Two years after the tOPV to bOPV switch: What happened to Poliovirus Type 2 ?

GVIRF, Bangkok, March 22, 2018

Dr. Ondrej Mach

Types of Polioviruses

Wild (WPV)	• Type 1 (22 cases in 2017) • Type 2 (eradicated worldwide in 1999) • Type 3 (none detected since November 2012)
Vaccine derived from OPV (VDPV)	• VDPVs are mutated Sabin (OPV vaccine) polioviruses • There are VDPVs type 1,2 and 3 • Epidemiology, transmissibility, neurovirulence and control measures for VDPVs are similar to wild polioviruses

Definitions

Vaccine-derived poliovirus (VDPV): OPV virus strains that are > 1% divergent (or >= 10nt changes, for types 1 and 3) or > 0.6% divergent (>= 6nt changes, for type 2) from the corresponding OPV strain in the complete VP1 genomic region

Circulating VDPV (*cVDPV*): Genetically linked VDPVs

Immune-deficiency associated VDPV (*iVDPV*): VDPVs isolated from persons with evidence of primary immunodeficiency (PID)

Ambiguous VDPV (*aVDPV*): VDPV isolate from individuals or from environmental samples, without evidence of circulation and from individuals with no known immunodeficiency

http://polioeradication.org/wp-content/uploads/2016/09/Reporting-and-Classification-of-VDPVs_Aug2016_EN.pdf

Assumptions vs observation

(1 May 2016 – 1 April 2018)

- Modelling forecast: (accepted for planning purposes prior to the switch by Eradication and Outbreak Management Group [EOMG])

Year Post Switch	cVDPV2 outbreaks (#)	VDPV2 events (#)
1	3	12
2	2	2
3	1	2
4	1	1

- Observation

Year post switch	cVDPV2 outbreaks (#)	VDPV2 events (#)
~2 years	7 (94 cases)	46 isolates/34 events

Modelling

RESEARCH ARTICLE Open Access

Managing the risk of circulating vaccine-derived poliovirus during the endgame: oral poliovirus vaccine needs

Radboud J. Duintjer Tebbens* and Kimberly M. Thompson

Abstract

Background: The Global Polio Eradication Initiative plans for coordinated cessation of oral poliovirus vaccine (OPV) use, beginning with serotype 2-containing OPV (i.e., OPV2 cessation) followed by the remaining two OPV serotypes (i.e., OPV13 cessation). The risk of circulating vaccine-derived poliovirus (cVDPV) outbreaks after OPV cessation of any serotype depends on the serotype-specific population immunity to transmission prior to its cessation.

Methods: Based on an existing integrated global model of poliovirus risk management policies, we estimate the serotype-specific OPV doses required to manage population immunity for a strategy of intensive supplemental immunization activities (SIAs) shortly before OPV cessation of each serotype. The strategy seeks to prevent any cVDPV outbreaks after OPV cessation, although actual events remain stochastic.

Results: Managing the risks of OPV cessation of any serotype depends on achieving sufficient population immunity to transmission to transmission at OPV cessation. This will require that countries with sub-optimal routine immunization coverage and/or conditions that favor poliovirus transmission conduct SIAs with homotypic OPV shortly before its planned coordinated cessation. The model suggests the need to increase trivalent OPV use in SIAs by approximately 40 % or more during the year before OPV2 cessation and to continue bOPV SIAs between the time of OPV2 cessation and OPV13 cessation.

Conclusions: Managing the risks of cVDPVs in the polio endgame will require serotype-specific OPV SIAs in some areas prior to OPV cessation and lead to demands for additional doses of the vaccine in the short term that will affect managers and manufacturers.

Risks of Paralytic Disease Due to Wild or Vaccine-Derived Poliovirus After Eradication

Authors: Tebbens, Radboud J. Duintjer; Pallansch, Mark A.[1]; Kew, Olen M.[1]; Cáceres, Victor M.[2]; Jafari, Hamid[2]; Cochi, Stephen L.[2]; Sutter, Roland W.[3]; Aylward, R. Bruce[3]; Thompson, Kimberly M.
Source: Risk Analysis, Volume 26, Number 6, December 2006, pp. 1471-1505(35)
Publisher: Wiley-Blackwell
DOI: https://doi.org/10.1111/j.1539-6924.2006.00827.x

After the global eradication of wild polioviruses, the risk of paralytic poliomyelitis from polioviruses will still exist and require active management. Possible reintroductions of poliovirus that can spread rapidly in unprotected populations present challenges to policymakers. For example, at least one outbreak will likely occur due to circulation of a neurovirulent vaccine-derived poliovirus after discontinuation of oral poliovirus vaccine and also could possibly result from the escape of poliovirus from a laboratory or vaccine production facility or from an intentional act. In addition, continued vaccination with oral poliovirus vaccines would result in the continued occurrence of vaccine-associated paralytic poliomyelitis. The likelihood and impacts of reintroductions in the form of poliomyelitis outbreaks depend on the policy decisions and on the size and characteristics of the vulnerable population, which change over time. A plan for managing these risks must begin with an attempt to characterize and quantify them as a function of time. This article attempts to comprehensively characterize the risks, synthesize the existing data available for modeling them, and present quantitative risk estimates that can provide a starting point for informing policy decisions.

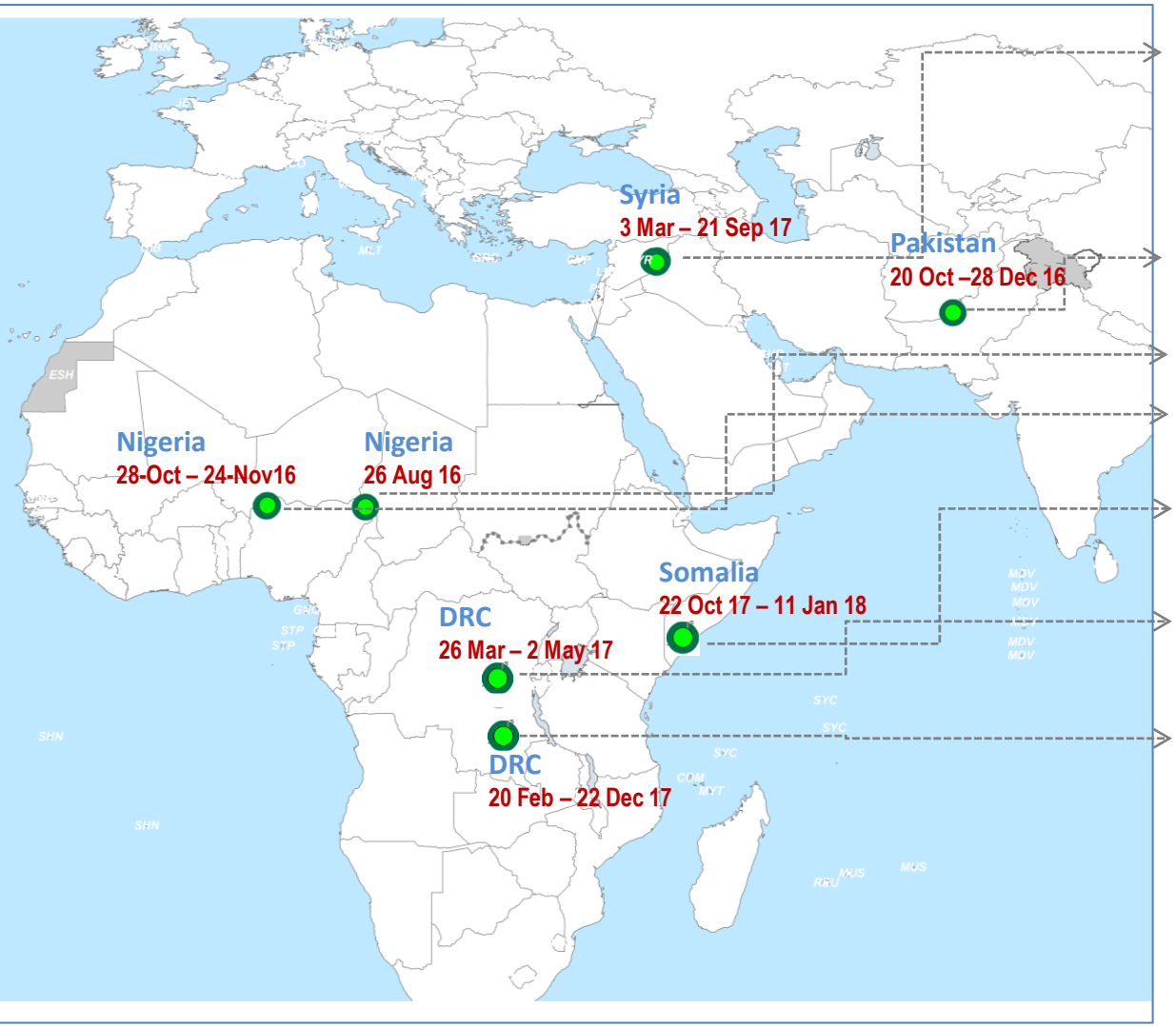
1. Duintjer Tebbens RJ, Thompson KM. Managing the risk of circulating vaccine-derived poliovirus during the endgame: oral poliovirus vaccine needs. BMC Infect Dis **2015**; 15:390. DOI: 10.1186/s12879-015-1114-6

2. Tebbens, Radboud J. Duintjer; Thompson, Kimberly Met al, Risks of Paralytic Disease Due to Wild or Vaccine-Derived Poliovirus After Eradication, Risk Analysis, Volume 26, Number 6, December 2006, pp. 1471-1505(35) DOI: https://doi.org/10.1111/j.1539-6924.2006.00827.x

http://polioeradication.org/wp-content/uploads/2016/09/Reporting-and-Classification-of-VDPVs_Aug2016_EN.pdf

Post switch* cVDPV2 outbreaks (n=7)

Total of 7 post-switch cVDPV type2 outbreaks in 5 countries



Syria (74 cases, mostly Deir ez-Zor)

Pakistan (1 case)

Nigeria Borno (1 case)
Nigeria Sokoto (1 case)

Somalia (4 Env isolates)

DRC Maniema (2 cases)

DRC Haut Lomami and Tanganyika (22 cases, 17 community contacts)

Using assumption of 1%nt change/year at a uniform rate, all VDPV2 except DRC, Maniema seeded before the switch.

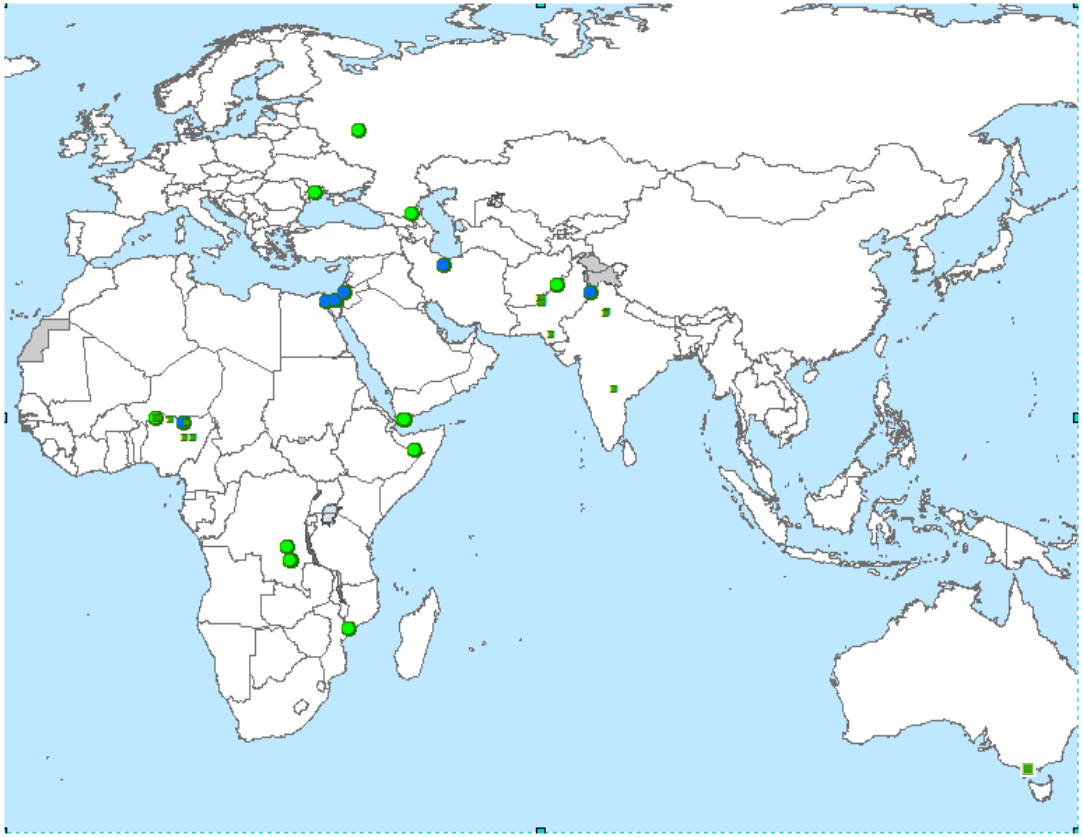
*Switch date: 01 May 2016

cVDPV2 outbreak (total 7 outbreaks)

Post-switch SIA containing mOPV2 vaccine was conducted or is planned.

Data in WHO HQ as of 06 Mar. 2018

Post switch[1] VDPV2 events[2]



44 a/i/ VDPV2 isolates from 34 'events' in 14 countries

aVDPV: *Australia, Afghanistan, DRC, Egypt, India, Iran, Mozambique, Nigeria, Pakistan, Russia, Somalia, Ukraine, West Bank, Yemen*

- 51% aVDPV2 seeded before the switch

iVDPV: *Egypt, Iran, West Bank, Pakistan*

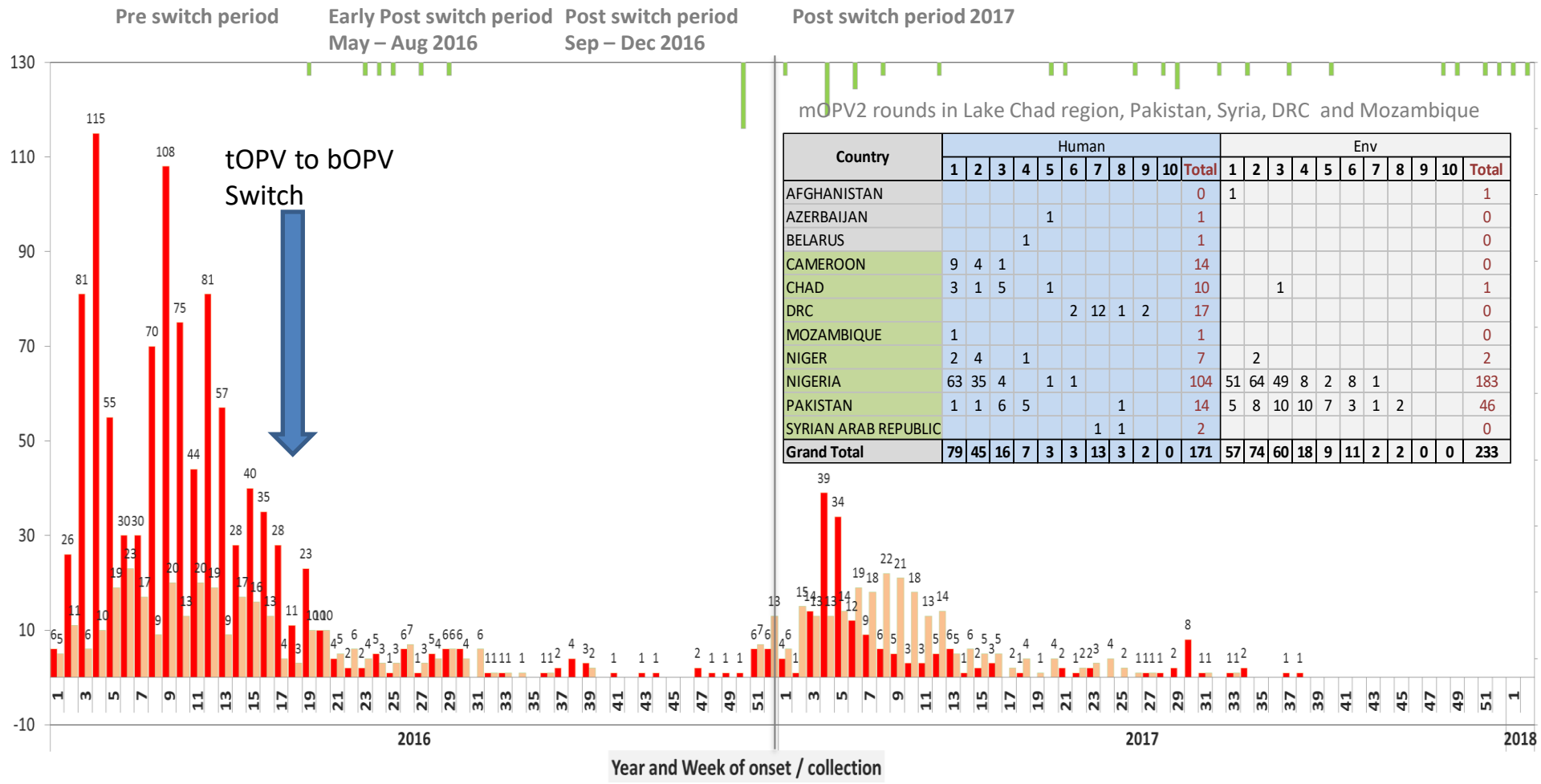
- All iVDPVs appear to have been seeded before the switch

[1]Switch date: 01 May 2016
[2]Event refers to all vaccine derived polioviruses, regardless of source, except those which have been classified as circulating

AFP, contact, healthy human VDPV2 events (n=12)
Environmental VDPV2 events (n=28)
iVDPV2s (n=6)

Data in WHO HQ as of 06 Mar. 2018

Distribution of SL2 by week from AFP and ENV, Global, 2016-2017

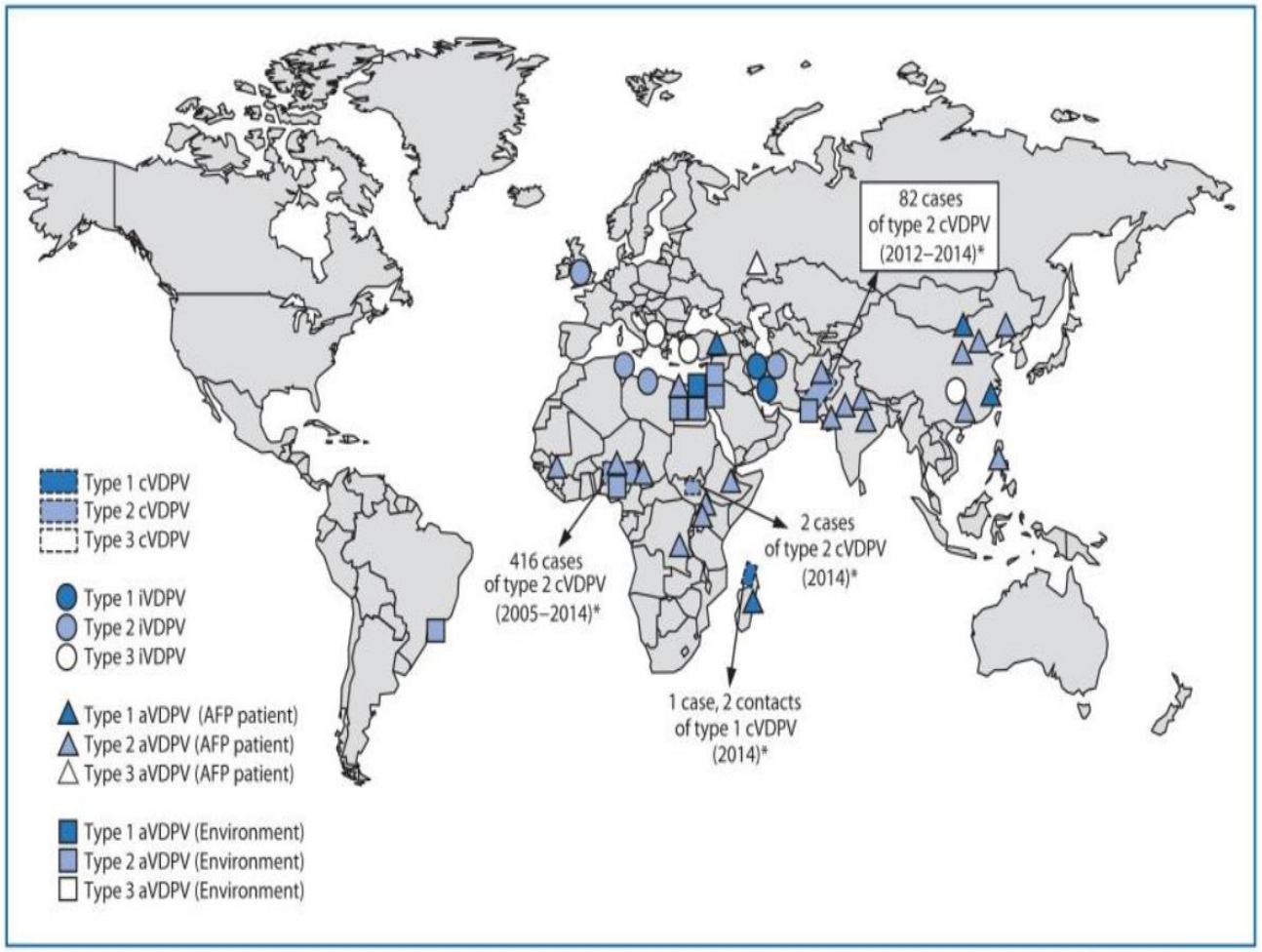


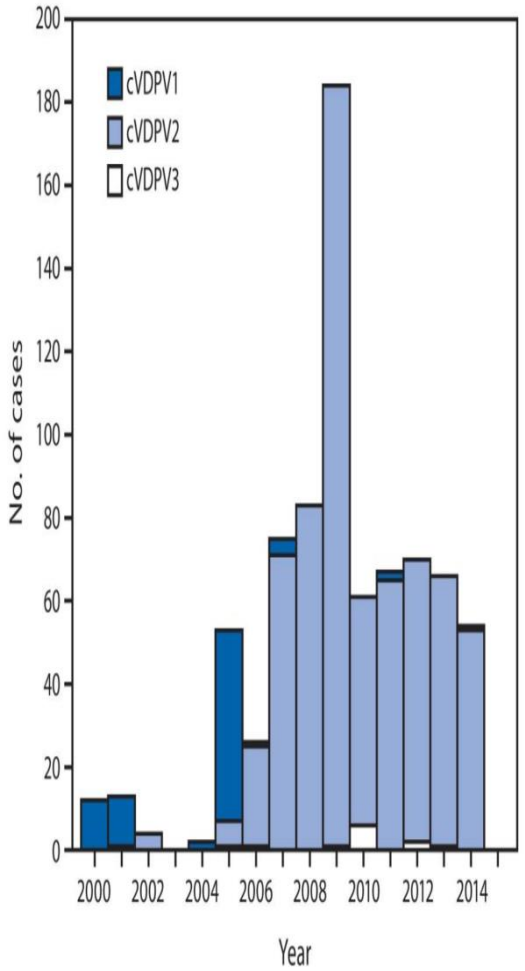
Country	Human											Env									
	1	2	3	4	5	6	7	8	9	10	Total	1	2	3	4	5	6	7	8	9	10	Total
AFGHANISTAN											0	1										1
AZERBAIJAN					1						1											0
BELARUS				1							1											0
CAMEROON	9	4	1								14											0
CHAD	3	1	5		1						10			1								1
DRC						2	12	1	2		17											0
MOZAMBIQUE	1										1											0
NIGER	2	4		1							7		2									2
NIGERIA	63	35	4		1	1					104	51	64	49	8	2	8	1				183
PAKISTAN	1	1	6	5				1			14	5	8	10	10	7	3	1	2			46
SYRIAN ARAB REPUBLIC							1	1			2											0
Grand Total	**79**	**45**	**16**	**7**	**3**	**3**	**13**	**3**	**2**	**0**	**171**	**57**	**74**	**60**	**18**	**9**	**11**	**2**	**2**	**0**	**0**	**233**

ENV
AFP / Contact
Type 2 containing SIAs

*Afghanistan SL2 is linked to mOPV2 use in Balochistan, Pakistan

VDPVs detected worldwide, prior to switch





Diop OM, Burns CC, Sutter RW, Wassilak SG, Kew OM. Update on Vaccine-Derived Polioviruses — Worldwide, January 2014–March 2015. *MMWR Morbidity and Mortality Weekly Report*. 2015;64(23):640-646.

Response with mOPV2

- **Mechanism of response:** The Advisory Group [AG] assesses each VDPV2 event/outbreak and recommends release of mOPV2; the release is authorized by WHO's Director General [DG] (within 24 hours of AGs recommendation)

- **Speed of response:** mOPV2 was available in the target country within 7 days of DG authorization in 5/6 outbreaks (exception: Syria) and 1st SIA carried out within 14 days of confirmation of outbreak in 3/6 outbreaks (Delay in DRC and in Syria)

- **Number and scope of mOPV2 SIAs for response:** varied**;** 5 mOPV2 SIAs implemented in Borno, 4 SIAs in Sokoto and 2 SIAs implemented each in Quetta, DRC, Syria, Mozambique; Target population average per round = 3.0 million (Range 0.2 - 48 million)

- **IPV use to complement response:** IPV used in combination with mOPV2 in four responses (Quetta, Borno, Sokoto, Syria)

Emergence of VDPV2 following mOPV2 campaigns

- **Pakistan**:
  - 2 mOPV2 rounds in early late 2016 and early 2017
  - Significant increase in SL2 starting one week post campaign
  - *5x emergences of new independent VDPV2 (6-8 ntd) in Q1 2017 (First VDPV2 detected 12 weeks after first mOPV2 SIA)*

- **Nigeria**:
  - Multiple mOPV2 campaigns in 2016
  - *Emergences of 8x new VDPV2 (6-7 ntd) after 8 weeks following first mOPV2 SIAs reported from multiple areas (Bauchi, Katsina, Gombe and Chad)*

None of these aVDPVs progressed to persistent cVDPV so far

Risks and Challenges

- Risk of cVDPV2 outbreak continuation and geographic spread in Syria and DRC
- Risk of mOPV2 seeding new VDPV (and subsequent cVDPV) at the areas bordering intervention – unstoppable snowball effect however modelling shows that risk of uncontrolled VDPV2 spread > risk of new emergence; *"VDPV2 is uglier virus than Sabin 2; and mOPV2 is the only weapon we have" Roland Sutter*
- Challenges:
  - Inaccessible and conflict affected areas (Borno, DRC and Syria)
  - Surveillance gaps
  - Quality of response (Speed vs SIAs quality)---Technical vs operational
  - Ensuring proper mOPV2 management, in difficult area: mOPV2 retrieval, disposal

Summary

- In the first 2 years post switch, polio program detected slightly higher number of cVDPV2 outbreaks and VDPV2 events, when compared to expectations

- Mechanisms governing mOPV2 release, use and disposal were followed; speed, type and scope of type2 outbreak response varied depending on the situation

- Evidence suggested that mOPV2 SIAs led to emergence of new VDPV2, and that the evolution of VDPV2 was faster than expected