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Original Article

Policy Decision Options During the First 5 Years Following Certification of Polio Eradication

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Abstract and Introduction

Abstract

Policy makers face a number of difficult choices as they develop policies to ensure maintenance of a polio-free world following global eradication and certification. These policy decisions include choices about immunization, outbreak response (including whether to create a vaccine stockpile), surveillance, containment, management of chronic excretors, and investment in future research. This paper focuses on identifying the categories of decisions and characterizing the actual factors that country-level policy makers must weigh to manage polio risks during the first 5 years after certification. Building on a comprehensive literature review, we report the results of the first qualitative analysis to: (1) systematically characterize each type of decision and the relevant options during the first 5 years after certification, (2) clearly identify critical factors that influence the choices, and (3) specifically demonstrate the interdependence among the decisions to produce a reduced set of decision options. This paper explicitly focuses on the different perspectives of developed and developing countries in characterizing the options. While the management of polio risk in the postcertification period presents important challenges, this comprehensive approach helps simplify the process by focusing on critical decisions.

Introduction

Successful polio eradication efforts continue to move the world closer to eradication and certification as free of wild poliovirus. Global certification will occur once all 6 World Health Organization (WHO) regions report finding no wild poliovirus under high-quality surveillance for at least 3 years and the Global Certification Commission becomes satisfied that sufficient laboratory containment exists,[1,2] a milestone already achieved by 3 regions. The achievement of polio eradication and certification will soon lead policy makers to face difficult choices to ensure maintenance of a polio-free world. These choices primarily include policies related to: routine and supplemental immunization, outbreak response (including whether to create a stockpile), surveillance, and containment of wild and vaccine-derived polioviruses (VDPVs). The combination of discrete policy choices forms an overall strategy, with the best strategy from the policy maker's perspective striking an optimal balance among the risks, costs, and benefits. In the context of global discussions of postcertification risk management strategies, few efforts to date have comprehensively described the complexity of choices and placed them within the context of developing and evaluating an overall national strategy. This paper builds on prior work to help fill this void.

Recent discussions predominantly focused on stopping immunization as the ultimate goal of the eradication initiative and on characterizing related issues. In March 1998, a WHO meeting on the scientific basis for stopping polio immunizations identified 4 strategies for stopping immunization that depended on the then unanswered question of whether VDPVs could persist in populations.[3,4] If VDPVs could persist, the preferred options would be to replace the current trivalent oral polio vaccine (tOPV) for a transition period or replace the tOPV indefinitely with either the enhanced inactivated polio vaccine (eIPV) or a new vaccine. If VDPVs could not persist, the preferred option involved a coordinated cessation of tOPV use, possibly including sequential removal of eradicated strains from tOPV (ie, using bivalent OPV [bOPV] or monovalent OPV [mOPV]).

Following clear evidence of the persistence of VDPVs and associated outbreaks,[5] Wood and colleagues[6] concluded that "discontinuation of OPV in a synchronized way remains the most plausible" option. Subsequent publications presented similar vaccination options[7-13] and discussed whether and how immunization should be stopped,[14-16] with one study emphasizing the differences in decisions between developed and industrialized countries.[15] Another study summarized available data addressing the option of using monovalent vaccines as part of the immunization policy,[17] and a recent report noted the interdependence of countries' decisions.[18]

In spite of clear recognition of the need for surveillance strategies, stockpiles, and contingency plans to respond to potential outbreaks in the postcertification era,[3,4,9,10,13,19,20] few articles have elaborated on these issues and related decision options.[10,21] Fine and colleagues[10] estimated the impact in the posteradication era of an outbreak in a population assuming various immunization and surveillance conditions

that might result from the implementation of different policies. From their analysis of the implications of delays in outbreak response, they recommended: (a) maintaining active surveillance for at least 5 years after ceasing all polio vaccination, (b) minimizing delays in diagnosis and confirmation of an outbreak, (c) restricting poliovirus work to a few high-level containment laboratories, (d) maintaining OPV manufacturing capacity, and (e) establishing a stockpile and a response protocol for outbreaks. Recently, Sangrujee and colleagues[21] estimated the potential immunization policy costs for continuing tOPV, switching to eIPV, and stopping immunizations, and developed general cost estimates for global programmatic activities such as maintaining stockpile, laboratory network, and surveillance capabilities. Finally, Fine[22] suggested the need to refine the scenarios presented by Wood and colleagues,[6] recognizing that probably the most important choice facing policy makers remains which vaccine to use, if any.

While these papers represent important progress in informing decision makers, considerable work remains. The decision makers at the 1988 World Health Assembly (WHA) resolved to eradicate polio,[23] and this paper anticipates that the success of the eradication initiative will lead a future WHA to discuss and determine global polio policies to implement after global certification. Clearly, the current (precertification) time period represents a critical time for research efforts focusing on scientific uncertainties, economics, and logistics to provide sufficient information to decision makers about the implications of policy challenges after certification.

This paper describes the policy options during the first 5 years after certification from the perspective of the decision maker for an individual country. We focus on the first 5 years after certification because it represents a critical time period for decisions about continuing OPV use. During this time, we expect both the highest population immunity and the greatest risk of VDPVs. We characterize the currently debated policy options and discuss how various factors (eg, cost, risks, risk perception, neighboring countries' policies) influence policy decisions. Through qualitative analysis and with the objective of providing focus and context to the debate, we narrow the list of potential policy options to those most likely for decision makers of either developed or developing countries. Section 2 describes the methodology used, while section 3 describes each category of decisions and the current country-level options that exist within that category. Section 4 discusses several factors likely to influence policy makers as they evaluate the options and presents our expectations about the reduced set of options available to decision makers in developed and developing countries. Section 5 discusses critical issues (eg, time); and sections 6 and 7 present the conclusions and references, respectively.

Methods

We conducted a thorough review of the literature on policy options following certification of polio eradication. A PubMed search of relevant keywords (ie, polio post certification, polio post eradication, polio post-eradication, polio policy, polio certification strategy and strategies, polio eradication strategy and strategies, and polio endgame) identified 304 unique articles. Review of the titles and available abstracts led to selection of 21 articles for complete review, from which we identified 19 articles or letters that discuss postcertification decision options. We also reviewed unpublished reports and operational guidelines provided by the WHO and the Centers for Disease Control and Prevention (CDC).

Based on our synthesis of the existing literature, we identified categories of current and future policies after certification. We listed all possible decision options within those categories from the perspective of a country-level policy maker and developed decision trees to characterize the set of options for each category. From these options, we eliminated any that appeared economically and technically impractical within the time period starting from the point of certification and ending 5 years after certification (ie, those for which financing would not likely exist and/or technical, regulatory, or other barriers suggested implausibility in the short-term). We also informally queried experts on several of the issues for more information and to ensure that we included relevant unpublished reports. We particularly benefited from helpful discussions with a number of experts involved with the Polio Eradication Initiative (PEI) at the WHO and the CDC. We further identified a number of critical factors that may influence a policy maker's choices. Finally, we conducted qualitative analyses of the decision options using the decision trees to identify any dependent relationships among the policy categories; this allowed us to eliminate any logically inconsistent policy combinations.

Categories of Policy Options for the First 5 Years Following Certification

We identified 8 categories of policy options that the following 8 subsections address independently. Each subsection identifies the current policies, to provide context for the unfamiliar reader, and the postcertification options. For each category, we provide a corresponding figure that shows the options in the form of a decision tree.

Routine Immunization

Current policies. The decision to vaccinate routinely requires choosing both the type of vaccine for use and the schedule for vaccine administration. Currently, the WHO recommends that each child receive 4 doses of tOPV (administered at 6, 10, and 14 weeks, with the fourth dose given either at birth or within the first year) in order to be fully protected against polio.[24,25] Consistent with this recommendation, most countries perform primary vaccination (defined as the first 3 doses of polio vaccination) with tOPV. However, currently, 16 developed countries use eIPV for primary vaccination (Andorra, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Iceland, Latvia, Lithuania, The Netherlands, Norway, Sweden, Switzerland and the United States).[24,25] In addition, 4 countries (Belarus, Croatia, Hungary, and Israel) currently use a primary sequential schedule of eIPV/tOPV.[24,25] Three countries (Andorra, Latvia, and Lithuania) give children a routine tOPV booster dose after the completion of the eIPV primary schedule,[24,25] and routine immunization schedules continue to change.

All countries currently using eIPV maintain high levels of routine coverage and good sanitation, resulting in no reported cases of wild polio in more than 10 years (The Netherlands last reported a case in 1993[26]). Most of these countries switched from tOPV to eIPV (some first transitioning with a sequential schedule) to avoid cases of vaccine-associated paralytic polio (VAPP), a rare adverse event associated with

tOPV.[27] Given lingering concerns about the risk of importation from countries where the wild poliovirus still exists, not all industrialized countries have switched to eIPV, mainly due to the better intestinal immunity with tOPV and the benefit obtained from secondary spread of tOPV to maintain high levels of population immunity. Variation currently exists among countries in terms of the number or scheduling of doses given. Policy decisions on scheduling tend to focus on harmonizing the vaccination schedule with other vaccinations. For example, in the United States, the current Advisory Committee on Immunization Practices recommends administering eIPV in a 4-dose schedule at 2, 4, 6-18 months, and 4-6 years of age, coordinating polio vaccination with the recommended schedules for DT(a)P and Hib vaccines.[27] Currently, Cuba relies only on mass immunization campaigns twice a year for its routine delivery of tOPV instead of regularly scheduled visits to a clinic.

Postcertification options. In the postcertification era, routine immunization policies include stopping vaccination altogether, using the same or a different vaccine, and changing or maintaining the vaccination schedule. Currently, tOPV is used to vaccinate against 3 types of wild poliovirus (types 1, 2, and 3), but policy makers may at some point in the future choose to use bOPV or mOPV as the different types are eradicated. Fine and colleagues[10] discussed some of the potential motivations and issues related to using mOPV or bOPV, with thorough discussions of both the risks and the benefits. Alternatively, countries may choose the current eIPV vaccine, available alone as a single vaccine (ie, single-antigen) or in a combination form (ie, combined with other antigens, such as in DTaP-IPV, DTaP-Hib-IPV, DTaP-Hep B-IPV, DTaP-Hep B-Hib-IPV). A new potential alternative IPV/Sabin vaccine, produced using the Sabin poliovirus strains instead of the wild strains now used, is being developed for bulk production. The choice of IPV/Sabin may offer some benefits related to containment during production, although licensing of an IPV/Sabin vaccine within the first 5 years after certification appears unlikely. Similarly, licensing of bOPV or mOPV for routine immunization appears unlikely. Finally, at some point, policy makers may benefit from research efforts leading to a new vaccine, although the complexities of evaluating such vaccine make the probability of licensure and production within the first 5 years after certification remote.

Figure 1 illustrates the set of decision options for routine immunization, with the options that we assume to be practical within the first 5 years after certification indicated in bold. The main decision countries face is whether to use OPV, IPV, or no vaccine. If the WHO recommends cessation of all vaccinations in a coordinated fashion, countries must decide whether to join the coordinated cessation or not. We assume that in the first 5 years following certification, only tOPV and eIPV are realistic vaccines for routine immunization, and those countries that continue to vaccinate will maintain their current vaccination schedules. Countries that plan to stop tOPV vaccination may also need to decide whether to conduct a mass immunization campaign just prior to stopping to boost population immunity.[6] Although some countries might decide to switch to a sequential schedule from an all-tOPV schedule immediately after certification, we treat this as a transitional choice to an all-eIPV schedule and do not include it explicitly in this analysis.
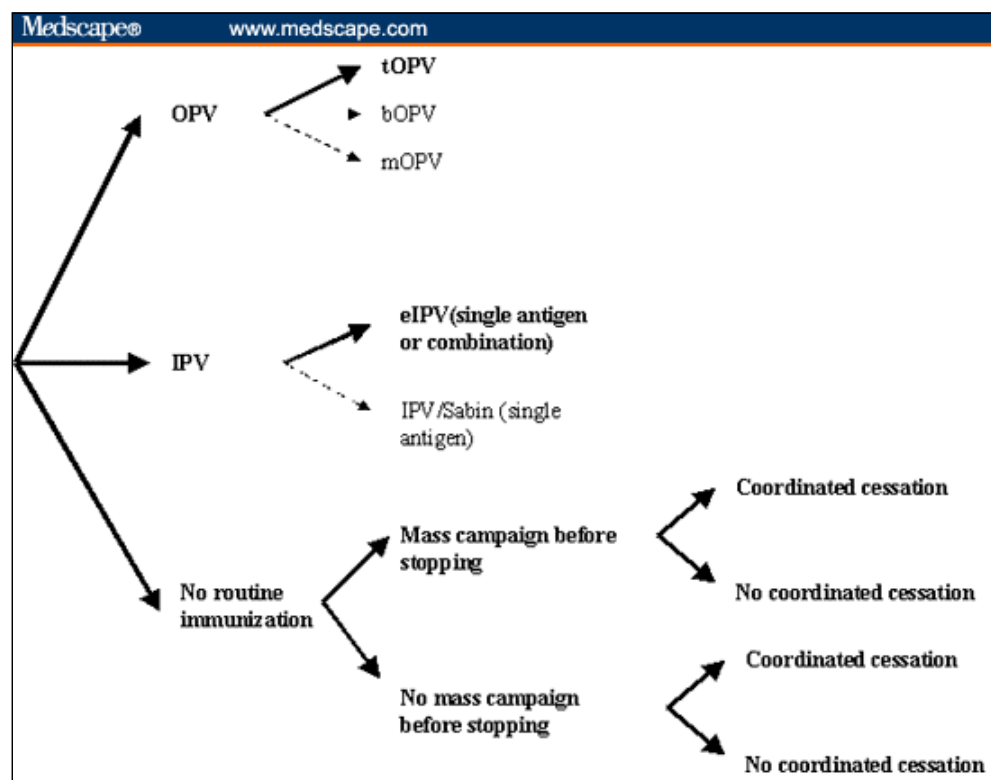

Figure 1. Routine vaccination decision options.

Supplemental Immunization Activities (SIAs)

Current policies. SIAs include national immunization days (NIDs), sub-NIDs (SNIDs), and mop-up campaigns that rapidly interrupt poliovirus transmission. The WHO Technical Consultative Group (TCG) on Polio Eradication recommended the maintenance of high-quality

SIAs in all polio endemic countries and developed criteria for determining when to conduct NIDs.[28] The WHO recommends NIDs at least annually in polio-endemic or recently endemic countries. Currently, all SIAs use tOPV, targeting all children under the age of 5 years (regardless of the child's immunization history). Two rounds of SIAs are conducted over a 4- to 6-week period. Other countries that border endemic countries may also conduct NIDs or SNIDs. Countries may target SNIDs in areas with particularly low routine vaccination coverage, and large, populous countries (eg, China, India) may conduct SNIDs on the scale of smaller countries' NIDs to target specific regions. During mop-up campaigns, vaccinators go door-to-door to immunize children in areas that are difficult to reach with a (fixed post) (S)NID campaign, have low immunization coverage, or are at highest risk. Finally, in the context of the PEI, countries often collaborate with neighboring countries to conduct synchronized regional NIDs to interrupt transmission in larger geographic areas.[29]

In April 2002, the TCG also recommended that: (1) polio-free countries that either border an endemic area or have routine coverage of 70% or less should continue to conduct NIDs or SNIDs, as appropriate, on an annual basis; and (2) countries that maintain polio-free status for at least 3 years but fail to achieve or maintain a level of 90% routine immunization coverage with 3 doses of tOPV among infants should continue to conduct NIDs at least every 3 years to prevent the accumulation of susceptible individuals and protect against the importation of wild polioviruses.[28] The WHO also recommends, where appropriate, that larger countries conduct SNIDs to cover those states or provinces with lower than 90% coverage. These recommendations support the goals of interrupting any continued transmission of the poliovirus and maintaining high levels of population immunity in areas with insufficient routine coverage.

Postcertification options. In the postcertification era, countries must decide whether to conduct NIDs, SNIDs, or no SIAs, as shown in Figure 2. If they continue SIAs, they must also decide how frequently to conduct them, the number of rounds, and the type of vaccine to use. We assume that the target group consistently remains children under 5 years of age and that the NID includes 2 vaccination rounds. We assume that the vaccine used in SIAs will be the same as the vaccine used for routine vaccination. However, due to regulatory constraints mentioned previously for bOPV, mOPV, and IPV/Sabin as well as potential supply constraints on eIPV, we assume that immediately after certification, only tOPV is used during SIAs. Immediately after certification, conducting NIDs may become the optimal choice for developing countries to prevent re-emergence of wild poliovirus or circulating VDPVs (cVDPVs), although some countries may opt to conduct only SNIDs based on WHO TCG recommendations.
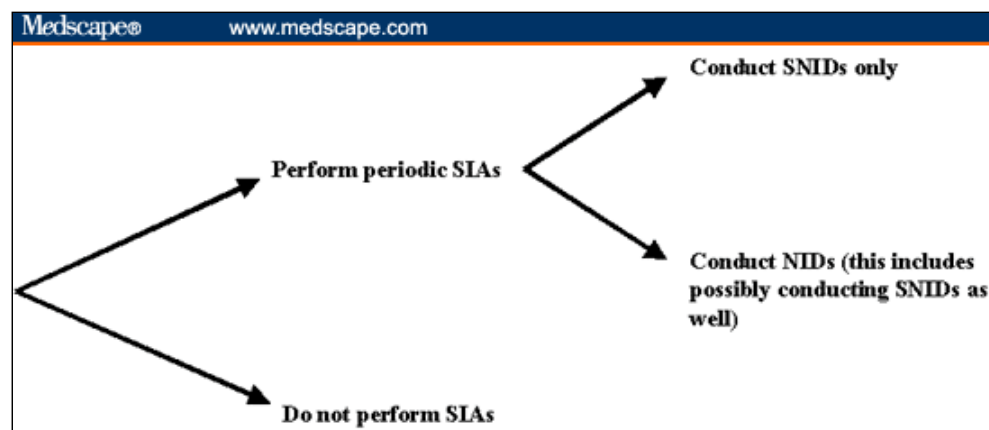

Figure 2. Supplemental immunization activities decision options.

Outbreak Response

Current policies. An outbreak response, as defined in the WHO guidelines,[30] consists of 2 parts: intensified surveillance (to detect new cases and identify subpopulations at high risk), and immunization response (currently with tOPV). Current guidelines aim to intensify acute flaccid paralysis (AFP) surveillance by introducing active case investigation and increased efforts to isolate additional polioviruses.[31-33] The immunization response generally consists of house-to-house mopping-up campaigns in the districts of the confirmed outbreak (or even in some cases prior to isolation of poliovirus, for example, in China[34]), followed by NIDs or SNIDs depending on the number of cases found and the size of the country (eg, NIDs in Albania[31] and Bulgaria,[33] SNIDs in China[34]). The WHO recommends notification of an outbreak to both the WHO and UNICEF within 48 hours of detection.[30] The WHO, in turn, can offer recommendations and assistance to countries in the context of the global PEI. Countries must decide how to respond to an outbreak at the national level.

Postcertification options. In the postcertification era, the likely immediate surveillance response includes performing a comprehensive outbreak investigation and surveillance enhancement (intensified AFP surveillance, active case search, retrospective hospital record reviews, etc.) until evidence shows the interruption of transmission. This effort essentially corresponds to a classical epidemiologic outbreak investigation, and we expect future WHO guidelines for postcertification outbreak response to include these efforts. We assume that each country would follow any WHO guidelines for the outbreak surveillance response, and we anticipate that the WHO would develop guidelines for the postcertification era before certification.

Given the current experience with outbreaks, we expect future guidelines to suggest some scale of mass immunization response. Countries may choose the size of the response, ranging from no response at all to a focal immunization response (eg, immunization of contacts to house-to-house immunization of children in the district or area of the outbreak), to SNIDs or NIDs, and finally to participation in a regional or global NID. We expect decisions about the appropriate size of the response to depend on time, with greater responses needed with lower

levels of population immunity, and all response strategies depending on the scale-up required to successfully interrupt transmission. We assume that the choice of outbreak response in any country increases in a discrete manner, and it depends on the size and characteristics of the outbreak, as shown in Figure 3. We assume that in the first 5 years after certification, evidence of an outbreak of circulating poliovirus will lead at least to an SNID if not an NID. Further, at some threshold, the scale of the response will rapidly increase to an NID to ensure interruption of transmission. We assume a very low threshold for a national response following certification of eradication, given the global repercussions of failing to contain the outbreak.
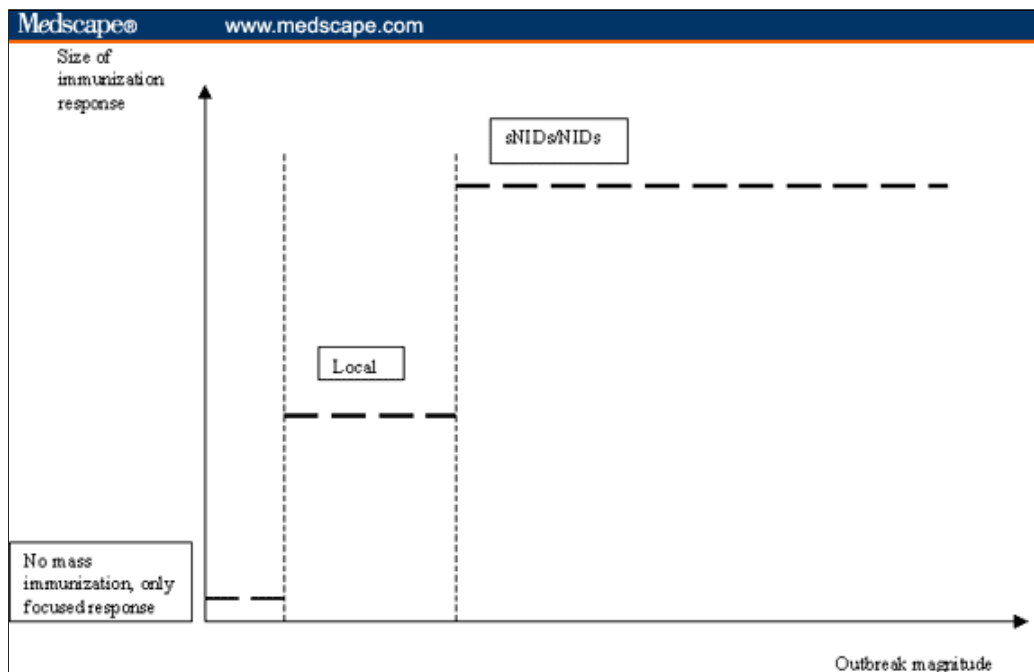

Figure 3. Size of outbreak immunization response as a function of outbreak magnitude.

From the country perspective, Figure 4 summarizes the vaccination options for responding to an outbreak, although we emphasize the likely role of the WHO and its guidelines in determining the size of the response. Figure 4 shows that the choices for those countries that stop routine immunization after certification include resuming routine immunization in addition to conducting response NIDs. Restarting routine immunization assumes resuming polio vaccination indefinitely using the country's current immunization schedule, whether with tOPV or eIPV, possibly with regularly conducted NIDs. We emphasize that the scale of the response may also depend on the availability of sufficient quantities of vaccine from suppliers or stockpiles, but we assume that during the first 5 years after certification, a sufficient supply of vaccines exists. We further assume that outbreak response will use tOPV, mOPV, or eIPV, and it will target children under the age of 5 years. As Fine and colleagues[10] discussed, the use of mOPV might become desirable in the postcessation era so as not to reintroduce nonoutbreak-related poliovirus serotypes into the environment.
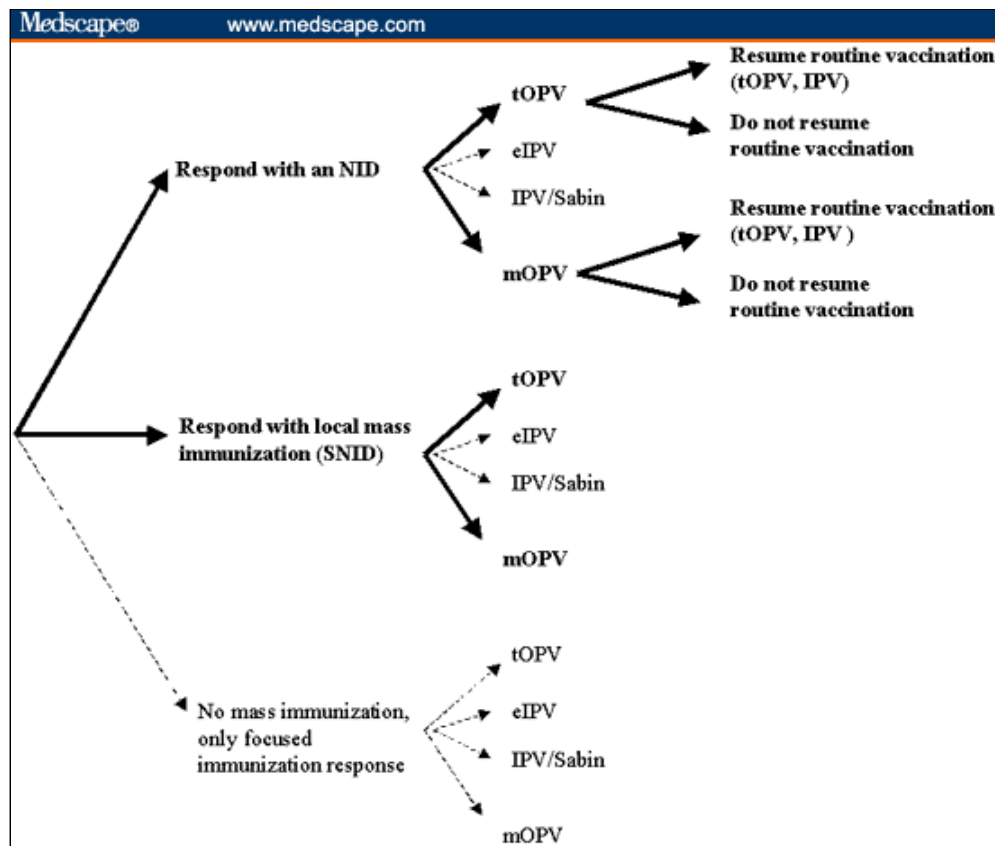
Figure 4. Outbreak response strategies decision options.

Stockpile

Current policies. The WHO and UNICEF currently have vaccine reserves, through the maintenance of funds and arrangements with manufacturers to purchase vaccine for outbreak response, but no formal global stockpile of polio vaccine currently exists. The TCG recommended that a global stockpile exist prior to discontinuation of OPV immunization.[9] Stockpile policy decisions must be made well before certification in order for cessation of immunization to be a realistic policy option at the time of certification. The WHO is currently researching the stockpile design and specifications and exploring issues related to governance and financing. The United States is considering the components of a US national stockpile and is reviewing critical regulatory issues. For example, tOPV needs relicensing in the United States because the prior license lapsed once the United States switched to eIPV for routine vaccination in 2000, and the facilities that manufacture tOPV for the stockpile must meet US Food and Drug Administration production regulations.

Postcertification options. Figure 5 shows the high-level stockpile choices that countries face. Note that the decision to create a stockpile necessitates a number of other critical decisions related to the design, specifications, and governance of a stockpile (not shown in Figure 5, but currently the subject of WHO and US research as noted above). If the WHO creates a global stockpile, then countries could presumably negotiate for explicit access to the global stockpile in the case of an outbreak. For some countries, this access would be implicitly assumed (ie, they assume that the WHO would give them access to the global stockpile in the event of an outbreak). We make the analogy here to the option of purchasing insurance, and we assume that arranging for coverage by the global stockpile essentially provides insurance in case of an outbreak, while not doing so essentially leaves a country uninsured. Some countries may decide to establish a national stockpile only or in addition to arranging for access to the global stockpile.
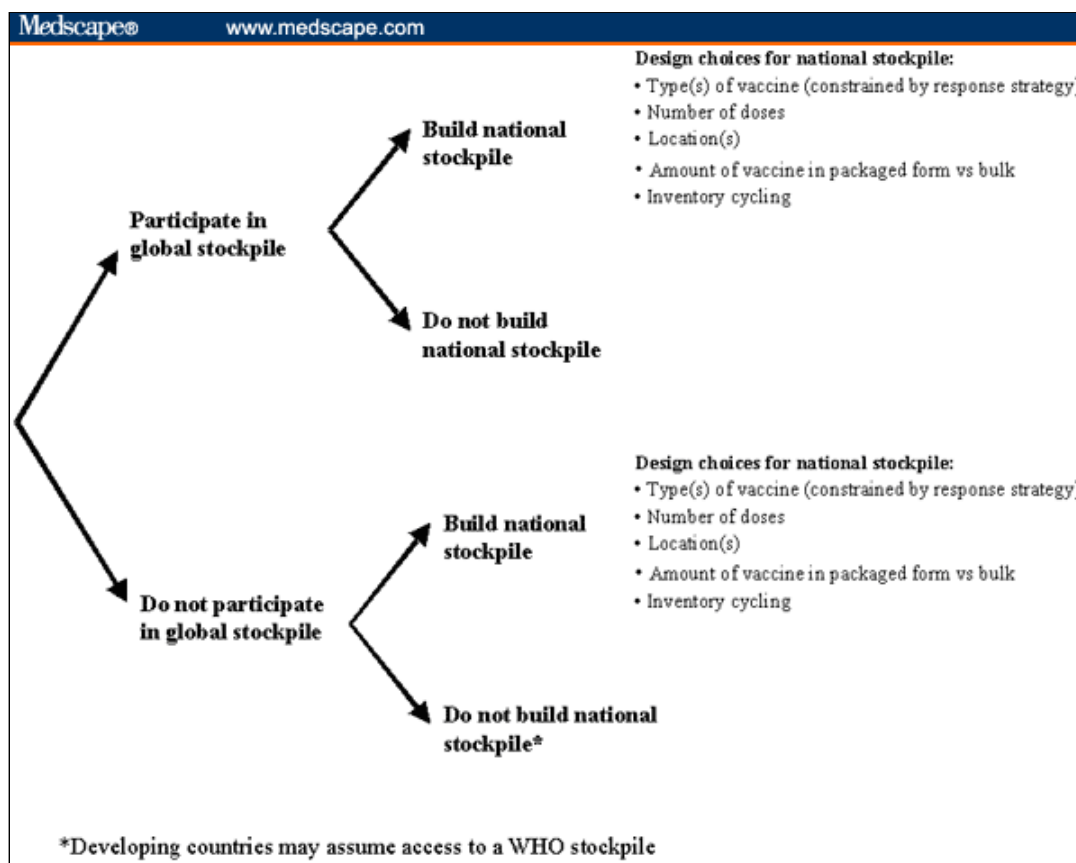
Figure 5. Stockpile decision options.

For countries that create their own stockpile, a number of important design decisions arise, including determination of the: (1) number of doses of 1 or more types of vaccine to keep in the stockpile, (2) number of locations in which to house the stockpile, (3) amount of vaccine to keep readily available in packaged form vs bulk, and (4) appropriate management policies related to cycling the inventory and ensuring that the stockpile size increases in accordance with changing risks and potential demands (ie, growth in the susceptible population). At the global level, for example, a stockpile during the period immediately after certification may in one scenario consist of sufficient doses of tOPV to cover 3 global birth cohorts with 3 doses,[10] although the existence of the global stockpile and numerous possible scenarios related to design issues currently remain under debate. At the national level, we treat the design questions as secondary decisions and we assume that the primary stockpile decisions include arranging for coverage by the global stockpile and/or building a national stockpile (which would include choosing the vaccine type and all other secondary decisions).

Surveillance

Current policies. The current surveillance system for polio started when the Pan American Health Organization initiated a regional laboratory network for AFP surveillance in 1986.[35] In 1989, the WHO Plan of Action (endorsed by the World Health Assembly in 1990 and revised in 1996) expanded this system globally under the WHO PEI.[36] AFP results from multiple causes, including infection by a poliovirus. However, even in the absence of poliovirus circulation, cases of AFP occur at a minimum background incidence rate of approximately 1 per 100,000 children under 15 years of age.[37] This surveillance system analyzes stool specimens from cases of AFP for the presence of poliovirus. Currently, the AFP surveillance system includes the placement of personnel dedicated to finding any wild poliovirus through the identification and investigation of cases of AFP and a global laboratory network of virologic laboratories.[37] The global polio laboratory network includes "7 global specialized laboratories, 15 regional reference laboratories, 83 national laboratories, and 40 subnational laboratories (in large countries)."[38] Currently, surveillance also includes characterization of strains as wild, vaccine, or vaccine-derived (ie, genetic variations of a vaccine strain, of most concern when they revert to virulent forms). A few industrialized countries, including the United States, do not conduct AFP surveillance, although they have laboratories that participate in the global polio laboratory network, choosing instead to include reporting of poliomyelitis as part of ongoing systems of passive and enterovirus surveillance.

Some experience exists with using alternative methods (eg, environmental surveillance) to enhance surveillance; in the future, countries or regions may also consider these alternatives as options. The report of the 6th TCG report stated that: "experience gained from environmental surveillance projects in Egypt, Georgia, India (Mumbai) and Turkey has demonstrated that it is possible to detect wild virus in the absence of AFP cases (Egypt, Mumbai)."[32] One recent study concluded that aseptic meningitis-based surveillance appears impractical as a substitute for AFP surveillance, but suggested the potential utility of environmental and enterovirus surveillance (eg, routine clinical diagnosis of cell cultures of stool specimens) as supplements to AFP surveillance.[39] As recommended at the 6th TCG meeting,[32] the WHO has developed global guidelines for environmental surveillance.[40]

Currently, no policy exists for the routine use of serologic surveillance. Serologic surveillance provides evidence of poliovirus population immunity, but it cannot distinguish between previous vaccine-related or wild poliovirus infections. Serosurveys provided additional evidence of the limited persistence of vaccine-derived polioviruses in an unvaccinated and polio-free population in Cuba[41] and may prove to be a useful tool for the PEI.[42] In a growing susceptible population (ie, following cessation of vaccination), serologic surveillance may offer an additional method for detecting exposure to poliovirus in the population.

Postcertification options. From the country perspective, Figure 6 shows the main options for the first 5 years after certification, including passive surveillance, which relies on the national routine passive disease reporting system, and dedicated AFP surveillance, which represents the current policy now used essentially globally (with the exception of a few developed countries). In some countries, AFP surveillance could eventually get incorporated into a national Integrated Disease Surveillance system, and we assume that such integration would not change the quality of the AFP surveillance, although the costs and details related to implementation require further study. In addition to a passive or dedicated surveillance system, countries may also opt to conduct some form of enhanced surveillance, including environmental surveillance, enterovirus surveillance systems, or serologic surveillance, either nationally or limited to targeted high-risk areas. In the short term, serologic surveillance is not useful following cessation of routine vaccination, given the presence of antibodies from previous vaccinations in most of the population in the 5 years after certification. Similarly, screening for enteroviruses also appears to be a limited option because few countries have the infrastructure to provide routine diagnostic services for the whole population, although this could be initiated. Thus, environmental surveillance remains the only realistic enhanced surveillance policy option for countries immediately following certification.
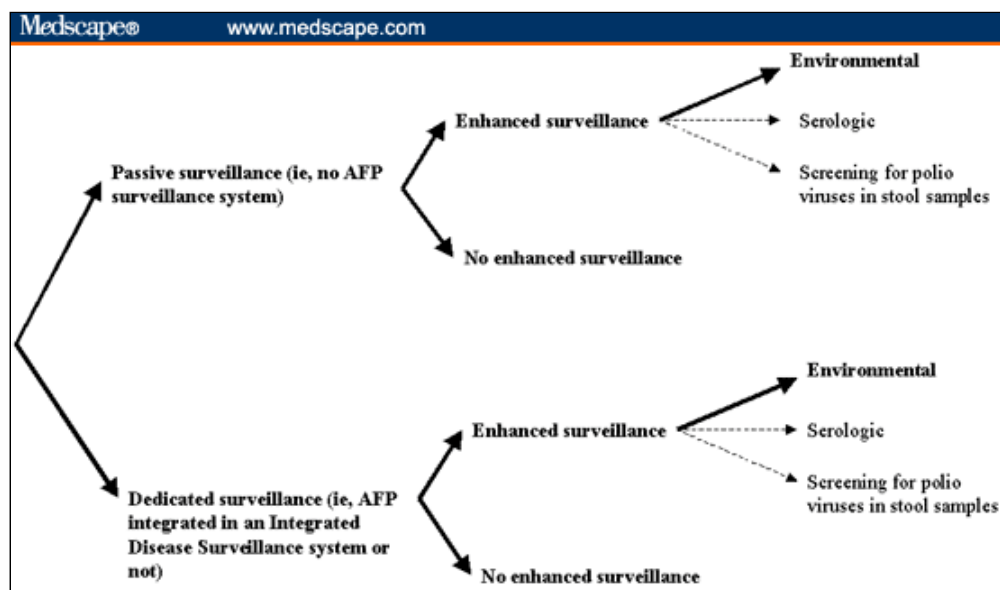

Figure 6. Surveillance decision options.

Containment Strategies

Current policies. Containment strategies focus on reducing the risk of reintroduction of poliovirus into the environment, notably through vaccine manufacturing facilities and laboratories that handle materials that could contain poliovirus (wild or vaccine-related). The WHO recommends that laboratories handle wild poliovirus infectious or potentially infectious materials under biosafety level (BSL-2/polio) procedures.[2] Current WHO policy requires countries to complete a national inventory of wild poliovirus infectious materials and potentially wild poliovirus infectious materials before global certification of eradication.[43] The WHO defines wild poliovirus infectious materials as clinical materials collected from persons with wild or VDPV infections, or materials that contain wild poliovirus isolates (ie, those treated and stored to preserve the virus). Potentially wild poliovirus infectious materials include "respiratory secretions, feces, and environmental samples collected for any purpose at a time and in a geographic area where wild poliovirus was known or suspected to be present."[44]

One year after detection of the last wild poliovirus, the WHO plans to ask countries to begin the implementation of procedures for containment of wild polioviruses. This process includes contacting all agencies and institutions on the national inventory to do one of the following with the materials: (1) implement laboratory containment procedures (BSL-3/polio for all laboratories with wild poliovirus infectious materials or laboratories that "perform activities involving poliovirus permissive cells or animals" for wild polioviruses and potentially poliovirus infectious materials, or BSL-2/polio for laboratories handling only potential poliovirus infectious materials and performing no such activities[2]); (2) transfer wild poliovirus infectious and potentially infectious materials to WHO-designated repositories; or (3) render such materials noninfectious or destroy them under appropriate conditions. These actions require completion prior to consideration of global certification of polio eradication. In the case of a global decision to cease tOPV administration, the WHO anticipates an increased stringency in the containment requirements for wild and vaccine-derived polioviruses for those countries that choose not to immunize, although the degree of increase remains under discussion.[2]

Postcertification options. As shown in Figure 7, given the condition of meeting containment requirements in order for global certification to

occur, the policy decision after certification for each country essentially becomes whether to enforce the WHO-suggested containment requirements.

Figure 7. Containment decision options.

Management of Chronic Excretors of Polioviruses

Current policies. No known cases exist of chronic excretion of wild poliovirus.[6] As of early 2003, WHO reports have catalogued a cumulative experience consisting of a total of 19 immunodeficient chronic excretors of vaccine-derived polioviruses (iVDPV) globally in more than 40 years of OPV use. These individuals live(d) in mid- to upper-level income countries, primarily in the United States and Europe. Of these 19 chronic excretors, 2 continue to excrete, while the others died or stopped excreting virus. Poliovirus type 2 represents the most frequently isolated serotype. Virtually all of these individuals suffered from severe primary (congenital) antibody deficiency diseases. Preliminary studies estimated extremely low (ie, on the order of 0.1% to 1%) upper limits of prevalence of chronic poliovirus excretion among patients with primary immunodeficiency.[45] The poor access to appropriate medical care and treatment dramatically limits the survival beyond early childhood of patients with primary immunodeficiency in developing countries.

An informal survey of prominent immunologists attending the 2002 Federation of Clinical Immunology Societies meeting gauged their support of a "standard of practice" recommendation that would lead to routine screening (for poliovirus excretion) of patients with primary immunodeficiencies. The immunologists declined endorsement of such a screening policy given the absence of adequate therapy for identified chronic excretors.

We did not identify any current global or country level policies for the specific surveillance of iVDPV. The existing AFP surveillance network has identified all iVDPV cases since 1998, but the sensitivity of the AFP surveillance system for detecting iVDPV remains unknown, given that prolonged excretion may occur prior to the development of paralysis.

Postcertification options. Figure 8 shows the options for managing chronic excretors. We expect that global and country level options for specific surveillance of iVDPVs may become more feasible with the identification of effective therapeutic measures. However, to manage the risk of reintroduction of poliovirus to the community from identified patients, countries may choose whether to conduct screening and/or offer education about strategies for minimizing exposure to others.
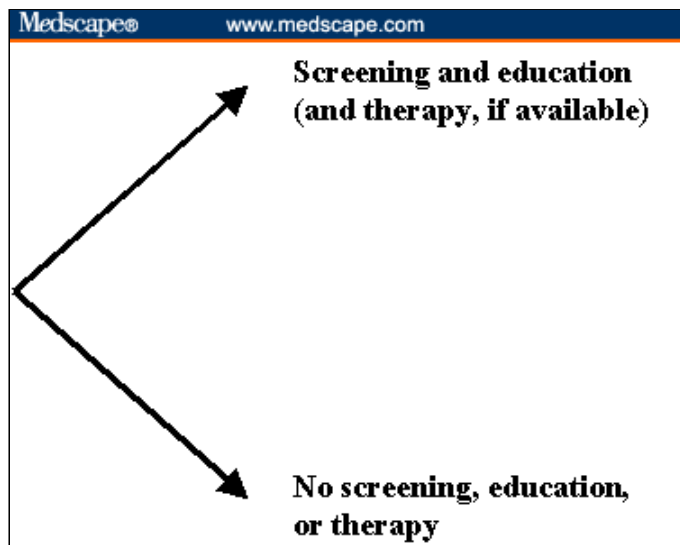
Figure 8. Management of chronic excretors decision options.

Investment in Research

In any risk management process, ongoing research continues to play an important role in resolving important uncertainties and in creating new (and often better) options (eg, safer, cheaper, and/or more effective vaccines). Although this section does not identify any specific research options, we note that countries may choose to invest some of their resources in research, although currently the WHO and the CDC have funded most research.

Characterizing the Set of Decision Options

Figure 9 combines decision categories and options discussed above as realistic during the first 5 years after certification to represent them in the form of a summary decision tree. This section begins by explicitly recognizing that several critical factors influence the relative attractiveness of the different options to various countries. Then, the following section focuses on identifying the interdependence among some of the options in Figure 9, enabling further narrowing of the decision tree to a realistic set of options.
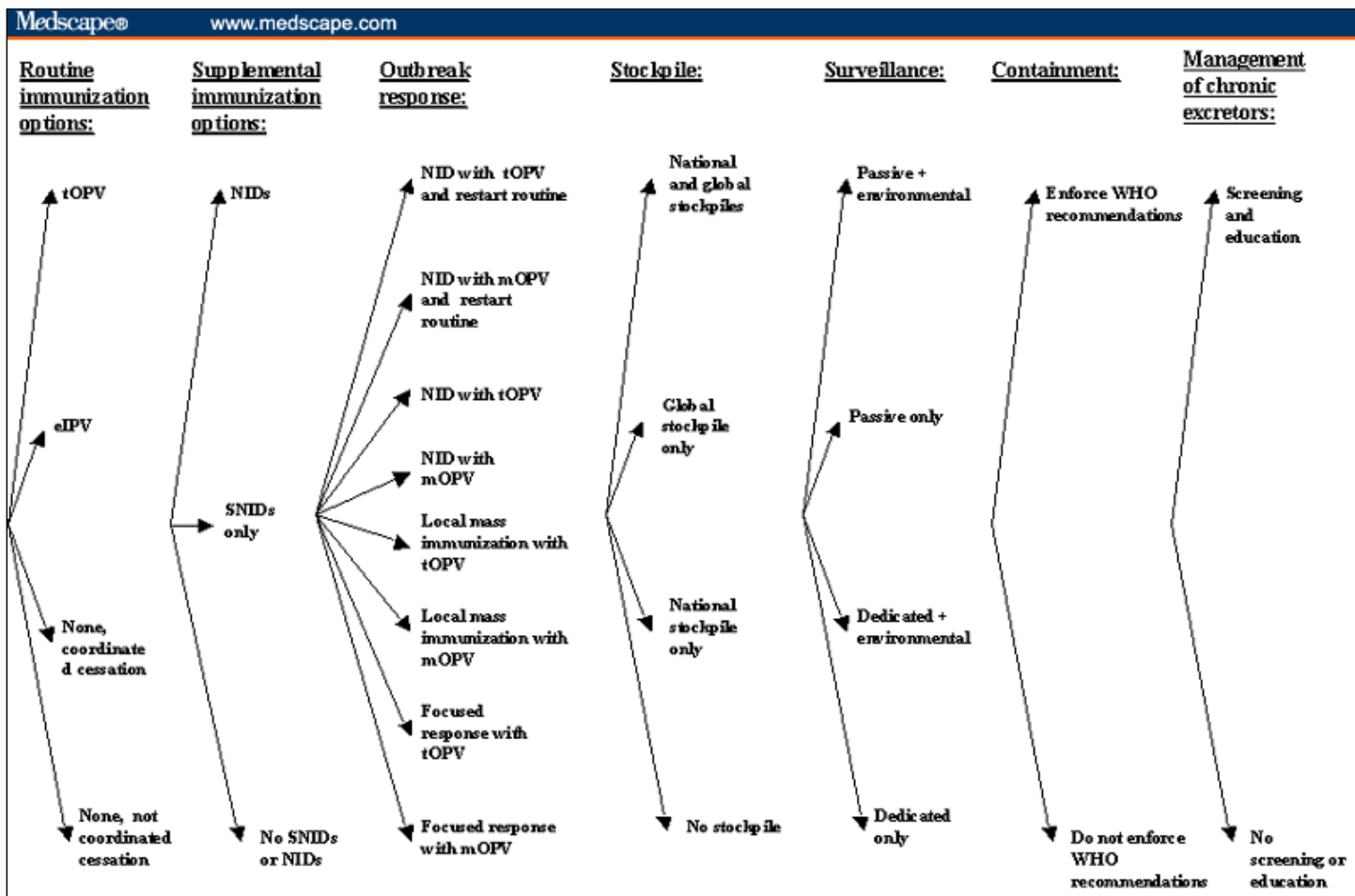
Figure 9. Country decision options -- first 5 years following certification

Critical Factors

Costs. Clearly, cost implications arise with each decision, and the implications of these resource requirements warrant serious consideration. In some cases, cost considerations may make some policy options unfeasible for countries with competing health and budget priorities. The cost of tOPV has ranged from $0.02 ($US, 2002) in China, which self-produces,[46] to $0.09 ($US, 2002) when purchased by UNICEF,[47] and $16.50 ($US, 2002) in the UK private market.[48] In the US public sector, eIPV vaccine costs $9.67 ($US, 2002) per dose and a DTaP-HepB-IPV combination vaccine costs $31.80 ($US, 2002) per dose; the price doubles in the private sector.[49] Additional costs for eIPV include needle, syringe, trained personnel, and disposal. SIAs represent large operations that involve high costs for planning, personnel, transport, and social mobilization. The cost of a response, including planning, cold chain, and training, could influence the size of the outbreak response, but we assume that, to some degree, the required size of the response will follow WHO recommendations. For countries that do not currently conduct enhanced surveillance, the establishment of an environmental surveillance system/program may potentially prove too costly in terms of human and financial resources.

Certain activities in developing countries currently benefit from support by external funders such as operational costs of NIDs and maintenance of an AFP surveillance system. Financing of these costs will play a large role in a national decision maker's policy choices.

Risk. The decision makers' perceptions of the risk of adverse events also influences their vaccine choice for routine immunization, SIAs, and outbreak response. Continued tOPV use implies a small (but measurable) risk of VAPP and the potential risk of emergence of cVDPVs into the population. Using mOPV may become increasingly desirable to eliminate the risk of reintroduction of particular poliovirus types.[10] eIPV use carries the risk of adverse events related to injection safety and greater impact of potential outbreaks because the level of individual immunity induced by eIPV when administered at the current WHO 6, 10, 14-week schedule appears lower than that induced by tOPV.[50] The option to stop all vaccinations inherently carries the risk of potentially large outbreak scenarios in the longer term, particularly with the impact of the outbreaks increasing as the size of the unvaccinated population increases. The level of risk aversion (where risk perception of an intentional release or catastrophic outcome influences decisions) will affect a country's containment policy decision to support the WHO's biosafety requirement guidelines. An increase in susceptible individuals over time may raise the relative importance of laboratory containment efforts.

Differing perceptions of the risk of an outbreak and likely consequences will affect a country's decision to rely on a global stockpile and/or develop a national stockpile. The change in the number of susceptible individuals and the changing perception of the risks of reintroduction

may also influence how the size of the stockpile changes over time. For example, changes in the perception of current risks of bioterrorism recently led US policy makers to re-establish a stockpile of smallpox vaccine. As seen in the case of smallpox, the decision to reduce and eventually abandon the global stockpile followed from changes in perceptions of the relative benefits of a stockpile compared with the costs of its maintenance.

Other countries' policies. The policies of neighboring countries also play an important role. For example, a country bordering a tOPV-using or eIPV-manufacturing country might face an increased risk of reintroduction of vaccine-associated poliovirus strains compared with countries in regions where all tOPV vaccination stops and no eIPV production occurs. Recent polio endemicity may increase the country and neighboring countries' desire for high-quality surveillance to provide additional evidence of continued maintenance of the country as polio free.

The establishment of a global stockpile with access for all countries clearly influences a country's choice to build a national stockpile. Although it remains unclear how countries would participate in a global stockpile, this participation will likely differ between developed and developing countries. For example, wealthier countries may contribute a vast majority of the funds, ensuring stocks for their own country as well as other countries.

Interdependence of Policy Decisions

The previous section provided a glimpse of some of the factors that influence national choices within the comprehensive perspective of the complexity of the set of choices that policy makers will face after certification. The significant differences between developed and developing countries play an important role in limiting the set of options that any single country would consider. In addition, the interdependence of policy decisions leads to a significantly narrowed set of realistic decision options, since some options make little sense when combined. This section summarizes what we find as the realistic set of options when considering interdependent options jointly for the first 5 years after certification. We discuss the narrowed set of options first for developed countries where we assume routine vaccination with eIPV continues, and then for developing countries where continued routine vaccination remains an open question.

Developed Countries

Clearly, a country's vaccine history and current policy provide important context for its future vaccine policy choices. In the context of developed countries (ie, those that switched from tOPV to eIPV to avoid the burden of VAPP), we do not foresee that these will either return to tOPV or stop vaccination during the first 5 years after certification. Further, we do not expect that developed countries will conduct SIAs (using tOPV), as their current policy also does not include SIAs. Policy makers in a developed country also face a smaller set of options associated with managing an outbreak. While outbreaks of different magnitudes will lead to a varying scale of responses, developed countries do not face the choice of restarting routine vaccination because they will already be routinely vaccinating with eIPV. Based on previous outbreaks, we assume that developed countries would use either tOPV, mOPV, or eIPV as vaccine options in outbreak response efforts.[10,26,51] We include eIPV as a policy option given that some countries may not wish to vaccinate with a live vaccine, or because regulatory hurdles may preclude the use of tOPV or mOPV. This implies that they must maintain access to supplies of tOPV, mOPV, or eIPV either from current supply production or from a stockpile. Thus, from a national perspective, each country will face the choice of either having a national stockpile or participating in any agreements related to the creation and maintenance of a global stockpile. Figure 10 reflects the more restricted set of decisions we expect policy makers in developed countries to face. Note that no reduction occurs in the decisions related to surveillance, laboratory containment, and management of chronic excretors and that the list of options for these decision categories is essentially independent of other choices.
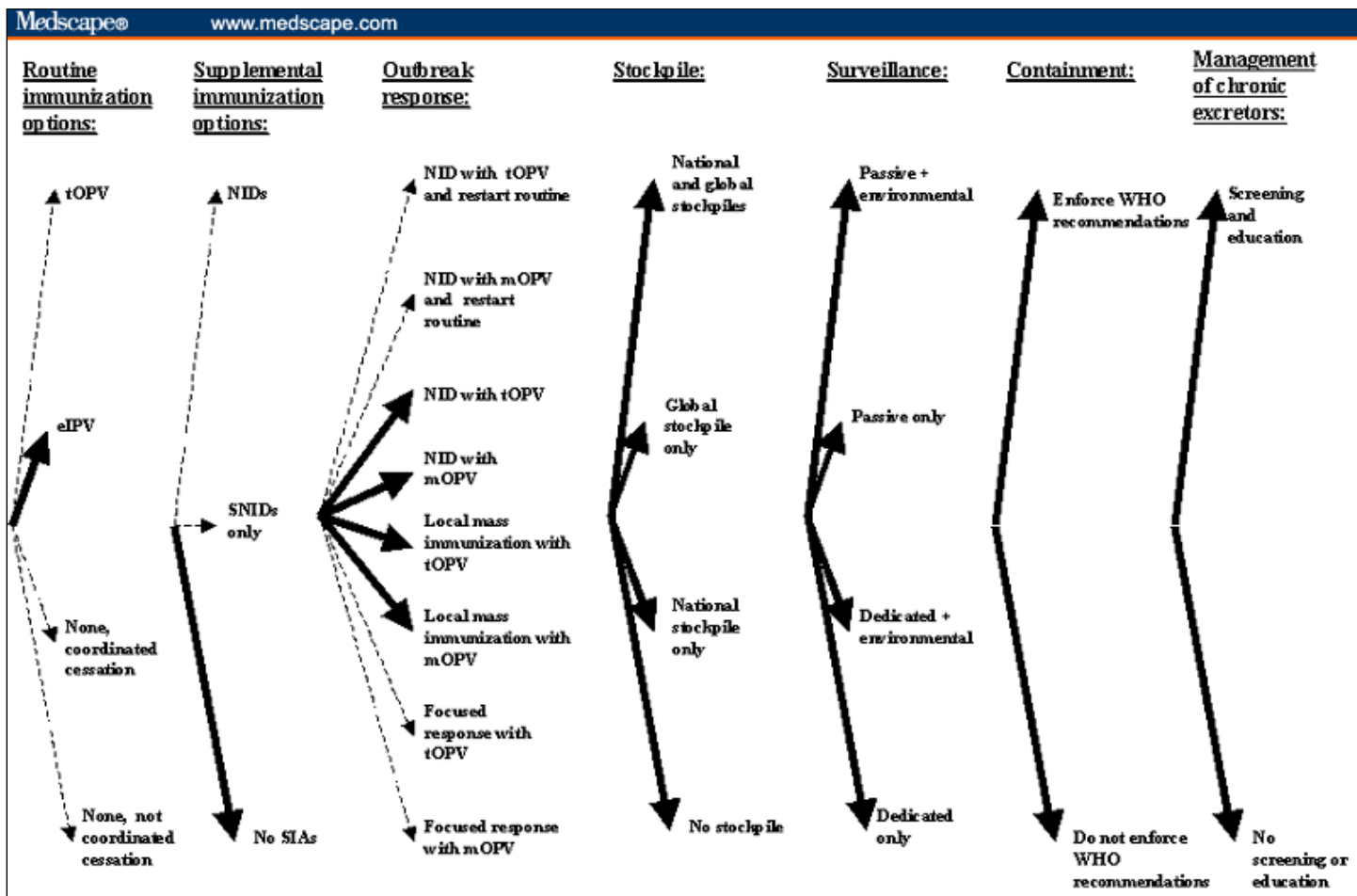
Figure 10. More restricted set of decision options for developed countries choosing routine IPV vaccination.

Developing Countries

Currently, all developing countries rely on tOPV for routine vaccination. While the eradication initiative began with the full expectation that all countries would stop vaccination following certification, that assumption no longer exists. Developing countries will choose between continuing routine vaccination with tOPV, switching to eIPV, or stopping routine vaccination (in coordinated fashion or not) during the first 5 years following certification.

For countries that decide to switch to eIPV, the reduced set of options is similar to the scenarios described for developed countries (shown in Figure 10). Although the set of options remains the same, the critical influencing factors for a developing country policy, and thus the likelihood of choosing an option, may differ.

Figure 11 shows the more restricted set of options for those countries that choose to continue vaccination with tOPV, assuming access to a supply of tOPV exists. We assume that with continued routine use of tOPV, these countries would not see a need to participate in a global stockpile, although they might decide to build a national stockpile to help ensure vaccine supply. We eliminate outbreak response options that include restarting routine immunization. WHO recommendations, current SIA policies, coverage rates, and other factors will affect the choice about whether to conduct SIAs. However, we assume that the vaccine used for SIAs and for outbreak response will be the same as the vaccine used for routine vaccination. As in the case of developed countries, all options for surveillance, laboratory containment, and management of chronic excretors remain possible.
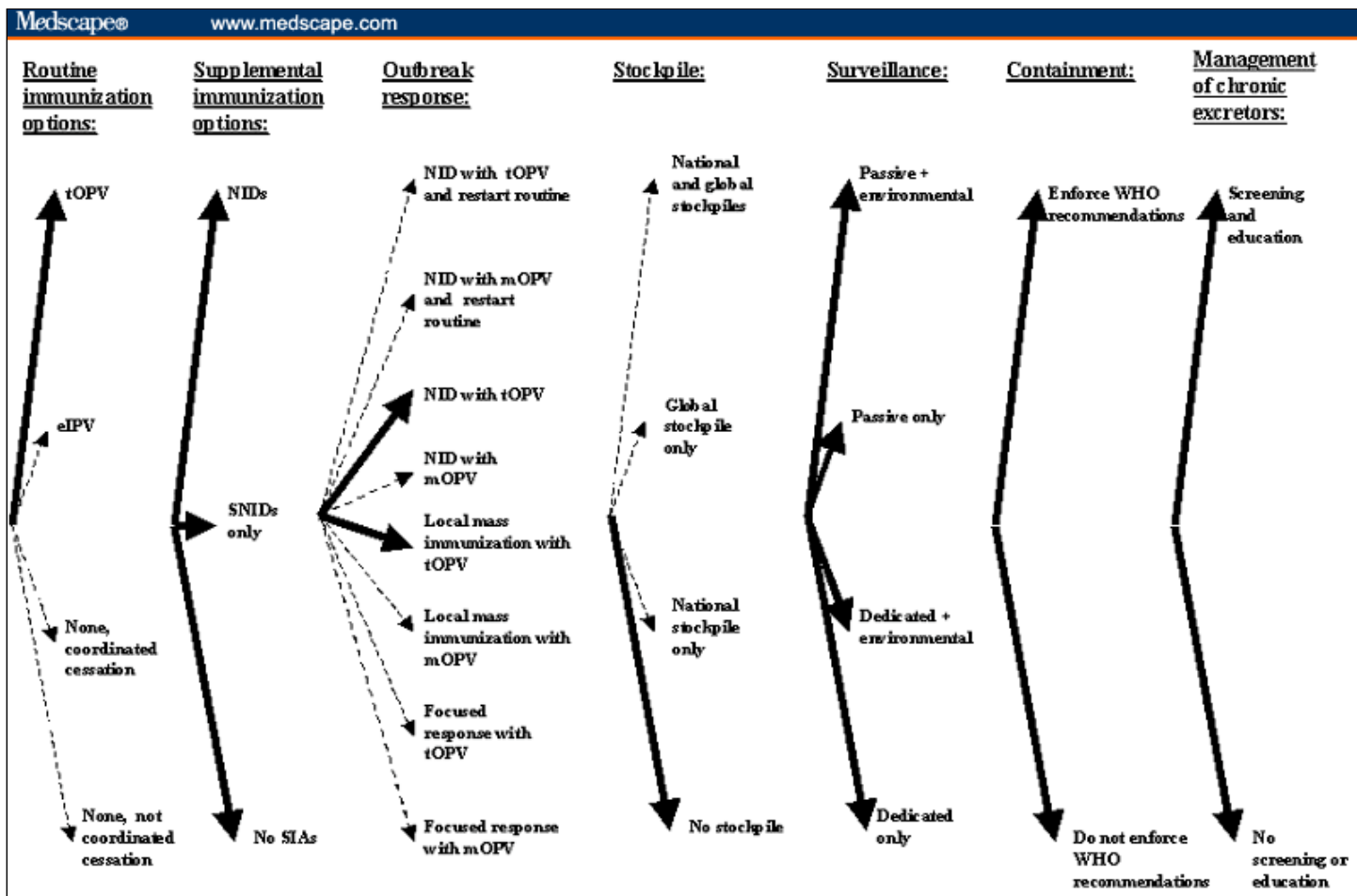
Figure 11. More restricted set of decision options for developing countries choosing routine OPV vaccination.

Figure 12 shows the more restricted set of options for those countries that choose to stop all routine polio vaccination. If countries decide to stop routine immunization, we assume that they would not continue to conduct SIAs, so we eliminate this set of options from the tree. However, additional choices arise in the set of outbreak response options to allow for the possibility of restarting routine vaccination. The country's policies with respect to vaccination may affect their choice of surveillance policy, with the potential need for a higher intensity and quality of surveillance than that used by a country with high levels of routine coverage.[10] In developing countries that stopped all immunizations, the policy makers must decide among all options for building a stockpile, surveillance, containment, and management of chronic excretors.
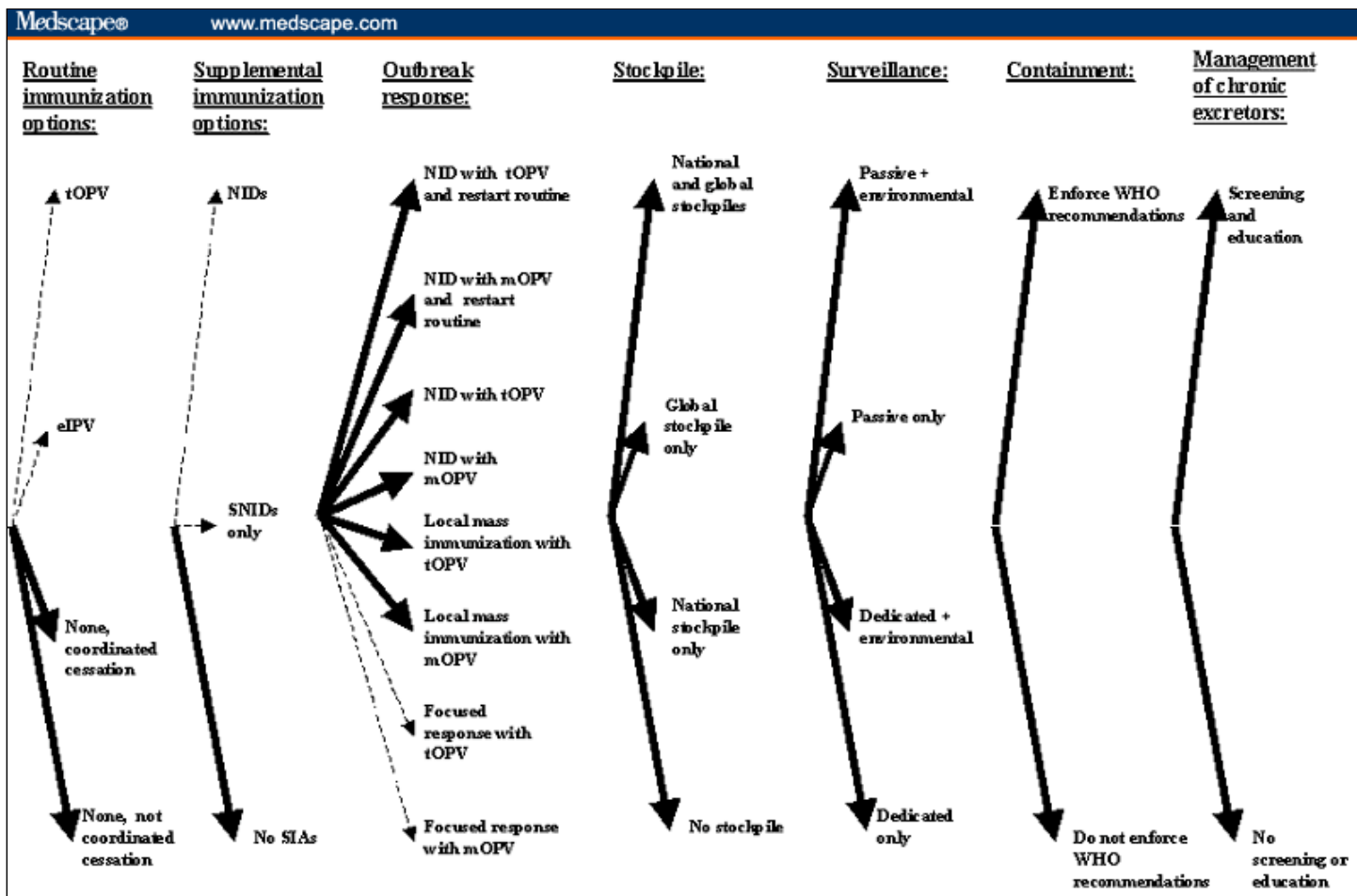
Figure 12. More restricted set of decision options for developing countries choosing to stop routine vaccination.

Discussion

The previous section focused on identifying the realistic set of decisions for policy makers in developed and developing countries over the limited period of 5 years after certification. The purpose is to help policy makers develop much needed communication tools as they evaluate and discuss their options within their countries and with the leaders of other countries. Although management of national and global polio eradication activities remains relatively complex, it is important to provide characterizations now of critical issues and the implications of various choices.

Future studies will need to consider the implications of the framework presented here and whether additional time periods following certification should be examined. After certification, manufacturers may stop producing tOPV, anticipating that the demand for the vaccine will greatly diminish. However, this may lead to initiatives to increase the production of eIPV. Finally, the licensing of mOPV, bOPV, and IPV/Sabin and/or the development of a new vaccine may present a more desirable future routine immunization or stockpiling options that avoid the need for containment of large stocks of wild poliovirus in the production of eIPV. The supply of vaccines and consequently the pricing of vaccines will also change over time. Given that a policy maker has a limited budget, these changes in prices and hence costs of different decision options (eg, vaccination, maintenance of stockpile) may change the likelihood of choosing certain options. Further out from certification, OPV use may become suboptimal because of high health-related and financial costs associated with greater numbers of VAPP cases and continued cVDPV risks.

In any country, the time elapsed since eradication influences the level of alarm caused by an outbreak and, therefore, the probability of a public demand for vaccination outside the indicated response boundaries. For countries that stop vaccination, the increasing cohort of susceptible individuals may influence the size of the response. Moreover, the priority of polio surveillance may decline as the risk of cVDPVs decreases over time. However, the potential consequences of an outbreak will increase over time with the growing susceptibility of the population, indicating an increasing importance of maintaining sensitive surveillance and timely detection of potential outbreaks (eg, perhaps shifting the relative attractiveness of environmental or serologic surveillance to detect polioviruses before they caused paralysis).

For countries using tOPV, the switch to eIPV becomes more likely after interruption of transmission or certification of global eradication. However, some countries in certified polio-free regions may begin to switch to eIPV as tOPV becomes the primary source of polio cases within the population. Although stopping routine immunization altogether in countries before certification seems unlikely, countries may in some cases decide to do so if they perceive that the risk and costs of VAPP or unsafe injections exceeds that from wild poliovirus.

The optimization of future options depends on current investments in research and analysis of current program data. For example, if the risks associated with cVDPVs appear significant after certification, then research conducted now to characterize the circumstances that increase or decrease the risk of cVDPV outbreaks can help identify appropriate efforts to minimize these conditions in the future. Research to identify more cost-effective ways to conduct environmental or serologic surveillance might make these options more attractive, particularly with respect to managing the potential risks of re-emergence due to a break in laboratory containment or bioterrorism. Anticipating that outbreak responders will face dilemmas about potentially reintroducing VDPVs into the population (ie, through responding with live vaccine), research done now that might improve the ability to understand the trade-offs could also be helpful.

The fact that neighboring countries' policies will influence a country-based policy maker's decision emphasizes the need for open discussion and coordination of policy making. The meeting in Annecy, France in April 2002 was the first forum for an open discussion that included individual country perspectives and the factors that influence their decisions (eg, costs, risk perception).[52] Without explicit coordination and commitment of containment, a country neighboring an eIPV-manufacturing country could perceive itself to be at increased risk for importations due to break in containment and choose to continue to vaccinate. The opportunity cost of those resources used to maintain a vaccination policy could exceed the cost of maintaining laboratory containment. Given that actions by a neighboring country affect a country's risk of reintroduction, coordinating country implementation of policy changes emerges as a critical issue for consideration and discussion. Finally, efforts to develop models that aid policy makers as they weigh the different alternatives and evaluate the risks, costs, and benefits of their choices will provide a means for stimulating dialogue and discussion of key issues and promote more informed decisions.

Conclusions

Although policy makers will face a complex set of choices in managing polio risks after certification, considering the logical relationships and feasibility leads to a more restricted set of practical options for the specific time period of 5 years following certification. We believe that our paper provides the first comprehensive synthesis of all potential choices at the country level and the factors that influence these choices. Policy makers must weigh these sets of policy options jointly. Moreover, discussions between countries regarding the implications of their policy choices for each other and globally must occur for policy makers at all levels to make the best policy decisions. Additional efforts to provide information to decision makers about the expected relative risks, costs, and benefits of these options and the trade-offs associated with making these choices are needed to inform the global policy discussions about polio risk management after certification.

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Editorial

Polio and Policy Options

William H. Foege, MD, MPH

Much of medicine is dependent on constant maintenance. Histories, physicals, laboratory tests, diagnosis, treatment plans, surgery, and daily medications need to be repeated endlessly. Constant attention is required to the details, to quality, and to the quest for improvement. Sometimes, as with surgery, a single encounter will be sufficient for the lifetime of that patient, but must be repeated for other patients.

On the community level, there are breakthroughs at times with medications or diagnostic tests that need be made only once. Even rarer is an opportunity to achieve an objective that never has to be repeated in the history of the world. Disease eradication fits in that category but has been realized only once to date. That happened 25 years ago with the last case of smallpox in the world. Now we face the possibility of accomplishing this goal for Guinea worm and for poliomyelitis.

Sangrujee and colleagues[1] have provided the most complete list of policy decision options for polio eradication to date. While there are some lessons available from smallpox, polio differs so markedly from smallpox that the overlap is not great. Most polio cases present no clinical signs or symptoms, and laboratory tests are required for polio while a clinical diagnosis could be made for most smallpox cases. Polio can roam a community undetected for periods of time while smallpox announced its presence with the first human infected in a community so that all were aware of the dangers.

The paper does us a favor by being explicit about options but then reaches the conclusion that the interdependence of policy decisions actually leads to a narrowed set of realistic decision options. Maybe there are even fewer real options than the authors have indicated.

What are the concerns? One constant worry is that interruption of transmission will not be achieved either because resources are insufficient or something goes wrong. What if a virus mutation produced a strain of polio no longer prevented by current vaccines? What if recent outbreaks due to vaccine strains lead to an outbreak that cannot be stopped with current vaccines? One option that must be discarded is any relaxation of effort at this stage. The window of opportunity must be seized before anything goes wrong. Since the time before interruption of transmission is resource-dependent, it is important to increase commitments at this time.

A second worry is that vaccine virus entering communities during waning immunity due to low coverage could lead to vaccine virus outbreaks. This seems to be the common factor with recent vaccine virus outbreaks. This would seem to limit the usefulness of two options. One is the use of oral polio vaccine (OPV) posteradication. The risks involved are untenable once the risk of wild virus is eliminated. A second option that might be excluded is the opportunity for country-by-country decisions on the use of OPV. Any country continuing OPV could constitute a risk to other countries. It would seem that a global approach to decision making is necessary.

A third worry concerns the reintroduction of wild virus after eradication is achieved. One source of virus could be the vaccine manufacturing process, which starts with wild virus. It should be possible to keep this risk to very low levels but it will be impossible to eliminate it totally. A second source of the virus might be from the thousands of laboratories world wide that have isolated the virus in the past. Every attempt is being made to purge laboratories of such specimens, but this can never be absolute since the virus may be in specimens collected for other reasons and laboratories would have no idea the virus is there. A third source could be deliberate release. While the use of polio virus by bioterrorists seems unlikely, the fact that it has been discussed makes it possible and must inform posteradication decisions. This is one lesson from smallpox eradication. We trusted everyone to follow civilized rules, and we now know that assumption has to be discarded. Whatever the source of virus, posteradication outbreaks constitute a risk for all countries, not just the country of virus release, another reason for global decisions rather than country-by-country decisions. Also, such outbreaks are likely to be monovalent, and it would be prudent for monovalent vaccine stockpiles to be developed. The FDA made a decision at one time that only trivalent vaccine would be licensed. That decision was logical at the time, but it is no longer of help and needs to be revised. While some countries may wish to have their own stockpiles, certainly the World Health Organization (WHO) should have global stockpiles located in various places around the world with the appropriate turnover in the stocks.

The use of inactivated polio vaccine (IPV) is already widespread in developed countries. It would have been reasonable for the WHO to have made combined programs of IPV and OPV the standard 10 years ago.[2] It would have speeded the course of eradication by reducing the number of visits required to each child and would have simplified the options now being discussed. It is now late, but not to late, to include IPV during the end game but also to provide continuing immunity when OPV is halted. The major reason for not including IPV in DTP in the past was cost. But the decision makers were looking only at the cost of vaccine. By reducing the number of visits to each child, the total campaign cost would have been reduced. The IPV vaccine cost is currently too expensive for routine use in developing countries; however, if it became the norm for the world, marginal prices would fall rapidly. If the incremental price of IPV would be reduced from the current level of dollars a dose to 15 cents per dose and assuming that 4 doses of DPT will become the global norm, the cost of polio maintenance in the future would drop to $60 million per year. Not only would this be a bargain for polio eradication maintenance, but it would also provide protection against a release of wild virus in the future. Outbreaks from future releases of the virus would be quickly contained with the background of all children having received IPV and an outbreak response using monovalent OPV.

On January 28, 2003, Dr. D. A. Henderson, speaking at the 35th anniversary of the National Institutes of Health's Fogarty International Center, said we should eradicate the notion of disease eradication and said, "The likelihood of ever truly eradicating polio [is] a near impossibility." This has led to understandable nervousness in the donor community but has also had an adverse impact on the many workers in polio eradication. The science is clear. The elimination of wild polio virus from large geographic areas has been predictable and successful. The elimination of wild polio virus from all populations is feasible. But oral polio vaccines, if used posteradication, provide unacceptable risks for individual cases and for vaccine virus outbreaks. It will have to be stopped. At the same time, the use of IPV in rich countries but not in poor countries would be untenable. The decision a decade ago to withhold IPV from poor countries was wrong but could now be corrected. But the window of opportunity is narrow and must be seized quickly. It will be another fine hour for global health.

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