GEMS Overview

The Global Enteric Multicenter Study (GEMS) is the largest, most comprehensive study of childhood diarrheal diseases ever conducted in developing country settings. Globally, diarrheal diseases are the second leading cause of death among children under five, despite the existence of effective interventions such as oral rehydration solutions (ORS), zinc supplements and rotavirus vaccines. Many different bacteria, viruses and other pathogens can cause diarrheal disease. However, it has been difficult to prioritize and target interventions because previous studies cannot be easily compared or combined due to differences and limitations in the methods used. By studying more than 22,000 children across two continents with consistent methods, GEMS provides important, new data that will help researchers, policymakers, donors and advocates make evidence-based decisions to help to reduce the global burden of diarrheal diseases.

Study Findings

GEMS was a three-year, case-control study conducted at seven sites in Africa and Asia that investigated (1) the cause, (2) the incidence and (3) the impact of moderate-to-severe diarrhea (MSD), which was characterized by severe dehydration, dysentery or hospitalization. Country-specific results are presented in the accompanying fact sheets. Key findings across sites published May 2013 in *The Lancet* include:

1. **Cause:** Just four pathogens were responsible for the majority of moderate-to-severe diarrhea cases. To determine the fraction of cases attributable to each pathogen, researchers tested stool samples from children diagnosed with MSD for nearly 40 pathogens and compared them to samples from age- and gender-matched control children.
   - **Rotavirus**, for which a vaccine already exists, was the leading cause of MSD during infancy across all study sites.
   - **Cryptosporidium**, a pathogen not expected to be a major contributor, was found to be the second leading cause of infant MSD at five sites.
   - **Shigella**, a type of bacteria, was the first or second leading cause of MSD among children 12-59 months of age at most of the field sites.
   - **Enterotoxigenic E. coli** (specifically ST-ETEC) was a significant pathogen in at least one age group at every site.

2. **Incidence:** Diarrheal diseases have a major impact across settings, especially on infants. GEMS researchers estimated the yearly number of new MSD cases (incidence) for each pathogen in the seven study countries by combining the causal data mentioned above with survey data from parents and caretakers designed to estimate the total number of MSD cases.
   - **Overall Burden:** GEMS estimated roughly 20 episodes of MSD each year per 100 children under the age of two years. This equates to roughly one episode per five children each year.
   - **Burden by Age:** Among the age groups investigated, infants showed the highest burden of MSD with approximately 30 cases per 100 children each year.
   - **Burden by Country:** Specific data for each country are included in supplemental fact sheets.
3. Impact: Moderate-to-severe diarrhea had lasting health repercussions even after the initial, acute phase of diarrheal disease. GEMS conducted 60-day follow-up visits to determine the longer-term impact of diarrheal diseases, which are often not measured since they occur outside the hospital setting. Researchers compared growth, mortality and other indicators between children with MSD and controls.

- **Mortality Risk:**
  - Children presenting with a single episode of MSD had a nearly 8.5-fold increase in risk of death over a two-month follow-up period compared to control children without MSD.
  - Notably, 61% of deaths occurred more than one week after children were diagnosed with MSD, when children may no longer be receiving care.
  - 56% of deaths among cases occurred at home, suggesting that earlier studies that focused only on deaths occurring in health centers may underestimate the total burden of MSD.

- **Growth Delays:** Children with moderate-to-severe diarrhea grew significantly less in length in the two months following their episode compared to age- and gender-matched controls.

### Implications for Diarrheal Disease Control

Although GEMS investigated diarrheal diseases in diverse settings, findings were largely consistent across study sites. This suggests that the key takeaways are broadly applicable for driving research and program implementation strategies in other high-burden areas. These takeaways include:

- **Expanding access to existing tools** to prevent and treat diarrhea – particularly rotavirus vaccines – can save a significant number of lives right now.
- **Changing the way diarrheal disease care is delivered** to include longer-term monitoring and nutritional rehabilitation could improve child health and survival. In particular, instituting a follow-up visit after the initial treatment, either in a healthcare setting or at home, could dramatically improve health outcomes.
- **Developing new tools** that specifically target the GEMS-identified top diarrheal pathogens – particularly *Cryptosporidium*, for which few interventions currently exist – is essential.

By building upon GEMS findings and infrastructure, researchers can accelerate progress toward reducing the diarrheal disease burden. GEMS established a well-equipped network of laboratories in high-burden areas that are prepared to conduct future studies or roll out diarrheal interventions, and GEMS researchers will provide open access to their data.

### Study Sites

![Study Sites Map]

### Additional Information

The Center for Vaccine Development at the University of Maryland School of Medicine coordinated GEMS, working in conjunction with field sites in seven African and Asian countries. GEMS was funded by the Bill & Melinda Gates Foundation. For more information, please visit: [http://medschool.umaryland.edu/GEMS/](http://medschool.umaryland.edu/GEMS/).