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Epidemiology of type 2 vaccine-derived poliovirus outbreaks between 2016 and 2020

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ABSTRACT

The number and geographic breadth of circulating vaccine-derived poliovirus type 2 (cVDPV2) outbreaks detected after the withdrawal of type 2 containing oral polio vaccine (April 2016) have exceeded forecasts. Using Acute Flaccid Paralysis (AFP) investigations and environmental surveillance (ES) data from the Global Polio Laboratory Network, we summarize the epidemiology of cVDPV2 outbreaks. Between 01 January 2016 to 31 December 2020, a total of 68 unique cVDPV2 genetic emergences were detected across 34 countries. The cVDPV2 outbreaks have been associated with 1596 acute flaccid paralysis cases across four World Health Organization regions: 962/1596 (60.3%) cases occurred in African Region; 619/1596 (38.8%) in the Eastern Mediterranean Region; 14/1596 (0.9%) in Western-Pacific Region; and 1/1596 (0.1%) in the European Region. As the majority of the cVDPV2 outbreaks have been seeded through monovalent type 2 oral poliovirus vaccine (mOPV2) use in outbreak responses, the introduction of the more stable novel oral poliovirus vaccine will be instrumental in stopping emergence of new cVDPV2 lineages.

1. Background

The Polio Eradication Endgame Strategic Plan 2013–2018 outlined a phased approach of oral polio vaccine (OPV) cessation, due to the risk of vaccine-associated paralytic poliomyelitis (VAPP) and reversion of OPV to vaccine-derived poliovirus (VDPV) [1]. In April 2016, there was global removal of type 2 containing OPV and a synchronised switch from trivalent OPV (tOPV, containing types 1, 2 and 3) to bivalent OPV (bOPV, containing types 1 and 3) vaccine. As a risk mitigation strategy, the World Health Organization's (WHO) Strategic Advisory Group of Experts (SAGE) recommended that at least one dose of inactivated poliovirus vaccine (IPV) should be used in routine immunization in all countries to protect against paralysis from all poliovirus, including serotype 2 [2].

Prior to the switch, supplementary immunisation activities (SIAs) were conducted with tOPV to increase population immunity against serotype 2 [3–5]. As OPV is the only currently available tool to prevent faecal-oral transmission of poliovirus, a global stockpile of monovalent OPV type 2 (mOPV2) was created for emergency use in response to outbreaks of circulating type 2 VDPV (cVDPV2) [6]. However, mOPV2 use retains a risk of generating new type 2 VDPV (VDPV2) emergences, particularly in outbreak response areas with low quality campaigns [3,7].

Due to the unprecedented nature of OPV2 withdrawal, there has been enhanced monitoring of the epidemiology of type 2 poliovirus isolates [5]. Outbreaks reported within a year of OPV2 removal were associated with low routine immunization and population immunity, consistent with previously identified risks [5,8,9]. Low coverage in mOPV2 outbreak response campaigns and the mixing of outbreak response target population and unvaccinated individuals from surrounding areas has resulted in persistence of Sabin 2-like virus transmission after outbreak response with mOPV2 and subsequent reversion of the Sabin-like virus into a neurovirulent VDPV2. Accordingly, an increasing number of new cVDPV2 outbreaks are attributable to mOPV2 use and the geographical spread of established cVDPV2 emergences is rapidly increasing

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with declining population immunity. To supplement the data analyses previously published on outbreaks between 2016 and 2019 [10]; five years after OPV2 cessation, this assessment of cVDPV2 epidemiology and outbreak origin is valuable for future management.

2. Methods

2.1. Data

The primary poliovirus surveillance sources of the Global Polio Eradication Initiative (GPEI) are cases of acute flaccid paralysis (AFP) targeted towards children aged < 15 years. As part of the case investigations stool specimens are collected to determine poliovirus infection. As part of the Global Environmental Surveillance Expansion Plan [11], environmental surveillance (ES) has been established within more than 30 countries where wastewater samples are collected from high-risk areas/populations and tested for polioviruses. Additional surveillance activities include contact sampling and community sampling [6,12]. All collected samples are tested in Global Polio Laboratory Network (GPLN) laboratories per World Health Organization (WHO) protocols to isolate, differentiate and characterize polioviruses to identify WPV, Sabin-like (vaccine) poliovirus, and VDPV[13,14]. Data on poliovirus isolates and reported AFP cases are stored in the GPEI Polio Information System (PolIS) database.

Polioviruses isolates are subsequently sequenced and classified by comparing the nucleotide sequence of the coding region for the 903 nucleotide viral capsid protein (VP1) with the corresponding vaccine strain: for serotype 2, Sabin-like virus (SL2) have $\geq$ 1 and < 6 nucleotides divergence; and VDPV2s have $\geq$ 6 nucleotides divergence to Sabin 2 [13]. VDPVs are further classified as 1) cVDPV, when evidence of person-to-person transmission in the community exists; 2) immunodeficiency-related VDPV (iVDPV), when they are isolated from persons with primary immunodeficiencies; and 3) ambiguous VDPV (aVDPV), when they are clinical isolates from persons with no known immunodeficiency and no evidence of transmission, or they are sewage isolates that are unrelated to other known VDPVs and whose source is unknown [15]. cVDPV2s are further classified into genetic emergence groups defined as viruses sharing four or more nucleotide mutations in VP1, compared to Sabin 2.

Data on poliovirus isolates with date of sample collection or onset of paralysis between 01 January 2016 and 31 December 2020 were exported from the GPEI PolIS database. Data was exported on 17 March 2022 and represents the cVDPV2 isolates reported to WHO headquarters on this date. In this paper, we classify an outbreak by country and genetic emergence group: a new cVDPV2 outbreak is either a new genetic emergence or detection of an existing emergence group in a new geographical location (country).

2.2. Statistical analysis

The date of seeding of VDPV2 is defined as the date that the infectious OPV2 dose was administered which subsequently evolved into cVDPV2. The date of seeding for each isolate was estimated with 95 % confidence interval by back-calculating from the date of sample collection (either AFP case or ENV), based on the number of nucleotide differences in the VP1 coding sequence from the Sabin 2 strain and VP1 mutation rates of approximately 1 % per year as described elsewhere [10].

For case-control analysis to estimate the effectiveness of IPV, controls were selected from AFP cases that had no poliovirus detected in stool samples (non-polio AFP case) from the same period of time. Controls were matched to cases on the year of AFP onset, age of child (to closest full year) and location at the Admin 1 level (subnational: province/state).

3. Results

A total of 2973 cVDPV2 isolates have been detected between 01 January 2016 and 31 December 2020. These isolates have been detected from multiple surveillance sources: 54 % (1596/2973) were through AFP surveillance, 27 % (789/2973) through environmental surveillance, and the remaining 19 % through stool sampling of case contacts, community members and healthy children.

The cVDPV2 viruses are classified into unique genetic emergence groups through the pattern of nucleotide mutations in VP1 genome. During this period, there have been 68 unique genetic emergence groups identified in 34 countries, resulting in 109 individual outbreaks. The number of cVDPV2 outbreaks, cVDPV2 AFP cases, unique genetic emergences and geographical extent of transmission for each year between 2016 and 2020 are summarised in Table 1.

3.1. Outbreaks

The 109 cVDPV2 outbreaks detected between 01 January 2016 and 31 December 2020 are described in Supplementary Table 1. They have been detected across 34 countries from the WHO African, Eastern Mediterranean, European and Western Pacific regions (Fig. 1): Afghanistan (n = 3), Angola (n = 5), Benin (n = 1), Burkina Faso (n = 2), Cameroon (n = 4), Central African Republic (n = 8), Chad (n = 3), China (n = 1), Congo (n = 3), Cote d'Ivoire (n = 2), DRC (n = 15), Egypt (n = 1), Ethiopia (n = 9), Ghana (n = 1), Guinea (n = 1), Iran (n = 1), Kenya (n = 1), Liberia (n = 1), Malaysia (n = 1), Mali (n = 2), Mozambique (n = 1), Niger (n = 1), Nigeria (n = 12), Pakistan (n = 15), Philippines (n = 1), Senegal (n = 1), Sierra Leone (n = 1), Somalia (n = 3), South Sudan (n = 1), Sudan (n = 2), Syrian Arab Republic (n = 1), Tajikistan (n = 1), Togo (n = 2), and Zambia (n = 2).

There are 39/109 outbreaks that have not had a detection within 12 months (since 01 January 2020) and are considered as closed, whilst 70/109 outbreaks are active with detection within the previous 12 months (Supplementary Table 1).

3.2. Genetic emergences

For each of the 68 genetic cVDPV2 emergences detected in the period 2016 to 2020, we estimate the date of seeding, shown in Fig. 2. We estimate that 7/68 (10.3 %) emergences were seeded prior to the removal of tOPV in May 2016, and 61/68 (89.7 %) emergences were seeded after May 2016, most likely though use of mOPV2 in outbreak response.

In 2016, three cVDPV2 emergences were detected in Nigeria (n = 2) and Pakistan (n = 1), that were seeded by pre-switch tOPV use (Table 1, Fig. 2). These emergences were rapidly controlled through mOPV2 outbreak response, with no subsequent detections beyond 2016. In 2017 and 2018, four and six new emergences were detected, respectively: 1/4 (25 %) in 2017 and 6/6 (100 %) in 2018 were seeded early after the Switch. Many of the emergences in this period (2017–2018) were not controlled: the NIE-JIS-1 and SOM-BAN-1 emergence groups have been circulating for over three years with international spread causing outbreaks in 14 and 3 countries, respectively (Supplementary Table).

In 2019, there were 40 new cVDPV2 new emergence groups detected, which 39/40 (97.2 %) were seeded after the switch (Table 1). In 2020 there have been only 15 new emergence groups detected, with 15/15 (100 %) seeded after the switch (Table 1).

Table 1
Prevalence of cVDPV2 detections, 01 January 2016 to 31 December 2020.

Year	Number cVDPV2 outbreaks detected			Number of new genetic emergences	Number of countries (administrative 0 area)	Number of provinces (administrative 1 area)	Number of AFP cases
	New outbreaks	Continuing outbreaks	Total				
2016	3	0	3	3	2	3	2
2017	4	0	4	4	3	7	96
2018	8	2	10	6	7	26	71
2019	52	5	57	40	19	105	366
2020	42	29	71	15	30	202	1061

Abbreviations: AFP – Acute flaccid paralysis; cVDPV2 – circulating vaccine-derived poliovirus type 2.

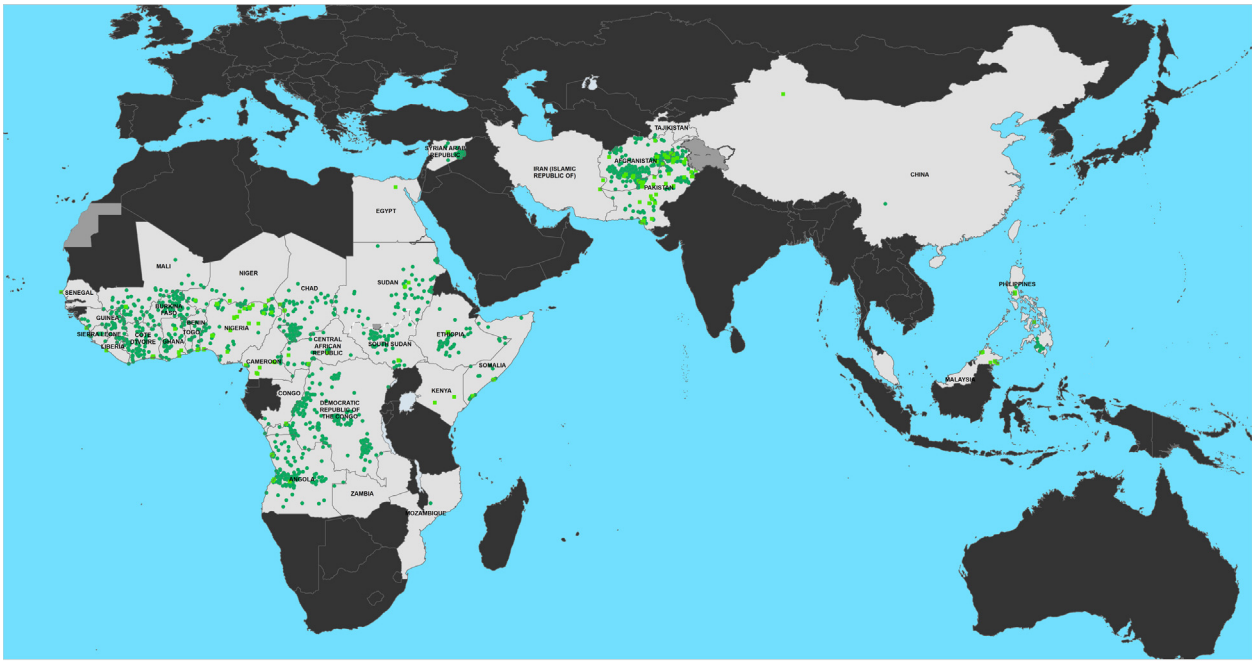

Fig. 1. Map of cVDPV2 AFP cases (circles) and ES positives (squares) detected 01 January 2016 to 31 December 2020.

The trend in geographic expansion of cVDPV2 outbreaks is evident in both the number of countries reporting outbreaks, and the number of infected provinces within countries. In 2020 there were 30 countries that reported cVDPV2 transmission, compared to 19 in 2019, 7 in 2018, 3 in 2017 and 2 in 2016 (Table 1). Furthermore, there were 202 infected provinces in 2020 compared to 105 in 2019, 26 in 2018, 7 in 2017 and 3 in 2016 (Table 1).

3.3. Paralytic cVDPV2 cases

Between 01 January 2016 and 31 December 2020 there have been 1596 AFP cVDPV2 cases reported: 962/1596 (60.3 %) cases occurred in African Region; 619/1596 (38.8 %) in the Eastern Mediterranean Region; 14/1596 (0.9 %) in Western-Pacific Region; and 1/1596 (0.1 %) in the European Region There were 2, 96, 71, 366 and 1061 AFP cases reported in 2016, 2017, 2018, 2019 and 2020, respectively (Table 2).

The age of cases was available for 1582/1596 AFP cases, with a median age of 1.92 [95 % CI: 0.5, 7.0] years. The median age has not significantly changed over time, despite increasing susceptibility in older age cohorts: the median age was 1.92 [95 % CI: 1.36, 2.47] years in 2016; 1.33 [95 % CI: 0.45, 5.84] years in 2017; 2.0 [95 % CI: 0.5, 8.75] years in 2018; 2.0 [95 % CI: 0.5, 6.01] years in 2019; and 2.0 [95 % CI: 0.45, 7.21] years in 2020. In total, 85 % (1343/1582) cVDPV2 AFP cases with age information available were born after the switch.

The number of IPV doses received were unknown in 55.2 % (881/1596) of AFP cases, zero doses in 37.9 % (605/1596) of AFP cases, one dose in 5.2 % (83/1596), and more than one dose reported in 2 % (27/1596) of AFP cases (Table 2).

There were 1033 cVDPV2 AFP cases that could be matched with non-polio AFP cases by geographic location, age at onset and paralysis onset date. In recall doses histories for children with cVDPV2 AFP cases, 550 investigations reported zero or one IPV dose, and 616 control investigations reported zero or one IPV dose. The proportion of IPV vaccinated cVDPV2 AFP cases was 16.5 % (91/550), compared to 32.3 % (199/616) of controls. This provides a vaccine effectiveness of one dose of IPV equal to 58.5 % [95 % CI: 40.0 % – 72.4 %].

4. Discussion

The international spread of poliovirus is declared a Public Health Emergency of International Concern (PHEIC) under the International Health Regulations (IHR) 2005, relating to WPV1 and cVDPV. At the meeting in February 2021, the emergency committee of IHR concluded a rising risk of cVDPV2 spread based on the increasingly large number of cases, environmental detections, and documented exportations across borders; the decreasing intestinal mucosal immunity against poliovirus type 2 since the withdrawal of tOPV in 2016; the impact of the COVID-19 pandemic; and lack of access to susceptible children [16].

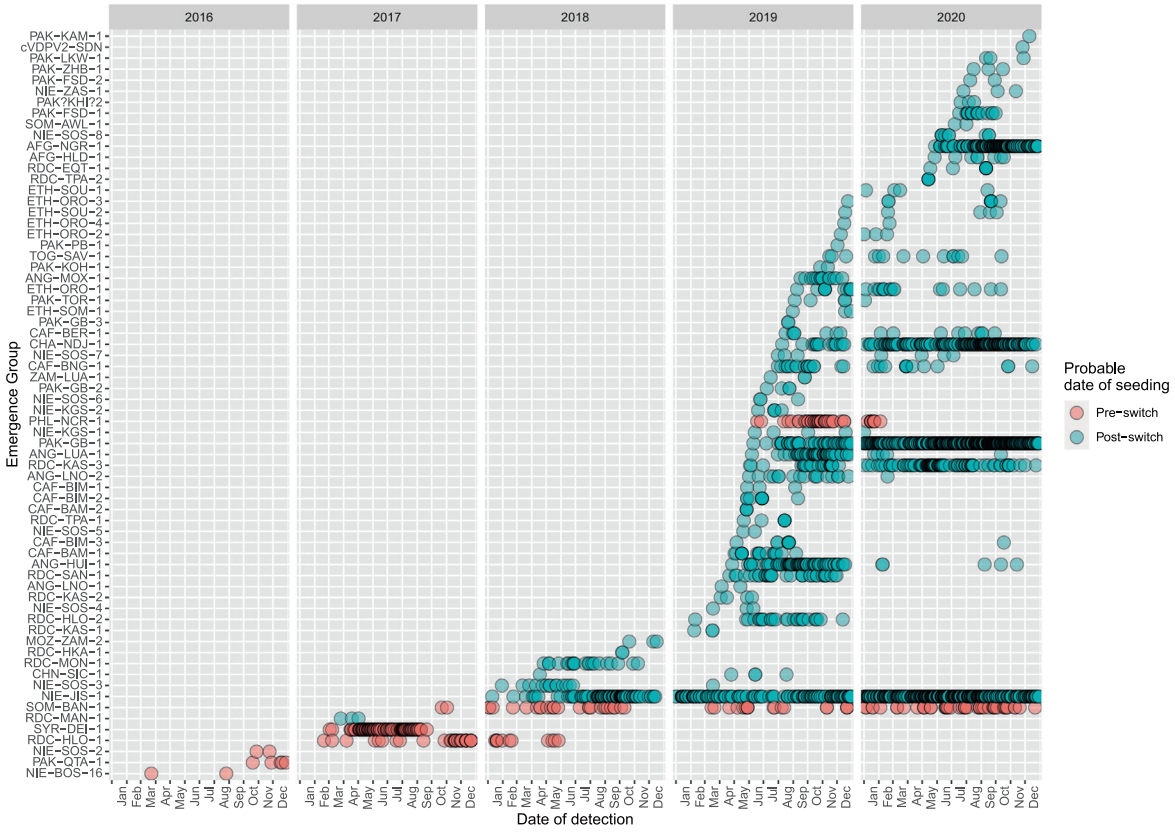

Fig. 2. Timeline of cVDPV2 emergences reported between 1 January 2016 and 31 December 2020, ordered by the date of first isolate detection. Each emergence is categorised by a probability greater than 0.5 that the date of seeding was after the Switch on 1 May 2016, shown by colour of circles.

Table 2
Demographics of cVDPV2 acute flaccid paralysis (AFP) cases reported between 01 January 2016 to 31 December 2020.

Variable	Number of cases (%)
Total	1596
WHO Region	
African	962 (60.3)
Eastern-Mediterranean	619 (38.8)
European	1 (0.1)
Western Pacific	14 (0.9)
Year of onset	
2016	2 (0.2)
2017	96 (6.0)
2018	71 (4.4)
2019	366 (22.9)
2020	1061 (66.5)
Gender	
Female	702 (44.0)
Male	877 (54.9)
Unknown	17 (1.1)
Age in years	
(0,1]	341 (21.4)
(1,2]	594 (37.2)
(2,3]	328 (20.6)
(3,5]	232 (14.5)
(5,15]	87 (5.5)
NA	14 (0.9)
Median age in years (95 % CI)	*1.9 [0.5, 7.0]*
Number of IPV doses reported	
0	605 (37.9)
1	83 (5.2)
>1	27 (3.8)
Unknown	881 (55.2)

Abbreviations: IPV – Inactivated poliovirus vaccine; WHO – World Health Organisation.

As our analysis shows, after a gradual increase in the incidence of outbreaks between 2016 and 2018, the number of cVDPV2 outbreaks amplified considerably in 2019. This was characterised by a large number of unique genetic emergences, that were seeded after the switch, likely from exposure to mOPV2 in outbreak response. In 2020, there have been substantially fewer new genetic emergences, but widespread transmission of established genetic lineages that have not been stopped by outbreak response. This geographic expansion has occurred both within the countries beyond the initial geographic areas identified for outbreak response with mOPV2, and across national borders into neighbouring countries. In 2020, the substantial increase in the number of AFP cVDPV2 cases and number of infected provinces, especially evident in Pakistan and Afghanistan, was notable given that the sensitivity of surveillance was impacted by the COVID-19 pandemic.

The increasing geographic expansion over time is likely linked to the rapidly declining population intestinal mucosal immunity levels against serotype 2 poliovirus, and more recently in 2020, the abrupt interruption of field activities due to the COVID-19 pandemic. Since March 2020, close to 60 scheduled preventive bOPV and outbreak response mOPV2 polio vaccination campaigns were delayed in more than 30 countries in compliance with global guidance on the pandemic. In addition, essential immunization activities were severely affected and the sensitivity of surveillance for polioviruses and field investigations significantly reduced.

The GPEI recommends that the response to cVDPV2 outbreaks should be at least two high-quality immunization campaigns with OPV within eight weeks of notification [6]. Whilst this is based on experience prior to the switch that two vaccination rounds with type 2 OPV are effective at stopping cVDPV2 transmission, we document that the majority of emergences have spread beyond the

initial outbreak response zone and established transmission in neighboring areas. The scope of outbreak response with mOPV2 has been restricted due to balancing the risk of seeding new cVDPV2 outbreaks and accounting for the limited vaccine supply available in the global stockpile. Our analysis suggests that reducing escape of the virus should be higher priority, especially as population immunity declines further, which would require larger geographic scope of response in the future.

Based on our case-control analysis, a single dose of IPV in routine immunization has provided around 60 % protection against paralytic disease, similar to immunogenicity data in clinical trials [17]. However, low coverage and delays in IPV introduction following the switch has left a large proportion of children unvaccinated. In October 2020, the SAGE recommended a second IPV dose to be introduced into routine immunization schedule [18]. Vigorous efforts should be made to improve IPV coverage in locations at risk of cVDPV2 outbreaks reduce the number of children susceptible to paralysis before outbreaks can occur, especially in the context of reduced coverage caused by the COVID-19 pandemic [19]. However, IPV is not recommended for cVDPV2 outbreak response because evidence demonstrates that IPV campaigns are unlikely to reach children not reached with OPV campaigns, have limited impact on stopping transmission and have a high programmatic cost [18]. The priority of outbreak response is to stop transmission; therefore, activities should focus on rapidly achieving high coverage with type-2 containing OPV.

A critical tool for cVDPV2 outbreak response is novel OPV2 (nOPV2), which received recommendation under WHO Emergency Use Listing procedure in November 2020 [20]. nOPV2 is a modified version of the Sabin mOPV2 strain, with enhanced genetic stability as a result of stabilizing key genomic segments of the vaccine virus. Therefore, this vaccine is expected to have significantly reduced risk of reversion to VDPV [21,22]. The vaccine has demonstrated comparable protection against poliovirus and increased genetic stability in Phase I and II clinical trials [23–25]. If nOPV2 performs as expected, it will be an imperative resource for controlling cVDPV2s.

In addition, in April 2020, SAGE recommended that the option of tOPV is available for cVDPV2 outbreak response in subnational areas with co-circulation or high risk of co-circulation of cVDPV2 with cVDPV1, cVDPV3 or WPV1[26]. Since October 2020, tOPV has been used for cVDPV2 outbreak response in the WPV1 endemic countries of Pakistan and Afghanistan, to avoid the need to conduct dual mOPV2 and bOPV campaigns.

In the context of multiple vaccination options for cVDPV2 outbreak response, SAGE recommends that countries should avoid delay and prioritize rapid, high-quality cVDPV2 outbreak response with whichever oral polio vaccine is available to them [19]. Conducting rapid and high-quality campaigns of sufficient scope will be essential to control and stop outbreaks. Persistent delays in responding and poor-quality campaigns will continue to obstruct the impact of outbreak responses with any vaccine.

CRediT authorship contribution statement

Grace Ruth Macklin: Methodology, Formal analysis, Writing – original draft, Writing – review & editing. **Ajay Goel:** Data curation, Visualization, Writing – review & editing. **Ondrej Mach:** Conceptualization, Supervision, Writing – original draft, Writing – review & editing. **Graham Tallis:** Conceptualization, Supervision, Writing – review & editing. **Kathleen O'Reilly:** Methodology, Supervision, Writing – review & editing. **Nicholas C Grassly:** Methodology, Supervision, Writing – review & editing. **Ousmane Diop:** Conceptualization, Investigation, Data curation, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2022.08.008.

References

[1] Global Polio Eradication Initiative. The Polio Eradication & Endgame Strategic Plan 2013-2018 Geneva: World Health Organisation2013. p. http://polioeradication.org/wp-content/uploads/2016/07/PEESP_EN_A4.pdf.
[2] Meeting of the Strategic Advisory Group of Experts on Immunization, November 2012 - conclusions and recommendations. Wkly Epidemiol Rec. 2013;88(1):1-16.
[3] Pons-Salort M, Burns CC, Lyons H, Blake IM, Jafari H, Oberste MS, et al. Preventing Vaccine-Derived Poliovirus Emergence during the Polio Endgame. PLoS Pathog 2016;12(7):e1005728.
[4] Thompson KM, Duintjer Tebbens RJ. Modeling the dynamics of oral poliovirus vaccine cessation. J Infect Dis 2014;210(Suppl 1):S475–84.
[5] Blake IM, Pons-Salort M, Molodecky NA, Diop OM, Chenoweth P, Bandyopadhyay AS, et al. Type 2 Poliovirus Detection after Global Withdrawal of Trivalent Oral Vaccine. N Engl J Med 2018;379(9):834–45.
[6] Global Polio Eradication Initiative. Standard Operating Procedures: Responding to a poliovirus event or outbreak Geneva2020 [updated March 2020. Version 3.1:[Available from: http://polioeradication.org/wp-content/uploads/2020/04/POL-SOP-V3.1-20200424.pdf.
[7] Famulare M, Chang S, Iber J, Zhao K, Adeniji JA, Bukbuk D, et al. Sabin Vaccine Reversion in the Field: a Comprehensive Analysis of Sabin-Like Poliovirus Isolates in Nigeria. J Virol 2016;90(1):317–31.
[8] Jorba J, Diop OM, Iber J, Henderson E, Zhao K, Sutter RW, et al. Update on Vaccine-Derived Polioviruses - Worldwide, January 2017-June 2018. MMWR Morb Mortal Wkly Rep 2018;67(42):1189–94.
[9] O'Reilly KM, Lamoureux C, Molodecky NA, Lyons H, Grassly NC, Tallis G. An assessment of the geographical risks of wild and vaccine-derived poliomyelitis outbreaks in Africa and Asia. BMC Infect Dis 2017;17(1):367.
[10] Macklin GR, O'Reilly KM, Grassly NC, Edmunds WJ, Mach O, Santhana Gopala Krishnan R, et al. Evolving epidemiology of poliovirus serotype 2 following withdrawal of the serotype 2 oral poliovirus vaccine. Science 2020;368(6489):401–5.
[11] Asghar H, Diop OM, Weldegebriel G, Malik F, Shetty S, El Bassioni L, et al. Environmental surveillance for polioviruses in the Global Polio Eradication Initiative. J Infect Dis 2014;210(suppl 1):S294–303.
[12] Macklin G, Liao Yi, Takane M, Dooling K, Gilmour S, Mach O, et al. Prolonged Excretion of Poliovirus among Individuals with Primary Immunodeficiency Disorder: An Analysis of the World Health Organization Registry. Front Immunol 2017;8.
[13] World Health Organization. Polio laboratory manual, 4th edition. Geneva: World Health Organisation; 2004 [Available from: http://polioeradication.org/wp-content/uploads/2017/05/Polio_Lab_Manual04.pdf.
[14] Global Polio Eradication Initiative. Polio environmental surveillance expansion plan. Geneva2015 [Available from: http://polioeradication.org/wp-content/uploads/2016/07/GPLN_ExpansionPlanES.pdf.
[15] Kew OM, Sutter RW, de Gourville EM, Dowdle WR, Pallansch MA. Vaccine-derived polioviruses and the endgame strategy for global polio eradication. Annu Rev Microbiol 2005;59(1):587–635.
[16] Statement of the Twenty-Seventh Polio IHR Emergency Committee [press release]. World Health Organisation,, 19 February 2021 2021.
[17] Macklin GR, Grassly NC, Sutter RW, Mach O, Bandyopadhyay AS, Edmunds WJ, et al. Vaccine schedules and the effect on humoral and intestinal immunity against poliovirus: a systematic review and network meta-analysis. Lancet Infect Dis 2019;19(10):1121–8.
[18] World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, October 2020–conclusions and recommendations. Wkly Epidemiol Rec 2020;95(48):585–607.
[19] World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, 22–24 March 2021: conclusions and recommendations. Wkly Epidemiol Rec 2021;96(22):197–216.
[20] World Health Organisation. Emergency Use Listing Procedure, Version 9 Geneva, Switzerland: World Health Organisation; 2020 [Available from: https://extranet.who.int/prequal/sites/default/files/documents/EUL_Procedure_Jan2020.pdf.
[21] Yeh MT, Bujaki E, Dolan PT, Smith M, Wahid R, Konz J, et al. Engineering the Live-Attenuated Polio Vaccine to Prevent Reversion to Virulence. Cell Host Microbe 2020;27(5):736–751.e8.
[22] Konopka-Anstadt JL, Campagnoli R, Vincent A, Shaw J, Wei L, Wynn NT, et al. Development of a new oral poliovirus vaccine for the eradication end game using codon deoptimization. npj Vaccines 2020;5(1).

[23] Van Damme P, De Coster I, Bandyopadhyay AS, Revets H, Withanage K, De Smedt P, et al. The safety and immunogenicity of two novel live attenuated monovalent (serotype 2) oral poliovirus vaccines in healthy adults: a double-blind, single-centre phase 1 study. The Lancet 2019;394(10193):148–58.

[24] De Coster I, Leroux-Roels I, Bandyopadhyay AS, Gast C, Withanage K, Steenackers K, et al. Safety and immunogenicity of two novel type 2 oral poliovirus vaccine candidates compared with a monovalent type 2 oral poliovirus vaccine in healthy adults: two clinical trials. Lancet 2021;397 (10268):39–50.

[25] Sáez-Llorens X, Bandyopadhyay AS, Gast C, Leon TD, DeAntonio R, Jimeno J, et al. Safety and immunogenicity of two novel type 2 oral poliovirus vaccine candidates compared with a monovalent type 2 oral poliovirus vaccine in children and infants: two clinical trials. Lancet 2021;397(10268):27–38.

[26] World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, 31 March–1 April 2020: conclusions and recommendations. Wkly Epidemiol Rec 2020;95(22):241–55.