# “Lessons Learned” in the Assessment of Health-Related Quality of Life:

## Selected Examples from the National Cancer Institute of Canada Clinical Trials Group

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**Quality of Life Committee, NCIC CTG**

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**For the QOL Committee, NCIC Clinical Trials Group**

# Outline

- Current Structure and Milieu
- *Brief* history

- The Decision to Collect PRO Data
- Planning Data Collection and Analysis
- Field operations
- Data analysis and interpretation

- Ancillary research examples
- Conclusions

# Brief History

1947: NCIC Created

1979: Decision to create NCIC Clinical Trials Group

1980: Dr. Joseph Pater named Director

1985: QOL working group created

1982: First Phase III Trial with QOL

# Brief History

## Historical Example: NCIC BR.5

**Chemotherapy Can Prolong Survival in Patients With Advanced Non–Small-Cell Lung Cancer—Report of a Canadian Multicenter Randomized Trial**

By Edna Rapp, Joseph L. Pater, Andrew Willan, Yvon Cormier, Nevin Murray, William K. Evans, D. Ian Hodson, David A. Clark, Ronald Feld, Andrew M. Arnold, Joseph I. Ayoub, Kenneth S. Wilson, Jean Latreille, Rafel F. Wierzbicki, and Donald P. Hill

*Journal of Clinical Oncology*, Vol 6, No 4 (April), 1988: pp 633-641

# BR.5 QOL

- Shortly after the trial started, centres were asked to participate in the QOL component of the trial
  - They were given the option to use both SIP and FLIC, only FLIC, or not participate
- Almost all centres agreed to participate and most chose to use both instruments

# After BR.5

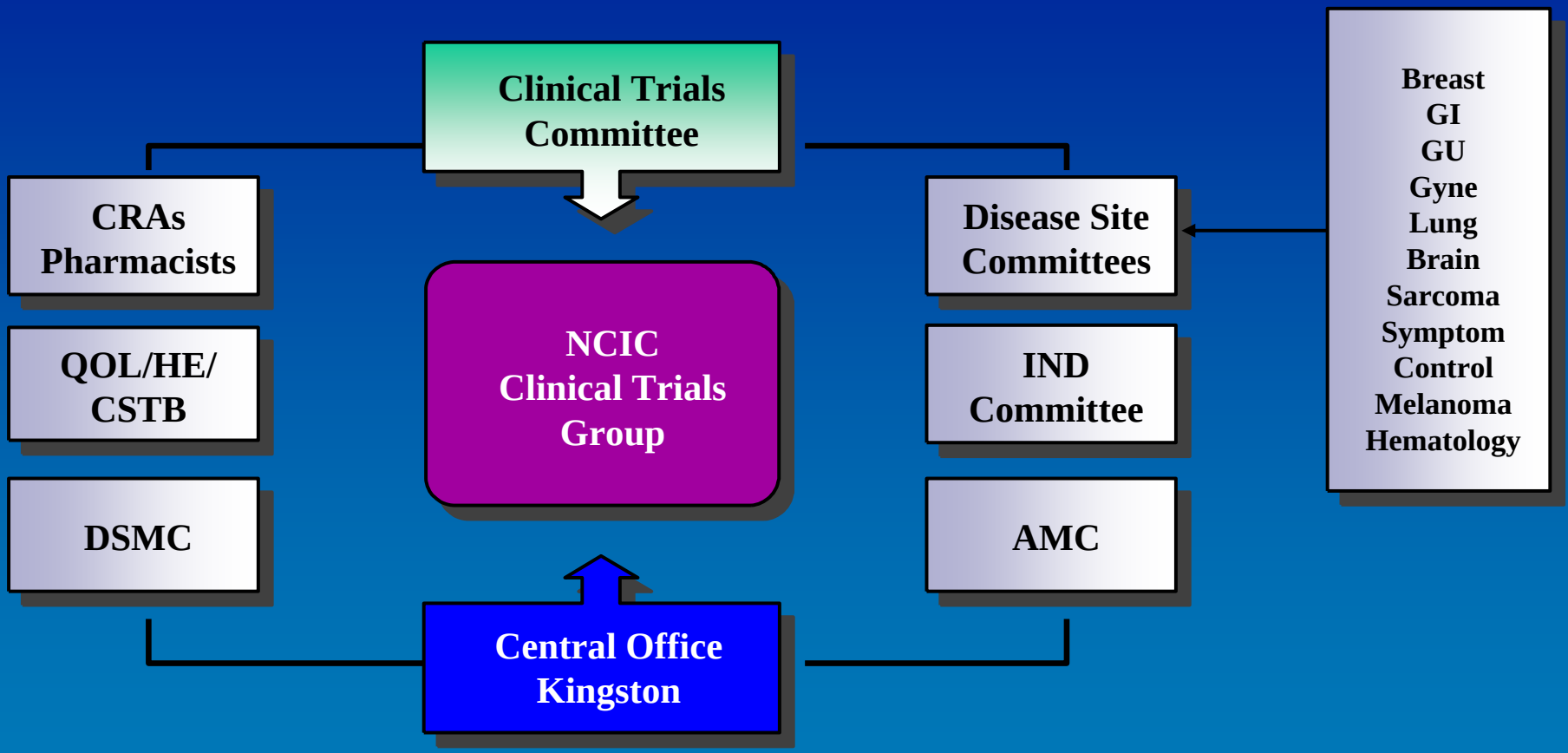
- Low compliance (<25%) with QOL collection in BR.5 was due to many factors

- It was evident that adequate QOL data collection would not just happen

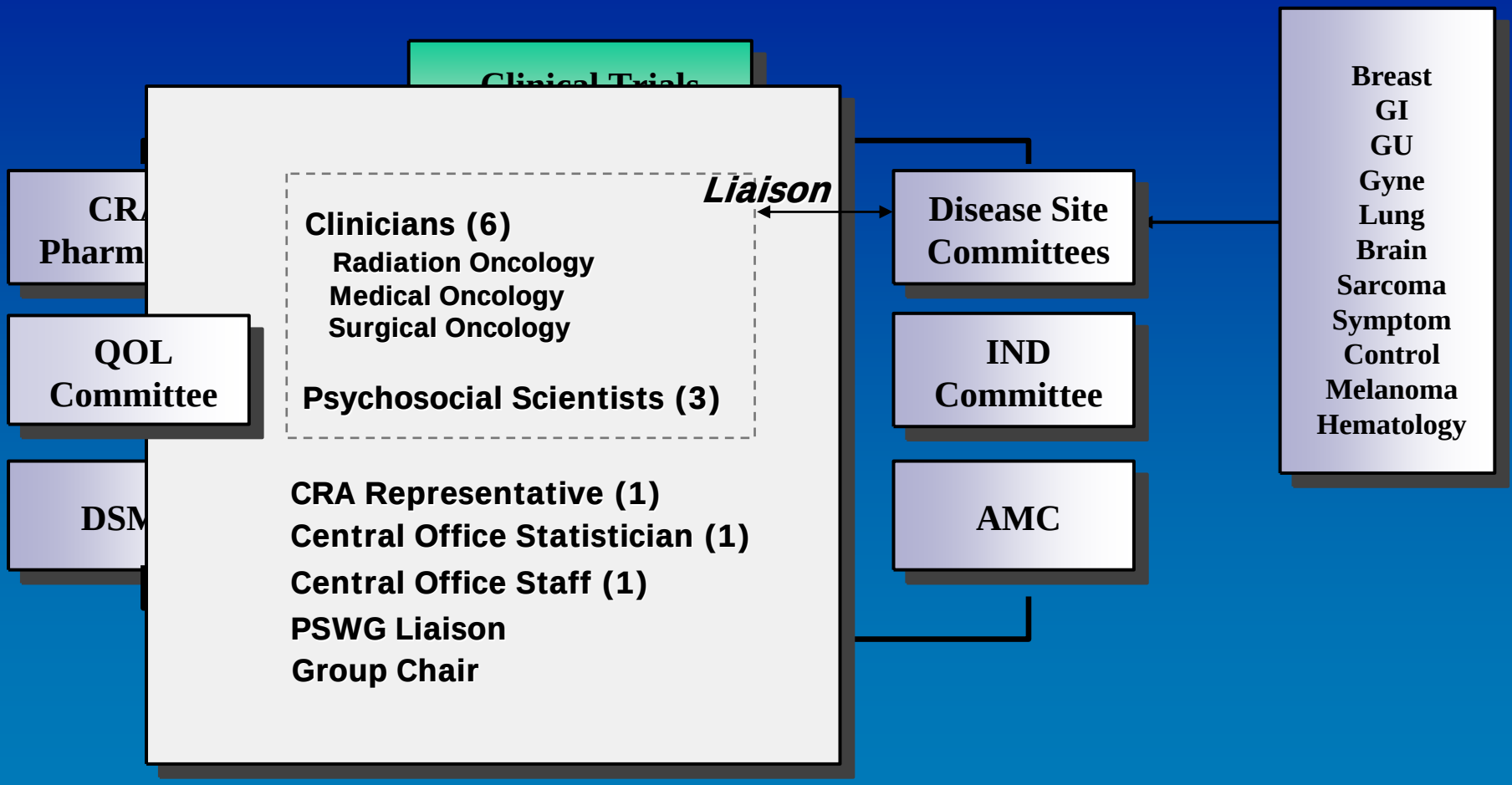
# After BR.5

- In order to stimulate interest in QOL and to discuss how the CTG should approach this area, a “scientific session” was held at the 1986 NCIC CTG Spring Meeting

# Current Structure



# Current Structure



# The Decision to Collect PRO Data in the Trial

## Some Key Points:

- Institution of Policy
- Focus on EORTC QLQ
- Organizational Infrastructure
  - QOL Committee
  - Strategic Planning
  - Disease Site Committees
  - Group Chair

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# The Decision to Collect PRO Data in the Trial

**Some Key Points:**

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- F
- C

- **There should be a statement about the anticipated impact of QOL with every proposed phase III clinical trial and whether or not QOL measures will be incorporated in the protocol**

- **If QOL is a selected study endpoint, all patients who are able to do so should be required to complete QOL assessments**

# The Decision to Collect PRO Data in the Trial

## Some Key Points:

- Institution of Policy
- **Focus on EORTC QLQ** and relevant modules
- Organizational Infrastructure
  - QOL Committee
  - Strategic Planning
  - Disease Site Committees
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| QOL questionnaire | Number of Studies |
| --- | --- |
| EORTC QLQ-C30 | 35 |
| SF-36 | 6 |
| FACT | 6 |
| 9 Others | 1 each |

# The Decision to Collect PRO Data in the Trial

## Some Key Points:

- Institution of Policy
- Focus on EORTC QLQ and relevant modules
- Organizational Infrastructure
  - **QOL Committee**
  - **Strategic Planning**
  - **Disease Site Committees**
  - Group Chair

# The Decision to Collect PRO Data in the Trial

- **Site liaisons**
- QOL committee representatives to a disease site group
- Role: consultation and advice regarding QOL

- **QOL coordinator for each trial**
- Formulating the design of the QOL aspect of the study
- Objectives of QOL measurement/hypotheses
- Choice of instrument
- Timing of administration
- Analysis
- Publication

Group Chair

# The Decision to Collect PRO Data in the Trial

## Some Key Points:

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## Some Key Benefits:

- Clear Expectations
- Cross-study comparisons
- Improved Integration
  - Multidisciplinary
  - Iterative improvement
  - Earlier involvement
  - Leadership

# Planning Data Collection and Analysis

## Some Key Points:

- Institution of Policy – Hypotheses / Sample Size
- QOL Committee – Intra-committee debate / Liaison
- Increased Familiarity with instruments
- Ad-hoc creation of symptom check lists
  - Systematic item bank
- Symptom control trials across disease sites

# Field operations (what worked?)

## Participation and Compliance:

- CRA Education and engagement
    - General
    - Trial specific
- Base line compliance monitoring
- Systematic quality assurance
- More recently – electronic feedback and monitoring

# Field operations (what worked?)

**Participation and Compliance:**

- **CRA Education and engagement**
  - **General**
  - **Trial specific eg. Cx.2**
- Base line compliance monitoring
- Systematic quality assurance
- More recently – electronic feedback and monitoring

# Field operations (what worked?)

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    - Trial specific
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# Q/A Feedback to Trial QOL Coordinator

## NCIC CTG TRIAL SC.20: QUALITY OF LIFE SUBMISSIONS

Eligible and Form 1 Received = 129 Patients

| Period | | Expected | Received (%) |
|---|---|---|---|
| Baseline - Prior to Randomization | | 126 | 125 (99.2) |
| Baseline - Day 1 of Radiotherapy | | 15 | 12 (80.0) |
| Follow-up | 1 | 120 | 110 (92.4) |
| | 2 | 94 | 84 (90.3) |
| | 3 | 83 | 65 (78.3) |
| | 4 | 71 | 58 (81.7) |
| | 5 | 59 | 46 (78.0) |
| | 6 | 45 | 39 (86.7) |
| | 7 | 3 | 2 (66.7) |

# Field operations

## Examples of Required Resources

- Central office QOL coordinator
- Central office QA processes
- Data entry and cleaning
- Forms/instrument costs
- Data analysis/other statistician input
- Clinician and scientist (QOL Committee) time
- Patient perspective
- Others

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} 0.2 FTE

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# Data analysis and interpretation

- The subject of continuous debate and education!
- NCIC CTG “basic” analysis development and implementation
- Site and context specific development
- “ancillary” research efforts

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- "ancillary" research efforts

# Data analysis and interpretation

ELSEVIER

European Journal of Cancer 41 (2005) 280–287

European Journal of Cancer

www.ejconline.com

## Analysis and interpretation of health-related quality-of-life data from clinical trials: basic approach of The National Cancer Institute of Canada Clinical Trials Group

David Osoba [a,*], Andrea Bezjak [b], Michael Brundage [c], Benny Zee [d], Dongsheng Tu [e], Joseph Pater [e], for the Quality of Life Committee of the NCIC CTG

[a] *QOL Consulting, 4939 Edendale Court, West Vancouver, Canada BC V7W 3H7*
[b] *Radiation Oncology, Princess Margaret Hospital, University of Toronto, Toronto, Ont., Canada*
[c] *Radiation Oncology, Queen's University, Kingston, Ont., Canada*
[d] *Chinese University of Hong Kong, Shatin, Hong Kong, China; Former Senior Statistician, NCIC CTG, Kingston, Ont., Canada*
[e] *NCIC CTG, Queen's University, Kingston, Ont., Canada*

Received 8 June 2004; received in revised form 18 October 2004; accepted 19 October 2004
Available online 19 November 2004

# Data analysis and interpretation

- Final compliance report
- For pre-specified time points:
  - Baseline scores
  - Change scores over time: Repeated measures ANOVA for all instrument domains
  - Clinically meaningful ‘response’ rates based on the threshold clinical difference specified in protocol

Received 8 June 2004; received in revised form 18 October 2004; accepted 19 October 2004
Available online 19 November 2004

# Ancillary research - examples

- **Clinical trial interpretation:**
  - **Metastatic setting (MA.8)**
  - **Symptom control setting (SC.15)**
- Subjective significance assessment
- Prognostic Factor assessment
- Communication of clinical trial QOL results
- Value of QOL data to patients

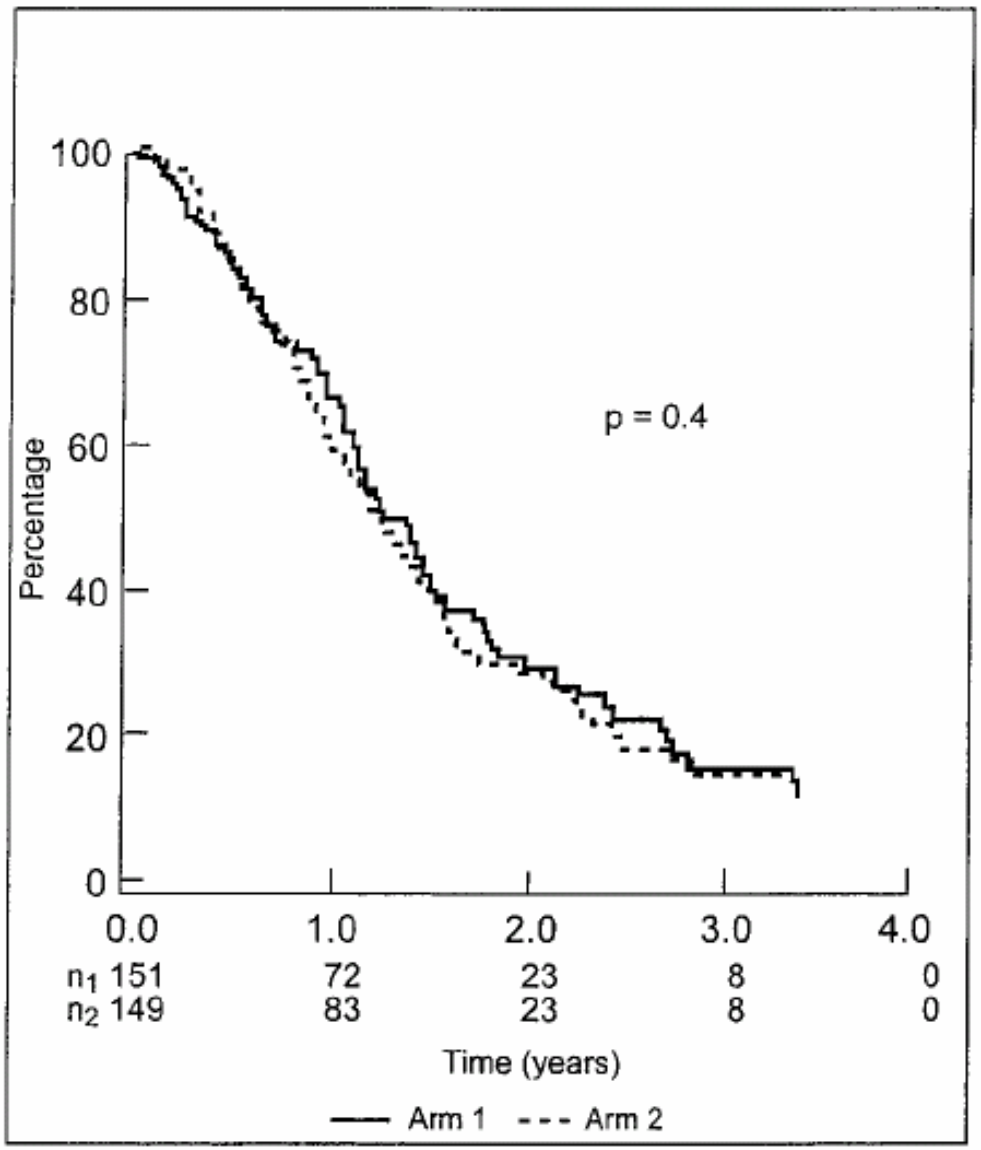
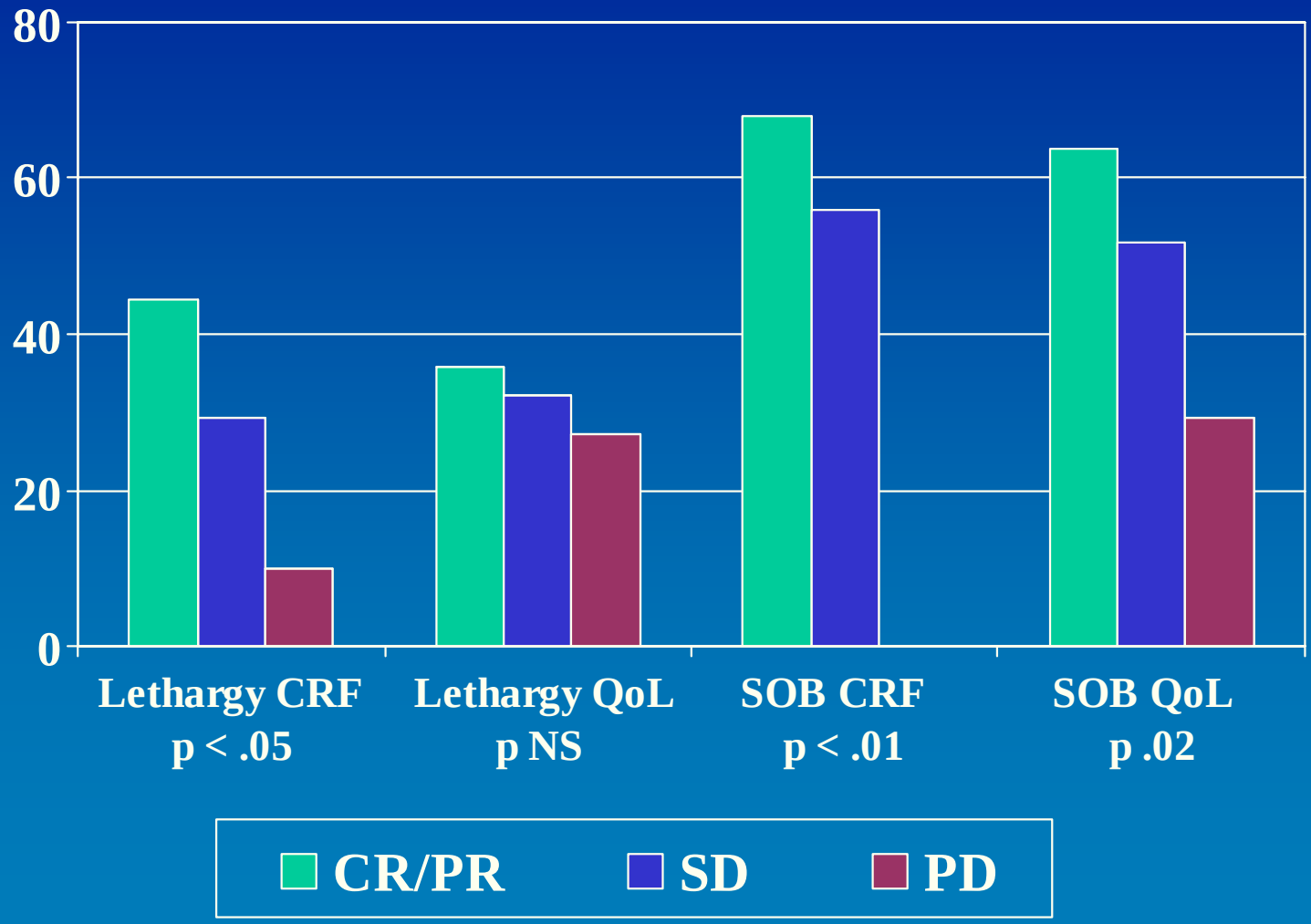



Fig 1. Overall survival by arm; $n_1$ = number of patients at risk, arm 1; $n_2$ = number of patients at risk, arm 2.

# Results (MA.8): Proportion of Patients with Symptom Improvement by Response Category



# QOL results – SC.15



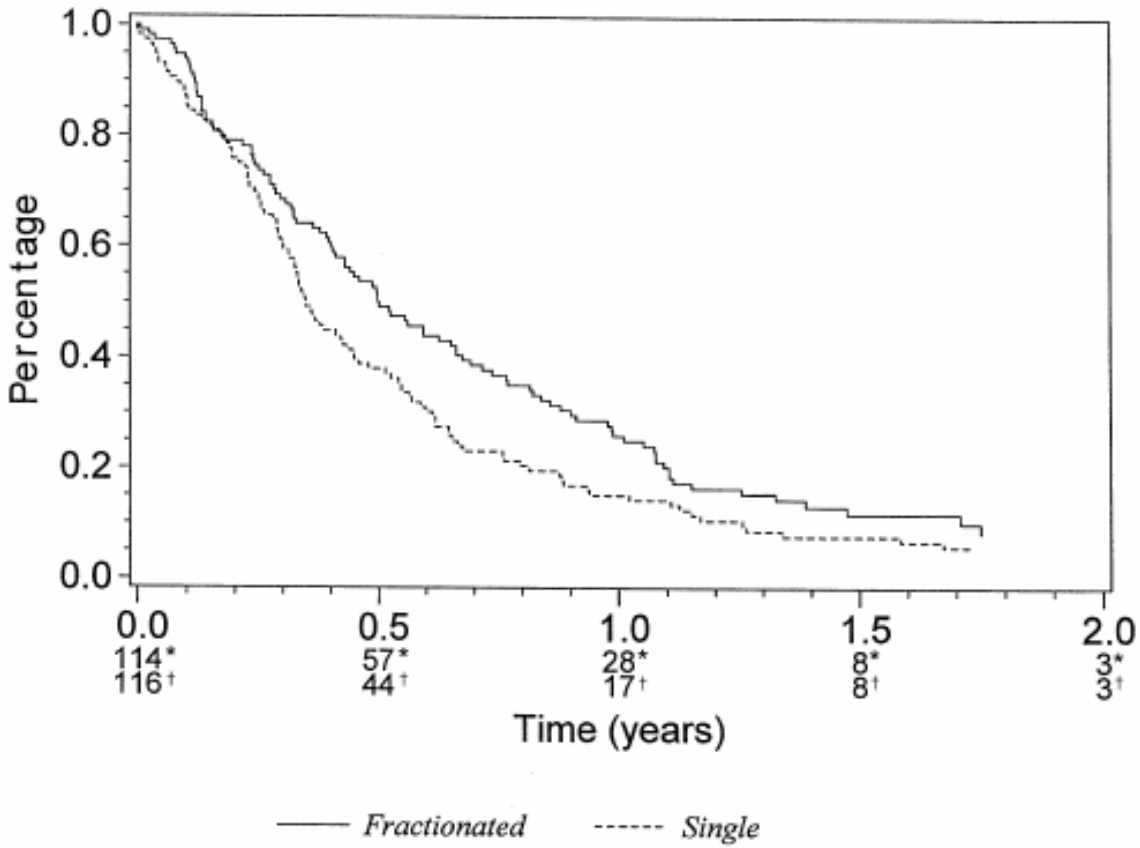
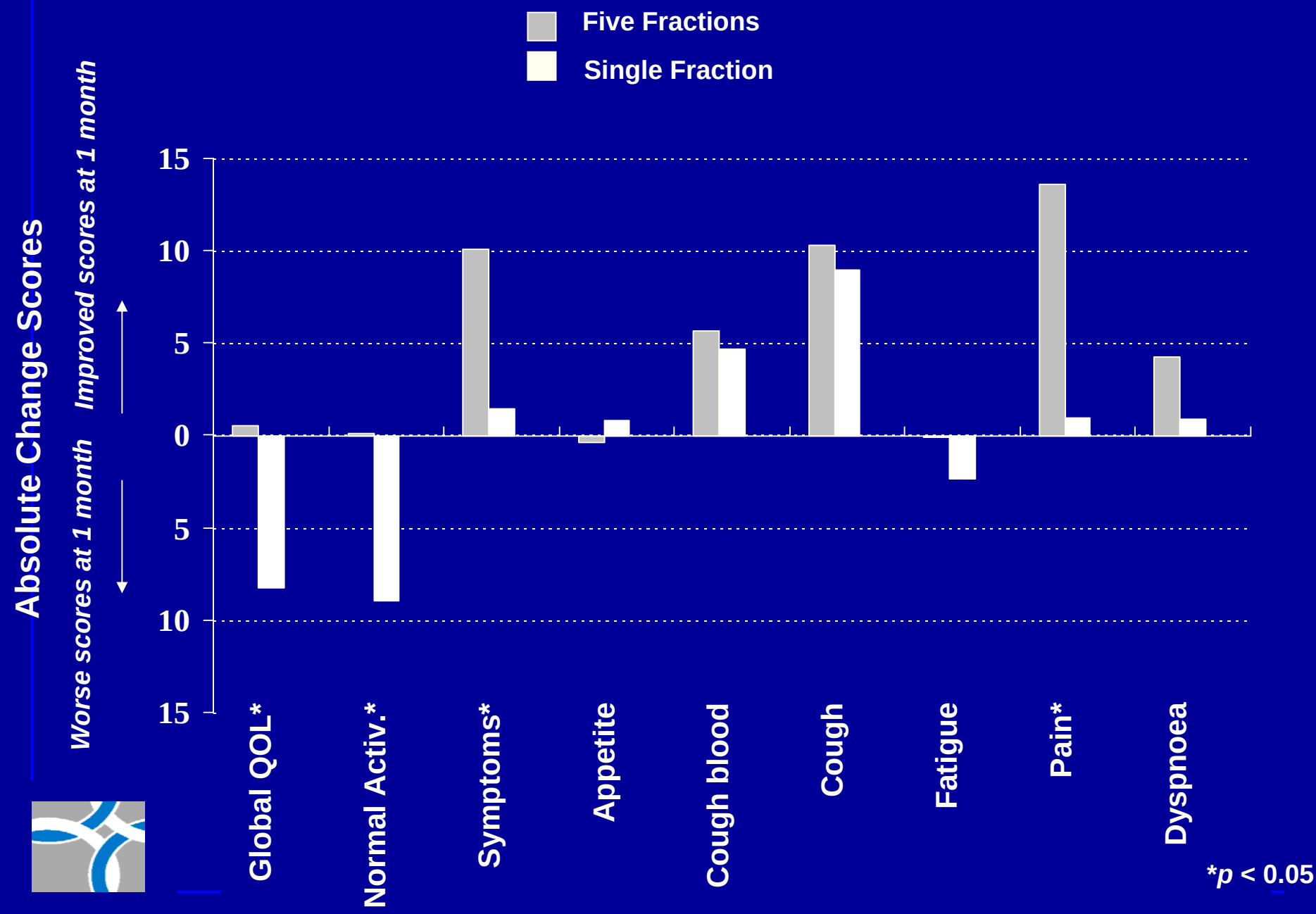



Fig. 4. Patient survival. *Number of patients at risk (fractionated arm). †Number of patients at risk (single arm).

# Change in Lung Cancer Symptom Scale Scores



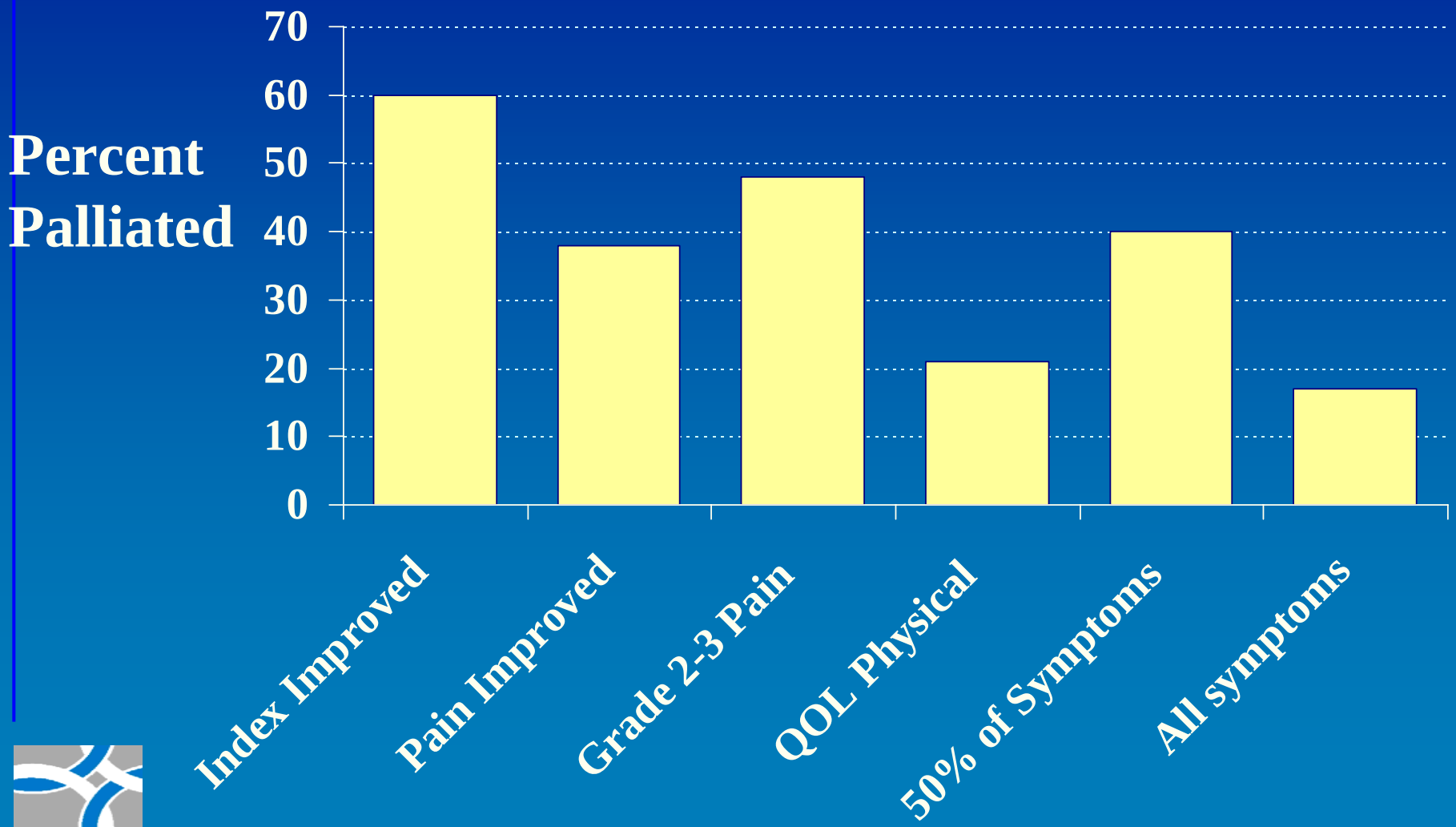

*$p < 0.05$

# SC.15 - conclusions

- Apparent extent of palliation depends on:
  - Outcome(s) of interest
  - Intent-to-evaluate analysis
  - Unit of analysis (Single symptom *vs.* single patient)

Substantive differences in apparent palliation result from the use of different approaches

# Apparent Extent of Palliation



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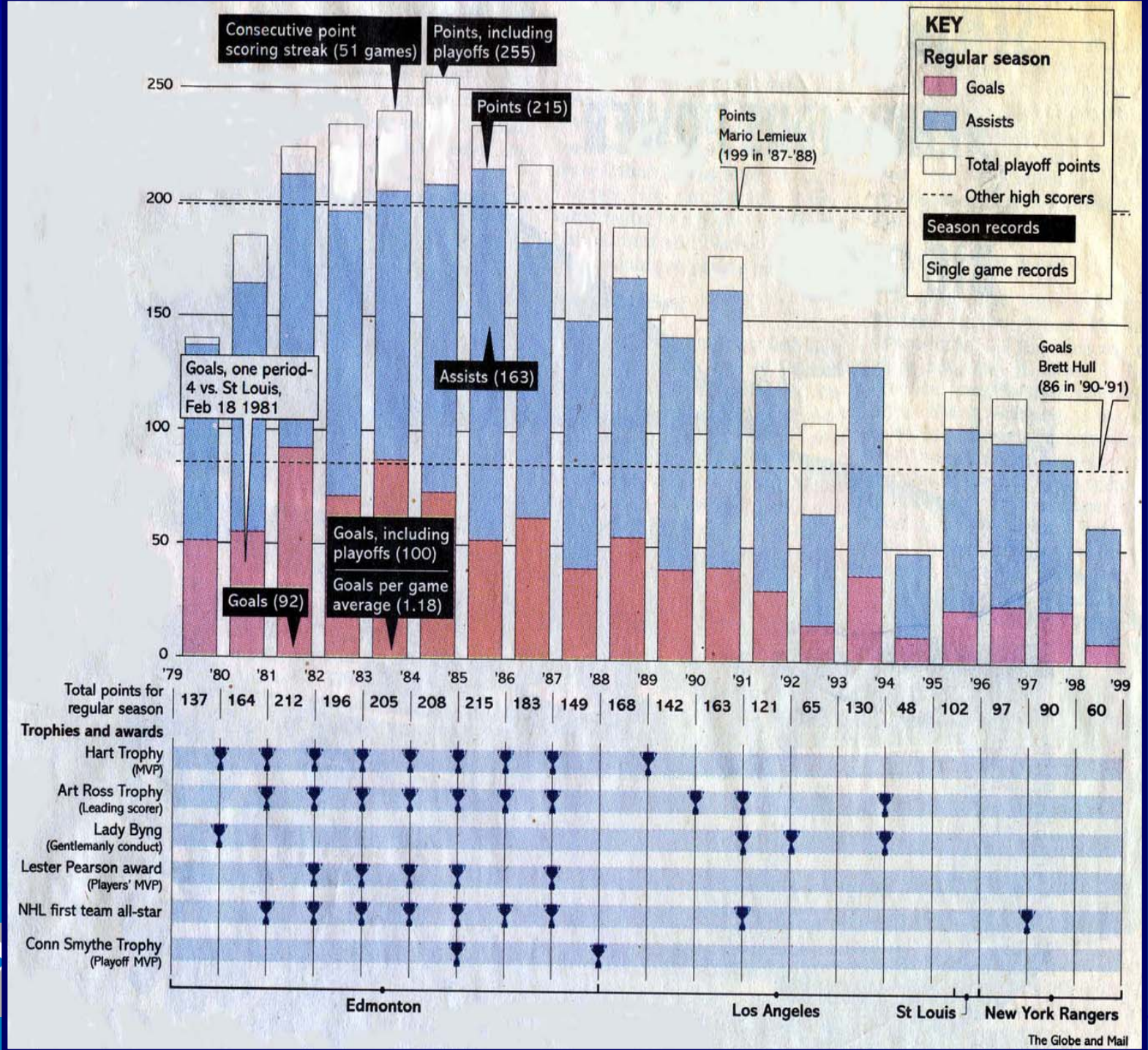
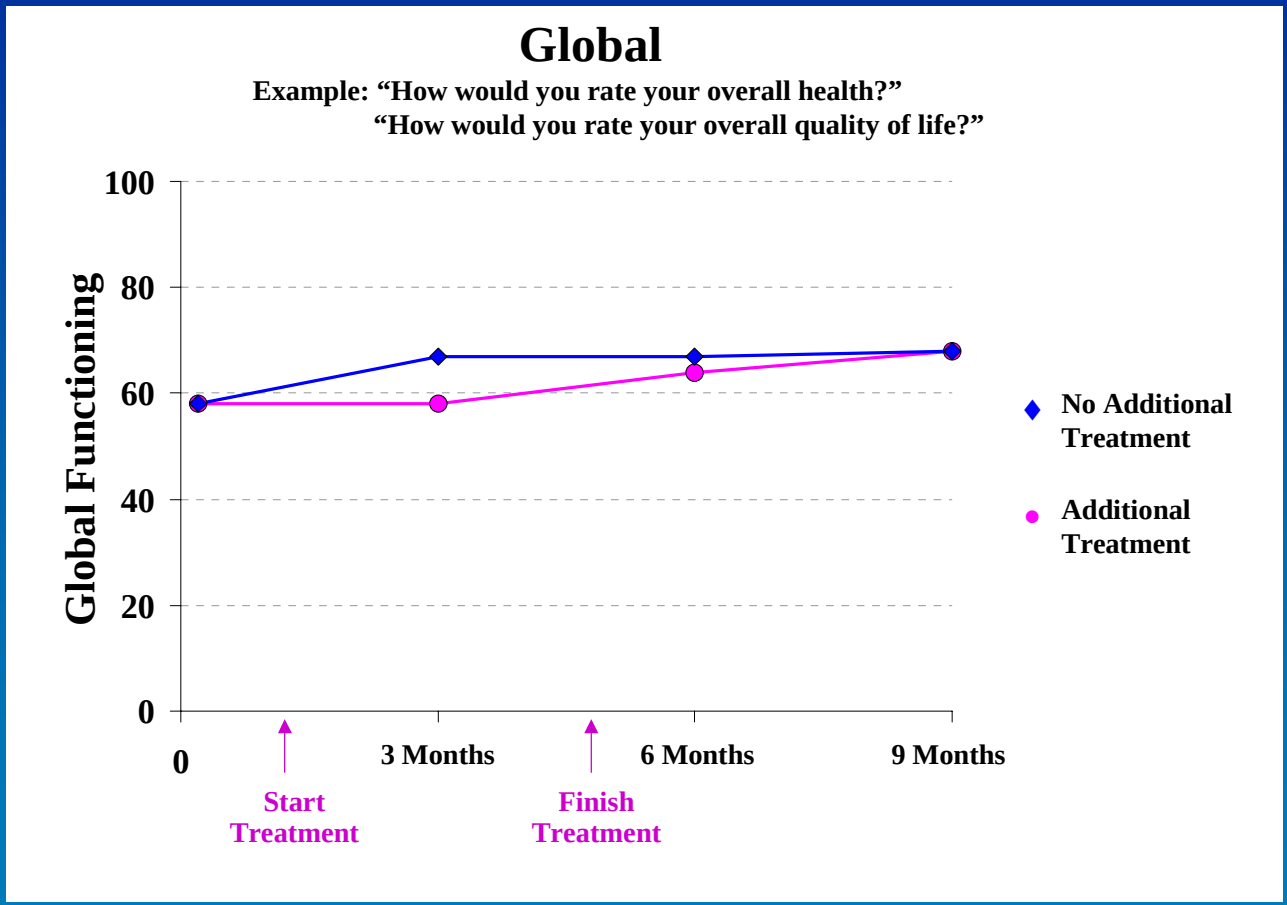
99
COMING MONDAY:
A special four-page tribute to Wayne Gretzky
and a chance to win a trip to the Stanley Cup finals.


KEY
Regular season
Goals
Assists
Total playoff points
Other high scorers
Season records
Single game records
Consecutive point scoring streak (51 games)
Points, including playoffs (255)
Points (215)
Points
Mario Lemieux
(199 in '87-'88)
Goals, one period-4 vs. St Louis, Feb 18 1981
Assists (163)
Goals
Brett Hull
(86 in '90-'91)
Goals, including playoffs (100)
Goals per game average (1.18)
Goals (92)
250
200
150
100
50
0
'79 '80 '81 '82 '83 '84 '85 '86 '87 '88 '89 '90 '91 '92 '93 '94 '95 '96 '97 '98 '99
Total points for regular season
137 164 212 196 205 208 215 183 149 168 142 163 121 65 130 48 102 97 90 60
Trophies and awards
Hart Trophy (MVP)
Art Ross Trophy (Leading scorer)
Lady Byng (Gentlemanly conduct)
Lester Pearson award (Players' MVP)
NHL first team all-star
Conn Smythe Trophy (Playoff MVP)
Edmonton
Los Angeles
St Louis
New York Rangers
The Globe and Mail

# Global Quality of Life Results



# Some Examples….

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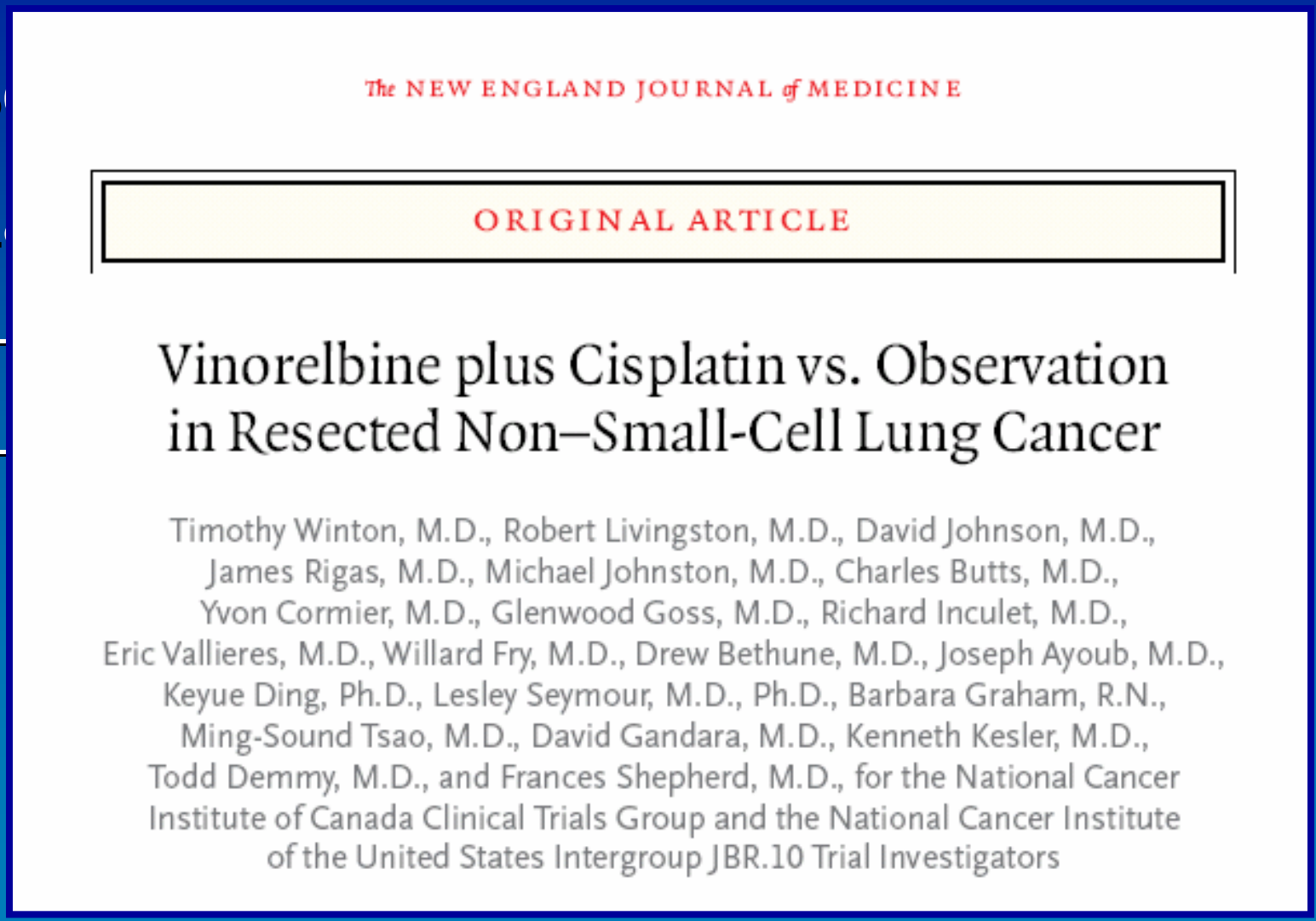


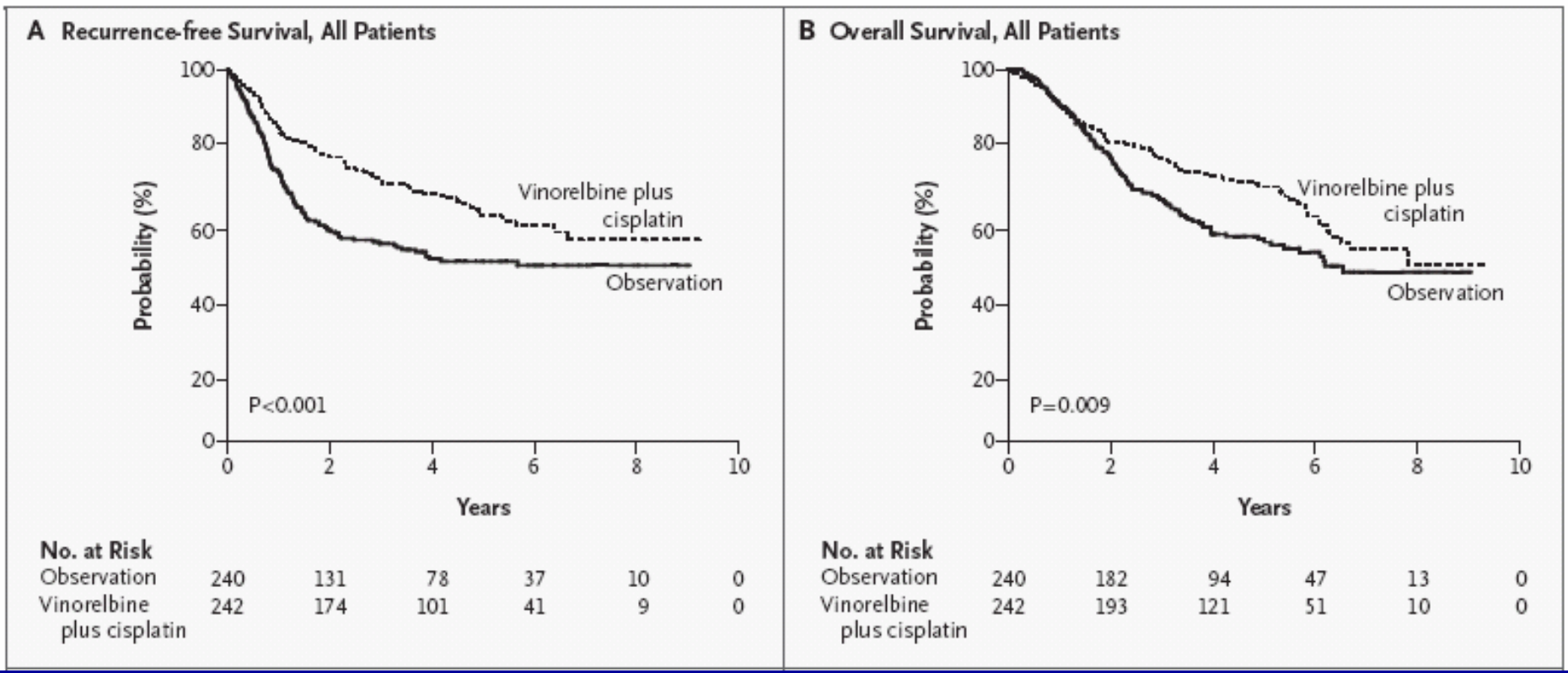
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

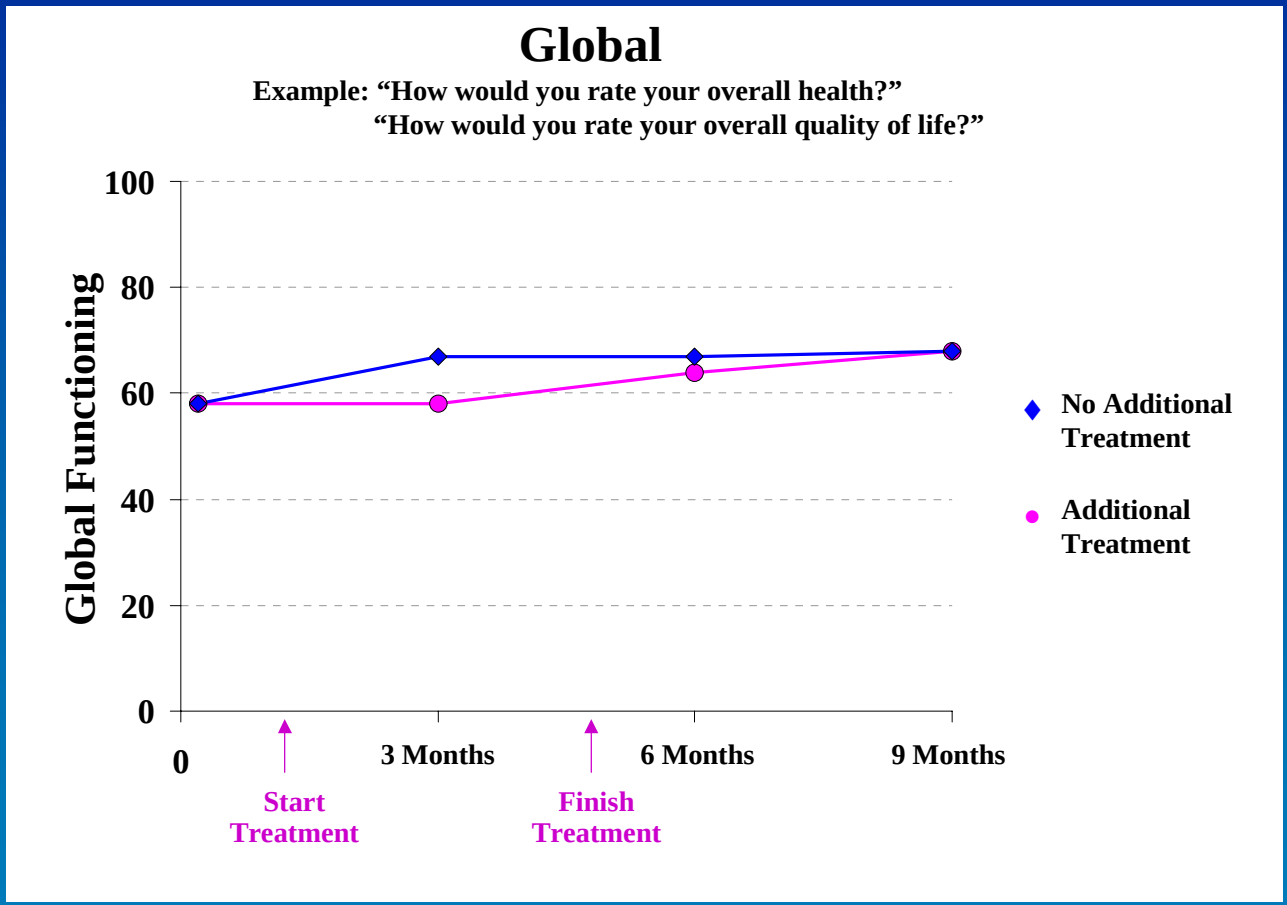
## Vinorelbine plus Cisplatin vs. Observation in Resected Non–Small-Cell Lung Cancer

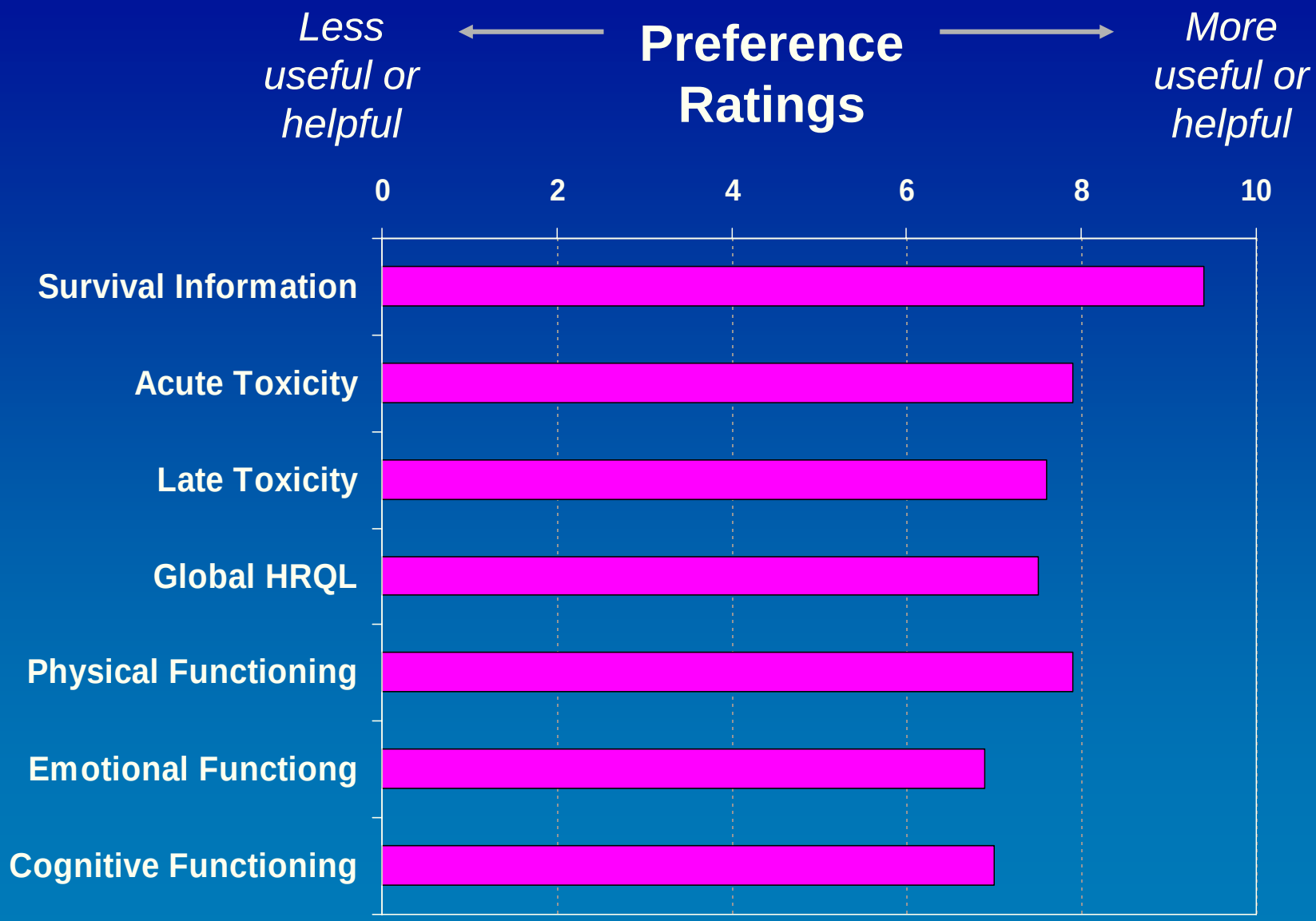
Timothy Winton, M.D., Robert Livingston, M.D., David Johnson, M.D., James Rigas, M.D., Michael Johnston, M.D., Charles Butts, M.D., Yvon Cormier, M.D., Glenwood Goss, M.D., Richard Inculet, M.D., Eric Vallieres, M.D., Willard Fry, M.D., Drew Bethune, M.D., Joseph Ayoub, M.D., Keyue Ding, Ph.D., Lesley Seymour, M.D., Ph.D., Barbara Graham, R.N., Ming-Sound Tsao, M.D., David Gandara, M.D., Kenneth Kesler, M.D., Todd Demmy, M.D., and Frances Shepherd, M.D., for the National Cancer Institute of Canada Clinical Trials Group and the National Cancer Institute of the United States Intergroup JBR.10 Trial Investigators

# Survival Outcome Results



# Global Quality of Life Results




Less useful or helpful
Preference Ratings
More useful or helpful
0
2
4
6
8
10
Survival Information
Acute Toxicity
Late Toxicity
Global HRQL
Physical Functioning
Emotional Functiong
Cognitive Functioning

# Continuing Education - examples

- Established CME events
  - CRAs
  - Annual Cooperative Group Meeting
  - QOL Committee
  - Workshops

# Conclusions

- Dedicated Group Chair
- Dedicated “Champions” of QOL outcome assessment
- Innovative integration
- Strong QA program
- Sustained efforts still required!