

Persistent circulating vaccine-derived poliovirus type 2 (cVDPV2) - current status in preparation of the tOPV to bOPV switch

Background paper for the meeting of SAGE, April 14-16, 2015

1 Introduction and background

Since the first outbreak due to a vaccine-derived poliovirus (VDPV) in 2000 on the island of Hispaniola,¹ it has become clear that live oral polio vaccine (OPV) viruses can, on rare occasion, circulate in communities and accumulate sufficient mutations to regain transmissibility and neurovirulence similar to wild-type polioviruses (circulating vaccine-derived polioviruses [cVDPVs]).² While VDPV outbreaks associated with each of the three components of trivalent OPV (tOPV) have been reported, from 2000-2015 the vast majority of VDPV outbreaks (97%) and related cases (>90%) have been associated with the type 2 component of OPV (OPV2).³ In addition, OPV2 is estimated to cause up to 40% of vaccine-associated paralytic polio (VAPP) cases.⁴

Since November 2012, all cases of polio related to wild virus have been type 1. Wild poliovirus type 2 (WPV2) has not been detected globally since October 1999, when the last case was reported from Aligarh, India.⁵ Therefore, at this point in the polio eradication effort, all type 2 polio cases are associated with the type 2 component of OPV. In order to manage the risks associated with the continued use of OPV,⁶ the 'endgame strategy' of the Global Polio Eradication Initiative (GPEI), as outlined in the 2013-2018 GPEI Strategic Plan,⁷ calls for the sequential withdrawal of OPV strains, starting with the withdrawal of OPV2 through a globally synchronized switch from tOPV to bOPV.⁸ To reduce the risk associated with OPV2 withdrawal, in November 2013 SAGE endorsed five readiness criteria,ⁱ as well as the global absence for at least 6 months of all persistent type 2 cVDPVs (cVDPV2).⁹

In April 2014, SAGE emphasized that the elimination of cVDPV2 must be a high priority for the polio eradication effort to remain on-track to achieve the major milestones of the 'endgame plan,' including the withdrawal of type 2 component of tOPV by April 2016.¹⁰ This background paper provides an update on the current status of persistent cVDPV2 transmission in Nigeria and Pakistan and information on VDPV2 outbreaks in other countries from 2010-2015; discusses immunization activities conducted and planned to interrupt currently persistent cVDPV2 transmission; and introduces detection and response scenarios for any new emergences of VDPV2.

2 Current status of persistent cVDPV2 transmission in Nigeria and Pakistan

Since 2005, 15 countries reported episodes of cVDPV2. However, since 2010, persistent cVDPV2 transmission (i.e., longer than 6 months after detection) has occurred in only 4 countries: Nigeria, Pakistan, Chad and Afghanistan. In Chad and Afghanistan, persistent cVDPV2 transmission has not occurred since 2012 and 2013, respectively. Persistent cVDPV2 transmission was detected only in Nigeria and Pakistan in 2014.¹¹

ⁱ (1) at least 1 dose of IPV included in the routine immunization programme in OPV-using countries; (2) bivalent oral polio vaccine (bOPV) licensed for routine immunization; (3) type 2 poliovirus surveillance and response protocols and monovalent OPV (mOPV) stockpile; (4) appropriate containment and handling of residual type 2 materials; and (5) verification of global eradication of wild poliovirus type 2.

2.1 Nigeria

Since 2005, more than 20 distinct emergences of cVDPV2 have been detected in Nigeria,^{12,13} including seven that established persistent circulation. These cVDPV2 outbreaks were restricted to the northern states, where immunization coverage with tOPV was low and SIAs using tOPV were infrequent. Repeated seroprevalence surveys conducted in Sokoto and Kano states indicated that population immunity to type 2 was low and had dropped significantly in Kano state between 2011 and 2013.¹⁴ Of the 20 emergences, only one lineage continued to circulate in 2014 in the northern states (see 'Nigeria Old' virus grouping, Figure 1) along with a cVDPV2 strain that was imported into northeastern Nigeria from Chad in 2011/2012 (see 'Nigeria-Chad' virus grouping, Figure 1). In 2014, 30 cVDPV2 polio cases were reported from Nigeria, compared to only 6 wild poliovirus type 1 (WPV1) cases. However, cVDPV2-related AFP cases or cVDPV2-positive environmental surveillance (ES) samples have not been identified since the most recent tOPV SNID conducted in November 2014.

From 2012 to mid-2014, the majority of SIAs conducted in Nigeria used bOPV to target remaining chains of WPV1 transmission – few tOPV campaigns were conducted. In each of 2012 and 2013, only one large-scale tOPV SIA was conducted in northern Nigeria. Moreover, vaccination efforts have been compromised due to insecurity and limited access in some critical areas, particularly in the northeastern states of Borno and Yobe. Since June 2014, IPV + tOPV campaigns have targeted high risk areas of Borno (June), Yobe (June) and Kano (November) states, and large-scale tOPV SIAs (SNIDs) were conducted in the northern states in August and November. For 2015, the Expert Review Committee on polio eradication in Nigeria has recommended an aggressive mopping-up response strategy to ensure that current persistent cVDPV2 transmission is interrupted within the first half of 2015. Two tOPV SIAs are planned for March (NID) and April (SNID), with IPV added in selected high-risk areas. Nigeria is planning to conduct additional immunization activities using IPV in April to address any areas of persistent virus circulation and ensure transmission is stopped, including raising immunity in internally displaced populations in Borno, Adamawa, Gombe, Nasarawa, Benue and Taraba; and raising immunity in other high-risk areas of northern states (including Kaduna and Sokoto). In addition, SIA plans in Nigeria include three tOPV SNIDs (July and October 2015, and January 2016) and two tOPV NIDs immediately before (February and March 2016) the planned OPV2 withdrawal.

2.2 Pakistan

Since mid-2012, there have been five distinct emergences of cVDPV2 in Pakistan. In 2014, two “old” lineages of cVDPV2 circulated causing 21 cases (compared to 306 WPV1 cases reported during the same year), with the majority of cases detected in the Federally Administered Tribal Areas (FATA) and adjacent districts of Khyber Pukhtunkhwa (KP) province, where insecurity and vaccination ban compromised access to children during SIAs. These two lineages have not been detected since June 2014. A new persistent lineage emerged in Gadaap, Karachi, in July 2014 and was last detected in January 2015 in an environmental surveillance sample.

Since mid-2014, there has been significant progress in vaccinating children displaced from inaccessible areas at transit vaccination posts, or through vaccination of internally displaced families in their accessible host communities. Two large tOPV SIAs were conducted in July (NID) and August (SNID) and small targeted campaigns with IPV were conducted between November 2014 and February 2015 in high-risk areas of Quetta, Killa Abdullah and Pishin districts (Balochistan province), FR Bannu (KP province) and high risk areas of Karachi (Sindh province). Pakistan will implement four tOPV campaigns during the first half of 2015 in areas

affected by persistent cVDPV2 in 2014: one in March (NID), one in April (SNID), and two in May (SNIDs), using tOPV + IPV in selected highest-risk areas. In addition, the SIA plan in Pakistan includes two tOPV SIAs (September and November 2015) and two tOPV SIAs immediately before (February and March 2016) the planned OPV2 withdrawal.

2.3 Pre-switch scenarios for cVDPV2 response in Pakistan and Nigeria

In October 2014, SAGE re-emphasized its previous recommendation that, in order to maintain the planned timeline towards the tOPV-bOPV switch in April 2016, the elimination of persistent cVDPV2 should have the same priority for the GPEI as the elimination of wild polioviruses.¹⁵ To reduce the risk of cVDPV2 emergence after withdrawal of OPV2, SAGE endorsed a risk-based approach for boosting population immunity to type 2 polioviruses prior to OPV2 withdrawal. The strategy ensures that sufficient tOPV SIAs are planned and conducted in areas at highest risk of cVDPV2 emergence.

The October 2015 meeting SAGE is expected to confirm April 2016 as the date for all OPV-using countries to withdraw OPV2. In April 2015, SAGE will review progress toward IPV introduction, OPV2 withdrawal, bOPV licensure and progress towards elimination of persistent cVDPV2. Prior to the April 2015 meeting, the SAGE Polio Working Group reviewed proposed scenarios of detection and response to persistent and emerging cVDPV2 in Nigeria and Pakistan for the periods before (April - September 2015) and after (November 2015 - March 2016) the October 2015 SAGE meeting.

Given the high risk in these countries, if persistent cVDPV2 is detected during April-September 2015 the response will include ensuring full implementation of all planned tOPV campaigns, the addition of intense mopping-up campaigns, addition of IPV to tOPV campaigns in specific areas, and further intensification/frequency of activities as needed. The SAGE WG agreed to review the epidemiology of persistent cVDPV2 in June 2015 and in greater detail during its meeting in September 2015. The final recommendations by the WG to SAGE will be given after the WG meeting in September 2015 and will be based upon whether or not there is clear evidence of progress in the two countries with persistent cVDPVs that would provide a high degree of confidence in October 2015 that by the time of the switch the criteria for elimination of persistent cVDPV2 circulation will be met. Detection of cVDPV2 following the October 2015 SAGE meeting will activate further escalation of tOPV/tOPV+IPV mopping-up in addition to planned tOPV campaigns.

3 cVDPV2 epidemiology and response in “other countries”

To provide a broader context of the outcome of cVDPV2 emergence and outbreaks and of the impact of GPEI response activities, the following is a brief description of the epidemiology and duration of cVDPV2 outbreaks during 2010-2015 in countries other than Nigeria and Pakistan (“other countries”).

There were 15 cVDPV2 events during 2010-2015, with 84 reported cases in 9 “other countries.”ⁱⁱ The median outbreak duration was 1.2 months (range: 0-32.2 months). The majority (13/15 or 87%) lasted <6 months, i.e., below the threshold used by the programme to define 'persistent transmission'. Regarding the origin of the outbreaks, 7/15 (47%) were new emergences and 8/15 (53%) were importations (4 from Nigeria, 1 from Chad, 1 from Somalia, and 2 from Pakistan). The size of the outbreaks involved primarily multiple-case

ⁱⁱ Afghanistan, Cameroon, Chad, China, DRC, Kenya, Niger, South Sudan and Yemen

events, 10/15 (66%) involving between 2-26 cases; however, there were 5/15 (33%) single-case events, 4 of which were importations from Nigeria.

Of the 15 cVDPV2 events, 73% were stopped by 2 or fewer campaigns and 87% were stopped by 4 or fewer campaigns: 7 (47%) stopped spontaneously; 2 (13%) after 1 SIA; 2 (13%) after 2 SIAs; 1 (7%) after 3 SIAs; and 2 (13%) after 4 SIAs. Only 1 (7%) outbreak (in Afghanistan) required 9 SIAs to stop the outbreak country-wide.

Based on the experience with cVDPV2 events in the past five years and anticipating the withdrawal of type 2 OPV in April 2016, scenarios in other countries for detection and response to VDPV2 were presented for the periods before (April-September 2015) and after (November 2015-March 2016) the October 2015 SAGE meeting. A risk-based approach was proposed that incorporated risk tiers for VDPV2 emergence and spread (Tier 1 vs. Tier 2-4 countries) and type of VDPV2 detected (cVDPV2 or aVDPV2) and proximity to the date of OPV2 withdrawal. The most intensive mopping up response would be implemented in the highest risk category scenario which would be the detection of cVDPV2 in a Tier 1 country during the October 2015-March 2016 timeframe. Based on the updated tOPV SIA calendar for preventative campaigns and this risk-based strategy, as we approach the OPV2 withdrawal date, a progressively intensified response would be undertaken following detection of any VDPV2.

Figure 1.

Nigeria: persistent cVDPV2 outbreaks, as of 18/3/15, and tOPV (IPV) SIAs conducted and planned from Jan/4 to Mar/16																															
As of 18 March 2015																															
Viral grouping	Source	State	2014												2015												2016				
			Jan.	Feb.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	
Nigeria-Old	AFP	Borno			•																										
		Katsina								•																					
		Kano					•	•		•		•																			
		Jigawa										•																			
	ENV	Jigawa										•																			
		Kano				•	•	•	•	•	•	•	•	•																	
		Kaduna						•		•		•	•	•	•																
		Sokoto		•		•	•	•	•	•	•																				
Nigeria-Chad		Borno		•	•	•	•	•			•																				
		Kano							•				•																		
		Jigawa										•																			
		Yobe										•	•																		
	ENV	Borno	•	•	•	•	•	•																							
		Kano				•																									
Nigeria 2014	ENV	Kaduna							•						•																
		SIAs using tOPV or IPV (conducted and planned)				SNID: bOPV + tOPV	bOPV SNID plus IPV in HR areas of Borno + Yobe		SNID: tOPV	HR area (which one?) IPV		SNID: tOPV + (IPV in HR areas of Yobe)	SNID: bOPV (+ IPV in 12 Kano LGAs)		•		NID: tOPV (+ IPV in 8 Kano LGAs)	SNID: tOPV		SNID: tOPV		SNID: tOPV		SNID: tOPV		SNID: tOPV	NID: tOPV	NID: tOPV	end OPV2		
			•	At least one cVDPV2 AFP case reported per given month																											
		•	At least one environmental site with a cVDPV2 reported per given month																												

Figure 2.

Viral grouping	Source	Province	Year / Month																										
			2014												2015												2016		
			Jan.	Feb.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.
Pakistan: 2 'old' groupings	AFP only	FATA	•	•	•	•	•																						
		KP	•	•			•	•																					
Pakistan-New	AFP	Sindh												•															
	ENV	Sindh							x		x	x	x	x	x														
		SIAs using tOPV or IPV (conducted and planned)		NID: bOPV + tOPV	NID: bOPV + tOPV				NID: tOPV	NID: tOPV			NID: bOPV +tOPV plus IPV (76,000) in Quetta		IPV (106,000) in K. Abd., FF Bannu, Karachi	IPV (25,000) in Pishin, BAL	NID: tOPV		NID: tOPV				NID: tOPV		NID: tOPV		NID: tOPV		NID: tOPV

4 References

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