Update: ClinicalTrials.gov Trial Registration and Results Reporting

Deborah A. Zarin, M.D.
National Library of Medicine, NIH
December 2010

Reasons to Register Clinical Trials and Report Results

- Human Subject Protections
  - Allows potential participants to find studies
  - Assists ethical review boards and others to determine appropriateness of studies being reviewed (e.g., harms, benefits, redundancy)
  - Promote fulfillment of ethical responsibility to human volunteers – research contributes to medical knowledge
- Research Integrity
  - Facilitates tracking of protocol changes
  - Increases transparency of research enterprise
- Evidence Based Medicine
  - Facilitates tracking of studies and outcome measures
  - Allows for more complete identification of relevant studies
- Allocation of Resources
  - Promotes more efficient allocation of resources

The good news: We have a lot of information

- 100,151 registered trials from 9,963 Sponsors
  - 45% US sites only
- 2,677 Results entries from 472 Sponsors
- Access to data about individual clinical trials
  - Powerful search tools
  - Users can identify and track trials and outcome measures
- Unique source of information about CRE

Content of ClinicalTrials.gov Records

- One record per trial
- Registration record
  - Submitted at trial initiation
  - Summarizes information from trial protocol
    - Condition
    - Interventions
    - Design, etc
  - Includes recruitment information (e.g., eligibility, locations)
- Results record
  - Submitted after trial completion
  - Summarizes trial results
    - Participant flow
    - Baseline characteristics
    - Outcome measures (including statistical analyses)
    - Adverse events

N Engl J Med. 2006 Oct 12;355(15):15

Effectiveness of atypica

Schneider LS, Tariot PN, Dagerma
Keck School of Medicine, University o

Abstract

BACKGROUND: Second-g
Alzheimer's disease, but the
antipsychotic drugs in outpa

METHODS: In this 42-site,
were randomly assigned to
mg per day), or placebo. Do
initial treatment to the discon
Impression of Change (CGI

RESULTS: There were no
olanzapine (median, 8.1 we
median time to the discontin
with quetiapine (9.1 weeks)
favored placebo. Overall, 24
risperidone, and 5% of patie
differences were noted amo
olanzapine, 26% of patients

CONCLUSIONS: Adverse effects offset advantages in the efficacy of atypical antipsychotic drugs for the treatment of psychosis, aggression, or agitation in patients with Alzheimer's disease. (ClinicalTrials.gov number, NCT00015548 [ClinicalTrials.gov].).

Secondary Source ID:

ClinicalTrials.gov/NCT00015548

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 12, 2006 VOL. 355 NO. 15

Effectiveness of Atypical Antipsychotic Drugs in Patients with Alzheimer's Disease

Lon S. Schneider, M.D., Pierre N. Tariot, M.D., Karen S. Dagerman, M.S., Sonia M. Davis, Dr.P.H., John K. Hsiao, M.D., M. Saleem Ismail, M.D., Barry D. Lebowitz, Ph.D., Constantine G. Lyketsos, M.D., M.H.S., J. Michael Ryan, M.D., T. Scott Stroup, M.D., David L. Sultzer, M.D., Daniel Weintraub, M.D., and Jeffrey A. Lieberman, M.D., for the CATIE-AD Study Group*

ABSTRACT

CONCLUSIONS

Adverse effects offset advantages in the efficacy of atypical antipsychotic drugs for the treatment of psychosis, aggression, or agitation in patients with Alzheimer's disease. (ClinicalTrials.gov number, NCT00015548.)

Full Text View

More Informati

Additional Informatio

Click here to fi

More informatic

Publications:

Schneider LS, DL, Weintraub disease. N Eng

Schneider LS, PV, Rosenheck RA, Small GW, Lebowitz B, Lieberman JA. National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE): Alzheimer disease trial methodology. Am J Geriatr Psychiatry. 2001 Fall;9(4):346-60.

510(k) Premarket Notification

CDRH SuperSearch

510(k) | Registration & Listing | Adverse Events | Recalls | PMA | Classification | Standards
CFR Title 21 | Radiation-Emitting Products | X-Ray Assembler | Medsun Reports | CLIA

New Search Back To Search Results

Device Classification Name	Lung Sound Monitor
510(k) Number	K091732
Device Name	VRLXP, MODEL XP
Applicant	DEEP BREEZE LTD. 2001 Pennsylvania Avenue Nw Suite 950 Washington, DC 20006
Contact	Jeff Baetz
Regulation Number	870.1875
Classification Product Code	OCR
Date Received	06/11/2009
Decision Date	03/04/2010
Decision	Substantially Equivalent (SE)
Classification Advisory Committee	Anesthesiology
Review Advisory Committee	Anesthesiology
Statement/Summary/Purged Status	Summary Only
Summary	Summary
Type	Traditional
Clinical Trials	NCT00473291 NCT00495430 NCT00506467 NCT00542282 NCT00672893
Reviewed By Third Party	No
Expedited Review	No

The bad news:

Somebody has to enter the data!

Legal and Other Requirements

FDAAA
Sec. 801 Expanded Clinical Trial Registry

- Enacted on September 27, 2007
- Requires Trial Registration (Dec 2007)
  - Phase II-IV drug and device trials for all diseases
  - Data elements: ClinicalTrials.gov + ~ WHO/ICMJE
- Requires Results Reporting (Sept 2008)
  - Trials of FDA-approved or cleared drugs and devices
  - "Basic" Results: Baseline Characteristics, Primary & Secondary Outcomes, Statistical Analyses
  - Adverse Events (Sept 2009)
  - "Expansion" of results by rulemaking (Sept 2010)
- Added enforcement provisions

Potential Enforcement Provisions

- Notices of non-compliance
- Civil monetary penalties (up to $10,000/day)
- Withholding of NIH grant funds

Key Terms

- Responsible Party
  - Sponsor, grantee
  - PI, if designated
- Applicable Clinical Trials
  - Interventional trials
  - Phase 2-4 drug, biologic, device
  - IND/IDE trial or ≥one site in U.S.
  - Ongoing as of 12/26/07, or later
- Primary Completion Date

Establishing the "Responsible Party"

- Who is the sponsor?
  - IND/IDE holder
  - NIH grantee
  - "Initiator of trial"
- Sponsor may designate the PI (under some conditions)
- RP has legal responsibilities for FDAAA
  - Others may help
  - Only one per trial!

Pitfalls in determining if your trial is an ACT

- Is it an interventional study?
  - Are the “interventions” a consequence of the research protocol, or vice versa?
  - Would the participants have received the interventions whether or not they were in the study?
- Does it include a device?
  - FDA regulatory definitions apply
  - Includes diagnostic devices

National Cancer Institute
U.S. National Institutes of Health | www.cancer.gov

Send to Printer

News

Contact the NCI Office of Media Relations | RSS Feed

Posted: 11/04/2010

Lung cancer trial results show mortality benefit with low-dose CT:

Twenty percent fewer lung cancer deaths seen among those who were screened with low-dose spiral CT than with chest X-ray

The National Cancer Institute (NCI) is today releasing initial results from a large-scale test of screening methods to reduce deaths from lung cancer by detecting cancers at relatively early stages.

The National Lung Screening Trial (NLST), a randomized national trial involving more than 53,000 current and former heavy smokers ages 55 to 74, compared the effects of two screening procedures for lung cancer -- low-dose helical computed tomography (CT) and standard chest X-ray -- on lung cancer mortality and found 20 percent fewer lung cancer deaths among trial participants screened with low-dose helical CT. The NLST was sponsored by NCI, a part of the National Institutes of Health, and conducted by the American College of Radiology Imaging Network (ACRIN) and the Lung Screening Study group. A paper describing the design and protocol of the NLST, "The National Lung Screening Trial: Overview and Study Design" by the NLST research team, was published yesterday by the journal Radiology and is openly available at http://radiology.rsna.org/cgi/content/abstract/radiol.10091808 [1].

National Lung Screening Trial (NLST)

This study is ongoing, but not recruiting participants.

First Received: October 3, 2002 Last Updated: June 15, 2010 History of Changes

Sponsor:	National Cancer Institute (NCI)
Collaborator:	American College of Radiology Imaging Network
Information provided by:	National Cancer Institute (NCI)
ClinicalTrials.gov Identifier:	NCT00047385

Purpose

RATIONALE: Screening tests may help doctors detect cancer cells early and plan more effective treatment for lung cancer. It is not yet known whether helical CT scan is more effective than chest x-ray in reducing death from lung cancer.

PURPOSE: Randomized clinical trial to compare the effectiveness of helical CT scan with that of chest x-ray in screening individuals who are at high risk for developing lung cancer.

(Device) (Device)

Condition	Intervention
Lung Cancer	Procedure: bronchoscopic and lung imaging studies Procedure: comparison of screening methods

Study Type: Interventional
Study Design: Allocation: Randomized
Control: Active Control
Primary Purpose: Screening

Official Title: National Lung Screening Trial

Basic Results Database

Basic Results Reporting Requirements

- Results of FDA-*approved/cleared* products
- Generally, submission within 12 months of the *earlier* of estimated/actual primary completion date
- Delayed Submission of Results
  - Seeking initial approval
  - Seeking approval of a new use
  - Extensions for “good cause”

Basic Results Modules

- Participant Flow
- Baseline and Demographic Characteristics
- Outcome Measures
- Adverse Events (summary data)
- Other Information
  - "Certain Agreements" *Restricting Results Disclosure*
  - Overall Limitations and Caveats
  - Results Point of Contact

Full Text View | Tabular View | Study Results | Related Studies

Docetaxel in Breast Cancer

This study is ongoing, but not recruiting participants.

Study NCT00312208 Information provided by Sanofi-Aventis
Study First Received: April 5, 2006 Last Updated: February 15, 2010 History of Changes
Results First Received: October 29, 2009

Study Type:	Interventional
Study Design:	Allocation: Randomized; Control: Active Control; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Open Label; Primary Purpose: Treatment
Condition:	Breast Cancer
Interventions:	Drug: docetaxel, doxorubicin, cyclophosphamide Drug: Docetaxel,doxorubicin, cyclophosphamide

Participant Flow: Overall Study

	Doxorubicin + Cyclophosphamide Followed by Docetaxel (AC -> T)	Docetaxel + Doxorubicin and Cyclophosphamide (TAC)
STARTED	1649 [1]	1649 [2]
COMPLETED	1477	1526
NOT COMPLETED	172	123
Adverse Event	97	61
Protocol Violation	5	3
Death	2	1
Lack of Efficacy		4
Lost to Follow-up	3	5
Withdrawal by Subject	53	42
Not specified	5	7

Reasons Not Completed

[1] 1649 patients randomized, 1634 patients treated
[2] 1649 patients randomized 1635 patients treated

Baseline Measures

	Doxorubicin + Cyclophosphamide Followed by Docetaxel (AC -> T)	Docetaxel + Doxorubicin and Cyclophosphamide (TAC)	Total
Number of Participants [units: participants]	1649	1649	3298
Age, Customized [units: Participants]			
> =65 years	85	83	168
Between 65 and 50 years	784	783	1567
Between 49 and 35 years	689	710	1399
< =35 years	91	73	164
Age [units: years] Median (Full Range)	50 (22 to 74)	50 (24 to 72)	50 (22 to 74)
Gender [units: participants]			
Female	1649	1649	3298
Male	0	0	0
Region of Enrollment [units: participants]			

"Default" Required Measures

User-Specified Baseline Measures

Hormonal Receptor Status [units: Participants]			
Positive	1348	1346	2694
Negative	301	303	604
Karnofsky Performance Status at Baseline [units: Participants]			
80 - Activity with effort; some signs of disease	36	33	69
90 - Normal activity; minor signs of disease	315	323	638
100 - Normal no complaints; no evidence of disease	1298	1293	2591
Menopausal status [units: Participants]			
Pre-Menopausal or Other age < 50 Years	866	863	1729
Post-Menopausal or Other age > 50 Years	783	786	1569
Number of Positive Lymph Nodes [units: Participants]			
[0]	0	1	1
[1 to 3]	1010	1005	2015
[4 to 10]	462	456	918
> 10	177	187	364
Patients with at least one surgery [units: Participants]			
Mastectomy	955	973	1928
Lumpectomy	283	276	559
Quadrantectomy/Segmental	411	400	811
Primary Tumor [units: Participants]			
pT1: Tumor < = 2cm	692	668	1360
pT2: Tumor in [2 - 5]	824	844	1668
pT3: Tumor > 5cm	131	135	266
pT4: Tumor with extension to chest			

Primary Outcome Measure: Local, Regional or Metastatic Relapse, or Second Primary Cancer, or Death From Any Cause (Disease-Free Survival)
[Time Frame: Median follow-up 65 months]

Measured Values

	Doxorubicin + Cyclophosphamide Followed by Docetaxel (AC -> T)	Docetaxel + Doxorubicin and Cyclophosphamide (TAC)
Number of Participants Analyzed [units: participants]	**1649**	**1649**
Local, Regional or Metastatic Relapse, or Second Primary Cancer, or Death From Any Cause (Disease-Free Survival) [units: Participants]	**356**	**352**

Statistical Analysis 1 for Local, Regional or Metastatic Relapse, or Second Primary Cancer, or Death From Any Cause (Disease-Free Survival)

Groups [1]	All groups
Method [2]	Log Rank
P Value [3]	0.978
Hazard Ratio (HR) [4]	1.00
95% Confidence Interval	(0.86 to 1.16)

Secondary Outcome Measure: Death From Any Cause (Overall Survival)
[Time Frame: Median follow-up of 65 months]

Measured Values

	Doxorubicin + Cyclophosphamide Followed by Docetaxel (AC -> T)	Docetaxel + Doxorubicin and Cyclophosphamide (TAC)
Number of Participants Analyzed [units: participants]	**1649**	**1649**
Death From Any Cause (Overall Survival) [units: Participants]	**187**	**202**

Statistical Analysis 1 for Death From Any Cause (Overall Survival)

Groups [1]	All groups
Method [2]	Log Rank
P Value [3]	0.371
Hazard Ratio (HR) [4]	0.91
95% Confidence Interval	(0.75 to 1.11)

Serious Adverse Events

	Doxorubicin + Cyclophosphamide Followed by Docetaxel (AC -> T)	Docetaxel + Doxorubicin and Cyclophosphamide (TAC)
Total, serious adverse events		
# participants affected / at risk	331/1634 (20.26%)	520/1635 (31.80%)
Blood and lymphatic system disorders		
Anemia † 1		
# participants affected / at risk	3/1634 (0.18%)	5/1635 (0.31%)
Coagulation disorders † 1		
# participants affected / at risk	1/1634 (0.06%)	0/1635 (0.00%)
Hemorrhage Vaginal † 1		
# participants affected / at risk	1/1634 (0.06%)	0/1635 (0.00%)
Leukopenia † 1		
# participants affected / at risk	18/1634 (1.10%)	56/1635 (3.43%)
Lymphadenopathy † 1		
# participants affected / at risk	0/1634 (0.00%)	1/1635 (0.06%)
Lymphedema † 1		
# participants affected / at risk	0/1634 (0.00%)	2/1635 (0.12%)
Pancytopenia † 1		
# participants affected / at risk	0/1634 (0.00%)	1/1635 (0.06%)
Thrombocytopenia † 1		
# participants affected / at risk	0/1634 (0.00%)	1/1635 (0.06%)
Cardiac disorders		
Arrhythmia † 1		
# participants affected / at risk	3/1634 (0.18%)	3/1635 (0.18%)
Arrhythmia Ventricular † 1		

† Events were collected by systematic assessment
1 Term from vocabulary, COSTART

Certain Agreements

"Whether there exists an agreement (other than an agreement solely to comply with applicable provisions of law protecting the privacy of participants) between the sponsor or its agent and the principal investigator (unless the sponsor is an employer of the principal investigator) that restricts in any manner the ability of the principal investigator, after the completion date of the trial, to discuss the results of the trial at a scientific meeting or any other public or private forum, or to publish in a scientific or academic journal information concerning the results of the trial."

[Sec. 282(j)(3)(C)(iv)]

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:** If no publication has occurred within 12 months of the completion of the study, the Investigator shall have the right to publish/present independently the results of the study. The Investigator shall provide the Sponsor with a copy of any such presentation/publication for comment at least 30 days before any presentation/submission for publication. If requested by the Sponsor, any presentation/submission shall be delayed up to 90 days, to allow the Sponsor to preserve its proprietary rights.

Public Archive for Records

- Changes can and should be made to records
  - Estimated dates become “actual” dates
  - Estimated enrollment becomes “actual”
  - Other protocol changes
  - Overall recruitment status changes
  - Results may be added or changed
- All changes are publicly “tracked”

How Are Results Reported?

- Tables are “constructed” by the data provider
  - Columns are pre-set as study arms, but can be changed by the data provider
  - Rows are measures—some are pre-set, others are customized for each study
  - Type of measure determines specific design of “cells”
- Attempt to balance fixed structure with flexibility

Results:Outcome Overview: **Edit Outcome Measure**

Title: Crossover Study Example: Drug A vs. Placebo ID: 1122

Outcome Measure Type* Primary

Outcome Measure Reporting Status* Indicate whether posting results data for this outcome measure. At least one outcome in each record must be "Posted".

Posted

Anticipated Posting Date If the Reporting Status is "Not Posted", please enter a month and 4 digit year for the anticipated posting date.

Month: -- Please Select -- Year:

Outcome Measure Title* change in diastolic blood pressure

Outcome Measure Time Frame* 3 months

Outcome Measure Description* -- Please Select --
Number
Mean
Median
Least Squares Mean
Geometric Mean
Log Mean

...inus value at baseline.

Safety Issue (FDAAA) ...e assessing a safety issue?

Measure Type* Mean

Measure of Dispersion* Please select "Not Applicable" if the Measure Type is "Number". Please do NOT select "Not Applicable" for other measure types.

95% Confidence Interval

Unit of Measure* -- Please Select --
Not Applicable
Standard Deviation
Inter-Quartile Range
Full Range
Standard Error
95% Confidence Interval

...mber", the Unit of Measure is typically "participants".

Statistical Test of Hypothesis:

P-Value: (e.g. <0.01) <0.04

If desired, provide additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance.

Two-sided

Method: Other

If other, please specify: Paired t-test

-- Please Select --
ANCOVA
ANOVA
Chi-squared
Chi-squared, Corrected
Cochran-Mantel-Haenszel
Fisher Exact
Kruskal-Wallis
Log Rank
Mantel Haenszel
McNemar
Mixed Models Analysis
Regression, Cox
Regression, Linear
Regression, Logistic
Sign test
t-test, 1 sided
t-test, 2 sided
Wilcoxon (Mann-Whitney)
Other

nt information, such as adjustments or degrees of freedom.

Statistics on Registration and Results Reporting[1] by Data Provider Class

(as of 12/2010)

	FDAAA Registration Analysis			FDAAA Results Analysis		All Studies
Data Provider	**Registered Applicable Clinical Trials (ACTs)[2]**	**"Responsible Party" Listed**	**"Primary Completion Date" Listed**	**Registered ACTs that Appear to Need Results, Certifications, or Extensions[3]**	**ACTs with Posted Results, Certifications, or Extensions**	**Total Results Submitted[4]**
Industry	14,609	12,057 (83%)	11,387 (78%)	5,236	1,689 (32%)	2,613
NIH	5,450	1,894 (35%)	2,605 (48%)	905	36 (4%)	82
Other	18,179	15,677 (86%)	15,506 (85%)	5,239	199 (4%)	816
NCI	3,681	838 (23%)	1,553 (42%)	604	0 (0%)	0

[1] All data as of November 3, 2010

[2] Includes registered interventional studies of drugs, biologics, and devices that are "not phase 0/1" with either a Primary Completion Date ≥1/2008 or Study Completion Date ≥ 1/2008 or both completion dates missing.

[3] Based on estimated registered Applicable Clinical Trials with a Primary Completion Date prior to December 2009

[4] Submitted includes all "posted" and "not yet posted" records that may not be subject to FDAAA. Results are reviewed by NLM prior to posting and most records require one or more revisions.

Issues in Reporting Results

ICJME

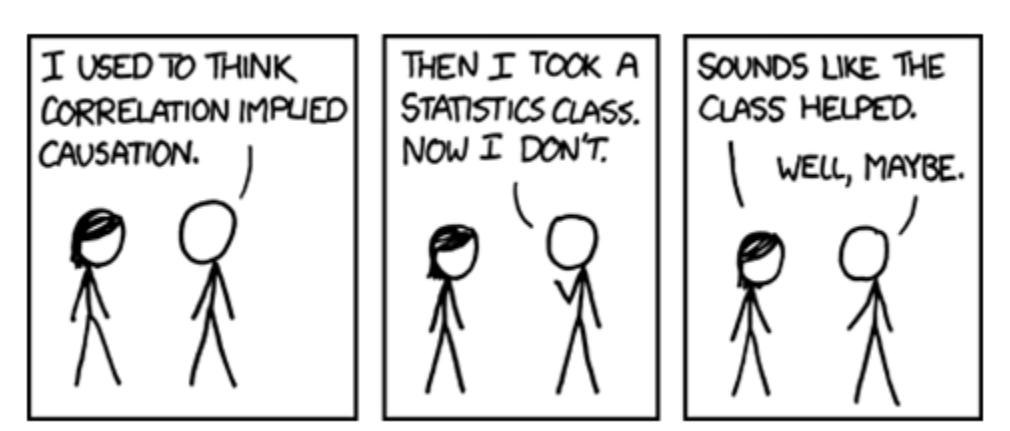
"…will not consider results posted in the same primary clinical trials register in which the initial registration resides as previous publication if the results are presented in the form of a brief, structured (<500 words) abstract or table."

[NOTE: About 53% of results records have associated publications in PubMed (11/2010)]

Quality Standards

- Tables should convey study design, conduct and analysis
- Data must make sense
  - Measure name, units, and data must match
  - No invalid entries
  - No illogical tables
  - No missing parameters or data

NEED FOR RIGOR AND PRECISION



Source: http://xkcd.com/552/

Problems with Entries

- Unclear/imprecise entries (% reduction: - 40%)
- Illogical entries (time to survival)
- Internal inconsistencies (enrollment does not match participant flow)
- Invalid entries (823 hours/day sleep)
- Data mismatch (time to response: 12 participants)
- Structure does not make sense
  - arms (and participants) come and go
- Inconsistent with other information about study
  - Randomized studies cannot have only one arm

Ambiguity of Language

Term

- "Frequency"
- "Rate"
- "Incidence" (*for # participants*)

Entered Value

- "33"
  - People?
  - Weekly events?
  - Percent?

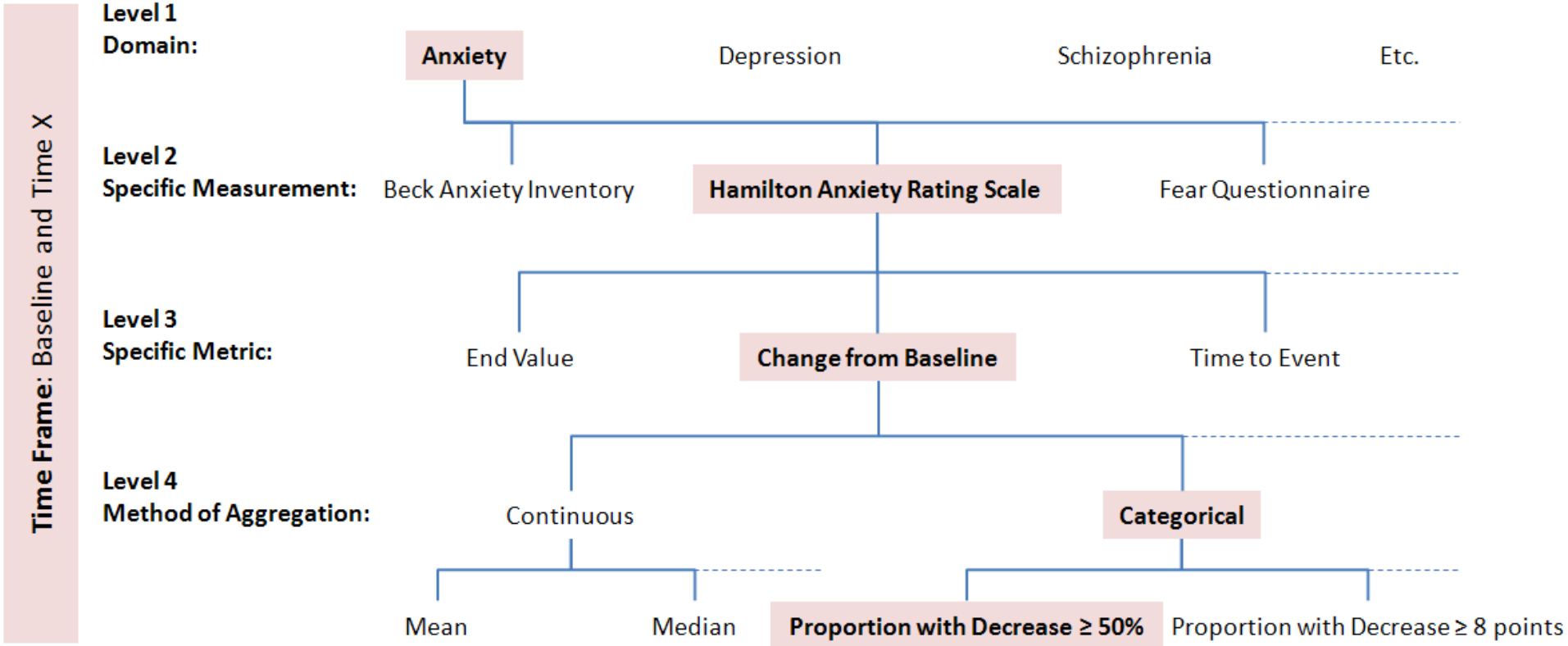
- "Percentage"

- "0.75"
  - 75%?
  - 0.75%?

Outcome Measure Statistics ClinicalTrials.gov (as of 9/27/10)

- 2,178 Clinical trial results records posted
- 2,178 Records with 4,376 Primary OMs
  - Mean: 2.0
  - Median: 1
  - Range: 1-71
- 1,639 Records w/ 12,509 Secondary OMs
  - Mean: 5.7
  - Median: 3
  - Range: 0-122

"Other Pre-specified": 119 Records, 424 OMs, Range: 0-31
"Post-Hoc": 43 Records, 84 OMs, Range: 0-6


Time Frame: Baseline and Time X
Level 1
Domain:
Anxiety
Depression
Schizophrenia
Etc.
Level 2
Specific Measurement:
Beck Anxiety Inventory
Hamilton Anxiety Rating Scale
Fear Questionnaire
Level 3
Specific Metric:
End Value
Change from Baseline
Time to Event
Level 4
Method of Aggregation:
Continuous
Categorical
Mean
Median
Proportion with Decrease ≥ 50%
Proportion with Decrease ≥ 8 points

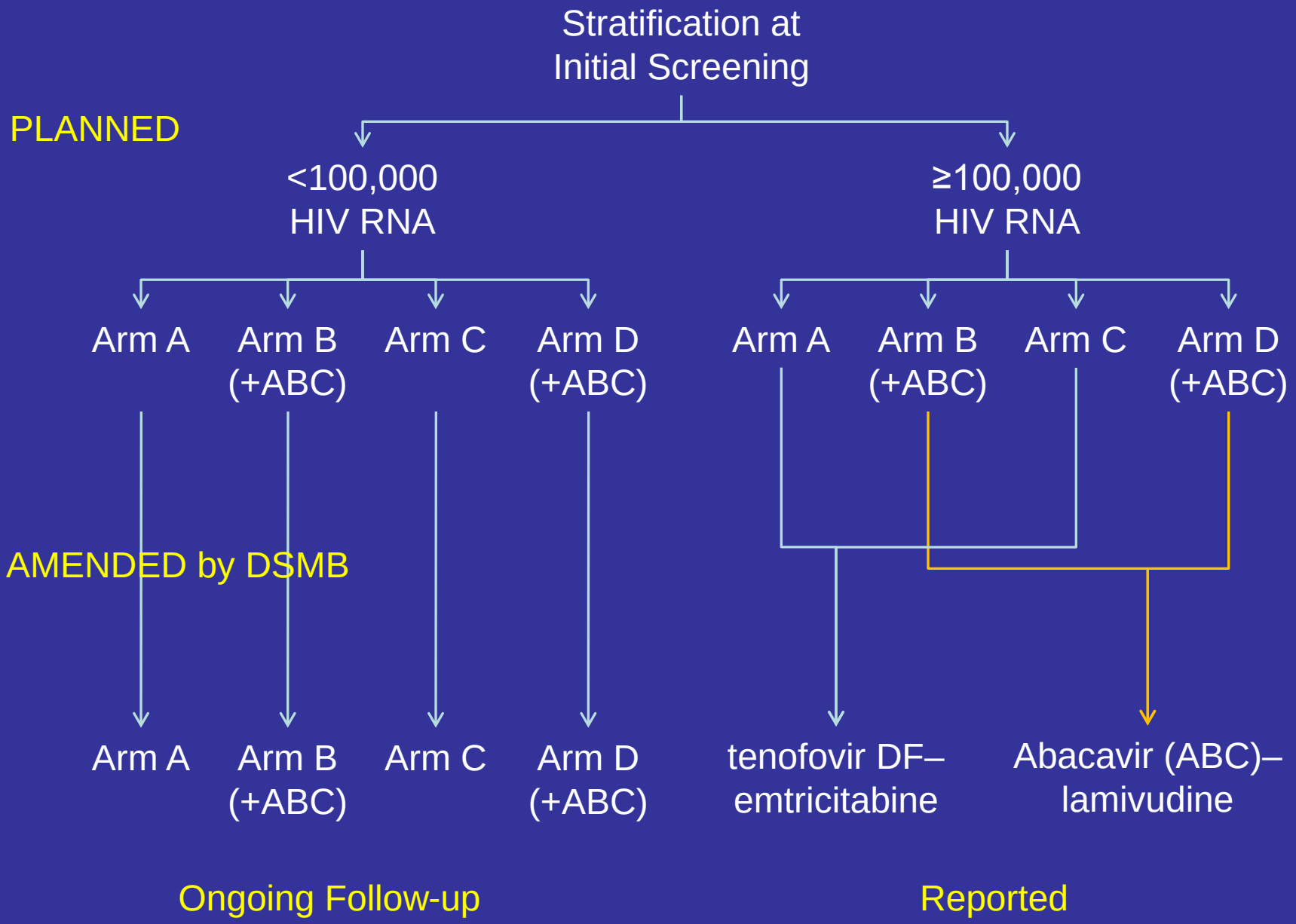
Structural Changes to Studies

- Arms come and go
- Participants come and go
- Participant Flow and Baseline Characteristics Tables describe different population than the Outcomes Tables
- Data providers cannot explain the “denominators”

Table 1. Baseline Characteristics of the Patients.*

Variable	Abacavir–Lamivudine (N = 398)	Tenofovir DF–Emtricitabine (N = 399)	Total (N = 797)
Sex — no. (%)			
Male	331 (83)	345 (86)	676 (85)
Female	67 (17)	54 (14)	121 (15)
Age — yr			
Median	38	40	39
Interquartile range	32–45	32–46	32–45
Age group — no. (%)			
16–19 yr	3 (1)	2 (1)	5 (1)
20–29 yr	77 (19)	68 (17)	145 (18)
30–39 yr	143 (36)	121 (30)	264 (33)
40–49 yr	121 (30)	142 (36)	263 (33)
50–59 yr	41 (10)	54 (14)	95 (12)
>59 yr	13 (3)	12 (3)	25 (3)
Race or ethnic group — no. (%)†‡			
White	170 (43)	202 (51)	372 (47)
Black	112 (28)	94 (24)	206 (26)
Hispanic	103 (26)	93 (23)	196 (25)
Asian or Pacific Islander	5 (1)	5 (1)	10 (1)
Native American or Alaskan Native	1 (<1)	1 (<1)	2 (<1)
Mixed race	7 (2)	3 (1)	10 (1)

Arms	Assigned Interventions
1: Experimental Participants will receive EFV, FTC/TDF, and placebo for ABC/3TC for 96 weeks	Drug: Efavirenz 600 mg tablet taken orally daily Drug: Emtricitabine/Tenofovir disoproxil fumarate 200 mg emtricitabine/300 mg tenofovir disoproxil fumarate tablet taken orally daily Drug: Abacavir/Lamivudine placebo Placebo tablet taken orally daily
2: Experimental Participants will receive EFV, placebo for FTC/TDF, and ABC/3TC for 96 weeks	Drug: Abacavir/Lamivudine 600 mg abacavir/300 mg lamivudine tablet taken orally daily Drug: Efavirenz 600 mg tablet taken orally daily Drug: Emtricitabine/Tenofovir disoproxil fumarate placebo Placebo tablet taken orally daily
3: Experimental Participants will receive RTV-boosted ATV, FTC/TDF, and placebo for ABC/3TC for 96 weeks	Drug: Atazanavir 300 mg tablet taken orally daily Drug: Emtricitabine/Tenofovir disoproxil fumarate 200 mg emtricitabine/300 mg tenofovir disoproxil fumarate tablet taken orally daily Drug: Ritonavir 100 mg tablet taken orally daily Drug: Abacavir/Lamivudine placebo Placebo tablet taken orally daily
4: Experimental Participants will receive RTV-boosted ATV, placebo for FTC/TDF, and ABC/3TC for 96 weeks	Drug: Abacavir/Lamivudine 600 mg abacavir/300 mg lamivudine tablet taken orally daily Drug: Atazanavir 300 mg tablet taken orally daily Drug: Ritonavir 100 mg tablet taken orally daily Drug: Emtricitabine/Tenofovir disoproxil fumarate placebo Placebo tablet taken orally daily


Stratification at Initial Screening
PLANNED
<100,000 HIV RNA
≥100,000 HIV RNA
Arm A
Arm B (+ABC)
Arm C
Arm D (+ABC)
Arm A
Arm B (+ABC)
Arm C
Arm D (+ABC)
AMENDED by DSMB
Arm A
Arm B (+ABC)
Arm C
Arm D (+ABC)
tenofovir DF–emtricitabine
Abacavir (ABC)–lamivudine
Ongoing Follow-up
Reported

Interventional or Observational?

- Key features of “interventional”
  - Investigator assigns participants to interventions
  - Interventions occur as the result of participation in a study with a protocol, and would not occur in the same manner if not in the study
- Example: Evaluation of PillCam™ Colon Capsule Endoscopy (PCCE) in the Visualization of the Colon

Alzheimer's Study: Is this interventional?

- Longitudinal study of a cohort of adults at high risk of AD
- All participants receive several diagnostic tests at varying intervals, including:
  - Regular, periodic PET scan for the PiB marker
  - Comparison with MRI markers of small vessel disease
  - Assessment of cognitive decline in patients

Device or Procedure?

- What Is the Intervention Type?
  - Device vs. Procedure/Surgery (e.g., imaging)
  - Drug vs. Procedure (e.g., Cell Therapy)
- Example: The Stress Incontinence Surgical Treatment Efficacy Trial
  - Burch Colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence
  - Albo ME et al. NEJM (2007)

Studies Involving Genetic Tests

- Study Title: “Genotype Based Personalized Prescription of Nevirapine (GENPART)” [NCT00986063]
  - Primary Outcome Measure: “…incidences of nevirapine-associated rashes” between
    - Genetic Test Group: “nevirapine, **guided by genetic tests**”
    - Control Group: “standard of care approach”
  - Study of a Drug or Device (i.e., genetic test)?

Genetic Counseling in Women at Risk for BRCA1 or BRCA2 Mutations

This study is ongoing, but not recruiting participants.

First Received: December 27, 2006 Last Updated: March 7, 2009 History of Changes

Sponsor:	Lombardi Cancer Research Center
Collaborator:	National Cancer Institute (NCI)
Information provided by:	National Cancer Institute (NCI)
ClinicalTrials.gov Identifier:	NCT00416754

Purpose

RATIONALE: Genetic counseling and using an interactive computer program may help women at risk for breast cancer make medical decisions about treatment.

PURPOSE: This randomized clinical trial is studying standard genetic counseling to see how well it works when given together with or without a medical decision-making computer program in women at risk for BRCA1 or BRCA2 mutations.

Condition	Intervention
Breast Cancer	Other: counseling intervention

Study Type: Interventional
Study Design: Allocation: Randomized
Primary Purpose: Screening

Official Title: Improving the Long-Term Outcomes of BRCA1/BRCA2 Mutation Testing

Preliminary Findings: Fidelity to Protocol

- Structure of trial
  - Arms come and go
  - Participants come and go
  - Definition of “trial” is fluid
- Outcome measures
  - Primary vs. secondary vs. ???
  - Content of outcome measure
- Analysis Population
  - Up to 25 different “denominators” for a single study arm in a trial
  - 24% trials reported results involving ≤ 90% of all participants

Examples of Discrepant Primary Outcome Measures

- Specific Measure
  - “Time to progression” [unit of time] vs. “progression-free survival” [# participants]
  - “Time to the first [event]” vs. number of events
  - “[unprotected and protected] Sexual activities with main male partner” vs. unprotected only
- Time Frame
  - “fortnightly” [q 2 weeks] vs. “4 weeks”
  - “1 and 3 month post-injection” vs. “at one month”

The Effect of Testosterone on Mood and Quality of Life

This study has been completed.

Study NCT00202462 Information provided by Seattle Institute for Biomedical and Clinical Research
First Received: September 12, 2005 Last Updated: September 30, 2008 History of Changes

Tracking Information

First Received Date ICMJE	September 12, 2005
Last Updated Date	September 30, 2008
Start Date ICMJE	November 2002
Current Primary Outcome Measures ICMJE (submitted: September 30, 2008)	Hamilton Depression Rating Scale [Time Frame: 12 and 24 weeks] [Designated as safety issue: No]
Original Primary Outcome Measures ICMJE (submitted: September 12, 2005)	• SCL-20 • Endicott Quality of Life Scale
Change History	Complete list of historical versions of study NCT0020246

POMs registered on 9/12/05

"The primary outcome measure was the change in the Hamilton Rating Scale for Depression (HAM-D) score from baseline to the end of the double-blind phase."

Study Completion Date: November 2006

J Clin Psychiatry. 2009 Jul;70(7):1009-16.

A Randomized, Double-Blind, Placebo-Controlled Study of Testosterone Treatment in Hypogonadal Older Men With Subthreshold Depression (Dysthymia or Minor Depression)

Molly M. Shores, M.D.; Daniel R. Kivlahan, Ph.D.; Tatiana I. Sadak, Ph.C.; Ellen J. Li, M.D.; and Alvin M. Matsumoto, M.D.

Objective: Hypogonadism and subthreshold depression are common conditions in elderly men.

12 weeks, followed by a 12-week open-label extension phase during which all subjects received 7.5 g of testosterone gel. The primary outcome measure was the change in the Hamilton Rating Scale for Depression (HAM-D) score from baseline to the end of the double-blind phase. Secondary outcome measures were remission of subthreshold depression (defined a priori as a HAM-D score ≤7) and changes in the Hopkins Symptom Checklist depression scale, the Medical Outcomes Study 36-Item Short-Form Health Survey, and the short-form 16-item Quality of Life Enjoyment and Satisfaction Questionnaire.

Received June 17, 2008; accepted August 22, 2008. From the Geriatric Research, Education, and Clinical Center (Drs. Shores and Matsumoto) and the Center of Excellence in Substance Abuse Treatment and Education (Dr. Kivlahan), Veterans Affairs (VA) Puget Sound Health Care System, Seattle, Wash.; and the Department of Psychiatry and Behavioral Sciences (Drs. Shores, Kivlahan, and Li), the School of Nursing (Ms. Sadak), and the Division of Gerontology and Geriatric Medicine, Department of Medicine (Dr. Matsumoto), University of Washington, Seattle.

Supported by the VA Geriatric Research, Education, and Clinical Center; the American Federation on Aging Research; and Solvay Pharmaceuticals, Inc. Solvay provided testosterone and placebo gels for the study and funding to support a research assistant. The funding agencies had no role in the design or analysis of the study results.

Presented at the 6th World Congress on The Aging Male, February 21–24, 2008, Tampa, Fla., and the annual meeting of the American Association of Geriatric Psychiatry, March 1–4, 2007, New Orleans, La.

The authors thank Margaret Moroz, A.A., and Brett T. Marck, B.S., who provided technical assistance. Ms. Moroz and Mr. Marck have no pertinent financial disclosures.

Dr. Matsumoto has been a consultant for Solvay, GlaxoSmithKline, GTx, Merck, Tokai, and Amgen and has received grant/research support from GlaxoSmithKline, Solvay, Ardana, Ascend, and Auxilium. Drs. Shores, Kivlahan, and Li and Ms. Sadak report no additional financial affiliations or other relationships relevant to the subject of this article.

Corresponding author and reprints: Molly M. Shores, M.D., VA Puget Sound Health Care System, 1660 S. Columbian Way, S-182GRECC, Seattle, WA 98108 (e-mail: mxs@u.washington.edu).

Androgen deficiency, as defined by a low serum testosterone level, is a common condition in elderly

Preliminary Findings: Oversight
(Clinical Trial Results Records Posted on 9/27/10)

- 24% (359/1,509) reporting having a DMC*
  - By Phase**
    - 23% (125/535) – up to Phase 2
    - 27% (142/520) – Phase 2/3 or 3
    - 15% (45/298) – Phase 4
  - By Lead Sponsor Class
    - 17% (195/1,164) – Industry
    - 48% (164/345) – Non-Industry
- Of 1,730 reporting having "Certain Agreements"
  - 8% (132/1,730) impose embargoes ≤60 days
  - 16% (280/1,730) impose embargoes >60 and <180 days
  - 76% (1,318/1,730) describe "other" restrictions

*Optional data element **156 records do not report Phase information

Issues to Consider in Determining Reporting Burden

- What's the starting point?
  - Which data points are not routinely calculated or determined at the end of a study?
- Heterogeneity of trials
  - Complexity of trial design/structure
  - # arms (1-16)
  - # outcome measures (1-124)
  - # statistical analyses (0-50)
- Status of existing data management system
  - Many sponsors upload registry data
  - Others upload AEs

Minimal Results Data Set
(all results reported by arm)

- Participant Flow
  - Number Started
  - Number Completed
- Baseline Characteristics
  - Number of Participants
  - Age and Gender
- Outcome Measures
  - Summary results for Primary and Secondary OMs
  - Statistical analyses, as appropriate
- Adverse Events
  - “Serious” and “Other” by Organ System

Three Components of Successful Results Data Entry

- Familiarity with the system
  - Initial (steep) learning curve
- Clinical trial expertise
  - Including knowledge of specific trial
- Relevant data from the trial

Efforts to Improve Compliance

- Ongoing outreach and educational efforts
- Better resource materials
- Informational Messages

Sample Message
(FDAAA Registration Data Element Missing)

ClinicalTrials.gov Records and FDAAA Requirements

Message generated by ClinicalTrials.gov Protocol Registration System

---

NOTE: Each ClinicalTrials.gov record below either lists a date for the final data collection of the primary outcome measure (currently, the "Primary Completion Date" field in ClinicalTrials.gov) that is more than 12 months in the past or is missing an entry for this field. Please be aware that, under FDAAA, results of certain "applicable clinical trials" involving FDA-regulated drugs, biological products, or devices must be reported to ClinicalTrials.gov within 12 months of this date. The Responsible Party is encouraged to take the following steps, as appropriate, if this trial is an "applicable clinical trial":

a. check that the "Primary Completion Date" and other items in the registry record are accurate and update if necessary; and, if appropriate,

b. enter results in the PRS if required; OR

c. consider the "delayed reporting" options at http://prsinfo.clinicaltrials.gov/DelayedSubmission.html.

EMA Requirements

- Publically Accessible Results Database
  - Required no later than 6 months after trial completion (i.e., last patient, last visit)
  - Applies to EU-regulated clinical trials of medicines, **regardless of authorization status**
  - Applies to trials of pediatric and adult drugs
- Interaction to harmonize EudraCT and ClinicalTrials.gov databases & *policies*

Issues for Academic Medical Centers

- Legal/regulatory issues related to RP and compliance
- Support for PIs who must report data
  - Help with system training
  - Provide appropriate biostatistical support
- Are trials becoming too complex?
- Are roles clear? (Who is responsible?)
- Emphasize clinical epidemiology principles in student and researcher training programs

Bottom Line

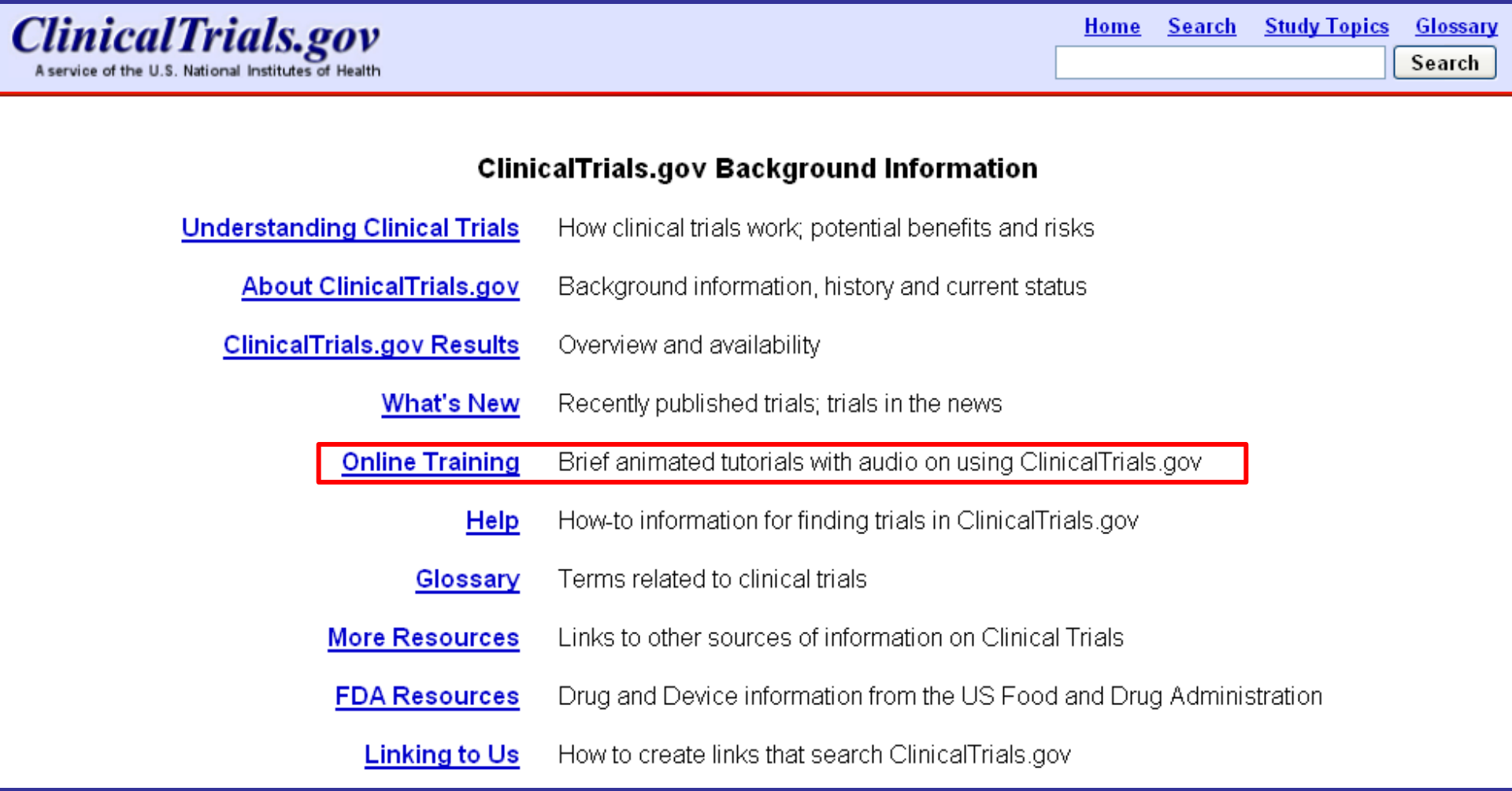
- Determine who is the Responsible Party
- Register prior to enrollment (or within 21d):
  - Phase 2-4 interventional trials that include a drug, device or biologic
  - Regardless of whether or not the trial is being used to support an FDA application
- Report results:
  - Any trial described above once the drug, device or biologic has been approved; OR
  - Within one year of “primary completion date”
- Keep all information up to date!

In Sum

- National (international) experiment
- System before FDAAA was not working (with regard to dissemination of trial information)
- Structured database complements journal publications
- Requires and reinforces knowledge of basic principles of clinical epidemiology
- We are here to help

Resources

Help for Users



http://clinicaltrials.gov/ct2/info

United States
National Library of Medicine
National Institutes of Health

Search NLM Web Site
Go
NLM Home | Contact NLM | Site Map | FAQs

Home > Training & Outreach > Distance Education Resources

ClinicalTrials.gov Online Training

Quick Tour

Return to ClinicalTrials.gov

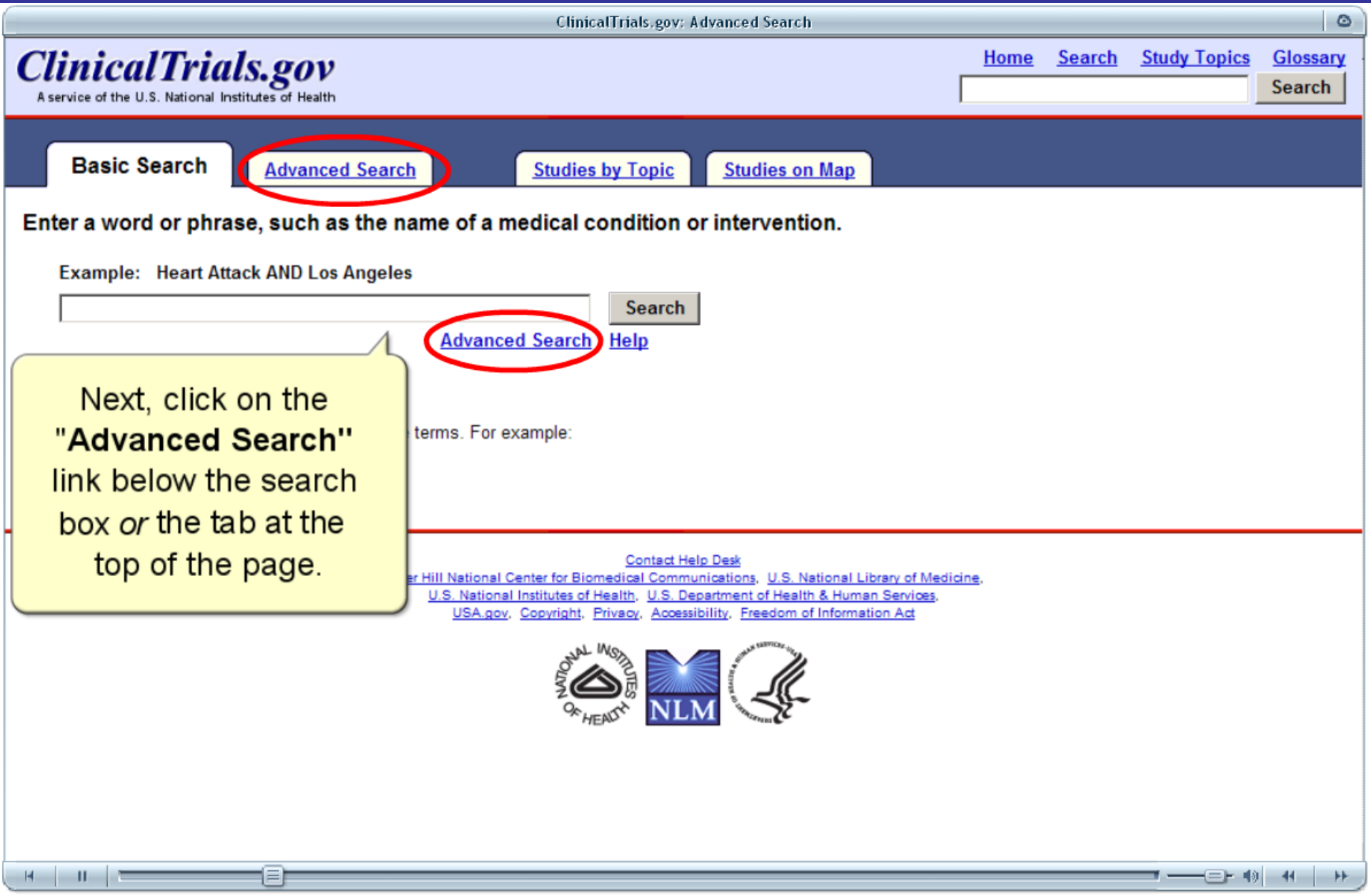
The following are brief animated tutorials with audio for using the ClinicalTrials.gov. Running times are rounded to the nearest minute. Click on the link to launch the tour.

- Basic Search (3 min., March 2010)
- Clinical Study Details (2 min., March 2010)
- Customize Your Display (2 min., March 2010)
- Advanced Search (3 min., March 2010)
- Refine a Search (2 min., March 2010)
- Downloading Search Results (4 min., March 2010)
- RSS Feed Setup for a Search (2 min., March 2010)

The above demos require the Adobe Flash™ Player. They were created using Qarbon Viewlet Builder™.

Last updated: 26 March 2010
First published: 26 March 2010
Metadata| **Permanence level:** Permanence Not Guaranteed

http://www.nlm.nih.gov/bsd/viewlet/ct/index.html


ClinicalTrials.gov: Advanced Search
ClinicalTrials.gov
A service of the U.S. National Institutes of Health
Home
Search
Study Topics
Glossary
Search
Basic Search
Advanced Search
Studies by Topic
Studies on Map
Enter a word or phrase, such as the name of a medical condition or intervention.
Example: Heart Attack AND Los Angeles
Search
Advanced Search
Help
terms. For example:
Next, click on the "Advanced Search" link below the search box or the tab at the top of the page.
Contact Help Desk
U.S. National Library of Medicine,
U.S. National Institutes of Health,
U.S. Department of Health & Human Services,
USA.gov,
Copyright,
Privacy,
Accessibility,
Freedom of Information Act
NATIONAL INSTITUTES OF HEALTH
NLM

Help for Trial Sponsors & Investigators

ClinicalTrials.gov
Protocol Registration System

PRS Information

Registration of Clinical Trials

Clinical trials are registered with ClinicalTrials.gov via a web based data entry system called the Protocol Registration System (PRS).

ClinicalTrials.gov allows the reporting of trials that:

- **Are in conformance with any applicable human subject or ethics review regulations (or equivalent) and**
- **Are in conformance with any applicable regulations of the national (or regional) health authority (or equivalent)**

ClinicalTrials.gov facilitates registration of trials in accordance with the International Committee of Medical Journal Editors (ICMJE) initiative requiring prior entry of clinical trials in a public registry as a condition for publication.

Multi-site trials and multi-sponsor trials are susceptible to duplicate registration, thus care must be taken in how the trials are registered. For multi-sponsor trials it is the lead sponsor who should take responsibility for registration. It is critical that investigators and sponsors work together to ensure that a trial is registered once and only once.

http://prsinfo.clinicaltrials.gov

ClinicalTrials.gov
Protocol Registration System

ICMJE Initiative

The International Committee of Medical Journal Editors (ICJME) has established a requirement that all clinical trials be entered in a public registry before the onset of patient enrollment, as a condition of consideration for publication.

ClinicalTrials.gov provides a vehicle which allows organizations and individuals to provide the data requested by ICMJE, which has adopted the World Health Organization (WHO) minimal registration data set.

See the following ICMJE resources for more information:

- ICMJE Web site
- ICMJE FAQ on Trial Registration
- Statement on Clinical Trial Registration (September 2004)

http://prsinfo.clinicaltrials.gov/icmje.html

ClinicalTrials.gov
Protocol Registration System

PRS and U.S. Public Law 110-85

General Requirements

U.S. Public Law 110-85 (Food and Drug Administration Amendments Act of 2007 or FDAAA), Title VIII, Section 801 mandates that a "responsible party" (i.e., the sponsor or designated principal investigator) register and report results of certain "applicable clinical trials":

> **Trials of Drugs and Biologics**: Controlled, clinical investigations, other than Phase I investigations, of a product subject to FDA regulation;
>
> **Trials of Devices**: Controlled trials with health outcomes of a product subject to FDA regulation (other than small feasibility studies) and pediatric postmarket surveillance studies.

"Applicable clinical trials" generally include interventional studies (with one or more arms) of drugs, biological products, or devices that are subject to FDA regulation, meaning that the trial has one or more sites in the U.S, involves a drug, biologic, or device that is manufactured in the US (or its territories), or is conducted under an investigational new drug application (IND) or investigational device exemption (IDE). For the complete statutory definitions and more detailed information on the agency's current thinking about their meaning, see this pdf document.

http://prsinfo.clinicaltrials.gov/fdaaa.html

Additional Background

- Tse T, Williams RJ, Zarin DA. Update on registration of clinical trials in ClinicalTrials.gov. *Chest* 2009;136:304-5.
- Tse T, Williams RJ, Zarin DA. Reporting basic results in ClinicalTrials.gov. *Chest* 2009;136:295-303.
- Zarin DA, Tse T. Moving toward transparency of clinical trials. *Science* 2008;319:1340-2.
- Wood AJ. Progress and deficiencies in the registration of clinical trials. *N Engl J Med* 2009;360:824-30.

Additional Information

- Email LISTSERV and other FDAAA information:
  - http://prsinfo.clinicaltrials.gov/fdaaa.html
- Other general information:
  - http://prsinfo.clinicaltrials.gov
- Questions?
  - register@clinicaltrials.gov

http://prsinfo.clinicaltrials.gov/fdaaa.html

"Basic Results" Database

- Pre-Submission Checklist (pdf) (DRAFT) - a short reminder checklist to assist in results data entry
- Common errors (pdf) (DRAFT) - overview of common types of errors identified in submitted records with "basic results"
- Helpful hints (pdf) - tips on entering results data, including three examples of common study models (parallel design, crossover design, and diagnostic accuracy studies), reporting measure types, including information on reporting outcomes measured with a scale.
- "Basic Results" Data Element Definitions (DRAFT) - details on the information that is entered about results via the PRS.
- Detailed Review Items (pdf) (DRAFT) - describes items evaluated by the Quality Assurance/Quality Control staff at ClinicalTrials.gov after results have completed high-level review.
- Basic Results Provisions - extracted from FDAAA 801.
- Delayed Submission of Results - information on submitting certifications or requests for extension
- Recorded Presentation (Adobe Flash: 37 minutes) and accompanying slides (pdf)
  - Module 1: ClinicalTrials.gov Overview and PL 110-85 Requirements
  - Module 2: "Basic Results" Data Entry
  - Module 3: Posted Results at ClinicalTrials.gov