

THE EPIDEMIOLOGY AND DISEASE BURDEN OF ROTAVIRUS

INTRODUCTION

Diarrhea is one of the world's leading killers of children, and rotavirus remains among the most common causes of severe diarrhea in children under the age of 5 years worldwide.

Rotavirus is a virus that causes gastroenteritis, an inflammation of the stomach and intestines. Rotavirus primarily infects the small intestine, destroying the surface tissue and preventing the absorption of nutrients, causing diarrhea. Typical symptoms can range from mild, watery diarrhea to severe diarrhea with vomiting and fever.

WHO-recommended treatment, such as zinc supplements, oral rehydration therapy (ORT) and treatment with intravenous (IV) fluids, when needed, can help rehydrate children until the intestine can repair and recover. In low-income countries, particularly in hard-to-reach areas where children do not have timely access to such medical care, severe disease can result in rapid dehydration, leading to electrolyte imbalance, shock and death. Yet many of the world's poorest children do not have access to ORT, despite it being inexpensive and effective. ORT coverage hovers around 40% in many of the places where the greatest number of diar-

rhea deaths occur.⁽¹⁾ While efforts to increase ORT use should continue, providing ORT to treat each episode of rotavirus diarrhea in resource-poor settings is challenging.

Because of the high transmissibility of the disease—which is often spread person-to-person and through contaminated objects, surfaces, food and water—it is found everywhere, including in high- and middle-income countries with advanced water and sanitation systems. In fact, nearly all children experience at least one rotavirus infection during the first two years of life in unvaccinated populations.⁽²⁾

SEVERE DIARRHEAL DISEASE IN YOUNG CHILDREN DUE TO ROTAVIRUS

While over 114 countries have introduced rotavirus vaccine into their national immunization program, an estimated 60%—over 80.9 million—of all children globally remain unvaccinated.⁽³⁾ Rotavirus was by far the most common pathogen found in a global review of studies of hospitalized diarrhea cases in countries that haven't yet introduced the vaccine, accounting for an estimated 38% of all cases in children under 5.⁽⁴⁾ Another global analysis estimated that 27% of severe diarrhea worldwide was due to rotavirus, with a range of 23–33% by WHO region.⁽⁵⁾

Rotavirus accounted for the highest proportion of cases of moderate to severe diarrhea in children under the age of 1 presenting at hospitals and health centers across sites participating in a seven-country prospective study (ranging from 22–35% of cases) (See Figure 1).^(6,7)

Among 16 low- and middle-income countries in Asia, Africa, and Eastern Europe that had not included rotavirus vaccine in their national immunization programs as of 2016, a median of 40% of hospitalized cases of diarrhea in children less than 5 years of age were due to rotavirus. In two countries—Afghanistan and the Democratic Republic of the Congo (DCR)—rotavirus accounted for two-thirds to three-quarters of all hospitalized cases of diarrhea in children under 5 found at the surveillance sites (Both countries have now introduced rotavirus vaccines) (See Figure 2). These rates compared to a median of 17.5% of hospitalized diarrhea due to rotavirus in 14 countries in the surveillance network that have introduced rotavirus vaccination in their childhood immunization schedule, which represents a greater than 50% difference.⁽⁸⁾

SEVERE ROTAVIRUS STRIKES THE VERY YOUNG, MOST VULNERABLE CHILDREN

Most cases of severe rotavirus gastroenteritis occur in children under the age of 2 years, with children under 12 months at highest risk. The disease can strike early in infancy, especially in low-income settings, as studies in India, Malawi, Nigeria, and Sudan have demonstrated.

Nigeria

In Enugu, 77% of children hospitalized with rotavirus in a major hospital were less than 1 year old and 20% were 5 months old or younger.⁽⁹⁾

India

By 6 months of age, more than half (56%) of all children in a population-based study in the slums of Vellore had been infected with rotavirus and 20% had had rotavirus diarrhea. By 12 months of age, 81% had been infected and 36% had become ill from the infection.⁽¹⁰⁾

Sudan

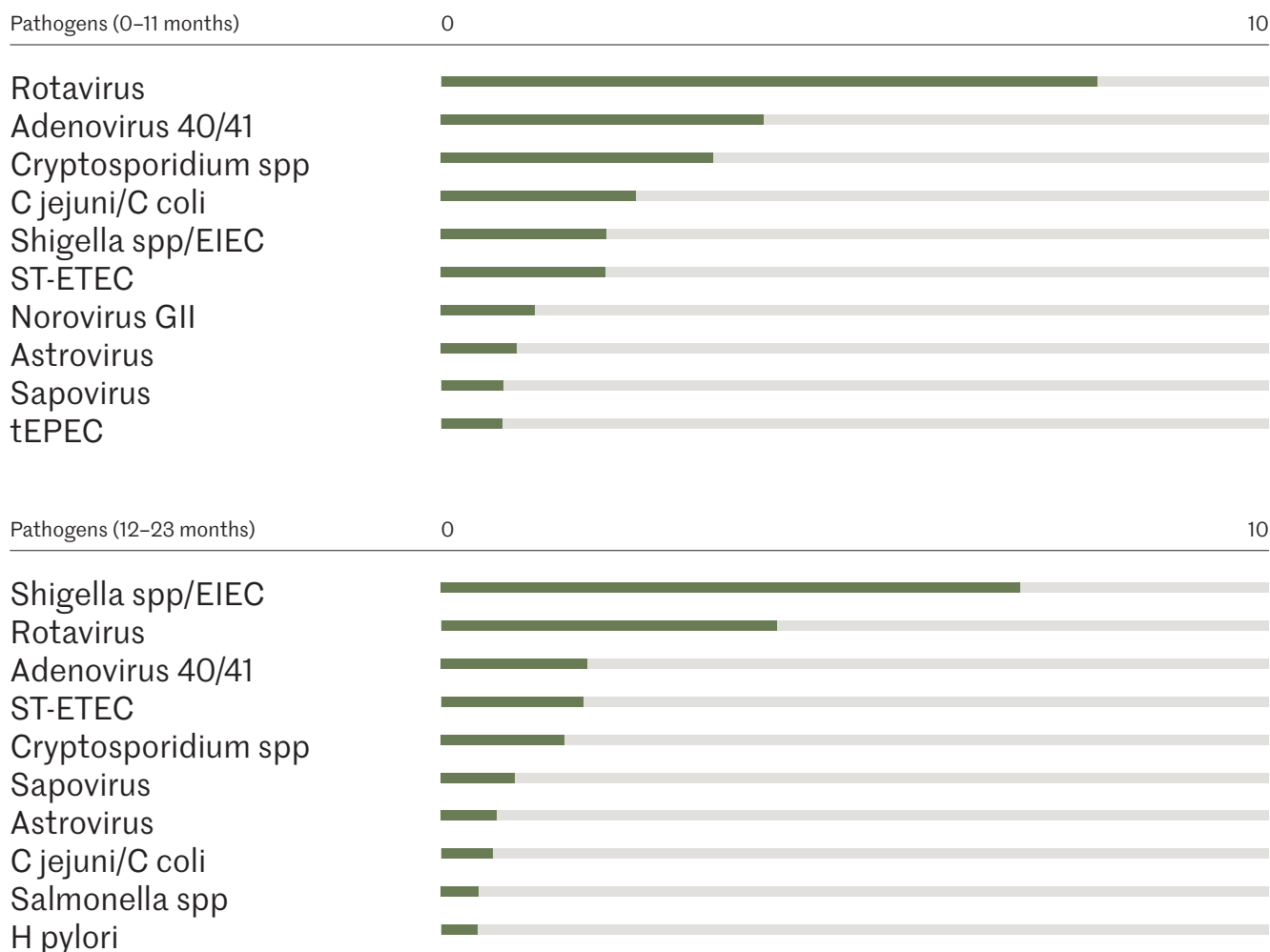
In an eight-hospital study, 19% of children hospitalized with rotavirus were less than 6 months of age and 61% were less than 1 year old.⁽¹¹⁾

Malawi

In a rotavirus vaccine trial, 44% of children in the placebo group had become infected with rotavirus by 5 months of age.⁽¹²⁾

FIG.1 CAUSES OF MODERATE TO SEVERE DIARRHEA AMONG CHILDREN UNDER 2 ACROSS SEVEN AFRICAN AND ASIAN SITES⁽⁷⁾

■ Incidence per 100 child-years (Global Enteric Multicenter Study [GEMS] reanalysis)



In unvaccinated populations, nearly all infants experience at least one rotavirus infection by 24 months of age.

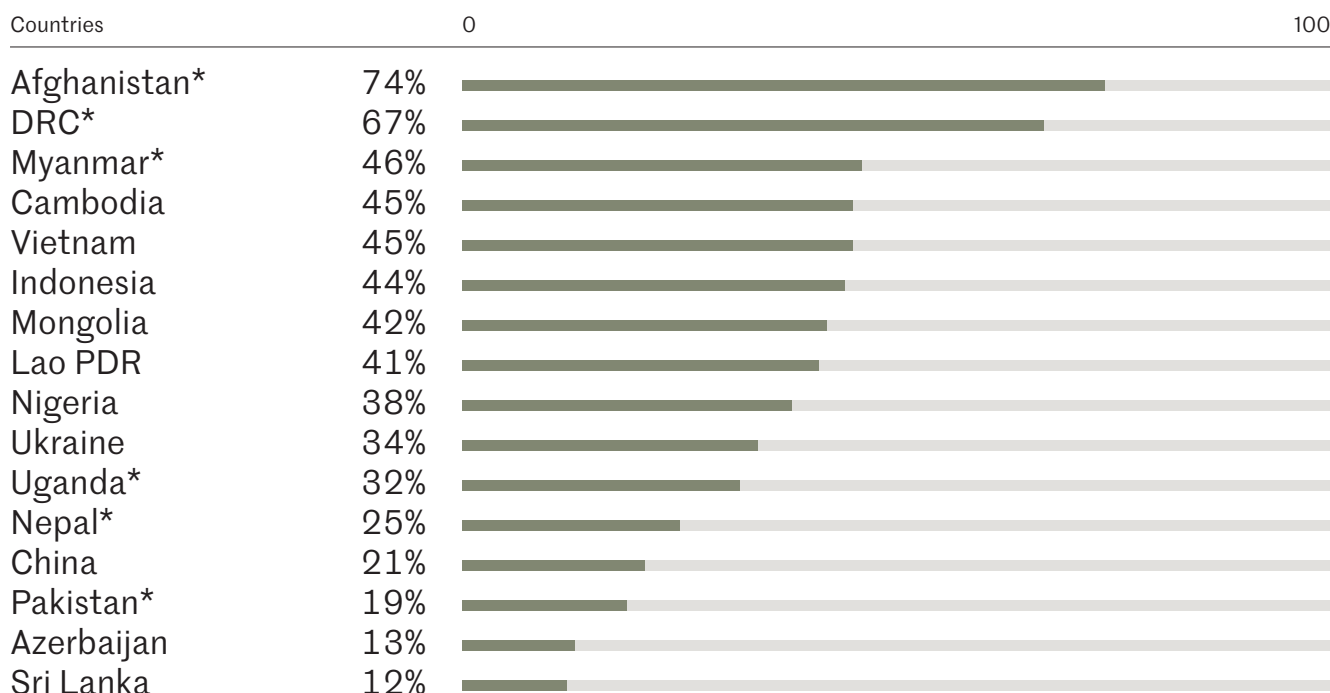
The morbidity caused by rotavirus—with its high economic costs and toll on children’s health—is often unrecognized and underappreciated. In 2017, for each rotavirus death, there were an estimated 12 hospitalizations and 2,000 episodes for each rotavirus death⁽⁷⁾. In 2019, an estimated 1.76 million hospitalizations were attributed to rotavirus. Rotavirus vaccination coverage and introductions at the time addressed just 41% of the preventable burden of rotavirus hospitalization yet still averted over 500,000 hospitalizations.⁽¹³⁾ Data from India suggests that prior to the start of their phased introduction of rotavirus vaccine, 1 in 31 children was at risk of

hospitalization from the disease by the age of 5.⁽¹⁴⁾

In low-mortality countries like the U.S. and Western European countries, the risk of severe illness from rotavirus in the absence of rotavirus vaccination is still great. Prior to vaccine introduction in the U.S., children had a 1 in 70 chance of being hospitalized for rotavirus before they reached the age of 5 years.⁽⁹⁾

The high risk of severe illness, coupled with high economic costs of rotavirus disease, were key reasons why high-income countries like the U.S. have introduced rotavirus vaccine into their national immunization schedules.

FIG.2 PERCENT OF <5 DIARRHEA HOSPITALIZATIONS DUE TO ROTAVIRUS IN COUNTRIES YET TO INTRODUCE THE VACCINE (2016)⁽⁸⁾



*These countries have since introduced rotavirus vaccine

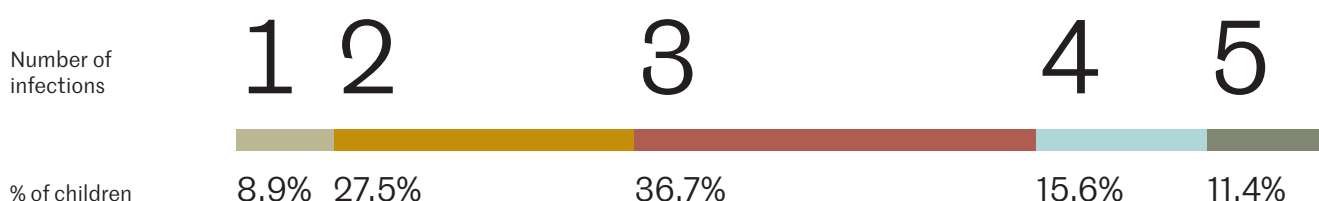
In WHO countries not yet using rotavirus vaccines in their immunization program, a median of 40% of diarrhea hospitalizations in children under 5 were due to rotavirus.

Children can also experience repeat rotavirus infections, particularly in impoverished settings. While the first infection may be more severe, it confers only partial protection against the disease.

In a study that followed children from birth living in the slums of Vellore, India, nearly two-thirds (63%) of children infected with rotavirus experienced at least three infections by their third birthday (Figure 3).⁽¹⁰⁾

FIG.3 CHILDREN IN LOW-INCOME COMMUNITIES OF VELLORE, INDIA HAD MULTIPLE ROTAVIRUS INFECTIONS⁽¹⁰⁾

Among 373 children who experienced at least one rotavirus infection, over a period of 3 years



ROTAVIRUS DEATHS IN CHILDREN

Rotavirus kills over 185,000 children under 5 every year and is responsible for over one-third of all child diarrheal deaths.

Estimates of diarrheal deaths in children less than 5 years old have declined sharply in the past 15 years or so, from around 1.24 million worldwide in 2000 to just over half a million in 2013.^(16,17) This reduction is partially due to improvements in living conditions, including in water, sanitation, and hygiene, and partially due to the use of new disease estimation methods.⁽¹⁷⁾ The estimated number of deaths from rotavirus in children under 5 also declined from 528,000 in 2000 to 215,000 in 2013—a nearly 60% reduction. Models currently estimate that about 185,300 children die annually from rotavirus.^(17,18) This recent decline is due to the revised estimates of overall diarrheal deaths as well as to the introduction of rotavirus vaccine into many national immunization programs since 2013.⁽¹⁹⁾

Nonetheless, rotavirus remains a leading cause of diarrheal deaths worldwide—accounting for an estimated 30% of all diarrheal mortality in children under 5.^(17,18) In fact, even as the overall number of rotavirus deaths has fallen, the proportional contribution of rotavirus to all diarrheal

deaths has only slightly declined.⁽¹⁷⁾ The sharpest reduction in the proportion of diarrheal deaths due to rotavirus—from 36% in 2000 to 26% in 2013—occurred in Latin America, where nearly all countries have included rotavirus vaccine in their national immunization program. India accounted for approximately 16% of global rotavirus deaths in children under 5 in 2017 but has since fully introduced rotavirus vaccines in their national immunization program and accounted for just 1% of deaths in 2019.

Where are children dying of rotavirus?

Nearly all rotavirus deaths occur in low- and middle-income countries.⁽¹⁸⁾ In fact, in 2019, four countries—Nigeria, Chad, Niger and Pakistan—were estimated to account for half of all rotavirus deaths. Almost three-quarters (70%) of all global deaths occurred in only 10 countries (see Figure 4).

FIG.4 THE COUNTRIES WITH THE GREATEST NUMBER OF ROTAVIRUS DEATHS AS A PROPORTION OF ALL GLOBAL ROTAVIRUS DEATHS IN CHILDREN UNDER 5⁽¹⁸⁾ (2019)

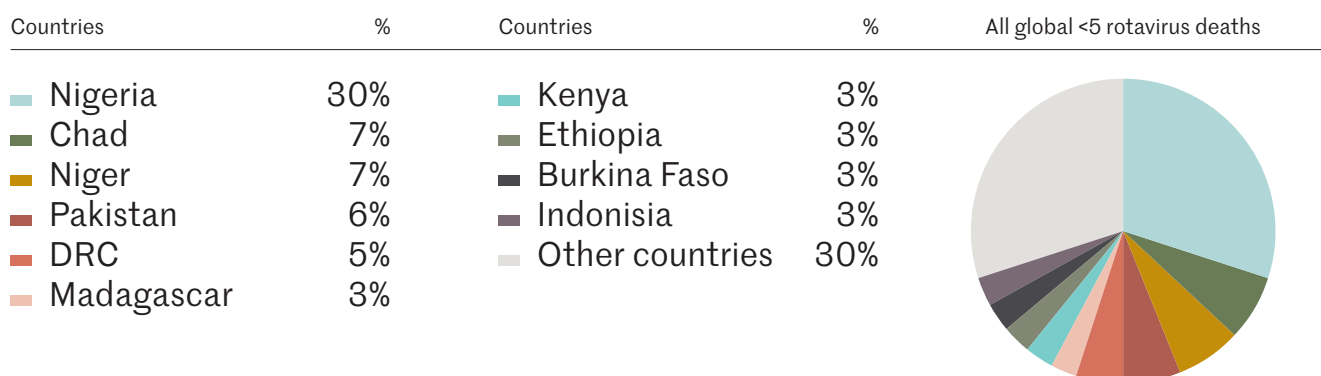


FIG.5 RATES OF ROTAVIRUS MORTALITY PER 100,000 CHILDREN UNDER AGE 5 IN 2019, BY COUNTRY⁽¹⁸⁾

■ >100 ■ 50-99 ■ 10-49 ■ <10

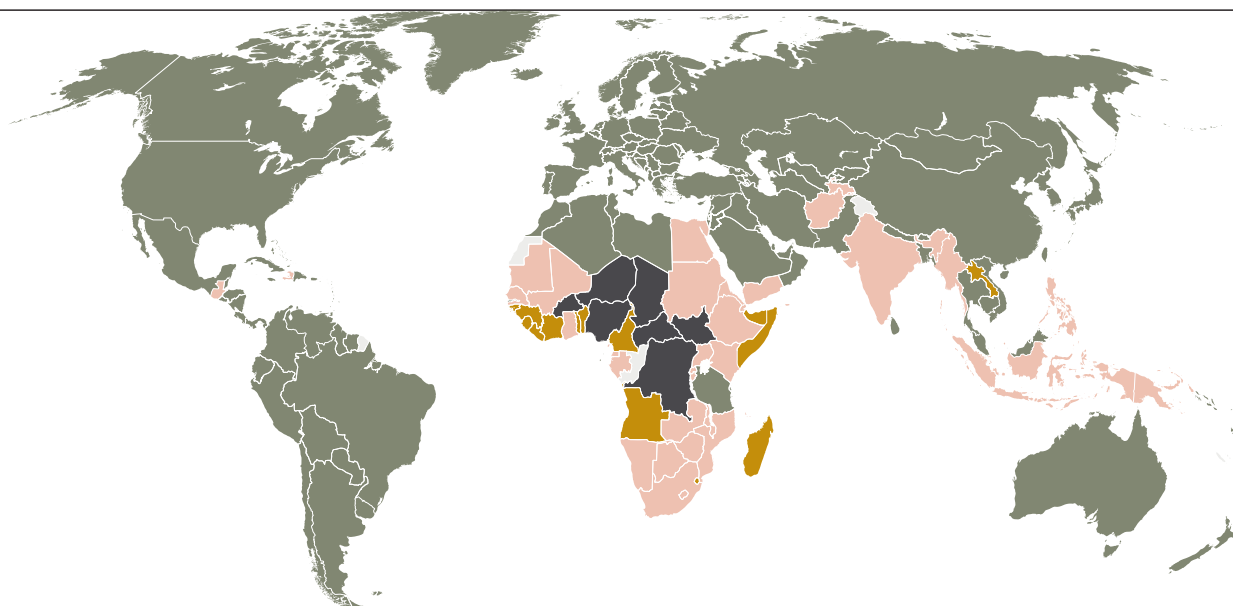


TABLE 1 HIGHEST GLOBAL RATES OF ROTAVIRUS MORTALITY PER 100,000 (2019)⁽¹⁸⁾

| | | | |
|--------------------------|-----|--------------|-----|
| Chad | 330 | Madagascar | 133 |
| Niger | 223 | Burkina Faso | 103 |
| Central African Republic | 215 | Somalia | 94 |
| Togo | 176 | South Sudan | 83 |
| Nigeria | 136 | Kenya | 75 |

Looking at rotavirus mortality rates instead of number of deaths, seven countries have rates exceeding 100 deaths per 100,000 children under 5—all of them in sub-Saharan Africa (Figure 5). Three countries had rates of more than 200 per 100,000, with the highest in Chad (330/100,000) (Table 1).

A key reason that nearly all rotavirus deaths occur in less developed countries—despite the fact that the disease is common in rich and poor countries alike—is the lack of timely access to health care in many places. In addition, rotavirus can be more severe in low-income countries due to frequent concurrent infections, malnutrition, and other factors. Year-round transmission due to climatic factors may also contribute to the much higher toll of the disease among children in low-income countries.^(20,21)



Mothers bring their children for vaccinations and health checks in Accra, Ghana on January 9, 2014.

Several of the countries with the highest burden of rotavirus diarrhea have recently introduced rotavirus vaccination into their immunization program nationally—such as the Democratic Republic of Congo, Pakistan, Angola, and India. Others, such as Nigeria, have announced plans to introduce the vaccine in the next few years.

REFERENCES

- UNICEF's global database. *Diarrhea data: Child health coverage 2015–2016*. 2016; Available from: <https://data.unicef.org/topic/child-health/diarrhoeal-disease/>.
- Kotloff, K.L., The Burden and Etiology of Diarrheal Illness in Developing Countries. 2017. p. 799–814.
- International Vaccine Access Center, *VIEW-hub Report: Global vaccine introduction and implementation*. Johns Hopkins Bloomberg School of Public Health, 2021.
- Lanata, C.F., et al., *Global causes of diarrheal disease mortality in children <5 years of age: a systematic review*. *PLoS One*, 2013. 8(9): p. e72788.
- Fischer Walker, C.L., et al., *Global burden of childhood pneumonia and diarrhoea*. *The Lancet*, 2013. 381(9875): p. 1405–1416.
- Kotloff, K.L., et al., *Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): a prospective, case-control study*. *The Lancet*, 2013. 382(9888): p. 209–222.
- Liu, J., et al., *Use of quantitative molecular diagnostic methods to identify causes of diarrhoea in children: a reanalysis of the GEMS case-control study*. *The Lancet*, 2016. 388(10051): p. 1291–1301.
- World Health Organization. *WHO Global Invasive Bacterial Vaccine Preventable Disease and Rotavirus Surveillance Network Bulletin*. 2017; Available from: <https://mailchi.mp/046b8f12e001/who-ib-vpd-and-rotavirus-surveillance-bulletin-june-15662452e225412eff9>.
- Tagbo, B.N., et al., *Epidemiology of Rotavirus Diarrhea among Children Younger Than 5 Years in Enugu, South East, Nigeria*. *The Pediatric Infectious Disease Journal*, 2014. 33: p. S19–S22.
- Gladstone, B.P., et al., *Protective effect of natural rotavirus infection in an Indian birth cohort*. *The New England journal of medicine*, 2011. 365(4): p. 337–46.
- Mustafa, A., et al., *Baseline Burden of Rotavirus Disease in Sudan to Monitor the Impact of Vaccination*. *The Pediatric Infectious Disease Journal*, 2014. 33: p. S23–S27.
- Bar-Zeev, N., et al., *Effectiveness of a monovalent rotavirus vaccine in infants in Malawi after programmatic roll-out: an observational and case-control study*. *Lancet Infect Dis*, 2015. 15(4): p. 422–428.
- Hallowell, B.D., et al., *Global Estimates of Rotavirus Hospitalizations Among Children Below 5 Years in 2019 and Current and Projected Impacts of Rotavirus Vaccination*. *Journal of the Pediatric Infectious Diseases Society*, 2021. doi:10.1093/jpids/piab114.
- John, J., et al., *Rotavirus gastroenteritis in India, 2011–2013: Revised estimates of disease burden and potential impact of vaccines*. *Vaccine*, 2014. 32(S1): p. A5–A9.
- Cortese, M., U. Parashar, and C. Centers for Disease, *Prevention of rotavirus gastroenteritis among infants and children: recommendations of the Advisory Committee on Immunization Practices (ACIP)*. *MMWR Morb Mortal Wkly Rep*, 2009. 58(RR-2): p. 1–25.
- WHO and Maternal and Child Epidemiology Estimation Group, *Estimates of child cause of death, diarrhoea 2018*. 2018.
- Tate, J.E., et al., *Global, Regional, and National Estimates of Rotavirus Mortality in Children <5 Years of Age, 2000–2013*. *Clinical Infectious Diseases*, 2016. 62 (suppl 2): p. S96–S105.
- Global Burden of Disease Collaborative Network. *Global Burden of Disease Study 2019 (GBD 2019) Results*. Institute for Health Metrics and Evaluation (IHME) 2020; Available from: <http://ghdx.healthdata.org/gbd-results-tool>.
- Global Burden of Disease Collaborators, *Estimates of global, regional, and national morbidity, mortality, and aetiologies of diarrhoeal diseases: a systematic analysis for the Global Burden of Disease Study 2015*. *The Lancet. Infectious diseases*, 2017. 17(9): p. 909–948.
- Glass, R.I., et al., *Rotavirus vaccines: Successes and challenges*. *Journal of Infection*, 2014. 68: p. S9–S18.
- Patel, M.M., et al., *Global seasonality of rotavirus disease*. *Pediatric Infectious Disease Journal*, 2013. 32(4): p. 1–25.

ROTA Council thanks the following organizations for their support: Bharat Biotech, Bill & Melinda Gates Foundation, CDC, GSK, PATH, and Sabin Vaccine Institute. Suggested Citation: ROTA Council at International Vaccine Access Center (IVAC), Johns Hopkins Bloomberg School of Public Health. (2022). Rotavirus Disease and Immunization: The Epidemiology and Disease Burden of Rotavirus.

Disclaimer: The presentation of maps is not by any means an expression of IVAC's opinion regarding the legal status of countries/territories, their governing authorities, or their official borders.

Photo credits:
Page 6: Bill & Melinda Gates Foundation/
Jiro Ose

THE EPIDEMIOLOGY AND DISEASE BURDEN OF ROTAVIRUS

KEY FACTS

Common

Rotavirus remains among the most common causes of severe and fatal diarrhea in children under 5 worldwide and is the leading cause of severe and fatal diarrhea in infants under 1. (See page 1)

Vulnerable

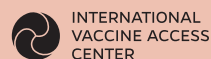
Children under 1 year of age suffer the highest rates of rotavirus diarrhea and, in high-incidence settings, a substantial proportion of cases occur in children less than 6 months of age. (See page 2)

Unrecognized

The morbidity caused by rotavirus—in terms of hospitalizations, outpatient visits and diarrheal episodes—is often underappreciated. (See page 3)

Deadly

An estimated 185,300 children died from rotavirus in 2017 worldwide—nearly all in low- and middle-income countries. (See page 5)



For more information please visit preventrotavirus.org.