



# **PATIENT OUTCOMES PERSPECTIVE: PATIENT REPORTED OUTCOMES (PROs) & PERSONAL COST OF CANCER**

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*There are no conflicts to disclose*

# Outline

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1. Defining PROs
2. How do PROs help stakeholders?
3. How PROs can enhance value models
4. Which PROs should be used?
5. Interventions for toxicity based on PROs
6. Call to action

# Patient-Reported Outcomes (PROs)

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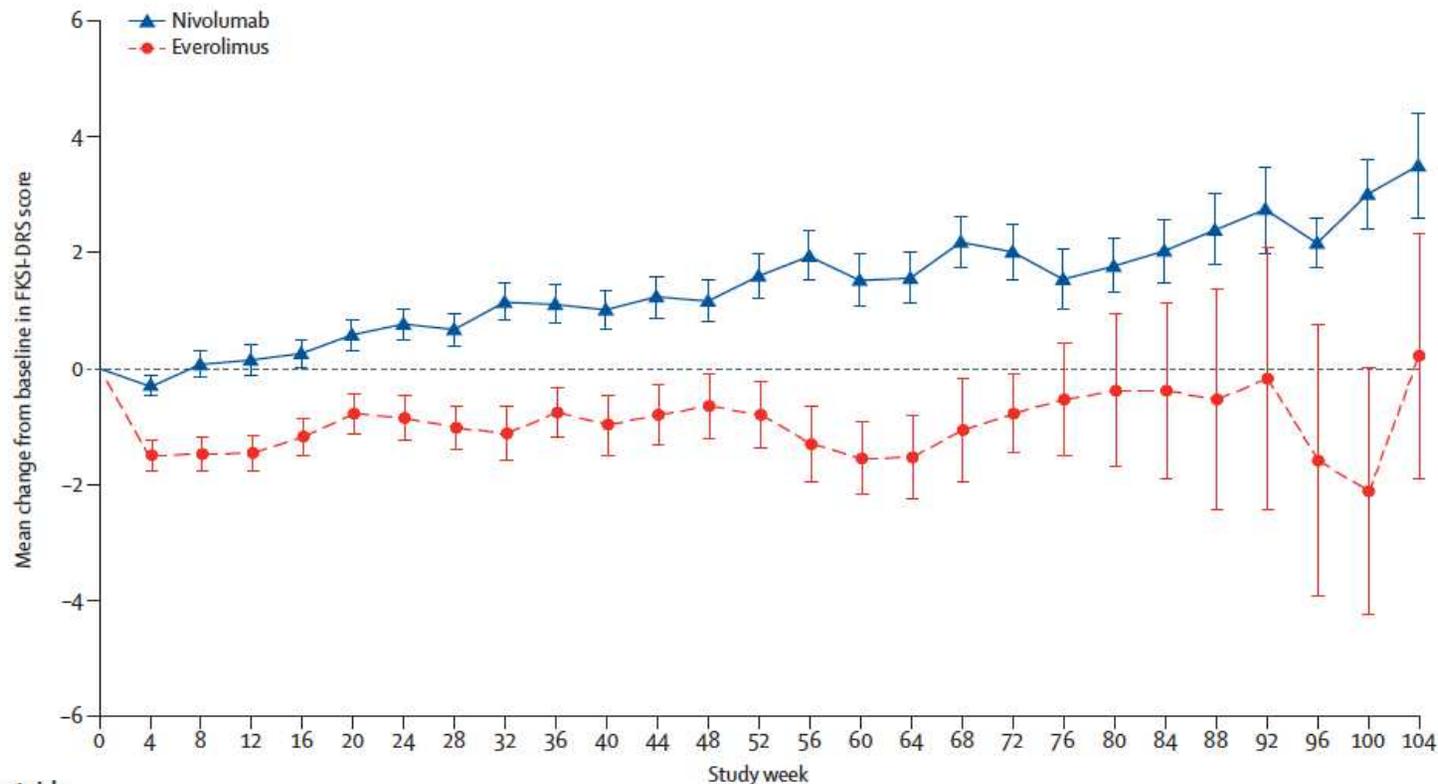
“Any report of the status of a patient’s health condition that comes directly from the patient, without interpretation of the patient’s response by a clinician or anyone else.”



# How Do PROs Help?

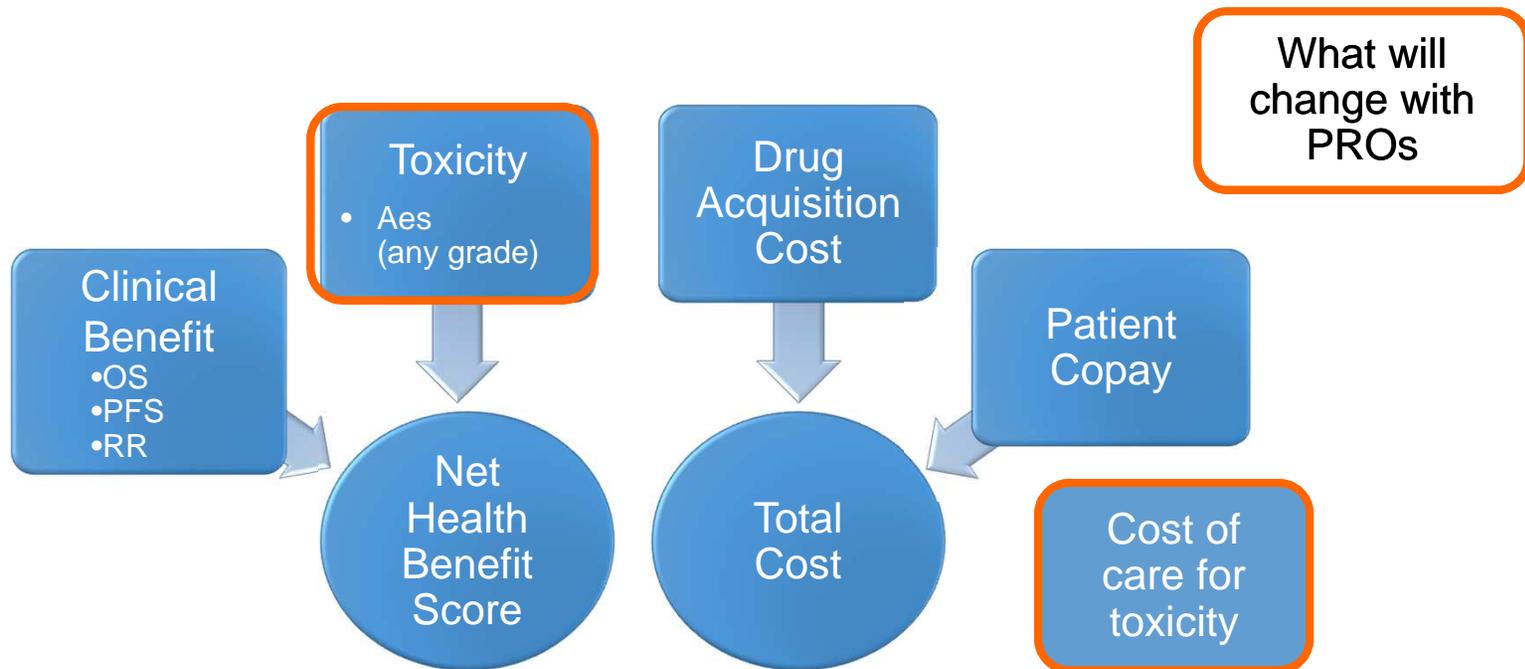
- Show **clinical benefit** in reducing disease-related symptomatology

Immunotherapy and Symptom Palliation: Checkmate 025: Change in HRQoL score FKSI-DRS



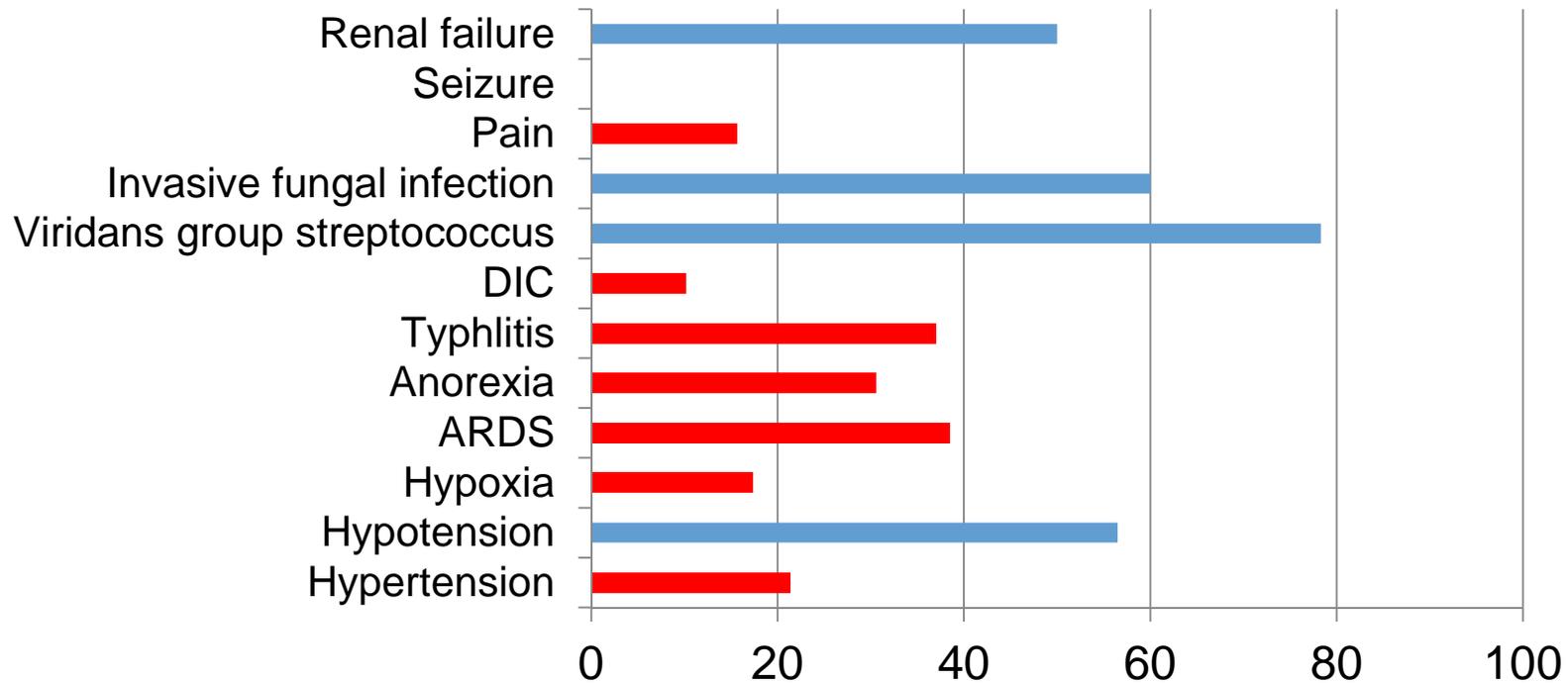
# How Do PROs Help?

- Show **clinical benefit** in reducing disease-related symptomatology
- Provide more accurate estimates of toxicity
  - Enhance value frameworks



# AEs Don't Accurately Capture Toxicity

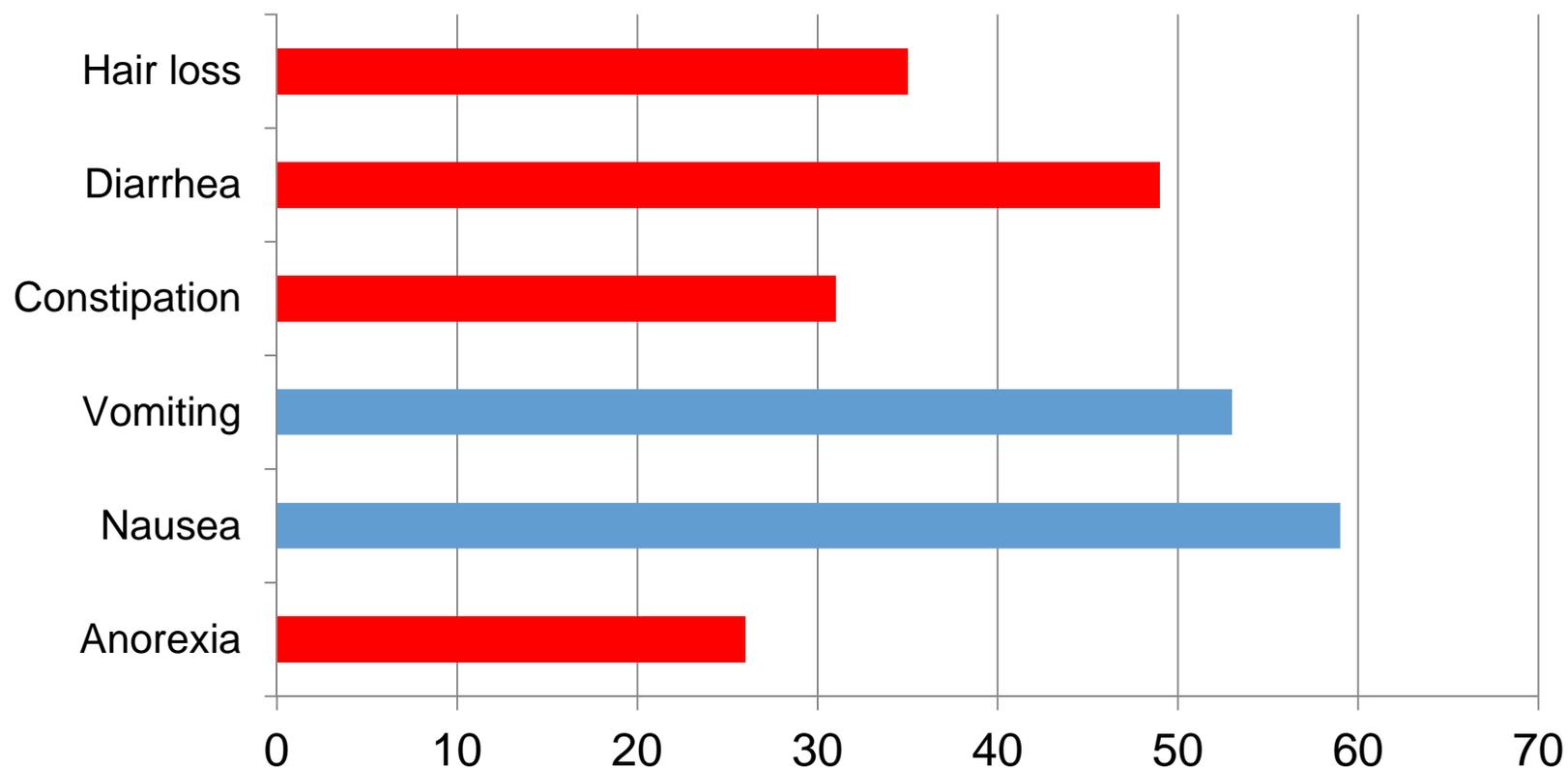
## Sensitivity of AEs Compared to EMR



ARDS: Adult respiratory distress syndrome, DIC: disseminated intravascular coagulation

# AEs Don't Accurately Capture Toxicity

## Sensitivity of AEs Compared to Patient Report



# PROs Can Help To Model Treatment Costs

| Toxicity             | ICD-9           | ICD-10                   | Incidence Ipilimumab | Incidence Nivolumab | Incidence Pembrolizumab | Estimated Cost      |
|----------------------|-----------------|--------------------------|----------------------|---------------------|-------------------------|---------------------|
| Anemia               | 285.3.<br>285.9 | D64.89                   | 42.9%                | 59.4%               | 34.0%                   | \$851 <sup>4</sup>  |
| Colitis              | 558.9           | K52.1<br>K52.89<br>K52.9 | 10.2%                | 10.9%               | 9.7%                    | \$8563 <sup>4</sup> |
| Dermatitis from drug | 692.9<br>693.0  | R21                      | 18.1%                | 10.9%               | 18.8%                   | \$764 <sup>7</sup>  |
| Diarrhea             | 787.91          | R19.7                    | 26.4%                | 15.8%               | 40.3%                   | \$775 <sup>4</sup>  |
| Dyspnea              | 786.09          | R06.00                   | 8.4%                 | 31.7%               | 8.3%                    | \$3345 <sup>4</sup> |
| Fatigue              | 780.79          | R53.83                   | 72.0%                | 87.1%               | 91.0%                   | \$2069 <sup>4</sup> |
| Fever                | 780.6           | R50                      | 17.8%                | 22.8%               | 20.8%                   | \$3304 <sup>4</sup> |

| Treatment     | # of Patients | Average # of Doses | Cost Per Dose | Estimated Cost of Therapy | Estimated Average Cost of Toxicities | Total Cost of Treatment | % of Total Cost Related to Toxicity |
|---------------|---------------|--------------------|---------------|---------------------------|--------------------------------------|-------------------------|-------------------------------------|
| Ipilimumab    | 382           | 3.3                | \$30,694      | \$101,290                 | \$8,216                              | \$109,506               | 6.3%                                |
| Nivolumab     | 101           | 6.3                | \$6,043       | \$38,078                  | \$9,616                              | \$47,686                | 17.6%                               |
| Pembrolizumab | 144           | 8.0                | \$7,251       | \$58,008                  | \$8,547                              | \$66,555                | 16.0%                               |

Mason et al., *JCO* 2016; 34:suppl; abstr 6627.

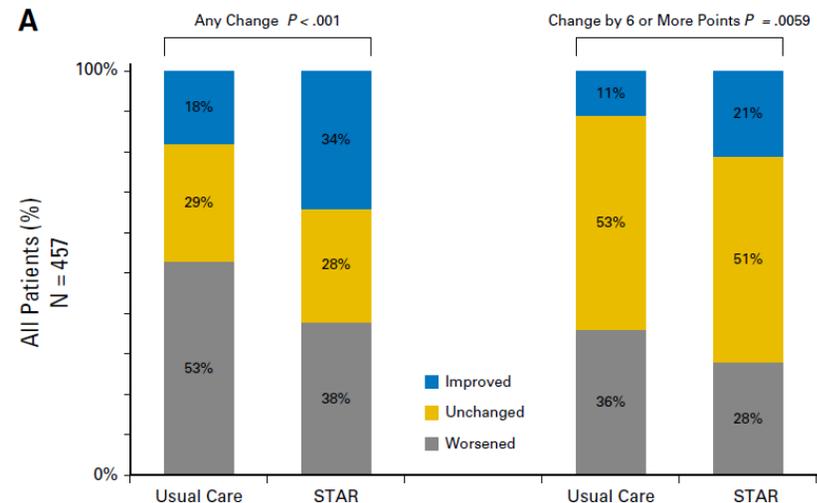
# How Do PROs Help?

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- Show **clinical benefit** in reducing disease-related symptomatology
- Provide more accurate estimates of toxicity
  - Enhance value frameworks
  - Patient education
  - Shared decision making
  - Improved symptom management to **help patients stay on drug longer with potential survival benefits**

# PROs Can Improve Outcomes

- High relevance for managing toxicity in combination trials
- Clinic-based monitoring of 12 common symptoms using the PRO-CTCAE in 766 patients
- Treated with chemotherapy for metastatic breast, genitourinary, gynecologic, or lung cancer
- Triggered email alerts to nurses with severe or significantly worsening symptoms



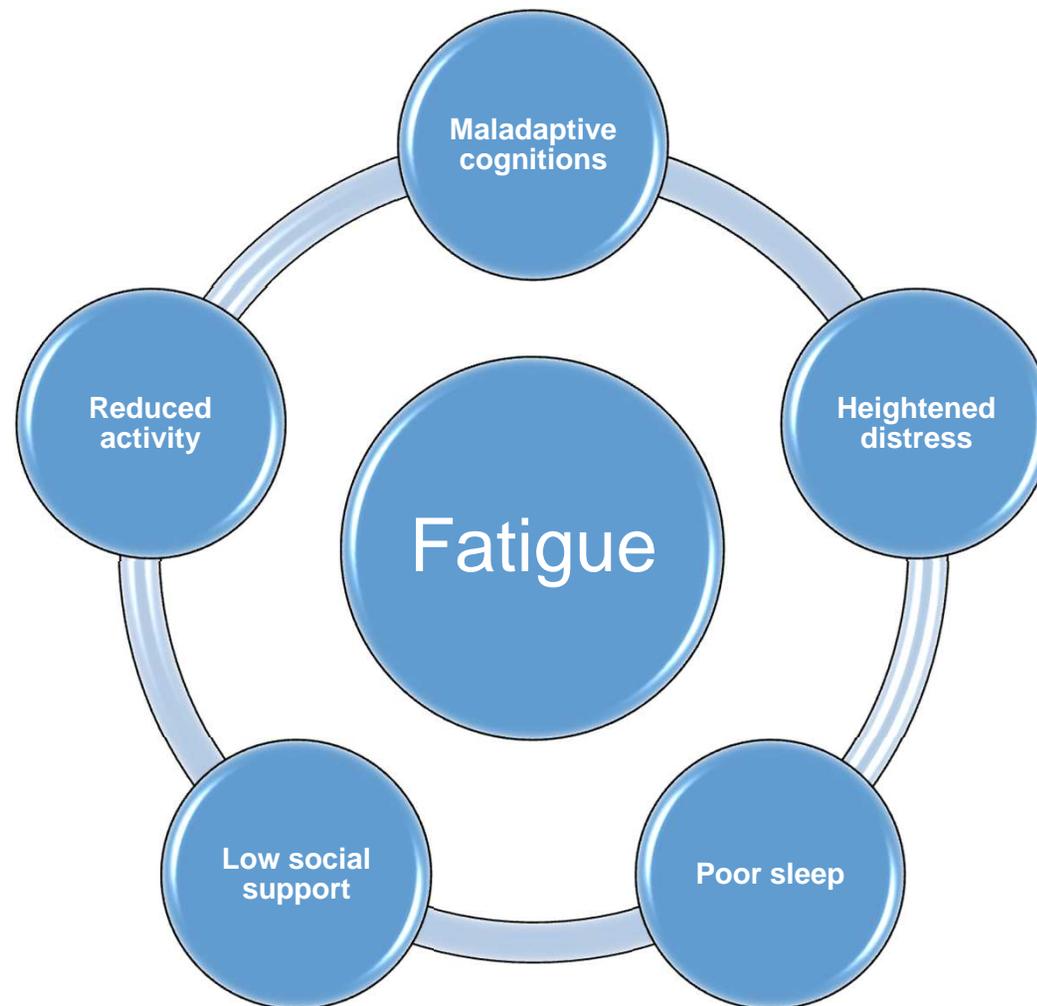
# PROs Can Improve Outcomes

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- ER visits at one year (34% vs. 41%) (p=.02)
- Median months on chemotherapy (8.2 vs. 6.3) (p=.002)
- Quality-adjusted one year survival (75% vs. 69%) (p=.05)
- More pronounced benefits for computer-inexperienced patients

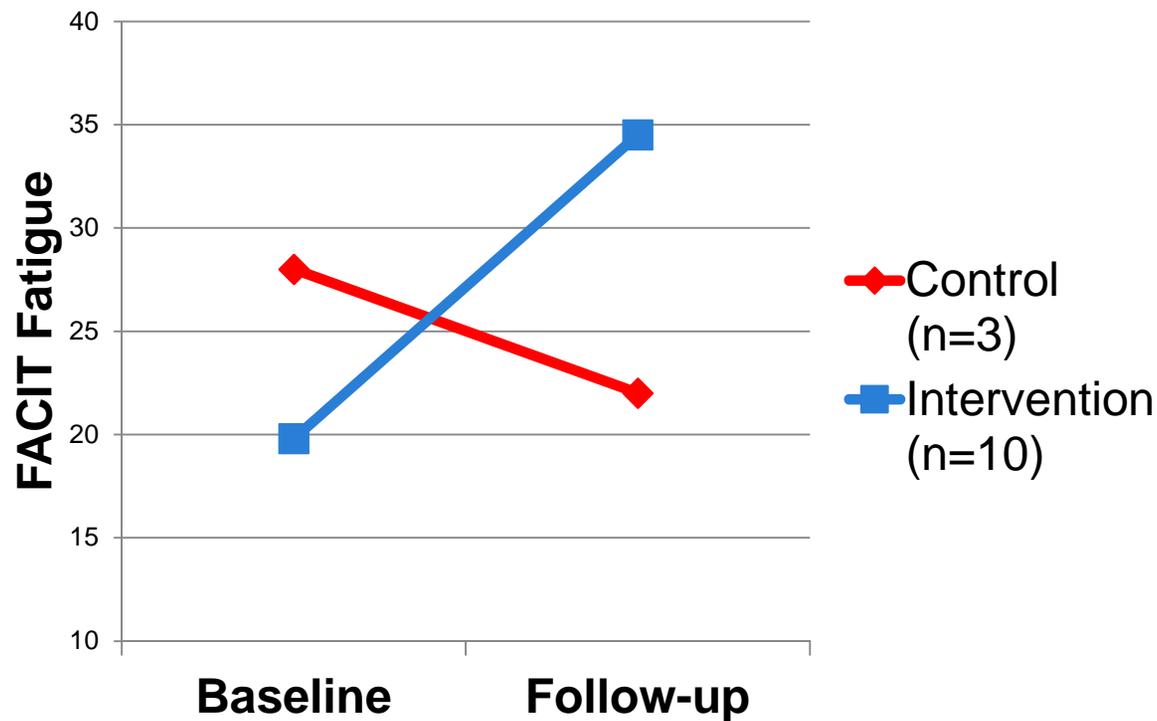
# Management of Treatment-Related Fatigue

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Poort et al., *Clin Nurs* 2016. Epub ahead of print.

# Cognitive Behavioral Intervention: Dramatic Improvements Pts on TKIs



# Current state of the science: EQ-5D

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1. Mobility
  - I have no problems
  - I have slight problems
  - I have moderate problems
  - I have severe problems
  - I am unable
2. Self-care (washing/dressing)
3. Usual activities
4. Pain/discomfort
5. Anxiety/depression

# Patient Reported Outcomes Version of the CTCAE (PRO-CTCAE)

| Oral   | Cardio/Circulatory        | Neurological           | Sleep/Wake                           | Sexual                                |
|--|---------------------------|------------------------|--------------------------------------|---------------------------------------|
| Dry mouth S  | Swelling FSI              | Numbness & tingling SI | Insomnia SI                          | Achieve and maintain erection S       |
| Difficulty swallowing S                                      | Heart palpitations FS     | Dizziness SI           | Fatigue SI                           | Ejaculation F                         |
| Mouth/throat sores SI  |                           |                        |                                      | Decreased libido S                    |
| Cracking at the corners of the mouth (cheilosis/cheilitis) S | Cutaneous                 | Visual/Perceptual      | Mood                                 | Delayed orgasm P                      |
| Voice quality changes P                                      | Rash P                    | Blurred vision SI      | Anxious FSI                          | Unable to have orgasm P               |
| Hoarseness S   | Skin dryness S            | Flashing lights P      | Discouraged FSI                      | Pain w/sexual intercourse S           |
|  | Acne S                    | Visual floaters P      | Sad FSI                              |                                       |
| Gastrointestinal   | Hair loss P               | Watery eyes SI         |                                      | Miscellaneous                         |
| Taste changes S  | Itching S                 | Ringing in ears S      | Gynecologic/Urinary                  | Breast swelling and tenderness S      |
| Decreased appetite SI  | Hives P                   |                        | Irregular periods/vaginal bleeding P | Bruising P                            |
| Nausea FS  | Hand-foot syndrome S      | Attention/Memory       | Missed expected menstrual period P   | Chills FS                             |
| Vomiting FS  | Nail loss P               | Concentration SI       | Vaginal discharge P                  | Increased sweating FS                 |
| Heartburn FS   | Nail ridging P            | Memory SI              | Vaginal dryness S                    | Decreased sweating P                  |
| Gas P  | Nail discoloration P      | Pain                   | Painful urination S                  | Hot flashes FS                        |
| Bloating FS  | Sensitivity to sunlight P | General pain FSI       | Urinary urgency FI                   | Nosebleed FS                          |
| Hiccups FS   | Bed/pressure sores P      | Headache FSI           | Urinary frequency PI                 | Pain and swelling at injection site P |
| Constipation S   | Radiation skin reaction S | Muscle pain FSI        | Change in usual urine color P        | Body odor S                           |
| Diarrhea F   | Skin darkening P          | Joint pain FSI         | Urinary incontinence FI              |                                       |
| Abdominal pain FSI   | Stretch marks P           |                        |                                      |                                       |
| Fecal incontinence FI  |                           |                        |                                      |                                       |
| Respiratory  |                           |                        |                                      |                                       |
| Shortness of breath SI                                       |                           |                        |                                      |                                       |
| Cough SI   |                           |                        |                                      |                                       |
| Wheezing S   |                           |                        |                                      |                                       |

| Attributes   |                             |
|--------------|-----------------------------|
| F: Frequency | I: Interference             |
| S: Severity  | P: Presence/Absence /Amount |



# The Mobile Health Platform

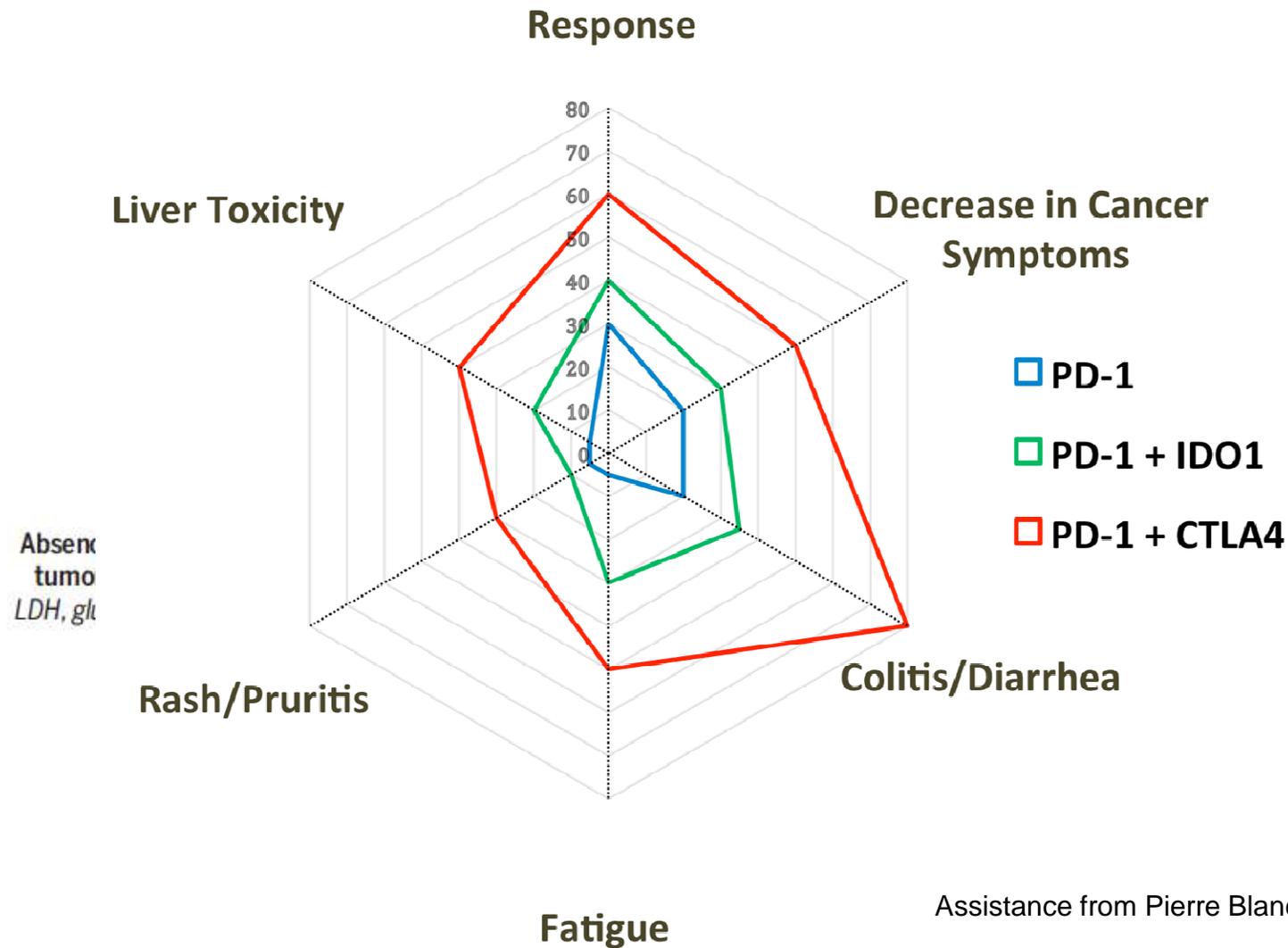


Secure Communication

Systems Integration

Clinical Innovation

# Communicating value in health care using Radar Charts (hypothetical data)



# PRO Monitoring for Immunotherapy Trials: Summary of Potential Benefits

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- Improve reporting to determine clinical benefit

- Adverse events
- Palliative benefits
- Treatment cost
- Time to return to work / ADL

Important for  
patients, shared decision  
making and regulatory  
approval, payers, etc

- Improve management of toxicity

- Better QOL
- Longer time on treatment
- Improved survival
- Fewer ER visits, hospitalizations
- Complements translational research

# Summary and call to action

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- SITC is well-positioned to:
  - Form a working group including; patients, providers, pharma, regulatory, etc
  - Develop a common PRO measure(s) to assess symptoms in immunotherapy trials and clinical care.
  - Incorporate measure(s) routinely into clinical trials

# This will create a future for:

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- Data warehouse of ePROs, an in-silico database
- Use machine learning to identify patterns of symptoms that predict cancer progression and life-threatening complications
- Develop and validate algorithms to treat toxicities detected by patient-reported symptoms
- Use technology to deliver solutions to patients and providers

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