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Stopping a polio outbreak in the midst of war: Lessons from Syria

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Abstract

Background: Outbreaks of circulating vaccine-derived polioviruses (cVDPVs) pose a threat to the eventual eradication of all polioviruses. In 2017, an outbreak of cVDPV type 2 (cVDPV2) occurred in the midst of a war in Syria. We describe vaccination-based risk factors for and the successful response to the outbreak.

Methods: We performed a descriptive analysis of cVDPV2 cases and key indicators of poliovirus surveillance and vaccination activities during 2016–2018. In the absence of reliable subnational coverage data, we used the caregiver-reported vaccination status of children with non-polio acute flaccid paralysis (AFP) as a proxy for vaccination coverage. We then estimated the relative odds of being unvaccinated against polio, comparing children in areas affected by the outbreak to children in other parts of Syria in order to establish the presence of poliovirus immunity gaps in outbreak affected areas.

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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.

Findings: A total of 74 cVDPV2 cases were reported, with paralysis onset ranging from 3 March to 21 September 2017. All but three cases were reported from Deir-ez-Zor governorate and 84% had received < 3 doses of oral poliovirus vaccine (OPV). After adjusting for age and sex, non-polio AFP case-patients aged 6–59 months in outbreak-affected areas had 2.5 (95% CI: 1.1–5.7) increased odds of being unvaccinated with OPV compared with non-polio AFP case-patients in the same age group in other parts of Syria. Three outbreak response rounds of monovalent OPV type 2 (mOPV2) vaccination were conducted, with governorate-level coverage mostly exceeding 80%.

Interpretation: Significant declines in both national and subnational polio vaccination coverage, precipitated by war and a humanitarian crisis, led to a cVDPV2 outbreak in Syria that was successfully contained following three rounds of mOPV2 vaccination.

Keywords

Polio; Outbreaks; Vaccine-derived polioviruses; Oral poliovirus vaccine; Syria; Conflict

1. Introduction

Poliomyelitis, commonly referred to as polio, is a paralytic disease caused by poliovirus infection,[1] which mostly affects children < 5 years of age. Among the three serotypes of wild poliovirus (WPV), only WPV type 1 (WPV1) remains in circulation and endemic transmission of the virus is now limited to only Afghanistan and Pakistan,[2] a direct result of deliberate efforts to eradicate polio by the Global Polio Eradication Initiative (GPEI).[3] Despite the successes of GPEI, several threats remain to the eradication of polio. One of the leading threats is the occurrence of outbreaks in previously polio-free countries as a result of importation of WPV1 from countries where transmission persists. During 2013–2014, several countries in the Middle East and Africa that had been previously polio-free experienced outbreaks.[4] In Syria, which eliminated indigenous WPV transmission prior to the initial GPEI target of the year 2000 for polio eradication[5], 36 children were paralyzed in a WPV1 outbreak linked to virus strains circulating in Pakistan, prompting a multi-country response in the Middle East that reached > 27 million children with poliovirus vaccines.[6,7] While Syria has since remained WPV1 free, disruption of a previously robust healthcare and immunization delivery system, precipitated by a civil war that began in 2011, has left the country vulnerable to recurrent disease outbreaks.[8–10] One such outbreak involved the emergence and circulation of vaccine-derived polioviruses (VDPVs) among a population of suboptimally immunized children in Deir-ez-Zor, Raqqa and Homs governorates, resulting in 74 paralytic cases in 2017.[11]

VDPVs emerge when the live, attenuated virus contained in Sabin oral poliovirus vaccine (OPV) replicates for an extended period of time either through protracted circulation of the vaccine virus within a suboptimally immunized population or prolonged replication of the vaccine virus within an individual with a primary immunodeficiency, both allowing for sequential genetic mutation. [12–14] When VDPVs emerge and spread as a result of prolonged community transmission, they are known as circulating VDPVs (cVDPVs). [12,15] Just like wild polioviruses, VDPVs are capable of causing paralysis in infected

persons and pose a threat to polio eradication. They can result from any of the three Sabin OPV serotypes (types 1, 2, and 3), but most commonly are due to type 2 poliovirus.[16]

The risk of emergence of cVDPV type 2 (cVDPV2) increased in selected areas following the synchronized global withdrawal of trivalent OPV (tOPV, containing types 1, 2, and 3) and switch to bivalent OPV (bOPV, containing types 1 and 3) in May 2016. [17–19] The 2016 withdrawal of type 2-containing OPV from the immunization schedules of all 155 OPV-using countries was undertaken after the 2015 certification of WPV type 2 eradication because of the large number of cVDPV2 outbreaks. However, in areas where vaccination coverage with tOPV had been suboptimal prior to its withdrawal, there was an elevated risk of emergence of cVDPV2s as predicted by modeling,[20] with a high proportion of multiple birth cohorts without mucosal or humoral immunity to type 2 poliovirus. The only opportunity for children to develop immunity to type 2 polioviruses after the global switch to bOPV would have been through administration of at least a single dose of inactivated poliovirus vaccine (IPV), which primarily protects against paralysis rather than infection. [21–22] As a consequence, individual immunity to type 2 polioviruses has waned more acutely in many countries since the switch.

Within the unique context of Syria, routine immunization coverage with three doses of OPV plummeted from > 80% prior to the onset of the civil war in 2011 to < 50% by the end of 2016, the year tOPV was withdrawn.[23] Coverage with IPV, introduced as a two-dose regimen into Syria's immunization schedule in 2008,[24] also has been suboptimal, with national level coverage consistently below 80% during 2015–2018.[23] Following the decline in immunization coverage, a cluster of acute flaccid paralysis (AFP) cases was identified in Deir-ez-Zor governorate during March-May 2017, and a cVDPV2 outbreak was confirmed in June of the same year.[11] The cVDPV2 outbreak in Syria was successfully curtailed within 120 days of its confirmation, as stipulated by GPEI.[25] We investigated how such an effective outcome was achieved under the extremely challenging circumstances of Syria's civil war. We also describe how the outbreak was detected and the epidemiology of cases and examine risk factors for spread of cVDPV2 in areas that were affected by the outbreak.

2. Methods

2.1. Poliovirus surveillance Methods

Poliovirus surveillance in Syria is conducted in line with GPEI guidance, which relies primarily on the reporting and investigation of AFP cases as a means of promptly identifying areas with poliovirus circulation.[26] During January 1, 2016-December 31, 2018, AFP cases in Syria were detected and reported through a network of sentinel surveillance sites in areas under the control of the Syrian government and the Early Warning, Alert, and Response Network (EWARN) of the World Health Organization (WHO) in opposition-controlled areas. EWARN comprises an informal network of healthcare providers and facilities engaged in surveillance for diseases of public health significance in conflict-affected areas of several countries, including in the Middle East and Horn of Africa. [27]

AFP cases reported through either surveillance system were investigated including through the collection of stool specimens, which were sent for laboratory testing for polioviruses. Stool specimens from an AFP case are adequate when two specimens are collected 24 h apart within 14 days of paralysis onset and transported to the polio laboratory in leak-proof containers under proper reverse cold chain conditions.[26] If the stool specimens collected from an AFP case were deemed inadequate, one stool specimen was collected from three close household or neighborhood contacts of the cases to improve virus detection. Beginning in December 2017, environmental surveillance sites were established in two governorates; expansion to all governorates was completed by early 2020. Sewage samples systematically collected at these sites were tested at the national polio laboratory in Damascus.

2.2. Laboratory testing and case detection

Stool specimens from AFP cases and contacts were tested for polioviruses at the polio laboratory in Damascus for government-controlled areas and at the GPEI network laboratory in Ankara, Turkey for opposition-controlled areas. Specimens in which polioviruses were isolated underwent further testing for intratypic differentiation at accredited laboratories within the GPEI network of laboratories. An AFP case was classified as cVDPV2 if a stool specimen from the case-patient or a close contact contained VDPV2 determined by sequencing and analysis of the VP1-coding region. Phylogenetic analysis was performed to demonstrate the relationship among sequenced viruses. AFP cases with stools that did not contain poliovirus were either classified as discarded, i.e., non-polio AFP cases, or clinically compatible with polio if stool specimens taken from these cases were inadequate and case-patients had residual paralysis 60 days after paralysis onset.

2.3. Data sources and statistical analysis

All data reviewed and analyzed were provided by government or opposition sources to the polio and emergency response hub of the WHO Regional Office for the Eastern Mediterranean, located in Amman, Jordan. We analyzed data on all AFP cases, including those confirmed as cVDPV2 cases, during January 1, 2016-December 31, 2018, taking into account the periods preceding, encompassing, and after the outbreak. We described demographic characteristics of confirmed cVDPV2 cases. Using SAS software version 9.4 [Copyright © 2013, SAS Institute Inc., Cary, N.C., USA], we analyzed non-polio AFP cases aged 6–59 months to determine their OPV vaccination status. To estimate differences in polio vaccination coverage and identify areas with gaps in polio immunity, we calculated the proportion of non-polio AFP cases aged 6–59 months that had not received OPV, i.e., zero-dose cases, comparing cases reported from governorates within the outbreak zone to other parts of Syria using the Chi-square test (statistical significance with p-value < 0.05). Using logistic regression, we then estimated the odds ratio for being unvaccinated with OPV comparing non-polio AFP cases reported within the outbreak zone to those reported from other parts of Syria in univariate and multivariate (adjusted for age and sex) models. Vaccination campaign data, including those from postcampaign monitoring, were analyzed to assess the level of coverage in the years preceding and during the outbreak response. Because this study was undertaken as part of the polio outbreak response and surveillance, it was not considered human subjects research following review at the U.S. Centers for Disease Control and Prevention, Atlanta, USA.

3. Results

Descriptive Epidemiology:

A total of 74 cVDPV2 cases were detected during the outbreak, with dates of onset ranging from 3 March to 21 September 2017 (Figs. 1, 2). A majority (62%) of case-patients were female (Table 1) and the median age of case-patients was 15 months (range: 4–155 months). The age distribution of case-patients indicated that nearly half (47%) of all cases occurred among children aged 12–23 months, 35% among children aged < 12 months, 15% among children aged 24–59 months, and only 3% in children 5 years or older. Taken together, this means that children < 2 years of age accounted for 82% of all cVDPV2 cases.

Ninety-six percent of the 74 cVDPV2 cases were reported from Deir-ez-Zor governorate (Fig. 2). Of the 71 cases reported from Deir-ez-Zor, 58 were from Mayadeen district, 12 from Bokamal, and one from the district of Dier-ez-Zor. The other three cases occurred in the districts of Tell Abyad and Thawra in Raqqa governorate and Tadmour district in Homs governorate. Genomic sequence analysis showed genetic linkage among all confirmed cVDPV2 cases, with 22–34 nucleotide substitutions in the VP1 coding region from the parent type 2 Sabin virus contained in OPV. This suggests emergence and circulation of this cVDPV2 strain for about two years prior to outbreak detection.

Poliovirus Surveillance:

Non-polio AFP rates, used to assess the sensitivity of a country's poliovirus surveillance system, exceeded the recommended target of ≥ 2 cases per 100,000 persons < 15 years at the national level during 2016–2018, encompassing the years preceding, during, and following the outbreak. The national stool adequacy rates also exceeded the target of ≥ 80% during the years under review. Subnationally, however, there were gaps in stool adequacy, notably in Deir-ez-Zor and Raqqa governorates, where stool adequacy rates were below 80% during 2016–2017. There were no cVDPV2 isolations from any of the environmental surveillance sites established as an ancillary means of poliovirus surveillance approximately six months after the outbreak was detected.

Polio Immunity Profile:

WHO/UNICEF estimated national routine immunization coverage with 3 doses of OPV in Syria as ranging between 48% and 53% during 2016–2018, a steep drop from prewar levels of 83%–86% during 2001–2010.[23] Official estimates of national coverage with IPV ranged from 58% to 67% during 2016–2018. Consequently, national coverage levels for both OPV and IPV have been well below the recommended target of ≥ 90% during the period under review. Among the 74 cVDPV2 cases, 30 (41%) children had never received OPV (i.e., zero-dose cases), 32 (43%) had received 1–2 doses, while only 12 (16%) had ≥ 3 OPV doses.

In the absence of reliable subnational data on OPV coverage, we used the self-reported OPV vaccination status of non-polio AFP cases aged 6–59 months to estimate the difference in the polio immunity profile of governorates affected by the outbreak (i.e., Deir-ez-Zor, Raqqa, and Homs), hereafter referred to as the outbreak zone, compared with other

governorates in Syria. There was no significant difference between the outbreak zone and the rest of Syria in the proportion of non-polio AFP cases that had not received OPV, i.e., zero-dose cases, in 2016 (6.7% v 5.9%; p-value: 0.8066) and 2018 (7.2 v 4.3%; p-value: 0.2149), both years straddling the year of the outbreak. However, during 2017 (the outbreak year), non-polio AFP cases reported from the outbreak zone were significantly more likely to be zero-dose cases compared with those reported from the rest of Syria (16.3% v 5.2%; p-value: <0.0006).

Using logistic regression to further assess the OPV status of non-polio AFP cases corroborated the differences in the polio immunity of children in the outbreak zone compared with the rest of Syria during 2017. Among 368 non-polio AFP cases aged 6–59 months reported during 2017, univariate logistic regression showed that cases in the outbreak zone had 3.6 (95% CI: 1.7–7.6) times increased odds of being unvaccinated with OPV compared with cases reported from the rest of Syria (Table 2). After adjusting for age and sex in a multivariate model, the magnitude of the comparative odds of being unvaccinated in the outbreak zone reduced to 2.5 (95% CI: 1.1–5.7) times that of the rest of Syria. Each additional month of age was associated with an 8% reduction in the odds of being unvaccinated with OPV after adjusting for geographic location and sex (Odds Ratio: 0.92; 95% CI: 0.87–0.96). Female children were at 2.3 (95% CI: 1.01–5.2) times increased odds of being unvaccinated with OPV compared with boys in the same age group.

Vaccination Response Activities:

In 2016, the year preceding the outbreak, six polio supplementary immunization activities (SIAs) were conducted in Deir-ez-Zor governorate, the epicenter of the outbreak. Trivalent OPV was used for two of these SIAs, conducted in March and April 2016, with poor administrative coverage being reported during the campaigns, i.e., 7% and 23%, respectively. These were the last campaigns prior to the global withdrawal of trivalent OPV and synchronized switch to bivalent OPV.

Vaccination activities in response to the outbreak were implemented according to GPEI guidelines for responding to type 2 vaccine-derived polioviruses in the post-switch era. In response to the cVDPV2 outbreak, which was confirmed in June 2017, three rounds of monovalent OPV type 2 (mOPV2) vaccination activities were conducted in the outbreak zone in two distinct phases. During the first phase of response activities, two rounds of mOPV2 vaccination campaigns targeting children < 5 years of age were conducted in Deir-ez-Zor (target population: 328,000) and Raqqa governorates (target population: 120,000–127,000). Campaigns in Deir-ez-Zor took place one month apart during July and August 2017; postcampaign monitoring data (based on parental recall) estimated coverage at 88% and 77% during the first and second rounds, respectively, of mOPV2 vaccination in the governorate. The first round of mOPV2 vaccination in Raqqa took place in mid-August 2017 but the second round was delayed until two months later in October 2017, owing to evolving political control of the governorate, which complicated and delayed negotiations with multiple local authorities in order to secure approvals for the campaign. Postcampaign monitoring data showed that coverage improved from 57% to 84% between the two rounds of campaigns.

Owing to detection of a new cVDPV2 case in Deir-ez-Zor governorate 14 days after the completion of two rounds of mOPV2 vaccination, a third round of mOPV2 vaccination campaigns was undertaken in January 2018 as part of the second phase of outbreak response activities. The campaigns were implemented in Deir-ez-Zor, Raqqa, and Homs (Tadmour district only) governorates, which reported cases, as well as Hasakeh governorate because of its geographic proximity to the outbreak zone. Postcampaign monitoring data indicated coverage levels ranging from 84% in Raqqa governorate to 91% in Hasakeh governorate. Coverage could not be accurately estimated for the<1000 children vaccinated in Tadmour district of Homs due to large-scale population displacement from the governorate during the campaigns.

IPV was adjunctively administered to children aged 2–23 months during the second and third rounds of mOPV2 vaccination in targeted areas within and outside the outbreak zone. In addition, IPV was used for risk-mitigation vaccination among internally displaced persons from the outbreak zone arriving in other parts of Syria and among refugees and high-risk groups in border areas of Turkey, Iraq, Lebanon and Jordan.

4. Discussion

Circulating vaccine-derived polioviruses pose a significant threat to the eventual eradication of all polioviruses.[13,28–29] The 2017 outbreak of cVDPV2 in war-torn Syria underscores this risk while providing useful lessons for mitigation. The strategic response to the outbreak highlights the importance of a prompt and coordinated approach to responding to disease outbreaks within settings of conflict and humanitarian crisis.

Since the onset of a civil war in Syria in 2011, the delivery of healthcare services in the country has been severely compromised owing to destruction of healthcare infrastructure and large-scale displacement of persons to areas within and outside Syria.[8–10,30] As a result, epidemics of infectious diseases in the country have been on the rise. Steep declines in the delivery of immunization services have led to a resurgence in vaccine-preventable diseases, including measles and polio.[31] Barely three years after a WPV1 outbreak paralyzed 36 children in Syria,[6] a cVDPV2 outbreak paralyzed twice as many children in the country.[11] Deir-ez-Zor governorate, and specifically Mayadeen district, was the epicenter of both outbreaks, though the WPV1 outbreak was more dispersed geographically than the subsequent cVDPV2 outbreak. Owing to its geographic dispersion across the northeastern and northwestern parts of Syria, and the risk of spread to neighboring countries, the WPV1 outbreak prompted a large, mass vaccination drive across eight countries in the Middle East using both bOPV and tOPV during 2013–2015. The extensive nature of the vaccination response to the WPV1 outbreak might have limited the geographic and demographic scope of the cVDPV2 outbreak that followed.

While both the WPV1 and cVDPV2 outbreaks predominantly affected children born after the onset of the civil war in Syria, the age distribution of children affected by the cVDPV2 outbreak was further narrowed to mostly children born after the 2013–2014 WPV1 outbreak. Of the 74 cases reported during the cVDPV2 outbreak in 2017, 82% were aged < 2 years and therefore mostly born after the cessation of response activities

to the WPV1 outbreak, which were concluded in 2015. Further, the quality of pre-switch tOPV vaccination campaigns in Deir-ez-Zor, the epicenter of the outbreak, was poor. Intermittent bans imposed by insurgent groups on vaccination activities in the intervening period between both outbreaks further deprived children born in the governorate during this period of opportunities to receive polio vaccines.

Given the above scenario, it is plausible that the poor quality of tOPV campaigns in Deir-ez-Zor created the enabling conditions for vaccine-derived polioviruses to emerge and circulate predominantly in multiple susceptible birth cohorts that lacked opportunities for protection against type 2 polioviruses, due to the withdrawal of trivalent OPV globally in April/May 2016. Our statistical analysis, which analyzed the odds of being unvaccinated with OPV among non-polio AFP cases as a proxy for the quality of immunization service delivery, supports this hypothesis. After adjusting for age and sex, non-polio AFP cases aged 6–59 months in the three governorates that reported cVDPV2 cases had 2.5 times increased odds of being unvaccinated with OPV compared with non-polio AFP cases in the same age group reported from elsewhere in Syria in 2017. This finding also likely explains why the outbreak in Deir-ez-Zor did not spread to other parts of the country prior to implementation of response vaccination activities despite large-scale population migration from the outbreak zone to other parts of the country.

Transmission of cVDPV2 within the outbreak zone itself was effectively curtailed and interrupted within 120 days through implementation of three mOPV2 SIAs with adjunct administration of IPV; governorate-level administrative coverage mostly exceeded 80%. Remarkably, these vaccination rounds went ahead despite active combat between government and opposition forces, changes in political control of some areas in the outbreak zone between rounds, and substantial logistical constraints in transportation and storage of vaccines. While contested sovereignty has been viewed as an obstacle to mounting effective public health responses in settings of conflict,[32] GPEI’s interagency structure allowed it to draw on the strengths of its different partners to play an intermediary role between warring factions to facilitate outbreak response activities while maintaining its political neutrality. This, of course, would not have been possible without the cooperation and resilience of the Syrian people across the political divide, who demonstrated strong acceptance of the need to vaccinate their children against polio.

Certain limitations should be taken into consideration in interpreting our findings. The OPV vaccination status of all cVDPV2 case-patients as well as all other non-polio AFP case-patients was ascertained based on caregiver recall and did not specify which type of OPV was received, and as such may be subject to recall and misclassification bias. Further, in the absence of reliable data on IPV vaccination, we used only the OPV vaccination status of non-polio AFP cases as a proxy for the quality of polio immunization coverage. While this could lead to inaccurate estimates of polio immunity within specific geographic areas of Syria, the poor vaccination status of cVDPV2 cases reported from outbreak-affected areas supports the metric’s usefulness as an indicator of polio immunity.

With the surge in the number of countries experiencing cVDPV outbreaks in Africa and elsewhere around the world,[16,33–34] the response to the cVDPV2 outbreak in Syria

provides several important lessons. First, while AFP surveillance remains the key method for poliovirus surveillance, it may not be sufficient for timely detection of cVDPV outbreaks owing to subnational gaps, especially in areas where access is limited by insecurity and bans on routine immunization or other polio activities. The possibility of prolonged poliovirus circulation in sequestered populations without the detection of paralytic cases should be a consideration in establishing environmental sewage sampling sites as an ancillary means of poliovirus surveillance, where feasible.[35–37] Second, high quality mOPV2 SIAs are effective in stopping cVDPV2 outbreaks, especially when implemented in a timely manner.[38] The demographic and geographic scope of these rounds should be informed not only by the areas where there is active virus transmission but also by the historical context of vaccination within the country as a whole. Historically high prewar vaccination coverage and the response to a previous WPV1 outbreak in Syria played a role in limiting the scope of the subsequent cVDPV2 outbreak. Consideration should be given to large-scale national or subnational mOPV2 vaccination campaigns in response to cVDPV2 isolation in countries with historically low vaccination coverage. Finally, the successful response to the cVDPV2 outbreak in Syria demonstrates that communities with positive attitudes towards vaccination are capable of overriding the seemingly insurmountable barriers of conflict and insecurity to halt disease outbreaks.

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References

[1]. Nathanson N, Kew OM. From emergence to eradication: the epidemiology of poliomyelitis deconstructed. Am J Epidemiol 2010;172:1213–29. [PubMed: 20978089]

[2]. Chard AN, Datta SD, Tallis G, et al. Progress Toward Polio Eradication — Worldwide, January 2018–March 2020. MMWR Morb Mortal Wkly Rep 2020;69:784–9. [PubMed: 32584798]

[3]. Wassilak SG, Oberste MS, Tangermann RH, Diop OM, Jafari HS, Armstrong GL. Progress toward global interruption of wild poliovirus transmission, 2010–2013, and tackling the challenges to complete eradication. J Infect Dis 2014;210:S5–S15. [PubMed: 25316873]

[4]. Moturi EK, Porter KA, Wassilak SGF, et al. Progress toward polio eradication—worldwide, 2013–2014. MMWR Morb Mortal Wkly Rep 2014;63:468–72. [PubMed: 24871252]

[5]. Thompson KM, Pallansch MA, Duintjer Tebbens RJ, Wassilak SGF, Kim JH, Cochi SL. Pre-eradication national vaccine policy options for poliovirus infection and disease3 control. Risk Anal 2013;33:516–43. [PubMed: 23461599]

[6]. Mbaeyi C, Ryan MJ, Smith P, et al. Response to a Large Polio Outbreak in a Setting of Conflict — Middle East, 2013–2015. MMWR Morb Mortal Wkly Rep 2017;66:227–31. [PubMed: 28253229]

[7]. Roberts L A war within a war. Science 2014;343:1302–5. [PubMed: 24653016]

[8]. Sharara SL, Kanj SS. War and infectious diseases: challenges of the Syrian civil war. PLoS Pathog. 2014;10(10):e1004438. [PubMed: 25393545]

[9]. Ozaras R, Leblebicioglu H, Sunbul M, et al. The Syrian conflict and infectious diseases. Expert Rev Anti Infect Ther. 2016;14(6):547–55. [PubMed: 27063349]

[10]. Stone-Brown K Syria: a healthcare system on the brink of collapse. BMJ 2013;347:f7375. [PubMed: 24327182]

[11]. Mbaeyi C, Wadood ZM, Moran T, et al. Strategic Response to an Outbreak of Circulating Vaccine-Derived Poliovirus Type 2 — Syria, 2017–2018. MMWR Morb Mortal Wkly Rep 2018;67:690–4. [PubMed: 29927908]

[12]. Burns CC, Diop OM, Sutter RW, Kew OM. Vaccine-derived polioviruses. J Infect Dis. 2014;210(Suppl 1):S283–93. [PubMed: 25316847]

[13]. Kew O, Pallansch M. Breaking the Last Chains of Poliovirus Transmission: Progress and Challenges in Global Polio Eradication. Annu Rev Virol. 2018;5(1):427–51. [PubMed: 30001183]

[14]. Macklin G, Liao Y, Takane M, et al. Prolonged Excretion of Poliovirus among Individuals with Primary Immunodeficiency Disorder: An Analysis of the World Health Organization Registry. Front Immunol. 2017;8:1103. [PubMed: 28993765]

[15]. Jorba J, Diop OM, Iber J, et al. Update on Vaccine-Derived Polioviruses — Worldwide, January 2017–June 2018. MMWR Morb Mortal Wkly Rep 2018;67:1189–94. [PubMed: 30359342]

[16]. Jorba J, Diop OM, Iber J, et al. Update on Vaccine-Derived Poliovirus Outbreaks — Worldwide, January 2018–June 2019. MMWR Morb Mortal Wkly Rep 2019;68:1024–8. [PubMed: 31725706]

[17]. Hampton LM, Farrell M, Ramirez-Gonzalez A, et al. Cessation of Trivalent Oral Poliovirus Vaccine and Introduction of Inactivated Poliovirus Vaccine — Worldwide, 2016. MMWR Morb Mortal Wkly Rep 2016;65:934–8. [PubMed: 27606675]

[18]. Koopman JS. Models and analyses to understand threats to polio eradication. BMC Med. 2017 22;15(1):221. [PubMed: 29268738]

[19]. Moffett DB, Llewellyn A, Singh H, et al. Progress Toward Poliovirus Containment Implementation — Worldwide, 2018–2019. MMWR Morb Mortal Wkly Rep 2019;68:825–9. [PubMed: 31557146]

[20]. Thompson KM, Duintjer Tebbens RJ. Modeling the dynamics of oral poliovirus vaccine cessation. J Infect Dis 2014;210:475–84.

[21]. Thompson KM, Pallansch MA, Duintjer Tebbens RJ, Wassilak SGF, Cochi SL. Modeling population immunity to support efforts to end the transmission of live polioviruses. Risk Anal 2013;33:647–63. [PubMed: 22985171]

[22]. Duintjer Tebbens RJ, Thompson KM. Modeling the potential role of inactivated poliovirus vaccine to manage the risks of oral poliovirus vaccine cessation. J Infect Dis 2014;210:485–97.

[23]. World Health Organization. Vaccine-preventable diseases: monitoring system 2019 global summary. Geneva, Switzerland: World Health Organization; 2019. http://apps.who.int/immunization_monitoring/globalsummary. Accessed 14 February 2020.

[24]. World Health Organization. Circulating vaccine-derived poliovirus type 2 – Syrian Arab Republic. Disease Outbreak News, 13 June 2017. https://www.who.int/csr/don/13-June-2017-polio-syrian-arab-republic/en/. Accessed 5 May 2021.

[25]. Global Polio Eradication Initiative. Standard operating procedures: responding to a poliovirus event or outbreak, November 2017. Geneva, Switzerland: World Health Organization, Global Polio Eradication Initiative; 2017. http://polioeradication.org/wp-content/uploads/2018/01/pol-sop-responding-polioevent-outbreak-part1-20180117.pdf.

[26]. Patel JC, Diop OM, Gardner T, et al. Surveillance to Track Progress Toward Polio Eradication — Worldwide, 2017–2018. MMWR Morb Mortal Wkly Rep 2019;68:312–8. [PubMed: 30946737]

[27]. World Health Organization. Outbreak surveillance and response in humanitarian emergencies: WHO guidelines for EWARN implementation Geneva, Switzerland: World Health Organization; 2012. https://www.who.int/diseasecontrol_emergencies/publications/who_hse_epr_dce_2012.1/en/. Accessed 14 February 2020.

[28]. Duintjer Tebbens RJ, Pallansch MA, Kew OM, et al. Risks of paralytic disease due to wild or vaccine-derived poliovirus after eradication. Risk Anal 2006;26:1471–505. [PubMed: 17184393]

[29]. Duintjer Tebbens RJ, Pallansch MA, Kim JH, et al. Oral poliovirus vaccine evolution and insights relevant to modeling the risks of circulating vaccine-derived polioviruses. Risk Anal 2013;33:680–702. [PubMed: 23470192]

[30]. Aburas R, Najeeb A, Baageel L, et al. The Syrian conflict: a case study of the challenges and acute need for medical humanitarian operations for women and children internally displaced persons. BMC Med. 2018;16:65. [PubMed: 29747641]

[31]. Doganay M, Demiraslan H. Refugees of the Syrian Civil War: Impact on Reemerging Infections, Health Services, and Biosecurity in Turkey. Health Secur. 2016;14(4):220–5. [PubMed: 27362427]

[32]. Kennedy J, Michailidou D. Civil war, contested sovereignty and the limits of global health partnerships: A case study of the Syrian polio outbreak in 2013. Health Policy Plan. 2017;32(5):690–8. [PubMed: 28453719]

[33]. Mbaeyi C, Alleman MM, Ehrhardt D, et al. Update on Vaccine-Derived Poliovirus Outbreaks — Democratic Republic of the Congo and Horn of Africa, 2017–2018. MMWR Morb Mortal Wkly Rep 2019;68:225–30. [PubMed: 30845121]

[34]. Bauri M, Wilkinson AL, Ropa B, et al. Notes from the Field: Circulating Vaccine-Derived Poliovirus Type 1 and Outbreak Response — Papua New Guinea, 2018. MMWR Morb Mortal Wkly Rep 2019;68:119–20. [PubMed: 30730867]

[35]. Eboh VA, Makam JK, Chitale RA, et al. Notes from the Field: Widespread Transmission of Circulating Vaccine-Derived Poliovirus Identified by Environmental Surveillance and Immunization Response — Horn of Africa, 2017–2018. MMWR Morb Mortal Wkly Rep 2018;67:787–9. [PubMed: 30024868]

[36]. Nnadi C, Damisa E, Esapa L, et al. Continued Endemic Wild Poliovirus Transmission in Security-Compromised Areas — Nigeria, 2016. MMWR Morb Mortal Wkly Rep 2017;66:190–3. [PubMed: 28233765]

[37]. Vallejo C, Pearson CAB, Koopman J, Hladish TJ. Evaluating the probability of silent circulation of polio in small populations using the silent circulation statistic. Infect Dis Model. 2019;4:239–50. [PubMed: 31312777]

[38]. Thompson KM, Duintjer Tebbens RJ, Pallansch MA. Evaluation of response scenarios to potential polio outbreaks using mathematical models. Risk Anal 2006;26:1541–56. [PubMed: 17184396]

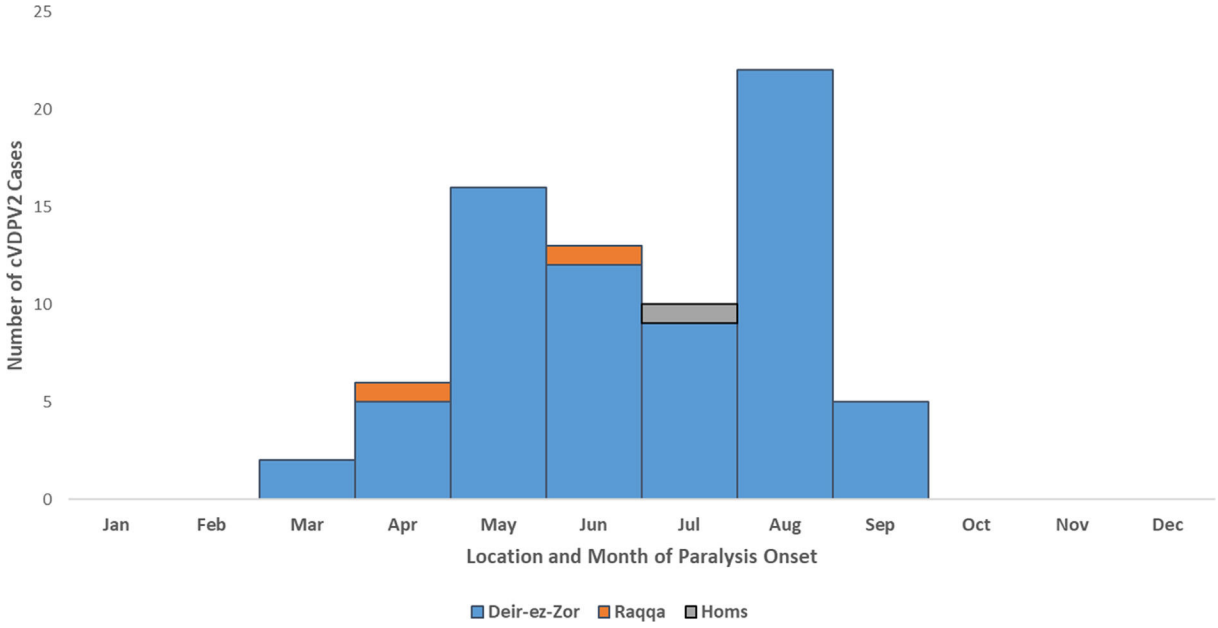

Fig. 1.

Distribution of cases of circulating vaccine-derived poliovirus type 2 (cVDPV2), by governorate and month of paralysis onset — Syria, 2017.

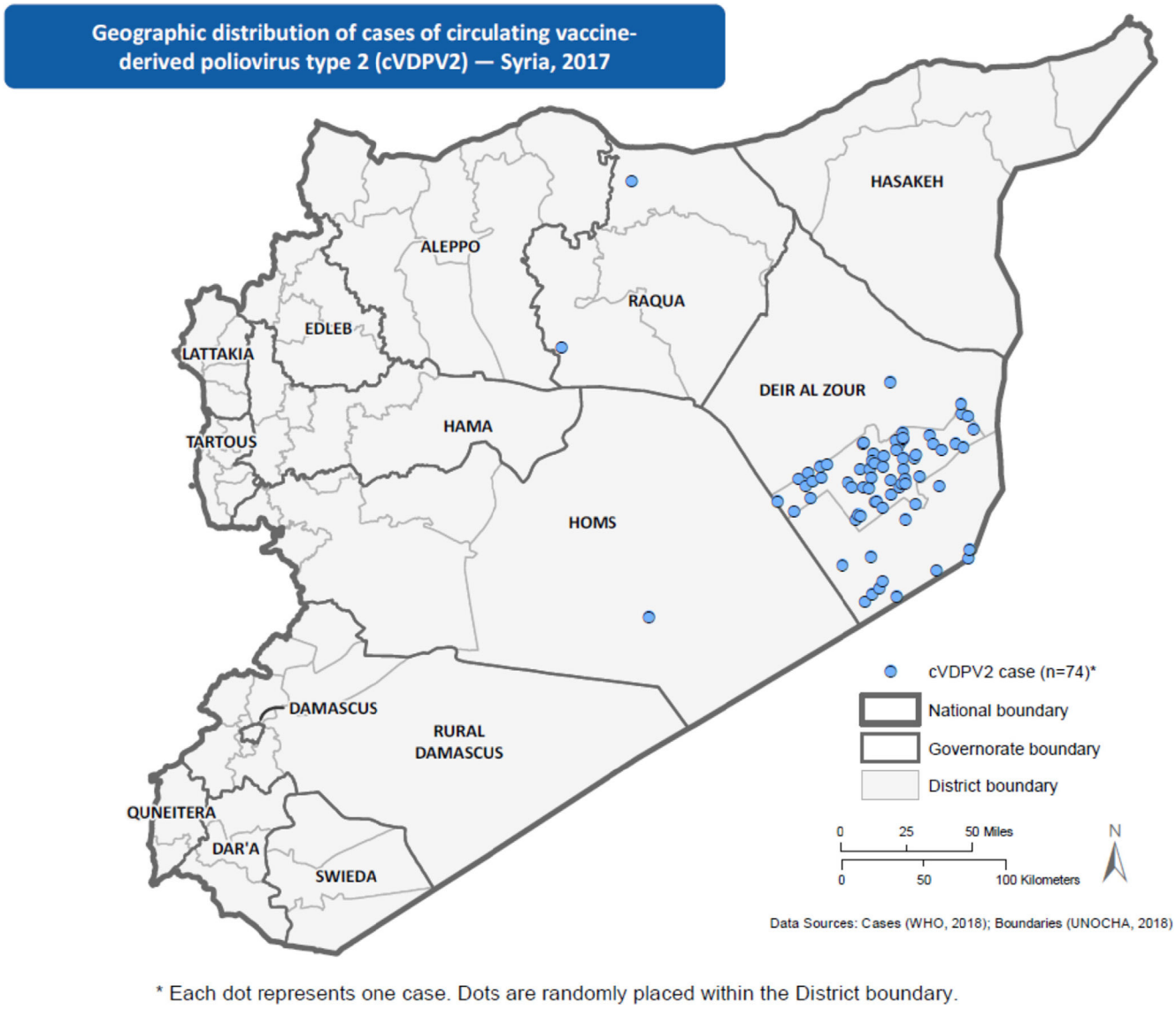

Fig. 2.

Geographic distribution of cases of circulating vaccine-derived poliovirus type 2 (cVDPV2) – Syria, 2017.

Table 1

Demographic characteristics and vaccination status of circulating vaccine-derived poliovirus type 2 (cVDPV2) and non-polio acute flaccid paralysis (AFP) cases reported in Syria during 2017.

Variable	cVDPV2 Cases (N = 74)		Non-polio AFP cases (N = 654)		Chi-square P-value
	Number	Percentage (%)	Number	Percentage (%)	
Sex					
Male	28	38	372	57	0.0018
Female	46	62	282	43	
Age					
<12 months	26	35	58	9	<0.0001
12–23 months	35	47	131	20	
24–59 months	11	15	194	30	
≥60 months	2	3	271	41	
OPV *doses					
0	30	41	47	7	<0.0001
1–2	32	43	76	12	
≥3	12	16	529	81	
Location					
Outbreak Zone **	74	100	159	76	<0.0001
Rest of Syria	0	0	495	24	

*OPV: Oral poliovirus vaccine

**Outbreak Zone: Deir ez Zor, Raqqa, and Homs governorates

Table 2

Univariate and multivariate logistic regression of the relative odds of being unvaccinated with oral poliovirus vaccine (OPV) comparing non-polio acute flaccid paralysis (AFP) cases aged 6–59 months in the outbreak zone to those reported in other areas of Syria in 2017.

Variable	Univariate Model		Multivariate Model	
	Odds Ratio	95% Confidence Interval	Adjusted Odds Ratio	95% Confidence Interval
Location				
Outbreak Zone *	3.57	1.67–7.62	2.53	1.13–5.66
Reference: Rest of Syria				
Sex				
Female	2.44	1.13–5.29	2.27	1.01–5.12
Reference: Male				
Age (months)	0.91	0.86–0.95	0.92	0.87–0.96

* Outbreak Zone: Deir ez Zor, Raqqa, and Homs governorates