

## **Rotavirus immunization: global coverage and local barriers for implementation.**

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## **ABSTRACT**

**Background:** Rotavirus (RV) is a major agent of gastroenteritis and an important cause of child death worldwide. Immunization (RVI) has been available since 2006. the Federation of International Societies of Gastroenterology Hepatology and Nutrition (FISPGHAN) identified RVI as a top priority for the control of diarrheal illness. A FISPGHAN working group on acute diarrhea aimed at estimating the current RVI coverage and identifying barriers to implementation worldwide.

**Methods:** A survey was distributed to national experts in infectious diseases and vaccinations, and health-care authorities (March 2015 -April 2016), collecting information on local recommendations, costs and perception of barriers to implementation.

**Findings:** RVI is recommended in 27/49 countries (55%) participating in the survey. Although five countries have recommended RVI since 2006, a large number (16, 33%) included RVI in a National Immunization Schedule between 2012 and 2014. The costs of vaccination are covered by the government (39%), by the GAVI Alliance (10%) or public and private insurance (8%) in some countries. However, in most cases, immunization is paid by families (43%).

Elevated costs (49%) and the limited perception of RV illness severity by the families (47%) and public-health authorities (37%) are the major barriers to large-scale RVI programs.

**Interpretation:** After 10 years since its introduction, the implementation of RVI is still unacceptably low and should remain a major target for global public health. Barriers to implementation vary according to setting. Nevertheless, public health authorities should promote education for caregivers and health-care providers and interact with local health authorities in order to implement RVI

**Key words:** Rotavirus, diarrhea, immunization, vaccine, implementation

**Abbreviations:** RV: Rotavirus, RVI: RV immunization, AGE: acute gastroenteritis, FISPGHAN: Federation of International Societies of Gastroenterology Hepatology and Nutrition, GAVI: Global Alliance for Vaccine Immunization, NIP: National Immunization Programs, WHO: World Health Organization,

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### **Evidence before this study**

Rotavirus infection has a relevant impact of child morbidity and mortality worldwide.

In countries where Rotavirus immunization (RVI) has been actively implemented, a significant reduction of morbidity, hospitalizations and costs has been reported.

Although RVI is currently recommended by all authoritative guidelines, data on coverage are available only in selected areas, and barriers to local implementation are unknown.

### **Added value of this study**

The present study estimates RVI coverage in 49 world countries and identifies the major barriers to local implementation. These findings may help to define possible interventions to reach the goal of global coverage.

### **Implications of all the available evidence**

Scientific societies and public-health authorities should promote education for families/caregivers and physicians and interact with local health organizations to develop strategies to spread RVI worldwide.

## INTRODUCTION

Rotavirus (RV) is the most common agent of acute gastroenteritis (AGE) in children under five years of age, and the most severe independent of age<sup>1,2</sup>. Despite a progressive decrease in diarrhea-related deaths, RV is still a major cause of mortality mainly in developing countries<sup>3</sup>. RV disease can be prevented by vaccination, and 95% of RV-induced deaths occurred in 72 countries, which were all eligible to receive Global Alliance for Vaccine Immunization (GAVI) support. As of January 1, 2016, 80 of the 195 countries worldwide have introduced RV vaccines in their National Immunization Programs (NIP)<sup>4</sup>. There are public health barriers to the implementation of RV immunization (RVI), but WHO and other authorities recommend universal immunization<sup>5</sup>. Two vaccines with high efficacy and good safety profiles are currently available (Rotarix™ and RotaTeq®). Both vaccines aim to prime broad immune responses followed by progressively broader protection developing through successive natural rotavirus infections<sup>6-9</sup>.

Thus far, RV vaccines have been introduced in United States, some European countries, and Australia and are being implemented in selected countries in Asia.

Potential major barriers to large-scale immunization are the need for administration within a limited time frame (six to eight weeks following birth) and a vaccination schedule that needs to be completed by six months of age so as to decrease the possible vaccine-related risk of intussusception. The likelihood of intussusception following RVI is low based on the results of both large clinical trials and post-marketing surveillance data. Furthermore, the benefit in lives saved by broadening age restrictions for immunization may well exceed the risk of potential deaths related to intussusception<sup>10</sup>.

In 2012, the Federation of International Societies of Pediatric Gastroenterology, Hepatology, and Nutrition (FISPGHAN) identified the spread of RV vaccination as a top priority for the control of diarrheal illness in childhood<sup>11</sup>.

In order to estimate current RVI coverage and identify the major barriers to local implementation, the FISPGHAN Working Group (WG) on AGE conducted a global survey aimed at collecting information on RVI worldwide.

## METHODS

### ***Working Group and survey***

The WG on AGE was created during the FISPGHAN World Congress held in Taiwan in 2012 and encompasses two experts of each continental Society of Pediatric Gastroenterology, Hepatology and

Nutrition: European (ESPGHAN), Asian Pan Pacific (APPSGHAN), Commonwealth Association (CAPGHAN), Latin American (LASPGHAN) and North American (NASPGHAN) Societies.

In order to identify and promote practical interventions that will help to reduce the burden of AGE in children worldwide, the WG on AGE collaborated with experts in the field of RVI actively involved in the dissemination of RVI around the world.

The WG coordinators developed a survey including information on the availability of RV vaccines, inclusion in the NIP, immunization coverage according to local available data, costs and financial support, main perceived barriers to implementation, possible interventions to achieve >90% global coverage (see Table 1 in Supplemental material). The survey successively was circulated among the WG members for approval.

### ***Study design***

National experts in infectious diseases and vaccination from several countries in the world were contacted between October 2015 and May 2016. Experts were identified among the members of national institutes for health, panels for local immunization programs, scientific societies working and/or reporting data on RVI (see Table 2 in Supplemental material).

All of them were asked to fill-in a survey to give information on inclusion of RV vaccination in their country's NIP, implementation programs, costs and their perception of local barriers to implementation. All participants were encouraged to provide original local evidence supporting their data and to report the source of information (see Table 2 in Supplemental material).

### ***Data analysis***

The WG planned to reach at least one referral expert for each world country. When more than one expert from the same country participated to the survey, the data were discussed and combined and analyzed as a single source.

Since data and opinions about local barriers may vary slightly according to the setting, rough data were analyzed and reported according to the Human Development Index (HDI) list of countries with advanced economy (<http://hdr.undp.org/en/content/human-development-index-hdi>) and countries were differentiated into high HDI countries, medium HDI countries and low HDI countries.

Data were summarized as means $\pm$ SD for continuous variables and as percentage and frequencies for categorical variables. Comparison of groups was performed using one-way analysis of variance (ANOVA) for multiple group comparisons. Chi-square test with Fisher's correction was used to

address any differences for categorical variables, as needed. A *p* value of 0·05 or less was considered as significant. Results were updated in December 2015.

### ***Role of the funding source***

Neither the WG nor single authors receive any economic support to carry out the study.

## **RESULTS**

Ninety-one experts in the field were contacted by e-mail or met personally at medical meetings, symposia and workshops worldwide. Among the 79 countries contacted, 49 provided a survey eligible for analysis (response rate 62%)(Figure 1). Forty-two of the 49 responders provided data for all required fields, but for other seven countries the data on RVI coverage were not available (Ireland, Lithuania, Portugal, Romania, Singapore, Slovenia, Switzerland) although the survey was completed in all other fields.

Responders were equally distributed between low- (23, 47%) and medium/high-income countries (26, 53%).

### ***Rotavirus immunization coverage and costs***

RVI is recommended in 27 out of the 49 countries (55%) participating in the global survey (Table 1). Although some countries have recommended RVI since 2006, most countries (16/49, 33·3%) first included RVI in the NIP between 2012 and 2014 (Table 1). RVI rates showed a scattered pattern from 0 to over 90% according to different countries. Overall RVI coverage is reported in Figure 2.

Rotarix™ and Rotateq® are both distributed worldwide, with 40 (81·6%) and 38 (77·5%) countries respectively, but Rotarix® is prevalent in African countries (Table 2).

The costs of vaccines are substantially different, being higher in European and American and lower in Asian and African countries (Table 2). Costs reported for a complete vaccination cycle with Rotateq® are slightly higher than those of Rotarix™ in average (176·8 vs 103·8USD, *p*=0.14).

These costs are covered by the government in 38·7% of countries included in the survey, by international organization such as the GAVI Alliance (10·2%) or public and private insurance (8·1%). However, in most cases, these costs are charged directly to families (42·8%)(Table 2).

It should be noted that national policies for reimbursement are often reassessed. For example, in Latvia, Europe, the government has partially reimbursed RV vaccination since September 2012 and full reimbursement was introduced in January 2015. In France the vaccination was available since 2006 and has been successively included in the NIP in 2013 at expenses of families. However, at

the moment the survey was collected the government was substantially reviewing the national recommendations and possible coverage of expenses for RVI due to a warning released by the National Agency of Drug Safety. In the United States of America, beginning September 2010, children 0 through 18 years that are enrolled in new private health plans are eligible to receive vaccines (including RV), without any cost-sharing requirements when provided by an in-network provider. Children covered by government insurance were already fully eligible. These major changes in local policy for RVI may well significantly impact future immunization coverage.

### ***Barriers to local implementation***

The direct and indirect costs for immunization and the limited perception of RV severity by the families are two major barriers for large-scale implementation of RVI programs (Figure 3, Table 3). Only eight countries reported the timing of first administration within six weeks as a major barrier (Figure 3, Table 3).

The underestimation of RV severity by public health authorities is a common barrier worldwide, however, it is particularly relevant in developing countries with low and medium HDI (Table 3). An impact of anti-vaccination movements and a general fear about vaccines' side effects was reported in the United States, Latvia, and Iraq. In France, the notification of serious side effects after RVI had a relevant impact on national agency recommendations and on local immunization coverage.

In Malaysia, the government did not consider RVI as a health priority and restricted funds for RVI implementation and reimbursement. In addition, two experts reported that the finding of porcine circovirus DNA fragments in vaccines available on the market<sup>12,13</sup> had a relevant negative impact on local implementation of RV vaccines for religious reasons.

In Zambia, the overall erratic distribution of vaccines has been reported as a major barrier to large-scale implementation of RVI.

### ***What FISP GHAN can do?***

To the question "How could FISP GHAN help to achieve the goal?" most experts suggested educational initiatives to be adopted as primary intervention (Figure 4). The majority of responders identified the need of public educational campaigns (33/49, 67.3%) or educational programs addressed to local health-care providers (24/49, 48.9%).

This is particularly true in low-income countries where the majority of responders indicated the education directed to caregivers (88%) or physicians (50%) as the major interventions to be

promoted (Figure 4). According to the result of our survey, the education programs for caregivers could be started in the third trimester of gestation or alternatively during first well-baby visits. The latter may also provide an optimal opportunity to administer the vaccine.

Countries with medium-high or very high income suggested FISPUGHAN could provide support for public health legislation aiming to reduce vaccination costs and simplify access to vaccination (Figure 4). In addition, FISPUGHAN should interact with national health authorities to promote the inclusion of RVI in the NIP and to enhance the cooperation amongst the active stakeholders to improve the spread of information.

## DISCUSSION

This study provides a worldwide overview of the status of RVI and outlines the main barriers to local implementation of RV vaccination with the final aim of identifying possible interventions that may help to reach a goal of global coverage. Our results showed that common barriers to the implementation of RV vaccine included its costs and the perception of a low disease burden as observed in a previously publication in European countries where potential safety concerns represented a third relevant barrier<sup>14</sup>.

### *RVI coverage and costs*

Oral RV vaccines can prevent severe cases of infection. Even if RV vaccination is currently recommended by WHO and all authoritative guidelines<sup>5,15-19</sup>, RVI coverage significantly varies in the world, and even within the same geographical area (from 0 to over 90%). In Europe only few countries such as Austria, Belgium and Finland have reached adequate vaccination coverage as high as 90%, despite the specific recommendations of European guidelines since 2008<sup>18</sup>. The inclusion in those countries of the RV vaccine in the NIP since 2006-2007 and the implementation of clinical studies conducted by local researchers<sup>20-22</sup> may well have positively impacted the current rate of immunization coverage.

The scenario in North and South America seems to be different: in almost all countries included in the survey the vaccine is recommended and the coverage rates range from 50% (Peru) to over 90% (United States). The only exception is represented by Canada, where recommendations vary according to regional provinces and coverage has been estimated <10%. Coverage in Asian countries is even lower and only Japan reported values above 10%, probably because in most Asian countries the RV vaccine is not nationally recommended by health authorities, with exception of Taiwan and Iraq, and more recently India.



High coverage rates have been reached in African countries where GAVI alliance supported RV vaccination campaign (Rwanda, Ghana, Tanzania and Botswana).

In addition, we observed that, after approval of the two RV vaccines and early endorsement by some countries in 2006, most countries recommended RVI very recently between 2012 and 2014. This two-peak distribution might be affected by the emergence of data on potential side effects, including the risk of intestinal intussusception (2008-2012)<sup>23</sup> and the presence of porcine circovirus in Rotarix™ (2009-2010)<sup>24</sup>.

There was no significant difference in the distribution of the two main types of vaccines, but RotaTeq® tended to be less employed in African countries confirming previous reports that identified Rotarix™ as a preferred choice due to a better cost-effectiveness, the requirement of fewer doses and less storage space, and proven thermo-stability<sup>25</sup>. Significant differences emerged in relation to costs, which are higher in European and American countries and lower in Asia and Africa. This represents a commitment that developed countries could support RVI in developing areas especially due to GAVI international support<sup>26</sup>. Up to 2014, GAVI supported the introduction of RVI in the NIP of 16 African and South American countries<sup>26</sup>.

### *Barriers to RVI implementation*

Elevated costs of immunization and a misperception regarding the potential severity of RV infection and its consequences have been identified as the major barriers to universal dissemination of RVI. However, the factors limiting local implementation vary greatly between countries and even within the same geographic area. In Europe, the opinion of experts varied country by country, from Finland where no barriers to implementation were reported to Slovenia where RVI “is not recognized by far as a priority among vaccine-preventable diseases”. Awareness of disease burden can drive vaccination uptake, as suggested in several studies<sup>14, 27-28</sup>. According to our results it was felt that a large percentage of caregivers are simply not aware of risks of RV infection probably because they received inadequate information. Many parents are aware of the risk of hospitalization or death, but most do not know about the advantages and availability of RV vaccines in their own country. Counseling can be an integral part of health education to the public and can provide useful information against vaccine-preventable diseases to families who accept to receive information by health-care personnel<sup>27</sup>.

Unfavorable cost-effectiveness has been put forward as a reason not to implement universal RV vaccination in several countries<sup>28</sup>. Because tender prices are unknown, some experts in health economics advise that the focus should be on threshold prices<sup>29</sup>. Indirect costs are also an important part of the economic burden of RV gastroenteritis. Universal vaccination has been estimated to be

cost-effective from a wider societal perspective, in particular in relation to the beneficial effects coming from herd immunity<sup>30</sup>. In keeping with our results, previous studies also identified the concerns about reimbursement issues and parental acceptance of the vaccine as major barriers to optimal implementation of RV vaccination. Copayment systems or funding by sickness funds have been implemented as an alternative to national funding in several high-income and medium-income countries<sup>14</sup>. However, guidelines were against the hypothesis of immunizing at risk populations only<sup>18,19</sup>.

A further barrier is represented by the overall concern of vaccine-related side effects that, together with anti-vaccination movements, impact on immunization campaign worldwide. In France, the notification in December 2014 of three deaths and about 50 intussusceptions after RV vaccine administration significantly changed government's attitude towards routine RVI and national agency recommendations (Letter reported at <http://www.bmj.com/content/350/bmj.h2867/rr-1>). Surprisingly, the RVI time schedule with the introduction of the first dose within the first six weeks of life, was not been identified as a major barrier. The first dose could be administered together with other vaccines starting from the second month of life, which could enhance RVI.

Other barriers have been reported by experts as a result of the direct interaction that FISPUGHAN had with local experts: one of these is related to a religious matter. In Malaysia, a country with a predominance of people practicing Islam (over 60%), the finding of DNA fragments of porcine circoviruses type-1 in RV vaccines Rotarix<sup>TM</sup> has been reported as a relevant barrier for local implementation of large-scale immunization programs.

The Strategic Advisory Group of Experts on immunization in 2010 reported to the World Health Organization that porcine circovirus type-1 is not known to cause disease in humans and is often found in food products, confirming the safety of Rotarix<sup>TM</sup><sup>5,24</sup>. However, according to our data, in an Islamic-prevalent country the potential assumption of pig derivate seems to overweigh safety reasons and this significantly impacts on regional health authorities, religious leaders and families' beliefs.

#### *Future prospective for RVI implementation*

Educational initiatives directed at health-care providers and caregivers have been identified as primary interventions that should be adopted and promoted. However the role of FISPUGHAN is likely to vary according to setting and countries needs. Countries with medium-high or very-high income asked FISPUGHAN to support public health legislation aimed at a reduction in vaccination costs and simplified access to vaccination. Systems involving different health-care workers were

effective. For example, in Norway the nurses, who are responsible for the child immunization program, provide information to caregivers using printed information material and web-pages. In developing areas, some experts suggested a role by FISP GHAN in supporting public health legislation and the introduction of RVI in NIP as well as in promoting the enhancement of cooperation and information flow between local health-care practitioners, regulatory authorities and field workers.

This survey was supposed to cover as many countries as possible to ensure a better view of RVI scenario in the world. Unfortunately, despite our commitment and efforts, we have been able to obtain reliable information from only a quarter of world countries, and this represents a limitation of our study. However, we observed a balanced distribution between high- and low-income countries and provided useful new information about RVI coverage and barriers to implementation of RVI. A further limitation of our survey is that data about RVI coverage are based on single person reports. However it should be considered that all enrolled health-care workers are experts in the field and provided supporting data including material from local literature, websites or published material (see Supplemental material).

In conclusion, immunization is the best approach for preventing RV infection.

After approximately 10 years since the introduction of RVI, the implementation of this major life saving intervention is still unacceptably low and remains a major target for reaching the Millennium Developmental Goal.

Barriers to implementation vary according to setting and local conditions, but the costs of RVI programs and perceptions about disease burden are major barriers for global dissemination of RVI. In order to sustain and implement RVI, medical professional societies and public health authorities should promote education for caregivers and physicians and interact with local health organizations to enhance networking among stakeholders and develop strategies to reduce RVI-related costs.

## **DECLARATION OF INTERESTS**

The authors have no financial relationships relevant to this article to disclose.

The authors have no conflicts of interest relevant to this article to disclose.

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## FIGURE LEGEND

**Figure 1.** Flowchart of study methodology.

FISPGHAN: Federation of International Societies of Pediatric Gastroenterology Hepatology and Nutrition, APPSGHAN: Asian Pan Pacific Society of Pediatric Gastroenterology Hepatology and Nutrition, CAPGHAN: Commonwealth Association of Paediatric Gastroenterology & Nutrition, ESPGHAN: European Society of Pediatric Gastroenterology Hepatology and Nutrition, LASPGHAN: Latin American Society of Pediatric Gastroenterology Hepatology and Nutrition, NASPGHAN: North American Society of Pediatric Gastroenterology Hepatology and Nutrition. CDC: Center for Disease Control and Prevention – Atlanta United States

**Figure 2.** Global coverage for Rotavirus Immunization.

**Figure 3.** Barriers to local implementation of Rotavirus immunization (Pareto Chart).

**Figure 4.** FISPGHAN activities to improve rates of Rotavirus immunization coverage.

## **CONTRIBUTORS' STATEMENT**

ALV and AG conceived and designed the study.

ALV and IL prepared the first draft of the survey.

JAD, JAB, CB, MBC, SC, ESL, BS, PMS, TS and AG revised and approved the survey before dissemination. AG coordinated the working group and the dissemination of the survey.

JAD, JAB, CB, MBC, SC, ESL, BS, PMS, TS as member of the working group on acute diarrhea of the Federation of International Societies of Gastroenterology Hepatology and Nutrition (FISPGHAN), helped to contact delegates for each participating country.

SP provided contacts for African countries and helped in collecting data.

ALV and IL developed the database, collected data and performed the statistical analysis.

ALV and IL wrote the first draft of the manuscript.

MBC, PMS, ESL and AG provided substantial contribution to draft the paper and review the tables and figures. JAD, JAB, CB, SC, BS, TS, SP reviewed the manuscript and provided intellectual content to the final draft.

All authors gave their final approval of the version to be published and agree to be accountable for all aspects of the work.

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**Table 1. Inclusion of Rotavirus Immunization in national immunization plans according to different countries.**

Continent	Country	Recommendation by National Immunization Plan	Year of start
Africa	Botswana	Recommended	2012
	Ethiopia	Recommended	2013
	Ghana	Recommended	2012
	Kenya	Recommended	2014
	Nigeria	Not recommended	
	Rwanda	Recommended	2012
	Senegal	Recommended	2014
	Tanzania	Recommended	2012
	Uganda	Not recommended	
	Zambia	Recommended	2013
Asia and Oceania	Bangladesh	Not recommended	
	Cambodia	Not recommended	
	China	Not recommended	
	Japan	Recommended*	2011
	India	Recommended*	2016
	Indonesia	Not recommended	
	Iraq	Recommended	2012
	Israel	Recommended	2011
	Malaysia	Not recommended	
	Singapore	Not recommended	
	South Korea	Not recommended	
	Taiwan	Recommended	2006
	Thailand	Not recommended	
Europe	Austria	Recommended	2007
	Belgium	Recommended	2006
	Estonia	Recommended	2014
	Finland	Recommended	2009
	France	Recommended	2013
	Germany	Recommended	2013
	Ireland	Not recommended	
	Italy	Not recommended	
	Latvia	Recommended	2010
	Lithuania	Not recommended	
	Netherlands	Not recommended	
	Norway	Recommended	2014
	Poland	Not recommended	
	Portugal	Not recommended	
	Romania	Not recommended	
	Russia	Not recommended	
	Slovenia	Not recommended	
	Switzerland	Not recommended	
	Turkey	Not recommended	

	United Kingdom	Recommended	2013
North America	Canada	Recommended*	2006
	Mexico	Recommended	2013
	USA	Recommended	2006
South America	Brazil	Recommended	2006
	Chile	Not recommended	
	Peru	Recommended	2009

\* RV vaccination is recommended only in some regions of the country.

**Table 2.** Rotavirus vaccines and relative costs according to continents.

Questions	Total (n=49)	Africa (n=10)	Asia (n=13)	Europe (n=20)	North America (n=3)	South America (n=3)	p
Inclusion in NIS (n, %)	27 (55.1)	8 (80)	5 (38.4) <sup>§</sup>	9 (45) <sup>§</sup>	3 (100)	2 (66.6)	0.116
<b>Available vaccine</b>							
Rotarix (n, %)	40 (81.6)	7 (70)	10 (76.9)	17 (85)	3 (100)	3 (100)	0.627
RotaTeq (n, %)	38 (77.5)	3 (30)	11 (84.6)	18 (90)	3 (100)	3 (100)	0.002
Other (n, %)	2 (4)	0 (0)	2 (15.3)	0 (0)	0 (0)	0 (0)	0.217
None (n, %)	3 (6.1)	1 (10)	2 (18.2)	0 (0)	0 (0)	0 (0)	0.422
<b>Costs in USD</b>							
Rotarix (mean+SD)	103.8 (70.1)	12.6 (18.5)	80.0 (56.1)	140.6 (56.4)	182 (45.3)	57.5 (61.5)	<0.001
RotaTeq (mean+SD)	176.8 (267.4)	15 (NA)	84.9 (47.8)	253.2 (363.3)	187.8 (53.4)	125.5 (44.5)	0.64
Other (mean+SD)	37.5 (48.8)	-	37.5 (48.8)	-	-	-	NA
<b>Payment charged to:</b>							
Family (n, %)	21 (42.8)	2 (20)	8 (61.5)	10 (50)	0 (0)*	1 (33.3)	0.149
Government (n, %)	19 (38.7)	4 (40)	3 (23)	7 (35)	3 (100)	2 (66.6)	0.054
GAVI Alliance (n, %)	5 (10.2)	4 (40)	1 (7.6)	0 (0)	0 (0)*	0 (0)	0.014
Insurance (n, %)	4 (8.1)	0 (0)	1 (9)	3 (15)	0 (0)*	0 (0)	0.638
No answer	1 (2.0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	NA

NIS = National Immunization Schedule, NA = Not assessable

\* Private Insurance may cover the cost of vaccination.

§One country changed recommendation in 2015-2016 (see text)

**Table 3.** Major barrier to the implementation of Rotavirus Immunization according to Human Development Index (HDI)

Barriers to RV immunization	Total (n=49)	Low HDI Countries (n=8)	Medium-High HDI Countries (n=16)	Very-High HDI Countries (n=25)	p
Elevated Costs (n, %)	24 (48.9)	1 (12.5)	10 (62.5)	13 (52)	0.06
Limited perception of RV severity by the family (n, %)	23 (46.9)	5 (62.5)	8 (50.0)	10 (40)	0.52
Limited perception of RV severity by public health authorities (n, %)	18 (36.7)	5 (62.5)	7 (43.7)	5 (20)	0.06
Limited perception of RV severity by physicians (n, %)	12 (24.5)	2 (25)	4 (25.0)	6 (24)	0.99
Timing of administration within 6 weeks (n, %)	8 (16.3)	1 (12.5)	5 (31.2)	2 (8)	0.14
Anti-vaccination movement/concern about side effects (n, %)	4 (8.1)	0 (0)	1 (6.2)	2 (8)	0.71
No protection against other diarrheal agents (n, %)	2 (4.1)	1 (12.5)	0 (0)	1 (4)	0.34
Erratic supply of vaccines (n, %)	1 (2.0)	1 (12.5)	0 (0)	0 (0)	0.07
Religious barriers (n, %)	1 (2.0)	0 (0)	1 (6.2)	0 (0)	0.07

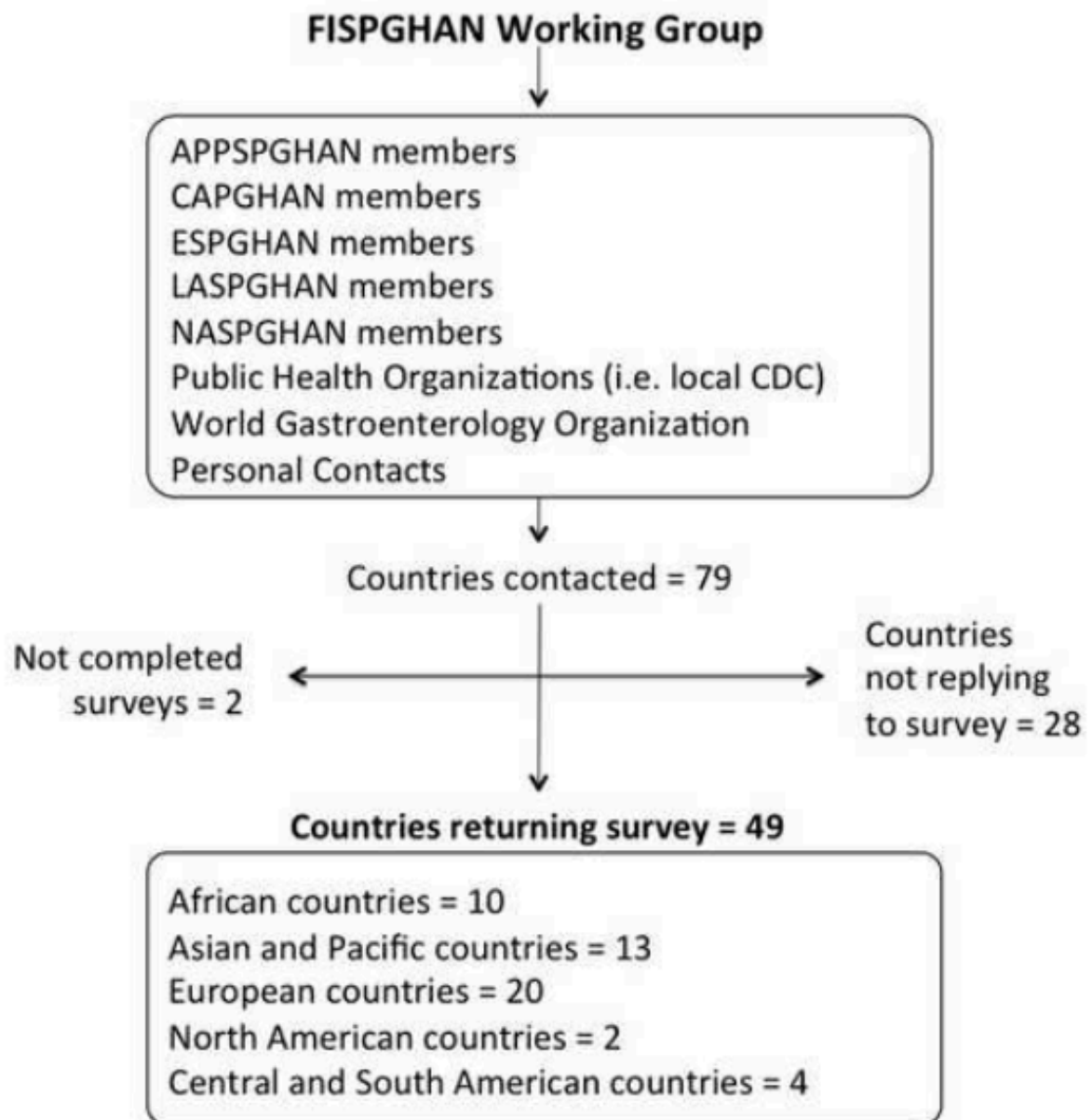


Figure 1

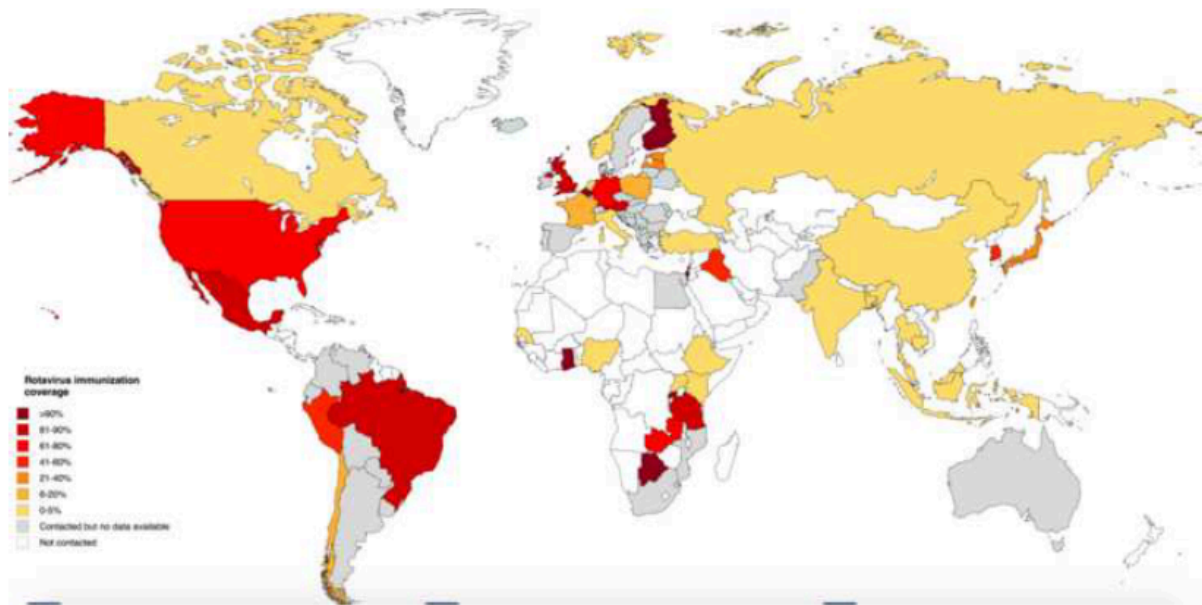


Figure 2

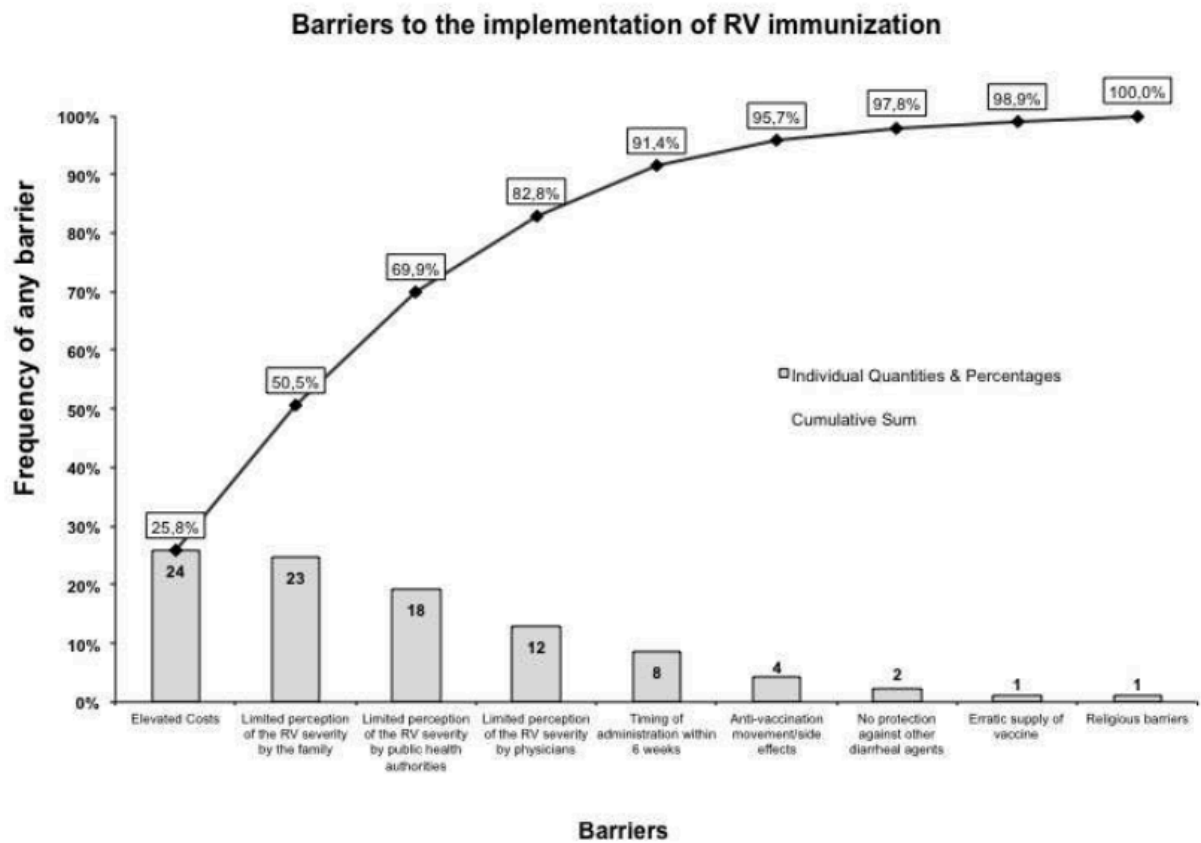


Figure 3

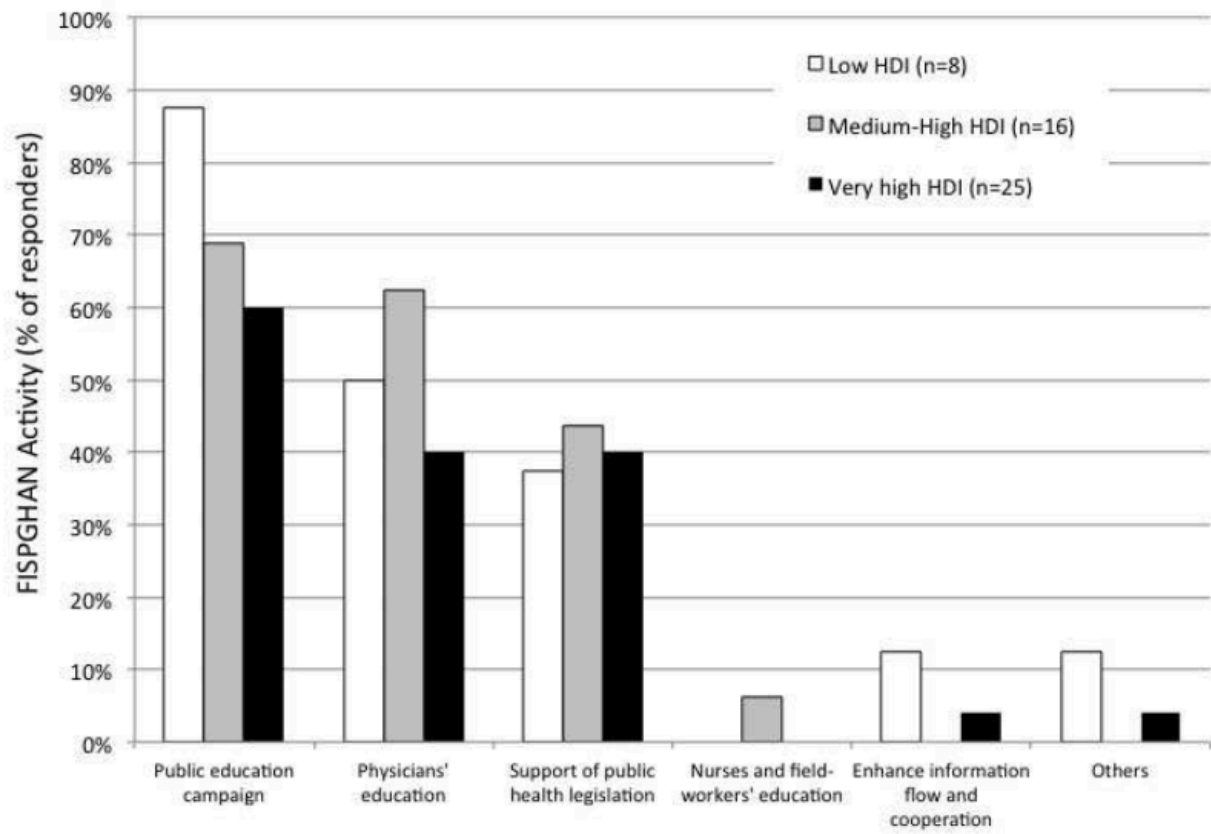


Figure 4

