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Rotavirus vaccines
Update on global impact and future priorities

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Abbreviations: SAGE, strategic advisory group of experts; WHO, World Health Organization; HIV, human immunodeficiency virus; GAVI Alliance, formerly known as the Global Alliance for Vaccines and Immunizations; RV1, monovalent rotavirus vaccine; RV5, pentavalent rotavirus vaccine

Early rotavirus vaccine adopter countries in the Americas, Europe, and in Australia have documented substantial declines in rotavirus disease burden following the introduction of vaccination. However, the full public health impact of rotavirus vaccines has not been realized as they have not been introduced into routine immunization programs in countries of Africa and Asia with the highest rotavirus disease morbidity and mortality burden. In this article, we review the epidemiology of rotavirus disease, the development and current status of rotavirus vaccines including newly available vaccine impact data from early-introducer countries, and future priorities for implementation and monitoring of rotavirus vaccination programs in developing countries.

Rotaviruses are the most common cause of severe infant and childhood gastroenteritis worldwide, responsible for an estimated 23 million outpatient visits, 2.3 million hospitalizations, and over half a million deaths annually among children under 5 y of age.[1,2] To mitigate this substantial burden of disease, two live, oral rotavirus vaccines—a monovalent rotavirus vaccine (RV1), Rotarix® (GSK Biologicals) and a pentavalent rotavirus vaccine (RV5), RotaTeq® (Merck and Company, Inc.,)—are now available for use in over 100 countries. Beginning in 2006, many countries in the Americas and Europe adopted rotavirus vaccines into their national immunization programs following availability of clinical trial data from these regions.[3,4] In 2009, after data on efficacy of rotavirus vaccines became available from Africa and Asia,[5-7] the Strategic Advisory Group of Experts (SAGE) of the World Health Organization (WHO) recommended inclusion of rotavirus vaccines in all national immunization programs worldwide.[8] In this paper, we review the epidemiology of rotavirus disease, the development and current status of rotavirus vaccines including newly available vaccine impact data from early-introducer countries and future priorities for implementation and monitoring of rotavirus vaccination programs in developing countries.

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Epidemiology of Rotavirus Disease

Rotaviruses are 100 nm, non-enveloped RNA viruses that are made up of a triple-layered protein capsid surrounding a viral genome of 11 segments of double-stranded RNA.[9,10] These RNA segments code for six structural proteins and six nonstructural proteins. Two outer layer structural proteins, the VP7 glycoprotein (i.e., G-type glycoprotein) and the VP4 protein (i.e., P-type protease activated protein) determine the G and P serotypes. These structural proteins are the principal targets of neutralizing antibodies that are believed to be important in protection against disease and hence are used in vaccine development. Globally, five G types (G1–G4, and G9) and three P types (P[4], P[6] and P[8]) predominate,[11-18] with G1P[8], G2P[4], G3P[8], G4P[8] and G9P[8] combinations accounting for more than 90% of circulating viruses (**Fig. 1**).[14]

Spread of the virus occurs primarily through the fecal-oral route, by close person-to-person contact,[10] and also likely through contaminated fomites. The latter may be especially important in out-of-home care settings and hospitals.[19-21] Very few infectious virions are needed to cause disease in susceptible hosts.[22] Clinical manifestations of illness range from mild, watery diarrhea to severe diarrhea with vomiting and fever that may result in severe dehydration.[23-27] Complications and fatalities are related almost exclusively to severe dehydration,[28] although rare cases of meningoencephalitis have been reported.[29] Other reported complications include acute myositis, hepatitis, hemophagocytic lymphohistiocytosis and polio-like paralysis, but their relationship to rotavirus infection remains unclear.[30] Rotavirus has also been detected in some surveys of children with intussusception, a form of bowel obstruction in which a portion of intestine invaginates into another, potentially resulting in bowel edema and ischemia. However, results have been equivocal and further study is needed to evaluate if rotavirus is associated with intussusception among children.[31-33] Additionally, although rotavirus infection was originally thought to be confined to the gut, rotavirus antigenemia and viremia have been identified in children with rotavirus disease,

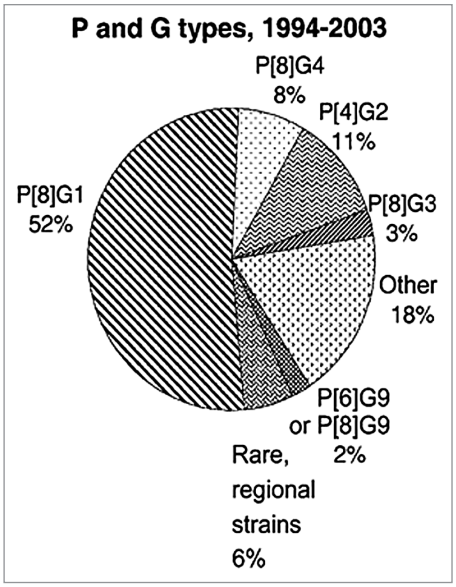

Figure 1. Global distribution of rotavirus strains, 1994–2003. Adapted from Gentsch J, et al.[11]

but the clinical significance of these findings is unclear.[34-36] Symptoms and asymptomatic viral shedding can be prolonged in patients with severely compromised immune systems, such as those with certain primary immunodeficiencies and those who have undergone bone marrow or solid organ transplantation;[37-40] infection does not appear to cause more severe disease in children with human immunodeficiency virus (HIV).[41-43]

Almost all children are infected with rotavirus at least once by the age of 5 y,[44,45] regardless of whether they live in industrialized or developing countries. The ubiquitous nature of rotavirus infection indicates that improvements in sanitation and hygiene will not adequately prevent transmission, and thus, vaccines remain the cornerstone of rotavirus disease prevention. The epidemiology of rotavirus disease, however, can differ among countries. Rotavirus infection has demonstrated winter seasonality in countries located in more temperate climates, but has demonstrated less distinct seasonality in countries located in more tropical climates.[46] In these countries, disease typically tends to occur year-round and there is often greater diversity in the number of circulating rotavirus strains. Also, children in developing countries tend to acquire their first rotavirus infection at an earlier age (approximately 75% are infected by their first birthday) vs. children in developed countries.[47,48] The rates of severe outcomes including mortality are greater in developing country settings possibly because children living in these settings tend to have more co-morbidity, such as co-infections and malnutrition, and limited access to medical care.[1]

Worldwide, an estimated 527,000 children under 5 y of age die each year from rotavirus disease, translating to approximately 1,440 deaths due to rotavirus per day, with more than 85% of these deaths occurring in low-income countries (**Fig. 2**).[1] Rotavirus is the most common cause of diarrhea requiring hospital care in young children. Data from a global rotavirus surveillance network of 43 countries demonstrated that, in 2009, approximately 25–47% of children under 5 y of age hospitalized with diarrhea tested positive for rotavirus. The lowest proportions occurred in countries in the Americas where rotavirus vaccines had already been introduced and reduced the overall rotavirus disease burden.[49]

Evolution of Rotavirus Vaccines

The development of rotavirus vaccines has been based on the premise that a live, attenuated rotavirus vaccine can mimic the immunologic response to natural infection without causing significant symptoms and therefore provide protection against clinical disease following subsequent wild-type rotavirus exposure.[50-52] First generation rotavirus vaccines used naturally attenuated animal strains, but efficacy of these monovalent vaccines against severe rotavirus disease was variable, and none were licensed for use after completion of clinical trials, with the exception of a lamb-derived vaccine that is currently used in China.[53-58] Second generation vaccines, including the currently licensed vaccines, use either naturally attenuated human-animal reassortant strains or an attenuated human strain to induce protection against disease.[59]

In 1998, a rhesus-human rotavirus vaccine (RotaShield®, Wyeth Lederle Vaccines) was licensed in the US after clinical trials in Finland, the US, and Venezuela demonstrated vaccine efficacy of 82–91% against severe rotavirus gastroenteritis.[60-63] However, the vaccine was withdrawn from the US market less than one year after its licensure due to an association with intussusception at a rate of 1 case per 10,000 vaccinated infants that occurred primarily after the first dose.[33,64-66] Fortunately, despite this setback, vaccine development continued due to recognition of the significant public health burden of rotavirus disease, and both currently licensed vaccines, RV1 and RV5, underwent large prelicensure safety trials with approximately 60,000 to 70,000 infants each.[3,4] No increased risk of intussusception was observed with either vaccine in these clinical trials.

Monovalent Rotavirus Vaccine (RV1)

RV1 is a live, monovalent vaccine that contains an attenuated, human G1P[8] rotavirus strain. Two doses are orally administered early in infancy (first dose may be given as early as six weeks of age). RV1 vaccine trials performed mainly in Latin America and in Europe demonstrated a 2-dose vaccine efficacy of 83% [95% Confidence Interval (CI): 67–92] and 96% (95% CI: 90–99), respectively, against severe rotavirus gastroenteritis through the first year of life. Efficacy against rotavirus disease of any severity was measured in Europe and was 87% (95% CI: 80–92) (**Table 1**).[3,67] In Latin America, efficacy against serotype-specific severe rotavirus gastroenteritis was approximately 92% (95% CI: 74–98) against G1P[8] strains and 87% (95% CI: 64–97) against pooled non-G1 strains (G3P[8], G4P[8] and G9P[8]).[3,70] Efficacy was 41% (95% CI: -79–82) against G2P[4] strains which do not share a G- or P-type with the vaccine. However, confidence intervals crossed zero and limited the interpretation of the lower efficacy of RV1 against disease from G2P[4] strains.

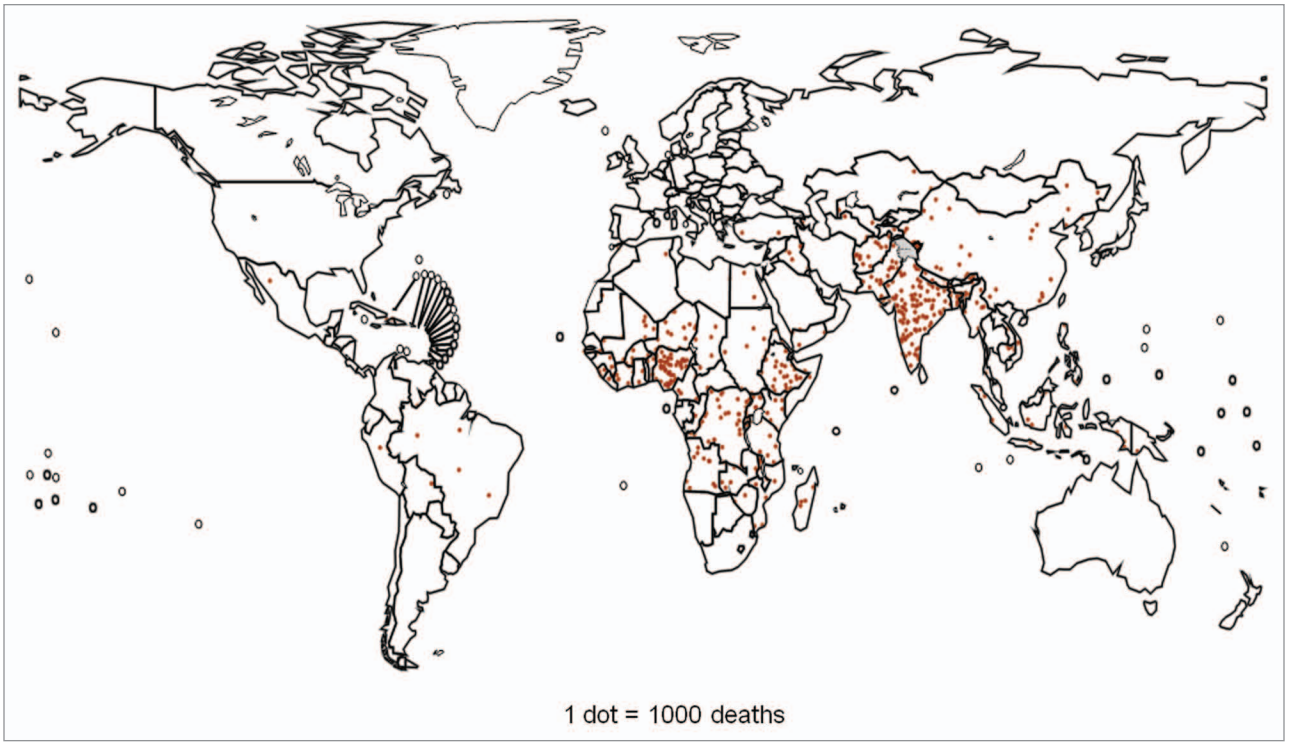

Figure 2. Estimated distribution of rotavirus deaths among children <5 y of age. Each dot represents 1,000 deaths. Dots are placed at random within each country according to the estimated number of deaths in that country. Adapted from Parashar UD, et al.[1]

Table 1. Summary of vaccine efficacy findings from clinical trials of rotavirus vaccines (RV1 and RV5)

Location	Vaccine	Vaccine Efficacy (95% CI)	Rotavirus Gastroenteritis Severity
High and middle income			
Latin America and Finland[3]	RV1	85% (72–92)	Severe (Vesikari score ≥11)
Europe[67]	RV1	87% (80–92)	Any severity
Asia (Hong Kong, Singapore, Taiwan)[68]	RV1	96% (85–100)	Severe (Vesikari score ≥11)
Japan[69]	RV1	92% (62–99)	Severe (Vesikari score ≥11)
United States and Finland[4]	RV5	98% (88–100) 74% (67–80)	Severe G1–G4 (Clark score >16) Any severity (G1–G4)
Middle-low and low income			
Africa (South Africa and Malawi)[7]	RV1	59% (36–74)	Severe (Vesikari score ≥11)
Africa (Kenya, Ghana, Mali)[5]	RV5	64% (40–79)	Severe (Vesikari score ≥11)
Asia (Vietnam and Bangladesh)[6]	RV5	51% (13–73)	Severe (Vesikari score ≥11)

In Europe, RV1 efficacy against severe rotavirus gastroenteritis through the second year of life was approximately 86% (95% CI: 80–92) against G2P[4] strains and >90% against non-G2 strains, demonstrating significant heterotypic cross-protection.[67] Clinical trials conducted in high income Asian countries demonstrated similar efficacy against severe rotavirus gastroenteritis of approximately 96% (95% CI: 85–100) in Hong Kong, Singapore and Taiwan, and 92% (95% CI: 62–99) in Japan through the second year of life (**Table 1**).[68,69] In Hong Kong, Singapore and Taiwan, efficacy against serotype-specific severe rotavirus gastroenteritis was approximately 100% (95% CI: 81–100) against G1P[8] strains and 94% (95% CI: 75–99) against pooled non-G1 strains. In Japan, efficacy against serotype-specific severe rotavirus gastroenteritis was approximately 92% (95% CI: 31–99) against G1 strains, 100% (95% CI: 24–100) against G3 strains, and non-significantly, 75% (95% CI: -382–100) against G9 strains. However, clinical trials conducted in Africa demonstrated lower vaccine efficacy through the first year of life against severe rotavirus gastroenteritis of approximately 72% (95% CI: 40–88) in South Africa and 49% (95% CI: 11–72) in Malawi (**Table 1**).[7] No difference in vaccine efficacy against severe gastroenteritis due to G1 strains and non-G1 strains was observed in either South Africa or Malawi. In Malawi, where greater strain diversity was encountered, almost 87% of strains circulating during the trial were non-G1.[7] Despite lower vaccine efficacy in these African countries, the number of rotavirus cases prevented per

Table 2. Summary of findings from vaccine impact studies from early-introduction countries

Location	Vaccine	Key Findings from Major Vaccine Impact Studies
The Americas		
Brazil	RV1	Vaccine effectiveness of 85% (95% CI: 54–95) against G2P[4] rotavirus gastroenteritis among children 6–11 mo of age;[71] ~22% reduction in diarrhea-associated mortality rates and ~17% reduction in diarrhea-associated hospitalization rates among children <5 y during postvaccine years 2007–2009[72]
El Salvador	RV1	Vaccine effectiveness of 74% against severe rotavirus gastroenteritis (Vesikari score ≥11) and 88% against very severe rotavirus gastroenteritis (Vesikari score ≥15);[73] ~69–81% decline in rotavirus hospitalizations rates and ~35–48% decline in all-cause diarrhea events (outpatient and inpatient) among children <5 y in 2008 and 2009[74]
Mexico	RV1	~35% reduction in diarrhea-related mortality rate among children <5 y in 2008; 75 ~11–40% reduction in all-cause diarrhea hospitalizations among children <5 y in 2008 and 2009[76]
Nicaragua	RV5	Vaccine effectiveness of 52–63% against severe rotavirus gastroenteritis (Vesikari score ≥11) and 73–86% against very severe rotavirus gastroenteritis (Vesikari score ≥15) in the first year post vaccine introduction[77]
Panama	RV1	~22–37% reduction in all-cause diarrhea hospitalizations among children <5 y in 2007 and 2008[78]
US	RV1 and RV5	RV5 vaccine effectiveness of 83–86% against rotavirus gastroenteritis ED visits or hospitalizations over 2 rotavirus seasons, 2008–2009;[79] ~46% decline in all-cause diarrhea hospitalization rates among children <5 y in 18 states in 2008 resulting in ~40,000 to 60,000 fewer gastroenteritis-related hospitalizations;[80] delayed, shorter rotavirus seasons and a sustained reduction in the number of rotavirus antigen-positive tests through the 2009–2010 rotavirus season[72]
Europe		
Austria	RV1 and RV5	Vaccine effectiveness of 60–97% against rotavirus hospitalization; ~79–87% reduction in rotavirus hospitalizations among children age-eligible to receive vaccine in 2008 and 2009[81]
Belgium	RV1 and RV5	~65–83% reduction in rotavirus hospitalizations during postvaccine years 2007–2010[82]
Australia	RV1 and RV5	Vaccine effectiveness of 89–94% against rotavirus hospitalizations; ~53–93% reduction in rotavirus hospitalizations among children ≤3 y[83]

100 person-years was substantial (6.7 cases per 100 person-years in Malawi; 4.2 cases per 100 person-years in South Africa) and was greater than estimates of cases prevented in Latin America and Europe, largely because of the substantially greater baseline rates of severe rotavirus disease.

Pentavalent Rotavirus Vaccine (RV5)

RV5 is a live, pentavalent human-bovine reassortant vaccine that contains 5 reassortant viruses, 4 expressing a unique human G-type protein (G1–G4) and one expressing a human P-type protein (P[8]).[4] Three doses are orally administered early in infancy (first dose may be given as early as 6 weeks of age). Pre-licensure clinical trials performed predominantly in the US and Finland demonstrated a vaccine efficacy of 98% (95% CI: 88–100) against severe G1–G4 rotavirus gastroenteritis and 74% (95% CI: 67–80) against G1–G4 rotavirus gastroenteritis of any severity through the first full rotavirus season following vaccination (**Table 1**); efficacy against G2 rotavirus gastroenteritis of any severity was approximately 63% (95% CI: 3–88).[4] Similar to the RV1 trials, vaccine trials performed in Africa and Asia demonstrated lower efficacy; vaccine efficacy against severe rotavirus gastroenteritis through the first year of life was 64% (95% CI: 40–79) in Africa (Ghana, Kenya and Mali) and 51% (95% CI: 13–73) in Asia (Bangladesh and Vietnam) (**Table 1**).[5,6] In these African and Asian countries, the majority (89–100%) of rotavirus strains circulating during the trials were of G and P genotypes contained in RV5. Similar to the RV1 results, despite lower vaccine efficacy, the number of rotavirus cases prevented per 100 person-years in Africa and Asia was substantial (2.7 cases per 100 person-years in Africa, 3.3 cases per 100 person-years in Asia).

Post-marketing Rotavirus Vaccine Impact and Effectiveness Studies

Many studies have demonstrated the real-world impact of rotavirus vaccines in early-introducer countries in the Americas, Europe and in Australia (**Table 2**). In the Americas, where rotavirus vaccines have been integrated into the national immunization programs of many countries since 2006, vaccine effectiveness in routine use has been similar to the vaccine efficacy seen in pre-licensure trials.[71,79,84] Sustained reductions in diarrhea-related mortality and/or morbidity have been observed in Brazil, El Salvador, Mexico, Panama and the US,[72,74-76,78,80,85] thus demonstrating the benefits of vaccination in countries of diverse socioeconomic status (**Figs. 3 and 4**). Similar findings have been observed in Europe, where Austria and Belgium were the earliest countries to introduce both rotavirus vaccines into their national immunization programs, and also in Australia.[81-83] Evidence of indirect benefits (i.e., herd immunity) for older children has been noted after vaccine introduction in several countries, including the US, Austria, Australia and El Salvador.[74,80,81,83]

Of specific interest to the global community are findings of significant reductions in under-5 mortality related to diarrhea in Mexico and Brazil after the introduction of rotavirus vaccine.[72,75]

In both settings, the reduction has been large, amounting to declines of over 1,300 childhood deaths annually, and sustained for more than 3 y since the introduction of vaccine. The effect of the vaccines on diarrhea mortality was not assessed in clinical trials. Thus, these findings provide welcome news for developing countries of Africa and Asia where over 85% of the global rotavirus mortality occurs.

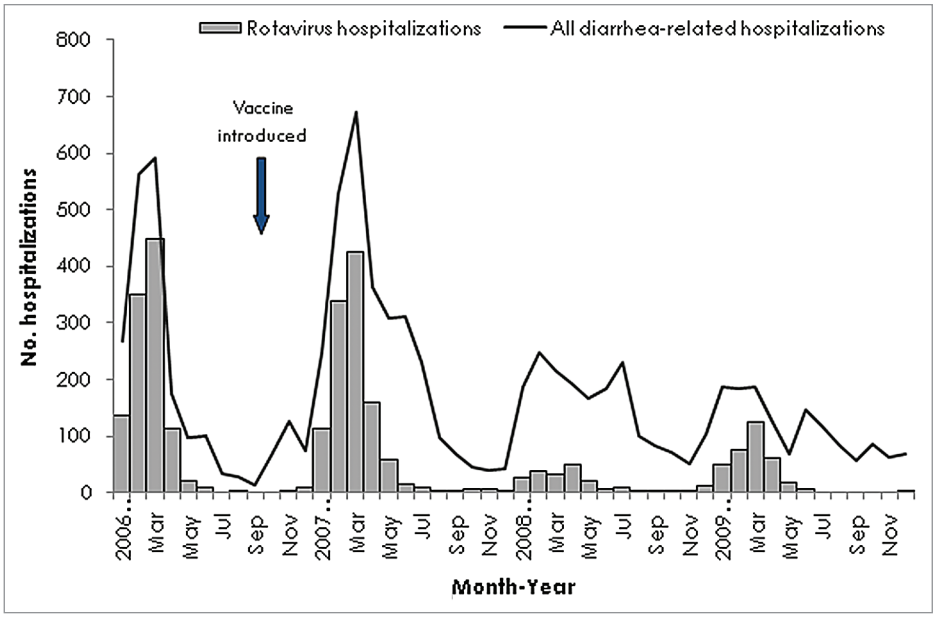

Figure 3. Number of diarrhea-related and rotavirus hospitalizations among children <5 y of age at 7 sentinel surveillance hospitals, El Salvador, January 2006—December 2009. Adapted from Yen C, et al.[74]

Post-Marketing Rotavirus Vaccine Safety Surveillance

As mentioned previously, no increased risk of intussusception was observed during large pre-licensure safety trials for either of both currently licensed vaccines, RV1 and RV5.[3,4] However, some post-marketing safety studies have detected a low risk of intussusception, primarily in the first week after the first vaccine dose. Studies conducted in Mexico (RV1) and Australia (RV1 and RV5) found a low-level, increased risk of intussusception of approximately 1 per 50,000 to 100,000 vaccinated infants following the first dose of vaccine, risks much lower than the 1 per 10,000 seen with Rotashield®.[86-88] A risk with the first dose was not observed in a similar study conducted in Brazil (RV1),[87] although a low-level risk with the second dose of vaccine was noted. Post-marketing data on RV5 available from the US have not demonstrated an increased risk of intussusception, although currently available US data cannot reliably exclude the level of risk seen in Mexico and Australia.[89,90]

The WHO Global Advisory Committee for Vaccine Safety reviewed available data in late 2010, and concluded that the substantial benefits of vaccination outweigh the small risk of intussusception seen in some post-licensure studies.[8] For example, in Mexico, rotavirus vaccination has prevented some 330 deaths and 280 hospitalizations related to rotavirus diarrhea for every death and hospitalization related to vaccine-associated intussusception. WHO continues to recommend universal rotavirus vaccination of infants.

Considerations and Future Priorities

Despite the WHO recommendation for inclusion of rotavirus vaccination in all national immunization programs and the well-documented benefits of vaccination, only 27 of 193 WHO member states have introduced rotavirus vaccines nationally to date.[49] As many countries weigh the introduction of rotavirus vaccines into their national immunization programs and as other countries decide whether to continue to fund their existing rotavirus vaccination programs, several areas of consideration and future priorities should be addressed. These include monitoring of the impact of rotavirus vaccination programs in other countries to support the introduction of rotavirus vaccines, monitoring of existing rotavirus vaccination programs to support sustained use, understanding vaccine effectiveness (including indirect effects and the economic benefits across different settings), understanding the impact on circulating strains, monitoring the safety of rotavirus vaccines, improving the performance of rotavirus vaccines in developing country settings, and improving financial access to rotavirus vaccines.

Evidence of the benefits of vaccination can be useful to help countries decide whether to introduce rotavirus vaccine into their national immunization programs and, once introduced, whether to provide continued support for the rotavirus vaccination program. In countries considering introduction of rotavirus vaccines, documentation of the burden of rotavirus disease and the cost-effectiveness of a vaccination program may provide decision makers the evidence required for prioritizing limited health care funding on a new vaccine. This will be particularly important for developing countries in Africa and Asia, where the impact of vaccination will likely be substantial even after taking into account the lower vaccine efficacies seen in the clinical trials, given high disease burdens.[5-7] In countries that have existing rotavirus vaccination programs, documenting the impact of the vaccination program can be achieved through studies assessing the field effectiveness of vaccination and the direct and indirect benefits of vaccination on diarrhea-related disease trends and healthcare costs. Targeted vaccine introduction projects may help demonstrate the health benefits of vaccination and allow appraisal of potential logistical or programmatic issues related to rotavirus vaccine introduction. Additionally, rotavirus strain surveillance can provide a better understanding of the impact of vaccination on strain diversity and evolution. These studies are important since it is not known whether vaccination will provide

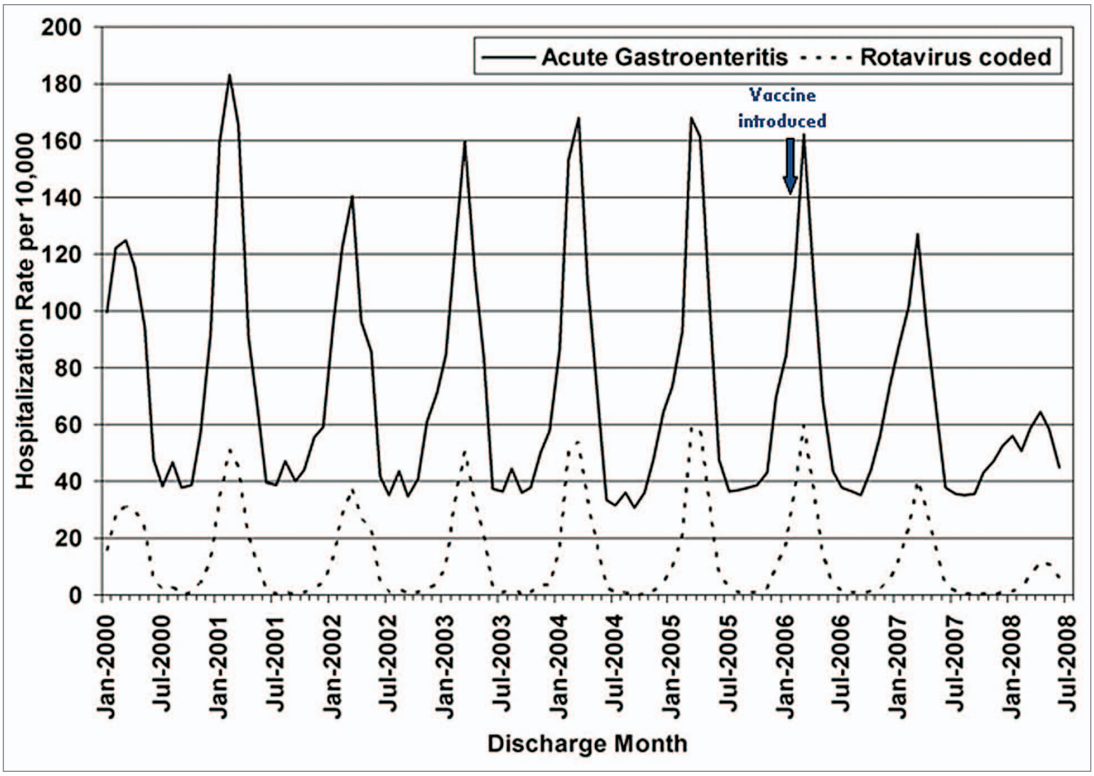

Figure 4. Monthly acute gastroenteritis and rotavirus—coded hospitalization rates among children aged <5 y from January 2000 through June 2008, in 18 states—US. Adapted from Curns AT, et al.[80]

protection against all circulating strains and there is a question of whether some of these strains may be selected over the long-term in highly vaccinated populations, either through reassortment events between different rotavirus strains, antigenic drift in viral antigens, or both. Documenting changes occurring in strains through whole genome sequencing may help elucidate potential rotaviral resistance mechanisms to vaccine immunity if they occur.

Understanding the overall balance between the benefits and possible risks of vaccination, especially with regards to intussusception, is essential. The reasons for the low-level risk of intussusception seen in recent studies in Mexico, Brazil and Australia are currently unclear.[86-88] Post-licensure assessments will help better characterize the potential risk of intussusception and may elucidate the potential mechanism of vaccine-associated intussusception. To do this, strong surveillance systems are necessary to help establish baseline rates of intussusception and to monitor for adverse events following the introduction of a new vaccine. However, given the limitations of passive reporting systems, relying on active surveillance at sentinel hospitals may be a more efficient and economical approach to assess the risk of intussusception following vaccination.

Optimizing the performance of rotavirus vaccines in developing country settings is a priority as data from studies in Africa, Asia, and the Americas indicate lower vaccine efficacy/effectiveness and suggest waning immunity against rotavirus disease in the second year of life that has not been seen in higher income countries.[5-7,77] In these settings, the immune response to oral vaccines in early infancy may be reduced because of higher levels of transplacental maternal antibody, interference by immune and nonimmune components of breast milk, micronutrient malnutrition (e.g., vitamin A and zinc), interfering gut flora, and the disease state of the infant (e.g., HIV infection or other concomitant infections).[91-93] More research in the area of immune response to oral rotavirus vaccines in early infancy is needed, and future studies with the aim of improving the immune response to vaccination, including the use of micronutrient supplementation (i.e., zinc and/or probiotics), withholding breastfeeding at the time of vaccination, and determining the optimal dosing schedule, including providing neonatal or booster doses of vaccine, will be important to determine if protection in low-resource settings during the first year of life can be improved and extended through the second year of life. Protection against severe rotavirus disease through the second year of life is necessary for maximal public health impact. Additionally, continued investment in the research and development of new rotavirus vaccines may lead to vaccines with greater effectiveness in developing countries, as well as lower cost vaccines. Currently, emerging vaccine manufacturers in Brazil, China, Germany, India, Indonesia and Vietnam are working on the development of new rotavirus vaccines. The original rhesus-based reassortant vaccine is also undergoing renewed development with a manufacturer in Germany.[94] Finally, there is renewed interest in exploring non-replicating, parenteral rotavirus vaccine candidates.[95] All of this work may lead to the development of better oral vaccines and/or oral

delivery systems or of vaccines with alternative delivery systems, such as inactivated vaccines, that may potentially have better efficacy and safety profiles.

One of the most significant barriers to the introduction of rotavirus vaccines is financial. Current rotavirus vaccines are more expensive than most other vaccines supplied by national immunization programs. Therefore, for those countries that are not eligible for new vaccine support through the GAVI Alliance (formerly known as the Global Alliance for Vaccines and Immunizations), the costs and benefits of a national rotavirus vaccination program must be weighed carefully. For rotavirus vaccines to have maximal public health impact globally, financial access to these vaccines must be improved, either through reduced prices or additional funding mechanisms. Recent successful fundraising efforts by the GAVI Alliance and the reduction in the price of RV1 to US$2.50 per dose by GlaxoSmithKline for GAVI-eligible countries are great steps toward improving access to these vaccines for populations in countries with the highest risk for the disease and in the greatest need of protection,[96,97] but these steps alone are not enough, particularly for populations not supported by the GAVI Alliance.

Conclusion

Substantial declines in rotavirus disease burden have been documented in early rotavirus vaccine adopter countries in the Americas, Europe, and in Australia. However, the full public health impact of these vaccines has not been completely realized as they have been introduced in few countries in Africa and Asia (i.e., those with the highest rotavirus disease morbidity and mortality). As rotavirus vaccines are adopted and used more widely, it is imperative that evidence of the benefits of vaccination be documented, the safety of these vaccines continue to be monitored, efforts to maximize the impact of current and future vaccines be made, and financial barriers to introduction and maintenance of vaccination programs be reduced to allow countries to make informed decisions that are in the best interest of public health. To monitor these parameters, sustainable surveillance systems will need to be established and maintained in more countries adopting rotavirus vaccines.

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Disclaimer

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