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Outcome Measures Module

Results Database Train-the-Trainer Workshop
October 2012

http://ClinicalTrials.gov

FDAAA - Outcomes

"…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."

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

FDAAA = Food and Drug Administration Amendments Act of 2007

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Description of Outcome Measures Module

The Outcome Measures module displays the results and associated statistical analyses for each pre-specified primary and secondary outcome measure. Other outcome measures may also be included.

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Outcome Measures
Journal Article Format

Table 2. Primary safety assessment of the number of patients with severe, life-threatening, or fatal treatment-related toxicities.

Variable	AmB (n = 47)	AmB+Fluc400 (n = 48)	AmB+Fluc800 (n = 45)
Related to either study drug			
Overall			
Patients with event	19 (40.4)	18 (37.5)	14 (31.1)
90% CI, %[a]	28.3–53.5	25.8–50.4	19.9–44.3
P[b]		.573	.794
By severity[c]			
Severe	13 (27.6)	13 (27.1)	9 (20.0)
Life-threatening	6 (12.8)	5 (10.4)	5 (11.1)
Fatal	0	0	0
By relatedness[c]			
Probably related	16 (34.0)	16 (33.3)	12 (26.7)
Definitely related	3 (6.4)	2 (4.2)	2 (4.4)
Related to fluconazole			
Overall			
Patients with event	0	0	2 (4.4)

Pappas PG, Chetchotisakd P, Larsen RA et al. Clin Infect Dis. 2009

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ClinicalTrials.gov Format

Measure Type	Primary
Measure Title	Number of Grade 3-5 Adverse Experiences That Are Definitely or Probably Related to Study Drug
Measure Description	Events are reported by MedDRA Preferred Term. Grade 3 - Severe. Incapacitating; inability to perform usual activities and daily tasks; significantly affects clinical status; requires therapeutic intervention. Grade 4 - Life-threatening. AE is life-threatening. Grade 5 - Death. AE causes death.
Time Frame	Day 100
Safety Issue	Yes

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.
The Regulatory Safety population includes all subjects who were randomized, who receive at least 1 dose of study drug, and who have any on-study data.

NCT00145249

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ClinicalTrials.gov Format (cont.)

Measured Values

	AmphoB Standard	AmphoB+Fluc400	AmphoB + Fluc800
Number of Participants Analyzed [units: participants]	45	47	49
Number of Grade 3-5 Adverse Experiences That Are Definitely or Probably Related to Study Drug [units: Events]			
Hypomagnesaemia	2	1	0
Hypokalaemia	0	0	1
Anaemia	1	1	0
Drug intolerance	1	0	0
Creatinine renal clearance increased	0	0	1
Psychotic disorder	0	0	1

NCT00145249

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Outcome Measures
Journal Article Format

" After the accrual of 144,103 person-years in the low-dose CT group and 143,368 person-years in the radiography group, 356 and 443 deaths from lung cancer in the two groups, respectively, had occurred …"

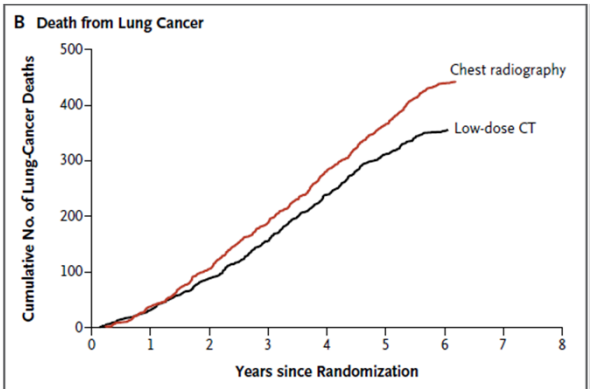

Figure 1. Cumulative Numbers of Lung Cancers and of Deaths from Lung Cancer.
The number of lung cancers (Panel A) includes lung cancers that were diagnosed from the date of randomization through December 31, 2009. The number of deaths from lung cancer (Panel B) includes deaths that occurred from the date of randomization through January 15, 2009.

N Engl J Med 365;5 August 2011

Outcome Measures
ClinicalTrials.gov Format

Measured Values

	LDCT Screening	CXR Screening
Number of Participants Analyzed [units: participants]	**26722**	**26732**
Lung Cancer Deaths [units: Participants]	**356**	**443**

Statistical Analysis 1 for Lung Cancer Deaths

Groups [1]	All groups
Method [2]	Weighted log-rank (details below)
P Value [3]	0.004
Hazard Ratio (HR) [4]	0.800
95% Confidence Interval	(0.733 to 0.932)

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NCT00047385

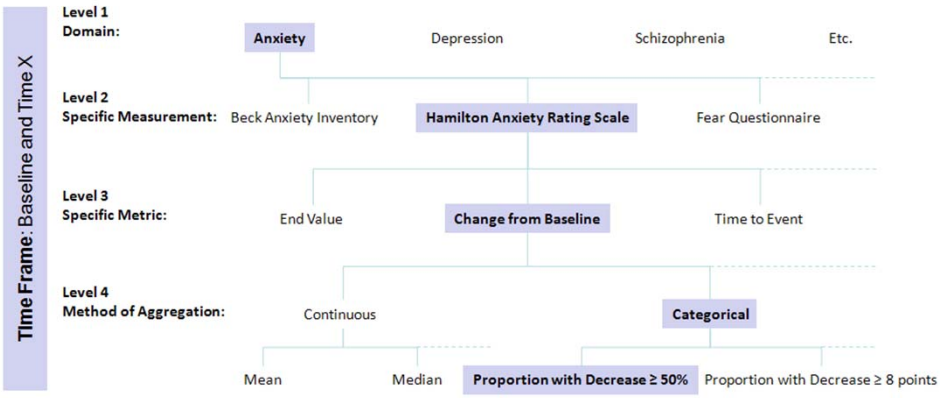
Outcome Measure Template

Measure Type*	*(Circle One)*	Primary	Secondary	Other Pre-specified	Post-Hoc	**Safety Issue?***	*(Circle One)*	Yes No
Measure Title*								
Measure Description								
Measure Timeframe*								
Analysis Population Description								

Outcome Data Table			[1]	[2]	[3]
Unit of Measure*		**Arm/Group Title***			
		Arm/Group Description*			
		Number of Participants Analyzed*			
Number / Central Tendency* (Circle One and Enter numeric value in each column)	Number Mean Median Least Squares Mean Geometric Mean Log Mean				
Dispersion/ Precision* (Circle One and enter values in each column)	Not Applicable (Use only with Number) Standard Deviation (Do NOT use with Number) Inter-quartile Range [Low to High] (Do NOT use with Number) Full Range [Low to High] (Do NOT use with Number) Standard Error (Do NOT use with Number) 95% Confidence Interval [Low to High] 90% Confidence Interval [Low to High]				

Outcome Measures
Conceptual Framework

Four Levels of Specification in Reporting Outcome Measures



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Zarin DA, Tse T, Williams RJ, Califf RM, Ide NC. N Engl J Med. 2011.

Specification of Outcome Measures in Protocol

Level	Primary OMs (% Total) n=100
1 – Domain (only)	36%
2 – Specific Measurement	25%
3 – Specific Metric	26%
4 – Method of Aggregation	13%
Included Specific Timeframe	63%

Zarin DA, Tse T, Williams RJ, Califf RM, Ide NC. N Engl J Med. 2011.

Best Practices

- If the Number of Participants Analyzed is not the same as a "row" (Started, Completed, Other Milestone) in Participant Flow, describe the population in the Analysis Population Description
- Use multiple Outcome Measures to report results for the same measure at multiple time points
- If the reporting groups are different from Participant Flow Arm/Groups, use Outcome Measure Arm/Group Title/Descriptions to explain and relate to Participant Flow Arm/Group Title/Descriptions

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Outcome Measures
Tutorial

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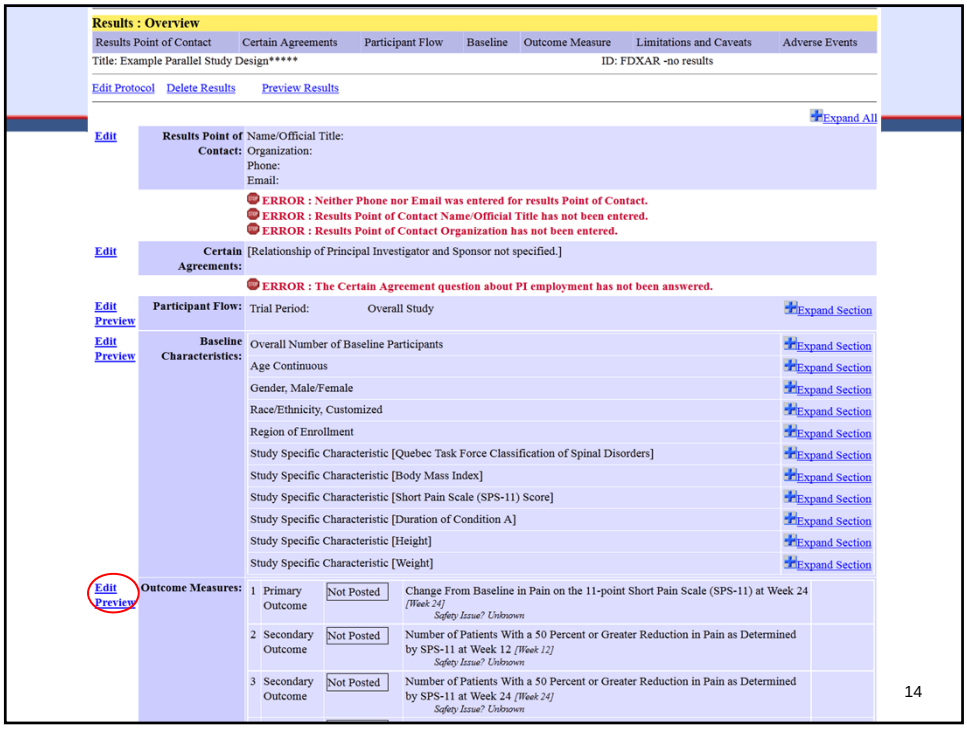

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Outcome Overview

Results

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	**Outcome Measure Outcome Overview**	Limitations and Caveats	Adverse Events

Title: Example Parallel Study Design***** ID: FDXAR -no results

Results Overview Preview Outcome Measures

Need help? The Outcome Measure Simplified Form Examples show the type of information needed to report Results for an Outcome Measure. Also, the webinar on the Outcome Measures and Statistical Analyses Module provides an overview of the purpose and specific, required data elements.

Add Outcome Measure **Reorder Outcome Measures** Expand All

ERROR : At least one Primary Outcome Measure must "Post" Results data.

1 **Not Posted**

Type : **Primary** *Title:* **Change From Baseline in Pain on the 11-point Short Pain Scale (SPS-11) at Week 24**
Time Frame: *Week 24*
Description:
Safety Issue? *Unknown*

Post Outcome Measure Edit Title Fields Delete

WARNING : Outcome Safety Issue? has not been entered.

2 **Not Posted**

Type : **Secondary** *Title:* **Number of Patients With a 50 Percent or Greater Reduction in Pain as Determined by SPS-11 at Week 12**
Time Frame: *Week 12*
Description:
Safety Issue? *Unknown*

Post Outcome Measure Edit Title Fields Delete

WARNING : Outcome Safety Issue? has not been entered.

Outcome Measure Arm/Groups

Results

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	**Outcome Measure Initial Outcome Measure Arm/Groups**	Limitations and Caveats	Adverse Events

Title: Example Parallel Study Design***** ID: FDXAR -no results

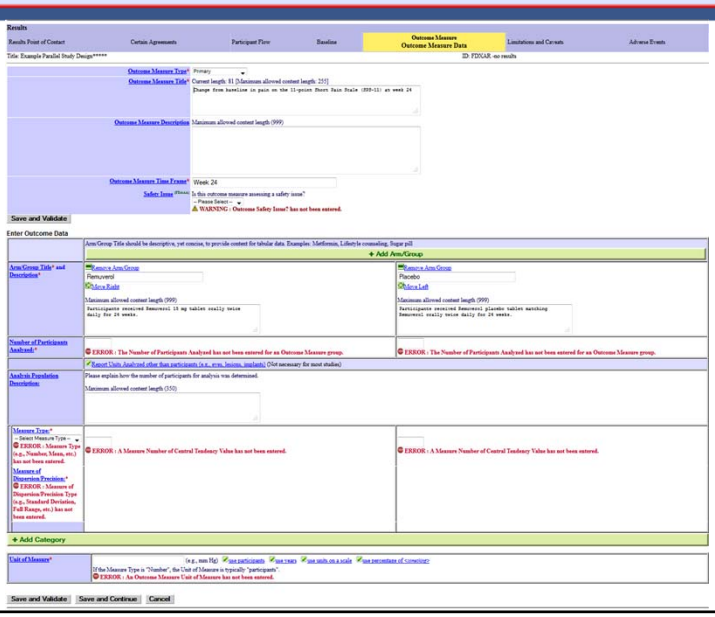
Arm/Group*

Select the Arm/Groups for this Outcome Measure. The Arm/Groups define columns for reporting tabular Outcome Measure data. You will be able to edit the Arm/Group Titles and Descriptions later, if desired.

(•) **Use Arm/Groups (i.e., columns) from** 2 Participant Flow	**Arm/Group Title**	Remuverol	Placebo
	Arm/Group Description	Participants received Remuverol 15 mg tablet orally twice daily for 24 weeks.	Participants received Remuverol placebo tablet matching Remuverol orally twice daily for 24 weeks.
( ) **Define New Arm/Groups (columns)**			

Continue Cancel

Outcome Measure Data



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Outcome Measure Data (cont.)

Results

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	**Outcome Measure** **Outcome Measure Data**	Limitations and Caveats	Adverse Events

Title: Example Parallel Study Design*****

ID: FDXAR -no results

Outcome Measure Type* Primary

Outcome Measure Title* Maximum allowed content length (255)

Change from baseline in pain on the 11-point Short Pain Scale (SPS-11) at week 24

Outcome Measure Description Current length: 202 [Maximum allowed content length: 999]

SPS-11 is a validated, self-reported instrument assessing average pain intensity over the past 24 hr period. The severity of pain scores on the SPS-11 range from 0 (no pain) to 10 (worst possible pain).

Outcome Measure Time Frame* Baseline and Week 24

Safety Issue (FDAAA) Is this outcome measure assessing a safety issue?

No

Save and Validate

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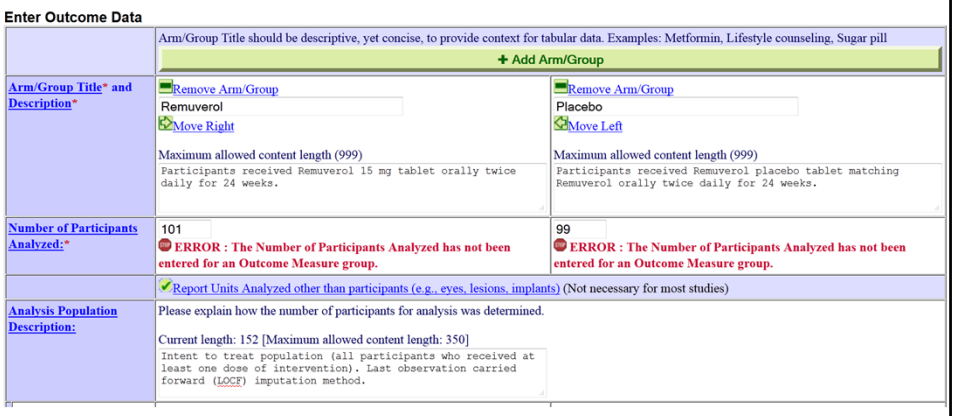
Outcome Measure Data (cont.)



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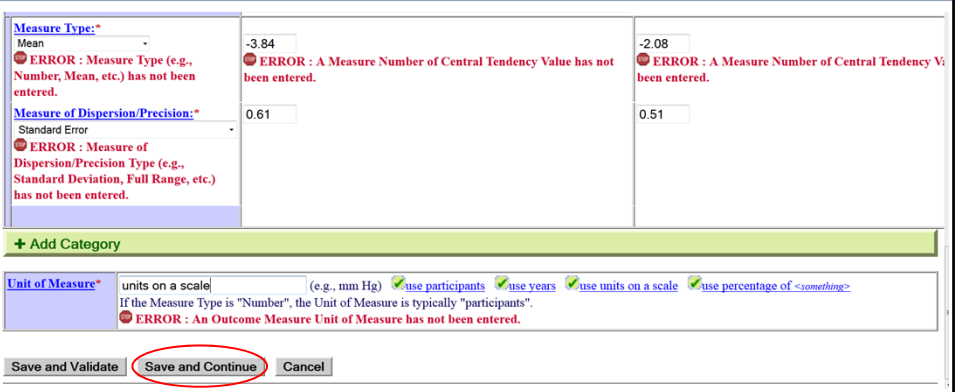
Outcome Measure Data (cont.)



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Outcome Overview

Results

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	**Outcome Measure Outcome Overview**	Limitations and Caveats	Adverse Events

Title: Example Parallel Study Design***** ID: FDXAR -no results

1

Posted

Type : **Primary** *Title:* **Change From Baseline in Pain on the 11-point Short Pain Scale (SPS-11) at Week 24**
Time Frame: Baseline and Week 24
Description: SPS-11 is a validated, self-reported instrument assessing average pain intensity over the past 24 hr...
Safety Issue? No

Un-Post/Delete Copy

Collapse Section

Edit

	Remuverol *Participants received Remuvero...*	Placebo *Participants received Remuvero...*
Number of Participants Analyzed	*101*	*99*
Number of Units Analyzed	*Same as Number of Participants Analyzed*	
Analysis Population Description	*Intent to treat population (all participants who received at least one dose of intervention). Last observation carried forward (LOCF) imputation method.*	
units on a scale	**Mean ± Standard Error**	**Mean ± Standard Error**
	-3.84 ± 0.61	*-2.08 ± 0.51*

Add Statistical Analysis

Add Outcome Statistical Analysis

Results

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	**Outcome Measure Add Outcome Statistical Analysis**	Limitations and Caveats	Adverse Events

Title: Example Parallel Study Design***** ID: FDXAR -no results

Posted **Primary Outcome: Change from baseline in pain on the 11-point Short Pain Scale (SPS-11) at week 24** *; Units: units on a scale [Baseline and Week 24]*

Statistical Analysis Overview:

Comparison Group Selection: *
Generally, at least 2 groups should be checked. Check all groups for an "omnibus" analysis.
☑ Remuverol ☑ Placebo
Please provide additional details about the analysis, such as null hypothesis and power calculation.
Current length: 272 [Maximum allowed content length: 500]

```
It was calculated for this study that, approximately 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 (α = 0.05). Assumptions
included a common standard deviation of 1.14 and a
discontinuation rate of 7%.
```

Is this a non-inferiority or equivalence analysis? * No

ERROR : Please enter whether the Statistical Analysis tested for Non-inferiority or Equivalence.

If yes, please describe details of power calculation (if not previously provided), definition of non-inferiority margin, and other key parameters.
Maximum allowed content length (500)

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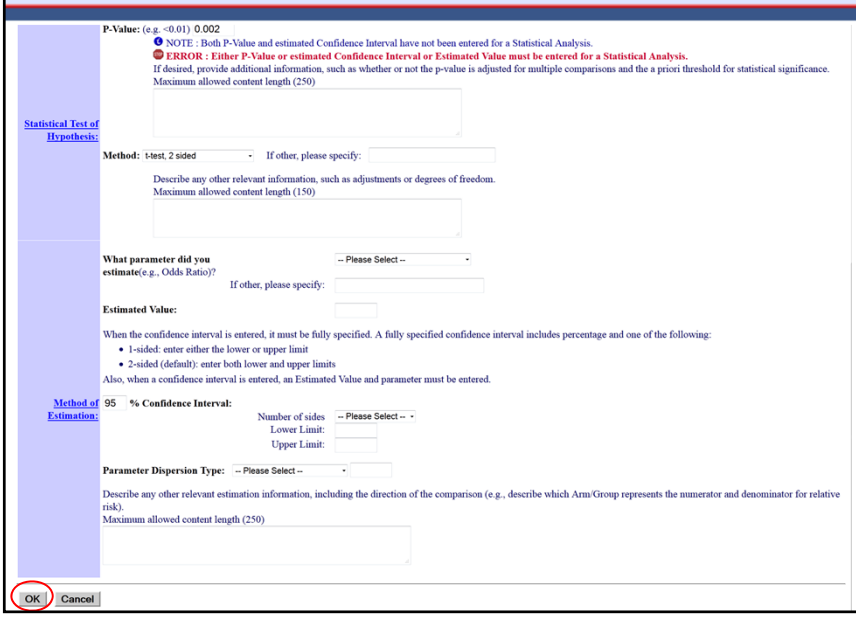
Add Outcome Statistical Analysis (cont.)



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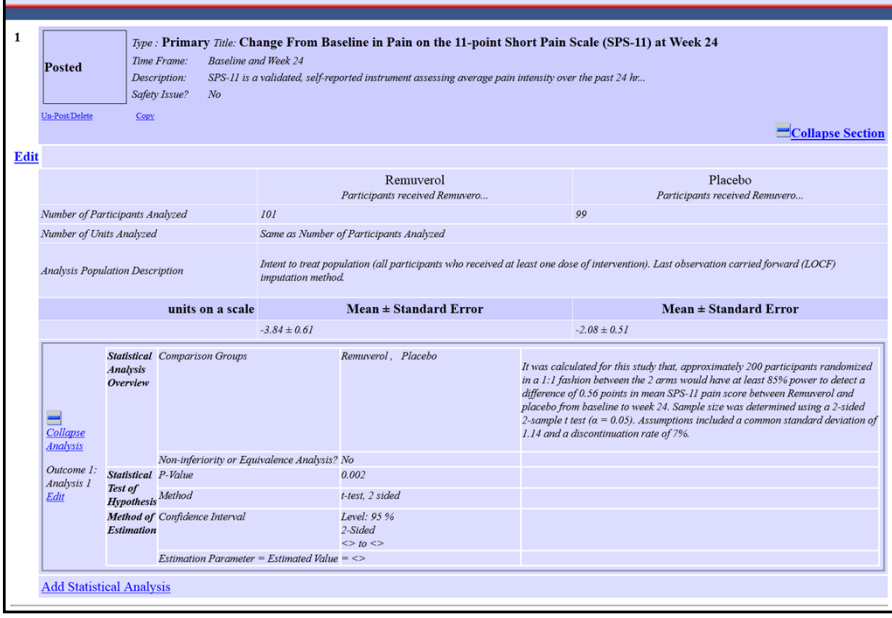
Outcome Overview



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Enter Primary Outcome Measure

- Example Study Designs
  - Crossover
  - Dose Escalation
  - Factorial
  - Multiple Period

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Additional Issues

- A pre-specified Outcome Measure is not analyzed (e.g., too few participants enrolled, equipment used for measurement not reliable)
- Certain data are not available (e.g., upper limit of 95% Confidence Interval, assays below detectable limit)
- Data collection is still ongoing and analysis not yet conducted for Secondary Outcome Measures

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