About IKP Centre for Technologies in Public Health

IKP Centre for Technologies in Public Health (ICTPH) is a research centre that aims to improve the health of poor populations by focusing on designing, developing and delivering innovative solutions in healthcare concerning India and the developing world through an inclusive process that scientifically integrates knowledge of factors influencing health and diseases in India, regular evaluation and impact assessment of existing health systems and integration of appropriate technology for optimal health care delivery. ICTPH aims to learn, discover and apply relevant innovative solutions for health care leading to improved health for the people of India and other developing countries and to integrate technological advances with delivery of affordable, accountable and accessible health care. ICTPH has prioritized the diseases of its interest as malaria, tuberculosis, reproductive health, diarrhoeal diseases and diabetes.

IKP Centre for Technologies in Public Health is structured as an autonomous centre within ICICI Knowledge Park (IKP), a not-for-profit Research Park in Hyderabad, India focusing on Life Sciences.

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Foreword

The IKP Centre for Technologies in Public Health (ICTPH) aims to identify the most important evidence gaps in the current knowledge that India and developing countries have about health technologies pertinent to diseases of interest. ICTPH has prioritized the diseases of its interest as malaria, tuberculosis, reproductive health, diarrhoeal diseases and diabetes. Pertinent to diarrhoeal diseases, ICTPH is interested in the current status of preventive and therapeutic interventions with a focus on determining gaps in knowledge as well as potential areas for improvement. This report will be utilized by ICTPH to explore potential product development and/or development of product diffusion and scale up strategies. We welcome comments and suggestions from our readers.

Reports on strategies for malaria, tuberculosis, reproductive health and diabetes are also available as a part of our Working Paper Series.

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Executive Summary

Diarrhoeal diseases remain among the top five preventable killers of children under 5 in developing countries. More than 113 million episodes of Shigella infection are estimated to occur each year in children under the age of 5 years. An estimated 600, 000 deaths occur from Shigella infection each year among children under five years; overall mortality from diarrhoea is estimated at 2.6 million deaths among children aged below 5 years between 1990 and 2000. Studies from India report 1.1 to 6 episodes of diarrhoea per child aged 0 to 4 years annually (Kosek 2003). 16.7% to 37.5% of mortality among children under 5 years were attributed to diarrhoea (Kosek 2003).

Microbiological culture and microscopy remains the mainstay of diagnosis, despite their limited sensitivity. The delay in lab identification including the time to culture is a major limitation. New tests to detect inflammatory mediators or white or red blood cells in stool may help distinguish between secretory and inflammatory disease. High background levels from previous infections currently limit the use of such tests in developing countries where they will be most useful. New immunologic and nucleic acid based tests may be useful to detect pathogen-specific factors but are too expensive or require specialized instrumentation and trained technicians.

Oral Rehydration Therapy (ORT) remains the cornerstone of diarrhoea management. New formulations of ORS (Oral Rehydration Salts) are being studied; the WHO (World Health Organization) now recommends a different formulation in which the glucose and sodium content are each reduced to 75 mmol/L to give a total osmolarity of 245 mmol/L (referred to as ORS-245). Utilization of ORS by different stakeholders remains suboptimal and hovers about the 50% mark. Use of unclean water or unclean hands to prepare ORS adds to the potential for infections that may adversely affect the status of diarrhoea. This is an important consideration in rural areas especially when one considers the home based preparations of ORS.

The role of zinc supplements has to be evaluated further. Several new antibiotics are under development as are vaccines. Several strategies exist for the prevention of diarrhoea. Breast feeding promotion {US $930 per DALY (Disability Adjusted Life Years)} and measles immunization (US$ 981 per DALY) administered during the first year of were the most cost effective interventions.

ORT (US$ 1,062 per DALY) and water and sanitation in rural areas (US $ 1,974 per DALY) were the next most cost effective, *but only if they were continuously implemented for five years.* Rotavirus immunization (US$2,478 per DALY), cholera immunization (US$ 2,945 per DALY), and water and sanitation in urban areas (US$6,396 per DALY) were the least cost effective.

From a public health perspective, ICICI Centre for Technologies in Public Health (ICTPH) may focus on three broad areas: low cost technologies to provide clean water in rural areas, vaccine development for Shigella and enteroinvasive Escherichia coli, and rapid diagnostic tests to determine causative agents of diarrhoea.

A. Diarrhoeal Diseases as a Public Health Priority

A.1 Definition

By convention, diarrhoea is defined as the passage of three or more stools within 24 hours that are sufficiently liquid to take the shape of the container in which they are placed. The interval between episodes is arbitrarily defined as at least 48 hours of normal stools. The frequent passage of formed stool is not diarrhoea.

A.2 Transmission

Diarrhoea is caused by several infectious organisms including viruses, bacteria, helminthes and protozoa. The mode of transmission is essentially fecal-oral, that is, from the stool of one individual to the mouth of another. The route from the stool to the mouth and the number of organisms required to cause diarrhoea differ between organisms. Additional factors include the ability to survive the acidity of the stomach, host species preference, and the virulence of the organism, which may have a genetic basis.

A.3 Morbidity and Mortality

The estimated median incidence of diarrhoeal diseases in children under five in developing countries has remained almost static over the past decade – 3.5 episodes per child in 1993[1] compared to 3.2 episodes per child aged below five years in 2003.[2] Incidence continues to show a peak in infants aged 6 to 11 months, and drops thereafter. More than 113 million episodes of Shigella infection are estimated to occur each year in children under the age of 5 years.[3] These data are limited by the lack of systematic data collection and diverse data definitions and data collection methods across countries. Mortality from diarrhoea shows a decreasing trend.

1. Jamison, D.T., H.W. Mosley, A.R. Measham, and J.L. Bobadilla. **1993**. *Disease Control Priorities in Developing Countries*. Oxford, U.K.: Oxford University Press

2. Parashar, U.D., E.G. Hummelman, J.S. Breese, M.A. Miller, and R.I. Glass. Global Illness and Deaths caused by Rotavirus disease in Children. *Emerging Infectious Diseases* **2003**; *4*: 561-70

3. Kotloff, K.L., J.P. Winickoff, B. Ivanoff, J.D. Clemens, D.L. Swerdlow, P.J. Sasonnetti and others. Global Burden of Shigella Infections: Implications for vaccine development and implementation of control strategies. *Bulletin of the World Health Organization* **1999;** *77*: 651-66

Estimates of mortality from diarrhoea have dropped from 4.6 million deaths per year before the 1980s to 3.3 million per year in the decade 1980 to 1990 and 2.6 million per year between 1990 and 2000.[4,5,6] An estimated 600, 000 deaths occur from Shigella infection each year among children under five years. Diarrhoeal diseases remain among the top five preventable killers of children under 5 in developing countries.

Studies from India report 1.1 to 6 episodes of diarrhoea per child aged 0 to 4 years annually (Kosek 2003). 16.7% to 37.5% of mortality among children under 5 years were attributed to diarrhoea (Kosek 2003)

A.4 Question of Interest

What are the current (established) modalities to diagnose manage and prevent diarrhoea?

A.5 Methodology

A systematic review of the scientific literature focused on the diagnosis and prevention of diarrhoea with special emphasis on oral rehydration strategies was performed. The search covered The Cochrane Library, PUBMED, MEDLINE and EMBASE as the central databases and also covered the WHO database of publications. The search was performed using one or a combination of the following key words: diarrhoea, diagnosis, prevention, oral rehydration solution, dehydration, and rehydration.

Studies on adults or children with any form of diarrhoea were considered eligible for inclusion. No restriction was placed on study settings and included studies from any country. The major proportion of studies was from developing countries mimicking the geographic distribution of diarrhoea. Randomized controlled trials were included for the review as randomized controlled trials are considered the highest level of evidence.

4. Snyder, J.D., and M.H. Merson. The magnitude of the global problem of acute diarrhoeal disease: A review of active surveillance data. *Bulletin of the World Health Organization* **1982**; *60*: 604-13.

5. Bern, C.J., J. Martines, I.de Zoysa, and R.I. Glass. The magnitude of the problem of diarrhoeal disease: A ten year update. *Bulletin of the World Health Organization* **1992**; *70*: 705-14

6. Kosek, M., C. Bern, and R.L. Guerrant. 2003. The global burden of diarrhoeal diseases, as estimated from studies published between 1992 and 2000. *Bulletin of World Health Organization 81*: 197-204

Only articles in the English language were considered for review. The initial review of articles was followed by a review of the cross referenced articles. The related article link in PUBMED was used sequentially to identify other similar articles of interest.

B. Diagnosis of Diarrhoea

B.1 Syndromic Diagnosis

Acute Watery Diarrhoea

Acute watery diarrhoea can be rapidly dehydrating, with stool losses of 250 milliliters or more, a quantity that rapidly exceeds total plasma and interstitial fluid volumes and is incompatible with life unless fluid therapy is instituted to keep up with the loss. Such dramatic dehydration is usually due to rotavirus, enterotoxigenic E.coli or Vibrio cholerae, and is very dangerous in the young.

Persistent Diarrhoea

This is typically associated with malnourishment either preceding or resulting from the illness. Persistent diarrhoea has a disproportionately increased risk of death. In India, persistent diarrhoea accounted for 5% of episodes but 14% of deaths, and a mortality rate three times higher than brief episodes.[7] In Pakistan, persistent diarrhoea accounted for 18% of episodes, but 54% of deaths.[8] In Bangladesh, persistent diarrhoea was responsible for nearly half of the deaths from diarrhoea and the relative risk for death among infants with persistent diarrhoea and severe malnutrition was 17 times greater than for those with mild malnutrition.[9] HIV infection is a risk for persistent diarrhoea among adults and children.[10]

Bloody Diarrhoea

Bloody diarrhoea is diarrhoea with visible or microscopic blood in the stools, is associated with intestinal damage and nutritional deterioration, often with secondary sepsis. Some mild dehydration is common, as is fever. Bloody diarrhoea is different from dysentery.

7. Bhan, M.K., N. Bhandari., S. Sazawal., J. Clemens and P. Raj. Descriptive epidemiology of persistent diarrhoea among young children in rural north India. *Bulletin of the World Health Organization* **1989**; *67*: 281-88

8. Khan, S.R.,F. Jalil, S. Zaman, B.S Lindblad., and J. Karlberg. Early Child Health in Lahore, Pakistan: X-Mortality. *Acta Paediatrica Supplement* **1993**; *390*: 109-17

9. Fauveau V., F.J Henry, A. Briend, M. Yunus., and J. Chakraborty. Persistent diarrhoea as a cause of childhood mortality in rural Bangladesh. *Acta Paediatrica Supplement* **1992**; *381*: 12-14

10. Keusch G.T., D.M. Thea., M. Kamenga., K. Kakanda., M. Mbala, and F. Davachi. Persistent diarrhoea associated with AIDS. *Acta Paediatrica Scandinavica* **1992**; *381* (suppl.):45-48

New bouts of infection can occur before complete restoration of nutrient stores and can initiate a downward spiral of nutritional status that may lead to fatal protein – energy malnutrition.

B.2 Laboratory diagnosis

Microbiological culture and microscopy remains the mainstay of diagnosis, despite their limited sensitivity. The delay in lab identification including the time to culture is a major limitation. Culture methods used for the diagnosis of Shigella are relatively inefficient and time consuming. The results often remain obscure due to the presence of low numbers of causative organisms, competition from other commensal organisms and inadequate or inappropriate sample collection. Samples collected after antibiotic therapy show impaired growth of the organisms. New tests to detect inflammatory mediators or white or red blood cells in stool may help distinguish between secretory and inflammatory disease. High background levels from previous infections currently limit the use of such tests in developing countries where they will be most useful. New immunologic and nucleic acid based tests may be useful to detect pathogen-specific factors but are too expensive or require specialized instrumentation and trained technicians.

The polynucleotide *ial* probe derived from the large invasion plasmid identifies Shigella and Entero Invasive Escherichia Coli (EIEC) through nucleic acid hybridization.[11] This probe is specific but is less sensitive when used directly with blotted blood specimens or with colonies from solid media blotted onto the membrane. Spontaneous loss of invasion plasmids and selective loss of invasion associated genes is a possibility that may give rise to false negative results.[12] Another DNA probe developed from Shigella Flexneri *ipah* gene is more sensitive in the detection of Shigella and EIEC.[13]. Several PCR (Polymerase Chain Reaction) based assays have also been developed to differentiate between species causing diarrhoeal diseases.

11. Small P.L, S. Falkow. Development of a DNA probe for the virulence plasmid of shigella spp and enteroinvasive Escherichia coli. In Lieve L, Bonventre PF, Morello JA, Silver SD, Wu WC (eds). Microbiology. Washington DC. *American Society for Microbiology* **1986**; 121-124.

12. Venkatesan, M., J.M. Buysse, E.V. Vandendries, and Kopecko D.J. Development and testing of invasion associated DNA probes for detection of Shigella spp and Enteroinvasive Escherichia Coli. *Journal of Clinical Microbiology* **1988**; *26*: 261-266

13. Venkatesan, M., J.M. Buysse, and Kopecko D.J. Use of Shigella Flexneri *ipac* and *ipah* gene sequences for the general identification of Shigella spp and enteroinvasive Escherichia coli. *Journal of Clinical Microbiology* **1989;** *27*: 2687-2691

Table 1: Direct PCR in Comparison with Conventional Techniques for Diagnosis of Shigella and enteroinvasive E. Coli infection[14]

Assay	*Sensitivity (CI*)*	*Specificity*	*PPV***	*NPV****	*Agreement*	*Time to result*
Stool PCR	96% (94-98)	100%	100%	99%	99%	7 hours (SD 0.8)
Colony Hybridization	60% (54-66)	100%	100%	93%	94%	34 hours (SD 5.6)
Culture	54% (48-60)	100%	100%	92%	93%	42 hours (SD 4.3)
Clinical Diagnosis of Bloody Dysentery	96% (94-98)	68%	37%	99%	73%	

* CI = Confidence Intervals
** PPV = Positive Predictive Value
*** NPV = Negative Predicted Value

14. Dutta A.S and others. Sensitivity and performance characteristics of a direct PCR with stool samples in comparison to conventional techniques for diagnosis of Shigella and enteroinvasive Escherichia Coliinfection in children with acute diarrhoea in Calcutta, India. *Journal of Clinical Microbiology* **2001**; *50*: 667-674.

C. Managing Diarrhoea

C.1 Antibiotics for Diarrhoea

Antibiotics remain the mainstay of managing the bloody diarrhoea. Antimicrobials have been indiscriminately used and have led to widespread resistance. The current choice of treatment of Shigella is Ciprofloxacin but the widespread and inappropriate use of this antibiotic has led to the development of resistance against Ciprofloxacin. Newer antibiotics may help overcome the problem of resistance. However, inability to correctly and rapidly diagnose the causative organism will lead to the indiscriminate use of these new antimicrobials and the development of resistance against these drugs. Vaccines are an option that is currently under exploration.

C.2 Zinc Supplementation

Reports indicate that Zinc supplements during an episode of acute diarrhoea reduce duration and severity of the diarrhoea and could prevent 300,000 deaths in children each year.[15] The WHO and UNICEF now recommend giving Zinc supplements for 10-14 days during and after diarrhoea to every child with acute diarrhoea.[16] The role of zinc is currently under evaluation in large community based trials.

C.3 Rehydrating the Dehydrated

Rehydration is the most important strategy in the management of diarrhoea. Oral rehydration solution (ORS) was introduced in 1979 by the World Health Organization (WHO) and it rapidly became the cornerstone of programmes for the control of diarrhoeal diseases.[17] The osmolality of the original formulation is 310 mmol/L (referred to as ORS-310) and consists of glucose (111 mmol/L), sodium (90 mmol/L), potassium (20 mmol/L), chloride (80 mmol/L), and citrate (10 mmol/L) or bicarbonate (30 mmol/L).

15 . Black RE. Zinc Deficiency, Infectious disease, and Mortality in the developing world. *Journal of Nutrition* **2003**; *133* (suppl 1): 1485S-89S.

16. WHO and UNICEF. Joint Statement: Clinical Management of Acute diarrhoea. WHO/FCH/CAH/04.7. Geneva: WHO; New York: UNICEF.

17. Claeson M,Merson MH. Global progress in the control of diarrhoeal diseases. *Pediatric Infectious Disease Journal* **1990**; *9(5)*: 345-55.

The ORS was shown to improve signs of dehydration, including thirst, sunken eyeballs, sunken fontanelles, poor skin turgor, or a decreased or absence of urine output.[18] ORS-310 is considered as both safe and effective[19] , and, since its introduction, it has been considered to be mainly responsible for the decrease in case-fatality rates from acute dehydrating diarrhoea. [20]

The physiological basis for the use of ORS-310 was the co-transport of glucose and sodium across the intestinal membrane. While this glucose-based ORS is effective in replacing the fluid from acute diarrhoea thus preventing further dehydration, it neither reduces stool loss nor shortens the duration of illness. Increasing the glucose concentration to greater than 111 mmol/L increases the osmotic load of the solution, which may further aggravate the fluid loss and induce hypernatraemia.[21] In 2004, the WHO recommended a different formulation in which the glucose and sodium content were each reduced to 75 mmol/L to give a total osmolarity of 245 mmol/L (referred to as ORS-245).[22] ORS-245 reduces stool volume, shortens duration of diarrhoea, and decreases the need for unscheduled intravenous therapy compared with ORS-310.[23]

In 1996, Gavin and colleagues published the results of a meta-analysis that evaluated the efficacy of glucose-based ORT among well-nourished children in developed countries. The review included six studies that compared ORT with intravenous therapy (IVT) and seven studies that compared ORS solutions with different sodium contents. They found that failure of ORT (defined as the need to revert to IVT) varied among trials, ranging from 0% to 18.8% with an overall failure rate of 3.6% (95% confidence interval 1.4 to 5.8).

18. Joint WHO/ICDDR, B Consultative Meeting on ORS Formulation. *25 years of ORS: Joint WHO/ICDDR,B Consultative Meeting on ORS Formulation, Dhaka, Bangladesh, 10-12 December 1994[CDR/CDD/95.2].* Geneva: World Health Organization, 1995.World Health Organization, 1995.

19. Santosham M, Greenough WB 3rd. Oral rehydration therapy: a global perspective. *Journal of Pediatrics* **1991**; *118(4 (Pt 2))*: 44{51.

20. Victora CG, Bryce J, Fontaine O,Monasch R. Reducing deaths from diarrhoea through oral rehydration therapy. *Bulletin of the World Health Organization* **2000**; *78(10)*: 1246{55.

21. Hunt JB, Elliott EJ, Fairclough PD, Clark ML, Farthing MJ.Water and solute absorption from hypotonic glucose-electrolyte solutions in human jejunum. *Gut* **1992**; *33(4)*: 479{83.

22. World Health Organization. Dept. of Child and Adolescent Health and Development. *Clinical management of acute diarrhoea: WHO/UNICEF joint statement [WHO/FCH/CAH/04.7].* Geneva: *World Health Organization*, **2004**.

23. Hahn S, Kim Y, Garner P. Reduced osmolarity oral rehydration solution for treating dehydration caused by acute diarrhoea in children.In: *Cochrane Database of Systematic Reviews*, 1, **2002**.

They found no significant difference in failure between different ORS solutions. They also found no higher risk of iatrogenic hypernatremia or hyponatremia with ORT compared with IVT and no significant differences in failure rates between inpatients and outpatients. The authors suggested that ORT may, in fact, be associated with more favorable outcomes such as increased weight gain and shorter duration of diarrhoea.

A recent review (2006)[24] concluded the lack of important clinical differences between ORT and IVT for rehydration secondary to acute gastroenteritis in children. It seems reasonable that children presenting for medical care with mild to moderate dehydration secondary to acute gastroenteritis should initially be treated with ORT. Should treatment fail, then IVT may be used. In children who have persistent vomiting, ORT may be used, but the child must be closely observed for proof of successful treatment. For every 25 children treated with ORT, one would fail and require IVT. Clinicians and families need to apply this evidence to individual situations in order to decide whether they are willing to accept this minimal risk.

A Cochrane Review of rice based rehydration compared with glucose Oral Rehydration Solution (ORS) showed that rice water was associated with lower stool volumes in cholera patients but not in diarrhoea from other causes.[25] The available data were however insufficient to make generalized conclusions.

A recent Cochrane review was done on trials of children admitted to hospital who were dehydrated because of diarrhoea.[26]

This review used unscheduled intravenous fluid infusion as the primary endpoint since it was pragmatic and provides a measure of failed oral rehydration and has implications for the healthcare resources. The authors found that reduced osmolarity ORS has beneficial effects over the WHO standard ORS in reducing needs for unscheduled intravenous fluid infusion, stool output during rehydration, and the number of patients with vomiting during oral rehydration treatment.

24. Hartling L, Bellemare S, Wiebe N, Russell K, Klassen TP, Craig W. Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children. *Cochrane Database of Systematic Reviews* **2006**, Issue 3. Art. No.: CD004390. DOI:10.1002/14651858.CD004390.pub2

25. Fontaine O, Gore SM, Pierce NF. Rice-based oral rehydration solution for treating diarrhoea (Cochrane Review). In: *The Cochrane Library*, 3, **2000**. Oxford: Update Software

26. Hahn S, Kim Y, Garner P. Reduced osmolarity oral rehydration solution for treating dehydration caused by acute diarrhoea in children. *Cochrane Database of Systematic Reviews* **2002**, Issue 1. Art. No.: CD002847. DOI: 10.1002/14651858.CD002847

Reduced osmolarity ORS has no further risk of developing hyponatraemia as compared to the WHO standard ORS. Findings from this review indicate reduced osmolarity ORS is more effective than WHO standard ORS in the first line treatment of dehydration in children with diarrhoea. It is not easy to be sure however, that this finding applies to a subgroup of patients with severe diarrhoea caused by cholera, where electrolyte loss is profound. This could increase the risk of hyponatraemia, result in adverse clinical events, and attenuate the advantages of reduced osmolarity ORS. A WHO expert group recommended that ORS for treating diarrhoea in children with non-cholera diarrhoea will be enhanced by shifting to a reduced osmolarity ORS, and propose a global shift to ORS with an osmolarity of 75 mEq/L of sodium (WHO 2001).

The issue of cleanliness of the water and the hand that prepares the ORS is to be kept in mind. Use of unclean water or unclean hands adds to the potential for infections that may adversely affect the status of diarrhoea. This is an important consideration in rural areas especially when one considers the home based preparations. It is important that the ORT (commercial or home based) is prepared with the appropriate mix of water such that the preparation does not contain too much electrolytes or glucose. Inappropriate preparation may not lead to appropriate replacement of electrolytes and may lead to shock and other complications.

D. Preventive Strategies

- *Exclusive Breastfeeding for Infants under 6 Months of Age*: Exclusive breastfeeding means that no other food or drink, not even water, is allowed during this period. Medicines and vitamin and mineral supplements may be given. Breastfed children under 6 months of age are 6.1 times less likely to die of diarrhoea than infants who are not breastfed.[27]

- *Improved Complementary Feeding*: Complementary feeding should be initiated at or after 6 months and should be supplemented with breast milk preferably till the age of two years (WHO 2003).Improved feeding practices to treat or prevent malnutrition can save as many as 800,000 lives per year.[28]

- *Rotavirus Vaccination*: Rotavirus accounts for at least one-third of severe and potentially fatal watery diarrhoea episodes-primarily in developing countries, where an estimated 440,000 vaccine preventable rotavirus deaths per year occur.[29]

- *Vaccines for Cholera*: Although scientific interest for a vaccine against cholera remains high, its public health importance is less than the development of a vaccine against Shigella. ORT is inexpensive and useful in preventing mortality from cholera as compared to the more expensive vaccines.

- *Vaccines for Shigella and E-Coli*: Given the high public health significance, the vaccines against Shigella and E. coli are in their developmental stage. However, the costs of these vaccines will be a major constraint for resource poor countries if the developmental costs are transferred to the consumers.

27. WHO collaborative study team, Effect of breastfeeding on infant and Child mortality due to infectious diseases in less developed countries: A Pooled Analysis. *Lancet* **2000**; *355*: 1104

28. Jones G R and the Bellagio Child Survival Study Group. How many Child Deaths Can we Prevent this year? *Lancet* **2003**; *362:* 65-71

29. Parashar and others. Global Illness and deaths caused by Rotavirus disease in children. *Emerging Infectious Diseases* **2003**; *9*: 565-72.

- *Immunization against Measles*: Immunizing 45 to 90% of infants against measles will prevent 44 to 64% of measles, 0.6 to 3.8% of diarrhoeal episodes, and 6 to 26% of diarrhoeal deaths among children under five.

- *Improved Water and Sanitary Facilities and Promotion of Personal and Domestic Hygiene*: Poor sanitation, inadequate access to clean and safe drinking water, and inadequate personal hygiene are responsible for an estimated 90% of childhood diarrhoea (WHO 1997). Hand washing reduces diarrhoea incidence by as much as 33% (Huttly and others 1997). Washing hands after defecation or handling feces of children, and before food is recommended but will entail an average of 32 hand washes per day and consumes 20 liters of water (Graef and others 1993). The supply of safe water and the safe disposal of fecal waste are the two strategies that can have the highest impact on diarrhoeal diseases. Low cost technologies for potable water and simple latrines with running water will be useful. However; these do not fall within the radar of policy makers given the importance of other infectious disease priorities.

Table 2: Cost along with Morbidity and Mortality Reduction on the Implementation of the Proposed Preventive Strategies[30]

Strategy	*Cost/Child Range (2001 US$)*	*Median Morbidity Reduction (%)*	*Median Mortality Reduction (%)*
Breast-feeding Promotion	0.46-17.50	4.5	10.5
Rotavirus Immunization with RRR-TV	3.33-104.30	8.54	24.1
Live Cholera Vaccine	1.70-5.60	0.095	1.5
Measles immunization	0.56-26.00	2.2	16
Improved water supply and sanitation	25-81	24	65
ORT	0.02-11	0	95

Breast feeding promotion (US $930 per DALY) and measles immunization (US$ 981 per DALY) administered during the first year of were the most cost effective interventions. ORT (US$ 1,062 per DALY) and water and sanitation in rural areas (US $ 1,974 per DALY) were the next most cost effective, *but only if they were continuously implemented for five years.* Rotavirus immunization (US$2,478 per DALY), cholera immunization (US$ 2,945 per DALY), and water and sanitation in urban areas (US$6,396 per DALY) were the least cost effective.[30]

30. Keusch GT et al. Diarrhoeal diseases. *Disease control Priorities in developing countries*. **2006**; 371-387

E. Potential Directions for ICTPH

- A focus on RDTs may be of interest considering that rapid and accurate diagnosis of causative organisms especially Shigella and EIEC is essential for the therapeutic interventions to become more optimal.

- On the preventive front, ICTPH can explore low cost technologies to provide clean and safe water (potable water) in rural areas. Such technologies can explore feasibility of converting existing water sources into potable water.

- The development of a vaccine against Shigella is another area of importance.

- ICTPH may also explore deployment strategies for optimal use of ORT.

However, it may be most useful from a public health perspective to develop low cost technologies for clean water in rural areas.

F. Abbreviations

DALY	Disability Adjusted Life Years
DNA	Deoxyribo Nucleic Acid
E. coli	Escherichia Coli
EIEC	Entero Invasive Escherichia Coli
HIV	Human Immunodeficiency Virus
IVT	Intra Venous Therapy
ORS	Oral Rehydration Solution
ORT	Oral Rehydration Therapy
PCR	Polymerase Chain Reaction
UNICEF	United Nations International Children's Emergency Fund
US	United States
WHO	World Health Organization