Acute Diarrhoeal Disease in Children

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Why are we talking about it?

Global and local context …….
Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000

Figure 2

Lancet 2012;379:2151-61
Global trends in Child Deaths 2000-2010

Lancet 2012;379:2151-61
Every death counts: use of mortality audit data for decision making to save the lives of mothers, babies, and children in South Africa

Figure 2: Cause of death in South Africa
(A) Primary causes of maternal death, (B) primary causes of stillbirths (more than 1000 g or 28 weeks), and (C) causes of death for children younger than 5 years and neonates (babies younger than 28 days). Reproduced from Every Death Counts report with permission from author and publisher. Data for primary causes of maternal deaths from Saving Mothers 2002–04 report; for primary causes of stillbirths from Saving Babies 2003–05 report; and for causes of death for children younger than 5 years and those younger than 1 month derived from the 2000 South Africa Burden of Disease estimates.
Reported cases of Diarrhoea in Cape Town
By month - Nov 2011 to Sep 2013

- Diarrhoea with dehydration under 5 years - new ambulatory
- Diarrhoea without dehydration under 5 years - new ambulatory
The setting in Africa

- Child spacing
- Breast feeding
- Education
- Weaning
- Water source
- Sanitation
- Deprivation
- Social disruption
- Women in society

3-9 episodes/child year in developing countries, vs. 1.3-2.3 in industrialised
WHO Enhanced Diarrhoeal Disease Control (EDDC): 1980

Figure 1: The Enhanced Diarrhoeal Disease Control (EDDC) framework: an integrated approach to Management of Diarrhoeal Disease.

Promotion ORS ↓ deaths 4.5 → 1.6 million/year

No BF vs EBF:
- 14.4xRR all cause mortality <6mo
- 4 x RR diarrhoea
- 10.5 x RR diarrhoea mortality

Water, water quality (point of use), sanitation and hygiene independently reduced DDx burden

Lancet 2008; 371:243-60
Lancet Infect Dis 2005; 5:42-52
What causes diarrhoea and how?
Common pathogens causing childhood diarrhoea

- **Viruses**
  - Rotavirus
  - Norovirus
  - Enteric adenovirus
  - Other: caliciviruses, astroviruses, enteroviruses

- **Protozoa**
  - Cryptosporidium parvum
  - *Giardia lamblia*
  - Entamoeba histolytica

- **Bacteria**
  - *Campylobacter jejuni*
  - Non-typhoid *Salmonella* *
  - Enteropathogenic *E. Coli*
  - Enterotoxigenic *E. Coli* (ETEC)
  - *Shigella spp*
  - *Salmonella typhi*
  - *Vibrio cholera*

- **Unidentified**

- **Mixed infections**

* Dysentery
Ingest organism

Intestinal colonisation and cellular adherence

Mucosal invasion

Villous cell destruction

Impaired sodium absorption

Toxin production

Cytotoxin/enterotoxin

Stimulate chloride secretion

DIARRHOEA
What causes it where?
FIG. 1. Geographical distribution of the main enteropathogens in European countries for which these data are available. The main agents of acute gastroenteritis (AGE) in European countries are listed in order of frequency. Rotavirus is the most common enteropathogen throughout Europe. Campylobacter is the second most frequent enteropathogen in northern countries, and Salmonella is in southern countries.
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


Summary
Background Diarrhoeal diseases cause illness and death among children younger than 5 years in low-income countries. We designed the Global Enteric Multicenter Study (GEMS) to identify the aetiology and population-based burden of paediatric diarrhoeal disease in sub-Saharan Africa and south Asia.
Findings of GEMS

- Study: 9439 cases 13 129 controls
  - 3 year prospective age-stratified case-control
  - 4 sites Africa (Kenya, Mali, The Gambia, Mozambique)
    - 3 sites Asia (India, Bangladesh, Pakistan)

- Most cases of moderate to severe diarrhoea were due to 4 pathogens
  - Rotavirus
  - Cryptosporidium
  - Enterotoxigenic E.Coli (ST-ETEC)
  - Shigella

- 72-83% of controls had 1 or more potential pathogens
Findings of GEMS

- Odds of dying
  - 8.5 x higher in pts with mod-severe dehydration

- Deaths
  - Most outside health facilities
  - 1/3 each within 0-7 days, 8-21 days and 21-60 days

- Pathogens associated with increased risk of death
  - Infants: ST-ETEC(HR 1.7) and typical EPEC(HR 2.6)
  - Toddler: cryptosporidium

- Nutritional impact
  - Enrolment HAZ inversely associated with risk of dying
  - HAZ scores decreased between enrolment and followup
GEMS: Conclusions and recommendations

- Rotavirus commonest cause at all sites in first year
- Cryptosporidium a significant pathogen regardless HIV status
- EPEC associated with persistent diarrhoea, nutritional faltering and death BUT many controls positive
- Potential 40% reduction incidence and sequelae of diarrhoea - focused preventative strategies vs 4 pathogens
- **Accelerate: rotavirus vaccination, zinc**
- ?new vaccines
- **Revitalise diarrhoea case management algorithms**
Why all this morbidity and mortality?
Complications of Diarrhoea

Acute

- **Dehydration**
  - Neurological sequelae
- **Metabolic acidosis**
- **Electrolyte disturbances**
- **Haemolytic uraemic syndrome**
- Iatrogenic – complications fluid administration
- **Death**

Longer term

- Susceptibility to re-infection
- **Malnutrition**
- **Carbohydrate (lactose, glucose) intolerance**
- Development of food (CMP, soya) intolerance
- **Death**

BMJ 2007;334:35–40
Indications for hospitalisation

- Severe dehydration with/without shock
- Altered neurological status
- Intractable vomiting or ORS failure
- Caregivers that cannot provide adequate care at home
- Young age, < 6 months with dehydration
- Assoc chronic illness
- Enteric fever: high fever/inflammatory diarrhoea
- Dysentery esp< 1 yr
- Tender abdomen /suspected surgical condition
- High output diarrhoea
- Persistent diarrhoea
Differential diagnosis in children presenting with acute diarrhoea

1. **Infections outside the GIT e.g.** meningitis, UTI
2. **Surgical conditions** eg intussusception, malrotation, especially bile-stained vomiting
3. **Underlying immunodeficiency** e.g. HIV disease
4. **Spurious diarrhoea** – faecal impaction with overflow
5. **Side-effects** of medications e.g. antibiotics
6. **Primary gastrointestinal tract pathology** e.g. inflammatory bowel disease, coeliac disease, cystic fibrosis
7. **Toddler’s diarrhoea**

*BMJ 2007;334:35–40*
How do we manage children with acute diarrhoea?
Approach to Management

- Thorough history and examination
  - Assess for shock then dehydration
- Nutritional evaluation
- Comprehensive clinical evaluation to identify
  - Complications
  - Associated illnesses
  - Exclude differential diagnosis
- **Prescribe fluids and feeds**
- Investigations
- **Pharmacologic therapy**
Diarrhoea and vomiting in children

Diarrhoea and vomiting caused by gastroenteritis: diagnosis, assessment and management in children younger than 5 years

THE TREATMENT OF DIARRHOEA

World Health Organization
A manual for physicians and other senior health workers

Review article: the management of acute gastroenteritis in children

M. Pieścik-Lech*, R. Shamir†, A. Guarino† & H. Szajewska*

European Society for Paediatric Gastroenterology, Hepatology, and Nutrition/European Society for Paediatric Infectious Diseases
Evidence-Based Guidelines for the Management of Acute Gastroenteritis in Children in Europe: Executive Summary

*Alfredo Guarino (Coordinator), *Fabio Albano, †Shai Ashkenazi, ‡Dominique Gendrel, §J. Hans Hoekstra, ||Raanan Shamir, and ¶Hania Szajewska: The ESPGHAN/ESPID Evidence-Based Guidelines for the Management of Acute Gastroenteritis in Children in Europe Expert Working Group
Fluid management options

- Intravenous or oral/enteral
- Rapid (over 4-6 hours) vs standard (24 hours)
- Large-volume vs standard-volume
- Feeding choice
secretory and absorptive processes in the intestine are separate

glucose-sodium co-transport unaffected in diarrhoea

Water passively follows the osmotic gradient generated by trans-cellular transport of electrolytes and nutrients
Reduced Osmolarity ORS

- Lower concentrations of sodium (60/75 mmol/l vs 90 mmol/l) and glucose (75 mmol/l vs 111 mmol/l)
  - [Cl⁻ 65mmol/l, K⁺ 20mmol/l, citrate 10mmol/l]

- Osmolarity 245 mOsm/l (vs 310mOsm/l)
  - lower use iv rescue (↓33%)
  - reduced vomiting
  - similar incidence hyponatraemia for cholera and non-cholera diarrhoea
### TABLE 3. Composition of commercial oral rehydration solutions (ORS) and commonly consumed beverages

<table>
<thead>
<tr>
<th>Solution</th>
<th>Carbohydrate (gm/L)</th>
<th>Sodium (mmol/L)</th>
<th>Potassium (mmol/L)</th>
<th>Chloride (mmol/L)</th>
<th>Base (mmol/L)</th>
<th>Osmolarity (mOsm/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>World Health Organization (WHO) (2002)</td>
<td>13.5</td>
<td>75</td>
<td>20</td>
<td>65</td>
<td>30</td>
<td>245</td>
</tr>
<tr>
<td>WHO (1975)</td>
<td>20</td>
<td>90</td>
<td>20</td>
<td>80</td>
<td>30</td>
<td>311</td>
</tr>
<tr>
<td>European Society of Paediatric</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Gastroenterology, Hepatology</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>and Nutrition</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enfalyte§†</td>
<td>16</td>
<td>60</td>
<td>20</td>
<td>60</td>
<td>30</td>
<td>240</td>
</tr>
<tr>
<td>PediaLyte§</td>
<td>30</td>
<td>50</td>
<td>25</td>
<td>45</td>
<td>34</td>
<td>200</td>
</tr>
<tr>
<td>Rehydralyte§</td>
<td>25</td>
<td>45</td>
<td>20</td>
<td>35</td>
<td>30</td>
<td>250</td>
</tr>
<tr>
<td>CeraLyte‡‡</td>
<td>25</td>
<td>75</td>
<td>20</td>
<td>65</td>
<td>30</td>
<td>305</td>
</tr>
<tr>
<td>Commonly used beverages (not</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>appropriate for diarrhea treatment)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apple juice§§</td>
<td>120</td>
<td>0.4</td>
<td>44</td>
<td>45</td>
<td>N/A</td>
<td>730</td>
</tr>
<tr>
<td>Coca-Cola§§Classic</td>
<td>112</td>
<td>1.6</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>13.4</td>
</tr>
</tbody>
</table>

* Actual or potential bicarbonate (e.g., lactate, citrate, or acetate).
§ Ross Laboratories (Abbott Laboratories), Columbus, Ohio. Data regarding Flavored and Freezer Pop PediaLyte are identical. Additional information is available at http://www.pediaLyte.com.
** Cera Products, L.L.C., Jessup, Maryland. Additional information is available at http://www.ceralyte.com/index.htm.
†† Not applicable.
§§ Meeting U.S. Department of Agriculture minimum requirements.
¶¶ Coca-Cola Corporation, Atlanta, Georgia. Figures do not include electrolytes that might be present in local water used for bottling. Base = phosphate.
ORS (vs ivi fluids)

- ORT first line Management for diarrhoea with “some dehydration” (AAP, ESPGHAN, Cochrane)
  - cheaper
  - less adverse events
  - shorter stay
  - more effective

- Enteral(NG) as alternative

**ORT CONTINUES TO BE UNDERUSED GLOBALLY**

*Oral rehydration should be used as first-line therapy for the management of children with AGE:

- When oral rehydration is not feasible, enteral rehydration by the nasogastric route is as effective if not better than IV rehydration (I, A).
- Enteral rehydration is associated with significantly fewer major adverse events and a shorter hospital stay compared with IV therapy and is successful in most children (I, A).
- Children who are able to receive oral rehydration therapy (ORT) should not be given IV fluids (I, A).*
Rehydration Fluids

- Rehydration over **four hours** in mild to moderate (IMCI “some”) dehydration
  - As effective as rehydration over 24 hours
- Rehydration should be slower over **8–24 hours** in
  - under three months of age
  - respiratory or cardiac disease
  - those with suspected or proven hypernatraemia
  - in malnourished children

The Cochrane Library 2006, issue 4
Aliment Pharmacol Ther 2013;37:289-303
How much to give

- **Rapid NG Rehydration**
  - 20ml/kg/hour for 4 hours (NICE:50ml/kg/4hrs)
  - Continue breastfeeding
  - Then reduce 10ml/kg/hour or oral ORS with usual feeds

- **Slow NG rehydration**
  - Usual maintenance feed
  - Rehydrate 50-100ml/kg/12-24hours
  - Always supplement ORS with each loose stool to replace ongoing losses to prevent dehydration
    - 50ml/kg/day or 50-100ml AELS or 10-20ml/kg AELS
Intravenous Fluids

- **Indications**
  - Shock and/or severe dehydration
  - failed oral/enteral therapy
  - avoid in children who are malnourished (unless shocked)

- Ultra-rapid (50ml/kg/hour) vs rapid (50ml/kg/3 hours) vs slow (50-100ml/kg over 24 hours)

- Large-volume (60ml/kg/hour) vs standard volume (20ml/kg/hour) rehydration

- Lack of consistency in evidence, stick to standard therapy 20ml/kg/hr
**Choice of intravenous rehydration fluids**

<table>
<thead>
<tr>
<th></th>
<th>½ Darrows dextrose</th>
<th>Ringers lactate +/- 5% dextrose</th>
<th>Normal saline +/- 5% dextrose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na+</td>
<td>61</td>
<td>130</td>
<td>154</td>
</tr>
<tr>
<td>K+</td>
<td>17</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Cl-</td>
<td>52</td>
<td>109</td>
<td>154</td>
</tr>
<tr>
<td>Lactate</td>
<td>27</td>
<td>28</td>
<td>0</td>
</tr>
<tr>
<td>Glucose</td>
<td>278</td>
<td>0 / 278</td>
<td>0 / 278</td>
</tr>
</tbody>
</table>

- **WHO**: Ringers lactate with/without 5% dextrose
- **SA**: ½ DD “in some countries special IV solutions produced for treatment of dehydration caused by diarrhoea….these are preferred….at least 90 mmol sodium….provide base and potassium similar to ORS….should contain glucose to prevent hypoglycaemia”
- **NICE,(UK) NSW(Australia)**: NS + 5% DW +/- 20mmol/l KCl
Nutritional Management in Diarrhoeal Disease

- Consensus from WHO, ESPGHAN and the AAP:
  - continue breastfeeding at all times
  - continue normal feeds in uncomplicated gastroenteritis within four hours
  - no role for dilution or gradual re-introduction of formula
  - no role for special formulae like soya-based or lactose free

- beverages with high sugar content should not be used
- an extra meal a day for at least a week following an episode of gastroenteritis should also be encouraged to allow catch-up growth

JPGN 2008; 46:S81–S122
BMJ 2007;334:35–40
Aliment Pharmacol Ther 2013;37:289-303
Modifying ORS

- ORS with improved taste
  - Sucralose sweetened more palatable than rice-based ORS
  - No change in resolution dehydration/weight gain — as effective
- ORS with honey
  - ? anti-microbial and anti-inflammatory properties
  - Egyptian study promising
- ORS with glucose polymer: rice/wheat
  - Slow release of glucose advantageous?
  - some advantage in cholera and non-cholera diarrhoea
  - Most studies compared with “old” ORS

Aliment Pharmacol Ther 2013;37:289-303
Other modified formulations of ORS

- No improved efficacy:
  - amylase-resistant starch, guar gum
    - Generates short chain fatty acids in colon which accelerate colonic sodium and fluid absorption
  - ORS with L-isoleucine
    - L-isoleucine enhances secretion antimicrobial peptides in intestinal epithelium
  - ORS with non-digestible carbohydrates, probiotics, zinc and glutamine
    - zinc: shelf life, not completing 10 days
Does medication help?
## Pharmacologic therapy

### (a) Antibiotics

<table>
<thead>
<tr>
<th>Indication for Antibiotics</th>
<th>Antibiotic regimen</th>
</tr>
</thead>
</table>
| **Empiric systemic antibiotics**  
  • Bacterial gastroenteritis with systemic sepsis  
  • Neonates  
  • Ill immunocompromised  
  • Assoc infection e.g. UTI, meningitis | Ampicillin and gentamicin OR Ceftriaxone |
| **Dysentery**  
  • *Shigella*  
  • *Salmonella* spp  
  • *Campylobacter* | • Nalidixic acid or ciprofloxacin or ceftriaxone  
  • Erythromycin or above |
| **Specific Infections**  
  • Amoebiasis  
  • *Giardia lamblia*  
  • *Vibrio cholera* – severe dehydration only  
  • *C. difficile* | • Metronidazole  
  • Metronidazole  
  • Doxycycline (>6 yrs) or fluoroquinolone  
  • Metronidazole or vancomycin |
Pharmacologic therapy

(b) **Zinc**

- Zinc deficiency
  - Impaired electrolyte and water absorption
  - Decreased brush border enzyme activity
  - Impaired cellular and humoral immunity

- Zinc supplementation
  - Reduces *severity & duration* of acute & persistent diarrhoea
  - Reduces *recurrent* episodes

UNICEF and WHO recommend zinc supplementation (10mg below 6 months of age and 20mg in older infants and children for 10–14 days) as a universal treatment for children with diarrhea.

Although there is no major safety issue regarding zinc supplementation, there is also no proven benefit of its use in European children with AGE (III, C). Given the WHO recommendation, zinc should be given to any malnourished child.

Gastroenterol 2006;130:2201–5
Nutrition 2007;23:498–506
JPGN 2008; 46:S81–S122
Aliment Pharmacol Ther 2013;37:289-303
Pharmacologic therapy

(c) Probiotics

- Useful adjunct: pooled data
  - *Lactobacillus GG* and *Saccharomyces boulardii* and *L.reuteri*
  - Reduced diarrhoea duration, stool frequency, persistence
  - Young infants
  - Viral gastroenteritis, early in course
  - Dose $10^{10}$ CFU/day

- Developing world
  - Effectiveness? Bacterial aetiology
  - Safety?

References:
- JPGN 2008; 46:S81–S122
- Nutrition 2007;23:498–506
- Cochrane 2010;issue 11
- Aliment Pharmacol Ther 2013;37:289-303
- Arch Dis Childhood Sept 2015(online)
### Composition of Probiotics:

<table>
<thead>
<tr>
<th>Probiotic</th>
<th>CFU*</th>
</tr>
</thead>
<tbody>
<tr>
<td>L. acidophilus</td>
<td>20b CFU*</td>
</tr>
<tr>
<td>L. rhamnosus GG, LGG®</td>
<td>1b CFU*</td>
</tr>
</tbody>
</table>

* CFU: Colony Forming Units; CFU at the time of manufacture.

### Composition of Electrolytes:

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Amount (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose, anhydrous</td>
<td>3.375 g</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>0.65 g</td>
</tr>
<tr>
<td>Potassium chloride</td>
<td>0.375 g</td>
</tr>
<tr>
<td>Citrate</td>
<td>0.725 g</td>
</tr>
</tbody>
</table>

* Contains artificial colours, sweeteners, and flavours (sucrose, sorbitol, tropical fruit).

**Children 1 year and older:**

Give 30-60 mL reconstituted HydraChoice™ after each bowel action and/or enough to quench thirst. May also be given as smaller amounts more frequently if large amounts are not tolerated.

**Adults:**

Give 75-150 mL reconstituted HydraChoice™ after each bowel action and/or enough to quench thirst. May also be given as smaller amounts more frequently if large amounts are not tolerated.

**Women who are pregnant or breastfeeding should consult a doctor before using this product.**

**Hansen LGG®**

Hansen LGG® is a registered trademark of Valio Ltd.
Pharmacologic therapy
(d) **Vitamin A**

- Reduces all cause mortality
- Prescribe if not given in preceding 6 months

JPGN 2008; 46:S81–S122
Cochrane 2011 Sep 7;9: CD005506
Pharmacologic therapy

(e) Potential agents

(i) Newer anti-emetics e.g. ondansetron ($5-HT_3$ serotonin antagonist)

- Reduced vomiting episodes immediately (not 24hrs) (PO & IV)
- Reduced need IV fluids and admission
- Increased diarrhoea (?toxin retention)
- No difference admission rates and repeat ED visits
- Safety issues: prolonged QT(IV)

Despite some clinical benefits, we suggest that anti-emetics should not be routinely used to treat vomiting during AGE in children (II, B).

Single dose

JPGN 2008; 46:S81–S122
Cochrane 2011 Sep 7;9: CD005506
Evid-Based Child Health 2013: 8;1123-1137
NICE 2014
Pharmacologic therapy

(e) **Potential agents**

(ii) **Smectite**

- Natural hydrated aluminomagnesium silicate (adsorbent)
- Binds to digestive mucous, endo- and exo-toxins, rotavirus
- Increases water and electrolyte absorption, restores barrier properties, modifies activity bile salts and gastric mucous
- India: Reduced duration and prevention prolonged course

*Smectite may be considered in the management of AGE (II, B).*

JPGN 2008; 46:S81–S12
Aliment Pharmacol Ther 2013;37:289-303
Pharmacologic therapy

(e) **Potential agents**

(iii) **Racecadotril** (acetorphan): 1.5mg/kg 8 hourly

- Inhibits intestinal enkephalinase: antisecretory
- Prevents breakdown of endogenous opioids $\rightarrow$ reduced water and electrolyte secretion

Racecadotril may be considered in the management of AGE (II, B).

However, well-designed prospective studies of efficacy and safety should be carried out in outpatient children.

- MA 2011 (9 RCTs, $n=1384$): reduced volume and frequency of stool output, and diarrhoea duration (<2 days)

NEJM 2000;343(7):463-7
JPGN 2008; 46:S81–S122
Acta Paediatrica 2008;97:1008-15
Dig Liver Dis 2011;43:717-13
Pharmacologic therapy
(e) **Potential agents**

- (iv) **Synbiotics**
  - Combinations of prebiotics and probiotics that beneficially affect the host
  - Improve survival and implantation of live microbial dietary supplements
  - Eg probiotics with fructo-oligosaccharides
  - “Promising”

[Aliment Pharmacol Ther 2011;34:862-7]
Pharmacologic therapy

(f) Not recommended

- Antimotility agents eg loperamide
- Older anti-emetics e.g. metoclopramide
- Routine antibiotics
- Prebiotics, glutamine, folic acid, kaolin-pectin, attapulgite, activated charcoal, bismuth

JPGN 2008; 46:S81–S122
BMJ 2007;334:35–40
### Table 2 | Summary of new evidence on the management of acute gastroenteritis in children

<table>
<thead>
<tr>
<th>Category</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral rehydration</td>
<td>Remains central to the management of children with AGE. Efforts to improve the taste and/or efficacy of ORS continue, and some interventions are promising.</td>
</tr>
<tr>
<td>Nasogastric rehydration</td>
<td>While standard (over 24 h) nasogastric rehydration is still being used, new evidence confirms that rapid (over 4 h) nasogastric rehydration is also effective.</td>
</tr>
<tr>
<td>Intravenous rehydration</td>
<td>New evidence is available regarding rapid or ultrarapid and large-volume vs. standard-volume rehydration. As the new evidence is not consistent, until more data are available, the administration of 20 ml/kg is appropriate.</td>
</tr>
<tr>
<td>Antiemetics</td>
<td>Ondansetron reduces the risk of vomiting in young children with AGE, but there is no evidence to support the use of other antiemetics. The FDA recommends electrocardiogram monitoring of the QT interval in patients receiving ondansetron.</td>
</tr>
<tr>
<td>Zinc</td>
<td>Evidence from one study in Europe, where zinc deficiency is rare, confirms no benefit from the use of zinc.</td>
</tr>
<tr>
<td>Racecadotril</td>
<td>Data, mainly from outside of Europe, have reconfirmed that racecadotril may be an effective adjunctive therapy to oral rehydration.</td>
</tr>
<tr>
<td>Smectite</td>
<td>Data, mainly from outside of Europe, have reconfirmed that smectite may be an effective adjunctive therapy to oral rehydration.</td>
</tr>
<tr>
<td>Probiotics</td>
<td>Certain probiotics, such as <em>Lactobacillus GG</em> or <em>S. boulardii</em>, are useful. It is likely that many more probiotics are effective; the current lack of clear evidence of efficacy does not mean that future clinical research will not establish significant health benefits for other probiotics (single or in combination). The same applies to synbiotics.</td>
</tr>
</tbody>
</table>
Figure 1: The Enhanced Diarrhoeal Disease Control (EDDC) framework: an integrated approach to Management of Diarrhoeal Disease.
Rotavirus

- Unaffected by socioeconomic status/sanitation
- Almost all deaths still in developing countries
- 2009: WHO recommended RV vaccination be included in all national EPIs: **progress towards achieving MDG**
- Success Europe: 65-84% reduction hospitalisations from RV*
- **Vaccine:** safe & effective (85%) in middle income countries but concerns in Africa
  - ?Interference maternal antibodies
  - ?Safety and immunogenicity in HIV
  - ?Interference gut microorganisms

*Vaccine Mar 2015:33;2097-2107
Key messages

- Significant burden of disease: morbidity and mortality
  - Nutritional impact
- Improved understand of aetiology: GEMS
- Primary prevention
  - Water, sanitation and hygiene
  - Rotavirus vaccination: ADVOCACY
- Much good evidence not practiced
- Zinc in Africa and Asia
- Some promising new drugs: Ondansetron, smectite
Thank you for your attention