Patient reported outcomes vs. clinician reported outcomes: what is the best to measure toxicities?

Universitätsklinikum Heidelberg, Innere Medizin V
Karin Jordan
Im Neuenheimer Feld 410, 69120 Heidelberg
DISCLOSURE SLIDE

Karin Jordan is consultant and/or received Honoraria from: MSD, Helsinn, Tesaro
Patient-reported-outcomes (PRO)

“Any outcome evaluated directly by the patient himself and based on patient’s perception of a disease and its treatment(s) is called patient-reported outcome (PRO).”

![Patient-reported outcomes example](image-url)
Clinician reported outcome (CRO)

- Classical example: Common Toxicity Criteria Adverse Events (CTCAE)

<table>
<thead>
<tr>
<th>GRADE</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCI Common Terminology Criteria for Adverse Events</td>
<td>None</td>
<td>Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function</td>
<td>Sensory alteration or paresthesia (including tingling), interfering with ADL</td>
<td>Sensory alteration or paresthesia interfering with ADL</td>
<td>Disabling</td>
</tr>
<tr>
<td>Neuropathy Sensory Subscale</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

....grade 2: „oh, that’s not too bad“

<table>
<thead>
<tr>
<th>Vomiting</th>
<th>1 - 2 episodes (separated by 5 minutes) in 24 hrs</th>
<th>3 - 5 episodes (separated by 5 minutes) in 24 hrs</th>
<th>&gt;=6 episodes (separated by 5 minutes) in 24 hrs; tube feeding, TPN or hospitalization indicated</th>
<th>Life-threatening consequences; urgent intervention indicated</th>
<th>Death</th>
</tr>
</thead>
</table>

Definition: A disorder characterized by the reflexive act of ejecting the contents of the stomach through the mouth.
Frequent pitfalls of CTCAE reporting in studies

Are grade III/IV toxicities the only one that matters?

Are PROMs and CRO (CTCAE) going well together?
1. PROs identified a higher incidence and severity of treatment-related toxicities

Basch E. 2010, NEJM, 362: 865-69
Universitätsklinikum Heidelberg | Karin Jordan
The association between clinician-based common terminology criteria for adverse events (CTCAE) and patient-reported outcomes (PRO): a systematic review

Thomas M. Atkinson\(^1\) • Sean J. Ryan\(^{1,2}\) • Antonia V. Bennett\(^3\) • Angela M. Stover\(^3\) • Rebecca M. Saracino\(^1\) • Lauren J. Rogak\(^1\) • Sarah T. Jewell\(^4\) • Konstantina Matsoukas\(^1\) • Yuelin Li\(^1\) • Ethan Basch\(^{1,3}\)

Conclusion: CTCAE and PRO ratings was moderate at best
Questions arising

• Who is right? CRO or PROM? Patient or clinician?
• Are PROMs really that helpful?
TWO potential views of the situation:

1. *more patient-centered view*: the patient is always right by definition because nobody (not even the most sensitive clinician) can truly know another person’s subjective experience.

2. *more traditional view*: the clinicians should be considered right because they have an “objective” perspective based on experience and training

Combination of these views possible?

Three potential approaches

1) “Independent reporting,” in which patient and clinician toxicity data are collected, analyzed, and reported completely separately from each other;

2) “Merged reporting,” in which patient and clinician data are collected separately and then merged analytically into a single metric; and

3) “Collaborative reporting,” in which patients directly report symptomatic toxicity information, which is then provided to clinicians to inform their CTCAE reporting.
Three potential approaches

1) “Independent reporting,” in which patient and clinician toxicity data are collected, analyzed, and reported completely separately from each other;

2) “Merged reporting,” in which patient and clinician data are collected separately and then merged analytically into a single metric; and

3) “Collaborative reporting,” in which patients directly report symptomatic toxicity information, which is then provided to clinicians to inform their CTCAE reporting.
SPECIAL ARTICLE

European Society for Medical Oncology (ESMO) position paper on supportive and palliative care

K. Jordan1*, M. Aapro2, S. Kaasa3,4,5, C. I. Ripamonti6, F. Scotté7, F. Strasser8, A. Young9, E. Bruera10, J. Herrstedt11,12, D. Keefe13, B. Laird14,15, D. Walsh16, J. Y. Douillard17 & A. Cervantes18

1Department of Medicine V, Hematology, Oncology and Rheumatology, University of Heidelberg, Heidelberg, Germany; 2Cancer Center, Clinique de Genolier, Genolier, Switzerland; 3Department of Oncology, Oslo University Hospital, Oslo; 4University of Oslo, Oslo; 5European Palliative Care Research Centre (PRC) NTNU, Oslo, Norway; 6Supportive Care in Cancer Unit, Department of Onco-Haematology Fondazione IRCCS, Istituto Nazionale dei Tumori, Milano, Italy; 7Medical Oncology and Supportive Care Department, Foch Hospital, Suresnes, France; 8Oncological Palliative Medicine, Clinic for Medical Oncology and Hematology, Departement Internal Medicine, Cantonal Hospital St.Gallen, St. Gallen, Switzerland; 9Warwick Clinical Trials Unit, University of Warwick, Coventry, UK; 10Department of Palliative, Rehabilitation and Integrative Medicine, The University of Texas, MD Anderson Cancer Center, Houston, USA; 11Department of Oncology, Zealand University Hospital, Roskilde; 12Department of Oncology, University of Copenhagen, Copenhagen, Denmark; 13Department of Medicine, Faculty of Health Sciences, University of Adelaide, Adelaide, Australia; 14Edinburgh Cancer Research Centre, University of Edinburgh, Edinburgh; 15St. Columba’s Hospice, Edinburgh, UK; 16Academic Department of Palliative Medicine, Our Lady’s Hospice and Care Services, Dublin, Ireland; 17ESMO, Lugano, Switzerland; 18CIBERONC, Department of Medical Oncology, Institute of Health Research INCLIVA, University of Valencia, Valencia, Spain
### Table 1. Key patient-centred care interventions (examples)

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Monitoring and intervention: regular changes in patients’ health status preferably assessed with PROMs or other validated assessment tools</th>
<th>Management of cancer-related symptoms and other needs</th>
<th>Management of anticancer treatment-related toxicities and complications, including prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cancer and anticancer-treatment related symptoms, toxicities, complications</td>
<td>• Treatment decision-making</td>
<td>• Pain</td>
<td>• Nausea and vomiting</td>
</tr>
<tr>
<td>• Psychological disorders, distress</td>
<td>• Advance care planning</td>
<td>• Fatigue</td>
<td>• Anaemia</td>
</tr>
<tr>
<td>• Sleep disturbances</td>
<td>• Preparation for end-of-life and dying</td>
<td>• Nausea and vomiting</td>
<td>• Febrile neutropenia</td>
</tr>
<tr>
<td>• Family distress and role of the caregiver</td>
<td>• Family distress and care-giving roles</td>
<td>• Constipation, diarrhoea</td>
<td>• Fatigue</td>
</tr>
<tr>
<td>• Professional support networks</td>
<td>• Professional support networks</td>
<td>• Anorexia, cachexia, early satiety</td>
<td>• Pain</td>
</tr>
<tr>
<td>• Loss of autonomy</td>
<td>• Loss of autonomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Distress</td>
<td>• Distress</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Existential, spiritual and religious needs</td>
<td>• Existential, spiritual and religious needs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Other monitoring and intervention issues</td>
<td>• Other monitoring and intervention issues</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PROMs, patient-reported outcome measures; CTIBL, cancer treatment-induced bone loss.
Are PROMs really that helpful?

2. PRO measurement linked to overall survival,
> 5 month survival benefit just through PRO measurement

Basch E. JAMA 2017 epub ahead

Universitätsklinikum Heidelberg | Karin Jordan
Conclusion

Assessment

• “Collaborative reporting,” in which patients report PROM directly, which is then provided to clinicians to inform their CTCAE reporting

Management!

• Assessment is not enough
• Need of a multidisciplinary team
That’s why we are here