HHS Public Access

Expected implications of globally-coordinated cessation of serotype 3 oral poliovirus vaccine (OPV) before serotype 1 OPV

Dominika A. Kalkowska[1], **Kimberly M. Thompson**[1,*]

[1.]Kid Risk, Inc., Orlando, FL, USA

Abstract

Globally-coordinated cessation of all three serotypes of oral poliovirus vaccine (OPV) represents a critical part of a successful polio endgame, which the Global Polio Eradication Initiative (GPEI) plans to conduct in phases, with serotype 2 OPV cessation completed in mid-2016. Although in 2016 the GPEI expected to globally-coordinate cessation of the remaining OPV serotypes (1 and 3) by 2021, continuing transmission of serotype 1 wild polioviruses to date makes those plans obsolete. With increasing time since the last reported polio case caused by serotype 3 wild poliovirus (in November 2012) leading to high confidence about its successful global eradication, the Global Commission for the Certification of Poliomyelitis Eradication recently certified its eradication. Questions now arise about the optimal timing of serotype 3 OPV (OPV3) cessation. Using an integrated global model that characterizes the risks, costs, and benefits of global polio policy and risk management options, we explored the implications of different options for coordinated cessation of OPV3 prior to COVID-19. Globally-coordinating cessation of OPV3 as soon as possible offers the opportunity to reduce cases of vaccine associated paralytic polio globally. In addition, earlier cessation of OPV3 should reduce the risks of creating serotype 3 circulating vaccine derived polioviruses after OPV3 cessation, which represents a significant threat to the polio endgame given current GPEI plans to reduce preventive OPV supplemental immunization activities starting in 2019.

Social media summary:

New study explores the option to end the use of serotype 3 oral poliovirus vaccine

Keywords

polio; eradication; dynamic modeling; oral poliovirus vaccine

Introduction

The Global Polio Eradication Initiative (GPEI) began the process of ending all use of oral poliovirus vaccine (OPV) with the globally-coordinated cessation of serotype 2 OPV (OPV2) in late April-early May 2016 (Hampton et al., 2016). The GPEI expected to subsequently coordinate the cessation of both serotypes 1 and 3 OPV (currently used in

*Correspondence to: Kimberly Thompson, Kid Risk, Inc., 7512 Dr. Phillips Blvd. #50-523 Orlando, FL 32819, USA, kimt@kidrisk.org.

bivalent OPV, bOPV), at the same time and shortly after OPV2 cessation (i.e., by 2021) (World Health Organization Global Polio Eradication Initiative, 2015). However, significant delays in stopping the transmission of serotype 1 wild poliovirus (WPV1), which continues to date (World Health Organization, 2020), combined with the absence of reported serotype 3 wild poliovirus cases since late 2012 (World Health Organization, 2013), leads to questions about whether and when to coordinate cessation of serotypes 1 and 3 OPV.

Modeling related to the dynamics of OPV cessation emphasized the importance of maintaining high population immunity with OPV supplementary immunization activities (SIAs) in OPV-using countries prior to homotypic OPV cessation to minimize the risks of circulating vaccine-derived polioviruses (cVDPVs) following cessation (Duintjer Tebbens, Hampton, & Thompson, 2016a, 2016b, 2018; Duintjer Tebbens, Hampton, Wassilak, et al., 2016; Thompson & Duintjer Tebbens, 2014, 2015a). Other modeling performed prior to OPV2 cessation explored different options and timing for stopping OPV for all 3 serotypes assuming maintenance of OPV SIAs prior to cessation, and reported expected reductions of vaccine-associated paralytic polio (VAPP) cases associated with earlier phased cessation of serotype 3 OPV (OPV3) compared to later cessation of bOPV (Thompson & Duintjer Tebbens, 2015b).

The Global Commission for the Certification of Poliomyelitis Eradication (GCC) emphasized in October 2018 (World Health Organization, 2018) that the absence of detection of serotype 3 wild poliovirus (WPV3) cases since late 2012 (World Health Organization, 2013) creates the opportunity to certify the world as free of WPV3, and it initiated the WPV3 certification process. Confidence about the absence about no circulation of WPV3 continues to increase, with now over 7 years since the last reported case in the last reservoirs (Duintjer Tebbens, Kalkowska, & Thompson, 2019) (Kalkowska, Duintjer Tebbens, Pallansch, & Thompson, 2019; Kalkowska & Thompson, 2020). In October 2019, the CC certified the eradication of WPV3 (World Health Organization, 2019), which will likely lead to discussions about the appropriate and optimal timing of cessation of OPV3. Given delays in the OPV production process, forecasting for the specific OPV formulations needed can significantly impact the availability of vaccine (Duintjer Tebbens & Thompson, 2015). Thus, separately phasing the cessation of serotypes 1 and 3 OPV requires sufficient planning since it can lead to logistical challenges for supply chains and health systems. However, cessation of one OPV serotype can free up scarce OPV bulk manufacturing capacity for the production of other serotypes (e.g., serotype 2), although filling and finishing capacity constraints may still pose logistical challenges (UNICEF, 2019). Modeling can support deliberations related to decisions about the optimal timing for OPV3 cessation.

Methods

No prior or post-OPV cessation modeling explored the risks and benefits of phased cessation of OPV3 within the next 10 years (i.e., 2020–2029). This analysis uses a global model that characterizes the dynamics of population immunity for each poliovirus serotype assuming a path consistent with current GPEI plans and budgeting as the reference case (RC2) (Kalkowska, Wassilak, Cochi, Pallansch, & Thompson, 2020), which we recently updated to

account for epidemiological experiences in late 2019 (Kalkowska, Pallansch, et al., 2020). Briefly, the updated global model (Kalkowska, Wassilak, et al., 2020) divides the word into 72 blocks of 10 subpopulations each (approximately 10.7 million people per subpopulation in 2019 (Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat, 2019)) that mix homogenously in space and heterogeneously by age. We characterize the blocks by income level (low-income, LI; lower middle-income, LMI; upper middle-income, UMI; high-income, HI (World Bank, 2019)) and current routine immunization (RI) vaccine use (i.e., OPV+IPV, IPV/OPV, IPV-only (Kalkowska, Wassilak, et al., 2020)) representing some of the global variability in conditions, costs, values, and preferences. The epidemiological, demographic, and transmission assumptions represent conditions existing in the world as of the end of 2019 (i.e., before the COVID-19 pandemic). The results of that model suggest that with the current GPEI strategy, WPV1 transmission will continue in RC2 through 2024, and the need to restart of OPV2 use in RI in many OPV-using countries appears probable (Kalkowska, Pallansch, et al., 2020; Kalkowska, Wassilak, et al., 2020). In addition, the model triggers a restart of homotypic OPV use in RI schedules when the cumulative paralytic case count reaches the threshold of 5,000 global cases following serotype-specific OPV cessation (Kalkowska, Wassilak, et al., 2020; Thompson & Kalkowska, 2019). However, the actual restart occurs with an assumed delay due to vaccine manufacturing and licensing time and national immunization program financing and operational delays post global OPV cessation (Kalkowska, Wassilak, et al., 2020; Thompson & Kalkowska, 2019).

For this analysis, we focus only on serotype 3. We explore the health, risk, and cost implications of globally-coordinated cessation of OPV3 on January 1 or May 1 of 2021 or 2024 distinguishing between serotype 3 cVDPV (cVDPV3) risks only and all post cessation risks (i.e., including immunodeficiency-associated long-term vaccine-derived poliovirus (iVDPV) excreters, containment breaches, etc. (Kalkowska, Wassilak, et al., 2020)). We considered January and May cessation dates to explore the impacts of different times of year relative to seasonality and planned SIAs. We considered 2024 since the GPEI current strategic plan assumes that timing (World Health Organization Global Polio Eradication Initiative, 2019) and 2021 as the earliest possible timing for OPV3 cessation. We include the use of reported acute flaccid paralysis (AFP) cases caused by polio as the trigger for outbreak response and also the possibility of detecting transmission prior to observing a case due to environmental surveillance (ES) and using that signal as the trigger for outbreak response (Kalkowska, Wassilak, et al., 2020). Consistent with the current GPEI strategic plan, both the RC2 of continued use of OPV3 (i.e., the comparator or *status quo*) and the alternative scenarios assume that all countries will continue to use at least one IPV dose in their RI schedules through 2029 (Kalkowska, Wassilak, et al., 2020). We do not increase the number of IPV doses in countries using one dose in 2019 to a minimum of two doses, because of the delays in WPV1 eradication. We also assume that countries with planned SIAs (pSIAs) will perform the number planned for each year, the model replaces bOPV doses used for RC2 with serotype 1 monovalent OPV (mOPV1) in any of the years after globally-coordinated OPV3 cessation. Although the GPEI began procuring and using some mOPV1 in pSIAs as of early 2019 in Pakistan and Afghanistan (World Health Organization and UNICEF, 2018), despite results from modeling that suggest the inadvisability of opening

up any immunity gaps for OPV serotypes still in use in RI and the ineffectiveness of the strategy for increasing population immunity for serotype 1 (Thompson & Duintjer Tebbens, 2017), we conservatively ignore the increases in cVDPV3 risks that the GPEI and countries induce with this strategy as part of the RC2. We emphasize, however, that using mOPV1 for pSIAs instead of bOPV while bOPV remains in use in RI or in other SIAs represents a form of uncoordinated OPV cessation that poses real risks. Table 1 summarizes the assumptions we used for the total doses for each type of vaccine for RI and for pSIAs for RC2 and the alternative scenarios. Consistent with current GPEI plans, we do not include any OPV3 or bOPV intensification activities for any of the alternatives that involve OPV3 cessation. We also do not include consideration of OPV1 cessation before 2024 given the model expectations of continued WPV1 transmission based on our understanding of the current GPEI plans and performance (Kalkowska, Wassilak, et al., 2020).

We consider a time horizon of 2019–2029. We run a single realization of the RC2 and alternative OPV3 cessation timing options considering the cVDPV3 risks only to explore the impacts of the current and expected future serotype 3 population immunity to transmission on cVDPV3 cases after OPV3 cessation. We then run 100 iterations of the RC2 and alternative OPV3 cessation times considering all post cessation risks on the Amazon Cloud. We controlled the iterations to ensure comparability.

Recognizing that our assumption of bOPV use for pSIAs does not appear consistent with some use of mOPV1 in Pakistan and Afghanistan, and we explore an alternative reference case (RC2$_{alt}$) in which we introduce the use of mOPV1 instead of bOPV for two pSIAs per year (in January and March) only in the last remaining block of our model that sustains indigenous WPV1 transmission from 2019 on. We repeat the set of scenarios that include cVDPV3 risks only to investigate the impact of these different amounts of OPV3 going into this block.

Finally, prior modeling recognized a substantial uncertainty about risks of reintroduction from iVDPV excreters (Duintjer Tebbens & Thompson, 2017a). Specifically, considering the lack of evidence of iVDPV reintroduction events following OPV2 cessation to date, the reference case assumes that iVDPV excreters reintroduce stage 10 reverted virus (Kalkowska, Wassilak, et al., 2020). We perform a sensitivity analysis (SA) that reintroduces iVDPV excreted viruses into the population assuming either: (1) a higher reversion stage (i.e., stage 19 instead of stage 10, SA1) or (2) at a random reversion stage (i.e., random stage between 1 and 19 instead of stage 10, SA2) for the alternative scenarios of globally-coordinated cessation of OPV3 on January 1 of 2021. We performed this modeling prior to the COVID-19 pandemic, which disrupted polio immunization activities in many countries in 2020. Consequently, after the impacts of COVID-19 become clear, further analyses will need to explore the timing options for OPV3 cessation in the context of disrupted immunization activities in 2020 (and potentially beyond).

Results

Table 2 shows the results of running the model to explore the impacts of earlier globally-coordinating cessation of OPV3 considering only cVDPV3 risks. As shown in the second

column of Table 2, earlier OPV3 cessation offers the opportunity to reduce cases of VAPP globally. Earlier OPV3 cessation also reduces the expected OPV3 RI and pSIA vaccine needs as shown in the fourth column of Table 2. Earlier cessation of OPV3 should reduce cVDPV3 risks after OPV3 cessation, which represents a threat to the polio endgame given current GPEI plans to reduce OPV pSIAs starting in 2019. However, the results in Table 2 (third and fifth columns) do not show cases of cVDPV3s after OPV3 cessation or any mOPV3 use to respond to outbreaks, so this impact appears small with respect to cVDPV3 events only, as long as the pSIAs continue at the modeled level.

Table 3 shows the percentage of OPV3 restarts triggered (and implemented) during the time horizon, the percentage of iterations with ongoing transmission of OPV3-related viruses at the end of time horizon, as well as the means and ranges of the estimates of cases and the average oSIA doses used from the 100 iterations for the RC2, the alternatives, and the sensitivity analysis. We separately show the results for the varying time period of 5 years after the OPV3 cessation date (top), which differ for the alternatives considered, and for the entire model time horizon (i.e., 2019–2029) (bottom), which effectively includes different numbers of years post-OPV3 cessation since the dates of OPV3 cessation change.

As shown in the second column of Table 3 (bottom), 0–4% of the iterations lead to triggering OPV3 restart, while 0% of the iterations implemented OPV3 restart within the time horizon. Within a five year period after OPV3 cessation, 0% of the iterations triggered or implemented OPV3 restart. The results for the sensitivity analysis scenarios show a substantial increase in OPV restarts if iVDPV introduction risks occur using more transmissible and more neurovirulent viruses than assumed in RC2. Moreover, the third column of Table 3 shows that transmission of OPV3-related viruses continues at the end of time horizon for additional iterations in all scenarios, indicating the possibility of more OPV3 restarts beyond 2029.

Since the model only allows for mOPV3 use for outbreak response SIAs (oSIAs) for 5 years after the OPV3 cessation date, the top part of Table 3 includes only the time during which mOPV3 use can occur for oSIAs. Consequently, the results in the bottom part of Table 3 for the full model time horizon show more IPV use for oSIAs for the scenarios with earlier OPV3 cessation dates, consistent with more time since OPV3 cessation. The fourth column of Table 3 shows that OPV3 cessation leads to lower expected VAPP cases than no cessation (i.e., the RC2), with the cases increasing as the time to the OPV3 cessation date increases. The results for 5 years after OPV3 cessation show increasing risks of cVDPV3 and expected cVDPV3 cases with OPV3 cessation dates in May compared to January (column 5 in the top of Table 3). Comparing the results of the scenarios that include only cVDPV3 risks (Table 2) to those scenarios that consider all post cessation risks (Table 3) shows the possibility of an increased number of cVDPV3 cases and mOPV3 doses used in outbreak response due to the potential reintroductions from iVDPV3 excreters and/or containment failures. The results for the full model time horizon (bottom of Table 3), remain more difficult to interpret due to the complexity of OPV restarts. The results of the sensitivity analysis that introduce iVDPVs as behaving like wild polioviruses (SA1) leads to significantly higher values, while introduction of iVDPVs at random reversion stages leads to mid-range values, which

demonstrates the importance of the uncertainty about the role of iVDPV risks in the polio endgame.

Discussion

The polio endgame continues to pose significant challenges (Kalkowska, Wassilak, et al., 2020), with the eradication of 3 separate pathogens (i.e., 3 serotypes) and cessation of 3 OPVs proving difficult to manage, and uncertainty remaining about whether the 2016 coordinated OPV2 cessation will ultimately succeed or if we will need to restart OPV2 (Thompson & Kalkowska, 2019). A global decision to restart OPV2 could significantly impact the willingness to pursue OPV cessation as a strategy overall or not, and thus, whether to stop other OPV serotypes, including OPV3 (Thompson & Kalkowska, 2019). Given limited and decreasing OPV manufacturing capacity, the need to restart OPV2 would likely significantly impact the availability of other serotypes of OPV, whereas earlier, planned and coordinated cessation of OPV3 could free up some OPV production capacity in the event of needing to produce more OPV2. Cessation of OPV3 will lead to containment requirements for all serotype 3 WPVs and cVDPVs, as previously occurred for all serotype 2 WPVs and cVDPVs (Duintjer Tebbens, Kalkowska, & Thompson, 2018). The containment of another serotype will likely ramp up containment activities, which will likely increase OPV costs, increase pressure on manufacturers to plan to stop all OPV production, and further tighten OPV supply if not managed well.

The logistics of globally-coordinated cessation of OPV3 will also require some activities on the part of health systems. The GPEI estimated that it provided approximately US$ 19.4 million to 67 relatively lower income countries to assist with the tOPV-bOPV switch planning, implementation, monitoring, and validation and tOPV disposal activities for the globally-coordinated cessation of OPV2 (personal communication, Diane Chang Blanc, February 2019). We assume actual total costs could be as much as approximately three times higher considering activities not supported by the GPEI (i.e., costs up to $60 million). In addition, for OPV2 cessation, countries reported removing over 100 million doses of tOPV from their supply chains and destroying these instead of finding opportunities to use them prior to OPV2 cessation. The GPEI also compensated vaccine manufacturers for the destruction of 80 million tOPV doses, although vaccine manufacturers destroyed many more doses that they produced without contracts (i.e., doses that they made in order to enable supporting a potential delay in OPV2 cessation that did not occur). OPV3 cessation will imply similar issues. Ideally, countries could learn lessons from OPV2 cessation and conduct sufficient immunization activities prior to OPV3 cessation to fully utilize the bOPV in their supply chains. In addition, in any countries that experience cVDPV3 outbreaks following OPV3 cessation while bOPV remains in their supply chain, given that these countries will likely also face immunity gaps for serotype 1, these countries should strongly consider the use of any remaining bOPV for outbreak response. Modeling suggested the benefits of using any available tOPV to respond to cVDPV2 outbreaks in the short time period after OPV2 cessation (Duintjer Tebbens, Pallansch, Wassilak, Cochi, & Thompson, 2016), but the GPEI and countries did not exercise this option.

Consistent with our prior analyses of the role of IPV in OPV cessation, IPV use plays little role in OPV3 cessation due to its limited role in preventing the transmission of serotype 3 live polioviruses (LPVs, i.e., WPV, OPV, OPV-related, VDPV, VAPP) in countries that use OPV (Duintjer Tebbens & Thompson, 2017b; Thompson, 2014). The extent to which IPV use reduces cases (and thus masks the ability to detect transmission through AFP surveillance) depends on the IPV-only coverage achieved and the nature and quality of the surveillance system (see further discussion elsewhere (Thompson & Kalkowska, 2020)).

Our results and insights depend on our assumptions about the pSIAs. If the GPEI and countries continue to perform a sufficient number of high-quality SIAs prior to OPV3 cessation, instead of scaling back as we modeled, or if they scale back but then perform OPV3 intensification SIAs to increase population immunity to transmission in the six to twelve months prior to OPV3 cessation, then the results would look different. Our reliance on a model implies all of its associated limitations (Kalkowska, Wassilak, et al., 2020), although our focus on comparisons between alternatives and the RC2 controls across these by using the same assumptions for inputs that do not change across the scenarios. The declaration of transmission of SARS-CoV-2 virus as pandemic and the impacts of COVID-19 already alter national and GPEI polio immunization activities, which future analyses will need to explore. We hope that this analysis provides context for the importance of carefully considering the options in the context of the population immunity to transmission for serotype 3 that exists once the GPEI begins to recover from the COVID-19 disruptions.

This analysis highlights some of the trade-offs associated with earlier global cessation of OPV3, which should support the deliberations by global health policy leaders as they continue to navigate the polio endgame. With the polio endgame extending far beyond expectations and modeling suggesting ongoing WPV1 transmission throughout the model time horizon given the current trajectory (Kalkowska, Wassilak, et al., 2020), the concept of waiting to simultaneously stop OPV3 and OPV1 use comes with the potential risk of never stopping either. At the same time, global health leaders may decide to restart OPV2 in RI in OPV-using countries due to the relatively high probability of needing to do so to stop the current and expected ongoing transmission of OPV2-related viruses (Kalkowska, Pallansch, et al., 2020), which the COVID-19 pandemic will likely further exacerbate. If global health leaders choose to abandon OPV cessation as a global polio endgame strategy, then for those countries that will need to use OPV to maintain sufficient population immunity in the polio endgame, restarting tOPV would offer the most cost-effective long-term polio immunization option.

Acknowledgments

References

Duintjer Tebbens RJ, Hampton LM, & Thompson KM (2016a). Implementation of coordinated global serotype 2 oral poliovirus vaccine cessation: Risks of inadvertent trivalent oral poliovirus vaccine use. BMC Infectious Diseases, 16, 231. [PubMed: 27230071]

Duintjer Tebbens RJ, Hampton LM, & Thompson KM (2016b). Implementation of coordinated global serotype 2 oral poliovirus vaccine cessation: Risks of potential non-synchronous cessation. BMC Infectious Diseases, 16, 237. [PubMed: 27246198]

Duintjer Tebbens RJ, Hampton LM, & Thompson KM (2018). Planning for globally coordinated cessation of bivalent oral poliovirus vaccine: risks of non-synchronous cessation and unauthorized oral poliovirus vaccine use. BMC Infect Dis, 18(1), 165. doi:10.1186/s12879-018-3074-0 [PubMed: 29631539]

Duintjer Tebbens RJ, Hampton LM, Wassilak SGF, Pallansch MA, Cochi SL, & Thompson KM (2016). Maintenance and intensification of bivalent oral poliovirus vaccine use prior to its coordinated global cessation. Journal of Vaccines and Vaccination, 7(5), 340. doi:10.4172/2157-7560.1000340 [PubMed: 28690915]

Duintjer Tebbens RJ, Kalkowska DA, & Thompson KM (2018). Poliovirus containment risks and their management. Future Virology, 13(9), 617–628. doi:10.2217/fvl-2018-0079

Duintjer Tebbens RJ, Kalkowska DA, & Thompson KM (2019). Global certification of wild poliovirus eradication: insights from modelling hard-to-reach subpopulations and confidence about the absence of transmission. BMJ Open, 9(1), e023938. doi:10.1136/bmjopen-2018-023938

Duintjer Tebbens RJ, Pallansch MA, Wassilak SGF, Cochi SL, & Thompson KM (2016). Characterization of outbreak response strategies and potential vaccine stockpile needs for the polio endgame. BMC Infectious Diseases, 16, 137. doi:10.1186/s12879-016-1465-7 [PubMed: 27009272]

Duintjer Tebbens RJ, & Thompson KM (2015). Managing the risk of circulating vaccine-derived poliovirus during the endgame: Oral poliovirus vaccine needs. BMC Infectious Diseases, 15(390), doi:10.1186/s12879-12015-11114-12876.

Duintjer Tebbens RJ, & Thompson KM (2017a). Comprehensive screening for immunodeficiency-associated vaccine-derived poliovirus: an essential OPV cessation risk management strategy. Epidemiology & Infection, 145(2), 217–226. doi:10.1017/S0950268816002302 [PubMed: 27760579]

Duintjer Tebbens RJ, & Thompson KM (2017b). Poliovirus vaccination during the endgame: Insights from integrated modeling. Expert Review of Vaccines, 16(6), 577–586. doi:10.1080/14760584.2017.1322514 [PubMed: 28437234]

Hampton LM, Farrell M, Ramirez-Gonzalez A, Menning L, Shendale S, Lewis I, … Immunization Systems Management Group of the Global Polio Eradication Initiative. (2016). Cessation of trivalent oral poliovirus vaccine and introduction of inactivated poliovirus vaccine - Worldwide, 2016. Morbidity and Mortality Weekly Report, 65(35), 934–938. doi:10.15585/mmwr.mm6535a3 [PubMed: 27606675]

Kalkowska DA, Duintjer Tebbens RJ, Pallansch MA, & Thompson KM (2019). Modeling undetected live poliovirus circulation after apparent interruption of transmission: Pakistan and Afghanistan. Risk Analysis, 39(2), 402–413, on-line October 408, 2018. doi:10.1111/risa.13214 [PubMed: 30296340]

Kalkowska DA, Pallansch MA, Cochi SL, Kovacs SD, Wassilak SGF, & Thompson KM (2020). Updated characterization of post-OPV cessation risks: Lessons from 2019 serotype 2 outbreaks and implications for the probability of OPV restart. Risk Analysis, In Press. doi:10.1111/risa.13555

Kalkowska DA, & Thompson KM (2020). Modeling undetected live poliovirus circulation after apparent interruption of transmission: Borno and Yobe in northeast Nigeria. Risk Analysis, 10.1111/risa.13486. doi:10.1111/risa.13486

Kalkowska DA, Wassilak SGF, Cochi SL, Pallansch MA, & Thompson KM (2020). Global transmission of live polioviruses: Updated integrated dynamic modeling of the polio endgame. Risk Analysis. doi:10.1111/risa.13447

Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat. (2019). World population prospects. The 2019 revision. . Retrieved from https:// population.un.org/wpp/

Thompson KM (2014). Polio endgame management: Focusing on performance with or without inactivated poliovirus vaccine. The Lancet, 384(9953), 1480–1482.

Thompson KM, & Duintjer Tebbens RJ (2014). Modeling the dynamics of oral poliovirus vaccine cessation. Journal of Infectious Diseases, 210(Suppl 1), S475–S484.

Thompson KM, & Duintjer Tebbens RJ (2015a). The differential impact of oral poliovirus vaccine formulation choices on serotype-specific population immunity to poliovirus transmission. BMC Infectious Diseases, 15(376), doi:10.1186/s12879-12015-11116-12874.

Thompson KM, & Duintjer Tebbens RJ (2015b). Health and economic consequences of different options for timing the coordinated global cessation of the three oral poliovirus vaccine serotypes. BMC Infectious Diseases, 15(374), doi:10.1186/s12879-12015-11113-12877.

Thompson KM, & Duintjer Tebbens RJ (2017). Lessons from the polio endgame: Overcoming the failure to vaccinate and the role of subpopulations in maintaining transmission. Journal of Infectious Diseases, 216(Suppl 1), S176–S182.

Thompson KM, & Kalkowska DA (2019). Logistical challenges and assumptions for modeling the failure of global cessation of oral poliovirus vaccine (OPV). Expert Review of Vaccines, 18(7), 725–736. doi:10.1080/14760584.2019.1635463 [PubMed: 31248293]

Thompson KM, & Kalkowska DA (2020). Review of poliovirus modeling performed from 2000–2019 to support global polio eradication. Expert Rev Vaccines, In Press. doi:10.1080/14760584.2020.1791093

UNICEF. (2019). Market Update: Oral Polio Vaccines UNICEF Vaccine Industry Consultation 19 September 2019. Retrieved from https://www.unicef.org/supply/media/3296/file/VIC-2019-Session-13-Presentation-2-OPV-update.pdf

World Bank. (2019). World Bank list of economies (June 2019). Retrieved from http:// databank.worldbank.org/data/download/site-content/CLASS.xls

World Health Organization. (2013). A year without type 3: Could type 1 be the only wild polio serotype left in the world? Available at: http://www.polioeradication.org/Mediaroom/Newsstories/ Newsstories2013/tabid/488/iid/336/Default.aspx#sthash.KwtoN8XJ.dpuf. Accessed 26 June 2014.

World Health Organization. (2018). Statement following the 18th meeting of the Global Commission for the Certification of Poliomyelitis Eradication, 29–30 October 2018, Amman, Jordan. Retrieved from http://polioeradication.org/wp-content/uploads/2016/07/GCC-report-29-31-Oct-20181031.pdf

World Health Organization. (2019). Two out of three wild poliovirus strains eradicated. Retrieved from https://www.who.int/news-room/feature-stories/detail/two-out-of-three-wild-poliovirus-strains-eradicated

World Health Organization. (2020). Polio this week as of 19 February 2020. Retrieved from http:// polioeradication.org/polio-today/polio-now/this-week/

World Health Organization and UNICEF. (2018). 17th WHO/UNICEF Consultation with OPV/IPV Manufacturers and National Authorities for Containment of Polio Vaccine Producing Countries. Retrieved from http://polioeradication.org/wp-content/uploads/ 2018/11/2018_WHO_UNICEF_Consultation_Mtg_Report_FINAL.pdf

World Health Organization Global Polio Eradication Initiative. (2015). Polio eradication & endgame: Midterm review July 2015. Geneva; 2015. Report No: WHO/POLIO/15.04. Retrieved from http:// polioeradication.org/wp-content/uploads/2016/07/GPEI-MTR_July2015.pdf

World Health Organization Global Polio Eradication Initiative. (2019). Polio eradication and endgame strategic plan (2019–2023). Geneva; 2019. Report No: WHO/POLIO/19.04. Retrieved from http:// polioeradication.org/wp-content/uploads/2019/05/polio-endgame-strategy-2019-2023.pdf

Table 1:

Vaccine doses (millions) for routine immunization (RI) and planned supplemental immunization activities (pSIAs) for countries that use OPV for the Reference Case (RC2) and alternative scenarios by vaccine type

Scenario	RI doses [millions]			pSIA doses [millions]	
	bOPV	mOPV1	IPV	bOPV	mOPV1
RC2 (comparator of continued bOPV use through 2029)	3,497	0	1,555	5,476	0
OPV3 stop January 2021	633	2,864	1,555	1,008	4,467
OPV3 stop May 2021	739	2,758	1,555	1,585	3,890
OPV3 stop January 2024	1,584	1,912	1,555	2,628	2,848
OPV3 stop May 2024	1,690	1,807	1,555	3,054	2,422
RC2alt (comparator of continued bOPV use through 2029) [*]	3,497	0	1,555	5,461	15
OPV3 stop January 2021	633	2,864	1,555	1,006	4,469
OPV3 stop May 2021	739	2,758	1,555	1,582	3,893
OPV3 stop January 2024	1,584	1,912	1,555	2,621	2,854
OPV3 stop May 2024	1,690	1,807	1,555	3,046	2,429

Notes:

[*]
RC2alt assumes the use of mOPV1 instead of bOPV for two pSIAs per year (in January and March) from 2019 on in the last remaining block of our model that sustains indigenous WPV1 transmission (representing conditions like those in WPV1 reservoir areas of Pakistan and Afghanistan)

Abbreviations: bOPV, bivalent oral poliovirus vaccine (containing serotypes 1 and 3); IPV, inactivated poliovirus vaccine; mOPV1, serotype 1 monovalent oral poliovirus vaccine; OPV, oral poliovirus vaccine; RC2, reference case; RI, routine immunization; SIAs, supplemental immunization activities

Table 2:

Results of simulations that globally-coordinate OPV3 cessation on different dates, with response to positive ES samples starting from 6 months post-OPV3 cessation, considering cVDPV3 risks only, and compared to reference case (RC2) and alternative reference case (RC2$_{alt}$).

Scenario	Estimated serotype 3 VAPP cases	cVDPV3 cases	OPV3 doses not required [millions]	mOPV3 doses used for outbreak response [millions]
RC2 (comparator of continued bOPV use through 2029)	586	0	0	0
OPV3 stop January 2021	107	0	7,331	0
OPV3 stop May 2021	132	0	6,648	0
OPV3 stop January 2024	268	0	4,760	0
OPV3 stop May 2024	293	0	4,229	0
RC2$_{alt}$ (comparator of continued bOPV/mOPV1 use through 2029) *	586	0	0	0
OPV3 stop January 2021	107	0	7,318	0
OPV3 stop May 2021	132	0	6,636	0
OPV3 stop January 2024	268	0	4,751	0
OPV3 stop May 2024	293	0	4,221	0

Notes:

*
RC2$_{alt}$ assumes the use of mOPV1 instead of bOPV for two pSIAs per year (in January and March) from 2019 on in the last remaining block of our model that sustains indigenous WPV1 transmission (representing conditions like those in WPV1 reservoir areas of Pakistan and Afghanistan)

Abbreviations: cVDPV3, serotype 3 circulating vaccine-derived poliovirus; mOPV3, serotype 3 monovalent oral poliovirus vaccine; OPV, oral poliovirus vaccine; OPV3, serotype 3 oral poliovirus vaccine; VAPP, vaccine-associated paralytic polio; VDPV, vaccine-derived poliovirus; WPV, wild poliovirus

Table 3:

Estimated probabilities of restart of OPV for serotype 3, cases and average vaccine doses used (millions) in outbreak response SIAs (oSIAs) from 100 iterations considering all post-cessation risks for globally-coordinated OPV3 cessation on different dates, with response to positive ES samples starting from 6 months post-OPV3 cessation, and compared to the reference case (RC2) for the full time horizon (top) and for a period of 5 years post the coordinated OPV3 cessation date (bottom).

Scenario	OPV3 restarts triggered during time horizon (implemented) [%]	Ongoing transmission of OPV3-related viruses at the end of time horizon [%]	Estimated serotype 3 VAPP cases (range)	Estimated cVDPV3 cases (range)	Average mOPV3 doses for oSIAs [millions]	Average OPV3 doses not required [millions]	Average IPV doses for oSIAs [millions]
RC2 (comparator of continued bOPV use through 2029)	0 (0)	100	589 (571–597)	0	0	0	0
5-year period post OPV3 cessation date shown in the scenario							
OPV3 stop January 2021	0 (0)	7	0 (0–3)	17 (0–1,266)	1.3	4,144	0
OPV3 stop January 2021 SA1 *	4 (0)	81	8 (1–18)	1,856 (70–10,700)	148.0	3,997	0
OPV3 stop January 2021 SA2 *	4 (0)	26	1 (0–9)	488 (0–6,450)	22.1	4,123	0
OPV3 stop May 2021	0 (0)	9	1 (1–5)	54 (0–2,098)	2.1	3,997	0
OPV3 stop January 2024	0 (0)	5	0 (0–2)	11 (0–601)	1.1	3,958	0
OPV3 stop May 2024	0 (0)	9	1 (1–3)	50 (0–1,875)	1.4	3,968	0
Full time horizon [2019–2029]							
OPV3 stop January 2021	3 (0)	7	106 (106–110)	1,083 (0–50,889)	1.3	7,330	13.9
OPV3 stop January 2021 SA1 *	62 (4)	81	120 (107–325)	12,533 (73–67,125)	175.0	7,130	130.1
OPV3 stop January 2021 SA2 *	16 (4)	26	113 (106–270)	3,738 (0–51,419)	53.7	7,252	0.6
OPV3 stop May 2021	4 (0)	9	132 (131–137)	642 (0–20,6791)	2.1	6,646	13.7
OPV3 stop January 2024	0 (0)	5	268 (267–269)	59 (0–3,375)	1.1	4,759	0.9
OPV3 stop May 2024	0 (0)	9	293 (292–295)	106 (0–4,374)	1.4	4,227	1.2

Notes:

*
SA(1,2) indicates sensitivity analyses results that assume iVDPV excreters reintroduce (1) fully-reverted VDPV viruses (stage 19) or (2) random reversion stage VDPV viruses (stage 1 to 19) for comparison to the row above

Abbreviations: cVDPV3, serotype 3 circulating vaccine-derived poliovirus; mOPV3, serotype 3 monovalent oral poliovirus vaccine; OPV, oral poliovirus vaccine; OPV3, serotype 3 oral poliovirus vaccine; SA, sensitivity analysis; VAPP, vaccine-associated paralytic polio; VDPV, vaccine-derived poliovirus; WPV, wild poliovirus