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Re-emergence of vaccine-derived polio in the demographic Republic of Congo: Causes and consequences

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ABSTRACT

Poliovirus is a deadly disease that needs to be eradicated in the world. Recently, issues with circulating vaccine-derived polioviruses (cVDPVs) in the Democratic Republic of the Congo (DRC) have been raised in the country. This article aims to determine the increase in Type 1 cVDPV1 and Type 2 cVDPV2 in the DRC. Relevant articles on PubMed, Google Scholar, ResearchGate, and Web of Science were searched from 2010 to 2023. Our findings indicate that the Democratic Republic of Congo has struggled with polio outbreaks, with the virus primarily linked to cVDPVs produced from vaccines rather than wild poliovirus. These cVDPVs have the potential to revert to their paralyzing capabilities by evolving from the weakened virus seen in the oral polio vaccination (OPV). Several regions in DRC have reported cVDPV outbreaks of cVDPVs. Numerous cVDPV2 outbreaks were documented in various provinces during the 2017–2018 period. Addressing the cVDPV outbreak in the DRC requires a concerted global effort, involving collaboration among governments, international health organizations, and donor agencies. There should be global support and collaboration among governments, international health organizations, and donor agencies to address the cVDPV outbreak in the DRC.

1. Introduction

The eradication of wild-type poliovirus type 2 (WPV2) is a significant milestone, but challenges persist with the rise of circulating vaccine-derived poliovirus type 2 (cVDPV2) outbreaks, posing a major hurdle for the Global Polio Eradication Initiative (GPEI) [1]. In 2020, there were 1062 reported cVDPV2 paralytic poliomyelitis cases across 30 countries in WHO regions such as Africa, Eastern Mediterranean, Western-Pacific, and Europe [2]. While the Democratic Republic of the Congo (DRC) achieved freedom from wild poliovirus (WPV) in 2011, progress faces setbacks in Afghanistan and Pakistan due to endemic transmission, further complicated by challenges brought about by the

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COVID-19 pandemic [2,3]. Vaccination efforts primarily target children under 5, the demographic most susceptible to poliomyelitis. However, an outbreak in the DRC in 2010–2011 revealed 16 % of cases among adults, highlighting the need to evaluate adult immunity against polioviruses and their potential role in transmission [3,4]. In response to outbreaks, national and sub-regional supplemental immunization activities (SIAs) broadened their scope to include the entire population, adapting strategies to reach adults [2]. Notably, cVDPV2 cases have been documented in adults, emphasizing the need for comprehensive vaccination strategies [4].

Serological protection among adults is crucial for preventing the transmission of wild and vaccine viruses [4]. In regions like the DRC, where routine immunization coverage was historically low and wild polioviruses were endemic, assessing adult immunity becomes paramount [4,5]. Historically, SIAs focused on under-5 children, but the 2010–2011 outbreak led to all-age campaigns in certain DRC provinces, making adults eligible for supplementary vaccination [5]. Oral polio vaccines (OPV) have been pivotal, but the persistent threat is evident in over 172 cVDPV outbreaks since 2016, with 51 % active in 2021–2022 [6]. Adaptations in response strategies, including the use of mOPV2, became necessary. Although OPV usage significantly reduced the number of polio-affected countries from >125 in 1988 to only 3 in 2018, it is associated with the emergence of vaccine-derived poliovirus (VDPV) and a low risk of vaccine-associated paralytic polio [6,7]. The Polio Eradication Endgame and Strategic Plan 2013–2018 recommended a sequential removal of all Sabin strains, starting with type 2, in all OPV-using countries with the introduction of ≥1 dose of inactivated poliovirus vaccine (IPV) in routine immunization (RI) [6].

The management of the mOPV2 stockpile evolved to include trivalent OPV and genetically stabilized 'novel OPV type 2' vaccines [7]. However, challenges like unpredictable vaccine demand, fixed production timelines, and varied resource requirements complicate ensuring sufficient vaccine availability for effective outbreak control [7,8]. Identifying high-risk areas with susceptible adult populations is crucial for planning and managing eradication efforts, preventing the continued emergence or importation of cVDPVs and the reintroduction of WPV. The complexity of these challenges underscores the need for ongoing vigilance and adaptability in the global pursuit of polio eradication in the DRC. This article aims to determine the rise of cVDPV1 and cVDPV2 in the DRC, lay more emphasis on their drivers of escalation, impact on health and society, as well as strategies for mitigation.

2. Historical landscape

The Expanded Program on Immunization (EPI) was implemented in the DRC in 1978, including four doses of trivalent Oral Polio Vaccine (tOPV) for infants at birth, 6, 10, and 14 weeks [9]. The DRC's Polio Eradication Program, initiated in 1996, conducted supplemental immunization activities (SIAs) in areas with high disease burdens. Until 2001, the DRC was endemic for Wild Poliovirus (WPV) transmission and considered a source of virus export. Between 2006 and 2011, outbreaks of WPV1 and WPV3 occurred in 10 of 11 provinces, mainly due to importations from Angola [9]. Multiple outbreaks of cVDPV2 were also observed from 2004 to 2012 [10]. The last confirmed WPV case in Maniema province was reported in December 2011. In 2016, two cVDPV2 outbreaks emerged from Maniema and Haut Lomami provinces [9].

The isolates from the cVDPV1 PHL-NCR-2 emergence group in the Philippines and Malaysia displayed a range of 30–40 nucleotide substitutions in the VP1 region from Sabin 1, indicating a divergence of 3.3–4.4 %. This suggests undetected replication for a minimum of three years. Through Bayesian phylogenetic analysis, assuming a consistent evolution rate of 1.1 % per year, the average estimated date of the initial seeding dose was in early 2016 [11]. All PV2 strains found in individuals with acute flaccid paralysis (AFP), their close contacts, and samples taken from the environment in Angola underwent sequencing specifically targeting the VP1 capsid region, encompassing 903 nucleotides. Based on guidelines, those with six or more nucleotide differences from the Sabin 2 strain were classified as VDPV2. 54 % of VDPV2 isolates had less than ten nucleotide differences from Sabin 2, indicating early detection [6]. Phylogenetic analysis identified five independent cVDPV2 emergences in different provinces: ANG-HUI-1, ANG-LNO-1, ANG-LNO-2, ANG-LUA-1, and ANG-MOX-1. The sequence analysis of the poliovirus strains isolated from cases in the southern province of Huila and the northern province of Lunda Norte, between April and June 2019, revealed that the Vaccine-Derived Poliovirus Type 2 (VDPV2) strains were closely linked to the Sabin 2 strain. These VDPV2 cases were identified as separate from the circulating VDPV2 (cVDPV2) occurrences previously documented in the Democratic Republic of Congo (DRC). All cVDPV2 isolates had a common nucleotide substitution in VP1 [6]. Sequence analysis revealed at least four to 12 shared nucleotide substitutions in VP1 from parental Sabin 2 within each cVDPV2 emergence group. The estimated dates of the originating Oral Polio Vaccine type 2 (OPV2) doses for the five cVDPV2 emergence groups in Angola were calculated based on the divergence of VP1 sequences from the Sabin 2 sequence, assuming a constant evolution rate of 1.1 % per year [6].

3. Present realities of cVDPV1 and cVDPV2 in the DRC

There were issues with cVDPVs in the DRC. But maybe things have changed since then. For many years, the DRC has struggled with polio outbreaks, with the virus primarily being linked to strains produced from vaccines rather than wild poliovirus. These strains have the potential to revert to their paralyzing capabilities by evolving from the weakened virus seen in the OPV. These strains may spread among populations with low immunization rates due to insufficient vaccine coverage [12]. Several DRC regions have reported outbreaks of cVDPVs. Numerous cVDPV2 outbreaks were documented in various provinces during the 2017–2018 period. According to WHO, these outbreaks revealed vaccine coverage gaps that let the virus proliferate [13]. In the DRC, vaccination efforts face significant hurdles, including armed conflicts, difficult terrain that makes it hard to reach remote areas, insufficient healthcare facilities, and difficulties in engaging communities and encouraging them to participate in immunization campaigns. Surveillance and containment of infectious diseases, such as COVID-19 and Ebola, provide significant challenges for the DRC. These difficulties stem from several variables that make it difficult for the region to carry out efficient containment and surveillance [14]. The DRC shares porous borders with multiple countries, making it vulnerable to cross-border transmission of diseases. Controlling and monitoring these borders to prevent the spread of infectious diseases poses significant challenges. Limited data collection, surveillance, and reporting mechanisms contribute to gaps in understanding disease epidemiology. This lack of comprehensive data impedes the formulation of effective containment strategies. Cultural practices and beliefs sometimes clash with disease containment measures. For instance, burial practices in some communities may increase the risk of disease transmission [15].

Efforts by international organizations, such as the World Health Organization (WHO) and Médecins Sans Frontières (MSF), along with governmental initiatives, aim to address these challenges. However, sustained progress requires overcoming the complex interplay of these hurdles, necessitating long-term investment, community engagement, and collaboration among various stakeholders [16].

Eradication strategies for cVDPVs in the Democratic Republic of Congo (DRC) have significant global ramifications due to the potential spread of these viruses beyond national borders and their implications for the global polio eradication initiative [17]. The DRC has faced challenges in controlling polio outbreaks, particularly cVDPV2, prompting intense efforts to contain and eliminate these strains [13]. The strategies employed and their success in the DRC have broader implications for global polio eradication efforts.

4. Drivers of escalation

The DRC is facing a major challenge in its efforts to eradicate polio. Circulating vaccine-derived poliovirus, a mutated form of the weakened poliovirus used in vaccines, has been circulating in the DRC since 2005 [18]. In recent years, the number of cVDPV cases has increased, and the virus has spread to new areas of the country. The main factor contributing to this is low routine vaccination coverage. The DRC has consistently struggled to achieve and maintain high routine vaccination coverage. A particular study revealed that living in rural areas, lack of available seating during vaccination sessions at health facilities, non-compliance with the order of arrival during vaccination in health facilities, and lack of a reminder system on days before the scheduled vaccination are the major causes of low vaccination coverage in the DRC. These were significantly associated with high dropout rates of vaccination among children aged 12–23 months [19]. The major indicators that need evaluation include poverty and inequality. In the DRC, poverty and inequality contribute to poor sanitation, malnutrition, and limited access to healthcare, all of which increase the risk of poliovirus transmission and vaccine-preventable diseases. Despite vast natural resources, widespread poverty persists in the DRC as evidenced by the low human development index (HDI) [20].

Furthermore, political instability and insecurity have hampered efforts to effectively implement and sustain polio eradication programs. Conflicts, such as the Kamwina Nsapu rebellion in the Kasai region, paralyzed polio and other health-related activities for some time due to the destruction of hospitals and health centres. Given the ongoing clashes between the government and Kamwina Nsapu's followers, health workers' access was often compromised [20]. Likewise, the DRC's healthcare system faces challenges due to weak governance, underfunding, and a shortage of trained healthcare workers. These factors hinder the effective implementation of vaccination programs, surveillance systems, and outbreak response measures. A study revealed that there is very poor coverage in Mongala, Sankuru, and Tshuapa provinces due to poor health infrastructure, including a weak cold chain system, which is a major barrier to accessing the immunization program. Similarly, Tanganyika also has low vaccination coverage [21].

5. Impacts on health and society

The Democratic Republic of Congo is among the countries that reported cases of cVDPV 1 and 2 between January 2021 and March 2023. DRC also accounted for up to 59 % of cVDPV cases [8]. Cases of cVDPV2 were linked to delays in implementing supplemental immunization activities, potentially leading to the virus spreading to new areas during this period [2]. Circulating vaccine-derived polio-virus poses many risks to vulnerable populations, these are in places where polio vaccination is low. Children who haven't received vaccinations are more likely to transmit the disease to others. Most cases of low vaccination are in low and middle-income countries where cases of open defecation occur, thus leading to the transfer of the disease to others [22]. The transmission pattern of Poliovirus depends on the socioeconomic situation of the affected country. In low-income countries, risk factors associated with the spread of the disease, which are also major indicators include lack of access to clean drinking water, poor hand hygiene, high population density, and poor sanitation, are commonly seen [22].

The impact of cVDPV outbreaks on the Congolese population is substantial. For instance, cVDPV2 outbreaks have been a recurrent issue. Between 2017 and 2021, 19 outbreaks were detected, resulting in 235 paralysis cases across a wide swathe of the country, affecting 84 health zones in 18 of the DRC's 26 provinces [2]. The largest outbreak during this period, DRC-KAS-3, resulted in 101 paralysis cases across 10 provinces [3]. These outbreaks demonstrate the significant health burden placed on the DRC by cVDPV.

The global elimination of poliovirus requires a comprehensive vaccination campaign that extends across diverse regions and populations. Firstly, the DRC has conducted numerous Supplemental Immunization Activities (SIAs) using the monovalent oral poliovirus vaccine type 2 (mOPV2) to control outbreaks of (cVDPV2) [23]. However, suboptimal mOPV2 coverage has led to the emergence of new cVDPV2 cases [24]. The introduction of the novel OPV type 2 (nOPV2), which has greater genetic stability, is expected to improve control efforts and reduce the risk of further cVDPV2 emergence [24]. Secondly, to maintain high population immunity, the DRC is working to enhance routine immunization programs. This includes the introduction of a second dose of inactivated poliovirus vaccine (IPV) to increase protection against paralysis and improve overall immunization coverage [23].

Additionally, effective surveillance systems, including acute flaccid paralysis (AFP) surveillance, are critical for early detection and response to polio cases [23]. This involves both epidemiologic and laboratory surveillance to monitor poliovirus transmission and guide immunization activities. Moreover, the DRC has implemented innovative public-private partnerships to strengthen immunization programs at the provincial level [23]. These partnerships aim to improve vaccine accessibility, increase immunization coverage, and manage/eliminate polio outbreaks through coordinated efforts with local governments and international partners.

Lastly, the Global Polio Eradication Initiative (GPEI), endorsed by the World Health Organization (WHO), includes the phased removal of OPVs starting with type 2 poliovirus-containing vaccines and the introduction of IPV into routine immunization schedules [25]. This strategy aims to mitigate the risk of vaccine-associated paralytic polio and cVDPVs.

The effectiveness of these protocols for the eradication of vaccine-derived polio in the DRC varies significantly between urban and rural areas due to differences in infrastructure, accessibility, and community engagement [25].

Such measures are essential for effectively eradicating cVDPV. However, in many developing nations, the capacity to execute these procedures is hindered by limited manpower, inadequate resources, and a shortage of healthcare facilities. Monitoring polio across the entire country is challenging due to a lack of sufficient manpower and healthcare professionals. As a result, ensuring appropriate surveillance for the disease becomes difficult to achieve [2]. Conflicts have further compounded in DRC's healthcare system, causing many people to be displaced [21]. Limited healthcare resources in the DRC could impede the efforts to eradicate circulating cVDPV. These include worker shortages, limited health worker capacity, lack of financial motivation, and lack of supervision of health workers [21].

6. Strategies for mitigation

The emergence and circulation of cVDPV1 and cVDPV2 in the DRC poses a significant public health threat, necessitating a comprehensive and multifaceted approach to mitigation [12,17,23].

National strategies for mitigating polio in the DRC have focused on several key areas, validated through various initiatives and studies.

One significant strategy involves the establishment of innovative sub-national public-private partnerships. These partnerships formalized through Memorandums of Understanding (MoUs) between the Bill and Melinda Gates Foundation and provincial governments, aim to enhance immunization coverage, manage and eliminate polio outbreaks, improve vaccine accessibility, and transfer immunization service management to provincial leadership. This approach has been piloted in the provinces of Haut Lomami, Tanganyika, and Lualaba, resulting in increased immunization coverage and reduced zero-dose children, although challenges such as COVID-19 and healthcare worker strikes have impacted progress [17].

Another validated strategy is derived from the Global Polio Eradication Initiative (GPEI), which has been instrumental in addressing implementation barriers such as political insecurity, population movement, and community hesitancy. The GPEI's approach includes adapting

service delivery, investing in health systems capacity, establishing planning and accountability mechanisms, and social mobilization [23]. These efforts have improved system infrastructure and service delivery, although there are still gaps in routine immunization and surveillance that need to be addressed to prevent polio resurgence. Government and polio eradication initiatives in DRC should intensify vaccination efforts by increasing the frequency and scope of polio vaccination campaigns to ensure accessibility in remote and high-risk areas within DRC [23]. Employment of mobile vaccination teams to reach underserved communities, particularly in conflict-affected or geographically challenging regions [17]. Engagement of local healthcare workers and community leaders to promote vaccination, address misconceptions and provide culturally relevant vaccination services [12].

Furthermore, the Congolese government should utilize community health workers, peer educators, and traditional healers in the country to build trust and address vaccine hesitancy, leveraging their trusted positions within their communities [23]. We believe that the best way to eradicate polio is by improving vaccine coverage through strengthening routine immunization programs to ensure a higher percentage of children in the DRC receive the full course of polio vaccinations, thereby reducing susceptibility to vaccine-derived strains [17]. Health authorities in the DRC should devise effective plans to ensure that nomadic communities and regions impacted by conflict receive necessary healthcare services. This could involve setting up mobile healthcare units and adapting vaccination schedules to accommodate the unpredictable movement patterns of these groups [23]. Additionally, it's crucial to closely monitor vaccination rates across the country and use this data to pinpoint areas where coverage is lacking. By identifying these areas, health interventions can be prioritized to ensure that vulnerable populations receive the immunizations they need [12].

Evaluating the long-term effectiveness of these mitigation strategies is essential.

Seroprevalence studies are critical for assessing immunity levels against poliovirus types 1, 2, and 3 over time. Monitoring these levels helps identify immunity gaps and the need for supplementary immunization activities (SIAs). For instance, a study found population immunity to be 81 %, 90 %, and 70 % for these types, respectively, among children aged 6–59 months (16). Continuous monitoring allows for early detection of waning immunity and ensures timely interventions. Effective disease surveillance systems are paramount for detecting poliovirus circulation. The cornerstone of this system is Acute Flaccid Paralysis (AFP) surveillance. Here, key indicators include the non-polio AFP rate, timely stool collection from suspected cases, and adequate stool specimen condition for analysis. While improvements in these indicators have been documented at national and provincial levels, gaps remain at the zone de santé (ZS) level (17). Strengthening surveillance at this local level is crucial for comprehensive detection and rapid response. Complementing AFP surveillance, environmental surveillance through testing sewage samples for polioviruses helps detect silent transmission, where infected individuals may not exhibit symptoms. This method is particularly valuable in areas with low AFP case detection rates (18). A robust combined approach using both AFP and environmental surveillance enhances the ability to identify and contain the virus.

The impact of polio eradication strategies extends beyond disease control, positively affecting society in the DRC in several ways. The effectiveness of the AFP surveillance system directly translates to better public health outcomes. Documented improvements in AFP surveillance performance, including timely stool collection and adequate specimen condition, contribute to early detection and response to potential poliovirus outbreaks (17). A strengthened surveillance system fosters a more proactive approach to public health threats. The ability to rapidly respond to and control outbreaks of both wild poliovirus (WPV) and vaccine-derived poliovirus (VDPV) is essential for preventing their spread. Historical data highlights the importance of robust outbreak response mechanisms, as gaps in surveillance and immunization can lead to reestablished transmission (19). Effective outbreak response safeguards public health by minimizing the impact of potential outbreaks. Public knowledge and acceptance of polio vaccination are vital for achieving and maintaining eradication goals. Surveys indicate that while outreach efforts are connecting with communities, there is still a need to improve understanding of polio transmission (18).

We urge the Congolese government to adopt various vaccination strategies in the DRC, such as tailoring vaccination strategies based on local epidemiology, mapping areas with low coverage, and targeting interventions accordingly [17] as well as utilising new and emerging vaccination technologies, such as inactivated polio vaccine (IPV), to supplement OPV and address limitations of OPV in preventing cVDPV outbreaks [23]. The following strategies can enhance surveillance and response measures in the DRC: Top of the list is to strengthen monitoring systems to promptly detect and respond to any suspected cases of cVDPV [25]. Secondly, enhancing laboratory capacities to rapidly diagnose poliovirus infections, and ensuring timely and accurate identification of cVDPV cases [23]. Additionally, training healthcare personnel to recognize and report signs and symptoms of polio, including surveillance of acute flaccid paralysis (AFP) cases [12]. Establish efficient reporting mechanisms to promptly notify public health authorities of suspected cVDPV cases, enabling rapid response and containment measures [25].

More emphasis should be placed on rapid response teams for polio eradication in the DRC. They should have the necessary resources and expertise to conduct immediate vaccination campaigns, implement containment measures, and carry out comprehensive epidemiological investigations [12].

7. Conclusion

Addressing the cVDPV outbreak in the DRC requires a concerted global effort, involving collaboration among governments, international health organizations, and donor agencies. There should be global support and collaboration among governments, international health organizations, and donor agencies to address the cVDPV outbreak in the DRC. Information, resources, and expertise should be available to strengthen vaccination programs, surveillance capacities, and response measures in the DRC. Partnerships and collaborations should be put in place to support the DRC's polio eradication efforts.

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CRediT authorship contribution statement

Malik Olatunde Oduoye: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Funding acquisition, Formal analysis, Conceptualization. **Samuel Chinonso Ubechu:** Writing – original draft, Visualization, Validation, Funding acquisition. **Marina Ramzy Mourid:** Writing – original draft, Visualization, Validation, Investigation, Formal analysis, Conceptualization. **Ahmad Ibrahim Ahmad:** Writing – original draft, Visualization, Validation, Funding acquisition. **Abdullahi Adeyemi Adegoke:** Writing – original draft, Visualization, Validation, Funding acquisition. **Umulkhairah Onyioiza Arama:** Writing – review & editing, Writing – original draft, Visualization, Validation, Data curation. **Muhammad Furqan:** Writing – original draft, Visualization, Validation. **Saiyad Ali:** Visualization, Funding acquisition. **Bashiru Muhammad Auwal:** Writing – original draft, Visualization, Validation. **F.N.U. Fariha:** Writing – original draft, Visualization, Validation. **Ankini Mukherjee:** Writing – original draft, Visualization, Validation. **Aymar Akilimali:** Writing – original draft, Visualization, Validation.

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There is nothing to disclose.

Declaration of competing interest

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List of Abbreviations:

(AFP) Acute Flaccid Paralysis
(cVDPVs) Circulating vaccine-derived polioviruses
(DRC) Democratic Republic of the Congo
(EPI) Expanded Program on Immunization
(GPEI) Global Polio Eradication Initiative
(HDI) Human Development Index
(MSF) Médecins Sans Frontières
(OBR) Outbreak Response
(OPV) Oral polio vaccines
(SIAs) Supplemental immunization activities
(SOPs) Standard Operating Procedures
(WPV2) Wild-type poliovirus type 2
(VDPV) Vaccine-Derived Poliovirus and
(WHO) World Health Organization

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