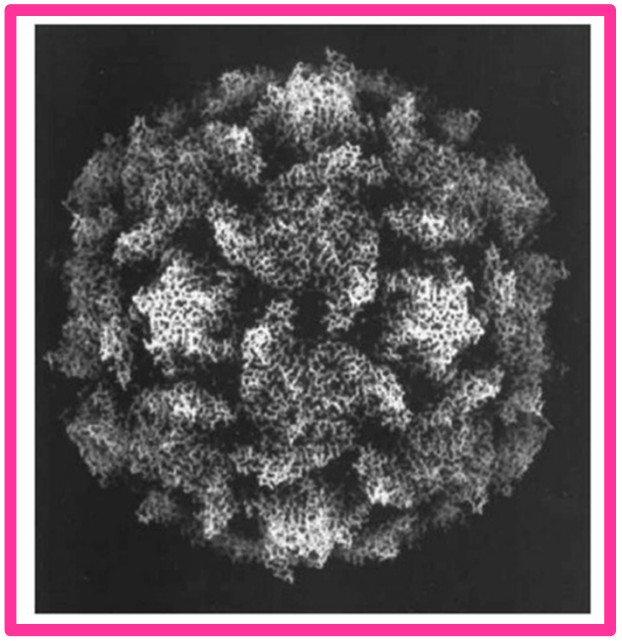
Global Polio Eradication: The Need for Inactivated Polio Vaccines (IPV)



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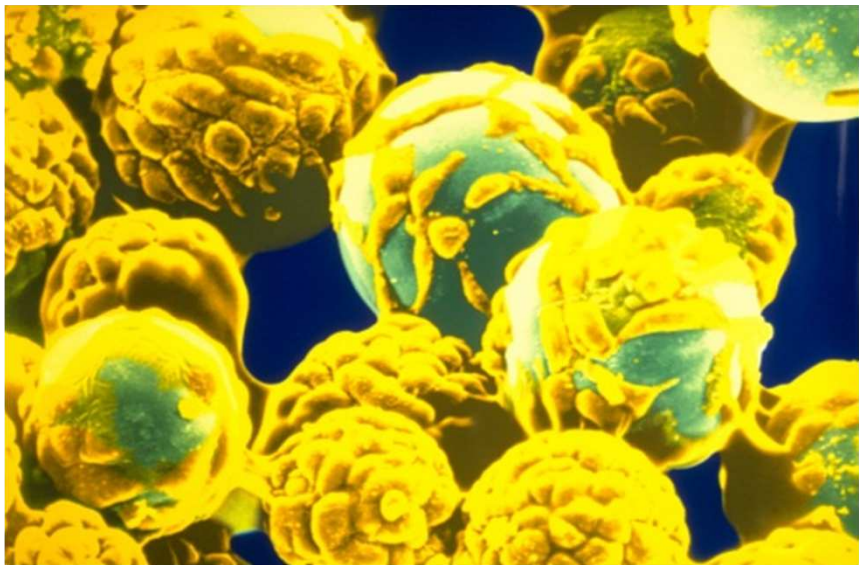
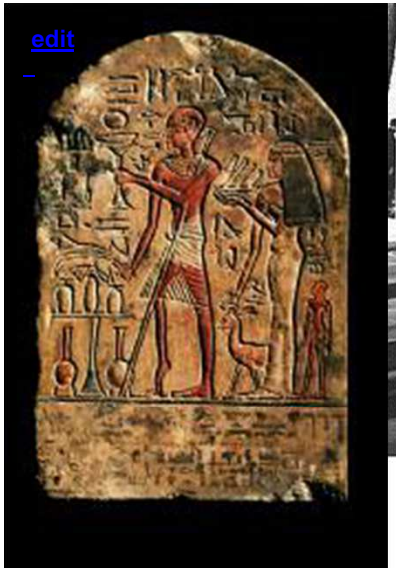
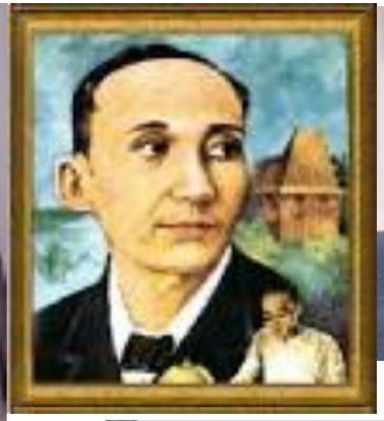
Outline:

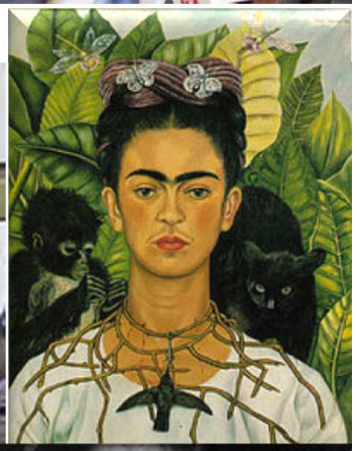
- Polio: Background
- Global Polio Eradication Initiative
- Role of Inactivated Polio Vaccines (IPV)
- Features/ Use of IPV

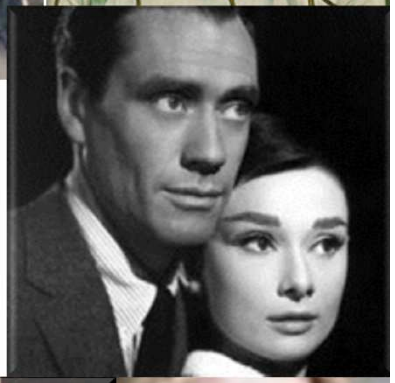











Anyone can be a victim …

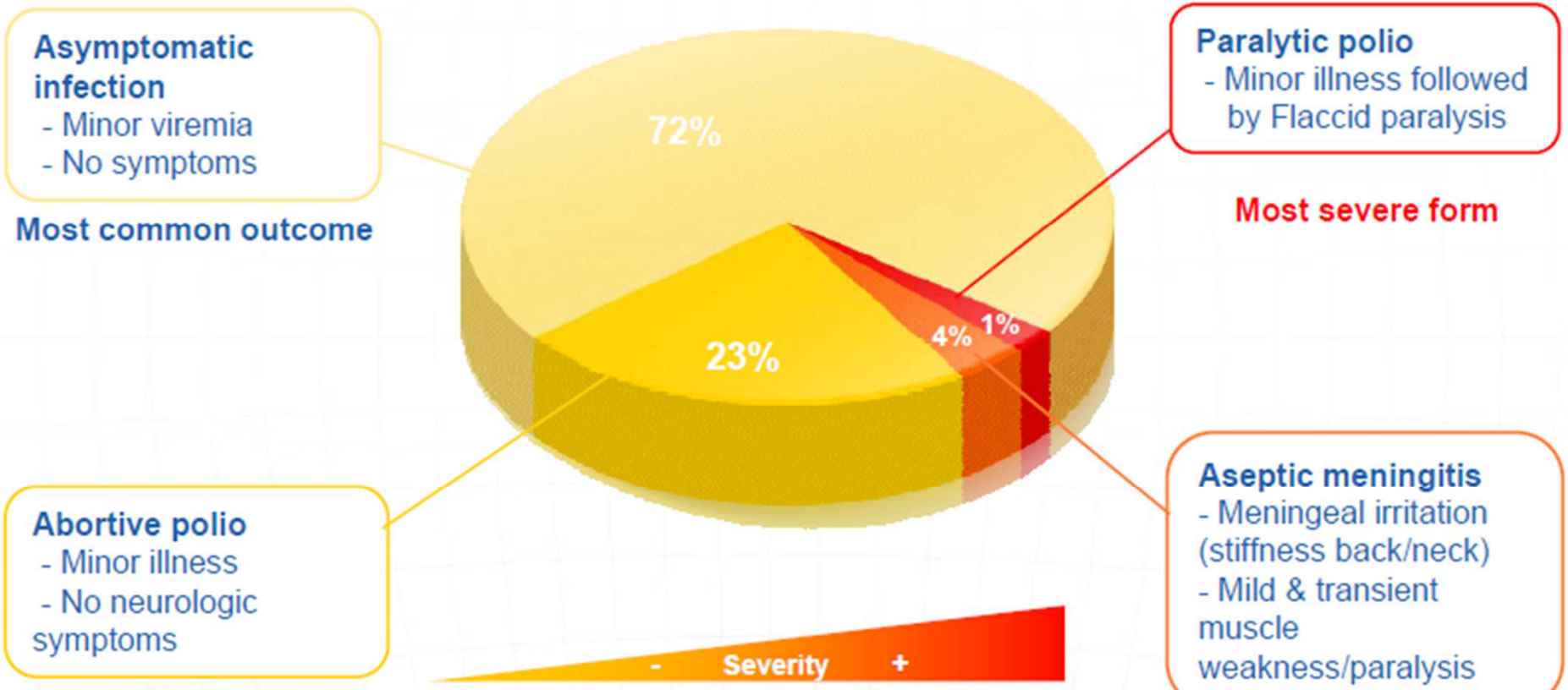
- US President Franklin D. Roosevelt
- Francis Ford Coppola
- Donald Sutherland, Mia Farrow, Mel Ferrer
- Arthur Guyton (physiologist), Jack Niclaus
- Frieda Kahlo (artist), Katherine Jackson
- Neil Young, David Sanborn (saxophone player)
- **Apolinario Mabini**
- **Ma. Gracia Cielo "Grace" Magno Padaca**

Background

POLIO:

- Highly contagious disease that causes permanent disability and even death.
- Caused by: **Poliovirus (types 1, 2, 3)**
  - **Wild poliovirus (WPV)**
  - **Vaccine -derived polio virus (OPV)** → **VAPP**, **cVDPV**
- Person-to-person spread
- 1 in 200 infections → irreversible paralysis
  - Among those paralyzed, 5% to 10% die
- Children <5 years old most at risk.
- No cure
- Polio vaccine, given multiple times, can protect a child for life.

Polio: Clinical Description



Sutter.R, Kew.O, Cochi. Stephen. Poliovirus vaccine-Live. 2008:651-705.pd

Polio: What you see is only the tip of the iceberg

The poliovirus is sneaky, silent and highly contagious.

It doesn't respect boundaries or social class – it is an equal opportunity paralyzer.

Even 1 case is an outbreak...

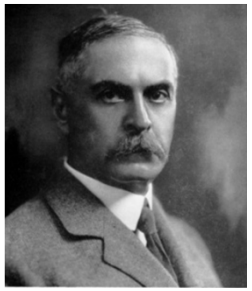
for every one case of polio

200 more kids are infected

http://www.cdc.gov/globalhealth/immunization/infographic/world-polio-day-2014.htm

The fight against Polio has lasted for over 70 years…

1908 — 1938 — 1955 — 1988 — 2012



Landsteiner (Vienna)
Viral etiology established

March of Dimes
Saving babies, together

The Thomas Francis Field Trial of Salk's Inactivated Polio Vaccine: the largest efficacy clinical trial ever done

POLIO GLOBAL ERADICATION INITIATIVE

Born from a coalition between WHO, Rotary, Unicef and US CDC, **GPEI initiative** is launched at 41st WHA with the objective to eradicate Polio by 2000.

Polio Eradication and End Game Strategic Plan 2013-2018 *launched by the GPEI*


More children will be receiving injected killed polio vaccine in a bid to finally eradicate the virus.

HEALTH
Vaccine switch urged for polio endgame
Inactivated virus vaccine could deliver the final blow.

Sources: Plotkin.S, Poliovirus vaccine-Live. Vaccines. 2013:598-645.pdf / Plotkin.S, Vidor.E. Poliovirus vaccine-inactivated. Vaccines. 2013:573-597 / CDC.Polio:unprotected story page. Available at http://www.cdc.gov/vaccines/vpd-vac/polio/unprotected-story.htm.Accessed April, 2012 / The March of Dimes. History page. Available at: http://www.marchofdimes.com/mission/history_indepth.html. Accessed April, 2012; ; Global Polio Eradication Initiative Fact File www.polioeradication.org

Before this …

News › World news › Ebola

WHO declares Ebola outbreak an international public health emergency

Director general Margaret Chan says west African countries' health systems need international help to manage infection

Maev Kennedy
The Guardian, Friday 8 August 2014 11.15 BST

May 26, 2012: World Health Assembly declared **ending polio** a **"programmatic emergency for global public health."**

Global Polio Eradication Initiative

The **Polio Eradication and Endgame Strategic Plan 2013-2018**

- developed to capitalize on this new opportunity to end all polio disease.

Are we really very close to eradicating Polio?

- **Eradication**, not only Elimination:
  - **Elimination**:

    Reduction to zero of the incidence of a specified disease in a defined geographical area as a result of deliberate efforts; continued intervention measures are required.

    Example: neonatal tetanus.
  - **Eradication:**

    Permanent reduction to zero of the worldwide incidence of infection caused by a specific agent as a result of deliberate efforts; intervention measures are no longer needed.

    Example: smallpox.

Are we really very close to eradicating Polio?

Polio in the world:

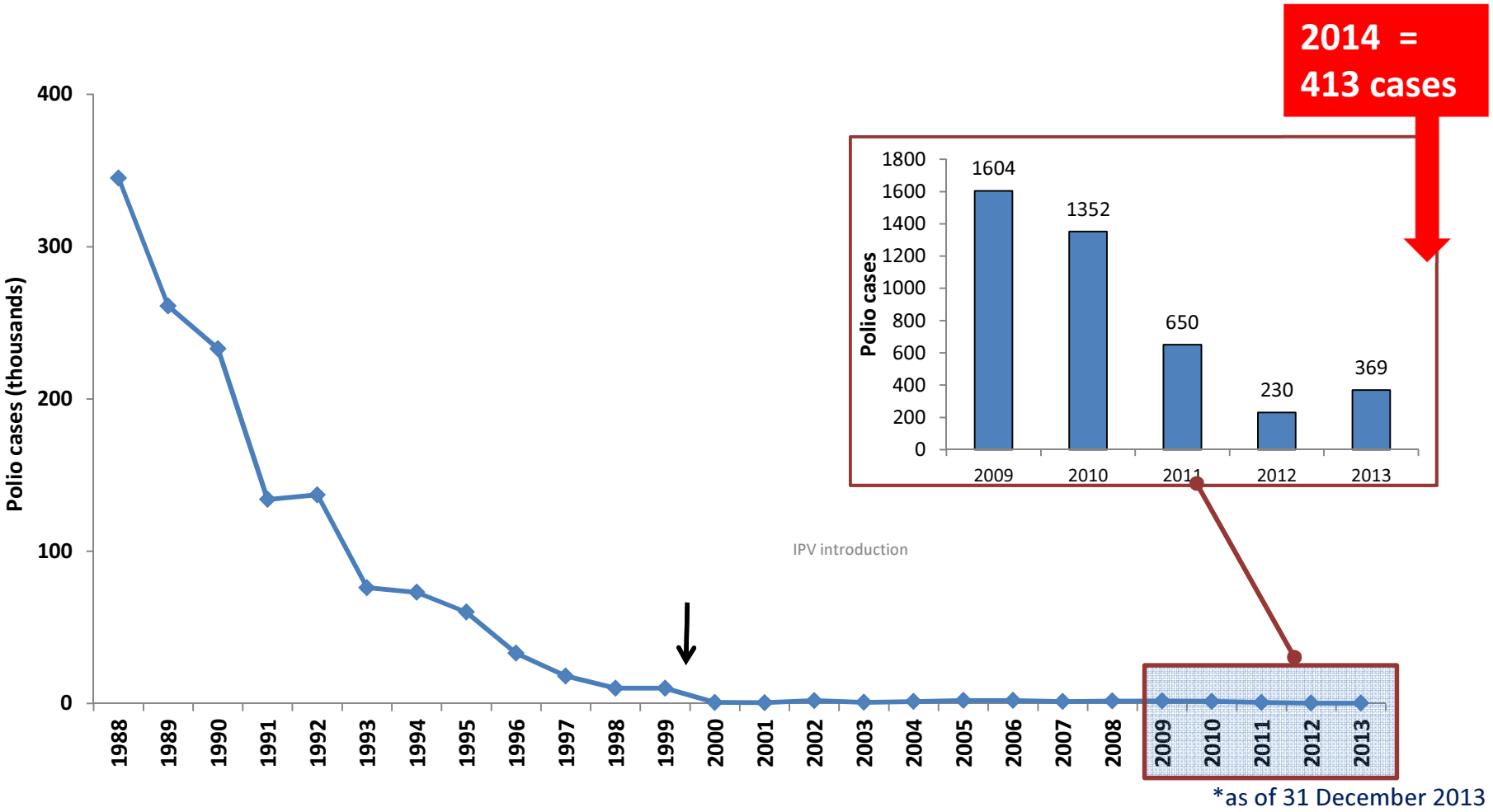
- Since the GPEI was launched in 1988:
  - Reduced global incidence of polio by > 99% (1988 to 2012)
  - Reduced number of countries with endemic polio (from 125 to 3) Pakistan, Afghanistan, and Nigeria
  - Prevented paralysis in >13 million people

Polio in the Philippines:

- Year 1993: last polio case was recorded in the Philippines.
- Year 2000: the Philippines was certified polio-free.

Answer: Yes

GPEI Accomplishment: Significant Decline in Polio-paralyzed Children, 1988-2013*

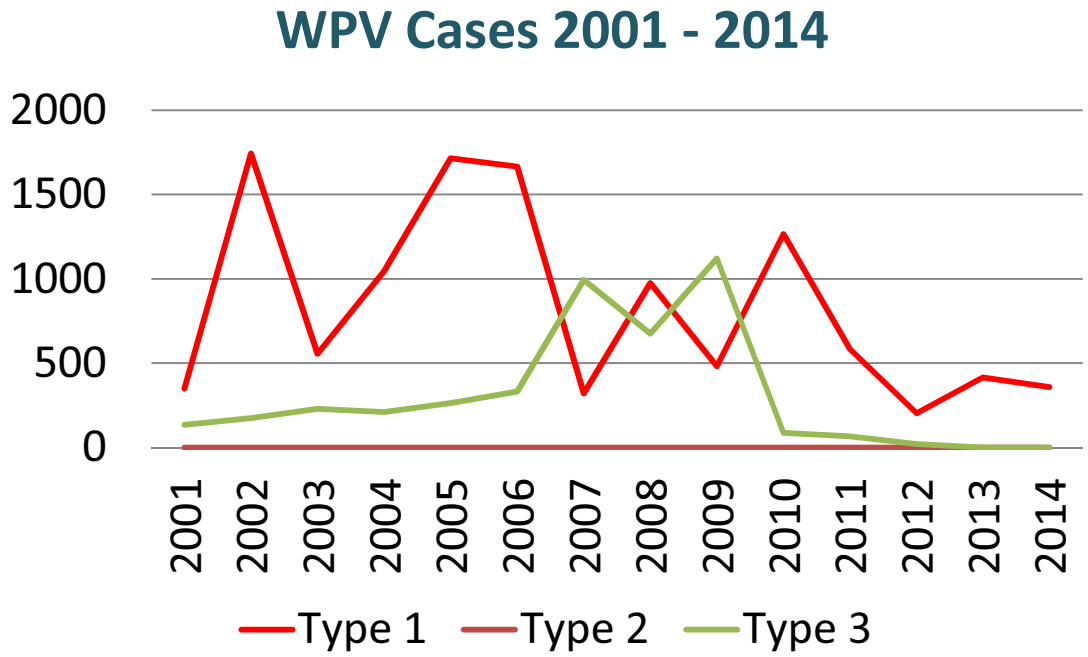


IPV Comprehensive Technical Module GPEI version date: Feb 10, 2014

Polio in 2014…

- **Wild Poliovirus (WPV) Cases**
  - Total: 359 cases, all WPV Type 1
    - Endemic countries: 340 cases (Pakistan, Nigeria, Afghanistan)
    - Non-endemic countries: 19 cases (Somalia, Cameroon, Equatorial Guinea, Syria, Iraq)

- 10 countries with active transmission, 4 have exported WPV to other countries.
- Not under control in Pakistan, (but shows significant progress in Nigeria and Afghanistan).
- Most recent: Jan 17, 2015



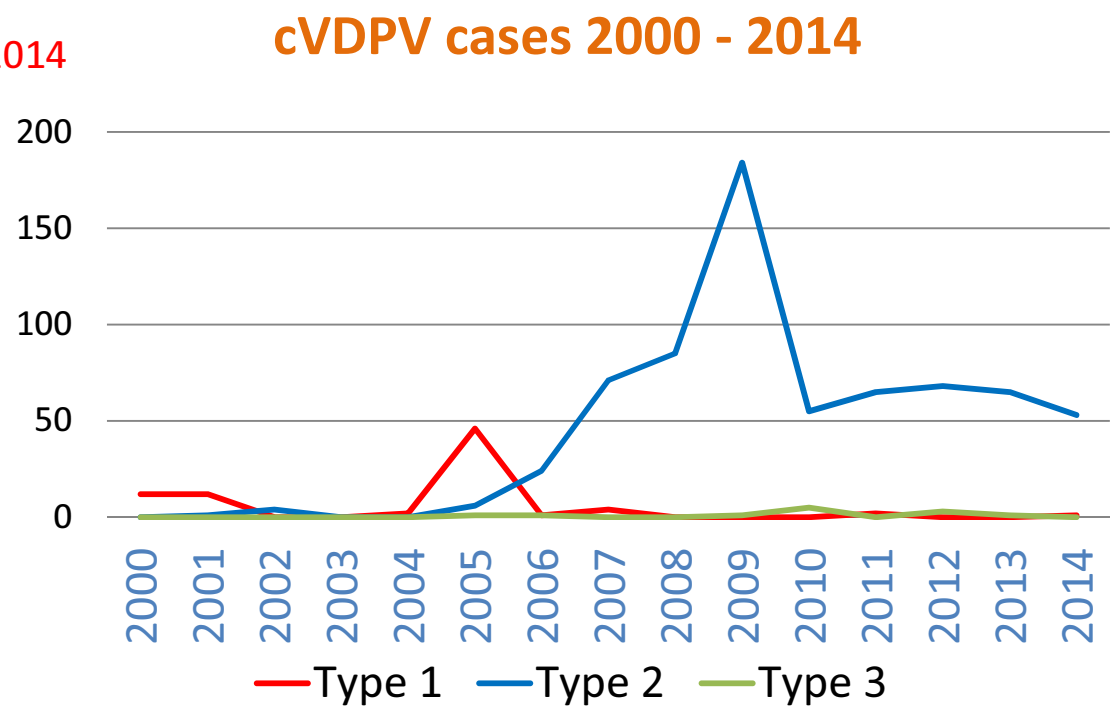
WHO WER 8 Aug 2014, 89, 357-368.; CDC MMWR July 7, 2014.
http://www.polioeradication.org/Dataandmonitoring/Poliothisweek/Wildpolioviruslist.aspx

Polio in 2014…

- **Circulating Vaccine-Derived Poliovirus (cVDPV) Cases**
  - Total: 54 cases
    - Endemic: 51 cases Non-endemic: 3 cases
    - all cVDPV **type 2** except …
    - cVDPV **type 1**:
      - 1 case Madagascar Sep 2014
      - 2011 previous case
    - cVDPV **type 3**:
      - Last case 2013

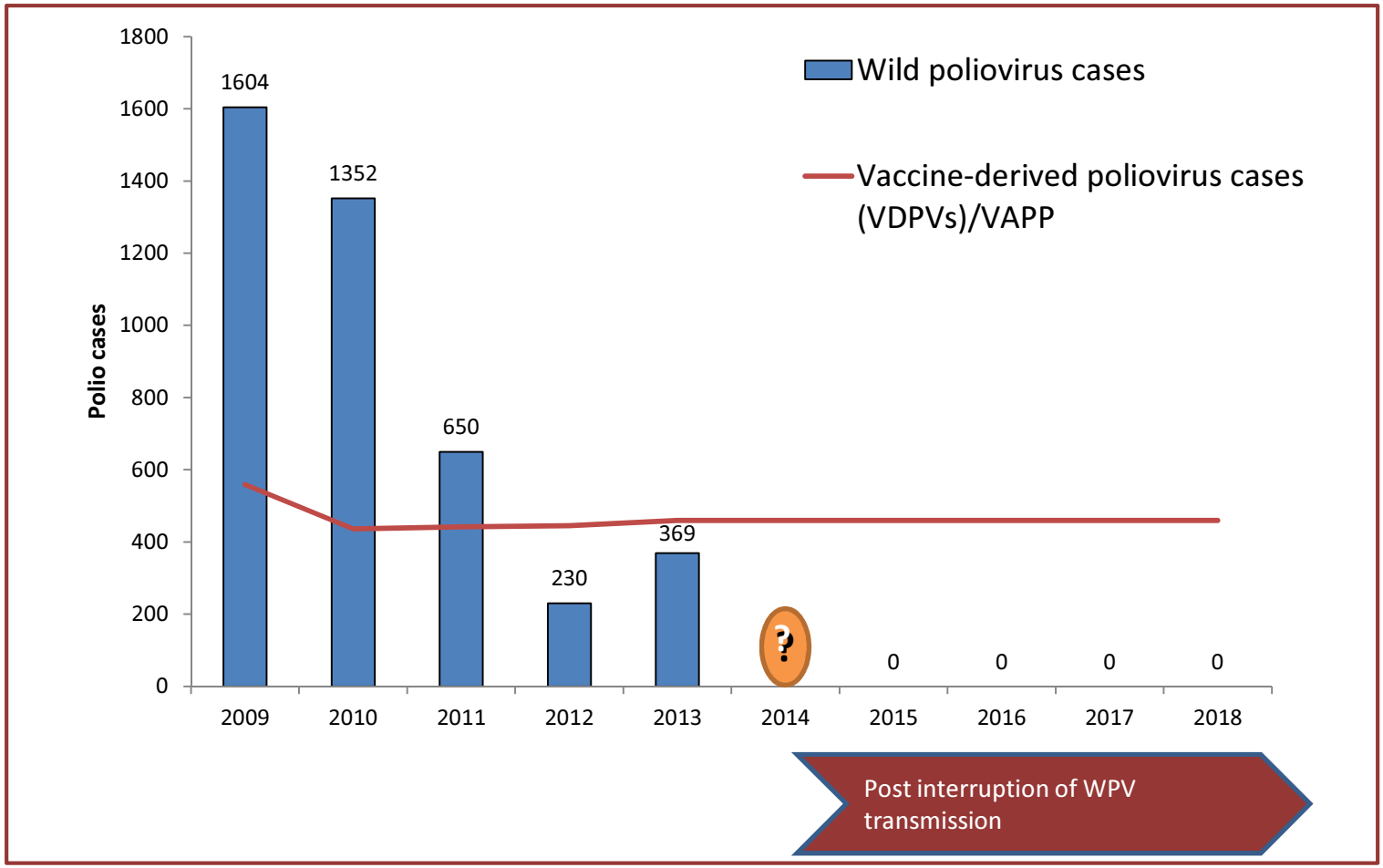
✓ General improvement in control

✓ Most recent: Dec 13, 2014



WHO WER 8 Aug 2014, 89, 357-368.; http://www.polioeradication.org/Dataandmonitoring/Poliothisweek/Circulatingvaccinederivedpoliovirus.aspx

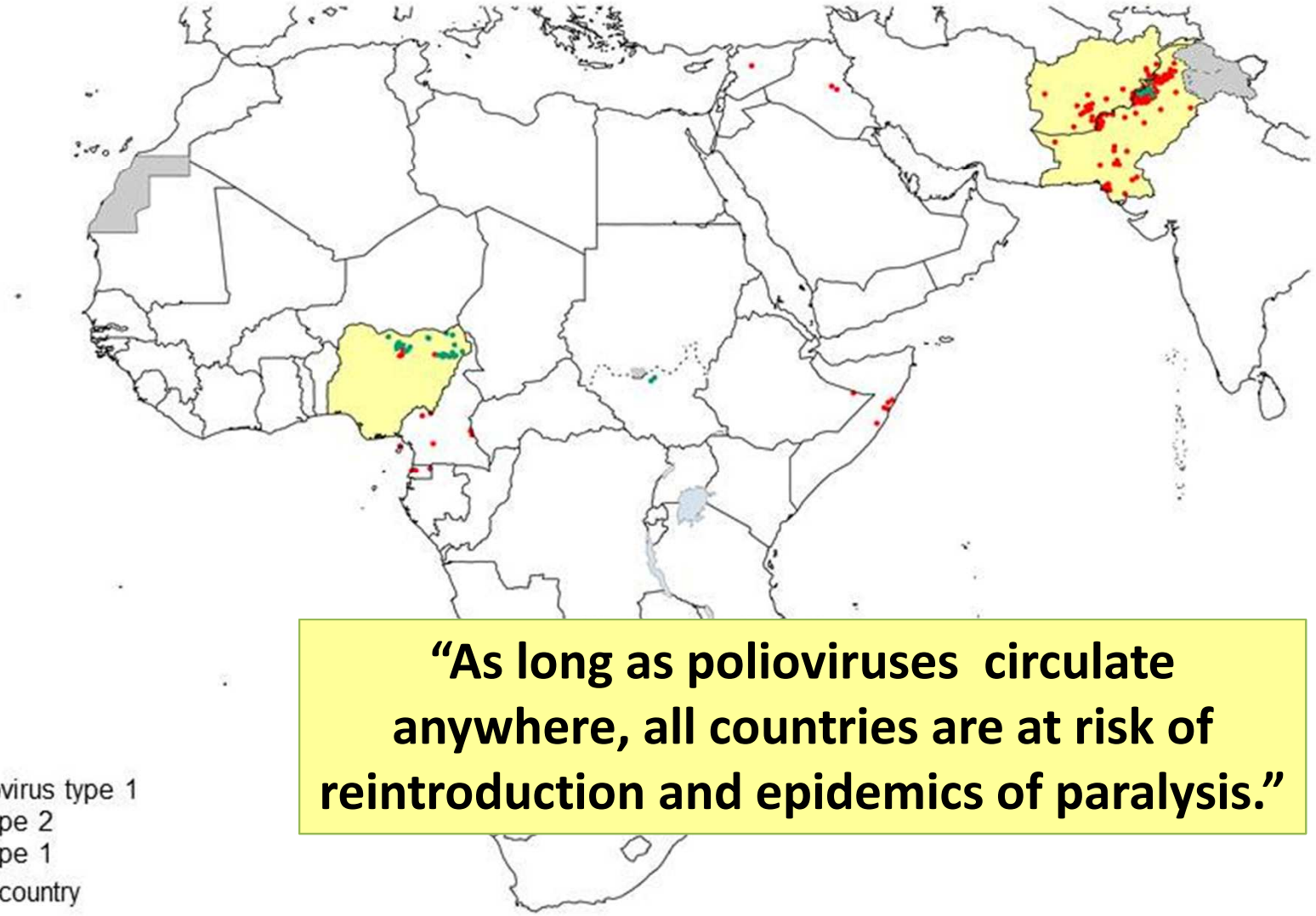
As wild polioviruses are eradicated, number of vaccine-derived cases exceeds wild poliovirus cases



A hypothetical scenario of estimated VDPV cases compared to reported cases of wild poliovirus (as of 31 December, 2013)

IPV Comprehensive Technical Module GPEI version date: Feb 10, 2014

Wild Poliovirus & cVDPV[1] Cases[2], 2014
01 January – 31 December



"As long as polioviruses circulate anywhere, all countries are at risk of reintroduction and epidemics of paralysis."

[1]cVDPV is associated with ≥ 2 AFP cases or non-household contacts. VDPV2 cases with ≥ 6 (≥ 10 for type1) nucleotides difference from Sabin in VP1 are reported here. [2]Excludes viruses detected from environmental surveillance.

Data in WHO HQ as of 03 February 2015

Orenstein W. PEDIATRICS vol 135 no 1 Jan 2015

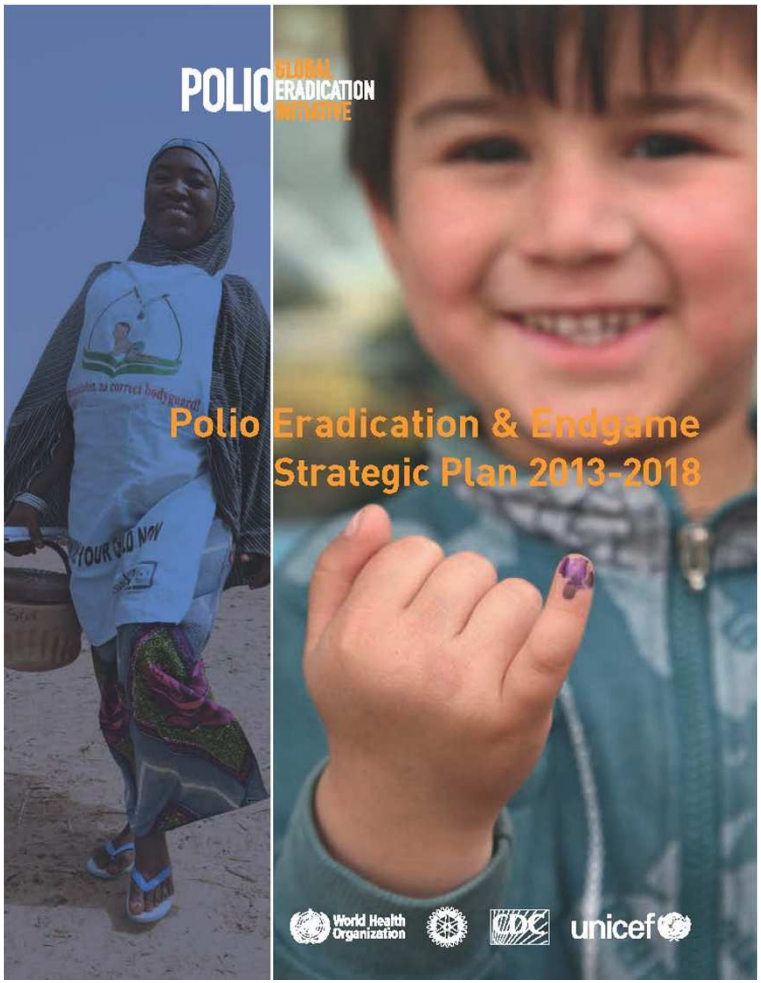
GPEI goal of interrupting transmission both WPV and cVDPV by end 2014 at extreme risk →

Security/political situation remains fragile in some countries

In May 2014, the international spread of poliovirus was declared a public health emergency of international concern.

CDC MMWR July 7, 2014.; http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6327a4.htm

Polio Eradication and Endgame Strategic Plan 2013–2018



The Plan differs from previous eradication plans

"complete the eradication and containment of all *wild*, *vaccine-related*, and *Sabin polioviruses* such that no child ever again suffers paralytic poliomyelitis."

IPV Comprehensive Technical Module GPEI version date: Feb 10, 2014

Polio Eradication and Endgame Strategic Plan 2013–2018

Objectives:

1. **Detect and Interrupt Poliovirus**
   - The plan provides a strategy to interrupt all wild poliovirus transmission by the end of 2014.
2. **Strengthen Immunization Systems and Withdraw OPV**
3. **Contain and Certify**
   - All regions must pass three years without a case to attain polio-free status, to be followed by global certification.
4. **Plan Polio's Legacy**

GPEI Fact File. www.polioeradication.org

World Health Organization

Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

28 FEBRUARY 2014, 89th YEAR / 28 FÉVRIER 2014, 89e ANNÉE
No. 9, 2014, 89, 73–92
http://www.who.int/wer

Polio vaccines: WHO position paper, January 2014

WHO Recommendations:

All children worldwide should be fully vaccinated against polio, and every country should achieve and maintain high levels of coverage.

WHO no longer recommends an OPV-only vaccination schedule.

For all countries currently using OPV only, at least 1 dose of IPV should be added to the schedule.

Review of Polio Vaccines: Difference between OPV and IPV

	OPV (Oral Polio Vaccine)	**IPV (Inactivated Polio Vaccine)**
Vaccine type:	Live attenuated	Inactivated "killed"
Contains:	tOPV: Polio Type 1, 2, 3 bOPV: Polio type 1, 3	Polio type 1, 2, 3
Pros:	Cheap, Easy to administer • Good oral and intestinal immunity • Confers transmission to contacts and secondary vaccination	• No risk of VAPP • Highly effective
Cons:	Causes paralysis in very rare cases (VAPP & cVDPVs)	More costly than OPV • Does not confer transmission to contacts and thus provide secondary vaccination
Protection:	≈ 50% immune after 1 dose >95% immune after 3 doses	≥90% immune after 2 doses ≥99% immune after 3 doses

CDC Pink Book 12th ed.; GPEI Planning for IPV Introduction – Implementation Facts March 2014 ; GPEI Background and Technical Rationale for Introduction of One dose of Inactivated Polio Vaccine (IPV) in Routine Immunization Schedule Feb 14, 2014

Why stop using OPV?

OPV protects vs transmission but challenges the eradication of polio…

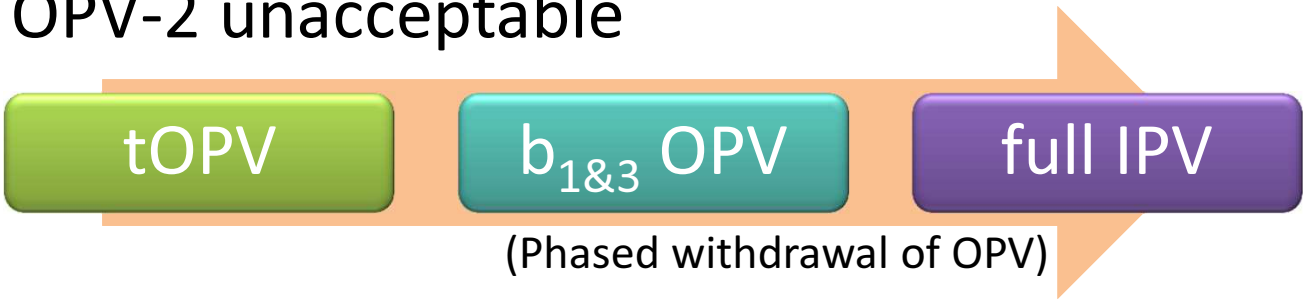
Rarely, OPV can cause:

- VAPP (Vaccine-associated Paralytic Polio)
- Vaccine-Derived Polioviruses (VDPV)

Polio type 2:

- Wild Polio Virus 2 eradicated globally in 1999
- OPV-related type 2 polio cases→ cause majority of cVDPV and VAPP cases
  - 40% of VAPP cases globally per year
  - 98% of cVDPV outbreaks in recent years

- OPV-2 now carries more risk than benefit
- Continuing OPV-2 unacceptable
- Plan: Shift:



Planning for IPV Introduction FAQs September 2013. IMG GPEI

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28 FEBRUARY 2014, 89th YEAR / 28 F
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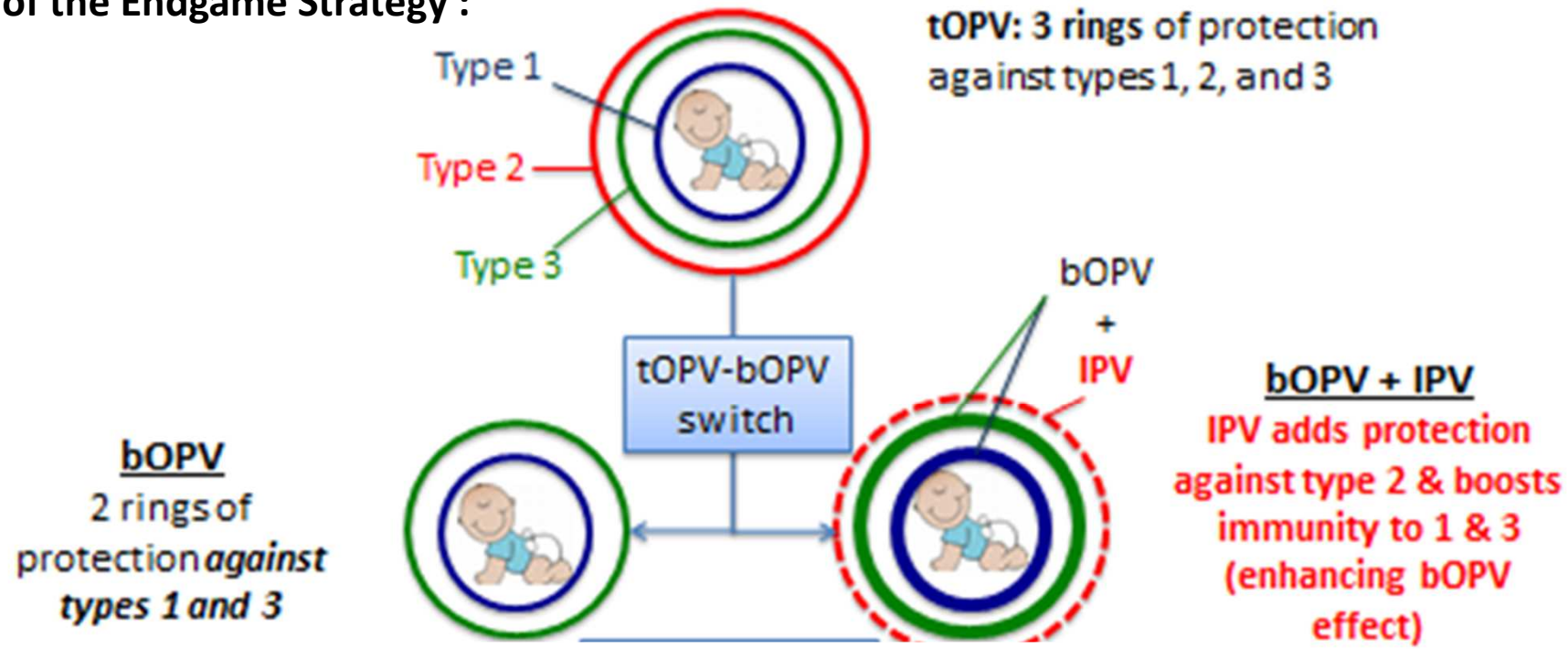
Polio vaccines: WHO position paper, January 2014

Primary purpose of the IPV dose:

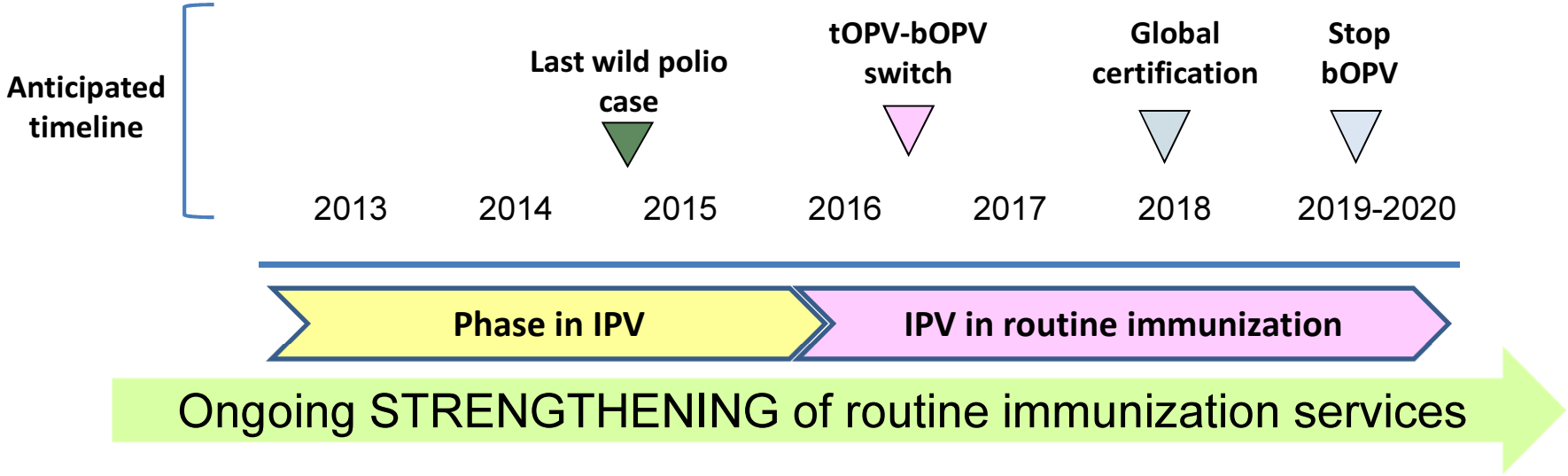
- To maintain immunity against type 2 polio during and after the global withdrawal of OPV2 and switch from tOPV to $b_{1\&3}$OPV
- To reduce VAPP risks (depending on the timing of the IPV administration)
- To boost immunity against polio types 1 and 3 → hasten the eradication of these WPVs

Schematic description of technical rationale for use of at least one dose of IPV as part of the Endgame Strategy :



Timeline for implementation of Objective 2:

Strengthen Immunization Systems and Withdraw OPV



3 Stages:

Introduction

- **Before end of 2015**: introduce **one dose of IPV** in immunization programs of all countries

Switch

- **2016**: **tOPV to $b_{1\&3}$OPV switch** globally

Withdrawal

- **2019-2020**: **withdrawal of bOPV** after the world is certified polio-free in 2018 (use all IPV)

IPV Comprehensive Technical Module GPEI version date: Feb 10, 2014

World Health Organization

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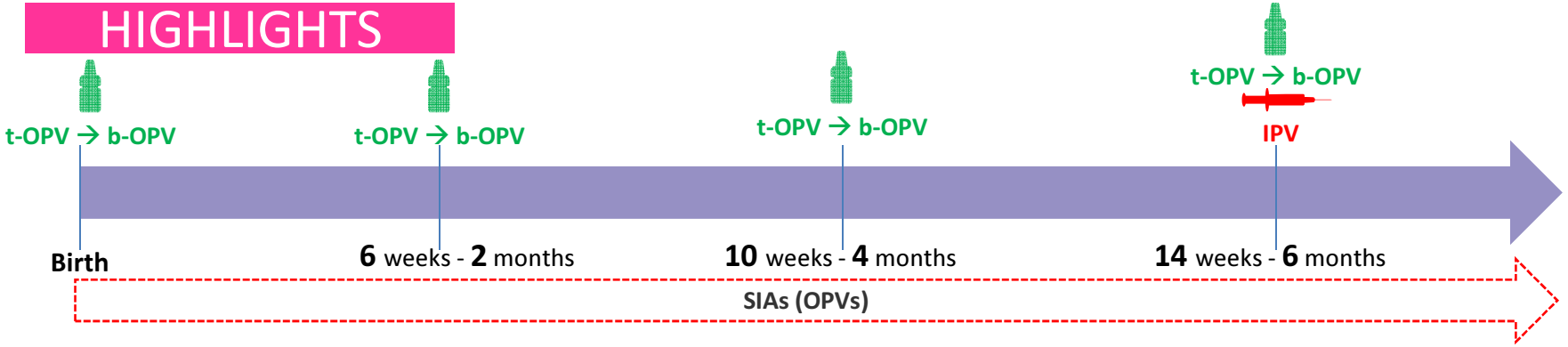
28 FEBRUARY 2014, 89th YEAR / 28 FÉVRIER 201
No. 9, 2014, 89, 73–92

Polio vaccines: WHO position paper, January 2014

HIGHLIGHTS



- IPV is an additional dose to OPV (not a replacement)
- Minimum interval: 4 weeks
- Single IPV dose at 14 weeks of age with DTP3/OPV3
  - → better immunogenicity of IPV vs earlier administration
- Late schedules (age > 3mos) → may give IPV on 1st visit
- Countries may consider alternative schedules
  - (e.g. VAPP risks)

Sources: WHO WER, 3rd January 2014, 89th year. No. 1, 2014, 89, 1–20

Inactivated Polio Vaccines (IPV)

Salk IPV
(Enhanced-potency IPV/Conventional IPV)

Sabin IPV
JPRI (Japan), Kunming (China), Intravacc (NL)

- Available as stand-alone or in combination
  - (tetra-, penta-, hexavalent with diphtheria, tetanus, pertussis, Hepatitis B, or Hib antigens)
  - No interferences reported when used in combination
- Most are WHO pre-qualified
- Considered very safe
- Main drivers of immunogenicity:
  - Number of primary series injections
  - Age at first dose
  - Interval between doses
  - Ethno-ecological factors (transient maternal antibodies, etc.)
- Less effective than OPV in inducing mucosal immunity, but reduces quantity and duration of viral shedding in stools due to a certain degree of intestinal protection.

Vidor E. & al. Poliovirus Vaccine – Inactivated VACCINES 6th ed. Plotkin ed. 2013; WHO. WER 2014; 89: 1–20

Impact of one dose of IPV

- **Primary role of 1- dose IPV**: **RISK MITIGATION** strategy
- **Seroconversion against type 2** after one dose of IPV: **32-63%**.
- **Seroconversion rates higher** when vaccine is **administered later in infancy** presumably because of waning maternal antibody

Author year	Country	Schedule	Type 2 Seroconversion
Intramuscular administration of 1 dose of IPV			
McBean 1988	US	2 mo	**35%**
Simasathien 1994	Thailand	2 mo	**39%**
Resik 2010	Cuba	6 wk	**36%**
Mohammed 2010	Oman	2 mo	**32%**
Resik 2013	Cuba	**4 mo**	**63%**

** Estı´variz CF et al. Lancet 2012; 12(2):128-35*

At least 2 doses of IPV (initiated ≥ 8 weeks of age) will give high protection against type 2 poliovirus when we shift from tOPV to bOPV.

IPV: Seroconversion against poliovirus Type 2

- 1 dose IPV: 32-63% (higher when given later)
- **2 dose IPV: >90%** when initiated after 8 weeks of age

Seroconversion rates following 1–3 doses of inactivated poliovirus vaccine (IPV) in different routine immunization schedules

Author year (Ref.)	Country	Schedule	*N*	% seroconversion[a]		
				Type 1	Type 2	Type 3
Intramuscular administration of 1 dose						
McBean 88 [45]	US	2 mo	309	42%	35%	54%
Simasathien 94 [46]	Thailand	2 mo	103	25%	39%	28%
Resik 10 [40•]	Cuba	6 wk	177	19%	36%	42%
Mohammed 10 [47•]	Oman	2 mo	186[b]	22%	32%	45%
Resik 13 [39••]	Cuba	4 mo	153	46%	63%	32%
Intramuscular administration of 2 doses						
WHO 97 [48]	Oman	6, 10 wk	136	71%	83%	81%
WHO 97 [48]	Thailand	6, 10 wk	141	40%	48%	79%
Cuba IPV group 05 [27]	Cuba	8, 16 wk	72	90%	89%	90%
Resik 10 [40•]	Cuba	6, 10 wk	177	63%	76%	93%
Mohammed 10 [47•]	Oman	2, 4 mo	186[b]	91%	91%	96%
Resik 13 [39••]	Cuba	4, 8 mo	153	100%	100%	99%

Estivariz C. & al. Poliovirus vaccination options for achieving eradication and securing the endgame. Current Opinion in Virology 2013, 3: 309-315.

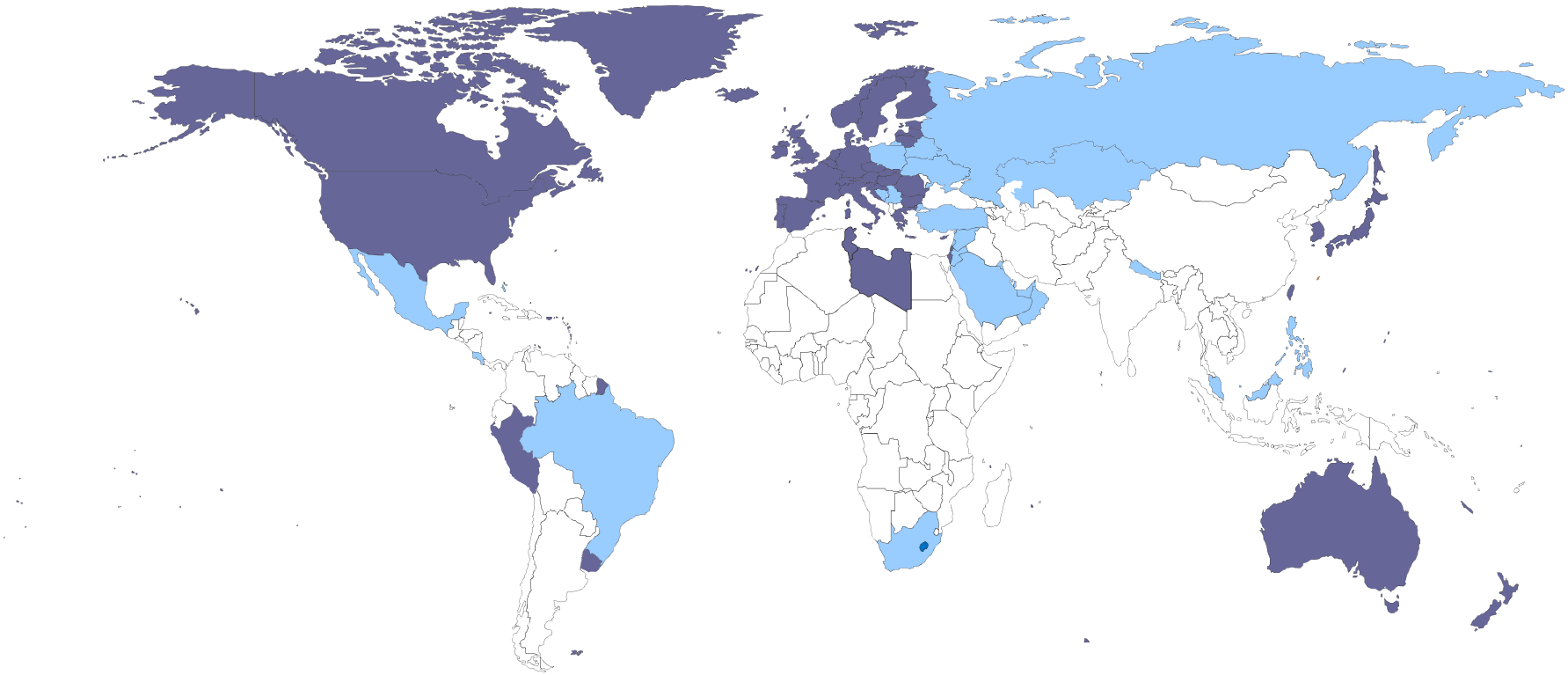
Salk IPV

- Efficacy
  - Proven in several studies (Houston 96%, Canada >90%, India 92%, etc.)
  - (Senegal study during outbreak of Polio type 1)
    - 1 dose: 36%
    - 2 dose: 89%
- Herd Immunity demonstrated
  - US experience upon IPV introduction → case reduction more than expected
- IPV-containing vaccines
  - Licensed in > 100 countries
  - Yearly: 25-30 million newborns, 15 mil children, adolescents, and adults vaccinated
- Used in different schedules
  - IPV-only
  - IPV/OPV sequential schedules
  - IPV/OPV combined schedules

Vidor E. & al. Poliovirus Vaccine – Inactivated VACCINES 6th ed. Plotkin ed. 2013 ; WHO. WER 2014; 89: 1–20

As of Jan. 2015, 75 countries have introduced IPV in their routine public infant/toddler National Immunization Program

(and much more countries in their private markets)



IPV-only (40 countries)

IPV-only supplemented with OPV SIAs
IPV-followed-by-OPV Sequential (35 countries)
Mixed / Combined IPV / OPV

WHO/IVB Database, as of 04 December 2014; Map production Immunization Vaccines and Biologicals (IVB), WHO

Different routine POLIO immunization regimens combining IPV & OPV can be implemented

IPV-only supplemented by OPV SIAs	Mixed / combined IPV and OPV with OPV optional at birth	IPV-followed-by-OPV
• **Mexico**: IPV at 2, 4, 6 and 15-18 months of age completed by OPV NIDs twice a year in all <5yrs • **Israel**: IPV at 2, 4, 6 and 15-18 months of age completed by OPV NIDs twice a year in all <5yrs	• **Turkey:** IPV at 2 and 4 months, and IPV & OPV at 6 and 18 months • **South Africa:** OPV at birth, IPV & OPV at 6 weeks, IPV at 10, 14 weeks	• **US (from 1997 to end of 1999):** IPV at 2 and 4 months and OPV at 6 to 18 months and at 4 – 6 years • **Russia:** IPV at 3 and 4.5 months and OPV at 6, 18 and 20 months • **Brazil (since 2012):** IPV at 2 and 4 months and OPV at 6 and 15 months + OPV SIAs

As of today 24 countries have implemented IPV-OPV combined regimen.

Sutter R. & al. Poliovirus vaccine-Live. Vaccines 6th ed. 2013: 598-645
Vidor E. & al. Poliovirus vaccine-inactivated. Vaccines 6th ed. 2013:573-597

Several countries use all IPV-only, relying on IPV-containing combination vaccines

Infant series: 3 (sometimes 2) doses during 1st year of life

Booster doses: toddler age and/or pre-school/early-adolescence (to ensure long term immunity)

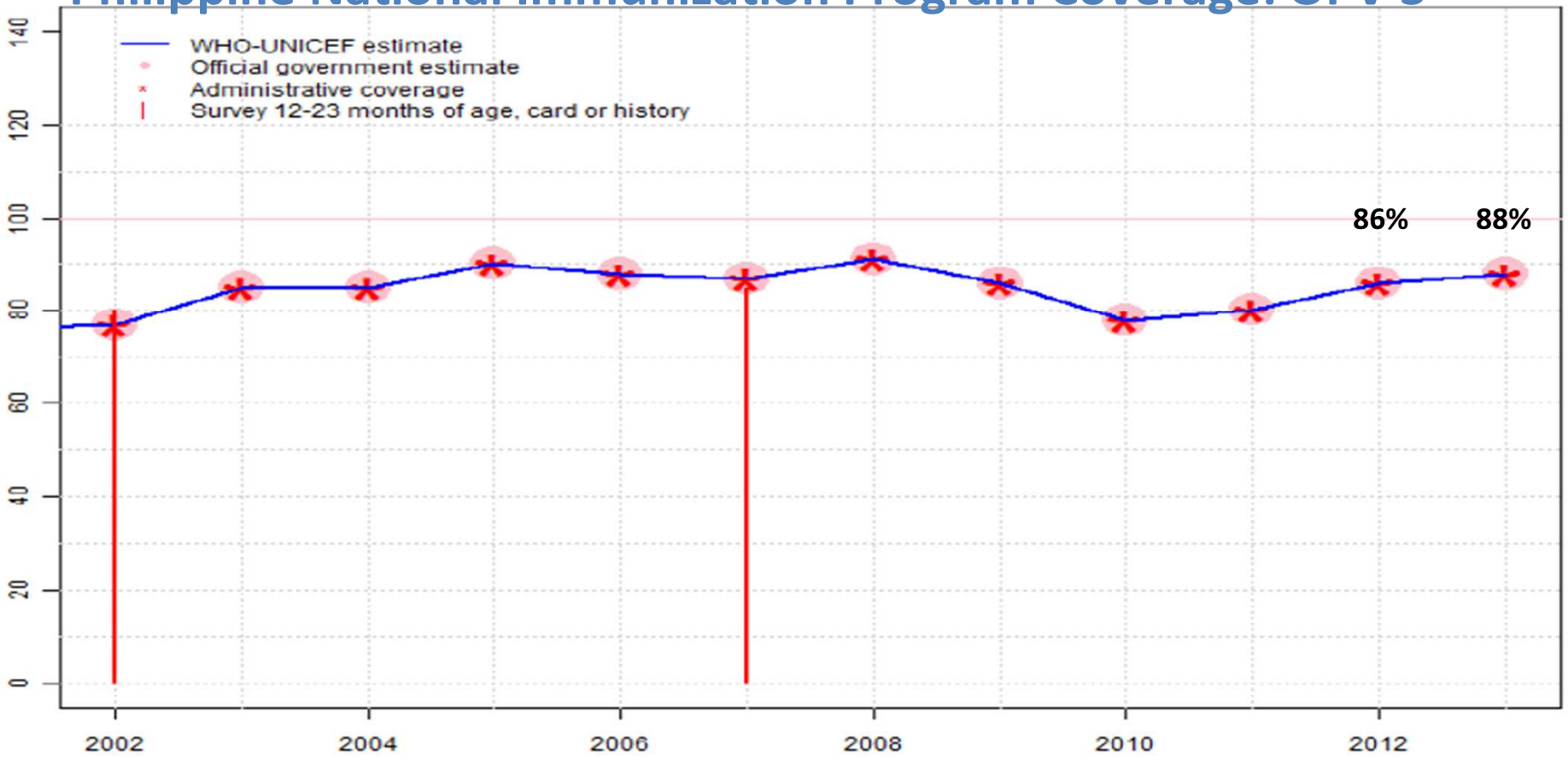
3 + 1 + 0	Spain, Slovenia, Japan, Uruguay
3 + 0 + 1	New Zaeland, United States*, Greece*, Australia, Ireland, Portugal, South Korea, UK
2 + 1 + 1	Austria, United States*, Greece*, France, Sweden, Slovakia, Italy, Norway, Denmark, Finland, Iceland
3 + 1 + 1	Switzerland, Canada, Croatia, Israel, Romania, Hungary, Belgium, Luxemburg, Germany, Czech Republic, Netherland, Estonia, Latvia, Lithuania, Bulgaria, Cyprus, Liechtenstein, Malta

* Official recommendations are for 3rd dose to be given any time between 6 and 18 months of age, therefore falling in the "2 + 1 + 1" or the "3 + 0 + 1" schedule. Consider also the "3 + 1 + 1" schedule as acceptable

http://vaccine-schedule.ecdc.europa.eu/pages/scheduler.aspx

Polio not included in combination vaccines used in Philippine NIP: can we improve coverage rates?

Philippine National Immunization Program Coverage: OPV 3



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Estimate	77	85	85	90	88	87	91	86	78	80	86	88
Estimate GoC	●●●	●	●●●	●●●	●●●	●●●	●●●	●●●	●●	●●	●●	●●

WHO and UNICEF estimates of national immunization coverage -June 27, 2014
http://www.childinfo.org/files/philippines_rev_13_FINAL.pdf

IPV-containing combination vaccines are now integrated in many routine public infant / toddler National Immunization Programs

(and much more countries in their private markets)

- **Most of European Union countries**
  - DTaP-IPV-Hib (1997) and DTaP-IPV-HepB-Hib (2000)
- **Canada**
  - DTaP-IPV-Hib (1997) and DTaP-HepB-IPV-Hib (2007)
- **Australia & NZ**
  - DTaP-IPV-HepB-Hib (2004)
- **USA**
  - DTaP-IPV-HepB (2005) and DTaP-IPV-Hib (2008)
- **Taiwan**
  - DTaP-IPV-Hib (2007)
- **Mexico, South Africa, Turkey, Costa Rica**
  - DTaP-IPV-Hib (2007)
- **Malaysia**
  - DTaP-IPV-Hib (2008)
- **South Korea**
  - DTaP-IPV (2010)
- **Japan**
  - DTaP-sIPV (2012)

Conclusions

- **WHO:**
  - **All countries currently using OPV only should add at least 1 dose of IPV to their NIP by 2015.**
  - **OPV cessation must occur for the world to be polio free.**
- **Need for IPV in Polio Eradication:**
  - Maintain immunity vs type 2 PV during/after the switch from tOPV to bOPV
  - Reduce VAPP risks
  - Boost humoral and mucosal immunity against PV types 1 and 3 → hasten the eradication of these WPVs
- **Salk IPV:**
  - No risk of VAPP or cVDPVs
  - Predictable, consistent high immunogenicity with at least 2 doses
  - Wealth of data have proven safety, efficacy, and effectiveness
  - Different schedules alone or in combination with OPV
  - Can be included in combination vaccines → improve coverage

PHILIPPINES: INTRODUCED IPV IN THE NIP LAST OCT 6, 2014

Courtesy of: World Health Organization. Retrieved from: http://www.vaccineinformation.org/polio/photos.asp

Unlikely hero: Polio victim saved 10 lives

Danny Petilla
@inquirerdotnet

Philippine Daily Inquirer 3:28 AM | Sunday, February 9th, 2014

Wendell Corregidor

- Polio victim: walks with crutches
- 36-year-old ex-paralympian
- Winner of gold medals from swimming competitions for the disabled.
- Saved 10 people, including six children, from drowning in gigantic storm surges during Supertyphoon “Yolanda” in in Palo, Leyte.
- **used his skills to save lives**

Photo by Caroline Gluck.
(courtesy rappler.com)

http://newsinfo.inquirer.net/575774/unlikely-hero-polio-victim-saved-10-lives#ixzz3RUcykzjY
http://www.rappler.com/move-ph/campaigns/54976-lifeguard-paralympic-swimmer-heroesofhaiyan

What can PEDIATRICIANS do?

1. Educate parents about importance of eradicating polio.
2. Ensure patients are vaccinated against polio (incorporate at least 1 dose IPV).
3. Ensure that all patients travelling internationally receive recommended vaccines (IPV when appropriate).
4. Consider polio in the ddx of child presenting with AFP.