ctgov: A suite of Stata commands for reporting trial results to ClinicalTrials.gov

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July 31, 2014

Outline

U.S. Public Law 110-85 (FDAAA)

The Food and Drug Administration Amendments Act of 2007 (FDAAA or US Public Law 110-85) was passed on September 27, 2007. The law requires mandatory **registration** and **results** reporting for certain clinical trials of drugs, biologics, and devices.

U.S. Public Law 110-85 (FDAAA)

(C) BASIC RESULTS

(i) DEMOGRAPHIC AND BASELINE CHARACTERISTICS OF PATIENT SAMPLE. A table of the demographic and baseline data collected overall and for each arm of the clinical trial to describe the patients who participated in the clinical trial, including the number of patients who dropped out of the clinical trial and the number of patients excluded from the analysis, if any.

(ii) PRIMARY AND SECONDARY OUTCOMES. The primary and secondary outcome measures as submitted under paragraph (2)(A)(ii)(I)(II), and a table of values for each of the primary and secondary outcome measures for each arm of the clinical trial, including the results of scientifically appropriate tests of the statistical significance of such outcome measures. Note: includes SAEs and AEs occurring at a frequency greater than a pre-defined threshold (5% is default).

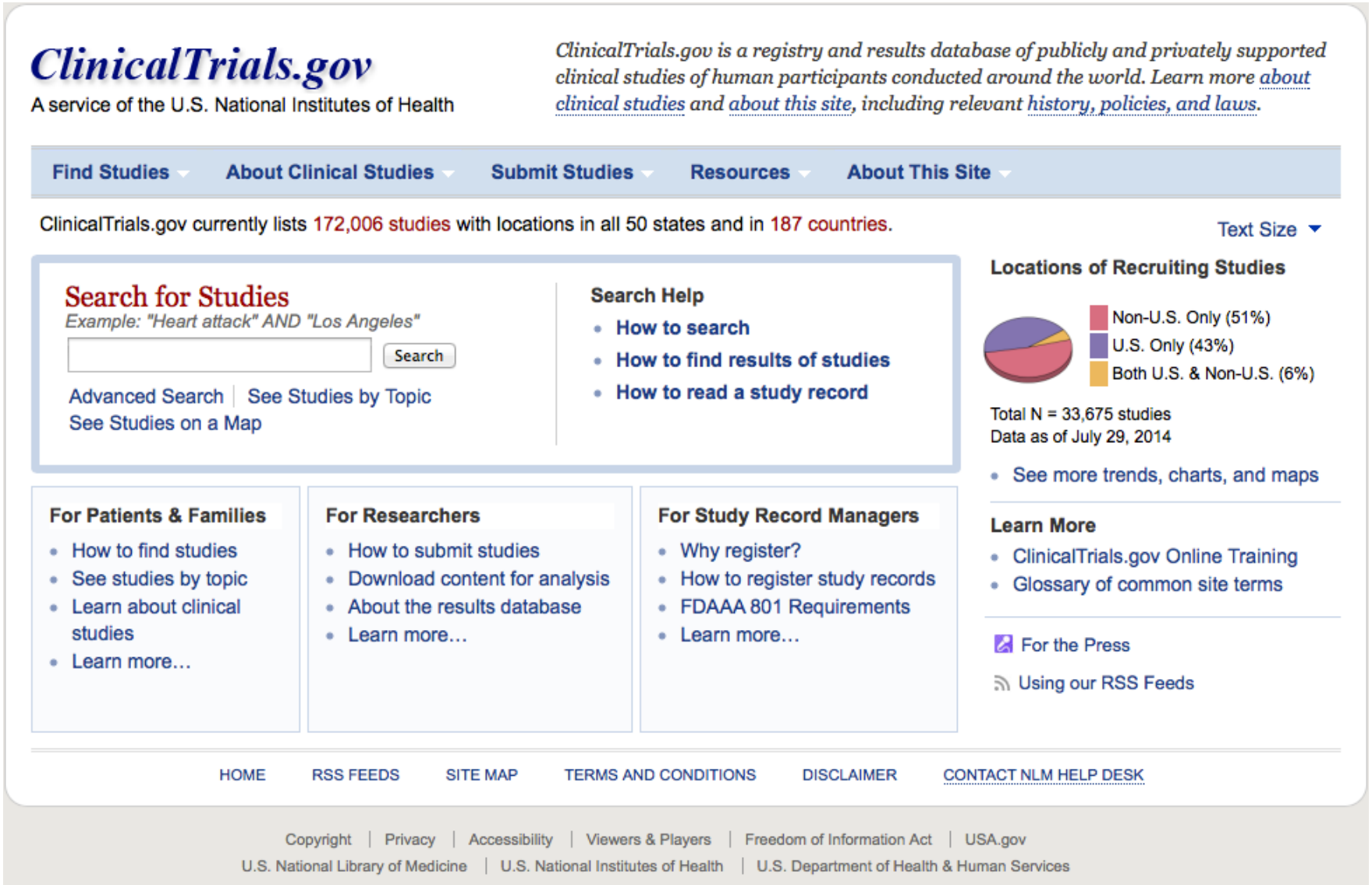
U.S. Public Law 110-85 (FDAAA)

(C) BASIC RESULTS (cont.)

(iii) POINT OF CONTACT. A point of contact for scientific information about the clinical trial results.

(iv) CERTAIN AGREEMENTS. Whether there exists an agreement [...] that restricts in any manner the ability of the principal investigator [...] to publish in a scientific or academic journal information concerning the results of the trial.

ClinicalTrials.gov



ClinicalTrials.gov
A service of the U.S. National Institutes of Health

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world. Learn more about clinical studies and about this site, including relevant history, policies, and laws.

Find Studies | About Clinical Studies | Submit Studies | Resources | About This Site

ClinicalTrials.gov currently lists 172,006 studies with locations in all 50 states and in 187 countries.

Text Size

Search for Studies
Example: "Heart attack" AND "Los Angeles"
Search
Advanced Search | See Studies by Topic
See Studies on a Map

Search Help
- How to search
- How to find results of studies
- How to read a study record

Locations of Recruiting Studies
Non-U.S. Only (51%)
U.S. Only (43%)
Both U.S. & Non-U.S. (6%)
Total N = 33,675 studies
Data as of July 29, 2014
- See more trends, charts, and maps

For Patients & Families
- How to find studies
- See studies by topic
- Learn about clinical studies
- Learn more…

For Researchers
- How to submit studies
- Download content for analysis
- About the results database
- Learn more…

For Study Record Managers
- Why register?
- How to register study records
- FDAAA 801 Requirements
- Learn more…

Learn More
- ClinicalTrials.gov Online Training
- Glossary of common site terms

For the Press
Using our RSS Feeds

HOME | RSS FEEDS | SITE MAP | TERMS AND CONDITIONS | DISCLAIMER | CONTACT NLM HELP DESK

Copyright | Privacy | Accessibility | Viewers & Players | Freedom of Information Act | USA.gov
U.S. National Library of Medicine | U.S. National Institutes of Health | U.S. Department of Health & Human Services

ClinicalTrials.gov (cont.)

- Trial registration (before trial opens)
  - Purpose
  - Eligibility
  - Contacts and Locations
  - More Information

ClinicalTrials.gov (cont.)

- Trial registration (before trial opens)
  - Purpose
  - Eligibility
  - Contacts and Locations
  - More Information
- Results (within 1 year of trial completion)
  - Participant Flow
  - Baseline Characteristics
  - Outcome Measures
  - Reported Adverse Events
  - More Information

Example: Parallel Study

Purpose

The purpose of this study is to assess the safety and efficacy of Remuverol for treatment of Condition A.

Condition	Intervention	Phase
Condition A	Drug: Remuverol Drug: Placebo	Phase 3

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Investigator), Randomized, Safety/Efficacy Study

Official Title: A 24-Week Double-Blind Trial of Remuverol in Adults With Condition A

Example: Parallel Study

Participant Flow

Recruitment Details -- *Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations:*

Participants were recruited based on physician referral at 3 academic medical centers between February 2010 and January 2011. The first participant was enrolled in March 2010, and the last participant was enrolled in December 2010.

Reporting Groups

	Description
Remuverol	Participants received Remuverol 15 mg tablet orally twice daily for 24 weeks.
Placebo	Participants received Remuverol placebo tablet orally twice daily for 24 weeks.

Example: Parallel Study

Overall Study

	Remuverol	Placebo
STARTED	101	99
Per Protocol Population Week 12	98	95
Per Protocol Population Week 24	76	81
COMPLETED	80	81
Not Completed	**21**	**18**
Adverse Event	10	8
Withdrawal by Subject	5	4
Protocol Violation	2	2
Lack of Efficacy	1	1
Physician Decision	1	1
Lost to Follow-up	1	2
Pregnancy	1	0

Example: Parallel Study

Baseline Characteristics

Reporting Groups

	Description
Remuverol	Participants received Remuverol 15 mg tablet orally twice daily for 24 weeks.
Placebo	Participants received Remuverol placebo tablet orally twice daily for 24 weeks.

Example: Parallel Study

Baseline Measures

	Remuverol	Placebo	Total
Number of Participants	101	99	**200**
Age Continuous *[units: years]* *Mean ± Standard Deviation*	34.78 ± 9.72	35.34 ± 10.71	**34.98 ± 9.89**
Gender, Male/Female *[units: participants]*			
Female	60	63	**123**
Male	41	36	**77**
Race/Ethnicity, Customized *[units: participants]*			
African	5	4	**9**
Caucasian	90	90	**180**
Hispanic	5	4	**9**
Native American	1	1	**2**

Example: Parallel Study

Region of Enrollment *[units: participants]*			
United States	44	47	**91**
Canada	35	35	**70**
Mexico	22	17	**39**
Study Specific Characteristic [Quebec Task Force Classification of Spinal Disorders] [1] *[units: participants]*			
Class 0 (no pain)	16	14	**30**
Class 1 (pain without radiation)	73	68	**141**
Class 2 (pain with proximal extremity radiation)	12	17	**29**
Study Specific Characteristic [Body Mass Index] *[units: kg/m^2]* *Mean ± Standard Deviation*	26.65 ± 4.50	27.41 ± 4.72	**26.91 ± 4.55**
Study Specific Characteristic [Short Pain Scale (SPS-11) Score] [2]	6.48 ± 1.34	6.57 ± 1.73	**6.52 ± 1.61**

Example: Parallel Study

Outcome Measures

1. Primary Outcome Measure:

Measure Title	**Change From Baseline in Pain on the 11-point Short Pain Scale (SPS-11) at Week 24**
Measure Description	SPS-11 is a validated, self-reported instrument assessing average pain intensity over the past 24 hour period. Possible scores range from 0 (no pain) to 10 (worst possible pain). Change = (Week 24 Score - Baseline score)
Time Frame	Baseline and Week 24
Safety Issue?	No

Population Description -- *Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate:*

Intent to treat population (all participants who received at least one dose of intervention).

Example: Parallel Study

Reporting Groups

	Description
Remuverol	Participants received Remuverol 15 mg tablet orally twice daily for 24 weeks.
Placebo	Participants received Remuverol placebo tablet orally twice daily for 24 weeks.

Measured Values

	Remuverol	Placebo
Number of Participants Analyzed	101	99
Change From Baseline in Pain on the 11-point Short Pain Scale (SPS-11) at Week 24 *[units: units on a scale]* Mean ± Standard Error	-3.84 ± 0.61	-2.08 ± 0.51

Example: Parallel Study

Statistical Analysis 1 for Change From Baseline in Pain on the 11-point Short Pain Scale (SPS-11) at Week 24

Groups	Remuverol, Placebo
Method	t-test, 2 sided
P-Value	0.002

Additional details about the analysis, such as null hypothesis and power calculation:

> It was calculated that 200 participants randomized in a 1:1 fashion between the 2 arms would have at least 85% power to detect a difference of 0.56 points in mean SPS-11 pain score between Remuverol and placebo from baseline to week 24. Sample size was determined using a 2-sided 2-sample t test ($\alpha = 0.05$). Assumptions included a common standard deviation of 1.14 and a discontinuation rate of 7%.

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

> [Not specified.]

Other relevant information, such as adjustments or degrees of freedom:

> [Not specified.]

Example: Parallel Study

Reported Adverse Events

Reporting Groups

	Description
Remuverol	Participants received Remuverol 15 mg tablet orally twice daily for 24 weeks.
Placebo	Participants received Remuverol placebo tablet orally twice daily for 24 weeks.

Time Frame
Additional Description

Serious Adverse Events

	Remuverol	Placebo
Total # participants affected/at risk	**4/101 (3.96%)**	**0/99 (0%)**
Blood and lymphatic system disorders		
Anemia Iron Deficiency † A		
# participants affected/at risk	1/101 (0.99%)	0/99 (0%)
Idiopathic Thrombocytopenic Purpura † A		
# participants affected/at risk	1/101 (0.99%)	0/99 (0%)

Example: Parallel Study

More Information

Certain Agreements:

All Principal Investigators ARE employed by the organization sponsoring the study.

Limitations and Caveats -- *Limitations of the study, such as early termination leading to small numbers of subjects analyzed and technical problems with measurement leading to unreliable or uninterpretable data:*

[Not specified.]

Results Point of Contact:

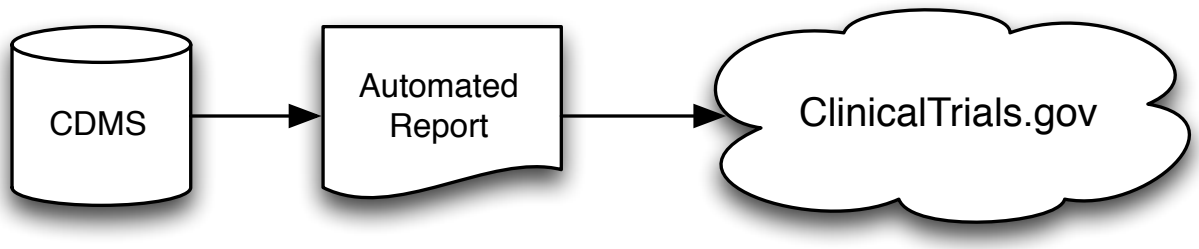
Name/Official Title: PRS Training Lead
Organization: PRS Training
Phone: 555-555-5555
Email: register@clinicaltrials.gov

Problems

- Unfunded mandate (12–16 hours required per protocol)
- Data completeness and quality
- Consistency with primary publication

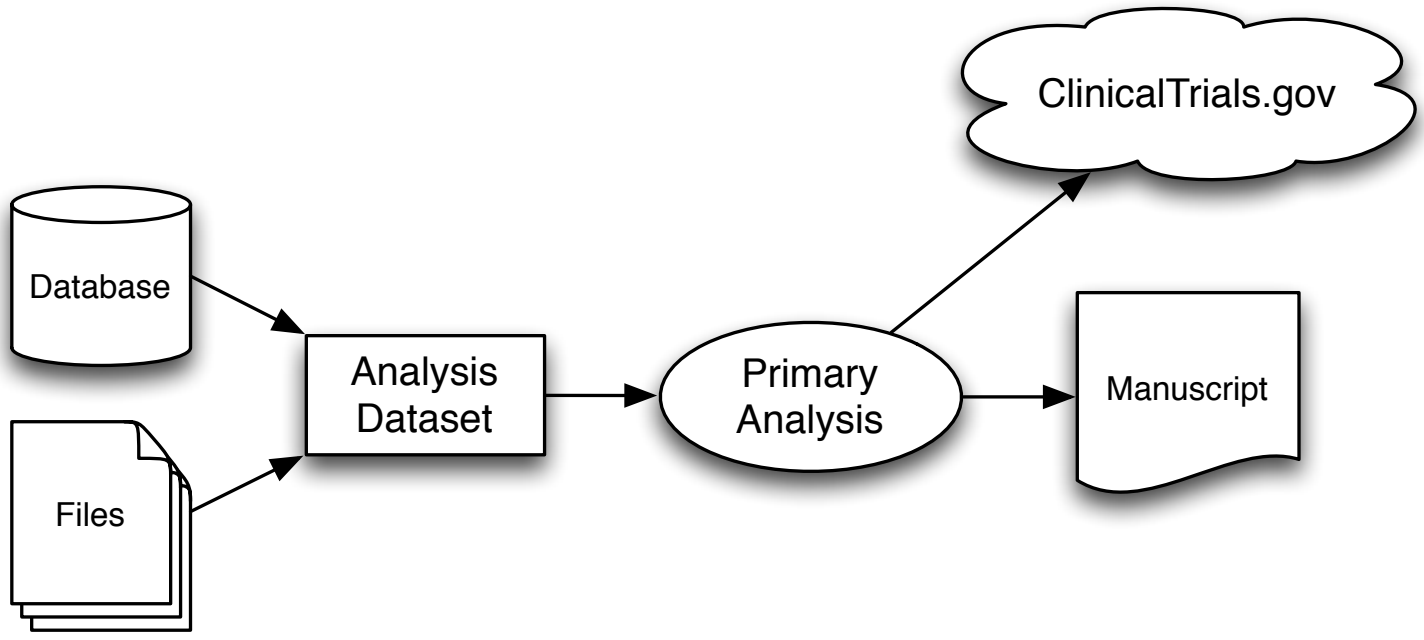
Problems (cont.)

Some drugs companies and cooperative groups pursued the following strategy:

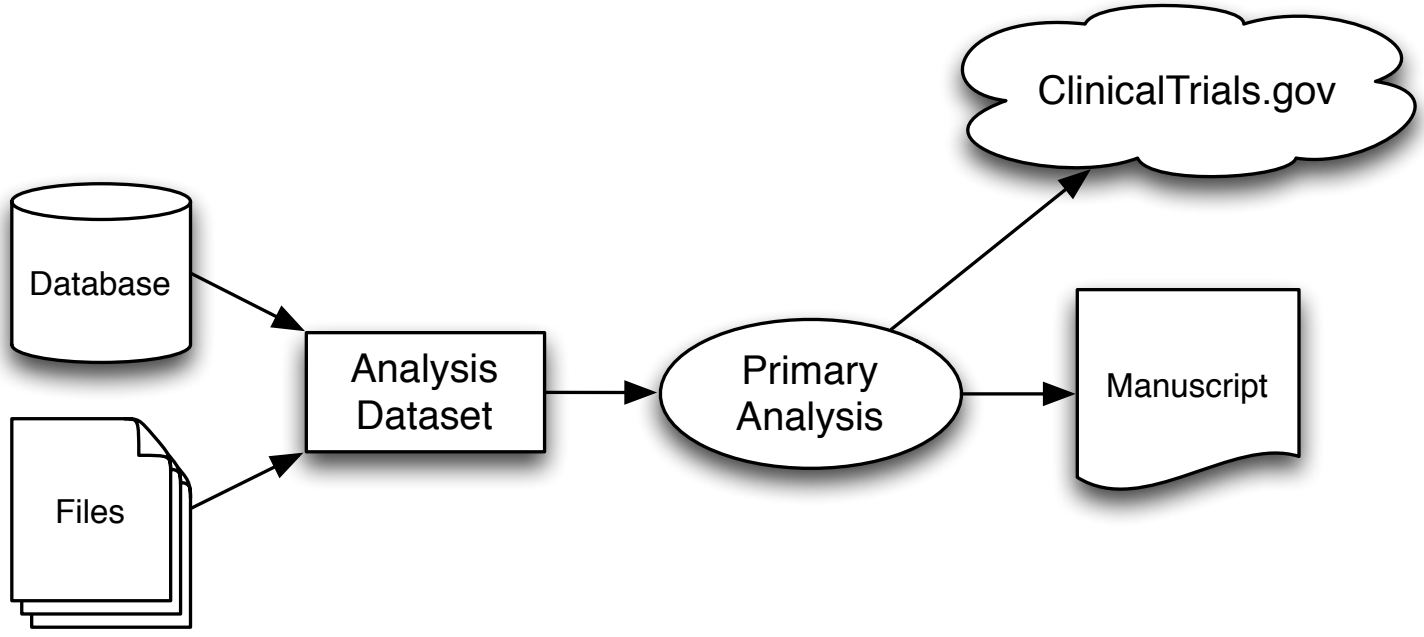


- Requires high quality and complete DB
- Requires programming expertise
- Outcomes difficult to automate

Incorporate ClinicalTrials.gov reporting into data analysis

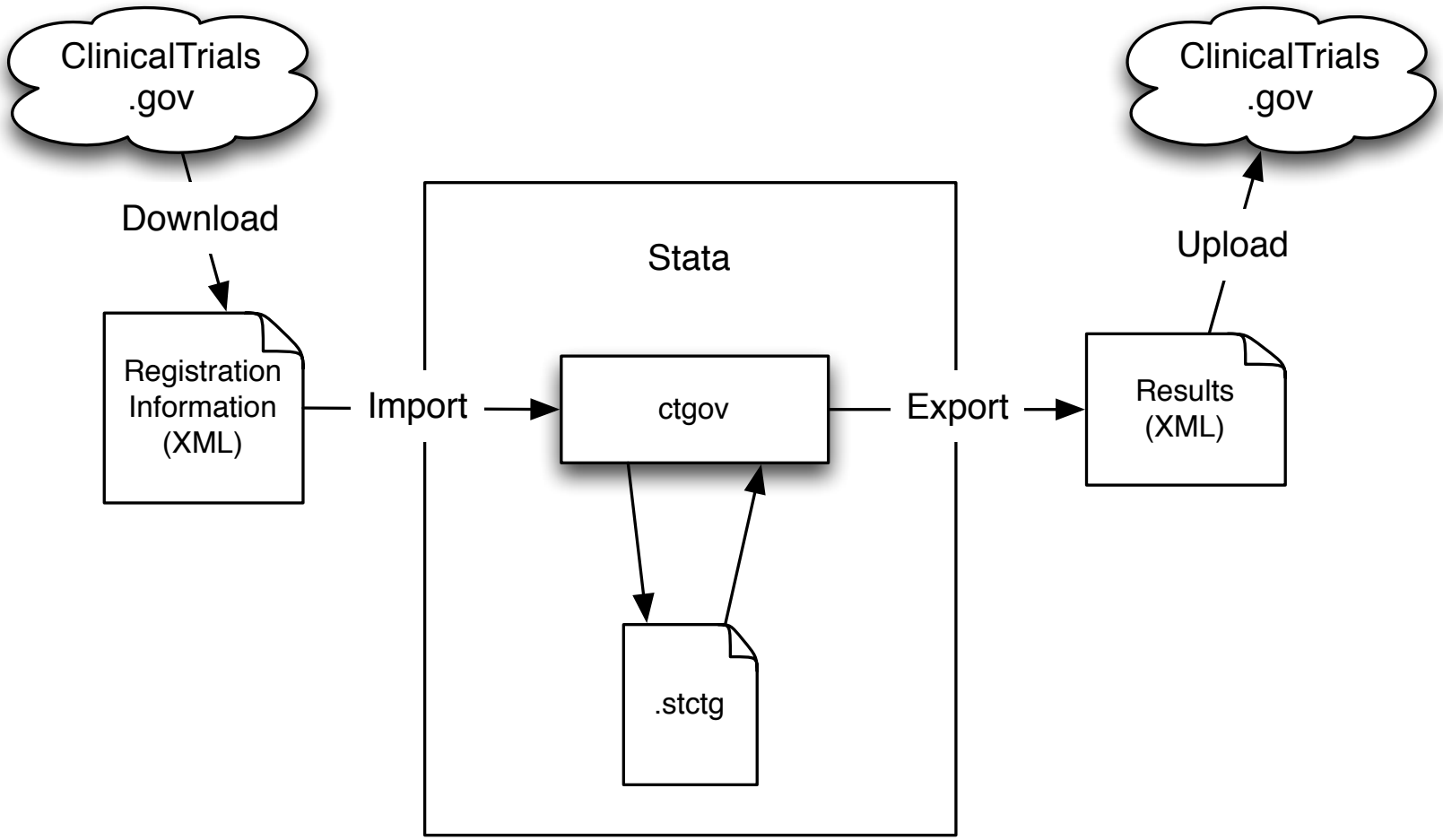


Incorporate ClinicalTrials.gov reporting into data analysis



- Requires little additional effort
- Requires no programming skill
- Reporting tied directly to primary manuscript and reproducible

Some more details



help ctgov

```
Title

    ctgov -- Generate study results for upload to ClinicalTrials.gov


Syntax

        ctgov subcommand ...  [, options ...]


    subcommand                      Description
    ---------------------------------------------------------------------------------------------------------
    Initialize and manage study
      init                          Initialize study from registration information
      describe                      Describe study in memory
      use                           Load study from file
      save                          Save study to file
      export                        Export study results to XML for upload

    Generate results from data
      flow                          Progression of subjects through trial
      baseline                      Demographic and baseline data
      outcome                       Outcome measures
      ae                            Adverse events

    Add study details
      contact                       Point of contact for information about results
      agreements                    Agreements between trial sponsor and Principal Investigator
      limitations                   Significant limitations of the trial
    ---------------------------------------------------------------------------------------------------------


Description

    The ctgov suite of commands facilitates reporting clinical trial results to ClinicalTrials.gov.
```

help ctgov

```
subcommand                      Description
-------------------------------------------------------------------------------
Initialize and manage study
  init                          Initialize study from registration information
  describe                      Describe study in memory
  use                           Load study from file
  save                          Save study to file
  export                        Export study results to XML for upload

Generate results from data
  flow                          Progression of subjects through trial
  baseline                      Demographic and baseline data
  outcome                       Outcome measures
  ae                            Adverse events

Add study details
  contact                       Point of contact for information about results
  agreements                    Agreements between trial sponsor and Principal Investigator
  limitations                   Significant limitations of the trial
-------------------------------------------------------------------------------
```

help ctgov flow

```
Title

    ctgov flow -- Summarize progression of subjects through trial


Syntax

    All subjects who started period also finished

        ctgov flow [if] [in] [weight] , by(groupvar[, description(groupdesc)]) [options]

    Number who completed period is less than the number who started

        ctgov flow reason_var [othreason_var] [if] [in] [weight] , by(groupvar[, description(groupdesc)]) [options]

    where reason_var is a numeric variable equal to 0 for those who completed the period and otherwise encoded using the standard
    ClinicalTrials.gov reasons for non-completion, and othreason_var is a string variable indicating reasons for non-completion not
    among the standard categories.


    options                       Description
    ------------------------------------------------------------------------------------------------------------------
    Main
      add                         add new period to existing periods; default is to replace any existing periods
      nostrict                    relax requirement that all reporting groups progress through each successive period
                                  (e.g., as with a dose escalation study)
      encoded                     indicates reason_var includes reasons for non-completion not included in standard categories
      milestones(varlist)         one or more indicator vars (i.e., 0/non-0) each representing a specific milestone
      title(string)               period title
      started(string)             additional information about the STARTED milestone
      recruitment(string)         key information relevant to the recruitment process
      preassignment(string)       significant events and approaches following enrollment but prior to group assignment
    ------------------------------------------------------------------------------------------------------------------
    Only fweights are allowed.
```

Example

```
. des

Contains data from tests/examples/parallel-design/flow.dta
  obs:            17
 vars:             5                          18 Mar 2014 18:36
 size:            85
-------------------------------------------------------------------------------
              storage   display    value
variable name   type    format     label      variable label
-------------------------------------------------------------------------------
grp             byte    %9.0g      grp
m1              byte    %9.0g                 Per Protocol Population Week 12
m2              byte    %9.0g                 Per Protocol Population Week 24
disp            byte    %21.0g     disp
n               byte    %9.0g
-------------------------------------------------------------------------------
Sorted by:  grp  m1  m2  disp
```

Example (cont.)

```
. li
```

	grp	m1	m2	disp	n
1.	Remuverol	0	0	Physician Decision	1
2.	Remuverol	0	0	Lost to Follow-up	1
3.	Remuverol	0	0	Pregnancy	1
4.	Remuverol	1	0	Completed	4
5.	Remuverol	1	0	Adverse Event	10
6.	Remuverol	1	0	Withdrawal by Subject	5
7.	Remuverol	1	0	Protocol Violation	2
8.	Remuverol	1	0	Lack of Efficacy	1
9.	Remuverol	1	1	Completed	76
10.	Placebo	0	0	Lack of Efficacy	1
11.	Placebo	0	0	Physician Decision	1
12.	Placebo	0	0	Lost to Follow-up	2
13.	Placebo	0	0	Pregnancy	0
14.	Placebo	1	0	Adverse Event	8
15.	Placebo	1	0	Withdrawal by Subject	4
16.	Placebo	1	0	Protocol Violation	2
17.	Placebo	1	1	Completed	81

Example (cont.)

```
. ctgov flow disp [fw=n], by(grp) milestones(m1 m2)

Reporting Groups
-------------------------------------------------------------------------------------------------------
                        | Description
------------------------+------------------------------------------------------------------------------
 Placebo                | Participants received Remuverol placebo tablet orally twice daily for 24 weeks.
                        |
 Remuverol              | Participants received Remuverol 15 mg tablet orally twice daily for 24 weeks.
-------------------------------------------------------------------------------------------------------

Overall Study
-----------------------------------------------------
                                |  Placebo   Remuverol
--------------------------------+--------------------
 STARTED                        |    99         101
 Per Protocol Population Week 12 |    95         98
 Per Protocol Population Week 24 |    81         76
 COMPLETED                      |    81         80
 Not Completed                  |    18         21
   Adverse Event                |     8         10
   Withdrawal by Subject        |     4          5
   Protocol Violation           |     2          2
   Lack of Efficacy             |     1          1
   Physician Decision           |     1          1
   Lost to Follow-up            |     2          1
   Pregnancy                    |     0          1
-----------------------------------------------------
```

Example (cont.)

Overall Study

	Remuverol	Placebo
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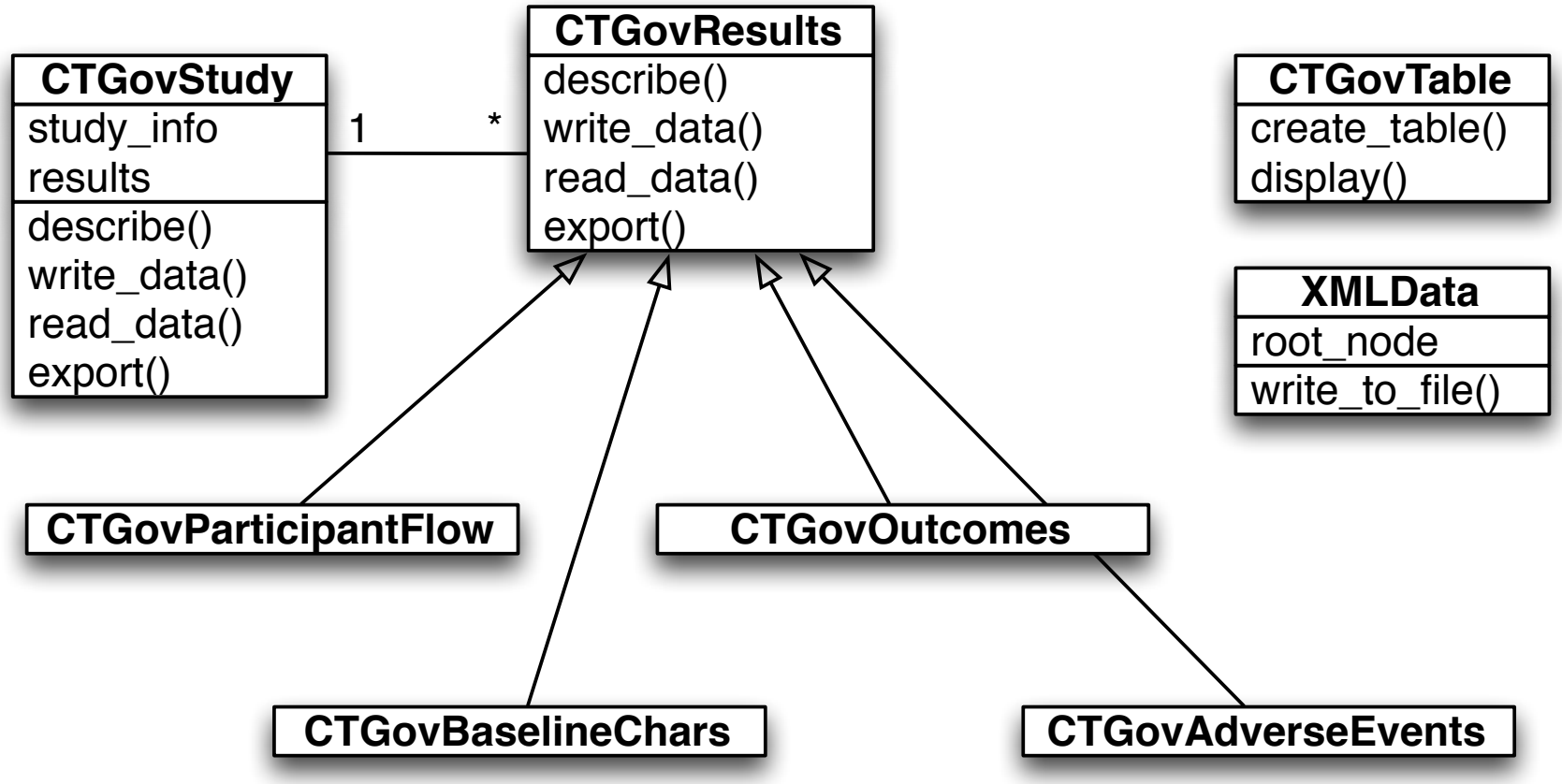
Per Protocol Population Week 12	98	95
Per Protocol Population Week 24	76	81
COMPLETED	80	81
Not Completed	**21**	**18**
Adverse Event	10	8
Withdrawal by Subject	5	4
Protocol Violation	2	2
Lack of Efficacy	1	1
Physician Decision	1	1
Lost to Follow-up	1	2
Pregnancy	1	0

Overview of program structure



IO

- XML import and export
- .stctg files for storing intermediate results

Table requirements

Mimic tables in Stata viewer as displayed on `ClinicalTrials.gov`

Table requirements

Outcome Measures

1. Primary Outcome Measure:

Measure Title	**Change From Baseline in Pain on the 11-point Short Pain Scale (SPS-11) at Week 24**
Measure Description	SPS-11 is a validated, self-reported instrument assessing average pain intensity over the past 24 hour period. Possible scores range from 0 (no pain) to 10 (worst possible pain). Change = (Week 24 Score - Baseline score)
Time Frame	Baseline and Week 24
Safety Issue?	No

Population Description -- *Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate:*

Intent to treat population (all participants who received at least one dose of intervention).

Table requirements

Region of Enrollment *[units: participants]*			
United States	44	47	**91**
Canada	35	35	**70**
Mexico	22	17	**39**
Study Specific Characteristic [Quebec Task Force Classification of Spinal Disorders] [1] *[units: participants]*			
Class 0 (no pain)	16	14	**30**
Class 1 (pain without radiation)	73	68	**141**
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Study Specific Characteristic [Body Mass Index] *[units: kg/m^2]* *Mean ± Standard Deviation*	26.65 ± 4.50	27.41 ± 4.72	**26.91 ± 4.55**
Study Specific Characteristic [Short Pain Scale (SPS-11) Score] [2]	6.48 ± 1.34	6.57 ± 1.73	**6.52 ± 1.61**

Table requirements

- Flexible row header structure, with dynamic indent
- Footnotes for column and table headers and individual cells
- Automatic wrapping and column resizing
- Control over horizontal and vertical justification

CTGovTable class:

- Uses `_tab`
- Easy to use
- Targeted to `ClinicalTrials.gov`

Table examples

Reporting Groups

	Description
Hypertena, Then Placebo	Participants first received Hypertena 20 mg tablet each morning in a fasting state for 2 weeks. After a washout period of 2 weeks, they then received Placebo tablet (matching Hypertena 20 mg) in a fasting state each morning for 2 weeks.
Placebo, Then Hypertena	Participants first received Placebo tablet (matching Hypertena 20 mg) in a fasting state each morning for 2 weeks. After a washout period of 2 weeks, they then received Hypertena 20 mg tablet in a fasting state each morning for 2 weeks.

Serious Adverse Events

	Hypertena	Placebo
Total # of participants affected/at risk	0/127 (0%)	1/127 (0.79%)
Cardiac disorders		
Myocardial Infarction [1,2]		
# participants affected/at risk	0/127 (0%)	1/127 (0.79%)

[1] Indicates events were collected by systematic assessment.
[2] Term from vocabulary, MedDRA 11.1

Outcomes

Reporting Groups

	Description
Remuverol	Participants received Remuverol 15 mg tablet orally twice daily for 24 weeks.
Placebo	Participants received Remuverol placebo tablet orally twice daily for 24 weeks.

Measured Values

	Remuverol	Placebo
Number of Participants Analyzed	101	99
Change From Baseline in Pain on the 11-point Short Pain Scale (SPS-11) at Week 24 *[units: units on a scale]* Mean ± Standard Error	-3.84 ± 0.61	-2.08 ± 0.51

Outcomes

Statistical Analysis 1 for Change From Baseline in Pain on the 11-point Short Pain Scale (SPS-11) at Week 24

Groups	Remuverol, Placebo
Method	t-test, 2 sided
P-Value	0.002

Additional details about the analysis, such as null hypothesis and power calculation:

> It was calculated that 200 participants randomized in a 1:1 fashion between the 2 arms would have at least 85% power to detect a difference of 0.56 points in mean SPS-11 pain score between Remuverol and placebo from baseline to week 24. Sample size was determined using a 2-sided 2-sample t test ($\alpha = 0.05$). Assumptions included a common standard deviation of 1.14 and a discontinuation rate of 7%.

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

> [Not specified.]

Other relevant information, such as adjustments or degrees of freedom:

> [Not specified.]

Handling outcomes via plugins

- Need to handle arbitrary analysis commands
- Need to have fully-functioning system from the start
- Possible to enter outcome results manually
- Plugins for specific command(s) facilitate reporting