Ebola and Emerging Infectious Diseases- how do we include children in research during times of crisis?

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Emerging infectious diseases in children
Children in the West African Ebola epidemic

- Approximately 20% of cases children under 16 years
  - ≈4600 cases

- Mortality rates
  - Neonates >99%
  - Age <1 year approx 89%
  - Age <5 years approx 79%
  - Age 5-9 years approx 60-67%
  - Age 10-15 years approx 52%

- Disease process
  - More rapid progression with subtler symptoms in younger children
  - Milder in teenagers
Ebola’s legacy for the children of West Africa

22,858 children have lost at least one parent
5714 have lost both parents

1368 child survivors of Ebola
  Some have gone blind
  Some have severe neurodisability
  Some have had further invasive infections

Based on estimates of incidence this means <30% of children survived, estimated actual survival should have been 34.5% – have some died since surviving?

?School access
?Food security
?Child labour

?How many
Other emerging infectious diseases in children
Zika virus

Countries that have past or current evidence of Zika virus transmission (as of January 2016)

www.cdc.gov

Figure 1. Notified cases of microcephaly in Brazil, 2010–2015

As of 17 November 2015

Figure 3. States of Brazil with reported confirmed autochthonous cases of ZIKV virus infection 2014–2015, and reported cases of microcephaly in 2015, as of 17 November 2015.
Dengue virus

Distribution of DENV-1 virus by decade. Messina et al. 2014

Distribution of DENV-2 virus by decade. Messina et al. 2014
Crimean Congo Haemorrhagic Fever

Geographic distribution of Crimean-Congo Haemorrhagic Fever

50° North latitude: Limit for geographic distribution of genus Hyalomma ticks

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS) World Health Organization

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Predicted geographic distribution of Lassa Fever

http://i.imgur.com/Bf52sv.jpg
# Pandemic Flu

## Known Influenza Pandemics

<table>
<thead>
<tr>
<th>Name of pandemic</th>
<th>Date</th>
<th>Deaths</th>
<th>Case fatality rate</th>
<th>Subtype involved</th>
<th>Pandemic Severity Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>1889–1890 flu pandemic (Asiatic or Russian Flu)</td>
<td>1889–1890</td>
<td>1 million</td>
<td>0.15%</td>
<td>possibly H3N8 or H2N2</td>
<td>N/A</td>
</tr>
<tr>
<td>1918 flu pandemic (Spanish flu)</td>
<td>1918–1920</td>
<td>20 to 100 million</td>
<td>2%</td>
<td>H1N1</td>
<td>5</td>
</tr>
<tr>
<td>Asian Flu</td>
<td>1957–1958</td>
<td>1 to 1.5 million</td>
<td>0.13%</td>
<td>H2N2</td>
<td>2</td>
</tr>
<tr>
<td>Hong Kong Flu</td>
<td>1968–1969</td>
<td>0.75 to 1 million</td>
<td>&lt;0.1%</td>
<td>H3N2</td>
<td>2</td>
</tr>
<tr>
<td>Russian flu</td>
<td>1977–1978</td>
<td>N/A</td>
<td>N/A</td>
<td>H1N1</td>
<td>N/A</td>
</tr>
<tr>
<td>2009 flu pandemic (worldwide)</td>
<td>2009–2010</td>
<td>18,000 to 284,500</td>
<td>0.03%</td>
<td>H1N1/09</td>
<td>N/A</td>
</tr>
<tr>
<td>Annual flu virus deaths (USA only)</td>
<td>1976-77 to 2006-07</td>
<td>3,000 to 46,000</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

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**Annual flu virus deaths (USA only)**

- 1976-77 to 2006-07: 3,000 to 46,000

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**Status as of 13 August 2009**

Countries, territories and areas with lab confirmed cases and number of deaths as reported to WHO.
Learning from Ebola – research in epidemics

- Rapid approval of clinical trials
  - But not quick enough
- Generally unprepared
- Inadequate standardised protocols in place
- No methods for rapid ethical approval on an international level
- No agreed standards for clinical trials in such settings
- Too many parties/poor collaboration
- No official oversight body
- Where were the basic trials of simple benefits of intravenous fluid management?
- **Clinical care must take priority but without losing benefits of clinical trials and interventions**
Clinical trials for Ebola

- **Favipiravir**
  - Age >1 year
  - Pregnant women excluded – potentially teratogenic

- **Brincidofovir**
  - 2 months-75 years
  - Withdrawn (?pregnancy – unclear)

- **Convalescent plasma (Liberia)**
  - Liberia - 18 years and older, not pregnant women
    - But WHO guidance for use in children under compassionate care
  - Sierra Leone & Guinea - children & pregnant women included
Clinical trials for Ebola

- **TKM Ebola**
  - Withdrawn, no benefit
  - ?Children/pregnant women excluded

- **ZMAPP**
  - All ages included
  - Pregnant women included
  - BUT seemingly not administered to young infants and pregnant women ?circumstantial
Vaccine trials for Ebola

- **VSV-EBOV ring vaccination trial**
  - Adults over 18
  - Children & pregnant women excluded even though potential contacts

- **cAd3-EBO Z vaccine (phase 2)**
  - Children originally excluded, GSK now including

- **Ad26-ZEBOV vaccine (phase 1 & 2)**
  - Children and HIV positive patients included

- **HPIV3-EbovZ GP (phase 1 & 2)**
  - Children excluded due to need for isolation (live attenuated vaccine)
How do we incorporate children in research in epidemic settings?

- We need to consider children a priority
  - Medicines for Children Research Network
  - Is it ethical? Is it ethical not to when they have the highest mortality?

- Standardised protocols and internationally agreed ethical standards

- Unaccompanied minors
  - Consent
  - Management
  - Follow up
Thank you

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West African health care workers, patients & survivors