ENTERIC AND DIARRHOEAL DISEASES

An Overview of Our Strategy

15 & 16 December 2015

Duncan Steele, Deputy Director and Strategic Lead for Enteric Vaccines

Global Burden of Foodborne Disease: From Data to Action

Amsterdam, The Netherlands

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ENTERIC & DIARRHOEAL DISEASES (EDD) GOAL

- To end diarrhoeal disease deaths* in children under age 5 in Gavi-eligible and Lower Middle Income Countries (LMIC);
- To significantly reduce the burden of ill health and impaired growth due to enteric infections in populations of LMICs
- To reduce typhoid incidence to <5/100,000 globally by 2035

* <1 diarrhoeal death per 1000 live births by 2030 is the actionable goal

A mother and children in Nairobi's Korogocho slum, Kenya

CONSIDERATIONS USED TO BUILD OUR STRATEGY

- Diarrhoeal diseases are associated with ~580,000 deaths in children under age 5 each year
- Rate of death is declining at 6.5% annually (2000-2013) - before rotavirus vaccine introductions
- Diarrhoeal incidence is also declining but is not as dramatic
  - 2.9 episodes per child annually (down from 3.4 episodes per child in 1990)[1]

A mother with a baby recovering from severe diarrhoeal disease at a hospital in Managua, Nicaragua

[1]*Fisher-Walker BMC Public Health, 2012*

OUR APPROACH

- We support the development and delivery of **vaccines** for the leading causes of enteric and diarrhoeal diseases.
- We work to ensure the availability of **treatments** and to improve case management in the highest-burden countries.
- We support research on the global and regional **burden** of these diseases to inform decisions on deploying new interventions and expanding the use of existing ones
- We are investing in understanding **environmental enteric dysfunction** and possible ways to address poor gut health

Countries with active EDD projects

Our partners worldwide include:

- Academic and research institutions
- Industry (MNCs, DCVMs)
- Multinational organizations, including WHO and UNICEF
- Nongovernmental organizations
- Product development partnerships
- Public-private partners, including Gavi

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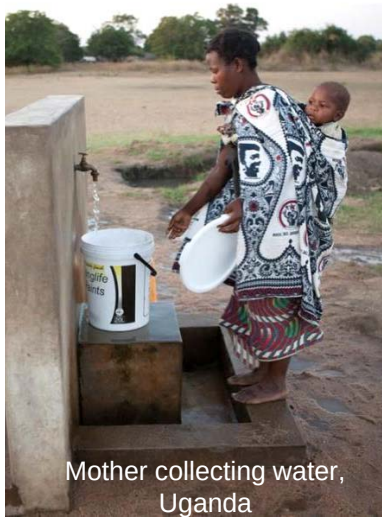
AREAS OF FOCUS

- **Enteric Vaccines**
  - Rotavirus
  - Cholera
  - ETEC and *Shigella*
  - Typhoid
- **Treatment Improvements and Delivery**
  - Research
  - Policy
  - Delivery
- **Health Gut**
  - Environmental enteric dysfunction (EED)
- **Evidence Generation**
  - Epidemiology and burden
  - *Cryptosporidium*
  - Learning agenda
    - Campylobacter, Norovirus, iNTS, Hepatitis E Virus
- **Advocacy**

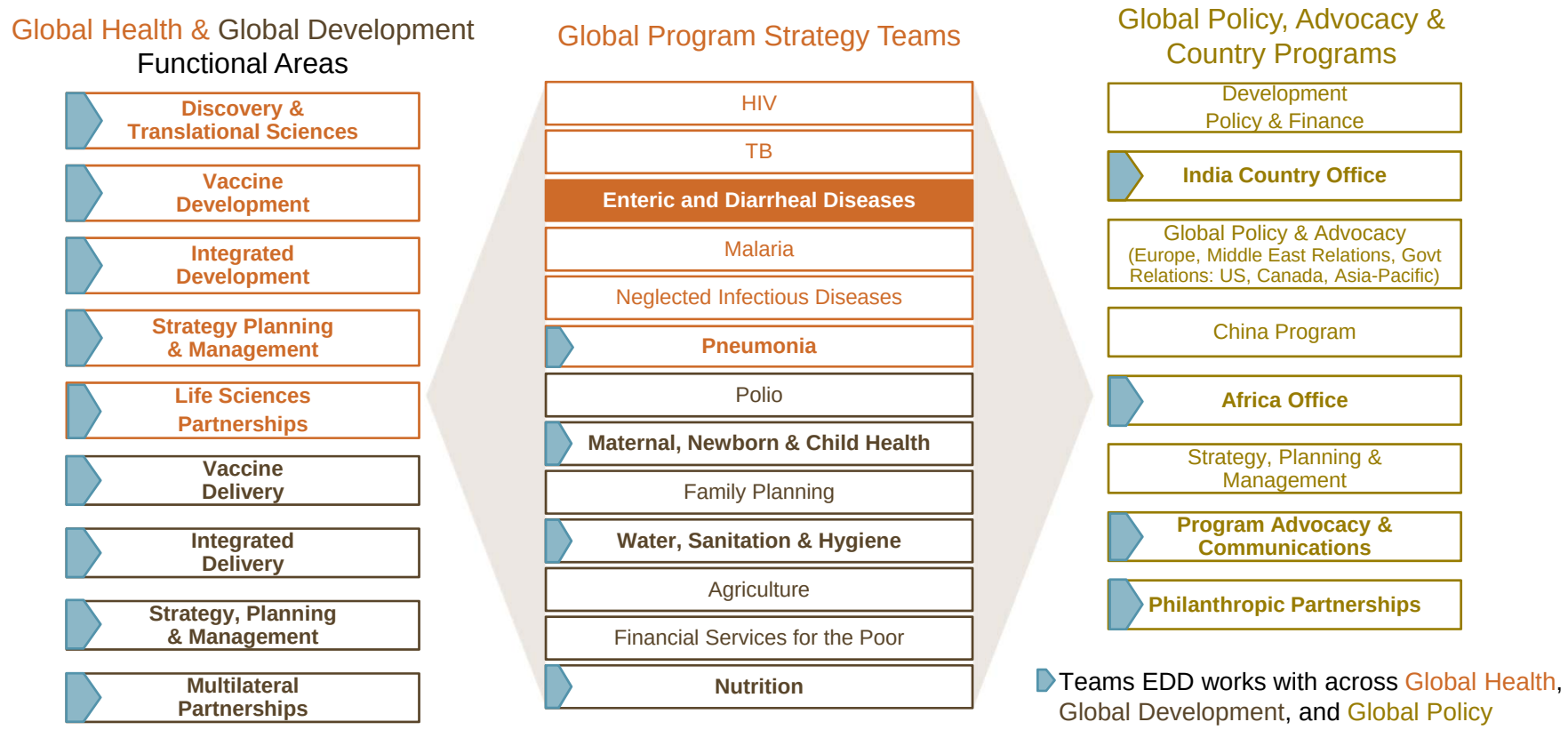
Research Scientist in laboratory at CMC, Vellore, India


Mother collecting water, Uganda

Mother feeding her child with ORS, Bangladesh

Rotavirus vaccine administration, Navrongo, Ghana

OUR WORK SUPPORTS BROAD GLOBAL HEALTH, DEVELOPMENT, AND ADVOCACY AGENDA



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EVIDENCE GENERATION: LANDMARK STUDIES

- **Global Enteric Multicenter Study (GEMS)**
  - Case control study on childhood diarrhoeal diseases in seven countries in Sub-Saharan Africa and South Asia.
  - Identified major causes of moderate to severe diarrhoea
  - GEMS 1A examined less severe diarrhoea
- **The Interactions of Malnutrition & Enteric Infections: Consequences for Child Health and Development (MAL-ED)**
  - Multi-country cohort study to understand the relationships between enteric infections, growth, gut function, cognitive development, and immune responses to vaccines.
- **Typhoid Surveillance in Africa Project (TSAP)**
  - 10 countries in Africa to elucidate typhoid and iNTS disease burden

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EVIDENCE GENERATION

- Epidemiology and burden
- *Cryptosporidium*
- Environmental enteric dysfunction (EED) leading to poor gut health and adverse consequences for child growth
- Learning agenda
  - Campylobacter
  - Invasive non-typhoidal salmonellosis
  - Norovirus
  - Hepatitis E Virus

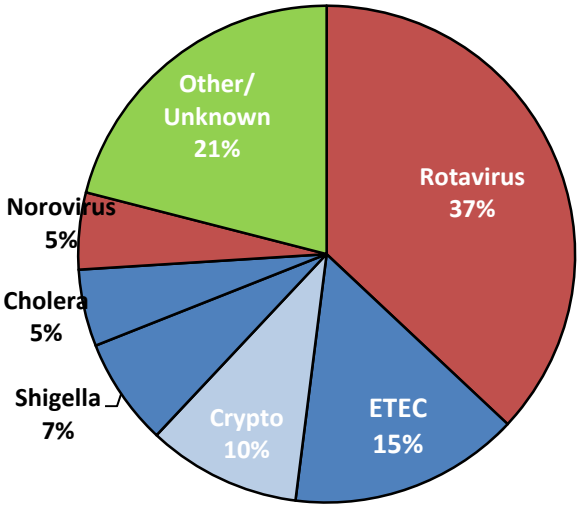
Children play outside the Joy Celebration Center for Nations church in Nairobi, Kenya on Wednesday December 16, 2009

GEMS IDENTIFIES HIGHEST BURDEN PATHOGENS

Likely under-represents overall burden of enteric and diarrhoeal disease:

- Diseases from enteric infections can lead to malnutrition, stunted growth, and impaired cognitive development, leading to diminished productivity over a lifetime for millions of people
- 8-fold mortality identified in GEMS sites 60-days post diarrhoea episode are not be captured as diarrhoea-related death

Estimated diarrhoeal deaths for U-5 children*
% of total deaths (~700K total**)



Kotloff KL. et al. Lancet. 2013;382(9888): 209-22

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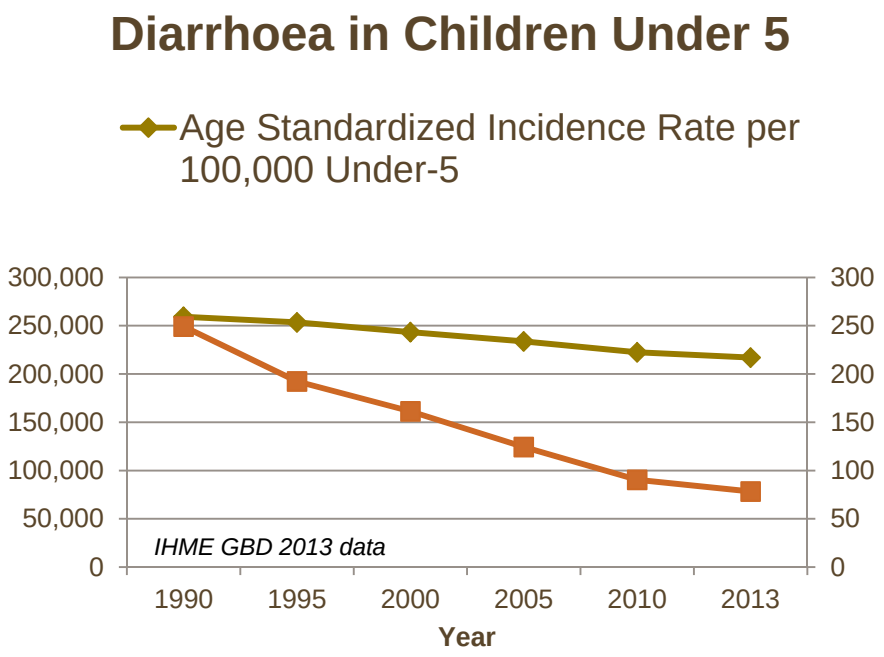
BURDEN OF DIARRHOEAL MORBIDITY IN INFANTS AND YOUNG CHILDREN



- Rate of death declining at 6.5% annually (2000-2013) - before rotavirus vaccine introductions
- Diarrhoeal incidence decline is not so dramatic - 2.9 episodes per child annually (down from 3.4 episodes per child in 1990)
- Increasing coverage of **treatment** has impacted death rates, yet incidence has not been largely impacted.
- Mortality burden has declined, but the burden of morbidity is relatively unchanged
- A focus on **treatment** alone will not sufficiently impact the significant morbidity of pathogens such as ETEC and *Shigella*

➢ Key to decreasing incidence *and* accelerating mortality declines is to focus on both **prevention** & **treatment** strategies

Fischer Walker C et al. BMC Pub Health 2013

CHOLERA VACCINE

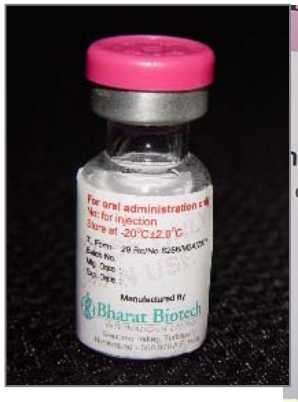
- Invested in the Shantha oral cholera vaccine (ShanChol®), which is WHO pre-qualified.
- Supported creation of global OCV stockpile in 2013
  - About 3.2 million doses of OCV distributed in the last two years via 14 disbursements
  - Supporting data collection for outbreak and endemic use guidelines
- Supporting vaccine development to achieve vaccine security
- Research on single-dose Shanchol® use in outbreak settings

Partners in Health: Cholera vaccination in Haiti

ROTAVIRUS VACCINE

ROTAVAC® licensure in India

- Shown to be safe and efficacious in Phase III trial in India
  - 54% efficacy against severe rotavirus gastroenteritis
  - Nearly 56% protection in the first year of life
- ROTAVAC ® products could achieve major impact in India and in Gavi countries
- First-generation product to be priced at ~$1 per dose

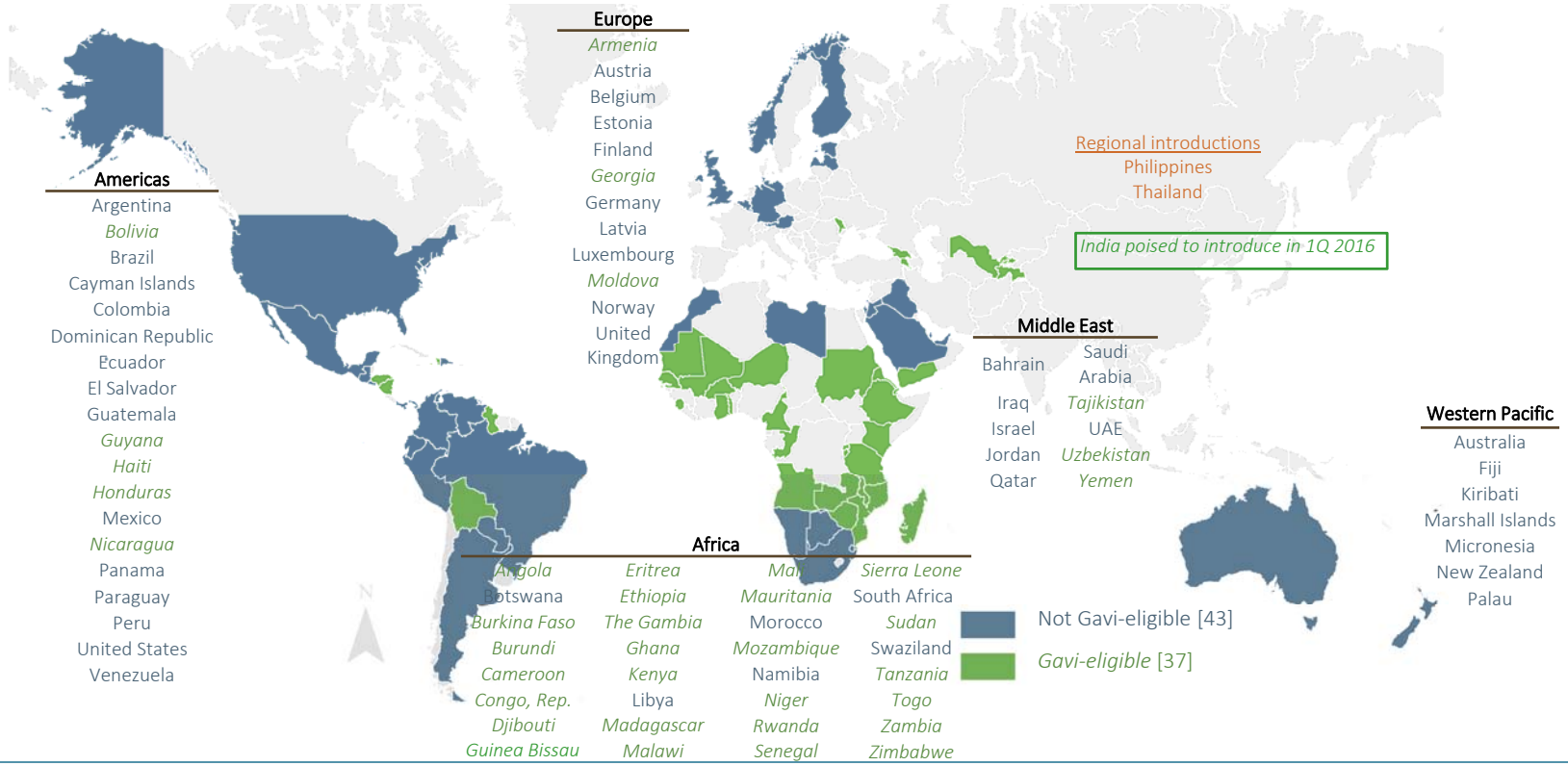


Bharat Biotech
Lead Innovation

Dr MK Bhan, former secretary, Department of Biotechnology, Dr K Vijay Raghavan, Secretary, DBT, Govt of India with Dr Krishna Ella, Chairman & Managing Director, Bharat Biotech, and Dr TS Rao, DBT at the release of Rotavac phase-III trial data in New Delhi

Bhandari N et al. Lancet 2014; 383: 2136-43

NATIONAL ROTAVIRUS VACCINE INTRODUCTIONS BY GEOGRAPHIC REGION - 80 COUNTRIES*



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TREATMENT INNOVATIONS AND DELIVERY

- Research to optimize treatment in resource-limited settings
- Policy advocacy and resource mobilization to support availability of ORS, zinc, and dysentery treatment
- Delivery of treatment to reduce diarrhoea deaths, with a focus on the highest-burden countries

A mother administers oral rehydration solution to her baby at a hospital in Dhaka, Bangladesh

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GROWING EVIDENCE OF NUTRITIONAL AND LONG-TERM EFFECTS

The impoverished gut—a triple burden of diarrhoea, stunting and chronic disease

Richard L. Guerrant, Mark D. DeBoer, Sean R. Moore, Rebecca J. Scharf and Aldo A. M. Lima

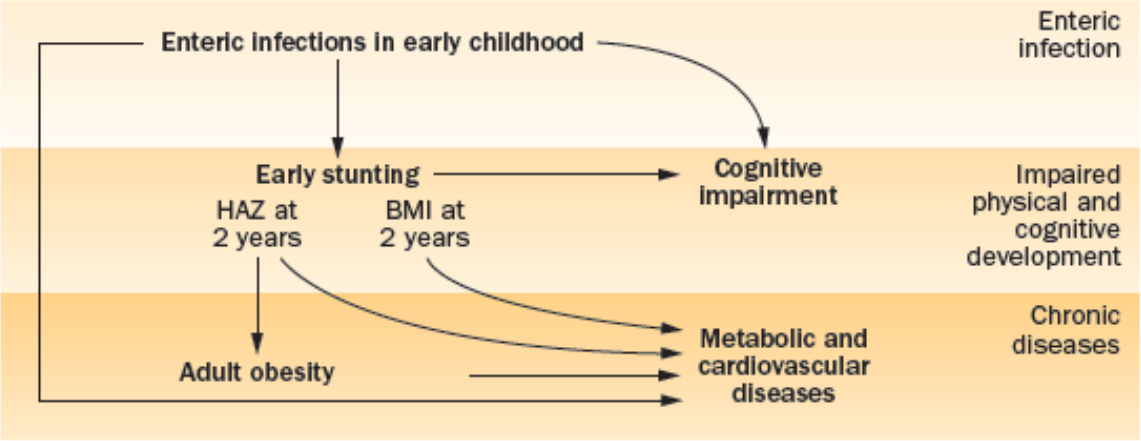

Figure 3 | Chronic consequences of early childhood enteric infections and stunting. The triple burden of enteric infections, impaired physical development (including low HAZ-2, or stunting and BMI-2) and cognitive development, and later life risk of obesity and its comorbidities are shown. Abbreviation: HAZ-2, height-for-age z-score at age 2 years.

Guerrant R et al, Nat Rev Gastrol Hepatol 2013; 10: 220-29

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THE WORK IS
COMPLICATED.
WHY WE DO IT IS NOT.