Quality of Life and Symptom Assessment: An Overview

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• **Purpose:**
  – Improve overall well-being: Quality of Life
  – Enhance symptom control and functional outcome
  – Modify health behaviors

• **Distinct Arena of Clinical Care and Research:**
  – Unlike Hospice, it does not concentrate on End-of-Life
  – Unlike Pain Clinics, the symptoms issues are broad in scope
  – Emphasis on the issues for cancer patients in active treatment and survivors
Biological and Physiological Variables

Symptom Status

Functional Status

General Health Perception

Overall Quality of Life

Psychological Supports

Social and Economic Supports

Social and Psychological Supports

Characteristic of the Environment

Nonmedical Factors
The Cancer Research Arena: More Than Just Drug Studies

- Clinical Research
  - Oriented towards treatment outcomes
- Biological Research
  - Underlying mechanisms
- Epidemiology
- Health Outcomes
- Cancer Control
Cancer Control:

• Vague term which encompasses the following:
  – Quality of life
  – Symptoms
  – Psychological Outcomes
  – Nutrition
  – Rehabilitation
  – Health Behaviors
  – ECT …..
Goal of this lecture . . .

• Provide exposure to this arena of research
• Provide an understanding of the basic constructs that underpin quality of life and symptom control research
• Dispel myths about the “soft science” of supportive care research
Defining Quality of Life:

• Global construct:
  – Perceptions of well-being as influenced by a patient’s experiences, perceptions, expectations and beliefs

• Reflects the patient’s point of view

• Multi-dimensional

• Health related issues are only one contributing factor to Quality of Life - HRQOL
Historical Framework:

• Until 1970’s research in QOL was limited:
  – Lack of interest among investigators
  – Lack of credibility
  – Lack of research tools

• During the 1980’s and early 1990’s:
  – Tool development
  – Key studies demonstrating the benefit of QOL assessment

• Late 1990’s and early 2000’s:
  – Ungoverned use of QOL tools
  – Recognition of limitations of QOL tools
  – Move to a more hypothesis driven approach
Quality of Life: The Challenge of Measurement

• How do you express general well-being in a way that is pertinent to all patients?

Answer: Ask the patient….
Commonly Assessed QOL Domains:

- Physical well being
- Functional well being
- Social well being
- Emotional well being
- Spiritual well being
- Financial well being
Types of Patient Reported Outcomes Measures:

- **General Health:**
  - Sickness Impact Profile
  - SF-36
- **Quality of Life Tools: Cancer Specific**
  - Functional Assessment of Cancer (FACT)
  - European Organization for Research and Treatment of Cancer (EORTC_QLQ 30)
- **Tumor Specific Symptom Surveys:**
  - Modules for specific cancers
  - Vanderbilt Head and Neck Symptom Survey
- **Symptom or Functional Specific Tools:**
  - Brief Pain Inventory
QOL Tool Parameters:

• Item generation
• Reliability
  – test-retest (5-7 days apart)
  – internal consistency
    • evaluative use - individual change over time (> .8)
    • discriminative use - group change (> .7)
• Validity
  – face validity
  – content validity
  – construct validity - scale behaves consistently with theoretical framework
• Responsiveness over time
Determining Clinical Significance

- Distribution-based methods
  - Examples: use of means, use of standard deviations
  - Compare difference in patient score to score of reference population
  - Difference converted into an effect size
- Anchor-based methods
  - Correspondence between change in QOL or symptom and other clinical parameter
  - Develop criterion for clinically significant change for a given parameter
Original QOL Report

• There is a reported change in ABC QOL Scale from 10 to 15
Original QOL Report

• There is a reported change in ABC QOL Scale from 10 to 15

• Range of ABC Scores: 10 to 20
Original QOL Report

• There is a reported change in ABC QOL Scale from 10 to 15

• Range of ABC Scores: 0 to 100
Anchor-based Reports

- Change in ABC QOL Scale from 10 to 15
- Anchors of meaning
  10 - “Poor” QOL
  50 - “Moderate” QOL
  90 - “Excellent” QOL
Anchor-based reports

- Change in ABC QOL Scale from 10 to 15
- Anchors of meaning
  - 10 – Typical ICU patients
  - 50 – PEG-dependent patients
  - 90 – Patients able to work
Clinical Interpretation

- Authors should provide scale’s range of scores
- Authors should provide anchors to guide clinical interpretation
What is clinically meaningful?
Minimally Important Clinical Difference

Can be calculated with:

• Internally-Based (distribution, or statistically based) techniques
• Externally-Based (anchor-based) techniques
Internally-based MCID

- Calculated after analysis of statistical distribution of data (Cohen’s effect size)
- Effect size of 0.20 (20% of standard deviation) is considered minimally important
- Effect size of 0.50 considered moderately important, 0.80 considered highly important
However

- Distribution-based MCID calculations are based in statistics
- Should develop method for calculating MCID based on clinical judgments
Externally-based MCID

- Use clinical ‘anchors’
- Compare changes in QOL to external clinical change or result
Calculating MCID

- Administer QOL scale twice prospectively.
- During second inquiry, administer ‘Changes’ questionnaire as well.
- Calculate MCID of QOL changes in patients indicating minimal change (2/7).
Revisit QOL Report

- Change in ABC QOL Scale from 10 to 15

- MCID: 12 points
Revisit QOL Report

• Change in ABC QOL Scale from 10 to 15

• MCID: 2 points
Commonly Used QOL Tools:

• **FACT-G**
  – 38 questions
  – Likert scale
  – Multiple tumor and symptom specific subscales

• **EORTC QLQ-C30**
  – 65 questions
  – Likert scale
  – Multiple tumor and symptom specific subscales
Why do we need QOL Measures and how are they used?

- Outcome measure in and of itself
- Compare treatment regimens
- Predictive factor for outcome
- Identify issues needing further evaluation and/or intervention
- Provide insight into specific issues for individuals or groups
General Lessons Learned from QOL Studies:

- QOL is a multi-dimensional construct
- Observers are a poor judge of how patients feel about QOL
- High rates of compliance can be achieved for QOL studies
- Aggressive therapy may enhance QOL
- Symptoms disrupt QOL
- QOL may predict survival

Osoba, David: JCO 1994
Examples:
Does Chemotherapy Palliate in the setting of Advanced Cancer

- Randomized trial of best supportive care versus systemic chemotherapy
- Patient population: advanced NSCLC
- Correlative study: QOL assessment

- Results:
  - Improved survival for chemotherapy arm
  - Improved QOL for chemotherapy arm
Does treatment of anemic cancer patients with red cell growth factors improve QOL?

- Randomized, double blind placebo controlled trial
- Patient population: cancer patients with a HGB <10.5
- Treatment: placebo vs Epoetin
- Measures:
  - FACT-an, SF-36, and CLAS
- Results:
  - Decrease in transfusions
  - Increase in HGB
  - Increase in QOL in all cancer and anemia specific domains
E1395: Phase III Trial of Cisplatin + 5FU vs Cisplatin Taxol in Met/Rec HNC

- **Patient Population:**
  - Chemo-naïve Metastatic or Recurrent Disease

- **Treatment:**
  - Arm 1 Cisplatin 100mg/m2 + 5FU 1gm/m2 x 4
  - Arm 2 Cisplatin 75mg/m2 + Taxol 175mg/m2

- **Endpoints:**
  - Response: no difference
  - Median survival and 1 year survival: no difference
  - Toxicity Profile: favored arm 2
FACT: Functional

Maximum score 35

A (n=42)
B (n=33)

p values
Interaction .03
Time .02
Tx .94
Head and Neck Subscale

Maximum score 40

A (n=32) vs B (n=25)

- Interaction p-value: 0.08
- Time p-value: 0.02
- Tx p-value: 0.99

Graph showing comparison of scores between Time 1, Time 2, and Time 3 for groups A and B.
Limitations of QOL as an Outcome Measure:
Quality of Life Over Time:

Response Shift:

“under the influence of a (highly significant) life event, such as getting a life threatening disease……there will be a concurrent change in the internalized standard on which the patient bases their perceptions.”

Symptoms and Function Outcomes:

• Symptoms perceived alterations in sensation
  – Some symptoms are purely subjective and must be measured by self-report (example: pain, fatigue, ect…)
  – Some symptoms are related to alterations in function (example: dysphagia, xerostomia, ect…) and may be measured by PROs or objective measures

• Function loss may or may not be perceived by the patient
  – Thus, function loss may require objective assessment
  – Asymptomatic function loss may clinically be significant
Symptoms and Function Outcomes:

- Symptoms and function loss may be secondary to disease state or treatment.
- Symptoms or function loss due to treatment is termed “adverse effects” or “treatment related toxicity”.
- Acute and late effects of therapy are the result of interactions between the host genetic make-up, treatment and the underlying tumor.
- Patient reports of QOL may return to baseline in the face of significant symptom burden.
  - Response shift
Toxicity Timeline:
Assessment Points

Baseline

Acute Toxicity

Chronic Toxicity

Treatment Duration (red)
Acute Toxicity (green)
Long Term Toxicity (pink)
Ideal Trial Design

- Prospective
  - Allows baseline comparison
- Longitudinal
  - Assessing acute and long term sequella
- Using repeated measure
  - Measures that have been validated
- Homogeneous patient population
- Uniform treatment
- Controlled for confounding factors
Measurement Issues:

• Subjective Measures:
  – Self-report

• Objective Measures:
  – Exercise testing
  – Actigraphs
  – Diet Recall
  – Modified Barium Swallow
Relationship Between QOL and Symptoms
Symptom Intensity and QOL

Cella, JPSM, 1994
Symptom Duration and Quality of Life

- Chronicity
- No Relationship
- Adaptation
Major Issues in Design & Method: Instrument Selection

• Do you want to study general QOL or a specific symptom or functional outcome?
• What is the purpose of obtaining data?
  – Change treatment or policy?
• What time burden will patients be able to tolerate?
  – How can you minimize subject burden.
<table>
<thead>
<tr>
<th>Type of Decision</th>
<th>Level of Instrument</th>
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<tbody>
<tr>
<td>• Policy decisions</td>
<td>• Generic</td>
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<tr>
<td>• Best treatment for</td>
<td>• Disease-specific (e.g., cancer)</td>
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<tr>
<td>patient population</td>
<td>• Symptom or treatment specific</td>
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<tr>
<td>• Individual patient</td>
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<tr>
<td>options</td>
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**Instrument Characteristics**

<table>
<thead>
<tr>
<th>Single item measures</th>
<th>Multiple item scales</th>
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<tbody>
<tr>
<td>• Numeric Rating Scale</td>
<td>• SF-36</td>
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<tr>
<td>• Visual Analogue Scale</td>
<td>• FACT-G</td>
</tr>
<tr>
<td></td>
<td>• Brief Pain Inventory – Interference Scale</td>
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**Benefits**

- Global
- Low subject burden

**Benefits**

- Comprehensive
- High subject burden