EORTC
European Organisation for Research and Treatment of Cancer

Evaluating cancer treatments based on overall survival and quality of life

Why improving patient's HRQoL is part of EORTC's core mission?

Winette van der Graaf, medical oncologist, Netherlands Cancer Institute Amsterdam
President of the EORTC

Conflict of interest

- Springworks advisory board
- Agenus advisory board
- PTC Therapeutics advisory board
- Eli Lilly research project

- All fees to the institute

Mission EORTC

To increase cancer patients' survival and improve their quality of life

Do this through:

- **Generating robust medical evidence**: design, coordinate and conduct multidisciplinary, clinical and translational trials, leading to therapeutic progress and new standard of treatment in care

- **Setting Standards**: being a reference for methodological research and an authority in establishing the standards of treatment in care

Multidisciplinary approach

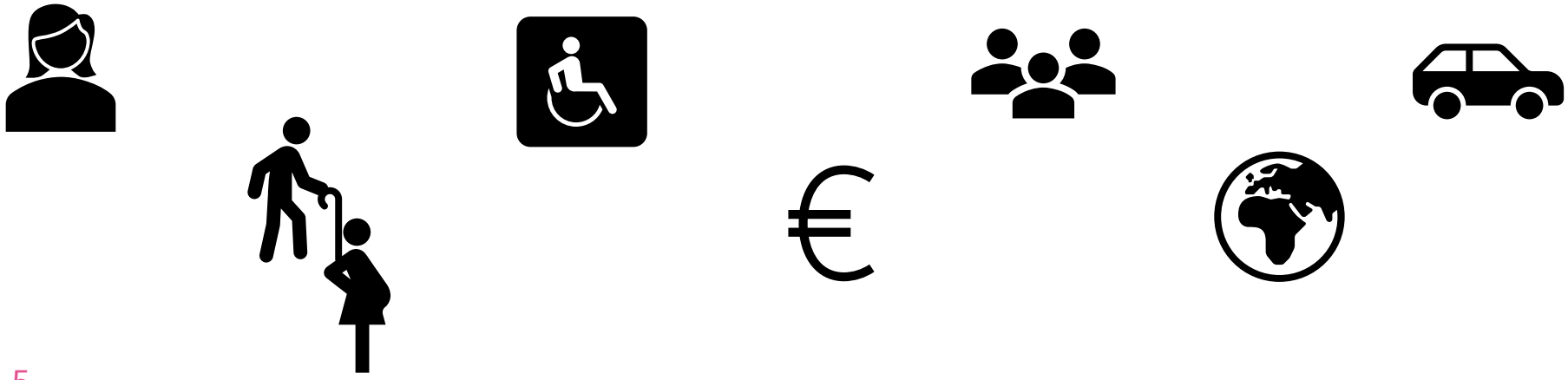
- EORTC aims ultimately to increase people's survival and quality of life by testing new therapeutic strategies based on existing drugs, surgery, and radiotherapy.

- EORTC also helps develop new drugs and approaches in partnership with the pharmaceutical industry and in **patients' best interests.**

What are patients' best interests and how to study patients' best interest?

- Activity of a treatment
- The balance of safety versus toxicity

➡ The impact of a treatment on patients' daily life, including health-related quality of life, depends on much more than the treatment alone



There is a notorious mismatch..

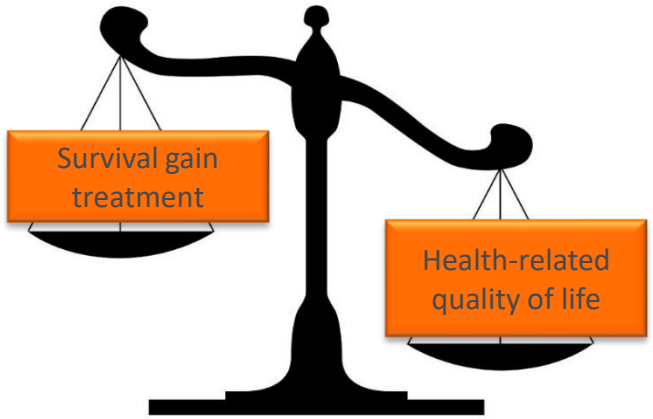
Doctors, despite their extended ears 

don’t listen well or know very well what the impact of cancer and its treatment on patient’s daily life and the impact on HRQol really is…

We need the patient’s voice

EORTC already long ago realised the relevance of the voice of patients and patients reported outcomes

Evaluation of clinical trials traditionally focus on objective outcomes such as disease-free, progression-free survival, overall survival, response rate, adverse events.



However, to get a more holistic overview we need to asses the patients' perspectives, which can provide important additional information to evaluate benefits and risks of interventions in cancer clinical trials.

Patient-reported outcomes (PROs)

"Refer to a host of outcomes coming directly from patients about how they feel or function in relation to a health condition and its therapy without interpretation by healthcare professionals or anyone else"[1]

- Symptoms (e.g. pain, fatigue)
- Perception of daily functioning (e.g. physically, socially)
- Health-related quality of life

We need instruments (mostly questionnaires and survey's) to capture information about PROs: patient reported outcome measures (PROMs)

[1] U.S. Department of Health and Human Services, Food and Drug Administration. Guidance for industry: Patient- reported outcomes measures: Use in medical product development to support labeling claims.

Is talking about HRQoL new?

No…

Already in 1986, the EORTC Quality of Life Group realised that a research program was necessary to develop a Quality-of-Life Instrument for Use in International Clinical Trials in Oncology.

At that time only a very few studies (in breast and lung cancer and sarcoma) had incorporated quality of life aspects.

The instrument to-be-developed should have core questions and an option for a modular approach.

The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology

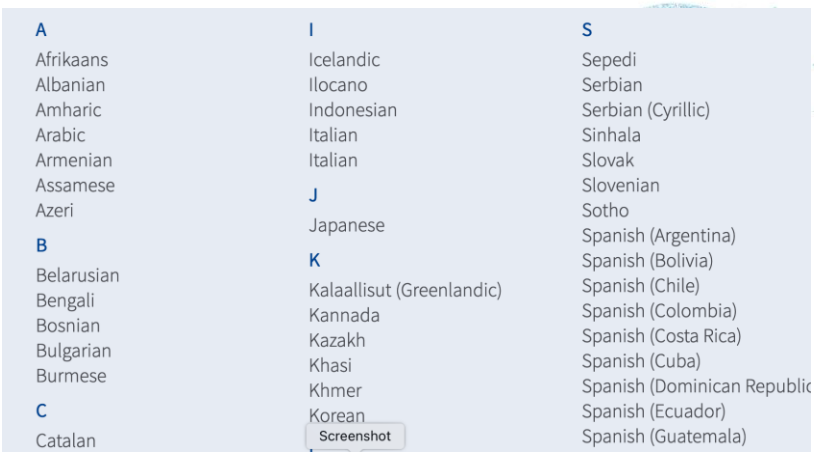
N K Aaronson, S Ahmedzai, B Bergman, M Bullinger, A Cull, N J Duez, A Filiberti, H Flechtner, S B Fleishman, J C de Haes, et al.

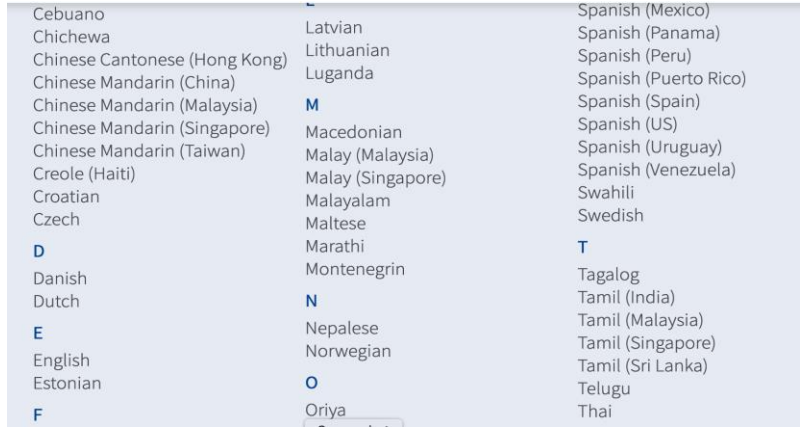
PMID: 8433390 DOI: 10.1093/jnci/85.5.365

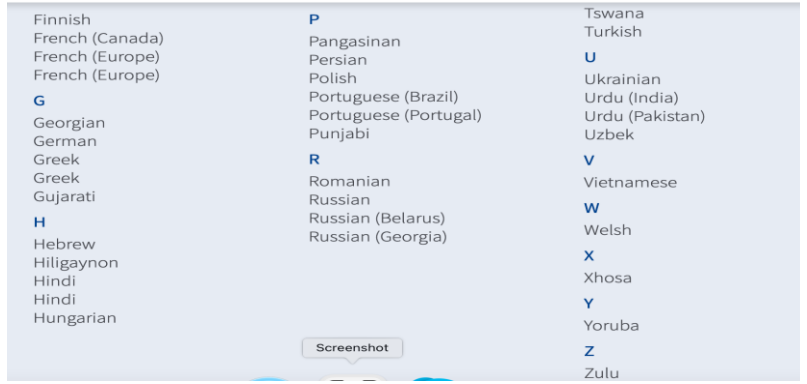
Abstract

Background: In 1986, the European Organization for Research and Treatment of Cancer (EORTC) initiated a research program to develop an integrated, modular approach for evaluating the quality of life of patients participating in international clinical trials.

Purpose: We report here the results of an international field study of the practicality, reliability, and validity of the EORTC QLQ-C30, the current core questionnaire. The QLQ-C30 incorporates nine multi-item scales: five functional scales (physical, role, cognitive, emotional, and social); three symptom scales (fatigue, pain, and nausea and vomiting); and a global health and quality-of-life scale. Several single-item symptom measures are also included.







	2018	2019	2020	2021	2022	Average per year	Total
Total	2,959	3,280	3,886	4,128	2,632	1,297.17	45,401
THE EUROPEAN-ORGANIZATION-FOR-RESEARCH-AND-TREATMENT-OF-CANCER QLQ-C30 - A QUALITY-OF-LIFE INSTRUMENT FOR USE IN INTERNATIONAL CLINICAL-TRIALS IN ONCOLOGY AARONSON, NK; AHMEDZAI, S; (...); TAKEDA, F Mar 3 1993 | JOURNAL OF THE NATIONAL CANCER INSTITUTE 85 (5) , pp.365-376	651	648	754	867	551	326.47	9,794

Chest. 1996 May;109(5 Suppl):110S-112S. doi: 10.1378/chest.109.5_supplement.110s.

Quality of life as a new end point

P Kosmidis [1]

Affiliations — collapse

Affiliation

1 Department of Medical Oncology, Metaxa Cancer Hospital, Piraeus, Greece.

PMID: 8635386 DOI: 10.1378/chest.109.5_supplement.110s

Abstract

Quality of life (QOL) is a relatively new clinical end point that is particularly relevant to the typically palliative therapy for non-small cell lung cancer. Patients' assessments of their QOL are shown to differ from their physicians', emphasizing the subjective nature of QOL. A number of relevant instruments and assessment techniques are employed. Results from a study using the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 instrument before and during chemotherapy are presented. Some parameters improved while others did not, preventing a simple interpretation. There are arguments for compiling indexes of QOL while retaining measures for individual parameters and a desire for the consistent international use of an instrument such as the EORTC questionnaire.

Next to the EORTC QLQ C30

2 other core instruments have been developed

- The EORTC-QLQ-C15-PAL for palliative care patients and
- The EORTC QLQ-F17 which includes only the functional scales and the global Health Status/Quality of Life scale of the EORTC C30

- Modules
- Validated questions (>1000) in the EORTC item library
- Translations in 120 languages

Back to the nineties

RECIST 2000 Patrick Therasse

- The response evaluation criteria in solid tumours **(RECIST)** was developed in the **late 1990s** to replace the WHO criteria for response evaluation. The new criteria included important changes such as unidimensional tumour measurement, selection of target lesions with a minimum size, details concerning imaging modalities and a new threshold for assignment of objective progression.

- **RECIST was published in February 2000 and very quickly came into operation first in clinical trials performed under the auspices of EORTC, US NCI or NCI Canada Clinical Trials Group but was adopted quickly thereafter by the entire cancer clinical research community.**

Therasse, et al, JNCI 2000: 205-16

Since RECIST 1.1 in 2009

Learning by doing…the place of ..

- (New) functional imaging?
- Immunotherapy assessment iRECIST
- Radiomics?
- The meaning of mixed responses?

- Still, the main question remains: How best to evaluate the benefit of clinical trials for patients?

Eisenhauer et al. Eur J Cancer 2009; 45: 228-47

Example of the complexity of endpoints (I)

Objectives:

1) To study if cancer drug trials that show improvement in OS or PFS also improve global QOL of patients with cancer compared with the control treatment,

2) to assess how unchanged or decreased QOL outcomes are reported in trial publications.

Methods:

Retrospective study

Patients with advanced stage of cancer - phase 3 RCTs which reported also QoL, published (in English) in 2019.

.

Samuel JN, JAMA Oncol. 2022;8:879-886.

QoL in clinical trials, review RCTs 2019 (II)

Results:

45 phase 3 RCTs: enrolled 24 806 participants (13 368 in the experimental arm and 11 438 in the control arm)

1) Improvement in global QOL with the experimental agent was reported in 11 (24%) RCTs.

The RCTs with improved QOL were more likely to also show improved OS vs trials with unimproved QOL : 7 of 11(64%) trials vs 10 of 34 (29%) ($p<0.04$).

Six trials (13%) reported a decrease in QOL, 3 of them were trials with targeted drugs,

11 trials reported an increase in QOL – 6/11 (55%) were trials with immunotherapy drugs.

2) Of the 34 trials in which QOL was not improved compared with controls, 16 (47%) reported these results in a positive frame.

Conclusion: Only a small proportion of RCTs of cancer drugs showed benefit in global QOL with the experimental agent, which had an association with OS (not with PFS).

There is a tendency to report negative trials regarding QoL more favourable.

The vision of Common sense Oncology (started 2023) ‘Outcomes that matter to patients’

EORTC: ‘outcomes that are in patients best interest’

Panel: Common Sense Oncology: outcomes that matter

Mission

To ensure that cancer care focuses on outcomes that matter to patients

Vision

Patients have access to cancer treatments that provide meaningful improvements in outcomes that matter, irrespective of where they live or their health system. To realise this vision, we aspire that:

- Patient outcomes that matter must be at the centre of every drug registration trial; and patient outcomes that matter should be the standard for every drug regulatory decision
- Reporting of trials is transparent and uses language that can be understood clearly by oncologists and patients
- Patients receive clear communication regarding treatment options that enables them to make informed decisions that are aligned with their personal goals and values
- The only treatments that are registered, reimbursed, and recommended are ones that meaningfully improve patients’ lives
- Common Sense Oncology that is grounded in evidence-based medicine and critical appraisal becomes a core curricular component for oncology training programmes
- Health systems invest in both developing new treatments and ensuring that patients have access to and benefit from proven effective treatments

Booth et al. Lancet Oncol. 2023 ;24:833-835.

To conclude

- We should collect data in clinical trials and make objective relevant assessments of patients' HRQoL next to imaging and survival endpoints to serve our patients and regulators.

- The long history of clinical trials, data collection and input from our patients' panel and experts in the Disease Oriented Groups and Taskforces and from HQ at EORTC enable a better insight into optimal trial design and analysis.

EORTC
European Organisation for Research and Treatment of Cancer

Thank you for your attention

w.vd.Graaf@nki.nl

Follow us on social media