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>
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</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>
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<tr>
<td>Feb 29, 2000</td>
<td></td>
<td>First version ClinicalTrials.gov publicly available</td>
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<td>September 2004</td>
<td>International Committee of Medical Journal Editors’ (ICMJE) policy established</td>
<td>Required studies published in their journals be registered in Clinicaltrials.gov or other equivalent publicly available registries.</td>
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<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>
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<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

For study NCT00zzzzzz

- Do any condition_browse or condition terms have a Y tag for Specialty X?
  - Y: Assign Y for Specialty X (GROUP 1)
    - Review study details, if desired
    - Exclude unrelated studies
    - Final subset for Specialty X manuscript.
  - N: Do any condition_browse or condition terms have ambiguous tags for Specialty X?
    - Y: Possibly assign to Specialty X (GROUP 2)
      - Review study details, if desired
      - Include related studies
    - N: Do all condition_browse terms and do all condition terms have a N tag for Specialty X?
      - Y: Assign N for Specialty X (GROUP 3)
        - Review study details, if desired
        - Include related studies
      - N: Possibly assign N for Specialty X (GROUP 4)
    - Y: Do any condition_browse terms or do any condition terms have a N tag for Specialty X?
      - N: Unclassified for Specialty X (GROUP 5)

40,970 “interventional” trials registered Oct 2007 to Sep 2010

3,502 potential CV studies using annotated terms

3012 with CV clinical condition

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

2344 studies

34 studies

53 studies of subjects <= 18 years

2325 studies for analysis
Study Start Year, Primary Completion Year

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

- **DMC**: Yes - No
- **Oversight**:
  - FDA - Non-FDA
  - US - Non-US
- **Randomized**: Yes - No
- **Masking**:
  - Open
  - Single - Double
- **# Arms**:
  - 1
  - 2
  - 3
  - 4+ (4+ not shown)
- **Model**:
  - Single - Parallel
  - X (X not shown)
Clinical Phase (n=2325)

- 802, 33%: Phase 0 or 1
- 113, 5%: Phase 2
- 470, 19%: Phase 3
- 596, 25%: Phase 4
- 444, 18%: Not Listed
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**: 25.8% < 50, 20.5% 51-100, 37.6% 101-500, 6.8% 501-1000, 9.4% >1000
- **Phase 4**: 16.8% < 50, 20.6% 51-100, 42% 101-500, 8.1% 501-1000, 12.5% >1000
- **Phase 3**: 12.5% < 50, 16.8% 51-100, 44.9% 101-500, 9.1% 501-1000, 16.8% >1000
- **Phase 0,1,2**: 47.1% < 50, 21.8% 51-100, 25.3% 101-500, 3.2% 501-1000, 3.4% >1000
- **Other**: 27% < 50, 21.8% 51-100, 37% 101-500, 6.4% 501-1000, 3.4% >1000

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Primary Outcomes for Completed Studies (n=511)

- **Clinical Event**: 157 (Overall), 38 (Phase 4), 24 (Phase 3), 45 (Phase 0,1,2), 50 (Other)
- **Biomarker**: 355 (Overall), 101 (Phase 4), 60 (Phase 3), 97 (Phase 0,1,2), 97 (Other)
- **Quality of Life**: Other (n=150)
- **Economic**: Other (n=150)
Intervention Type (n=2325 studies)

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

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Specialty Subtype  
(n=2325 studies)
Intervention Type by Subspecialty

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

CAD/IHD
- Drug: 492
- HF/CM: 220
- EP: 114
- Surgery: 80
- Congenital: 15
- Peripheral: 27
- Other: 88

HF/CM
- Drug: 351
- HF/CM: 178
- EP: 160
- Surgery: 70
- Congenital: 11
- Peripheral: 83
- Other: 60

EP
- Drug: 11
- HF/CM: 45
- EP: 11
- Surgery: 8
- Congenital: 1
- Peripheral: 5
- Other: 13

Surgery
- Drug: 8
- HF/CM: 20
- EP: 11
- Surgery: 79
- Congenital: 1
- Peripheral: 5
- Other: 39

Congenital
- Drug: 1
- HF/CM: 13
- EP: 11
- Surgery: 1
- Congenital: 5
- Peripheral: 27
- Other: 88

Peripheral
- Drug: 15
- HF/CM: 83
- EP: 1
- Surgery: 1
- Congenital: 5
- Peripheral: 27
- Other: 88

Other
- Drug: 79
- HF/CM: 45
- EP: 11
- Surgery: 8
- Congenital: 1
- Peripheral: 5
- Other: 39
Lead Collaborator/Sponsor by Subspecialty

- **Gov't US**
  - CAD/IHD: 265
  - HF/CM: 107
  - EP: 59
  - Surgery: 50
  - Congenital: 7
  - Peripheral: 25
  - Other: 51

- **Gov't OUS**
  - CAD/IHD: 264
  - HF/CM: 170
  - EP: 124
  - Surgery: 57
  - Congenital: 7
  - Peripheral: 60
  - Other: 63

- **Industry**
  - CAD/IHD: 265
  - HF/CM: 92
  - EP: 70
  - Surgery: 37
  - Congenital: 6
  - Peripheral: 20
  - Other: 40

- **Academic US**
  - CAD/IHD: 138
  - HF/CM: 95
  - EP: 39
  - Surgery: 24
  - Congenital: 7
  - Peripheral: 18
  - Other: 39

- **Academic OUS**
  - CAD/IHD: 170
  - HF/CM: 124
  - EP: 57
  - Surgery: 7
  - Congenital: 6
  - Peripheral: 20
  - Other: 40

**Subspecialties**
- CAD/IHD
- HF/CM
- EP
- Surgery
- Congenital
- Peripheral
- Other

**Organizations**
- Gov't US
- Gov't OUS
- Industry
- Academic US
- Academic OUS
- Institute / Foundation
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.