Assessing and Supporting Outcome Assessments

Categories, Context, and Evidence

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The views expressed are those of the author, and do not necessarily represent a Janssen position
Outline

• Outcomes and Endpoints
• Major categories of OAs
• Relationships related to outcome assessments in clinical trials
• Indirect and direct relationship
• Overarching aspects of OA evaluation
• Key performance aspects of an OA
• Context of Use
• Good Outcome Assessment Principles
Outcomes and Endpoints

• Outcome Assessment
  ➢ An evaluation or measurement of the person’s health or health-related state that is used to form an endpoint for a clinical study
  ➢ Part of, not the entirety of an endpoint

• Study Endpoint
  ➢ Defined by a specified outcome assessment, measured in a specified manner at one or more specific times during a study, and analyzed in a specified way
Overarching Relationships

- **Meaningful Health Aspect (MHA)**
  - An aspect of feels or functions as occurs in ‘typical’ daily life; or survival
  - The nature of the Treatment Benefit

- **Concept of Interest for Measurement (COI)**
  - Concept thought related to the MHA and is measurable
  - Clinical COI - often a more basic (simpler) element of the MHA
  - Biomarker COI – often thought causative of the MHA

- **Assessment** = Practical expression of the COI enabling measurement (an operationalized definition for COI)
Overarching Relationships

Meaningful Feelings, Functions, or Survival Concept (Meaningful Aspect of Health) → Concept of Interest to be Measured

Specific Feelings or Activities Occurring in a Person's Typical Life

Specific Outcome Assessment
**Relationship Examples**

- **Meaningful Aspects of Health**
  - Comprehensive Function (All Activities Affected by Disorder)
  - Arm & Hand Dependant Activities
  - Ambulation Dependant Activities
  - Cognition Dependant Activities

- **Concepts of Interest for Measurement (COI)**
  - Walking Capacity
  - Leg Muscle Strength
  - Walking Speed
  - Maximal Isometric Quadriceps Force
  - Timed 25 Foot Walk
  - 6 Minute Walk Test
  - Defined Clinical Outcome Assessments

- **Group of Related Meaningful Activities**
  - Walking in shopping mall
  - Walking from bus stop to office or home
  - Walking from building to building along a street
  - Walking from room to room inside house
Two Major Categories of OAs

• Clinical Assessment
  ➢ Affected by evaluator judgment or patient volition
  ➢ “Clinical” as *term of art* – not general language manner of use
  ➢ Several types of COA – prior presentation

• Biomarker Assessment
  ➢ Does not rely on judgment or volition
  ➢ An ‘analyte’ that exists outside of patient choices
• OA can directly describe meaningful feeling or function or indirectly reflect it.

• Indirectness is a graded characteristic.

• Type of evidence and amount of effort to obtain evidence establishing relationships can vary.

### Direct COA
(Direct measures of feeling, function or survival)
- Direct COA
- Brief Pain Inventory
- McGill Pain Questionnaire
- St. George Respiratory Questionnaire
- Beck Depression Inventory
- Epworth Sleepiness Scale

### Mildly Indirect COA
- 6-Minute Walk Test
- PANSS
- ALS Functional Rating Scale
- Sleep onset (time to)
- Visual acuity – ETDRS Scale
- BPRS (brief psych rating)
- Psoriasis Area and Severity Index
- Montgomery-Asberg Depression Scale
- Rankin Stroke scale
- Pulmonary Function Test (FVC, FEV1)
- Ashworth Spasticity Scale
- ADAS-COG
- SDMT

### Very Indirect COA
- Serum Cholesterol
- HIV Viral Load
- Phenylalanine
- XRay Feature
- HgbA1c
- Hgb
- MRI Brain Lesion Volume

### Biomarkers: Highly Indirect Outcomes
Assessment Categorization: Characteristics
Overarching Aspects of OA Evaluation

• Content Validity
  ➢ Does the OA actually represent the intended COI?

• Interpretability
  ➢ Does the COI actually reflect the meaningful health aspect?
    ❖ When does the MHA benefit occur relative to when the COI is measured? --- Important difference between OA reflecting current state of the patient and OA predicting some future state
  ➢ If COI is the exact MHA answer is self-evident
Key Performance Characteristics of the OA

- Reliability
  - Consistency of measurement
    - Within and between patients
    - Between observers (reporters) or study staff
    - Over time

- Responsiveness (sensitivity)
  - Does the measurement change when the COI changes

- Quantitative interpretation
  - What is a meaningful change
  - Not self-evident even if the COI = MHA
Context of Use

• OA utility varies in different contexts of use
• A comprehensive statement of
  ➢ Circumstances and manner of use
  ➢ Purpose of use in clinical trial
  ➢ How results applied to decision making
• Evidence used to justify use should be relevant to the intended context of use

• Patient population or subpopulation fully specified
• What is sampled
• How sample is measured (including study features)
• When measured
• How measurements analyzed
• How interpreted and results applied
Good Outcome Assessment Principles

• Define context of use (COU)
• Identify the meaningful health aspect that will be affected (treatment benefit)
• Identify (define) the concept of interest
• Evaluate the relationship of the MHA to the COI
• Define the OA
• Evaluate content validity of OA
• Evaluate performance characteristics of OA
• Re-evaluate intended conclusions/actions based on OA and other parts of COU