The role of risk analysis in polio eradication: modeling possibilities, probabilities and outcomes to inform choices


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Thinking big
Can we imagine a world with no new cases of any vaccine-preventable diseases? What would it take for such an exciting possibility to become a reality? In 1988, the World Health Assembly took a step in that direction following the successful eradication of smallpox when it committed to the ambitious goal of eradicating poliomyelitis by ending the transmission of wild polioviruses (WPVs) and set a target for the year 2000 [1]. Remarkably, the world succeeded in eradicating type 2 WPVs [2] and the annual burden of all paralytic polio cases dropped by approximately 99% between 1988 and 2000, which yielded significant health and economic benefits [3]. This progress occurred despite the reality that some countries did not begin active surveillance for paralytic cases and aggressive vaccination until shortly before the year 2000, and some regionally coordinated vaccination efforts only began after the year 2000 [4]. Now, 12 years after the initial target, unfortunately we still face challenges with respect to eradicating WPV types 1 and 3, and planning for the final stages (or ‘end game’) reveals previously un(appre)ciated complex and dynamic risks, and difficult choices [5,6]. For example, although the Global Polio Eradication Initiative (GPEI) continues to use the live-attenuated oral poliovirus vaccine (OPV) as its primary tool for eradication, its use leads to cases of vaccine-associated paralytic polio (VAPP) and potential outbreaks from circulating vaccine-derived polioviruses (cVDPVs) [7,8]. Consequently, the World Health Assembly formally recognized in 2008 that obtaining the goal of eradicating all cases of poliomyelitis depends on eradication of WPVs and cessation of OPV [9].

Investment
Eradication represents an ambitious goal and, like all major projects, its achievement depends on successfully managing risks in the context of a variable, uncertain and dynamic complex system [10,11]. Unlike most major projects, however, financing for the GPEI to date has occurred using a pay-as-you-go approach, such that activities occur using donated funds in hand, thus making financial risks one of the most significant ongoing threats to polio eradication specifically [11–13], and disease control and eradication efforts more broadly [14]. In today’s highly connected world, eradicating a vaccine-preventable disease requires immunizing enough people in every area to build up immunity in that population to high enough levels that transmission dies out locally and widespread circulation cannot (re)start following importation. Since countries achieve ‘high enough’ population immunity levels to eliminate indigenous transmission at different times, eradication requires those countries that succeed to continue to maintain high levels of population immunity until all countries contemporaneously eliminate circulating infections [1,11]. Not surprisingly, maintaining very high

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levels of vaccination coverage globally comes at a significant cost, but completion of polio eradication continues to represent a better humanitarian and financial option than switching to control (i.e., stopping short of eradication and allowing WPV types 1 and 3 to continue to circulate) [13].

**Modeling**

Given the complexity that exists and the reality of limited resources, modeling polio risks and management options can provide useful information for national, regional and global policy decisions. Overall, modeling risks can improve both communication and management, and risk analysts can play a key role in supporting policy decisions by providing structure that promotes shared understanding of key issues and uncertainties [15,16]. The effectiveness of risk analysis efforts depends heavily on the extent to which the analyses explicitly recognize important sources of variability (i.e., real differences that exist, for example between countries or income groups) and uncertainty (i.e., knowledge gaps due to imperfect evidence and the need for forecasting) [15], and deal with time [11]. For example, quantitative modeling of outbreaks demonstrated the importance of responding very quickly to paralytic polio cases in previously polio-free countries [17], which led the GPEI to invest in research and identify opportunities to speed up its detection and confirmation of cases and its response to outbreaks. In addition, modeling the risks, costs and benefits of various posteradication vaccination options demonstrated the importance of stopping the use of OPV after WPV eradication, and the need for innovations to make the inactivated poliovirus vaccine (IPV) a less expensive option for any countries wishing to continue polio vaccination after OPV cessation [6].

**Complex choices**

Currently, national and global health leaders face several critical issues as they manage polio risks to achieve eradication and transition to a polio-free world. Countries must determine their best strategies for achieving or maintaining high levels of vaccine coverage with OPV and/or IPV. OPV represents a relatively low-cost and easier to administer option that infects the vaccine recipient with an attenuated virus that can spread to others and produce direct secondary protection. However, as countries reach very high levels of OPV coverage and eliminate circulation of WPVs, they reach the point at which they begin to observe more cases of paralytic polio from oral poliovirus vaccine … than occur due to WPVs.

The continued use of the current formulation of trivalent OPV (tOPV) implies ongoing introduction of live type 2 polioviruses, and this leads to risks associated with cVDPVs. Prior work demonstrated the higher expected costs and/or cases associated with continued use of OPV following WPV eradication compared to OPV cessation [6], and this insight applies by extension to each serotype of OPV. However, OPV cessation requires coordinated efforts (e.g., containment, development of an appropriate vaccine stockpile and preparedness for emergency outbreak response) [20]. Although the option of switching from tOPV to IPV continues to remain available, the option of switching from tOPV to bivalent OPV types 1 and 3 (bOPV) only recently became a potential reality with the licensure of bOPV products. Thus, globally, we currently face a difficult choice about whether to continue to pursue the eradication of WPV types 1 and 3 using tOPV or to switch to bOPV and/or IPV. Switching to bOPV (i.e., cessation of OPV type 2 or OPV2) to manage cVDPV type 2 risks and improve overall type 1 and type 3 take rates (by eliminating competition from type 2) would require coordination and preparation of containment and outbreak response efforts similar to those anticipated for tOPV cessation [20]. In addition, several ongoing research efforts seek to identify opportunities to significantly reduce the costs of IPV, but large uncertainties currently exist about their potential and actual costs, effects, availability for large-scale use and anticipated coverage, which makes these options difficult to characterize and evaluate. A low-cost and easy-to-administer IPV option could dramatically change the relative desirability of IPV for managing posteradication risks, and possibly for achieving eradication as well, particularly for relatively low-income countries. Modeling the risks and options may play an important role in characterizing the expected costs and benefits of the various current global policy alternatives, but more importantly, it may also help manage expectations and motivate research and other efforts to improve the set of options available.

**Doing more**

Although modeling risks provides real value by answering specific questions, models often provide their greatest value by engaging stakeholders in a process that leads to understanding,
shared insights, asking the ‘right’ questions, and opportunities to avoid and minimize potential crises [16]. As the global population grows and we increasingly recognize the costs of disease and benefits of prevention, models will play an essential role by helping policy makers see and value the cases that do not occur as a result of vaccination. The lessons we learn from modeling polio risks may lead to better management of other vaccine-preventable diseases, and ultimately may help us ask better questions. While some people may question whether investments in vaccines represent a good use of resources, perhaps we should also ask: what are the risks of failing to invest sufficient resources? Is it time to do more?

Financial & competing interests disclosure
The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

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