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Polio inactivated vaccine costs into routine childhood immunization in Brazil

Custos da vacina inativada de pólio na imunização infantil de rotina no Brasil

ABSTRACT

OBJECTIVE: To analyze the costs of vaccination regimens for introducing inactivated polio vaccine in routine immunization in Brazil.

METHODS: A cost analysis was conducted for vaccines in five vaccination regimens, including inactivated polio vaccine, compared with the oral polio vaccine-only regimen. The costs of the vaccines were estimated for routine use and for the “National Immunization Days”, during when the oral polio vaccine is administered to children aged less than five years, independent of their vaccine status, and the strategic stock of inactivated polio vaccine. The presented estimated costs are of 2011.

RESULTS: The annual costs of the oral vaccine-only program (routine and two National Immunization Days) were estimated at US\$19,873,170. The incremental costs of inclusion of the inactivated vaccine depended on the number of vaccine doses, presentation of the vaccine (bottles with single dose or ten doses), and number of “National Immunization Days” carried out. The cost of the regimen adopted with two doses of inactivated vaccine followed by three doses of oral vaccine and one “National Immunization Day” was estimated at US\$29,653,539. The concomitant replacement of the DTPw/Hib and HepB vaccines with the pentavalent vaccine enabled the introduction of the inactivated polio without increasing the number of injections or number of visits needed to complete the vaccination.

CONCLUSIONS: The introduction of the inactivated vaccine increased the annual costs of the polio vaccines by 49.2% compared with the oral vaccine-only regimen. This increase represented 1.13% of the expenditure of the National Immunization Program on the purchase of vaccines in 2011.

DESCRIPTORS: Poliomyelitis, prevention & control. Poliovirus Vaccine Inactivated, supply & distribution. Poliovirus Vaccine Oral, supply & distribution. Immunization Programs, organization & administration. Cost analysis.

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RESUMO

OBJETIVO: Analisar os custos de esquemas de vacinação para a introdução da vacina inativada de pólio na imunização de rotina no Brasil.

MÉTODOS: Foi realizada análise de custos das vacinas de cinco esquemas de vacinação, incluindo vacina pólio inativada, comparados ao esquema apenas-vacina oral de pólio. Foram estimados custos das vacinas para rotina, para os “Dias Nacionais de Imunização”, quando a vacina de pólio oral é administrada para menores de cinco anos, independentemente da situação vacinal, e do estoque estratégico de vacina pólio inativada. Os custos estimados foram os de 2011.

RESULTADOS: Os custos anuais do programa apenas-vacina de pólio oral (de rotina e de dois Dias Nacionais de Imunização) foram estimados em US\$19.873.170. Os custos incrementais da inclusão da vacina pólio inativada dependeram: do número de doses da vacina, da apresentação da vacina (frascos com dose única ou dez doses) e do número de “Dias Nacionais de Imunização” realizados. O esquema adotado, com duas doses de VIP seguidas de três doses de VOP e um “Dia Nacional de Imunização”, foi estimado em US\$29.653.539. A concomitante substituição das vacinas DTPw/Hib e HepB pela vacina pentavalente permitiu a introdução da vacina pólio inativada sem aumento do número de injeções ou visitas necessárias para completar a vacinação.

CONCLUSÕES: A introdução da vacina pólio inativada aumentou os custos anuais das vacinas de pólio em 49,2%, comparado ao esquema apenas-vacina de pólio oral. Esse aumento representou 1,13% dos gastos do Programa Nacional de Imunização com a compra de vacinas em 2011.

DESCRIPTORIOS: Poliomielite, prevenção & controle. Vacina Inativada de Pólio, provisão & distribuição. Vacina Oral de Pólio, provisão & distribuição. Programas de Imunização, organização & administração. Análise de Custos.

INTRODUCTION

With the Global Polio Eradication Initiative of the World Health Organization (WHO), the number of paralytic poliomyelitis (polio) cases decreased more than 99.0% (from 350,000 in 125 endemic countries in 1988 to 416 cases in 2013). Four WHO regions have been certified to be polio-free; wild poliovirus type-2 was globally eliminated in 1999, and no new cases of wild poliovirus type-3 have been reported since November 2012.²³

Despite huge advances toward polio eradication, achieving total success has been more difficult than anticipated. Infection continues occurring due to suboptimal effectiveness of the oral polio vaccine (OPV) in tropical countries; and, mainly due to difficulties in achieving and sustaining sufficiently high vaccine coverage, particularly in conflict zones or difficult-to-access areas.²¹ Many countries still lack basic sanitation, which is important for controlling polio transmission. Three countries (Afghanistan, Pakistan, and Nigeria)

have never interrupted wild poliovirus transmission.²³ Viruses from these countries have caused outbreaks in neighboring countries that had already eliminated polio, such as the 2013 outbreaks in Somalia and Syria.^{4,22}

The WHO polio eradication strategy is based on the use of OPV. Although effective and safe, in rare cases, this attenuated vaccine strain may cause vaccine-associated paralytic poliomyelitis (VAPP), which is clinically indistinguishable from polio caused by wild poliovirus.^{15,23} Annual VAPP incidence is estimated at two to four cases per million births in countries using OPV.^{10,15,19,23}

The vaccine strain is transmitted to the vaccinees' contacts by the fecal-oral or oral-oral route and may spread in populations with low vaccine coverage. This strain is genetically unstable and may regain neurovirulence during the transmission chain in the community.^{6,15} This circulating vaccine-derived poliovirus (cVDPV) has been associated with outbreaks of paralytic polio.⁶ Although the three types of polio vaccine

strains may convert to cVDPV, most reported cVDPV outbreaks are related to the type-2 virus.^{6,23} Seven countries reported cases of paralytic polio caused by cVDPV in 2013, all of them caused by the type-2 virus. Polio eradication will be fully achieved only when OPV ceases to be used in the world.^{15,23}

Wild poliovirus transmission was interrupted in Brazil in 1989 and the Americas were declared polio-free in 1994. The immunization actions after 1994 have been aimed at preventing reintroduction of the wild poliovirus in the region.^{7,14} The polio vaccination strategy of the Brazilian National Immunization Program (NIP) comprised five OPV doses during routine immunization of children, along with two annual campaigns [National Immunization Days (NID)] for administering OPV to all children under five years of age, independent of their vaccination status. This strategy remained the same from the 1980s up to 2012.^{7,14} OPV is widely accepted by the Brazilian population, and high vaccine coverage has been maintained. A National Vaccination Coverage Survey reported 96.0% coverage for the third dose of polio vaccine among 18-month-old children in 2007.⁵ In March 2014, for the first time since polio elimination, wild poliovirus type-1 was detected in sewage samples collected at Viracopos International Airport in Campinas, SP, Southeastern Brazil.^a However, to date, no cases of paralytic polio due to wild poliovirus have been detected in Brazil.^a

Vaccine polio strains have been the only cause of paralytic polio in Brazil in the post-elimination period. The Surveillance of Acute Flaccid Paralysis program registered 46 confirmed VAPP cases between 1989 and 2010; this reflects an average of 2.1 cases per year, with an estimated risk of one VAPP case per 4.5 million initial OPV doses. As in other polio-free countries and regions, the risk of VAPP in Brazil has been higher than the risk of wild poliovirus importation.

A safer inactivated polio vaccine (IPV) is available; studies have demonstrated IPV's high immunogenicity and efficacy in tropical areas.^{3,8,23} However, IPV is more expensive than OPV, and switching from all-OPV immunization schedules to schedules including IPV would not be cost-effective.^{2,9,12,20} Many high- and medium-income countries have already replaced the all-OPV schedule with sequential IPV-OPV or all-IPV schedules.^{17,18} These countries switched to IPV to avoid VAPP despite the additional cost.^{1,18}

Until 2012, IPV was available in Brazil at public health immunization referral centres only for children with OPV contraindication: immunocompromised children, HIV-exposed children, and children in contact with immunocompromised persons. IPV was also available from

private clinics. Both the *Brazilian Paediatric Society* and the *Brazilian Immunization Society* recommended IPV use for routine polio immunization, particularly for the first two doses. Nevertheless, children from the higher socioeconomic strata were vaccinated with IPV in the private sector; low-income children, dependent on the Brazilian Unified Health System, continued to receive OPV and were at risk of VAPP, increasing inequities. Brazilian medical societies exerted pressure on the Ministry of Health for changes in the national polio immunization policies. The Brazilian Ministry of Health decided to introduce a sequential IPV-OPV schedule in routine immunization in August 2012. This routine included administration of IPV in the first two doses, followed by three OPV doses and one annual NID, with OPV administered to all children aged 6-59 months, independent of their immunization status.

Countries considering incorporating IPV into their NIP should evaluate its epidemiological, financial, and operational implications. Before adopting the new polio vaccination program, the Brazilian Ministry of Health commissioned a broad-spectrum health technology assessment of IPV introduction in routine childhood immunization.

The present study is part of this assessment; its purpose was to analyze the costs of including IPV in routine immunization vaccine schedules in Brazil.

METHODS

We conducted a search of the WHO website to identify polio immunization schedules including the use of IPV in different countries; our findings are shown in Table 1. Five different schedules were considered as effective alternatives for including IPV in routine childhood immunization: (1) a sequential schedule with one IPV dose followed by four OPV doses; (2) a sequential schedule with two IPV doses followed by three OPV doses; (3) a sequential schedule with three IPV doses followed by two OPV doses; (4) an all-IPV schedule composed of four IPV doses; and (5) all-IPV schedule composed of five IPV doses.

Cost estimates of different vaccination schedules including IPV were developed on the basis of the NIP Information System and NIP Coordination information. These estimates were then compared with the national annual costs of the all-OPV schedule (routine immunization + two NID).

The study was performed from the perspective of the health care system and only the vaccine purchase costs were considered. All costs were estimated in the 2011 Brazilian real (R\$) and presented in United States dollars (US\$) at the December 30, 2011, exchange rate of US\$1.00 = R\$1.88.^b

^a WHO Global Alert and Response. Detection of poliovirus in sewage, Brazil. Geneva; 2014 [cited 2014 Jul 28]. Available from: http://www.who.int/csr/don/2014_6_23polio/en/

^b Banco Central do Brasil. Taxas de câmbio. Brasília (DF); 2011 [cited 2012 Nov 15]. Available from: <http://www.bcb.gov.br/txcambio>

Table 1. 2011 polio vaccination schedules including IPV, by country.

Immunization Schedules	Country or Countries (number of vaccine doses)
Sequential schedules with 2 doses of OPV followed by IPV (4 doses)	South Africa (2 OPV, 4 IPV)
Sequential schedules with 1 dose of IPV followed by OPV (4-6 doses)	Bahrain (1 IPV, 4 OPV), Kuwait (1 IPV, 4 OPV), Oman (1 IPV, 5 OPV), Qatar (1 IPV, 4 OPV), Saudi Arabia (1 IPV, 4 OPV), United Arab Emirates (1 IPV, 4 OPV)
Sequential schedules with 2 doses of IPV followed by OPV (3-5 doses)	Bermuda (2 IPV, 4 OPV), Jordan (2 IPV, 4 OPV), Syrian Arab Republic (2 IPV, 4 OPV), Ukraine (2 IPV, 4 OPV)
Sequential schedule with 3 doses of IPV followed by OPV (1-5 doses)	Belarus (3 IPV, 3 OPV), Poland (3 IPV, 1 OPV), Russian Federation (3 IPV, 3 OPV), Marshall Islands (3 IPV, 5 OPV), Indonesia (part of the country has implemented 3 doses of IPV)
Sequential schedule with 4 doses of IPV followed by OPV (2 doses)	Malaysia (4 IPV, 2 OPV), Russia (4 IPV, 2 OPV), Turkey (4 IPV, 2 OPV)
All-IPV schedule in routine and OPV in campaigns	Costa Rica (4 IPV, 1 annual campaign for children aged 2 months to < 5 years, independent of previous vaccination history), Mexico (4 IPV, 3 annual campaigns for children aged 6 months to < 5 years with at least 2 previous doses of IPV)
All-IPV schedule	Andorra (4), Australia (3 or 4 ^a), Austria (4), Belgium (3 or 5 ^b), Bosnia and Herzegovina (4 ^c), Bulgaria (4), Canada (5), Croatia (6), Cyprus (5), Czech Republic (5), Denmark (4), Estonia (5), Finland (4), France (6), Germany (4 or 5 doses ^b), Greece (4), Hungary (5), Iceland (4), Ireland (4), Israel (5), Italy (4), Latvia (6), Lithuania (5), Luxembourg (5), Malta (5), Monaco (3), Netherlands (6), New Zealand (4), Niue (4), Norway (5), Palau (4), Portugal (4), Romania (5), San Marino (4), Slovakia (5), Slovenia (4), Spain (4), South Korea (4), Sweden (4), Switzerland (5), United Kingdom (5), United States of America (4)

Source: World Health Organization. Available from: <http://www.who.int/countries/en/> Accessed on May 1, 2012.

OPV: oral polio vaccine; IPV: inactivated polio vaccine

^a Different regions of the country use different schedules.

^b Higher number of doses if combined vaccine, lower number of doses if IPV separately.

^c Only part of the country uses all-IPV, another part of the country uses OPV.

Lebanon would start immunization with IPV in 2011, but no further information could be found.

Costs of vaccines for routine immunization (OPV and IPV) and NID (only OPV) were estimated separately. One or two yearly NID were considered as equally valid alternatives to assure high vaccination coverage during transition from all-OPV to a schedule including IPV. The mean number of OPV doses administered in the two NID conducted in 2010, reported by NIP Coordination, was considered as the reference for estimating costs of one NID.

To estimate the number of doses needed in a routine polio immunization protocol, we used the numbers of OPV and IPV doses administered in Brazil in 2010. These data were obtained from the NIP Information System.^c We assumed that the vaccination coverage of IPV-including schedules would be the same as for all-OPV schedules.

We assumed that a complete series of IPV doses would be administered to all children for whom OPV is contraindicated, according to the IPV doses administered in 2010.

The estimated number of vaccines needed included the number of administered doses plus a wastage rate. The OPV wastage rate was estimated on the basis of the number of doses distributed throughout Brazil in 2010 (reported by NIP Coordination) and the number of administered doses, as obtained from DATASUS^c:

$$\text{Oral polio vaccine wastage rate (\%)} = \frac{\text{Number of distributed doses} - \text{Number of administered doses}}{\text{Number of distributed doses}} \times 100$$

IPV wastage rate estimates were based on WHO recommendations.^d Two different wastage rates were considered depending on the IPV dose presentation: 5.0% for single-dose vials and 25.0% for liquid vaccines in 10-20-dose vials.

A strategic vaccine stock was included in the estimated number of doses required for the first year of the vaccination program. The extra vaccine supply is intended to

^c Ministério da Saúde, DATASUS. Informações de Saúde (TABNET): Assistência à Saúde: imunizações desde 1994: doses aplicadas [tabela]. Brasília (DF); 2014 [cited 2014 Nov 24]. Available from: <http://www2.datasus.gov.br/DATASUS/index.php?area=0202&VObj=http://tabnet.datasus.gov.br/cgi/deftohtm.exe?pn/cnv/dpni>

^d World Health Organization. Immunization service delivery: projected vaccine wastage. Geneva [cited 2014 Mar 19]. Available from: http://apps.who.int/immunization_delivery/systems_policy/logistics_projected_wastage/en/index.html

^e World Health Organization, Department of Vaccines and Biologicals. Guidelines for estimating costs of introducing new vaccines into the national immunization system. Geneva; 2002 [cited 2014 Mar 19]. Available from: http://whqlibdoc.who.int/hq/2002/WHO_V&B_02.11.pdf

be distributed throughout Brazil.^e Costs of a strategic IPV vaccine stock, set at 25.0% of the vaccine needs for routine immunization, were estimated separately.

OPV costs were estimated on the basis of the price paid by the Brazilian Ministry of Health in 2011 (US\$0.36 per dose in 20- or 25-dose presentation) (NIP Coordination). IPV costs were estimated on the basis of different prices according to the presentation size: the price paid by the Brazilian Ministry of Health in 2011 to conduct target group vaccination (US\$4.63 per dose) for IPV presented in single-dose vials and the price negotiated between the Ministry of Health and the vaccine producer for IPV introduction in routine childhood immunization (US\$2.67 per dose) for IPV presented in 10-dose vials.

Vaccine cost estimates were based on the following steps: identification, estimation of necessary resources, and valuation. The estimated resources were multiplied by the prices (unit costs) to estimate total vaccine costs:

- OPV costs = (Number of estimated administered doses + OPV wastage rate) × price of the OPV dose
- IPV costs = (Number of estimated administered doses + IPV wastage rate) × price of the IPV dose
- Total costs for routine immunization schedule = OPV (routine) costs + IPV costs

IPV introduction in childhood immunization was planned to occur simultaneously with substitution of the diphtheria-tetanus-whole cell pertussis/*Haemophilus influenzae* b (DTPw/Hib) and hepatitis B (HepB) vaccines for a pentavalent vaccine (DTPw/Hib/HepB). The numbers of required injections for each child would not change due to this change. Costs of syringes, safety boxes, and health professionals' vaccine administration time were considered to remain the same using the new immunization protocol as in the old and were not included in the analysis.

We estimated the vaccine volume per fully-immunized child for the "former immunization schedule" (DTPw/Hib + HepB + OPV) and for the "new schedule" (pentavalent + IPV-OPV) to assess the need for expanding the cold storage chain needed to support IPV introduction.

Vaccine volume per fully-immunized child was calculated by multiplying vaccine volume-per-dose (with vaccines stored in secondary packaging) by the number of doses per child, multiplied by a wastage factor.^f Volume-per-dose was estimated for the vaccines produced in Brazil (DTPw/Hib and hepB) according to the size of the secondary

package and the number of doses per box. In cases of internationally produced vaccines, we considered the volume-per-dose published in literature.

The wastage factor was calculated by the formula:

$$\text{Wastage factor} = 1/(1 - \text{wastage rate})$$

The wastage rates used for these estimates were as follows: 5.0% for all single-dose vials; 10.0% for liquid and lyophilized vaccines in 5-dose vials; and 25.0% for liquid vaccines in 10-dose vials. The wastage rate of OPV was estimated on the basis of the number of doses administered and distributed in Brazil in 2010.

RESULTS

According to NIP Coordination, 59,376,500 OPV doses were distributed for both routine immunization and NID. As shown in Table 2, a total of 41,783,381 OPV doses were administered; the wastage rate was 29.6%.

The cost of OPV administered in each NID was estimated at US\$6,800,740.00, depending on the average number of doses (14,691,390) administered during the two NID conducted in 2010 and the wastage rate.

Compared with the all-OPV schedule, including IPV in routine childhood immunization may change annual vaccine costs from -26.5% to +275%, depending on the number of IPV doses in the schedule, the IPV presentation size, and the number of NID conducted, not considering the strategic stock. These changes are shown in Table 3.

As illustrated in Schedule 2, Table 3, for scheduling 1 annual polio NID, the Ministry of Health purchased IPV in 10-dose vials and adopted a routine sequential immunization schedule with two IPV doses followed by three OPV doses. This program annually cost US\$29,653,539 for purchasing the vaccine, a 49.2% increase compared with the all-OPV program (US\$19,873,170), not considering the cost of the IPV strategic stock: US\$3,962,975 in the first year of the program (Table 3). This increase (US\$9,780,369) represented 1.1% of the 2011 NIP vaccine purchase expenditure (US\$862,355,593, as reported by NIP Coordination). Considering IPV purchased using the 10-dose presentation and 1 annual NID, the incremental costs of each additional dose of IPV in the schedule would be US\$1,535,989 for the first dose; US\$8,244,380 for the second dose; US\$8,430,273 for the third dose; US\$7,653,475 for the fourth dose, and US\$2,744,712 for the fifth dose.

^f Brenzel L, Jones A, et al. Immunization financing toolkit: a resource for policy-makers and program managers. Washington (DC): The World Bank; 2010 [cited 2014 Mar 19]. Available from: http://www.who.int/immunization_financing/tools/final_toolkit_2011.pdf

Table 2. Numbers of oral and inactivated polio vaccine doses administered in routine childhood immunization and NID. Brazil, 2010.*

Vaccine	1 st dose	2 nd dose	3 rd dose	4 th dose	5 th dose	Total Routine	1 st NID	2 nd NID	Total Routine + 2 NID
OPV	2,964,284	2,873,602	2,938,396	2,807,857	816,461	12,400,600	14,475,967	14,906,814	41,783,381
IPV	42,710	23,312	19,866	15,921	7,304	109,113	0	0	109,113
OPV + IPV	3,006,994	2,896,914	2,958,262	2,823,778	823,765	12,509,713	14,475,967	14,906,814	41,892,494

Source: DATASUS. Available from: www.datasus.gov.br >Informações em Saúde(TABNET)>Assistência à Saúde/>Imunizações/Doses Aplicadas

OPV: oral polio vaccine; IPV: inactivated polio vaccine; NID: National Immunization Day

* Routine childhood immunization was based on OPV. IPV was available at public health immunization referral centres only for immunocompromised children, HIV-exposed children, and children in contact with immunocompromised persons. In NID, OPV was administered to all children aged 0-5 years, independent of their immunization status.

As shown in Table 4, the cold chain needs assessment revealed that the new polio vaccination schedule saved space in the cold storage chain.

DISCUSSION

The decision to introduce IPV in the Brazilian childhood routine immunization program was driven by ethical issues. VAPP is unacceptable in the absence of wild poliovirus circulation. Considering the high acceptability of OPV in Brazil and its substitution by an injectable vaccine, retaining use of OPV in the early phases of the new polio immunization program is deemed important to ensure high vaccination coverage in Brazilian society. Sequential IPV-OPV schedules reduce the risk of VAPP while maintaining high levels of intestinal mucosal immunity conferred by OPV.²³ The effectiveness of two doses in preventing paralytic polio was estimated at 89.0% (95%CI 62.0;97.0).¹⁶ In the US, switching from an all-OPV to a sequential IPV-OPV schedule, with IPV used in the first two doses, led to a 54.3% reduction in VAPP cases.¹ No VAPP cases occurred in recipients of the sequential IPV-OPV schedule.¹

Among the 46 VAPP cases reported in Brazil from 1989 to 2010, 17 occurred after the first OPV dose, 10 after the second, 4 after the third, and four after the fourth dose; eight occurred among those in contact with a vaccinated child and in three cases, information was not available (Surveillance of Acute Flaccid Paralysis). The sequential schedule with IPV in the first two doses would avoid at least 58.7% of such cases. However, studies report that the risk of VAPP and cVDPV will cease only by eliminating OPV use.^{15,23}

As illustrated in Table 1, vaccination schedules including IPV are not mutually exclusive; they may be seen as steps for switching from an all-OPV to an all-IPV program. More doses of IPV may be introduced as soon as higher vaccination coverage is assured, provided there is sufficient funding and sustainable

vaccine supply. This transition strategy has already been successfully used by other countries such as the US.¹

This study is part of a collaboration with NIP managers to support decision making regarding the incorporation of new vaccines. Countries considering including IPV in routine childhood immunization must be able to guarantee long-term IPV supply, and price is definitely a relevant factor. Assessment of the financial impact of immunization interventions is important to determine long-term resource requirements and their impact on the government budget.

A trade-off between price (higher for single-dose vials) and wastage rate (higher for multi-dose vials) should be considered when choosing vaccine presentation. Ten-dose presentation saved the Brazilian government money as compared with a single-dose presentation. However, our costs of vaccination schedules with IPV in single-dose presentation could be overestimated, because we considered the price (US\$4.63 per dose) paid by the Ministry of Health in 2011 to purchase IPV for immunizing target groups. The Ministry of Health would probably get a lower price for utilizing IPV in universal childhood immunization, although it would not be as low as in the 10-dose presentation. On the other hand, cost estimates of vaccination schedules with IPV in 10-dose presentation were based on the price (US\$2.67) negotiated between the Ministry of Health and the producer to introduce IPV in routine immunization.

An important cost and operational factor of IPV introduction in Brazil was the concomitant substitution of DTPw/Hib and HepB vaccines by a pentavalent combination vaccine. This strategy allowed the Ministry of Health to introduce IPV in childhood immunization without increasing the number of clinic visits or the number of injections necessary to complete immunization and without additional vaccine administration costs. Increasing the numbers of visits or injections required for basic immunization increases the likelihood

Table 3. Annual estimated vaccine costs for different polio vaccination schedules in Brazil and proportion of increase in polio immunization program costs compared with the former all-OPV schedule (routine + 2 NID)^a, considering IPV presented in single-dose and 10-dose vials, and costs of IPV strategic stock (included only in the first year of the vaccination program), 2011.

Vaccination Schedule	IPV in single-dose vial, IPV price = US\$4.63/dose, wastage rate 5% ^b					IPV in 10-dose vial, IPV price = US\$2.67/dose, wastage rate 25% ^b					
	Routine Immunization ^a	Total routine + 1 annual NID ^b	Total routine + 2 annual NID ^c	IPV strategic stock (25%)	Routine immunization ^a	Total routine + 1 annual NID ^b	Total routine + 2 annual NID ^c	IPV strategic stock (25%)	Total routine + 1 annual NID ^b	Total routine + 2 annual NID ^c	IPV strategic stock (25%)
All-OPV ^a	6,271,690	NA	19,873,170	NA	NA	NA	NA	NA	NA	NA	NA
1 (1 IPV and 4 OPV)	19,335,336 (-2.7%)	26,136,076 (+31.5%)	32,936,816 (+65.7%)	3,563,620	14,608,419 (-26.5%)	21,409,159 (+7.7%)	28,209,899 (+41.9%)	2,048,057			
2 (2 IPV and 3 OPV)	31,999,345 (+61.0%)	38,800,085 (+95.2%)	45,600,825 (+129.5%)	6,895,577	22,852,799 (+15.0%)	29,653,539 (+49.2%)	36,454,279 (+83.4%)	3,962,975			
3 (3 IPV and 2 OPV)	44,948,902 (+126.2%)	51,749,642 (+160.4%)	58,550,382 (+194.6%)	10,302,662	31,283,072 (+57.4%)	38,083,812 (+91.6%)	44,884,552 (+125.9%)	5,921,070			
4 (4 IPV)	56,909,657 (+186.3%)	63,710,397 (+220.6%)	70,511,137 (+254.8%)	13,549,918	38,936,547 (+95.9%)	45,737,287 (+130.2%)	52,538,027 (+164.4%)	7,787,309			
5 (5 IPV)	60,921,328 (+206.6%)	67,722,068 (+240.8%)	74,522,809 (+275.0%)	14,505,078	41,681,259 (+109.7%)	48,481,999 (+143.9%)	55,282,740 (+178.2%)	8,336,252			

OPV: oral polio vaccine; IPV: inactivated polio vaccine; NID: National Immunization Day; NA: not applicable

US\$1.00 = R\$1.8758 (real, the Brazilian currency) on December 30, 2011

^a OPV was administered in routine immunization up to August 2012 and IPV was available (in single-dose vials) in public health immunization referral centers (Reference Centers for Special Immunobiologicals) only for children with OPV contraindication, such as immunocompromised children, HIV-exposed children, and children in contact with immunocompromised persons. Two NID were conducted annually, when OPV was administered to children aged 0-5 years, independent of their vaccination status.

^b OPV wastage rate was estimated as 29.6% in both routine vaccination and NID, according to the distributed and administered doses in Brazil, in 2010.

^c OPV costs for each NID were estimated at US\$6,800,740.00 according to the mean number of doses administered in both NID conducted in 2010 plus the wastage rate. Vaccine price per dose: OPV = US\$0.36; IPV = US\$2.67 for 10-dose presentation and IPV = US\$4.63 for single-dose presentation.

Table 4. Characteristics of vaccine presentation and the estimated vaccine storage volume per fully-immunized child for the “former immunization schedule” (all-OPV + DTPw/Hib + HepB) and for the “new schedule” (IPV-OPV + DTPw/Hib/HepB). Brazil, 2011.

	Number of doses per vial and number of vials per package	Vaccine volume per dose (cm ³)	Number of doses per FIC	Wastage factor ^a	Vaccine storage volume per FIC ^b (cm ³)
Liquid + lyophilized tetra: DTPw/Hib (Butantan/BioManguinhos)	5-dose vials in a box of 5	18.8	3	1.1	62.8
HepB (Butantan)	10-dose vial in a box of 20	4.1	3	1.3	16.3
OPV (BioManguinhos)	25-dose vial in a box of 100	1.0	3	1.4	4.3
Former schedule (DTPw/Hib + HepB + OPV)					83.4
Liquid penta (DTPw/Hib/HepB)	1-dose vial in a box of 50	12.9	3	1.0	40.7
IPV	1-dose vial in a box of 50	12.9	2	1.0	27.2
IPV	10-dose vial in a box of 10	2.46	2	1.3	6.6
OPV	25-dose vial	1.0	1	1.4	1.4
New schedule (Liquid penta + 2 IPV + 1 OPV) with IPV in a 1-dose vial					69.3
New schedule (Liquid penta + 2 IPV + 1 OPV) with IPV in a 10-dose vial					48.7

OPV: oral polio vaccine; DTPw: diphtheria-tetanus-whole cell pertussis; Hib: *Haemophilus influenzae* b; HepB: hepatitis B; IPV: inactivated polio vaccine; FIC: fully-immunized child

^a Wastage factor = 1/(1 - wastage rate). The following wastage rates were used: single-dose vials, 5.0%; 5-dose vials, 10.0%; liquid vaccine in 10-dose vials, 25.0%. OPV wastage rate was estimated as 29.6%, according to the distributed and administered doses in Brazil in 2010.

^b Vaccine volume per fully-immunized child = packed volume per dose multiplied by the number of doses, multiplied by the wastage factor.

of a missed vaccination. This is particularly important when considering the large number of new vaccines recently introduced in childhood immunization. New vaccine introduction also places significant pressure on the cold storage chain; as illustrated in Table 4, combination vaccines save space in the cold storage chain. Combination vaccines may facilitate the incorporation of IPV into the NIP.¹⁸ They simplify vaccine purchase, storage, and handling, reduce costs of labor and supplies, and reduce the need for additional clinic visits to avoid multiple injections, thereby improving compliance with vaccine recommendations.^{11,18}

In recent years, Brazil has strengthened its public health capability to deliver domestic immunobiological products by developing research and technology transfer agreements, allowing it to avoid dependence on importation of essential public health products. In 2007, approximately 83.0% of the vaccines used in the NIP were produced in Brazil.¹³ Production of an IPV-containing hexavalent combination, difficult but feasible, would allow Brazil to further reduce the number of injections and administration costs.

Our study has limitations. Costs of other combination vaccines containing IPV, such as diphtheria-tetanus-acellular pertussis/IPV (DTPa/IPV), DTPa/HepB/IPV, or DTPa/Hib/IPV, were not taken into account in this analysis because they were not being considered by the Ministry of Health. Administration costs were also not taken into account. Because of the concomitant switch from DTP/Hib and HepB to a pentavalent combination vaccine, the main driver of the cost for IPV introduction in Brazil was the cost of the vaccine. This may not be the case in other countries considering IPV introduction.

The costs of the NID involve more than purchasing vaccines, estimated in this study as US\$6,800,740.00 per NID. The costs of the two NID amounted US\$24.8 million in 2010, on average US\$12.4 million for each NID, including vaccine supply. The efforts to conduct an NID almost doubles vaccine costs (NIP Coordination information), and these costs were not considered in our study.

Replacing an all-OPV with an IPV-based immunization schedule poses many programmatic challenges; these include ensuring vaccine supply, training health

care staff to administer the new vaccine, and assuring high vaccination coverage. Incorporating IPV in routine immunization would incur costs related to social mobilization, educational initiatives, health care staff training and supervision, and redesign of stationery, which were not included in this study.

In May 2012, the World Health Assembly (the decision-making body of the WHO) declared eradication of polio as a programmatic emergency for global public health. The Polio Eradication Endgame Strategic Plan (2013-2018) outlines a comprehensive approach to complete polio eradication, including eradication of both wild and vaccine-related viruses.²³ Introducing at least 1 dose of IPV in routine immunization is a key point in this strategy; its primary aim is to preserve immunity against type-2 poliovirus while globally replacing trivalent OPV (tOPV) with bivalent

OPV (bOPV) containing types 1 and 3 vaccine poliovirus.²³ In April 2014, 36.0% of the 194 WHO Member States reported they have already introduced IPV in their immunization initiatives.²⁴

IPV prices are dropping in the international market. IPV cost US\$5.98 per dose in 2012 and US\$2.80 in the 2014 Revolving Funding Program of the Pan American Health Organization (PAHO). IPV is becoming available at approximately US\$1.00 per dose in 10-dose vials for GAVI Alliance (formerly the Global Alliance for Vaccines and Immunizations) eligible countries in 2014.²⁴ For middle-income countries, IPV will be available at US\$2.10-US\$3.30 per dose in 10-dose presentation. Another supplier is offering IPV at US\$1.90 per dose in 5-dose presentation.²⁴ This price reduction will allow more countries to be able to introduce at least one dose of IPV in routine childhood immunization.

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