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Another look at silent circulation of poliovirus in small populations

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ABSTRACT

Background: Silent circulation of polioviruses complicates the polio endgame and motivates analyses that explore the probability of undetected circulation for different scenarios. A recent analysis suggested a relatively high probability of unusually long silent circulation of polioviruses in small populations (defined as 10,000 people or smaller).

Methods: We independently replicated the simple, hypothetical model by Vallejo et al. (2017) and repeated their analyses to explore the model behavior, interpretation of the results, and implications of simplifying assumptions.

Results: We found a similar trend of increasing times between detected cases with increasing basic reproduction number (R_0) and population size. However, we found substantially lower estimates of the probability of at least 3 years between successive polio cases than they reported, which appear more consistent with the prior literature. While small and isolated populations may sustain prolonged silent circulation, our reanalysis suggests that the existing rule of thumb of less than a 5% chance of 3 or more years of undetected circulation with perfect surveillance holds for most conditions of the model used by Vallejo et al. and most realistic conditions.

Conclusions: Avoiding gaps in surveillance remains critical to declaring wild poliovirus elimination with high confidence as soon as possible after the last detected poliovirus, but concern about transmission in small populations with adequate surveillance should not significantly change the criteria for the certification of wild polioviruses.

1. Introduction

The detection of a wild poliovirus (WPV) in Borno state in Northeast Nigeria in 2016 (Nnadi et al., 2017), at a time when many hoped WPV circulation had stopped in Africa, raised questions about the possibility of prolonged undetected poliovirus circulation in small populations. The serotype 1 WPV detected in 2016 in Borno occurred almost two years after the prior most

Abbreviations: AFP, acute flaccid paralysis; CFP, case-free period; CNC, confidence about no circulation; CNCx%, time when the confidence about no circulation exceeds x%; DEFP, detected-event-free period; OPV, oral poliovirus vaccine; POE, Probability of eradication; TBC, time between detected cases; TUC, time of undetected circulation after the last detected-event; TUCx%, xth percentile of the TUC; WPV, wild poliovirus.

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recent case in Nigeria in 2014, although it likely originated from a distinct lineage last detected in Borno in 2013 (Nnadi et al., 2017). Due to civil unrest, polio eradication efforts could not reach parts of Borno with vaccination or surveillance for several years, and some areas remain inaccessible (Nnadi et al., 2017). Similar resurfacing of a WPV after multiple years without detection previously occurred in the Sudan and Chad (World Health Organization, 2005a, 2005b), and surveillance continues to occasionally detect WPVs with no closely linked ancestors in Pakistan and Afghanistan (i.e., orphan viruses) (Cowger et al., 2017). Poliovirus surveillance primarily relies on the detection of symptomatic cases of acute flaccid paralysis (AFP) and tests of their stool for the presence of poliovirus. However, only less than 1% of WPV infections in susceptible individuals result in paralytic symptoms (i.e., approximately 1/200, 1/2,000, and 1/1,000 for WPV serotypes 1, 2, and 3, respectively) (Nathanson & Kew, 2010). This implies that hundreds to thousands of infections can occur between successive cases, leading to a situation of silent circulation. While all documented instances of prolonged undetected circulation occurred in the context of likely gaps in surveillance, the possibility of silent poliovirus circulation contributes to the ability of transmission to go undetected.

Motivated by the re-emergence in Borno, a recent study used a stochastic model to examine whether simple, small, hypothetical populations not reached at all by vaccination can perpetuate WPV transmission while experiencing very long intervals between polio cases (Vallejo, Keesling, Koopman, & Singer, 2017). The potential for silent circulation influences the confidence about the interruption of poliovirus transmission as a function of time after the last detected poliovirus, which informs the decision to certify wild poliovirus eradication in a country, region, and globally. Global certification of a wild poliovirus serotype affects when the world can coordinate the cessation of the use of homotypic oral poliovirus vaccine (OPV), which represents a necessary step to end all paralytic poliomyelitis disease (polio) caused by polioviruses, because OPV itself can in rare instances cause polio (Duintjer Tebbens et al., 2006; World Health Organization, 2005a, 2005b, 2013). Delaying OPV cessation leads to substantial additional costs (Duintjer Tebbens et al., 2011), but premature OPV cessation implies a risk of a WPV reemergence that could become very difficult to control. As of early 2018, of the six World Health Organizations (WHO) regions, only the African and the Eastern Mediterranean regions remain not certified as polio-free due to the possibility of continued WPV transmission in Borno (African region) and continuing polio cases in Pakistan and Afghanistan (Eastern Mediterranean region) (World Health Organization, 2018). Moreover, of the three WPV serotypes, the world certified serotype 2 WPV eradication in 2015 (Global Polio Eradication Initiative, 2015) and did not report any polio cases due to serotype 3 WPV since 2012 (Kew et al., 2014), with only serotype 1 WPV continuing to cause reported polio cases.

Based on epidemiological experience and modeling, certifying a region or the world as polio-free requires no observed polio cases for at least three years (Debanne & Rowland, 1998; Eichner & Dietz, 1996; Kalkowska, Duintjer Tebbens, Pallansch, et al., 2015; World Health Organization, 2017). Prior to Vallejo et al. (2017), numerous modeling studies addressed the possibility of prolonged poliovirus circulation without any detected polio cases in different populations using different metrics, and spanning different model structures and assumptions about surveillance, vaccination, transmissibility, and demographics (Berchenko et al., 2017; Eichner & Dietz, 1996; Famulare, 2016; Houy, 2015; Kalkowska, Duintjer Tebbens, Pallansch, et al., 2015; Kalkowska, Duintjer Tebbens, & Thompson, 2012). These models generally agree that in most realistic situations, 3 years without any detected cases implies at least 95% confidence about no circulation, although our studies show that results depend on surveillance quality, serotype, seasonality, and vaccination strategies (Kalkowska, Duintjer Tebbens, Pallansch, et al., 2015; Kalkowska et al., 2012). In contrast to the prior literature, Vallejo et al. (2017) prominently reported (in their abstract) a 22% chance of at least 3 years between successive polio cases in a population of 10,000 people despite a 100% case detection rate. In a correction, Vallejo, Keesling, Koopman, and Singer (2018) report an error in the calculation of the average age of infection that resulted in the use of unrealistically high values for the basic reproduction number (R_0), which led them to note the limited applicability of their findings to real-world situations. Nonetheless, the potential use of their findings in deliberations about polio certification motivated us to replicate the Vallejo et al. (2017) analyses to take a closer look at the model behavior, the interpretation of the results (particularly in the context of the relevant prior literature that they did not consider), and the implications of some of their simplifying assumptions. Although they issued a correction that highlighted one unrealistic model input assumption (Vallejo et al., 2018), we highlight multiple other attributes that they did not consider that further limit the utility of their approach and model for supporting policy, including the unrealistic assumptions about the existence of completely isolated small populations that remain at the endemic equilibrium with no vaccination and yet benefit from perfect surveillance.

2. Material and methods

We used the model structure, notation, input values, and microsimulation algorithm descriptions provided by Vallejo et al. (2017) to reconstruct their model in Java using the Eclipse open development platform (Eclipse Foundation, Inc., Ottawa, Ontario, Canada). The first two authors independently reconstructed the model. The model assumes a constant population (i.e., birth rate = death rate) distributed over five compartments: susceptible (i.e., never infected), first infection (susceptible to paralysis), temporary full immunity to infection after recovery from infection, partial susceptibility to infection but not paralysis after waning, and reinfection of partially susceptible individuals. The paralysis-to-infection ratio determines the probability of a first infection leading to a polio case, and the detection rate determines the probability that surveillance would detect a polio case. The model ignores the 1–3-day latent period between virus exposure and becoming infectious to others (Duintjer Tebbens, Pallansch, Kalkowska, et al., 2013), and characterizes the infectious period using a single stage, which implies an exponential recovery process with an unrealistically long tail (Duintjer Tebbens, Pallansch, Kalkowska, et al., 2013; Lloyd, 2001). The model uses the Gillespie algorithm (Gillespie, 1976), which randomly generates when transition