reservoirs for WPV circulation and spread**
- ❑ **Circulating strains in the two endemic states have frequently spread to each other**
 - Bihar stopped WPV3 transmission for 3.5 years (2004-07); WPV3 then reintroduced from UP
 - Western UP stopped WPV1 transmission for 16 months (Jan 2007 – May 2008); WPV1 then reintroduced from Bihar
- ❑ **There is extensive population movement from UP and Bihar and between the two states; imperative that elimination of poliovirus is concurrent in these states**

Importance of Uttar Pradesh and Bihar in Polio Eradication (cont'd)

- ❑ **During statewide supplementary immunization activities (SIAs) in UP and Bihar:**
 - 49 million houses are visited during house-to-house vaccination
 - 5 million children are vaccinated while in transit – train stations, bus terminals, major crossings, etc.
 - A total of 58 million children <5 years of age are vaccinated
- ❑ **The assessed routine immunization coverage with 3 tOPV doses in UP and Bihar is 40% and 53%, respectively**

DEFINING THE CHALLENGES IN INDIA AND REFINING THE STRATEGIES AND TOOLS TO ACHIEVE POLIO ERADICATION

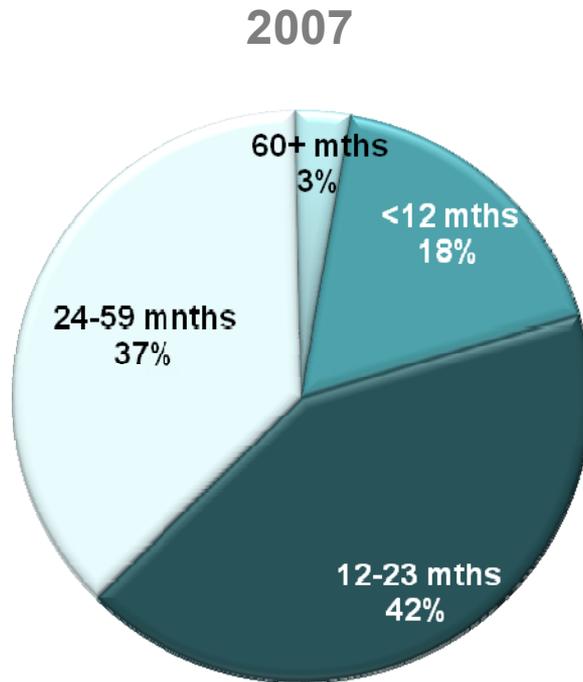
- Recent History of Polio in India
- **Current Status of Polio in India**
- Challenges
- Strategy Adjustments in 2010 to Achieve Polio Eradication in India



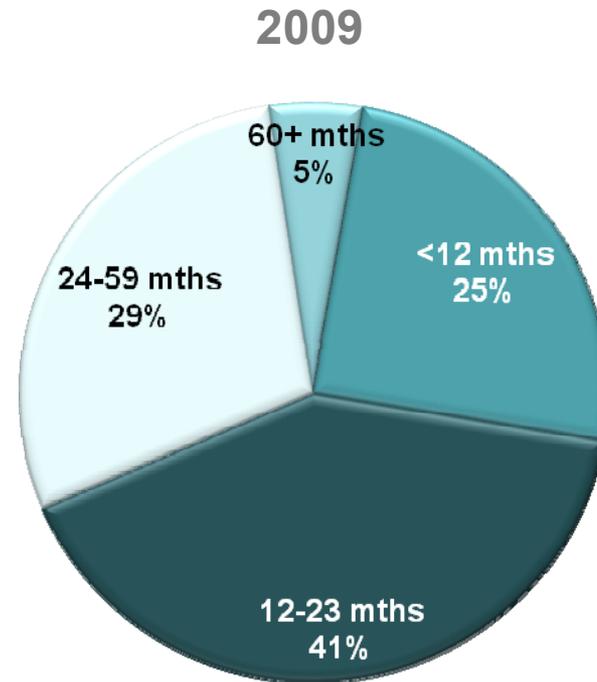
Current Status of Polio in India

- ❑ **89% of all polio cases in 2007-2009 were due to WPV3**
- ❑ **The WPV3 epidemiology is explained by the vaccination strategy – preferential use of type 1 mOPV**
- ❑ **Extensive use of mOPV1 in UP and Bihar has resulted in reduction of WPV1 geographic spread and genetic diversity**
- ❑ **Yet, transmission has persisted and ~80 WPV1 cases have occurred annually during 2007-2009**
- ❑ **Rest of India has maintained polio control using routine immunization and only two tOPV SIA activities per year**

Distribution of Polio Cases by Age India, 2007-2009



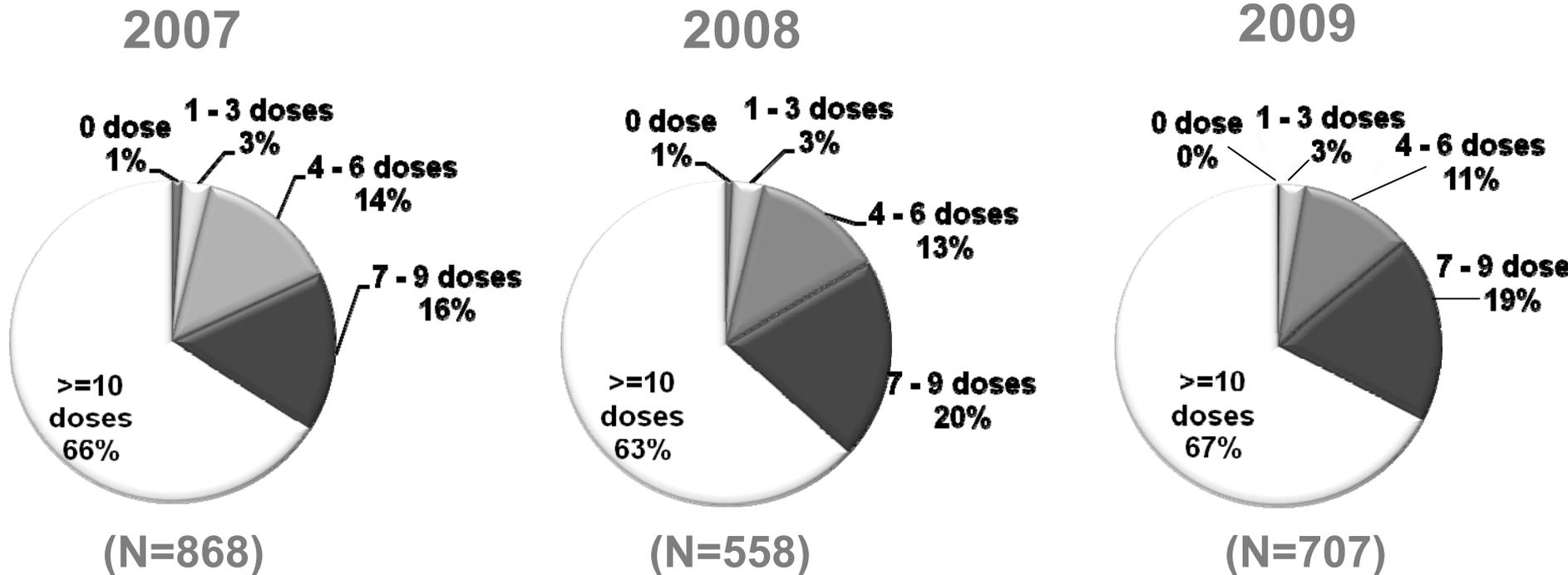
(N=874)



(N=721)

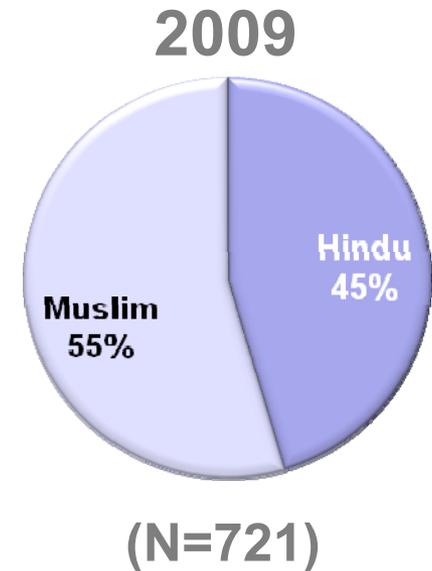
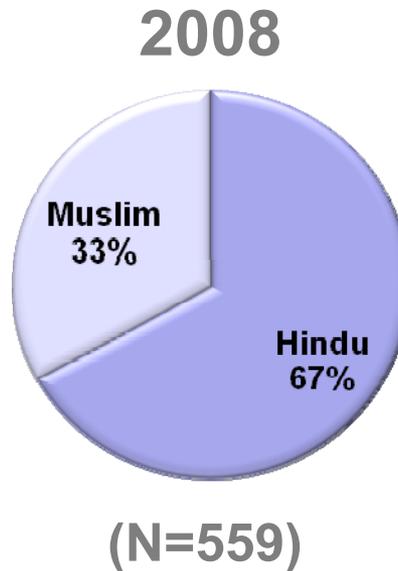
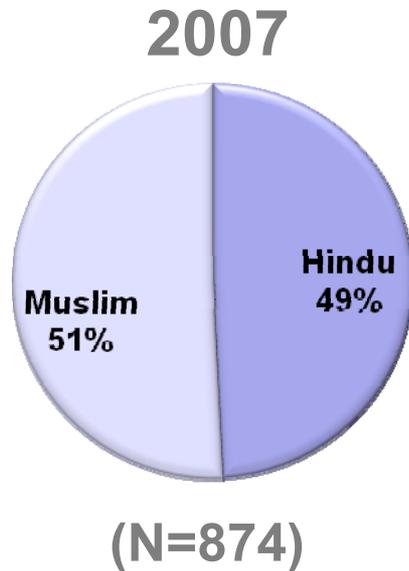
60% of Polio Cases are Less Than 24 Months of Age

OPV Vaccination Status of Polio Cases India, 2007-2009



>80% of Polio Cases in India during 2007-09 have reportedly received 7 or more doses of OPV

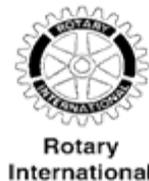
Distribution of Polio Cases by Religion India, 2007-2009



13% of the population in India is Muslim; proportion of Muslims among cases mainly related to population distribution in areas of transmission

DEFINING THE CHALLENGES IN INDIA AND REFINING THE STRATEGIES AND TOOLS TO ACHIEVE POLIO ERADICATION

- Recent History of Polio in India
- Current Status of Polio in India
- **Challenges**
- Strategy Adjustments in 2010 to Achieve Polio Eradication in India





Main Challenges to Polio Eradication in India

Challenge 1: Failure to Vaccinate

- ❑ Community resistance
- ❑ Poor quality of SIAs in some areas
- ❑ Reaching hard-to-reach sub-populations

Challenge 2: Vaccine Failure due to Sub-optimal OPV Effectiveness



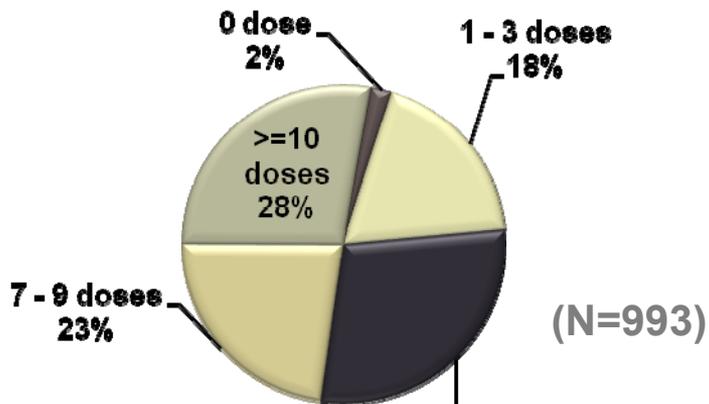
Progress in Addressing Failure to Vaccinate: Community Resistance

- ❑ **Until 2004, there was substantial resistance to OPV in many Muslim minority communities of western UP**
- ❑ **Muslim children were under-vaccinated compared to their Hindu counterparts**
- ❑ **Following extensive social mobilization and engagement of local leaders and institutions, the disparity in vaccination rates has been eliminated**
- ❑ **Refusal to vaccinate is now at very low levels; less than 0.1% families in high-risk areas of western UP refuse vaccination in SIA rounds**

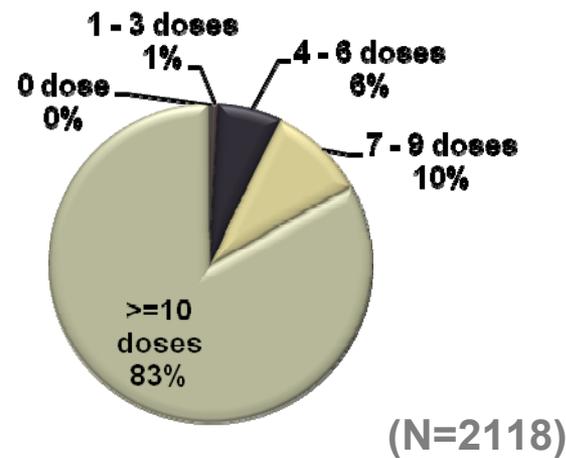
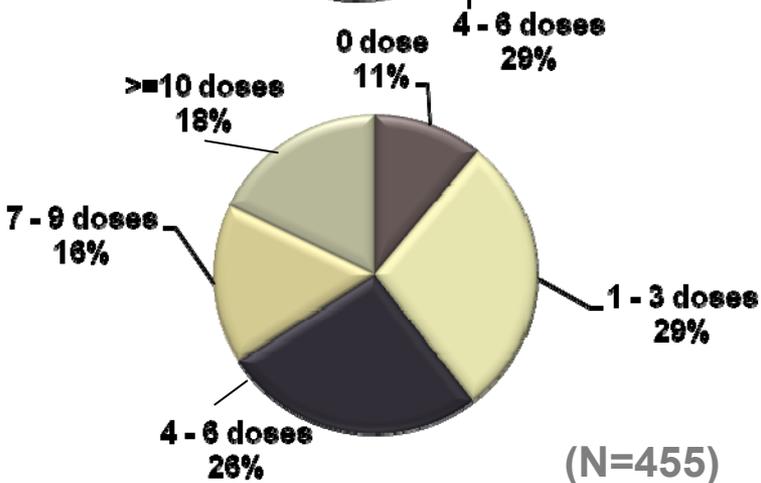
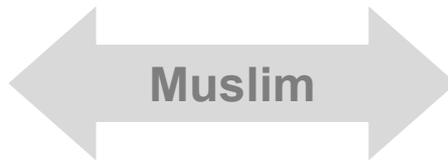
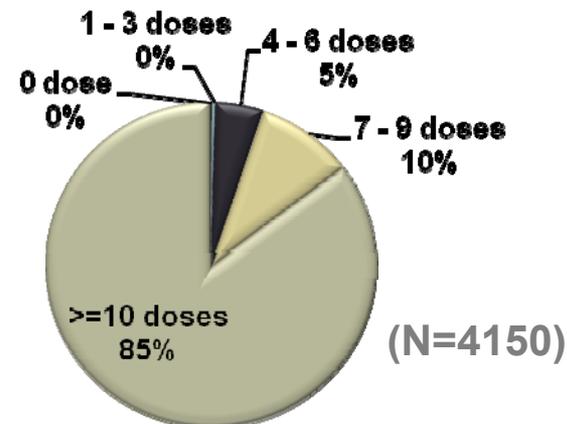
Reported OPV Doses among Non-Polio Cases of Acute Flaccid Paralysis, Uttar Pradesh

Children 6-59 Months of Age

2002



2008

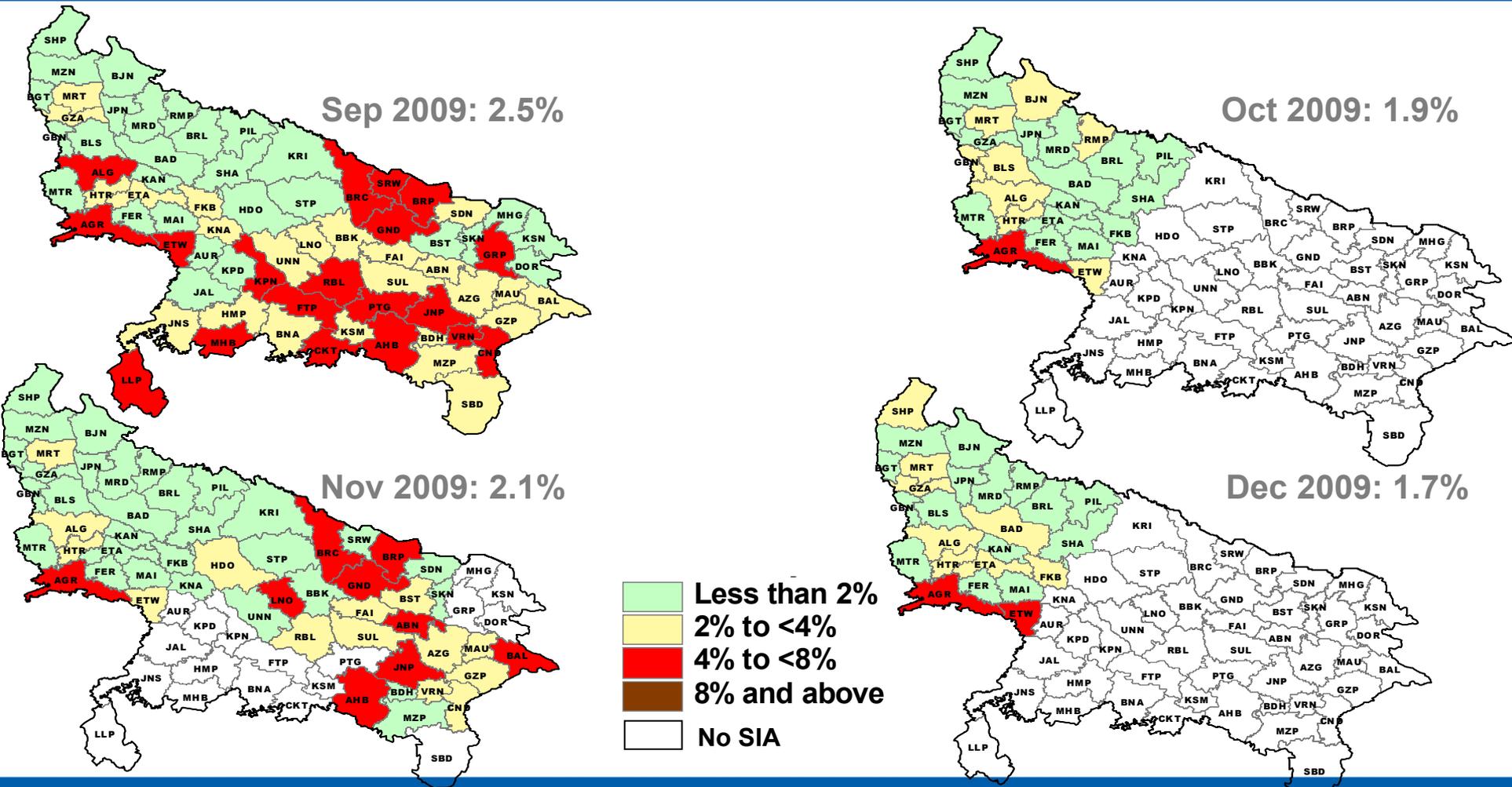


OPV, Oral Polio Vaccine



Progress in Addressing Failure to Vaccinate: Overall Improved Quality of SIAs

Surveys to Assess Percent Children Missed, Uttar Pradesh



Monitoring Data, National Polio Surveillance Project

SIAs, Supplementary Immunization Activities



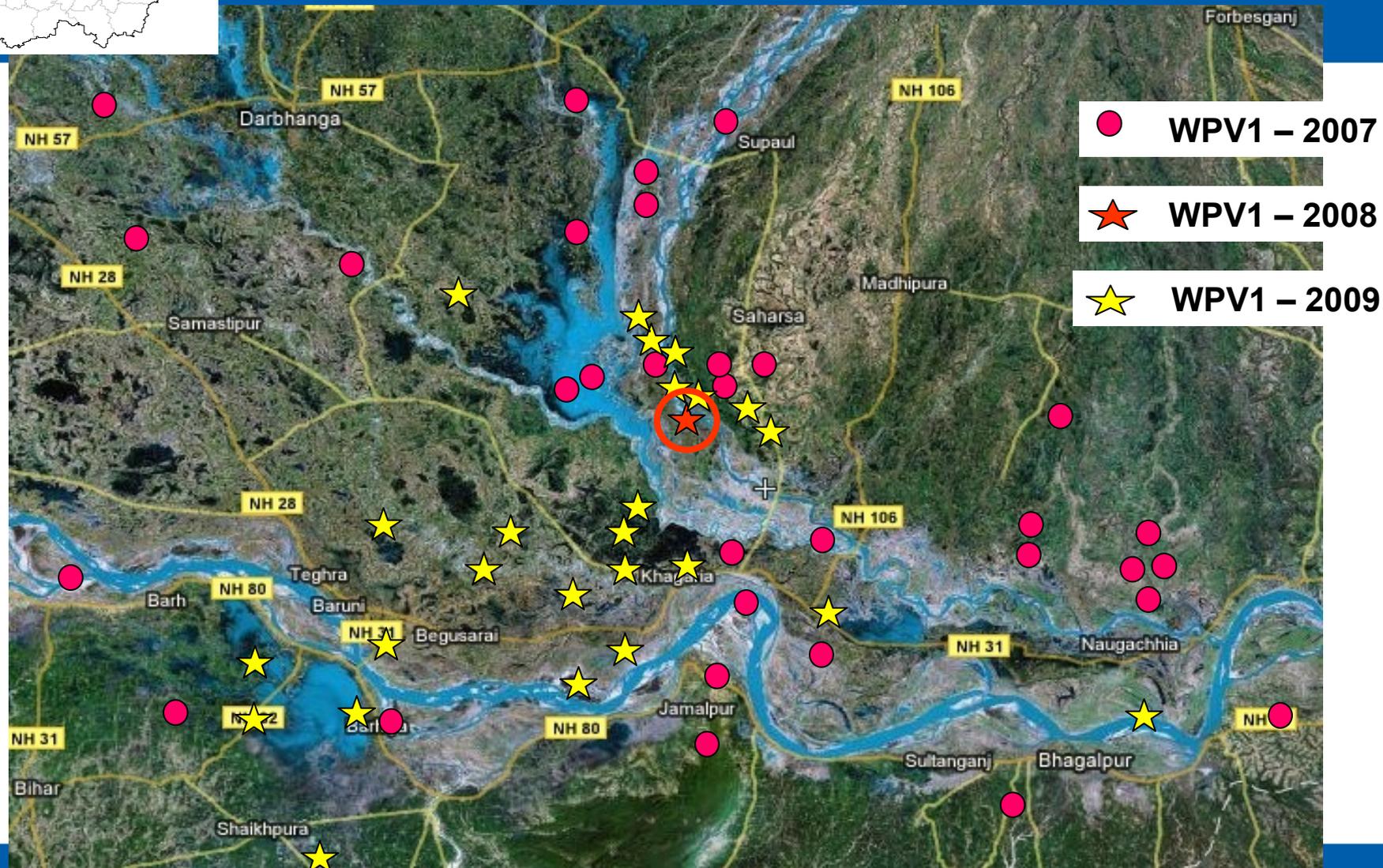


Progress in Addressing Failure to Vaccinate: Accessing Hard-to-Reach Children

- ❑ **Annual flooding of underserved Kosi River districts of central Bihar**
 - Population migration to higher grounds and other states
 - Farming in dry months with families in scattered field huts
- ❑ **Mobile populations in general**
 - Migrant labor families: construction sites, brick kilns, farms
 - Nomads



Kosi River Flood Plain, Bihar, India



Data as of 23 October 2009



Kosi River Area, Bihar, India



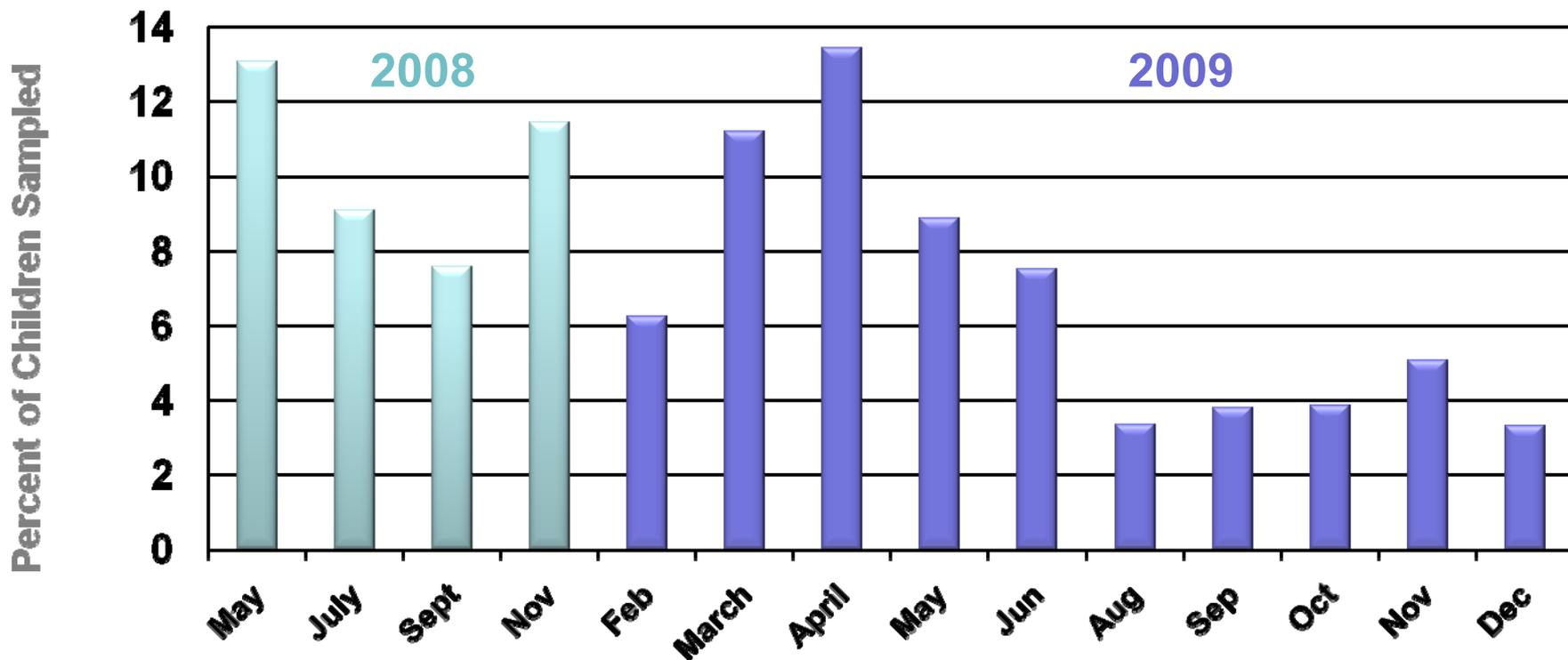
Difficult terrain to access children in widespread farming huts. Extremely challenging to supervise and monitor

Photographs courtesy of National Polio Surveillance Project

Percent of Sampled Children Remaining Unimmunized on Monitoring of Field Huts after SIAs

Kosi Area, May 2008 – Dec 2009

3,000 Children Checked Each Round

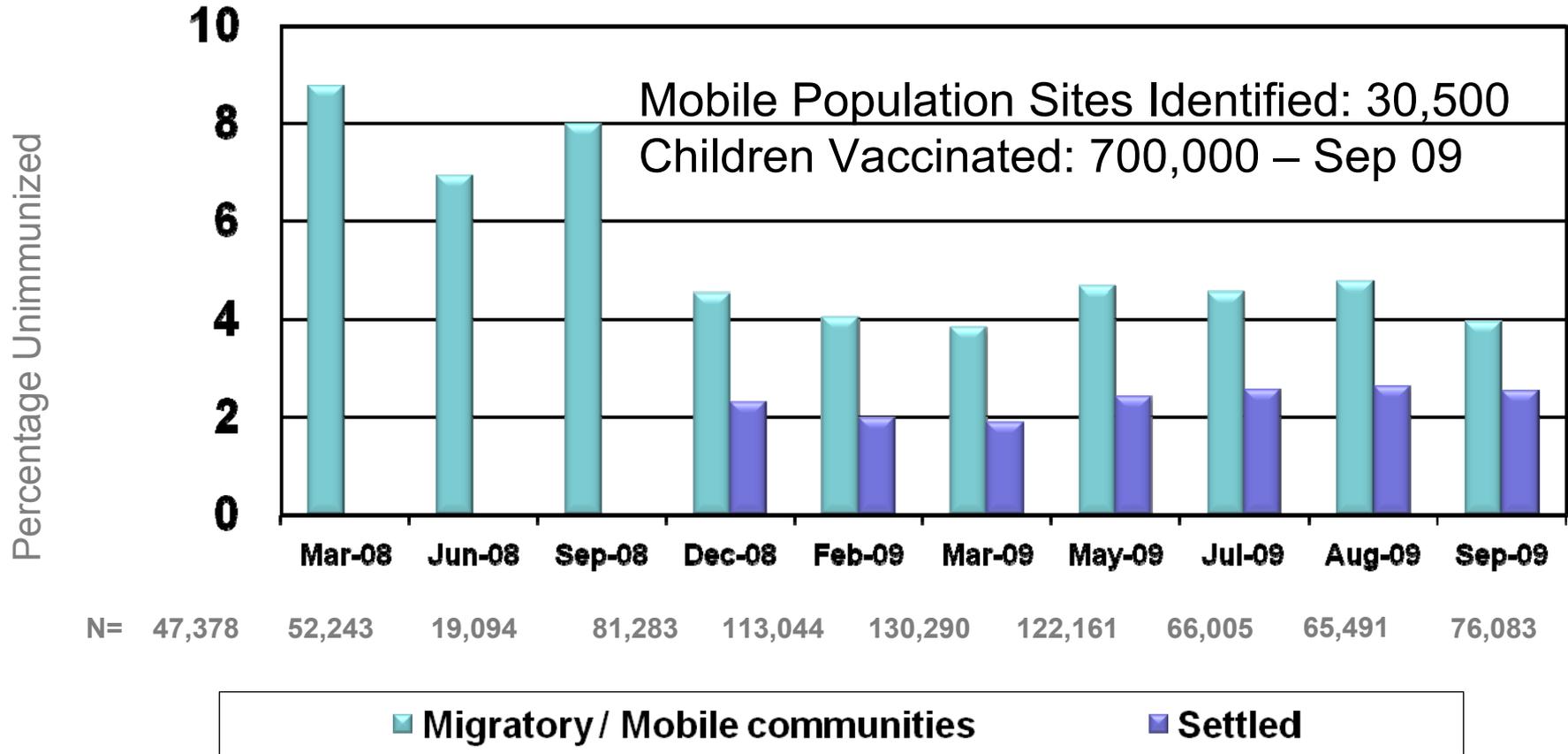


Data as of 13 Jan 2010, National Polio Surveillance Project



Percent of Sampled Children Missed Among Mobile and Settled Populations

Uttar Pradesh, March 2008 – September 2009, UP



Summary of Progress in Addressing Failure to Vaccinate

- ❑ **The resistance to vaccination in minority communities has been largely overcome**
- ❑ **Overall high coverage is being achieved in SIAs**
 - <3% children in UP and <1% in Bihar overall, are found unimmunized at the end of an SIA round
 - >80% of polio cases have received 7 or more OPV doses
- ❑ **The coverage among hard to reach populations has improved considerably, only around 4% are being missed per round**

The challenge of failure to vaccinate has largely been addressed; coverage levels in India are higher than almost anywhere else in the world



Main Challenges to Polio Eradication in India

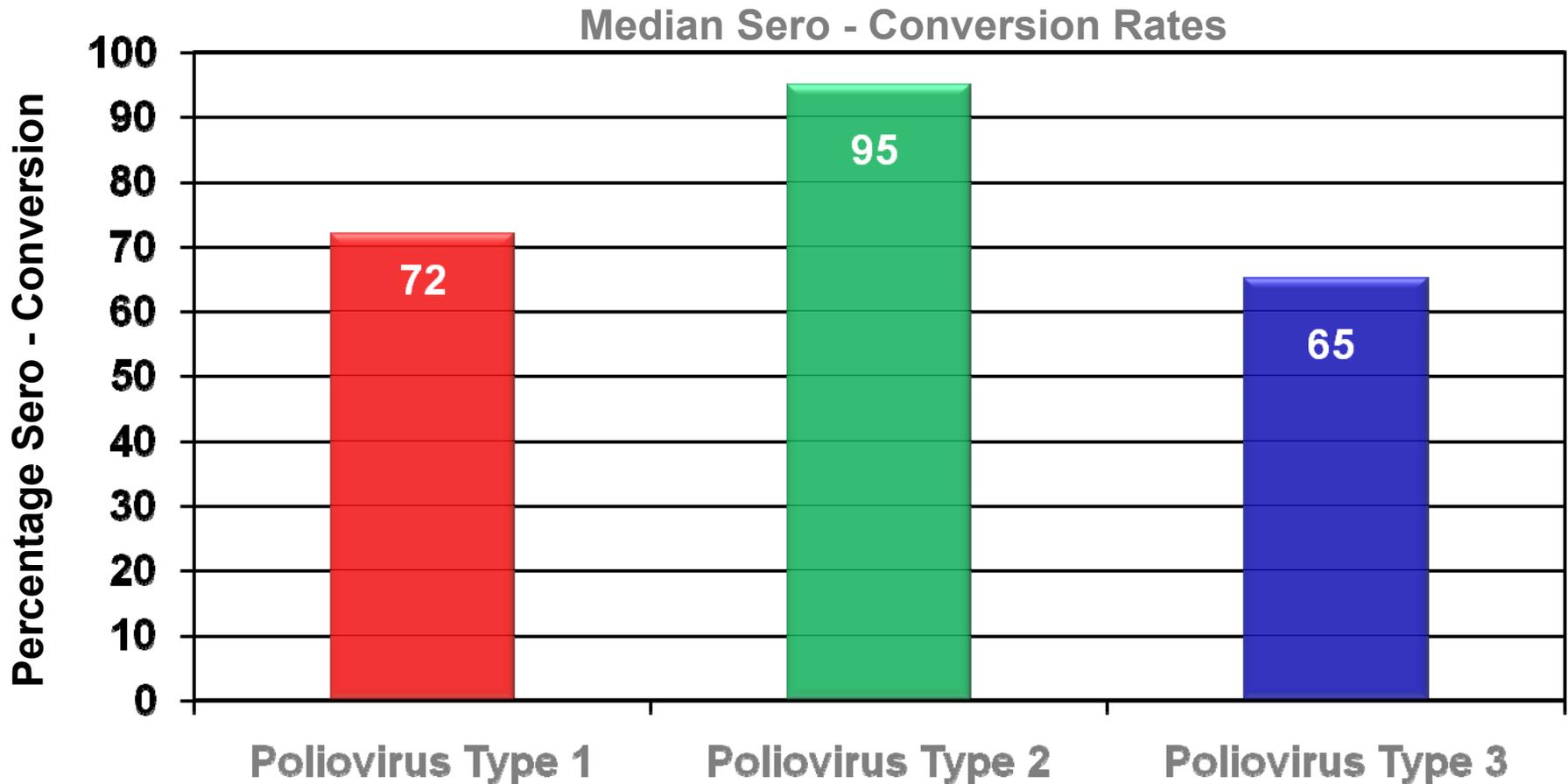
Challenge 1: Failure to Vaccinate

- Community resistance
- Poor quality of SIAs in some areas
- Reaching hard-to-reach sub-populations

Challenge 2: Vaccine Failure due to Sub-optimal OPV Effectiveness



Vaccine Failure: 3-Dose tOPV Immunogenicity in Developing Countries



Vaccine Failure: Per Dose Effectiveness of tOPV Compared with mOPV1 against WPV1

Case-Control Study Using AFP Surveillance Data 1997-2006

Vaccine	Location	Vaccine effectiveness (%) (95% CI)
Trivalent	Uttar Pradesh	11 (7 - 14)
	Bihar	19 (8 - 29)
	Rest of India	23 (17 - 29)
Monovalent	Uttar Pradesh	30 (19 - 41)**
	Bihar	18 (0 - 43)
	Rest of India	36 (0 - 72)

** Significantly Higher Than Trivalent Vaccine in UP



Strategies to Address Sub-optimal OPV Effectiveness

- ❑ **Increased frequency of SIAs since 2005**
- ❑ **Improved coverage of SIAs**
- ❑ **Use of monovalent OPVs since 2005**

Confirming Impact on Serologic Immunity

- ❑ **Is high vaccination coverage being achieved?**
- ❑ **Is the mOPV1 effective?**
 - Serosurveys in 2007 and 2009 of children in an endemic district of western UP
 - Serosurvey of acute flaccid paralysis case-patients 2008-09 in 25 districts of western UP

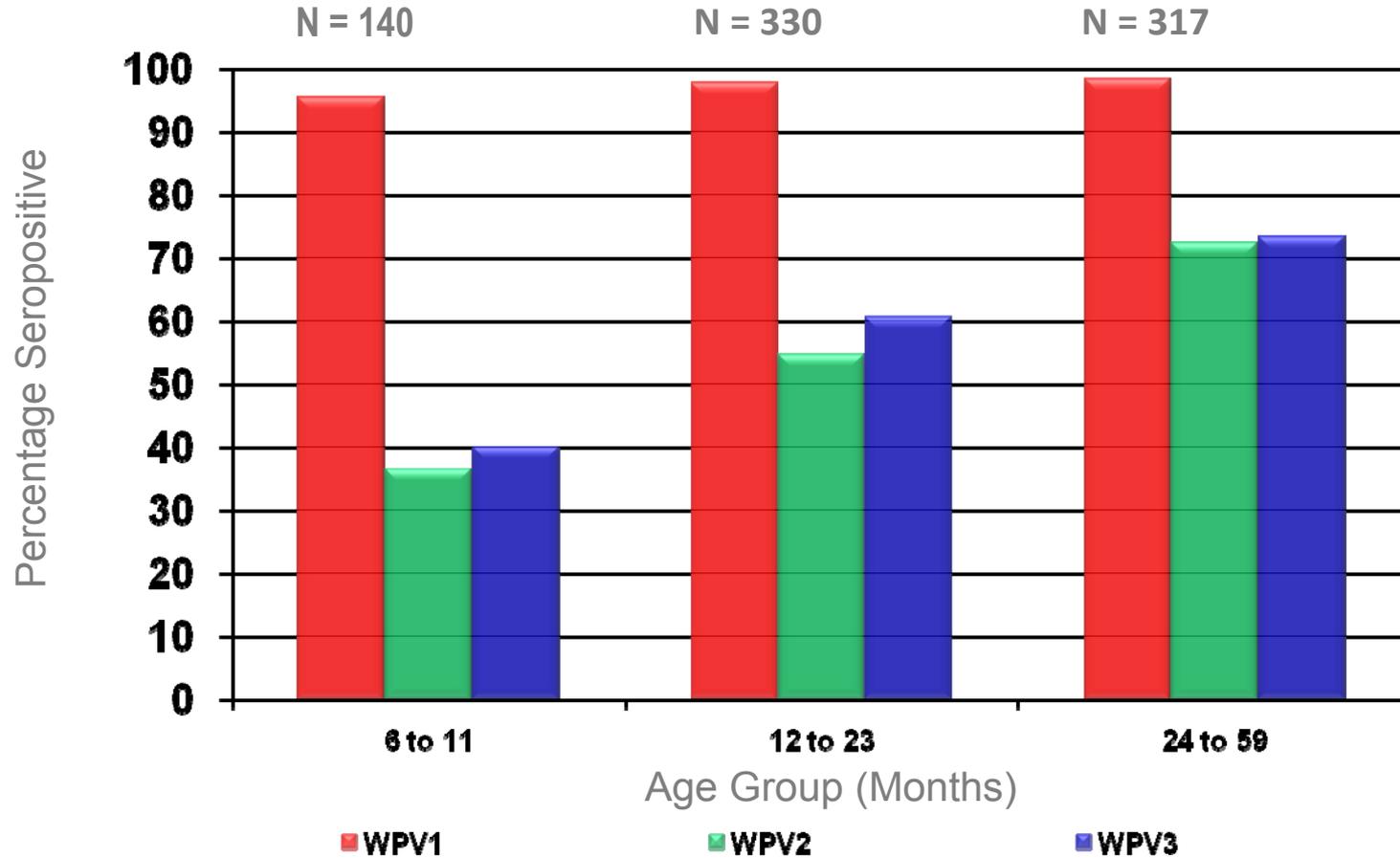
Seroprevalence in Children 6-9 Months Old, by Serotype, Western UP, 2007 and 2009

Study	November 2007 N=923	April 2009 N=1002
WPV1	81%	99%
WPV2	63%	72%
WPV3	71%	48%



Seroprevalence Against WPV among Children with Non-Polio AFP

Western Uttar Pradesh, Nov 2008 – Aug 2009



Major Findings on Serologic Immunity

- ❑ Evidence of high immunogenicity of mOPVs in endemic and non-endemic settings in India
- ❑ High levels of serological immunity against WPV1 in western UP
- ❑ Low levels of serological immunity against WPV2 and WPV3 in western UP

Impact of Increased SIA Frequency & Quality and mOPV1 Use

❑ Reduction in genetic diversity and geographic spread of WPV1

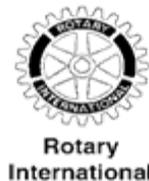
- 12 distinct genetic clusters in 2005
- 3 clusters remained in 2008
- Only 1 cluster detected in 2009

❑ Yet, low level transmission of WPV1 has persisted

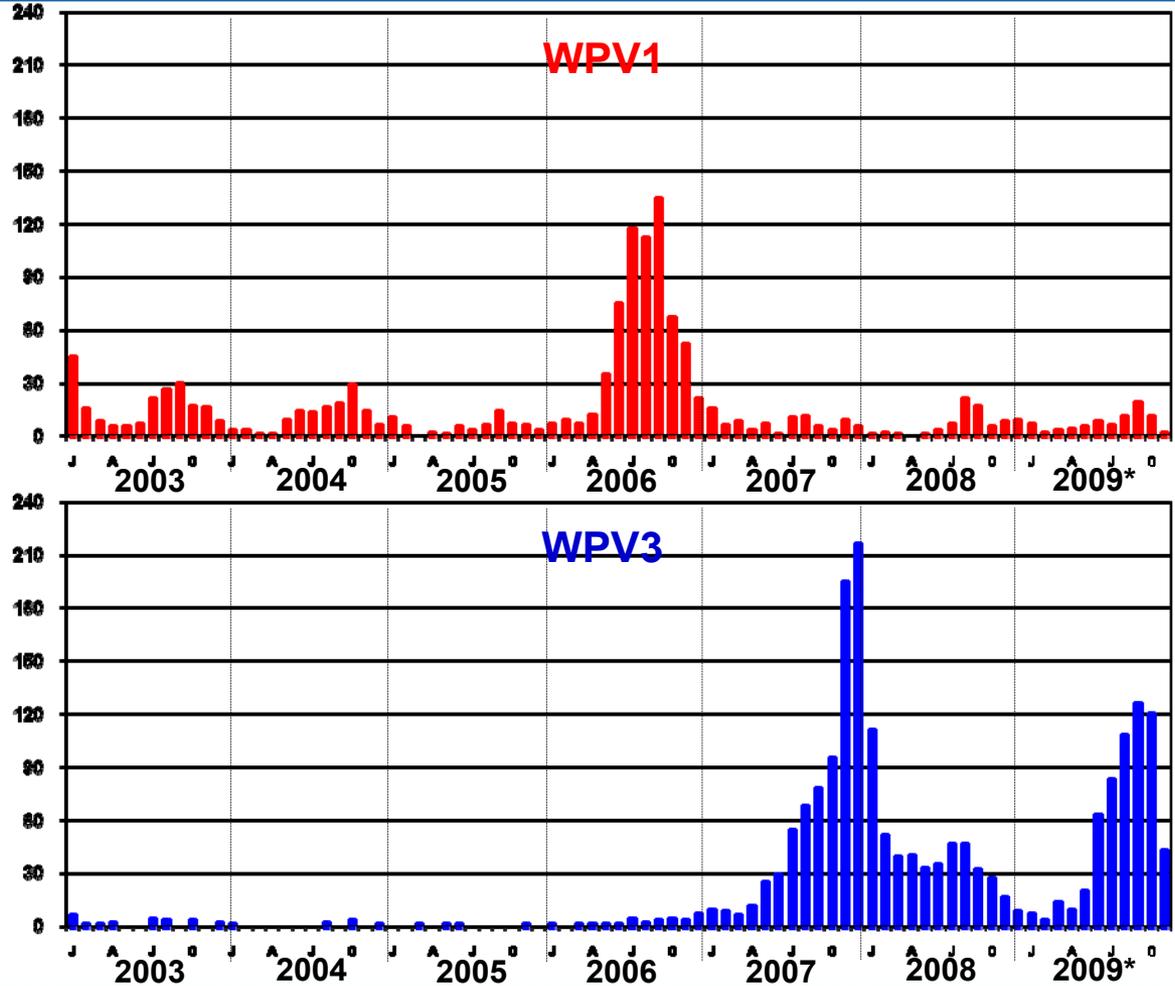
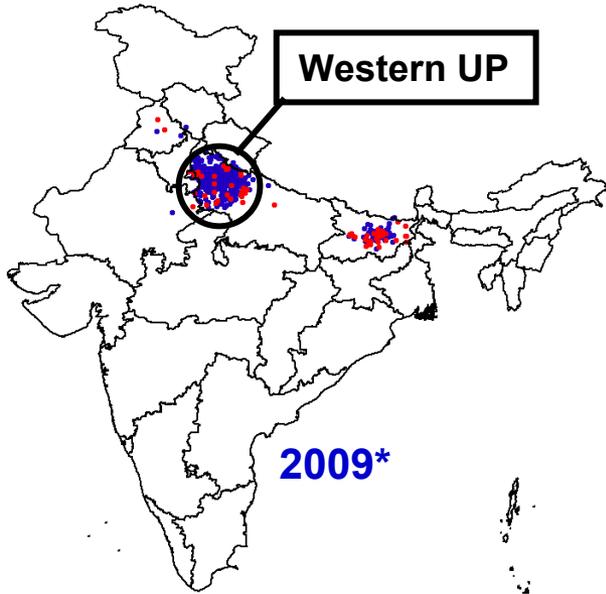
**The persistence of WPV1 remains
a major concern**

DEFINING THE CHALLENGES IN INDIA AND REFINING THE STRATEGIES AND TOOLS TO ACHIEVE POLIO ERADICATION

- Recent History of Polio in India
- Current Status of Polio in India
- Challenges
- **Strategy Adjustments in 2010 to Achieve Polio Eradication in India**



Current Status: Persistent Transmission & Alternating Outbreaks, India 2006-2009



Data as of 12 December 2009, National Polio Surveillance Project

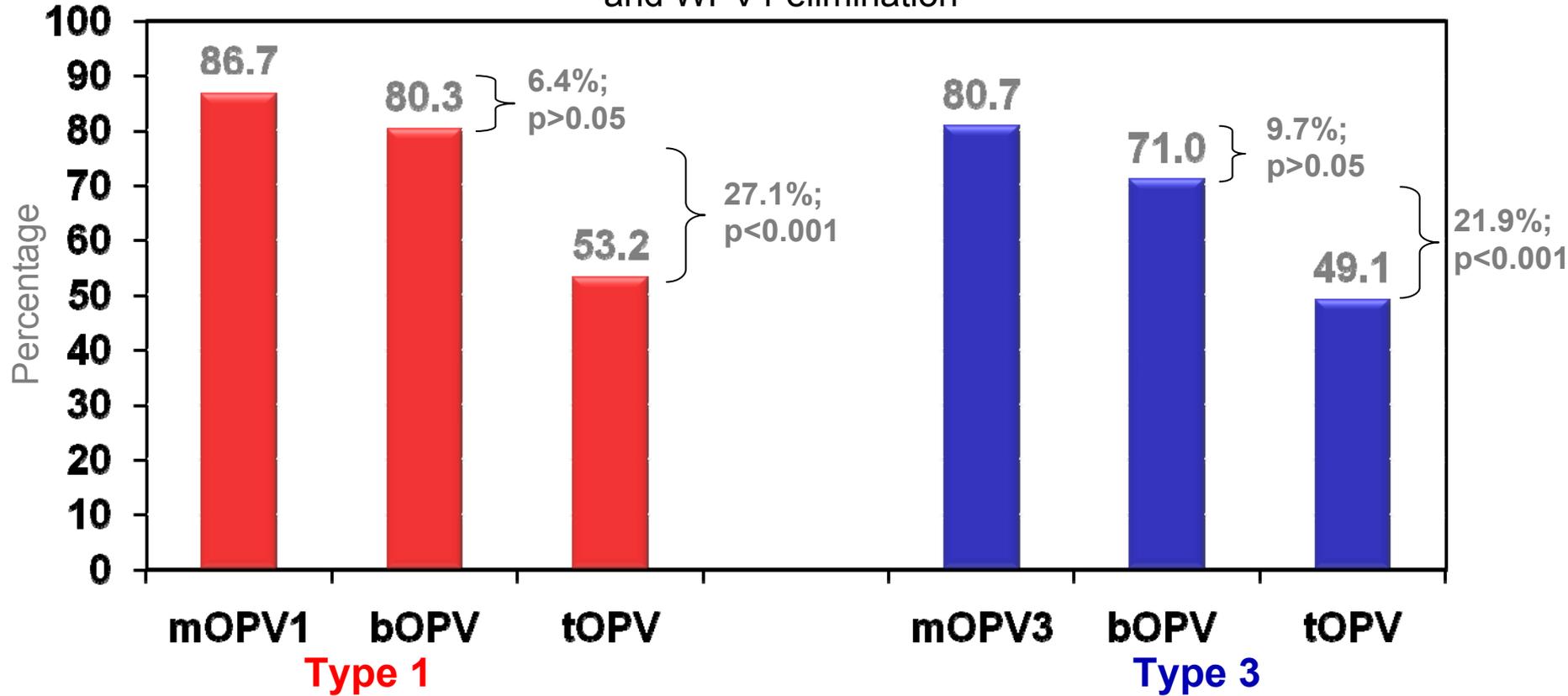




Seroconversion After 2nd Dose, by Study Arm, bOPV Trial

Multi-site, India, 2008-09

bOPV use will enable concurrent WPV3 control
and WPV1 elimination



mOPV, Monovalent Oral Polio Vaccine
bOPV, Bivalent Oral Polio Vaccine





Government of India Strategy Adjustments in 2010

- ❑ **Continue with current intensified vaccination strategy and add bOPV**
 - Encouraged by evidence of high WPV1 immunity and past cessation of transmission in UP
- ❑ **Reluctant to make major changes in strategy**
 - IPV risks: Operational feasibility; loss of confidence in OPV, impact on transmission unclear
 - Change in OPV target age group: insufficient evidence, operational feasibility
- ❑ **Increasing interest in a multi-pronged approach with focus on environment (sanitation, clean water)**
- ❑ **Reassess continuation of eradication program in 24 months**



Summary

- ❑ **High levels of vaccine coverage achieved in India**
- ❑ **High frequency of SIAs has largely overcome the limitations of lower vaccine effectiveness**
- ❑ **There remains a fundamental lack of understanding why it is so difficult to stop transmission in parts of UP and Bihar**
- ❑ **Additional substantial changes to India program strategy should be plausible, feasible and evidence-based**
- ❑ **Research is a current program priority to better understand transmission risk factors and potential options for changes in strategy**



RESEARCH NEEDED TO ACCELERATE POLIO ERADICATION IN INDIA



Mark Pallansch, PhD
Chief, Polio and Picornavirus Laboratory Branch
Division of Viral Diseases,
National Center for Immunization and Respiratory Diseases



Key Research Questions Under Discussion

❑ Serologic immunity

- Can addition of IPV result in high rates of seroconversion faster and with fewer OPV doses among infants?

❑ Mucosal immunity

- Given the intensity of poliovirus transmission in UP and Bihar, is current mucosal immunity insufficient to prevent infection and further transmission among serologically immune children?
- Is there a role for IPV in filling gaps in mucosal immunity?
- Does mucosal immunity wane in older individuals not in the SIA target group? Should it be boosted with OPV?

❑ What are the specific environmental, social, and host risk factors associated with poliovirus transmission?

IPV, Inactivated Polio Vaccine
OPV, Oral Polio Vaccine



Critical Role of Research

- ❑ **Re-examining Assumptions Related to Current Strategies**
- ❑ **Evaluating the Effectiveness of New Interventions**
- ❑ **Addressing New Research Questions on Vaccine Effectiveness**



Providing Science-based Evidence to Inform the Policy Decisions

Critical Role of Research

- Re-examining Assumptions Related to Current Strategies**
- Evaluating the Effectiveness of New Interventions
- Addressing New Research Questions on Vaccine Effectiveness

Re-examining Assumptions: Example 1

□ Assumption

- Rapid acquisition of immunity in the young infants will interrupt transmission because of the critical role of infants in sustaining virus circulation

□ Observations

- Routine immunization of young infants is very poor in areas of remaining polio circulation
- Vaccine effectiveness per dose can be generalized as:
IPV > mOPV ≈ bOPV > tOPV

□ Expectation

- Use of more effective vaccines will lead to acquisition of immunity more quickly leading to stopping polio transmission

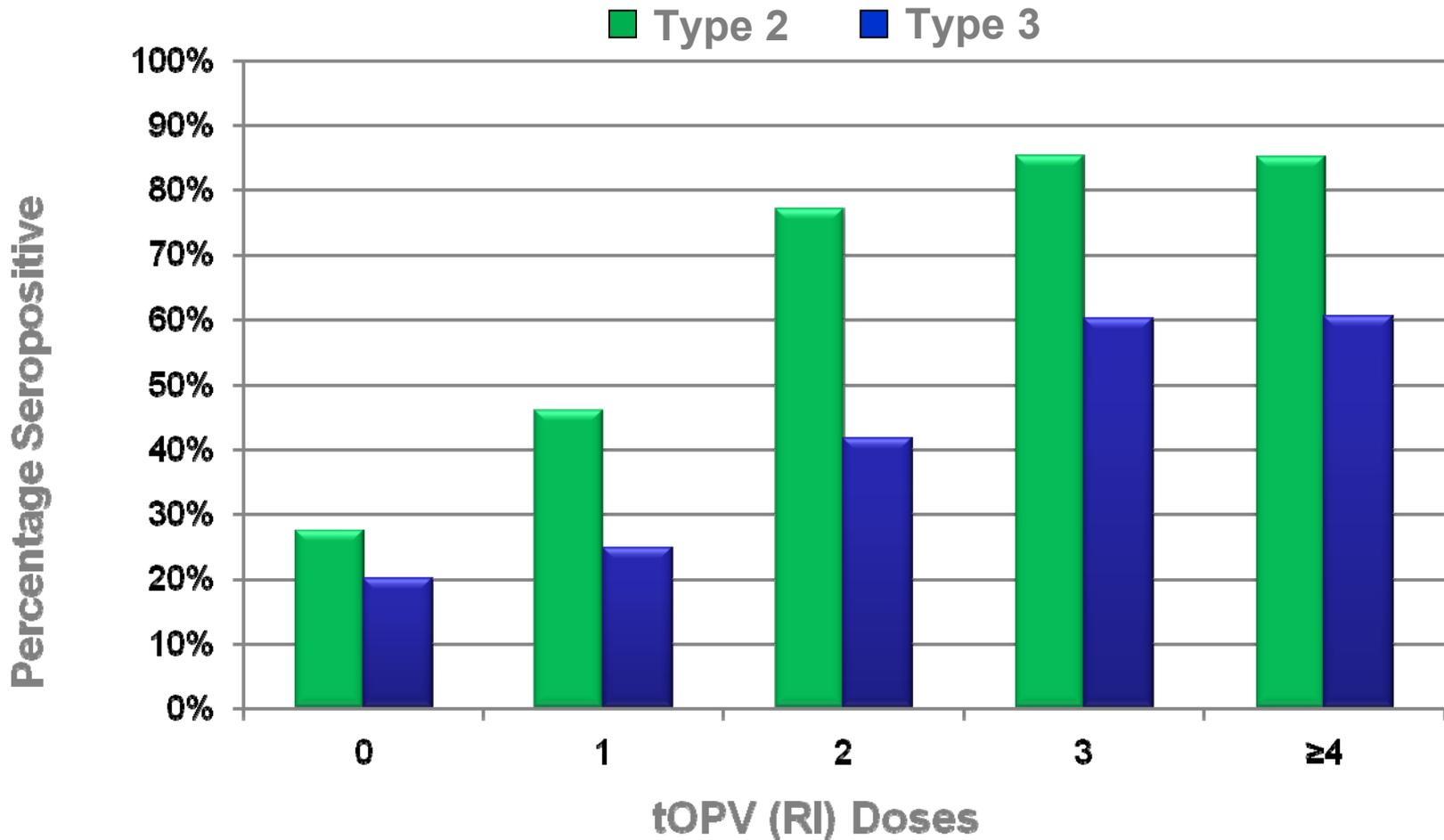
IPV, Inactivated Polio Vaccine
mOPV, Monovalent Oral Polio Vaccine
bOPV, Bivalent Oral Polio Vaccine
tOPV, Trivalent Oral Polio Vaccine





Baseline Seroprevalence in Western UP, 2009

6-9 Month-old Children, by Number of Routine tOPV Doses (N=1002)



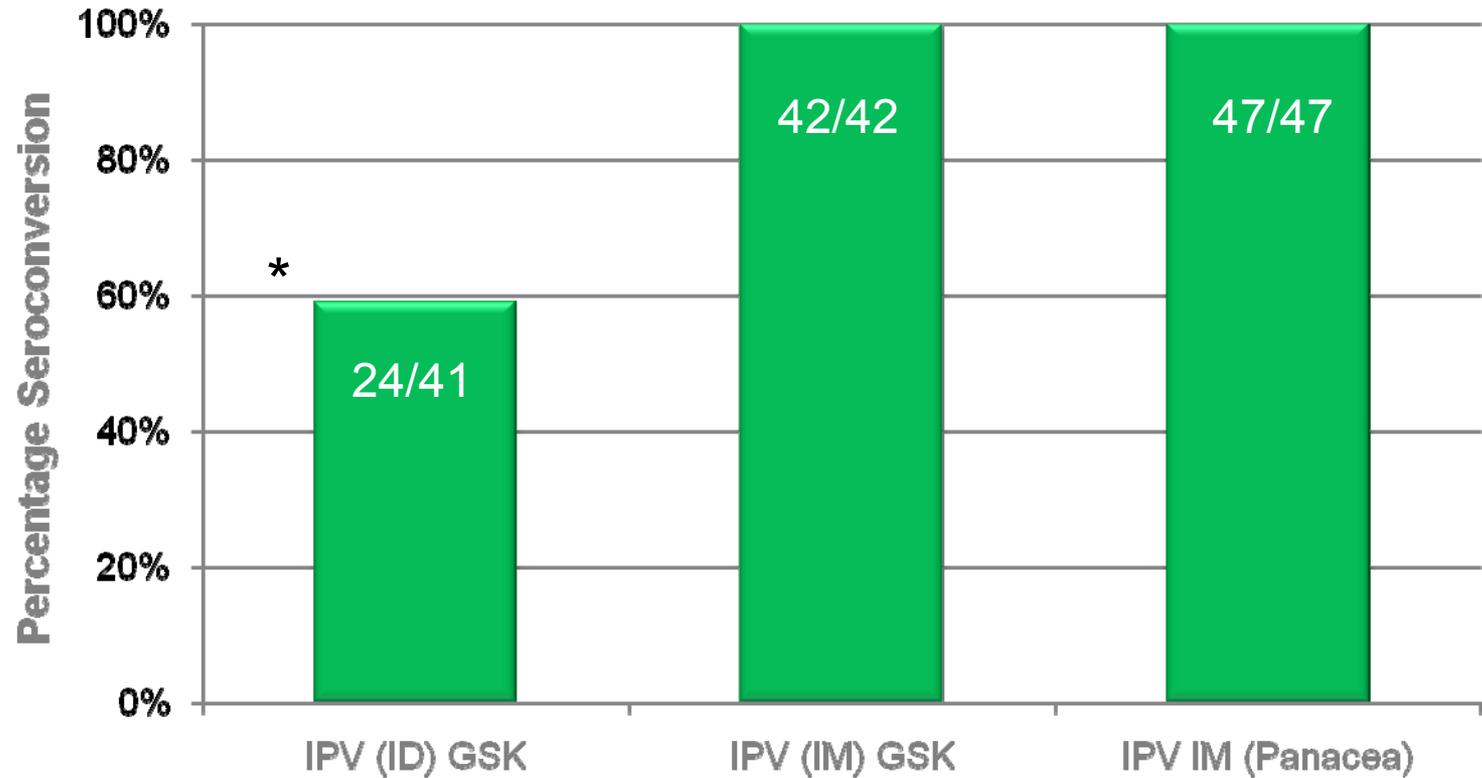
CMC books (96%) or immunization cards (4%)

tOPV, Trivalent Oral Polio Vaccine



Seroconversion to IPV Type 2 Poliovirus at 28 Days

6-9 Month-old Children



P < .0001 compared to IPV (IM) GSK

IPV, Inactivated Polio Vaccine
ID, Intradermal
IM, Intramuscular





Re-examining Assumptions: Example 1 Findings

□ Assumption

- Rapid acquisition of immunity in the young infants will interrupt transmission because of the critical role of infants in sustaining virus circulation

□ Findings

- Despite poor routine immunization, acquisition of immunity in young infants is better than previously suggested
- IPV demonstrates very high vaccine effectiveness per dose in boosting immunity in previously vaccinated seronegative children

□ Potential Interventions

- Use of IPV to accelerate immunity in young infants and/or boost immunity

Re-examining Assumptions: Example 2

❑ Assumption

- The age of polio cases is a reflection of the age for the majority of virus transmission, defining the age of immunization activities, and that boosting of immune individuals (e.g. older children) is unnecessary

❑ Observations

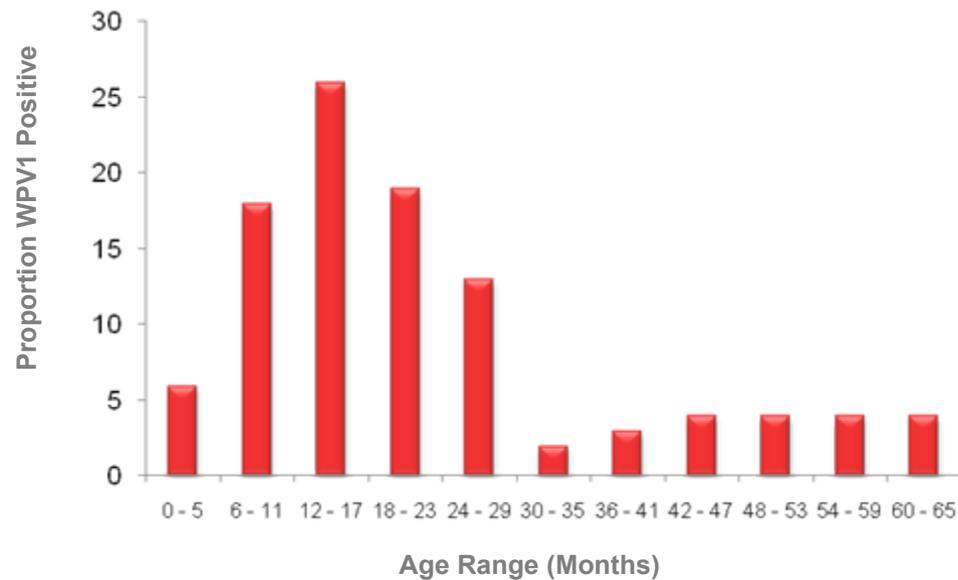
- In UP and Bihar, the median age of WPV cases is around 18 months
- Serologically, children between 36 and 60 months of age are almost universally positive for polio neutralizing antibodies
- SIA activities target children <60 months of age

❑ Expectation

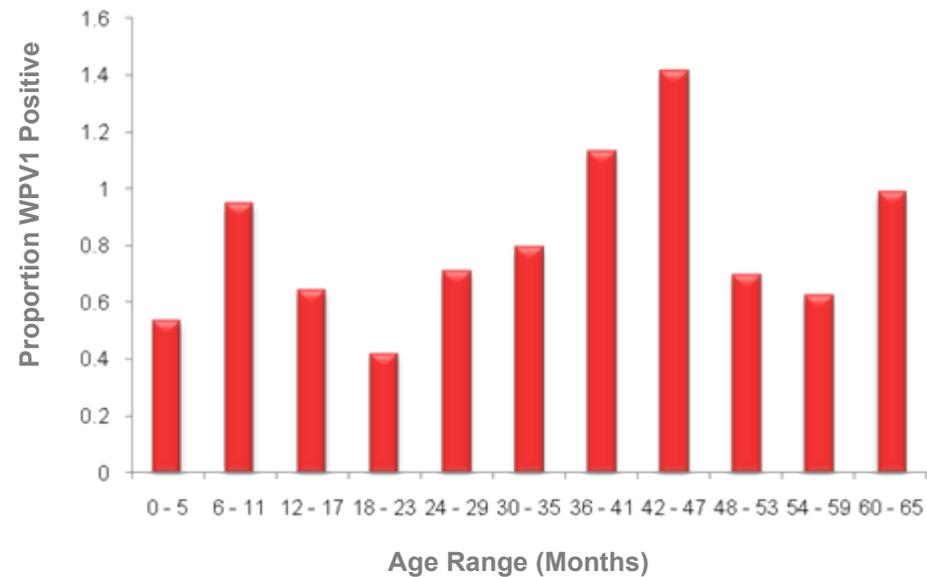
- Infection in immune/older children should be “insignificant” for transmission

Age Distribution of Children with Asymptomatic Wild Poliovirus Excretion Compared to Confirmed Wild Poliovirus Cases

WPV1 Cases



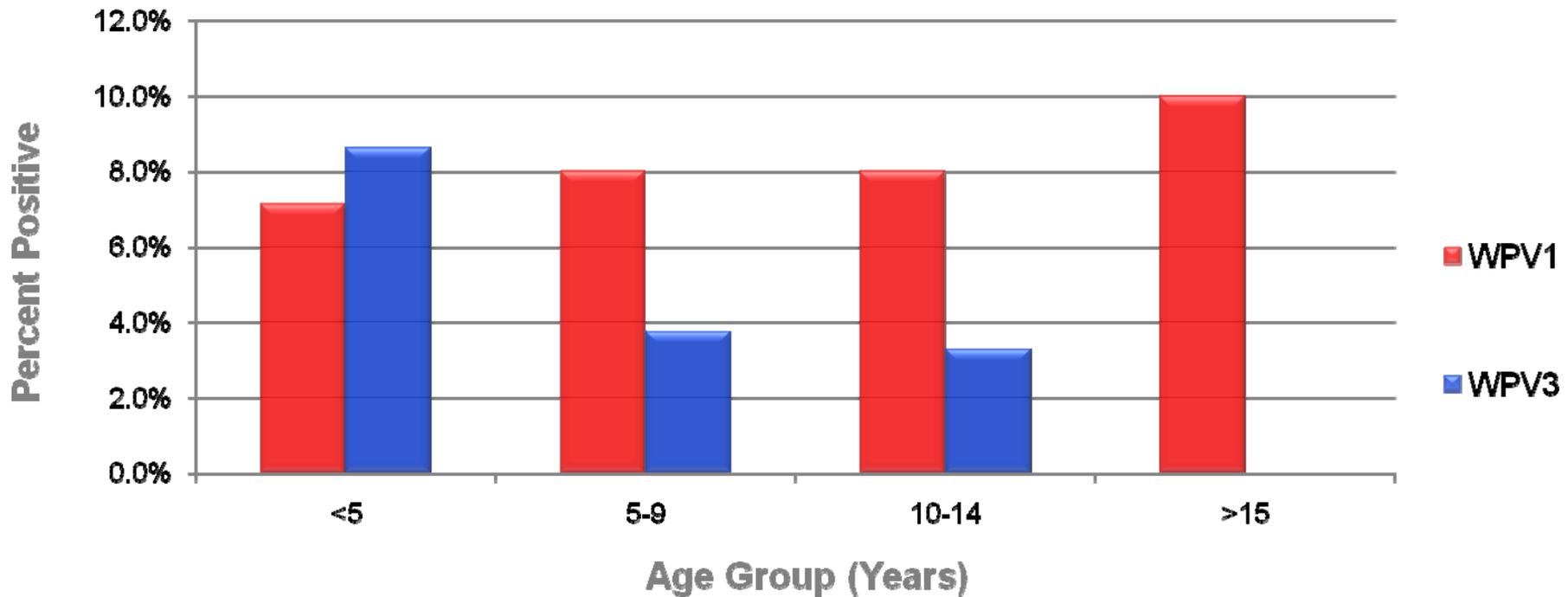
WPV1 Contacts



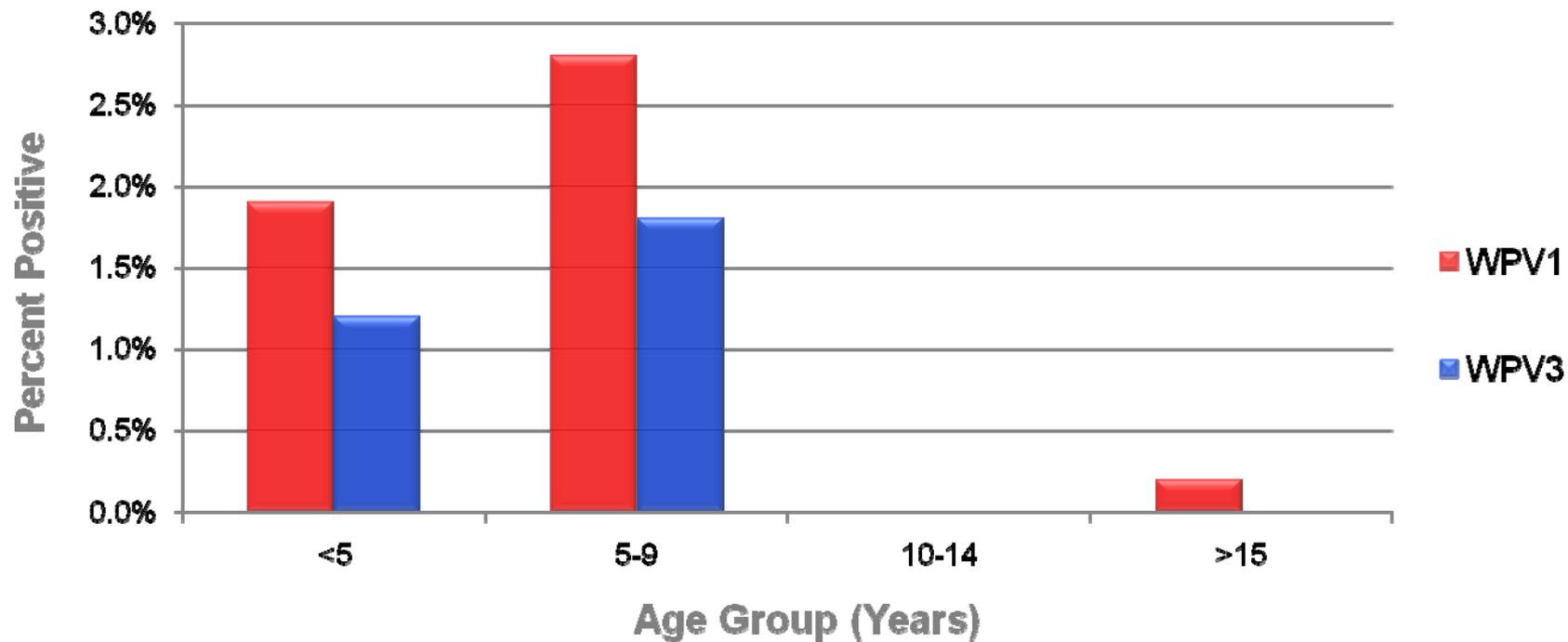
Source: NPSP Surveillance Data



WPV Positive Contacts of WPV Cases, by WPV Type, Uttar Pradesh



Rates of WPV Positive Fecal Specimens Among Randomly Selected Individuals in Bihar Transmission Zone by Age and WPV Type



Re-examining Assumptions: Example 2 Findings

□ Assumption

- The age of polio cases is a reflection of the age for the majority of virus transmission, defining the age of immunization activities, and that boosting of immune individuals (e.g. older children) is unnecessary

□ Findings

- Age distribution of cases does not equal the age distribution of infections
- Infections in older children are not insignificant, may even be comparable or greater

□ Potential Intervention

- Target older children in SIA activities

Critical Role of Research

- ❑ Re-examining Assumptions Related to Current Strategies
- ❑ Evaluating the Effectiveness of New Interventions
- ❑ Addressing New Research Questions on Vaccine Effectiveness



Research to Address Potential New IPV Intervention

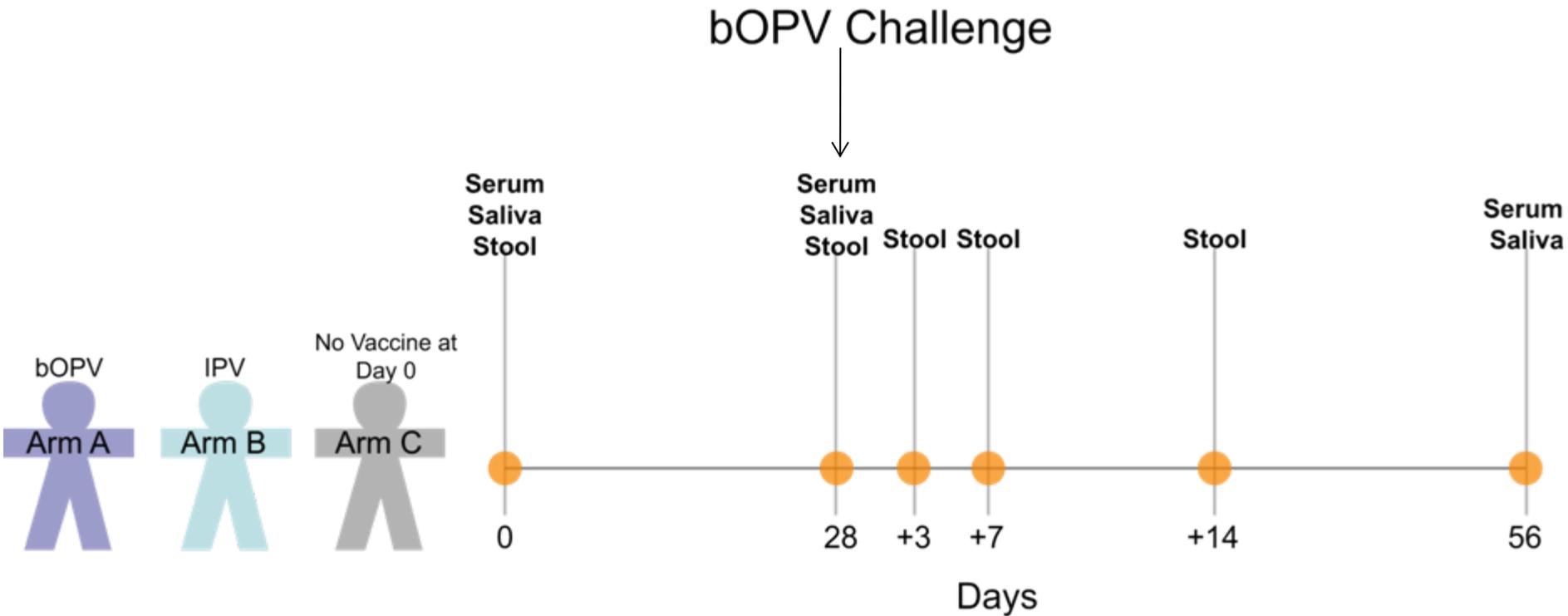
□ Inactivated polio vaccine (IPV)

- Does accelerated acquisition of humoral immunity in young infants result in reduced transmission?
- Demonstrated to have superior per dose effectiveness immunologically

□ IPV effectiveness in UP and Bihar will be related to vaccine coverage

- An operational pilot study could be done to look identify ways to achieve high coverage with IPV

Research to Measure Impact on Virus Shedding by IPV and OPV in Older Children



IPV, Inactivated Polio Vaccine
OPV, Oral Polio Vaccine
bOPV, Bivalent Oral Polio Vaccine



Critical Role of Research

- ❑ Re-examining Assumptions Related to Current Strategies
- ❑ Evaluating the Effectiveness of New Interventions
- ❑ **Addressing New Research Questions on Vaccine Effectiveness**



Other Factors that Potentially Influence Vaccine Effectiveness or Exposure

- ❑ Diarrhea
- ❑ Enteric Infections (viruses, bacteria, parasites)
- ❑ Micronutrients (indirect immunological/infection effects)
- ❑ Environmental exposure (clean water)



Priority Potential Research Activities for Northern India

- ❑ **Further assessment of the age distribution of poliovirus infections**
- ❑ **Measure virus shedding following boosting with OPV and/or IPV in older children**
- ❑ **Need to synthesize data, logistical requirements, resource needs, and estimates of cost effectiveness for policy makers**

POLIO ERADICATION IN PERSPECTIVE



Walter Dowdle, PhD
Task Force for Global Health, Atlanta

Disease Eradication is Made Possible by a Constellation of Four Conditions

- ❑ **Biologic feasibility (effective intervention measures)**
- ❑ **Adequate public health infrastructure**
- ❑ **Sufficient funding**
- ❑ **Political will**



Where the Constellation Exists, the Disease Doesn't

- ❑ **Developed countries eradicated smallpox and polio without need of an international declaration**
- ❑ **Global eradication requires an international declaration and commitment to assist developing countries to fill the constellation gaps**
- ❑ **Current international eradication goals:**
 - Guinea worm
 - Polio

Global Eradication of Polio Is Most Difficult

- ❑ **Smallpox was far less complex biologically and logistically than is polio (3 types, unapparent infections, less effective vaccines)**
- ❑ **22 years and ~\$7 billion after the World Health Assembly Resolution, eradication remains elusive**
- ❑ **Some see polio as no longer a problem, having been reduced from >350,000 cases/year in 1988 to 1,579 cases in 2009**
- ❑ **Why not declare victory, forget eradication, and revert to control?***

* Arita et al, Science 2006



Control is Not the Answer

- ❑ For 30 years, control through routine immunization in developing countries failed to prevent recurring major epidemics
- ❑ Epidemics result from pools of susceptible persons accumulating in high risk populations through vaccine failure and failure to vaccinate
- ❑ Even countries with high immunization coverage (>85%) have immunization gaps among high risk sub-populations
- ❑ 25 countries have routine immunization coverage of <60%

Outbreak Risks Remain as Long as Polioviruses Remain

Northern Nigeria stopped polio immunization in 2003-4. The Result:

- ❑ Polio was exported into 27 polio-free countries in 92 separate incidents**
- ❑ >\$500 million was required in additional emergency funding**
- ❑ >5,000 children were needlessly paralyzed**

High Control at Current Case Levels Will Require

- ❑ **No reduction in vaccine coverage**
- ❑ **Continued global surveillance network**
- ❑ **Emergency vaccine stockpiles**
- ❑ **Aggressive outbreak response**
- ❑ **In short, the same strategy as for eradication,
but indefinitely**

The Costs of High Control Over a 20-year Period

- ❑ **\$10 billion to maintain polio at current level of 1,500 cases/yr**
- ❑ **High control is never [economically] optimal if eradication is feasible**



Costs of Low Control (Routine Immunization Only) Over a 20-year Period

- ❑ **\$3.5 billion for vaccine**
- ❑ **~200,000 cases/yr, placing the polio burden on the poorest of the poor**
- ❑ **Low cost effective control is not possible**



Indefinite High Polio Control Using OPV

□ Means

- **Continuing OPV-associated paralytic poliomyelitis (250-500 cases/yr)**
- **Periodic polio outbreaks caused by OPV-derived viruses (1-2/yr)**
- **Chronic shedding of OPV-derived viruses by immunodeficient persons (?/yr)**

The Final WHO Goal is Eradication of Poliomyelitis of Any Origin

- ❑ Routine use of Sabin OPV must stop
- ❑ Affordable IPV must be available
- ❑ The absence of residual circulating OPV-derived polioviruses must be assured through continued surveillance and rapid response
- ❑ Polioviruses must be either destroyed or contained in a limited number (<20) of essential facilities

OPV, Oral Polio Vaccine
IPV, Inactivated Polio Vaccine



Polio Eradication Is Achievable

- ❑ The last stretch is most challenging
- ❑ Only in parts of 4 countries has eradication never been achieved
- ❑ Targeted research, innovation, and program flexibility are critical
- ❑ The polio program must reach out to other international health initiatives and partners
- ❑ All international health initiatives must recognize the mutual benefits of supporting polio eradication

Polio Eradication Is Crucial

- ❑ For all children at risk now and in the future in the developing world
- ❑ For all diseases where eradication is a potential goal
- ❑ For all international health initiatives that will share directly or indirectly in this remarkable global achievement



The Benefits of Polio Eradication Will Be Shared by All