Quality of Life Measurement for NCIC CTG - Clinical Trials

Alice Wei

QOL Committee– GI site liaison

NCIC-CTG

The Princess Margaret Hospital, Toronto

Thank you

- Input: NCIC-CTG QOL Committee
- Slides:
  - Jolie Ringash
  - Andrea Bezjak
  - Michael Brundage
  - David Osoba
  - Joe Pater

NCIC CTG
NCIC GEC

Learning Objectives

- Understand the meaning of “QOL”
- Learn basics of QOL measurement
- Interpret of QOL Results
- Learn the history of the CTG QOL Committee

NCIC CTG
NCIC GEC

What is QOL?

- “the goodness of life”
- patient’s perspective
- multi-dimensional assessment
  - physical, emotional, social +/- functional, sexual, spiritual
- includes hope/ hopefulness
- HRQoL as related to health (not housing, income, environment, etc)

NCIC CTG
NCIC GEC

What is QOL?

- “Optimum levels of physical, role and social function, including relationships, and the perception of health, fitness, life satisfaction and well-being. It should also include some assessment of the patient’s level of satisfaction with treatment, outcome and health status and with future prospects.”

Bowling, 1995

Why is QOL an increasingly frequent outcome in clinical trials?

- Disease-centered outcomes (response rates, cause-specific survival) are not the only clinically relevant outcomes
- Toxicity has traditionally been assessed from the view-point of medical staff
- Patient-centered outcomes have become an important measure of the patient experience of their illness and treatment

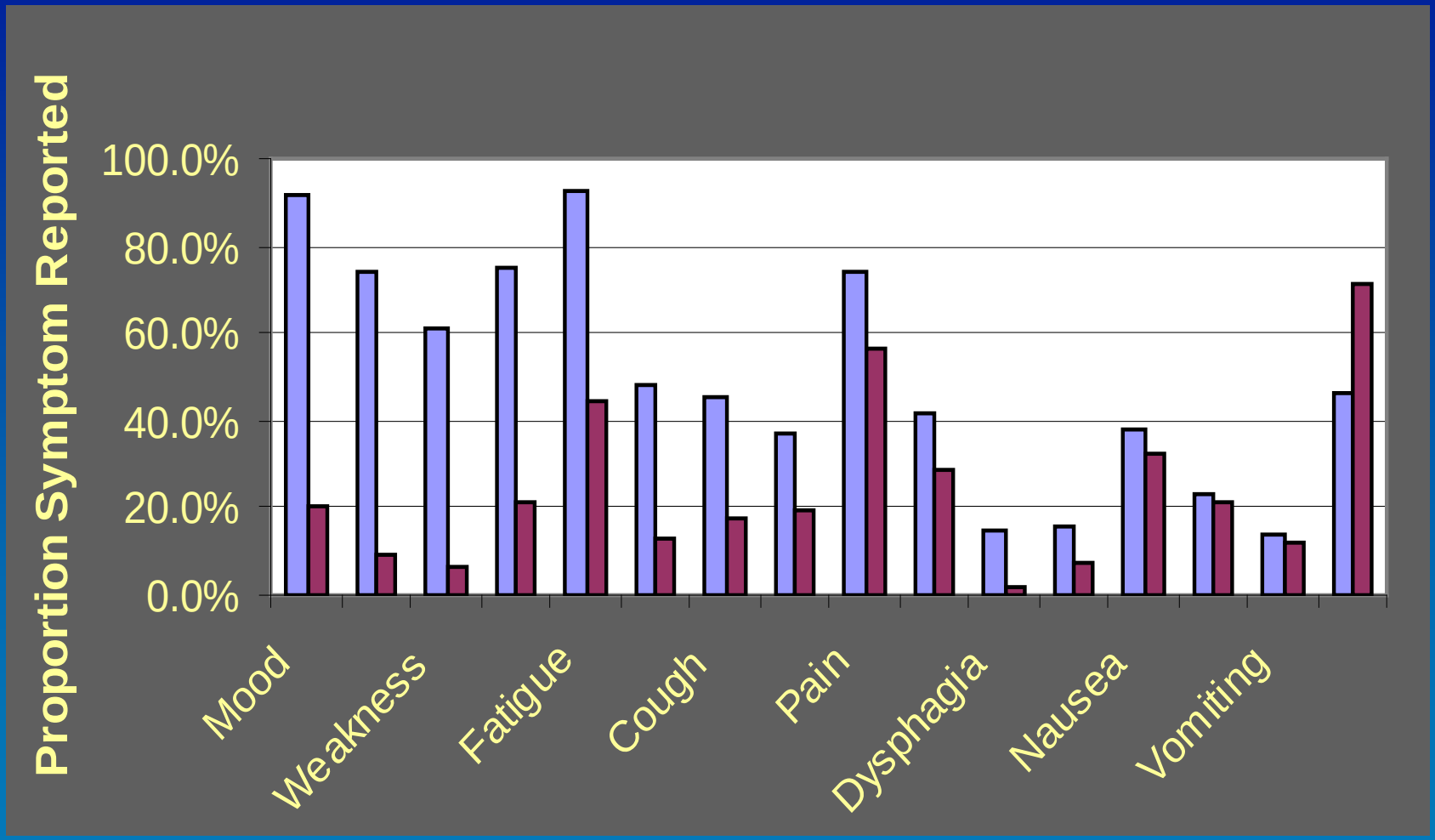
HRQL vs. Toxicity

Comparison of toxicity to HRQL data (advanced breast cancer):

- Agreement was found to be fair to slight
- (kappa 0.012 to 0.378)
- Patient's reported far more symptoms (by HRQL) than noted by toxicity scores.

These differences influenced the interpretation of trial results

HRQL vs. Toxicity



Savage C, Proc Am Soc Clin Oncol 21: 386a (abstract 1540)

NCIC CTG
NCIC GEC

Why QOL is important

- Different treatments have similar survival
- Treatment improves survival but has severe side effects
- Treatment has no effect on survival but may improve QOL
- Cure is not possible
- Chronic diseases with high survival rates

Issues to Consider

- The 5 W's: Who, What, When, Where, Why, How
  - Who are the patients (cancer type, age, etc)
  - What are their concerns or issues
  - When & where will QOL be measured
  - Why measure QOL?
  - How? Self-completed, computerized, interview

NCIC CTG
NCIC GEC

Who and What?

- Consider cancer type, gender, age, level of education, stage, treatment, and point in disease course
- Review literature or interview patients about their issues and concerns
- Are there existing, validated instruments?
- Consider emotional, social, cognitive, role-fulfillment and spiritual issues as well as physical condition

When & Where?

- Cross-sectional vs. longitudinal design
- Do you want to describe a state, or measure change?
- Beware pitfalls of missing or untimely data
- Respondents may be more comfortable in their own homes, but the clinic may be more practical
- Timing with respect to doctors' visits

How? Administration

- Self-completion is the gold standard
- Interviews must be standardized
- Use of computers is promising
- Use of proxy information is difficult

NCIC CTG
NCIC GEC

How important is it to get all patients to complete QOL questionnaires?

- Extremely important!!
- The biggest problem with analyzing QOL information from clinical trials is missing data - are pts whose QOL data are missing different from pts supplying QOL data? Or is QOL data missing because pts are sicker that those providing info?
- Analysis can try to account for missing data but it is best trying to prevent missing data

Reliability

- Are the results reproducible?
  - Internal consistency (similar items score similarly, eg. Cronbach's alpha)
  - Test-retest reliability (5-7 days) – ideally concordance (ICC) rather than correlation
  - Longer questionnaires are more reliable

Validity

- Does the questionnaire really measure QOL?
- Face and content validity
  - Do the questions make sense? Are they relevant? Is the administration and scoring sensible?
- Criterion validity
  - Compare to a “Gold Standard”

Construct Validity

- Also called: Concurrent validity, convergent validity, divergent validity
- Formulate and test hypotheses
  - Eg. CAROT score will be higher in younger patients and those with stage I toe cancer
  - Eg. CAROT score will correlate positively with EORTC QOL score and negatively with HAD (anxiety) score

Sensitivity (Responsiveness)

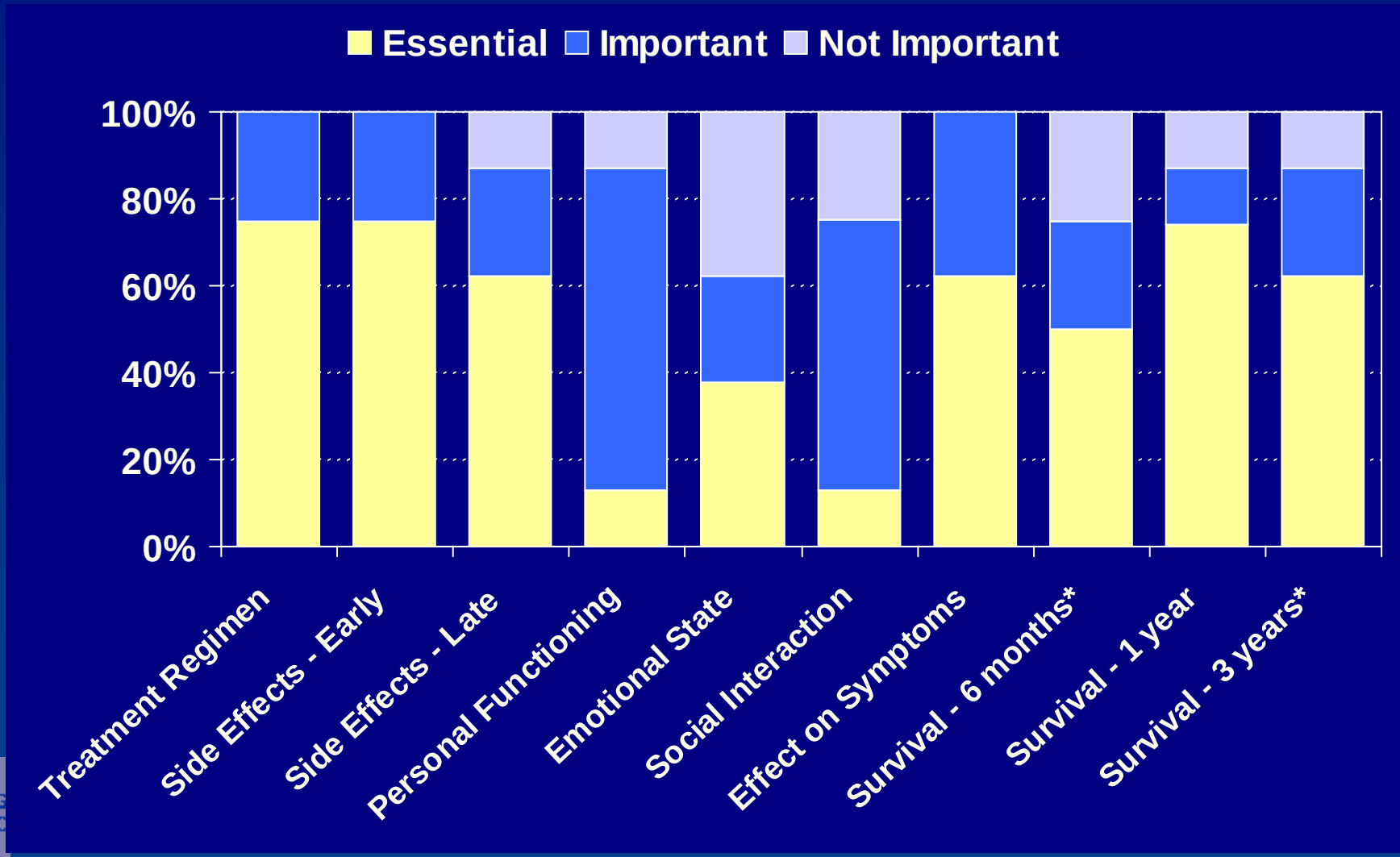
- Do scores accurately reflect change over time?
  - Usually measured in a group expected to change, eg. During toxic therapy, after cure
- The more specific the questionnaire, the better its responsiveness

Patients' Information Needs

- Patients have a extensive list of information needs
  - collectively and individually
- Information may be needed for one or more of several purposes
  - Decision making, planning, preparing, understanding, and so on

NCIC CTG
NCIC GEC

Patients' Information Needs

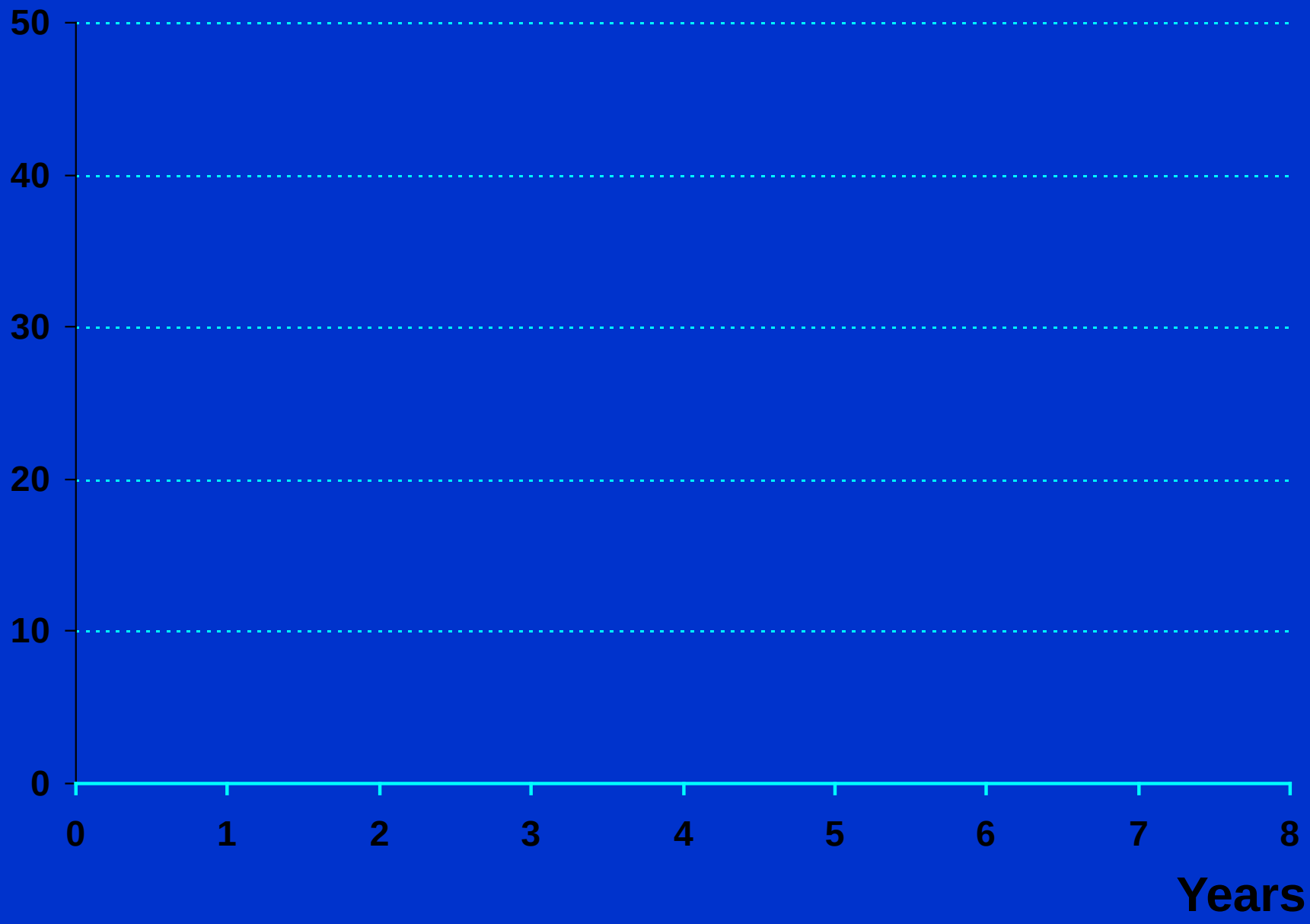


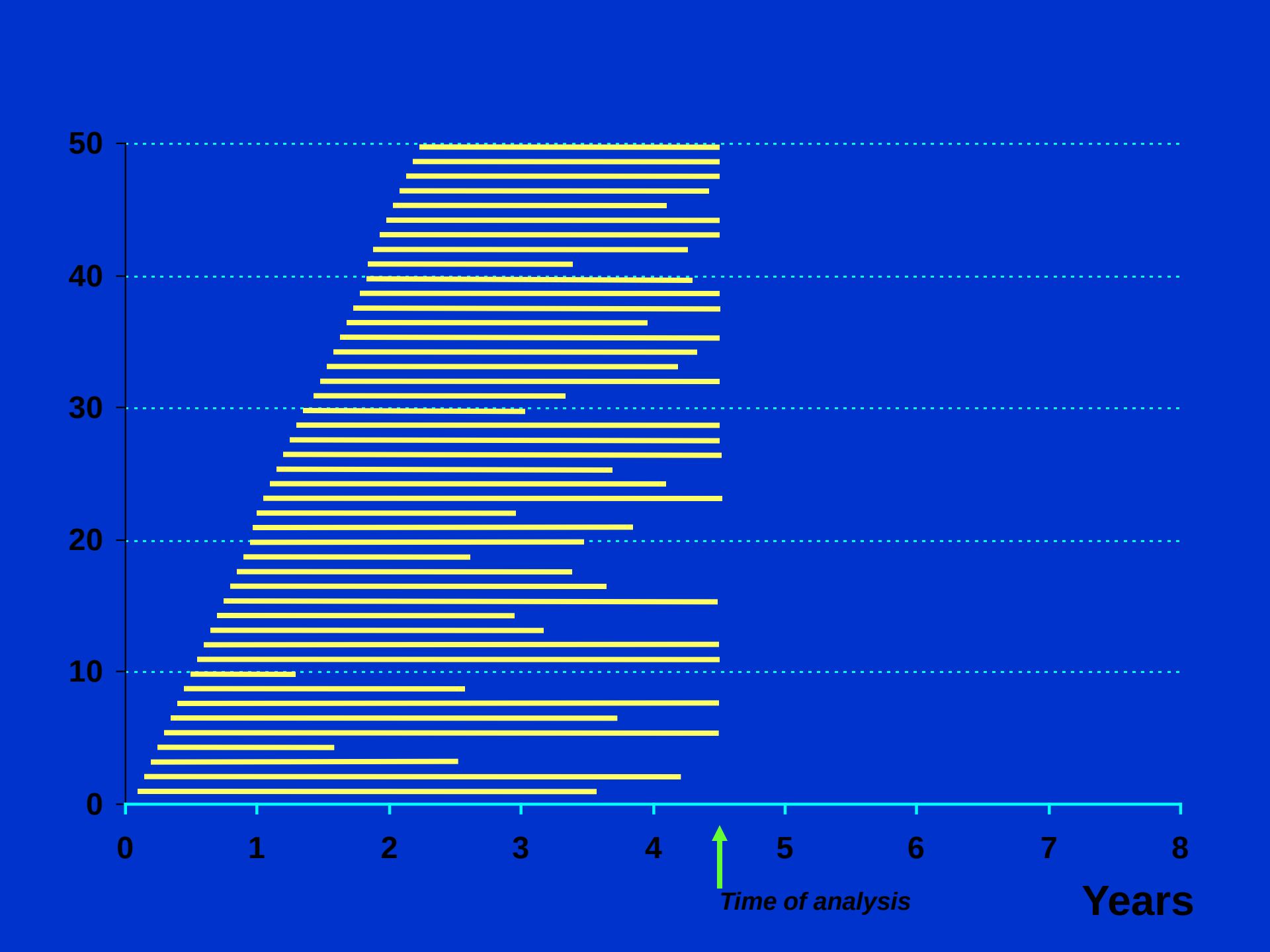
Interpretation of QOL Results: Example

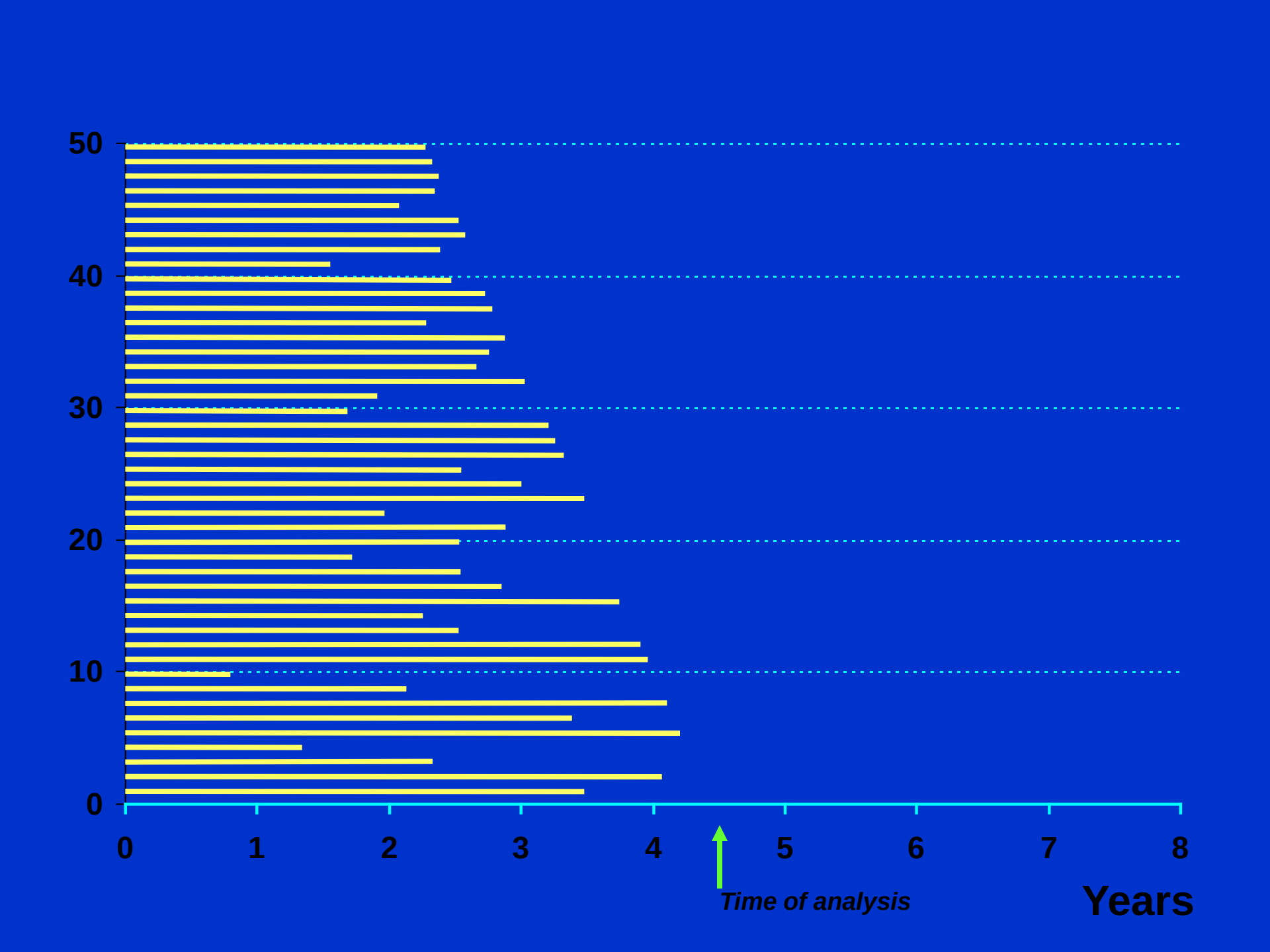
- A RCT claims to demonstrate that one treatment approach resulted in clinically superior QOL when compared with the other approach. How do you interpret this finding?
- Compare approach with a more familiar metric: survival

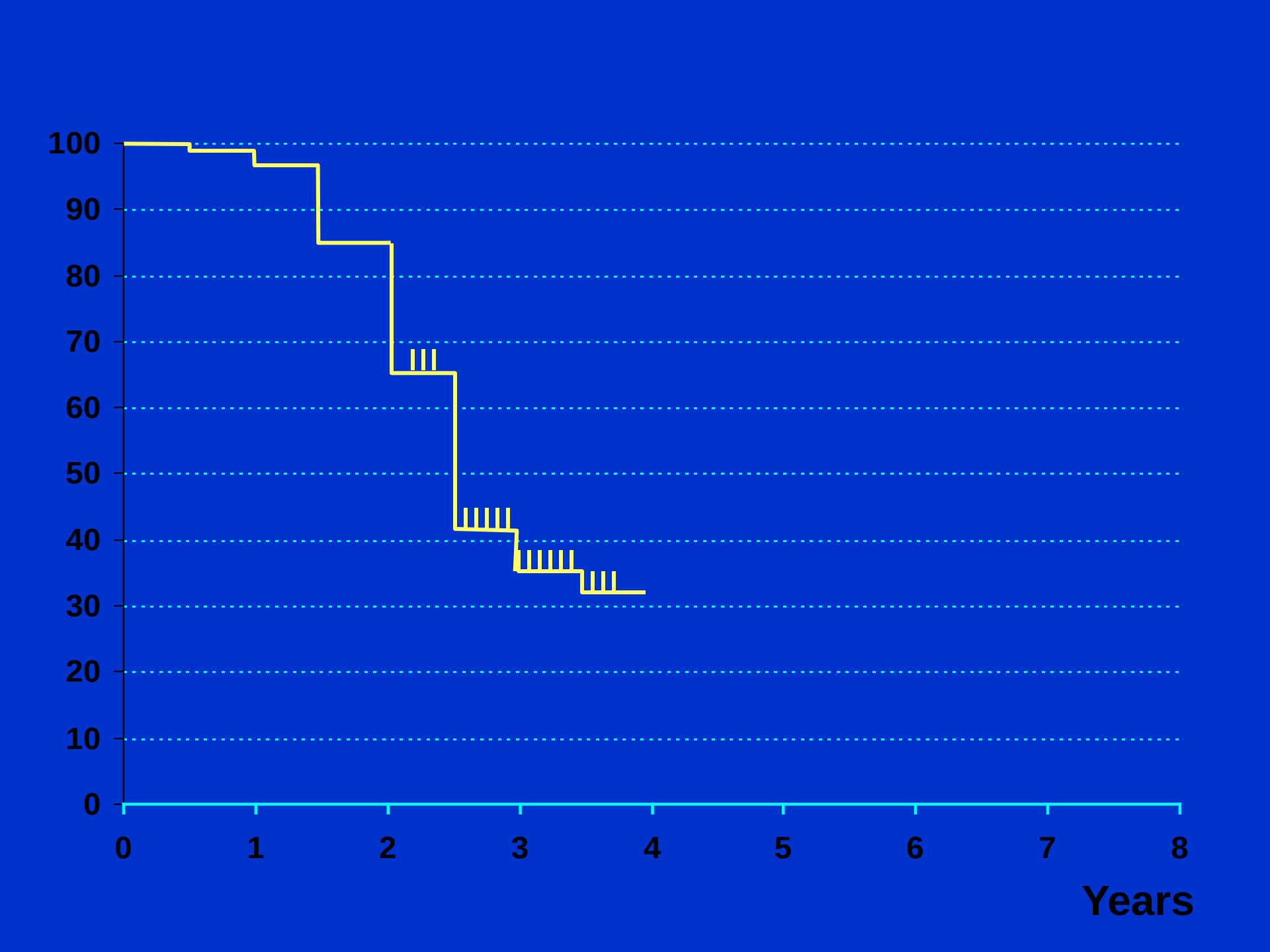
Example of an objective endpoint: Survival

- Patterns of survival on clinical trials are usually quite complex
- Clinically conveniently summarized by one or two statistics
  - E.g. Median survival, 3 year survival

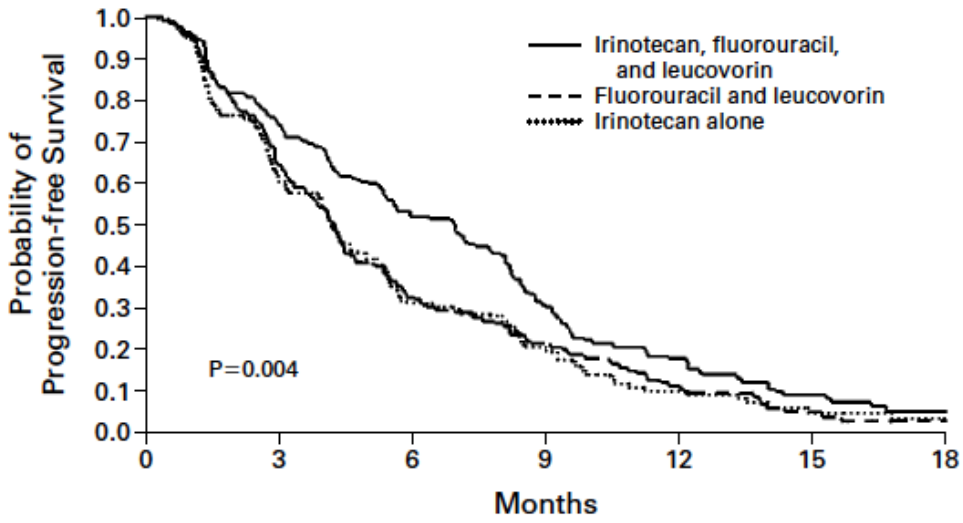

50
40
30
20
10
0
0
1
2
3
4
5
6
7
8
Years


50
40
30
20
10
0
0
1
2
3
4
5
6
7
8
Time of analysis
Years


50
40
30
20
10
0
0
1
2
3
4
5
6
7
8
Time of analysis
Years


100
90
80
70
60
50
40
30
20
10
0
0
1
2
3
4
5
6
7
8
Years

Level 1 Evidence



No. at Risk							
Irinotecan, fluorouracil, and leucovorin	231	154	99	49	23	11	5
Fluorouracil and leucovorin	226	124	54	32	15	5	2
Irinotecan alone	226	112	51	29	12	4	1

Figure 1. Kaplan–Meier Estimates of Progression-free Survival.
The P value was derived from a log-rank test comparing the triple-drug group with the two-drug group.

Saltz L et al, NEJM 2000

NCIC CTG
NCIC GEC

Example of a QOL “result”

- EORTC QLQ-C30+3 Instrument
- Domain: Global quality of life
- Patient questionnaire items:

How would you rate your overall health during the past week?

1 2 3 4 5 6 7

Very poor Excellent

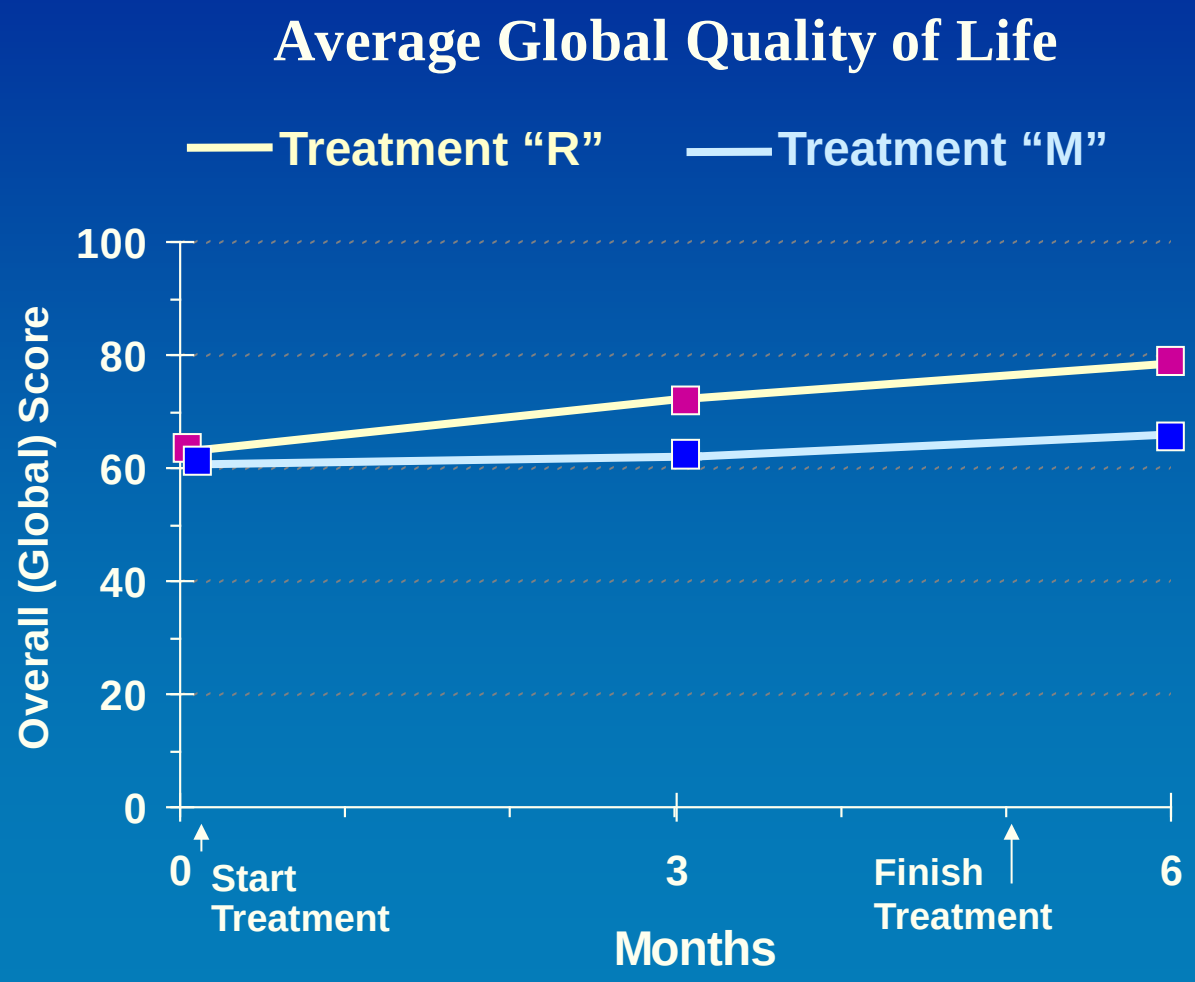
How would you rate your overall quality of life during the past week?

1 2 3 4 5 6 7

Very poor Excellent

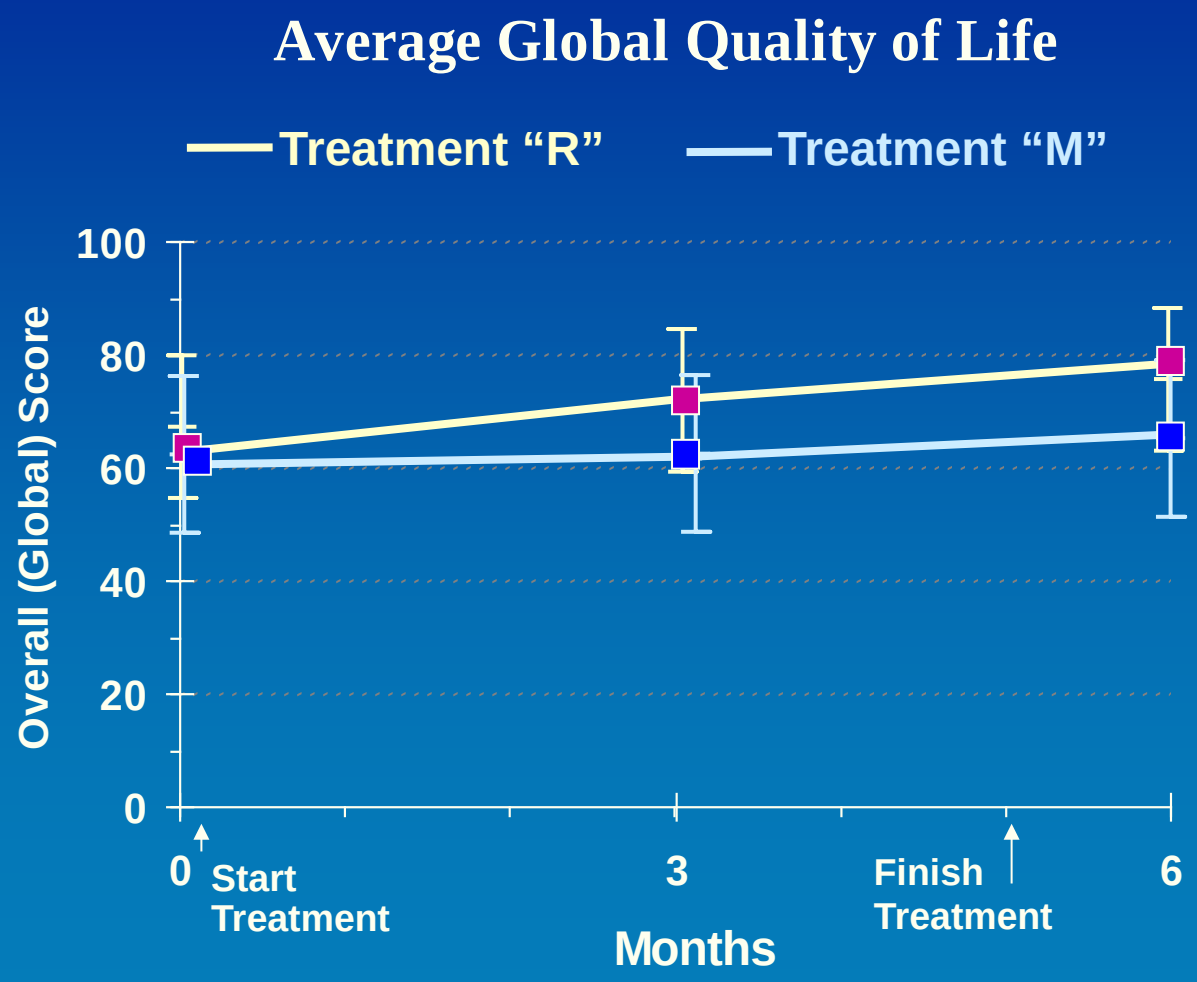
NCIC CTG
NCIC GEC

Example of a QOL “result”



NCIC CTG
NCIC GEC

Example of a QOL “result”

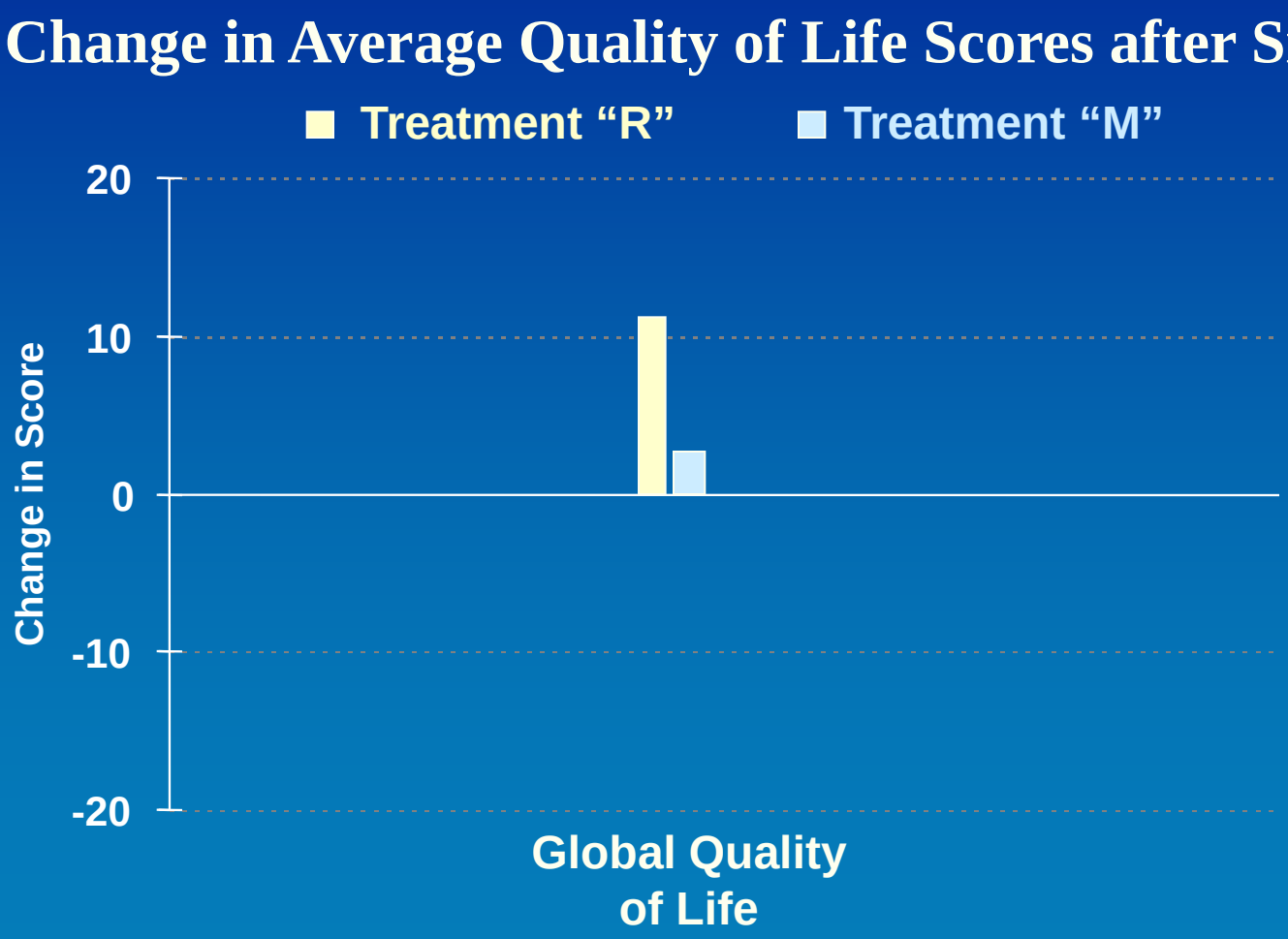


NCIC CTG
NCIC GEC

What “difference” is clinically significant?

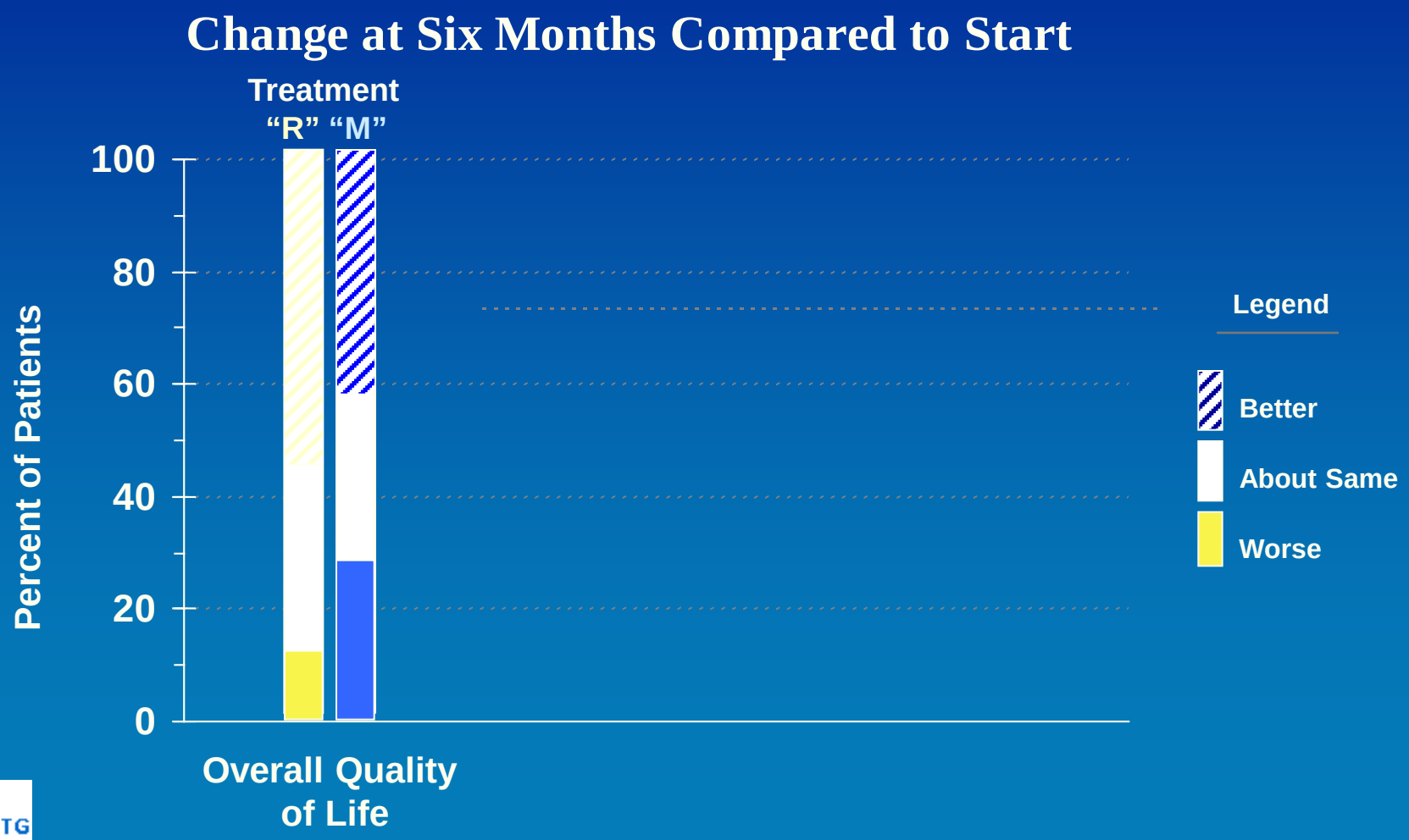
- E.g.: Osoba et al, JCO 1998
  - Minimal change: 5-10 points
  - Moderate change: 10-20 points
  - Large change: >20 points

Same Data Presented Differently



NCIC CTG
NCIC GEC

Same Data Presented Differently



NCIC CTG
NCIC GEC

Some final thoughts…

Is there bias in the results?

Look for:

- Statement of a clear hypothesis for assessing HRQL
- An explanation of the choice of HRQL instruments
- A clear description of methodology
- Appropriate planning for handling and analyzing data

NCIC CTG
NCIC GEC

History of the NCIC CTG Quality of Life Committee

With thanks to Joe Pater and David Osoba

NCIC Clinical Trials Group - History

- 1979 - NCIC decides to establish a Clinical Trials Group
- 1980 - Joe Pater named Director of Group and headquarters moved to Kingston, Ontario
- 1982 - IND program established
- 1982 – BR.5 (1st QOL trial)
- 1981 - 2004 - Program expands through a series of site visits
- 2005 – Ralph Meyer appointed to succeed Joe Pater in 2007

NCIC CTG
NCIC GEC

BR.5

- 1982: two trials in advanced NSCLC appeared to show a survival advantage for chemotherapy
  - Cormier – MACC
  - Gralla - cisplatin/vindesine
- Best supportive care control arm
- Reviewer suggests should have a QOL endpoint
- “gold standard” instrument (the Sickness Impact Profile) along with a newly developed cancer instrument (FLIC)

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 instruments, only FLIC or not participate
- Almost all centres agreed to participate and most chose to use both instruments
- Study completed 1986
- Survival benefit of chemotherapy

NCIC CTG
NCIC GEC

Audience Feedback

- What was the compliance rate with QOL questionnaire completion on BR.5?
  - >90%
  - 50-75%
  - 25-49%
  - <25%

NCIC CTG
NCIC GEC

Audience Feedback

- What was the compliance rate with QOL questionnaire completion on BR.5?
  - >90%
  - 50-75%
  - 25-49%
  - <25%

  Answer <25%

NCIC CTG
NCIC GEC

After BR.5

- The low compliance with QOL collection in BR.5 was due to many factors, including the fact the one of the key central office personnel had to leave due to illness in her family
- It was evident, though, the adequate QOL data collection would not just happen
- a “scientific session” was held at the 1986 spring meeting

Growth of QOL Committee

- Began as a Working Group in 1986
  - Symposium 1986 – Prof. Frits van Dam
  - Symposium 1987 – Dr. Neil Aaronson
  - Spring meeting 1988 – Dr. Jerome Yates
- Named as QOL Subcommittee in 1987
- Full Standing Committee - 1989 – present
  - Interim Chair, then Chair – D. Osoba ’86-’95
  - Chair – Andrea Bezjak ’95- 2006
  - Co-Chair – Michael Brundage ’03 - present
    - Jolie Ringash 2006-present

NCIC CTG
NCIC GEC

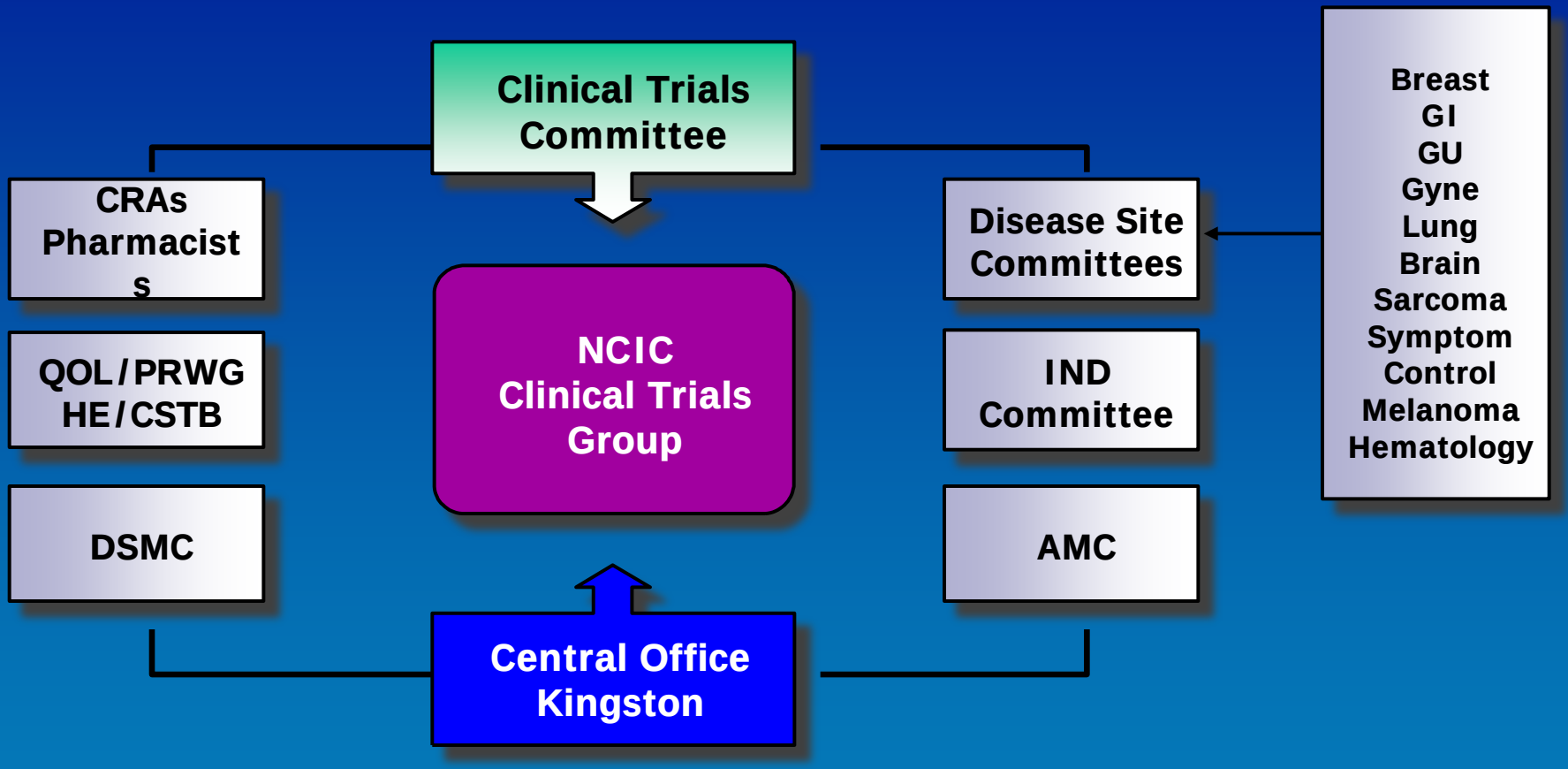
Developments Within QOL Committee

- Chose EORTC QLQ-C30
- Developed a policy re: QOL assessment in 1988; adopted in 1989
- “There should be a statement about the anticipated impact on QOL with every proposed phase III clinical trial and whether or not QOL measures will be incorporated in the protocol.”

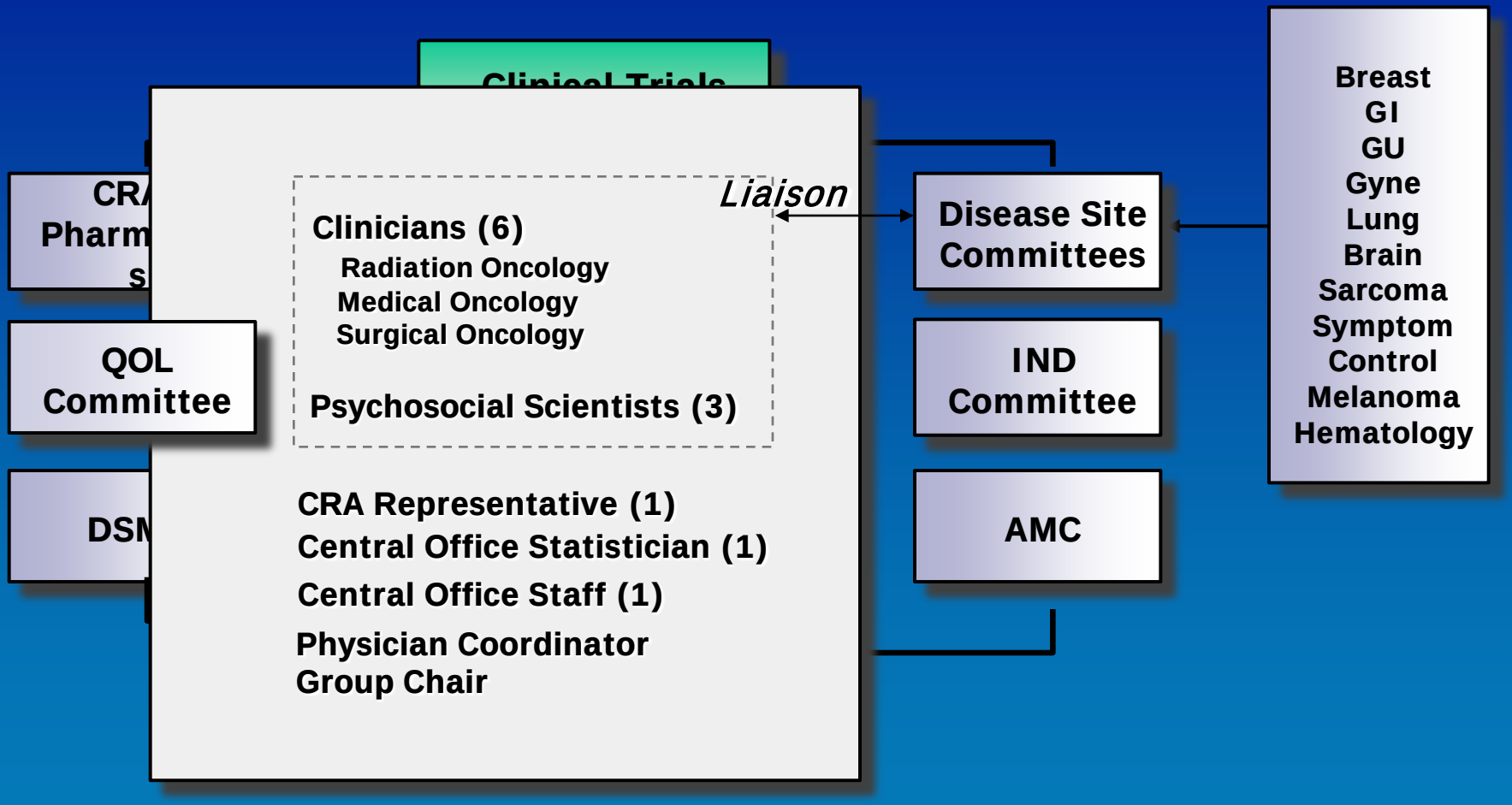
Developments Within QOL Committee

- Named members of the QOL Committee to act as Disease Site liaisons – usually as members of Disease Site Committees
- Maintained a liaison with the EORTC Quality of Life Study Group since 1987
- Maintained contact with several cooperative CTGs and NCI in USA
- First trial, ME.7 – an adjuvant trial of levamisole vs gamma interferon in malignant melanoma - November, 1988

Current Structure



Current Structure



NCIC CTG
NCIC GEC

QOL questionnaire	Number of Studies
EORTC QLQ-C30	35
SF-36	6
McMaster BCQ	1
FACT	6
SWOG Distress scale	1
Spitzer QOL index	1
Lung Cancer Symptom Scale (LCSS)	1
Brain Tumor QOL questionnaire	1
Menopause QOL questionnaire	1
PROSQUALY	1
Toronto Extremity Salvage Score	1
McMaster Head and Neck XRT questionnaire	1
NCCTG Symptom Distress Scale	1

Summary

- QOL refers to overall well-being, as reported by the patient
- There is a science of measurement which applies to QOL
- Interpretation of results is important
- NCIC-CTG has been a leader in QOL research

NCIC CTG
NCIC GEC