Pathogen Specific Diarrheal Diseases

Review Process, Preliminary Results and Plans for Finalization

Christa Fischer Walker

Johns Hopkins Bloomberg School of Public Health
Department of International Health
Search Objective: published and unpublished literature meeting inclusion/exclusion criteria

Search terms included combinations of:
- “diarrhea”, “morbidity”, “incidence”, “prevalence”, “mortality”, “etiology”, “cause of death”
- Key words and MeSH terms

Databases searched:
- PubMed
- WHO library (WHOLIST)
- SIGLE (System for Information on Grey Literature in Europe)
- CAB Abstracts
Inclusion / Exclusion Criteria
(not comprehensive)

Inclusion:
• Prospective studies conducted in representative populations
• Studies with > 12 mo of surveillance

Exclusion:
• Special populations (travelers, cancer patients, etc), except HIV
• Patients hospitalized for reasons other than diarrhea
• Antibiotic associated diarrhea
• Studies that do not articulate age ( < 5 / ≥ 5 years)
• Case reports of outbreaks
• Recall periods > 2 wks for morbidity
Mortality
MORTALITY: Modeling Goal

- Goal: Calculate diarrhea proportionate mortality for 2008 and 1990 using single cause model for all countries lacking appropriate VR data including:
  - 119 countries lacking all VR data or < 90% coverage of VR data
- Model has been tested for 2008. A similar model will be run for 1990
- Final results have been submitted for publication.
- Results will be available on CHERG website following publication
Selection Process for Mortality

10646 Titles identified for possible inclusion

Titles screened

1871 Abstracts identified

Abstracts screened

443 Full Papers screened

90 Papers Included in Final MORTALITY database
Mortality Model Inputs
90 studies, including 96 Data Points & > 650,000 Deaths
Morbidity
Goal: Calculate diarrhea incidence rates for 2010 and 1990 using age specific incidence data from cohort

Final results have been submitted to the Global Burden of Disease Project and have been submitted for publication

Results will be available on CHERG website following publication
Selection Process for Morbidity Systematic Review

10646 Titles identified for possible inclusion

Titles screened

1871 Abstracts identified

Abstracts screened

443 Full Papers screened

70 Papers Included in Final MORBIDITY database
Children < 5 years: Distribution of Morbidity Studies
Model Inputs
Diarrhea Duration & Severity
Systematic Review

GOAL: Describe the proportion of diarrhea episodes for children under 5 that are mild, moderate, and severe for better understanding of the burden of diarrhea disease

• Literature search for peer-reviewed publications on the duration and/or severity of diarrhea in children and adults

• Pubmed Mesh search terms: diarrhea, gastroenteritis, duration, persistence, severity, infant, child, teenage, adult

• Published from 1990-present in any language

• Reviewed the full papers of unique publications with relevant title/abstract
Diarrhea Duration in Children

- 1,604 unique publications -> 121 relevant titles/abstracts -> 49 included studies

<table>
<thead>
<tr>
<th>Measure of Duration Reported</th>
<th># Studies*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Duration</td>
<td>34</td>
</tr>
<tr>
<td>Median Duration</td>
<td>5</td>
</tr>
<tr>
<td>Proportion Persistent (≥14 days)</td>
<td>18</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study Location by WHO Region</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>6</td>
</tr>
<tr>
<td>Europe</td>
<td>0</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
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<td>Americas</td>
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<td>South East Asia</td>
<td>15</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>2</td>
</tr>
</tbody>
</table>

* Single studies may report multiple measures and/or study locations
Diarrhea Severity

• 3,061 unique publications -> 284 relevant titles/abstracts
• Review of relevant publications currently in progress
• According to preliminary data abstraction, the measures of severity implemented include:
  – Level of dehydration (mild, moderate, severe)
  – Daily frequency of loose stool passage
  – Presence of vomiting & blood and/or mucus in stool
  – 20-point Vesikari scoring system, combining the above indicators and episode duration
Duration and Severity Next Steps

- Final duration and severity results have been submitted for publication and will be available on the CHERG website after publication
Etiology
15,881 potential relevant citations in electronic search

15,203 references excluded

678 articles for further evaluation
+ 94 from hand search
TOTAL = 772

548 articles excluded

69 articles excluded as inpatient/outpatient

155 articles from which 205 studies selected (115 inpatients + 46 outpatients + 44 community)

Under triple review
ETIOLOGY: Model Inputs
Goal: Estimate median prevalence proportion for each pathogen for all children 0-59 mo by type of study (outpatient, inpatient, and community).

Age adjustments: Studies that do not directly report prevalence by pathogen for all ages 0-59 mo

- Step 1: Calculate age group conversion factors using all studies that report both prevalence for all 0-59 and smaller age groups. The conversion factor for age group $X$ is calculated as the median of $\text{prev}_{0.59}/\text{prev}_X$
- Step 2: Proportion reported for each age group given in the study is converted to a full 0-59 mo estimate
Median pathogen prevalence = median of age - converted rates by study population (in-, out-patient, and community)

Uncertainty estimates:
• Bootstrap confidence intervals are calculated for those estimates based on a minimum of 3 studies.
• ‘Pseudo-datasets’ created by sampling studies with replacement from the real dataset. Each of the 1000 pseudo-datasets is used in the estimation procedure described above to generate a corresponding 1000 prevalence proportions. The 2.5th and 97.5th percentile of these proportions give the 95% CI.
Moving Forward

- Final results have been submitted for publication and will be available on the CHERG website after publication