What does the patient want?

- to be cured (duh!)
- If not cured, then to be taken care of:
  - Via the best treatment
  - With empathy and dignity
  - To be heard and informed
What is a PRO?

• Measurement of any aspect of a patient’s health status that comes directly from the patient

Examples:
• Function
• Symptoms (intensity, frequency)
• Satisfaction (with medication)
• Well-being
• Quality of life (QOL).

...so our goal is...

• To establish an ongoing conversation of “how are you” with all stakeholders
• Do it without overburdening the patient, clinician or the system
• Accomplish this in an environment where everyone is stressed and has no time
• Sounds simple, right?
Everyone in this room cares about what the patient has to say in theory but how do we use PROs in reality?

1) Make assessing PROs simple (burden)
2) Make PROs easy to understand
3) Link PROs to “hard outcomes”
4) Answer “what do I do with PRO data?”
5) Treat PROs like any other vital sign/lab test

Too many surveys: too little time


- “A survey, again? You are the third survey team who visited us during these couple of months. I am fed up with ...”

- These words greeted me and my assistant at a house in Zalingei Internally Displaced Persons (IDPs) camp in Darfur in 2004. Health surveys play an increasingly critical role in responses to humanitarian crises and in monitoring progress towards the Millennium Development Goals, yet survey ethics are rarely discussed.

Heard in clinics across the world...

“[Cartoon image]: ‘You’ve got six months, but with aggressive treatment we can help make that seem much longer.’”
And clinicians do not have extra time in visits

Can we demonstrate the pay-off?

Genesis

- Affordable Care Act Beacon Project
- SE MN Health care agencies share data in the clinic in real time
- Include PRO data
- Focus groups and literature developed a list of 25 questions
- “Great! But there is no way in **** that will work…”

Fifteen Years Ago
(September, 1995)

- Plethora of assessment tools for quality of life (QOL) and patient-reported outcomes (PROs)
- Disappointing recent clinical trial results in terms of missing data, clinical significance, reliability issues
- “…so you’re suggesting we should all do with QOL what a dog does to a fire hydrant…”
Today

• Guidelines for virtually all outstanding issues
  • missing data (Fairclough, Design and Analysis of Quality of Life Studies in Clinical Trials, Chapman-Hall, 2010)
  • clinical significance (Sloan et al. MCP, 2002)
  • psychometrics (Sloan et al. Current Problems in Cancer, 2006)
  • regulatory issues (Sloan et al. Value in Health, 2008)
  • item response theory (Reeve et al. QOLR, 2007)
  • Inclusion in clinical practice (Guyatt et al. MCP/VIH, 2008)
  • Genetics (Sloan et al. December 2010, QOLR)

Hold that thought…

I have data relating to a new biomarker
A prognostic factor for cancer patient survival

It is called BMA

Biomarker Assay (BMA) Positive versus Negative
23 trials (3,704 patients)
Median survival (months) across sites

<table>
<thead>
<tr>
<th>Site</th>
<th>BMA-</th>
<th>BMA+</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI</td>
<td>9.1</td>
<td>16.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>GU</td>
<td>15.5</td>
<td>52.4*</td>
<td>0.0032</td>
</tr>
<tr>
<td>Lung</td>
<td>7.0</td>
<td>10.8</td>
<td>0.0003</td>
</tr>
<tr>
<td>Breast</td>
<td>16.6</td>
<td>26.2</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

* Not reached (projected)

Multivariate Cox Model for Survival

<table>
<thead>
<tr>
<th>Variable</th>
<th>P-Value</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMA-</td>
<td>&lt;.001</td>
<td>1.56 (1.40, 1.75)</td>
</tr>
<tr>
<td>Performance</td>
<td>&lt;.001</td>
<td>1.77 (1.62, 1.93)</td>
</tr>
<tr>
<td>Score (1-2 versus 0)</td>
<td>&lt;.001</td>
<td>1.37 (1.14, 1.65)</td>
</tr>
<tr>
<td>Age</td>
<td>0.075</td>
<td>1.00 (1.00, 1.01)</td>
</tr>
<tr>
<td>Minority</td>
<td>0.219</td>
<td>0.91 (0.79, 1.06)</td>
</tr>
<tr>
<td>GI</td>
<td>&lt;.001</td>
<td>2.02 (1.65, 2.47)</td>
</tr>
<tr>
<td>Lung</td>
<td>&lt;.001</td>
<td>0.64 (0.47, 0.88)</td>
</tr>
<tr>
<td>Breast</td>
<td>0.006</td>
<td>1.46 (0.96, 2.21)</td>
</tr>
<tr>
<td>GU</td>
<td>0.078</td>
<td>1.46 (0.96, 2.21)</td>
</tr>
</tbody>
</table>

Replication of results

- A recent meta-analysis (n=13,874) indicated that 36 of 39 studies indicated that analogues of BMA+ were significantly associated with overall survival (Gotay, JCO, 26: 1355–1363, March 2008)
- Another meta-analysis involving over 10,000 patients indicated that BMA+ analogue was prognostic for survival (Efficace, ASCO 2008)
- A literature review of over 100 studies from 1982 to 2008 indicated that BMA+ measures were significant independent predictors of survival duration (Montazeri, HOLO, 7:102, 2009)
Is this convincing evidence that BMA+ is a promising prognostic factor for cancer patient survival?

• What is BMA+?

BMA- = a score of 5 or less in patient-reported QOL on a 0-10 scale

Directions: Please circle the number (0-10) best reflecting your response to the following that describes your feelings during the past week, including today.

How would you describe:

d. your overall Quality of Life?

10: as bad as it can be
9:...
8:...
7:...
6:...
5:...
4:...
3:...
2:...
1:...
0: as good as it can be

This is a reliable and valid measure for cancer patient populations

(Sloan, MCF, 2002 & JCO, 2012; Huschka, Cancer, 2005; Locke, JPSM, 2007)

cut-off validation:

Butt, JPSM,2008; Sloan, Value in Health, 2007; Temel, J Thorac Oncol, 2006

Clinically Deficient Fatigue (CF) vs not Clinically Deficient Fatigue (nCF):

43 trials (3,915 patients)

<table>
<thead>
<tr>
<th>nCF</th>
<th>Median Survival (Months)</th>
<th>95% CI</th>
<th>Log-rank P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF</td>
<td>31.5 (25.9, 42.4)</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>nCF</td>
<td>&gt;83.9 (NA)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Long history of development and validation of questions for diagnostic use

LASA
Linear Analog Self Assessment
12 questions

Putting PROs into Practice Real time

Realtime Output: Intervention Triggers
Single-item QOL, fatigue and pain

Please circle the number (0-10) best reflecting your response to the following that describes your feelings during the past week, including today.

How would you describe:

1. your overall Quality of Life?
   1 2 3 4 5 6 7 8 9 10
   No benefit
   As good as it can be

2. the severity of your pain, on the average?
   0 1 2 3 4 5 6 7 8 9 10
   No pain
   Pain as bad as it can be

3. your level of fatigue, on the average?
   0 1 2 3 4 5 6 7 8 9 10
   No fatigue
   Fatigue as bad as it can be

How are you Doing?
An empirically-based model of prognostic factors for survival

Fatigue
Overall QOL
Performance Status

5-15%
10-20%
10-25%

Routinely collected in all phase III clinical trials NCCTG/Alliance

Clinical Pathway for Overall QOL Deficit Management
Case Study

- 8 year cancer survivor annual visit
- Rated QOL as a 2 out of 10
- Initiated conversation
- Insomnia
- “stupid thoughts”
- Suicidal ideation

Case Study

- Psych referral
- Anti-depressant
- 1 month later QOL was 7

Case Study

- 57 year old colorectal cancer patient, halfway through chemo (folfiri)
- Patient’s labs, tx look fine
- Fatigue of 2 (bad)
- Try dose modification
- Labs, tx remain fine, fatigue score improves to 8 for remainder of Tx
Case Study

- Surgical patient says pain is 7
- Objective test for mobility indicates level associated with no pain
- Surgeon combines PRO and test data
  - Will give you more pain meds because you seem to be saying you need them
  - Watch for cognition and constipation

Findings (Hubbard, JOP, May, 2014)

- QOL and fatigue measured in over 30,000 clinical visits
- Oncology staff provided feedback:
  - 86% endorsed the use of PROs
  - Over 90% indicated that it did not change clinic visit time nor did it add more work
  - Allowed for a validation of their perception of patient well-being
  - Enhanced their practice, established more goals
  - They felt more prepared for the visit
  - Raised issues otherwise undiscovered in 25%-40% of cases

We know incorporating PROs into Oncology Practice improves communication (Detmar, JAMA, 2002; Velkova, JCO, 2012)

- Incorporating standardized QOL assessments in daily clinical oncology practice facilitates the discussion of QOL issues and can heighten physicians' awareness of their patients' QOL.
- But what do we do with PRO information?
So how do we use this clinical trial science to make it real in the clinic?

- We know that a deficit in patient-reported overall QOL is associated with a doubling of the risk of death across a broad spectrum of cancer patients.
- We know the cutoff is similar across many PRO domains.
- We also know that a change of two points on a 0-10 scale is non-ignorable.

Testing Real-time QOL assessment in a radiation oncology clinical practice
(MCS1065, PI: Halyard; ASCO, 2012)

- 96% of patients would participate in this study again or recommend others to use the system
- 90% of physicians/nurse/nurse practitioners are satisfied/highly satisfied with the communication with their patient during the visit

...meanwhile in the Mayo oncology clinic....

- September 1, 2010: all oncology patients administered overall QOL and fatigue single items upon intake
- As part of a quality improvement project, the QOL and fatigue measures became part of the EMR, right after the pain assessment.
A Theoretical Model for Quality of Life

Molecular and genetic factors

Characteristics of the individual

- Psychological and psychosocial factors
- Symptoms status
- Functional status
- General health perceptions
- Overall quality of life

Characteristics of the environment

Sprangers & Sloan, QOLR, Dec. 2010

PRO-driven patient-centered integrated care

PRO-driven patient-centered integrated care

- Problems playing your role in life
- Caring for child
- Dealing with stress, anxiety, or fear

Supportive care needs

- Contact clinic
- Refer to Financial Services
- Refer to local support groups
- Refer to pharmaceutical programs
- Contact community financial aid
- Provide web support links
- Alert case manager

Financial Services

- Consult community financial aid
- Refer to pharmaceutical programs
- Refer to local support groups
- Contact community financial aid
- Provide web support links
- Alert case manager

How is your QUALITY OF LIFE?