Contemporary Clinical Research in Adult Cardiovascular Medicine: A Perspective from ClinicalTrials.gov

Society for Clinical Trials
33rd Annual Meeting

Associate Professor of Medicine
Duke University Medical Center / Duke Clinical Research Institute
Disclosures

- Financial support for this work was provided by grant U19FD003800 from the U.S. Food and Drug Administration awarded to Duke University for the Clinical Trials Transformation Initiative.

- Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organizations listed below:
  Abbott Vascular, Allmed Healthcare, American College of Cardiology Foundation, Eli Lilly, FDA, IBM, Irvine Scientific, Medtronic, Sanofi-Aventis, Terumo Corp.
- A public private partnership co-founded by FDA and Duke in late 2007
- All stakeholders involved
- Through a memorandum of understanding with FDA, Duke “hosts” the initiative
- Website: www.ctti-clinicaltrials.org

Mission: To identify practices that through broad adoption will increase the quality and efficiency of clinical trials
## ClinicalTrials.gov History

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nov 21, 1997</td>
<td>Food and Drug Modernization Act of 1997 (FDAMA) section 113 enacted</td>
<td>Mandated the creation of the clinicaltrials.gov registry for efficacy trials in serious and life-threatening conditions and interventions regulated by the FDA</td>
</tr>
<tr>
<td>Feb 29, 2000</td>
<td></td>
<td>First version ClinicalTrials.gov publicly available</td>
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<tr>
<td>September 2004</td>
<td>International Committee of Medical Journal Editors’ (ICMJE) policy</td>
<td>Required studies published in their journals be registered in Clinicaltrials.gov or other equivalent publicly available registries.</td>
</tr>
<tr>
<td></td>
<td>established</td>
<td></td>
</tr>
<tr>
<td>September 27, 2007</td>
<td>US Public Law 110-85 FDA Amendments Act (FDAAA) section 801 enacted</td>
<td>Created a legal requirement for the registration of trials of drugs, biologics, and devices,</td>
</tr>
<tr>
<td>September 23, 2008</td>
<td></td>
<td>Results reporting launched</td>
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<tr>
<td>September 28, 2009</td>
<td></td>
<td>Adverse Event reporting launched</td>
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Aggregate Analysis of ClinicalTrials.gov (AACT)

Developing Clinical Specialty Datasets

Assigning Studies to a Specialty

Study selection

- 40,970 “interventional” trials registered Oct 2007 to Sep 2010
- 3,502 potential CV studies using annotated terms
  - 3012 with CV clinical condition
  - 2344 studies
  - 53 studies of subjects <= 18 years
- 37,467 pertained to other medical specialties
- 490 studies without CV clinical condition
  - 199 studies with CV MeSH
  - 165 studies in non-CV populations
  - 668 studies of venous and pulmonary embolic disease, general risk factors in patients without CV disease, and non-CV populations or conditions
- 2325 studies for analysis
- 34 studies
Study Start Year, Primary Completion Year

Ongoing and Completed Studies (N=2,233)
Study Design Characteristics

- **DMC**: Yes | No
- **Oversight**: FDA | Non-FDA
- **Oversight**: US | Non-US
- **Randomized**: Yes | No
- **Masking**: Open | Single | Double
- **# Arms**: 1 | 2 | 3 | 4+
- **Model**: Single | Parallel | X

0% | 20% | 40% | 60% | 80% | 100%
Clinical Phase (n=2325)

- Not Listed: 113, 5%
- Phase 0 or 1: 802, 33%
- Phase 2: 470, 19%
- Phase 3: 444, 18%
- Phase 4: 596, 25%
Actual Enrollment

- Overall
  - < 50: 35.2%
  - 51-100: 19.6%
  - 101-500: 32.7%
  - 501-1000: 6.3%
  - >1000: 6.3%

- Phase 4
  - < 50: 29.4%
  - 51-100: 22.2%
  - 101-500: 33.3%
  - 501-1000: 6.3%
  - >1000: 4.8%

- Phase 3
  - < 50: 28.4%
  - 51-100: 13.6%
  - 101-500: 37.5%
  - 501-1000: 14.8%
  - >1000: 3.4%

- Phase 0,1,2
  - < 50: 52.9%
  - 51-100: 17.6%
  - 101-500: 24.5%
  - 501-1000: 2.9%

- Other
  - < 50: 28.6%
  - 51-100: 22.4%
  - 101-500: 36.6%
  - 501-1000: 4.3%
  - >1000: 3.7%
Anticipated Enrollment

Overall

- < 50: 25.8%
- 51-100: 20.5%
- 101-500: 37.6%
- 501-1000: 6.8%
- >1000: 9.4%

Phase 4

- < 50: 16.8%
- 51-100: 20.6%
- 101-500: 42%
- 501-1000: 8.1%
- >1000: 12.5%

Phase 3

- < 50: 12.5%
- 51-100: 16.8%
- 101-500: 44.9%
- 501-1000: 9.1%
- >1000: 16.8%

Phase 0,1,2

- < 50: 47.1%
- 51-100: 21.8%
- 101-500: 25.3%
- 501-1000: 3.2%
- >1000: 3.4%

Other

- < 50: 27%
- 51-100: 21.8%
- 101-500: 37%
- 501-1000: 6.4%
- >1000: 3.4%
Primary Outcomes for Completed Studies (n=511)

<table>
<thead>
<tr>
<th>Category</th>
<th>Clinical Event</th>
<th>Biomarker</th>
<th>Quality of Life</th>
<th>Economic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (n=511)</td>
<td>157</td>
<td>355</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 4 (n=147)</td>
<td>38</td>
<td>101</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 3 (n=81)</td>
<td>24</td>
<td>60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 0,1,2 (n=133)</td>
<td>45</td>
<td>97</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (n=150)</td>
<td>50</td>
<td>97</td>
<td></td>
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</tbody>
</table>
Intervention Type (n=2325 studies)

- Drug: 913, 39%
- Device, Procedure or Radiation: 1036, 45%
- Biological or Genetic: 119, 5%
- Dietary Supplement/Behavioral: 188, 8%
- Other: 69, 3%

Duke Clinical Research Institute
Specialty Subtype
(n=2325 studies)

- CAD/IHD: 987, 42%
- HF/CM: 502, 22%
- EP: 304, 13%
- Surgery: 176, 8%
- Congenital: 27, 1%
- Peripheral: 129, 5%
- Other: 200, 9%
**Intervention Type by Subspecialty**

- **Drug**
- **Biological or Genetic**
- **Device, Procedure or Radiation**
- **Dietary Supplement/Behavioral**
- **Other**

### Categories

- **CAD/IHD**
  - Drug: 492
  - Biological or Genetic: 20
  - Device, Procedure or Radiation: 178
  - Dietary Supplement/Behavioral: 114
  - Other: 351

- **HF/CM**
  - Drug: 220
  - Biological or Genetic: 21
  - Device, Procedure or Radiation: 160
  - Dietary Supplement/Behavioral: 11
  - Other: 178

- **EP**
  - Drug: 114
  - Biological or Genetic: 11
  - Device, Procedure or Radiation: 80
  - Dietary Supplement/Behavioral: 8
  - Other: 11

- **Surgery**
  - Drug: 83
  - Biological or Genetic: 11
  - Device, Procedure or Radiation: 15
  - Dietary Supplement/Behavioral: 27
  - Other: 60

- **Congenital**
  - Drug: 39
  - Biological or Genetic: 5
  - Device, Procedure or Radiation: 13
  - Dietary Supplement/Behavioral: 8
  - Other: 88

- **Peripheral**
  - Drug: 15
  - Biological or Genetic: 5
  - Device, Procedure or Radiation: 8
  - Dietary Supplement/Behavioral: 39
  - Other: 60

- **Other**
  - Drug: 15
  - Biological or Genetic: 5
  - Device, Procedure or Radiation: 13
  - Dietary Supplement/Behavioral: 8
  - Other: 88
Summary

- Cardiovascular medicine is widely regarded as a vanguard for evidence-based drug and technology development.
- Prevalent diseases do not automatically translate into large, controlled trials of clinical endpoints.
- There exists substantial heterogeneity in study design and sponsorship.
- Registration in clinicaltrials.gov, while an important step forward, provides little assurance of study quality or scientific validity.
- A preponderance of small trials represents an opportunity to encourage collaboration and foster research networks.