

# Can patient self-reporting of symptoms complement clinician ratings in estimating cancer survival?

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## Estimating cancer survival. A challenge!

- Predicting survival and disclosing the prediction to the patients is among the most difficult tasks the physicians face
- Which information do they need to make appropriate survival estimates?
  - Clinical data
    - Performance status, cancer site, metastasis
  - Socio-demographic
    - Age, gender, country
  - **Disease side effects**
    - **pain, fatigue, constipation, etc**

- **NCI-CTCTA (Developed in 1982. Fourth edition)**
  - A standard classification for defining Adverse Events (AE) in oncology trials
  - AE is an unfavorable and unintended sign, symptom, or disease associated with the use of a medical treatment or procedure

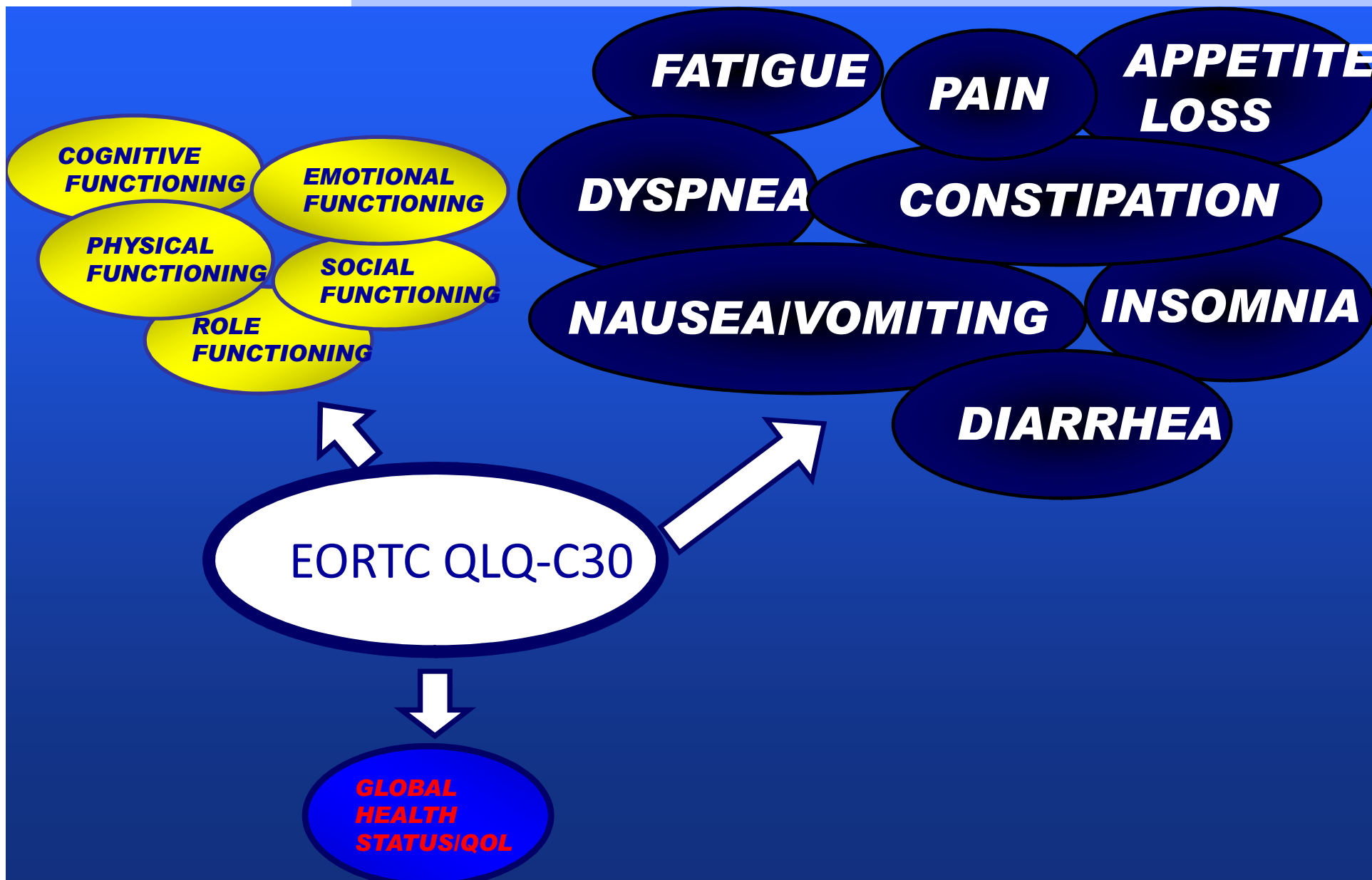
## NCI - Common Terminology Criteria Adverse Events

	Grade				
	1	2	3	4	5
<b>Pain</b>	Mild pain not interfering with function	Moderate pain; pain or analgesics interfering with function, but not with interfering with ADL	Severe pain; pain or analgesics severely interfering with ADL	Disabling	Dead

## Flaws in CTCAE ratings (Bruner et al., 2007)

- No standardized training for the implementation of the tool
- No standardized recording
  - Inter rater variability
- Lack of psychometric validation
  - No formal evidence that what separates grade 1 from grade 2 and 3 is clinically meaningful
- **SOLUTION!!**
- **Disease side effects by validated PRO instruments**

# Disease side effects obtained from patient (EORTC QLQ-C30)







## Research question (1)

- **Do clinicians and patients ratings are in agreement with regard to the scoring of disease side effects?**
- **If yes? Which ratings do we use?**
- **If not? Can they be complementary? How can their value be quantified?**

## The level of exact agreement between clinician and patient ratings

- Spearman correlation coefficient ( $\rho$ )

- Kappa correlation coefficient ( $\kappa$ )

QLQ-C30 Score 4		NCI-CTCAE Score 4
QLQ-C30 Score 3		NCI-CTCAE Score 3
QLQ-C30 Score 2		NCI-CTCAE Score 2
QLQ-C30 Score 1		NCI-CTCAE Score 1

- Kappa less than 0.00 (poor), 0.00 to 0.20 (slight), 0.21 to 0.40 (fair), 0.41 to 0.60 (moderate), 0.61 to 0.80 (substantial), and 0.81 to 1.00 (almost perfect)

# Information on symptoms by NCI-CTCAE (clinician) and EORTC QLQ-C30

- 6 disease side effects were collected simultaneously from both the EORTC QLQ-C30 and the CTCAE
- for each disease side effect, closed RCTs were pooled

Pain	Fatigue	Vomiting	Nausea	Diarrhea	Constipation
Number of closed RCTs pooled for each symptoms					
9	5	5	6	6	4
Number of patients					
1,467	1,237	824	813	815	751

Clinician (NCI-CTCAE)	Patient (EORTC QLQ-C30)	$\rho$	$\kappa$
<b>Pain</b>	Have you had pain?	0.58	0.29 (0.26-0.33)
	Did pain interfere with your daily activities?	0.50	0.27 (0.23-0.30)
<b>Fatigue</b>	Did you need to rest?	0.30	0.07 (0.03-0.10)
	Have you felt weak?	0.28	0.07 (0.03-0.10)
	Were you tired?	0.30	0.08 (0.04-0.11)
<b>Vomiting</b>	Have you vomited?	0.32	0.22 (0.13-0.30)
<b>Nausea</b>	Have you felt nauseated?	0.32	0.14 (0.10-0.18)
<b>Diarrhea</b>	Have you had diarrhea?	0.20	0.14 (0.07-0.20)
<b>Constipation</b>	Have you been constipated?	0.38	0.16 (0.11-0.21)

## Previous evidence supporting findings

- **Basch et al. (JNCI, 2009)**
  - The clinician brings in personal experience which is more associated with clinical outcomes
  - The patient is in a better position to communicate their own subjective experiences which are more associated with the daily health status
- **Fromme et al. (JCO, 2004)**
  - The clinician did not report half of the symptoms identified by the patient as AEs.
  - Thy patient did not detect approximately one half of the symptoms as reported by the physician.
- **Petersen et al. (EJC, 2006)**
  - Poor agreement between patient for psychosocial scales and emotional functioning
  - Best agreement for nausea/vomiting and constipation

## Research question (2)

- **What is the added value of both ratings in the survival prognostication?**
  - **Common clinical and socio-demographic prognostic variables for survival routinely collected in oncology clinical trials should be accounted for.**

- Linear models accounted for age, gender, metastasis, WHO performance status and cancer site
- Predictive accuracy
  - Harrel's discrimination c-index
    - Consider all possible pairs of observations (derived from the dataset)
    - Determine which patient in the pair survived longer
    - Compare with the largest predicted probability of surviving (derived from the model)
    - Range: 0-1
      - 0.5 indicates no predictive discrimination
      - 1 indicates perfect discrimination

# Results Predictive accuracy

	Pain	Fatigue	Vomiting	Nausea	Diarrhea	Constipation
	<b>C-index and (P-values)</b>					
<b>Model 1</b>	<b>0.60</b>	<b>0.60</b>	<b>0.62</b>	<b>0.62</b>	<b>0.61</b>	<b>0.60</b>
<b>Model 2</b>	<b>0.62</b>	<b>0.65</b>	<b>0.62</b>	<b>0.63</b>	<b>0.62</b>	<b>0.62</b>
<i>Model 2 vs. Model 3</i>	<i>(0.171)</i>	<i>(&lt;.001)</i>	<i>(0.216)</i>	<i>(0.512)</i>	<i>(0.492)</i>	<i>(0.034)</i>
<b>Model 3</b>	<b>0.62</b>	<b>0.63</b>	<b>0.62</b>	<b>0.62</b>	<b>0.62</b>	<b>0.61</b>
<i>Model 3 vs. Model 4</i>	<i>(&lt;.001)</i>	<i>(0.006)</i>	<i>(0.047)</i>	<i>(0.043)</i>	<i>(0.444)</i>	<i>(0.014)</i>
<b>Model 4</b>	<b>0.64</b>	<b>0.67</b>	<b>0.63</b>	<b>0.64</b>	<b>0.62</b>	<b>0.62</b>

## Discussion and further research

- Comparing patient versus clinician reporting
  - Patient reporting of fatigue and constipation had a significantly better survival prediction than clinician rating
- Comparing patient and clinician reporting versus clinician reporting
  - Except for diarrhea, **including both patient and clinician rating of symptom improved the predictive accuracy compared to clinician assessment alone.**
- Future analysis is planned using clinical data from Medical Research Council (MRC), National Cancer Institute Canada – Clinical Trial Group (NCIC-CTG) and German Onkologie Group (AGO)

- **Basch E, Jia X, Heller G et al. Adverse Symptom Reporting by Patients versus Clinicians: Relationship with Clinical Outcomes. Journal of the National Cancer Institute 2009; 101: 1624-1632.**
- **Harrel F.E. et al. Multivariable prognostic models; issues in developing models, evaluating assumptions and measuring and reducing errors. Statistics in Medicine 1996; 15: 361-87.**
- **[http://outcomes.cancer.gov/tools.pro-ctcae](http://outcomes.cancer.gov/tools/pro-ctcae)**

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