Clinical Research – State of the Art
A View as a Clinical Trialist, Registry Researcher, Educator, Physician

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Our Goals as Physicians

• Improve patient care
  – Find effective and safe new treatments (drugs, devices and strategies)
  – Apply proven therapies to all appropriate Patients

• Improve cost-effectiveness
  – Don’t use therapies when unnecessary
Clinical Research Types

**Clinical trials**
- Provide evidence
- Initial dose finding, then outcomes trials
- Currently—many are Pharma sponsored for new drugs, Some treatment strategies
- High quality data
- Expensive

**Registries**
- Evaluate practice
- Various sponsors: Pharma, academic, Health plan data
- Good quality data
- Less expensive
- NOT randomized → confounding!
What Changes Clinical Care?

• Randomized trials
  – Identify treatments and change guidelines
  – Identify dosing, clinical efficacy, safety,

• Traditional registration pathway trials
  – Large amounts data, great detail on everything.
  – Generally more limited population
  – VERY Expensive – (amount AE data, monitoring)

• Large simple trials -
  – Better estimate of effect on outcomes, broader populations less detail, lower cost
Registries - Large Databases

Issues

- Comparing treatments - Supposedly evaluate “effectiveness” – BUT confounding clouds comparison of Rx
- Incorrect assessment of “benefit” of
  - Hormone Repl. Therapy, Vitamin E, Folate,
  - And incorrect “harm” DES, PPI + Clopidogrel

- Strengths:
  - Identify current practice – gaps in care
  - Can serve as Quality Improvement tools
  - Could be used as data collection method for simple randomized trials
TIMI TRIALS
1984-2009

50 ACS Trials (45 completed)

ACS

STEMI n=25

PCI n=4

NSTEMI/UA n=22

More Than:

• ~200,000 Pts enrolled to date
• 4000 Hospitals worldwide
• 8000 Investigators worldwide
• 52 Countries
• 6 Continents

TIMI BIBLIOGRAPHY- 450 PUBLICATIONS IN PEER REVIEWED JOURNALS
PROJECT ORGANIZATION OF MAJOR COMPONENTS

STEERING:
- Scientific Design
- Primary/Secondary Goals

OPERATIONS: Project Management
(Sponsor/TIMI/CRO Group)

Clinical Sites
- Site Management – North America
- Site Identification – Worldwide – NLI
- Training
- Enrollment
- Medical Hotline
- SAEs
- Protocol Questions
- Manual of Operations

CEC
- Angiography
- ECG
- Hematology Biomarkers
- Holter
- Echocardiograph
- MRI

Core Labs

Randomization/Drug
- CRF Flow
- Analyses

Database
- CRO

Monitoring
- Publications

Independent Statistical Group

Data Safety Board

Study Chairman
What is the National Cardiovascular Data Registry?

- Suite of Hospital and Office-Based Quality Improvement Programs
  - measure and quantify outcomes
  - Identify gaps in the delivery of quality cardiovascular patient care

- Our Mission is to:
  - improve patient care
  - Provide knowledge and tools
  - Implement quality initiatives
  - Support research
NCDR at a Glance Today...

Registries
- CathPCI
- ICD
- CARE
- ACTION- GWTG

Registry Studies
- SPECT MPI
- CCTA
- ICD Longitudinal

Analytic Reporting Services
- United
- BCBSA
- WellPoint
- CMS

- PA
- MI
- WV
- HCA
- MA
- Tenet

Research & Publication Services
- Analytic Centers
- Yale – MAHI – DCRI
- Open to all

Quality Improvement
- QI Tools
- Phone Consultation
- Benchmark Reports
- Training and Orientation
## Participants and Patient Records

<table>
<thead>
<tr>
<th>Name</th>
<th># of Participants</th>
<th># of Patient Records</th>
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<td>1100</td>
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CRUSADE Excessive Dosing of Acute Medications by Age


% Excessive Dose

< 65 yrs | 65-75 yrs | >75 yrs

LMW Heparin: 12.5, 12.5, 16.5
UF Heparin: 28.7, 37, 38.5
GP IIb-IIIa: 8.5, 33.1, 64.5
CRUSADE Cumulative Impact of Dosing Errors: Combined Use of Heparin (UFH/LMWH) and GP IIb-IIIa


% RBC Transfusions

- Both Right: 4.1%
- 1 Excessive: 9%
- Both Excessive: 18.5%

Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER

Personalized And Targeted QI

Registry SITES

STANDARD QI FEEDBACK

Individualized GAP Analysis

Top 3 Quality or Safety Targets

Targeted Data Reports

Educational Modules and QI Tools

EVALUATION

• Composite Metrics of Quality and Safety
• Benchmarks Achieved
• Surveys assessing implementation and usability
Evaluation of a new Drug

We want:
- Clinical outcomes (Death, MI, stroke)
- Safety assessment
- Broad populations

Current FDA pathway for DM drugs:
- Show efficacy on glycemic control
- Demonstrate no CV harm (upper CI of Hazard ratio 1.8 at approval, later 1.3)
- Need about 500 events; Trials now 5000-8000 Pts
- BUT – underpowered for seeing CV benefit
Proposal for CV Research 2010+

- **Focus on Randomized trials** -
  - Keep traditional trials, but simplify
  - Create new type – large simple (registration) trials
- **Traditional trials**
  - Initial assessment of efficacy and safety: approval
  - Focus detailed safety on a “safety” cohort - ~5000 patients with detailed bloods, AE’s etc
- **New trials – large simple trials** (drugs, devices, strategies)
  - Get CV outcomes in larger cohort – w/ simpler data
  - Use registries to do simple, ongoing data collection
- **Registries** – 1) Assess Quality of care  2) Do QI programs
  Help apply therapies where beneficial and avoid over utilization