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## Theme 2: Water and Disease

Diarrheal disease as a key disease control priority

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# DCP, 2<sup>nd</sup> Edition



## Chapter 19 Diarrheal Diseases

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# Identifying options for diarrheal disease control and the issues our writing team explored

- Determine intervention options based on:
  - Pathophysiology, as presently understood
  - Target pathogens, as presently known
  - Transmission routes, as presently appreciated
- Specific or non-specific mechanisms
- Prevention or intervention
- Immediate or long-term impact
- Clinical and/or social concerns
- Finally, what will we need to know to further improve control when what we know has already been implemented, that is, what are the research needs now?

# Perspective from pathophysiology: 3 major mechanisms for diarrhea

- 1. *Acute watery diarrhea*** – altered transport of salts and water leading to dehydration
- 2. *Inflammatory diarrhea*** – intestinal damage leading to bloody diarrhea and dysentery
- 3. *Persistent diarrhea*** leading to malabsorption of nutrients and diarrhea lasting > 14 days and increasingly severe malnutrition

# What we knew when DCP2 started

1. There are many pathogens, including bacteria, viruses, protozoa and parasites
2. Acute watery diarrhea is self limited if fluid balance can be maintained, even in prodigious cholera diarrhea
3. Oral rehydration solution, ORS (based on the continued function of one Na transport system in watery diarrhea) can correct all but severe dehydration and maintain hydration after initial stabilization
4. Inflammatory and persistent diarrhea are not primarily dehydrating illnesses – ORS doesn't harm but does not affect the principal events in morbidity and mortality
5. Inflammatory diarrhea generally needs antibiotic therapy but drug resistance is an increasingly prevalent problem
6. Few vaccines are available – and not an easy R&D issue
7. Malnutrition is a significant co-morbidity, *only in part* related to the popular topic of micronutrient deficiencies

We also knew that diarrheal disease has social determinants that must be explored..

- Poverty
  - Housing
  - Crowding
  - Diet
- Environment
  - Sanitation
  - Refrigeration
  - Safe water supplies
- Social
  - Availability of medical care
  - Education, know-how and adaption o f best practices



# What we wanted...

1. Cost-effective (C/E) interventions that are feasible to implement in the near term, as well as longer term prevention (vaccines) and interruption of transmission (water and sanitation) based strategies that may require more research and/or infrastructure improvements
2. Decisions informed by C/E analysis but not entirely dependent on favorable C/E ratios
3. Geographically targeted packages aligned with major clinical/disease challenges in countries or regions
4. Improved and simplified case management as close to the household level as possible and a functioning referral capacity from the periphery to sophisticated health care facilities, including appropriate/sensible use of antibiotics

# Challenges to pathogen based strategies

1. Limited availability of pathogen specific diagnostics at the point of care – especially the lack of cheap specific/sensitive rapid tests
2. Increasing prevalence of microbial resistance to effective, inexpensive, oral antibiotics on a genus/species, time and place basis
3. Need for clear and rationale decisions on when to use, and equally important, when not to use, antimicrobials
4. Proven utility of syndromic based algorithms

# **Challenge to transmission based interventions: multiple mechanisms and possible interventions**

1. In food

2. In fluids

3. On the skin (fingers, nipple  
etc)

4. On contaminated inanimate  
objects (fomites)

5. On the feet of flies

6. Through anal-oral sex

1. Food safety (cooking,  
storing, refrigeration)

2. Safe water supplies

3. Handwashing and hygiene

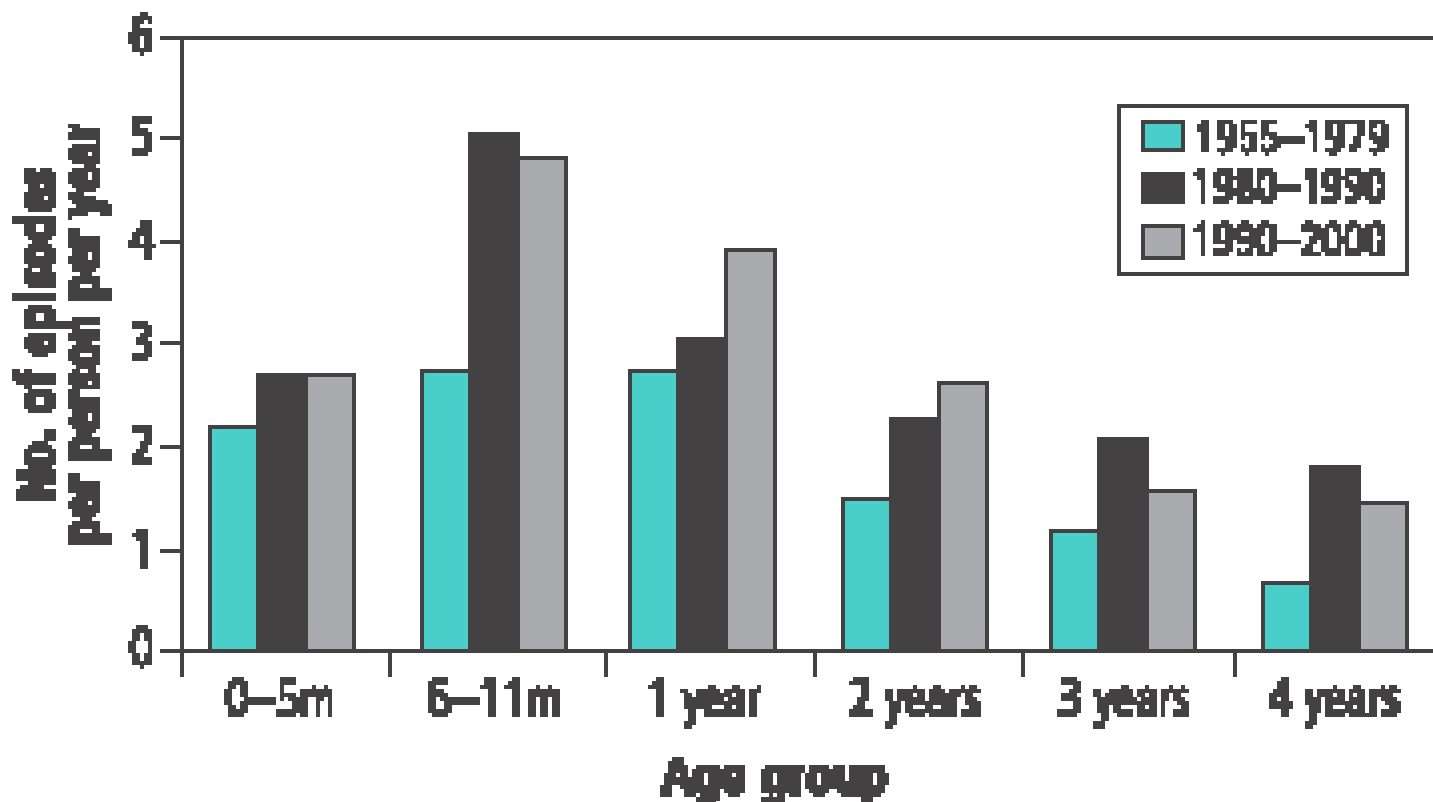
4. General hygiene, washing  
cups, dishes, bottles

5. Sanitary disposal of feces

6. Safer sex practices

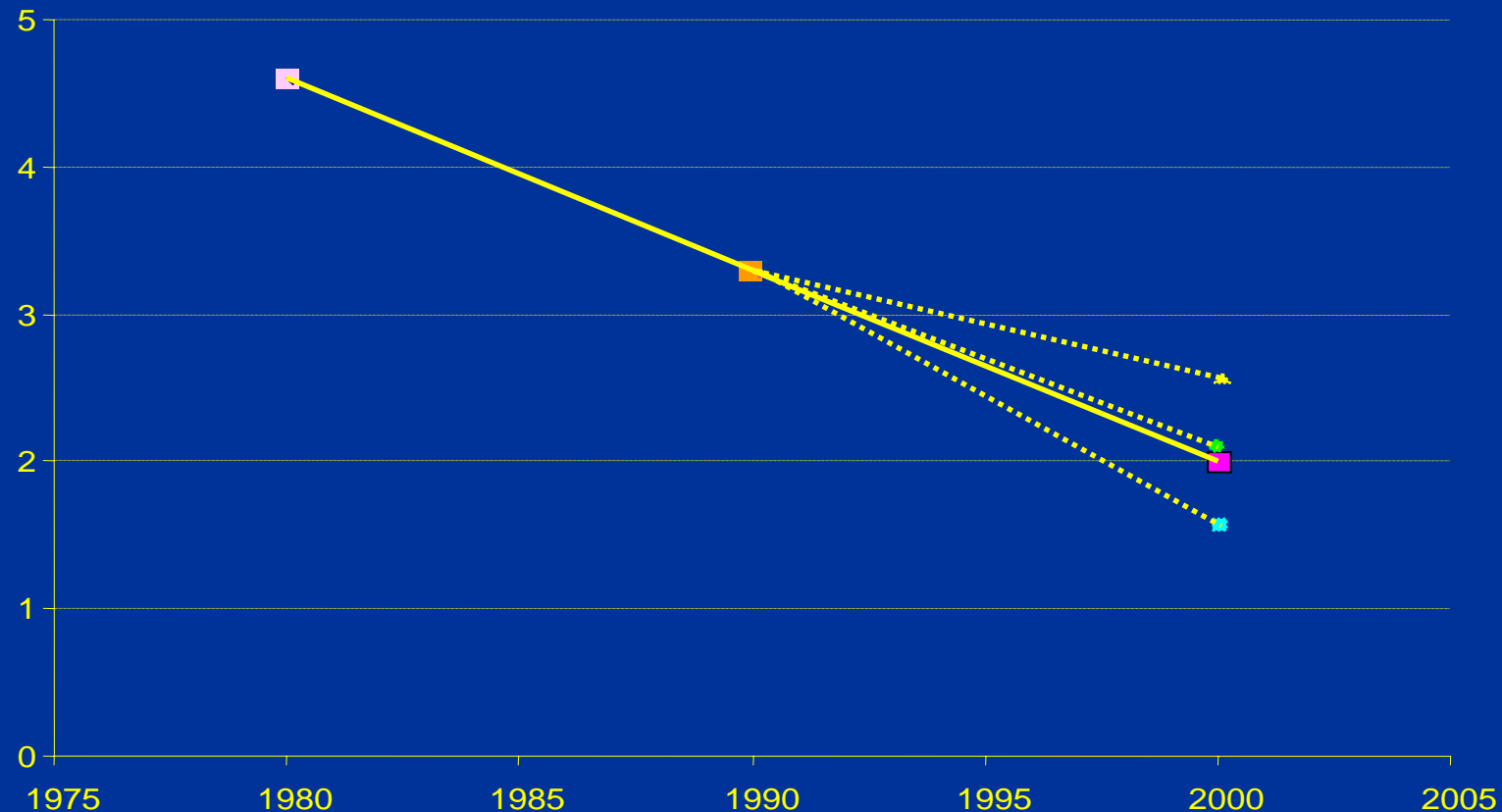
# Data: Diarrhea incidence hasn't changed in 50 years

**Fig. 1. Median age-specific incidences for diarrhoeal episodes per child per year from three reviews of prospective studies in developing areas, 1955–2000**



Data: Diarrheal mortality is clearly lower with residual of 1.5-2.5 million deaths/year

## Comparison of estimates



■ Snyder & Merson 1982

■ Bern et al. 1992

▲ Kosek et al. 2003

■ Trend estimate

● Parashar et al. 2003

■ Boschi-Pinto, submitted



# Interventions considered:

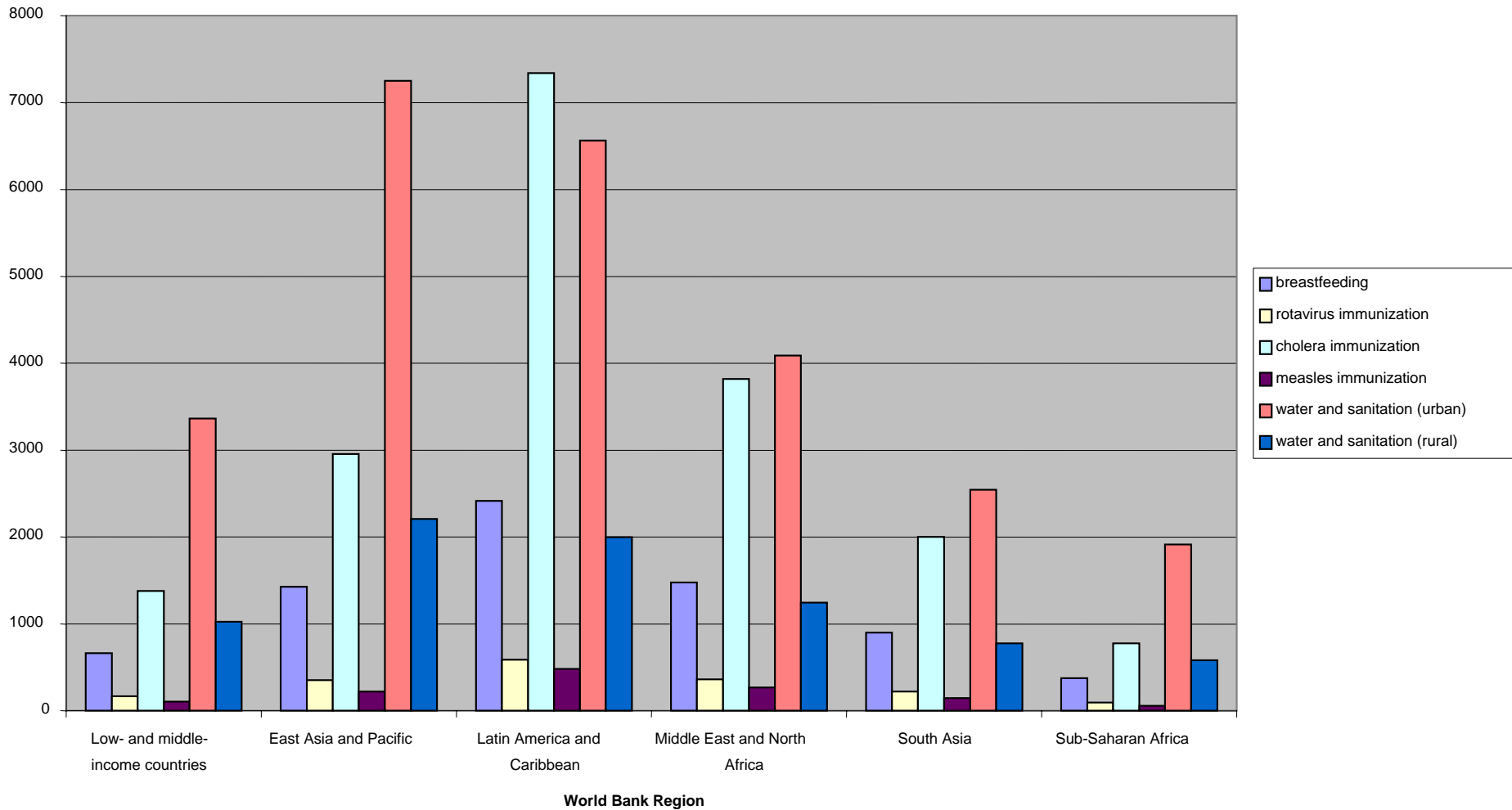
- Oral rehydration therapy
- Exclusive breast feeding for 6 months
- Improved complementary feeding practices
- Zinc supplementation
- Rotavirus immunization
- Cholera immunization
- Measles immunization
- Management of bloody diarrhea
- Improved water and sanitation infrastructure
- Promotion of personal and domestic hygiene

# Cost-effectiveness analysis decisions:

- Focus on under 5 year old target group
  - Cost of interventions in the 1<sup>st</sup> year of life and their impact on DALY's over 5 years
  - Cost of Interventions that must be implemented continuously for 5 years and their impact on DALY's over 5 years
- Input variables: (a) region-specific diarrhea morbidity rates adapted from Kosek, Bern, and Guerrant (2003); (b) region-specific underlying mortality rates and age structures provided by the DCP project; (c) median intervention effectiveness rates (% of diarrheal morbidity and mortality reduction); and (d) median per capita intervention costs gathered from the literature and personal communications
- Assume uniform intervention effectiveness rates for all regions because region-specific data were not available

# Cost-effectiveness: Intervention at birth continuing over 5 years with benefits over 5 years

C/E \$/DALY



# Conclusions from C/E analysis

1. Breastfeeding promotion was less effective than other early interventions (vaccines) but also less expensive than rotavirus and measles vaccination
2. Cholera vaccine was less expensive than breastfeeding promotion, but many times less effective because of the significantly higher prevalence of non-cholera diarrhea.
3. Oral rehydration therapy and water and sanitation interventions were more effective than breastfeeding interventions and vaccines in reducing morbidity and mortality but were also more expensive.
  - Caveat: the analysis for water and sanitation did not consider non-health benefits and the high cost-effectiveness ratio is more a limitation of the methodology employed than the intervention itself.

Non-economist authors challenged the economists C/E analysis. Result: reanalysis looking at the range of costs for ORS products

	Minimum	Median	Maximum
LMIC	4	1,062	2,124
EAP	4	132	260
LAC	20	2,570	5,120
ME/NA	10	2,564	5,113
SoA	4	642	1,279
SSA	4	988	1,972

The following text was added to the section on ORT:

The high cost-effectiveness ratio for ORT is attributable to the high variation in reported treatment costs, which may inflate the median cost used in this analysis. Given the range of reported treatment costs the cost-effectiveness ratio of ORT could be as low as US \$4 per DALY or as high as US \$2,124 per DALY in low- and middle-income countries. High variation in reported treatment costs results in high variation in cost-effectiveness for the other regions as well. *There remains little doubt, however, about the effect of widespread use of ORT on diarrhea morbidity and mortality and about the associated direct and indirect cost savings for treatment and hospitalization.*

# Finally, research priorities

1. How to best scale up known existing interventions
2. Better tracking of inflammatory diarrhea, prevalence, deaths, and long-term disability
3. How to control use of antimicrobials by health care workers and by individuals in the market place
4. Effective low cost vaccines
5. Technology for point of use clean water and simple methods for the safe disposal of feces
6. Pharmacological interventions in the pathophysiology cascade for watery, inflammatory or persistent diarrhea