

Clinical Research Networks: A Discussion



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Outline

- CRNs
- DTN
- Discussion

CRN Overview

Single Site Research

- CI time burden (admin, contracts, QA, data management, etc)
- Staff development and turnover
- Inefficient
- QC rare
- Prolonged study durations
- Limited authorship options
- Limited scientific opportunities

What is a CRN?

- WHO: Clinical, Research, and Administrative professionals
- WHAT: Design, conduct, analyze, and publish high impact studies
- HOW: Pre-established fiscal, legal, administrative, and management agreements and SOPs
- HOW: Contentious issues resolved (e.g. IP, authorship, data ownership, etc.)
- HOW: Procedural and regulatory integrity

CRN Benefits

- Reduced investigator burden
- Increased impact and number of research pubs
- Scientific career advancements (primary/secondary analyses, ancillary studies)
- Time and cost efficient
- Shortened study periods
- Unique scientific opportunities (e.g. biomarker studies) in informative samples
- Conduct cost efficient NMRC/BMRC multi site studies
- Attract commercial business

CRN Challenges

- Governance
- Regulatory Adherence
- PI Roles
- Unit Pricing in Country
- Authorship
- Intellectual Property
- Liability
- Clinical Management
- Quality Control
- Contract Issues
- Business Management
- Payments to Site PIs
- Data Capture
- Data Management
- Data Analysis
- Data Ownership
- Between Study Support

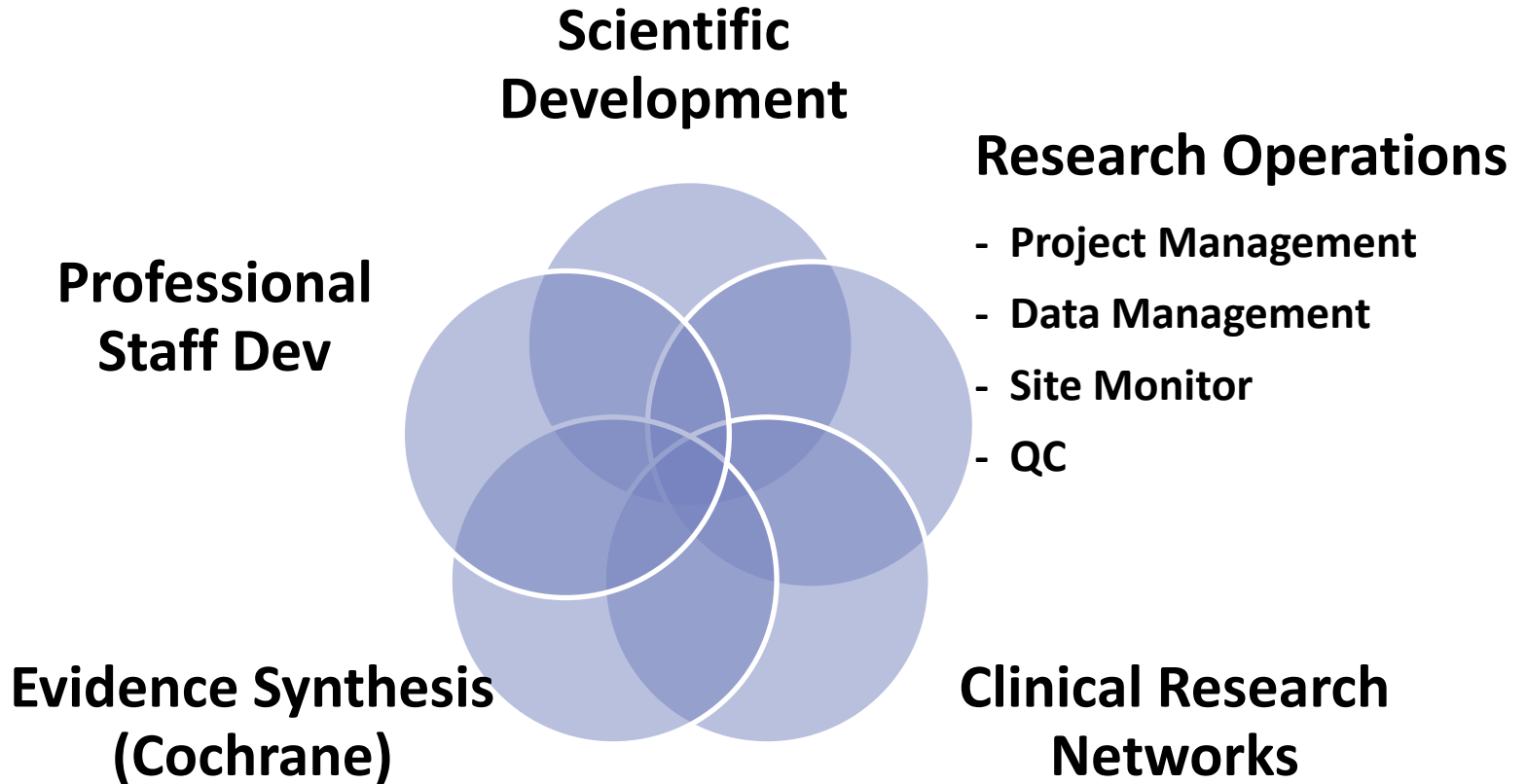
CRN Inducements

- Network Management
- Study Management
- Data Management
- Site Monitoring
- Regulatory QC
- Commercial Draw
- Study Design
- CRF Design
- Investigator Studies
- **Primary Analyses**
- **Secondary Analyses**
- **Ancillary Studies**
- **Publication Support**
- **CRC Training & QA**
- **EDC**
- **? CME**

CRNs Based on :

- Domains/disorders (e.g. diabetes, oncology, dementia, depression)
- Technologies (e.g. functional MRI, PET)
- Treatments (e.g. renal transplants, stents)
- Capacities (e.g. inpt, ER)

SCRI Activities



Case example – DTN

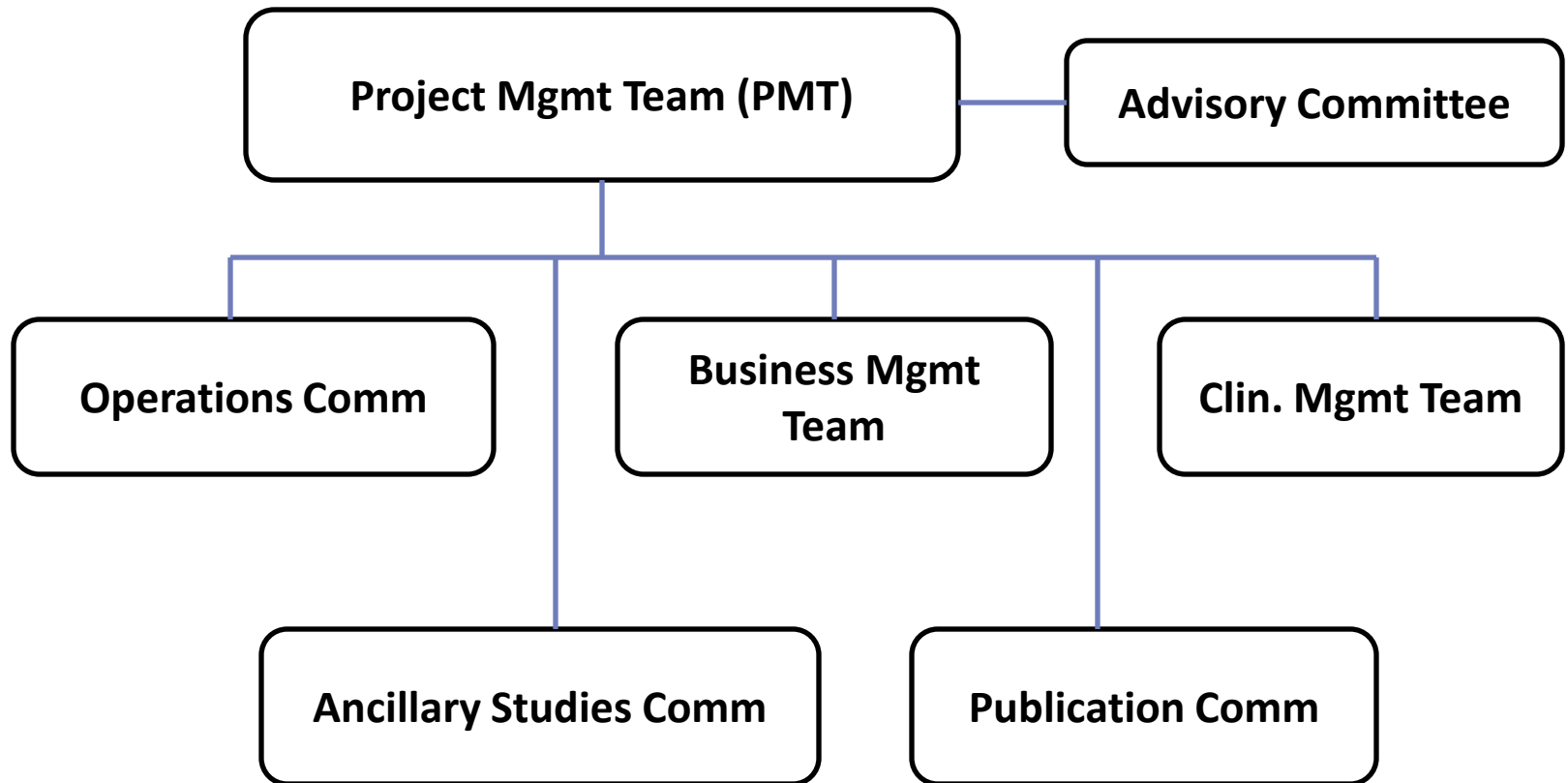
DTN : Overview

- 1999 – 2009
- \$30 million – STAR*D (4000)
 - \$2 million – SAMS (260)
 - \$8 million – COMED (660)
- Competitive Contract Bid
- 15 RCs
- 42 CSs

DTN: Contract & Funding

- One contract from (NIH to UTSWMC)
- Multiple subcontracts UTSWMC to
 - EDC
 - Pharmacy Benefit Management
 - RCs
 - CSs
- Hybrid funding (fixed cost PLUS by events)
 - CRC
 - CS Director
 - RC Director
- Research tasks : by event
- Research personnel : fixed (but can be stopped)

DTN: Organization



*All meetings by phone. Bi-annual face to face meetings of study team (PMT + Site PIs)

DTN: Participants

- 15 IRBs
- 1 DSMB
- 2 Safety Officers (FDA reports)
- Weekly SAE Adjudication

DTN: Products

- 120+ publications
 - Findings
 - Ancillary studies (DNA; measurement tools)
 - Secondary analyses
 - Design and statistical innovations
- Web dissemination (www.star-d.org; www.comed.org)
- All data and samples in public domain

DTN: Publications

- **Publication Committee** (Co-chairs: Biostats and Study PI or Co-PI) Plan primary + secondary analyses
- **All Hands Meetings** (Site PIs, Study Team) : for trial mgnt; QC; secondary analyses
- **Authorship policies** established for all primary and planned secondary analyses at outset (slot to CSs by performance + expertise)
- **Medical writer** engaged after first drafts
- **Publications cleared** by Publication Comm

The Ontario Prehospital Advanced Life Support Study



CAEP 2005

The OPALS Study

- The largest prospective pre-hospital study yet conducted
- Evaluates the impact of rapid defibrillation and ALS programs on survival and morbidity
- Over 9 years (1994-2003) involved 34,000 patients:
 - Cardiac arrest (10,000)
 - Major trauma (3,000)
 - Respiratory distress (8,000)
 - Chest pain (13,000)

CARE Study

↓ *Cardiac Arrest and Resuscitation Epidemiology in Singapore: A Pre-hospital Study*

↓ *Largest and most comprehensive OHCA study to date*

↓ *Prospective, Observational study*

↓ *Multi-center, covers whole of Singapore*





Co-investigators



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Co-investigators



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Dr Ng Kheng Siang

CARE Study

↓ *Period of study:*

↓ *CARE I: 1 Oct 2001 to 30 Apr 2002*

↓ *CARE II: 1 Oct 2002 to 14 Oct 2004*

↓ *CARE III: 1 January 2006 to 31 May 2006*

↓ *CARE IV: Ongoing*

↓ *Number of Cases Recruited: >28, 000*



CARE Study

- Ong EHM, Chan YH, Anantharaman V, Lau ST, Lim SH, Seldrup J. Cardiac Arrest and Resuscitation Epidemiology in Singapore (CARE I study). *Prehospital Emergency Care* 2003; 7: 427-433
- Ong ME, Chan YH, Srither DE, Lim YH. Asian Medical Staff Attitudes Towards Witnessed Resuscitation; *Resuscitation*; Jan 2004;60(1):45-50
- Ong MEH, . Chan YH, Ang HY, Lim SH, Tan KL. Resuscitation of out-of-hospital cardiac arrest by Asian primary health care physicians. *Resuscitation* 2005, 65:191-195
- Ong MEH, Chan YH, Anantharaman V. Improved response times with motorcycle based Fast Response Paramedics. *SGH Proceedings* 2003; 12(3): 114-119
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Obstacles and Solutions

- Authorship
 - Publication Comm + Policies
 - Planned Primary and Secondary Analyses
 - Rotation of Authors Over Time
 - Performance - Key to Authorship
 - Brand the Study or Network

- Scholarship
 - Ancillary Studies Committee
 - Planned Secondary Analyses
 - Methods Development

- Resources
 - Executive Comm
 - Project Management Teams
 - Publication Comm
 - Ancillary Studies Comm
 - Secretariat Functions

Obstacles and Solutions

- Contracts/Mgmt - Secretariat Reports to EC
- Project Management Meetings (Telephone)
- Communications - Newsletters; Face-to-face, Teleconferences
- Morale - Define Benefits, Rewards, Recognition
- Education - Key Presenter (CME; Research Foci; Others)

Issues for Discussion

- Intellectual Property
- Options to Contract Outside PAROS
- “National” Hubs
- Data Analyses Priorities
- Analyzing Ones Own Site or Country Data (Policy)
- Data Analyses for Workshops/Posters/Oral Presentations
- Promoting junior colleagues as co-authors/authors
- EC/Publication Comm Clearance
- Unplanned Secondary Analyses
- Regional/National Ancillary Studies

Types of Research Products

- Potential PAROS Studies
 - Describe services and treatments for specific conditions (cross sectional)
 - Describe acute (or longer term) outcomes of specific conditions
 - Test different interventions or treatments (system level and patient level)
 - Evaluate standard or new measures/scales
 - Identify “active ingredients” in a multi-step package
 - Identify predictors, moderators or mediators

Definitions

Predictor: Baseline feature that predicts outcome for a disease/condition independent of Rx (e.g. Edinburgh Coma Score)

Moderator: Baseline feature(s) that are associated with different outcomes of two different treatments for the same condition (e.g. liver cancer status and liver resection vs chemo Rx&D)

Mediator: Parameter(s) following the onset of an intervention that affects the outcome of the intervention (e.g. drug dose; frequency of treatment)

Management Issues

Publication Committee

Project Management Team

Ancillary Studies Committee

Secondary Analyses (? Committee)

Country Representatives

Communications Committee ?

Site Initiation

Site Monitoring

EDC Methods/Integration

Policies for approach by Pharma, CROs, or

Scientists to use PAROS

DISCUSSION

- Issues
- Next Steps

www.scri.edu.sg

www.star-d.org

www.ids-qids.org

www.co-med.org

THANK YOU!