Substance Use Treatments: Secondary Analyses Using the CTN Data Share

NIDA International Forum

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Overview of CTN Data Share

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Data Sharing

- Policy (NIH, EMA, Journals, PHRMA)
  - FDA considering sharing some data
- IOM : Discussion Framework for Clinical Trial Data Sharing: Guiding Principles, Elements, and Activities (for responsible data sharing, (Jan 22 2014) [Draft recommendations for public comment]
  - Proposes models of data sharing as starting point
    - Open access: all data available to anyone
    - Limited data access: data available to members of a consortium/defined group
    - Controlled access: data available by data use agreements, data pooled across multiple data sources or from individual entity
  - Discusses models in light of the challenges with data sharing
    - Balance between advancing research while maintaining privacy of research participants
    - Competitiveness of drug companies
    - Legal issues in different countries regarding intellectual property, informed consent, data privacy and antitrust laws

IOM Cont.

- *IOM : Discussion Framework for Clinical Trial Data Sharing: Topics for feedback
  - Global implementation/practical considerations
    - Different privacy protections/regulations; drug approval, data exclusivity, intellectual property laws, resources and health priorities
  - Timing/Prioritization
    - Different types of data, uses; what rationale for certain data/analyses; advantages; apply to new trials only
  - Risks
    - Invalid analyses, privacy/confidentiality, need for identifiable data, can participants be re-identified, what is impact
  - Incentives
    - Sponsors, researchers, responsibilities
  - Impact
    - How to assess different models of data sharing

*http://iom.edu/~/media/Files/Report%20Files/2014/Data-Sharing-Framework/clinicaltrialdata_topics.pdf

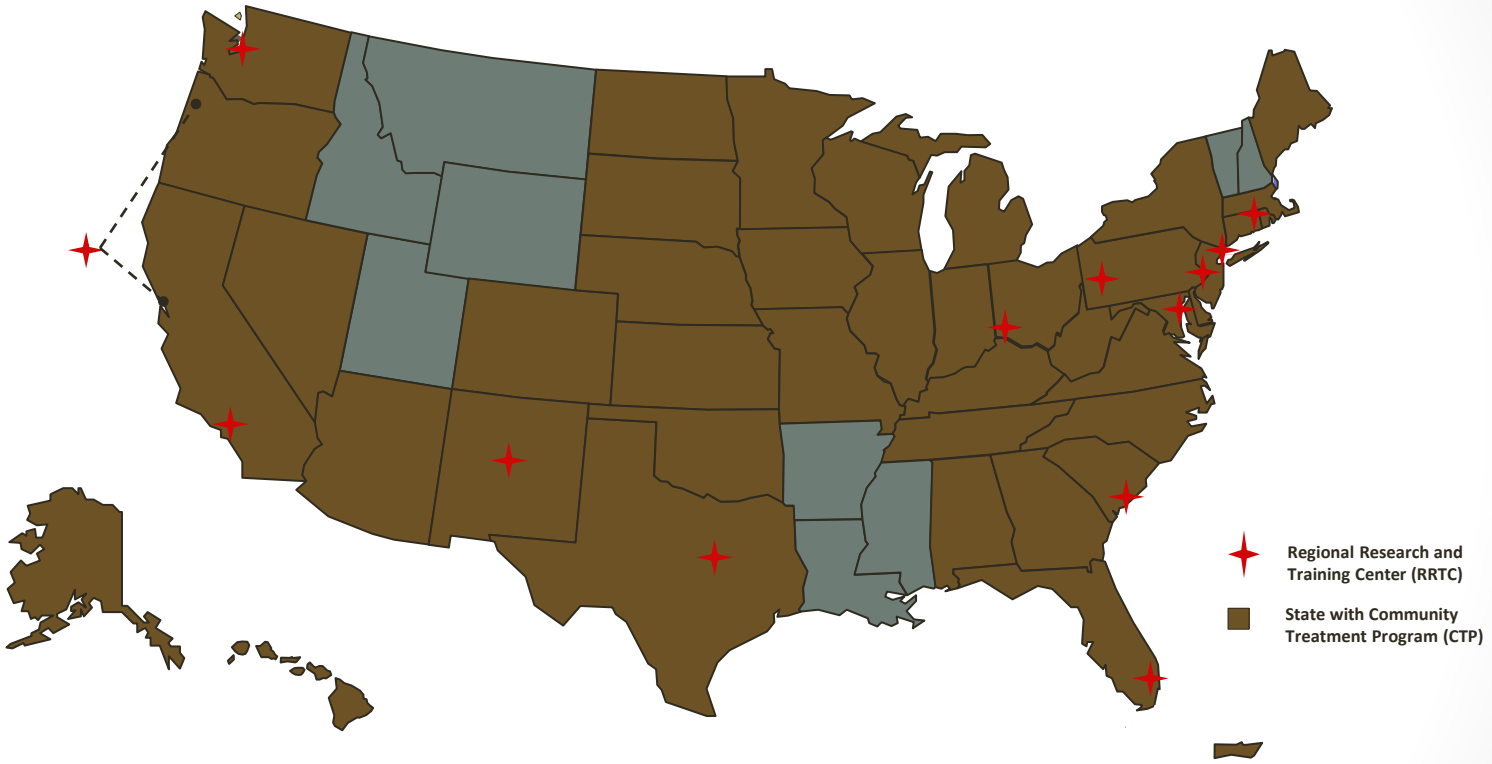
Issues

- Reproducibility
- Sharing analytic dataset
- Ethical/sensitivity concerns
- Sharing data from EHR/Health Learning Systems
  - Waiver of consent
  - HIPAA

CTN: Snapshot

- Established in 1999
- 42 multi site studies (1 trial in China)
  - 37 RCTs completed or recruiting
    - >16,700 participants recruited
    - Additional ~5000 in HIV testing platform study
    - 39% female
  - 2 studies in development (Vancouver a site)
  - 2 Surveys
  - 1 Quality Improvement
- ~25 ancillary studies
- 5 formal secondary analyses
- >300 papers reviewed by Publications Committee (more related)

National Drug Abuse Treatment Clinical Trials Network



Appalachian Tri-State Node
University of Pittsburgh

Delaware Valley Node
University of Pennsylvania

Florida Node Alliance
University of Miami

Greater New York Node
New York State Psychiatric Institute
New York University

Mid-Atlantic Node
The Johns Hopkins University
Friends Research Institute, Inc.

New England Consortium
McLean Hospital
Yale University

Ohio Valley Node
University of Cincinnati

Pacific Northwest Node
University of Washington
Washington State University

Pacific Region Node
University of California, Los Angeles

Southern Consortium Node
Medical University of South Carolina
Duke University Medical Center

Southwest Node
University of New Mexico

Texas Node
Univ. of Texas, Southwestern Med Cen.

Western States Node
University of California, San Francisco
Oregon Health & Science University

CTN International Collaborations

Australia (2009)
Canada (2013)
China (2007, 2010)
Colombia (2008)
Chile (2009)
France (2010)
Georgia (2007)
India (2007, 2009)
Iran (2010)
Italy (2013)
Kosovo (2010)
Mexico (2010)
Peru (2014)
Philippines (2008)
Switzerland (2011)
Ukraine (2010)

CTN Data Share

- **CTN Policy**: Data sets for CTN protocols are available after (1) the primary paper has been accepted for publication, or (2) the data is locked for more than 18 months, whichever comes first
- **Goals of the CTN Data Share:**
  - archiving and managing de-identified research data;
  - increase scientific productivity and optimize the use of resources originally invested in the trials;
  - encourage further analyses and promote new research:
    - apply different analytic plans to stored data regarding safety and effectiveness;
    - expand knowledge about demographic and clinical characteristics
  - teaching;
  - grant/fellowship/career development.

Cont.

- Data is de-identified to protect participants
  - No PHI or indirect identifies (site numbers, comment fields)
- The trial data sets are derived from the complete trial database.
  - **Analysis data sets such as those utilized to develop publications are not included on this website. Please see the primary manuscript or contact the lead investigator for details**

Available Files*

- The following information is posted, per protocol and is available to download:
  - Data files intended to allow researchers to perform statistical analyses are available in two formats: comma-separated variable files (American Standard Code for Information Interchange (ASCII)) and Statistical Analysis System (SAS) format transport files;
  - Descriptive metadata such as data dictionaries and annotated case report forms are provided for the data files, as well as overall descriptive data, such as study number, title, and a summary of the design

Files, Cont.*

- Study protocol, a document that describes the scientific rationale, objectives, design, methodology, planned analyses, and organization of the study
- De-identification notes, which describe in detail the study-specific de-identification process;
- Primary manuscript reference, when available;
- Website links external to Data Share integrated into the website to reference study summaries provided on the CTN website and the study description on clinicaltrials.gov.

Cont*

- In addition, taxonomy fields are provided for study keyword, investigator, and assessments associated with the study to aid in searching the Data Share website.
  - This taxonomy creates relationships between the various data points and links content across studies using vocabulary categorization.
  - This classification system links data in such a way that users can find content (e.g., studies) they may not have been aware existed or were applicable to their search.

*Shmueli-Blumberg, D, Hu, L, Allen, C, Frasketi, M, Wu, L, VanVeldhuisen, P. The National Drug Abuse Treatment Clinical Trials Network Data Share project: Website design, usage, challenges, and future directions, *Clin Trials* 2013 10: 977

Data Share

- CTN data share site available since 2006
  - In 2011 added detailed and categorized assessment information for all studies, ability to search across studies
- 31 data sets available (5 more by Dec 2014)– Open Access, only need to agree to the terms and conditions for use of the data:

  (1) not to attempt to establish the identity of any study participant;

  (2) retain control of the data and not to transfer it to other entities;

  (3) obtain IRB approval of the planned research, when applicable;

  (4) acknowledge the CTN in any publications or presentations;

  (5) maintain security and privacy of the data;

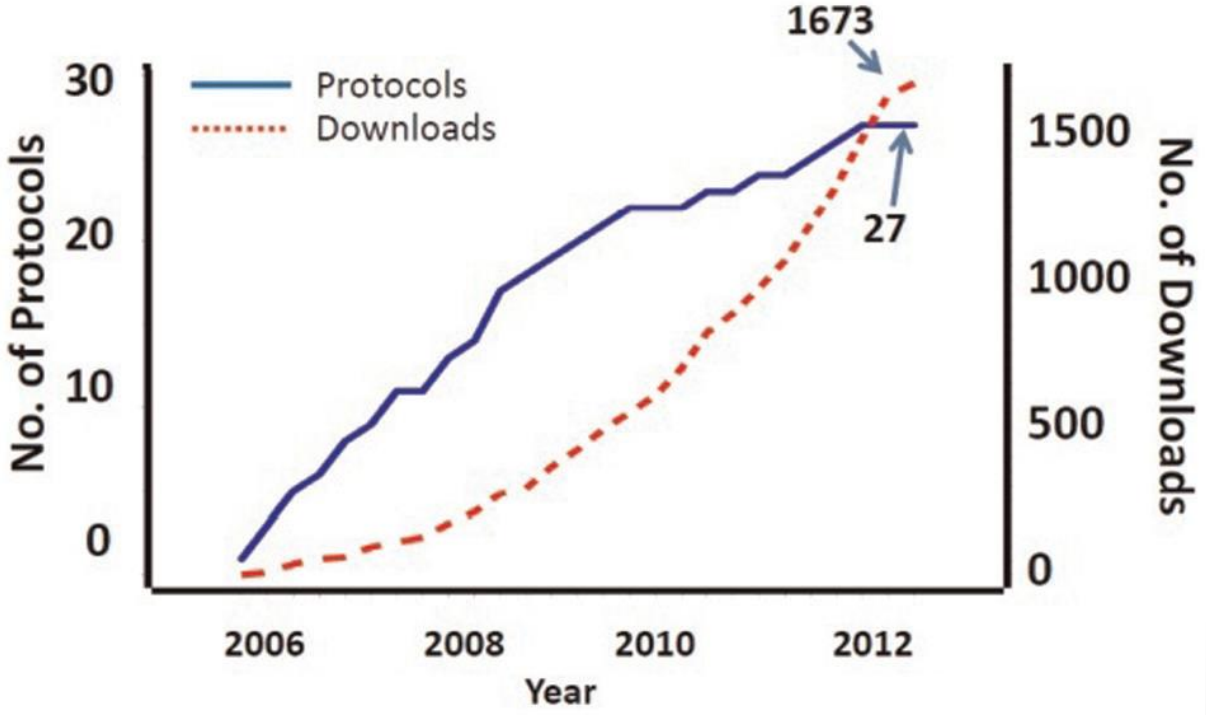
  (6) inform the NIDA Center for Clinical Trials Network (CCTN) when the research that uses the data is published;

  (7) CCTN may contact the recipient regarding the use of the data.

Cont.

- 2465 files downloaded from >50 countries (as May 8 2014)
  - CTN 0001 Bup/Nx vs. Clonidine Inpatient: 459
  - CTN 0030 POATS (Prescription Opiate Addiction Treatment Study): 181
  - CTN 0002 Bup/Nx vs. Clonidine Outpatient: 130
  - CTN 0015 Women's Treatment for Trauma and Substance Use Disorders: 126

Data Share website usage over time*



Publications

- At least 13 papers (that we know of)
  - Secondary analyses of individual studies
  - Analysis of merged data from several CTN studies
- Wu et al: applied factor and item response theory analyses to evaluate psychometric information and the quality of diagnostic tools in CTN studies
  - Results support diagnostic assessments used by the CTN and generate empirical data about the classification of Diagnostic and Statistical Manual of Mental Disorders– Fourth Edition (DSM-IV) substance-use disorders to inform DSM–Fifth Edition (DSM-V).

Some Examples (Cont)

- Lindblad et al: examined the safety data (adverse events and serious adverse events) from 17 completed CTN studies and developed a tailored safety strategy to reduce reporting burden of irrelevant safety events in clinical trials.
- Brooks et al: examined gender, racial/ethnic differences in the rates of HIV risk behaviors in clients participating in seven CTN trials.
  - Present results later in this session

Useful links Data Sharing

- PHRMA Principles for Responsible Clinical Trial Data Sharing
  - http://www.phrma.org/sites/default/files/pdf/PhRMAPrinciplesForResponsibleClinicalTrialDataSharing.pdf
- European Medicines Agency
  - http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000556.jsp
- IOM Outlines Framework for Clinical Data Sharing, Solicits Input, Bridget M. Kuehn, JAMA, 2014;311(7):665
- Preparing for Responsible Sharing of Clinical Trial Data, Michelle M. Mello, J.D., Ph.D., Jeffrey K. Francer, J.D., M.P.P., Marc Wilenzick, J.D., Patricia Teden, M.B.A., Barbara E. Bierer, M.D., and Mark Barnes, J.D., LL.M. N Engl J Med 2013; 369:1651-1658,
- October 24, 2013, FDA Notice: Masked and De-identified Non-Summary Safety and Efficacy Data:
  - https://www.federalregister.gov/articles/2013/06/04/2013-13083/masked-and-de-identified-nonsummary-safety-and-efficacy-data-availability
- NIH Sharing Policies and Related Guidance:
  - http://grants.nih.gov/grants/sharing.htm

For More Information: CTN

http://datashare.nida.nih.gov/index

CTN Dissemination Library:

http://ctndisseminationlibrary.org/

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Agenda

Practical Approaches for Using the CTN Data Share: Proposing Parameters, Creating Data Tables, and Analyzing Results

- Abigail G. Matthews, *The EMMES Corporation*

Using the CTN Data Share: An Example Utilizing Data From Multiple Protocols

- Audrey J. Brooks, *University of Arizona*

Secondary Analyses: Value and Limitations

- Daniel J. Feaster, *University of Miami Miller School of Medicine*