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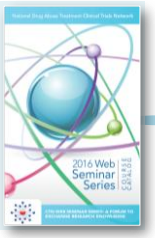

Demonstrating Practical Use of Data Share and Secondary Analyses

Presented by:
Dee Blumberg, PhD
Abigail G. Matthews, PhD

CTN WEB SEMINAR SERIES:
A FORUM TO EXCHANGE RESEARCH KNOWLEDGE
Produced by CTN Training

This training has been funded in whole or in part with federal funds from the National Institute on Drug Abuse, National Institutes of Health, Department of Health and Human Services, under Contract No. HHSN271201500065C

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Learning Objectives

- Review the structure of the NIDA Data Share website.
- Understand the information provided, how to navigate through the website, and obtain all the relevant information
- Demonstrate the technical procedures for using SAS or ASCII data sets for conducting secondary analyses.

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Polling Question

Have you been to the Data Share website?

❑Yes

❑No

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Introduction to Data Share

What is Data Share?

- Repository of publically available studies funded by NIDA
- CTN trials: ~34, plus 2 follow up studies
- Non-CTN trials: ~ 15 studies from the Division of Therapeutics and Medical Consequences (DTMC)

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Over 80 countries have downloaded data from Data Share

United States • India • UK • Canada • China • Spain • France • Malaysia • Bangladesh Turkey • Egypt • Poland • Nepal • Brazil • Afghanistan • Mexico • South Korea • Australia • Canary Islands • Croatia • Denmark • Ecuador • Netherlands • Pakistan • Singapore • South Africa •

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Goals of Data Share

- Optimize research productivity and use of resources
- Promote new research and secondary analyses
- Facilitate career development

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Funding Opportunity for Data Share

Accelerating the Pace of Drug Abuse Research Using Existing Data (R01)

- "*Of particular interest are analyses of data that have been harmonized and merged across multiple different datasets, such as those with PhenX measures… as well as data from NIDA Data Share for clinical trials…*"
- Deadline October 5, 2016 ☹

http://grants.nih.gov/grants/guide/pa-files/PAR-16-234.html

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Goals of Data Share

For example, it can be used for:

- Grant applications:
  - Preliminary data
  - Power/sample size calculations
- Secondary analyses:
  - Subgroup analyses
  - Mediation and moderation
- Secondary outcomes:
  - Harm reduction
  - Quality of Life

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Data Share Policies

- Trial data posted 18 months after database lock or after primary manuscript published, whichever comes first
- All CTN studies are posted to Data Share
- Only de-identified data is included
- Only raw data are provided

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Data Share Policies

- Truly open access:
  - No proposal necessary
  - Must agree to terms and conditions of use
- When publishing or presenting, must recognize the data source (NIDA Data Share)

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Overview of Posted Studies

- Most studies are:
  - Multi-site randomized controlled trials
  - Primary outcome usually substance-use related
  - Duration: intervention and follow-up are short (3-6 months)
  - Sample size: usually 100-500
- Types of interventions:
  - Behavioral (e.g., CTN-0037- Stimulant Reduction Intervention using Dosed Exercise (STRIDE))
  - Medication (e.g., CTN-0001- Buprenorphine/Naloxone versus Clonidine for Inpatient Opiate Detoxification)
  - Both behavioral and medication (e.g., CTN-0030- Buprenorphine/Naloxone Treatment Plus Individual Drug Counseling for Opioid Analgesic Dependence)

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Assessments

- Demographics
- Substance Use
- Mental Health
- Impulsivity and General Trait and Behavior Scales
- Interpersonal Relationships/Culture
- Physical/General Health
- Health Cognitions and QOL
- Clinical Measures
- Sexual Behavior/HIV
- Clinic Related Surveys

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Available Information

- Study documentation:
  - Brief study description
  - Protocol
  - Link to primary manuscript (available from CTN Dissemination Library)
- Data documentation:
  - Annotated CRFs
  - Data dictionary
  - De-identification notes

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Some examples

- Secondary analysis of individual studies
- Analysis of merged data from several CTN studies

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Examples

Journal of Substance Abuse Treatment 70 (2016) 73–80

Contents lists available at ScienceDirect

Journal of Substance Abuse Treatment

ELSEVIER

Mortality Rates Among Substance Use Disorder Participants in Clinical Trials: Pooled Analysis of Twenty-Two Clinical Trials Within the National Drug Abuse Treatment Clinical Trials Network☆,☆☆

Robert Lindblad, M.D. [a], Lian Hu, Ph.D., M.P.H. [a], Neal Oden, Ph.D. [a], Paul Wakim, Ph.D. [b], Carmen Rosa, M.S. [c], Paul VanVeldhuisen, Ph.D. [a]

ARTICLE INFO

ABSTRACT

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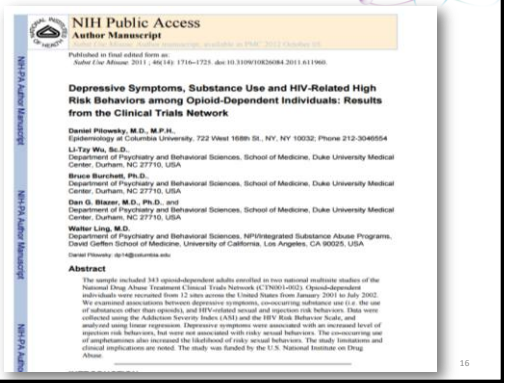

NIH Public Access
Author Manuscript

Published in final edited form as:
Subst Use Misuse. 2011 ; 46(14): 1716–1725. doi:10.3109/10826084.2011.611960.

Depressive Symptoms, Substance Use and HIV-Related High Risk Behaviors among Opioid-Dependent Individuals: Results from the Clinical Trials Network

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Daniel Pilowsky: dp146@columbia.edu

Abstract

The sample included 343 opioid-dependent adults enrolled in two national multisite studies of the National Drug Abuse Treatment Clinical Trials Network (CTN001+002). Opioid-dependent individuals were recruited from 12 sites across the United States from January 2001 to July 2002. We examined associations between depressive symptoms, co-occurring substance use (i.e. the use of substances other than opioids), and HIV-related sexual and injection risk behaviors. Data were collected using the Addiction Severity Index (ASI) and the HIV Risk Behavior Scale, and analyzed using linear regression. Depressive symptoms were associated with an increased level of injection risk behaviors, but were not associated with risky sexual behaviors. The co-occurring use of amphetamines also increased the likelihood of risky sexual behaviors. The study limitations and clinical implications are noted. The study was funded by the U.S. National Institute on Drug Abuse.

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Substance Abuse and Rehabilitation
Dovepress
ORIGINAL RESEARCH

Gender and racial/ethnic differences in addiction severity, HIV risk, and quality of life among adults in opioid detoxification: results from the National Drug Abuse Treatment Clinical Trials Network

Li-Tzy Wu[1,2]
Walter Ling[3]
Bruce Burchett[1]
Dan G Blazer[1,2]
Jack Shostak[3]
George E Woody[4]

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Purpose: Detoxification often serves as an initial contact for treatment and represents an opportunity for engaging patients in aftercare to prevent relapse. However, there is limited information concerning clinical profiles of individuals seeking detoxification, and the opportunity to engage patients in detoxification for aftercare often is missed. This study examined clinical profiles of a geographically diverse sample of opioid-dependent adults in detoxification to discern the treatment needs of a growing number of women and whites with opioid addiction and to inform interventions aimed at improving use of aftercare or rehabilitation.

Methods: The sample included 343 opioid-dependent patients enrolled in two national multisite studies of the National Drug Abuse Treatment Clinical Trials Network (CTN001-002). Patients were recruited from 12 addiction treatment programs across the nation. Gender and racial/ethnic differences in addiction severity, human immunodeficiency virus (HIV) risk, and quality of life were examined.

Results: Women and whites were more likely than men and African Americans to have greater psychiatric and family/social relationship problems and report poorer health-related quality of life and functioning. Whites and Hispanics exhibited higher levels of total HIV risk scores and risky injection drug use scores than African Americans, and Hispanics showed a higher level of unprotected sexual behaviors than whites. African Americans were more likely than whites to use heroin and cocaine and to have more severe alcohol and employment problems.

Conclusions: Women and whites show more psychopathology than men and African Americans. These results highlight the need to monitor an increased trend of opioid addiction among women and whites and to develop effective combined psychosocial and pharmacologic treatments to meet the diverse needs of the expanding opioid-abusing population. Elevated levels

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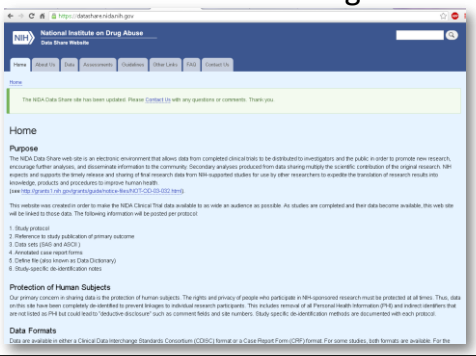
Website Home Page



National Institute on Drug Abuse
Data Share Website

Home | About Us | Data | Assessments | Guidelines | Other Links | FAQ | Contact Us

Home

The NDA Data Share site has been updated. Please Contact Us with any questions or comments. Thank you.

Home

Purpose

The NDA Data Share web site is an electronic environment that allows data from completed clinical trials to be distributed to investigators and the public in order to promote new research, encourage further analyses, and disseminate information to the community. Secondary analyses produced from data sharing multiply the scientific contribution of the original research. NIH expects and supports the timely release and sharing of final research data from NIH-supported studies for use by other researchers to expedite the translation of research results into knowledge, products and procedures to improve human health.
[see http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html].

This website was created in order to make the NDA Clinical Trial data available to as wide an audience as possible. As studies are completed and their data become available, this web site will be linked to those data. The following information will be posted per protocol:

1. Study protocol
2. Reference to study publication of primary outcome
3. Data sets (SAS and ASCII)
4. Annotated case report forms
5. Define file (also known as Data Dictionary)
6. Study-specific de-identification notes

Protection of Human Subjects

Our primary concern in sharing data is the protection of human subjects. The rights and privacy of people who participate in NIH-sponsored research must be protected at all times. Thus, data on this site have been completely de-identified to prevent linkages to individual research participants. This includes removal of all Personal Health Information (PHI) and indirect identifiers that are not listed as PHI but could lead to "deductive disclosure" such as comment fields and site numbers. Study specific de-identification methods are documented with each protocol.

Data Formats

Data are available in either a Clinical Data Interchange Standards Consortium (CDISC) format or a Case Report Form (CRF) format. For some studies, both formats are available. For the

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Guidelines Tab

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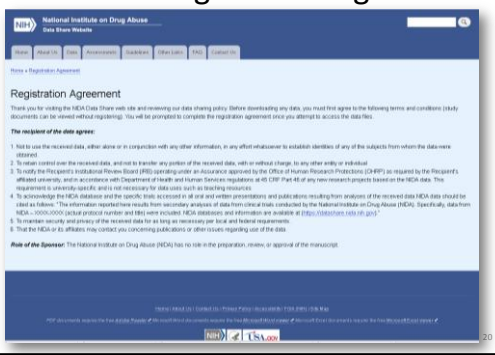
Data Share Registration Agreement



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Data Share Policy

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Other Links Tab

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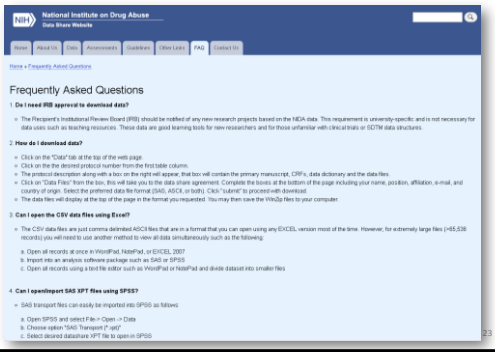
FAQ Tab



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CTN Web Seminar Series: *A Forum to Exchange Research Knowledge*

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LIVE DEMONSTRATION

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Assessments Tab

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Assessments- Main

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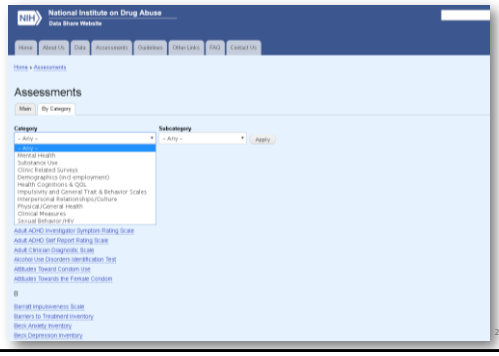
Assessments- by category



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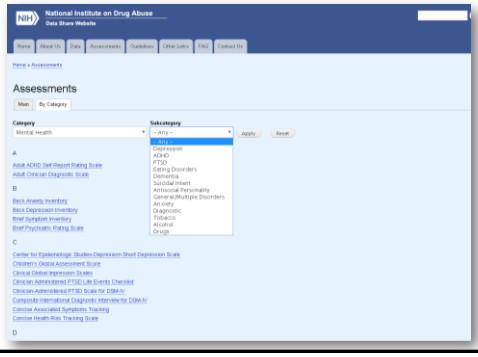
Mental Health Assessments



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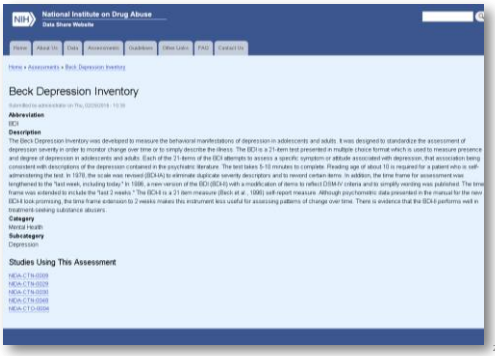

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A Research Example

- A researcher interested in the comorbidity, between **drug addiction** and **depression**…

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Questions

Any questions so far before we move on to the next section …

TIPS AND TRICKS

Documentation

- Read each protocol to understand:
  - Eligibility criteria
  - Visit timing/windows
  - Procedures for data collection
- Review annotated CRFs to:
  - Determine data elements
  - Evaluate codelists (commonality/harmonization)
  - Identify corresponding data files
- Read de-identification notes/nulled values docs
  - What information has been deleted*
  - What fields have been removed

** Contact study PI for access to raw data*

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Data Structure

- **CRF Level** – wide data files
  - One dataset per case report form
  - Each question/variable is a separate column
  - Requires substantial merging of different datasets
- **CDISC** – long and narrow data files
  - One row per question on CRF
  - Variable name/question described in one or more columns
  - All values/answers in one column
  - Minimizes amount of merging
  - Data from one case report form can be mapped to more than one dataset

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CRF-level data (CTN-0052)

PROT	PATID	VISNO	UDTSTPRF	UDCOLDT	UD1TMP	UD1ADULT	UD1THC	UD1OPI	UD1COC	UD1MDMA	UD1OXY	UD1MTD	UD1BAR
0052	193369	30	1	100	1	0	0	0	0	0	0	0	0
0052	193369	29	1	98	1	0	0	0	0	0	0	0	0
0052	193369	28	1	93	1	0	0	0	0	0	0	0	0
0052	193369	27	1	91	1	0	0	0	0	0	0	0	0
0052	193369	26	1	87	1	0	0	0	0	0	0	0	0
0052	193369	25	1	85	1	0	0	0	0	0	0	0	0
0052	193369	24	1	80	1	0	0	0	0	0	0	0	0
0052	193369	23	1	77	1	0	0	0	0	0	0	0	0
0052	193369	22	1	72	1	0	0	0	0	0	0	0	0
0052	193369	21	1	70	1	0	0	0	0	0	0	0	0
0052	193369	20	1	67	1	0	0	0	0	0	0	0	0
0052	193369	19	1	65	1	0	0	0	0	0	0	0	0
0052	193369	18	1	60	1	0	0	0	0	0	0	0	0
0052	193369	17	1	56	1	0	0	0	0	0	0	0	0
0052	193369	16	1	51	1	0	0	0	0	0	0	0	0
0052	193369	15	1	49	1	0	0	0	0	0	0	0	0
0052	193369	14	1	44	1	0	0	0	0	0	0	0	0
0052	193369	13	1	42	1	0	0	0	0	0	0	0	0
0052	193369	12	1	37	1	0	0	0	0	0	0	0	0

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CDISC Data (CTN-0009)

DOMAIN	USUBJID	EPOCH	VSTESTCD	VSTEST	VSORRES	VSORRESU	VISIT	VISITNUM	VSDY
VS	09_000748	SCREENING	DBP	DIASTOLI	76	MMHG	SCREENING	-3	-23
VS	09_000748	BASELINE	DBP	DIASTOLI	86	MMHG	BASELINE	-2	-14
VS	09_000748	PRETOD	DBP	DIASTOLI	77	MMHG	PRE-TOD	-1	6
VS	09_000748	TREATMENT	DBP	DIASTOLI	71	MMHG	TREATMENT	1	14
VS	09_000748	TREATMENT	DBP	DIASTOLI	79	MMHG	TREATMENT	2	21
VS	09_000748	TREATMENT	DBP	DIASTOLI	83	MMHG	TREATMENT	3	27
VS	09_000748	TREATMENT	DBP	DIASTOLI	74	MMHG	TREATMENT	4	34
VS	09_000748	TREATMENT	DBP	DIASTOLI	71	MMHG	TREATMENT	5	42
VS	09_000748	TREATMENT	DBP	DIASTOLI	79	MMHG	TREATMENT	6	49
VS	09_000748	TREATMENT	DBP	DIASTOLI	74	MMHG	TREATMENT	7	57
VS	09_000748	TREATMENT	DBP	DIASTOLI	84	MMHG	TREATMENT	8	63
VS	09_000748	FOLLOW UP	DBP	DIASTOLI	84	MMHG	FOLLOW UP	9	69
VS	09_000748	FOLLOW UP	DBP	DIASTOLI	83	MMHG	FOLLOW UP	13	105
VS	09_000748	SCREENING	PULSE	PULSE	93	BEATS/MIN	SCREENING	-3	-23
VS	09_000748	BASELINE	PULSE	PULSE	88	BEATS/MIN	BASELINE	-2	-14
VS	09_000748	PRETOD	PULSE	PULSE	87	BEATS/MIN	PRE-TOD	-1	6
VS	09_000748	TREATMENT	PULSE	PULSE	83	BEATS/MIN	TREATMENT	1	14
VS	09_000748	TREATMENT	PULSE	PULSE	90	BEATS/MIN	TREATMENT	2	21
VS	09_000748	TREATMENT	PULSE	PULSE	82	BEATS/MIN	TREATMENT	3	27
VS	09_000748	TREATMENT	PULSE	PULSE	72	BEATS/MIN	TREATMENT	4	34
VS	09_000748	TREATMENT	PULSE	PULSE	86	BEATS/MIN	TREATMENT	5	42
VS	09_000748	TREATMENT	PULSE	PULSE	79	BEATS/MIN	TREATMENT	6	49
VS	09_000748	TREATMENT	PULSE	PULSE	95	BEATS/MIN	TREATMENT	7	57
VS	09_000748	TREATMENT	PULSE	PULSE	84	BEATS/MIN	TREATMENT	8	63
VS	09_000748	FOLLOW UP	PULSE	PULSE	65	BEATS/MIN	FOLLOW UP	9	69

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Data Formats

- **ASCII**
  - Text files
  - CSV – comma separated values
  - Can be read into SAS, SPSS, Excel, Stata, etc.
- **SAS**
  - Usually SAS transport file (.xpt)
    - Can be read into SPSS, SAS, DBMS Copy, and other programs
    - Some studies have formats catalogue
  - Sometimes standard SAS file (.sas7bdat)
    - Can be read into SPSS and SAS

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Notes on De-identification

- Participant IDs are *not* those of the actual study
- Site is dropped
- All free text fields removed
- Dates converted to study day or days since informed consent

If you find any of the above information – please inform DSC, IGNORE and DELETE it

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- Pay special attention to CDISC data
  - "Epoch" and "Visit Name" usually have to be combined or use study day
  - "Domain" is defined on each CRF
- These are raw data
  - Data cleaning not perfect – check for inconsistencies and outliers
  - Note how missing data is coded – varies from study to study and form to form
- Be very careful when merging datasets
- When publishing/presenting, make sure to reference primary manuscript

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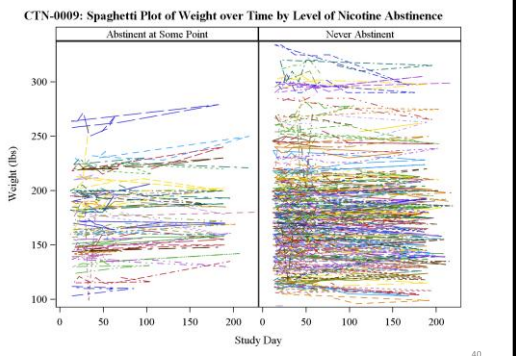

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Statistical Considerations

Secondary analyses have several pitfalls:

- Type I error (false positives)
- Underpowered
- Must be interpreted with caution
  - Cannot imply causality
  - Analyses are exploratory in nature and hypothesis-generating
- Analyses from Data Share will likely be *post hoc* – must acknowledge

Despite these pitfalls, secondary analyses are powerful tools and, as long as they are reported in a transparent manner, will contribute significantly to the literature

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CTN Web Seminar: Secondary Analyses

Secondary Analyses Clinical Trials

- Presenters: George Bigelow, Abigail G. Matthews, Daniel Feaster
- Learning objectives:
  - Review statistical issues with analyzing and reporting secondary analyses
  - Explore importance of pre-specification
  - Discuss reporting and interpreting secondary analyses, including PC perspective

http://ctndisseminationlibrary.org/display/1039.htm

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CDISC Resources

- Official website:
  http://www.cdisc.org/
- Standards:
  https://www.cdisc.org/standards/foundational/sdtm
- SAS import:
  http://support.sas.com/documentation/cdl/en/cdisc/60755/HTML/default/viewer.htm#titlepage.htm

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References

- Matthews, A., Feaster, D., & Bigelow, G. (2013). Secondary analyses for clinical trials in development. *CTN Web Seminar Series*. http://ctndisseminationlibrary.org/display/1039.htm
- Shmueli-Blumberg, D., Hu, L., Allen, C., Frasketi, M., Wu, L.T., Vanveldhuisen, P. (2013). The national drug abuse treatment clinical trials network data share project: website design, usage, challenges, and future directions. *Clinical Trials*, 10 (6): 977-986.
- Funding opportunity: Accelerating the Pace of Drug Abuse Research Using Existing Data. http://grants.nih.gov/grants/guide/pa-files/PAR-16-234.html

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Questions / Comments

Alternatively, questions can be directed to the presenter(s) by sending an email to CTNtraining@emmes.com.

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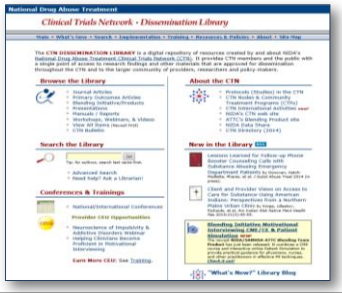
http://ctndisseminationlibrary.org/ctntraining.htm

A recording of this presentation will be available electronically.



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Next Topic…

Preparation for Drug Management and Accountability in a CTN Clinical Trial

October 19, 2016
1:00 pm ET

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CTN Web Seminar Series: *A Forum to Exchange Research Knowledge* WEB SEMINAR SERIES 2016

THANK YOU FOR YOUR PARTICIPATION