Help: Outcome Measures

Introduction

The Outcome Measures module includes measurements or observations used to assess the effect of experimental variables in a study, or for observational studies, to describe patterns of diseases or traits or associations with exposures, risk factors or treatment.

Outcome Measures EXAMPLE

Primary Outcome Measure:

1. 4-Item Pain Intensity Measure (P4)
   [Time Frame: 2 days] [Safety Issue: No]
   Self reported pain intensity in the morning, afternoon, evening and with activity over the past 2 days. Each item is scored 0-10 (0 = no pain; 10 = pain as bad as can be), yielding a total between 0 and 40.

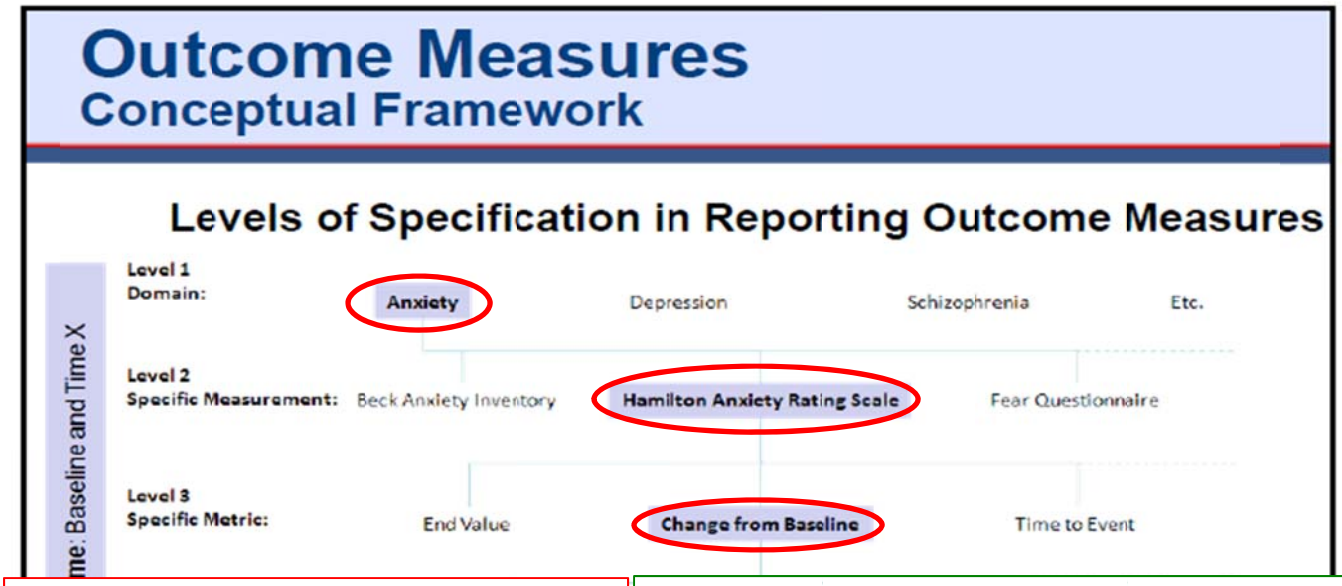
Secondary Outcome Measures:

2. Recurrence of Pain
   [Time Frame: 24 and 48 hours] [Safety Issue: No]
   Return of any migraine headache pain during the specified post-dose period, following a pain-free response at 2 hours.
3. Sustained Freedom from Migraine
   [Time Frame: 7 days] [Safety Issue: No]
   Pain free, with no migraine associated symptoms (photophobia, phonphobia, nausea) at the time of assessment, following a symptom-free response within 1 day of initial dose.

Specifying Outcome Measures in the Protocol Registration System (PRS) for ClinicalTrials.gov:

- A study typically has one (or very few) Primary Outcome Measure(s), indicating key observation(s) to be used in assessing study results.
- Make each Outcome Measure Title unique and descriptive, indicating the metric to be used. Examples:
  - Change in Systolic Blood Pressure
  - Area under the plasma concentration versus time curve (AUC) of [DRUG NAME]
  - Peak Plasma Concentration (Cmax) of [DRUG NAME]
- Time Frame is usually a single point in time, with these exceptions:
  - Change measures (e.g., "baseline and 8 weeks")
  - Time-to-Event measures (e.g., "up to 100 weeks," "from date of randomization until date of first documented progression or date of death from any cause, whichever came first, up to 100 months")
  - Pharmacokinetic measures (e.g., "0, 1, 2, 3, 4, 6, 8, 24 hours post-dose")
  - Measures assessed at time of intervention (e.g., "at time of surgery")
  - Outcome Measure Description may be left blank if Title is sufficiently descriptive.
- Specify each Outcome Measure separately. The same measurement taken at different time points must be specified as unique Outcome Measures.
- If measure is assessed using a scale (e.g., VAS for pain, Beck Depression Inventory), provide scale information:
  - Specify Full Scale Name and Construct (i.e., state what the scale measures if not clear from name).
  - State scale range (i.e., minimum and maximum score) and values considered to be a better or worse outcome (i.e., do higher values represent a better or worse outcome?).
  - If subscales will be combined to compute a total score, consider indicating how subscales are combined (summed, averaged, etc.).

Example Outcome Measure Specification



NOT Specific ⊘
Title: To compare Anxiety of Arm A to Arm B
Description: Hamilton Anxiety Scale
Time Frame: Baseline, Time X

NOT Specific ⊘
Title: Anxiety
Description: Hamilton Anxiety Scale
Time Frame: Baseline, Time X

Specific 👍
Title: Change in Anxiety score from Baseline to Time X
Description: Hamilton Anxiety Scale: 14 sets of symptoms are rated by participant on a 5-point scale (0=Not present, 4=Very severe), yielding a total score between 0 and 56.
Time Frame: Baseline, Time X

Specific 👍
Title: Proportion of Participants with Decrease in Anxiety ≥ 50% on the Hamilton Anxiety Rating Scale (HAM-A)
Description: The HAM-A contains 14 sets of symptoms rated by participants on a 5-point scale (0=Not present, 4=Very severe), yielding a total score between 0 and 56.
Time Frame: Baseline, Time X

Review Checklist for Outcome Measures

- The Outcome Measure information describes WHAT will be measured, not why it is measured.
  - Hint: Generally, do not include verbs (“to examine”, “to evaluate”) in the Outcome Measure Title.
- The Outcome Measure Titles and Descriptions (if provided) are as specific as possible.
  - Outcome Measure Titles are NOT overly general (e.g., "bioequivalence," "safety," and "feasibility" are not specific).
- The Outcome Measure information includes the name of the specific measure (e.g., Systolic Blood Pressure) and a description of the metric that will be used to characterize the measure (e.g., Change in Systolic Blood Pressure).

[Review Checklist continued on next page]

  - Hint: “Bioequivalence,” “pharmacokinetics,” and “pharmacodynamics” are not specific descriptions of an Outcome Measure because they do not specify by which measures bioequivalence, pharmacokinetics or pharmacodynamics will be assessed.
    - Examples of Outcome Measure Titles to assess these parameters include:
      - “Area under the plasma concentration versus time curve (AUC) of ‘drug x’”
      - “Peak Plasma Concentration (Cmax) of ‘drug x’”
  - Hint: “Safety,” “tolerability,” and “feasibility” are not specific measures. Similarly, “Adverse events” by itself is not sufficient. “Number of participants with adverse events” is specific.
  - Any assessment instruments or scales are described, including the number of scale items, scoring system, score range, and significance of higher vs. lower scores.

- Outcome Measure Time Frame specifies one time point of assessment; if more than 1 time point is specified, the title &/or description explains how multiple assessments will be combined into one reportable outcome measure (e.g., change between 2 time points, average of all measures, minimum, maximum, Cmax, AUC, time-to-event).
  - “At follow-up” or “end of study” is **not** an adequately stated Time Frame.

Common “Reviewer Comments” for Outcome Measures in ClinicalTrials.gov:

1. The Outcome Measure Title is vague; it is unclear *what will be measured and reported*. In the Title field, specify the measurement that will be used (e.g., descriptive name of scale, physiological parameter, questionnaire) and, if relevant, how the collected measurement data will be aggregated. Use the Description field, for any additional information about the measurement or metric for summarizing the data. For example, an Outcome Measure Title of "Safety and Tolerability" does not sufficiently describe how quantitative data will be reported. A specific Title would instead be "Number of participants with treatment-related adverse events as assessed by CTCAE v4.0".
2. The Outcome Measure Titles describe the goal or objective of each assessment, rather than what will be assessed. The Outcome Measure Title should define what will be measured, not why it will be measured. For example, phrases such as "to assess", "to examine", and "to determine" should be deleted and replaced by an accurate description of what will be measured and reported (e.g., Number of Participants With Treatment-Related Adverse Events as Assessed by CTCAE v4.0, or Change From Baseline in Pain Scores on the Visual Analog Scale).
3. Limit the Outcome Measure Title to WHAT was measured not why it was measured. For example, please remove verbs and/or phrases such as "To assess", "To Examine", or "To Determine".
4. The Outcome Measure appears to include multiple measures. If the entered information represents multiple outcome measures, then each measure must be entered separately (by using the "Add Outcome Measure" link) to clearly indicate each unique pre-specified outcome measure in this study. If the measure is a composite outcome measure consisting of multiple measures (results to be reported as a single value for each Arm/Group), then no changes are required, but it is recommended that the Outcome Measure Title or Description more clearly indicate that the measure is a composite.
5. The Outcome Measure describes multiple assessments with potentially different Units of Measure. Assessments with different Units of Measure (e.g., BMI in kg/m^2, weight in kilograms, height in meters) must be presented in separate Outcome Measures. Please revise to present these assessments in separate Outcome Measures, as appropriate, or to clarify how multiple measurements will be aggregated to arrive at one reported value (e.g., Number of Participants With Abnormal Laboratory Values and/or Adverse Events That Are Related to Treatment).
6. The Outcome Measure Time Frame includes more than one time point. Each Outcome Measure should typically only specify a single time point of assessment. A common exception to this is a measure assessing change between two time points (e.g., "Change from Baseline Systolic Blood Pressure at 6 months"). If the Outcome Measure(s) are assessing a change, please revise the Outcome Measure Title(s) to specify that "change" is being assessed. If not assessing change, please revise and enter additional Outcome Measures so that there is only one Time Frame per Outcome Measure.

Examples - Before/After - Outcome Measures revised in response to reviewers' comments:

QA Comment: The Outcome Measure Title is vague. It is unclear what will be measured and reported. Please change the Measure Title to accurately reflect what will be measured and reported (e.g. "Number of Participants with Adverse Events as a Measure of Safety and Tolerability" or "Pain Scores on the Visual Analog Scale" or "Tmax" or "Cmax"). Limit the Outcome Measure Title to WHAT was measured not why it was measured. For example, please remove verbs and/or phrases such as "To assess", "To Examine", or "To Determine". Please use the Description field to explain the outcome measure further, if needed.

Before QA: Outcome Measure Title[Description]	After QA: Outcome Measure Title [Description]
To evaluate the safety and efficacy of the xxx as a novel site for transplantation. The site has several physiologic attributes that may improve the outcomes of transplantation compared with the conventional transplant site.	Number of Adverse Events, ≥ Grade 3, as a measure of safety
Retention in care	Participants eligible for treatment who initiated treatment and who remain on treatment 12 months from enrollment, as a measure of retention
Adherence	Days covered by medication in the 12-month period after enrollment as assessed by pharmacy refill records
Functional recovery after transplant	1. Change in Fried Frailty Assessment [as a measure of functional recovery after transplant] 2. Change in Short Physical Performance Battery (SPPB) [as a measure of functional recovery after transplant]
Assess feasibility of recruitment strategy	Number of participants successfully enrolled
Compare mean number of migraine/migrainous days in melatonin group vs. placebo	Number of migraine/migrainous days per 28 day period [By participant self-report, using an online/mobile device headache diary]
Compliance	Proportion of participants with ≥85% symptom diary compliance during weeks 12-16 of the study

QA Comment: It seems that more than one outcome measure is listed in the Outcome Measure. Please list each Outcome Measure separately, using "Add an Other Pre-specified Outcome Measure" feature, or clarify how the listed outcomes will be combined into a single reportable outcome.

Before QA: Outcome Measure Title[Description]	After QA: Outcome Measure Title [Description]
cost-effectiveness [direct costs: treatments costs, adverse events, health care utilized (including rehospitalizations, and remission indirect costs: missed school and work days]	Cost per adolescent recovered [combined direct and indirect costs divided by number of recovered adolescents]
Retention and adherence	Feasibility [Feasibility will be defined by ≥90% retention of enrolled participants through week 12 AND no more than 2 missed visits among participants retained through week 12.]

QA Comment: The Time Frame provided "Immediately post-transplant" is not specific. The Time Frame should specify the specific time point(s) at which the outcome measure will be assessed and for which data will be presented. (e.g., "1 year" or "up to 24 weeks"). An average time period may also be acceptable but the Time Frame should specify that it is an average (e.g., "participants will be followed for the duration of hospital stay, an expected average of 5 weeks").

Before QA: Time Frame	After QA: Time Frame
Throughout the study	During the enrollment period, approximately 1 year
Throughout active phase of the study	During the "At Home Active Study Period" or Weeks 5-16

QA Comment: Please clarify the time frame "over 1 year". Do you mean over the course of one year as in up to one year? Or past one year as in 13 + months? Please revise as appropriate.

Before QA: Time Frame	After QA: Time Frame
[Time Frame: Over 1 year]	[Time Frame: up to 12 months]