The State of Infectious Diseases Clinical Trials: A Systematic Analysis of ClinicalTrials.gov

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Background

Clinical trials provide information about infection prevention, diagnosis, prognosis, and treatment. However, many questions uniquely ID specialists are not addressed by evidence-based medicine:

- 15% of recommendations contained in the Infectious Diseases Society of America (IDSA) practice guidelines are based solely upon expert opinion
- 23% of these recommendations are based on evidence from randomized controlled trials (RCTs)

The current spectrum of ID clinical trials has largely gone without systematic scrutiny regarding patterns of topical focus, geographical distributions, and levels of industry involvement. ClinicalTrials.gov, a registry of over 180,000 trials from 174 countries, provides a unique opportunity to take a "snapshot" of ID clinical trials.

Timeline of Clinical Trials.gov:

- 1997: FDA Modernization Act (FDAMA) of 1997 transferred oversight of the ClinicalTrials.gov registry
- 2001: International Conference of Medical Journal Editors’ (ICMEC) established policy to require public registration of phase III trials (as ClinicalTrials.gov or similar registry)
- 2007: FDA Amendments Act (FDAAA) created a legal requirement for the registration of all phase III trials, and derivatives with ClinicalTrials.gov

About Clinical Trials Transformation Initiative (CTTI):

- Initiated in Nov 2007 as a public-private partnership funded by FDA and Duke University and comprises >60 organizations across the clinical trials enterprise.
- Mission: Identify practices that through broad adoption will increase the quality and efficiency of clinical trials.
- To improve visibility of ClinicalTrials.gov, CTTI had two relational databases, the Aggregate Analysis of Clinical Trials (AACT), and regrouped studies by national library of medicine (NLM) algorithm.

Further Subcategorization and other Definitions

- ID trials were subcategorized based on study type and description. World Health Organization (WHO) cause-of-death categories were used when possible.
- WHO Global Burden of Disease team used to calculate the % of ID-related mortality and disability-adjusted life years (DALYs)
- Probable funding source algorithms

Industry-funded: lead sponsor from industry or collaboration from industry with NIH without NIH involvement
- NIH-funded: NIH either lead sponsor or collaborator and not the lead sponsor
- Descriptive statistical analysis was performed using SAS version 9.2 (Duke Institute, Cary, NC)

Methods

ClinicalTrials.gov through a systematic analysis of clinical trials, the Infectious Diseases Society of America (IDSA) practice guidelines are based solely upon expert opinion, 23% of these recommendations are based on evidence from randomized controlled trials (RCTs)

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Results

Table 1: Characteristics of ID Trials

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease type</td>
<td>Infectious Diseases</td>
</tr>
<tr>
<td>Study type</td>
<td>Treatment</td>
</tr>
<tr>
<td>Study size</td>
<td>Median enrollment size of 125 (IQR 44-400) subjects vs. 60 (IQR 18-193)</td>
</tr>
<tr>
<td>Industry</td>
<td>73.2% funded</td>
</tr>
<tr>
<td>HIV/AIDS trials</td>
<td>33.8%</td>
</tr>
<tr>
<td>Study phase</td>
<td>60% phase III</td>
</tr>
<tr>
<td>Treatment</td>
<td>80% of treatments are biologics, and devices</td>
</tr>
<tr>
<td>Funding source</td>
<td>10% Industry funded, 90% Other</td>
</tr>
</tbody>
</table>

Figure 1: 10 Characteristics of ID Trials

Figure 2: 10 characteristics compared to mortality and DALYs

Conclusions

- ID trials are well represented in the overall clinical trials enterprise, but tend to be larger than non-ID trials; and are less likely to be funded by NIH outside of the U.S.
- There are discrepancies between the number and quality of clinical trials in some disease states compared to the burden of disease.
- This "snapshot" of ID clinical trials should prompt examination of how best to prioritize and coordinate future clinical research efforts.

References


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Disclosures

None of the authors has any conflicts of interest to declare.