SAGE Polio Working Group Report

# *Role of IPV in OPV2 cessation*

*6 November, 2012*

# *Presentation outline*

- Rationale and evidence base for IPV
- IPV products and prices
- Programmatic consultations
- Proposed SAGE recommendations

# Rationale and evidence base for the use of IPV to manage risks associated with OPV2 cessation

## Rationale for introduction of 'at least 1 IPV dose prior to OPV2 cessation':

- possibility of continued silent circulation of cVDPV2 and of new cVPDV2 emergences following OPV2 cessation
- low but real risk of type 2 polio outbreaks following OPV2 cessation (i.e. due to cVDPV, chronic VDPV excretors, containment failure)

**Benefits of 'at least 1 IPV dose prior to OPV2 cessation':**

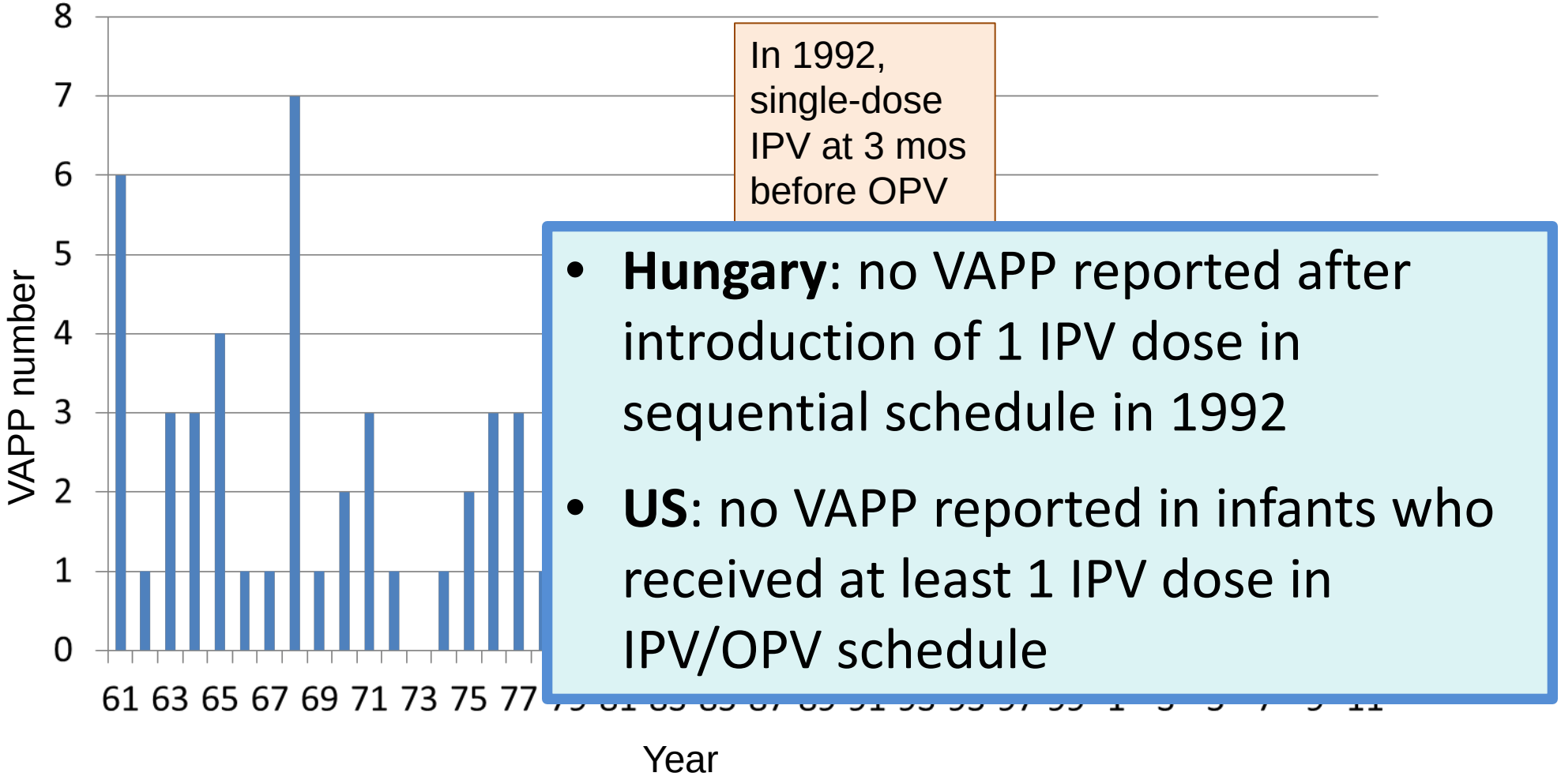
a) prevent polio if exposed to a VDPV2 or WPV2

b) improve response to mOPV2 in an outbreak

c) reduce transmission of a reintroduced type 2

d) boost immunity to WPV1 & 3

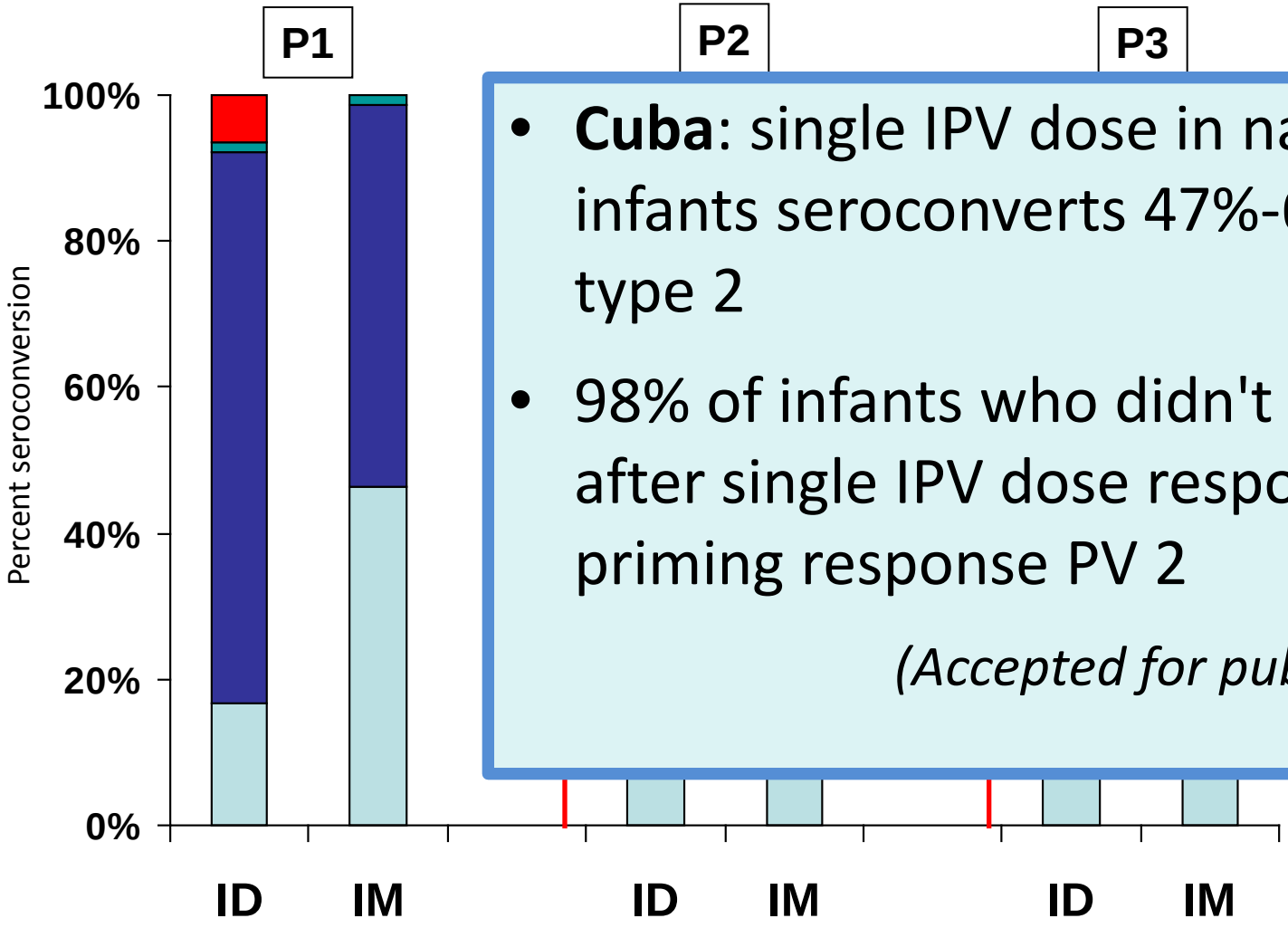
# a) 'prevent polio if exposed to a VDPV2 or WPV2'




- **Hungary**: no VAPP reported after introduction of 1 IPV dose in sequential schedule in 1992
- **US**: no VAPP reported in infants who received at least 1 IPV dose in IPV/OPV schedule

# b) 'improve response to mOPV2 in an outbreak'

*IPV priming effect, measured 7 d after 2nd IPV dose, Cuba, 2010*



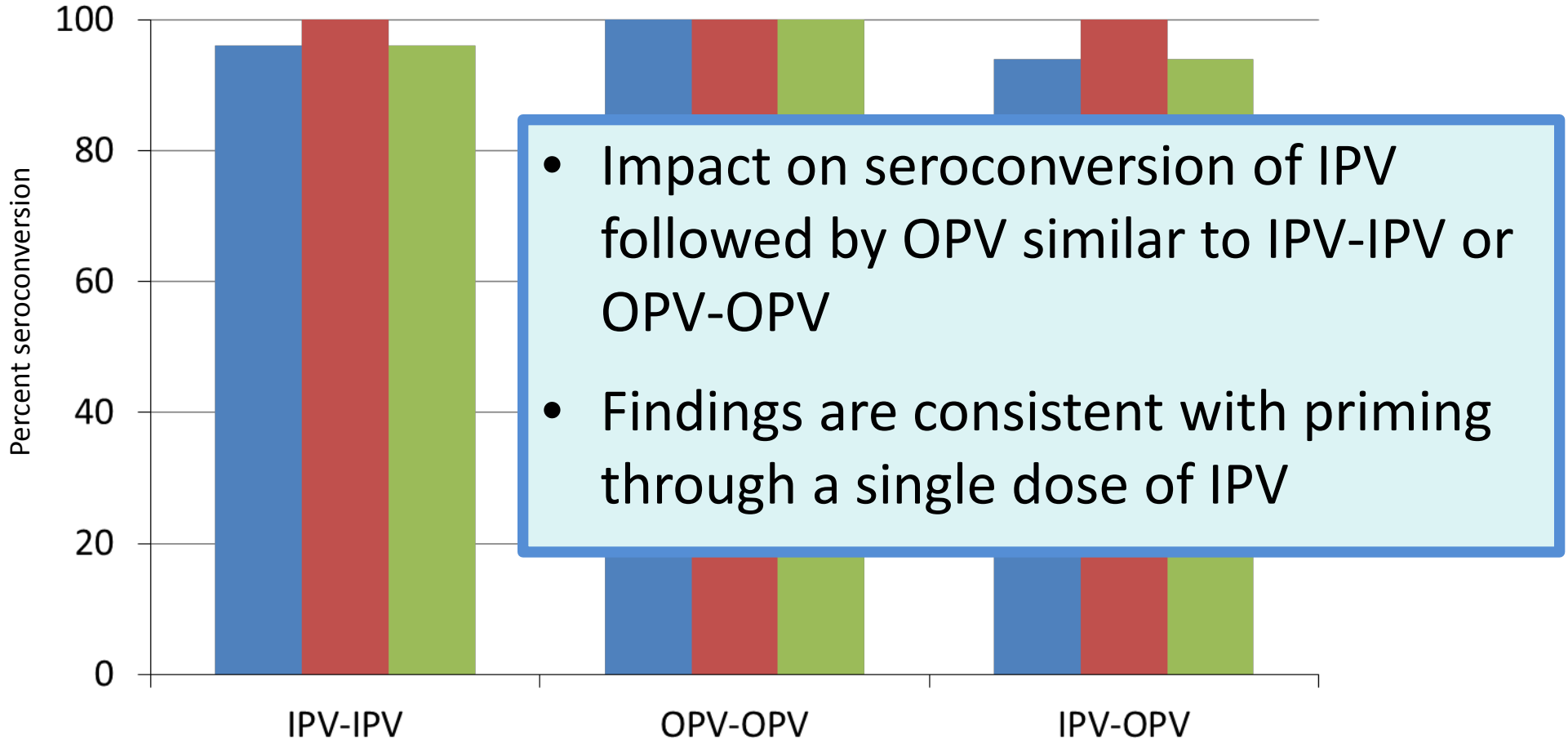

- **Cuba**: single IPV dose in naive 4-mo old infants seroconverts 47%-63% against type 2
- 98% of infants who didn't seroconvert after single IPV dose responded with priming response PV 2

*(Accepted for publication - NEJM)*

POLIO GLOBAL ERADICATION INITIATIVE

# b) 'Improve response to mOPV2 in an outbreak'

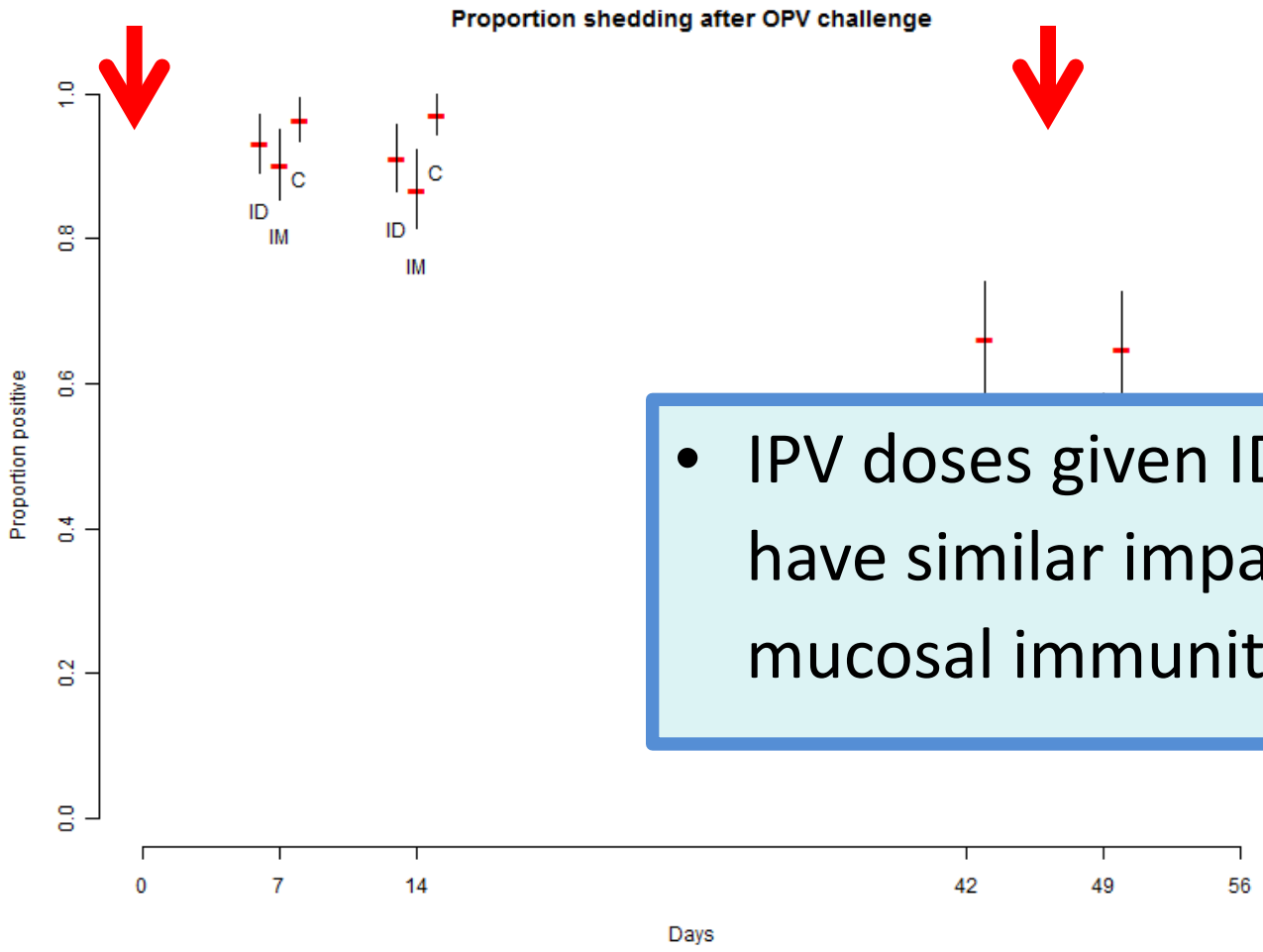
*Comparison of 2-dose response, Faden et al, JID, 1990*




- Impact on seroconversion of IPV followed by OPV similar to IPV-IPV or OPV-OPV
- Findings are consistent with priming through a single dose of IPV

# c) 'reduce transmission of a re-introduced type 2'

*IPV & mucosal immunity, Cuba, 2012*




tOPV challenges

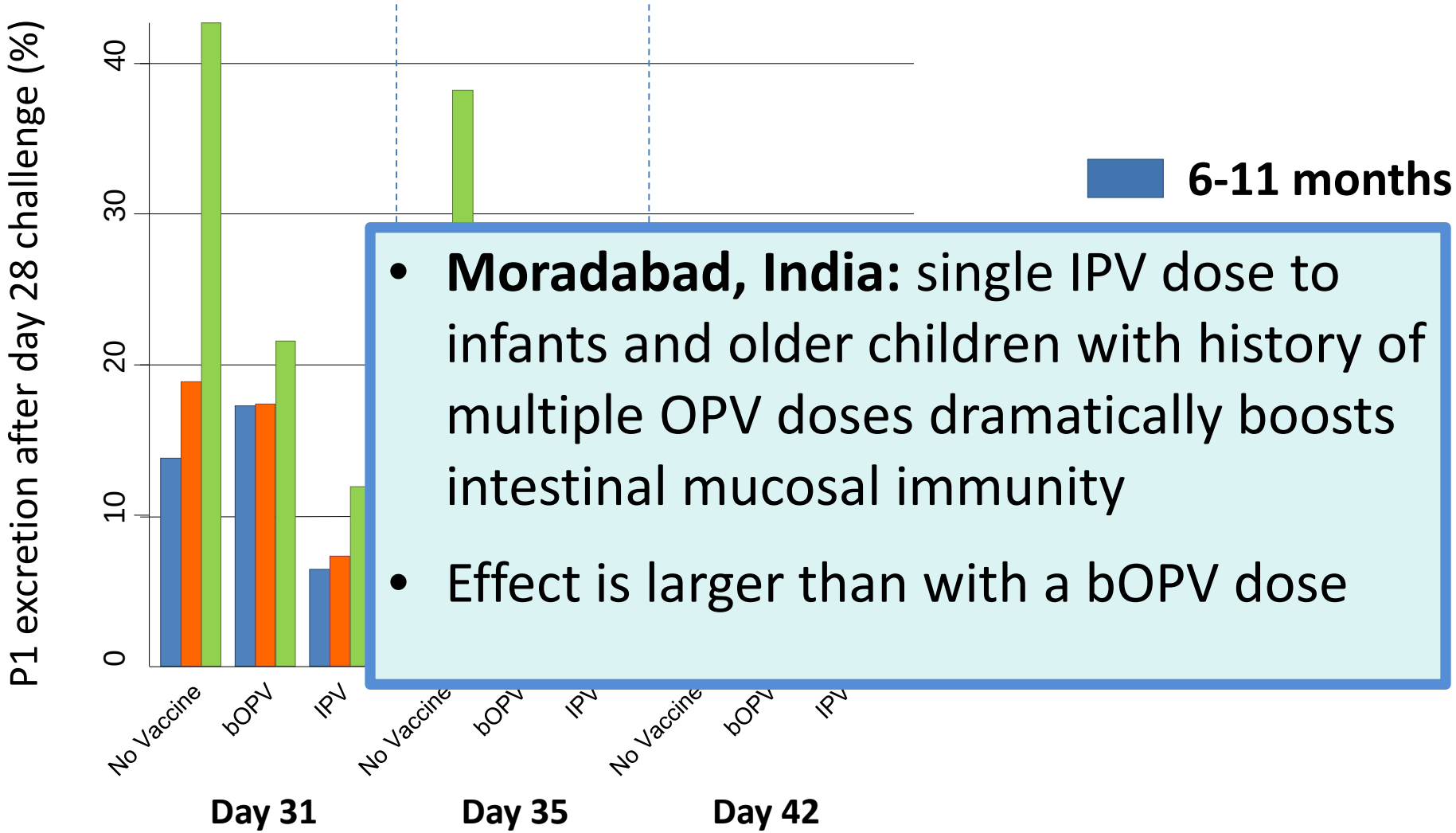
after 2 x IPV

n ID vs. IM

- IPV doses given ID and IM have similar impact on mucosal immunity

# c) 'reduce transmission of a re-introduced type 2'

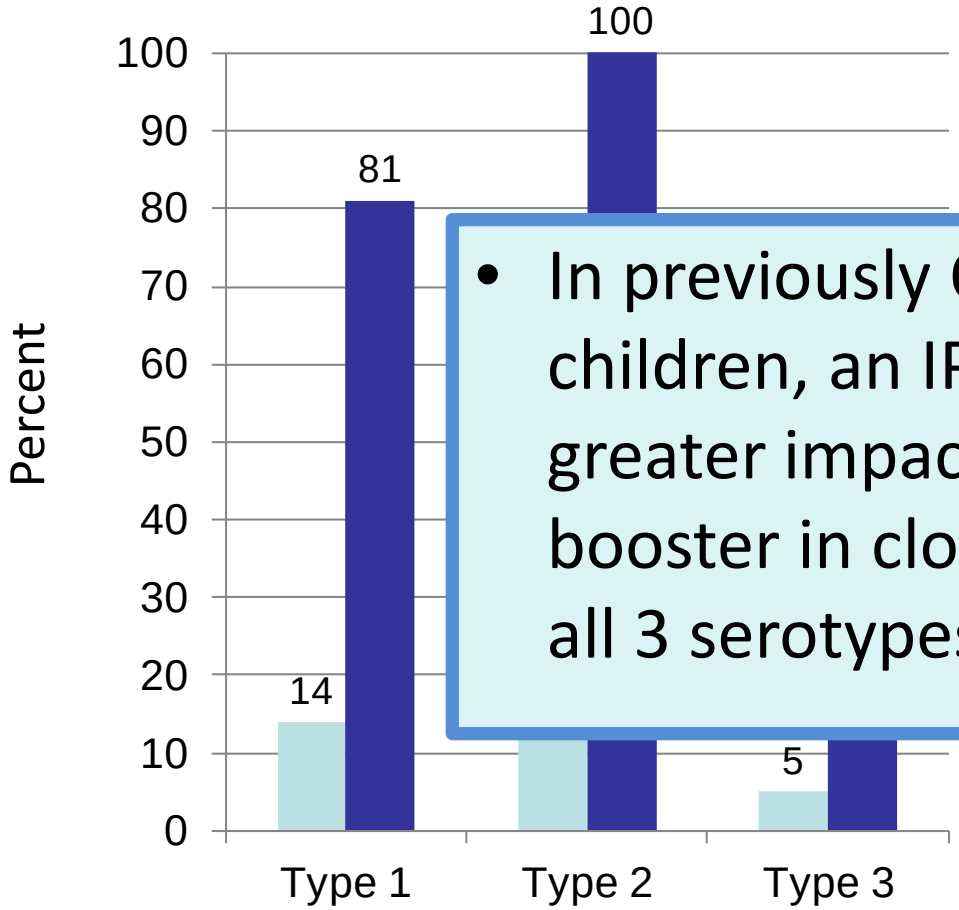
*Impact of IPV vs. bOPV booster, Moradabad, India, 2012*




- **Moradabad, India:** single IPV dose to infants and older children with history of multiple OPV doses dramatically boosts intestinal mucosal immunity
- Effect is larger than with a bOPV dose

# d) boost immunity to wild poliovirus 1 & 3

*Impact of IPV vs. OPV booster after OPV3 in seronegative individuals at 9 months of age, Côte d'Ivoire (Lancet, 1993)*




- In previously OPV-immunized children, an IPV booster dose has greater impact than an OPV booster in closing immunity gap to all 3 serotypes

*Proposed SAGE recommendation:*

All countries should introduce at least 1 dose of IPV ahead of the planned cessation of OPV2 (the 'tOPV-bOPV switch')

# IPV products and prices

# Consultative process with IPV manufacturers and regulatory authorities

- 3-4 Sept: WG meeting - consultation with IPV manufacturers
  - Four manufacturers invited, list of key questions shared ahead of time
  - 45-min discussions between WG and each manufacturer
  - Also: update from GATES foundation on their IPV-related activities
  - Follow-up letter to manufacturers requesting plans on IPV products and pricing in writing; detailed responses received from all 4 manufacturers
- 28 Sept: WG conference call
- 26 Oct: WG conference call (after receiving manufacturers replies)
- 25 Oct: Follow-up meeting of ADG + POL/WHO with manufacturers and regulatory authorities (global polio vaccine manufacturer's meeting)
- 31 Oct: ADG, POL + IVD/WHO meet with French and Belgian national regulatory authorities

# Volume purchasing

- Volume purchasing and guaranteed procurement can substantially reduce the price of current IPV products below the current 'awarded UNICEF price' (US$3.30/dose)
- However, volume purchasing alone cannot achieve a target price substantially below US$1.00/dose

# Dose-sparing IPV options

- Two viable approaches:
  - intradermal (ID) fractional (1/5$^{th}$) dose and
  - intramuscular (IM) adjuvanted dose IPV
- Regulatory and/or development challenges for both could potentially be addressed within 2 to 3 years by:
  - active engagement of and intensive collaboration with manufacturers
  - rapid mapping of regulatory pathways and options
  - development of a multi-dose vial policy

# Dose-sparing IPV products

- 3 of 4 producers will work on ID (1/5 dose) use
  - 1 producer will work on ID option for primary series and boosting; 2 producers will work on ID option for emergency response boosting only
  - estimated timeline for availability of ID option: 24 to 36 months
- All 4 manufacturers are working on adjuvanted IPV products
  - 2 producers working on stand-alone IM adjuvanted IPV - estimated timeline at least 36-48 months
  - 2 producers working on IPV-containing hexavalent option - estimated timeline 6 years

# Regulatory pathways - dose-sparing options

- Preliminary discussions held with French, Belgian and Indian regulators
- Main outcomes:
  - agreement in principle to clear regulatory pathways for I.D. fractional dose (for boosting), possibly using a 'line extension' to existing licenses
  - agreement in principle to non-inferiority studies as the basis for licensure of adjuvanted IPV products (both standalone and hexavalent)

# *Standalone IPV prices/dose*

**Existing product (2012)**

Whole-dose IM Salk IPV

US$3.30

US$1.25

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**Pipeline products (2015-17)**

*Adjuv*
*dose*

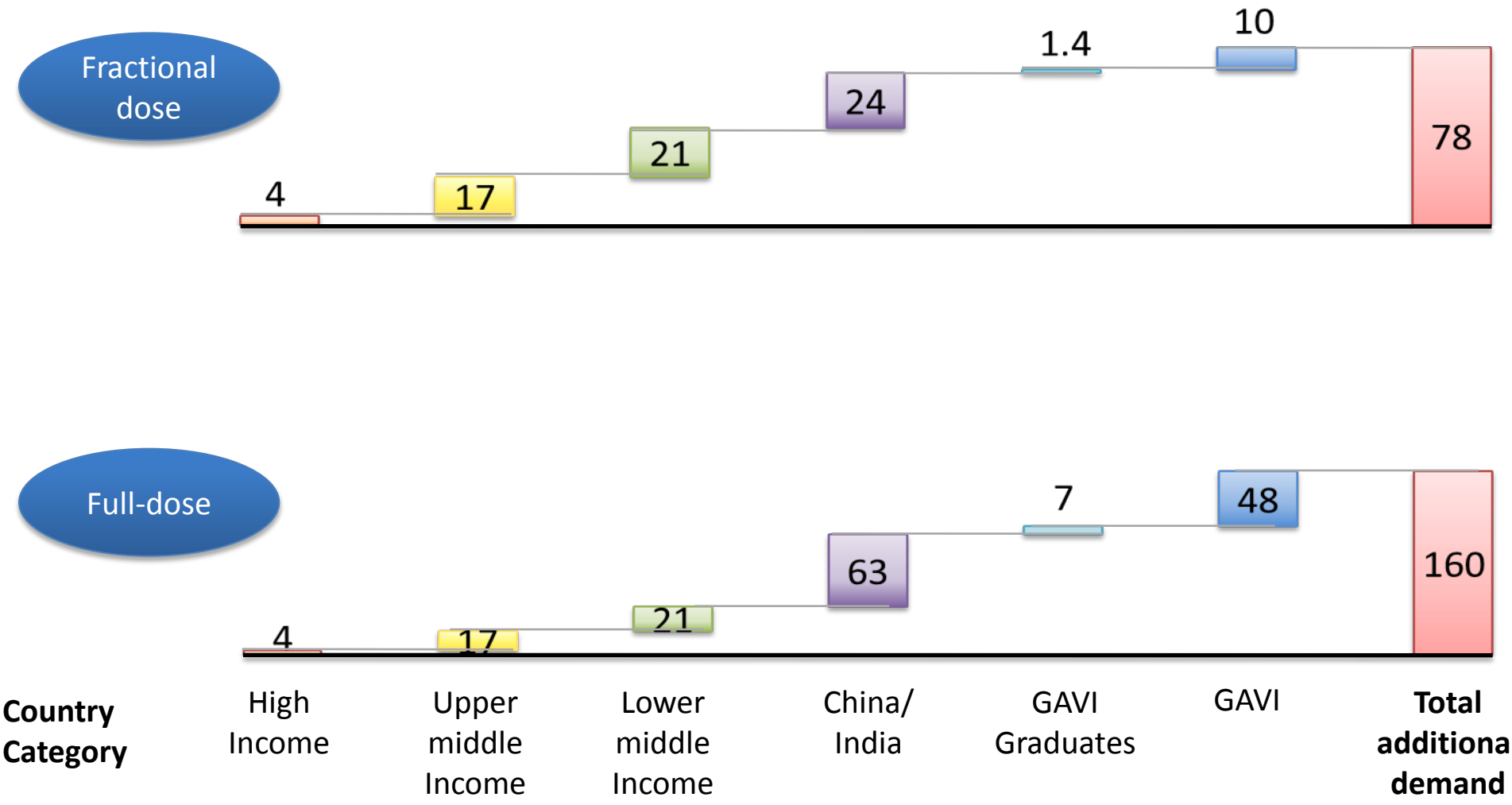
*Fract*
*intrade*

- Clear policy is essential to accelerate product development and licensure and establishing firm pricing

*NOTE: prices & timelines are best 10-dose vial estimates at Oct 2012*

# Expected Annual IPV Demand by Country Segment

## Million doses, Full year after universal IPV introduction



## *Proposed SAGE recommendations:*

- SAGE will review progress on IPV products and prices and other pre-requisites for OPV2 cessation every 6 months to finalize a target date for OPV2 cessation, with a minimum 24 months lead time.
- GPEI should establish a supply strategy for early IPV introduction using whole-dose SALK products for a transition period if needed.

# Programmatic considerations

# Programmatic consultations to date

4 Sept: Review of **implications of IM vs ID application of IPV** (based interviews with EPI managers of selected countries), SAGE Polio WG meeting, Geneva

19 Sept: Consultation on OPV2 cessation and IPV introduction at **EMRO EPI managers meeting**, Sharm-el-Sheikh, Egypt

2 Oct: **IPAC session** on programmatic aspects of IPV introduction, Geneva

10 Oct: Discussion on OPV2 cessation at **SEARO EPI TAG** meeting, New Delhi, India

16 Oct: **WHO/AFRO expert consultation** on regional perspectives for the use of IPV in routine immunization, Luanda, Angola

18 Oct: Consultation on OPV2 cessation and introduction of IPV at the **PAHO EPI TAG** meeting, Washington, USA

# Main outcomes

- Countries accept, in principle, the role of IPV for OPV2 cessation
- Strong demand for clear recommendation on universal IPV use
- Majority of countries prefer IM delivery of IPV; some opt for ID fractional dose
- More clarity needed on optimal timing of routine IPV dose and other policy considerations
- Low and low-middle income countries require external financing
- Strong demand for technical guidance and support for implementation
- Consider using 'Global Immunization Week' to facilitate the synchronization of OPV2 cessation

## *Proposed SAGE recommendations:*

- WHO should, by June 2013, establish the capacity to provide comprehensive technical guidance for countries and Regions on programmatic issues for the introduction of at least 1 dose of IPV.

- Consideration should be given to use the 'Global Immunization Week' to facilitate the synchronization of OPV2 cessation

# Summary of proposed SAGE recommendations

1. All countries should introduce at least 1 dose of IPV ahead of the planned cessation of OPV2 (the 'tOPV-bOPV switch')
2. SAGE will review progress on IPV products and prices and other pre-requisites for OPV2 cessation every 6 months to finalize a target date for OPV2 cessation, with a minimum 24 months lead time.
3. GPEI should establish a supply strategy for early IPV introduction using whole-dose SALK products for a transition period if needed.
4. Planning for OPV2 cessation should consider using the annual global immunization week (April) for the synchronized tOPV to bOPV 'switch' (i.e. April 2016?)
5. WHO should, by June 2013, establish the capacity to provide comprehensive technical guidance for countries and Regions on programmatic issues for the introduction of at least 1 dose of IPV.

# Next steps:

***Apr 2013:*** *WG to report back to SAGE on further review of pre-requisites for OPV2 cessation (**affordable IPV**, interruption of persistent cVDPV, laboratory containment, surveillance and outbreak response capacity) towards establishing the time frame for OPV2 cessation*

*- WG to conduct 6-monthly review of main pre-requisites and 'triggers' for OPV2 cessation until all are in place*