



Patient Reported Outcomes in Kidney Cancer

Vision of Hope: A Kidney Cancer Educational Symposium

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Agenda

- What are patient-reported outcomes?
- Unique data obtained using PROs
- What have we learned about kidney cancer and its treatment using PROs?
- Moving from PROs as observational to actionable



Assessment Options

- Observation
- Clinical examination
- Labs
- Imaging
- Clinician-rated toxicities
- Patient-reported outcomes (PROs)



What are patient-reported
outcomes?

Patient-Reported Outcomes: PROs

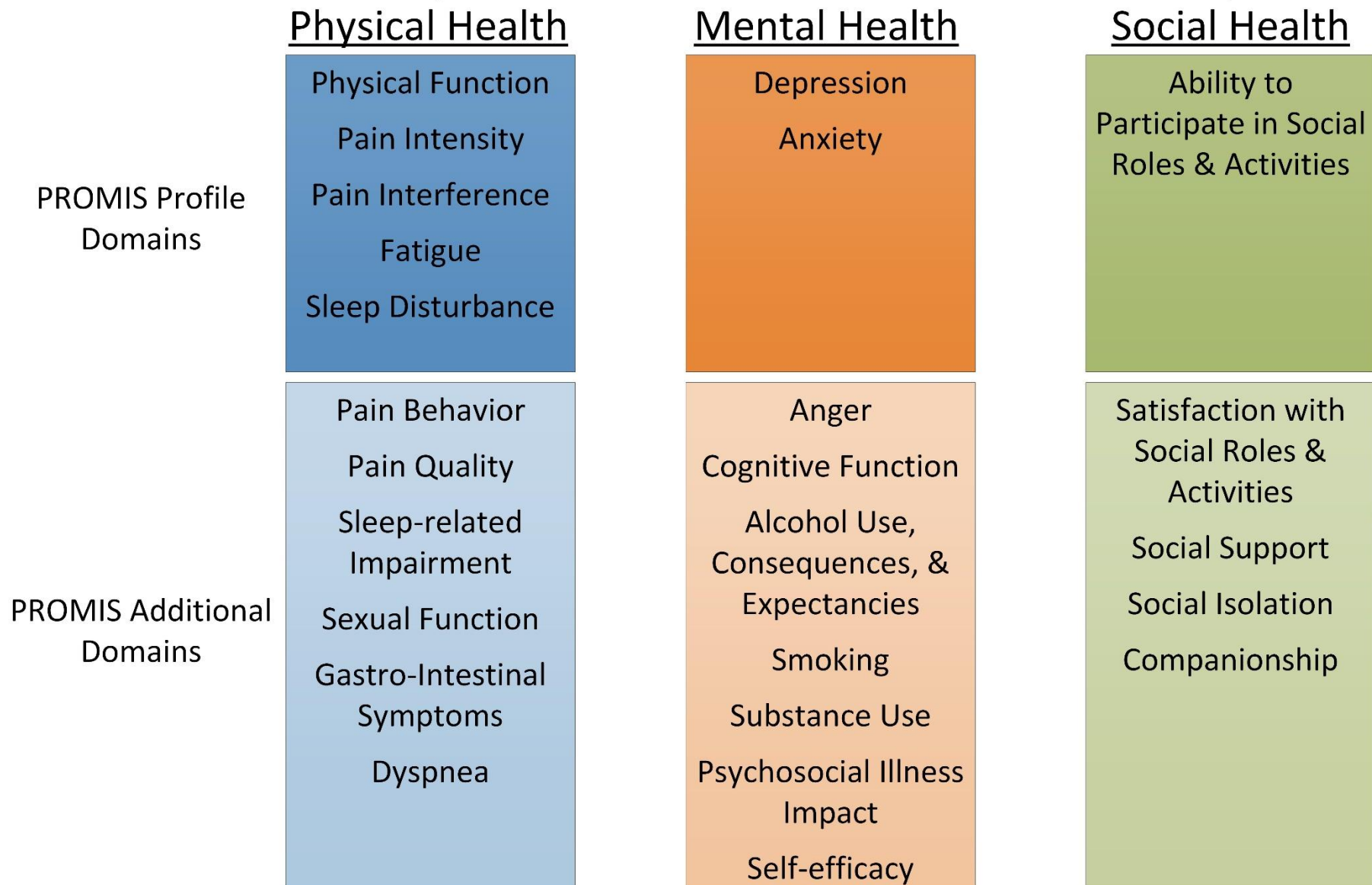
Food and Drug Administration (FDA) defines PROs as
“outcomes reported directly by patients without
interpretation by clinicians”

- BMJ 2010



PROMIS Adult Self-Reported Health

Global Health



PROMIS Pain Interference Short Form



In the past 7 days...

| | | Not at all | A little bit | Somewhat | Quite a bit | Very much |
|---|--|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| 1 | How much did pain interfere with your day to day activities? | <input type="checkbox"/> 1 | <input type="checkbox"/> 2 | <input type="checkbox"/> 3 | <input type="checkbox"/> 4 | <input type="checkbox"/> 5 |
| 2 | How much did pain interfere with work around the home?..... | <input type="checkbox"/> 1 | <input type="checkbox"/> 2 | <input type="checkbox"/> 3 | <input type="checkbox"/> 4 | <input type="checkbox"/> 5 |
| 3 | How much did pain interfere with your ability to participate in social activities? | <input type="checkbox"/> 1 | <input type="checkbox"/> 2 | <input type="checkbox"/> 3 | <input type="checkbox"/> 4 | <input type="checkbox"/> 5 |
| 4 | How much did pain interfere with your household chores?..... | <input type="checkbox"/> 1 | <input type="checkbox"/> 2 | <input type="checkbox"/> 3 | <input type="checkbox"/> 4 | <input type="checkbox"/> 5 |
| 5 | How much did pain interfere with the things you usually do for fun? | <input type="checkbox"/> 1 | <input type="checkbox"/> 2 | <input type="checkbox"/> 3 | <input type="checkbox"/> 4 | <input type="checkbox"/> 5 |
| 6 | How much did pain interfere with your enjoyment of social activities?..... | <input type="checkbox"/> 1 | <input type="checkbox"/> 2 | <input type="checkbox"/> 3 | <input type="checkbox"/> 4 | <input type="checkbox"/> 5 |

Unique Perspectives Gained from PROs

- PRO measures are the gold standard for assessing subjective concerns
 - Symptoms: pain, fatigue, distress
 - Impact of symptoms on continuing meaningful activities
 - Knowledge, attitudes, behavior
- Same biological value in 2 patients \neq same impact
- Health-related QOL scores predict survival in many conditions
- PROs signify risk for issues with treatment-related tolerability



Patient-Generated Symptom Data More Accurate than Clinician Ratings

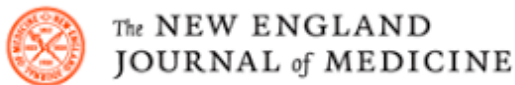
- PROs more accurate than clinician-rated toxicities in assessing symptom burden and quality of life
- Symptom ratings directly from patients provide more precise and reliable symptomatic adverse event detection in clinical trials
- Clinical investigators miss nearly half of symptomatic adverse events



Basch NEJM 2010
Basch et al JNCI 2009
Fromme et al JCO 2004
Velikova et al JCO 2001

Complex Factors Affect Patient-Provider Communication

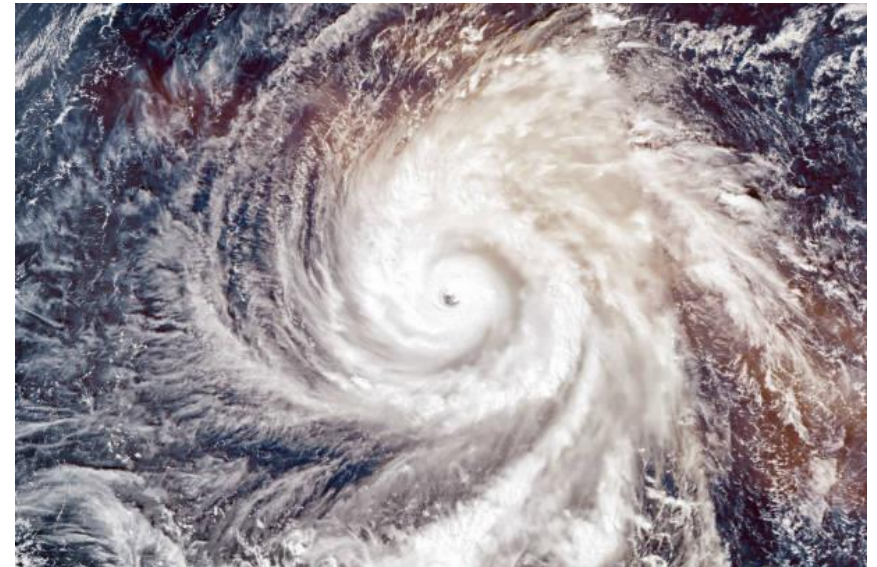
- Patients face inherent disincentives to reporting symptoms, toxicities
 - Desire to preserve rapport
 - Concerns about dose reductions, dose delays
- Providers assume patients will raise concerns



Talking about Toxicity — “What We’ve Got Here Is a Failure to Communicate”

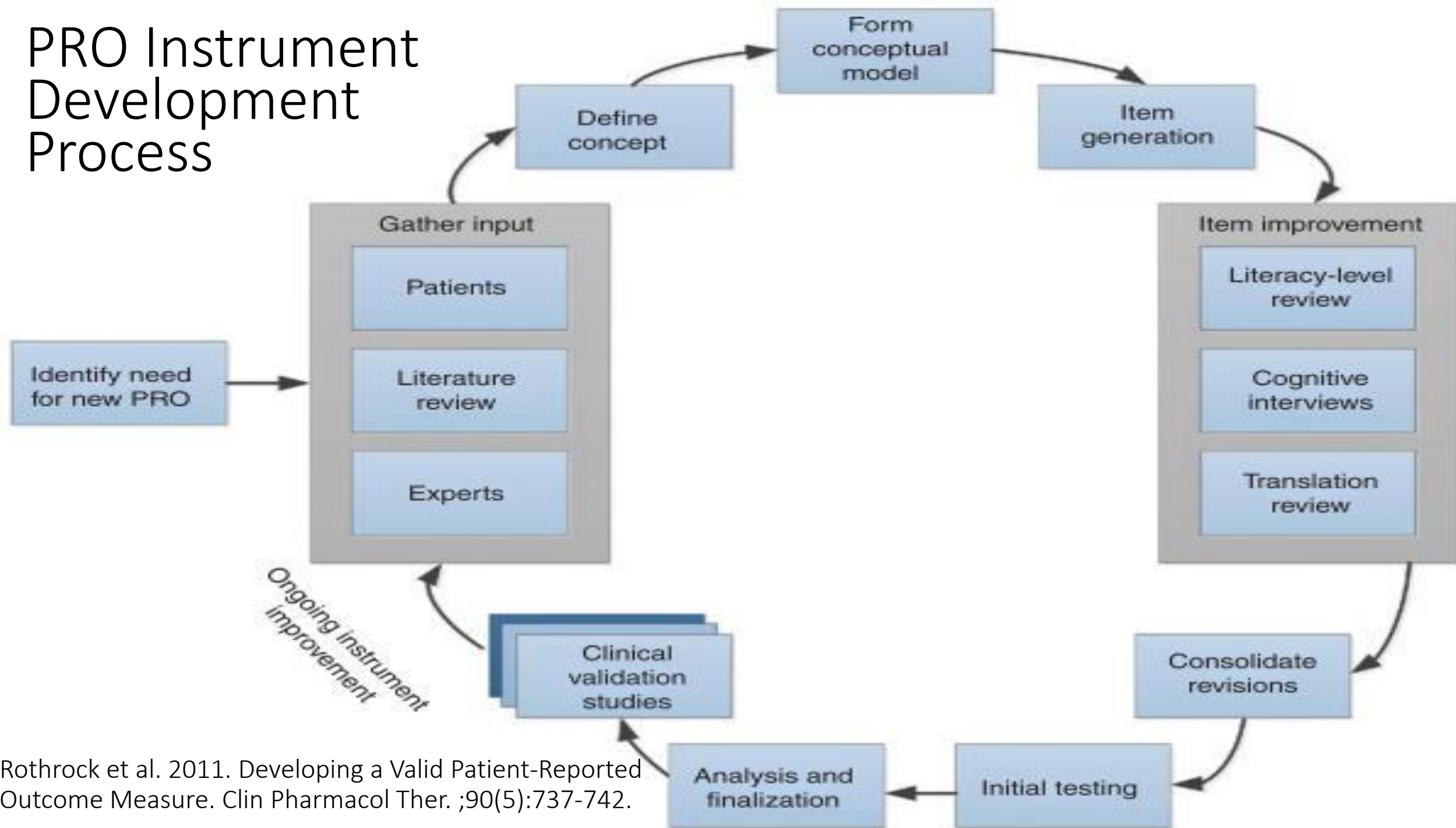
Chana A. Sacks, M.D., M.P.H., Pamela W. Miller, B.A., and Dan L. Longo, M.D.

October 10, 2019



How can you get high quality
information from patients?

PRO Instrument Development Process



Rothrock et al. 2011. Developing a Valid Patient-Reported Outcome Measure. Clin Pharmacol Ther. ;90(5):737-742.

What have we learned about
kidney cancer and treatment
using PROs?

Value Added: PRO Data

- Quantify domains important to the patient
- Facilitate patient-centered care
- Facilitate shared decision-making
- Inform expectations during and following treatment
- Inform role of new agents in treatment
- Enable cost utility analyses to guide health policies



PRO Outcomes: Localized renal cancer

- Laparoscopic nephrectomy vs Open surgery
 - > short-term physical function
- Nephron-sparing surgery vs Radical nephrectomy
 - > Physical function
 - ↓ intrusive thoughts, avoidance behavior, anxiety, worry
 - RN associated with greater worry regarding loss of kidney function
- Partial nephrectomy vs Radical nephrectomy
 - > Physical function
 - ↓ fatigue, sleep disturbance, pain
- Patient perception of remaining renal function significant and independent predictor of HRQL

PRO Outcomes: Localized renal cancer

- Ablative therapy, active surveillance vs Operative management
 - Comparable psychological outcomes
 - Caveat: sparse data
- HRQL returns to baseline following surgical management
 - 50% by 4 weeks
 - 80% by 12 weeks

PRO Outcomes: Localized renal cancer

Research gaps

- PRO data on robotic surgery, ablation, and active surveillance
 - European Active Surveillance of Renal cancer (EASE) currently underway
- Long-term impact of cancer survivorship
- Sexual function

ECOG-ACRIN E2805: PRO findings

- Adjuvant sunitinib or sorafenib for high-risk, non-metastatic renal-cell carcinoma
 - Hass et al. Lancet 2016

1B: PROMIS Fatigue T score

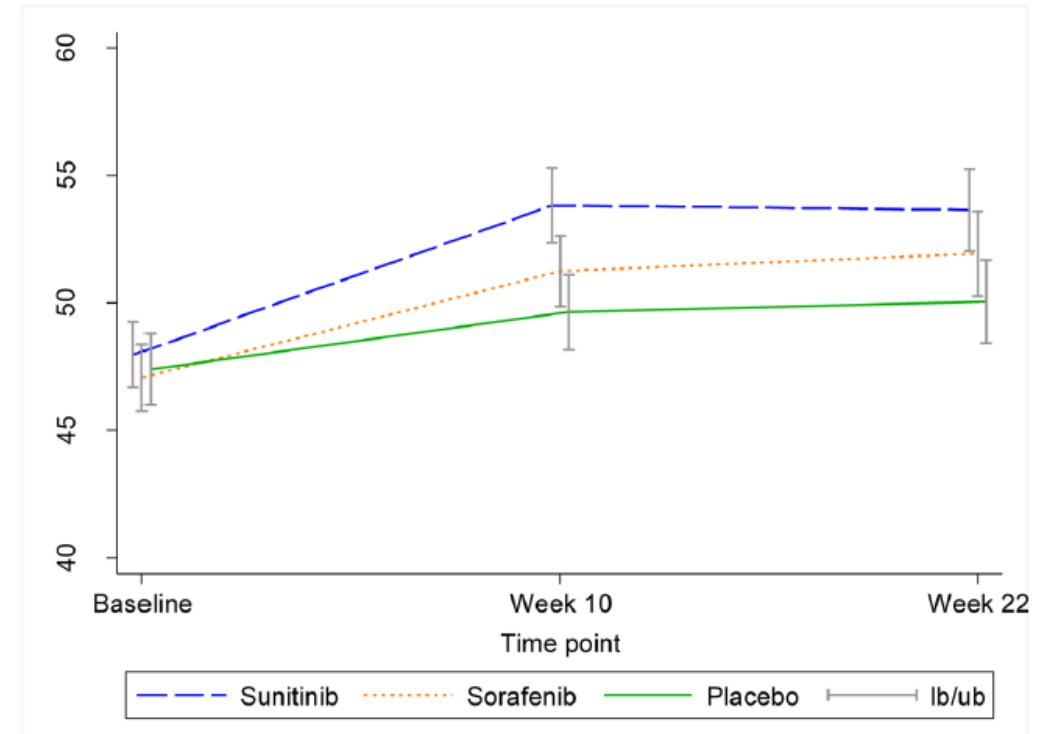


Figure 1.

Mean score and 95% CI of fatigue score by treatment arm

PROs to Inform Treatment Options: mRCC

- Increasing availability of molecular targeted therapies for mRCC
- Efficacy of new agents:
 - Relieve disease-related symptoms
 - Tolerability of treatment-related adverse events
 - Availability of interventions to manage AEs

➤ HRQL

PRO Outcomes: Metastatic renal cancer

| Sunitinib | Sorafenib | Pazopanib | Everolimus |
|---|---|------------------------------------|---|
| Improvement in disease-related symptoms compared to IFN-alpha | FKSI-10 score comparable to placebo, maintained HRQL comparable to placebo | Maintained HRQL similar to placebo | Maintained HRQL similar to placebo |
| Fewer severe disease-related symptoms than with IFN-alpha | Improvement in some symptoms: coughing, loss of breath, fever, enjoyment of life, worry | | Prolonged time to deterioration in HRQL and functional status |
| Greater toxicity-adjusted PFS rate than with IFN-alpha | No worsening in symptoms: fatigue, sleep quality, pain, weight loss | | |
| | Prolonged median time to health status deterioration | | |
| | Baseline FKSI predictive of OS rate | | |

PRO Outcomes: Advanced renal cancer

- METEOR phase III RCT: Cabozantinib and everolimus comparable
 - Disease related symptoms
 - Overall HRQL

| Cabozantinib Superior | Everolimus Superior |
|--------------------------------|---------------------|
| Less shortness of breath | Less diarrhea |
| Improved Time to deterioration | Less nausea |

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ORIGINAL REPORT

Quality of Life Outcomes for Cabozantinib Versus Everolimus in Patients With Metastatic Renal Cell Carcinoma: METEOR Phase III Randomized Trial

David Cella, Bernard Escudier, Nizar M. Tannir, Thomas Powles, Frede Donskov, Katriina Peltola, Manuela Schmidinger, Daniel Y.C. Heng, Paul N. Mainwaring, Hans J. Hammers, Jae Lyun Lee, Bruce J. Roth, Florence Marteau, Paul Williams, John Baer, Milan Mangeshkar, Christian Scheffold, Thomas E. Hutson, Sumanta Pal, Robert J. Motzer, and Toni K. Choueiri

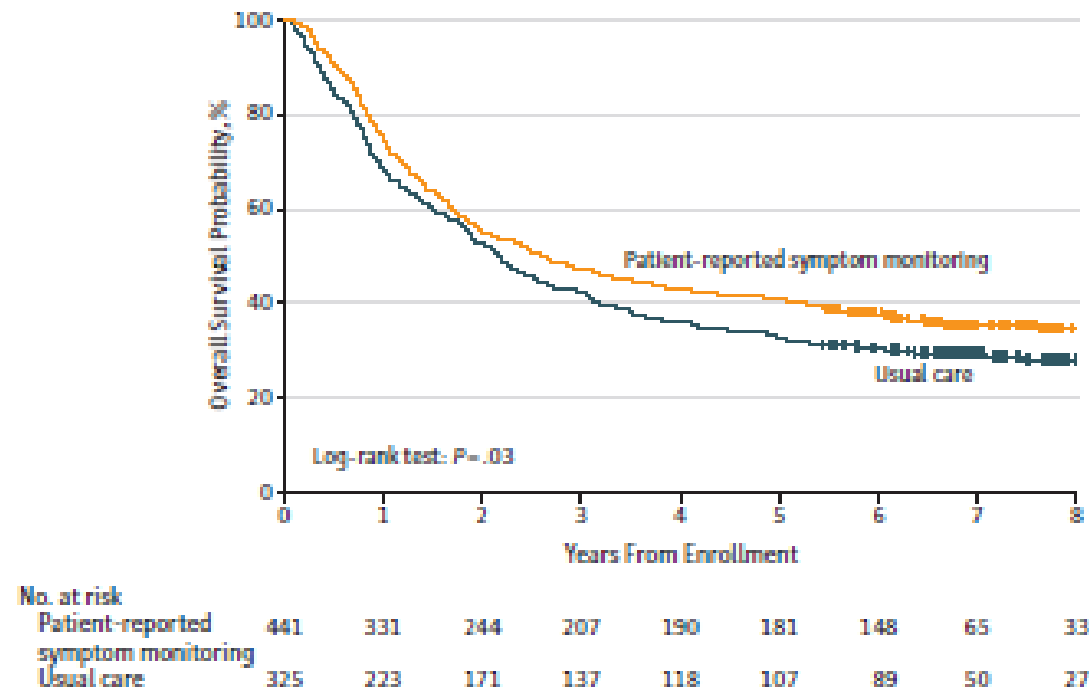
Moving from PROs as
Observational to PROs as
Actionable

Basch et al STAR Trial

- 766 patients randomized to Symptom Tracking and Reporting (STAR) or usual care
- Patients initiating chemotherapy at MSK for metastatic breast, genitourinary, gynecologic, or lung cancers
 - Types selected to represent spectrum of symptoms, metastatic for continuous tx/sx burden
- STAR = 12 PRO-CTCAE items, remote access or use of tablet or kiosk in clinic
 - Email alert to nurses ≥ 2 pts or grade ≥ 3
- Report printed for MD, nurse at each clinic visit

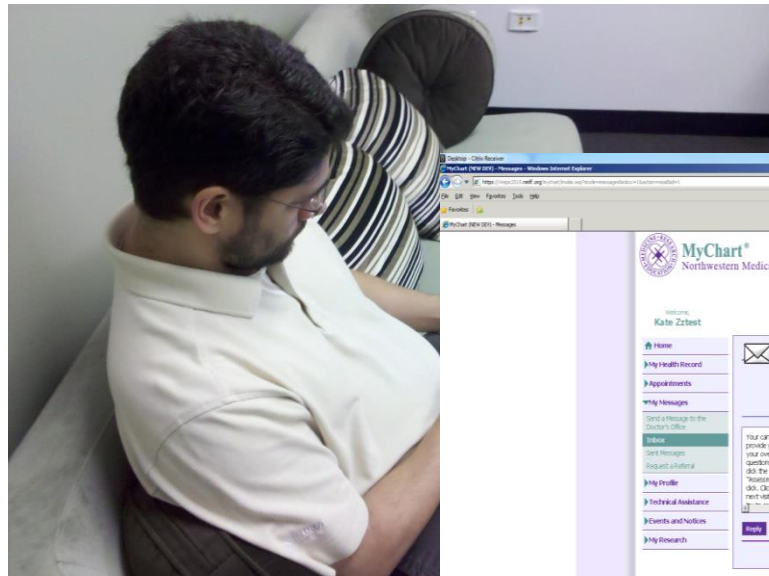
ePRO Symptom Monitoring: Survival Benefit

Figure. Overall Survival Among Patients With Metastatic Cancer Assigned to Electronic Patient-Reported Symptom Monitoring During Routine Chemotherapy vs Usual Care



Crosses indicate censored observations. Enrollment in the patient-reported symptom monitoring group was enriched for a preplanned subgroup with low baseline computer experience as part of a feasibility substudy with a 2:1 randomization ratio in that subgroup ($N = 227$) and a 1:1 ratio in the computer-experienced subgroup ($N = 539$), yielding 441 participants in the patient-reported symptom monitoring group, and 325 in the usual care group. With a minimum follow-up of 5.4 years, median follow-up was 6.9 years (interquartile range, 6.5–7.7) for the electronic patient-reported symptom monitoring group and 7 years (interquartile range, 6.6–8.1) for the usual care group.

Levering Informatics to Implement ePRO Symptom Monitoring

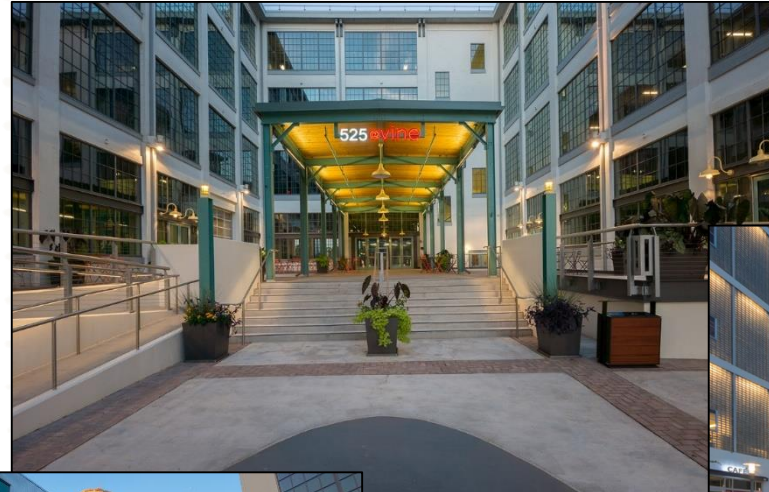


| Results | | | CC PATIENT SYMPTOM ASST (Order 75418233) |
|--|--|---|---|
| Result Information | | | |
| Exam Date and Time 5/20/2012 12:00 AM | | Status Final result -- Abnormal | Result Date and Time 5/20/2012 9:25 PM |
| Assessment Results | | | |
| Question | | Response | |
| In the past 7 days How often did you have to push yourself to get things done because of your fatigue? | | 5-Always | |
| In the past 7 days How run-down did you feel on average? | | 5-Very much | |
| In the past 7 days How fatigued were you on average? | | 5-Very much | |
| In the past 7 days What was the level of your fatigue on most days? | | 4-Severe | |
| Fatigue bank score | | 73.94 Severe | |
| In the past 7 days how much did pain interfere with your day to day activities? | | 3-Somewhat | |
| In the past 7 days how much did pain interfere with your ability to participate in social activities? | | 5-Very much | |
| In the past 7 days how much did pain interfere with your enjoyment of social activities? | | 3-Somewhat | |
| In the past 7 days how much did pain interfere with work around the home? | | 3-Somewhat | |
| Pain Intensity bank score | | 63.09 Moderate | |
| Does your health now limit you in doing two hours of physical labor? | | 1-Cannot do | |
| Are you able to do chores such as vacuuming or yard work? | | 1-Unable to do | |
| Are you able to carry a shopping bag or briefcase? | | 1-Unable to do | |
| Does your health now limit you in walking about the house? | | 2-Quite a lot | |
| Physical Function bank score | | 23.47 Severe | |
| Lab and Collection | | | |
| CC PATIENT SYMPTOM ASST (Order#75418233) on 5/20/12 - Lab and Collection Information | | | |
| Result History | | | |
| CC PATIENT SYMPTOM ASST (Order#75418233) on 5/20/12 - Order Result History Report | | | |
| Downloaded by I list | | | |

Bringing PROMIS to Practice: Brief and Precise Symptom Screening in Ambulatory Cancer Care

Lynne I. Wagner, PhD^{1,2}; Julian Schink, MD³; Michael Bass, MS¹; Shalini Patel, BS¹; Maria Varela Diaz¹; Nan Rothrock, PhD^{1,2}; Timothy Pearman, PhD^{1,2}; Richard Gershon, PhD¹; Frank J. Penedo, PhD^{1,2}; Steven Rosen, MD⁴; and David Cella, PhD^{1,2}

Thank you!



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