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Modeling and managing poliovirus risks: We are where we are...

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Abstract

This introduction for the third special issue on modeling poliovirus risks provides context for the current status of global polio eradication efforts and gives an overview of the individual papers included in the issue. Although risk analysis continues to support polio eradication efforts, efforts to finish the job were off track at the beginning of 2020 and prior to the COVID-19 pandemic, as discussed in the special issue. The disruptions associated with COVID-19 occurring now will inevitably change the polio eradication trajectory, and future studies will need to characterize the impacts of these disruptions on the polio endgame.

Keywords

polio; modeling; eradication

1. CONTEXT

Despite the 1988 World Health Assembly (WHA) resolution to eradicate polio by 2000 (World Health Assembly, 1988), polio eradication efforts continue. This third special issue of *Risk Analysis* on managing the risks of polioviruses follows related 2006 (Thompson, 2006) and 2013 (Thompson, 2013) special issues with a 7-year interval. The 1988 WHA led to the launch of the Global Polio Eradication Initiative (GPEI), which organizes key partners and manages their shared activities. Achieving the WHA mission of ending all cases of poliomyelitis caused by wild polioviruses (WPVs) requires stopping and permanently preventing the transmission of all three serotypes (1, 2, and 3) of WPV (i.e., WPV1, WPV2, and WPV3). The last reported global case caused by WPV2 occurred before 2000 and Nigeria reported the last WPV3 case in November 2012 (World Health Organization, 2016). The Global Certification Commission (GCC) formally declared indigenous WPV2 eradication in September 2015 (Global Polio Eradication Initiative, 2015) and indigenous WPV3 eradication in October 2019 (World Health Organization, 2019b). These successes still represent a partial victory, however, with indigenous WPV1 transmission continuing to date in Pakistan and Afghanistan, with notably increasing reported cases since 2017 (World Health Organization, 2020b).

National immunization programs in 2020 still use one or both of two types of poliovirus vaccines: oral poliovirus vaccine (OPV) and inactivated poliovirus vaccine (IPV). The

vaccines differ in their immunological benefits, costs (for the vaccine and administration), and risks (Thompson & Duintjer Tebbens, 2014). Meeting the goal of preventing all cases of poliomyelitis requires successfully ending all use of OPV after certification of WPV eradication, because OPV can cause rare cases of vaccine-associated paralytic polio (VAPP) in fully susceptible OPV vaccine recipients and their close contacts. In addition, secondary spread of OPV can lead to cases in fully susceptible individuals who become infected by transmission of OPV-related viruses, known as vaccine-derived polioviruses (VDPVs). All live polioviruses (LPVs, i.e., OPV, OPV-related viruses, and VDPVs) can cause infection, but they vary in transmissibility and neurovirulence. Delays in eradicating all WPVs led the GPEI to pursue a strategy of phased globally-coordinated OPV cessation, starting with serotype 2 OPV (OPV2). In late April and early May 2016, the GPEI coordinated a global switch of trivalent OPV (tOPV, which contains all 3 OPV serotypes) to bivalent OPV (bOPV, which contains serotypes 1 and 3). OPV2 cessation ended all use of OPV2 by national immunization programs, except for emergency use of monovalent serotype 2 OPV (mOPV2) to respond to serotype 2 VDPVs (VDPV2s) after the tOPV-bOPV switch (World Health Organization, 2016b). As of early 2017, most OPV-using countries stopped OPV2 use successfully and observed die out of all serotype 2 LPVs (Thompson & Duintjer Tebbens, 2017). However, not all countries succeeded (Duintjer Tebbens & Thompson, 2018), and the reported cases caused by VDPV2s substantially exceeded the number of reported WPV1 cases since 2017 (World Health Organization, 2020b). The need to respond to cVDPV2 outbreaks leads to continued use of mOPV2 for outbreak response and questions about whether the mid-2016 OPV2 cessation will ultimately succeed (Duintjer Tebbens & Thompson, 2018; Thompson & Kalkowska, 2019). As of 2020, the GPEI partners ordered the production of more OPV2, which signaled that the GPEI would not succeed without restarting some OPV2 production (Thompson, 2020).

Since the 2013 special issue, *Risk Analysis* published a small series of papers in 2018–2019 focused on the risks of poliovirus transmission in Pakistan and Afghanistan (Duintjer Tebbens et al., 2018; Duintjer Tebbens & Thompson, 2019; Kalkowska, Duintjer Tebbens, Pallansch, & Thompson, 2019; Kalkowska & Thompson, 2019). These papers modeled Pakistan and Afghanistan as an epidemiological block with subpopulations of under-vaccinated individuals that preferentially mix, and demonstrated the ability of the under-vaccinated individuals to sustain transmission (Duintjer Tebbens et al., 2018). Building on recognition of the need for significant improvement in OPV coverage using supplementary immunization activities (SIAs) in these under-vaccinated subpopulations to stop transmission (Duintjer Tebbens et al., 2018), additional modeling emphasized the importance of proactive strategies (as opposed to reactive ones) (Duintjer Tebbens & Thompson, 2019). Further studies explored the potential for silent poliovirus transmission and the role of different types of surveillance information in providing confidence about the absence of transmission for different durations of no reported cases found by active surveillance (Kalkowska et al., 2019) as well as the tradeoffs in key characteristics of the poliovirus surveillance system in Pakistan and Afghanistan (Kalkowska & Thompson, 2019).

In early 2019, faced with the reality of ongoing WPV1 transmission in Pakistan and Afghanistan and the need to raise additional funds to support ongoing and necessary

activities (despite extending its prior 2013–2018 Strategic Plan (World Health Organization Global Polio Eradication Initiative, 2013) to 2019 (World Health Organization Global Polio Eradication Initiative, 2015)), the GPEI released a new Strategic Plan for 2019–2023 (World Health Organization Global Polio Eradication Initiative, 2019). By necessity, this plan contrasted with earlier expectations of transitioning all GPEI assets and responsibilities to all countries by 2019 (World Health Organization Global Polio Eradication Initiative, 2013, 2015), with some GPEI transition activities implemented prior to 2019 leading to reduced resources and capacity to manage polio in some countries (Diop, Kew, de Gourville, & Pallansch, 2017). In early 2020, recognizing the ongoing VDPV2 transmission occurring nearly 4 years after globally coordinated OPV2 cessation, the GPEI issued an addendum to its 2019–2023 Strategic Plan (World Health Organization Global Polio Eradication Initiative, 2020). A separate review of polio modeling papers published in English between 2000–2019 describes the different approaches taken by a different modelers (Thompson & Kalkowska, 2020c).

The contents of this special issue focus on the status of polio eradication efforts at the beginning of the new strategic plan (World Health Organization Global Polio Eradication Initiative, 2019) and the GPEI expected trajectory before the SARS-CoV-2 virus led to the declaration of Coronavirus Disease (COVID-19) as a global pandemic in 2020. The disruptions associated with COVID-19 occurring now will inevitably change the polio eradication trajectory, and we leave it to future studies to characterize these impacts. This introduction for the third special issue on modeling poliovirus risks provides context for the pre-COVID-19 status of global polio eradication efforts and gives an overview of the individual papers included in the issue.

2. OVERVIEW OF THE SPECIAL ISSUE CONTENTS

The first paper in this third special issue on managing poliovirus risks provides this introduction to the 13 other papers. The second paper provides a reflection (Thompson & Kalkowska, 2020b) on prior modeling (i.e., built on the 2013 (Thompson, 2013) *Risk Analysis* special issue papers and performed to support the 2013–2018 GPEI Strategic Plan (Duintjer Tebbens, Pallansch, Wassalik, Cochi, & Thompson, 2015)) in the context of the situation at the time of the new GPEI Strategic Plan (World Health Organization Global Polio Eradication Initiative, 2019, 2020). In contrast to a systematic review of polio modeling papers published 2000–2019 (Thompson & Kalkowska, 2020c), the second paper (Thompson & Kalkowska, 2020b) focuses on the for the Kid Risk, Inc. polio modeling only and on areas in which the prior model assumptions did not match observed experience. A key observation of that reflection reveals that the prior model framing and assumptions about optimal behavior by national, regional, and global decision makers do not match the available evidence and suggest the need for updated modeling that characterize of the actual poor performance that occurred and will likely continue to occur in some areas (Thompson & Kalkowska, 2020b). This insight led to a shift in the framing of the modeling in this special issue to focus on realistic expected performance (i.e., modeling what countries would likely do and experience instead of how well they could do). The third paper presents an updated assessment of global transmission of live polioviruses (Kalkowska, Wassilak, Cochi, Pallansch, & Thompson, 2020), which builds directly on the 2013 global model (Duintjer

Tebbens et al., 2015) and focuses on updating the epidemiological, immunization, and virology-related inputs based on evidence available as of the end of 2019. In the context of this framing, the updated model suggests that polio eradication remains off track and suggests that WPV1 eradication would not occur by 2023 if countries followed the expected trajectory (even before COVID-19) (Kalkowska, Wassilak, et al., 2020).

The fourth and fifth papers in this special issue focus on Pakistan and Afghanistan. The fourth paper builds on insights from the prior series (Duintjer Tebbens et al., 2018; Duintjer Tebbens & Thompson, 2019; Kalkowska et al., 2019; Kalkowska & Thompson, 2019) and demonstrates that improvements in OPV SIAs in subpopulations that currently sustain transmission, if feasible, could interrupt transmission of WPV1 and thus support global WPV eradication by 2023 (Kalkowska & Thompson, 2020c). The fifth paper explores the impact of using surveillance data to better manage resource prioritization in Pakistan and demonstrates limited value of the information in this context, most likely due to other factors driving resource allocation decisions (Scott, Cullen, & Chabot-Couture, 2020).

With poliovirus transmission apparently stopped in Africa, the sixth and seventh papers of this special issue characterize transmission of polioviruses in the last known reservoirs of types 1 and 3 WPV (i.e., the Borno and Yobe states of Nigeria). The sixth paper focuses on characterizing the transmission dynamics using the available information, which remains limited in some areas due to inaccessibility (Kalkowska, Franka, et al., 2020). The seventh paper builds on the sixth paper and applies a stochastic model to characterize the risks of potential undetected transmission given the available surveillance evidence (Kalkowska & Thompson, 2020d). In August 2020, the WHO African Region certified its regional elimination of WPVs (World Health Organization, 2020a).

The results of the analysis of confidence about no circulation of WPV1 and WPV3 in Borno and Yobe (Kalkowska & Thompson, 2020d) in the seventh paper, combined with prior publications for other last reservoirs (Kalkowska et al., 2015; Kalkowska et al., 2019; Kalkowska, Duintjer Tebbens, & Thompson, 2018), provided support for the October 2019 certification of the global eradication of indigenous WPV3 (World Health Organization, 2019a). Recognizing that the certification of WPV3 eradication opens up the possibility of globally-coordinated cessation of type 3 OPV (OPV3) use, similar to the global cessation of type 2 OPV (OPV2) use that occurred in 2016, the eighth paper in the special issue explores some options for OPV3 cessation prior to OPV1 cessation (Kalkowska & Thompson, 2020a). The analysis shows that given expected continued transmission of WPV1 through at least 2023 (Kalkowska, Wassilak, et al., 2020), earlier OPV3 cessation reduces the expected number of vaccine-associated paralytic polio cases associated with OPV3, the doses of OPV3 required, and the prospective risks of cVDPV3s (Kalkowska & Thompson, 2020a).

The updated global model results follow global OPV2 cessation, and demonstrate the failure to stop all transmission of type 2 live polioviruses in the 4 years after cessation (Kalkowska, Wassilak, et al., 2020). Prior modeling (based on the 2013 framing (Thompson & Kalkowska, 2020b) of how well things could go with optimal actions and performance) suggested a relatively low probability (i.e., approximately 6% (Duintjer Tebbens et al., 2015)) of failing to stop all transmission of type 2 live polioviruses after OPV2 cessation and

thus needing to restart OPV2 use in national immunization programs. The ninth paper in this special issue updates the risks in the global model to include the unexpected OPV2 use that results in observed incidence of cVDPV2s in 2019 (Macklin et al., 2020) and provides updated estimates of the probability of needing to restart OPV2 use in national immunization programs (Kalkowska, Pallansch, Cochi, et al., 2020). This analysis explored the role of mOPV2 use in outbreak response to stop and prevent cVDPV2s (Kalkowska, Pallansch, Cochi, et al., 2020). Since the amended 2019–2023 Strategic Plan to manage cVDPV2s proposes to use novel OPV2 (nOPV2) strains for outbreak response (World Health Organization Global Polio Eradication Initiative, 2020), the tenth paper reviews the available information about the properties of nOPV2 to bound its likely behavior (Kalkowska, Pallansch, Wilkinson, et al., 2020). The amended GPEI strategy (World Health Organization Global Polio Eradication Initiative, 2020) anticipates that using nOPV2 for outbreak response will stop current and prevent future cVDPV2s. The tenth paper compares the use of nOPV2 to mOPV2 use for outbreak response and demonstrates that even before COVID-19, the probability of outbreak response alone stopping cVDPV2s remains very low (Kalkowska, Pallansch, Wilkinson, et al., 2020). The analysis explores how using nOPV2 may significantly decrease the risks of seeding new cVDPV2 events, but that this may come with the trade-off of less secondary spread (Kalkowska, Pallansch, Wilkinson, et al., 2020).

The final four papers of the special issue include both health and economic estimates. The integrated model relies on the updated estimates of poliovirus vaccine costs and the valuation of the benefits of their use provided in the eleventh paper. The eleventh paper highlights the higher costs of IPV and the challenges that countries face as they select poliovirus vaccines to manage the risks of poliovirus transmission in their populations (Thompson & Kalkowska, 2020a). Building on these results, the twelfth paper explores the global health and economic impacts of prospective immunization policy options for 2019–2029 (Kalkowska & Thompson, 2020b). The thirteenth paper in the special issue explores a hypothesis that OPV use provides non-specific health benefits, and characterizes the health economics of potentially reintroducing OPV into the US to reduce the transmission of COVID-19 (Thompson, Kalkowska, & Badizadegan, 2020). Finally, adopting the same framing as a 2011 paper (Duintjer Tebbens et al., 2011), the last paper in the special issue provides an updated economic analysis of the GPEI (Thompson & Kalkowska, 2020d). The updated health economic analysis of the GPEI (Thompson & Kalkowska, 2020d) shows a substantial decrease in the expected incremental net benefits of the GPEI compared to the 2011 estimates (Duintjer Tebbens et al., 2011).

3. WE ARE WHERE WE ARE...

Eradication represents a major global undertaking that depends on global cooperation and commitment to the goal at multiple levels, from local to global. Time will tell whether another 7 years from now *Risk Analysis* will publish another special issue on polioviruses. Each of the first three special issues implicitly expected a successful polio endgame within a few years of their publication, but we are where we are. The question remains, will the GPEI get on track to eradicate WPV1, successfully stop all OPV use, and end all cases of poliomyelitis?

During 2020, the COVID-19 pandemic substantially changed the dynamics of population mixing and disrupted polio immunization activities. The net impacts of these remain uncertain, and future analyses will need to start with an additional update to account for the 2020 epidemiological experience. Going forward, the GPEI will also likely need to reconsider and update its strategic plan to manage expectations and better forecast resource needs. Integrated modeling offers a tool to support national and global health leaders as they evaluate the increasingly complicated choices in the polio endgame.

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