

22th March 2012

**Endpoints and their relevance to older people:
Cancer and Palliative Care and work of EORTC**

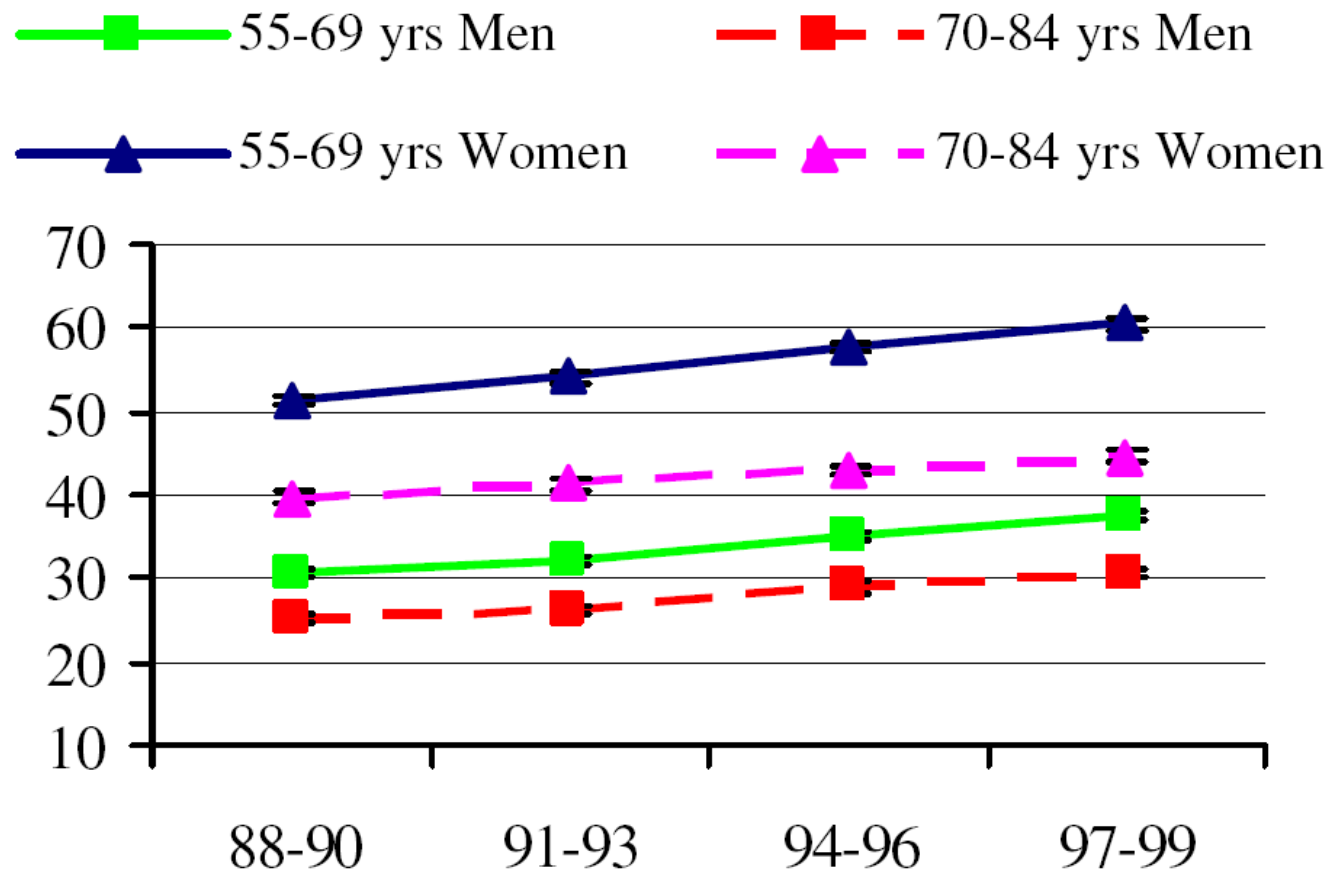
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Structure

- **Decision making in elderly cancer patients**
- **Geriatric Assessment in elderly cancer patients**
- **Endpoints and Clinical trials**
- **Research strategy**

Improvement in cancer care

All cancers combined (both sexes)*

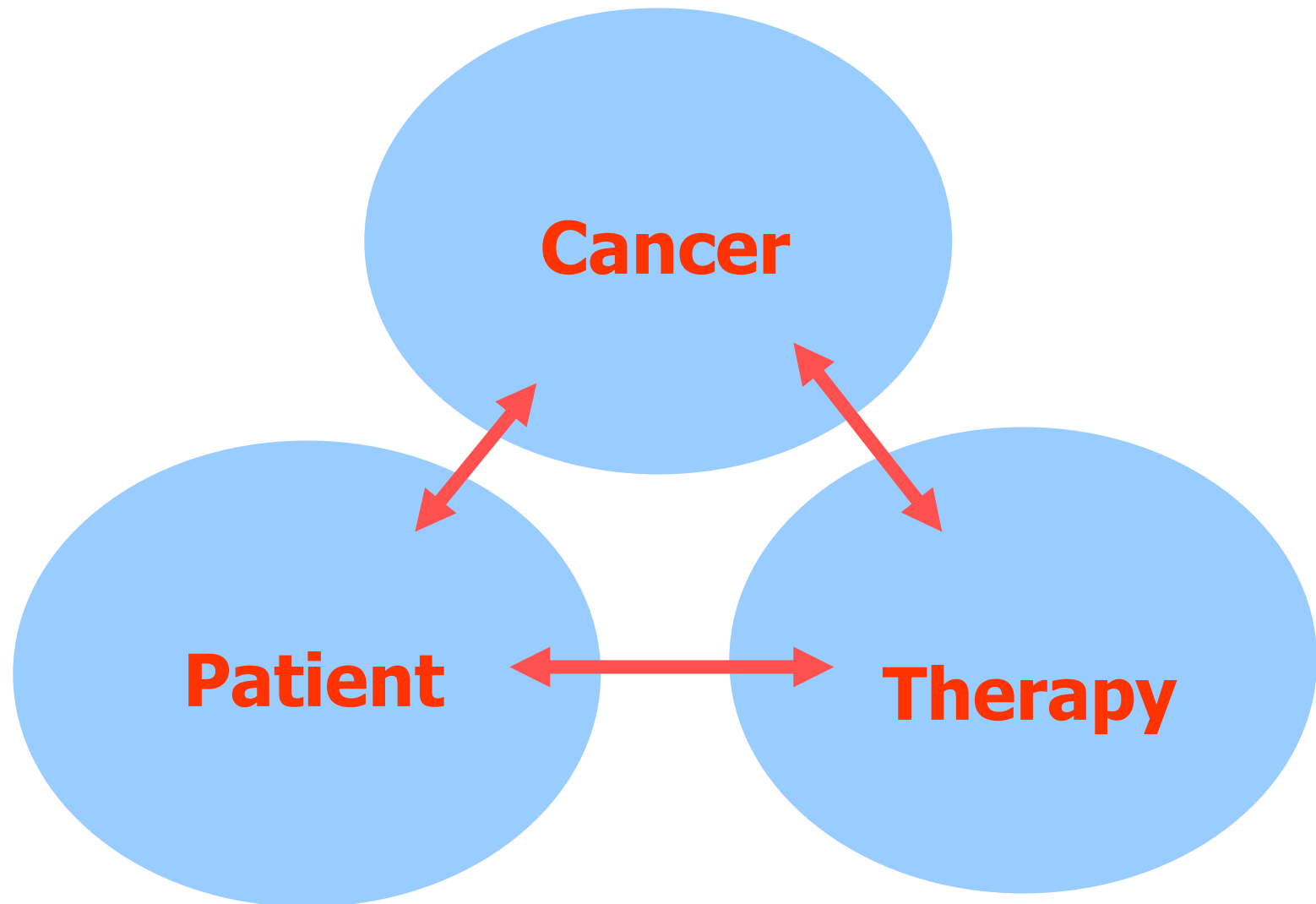


Main task in the treatment of elderly cancer patients

**less aggressive – lost chance
of cure,
of prolongation of life,
of symptome control**

**too aggressive – risk
of toxified natural course
resulting in therapy associated
mortality, morbidity, and
compromised quality of life**

Treatment decision: Medical treatment



Toxicity of medical treatment

- **Allogeneic bone marrow transplantation**
-> old patients aged 55-60+ years
- **Induction chemotherapy, e.g. of acute leukemia**
-> old patients aged 60-70+ years
- **Polychemotherapy**
-> old patients aged 70+ years
- **Monochemotherapy**
- **Monoclonal Antibodies**
- **IMiDs**
- **Hormonotherapy**

Aims of treatment

- **curative:**
 - **curative itself**
 - **adjuvant in addition to other treatment**
 - = **prolongation of survival without the disease**
- **non-curative / palliative:**
 - **prolongation of survival with the disease**
 - **prolongation of time without symptoms / deterioration of HRQoL**
 - **improvement of symptoms / HRQoL**
 - **dying in dignity**

Assessment in Oncology and Geriatrics

Oncology	Geriatrics
Age	functional status (e.g. ADL, iADL, aADL)
Performance Status, e.g. Karnofsky-PS or ECOG-PS	depression (e.g. Geriatric Depression Scale)
	dementia (e.g. Mini-Mental-Status-Examination)
	mobility (e.g. Tinetti, Timed Up and Go-Test)
	nutrition (e.g. Mini-Nutritional Assessment)
	social situation (e.g. F-Sozu)
	Comorbidities and polyparmacy (e.g. Charlson-Score)

Current evidence to perform a CGA* in oncological patients

- **detects changes missed in routine**
- **changes are of prognostic importance regarding survival, toxicity and HRQoL**
- **knowledge of changes can result in changed treatment recommendations**

- **data from RCTs that care based on CGA results improve outcome are missing**

*comprehensive geriatric assessment



available at www.sciencedirect.com



journal homepage: www.ejconline.com

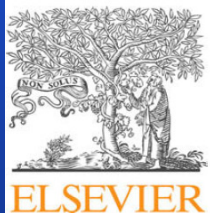


Position Paper

EORTC elderly task force position paper: Approach to the older cancer patient

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D. Lacombe ^a, S. Monfardini ^f, P. Scalliet ^g, H. Wildiers ^h

**Eur J Cancer 2010
Apr;46(6):1019-25**



available at www.sciencedirect.com



journal homepage: www.ejconline.com



Review

Questionnaires and instruments for a multidimensional assessment of the older cancer patient: What clinicians need to know?

A.G. Pallis ^{a,*}, U. Wedding ^{a,b}, D. Lacombe ^a, P. Soubeyran ^{a,c}, H. Wildiers ^{a,d}

**Eur J Cancer 2010
Jun;46(9):1502-13**

Bottle necks for clinical trial development in elderly

- **Medical community bottlenecks:**
 - poor collaboration with geriatric medicine
- **Clinical trial methodology issues**
 - no upper age limit vs. specific trials
 - definition of appropriate end-points
 - integration of geriatric assessment
 - inclusion of biomarkers
- **Infrastructures limitations**
 - local – national – international
- **Inadequate regulatory framework**
 - ICH E7, EFGCP, ...
- **Industry limited interest**
 - like to have homogeneous study populations vs. heterogeneous ageing population

Endpoints (1)

- **Classical endpoints are inadequate**
 - Overall survival, progression-free survival, ...
- **Overall treatment utility** (Seymour et al. Lancet 2011)
 - good OTU: no clinical or radiological evidence of disease progression, and no major negative treatment effects in terms of toxicity or patient acceptability
 - Intermediate OTU: either clinical deterioration but no negative treatment effect, or a significant negative treatment effect but no clinical deterioration
 - poor OTU: both clinical deterioration and a major negative treatment effect, or death
- **Therapeutic success** (Ardizzoni et al. JCO 2005)
 - combination of activity, toxicity and compliance
- ...

Endpoints (2)

- **Alternative endpoints: to avoid discomfort related to/ caused by cancer progression AND treatment**
 - ***Health Related Quality of Life (HRQoL)***
 - ◆ For older patients: anti-cancer treatment is not just how much additional time they can gain, but how valuable is that time
 - ◆ How to measure/quantify HRQoL optimally? Which cut-offs?
 - ***Quality-Adjusted Survival: Q-TWIST approach***
 - ◆ Survival time in 3 consecutive health states (time with toxicity from treatment; time without symptoms of disease or toxicity; time from progression/relapse to death) and utility weights assigned to each state
 - ◆ How to determine/quantify the weight factor?
 - ***Preservation of functional capacity/independence***
 - ◆ Maintenance of function and independence should be one of the major principles of cancer management.
 - ◆ Definition of functional dependence, optimal cut-off?
 - ◆ **Example:** GERICO: decrease of 2 points in IADL

- **‘Treatment regimen’ trials**
 - CALGB ‘Muss’ trial: therapy A vs drug B
 - Test ‘new’ drug in ‘old’ population; e.g. bevacizumab
 - ◆ Big market for industry!
 - ◆ Industry afraid of negative results

- **‘Strategic’ trials:**
 - No therapy versus therapy (prostate cancer wait and see ...)
 - Adjuvant chemotherapy versus no chemotherapy (CASA)
 - Need for observational studies!
 - ◆ Much less selection bias
 - ◆ Need for uniform evaluation of elderly!

- **Specific trials for older patients or...**
 - Design difficulties: elderly patients display much greater heterogeneity compared to younger patients
 - Jatoi et al. J Clin Oncol 2005
- **... clinical trials with no upper age limit?**
 - Selection bias only fit old patients are enrolled
- **Optimum: Combination of both and inclusion in a prospective register trials including a geriatric assessment**
 - Selection bias can be demonstrated, ...

- 1. Obligatory reporting of age related **subgroup analysis** including number of patients, **efficacy** and **toxicity** data and, if possible, pooled age analysis
- 2. Obligatory **post marketing studies** in elderly patients, with age specific trial design if applicable
- 3. Obligatory inclusion of a **minimum data set** for geriatric patients in registration trials and post-marketing trials.

original article

Annals of Oncology 22: 1922–1926, 2011

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EORTC workshop on clinical trial methodology in older individuals with a diagnosis of solid tumors

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- **G8 Questions (Bellera et al. Ann Oncol 2012)**
- **IADL Questions (Lawton et al. Gerontologist 1969)**
- **Charlson Comorbidity Scale (Charlson et al. J Clin Epidemiol 1987)**
- **Social situation**

Within a registry: Fitness of old cancer patients - from gut feeling to assessment based decision making

Group 1 'Fit'

organ function ↑
functional status ↑
life expectancy ↑
co-morbidity ↓
risk of toxicity ↓

Group 2 'Compromised'

Organ function ↓
functional status ↓
life expectancy →
co-morbidity ↑
risk of toxicity ↑

Group 3 'Frail'

organ function ↓ ↓
functional status ↓ ↓
life expectancy ↓ ↓
co-morbidity ↑ ↑
risk of toxicity ↑ ↑

'Go go'

Classical endpoints
Standard-treatment

'Slow go'

Special
endpoints
and protocols

'No go'

Other specific
endpoints
palliative care
only