Patient Reported Outcomes: What Does the Patient Want?

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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

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Too many surveys: too little time

- Hirotsugu Aigaa. Bombarding people with questions: a reconsideration of survey ethics. Bull World Health Organ. Nov 2007; 85(11): 823.
- "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.

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Heard in clinics across the world…

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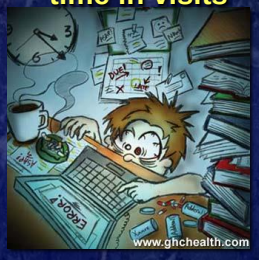
And clinicians do not have extra time in visits



Can we demonstrate the pay-off?

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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…"

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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…"

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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, 2005/2006)
  - 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)*

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Hold that thought…

I have data relating to a new biomarker

A prognostic factor

for cancer patient survival

It is called BMA

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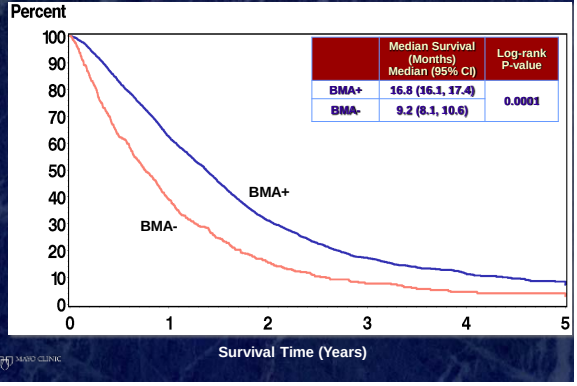
Biomarker Assay (BMA) Positive versus Negative

23 trials (3,704 patients)



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Median survival (months) across sites

Site	BMA-	BMA+	P-value
GI	9.1	16.7	<0.0001
GU	15.5	52.4*	0.0032
Lung	7.0	10.8	0.0003
Breast	16.6	26.2	0.0002

* Not reached (projected)

Multivariate Cox Model for Survival

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

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, HQLO, 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:

1. your overall Quality of Life?

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

This is a reliable and valid measure for cancer patient populations

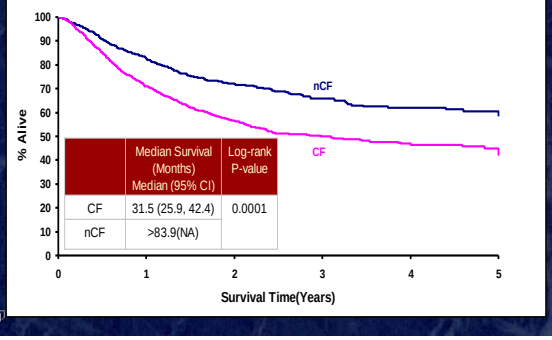
(Sloan, MCP, 2002 & JCO, 2012; Huschka, Cancer, 2005; Locke, JPSM,2007)

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)



	Median Survival (Months) Median (95% CI)	Log-rank P-value
CF	31.5 (25.9, 42.4)	0.0001
nCF	>83.9(NA)	

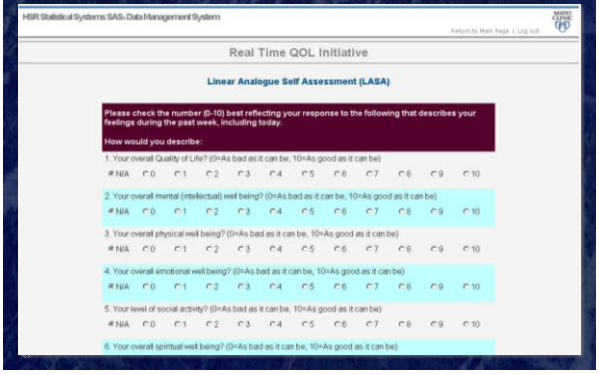
Long history of development and validation of questions for diagnostic use

LASA

Linear Analog Self Assesment

12 questions

Putting PROs into Practice Real time



Realtime Output: Intervention Triggers

Pt ZZ111111: LASA Scores by Week Since Treatment Started

Please click on the QOL domain links for Disease Management Pathways.

Items in **MAROON** represent complaints that are worse than average (5 points or below) and may warrant attention.
Items in **RED** represent a drop of 2 points or more
Items in **GREEN** represent a 2 points or more improvement on the measure since the last visit.

Factor Measured (0=worst QOL and 10=best QOL)	Baseline	Week 1	Week 3	Week 5	Last Week of Rx	Last Week of Rx Minus Week 5
Quality of Life	9	7	10	7	8	1
Mental (Intellectual) WB	8	10	7	6	9	3
Physical WB	7	6	7	9	3	-6
Emotional WB	9	8	6	8	7	-1
Social Activity Level	7	4		10	10	0
Spiritual WB	6	10	6	7	9	2
Pain Frequency	2	2		4	2	-2
Pain Severity	3	5		0	3	3
Fatigue Level	2	6	1	1	1	0
Level of Support	9	8	5	10	8	-2
Financial Concerns	7	7	9	9	10	1
Legal Concerns	10	8	9	8	7	-1

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?**

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

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

Fatigue	5-15%
Overall QOL	10-20%
Performance Status	10-25%

Routinely collected in all phase III clinical trials NCCTG/Alliance

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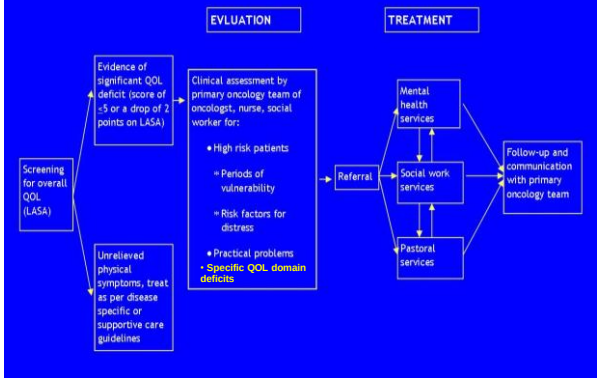
Clinical Pathway for Overall QOL Deficit Management



Case Study

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

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Case Study

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

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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

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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

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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

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We know incorporating PROs into Oncology Practice improves communication (Detmar, *JAMA, 2002; Velikova, 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?

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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.

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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

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…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.

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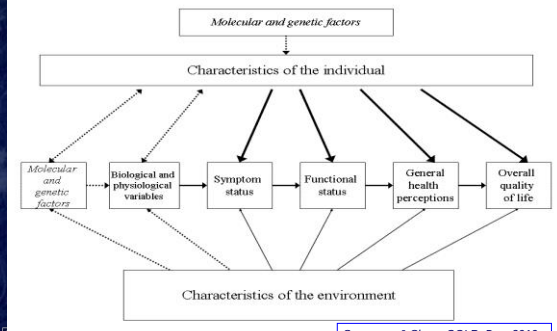
A Theoretical Model for Quality of Life



Sprangers & Sloan, QOLR, Dec. 2010

PRO-driven patient-centered integrated care