

Symptoms in Oncology Evaluation and Impact

- **Reviewer**

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Disclosure

- Advisory boards: Janssen Pharmaceutical Companies
- Studies: Janssen Pharmaceutical Companies, Amgen

Symptoms in Oncology

Introduction

- Disease-related symptoms
 - Curable disease
 - Local
 - Systemic
 - Incurable disease
 - Local
 - Systemic
 - Fatigue, pain, lack of energy, weakness, appetite loss > 50% of patients¹

Symptoms in Oncology

Introduction

- Treatment-related symptoms
 - Surgery
 - Radiotherapy
 - Medication

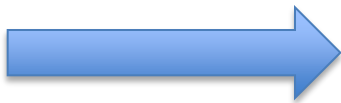
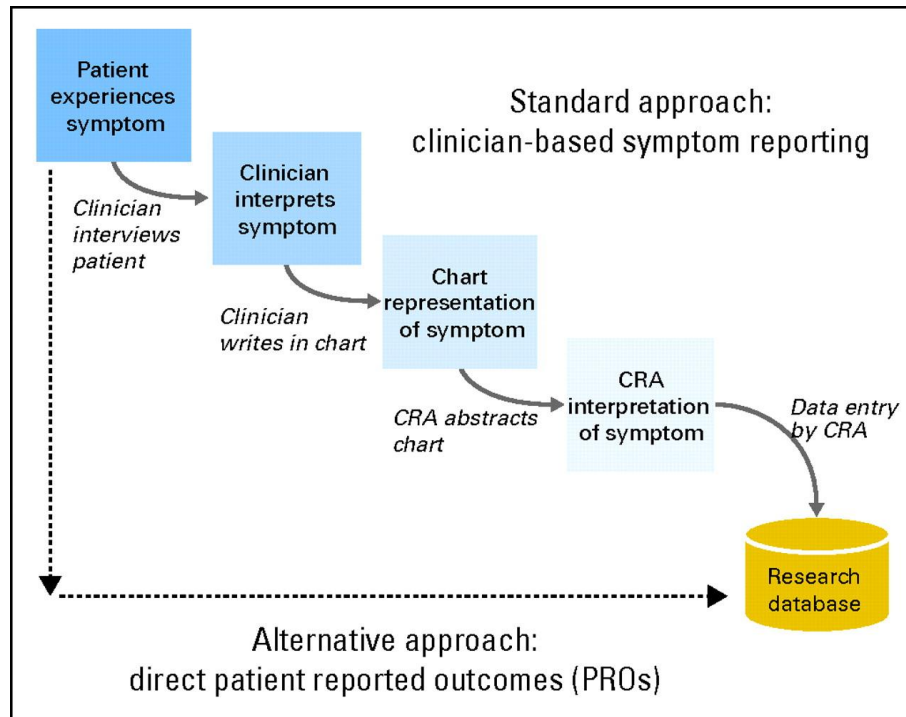
Symptoms in Oncology

Evaluation Instruments in Clinical Studies

- General evaluation instruments
 - EORTC QLQ-C30
- Disease-specific evaluation instruments
 - EORTC QLQ - H&N35
- Symptom-specific evaluation instruments
 - Hospital Anxiety and Depression Scale (HADS)
 - Edmonton Symptom Assessment Scale (ESAS)
- Treatment-related evaluation instruments
 - Common Terminology Criteria for Adverse Events (CTCAE)
 - Late effects in normal tissues subjective, objective, management and analytic scales (LENT-SOMA)

Symptoms in Oncology

Problems of Evaluation



Patient-reported outcomes measures

Patient-reported Outcome Definition

- A patient-reported outcome (PRO) = questionnaire used in a clinical trial or a clinical setting, where the responses are collected directly from the patient

Patient-reported Outcome Impact

- Prognosis: PRO related to survival**

Tumor type	PROs assesment	PRO related to survival
Bladder	EORTC QLQ-C30	Physical function, role function, appetite loss
Brain	FACT-Brain	Digit span (battery), fatigue
Breast	EORTC QLQ-C30	Appetite loss, pain
Cervical	FACT-Cervical (Cx)	FACT-Cx
Colorectal	EORTC QLQ-C30	Global QOL, social, physical, role and emotional function, nausea, pain, dyspnea, sleep disturbance
Lung	EORTC QLQ-C30 FACT-Lung FLIC	Global QoL, pain, dysphagia, IADL, ADL, fatigue Physical function Global QoL
Prostate	EORTC QLQ-C30 + FACT-G/FACT-P	Global QoL, insomnia, appetite loss, FACT-G/FACT-P composite, physical function, pain, fatigue, constipation, social function, appetite loss

PRO: patient-reported outcome; FACT/FACT-G: functional Assessment of Cancer Therapy; FACT-P: functional assessment of cancer therapy, prostate module; FLIC: Functional Living Index-Cancer; QoL: quality of life; QLQ-C30: Quality of Life Questionnaire Core-30; EORTC: European Organisation for Research and Treatment of Cancer, IADL: instrumental activity of daily living; ADL: activity of daily living

Patient-reported Outcome Impact

- **Prognosis: fatigue related to overall survival**
 - Brain tumors
 - Multiple myeloma
 - Prostate cancer
 - Lung cancer

Patient-reported Outcome Impact

- **Prognosis: anemia related to overall survival**

Author	Cancer type	Line of treatment	Type of treatment	OS
Tampellini	Colorectal	1	5FU-based	+
Altun	Nasopharyngeal	1	Platinum-based + RT	+
Berardi	Colorectal	1	CRT	+**
Prosnitz	Head and neck	1	Platinum-based + RT	+*
Zenda	Esophageal	1	5FU-based + RT	+

OS: overall survival; 5FU: 5-fluoruracil; RT: radiotherapy; CRT: chemoradiation; *:5-year failure-free survival;
 **: disease-free survival

Patient-reported Outcome Impact

- **Prognosis: other factors related to overall survival**
 - Patient-related factors
 - Performance status
 - Co-morbidity
 - Organ function
 - Specific symptoms (e.g. pain, dyspnea)
 - Hematological parameters (e.g. LDH)
 - Tumor-related factors
 - Histology (e.g. type, grading)
 - Stage
 - Molecular markers

Patient-reported Outcome Impact

- **Fatigue and anemia scores for overall survival (Gornadha et al)**
 - Findings
 - Correlation between fatigue and anemia scores and overall survival
 - Problems
 - Prospective or retrospective study design?
 - PROCHE study endpoints: time between scheduled treatment administration and actual administration and patient satisfaction
 - Patient selection?
 - Validated instrument for fatigue?
 - Impact other prognostic factors?
 - Merits
 - Implementation PRO in daily clinical practice situation

Patient-reported Outcome Impact

- **Toxicity evaluation**

Author	Cancer type/Toxicity	Evaluation instruments	Result
Ho	Head and neck/late toxicity	LENT-SOMA/ EORTC QoL-H&N35	Good agreement between LENT-SOMA and EORTC QLQ-H&N35 except for analgesic endpoints
Neben-Wittich	Breast/radiodermatitis prevention	Skindex-16 + STAT/ CTCAE	PRO positive/Provider–assessed negative

EORTC, European Organisation for Research and Treatment of Cancer; QoL: quality of life; H&N: head and neck, LENT-SOMA: late effects in normal tissues subjective, objective, management and analytic scales; STAT: Skin Toxicity Assessment Tool; CTCAE: Common Toxicity Criteria for Adverse Events

Patient-reported Outcome Impact

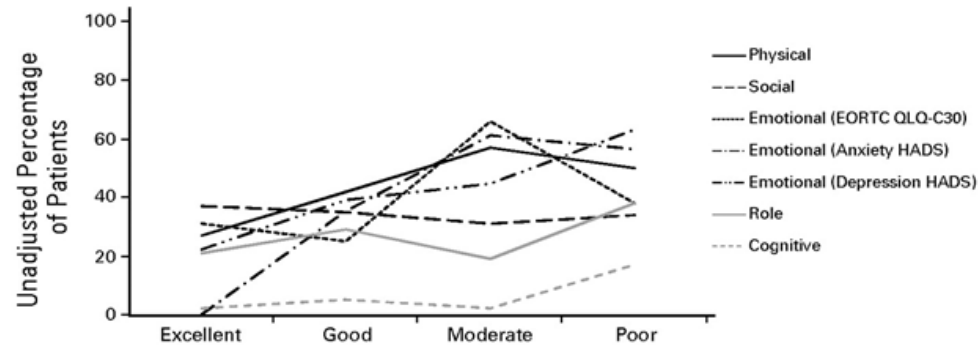
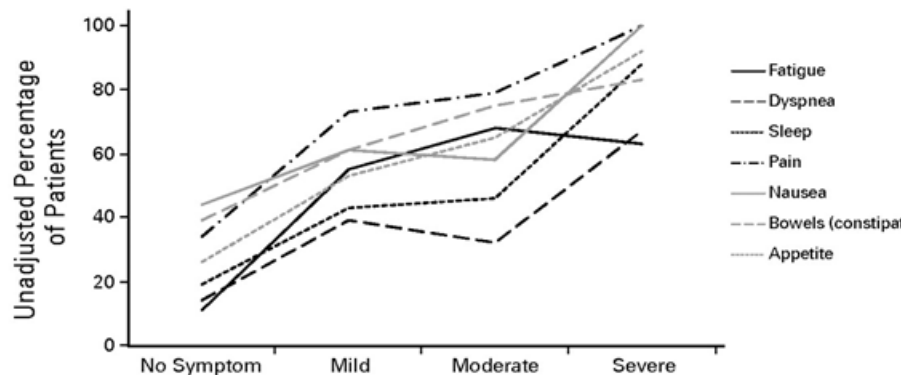
- Registration medication

Year	FDA					EMA				All oncology approvals
	HRQoL	Signs and symptoms	Multiple labels	Any PRO†	All oncology approvals	HRQoL	Signs and symptoms	Multiple labels	Any PRO†	
Pre-draft guidance										
1995–1996		2	1		—		1	1		5
1997–1999		1		1	10	1				8
2000–2002	1	1			11					14
2003–2005		1	1	1	13		2	2		10
Post-draft guidance										
2006–2008	1	1			19					23
2009–2010‡		1	1		7	2	1	1		8
						1	4			
Total	2	7	3	2	60	4	10	4		68
†Includes treatment satisfaction, use of rescue meds. ‡Until 31 September 2010.										

Patient-reported Outcome Impact

- Improved communication?

Relationship between EORTC QLQ-C30 and HADS scores and symptoms/functions being discussed in consultation



- Discussion topics predominantly raised by patients/relatives
- Discussions associated with severity of patient-reported symptoms/not with functional concerns

Patient-reported Outcome Impact

- **Improved patient outcome?**
 - Findings
 - PRSS improved SYM distress and a trend to better SYM management, communication and QoL
 - Problems
 - Recruitment
 - Training oncologists?
 - Nurse reporting of interventions?
 - Primary endpoint (Δ between baseline and week 6 in G-QOL (EORTC-QLQ-C30,29&30)): no difference between intervention and control group
 - Merits
 - Randomized prospective controlled trial
 - Validated PRO tools
 - Electronic tool

Patient-reported Outcome Applications in Daily Clinical Practice

- Screening tools
- Monitoring tools
- Patient-centered care
- Decision aids
- Facilitating multidisciplinary team communication
- Evaluating quality of care

Patient-reported Outcome Applications in Daily Clinical Practice

- Which groups of patients?
- Which questionnaires?
- Frequency of registration?
- Administration and scoring?
- Interpretation?
 - Multi-symptom outcome
- Impact?



Education of patients and professionals