

Methods and measures for assessing the health-related quality of life of mid- to long-term survivors of testicular and prostate cancer from EORTC phase III clinical trials

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Who is a cancer survivor?

National Coalition of Cancer Survivors:

"From the time of its discovery and for the balance of life, an individual diagnosed with cancer is a survivor."

U.S. National Cancer Institute:

"An individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life. Family members, friends, and caregivers are also impacted by the survivorship experience and are therefore included in this definition."

Three seasons of survival

Mullan F, 1985 NEJM 313:270-273

- **Acute survival:** begins with diagnosis and is dominated by diagnostic and therapeutic efforts
- **Extended survival:** period of remission following initial treatment; dominated by concern about recurrence and residual side-effects of disease and treatment
- **Permanent survival:** roughly equated with “cure” Focus on long-term risks (e.g., 2nd primaries) and effects (e.g., chronic fatigue)

Background

- Currently more than 10 million cancer survivors
(Ganz, 2007)
- Large cohorts of patients enjoy disease-free survival of 5 years or longer
- Disease-free status is not synonymous with a life free of physical and psychosocial health problems related to the cancer and/or its treatment.

Range of survivorship issues

- Treatment-induced morbidity (e.g., cardiovascular damage due to chemotherapy or radiotherapy; second tumors, etc.)
- Chronic disease- and treatment-related symptoms (e.g., fatigue)
- Functional impairment (e.g., sexual, cognitive)
- Psychosocial problems (e.g., fear of disease recurrence, difficulty in developing intimate relationships, depression)
- Practical problems (e.g., work disability, educational deficits, difficulty in obtaining health or life insurance, mortgage, etc.)

Survivorship literature

- Primarily focused on hematologic cancers, testicular cancer and breast cancer
- Primarily U.S., Scandinavian, and Dutch studies
- No international, cross-cultural comparisons of the survivorship experience

Potential contribution of EORTC to survivorship research

- Large, mature databases of patients treated in the context of controlled clinical trials
- RCT context facilitates controlling for disease- and treatment-related factors (i.e., case mix problem)
- EORTC uniquely positioned to investigate cross-cultural differences in survivorship experience

Research goals and objectives

- Long-term goal is to establish an EORTC cancer survivorship research program
- Current pilot study objectives:
 - to develop and test the logistics required to conduct survivorship studies within the context of the EORTC
 - to translate (where necessary) and pilot test questionnaires for assessing the HRQL of mid- to long-term cancer survivors (> 5 years disease free)

Choice of patient populations:

(1) Testicular cancer

- Collaboration with the EORTC GU Group
- Well-suited for HRQL survivorship studies
 - affects young adults
 - has a very high cure rate (90%)
 - large majority of TC survivors enjoy an HRQL similar to that of the general population (U.S., Norwegian and Dutch studies)
 - evidence of heightened levels of anxiety, sexual problems, and practical problems
- However, it is a rare disease

Choice of patient populations:

(2) Prostate cancer

- Collaboration with the EORTC GU Group
- Also well-suited for HRQL survivorship studies
 - most prevalent cancer among men in Western countries
 - modern methods of detection and treatment have resulted in earlier diagnose, and earlier and more effective treatments
 - relative 5 and 10 year survival rates for local and loco-regional prostate cancer are 99% and 91%, respectively
 - HRQL problems include bowel, urinary and sexual problems, fear of disease recurrence and psychological distress

Target trial testicular cancer: EORTC 30941

- Phase III study initiated in April 1995
- Investigated 4 different schedules of bleomycin, etoposide, and cisplatin (BEP) chemotherapy (four v three cycles given over 5 v 3 days)
- Primary study endpoint = progression free survival (PFS) and equivalence of treatment regimens and schedules
- Closed to patient recruitment in 1998
- Of the 818 patients in the trial, 799 are currently alive; median follow-up = 6.2 years

Target trial prostate cancer: EORTC 22911

- Phase III study of post-operative external radiotherapy in pathological stage T3 NO prostate cancer
- In total, 1005 patients from 8 countries were randomized to either post-surgical local radiotherapy or to a wait-and-see arm
- Primary endpoints = progression-free survival at 5 years and overall survival
- 825 patients (82%) are currently alive. Median duration of follow-up is 8.53 years (95% CI 8.32- 8.77)

Study methods and procedures (1)

- Based on the up-to-date EORTC databases for these trials, a provisional list of patients who are alive and disease-free will be generated.
- Local investigators from 5 countries (Belgium, Italy, the Netherlands, Norway and the United Kingdom) will be contacted to determine the most appropriate, efficient and ethically acceptable method for obtaining approval to contact these survivor cohorts.
- Procedures will be developed for confirming vital and disease status of those patients on the EORTC provisional list (e.g., via local hospitals' medical records, family physicians, municipal registries, etc.).

Study methods and procedures (2)

- Patients (25 per trial per country; total N = 250) will be mailed a battery of questionnaires with a follow-up mailing to initial non-respondents after 3 weeks:
 - SF-36 Health Survey (generic) and/or EORTC QLQ-C30
 - EORTC QL-PR25 and EORTC Testicular Cancer Module (condition-specific)
 - Impact of Cancer Questionnaire (survivorship-specific)
 - 41-item questionnaire organized into 10 domains: health awareness, body changes, health worries, positive and negative self-evaluation, positive and negative life outlook, social life interferences, relationships, and meaning of cancer.
 - Debriefing questions
- Qualitative interviews with 10-15 patients (Netherlands only)

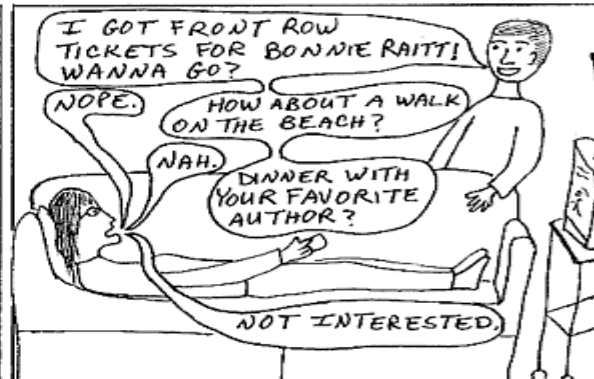
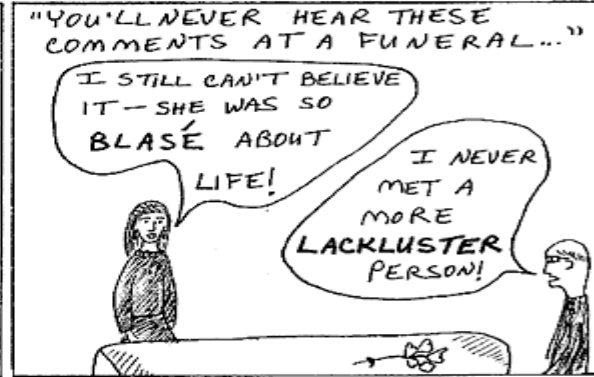
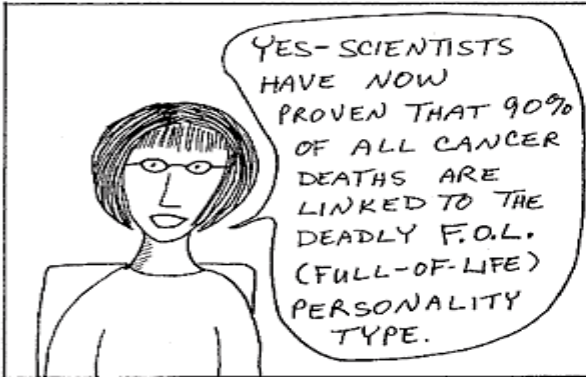
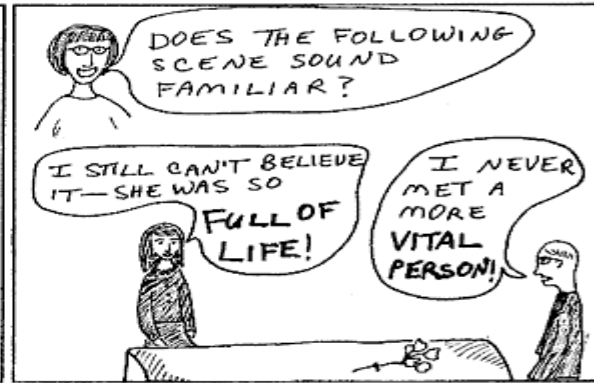
Analysis plan

- Descriptive statistics (% missing data, means and standard deviations, floor and ceiling effects, etc.)
- Scale structure and scale reliability
- Particular attention will be paid to the IOC
- The data from the debriefing questions and interviews will be reported qualitatively
- Initial analysis of cross-cultural differences (although n is relatively small).

Expected results

- Identification of practical and ethically acceptable procedures for recruiting patients from EORTC clinical trials for long-term HRQL survivorship studies
- Creation of an HRQL assessment package including generic, cancer-specific and survivor-specific questionnaire elements
- Lays groundwork for future, substantive studies on the cross-cultural differences in the survivorship experience of cancer patients.

THE FOL GENE



Miriam Engelberg, 1958-2006, "Cancer made me a shallower person"