OPV vs IPV: Past and Future Choice of Vaccine in the Global Polio Eradication Program

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Abstract

With the world approaching the post-eradication phase of polio control, two questions have been raised: (1) should polio vaccination be stopped or continued after global certification of polio eradication? (2) if vaccination is continued, what vaccine should be used? There has been no decisive answer to the first question. However, the possibility of a global switch from current oral polio vaccine (OPV) to inactivated polio vaccine (IPV) after global eradication of polio (the second question) is being debated. One of the barriers to such a switch is that the cost is thought to be prohibitively high for developing countries. This study estimates the incremental cost of a vaccine switch in developing countries.

The estimates show that the switch from OPV to IPV in its current presentation for all developing countries together will result in an increase in total annual cost of $317 million, averaging $2.91 per child. Overall, in developing countries the switch will need $1 million to avoid a case of vaccine-associated poliomyelitis paralysis through the switch of vaccines. For the low-coverage countries, the vaccine switch will lead to a net increase in costs of about $26 million, averaging about $2.42 per target child. For intermediate-coverage countries, the switch will result in an increase in total cost of $129 million, averaging about $2.68 per target child. For high-coverage countries, it will result in an increase in the total cost of $162 million, an average of about $3.26 per target child.

A switch to an IPV only (or, IPV-only strategy, program, etc.) would entail significant incremental costs and introduce additional epidemiological risks, including unsafe injections and the release of wild virus in the IPV production process. The benefit of the switch would come from elimination of: (1) a limited number of vaccine-associated polio paralyses and (2) a few polio cases caused by circulating vaccine-derived poliovirus. These benefits ultimately will need to be weighed against the high incremental costs and increased risks that would come with the switch. There are reasons to challenge either continuing to use OPV or to switch to IPV post eradication in developing countries. Another option would be to cease all polio vaccination for those countries deciding not to switch to IPV. This option relates to the first question above and needs further investigation that is beyond the scope of this analysis.

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Acronyms

ACIP	Advisory Committee on Immunization Practice
AFP	Acute Flaccid Paralysis
cVDPV	Circulating Vaccine-Derived Poliovirus
DTP	Diphtheria, Tetanus, Pertussis
EPI	Expanded Program on Immunizations
GNP	Gross National Product
Hib	Haemophilus Influenzae Type B
HIV	Human Immunodeficiency Virus
IPV	Inactivated Polio Vaccine
NID	National Immunization Day
OPV	Oral Polio Vaccine
TCG	Technical Consultative Group
VAPP	Vaccine-associated Poliomyelitis Paralysis
WHO	World Health Organization

Acknowledgments

Executive Summary

With the world approaching the post-eradication phase of polio control, public health experts and health care policymakers are debating the issue of appropriate endgame vaccine strategies following the global certification of polio eradication. Four vaccine strategy options have been outlined (Wood, Sutter, and Dowdle 2000; Vaccines and Biologicals of the World Health Organization 2002): (1) continued OPV vaccination; (2) coordinated discontinuation of OPV (with or without IPV, depending on national decisions); (3) replacement of OPV with IPV in all countries before final cessation of polio immunization; and (4) development of new live vaccines that would not cause vaccine-associated poliomyelitis paralysis (VAPP) and would not be transmissible.

This study was undertaken to address the third option and contribute to the debate over the choice of vaccine strategy – OPV or IPV (in its current presentation, which consists of all three serum types of polio vaccine) – during the post-eradication era of the polio control program. The objectives of this paper are to review the choices of polio vaccines at different stages of polio control program; to inform policymakers who must choose appropriate vaccine strategies in developing countries in the post-eradication period about the effectiveness and incremental cost of a vaccine switch; and to provide policymakers with suggestions for the appropriate use of study findings as well as other, non-financial considerations in making their decisions of vaccine choice.

The review of historical vaccine choices found that during the period of pre-eradication the vaccine choice between OPV and IPV by individual countries varied. Evidence shows that both vaccines are able to bring wild virus transmission under control. Once polio had been eradicated at the country level, some countries that had used OPV exclusively switched to IPV to avoid the occurrence of VAPP, but they did so at a significant incremental cost; others continued to use OPV, bearing the risk of VAPP. At the international level, the global polio control program has used OPV exclusively. While this strategy has succeeded in ending the transmission of wild poliovirus, it is being challenged by the fact that, after the global eradication of polio, all cases of paralytic poliomyelitis will be VAPP associated with the use of OPV. Policymakers are thus facing the difficult task of choosing a vaccine strategy for the global program in the post-eradication era.

If the choice is to continue with the status quo (routine OPV immunizations, and National Immunization Days conducted every three years in countries with OPV3 coverage less than 90 percent) in the post-eradication era in developing countries, the expected results are that (1) there will be about 300 cases of VAPP per year due to the infection from the vaccine virus, and (2) there will be persistent risk of vaccine-derived polio outbreak due to continuous introduction of vaccine virus and the existence of circulating vaccine-derived poliovirus (cVDPV). If the choice is to switch from an OPV-only program to an IPV-only regimen, the 300 cases of VAPP can be avoided and the risk of outbreak resulting from cVDPV can be greatly reduced, but at a significant incremental cost. Overall, $1 million will need to be spent on IPV per case of VAPP avoided in developing countries.

The incremental cost of a vaccine switch primarily depends on the price of IPV (in its current presentation). The total annual incremental cost can be as low as $128 million if the price of IPV is $0.50, and as high as $678 million if the price is $2.00. At an IPV price of $1.00 per dose for all developing countries, the vaccine switch will result in increased total costs of $317 million per year,

and an average incremental cost per target child of $2.91. For low-coverage countries, the total increase in cost will be about $26 million, averaging about $2.42 per target child. For intermediate-coverage countries, the total increase in cost will be $129 million, averaging about $2.68 per child. For high-coverage countries, the total increase in cost will be $162 million, averaging $3.26 per target child.

The analysis considered the cost of treatment of VAPP in the estimation of incremental costs of a vaccine switch. However, due to a lack of data, the analysis does not account for costs avoided with reduced risk of cVDPV, nor for the increased costs of unsafe injections. A switch to a policy of IPV-only would entail significant incremental costs and introduce additional epidemiological risks, including unsafe injections and the possible release of wild virus in the IPV production process. The benefits of the switch would come from the elimination of: (1) a limited number of VAPP cases; and (2) a few polio cases caused by cVDPV. These benefits ultimately will need to be weighed against the incremental costs and increased risks that would come with the switch.

However, the possibility of a vaccine switch in individual countries could be considered. Due to differences in incremental costs of a vaccine switch, the perception of benefits and risks, and ability to pay extra costs, the acceptance of a vaccine switch will be different, and so some countries may conduct a vaccine switch while others may not. The results suggest that high-coverage countries have an advantage over low-coverage countries for a vaccine switch because they can more easily afford the additional cost since they are likely to have higher per capita income, and they also have a lower risk of polio outbreak with a vaccine switch. If the benefits of switching to IPV are considered to be greater than costs for all countries, an ethical argument could be made for richer countries to subsidize costs of the switch for poorer countries.

Policymakers should interpret the findings of this study with caution. Changes in the input data used in the analysis could change results and recommendations. In addition, policymakers should consider issues beyond the financial ones explicitly addressed in this paper. The potential supply of IPV (which is affected by technical production capacity, the predicated price of vaccine, the expected life years of production, and possible public intervention in vaccine production), the epidemiological risks and health benefits of a vaccine switch, as well as the different approaches to the vaccine switch (a global switch vs. individual country switch) need to be carefully considered in choosing vaccines for the post-eradication era of the polio eradication program.

The weak support provided for a switch to IPV does not mean a strong support for continuing OPV, since both continuing with OPV and switching to IPV are costly options. Further, both options mean uncertain and, possibly, small benefits. Another option is to cease polio immunization altogether for countries deciding not to switch to IPV. This option would require maintaining a stockpile of vaccine sufficient to respond to emergencies. However, this is not the focus of this report and would merit further investigation.

1. Introduction

The choice between live attenuated oral polio vaccine (OPV) and inactivated polio vaccine (IPV) for the prevention of poliomyelitis has been the subject of a longstanding debate between the Sabin (1987) and Salk (1987) schools. The two schools advocate OPV-only and IPV-only vaccination policies, respectively, and neither has been able to convince the other (Plotkin 1997; Henderson 1997). The reason behind the debate is that each vaccine has advantages and disadvantages (see Annex A) as specified by a number of authors (Eichner and Hadeler 1995; Chin 1984; World Health Organization 1997a; and Willis et al. 1997). Because of lack of worldwide consensus, the choice between these two vaccines has varied among countries and at different stages of the polio control program. Currently the debate on choice of vaccines is becoming intense because the global polio eradication program is approaching a time when public health experts and policymakers will have to choose a vaccine strategy that will be used after global certification of poliomyelitis eradication.

Polio eradication has required a huge global investment. Estimates of total spending range from $3 to $5 billion. Although countries will ultimately have to choose which vaccine, or none, to select in the post-eradication era, they will be looking to the Global Polio Technical Consultative Group (TCG) for guidance and recommendations. A policy statement and recommendation will be needed within the next few years to help guide vaccine selection, prioritize limited IPV supply, and coordinate plans for stopping immunization.

The objective of the paper is to inform policymakers about financial implications as one element in their choice of vaccine for the post-eradication era by analyzing the incremental cost of a vaccine switch from OPV to IPV (in its current presentation, which consists of all three serum types of polio vaccine) in developing countries[1]. The report consists of four sections. Following this brief introduction, the second section reviews the history of vaccine choice at different stages of the polio control program and describes the choices now facing policymakers. The third section provides an estimation of the number of vaccine-associated paralytic poliomyelitis (VAPP) cases under OPV immunization and an analysis of the incremental cost of a vaccine switch to IPV (in its current presentation) in developing countries. The fourth section is a discussion of and suggestions on how to interpret the results and what other factors need to be considered by policymakers. It also summarizes the main findings and implications.

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[1] Developing country is defined as low-(with annual per capita income of $755 or less) and middle-income countries (with annual per capita income of $756-9265) in which most people have a lower standard of living with access to fewer goods and services than do most people in high-income countries (World Bank 2001). This study included 125 developing countries. There are 19 in the low immunization coverage group (50 percent or less), 30 in the medium coverage group (51-79 percent), and 76 in the higher coverage group (80 percent or higher).

2. Reviewing the History of Vaccine Choice

The history of vaccine choice can be divided into four non-consecutive stages: pre-eradication for individual countries; post-eradication for individual countries; pre-eradication worldwide; and post-eradication worldwide. Pre-eradication for an individual country covers a long period of time, from the development of polio vaccines until the interruption of wild poliovirus transmission in that country. Post-eradication for individual countries refers to the period during which wild poliovirus transmission is interrupted in certain countries but not in others. The stage of pre-eradication worldwide overlaps with post-eradication for individual countries. It covers the period from the start of the Global Polio Eradication Initiative to the interruption of wild poliovirus transmission worldwide. Post-eradication worldwide refers to the era after the global interruption of wild poliovirus transmission.

2.1 Pre-eradication for Individual Countries

Two vaccines are available to prevent and control polio epidemics: oral polio vaccine and inactivated polio vaccine. Due to lack of worldwide consensus on which offers the best overall net benefit, national-level public health experts and policymakers have had to balance the advantages and disadvantages of each vaccine when making their nation's vaccine choice. As would be expected, the choice across countries has not been uniform (Murdin, Barreto, and Plotkin 1996). Some countries (such as Finland and the Netherlands) use IPV in their routine immunization programs, while others (such as the United States and Cuba) have used OPV in their programs.

Interestingly, epidemiological evidence has shown that both vaccines worked well. By the 1970s, transmission of wild poliovirus had been interrupted in the northern European countries (Murdin, Barreto, and Plotkin 1996), where IPV was exclusively used. In Cuba and the United States, where OPV was exclusively used at that time, wild poliovirus transmission was also successfully interrupted (John 2000).

In addition, a review of 48 outbreaks of paralytic poliomyelitis worldwide from 1979 to 1995 (Patriarca, Sutter, and Oostvogel 1997) suggested that outbreaks had occurred in both OPV-only and IPV-only countries, but the documented reason for the outbreaks was inadequate immunization coverage. There was no evidence that the outbreaks were associated with the choice of vaccine.

Furthermore, in countries where IPV was the choice for routine immunization, OPV has consistently been used for immunization campaigns. The countries used this approach because of OPV's advantage in stimulating intestinal immunization, which limits the multiplication and transmission of poliovirus. For example, in 1984, there was an outbreak of poliomyelitis (10 cases of paralysis and 100,000 infections) in Finland where IPV had been used for 25 years and there had been no cases of poliomyelitis for 20 years. OPV was used for the immunization campaign during the outbreak, and 94 percent of the population was immunized (Hovi 1995). In the Netherlands, OPV was used for immunization campaigns to combat poliomyelitis outbreaks in 1977 and 1992 (Wood, Sutter, and Dowdle 2000). Evidence suggested that the immunization campaign using OPV could effectively terminate the outbreak and interrupt wild poliovirus transmission.

However, many investigations show that while in developed countries three doses of IPV or OPV can produce a protection rate of 98 percent, in developing countries it was consistently found that OPV is much less effective than IPV. Two doses of IPV can generate a protection rate of 89 percent, while the protection rate of two doses of OPV is only 72 percent. Three doses of IPV can protect almost 100 percent of the children, while three doses of OPV protect less than 85 percent of the children (Beale 1990; Moulia-Pelat, Garenne, Schlumberger, and Diouf 1988). The reasons for the difference in OPV efficacy in developed and developing countries are not clear. Problems with the cold chain explain only a small part of the difference. The major reason might be the interference of other virus infection, e.g., diarrhea caused by viruses, which hinders the uptake of OPV (Tulchinsky et al. 1994).

2.2 Post-eradication for Individual Countries

OPV-only countries where wild poliovirus transmission has been stopped once again face a difficult choice. Once wild virus transmission is stopped, all the cases of paralytic poliomyelitis are caused by OPV vaccinations, that is, by VAPP. In other words, protecting children against the risk of poliomyelitis caused by wild poliovirus incurs two types of costs: (1) the cost of vaccination, and (2) the cost of the occurrence of VAPP. The switch of vaccine from OPV to IPV is a hard choice since the current price of IPV is much higher than the price of OPV (Bart, Foulds, and Patriarca 1996; World Health Organization 1999).

In the history of polio vaccination, countries such as the United States, Canada, France, Germany, Sweden, Finland, and the Netherlands made the switch from OPV to IPV or never used OPV, either because these countries had been polio-free for many years and most had excellent routine immunization coverage, or because they perceived a lower risk of wild poliovirus transmission and higher perceived risk of VAPP (World Health Organization 2000a). Also, these countries were developed countries and could more easily afford to pay the higher costs of IPV.

The United States is a typical case. Soon after the introduction of OPV in 1961, the United States began using it in place of IPV. Polio immunization entered into an OPV-only era. The use of OPV brought the transmission of wild poliovirus to an end in 1979, when the last case of indigenously acquired wild poliovirus disease was reported (U.S. Centers for Disease Control and Prevention 1986). Nevertheless, from 1980 to 1994, 133 cases of paralytic poliomyelitis were reported, among which 125, an average of eight cases each year, were associated with the use of OPV (Sutter et al. 2000).

The continued occurrence of VAPP, coupled with the absence of disease due to wild poliovirus, led to renewed debate in the early 1980s as to whether OPV or IPV was the more appropriate formulation for routine use in the United States. The debate continued to the 1990s. In January 1997, the Advisory Committee on Immunization Practice (ACIP) (1997) in the United States recommended the adoption of a sequential IPV/OPV vaccination schedule (injections of IPV at 2 months and 4 months of age, followed by OPV at 12 to 18 months and again at 4 to 6 years). This schedule was intended to minimize the risk for VAPP (because the risk of VAPP for the birth dose of OPV is much higher than for the subsequent doses), while maintaining population immunity to the potential introduction of wild-type poliovirus (U.S. Centers for Disease Control and Prevention 1999). The 1997 change in the polio immunization schedule resulted in a reduction of the number of VAPP from eight cases per year before 1997 to five cases in 1997 and one case in 1998 (U.S. Centers for Disease Control and Prevention 1998).

Along with the increasing use of IPV and the continued existence of the risk of VAPP, in June 1999, the ACIP recommended the IPV-only regimen for routine immunization. On January 1, 2000, the transition from the IPV/OPV sequential immunization schedule to the IPV-only schedule took place, and was completed by June 30, 2000 (American Academy of Pediatrics, Committee on Infectious Disease 1999).

The two changes of polio vaccination policy in the United States resulted in about a 20 percent increase in costs. The switch from the OPV-only to the IPV-OPV sequential vaccination added an extra $20 million a year to the $230 million OPV-only program. The switch from the IPV-OPV sequential vaccination to the IPV-only vaccination added another $20 million to the program. The cost per case of VAPP avoided was estimated as $3.1 million for the change to a sequential schedule, and $3.0 million for the change to an all-IPV schedule (Sutter et al. 2000).

The switch from OPV to IPV following polio interruption typically has been made in developed countries. To date no switch has been reported in developing countries where poliomyelitis has been interrupted. OPV alone is still used in developing countries. The reasons for not making a switch are unclear; they probably include inertia, the increased cost of using IPV, the fear of an outbreak associated with possible lower immunization coverage after the switch,[2] and the lack of registration of IPV in the countries. The reason is clearly not due to a lower rate of VAPP than in developed countries. Generally, risk of VAPP in developing countries falls between 1 case per 1.4 million doses of OPV to 1 case per 2.5 million doses, which is equivalent to the rate in the United States and the United Kingdom. For example, a study in Latin American countries showed that from 1989 to 1991 the risk of VAPP was one case per 1.5-2.2 million doses (Andrus et al. 1995).

2.3 Pre-eradication Worldwide

The global program of polio control began when the Expanded Program on Immunizations (EPI) was established by the World Health Organization (WHO) in 1974. At that time WHO made a policy choice for OPV, to the exclusion of IPV, for good and obvious reasons: it was easy to give; it was more suitable for developing countries due to its secondary immunization effect; and its price was low. While the debate has never stopped (Plotkin 1997; Henderson 1997), the World Health Assembly again chose OPV when the Global Poliomyelitis Eradication Initiative was launched in 1988.

The goal of the global polio eradication initiative was that by the end of 2000, poliomyelitis transmission would be interrupted; and by the end of 2005, the world would be certified as polio-free (World Health Organization 1997a; John 2000). The most important criterion for certification of a country, a region, or indeed the world is the absence of poliovirus under conditions of adequate surveillance isolation for at least three years (Wood, Sutter, and Dowdle 2000).

Four operational approaches have been used in the eradication initiative (World Health Organization 2000a): high routine immunization coverage with at least four doses of OPV in the first year of life; annual National Immunization Days (NIDs), during which two supplemental OPV doses in an interval of a month are given to all children less than 5 years of age regardless of prior immunization status; laboratory-based surveillance for all cases of acute flaccid paralysis (AFP) under the age of 15; and house-to-house mop up.

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[2] The immunization coverage with IPV might not be as high as with OPV since the former requires a higher level of resource input and is less easy to deliver.

Evidence suggests that the exclusive use of OPV for EPI and the global polio eradication initiative is the right choice. The OPV-based polio eradication initiative has been proven to be highly effective (Vaccines and Biologicals of the World Health Organization 2002; World Health Organization 2000a): In 1994, WHO certified the Americas as polio-free; the WHO Western Pacific region was certified in October 2000; the WHO European region was certified in June 2002. Widely endemic on five continents in 1988, polio at the end of 2002 was concentrated only in parts of sub-Saharan Africa and the Indian subcontinent. In the first 12 years of the eradication initiative, the number of cases fell by more than 95 percent from an estimated 350,000 cases per year; the number of polio-infected countries fell from 125 in 1988 to 20 in 2000; and more than 190 countries and territories had interrupted poliovirus transmission. Between 2000 and 2001, the number of reported polio cases fell from 2971 to 480, with only 10 countries remaining polio-endemic at the start of 2002.

2.4   Post-eradication Worldwide

Within two years it is hoped that transmission of wild poliovirus in the remaining handful of countries can be stopped. Three polio-free years need to follow the last case before global certification can be considered. This brings the earliest possible date for global certification to 2007 under the best circumstances. Only after global certification, would the world enter into the post-eradication era.

Once again, the choice of vaccine is on the agenda. Four vaccine strategy options have been outlined (Wood, Sutter, and Dowdle 2000; Vaccines and Biologicals of the World Health Organization 2002): (1) continued OPV vaccination; (2) coordinated discontinuation of OPV (with or without IPV, depending on national decisions); (3) replacement of OPV with IPV in all countries before final cessation of polio immunization; and (4) development of new live vaccines that would not cause VAPP and would not be transmissible. This study was undertaken to assist in addressing the third option and contribute to the debate over the choice of vaccine strategy – OPV or IPV during the post-eradication era of the polio control program.

There are multiple reasons for reconsidering the value of IPV. Firstly, the continued use of OPV will result in the continuous occurrence of VAPP. This adverse effect will become more prominent when paralytic poliomyelitis caused by wild poliovirus is non-existent. Secondly, the continued use of OPV means the continuous transmission of vaccine virus, which may cause the reversion of the vaccine virus to the wild-type virus – circulating vaccine-derived poliovirus (cVDPV) – with neurovirulence (Fine and Carneiro 1999). This has already resulted in polio outbreaks in a number of countries (U.S. Centers for Disease Control and Prevention 2001a, and 2001b; CDC 2001; Wood 2002). The occurrence of VAPP and the risk of cVDPVs are considered unacceptable in the post-eradication era. Thirdly, because of the possibility of prolonged transmission of vaccine virus, the eventual cessation of vaccination following the use of OPV would put the population at greater risk than if the cessation follows the use of IPV.

Although the switch from OPV to IPV can eliminate the problems of OPV, IPV has its own shortcomings. Firstly, it needs a higher level of resource input since the current price of IPV is much higher than that of OPV; and vaccination with IPV, unlike OPV, requires use of trained health workers and injection supplies. Secondly, the use of IPV might result in an increase in both the number of susceptible persons if, because of more complex vaccine administration, the coverage achieved with IPV is not as high as it would be with OPV (hence increasing the risk of transmission of wild poliovirus), and the number of blood-borne infections (e.g., Hepatitis B and HIV) due to unsafe injections. Thirdly there is a risk of escape of the wild poliovirus from IPV production.

WHO has decided that immunization and high-quality surveillance need to continue for a number of years after the last case of poliomyelitis is detected (World Health Organization 2000a). What has not been decided is which vaccine or combination of vaccines will be recommended for use. Another issue related to the choice of vaccine is that even after the certification of polio-free world (three years after the last case is detected), there will still be a need for vaccination (World Health Organization 1998; Wood, Sutter, and Dowdle 2000). The choice between OPV and IPV has to be made.

Individual countries as well as global effort in the past have made their choice of vaccine for the eradication of poliomyelitis. While the choice of vaccine in the worldwide program was consistently OPV, the choices by individual countries varied. With the approach of global eradication of poliomyelitis, a new and probably harder choice of vaccine faces health experts. It is more serious because it goes beyond the trade-off between the traditional advantages and disadvantages of OPV and IPV, and because it is part of the technical preparation for the worldwide cessation of polio vaccination. This paper contributes to the decision process by examining the financial implications of the choice.

3. Informing the Future Choice

This section first lays out the scenarios of vaccine choice and specifies the cost and effectiveness information needed to help inform the choice. It then estimates the effectiveness and cost based on data available plus some assumptions. The information generated in this section is intended to assist decision makers in choosing the most appropriate scenario for developing countries when global polio control enters the post-eradication era.

3.1 Scenarios of Vaccine Switch and Information Needed to Make the Choice

The scenarios of vaccine switch can be classified based on the choice of vaccine (OPV-only strategy, IPV-only strategy, and a sequential use of both OPV and IPV), the pattern of vaccine switch (global vaccine switch vs. vaccine switch in individual countries), and vaccine presentation (IPV vs. IPV in combination presentations or combos, such as IPV-DTP and IPV-Hib). To simplify the analysis procedures, this report focuses on two vaccine choices – either OPV-only (baseline scenario) or IPV-only strategy (alternative scenario) – firstly because this is the focus of current debate, and secondly because sequential use of the two vaccines cannot eliminate the problem of VAPP occurrence and is considered to be an interim approach. In addition, IPV refers to its current presentation because IPV in other presentations, combinations, etc. are not currently available. The development, licensing and introduction of new vaccines and presentations are years away and not anticipated before the post-eradication era would start. In addition, the final price of a combination vaccine is uncertain.

To choose a vaccine strategy, decision makers will have to balance the costs and effectiveness associated with the alternatives. In choosing the cost and effectiveness measures, this analysis considers the following characteristics. First, the choice is conditioned by the existing program. That is, the concern is whether the switch from the existing OPV-only to an IPV-only program is economically desirable, rather than a comparison of starting a new program with either OPV or IPV. Thus, the relevant cost is the incremental cost of vaccine switch, rather than the full cost of the program using IPV (in its current presentation). Second, effectiveness cannot be measured by the occurrence of poliomyelitis caused by wild poliovirus because poliomyelitis transmission soon will have been interrupted worldwide and three years hence the world is expected to be certified polio-free. The continued use of vaccine is to protect against a very small risk of outbreak. It is expected that the effective and sufficient use of either vaccine can provide enough protection to prevent any outbreak caused by wild virus. Third, the continued use of OPV will mean continued occurrence of VAPP and the circulation of cVDPV. These represent costs associated with the use of OPV.

The major focus of this analysis is to look at the additional cost incurred to avoid the occurrence of VAPP and to reduce the risk of cVDPV by switching vaccines in developing countries. Two questions will be answered: First, what is the expected number of VAPP per year if OPV is continued in the developing world? Second, what are the incremental costs of the polio immunization program and the incremental cost per immunized child if vaccination is switched from OPV to IPV?

In the analysis, the baseline scenario following the global certification of polio eradication is assumed to be the projected status-quo in which OPV will still be used in both routine immunizations and National Immunization Days (NIDs), conducted every three years in countries with OPV3 coverage less than 90 percent, as recommended by TCG (Vaccines and Biologicals of the World Health Organization 2002). In the alternative scenario, IPV will be exclusively used and IPV NIDs will be conducted in low-coverage countries. In the estimation of incremental costs of a vaccine switch, the avoided treatment cost of VAPP is deducted from the increase in immunization costs. The reduced cost associated with the decrease in risk of cVDPV resulting from a vaccine switch is not considered due to lack of data. Thus, the results slightly overstate the net cost of the switch to IPV.

3.2   Estimation of VAPP

The method for estimating the number of VAPP cases appears straightforward. It equals the risk of VAPP (measured by the case/dose ratio) multiplied by the total number of doses of OPV vaccination. The latter is the product of the number of OPV doses per child and the number of target children in developing countries. However, the following issues complicate the estimation. (1) The risk of VAPP varies across countries and for different sequential doses (Fescharek et al. 1997). (2) The number of doses of OPV per fully immunized child varies depending on different routine immunization schedules and variations in the actual number of NIDs conducted. (3) The occurrence of VAPP can take place among both OPV recipients and their contacts. (4) The risk of VAPP is high among the immuno-compromised. To simplify the methods of estimation and produce a reasonable estimate for the number of VAPP in developing countries, the following methods and data are used:

- ▲ The total number of VAPP cases is estimated based on the average number of OPV doses given and the overall risk of VAPP described in the literature, assuming that all children in developing countries are immunized with OPV.

- ▲ The scheduled number of OPV doses per infant is four from routine immunization plus an additional two doses from NIDs, which are supposed to be conducted every three years after global certification of polio as recommended by WHO (Vaccines and Biologicals of the World Health Organization 2002).

- ▲ The average number of doses of OPV given is the sum of total number of doses for routine immunization and the total number of doses given during NIDs. It is calculated using this formula: the total number of OPV doses per year = [(total number of surviving infants of the birth cohort × the number of routine doses per infant) × routine immunization coverage rate] + [[(the number of 0-year children + the number of 1-year-old children + the number of 2-year-old children + the number of 3-year-old children + the number of 4-year-old children) × the number of doses per child per NID] × NID coverage rate × 1/3.]

- ▲ The total number of surviving infants of the birth cohort in developing countries is estimated at 108,944,000 (UNICEF 2001), which is the number of live births (116,269,000) adjusted by the infant mortality rate (63 per 1000 live births) as specified by UNICEF (2001).

- ▲ The number of doses per child 0-to 4-years-old during NIDs is two per child, and the routine immunization coverage rate is 74 percent (UNICEF 2001). It is believed that the coverage rate for NIDs is higher than that of routine immunization, ranging from 80 percent to 90 percent. Here we assume a coverage rate of 85 percent for NIDs.

The reported risk of VAPP ranges from as high as 1 per 183,000 doses of OPV in Romania (Strebel et al. 1994) and as low as 1 per 4.5 million doses in India (Kohler et al. 2002). Based on the figures in Table 1, we used an overall risk of 1 case of VAPP per 2.0 million doses of OPV delivered.

Table 1. The Reported Risk of VAPP of OPV Immunization by Countries

Sources	Country	Risk of VAPP of OPV
Andrus JK et al. (1995)	UK	1 per 1.4 million
CDC (1997)	United States	1 per 2.4 million
Strebel et al. (1994)	Romania	1 per 183,000 doses
Lei, Li, and Xu (1996)	China	1 per 1.25 million doses
Kohler et al. (2002)	India	1 per 4.1 to 4.6 million doses
Andrus JK et al. (1995)	Latin America	1 per 1.5-2.2 million doses

Table 2. The Numbers of Target Children and the Numbers of Doses of OPV from Routine Immunization and National Immunization Days in Developing Countries

Types of immunization	Age groups	Number of children (000)	Number of doses per child	Immunization coverage rate	Number of doses (000)
Routine	0-year old	108,944	4 + 2/3	74%	376,220
National immunization days	1-year old	108,209	2/3	85%	61,318
	2-year old	107,474	2/3	85%	60,902
	3-year old	106,749	2/3	85%	60,491
	4-year old	106,028	2/3	85%	60,083
Total	----------------	----------------	-----------------	------------------	619,014

Based on the above methods of estimation and data available (as shown in Table 2), it is estimated that if all the children in developing countries are immunized exclusively with OPV, there will be about 619 million doses of OPV delivered to children in developing countries and about 300 cases of VAPP per year.

3.3   Incremental Cost of the Vaccine Switch in Developing Countries

The incremental cost of the vaccine switch is defined as the net increase in the total annual cost of the polio eradication program due to the change from the OPV-only strategy to an IPV-only strategy (in IPV's current presentation). This section estimates the incremental cost associated with such a switch in developing countries. In the analysis, developing countries are divided into three groups according to their 2000 OPV3 coverage rate: low-coverage countries with a coverage rate of 50 percent and below; intermediate-coverage countries with a rate of 51-79 percent; and high-coverage countries with a rate of 80 percent and above.

There are three reasons for this grouping. First, a vaccine production capacity constraint may make it impossible for all countries to switch at once. Thus there is a question of in which countries is it more feasible to conduct a vaccine switch. Second, the coverage rate is associated with and thus

may be used as a proxy for the economic development level of the country.[3] This is important because the incremental costs of a vaccine switch differ when labor costs for administering vaccines differ. Countries with lower per capita income will have lower labor costs per dose of vaccine delivered. Third, to assure a high level of protection, low-coverage countries need NIDs to increase coverage, while high-coverage countries do not. These factors cause differences in costs among countries.

To estimate the incremental cost, the approach is to identify the types of costs that will increase and the types of costs that will decrease with the switch. The total incremental cost equals the difference between the increased costs and the decreased costs.

The switch to IPV leads to the following increases and decreases in costs. (1) The cost of vaccine will increase because the current price of IPV is at least five times higher than that of OPV and the decrease in the number of vaccine doses when using IPV does not cancel the effect of the higher vaccine price. (2) The cost of vaccination supplies will increase because of the need for injection supplies including syringes, needles, and cotton. (3) There will be an increase in the transportation cost of supplies. (4) The cost of sterilization and waste disposal will increase due to the increase in the use of vaccination supplies associated with injections. (5) The cost of training will increase, because the switch requires start-up training for health workers in order to administer IPV and safely dispose of associated wastes. (6) The cost of vaccine storage and transportation may decrease or increase depending on the total volume of each vaccine needed. (7) The cost of vaccination visits is expected to decrease because of the decrease in the number of vaccinations (because the number of vaccinations per child with IPV is less than that with OPV). (8) The cost of VAPP would be eliminated. The total incremental cost of the vaccine switch would be the sum of the net changes of the above items.

The values used in the analysis for the above-listed cost elements are based on reported data as well as educated estimates. The types of data used in the incremental cost estimates, the sources of data, and the methods of estimation are specified as follows:

- ▲ The number of target children for routine immunization of both OPV and IPV is assumed to be equal to the number of surviving infants of the birth cohort. The number of target children for OPV NIDs is assumed to be the sum of children under 5-years old. The target children for IPV NIDs are those under 5-years old who have received fewer than three doses of IPV.

- ▲ The number of doses per immunized child for the OPV-only program is four doses for an infant from routine immunizations and two doses for a child of 0-to 4-years old from NIDs, which are conducted every three years in low-coverage (less than 90 percent) countries. The number of doses of IPV is three for an infant from routine immunizations. The number of doses of IPV per child (only for those not receiving three routine doses) from NIDs is on average two (assuming the incompletely immunized children are evenly distributed between zero, one, and two doses). The individual protection rate of the current OPV strategy is assumed equivalent to three doses of IPV. There is no need to provide more than three doses of IPV, because reports have shown that three doses of IPV provide very high protection in both developing and developed countries (Beale 1990).

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[3] Regression analysis for 125 developing countries for which data are available show that immunization coverage (OPV3) is correlated with the log value of GNP per capita (F=60.97 P<0.0001). According to the regression model, countries with a low level of coverage usually have a GNP per capita of less than $300; countries with intermediate coverage usually fall in the GNP per capita range of $301 to 999; countries having a GNP per capita of more than $1000 tend to have a higher level of immunization coverage.

▲ It is assumed that, after the vaccine switch, (1) for the high-coverage countries, the IPV immunization target (90 percent) can be achieved through routine immunization; (2) for the intermediate-coverage countries additional social mobilization is needed to strengthen the routine immunization to reach the target of 90 percent; (3) for low-coverage countries, IPV NIDs are needed to achieve the target. The coverage rate for NIDs using either OPV or IPV is assumed to be 85 percent, as stated earlier. For both OPV and IPV a NID is supposed to be conducted every three years.

▲ The wastage rate of OPV is assumed to be 20 percent, based on a predicted reduction of the reported wastage rate of 40 percent (World Health Organization 1997a) resulting from increased use of Vaccine Vial Monitors.

▲ The vial volume per dose is 0.2 *ml* for OPV (two drops of OPV liquid per vaccination) and 0.5 *ml* for IPV based on current practice.

▲ The prices of the vaccines used in the analysis are $1.00 per dose for IPV[4] in its present presentation; $0.10 per dose for OPV including the unit cost of freight (Bart, Foulds, and Patriarca 1996; World Health Organization 1999; UNICEF Office in Ghana 2001). (See Annex B for a discussion of expected changes in vaccine prices). In the sensitivity analysis, the price of IPV is varied between $0.50 and $2.00 per dose.

▲ Data on the unit costs of vaccination supplies (syringes, needles, and cotton) per vaccination injection are limited. Because of the variation in types of syringes, and the possible large difference in their prices, it is difficult to provide a precise estimate of the unit cost. It is assumed that auto-destruct syringes will be used by all countries as is being promoted by UNICEF and WHO. Based on the study of Kaddar, Levin, Dougherty, and Maceira (2000) in Côte d'Ivoire, and the UNICEF Office in Ghana (2001) the cost of auto-destruct syringes per vaccination is about $0.08.

▲ The unit cost of transportation of supplies per injection is $0.01, about 10 percent of the cost of supplies (UNICEF Office in Ghana 2001).

▲ The unit cost of sterilization and waste disposal per injection may vary depending on the types of syringes and the methods of waste disposal. It is assumed that a cost of $0.01 per injection is added for necessary sterilization and wastage disposal that is required for injection safety (UNICEF Office in Ghana 2001).

▲ The unit cost for vaccine storage per liter is based on the estimate provided by Lloyd (2001) in his draft tool for the estimation of the cost of vaccine storage and distribution. The estimate is $4.09 per liter of vaccine, which includes the costs at all levels of vaccine storage from the time of vaccine purchase to the time of vaccine consumption. It is assumed that there is no difference in the unit cost of maintaining the vaccines at the appropriate temperature because both vaccines are to be stored at a temperature of 0-8C.

▲ The unit cost for vaccine transportation per M^3 is also estimated based on the work of Lloyd (2001). He estimated that the cost of vaccine transportation is $0.91 per M^3 per kilometer.

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[4] The current price of IPV is $2.50 per dose in the public sector of developing countries (Milstien 2001). The $1.00 estimation is based on the assumption that the increased use of IPV will enable the vaccine buyers to negotiate a better price. We use $1.00 per dose, rather than $0.50 per dose as estimated by WHO (1997b) to avoid underestimation of the incremental cost of vaccine switch.

We assume that the vaccine has to travel on average 500 kilometers from central storage to the point of vaccination; the unit cost per M^3 is $455.

▲ For the estimation of the labor cost per OPV dose for the three groups of countries, we assume the income of an average health worker is two to three times the country's per capita GNP. Based on the relationship between per capita GNP and immunization coverage (see footnote 3), the average annual income of health workers in low-coverage countries is estimated to be $1000; in intermediate-coverage countries, $2000; and in high-coverage countries, $3000. Based on a number of studies (Kaddar, Levin, Dougherty, and Maceira 2000; Zhang et al. 1998), we estimate that an average health worker does 12 vaccinations per hour, including the time for travel and record preparation. Thus the estimated unit labor cost per routine OPV dose is $0.04 in low-coverage countries ($1000 per year/12 injections per hour × 50 weeks per year × 5 days per week × 8 hours per day), $0.08 in intermediate-coverage countries, and $0.12 in high-coverage countries.

▲ The labor cost per IPV dose is assumed to be equal to that of OPV vaccinations since a vaccine switch is not likely to lead to changes in per diem payment, although there might be increased use of trained health workers. The labor cost per NID vaccination is assumed to be twice the cost of a routine immunization due to increased labor inputs associated with (1) intensified social mobilizations, which involve the use of large number of non-health professionals, and (2) increased travel time of health workers.

▲ In the estimation of the labor costs, the rule of thumb used in the analysis is that a labor charge must be made for each dose administered at an independent visit. If a dose of the vaccine can be delivered simultaneously with other vaccines, we do not count any labor cost of vaccination because the marginal labor cost of vaccination is close to zero. In this study, we assume that routine vaccination with OPV and IPV will be done simultaneously with other immunizations and thus do not incur extra labor costs. NIDs vaccination with OPV needs two visits per child under 5-years old. NIDs vaccination with IPV needs an average of two visits per child missed in routine vaccinations as discussed above.

▲ The switch of vaccine requires start-up training that for cost allocation purposes should be spread over several years. According to estimated budgets for training for the introduction of new vaccines in developing countries, the cost of start-up training per target child is $0.18, adjusted to $0.06 per child, assuming the cost may be spread over a period of three years. We also assume that in intermediate-coverage countries, in order to increase routine coverage of IPV to 90 percent, $0.02 per target child is needed for extra social mobilization.

▲ The estimated cost of treatment per case of poliomyelitis in developing countries varies a great deal: Bart et al. (1996) assumed $250 per case; Musgrove (1988) used $5800 per case as a cost estimate for Latin American countries; Acharya et al. (2002) assumed that the cost of treatment in low-and middle-income countries was $4200; and Dai and Zhang's (1996) investigation showed a treatment cost of $450 in China. As was done by the above authors, the cost of VAPP in this study includes only treatment costs, and other costs, such as costs associated with reduction in productivity (an indirect cost) and suffering, are not considered due to a lack of data. In addition, we assume that there is no significant difference between the costs of treating polio cases and VAPP cases, and that all of the VAPP cases will receive treatment. Most importantly, we assume that the per case treatment in low-coverage countries is about $1000, in intermediate countries is about $2000, and in high-coverage countries, $4000, considering the association between income and immunization coverage, and the varying cost estimates used by the authors in the literature. Some reviewers of earlier

versions of this analysis thought that $1000 per case treated in low coverage countries is too high. In any case, when using this figure the economic cost of VAPP is minimal relative to the total incremental cost. Thus, using a lower cost of treatment for VAPP would not lead to changes in the conclusions of the analysis.

The estimated changes of poliomyelitis immunization costs due to a vaccine switch from OPV to IPV in developing countries grouped by level of OPV3 coverage are shown in Table 3 (detailed analytical methods and calculations are shown in Annexes C, D, and E). The estimates show that the vaccine switch from OPV to IPV for the low-coverage countries will lead to a net increase in costs of about $26 million, averaging about $2.42 per target child. For intermediate-coverage countries, the vaccine switch will result in an increase in total cost of $129 million, averaging about $2.68 per target child. For high-coverage countries, the vaccine switch will result in an increase in the total cost of $162 million, an average of about $3.26 per target child. For all developing countries together, this study estimates that the vaccine switch will result in an increase in total cost of $317 million, averaging $2.91 per child.

The cost per VAPP case averted in all developing countries is about $1.05 million. This is lower in low-coverage countries ($881,000) and intermediate-coverage countries ($970,000), and higher in high-coverage countries ($1.18 million). The cost of a vaccine switch from OPV to IPV per VAPP avoided is much lower than that in the United States, where $3 million is needed to avoid one case of VAPP (Sutter et al. 2000).

Table 3. Changes of Poliomyelitis Immunization Costs from a Switch from OPV to IPV (in its current presentation) in Developing Countries Grouped by Level of OPV3 Coverage

Items of cost change	Low coverage	Intermediate coverage	High coverage	All countries
Change on cost of vaccine ($)	24,705,605	131,828,189	145,526,487	302,060,281
Change in cost of supplies and transporation ($)	2,192,219	11,723,398	12,089,893	26,005,510
Change in cost of sterilization and disposal ($)	243,580	1,302,600	1,343,321	2,889,501
Change in cost of vaccine storage ($)	15,297	79,423	160,247	254,967
Change in cost of vaccine transportation ($)	1,702	8,836	17,827	28,364
Change in labor cost of vaccination visits ($)	-1,375,864	-19,704,227	0	-21,080,091
Change in cost of training ($)	656,815	3,859,555	2,985,159	7,501,529
Change in cost of VAPP	-30,145	-265,702	-548,017	-843,864
Total incremental cost ($)	26,439,353	129,097,774	162,122,934	316,816,197
Average incremental cost per target child ($)	2.42	2.68	3.26	2.91

The change in total cost from the switch is made up of some increased costs and some decreased costs, with the increases ending up much bigger than the decreases. It can be seen that the largest share of the increases comes from vaccine (more than 85 percent of the total increase), and that the largest share of the decreases comes from the cost of vaccination visits associated with OPV NIDs (more than 95 percent of the total decrease).

Because vaccine cost represents a major portion of the total increase in costs and the future price of IPV is uncertain, we performed a sensitivity analysis by allowing the price of IPV to vary between $0.50 per dose (the lowest expected price) and $2.00 per dose (the highest expected price). In

addition, since the cost of vaccination visits represents a major portion of the total cost decrease and the number of visits depends on whether there will be IPV NID, we analyzed the difference in incremental costs between scenarios with and without IPV NIDs in low-coverage countries.

The results of the sensitivity analysis are shown in Table 4. Even in the least cost situation, where the price of IPV is the lowest and NIDs are not conducted anywhere (maximum saving from the reduction in the number of vaccination visits), the increase in costs of a switch to IPV cannot be cancelled out by the decrease in costs, resulting in a net increase in costs. The average incremental cost in a low-coverage country is $0.28 per child; in intermediate-coverage countries, the average incremental cost is $0.99 per child; in high-coverage countries, $1.57; overall for all countries together, the total incremental cost is $128 million, averaging $1.18 per child.

In the highest cost-saving situation, where the price of IPV is the highest and NIDs are conducted in low-coverage countries, the incremental cost is large. All countries together are expected to incur an additional cost of $6.22 per child from a vaccine switch. The average incremental cost per target child in low-coverage, intermediate-coverage, and high-coverage countries are $5.20, $6.05, and $6.63, respectively. For all countries, the total incremental cost will be $678 million.

Table 4. Results of Sensitivity Analysis by (1) Varying IPV NID from None to Once Every Three Years in Low-coverage Countries (LCC), and (2) Varying the Price of IPV to $0.5 and $2.0 per Dose

Items of cost change	Low coverage		Intermediate coverage		High coverage		All countries	
	$0.5/dose without NID	$2.00/dose with NID	$0.5/dose	$2.00/dose	$0.5/dose	$2.00/dose	$0.5/dose without NID	$2.00/dose with NID in LCC
Change in cost of vaccine ($)	2,468,307	55,153,091	50,415,704	294,653,161	61,568,898	313,441,664	114,452,909	663,247,916
Change in cost of supplies and transportation ($)	1,182,267	2,192,219	11,723,398	11,723,398	12,089,893	12,089,893	24,995,558	26,005,510
Change in cost of sterilization and disposal ($)	131,363	243,580	1,302,600	1,302,600	1,343,321	1,343,321	2,777,284	2,889,501
Change in cost of vaccine storage ($)	-13,389	15,297	79,423	79,423	160,247	160,247	226,282	254,967
Change in cost of vaccine transportation ($)	-1,489	1,702	8,836	8,836	17,827	17,827	25,173	28,364
Change in cost of vaccination visits ($)	-1,375,864	-1,375,864	-19,704,227	-19,704,227	0	0	-21,080,091	-21,080,091
Change in cost of training ($)	656,815	656,815	3,859,555	3,859,555	2,985,159	2,985,159	7,501,529	7,501,529
Change in cost of VAPP ($)	-30,145	-30,145	-265,702	-265,702	-548,017	-548,017	-843,864	-843,864
Total incremental cost ($)	3,048,010	56,886,840	47,685,289	291,922,746	78,165,345	330,038,110	128,054,780	678,003,832
Average incremental cost per target child ($)	0.28	5.20	0.99	6.05	1.57	6.63	1.18	6.22

4. Making the Choice

The polio eradication program is at a crossroads where a decision has to be made on whether polio vaccination should be stopped following global eradication of poliomyelitis. If the decision is to continue vaccination, then another decision must be made: whether OPV or IPV, in its present presentation, should be recommended for use. This paper focuses on the latter – the choice of vaccine – currently a hot topic for the global polio eradication program. This paper has described the methods used for estimating the incremental cost and effectiveness of a switch from OPV to IPV, provided estimates that can be judged and used by decision makers, and contributed to the literature on the debate over vaccine choice.

The results of incremental cost analysis provide weak support for a vaccine switch on a cost-saving basis. While decision makers should consider these results when choosing a vaccine strategy, additional factors should weigh the decision: (1) the limitations of this study should be well understood, and the results should be interpreted carefully; (2) the potential future availability of IPV should be taken into account; (3) the epidemiological risks and benefits of a vaccine switch need to be considered; and (4) different approaches to a vaccine switch (should it occur) need to be considered in advance.

Because the cost of vaccine makes up a dominant proportion of the estimated cost increases, the results related to the cost of vaccine should be understood clearly and interpreted carefully.

The cost of vaccine is associated with a number of variables, which include the price of OPV and IPV, the number of children in the target population, the immunization coverage rate, and the vaccine wastage rate. While we have little doubt about the accuracy of the number of children in the target population, the values used for the other variables are less certain.

- ▲ An increase in the price of OPV would increase the financial desirability of the vaccine switch. The price of OPV could increase because of (1) a loss of economies of scale from reductions in purchases and (2) litigation associated with VAPP in highly legalized developing countries (Beale 1990).

- ▲ Data on which to project the future price of IPV in its present presentation in developing countries are limited. The price estimate of IPV in the literature is primarily based on manufacturers' opinions. Any higher IPV price per dose above the projected estimates (assumed likely price of $1.00 per dose, with a range between $0.50 and $2.00) will greatly increase the cost of the vaccine switch.

- ▲ The wastage rates of OPV and IPV are both assumed to be 20 percent. If the wastage rate of IPV is lower than that of OPV, for example from a change in the open vial policy, there will be a reduction in the incremental cost of the vaccine switch.

- ▲ This study assumes that the coverage rate of IPV should be 90 percent or higher to achieve a level of prevention equivalent to the current OPV strategy. This rate may be higher than the actual achievable rate for some countries and lower for others. If the actual coverage rate

needed to achieve the equivalence is higher (lower) than 90 percent, we may have underestimated (overestimated) the cost increase.

The labor cost of vaccination visits makes up a predominant proportion of the costs that decrease. The estimated results need to be carefully judged by readers. The cost of vaccination visits is a function of the unit cost per visit and the number of visits. The number of vaccine-specific visits is difficult to estimate because the delivery of one dose of one vaccine can be done with other vaccines. Although the rule of thumb used in this study is thought to be the best approach, if routine administration of either OPV or IPV requires vaccination visits separate from those for other vaccines, then these estimates will be inaccurate. Separate visits for routine OPV would make the switch more financially favorable. Separate visits for IPV would make the switch less financially favorable.

In estimating the cost of vaccination visits, we include only the cost of labor. The exclusion of capital cost (e.g., the office space) may underestimate the true cost of vaccination visits. However, since personnel cost is by far the greatest share of the cost of vaccination visits (90 percent) (Kaddar, Levin, Dougherty, and Maceira 2000), and capital costs are not expected to change in the short run with the switch, the exclusion of capital cost is not expected to introduce significant errors.

Finally, the unit cost of storage and the unit cost of transportation are subject to scrutiny. These costs are estimated based on studies in only a few countries because universal data are not available. In addition, we do not vary unit costs of storage among the three groups of countries. We recognize that the delivery of vaccine in some countries (e.g., countries in conflict or with dispersed populations) may be more costly though the unit cost of delivery is not related to the level of immunization coverage, our method of grouping countries. This approach of using a single delivery cost for all may introduce errors for specific countries that are far from the mean, but this should not change the overall conclusions of this study because the decrease in transportation and storage costs of vaccine from the vaccine switch accounts for only a small portion of the total decrease in cost.

4.1   Vaccine Availability

The decision whether to switch to IPV in its present presentation should also take into account the availability of IPV. A major concern is whether manufacturers can meet the global demand if the switch to IPV happens. The availability of vaccine is associated with a number of factors, which include the technical production potential or capacity, the price of the vaccine, and the expected number of years of production, as well as the absence or existence of public intervention. All of these factors need to be considered by decision makers in the process of vaccine choice.

The technical production capacity for IPV is a concern because it is relevant to the degree to which the global need for IPV can be satisfied if the decision is made to replace OPV with IPV. Holding other factors constant, the future technical capacity of IPV production will determine whether there should be a vaccine switch and whether the switch should be conducted for all countries at once or country by country on an individual country basis. In addition, the pace of increase in IPV production capacity will determine the timeframe of the vaccine switch. With an IPV-only strategy, the global need for IPV for all countries would be about 500 million doses per year.

A study commissioned by the World Health Organization (1997b) showed that (1) the 1997 capacity of production was about 65 million doses; (2) without significant capital expansion, capacity could increase by fivefold (estimated 300 million doses) within three years; (3) with capital expansion, the capacity of production could increase to 600 million doses within four years. Because

an earlier study suggested that the capacity of IPV production had already reached 60 million doses per year in 1988 (Montagnon 1989), and the capacity of production could easily be expanded by using larger tanks for vaccine production (Montagnon 1985; van Wezel et al. 1984), the 1997 estimates of the production capacity and the timeframe needed for meeting the global demand for vaccine seem to be conservative.

Based on available studies, it can be said that potential production can meet the global need for IPV with three years lead time. The implication of this observation is that if the decision on a vaccine switch had been made in 1997, the production capacity of IPV could have reached 500 million doses by 2001; and if the decision can be made this year (2003), the capacity of production can increase to the level of vaccine needed in approximately 2005, when poliomyelitis is just eradicated – the right time for the vaccine switch. The time needed for capacity development is constrained by the time needed for production expansion as well as by the time needed to make the decision on vaccine choice. The latter will be the first bottleneck because manufacturers will not make the effort to expand the production capacity until the decision to switch is made.

The expected price of the vaccine is a major factor affecting producers' decisions on how much IPV to supply. The higher the price of the vaccine, the more likely manufacturers will be willing to expand their production capacity. However, if the price of the vaccine is high, the incremental cost of the vaccine switch will be high. If the increase in vaccine price drives the incremental cost of a vaccine switch to a point where it is prohibitive, there will be no demand for additional vaccine and the capacity will go unused. The implication of this discussion is that the supply will be insufficient if the price offered by bulk purchasers, such as WHO and UNICEF, is too low; and the vaccine switch will not occur if the price asked by manufacturers is prohibitively high. Negotiations on the price of vaccine among large vaccine purchasers, international vaccination policymakers, and vaccine manufacturers definitely are needed before a decision to a vaccine switch can become a reality.

The expected life years of production is a major concern of the manufacturers in deciding whether they should expand capital investment. Their rate of return will be low for a given price if the number of years of production is not long enough to spread the capital cost of expanded capacity over a long enough period of time. The fewer the years of post-eradication polio vaccination, the less likely manufacturers will be willing to expand their production capacity. As a result, the price they will demand will be higher and the cost of vaccination switch will be high. This consideration implies that if vaccination ceases right after the global certification of polio eradication, the length of production of vaccine may not be long enough to induce a boost in the supply of vaccines. However, how many years to vaccinate post-eradication should be a technical and epidemiological decision, not a financial one.

Public intervention into vaccine production may play a major role in vaccine supply. Public intervention may simply take the form of public production or subsidization of private manufacturers to produce vaccines. In the case of the former, policymakers determine the volume and price of vaccine; in the case of the latter, private manufacturers will be financially motivated to produce vaccine and sell it at a lower price.[5] Whether through government production, subsidies to private producers, or negotiating a price, governments[6] must pay more for IPV. They should choose the means that would allow them to pay the least amount more. If this amount is worth the VAPP

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[5] Note that public-sector producers who price a vaccine below the cost of production must still pay for the difference between cost and price.

[6] Government payment may take the form of richer-country governments paying on behalf of poorer-country governments, sometimes through multilateral institutions.

averted, adjusted for the other risks such as cVDPV, they should pay it. If not, then they should stick with OPV, or pay it for some countries where the financial burden caused by VAPP and cVDPV is higher, not for others.

4.2 Epidemiological Risks and Benefits

The epidemiological risks and benefits associated with a vaccine switch are important pieces of information for decision makers to consider. Adequately addressing this set of issues in detail is beyond the scope of this paper. Nevertheless, we sketch some of the issues below.

The epidemiological benefits of a vaccine switch to IPV include the elimination of VAPP, the discontinuation of the transmission of the vaccine virus, and the reduction of cVDPV. While the cost savings from elimination of VAPP were considered in the estimation of incremental cost, the cost savings from reduction in risk of cVDPV were not. It has been reported that outbreaks due to vaccine-derived poliovirus have occurred in Egypt, the Dominican Republic, Haiti, the Philippines, and Madagascar; and globally there were 61 cases in the history of OPV vaccination, averaging about three cases per year (U.S. Centers for Disease Control and Prevention 2001a and 2001b; CDC 2001c; Wood 2002). A switch to IPV may be needed to interrupt the transmission of cVDPV in preparation for the global cessation of polio vaccination. Countries must chose their vaccine strategy with full understanding that if they continue OPV, they risk the development of cVDPV in their country and potentially could export this virus to neighboring countries.

The epidemiological risks of the switch include the increased risk of transmission of existing wild virus due to inadequate vaccination coverage and the escape of wild virus in the process of IPV production. However, the increased risk of transmission of other blood-borne diseases (Hepatitis B and HIV) associated with unsafe IPV injections should not be ignored. In this study we assumed that all IPV vaccinations are delivered using auto-destruct syringes, hence unsafe injections and associated transmission of diseases are minimal. This assumption is optimistic. It was reported (Kane et al. 1999) that in developing countries at least one-third of the injections are unsafe and carry the risk of transmission of blood-borne infections. It was estimated that at least 8 million Hepatitis B, 2 million Hepatitis C, and 80,000 HIV infections may result every year from unsafe injections, and at least 20 percent of all new Hepatitis B infections are attributable to unsafe injections in developing countries. If a significant proportion of the IPV injections in developing countries are unsafe, the cost associated with unsafe injections will be high and will greatly increase the total incremental cost of a vaccine switch.

4.3 The Approaches to a Vaccine Switch

While the results do not support a global vaccine switch on a cost-saving basis, we do not exclude the possibility of a vaccine switch on individual country basis. Due to differences in the incremental costs of a vaccine switch, the perception of benefits and risks, and the ability to pay for the extra costs, the decision to make a vaccine switch is likely to be different for different countries.

A switch in higher coverage countries is likely to be more feasible than in lower coverage countries. First, a switch in countries with higher levels of coverage will involve a lower risk of outbreak. Second, countries with higher coverage often have higher incomes and thus are willing to spend more for a given epidemiological benefit. A vaccine switch starting with higher income developing countries could increase the acceptability of the switch. Third, as higher income countries switch, the volume of IPV purchased will increase (especially through bulk purchasing mechanisms

like UNICEF and the Pan American Health Organization), tending to push down its price. This would make the switch more attractive financially to the lower income countries that have yet to switch. Fourth, the vaccine switch in only some countries would give manufacturers time to increase production capacity that would allow for the vaccine switch in other countries. Last, a vaccine switch on an individual country basis is more likely to assure high polio immunization coverage rates because the countries with greater ability to pay can start first and donors' support can be concentrated on those that lack the ability to pay. However, where the benefits of switching to IPV are considered to be greater than costs for all countries, an ethical argument could be made for richer countries to subsidize costs of the switch for lower-income countries at a level sufficient to allow them to do so at the same time as higher-income developing countries.

The decision to switch should also consider options related to vaccine presentations (IPV in its current presentation vs. IPV combos, such as IPV-DTP and IPV-Hib). Financially, IPV combos are better if the price of a combo is equivalent or lower than the sum of the prices of the individual vaccines. However, the IPV combo-only switch is not likely to happen for three reasons. First, the price of an IPV combo is likely to be much higher than the prices of individual vaccines summed, so the saving from reduced vaccination visits and injections is unlikely to be sufficient to make it financially attractive. Second, many countries have already switched to IPV and they will not find a further switch to IPV combos before the worldwide cessation of polio vaccination to be desirable or necessary. Third, the production capacity of IPV combos is much more limited than the capacity for production of IPV. A global IPV-only strategy also is not likely because IPV-DTP is already in use in some countries, such as Canada, France, and the Netherlands (Beale 1990). The most likely scenario is a mixed use of IPV and IPV combos, if the switch eventually occurs. Also to be noted is that even if a complete switch occurs, a stock of OPV is still needed to deal with possible outbreaks and NIDs in low-performing areas.

The weak support provided for a switch to IPV does not mean a strong support for continuing OPV, since both continuing with OPV and switching to IPV are costly options. Further, both options mean uncertain and, possibly, small benefits. Another option is to cease polio immunization altogether for countries deciding not to switch to IPV. This option would require maintaining a stockpile of vaccine sufficient to respond to emergencies. However, the emergency stockpiling of OPV or IPV is not the focus of this report and needs further study.

Whether the final decision is vaccination cessation or a switch to IPV, a stockpile of OPV and potentially, IPV, and contingency funds to respond to outbreaks of cVDPVs and any intentional or unintentional release of wild virus is being planned for the post-eradication era. The amount of vaccine in the stockpile should take into consideration the lower immunity of countries that have stopped immunizing.

4.4   Summing Up

This paper reviews the historical choices of polio vaccines at different stages of the polio control program. To inform policymakers in choosing the appropriate vaccine strategies during the coming global post-eradication era, incremental cost analysis was undertaken. Policymakers should interpret the results of the analysis carefully and consider several other factors in making their vaccine choice.

In the review of vaccine choices, it was found that at the national level during the period of pre-eradication, the vaccine choice between OPV and IPV in its present presentation by individual countries varied. Evidence showed that both vaccines were able to bring wild virus transmission under control. When polio was eradicated at a national level, some countries where OPV had been exclusively used switched to IPV to avoid the occurrence of VAPP, but at a significant incremental

cost; others continued the use of OPV in their polio control program, bearing the risk of VAPP. At the international level, OPV was chosen throughout the history of the global polio control program because it is cheap, easy to give, and produces secondary immunization and intestinal immunity. While the global OPV-only strategy proved successful in bringing the transmission of wild poliovirus to an end, continuation of this strategy is challenged by the fact that after the global eradication of polio, all cases of paralytic poliomyelitis will be associated with the use of OPV. Policymakers face a difficult choice of vaccine in post-eradication era of the global polio eradication program.

The analysis shows that if the choice is to maintain the exclusive use of OPV, there will be about 300 cases of VAPP per year due to infection from vaccine virus. A switch to IPV can avoid the occurrence of VAPP. However, the avoidance of VAPP comes at an increased price of IPV. This raises a question of whether a vaccine switch from OPV to IPV is financially worthwhile. This study estimated the incremental cost of a vaccine switch.

The analysis shows that if the price of IPV is $1.00 per dose (below its current price, but possible as the volume of production increases) for all developing countries together, the vaccine switch is expected to result in an increase in annual total cost of $317 million. The average incremental cost per target child is $2.91. Overall, developing countries will need $1 million to avoid a case of VAPP through the switch of vaccines. The incremental cost of a vaccine switch is different across countries. The switch for the low-coverage countries will lead to a net increase in costs of about $26 million, averaging about $2.42 per target child. For intermediate-coverage countries, the vaccine switch from OPV to IPV will result in a total increase in cost of $129 million, averaging about $2.68 per target child. For high-coverage countries, however, the vaccine switch will result in an increase of $162 million, an average of about $3.26 per target child.

The incremental cost is particularly sensitive to the possible variation in IPV price and whether there will be NIDs. Sensitivity analysis was done by allowing the price of IPV to change between $0.5 per dose (the lowest expected) and $2.0 per dose (the highest expected) and by not conducting IPV NIDs in low-coverage countries. The results of the sensitivity analysis showed the most favorable situation, where the price of IPV is the lowest and there are no NIDs in low-coverage countries (maximum saving due to reduction in the number of vaccination visits), as well as the most unfavorable situation, where the price of IPV is the highest and NIDs are conducted in low-coverage countries.

The significant incremental costs and limited epidemiological benefits found by this study do not favor a global vaccine switch in developing countries. However, the benefit of such a switch comes from elimination of a limited number of vaccine associated polio paralyses and a few polio cases caused by circulating vaccine-derived poliovirus. These benefits ultimately need to be weighed against the incremental costs and increased risks associated with the switch.

If the decision is to conduct a switch as a preparation for the global cessation of polio immunization, the results support a vaccine switch on an individual-country basis, with higher coverage countries likely to go first. The reasons are as follows: (1) higher coverage countries can more easily afford the cost of a vaccine switch; (2) higher coverage countries would have a lower risk of polio outbreak should coverage dip when the vaccine switch occurs; and (3) the capacity of IPV production may not permit an all-countries-at-once vaccine switch.

The validity of the results is limited by the difficulty of obtaining data on costs of providing immunization services and the accuracy of the assumptions made for the analysis. Policymakers are urged to interpret the results carefully because changes in the input data could lead to changes in results and recommendations. In addition, it was suggested that the information that should be

considered by policymakers go beyond that explicitly addressed in this paper. The potential supply of IPV (which is affected by the technical production capacity, the expected price of vaccine, the expected life years of production, and public intervention in vaccine production), the epidemiological risks and benefits of a vaccine switch, as well as the different possible approaches for a vaccine switch need to be carefully considered in choosing vaccines for the post-eradication era of the polio eradication program.

Annex A: OPV vs. IPV: Their Advantages and Disadvantages

OPV was developed in 1960 by Dr. Albert Sabin (World Health Organization 1997a). It consists of live polioviruses attenuated by extensive passage of the original wild-type stains of poliovirus in cell cultures or in monkeys in vivo. This results in mutation of the virus, which weakens its potential to cause paralysis, while maintaining the antigenity by inducing the production of antibodies by the immune systems of the human body. The advantages of OPV are as follows:

- OPV can protect children against paralysis once infected as well as limit the spread of wild virus among their contacts because OPV induces both serum immunity and intestinal immunity. Intestinal immunity limits the multiplication of wild virus inside the gut and thus reduces fecal excretion (hence possible transmission) of the wild virus.

- The use of OPV can produce secondary immunization through the spread of a vaccine virus in stools, which indirectly immunizes those with secondary contacts. This is particularly important in developing countries where the sanitation status permits this spread and the immunization coverage is low.

- OPV can be delivered with low cost, firstly because the price is lower than that of IPV, secondly because OPV is administered orally, and thus the vaccination does not need professionally trained health workers and injection-related supplies (e.g., syringes).

- OPV is delivered orally, so unsafe injection is not an issue.

The disadvantages of OPV are as follows:

- It can cause vaccine-associated paralytic poliomyelitis (VAPP), although the probability is very low (1 case per 2.5 million doses), because some people are sensitive to vaccine virus, especially those who are immunodeficient.

- OPV may be less potent than IPV in inducing serum immunity in developing countries, where the infection of the intestines by other viruses may prohibit the intake of OPV. Thus it often needs repeated vaccination of up to five to 10 doses to protect all children (Moriniere et al. 1993). These kinds of limitations to OPV were particularly reported in India and Africa (John 1972; Oduntan et al. 1978).

IPV was developed in 1955 by Dr. Jonas Salk (World Health Organization 1997a). It consists of killed viruses, which are cultivated in monkey kidney cells and activated by incubation of the viruses in 1:1000 formalin for 12-14 days at 37 C. IPV is delivered via injection. The advantages of IPV are as follows:

- It can effectively protect individual children against paralysis after three doses with a protection rate of nearly 100 percent.

▲　It does not cause VAPP because the vaccine consists of killed poliovirus.

▲　IPV can be combined with other injectable vaccines (such as DTP and Hib) to reduce the cost of administration and increase immunization coverage.

The disadvantages of IPV are as follows:

▲　IPV only induces serum immunity, not intestinal immunity. Thus, IPV vaccination can effectively protect the vaccinated individuals against paralysis, but does not readily protect all of them against infection with the wild virus. If vaccinated children are infected, they can become a source of infection by wild virus if their antibody levels are not high enough to stop virus excretion.

▲　There is not a secondary immunization effect.

▲　The cost of IPV vaccination is higher than OPV because its price is higher and it requires injections by trained health workers.

▲　Wild poliovirus could escape from the production process.

▲　There is a risk of unsafe injections, which can lead to transmission of blood-borne diseases.

From the list of advantages and disadvantages of OPV and IPV (which are summarized in Table A1), it can be seen that both vaccines are effective, but not perfect. Neither of them can be easily judged as preferable to the other. These characteristics of the two vaccines have made the choice between them extremely hard, and have led to variation in choice among countries and across different stages of a polio control program.

Table A1: Comparison of Advantages and Disadvantages of OPV and IPV

Attributes	OPV	IPV
Potency	Low (needs 4 or more doses)	High (needs 2 or 3 doses)
VAPP	1 case/2.5 million doses	None
Intestinal immunity	High (community protection)	Low (individual protection)
Secondary immunization	Yes	No
Extra injection	No	Yes
Possible combination vaccine	Unlikely	Likely
Risk of escape of wild virus	Non-existent	Possible (if produce with wild virus seeds)
Price	Low	High
Injection safety	No issue	A risk

Annex B: Expected Changes in Vaccine Prices

Changes in vaccine prices depend on at least two factors. One is the average cost of production and the other is the demand for vaccines. The average cost of production is a function of at least two variables: the cost of inputs and the scale of production. The demand for vaccine is associated with the size of target population and the choice of vaccines.

We assume the costs of inputs (such as labor, capital, and most items of supplies) will not change much or will follow the trend of the economy; a change in production capacity due to the development of production technology can be expected to have the greatest impact on the average cost of production.

IPV has been produced according to the methods originally developed by Salk et al. (1954). The general process of production are the following (Van Wezel et al. 1984): (1) cultivation of three seed viruses (type 1 Mahoney, type 2 MEF, and type 3 Saukett); (2) clarification, concentration, and purification of the viruses; (3) virus inactivation by incubating of the viruses in 1:1000 formalin for 12-14 days at 37 C; (4) a mixing of the three types of inactivated viruses and produce trivalent IPV; (5) a combining process if combined vaccines are produced (e.g., DTP-IPV).

Initially, the viruses were produced on monolayer cultures of the kidney cells of primary monkeys. During this time period, the production of vaccines was limited by the storage of monkey kidneys. However, the production methods underwent a revolutionary change in the early 1980s. Vero cells that can be subcultured in vitro were invented. The Master-Cell-Bank and Working-Cell-Banks prepared by Montagnon and his colleagues gave a practically inexhaustible cell source (Montagnon 1981). In addition, the development microcarrier culture technique, which was adopted for cultivating cells and virus in a fully controlled bioreactor, made the production of cells and viruses on an industrial scale a reality (van Wezel et al. 1984). In 1982, the use of these new technologies in the production of IPV was licensed in France. The virus was produced in Vero cell cultures that can grow well on microcarriers in 1000-liter or even 10000-liter tanks (Montagnon 1985; van Wezel 1984). The Vero cell line has been used by Pasteur-Merieux-Connaught since 1982 with the Cell Bank's system to produce IPV and OPV (Montagnon et al. 1999). The production capacity of IPV was already 60 million doses per year in 1988 (Montagnon 1989). Recently, the World Health Organization recommended the use of non-wild strains in the production of IPV (World Health Organization 2000b) and claimed that some manufacturers had already had limited experience with it. If that is the case, the cost of production can only decline because the strategy for prevention of virus escape will not need to be as strict as in the case of IPV production with wild viruses.

While the development of vaccine production technology removed the supply-side constraint of large-scale production, the actual volume of production is then limited by the demand-side constraint. While the size of the target population is relatively fixed, the choice of vaccines matters a great deal. If IPV is chosen, the worldwide demand for IPV will drive the actual production to the upper limit of capacity, allowing the cost of production to fall significantly because of the spreading of fixed costs.

The increase in demand following the global choice of IPV could be expected to reduce the price of IPV to a level that allows manufacturers to profit at prices only a little above the average cost of production. However, precisely what the likely price of IPV will be if it is chosen for post-eradication production is unknown. A study commissioned by the World Health Organization showed that the manufacturers predicted a price of $0.50 per dose (World Health Organization 1997b), which is close to the price estimate provided by Martin (1984), who stated that "on the basis of our present experience and providing that the level of applicable prices in developed countries allows a satisfactory return on the expenditure for research and development, we believe we can offer the new IPV at $0.45 per dose in a multi-dose vial." In this paper we assume that the future price for IPV will be $1.00 to avoid underestimation of the incremental cost of a vaccine switch.

Annex C: Calculations of the Incremental Cost of a Vaccine Switch from OPV to IPV in Low Immunization Coverage Developing Countries

Items and their calculations	OPV	IPV
(1) Number of target children for routine immunization	10,946,919	10,946,919
(2) Number of doses per immunized child for routine immunizations	4	3
(3) Number of target children for NIDs	50,152,920	19,704,454
(4) Average number of doses per child per year for NIDs	2/3	2/3
(5) Immunization coverage rate for routine immunizations	40%	40%
(6) Immunization coverage rate for NIDs	85%	85%
(7) Vial volume per dose (ml)	0.2	0.5
(8) Total number of vaccination injections (2) ×(1)×(5)+ (4)×(3) ×(6)	0	24,357,989
(9) Price per dose ($)	0.1	1
(10) Vaccine wastage rate (%)	20%	20%
(11) Total number doses needed = [(2) × (1) × (5) + (3) × (4) × (6)]/[1-(10)]	57,418,823	30,447,487
(12) Total cost of vaccine ($) = (9) × (11)	5,741,882	30,447,487
(13) Unit cost of supplies per injection + unit cost of supplies transportation ($)	0	0.09
(14) Total cost of vaccination supplies and transportation ($) = (13) × (8)	0	2,192,219
(15) Unit cost of sterilization & wastage disposal per injection ($)	0	0.01
(16) Total cost of sterilization & wastage disposal ($) = (15) × (8)	0	243,580
(17) Unit cost vaccine storage per liter ($)	4.09	4.09
(18) Total volume of vaccine (*l*) = [(7) × (11)]/1,000	11,484	15,224
(19) Total cost of vaccine storage ($) = (17) × (18)	46,969	62,265
(20) Unit cost vaccine transportation per m3 ($)	455	455
(21) Total cost of vaccine transportation = (20) × [(18)/1,000]	5,225	6,927
(22) Unit cost per vaccination visit for routine immunization ($)	0.04	0.04
(23) Unit cost per vaccination visit for NIDs ($)	0.08	0.08
(24) Number of vaccination visits per immunized child (routine immunization)	0	0
(25) Number of vaccination visits per immunized child (NIDs)	0.67	0.67
(26) Total cost of vaccination visits ($) = (22) × (24) × (1) × (5) + (23) × (25) × (3) × (6)	2,273,599	897,735
(27) Cost of start-up training for vaccine switch ($) = $0.06 × (1)	0	656,815

(28) Treatment cost of VAPP	30,145	0
(29) Change in cost of vaccine due to vaccine switch ($)	-------------------	24,705,605
(30) Change in cost of vaccine supplies and transportation due to vaccine switch ($)	-------------------	2,192,219
(31) Change in cost of sterilization and wastage disposal due to vaccine switch ($)	-------------------	243,580
(32) Change in cost of vaccine storage due to vaccine switch ($)	-------------------	15,297
(33) Change in cost of vaccine transportation due to vaccine switch ($)	-------------------	1,702
(34) Change in cost of vaccination visits due to vaccine switch ($)	-------------------	-1,375,864
(35) Change in cost of training ($)	-------------------	656,815
(36) Change in cost of VAPP	-------------------	-30,145
(37) Total incremental cost due to vaccine switch in developing countries ($)	-------------------	26,439,353
(38) Average incremental cost per immunized child ($)	-------------------	2.42

Annex D: Calculations of the Incremental Cost of a Vaccine Switch from OPV to IPV in Intermediate Immunization Coverage Developing Countries

Items and their calculations	OPV	IPV
(1) Number of target children for routine immunization	48,244,436	48,244,436
(2) Number of doses per immunized child for routine immunizations	4	3
(3) Number of target children for NIDs	216,244,805	0
(4) Average number of doses per child per year for NIDs	2/3	0
(5) Immunization coverage rate for routine immunizations	65%	90%
(6) Immunization coverage rate for NIDs	85%	0%
(7) Vial volume per dose (ml)	0.2	0.5
(8) Total number of vaccination injections (2) ×(1)×(5)+ (4)×(3) ×(6)	0	130,259,977
(9) Price per dose ($)	0.1	1
(10) Vaccine wastage rate (%)	20%	20%
(11) Total number doses needed = [(2) × (1) × (5) + (3) × (4) × (6)]/[1-(10)]	309,967,821	162,824,972
(12) Total cost of vaccine ($) = (9) × (11)	30,996,782	162,824,972
(13) Unit cost of supplies per injection + unit cost of supplies transportation ($)	0	0.09
(14) Total cost of vaccination supplies and transportation ($) = (13) × (8)	0	11,723,398
(15) Unit cost of sterilization & wastage disposal per injection ($)	0	0.01
(16) Total cost of sterilization & wastage disposal ($) = (15) × (8)	0	1,302,600
(17) Unit cost vaccine storage per liter ($)	4.09	4.09
(18) Total volume of vaccine (*l*) = [(7) × (11)]/1,000	61,994	81,412
(19) Total cost of vaccine storage ($) = (17) × (18)	253,554	332,977
(20) Unit cost vaccine transportation per m3 ($)	455	455
(21) Total cost of vaccine transportation = (20) × [(18)/1,000]	28,207	37,043
(22) Unit cost per vaccination visit for routine immunization ($)	0.08	0.08
(23) Unit cost per vaccination visit for NIDs ($)	0.16	0.16
(24) Number of vaccination visits per immunized child (routine immunization)	0	0
(25) Number of vaccination visits per immunized child (NIDs)	0.67	0
(26) Total cost of vaccination visits ($) = (22) × (24) × (1) × (5) + (23) × (25) × (3) × (6)	19,704,227	0
(27) Cost of start-up training and social mobilization ($) = $0.08 × (1)	0	3,859,555

(28) Treatment cost of VAPP	265,702	0
(29) Change in cost of vaccine due to vaccine switch ($)	------------------	131,828,189
(30) Change in cost of vaccine supplies and transportation due to vaccine switch ($)	------------------	11,723,398
(31) Change in cost of sterilization and wastage disposal due to vaccine switch ($)	------------------	1,302,600
(32) Change in cost of vaccine storage due to vaccine switch ($)	------------------	79,423
(33) Change in cost of vaccine transportation due to vaccine switch ($)	------------------	8,836
(34) Change in cost of vaccination visits due to vaccine switch ($)	------------------	-19,704,227
(35) Change in cost of training and social mobilization ($)	------------------	3,859,555
(36) Change in cost of VAPP	------------------	-265,702
(37) Total incremental cost due to vaccine switch in developing countries ($)	------------------	129,097,774
(38) Average incremental cost per immunized child ($)	------------------	2.68

Annex E: Calculations of the Incremental Cost of a Vaccine Switch from OPV to IPV in High Immunization Coverage Developing Countries

Items and their calculations	OPV	IPV
(1) Number of target children for routine immunization	49,752,645	49,752,645
(2) Number of doses per immunized child for routine immunizations	4	3
(3) Number of target children for NIDs	232,725,336	0
(4) Average number of doses per child per year for NIDs	0	0
(5) Immunization coverage rate for routine immunizations	90%	90%
(6) Immunization coverage rate for NIDs	85%	0%
(7)Vial volume per dose (ml)	0.2	0.5
(8) Total number of vaccination injections (2) ×(1)×(5)+ (4)×(3) ×(6)	0	134,332,142
(9) Price per dose ($)	0.1	1
(10) Vaccine wastage rate (%)	20%	20%
(11) Total number doses needed = [(2) × (1) × (5) + (3) × (4) × (6)]/[1-(10)]	223,886,903	167,915,177
(12) Total cost of vaccine ($) = (9) × (11)	22,388,690	167,915,177
(13) Unit cost of supplies per injection + unit cost of supplies transportation ($)	0	0.09
(14) Total cost of vaccination supplies and transportation ($) = (13) × (8)	0	12,089,893
(15) Unit cost of sterilization & wastage disposal per injection ($)	0	0.01
(16) Total cost of sterilization & wastage disposal ($) = (15) × (8)	0	1,343,321
(17) Unit cost vaccine storage per liter ($)	4.09	4.09
(18) Total volume of vaccine (*l*) = [(7) × (11)]/1,000	44,777	83,958
(19) Total cost of vaccine storage ($) = (17) × (18)	183,139	343,387
(20) Unit cost vaccine transportation per m3 ($)	455	455
(21) Total cost of vaccine transportation = (20) × [(18)/1,000]	20,374	38,201
(22) Unit cost per vaccination visit for routine immunization ($)	0.12	0.12
(23) Unit cost per vaccination visit for NIDs ($)	0.24	0.24
(24) Number of vaccination visits per immunized child (routine immunization)	0	0
(25) The number of vaccination visits per immunized child (NIDs)	0	0
(26) Total cost of vaccination visits ($) = (22) × (24) × (1) × (5) + (23) × (25) × (3) × (6)	0	0
(27) Cost of start-up training ($) = $0.06 × (1)	0	2,985,159

(28) Treatment cost of VAPP	548,017	0
(29) Change in cost of vaccine due to vaccine switch ($)	------------------	145,526,487
(30) Change in cost of vaccine supplies and transportation due to vaccine switch ($)	------------------	12,089,893
(31) Change in cost of sterilization and wastage disposal due to vaccine switch ($)	------------------	1,343,321
(32) Change in cost of vaccine storage due to vaccine switch ($)	------------------	160,247
(33) Change in cost of vaccine transportation due to vaccine switch ($)	------------------	17,827
(34) Change in cost of vaccination visits due to vaccine switch ($)	------------------	0
(35) Change in starting-up cost ($)	------------------	2,985,159
(36) Change in cost of VAPP	------------------	-548,017
(37) Total incremental cost due to vaccine switch in developing countries ($)	------------------	162,122,934
(38) Average incremental cost per immunized child ($)	------------------	3.26

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