

FDA Perspectives on Patient-Reported Outcomes in Cancer Trials

Patient-Reported Outcomes in Clinical Trials:
Evaluating and Enhancing the Payoff to Decision Making

NCI, NIH

September 21, 2006—North Bethesda

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Basis of US FDA drug approval

- Substantial evidence of efficacy from adequate and well-controlled trials
 - Efficacy must represent a clinical benefit
 - Prolongation of life
 - Better life
 - Effect on an established surrogate
- Evidence that the risk does not outweigh the benefit when used as intended

Better life measured with PROs

- Direct assessment of clinical benefit
 - Not a surrogate
 - Elicited without clinical interpretation
 - Part of a general movement toward the thought that patients should participate in decisions about their health
 - Patients are the best source of information about how they feel and function as a result of treatment

Is PRO a synonym for HRQL?

- NO!
- “HRQL” is a multi-domain concept that represents the patient’s overall perception of the impact of a condition and its treatment
- HRQL is measured using complex instruments
- “PRO” is NOT a measurement concept
- A PRO concept can be single or multi-domain
- A PRO can be measured using simple or complex measures

Why are these definitions important?

- If we're not clear in our own discussion, how can we expect the research community to understand what we want to accomplish?
- Evidence that we're not communicating well:
 - "...PRO measurement is ancillary to our real job..."
 - "...MOST clinicians support the value of PROs..."
- **DON'T USE "PRO" WHEN YOU MEAN "HRQL"**

Quote from J. Tukey

- "It is often much worse to have good measurement of the wrong thing-- especially when, as is so often the case, the wrong thing will in fact be used as an indicator of the right thing--than to have poor measurement of the right thing."

How do we know we're measuring the right thing????

- Content validity
 - Patient input early in the instrument development process
 - Confirm that the target concepts represent what the target population considers important regarding their condition and treatment
 - Confirm that the data captured actually represent the intended concepts
- Other measurement properties (construct validity, reliability, ability to detect change, interpretability) cannot make up for inadequate content validity

What constitutes evidence of content validity?

- Summaries and results from patient interviews and focus groups
- Criteria used for item selection
- History of item origin, modification, deletion or addition
- Record of the path to PRO instrument finalization

Does content validity apply to complex measures only?

- NO!
- Simple measures also must be “well-defined and reliable” per regulation

Is the guidance harmful???

- YES! It's harmful to:
 - The practice of measuring undefined constructs
 - Study results that cannot be explained to patients in their own terms
 - Studies that cherry-pick domains without including patients' most important QOL concerns