Learning at the Bedside to Inform Clinical Research in Outbreaks

Translating Anecdote to Evidence

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Key Messages

• Clinical information needed for clinical trials and outbreak response is routinely collected at the bedside but RARELY shared

• We won’t be prepared for tomorrow if we don’t do the work TODAY
  • Pandemic preparedness must be integrated into daily clinical care
  • Streamline regulatory processes
  • Leverage existing data platforms to tell us WHO is infected and WHAT happens
  • Learn the rules of the disease (pathogen/immune response kinetics)

• Pandemics are global problems – data, like diagnostics, vaccines, and therapeutics must be shared rapidly and widely
Patients tell us what we need to know…

WHO, WHAT, WHEN

The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) — China, 2020

The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team

Zou, L NEJM 2020

LONG-HAULERS ARE REDEFINING COVID-19

Without understanding the lingering illness that some patients experience, we can't understand the pandemic.

SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients

This is an official CDC HEALTH ADVISORY

COVID-19 Rebound After Paxlovid Treatment

Distributed via the CDC Health Alert Network
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Zou, L NEJM 2020
What are the Barriers to Transforming this Information into Action?

Clinical presentation → Case definition
Demographics → RF for severe disease/death
Natural history → Clinical complications
Clinical excess of lab samples → kinetics/pathogen-specific endpoints
Ebola Epidemic Timeline

INTEGRATING CLINICAL RESEARCH INTO EPIDEMIC RESPONSE

THE EBOLA EXPERIENCE

6 Major Capacity Challenges

1. Lack of clinical experience with Ebola
2. Poor surveillance/laboratory capacity
3. Deficiency of healthcare infrastructure and HCWs
4. Limited research experience
5. Under supported ethics review boards
6. Delays in legal/bureaucratic steps
**Problem 1:** Sustainable health systems including research capacity
→ Diagnostics, Data collection systems, and better supportive care
→ Leverage existing clinical databases to provide high level information (Who, What)
→ Smaller more granular studies of pathogen kinetics and immune responses (When)

**Problem 2:** Regulatory pathways
→ Memoranda of understanding
→ Facilitate rapid ethics review in a public health emergency
→ Provide resources to support local data collection/analysis/sharing (public health agencies)

**Problem 3:** Data sharing - ACCESS
→ Public health dashboards (UKHSA, WHO, CDC)
→ Pre-print/GISAID

**Problem 4:** We have to create systems that allow us to learn what we don’t know
→ Learn the WHO, WHAT, WHEN + rules of the virus
→ “Outbreak response must evolve from crisis response to integrated cycles of preparation, response and recovery*”

*Bedford, J et al. Nature 2019*
Coordination – Gov’t/Academic Partnership

**UK Health Security Agency**

**Confirmed cases in England by specimen data**

<table>
<thead>
<tr>
<th>Metric</th>
<th>Count</th>
<th>Denominator (excluding cases with missing responses)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gay, bisexual, or men who have sex with men</td>
<td>857</td>
<td>886</td>
<td>96.7%</td>
</tr>
<tr>
<td>History of STI in the last year</td>
<td>481</td>
<td>899</td>
<td>53.5%</td>
</tr>
<tr>
<td>4 to 9 sexual partners in the last 3 months</td>
<td>312</td>
<td>904</td>
<td>34.5%</td>
</tr>
<tr>
<td>10+ sexual partners in last 3 months</td>
<td>267</td>
<td>904</td>
<td>29.5%</td>
</tr>
<tr>
<td>Living with HIV</td>
<td>228</td>
<td>867</td>
<td>26.3%</td>
</tr>
<tr>
<td>Ever used PrEP (among HIV negative)</td>
<td>490</td>
<td>624</td>
<td>78.5%</td>
</tr>
</tbody>
</table>

What are We Willing to Spend?

Systems  Staff  Stuff

The economic impact of epidemics

Ebola 2014-16: $2.2bn  ZIka 2016: $3.5bn  SARS 2003: $40bn

The COVID-19 Pandemic and the $16 Trillion Virus

David M. Cutler, PhD; Lawrence H. Summers, PhD

Author Affiliations  Article Information

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