Vaccine xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Modeling the costs and benefits of temporary recommendations for poliovirus exporting countries to vaccinate international travelers

Radboud J. Duintjer Tebbens *, Kimberly M. Thompson

Kid Risk, Inc., Orlando, FL, USA

ARTICLE INFO

Article history:
Received 22 April 2017
Received in revised form 31 May 2017
Accepted 31 May 2017
Available online xxxx

Keywords:
Traveler vaccination
Health economics
Polio eradication
Outbreaks
International Health Regulations

ABSTRACT

Recognizing that infectious agents readily cross international borders, the International Health Regulations Emergency Committee issues Temporary Recommendations (TRs) that include vaccination of travelers from countries affected by public health emergencies, including serotype 1 wild polioviruses (WPV1s). This analysis estimates the costs and benefits of TRs implemented by countries with reported WPV1 during 2014–2016 while accounting for numerous uncertainties. We estimate the TR costs based on programmatic data and prior economic analyses and TR benefits by simulating potential WPV1 outbreaks in the absence of the TRs using the rate and extent of WPV1 importation outbreaks per reported WPV1 case during 2004–2013 and the number of reported WPV1 cases that occurred in countries with active TRs. The benefits of TRs outweigh the costs in 77% of model iterations, resulting in expected incremental net economic benefits of $210 million. Inclusion of indirect costs increases the costs by 13%, the expected savings from prevented outbreaks by 4%, and the expected incremental net benefits by 3%. Despite the considerable costs of implementing TRs, this study provides health and economic justification for these investments in the context of managing a disease in advanced stages of its global eradication.

1. Introduction

Recognizing that infectious agents readily cross international borders, the World Health Organization (WHO) International Health Regulations Emergency Committee (IHREC) issues Temporary Recommendations (TRs), which include requirements to vaccinate travelers from countries affected by public health emergencies. Between May 2014 and the end of 2016, the IHREC for polio issued TRs to five countries experiencing WPV1 transmission (i.e., Afghanistan, Cameroon, Equatorial Guinea, Pakistan, and the Syrian Arab Republic) [1,2]. Of these, only Pakistan, Afghanistan, and Cameroon provided evidence to the WHO of substantive implementation of the TRs, with Pakistan demonstrating the most extensive efforts. To date, no known new WPV1 outbreaks occurred as a result of WPV1 exportations from these countries, although cross-border transmission between Pakistan and Afghanistan continued to occur on a background of ongoing indigenous WPV1 transmission in both countries. In contrast, outbreaks associated with WPV1 importations regularly occurred in previously polio-free countries in the 10-year period preceding the first polio TRs [3]. This could reflect the reduced overall incidence of WPV1 (possibly in part motivated by the TRs), improvement by polio-free countries to manage their population immunity to serotype 1 poliovirus transmission, and/or effectiveness of the TRs in reducing WPV1 exportation risks. The TRs may reduce WPV1 exportations by immunizing previously unvaccinated travelers or boosting the immunity of travelers with waned immunity, both of which reduce the probability and duration of any WPV1 infections they may acquire before traveling to another country [4].

Few studies estimate the costs and benefits of traveler recommendations for infectious diseases [5,6], and no prior published studies explore the economics of TRs for polio, although some assessed the risk of international poliovirus spread [7,8]. The WHO compiled unpublished data that estimated TR vaccination costs of approximately $1.5 million per year including vaccine and personnel costs at points of entry (POEs), but only vaccine

Abbreviations: cMYP, comprehensive multi-year plan; cVDPV(2), circulating vaccine-derived poliovirus (of serotype 2); HF, health facility; IHREC, International Health Regulations Emergency Committee; INB, incremental net benefit; IPV, inactivated poliovirus vaccine; POE, point of entry; OPV, oral poliovirus vaccine; oSIA, outbreak response supplemental immunization activity; pSIA, planned preventive supplemental immunization activity; TR, temporary recommendations; WHO, World Health Organization; WPV1, serotype 1 wild poliovirus; $, year 2015 United States dollars.

* Corresponding author at: Kid Risk, Inc., 10524 Moss Park Rd., Ste. 204-364, Orlando, FL 32832, USA.

E-mail address: rdt@kidrisk.org (R.J. Duintjer Tebbens).

http://dx.doi.org/10.1016/j.vaccine.2017.05.090
0264-410X/

costs for traveler vaccinations administered at health facilities (HFs). WHO data further suggest costs to respond to outbreaks in previously polio-free countries of $850 million during 2003–2009 [8] and $1.15 billion during 2003–2014 [9]. Recognizing that countries need to budget for the costs of implementing TRs, but not for the unobservable benefits of prevented outbreaks and cases, questions remain about how the costs of the TRs compare to their health and economic benefits. This analysis used a decision analytic model to estimate the economic trade-offs associated with implementation of the recent polio TRs.

2. Methods

We focus on the costs and benefits of the TRs during the 3 years 2014–2016 because the IHREC for polio issued the first TRs for polio in May 2014. We consider the possibility of prevented outbreaks (defined as one or more reported polio cases linked to a WPV1 importation into a previously polio-free country and excluding circulating vaccine-derived poliovirus (cVDPV) outbreaks) for up to 10 years (i.e., through the end of 2023) and the expected lifetime societal benefits of prevented polio cases. We report all monetary outcomes in year 2015 US dollars ($) and discount using a rate of 3% [10] from the perspective of a decision maker in 2014. We include all costs regardless of who pays for them (e.g., country, Global Polio Eradication Initiative).

Fig. 1 shows a causal loop diagram of the main components that dynamically interact in the context of TRs (see the Appendix A for a decision tree representation). Fig. 1a shows the fundamental feedback loop that represents the propagation of outbreaks: more new outbreaks lead to more polio cases, which lead to a higher rate of exportation events, which lead to more new outbreaks. Issuing TRs decreases the rate of WPV1 exportation events, which will effectively dampen (i.e., slow down) the outbreak propagation feedback loop. Fig. 1b explicitly characterizes the realization of new outbreaks as random events (depicted using an oval). Each realization implies different numbers of polio cases and outbreak response supplemental immunization activities (oSIAs), which lead to different outbreak costs. Issuing TRs carries costs for each country that needs to implement the TRs, and thus Fig. 1c shows that the occurrence of outbreaks increases the TR costs. Finally, Fig. 1d shows the full diagram with both the costs in the presence of the TRs and the counterfactual outbreak costs in their absence. The difference between these costs represents the incremental net benefits (INBs) of the TRs.

We dynamically and probabilistically account for the relationships depicted in Fig. 1. The model focuses on the effect of TRs on new WPV1 outbreaks in previously WPV1-free countries. Given that no known new WPV1 outbreaks in polio-free countries occurred during 2014–2016 from any of the countries that implemented TRs, the dynamic outbreak propagation model focuses on simulating the occurrence of potential hypothetical outbreaks in the absence of these TRs for the counterfactual scenario. We base these simulations on the average historical rate of 1 WPV1 importation outbreak to polio-free countries per 140 reported WPV1 polio cases during 2004–2013 (i.e., the 10-year time period before the beginning of polio-related TRs) (see Appendix A) [3,11–15].

We assume that the number of WPV1 importation outbreaks in any given month follows a Poisson distribution with a rate equal to the number of reported WPV1 cases in countries that implemented TRs (Fig. 2), multiplied by the average rate of WPV1 importation outbreaks per reported WPV1 case (i.e., 1/140). For every outbreak that occurs, we randomly select an outbreak realization from the 58 outbreaks that occurred during 2004–2013 (see Appendix A). Each outbreak implies a number of oSIA doses used to respond to the outbreak, from which we estimate the vaccination costs of the outbreak, and a list of monthly cases, which we combine with some delay (best estimate 6 months) to characterize the monthly incidence of WPV1 cases that contribute to the probability of generating new outbreaks in future months. We continue until no future cases remain or until reaching the end of the time horizon (i.e., end of 2023), whichever comes first.

Table 1 lists all model inputs and sources, including broad uncertainty bounds for most of the inputs. For each outbreak, we compute the expected direct costs from the number of oSIA doses and the direct treatment costs associated with polio cases using unit costs inputs from prior work [16–18]. We estimate the TR cost from estimates about the number of travel vaccinations provided to the WHO by countries subject to the TRs, complemented with publicly available national unit costs estimates and estimates from prior publications [16–18]. We also compute the indirect lifetime costs of lost productivity for each polio case using existing methods that multiply the average number of disability-adjusted life-years per polio case with the income level-specific average annual per-capita gross national income (GNI) [16,19]. To value the indirect (opportunity) costs of lost productivity associated with time to receive vaccination, we make assumptions about the amount of time spent by travelers to receive vaccine and prorate this time cost by the country-specific GNI [20]. In the absence of detail about the age or employment of travelers, we effectively average over all incomes in the country. Finally, to compute the INBs, we subtract the TR costs from the savings associated with prevented outbreaks.

We performed 1000 stochastic iterations of the model with a monthly time step for the outbreak simulation. Each iteration involves both random realizations from all uncertain model inputs and random realizations of outbreaks, which depend on the realized outbreak rate per reported WPV1 case and the delay between exportations and onset of paralysis of the first case.

3. Results

With all model inputs at their best estimates (Table 1), the direct costs of implementing the TRs equal almost $24 million, with 87% of these coming from Pakistan (see Appendix A). The indirect costs remain relatively minor at $2.4 million, or 9% of the total direct and indirect costs. These percentages remain similar when fully accounting for model input uncertainty. Fig. 3 shows the distribution of direct outbreak-related costs, which reflect uncertainty in model inputs as well as random variability related to outbreak realizations. If outbreaks directly triggered by the cases in Fig. 2 by chance remain small, as most outbreaks during 2004–2013 (see Appendix A), then with high probability they also end quickly without triggering further outbreaks. However, some WPV1 important outbreaks that occurred during 2004–2013 behaved either explosively or continued for many years, both of which lead to large numbers of WPV1 cases likely to trigger further outbreaks (i.e., they exhibit the outbreak propagation feedback behavior explained in Fig. 1). Of the 1000 model iterations, 75 (7.5%) resulted in no new outbreaks at all, 437 (44%) resulted in 1–4 outbreaks, and 137 (14%) resulted in more than 10 outbreaks. The simulation suggested a very long tail, with a 95th percentile of 18 outbreaks and a maximum of 69 outbreaks through 2023. Outbreaks continued until the end of 2023 in 41 model iterations (4.1%). Fig. 3 shows a very long tail in direct outbreak costs, with a 95th percentile of $960 million and a maximum of $4.5 billion. The largest number of simulated outbreak cases equaled almost 6000.

Table 2 summarizes the expected costs of implementing the TRs during 2014–2016, the expected savings associated with outbreaks prevented, and the expected INBs of the TRs based on all 1000

Please cite this article in press as: Duintjer Tebbens RJ, Thompson KM. Modeling the costs and benefits of temporary recommendations for poliovirus exporting countries to vaccinate international travelers. Vaccine (2017), http://dx.doi.org/10.1016/j.vaccine.2017.05.090