Quality of Life (QOL)
Results from Clinical Trials

(A primer for New Investigators)

M. Brundage MD MSc FRCPC
Queen's Cancer Research Institute
Cancer Care and Epidemiology Division

Quality of Life Committee Co-Chair
Canadian Cancer Trials Group

Overview: Objectives

- Be familiar with the CCTG structure re: QOL Committee
- Understand the nature of QOL data
  - Philosophy
  - Source Questionnaires
  - Data collection
- Become familiar with Scale/instrument interpretation issues
  - Reliability, validity, responsiveness
- Become familiar with clinical utility of QOL data
- New Directions of CCTG QOL Committee

Brief History

1979: NCIC (now CCSRI) decides to have a formal cooperative clinical trials group

1980: NCIC Clinical Trials Group established at Queen's University (Dr. Pater)

1982: First Phase III Trial with QOL (BR.5)

1989: Establishment of a QOL committee (Dr. J. Pater)

- Dr. David Osoba and Dr. Benny Zee
- Dr. Andrea Bezjak
- Drs. Jolie Ringash/Michael Brundage

Brief History

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

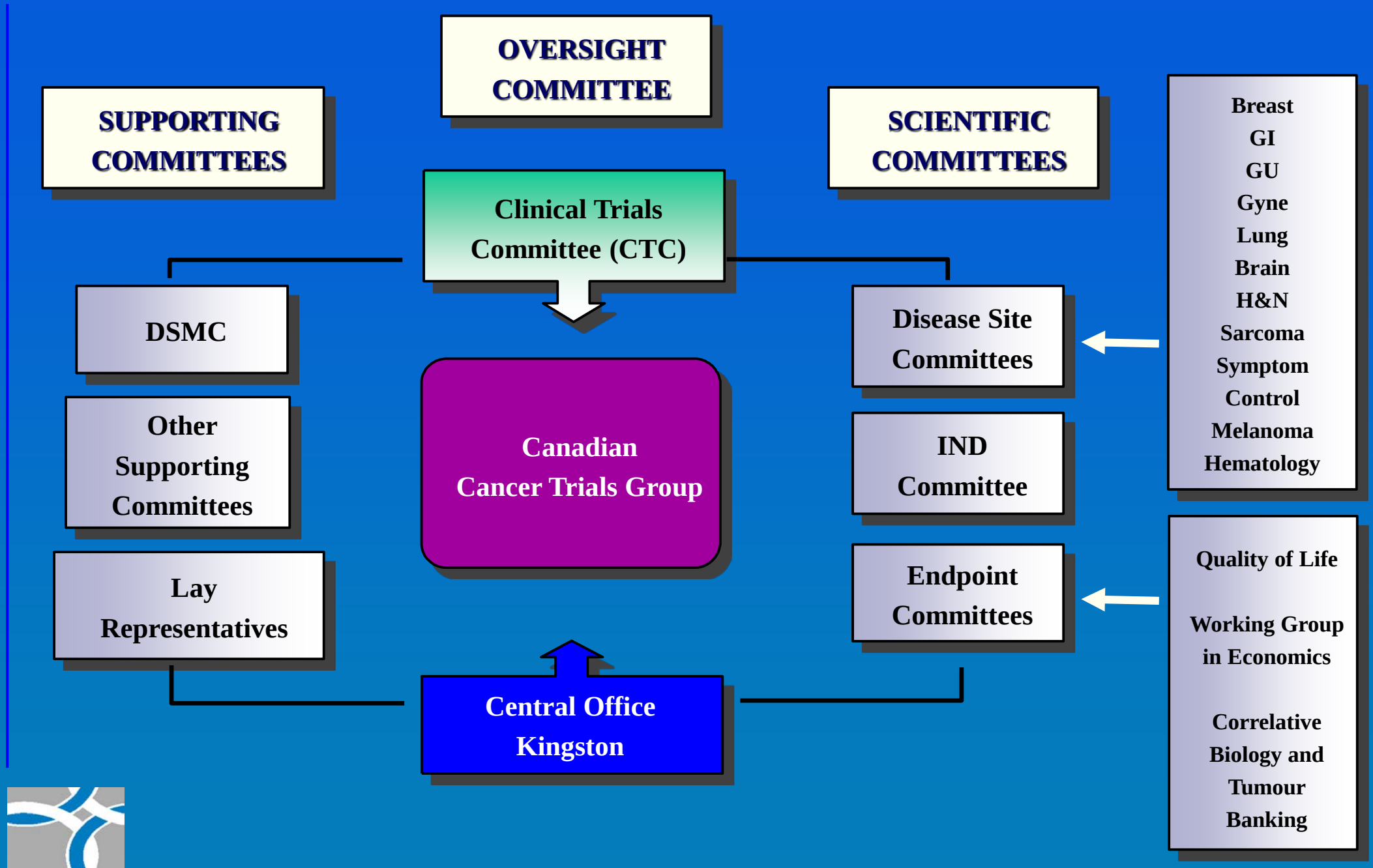
BR.5 QOL

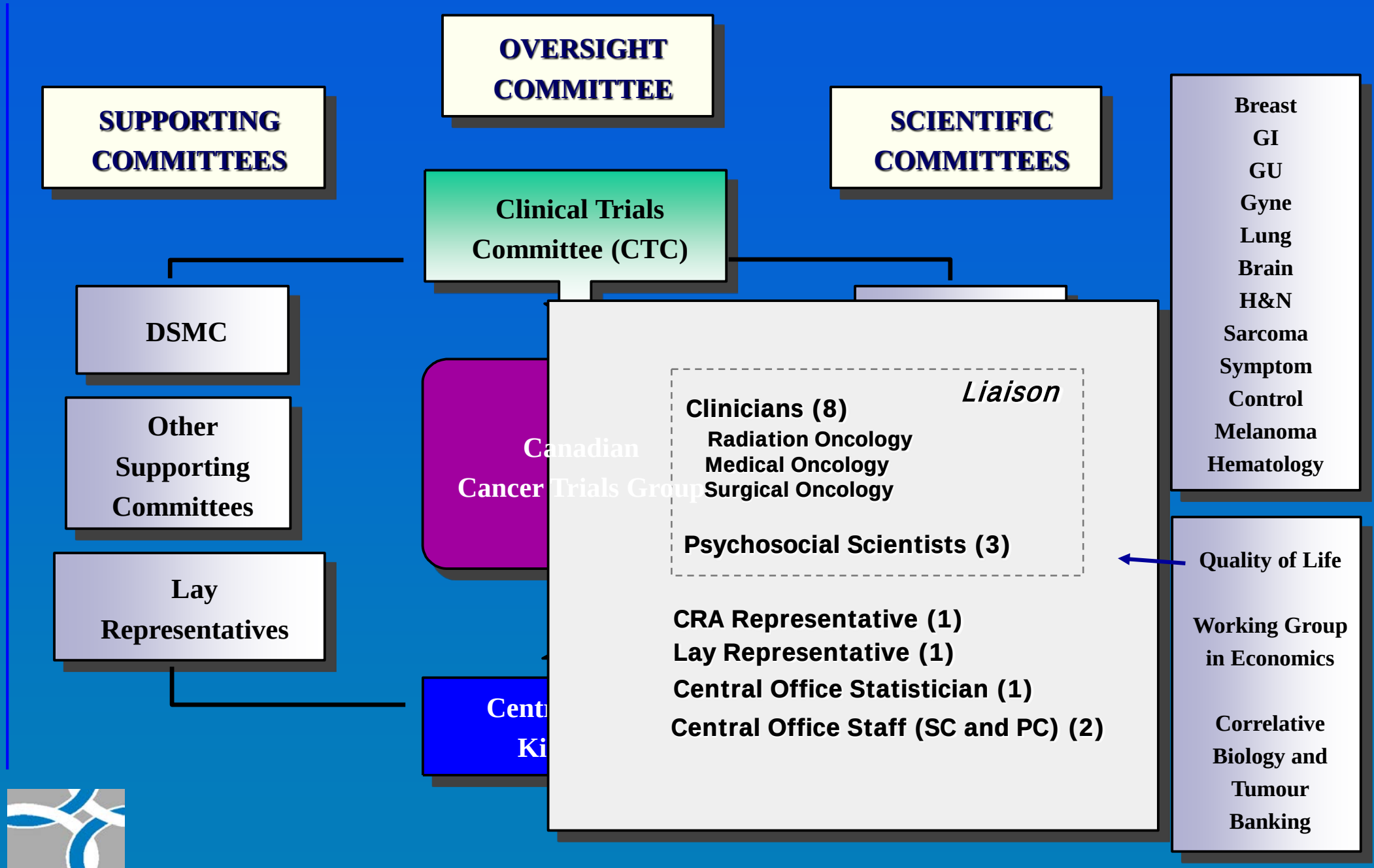
- Shortly after the trial started, centres were asked to participate in the QOL component of the trial
  - They were given the option to use both Sickness Impact Profile (SIP) and Functional Living Index – Cancer (FLIC) questionnaires, only FLIC, or not participate
- Almost all centres agreed to participate and most chose to use both instruments

After BR.5

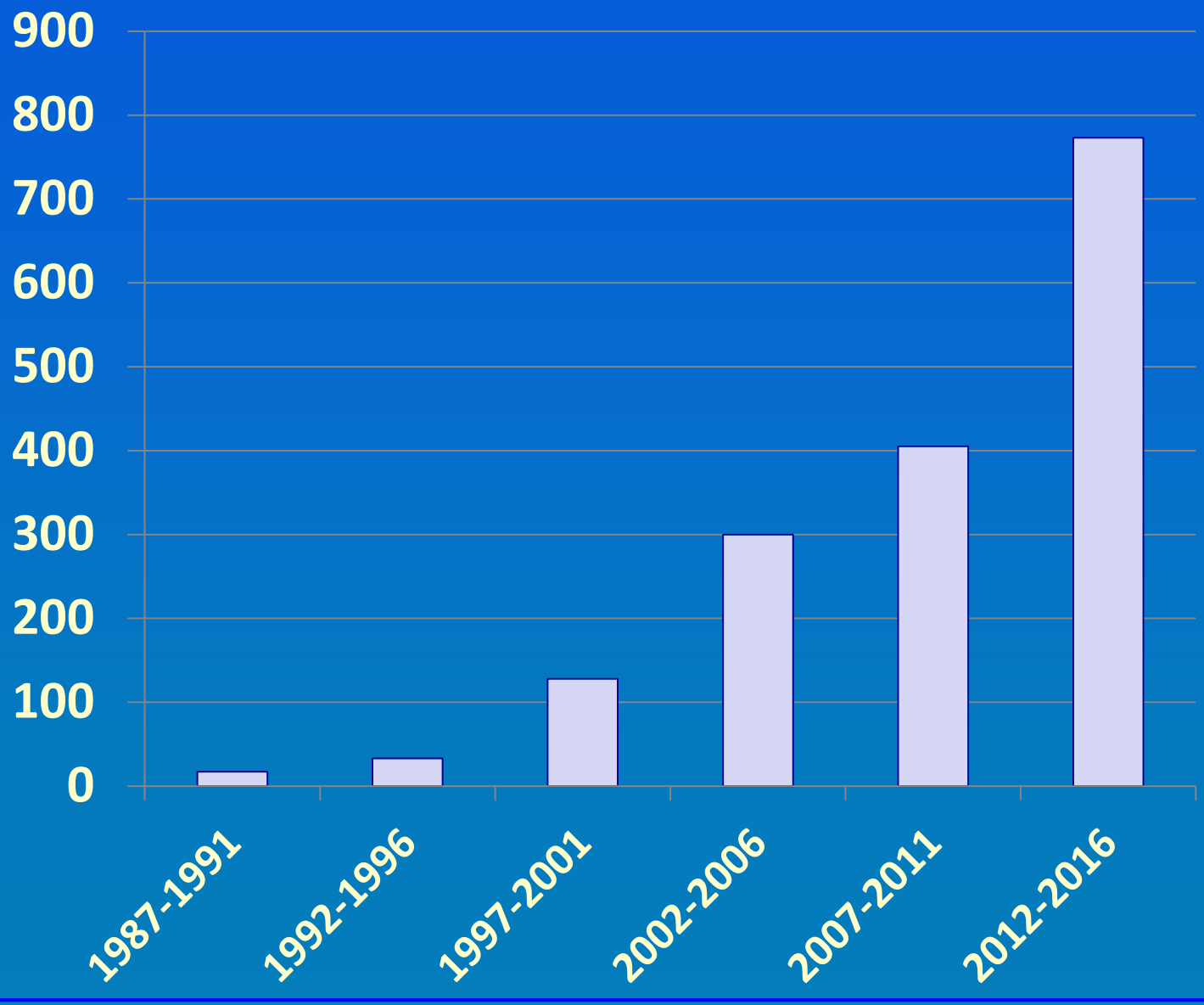
- Low compliance (<25%) with QOL collection in BR.5 was due to many factors

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


OVERSIGHT COMMITTEE
SUPPORTING COMMITTEES
SCIENTIFIC COMMITTEES
Clinical Trials Committee (CTC)
DSMC
Other Supporting Committees
Lay Representatives
Canadian Cancer Trials Group
Central Office Kingston
Disease Site Committees
IND Committee
Endpoint Committees
Breast
GI
GU
Gyne
Lung
Brain
H&N
Sarcoma
Symptom Control
Melanoma
Hematology
Quality of Life
Working Group in Economics
Correlative Biology and Tumour Banking


OVERSIGHT COMMITTEE
SUPPORTING COMMITTEES
SCIENTIFIC COMMITTEES
Clinical Trials Committee (CTC)
DSMC
Other Supporting Committees
Lay Representatives
Canadian Cancer Trials Group
Cent
Ki
Liaison
Clinicians (8)
Radiation Oncology
Medical Oncology
Surgical Oncology
Psychosocial Scientists (3)
CRA Representative (1)
Lay Representative (1)
Central Office Statistician (1)
Central Office Staff (SC and PC) (2)
Breast
GI
GU
Gyne
Lung
Brain
H&N
Sarcoma
Symptom Control
Melanoma
Hematology
Quality of Life
Working Group in Economics
Correlative Biology and Tumour Banking

Randomized Trials with QOL Published Results



Some High-Impact Trials

- **CE.6** - Temozolomide and Short-Course Radiation in the Treatment of Glioblastoma Multiforme in Elderly Patients **J Clin Oncol**
- **MA.17R** - Extending Aromatase-Inhibitor Adjuvant Therapy to 10 Years. **N Engl J Med**
- **MA.20** - Regional Nodal Irradiation in Early-Stage Breast Cancer. **N Engl J Med**
- **HD.6** - ABVD Alone versus Radiation-Based Therapy in Limited-Stage Hodgkin's Lymphoma **N Engl J Med**
- **SC.23** - Dexamethasone in the prophylaxis of radiation-induced pain flare after palliative radiotherapy for bone metastases **Lancet Oncol**
- **PR.7** - Intermittent Androgen Suppression for Rising PSA Level after Radiotherapy. **N Engl J Med**

PROs and HRQoL

Patient-Reported Outcomes (PROs):

Provide a standardized method of measuring the patient perspective on “any outcome based on data provided by patients or patient proxies as opposed to data provided by other sources”

First – A Brief Bit of Background

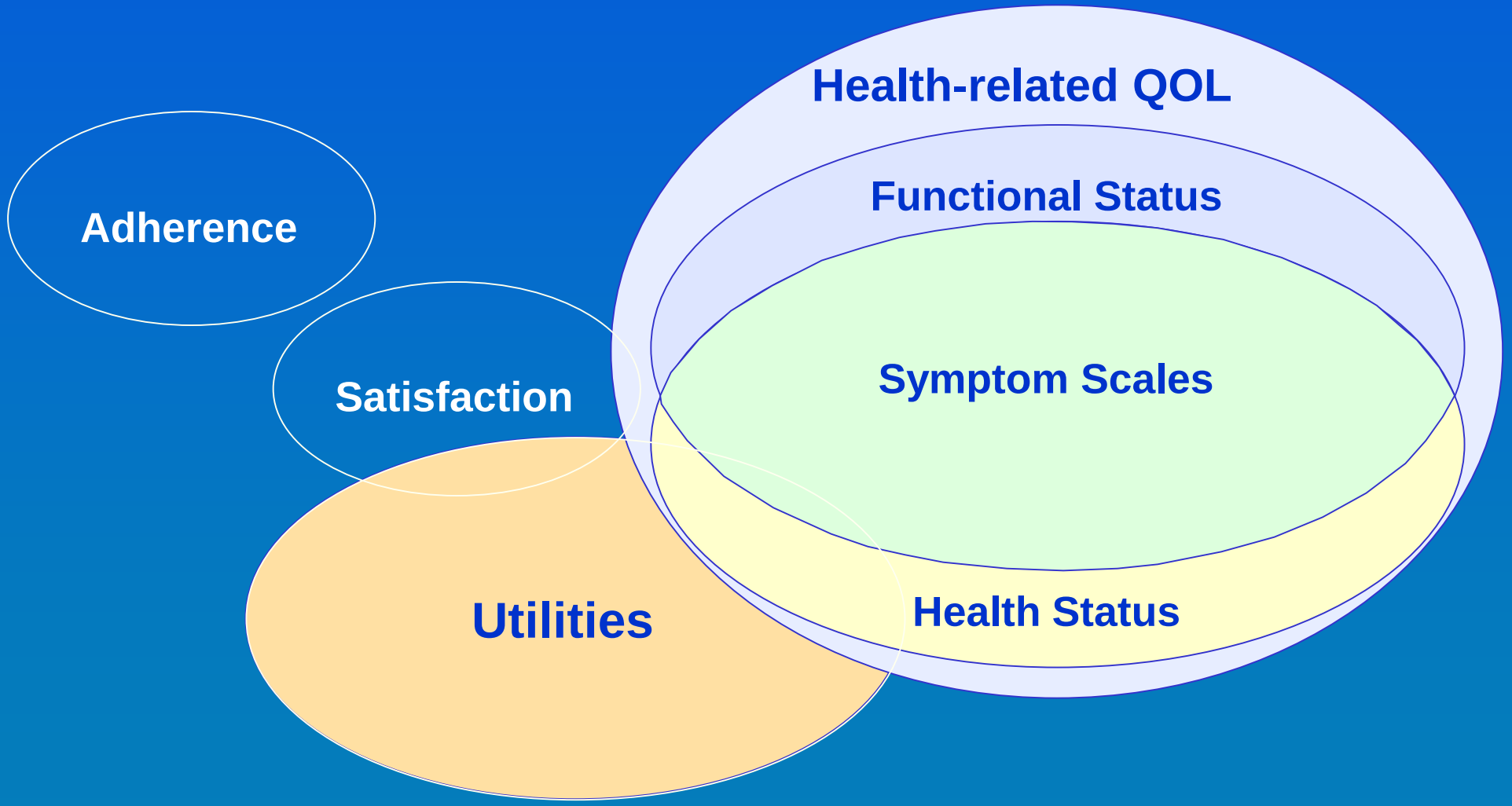
Patient-Reported Outcomes (PROs):

Provide a standardized method of measuring the patient perspective on "any outcome based on data provided by patients or patient proxies as opposed to data provided by other sources"

Health-related quality of life (HRQoL):

"The extent to which one's usual or expected physical, emotional, and social well-being is affected by a medical condition and/or treatment."

Examples of Patient-Reported Outcomes



What is QOL?

Overall QOL?

- **"the goodness of life" or person's overall well-being**
- Influenced by:
  - **patient's perspective (subjectivity)**
  - **multi-dimensional (many dimensions of life experience relating to specific "domains")**
  - **Sociocultural context (culture and value systems)**

Health-related QOL?

- **As related to health (not housing, income, environment, etc)**

What is health-related QOL?

- “Optimum levels of physical, role and social function, including relationships, and the perception of health, fitness, life satisfaction and well-being.”

Bowling, 1995

60

60

- Indicator of patient status
- Measurement method is familiar
- Measurement scale is familiar
- Clinical interpretation is familiar

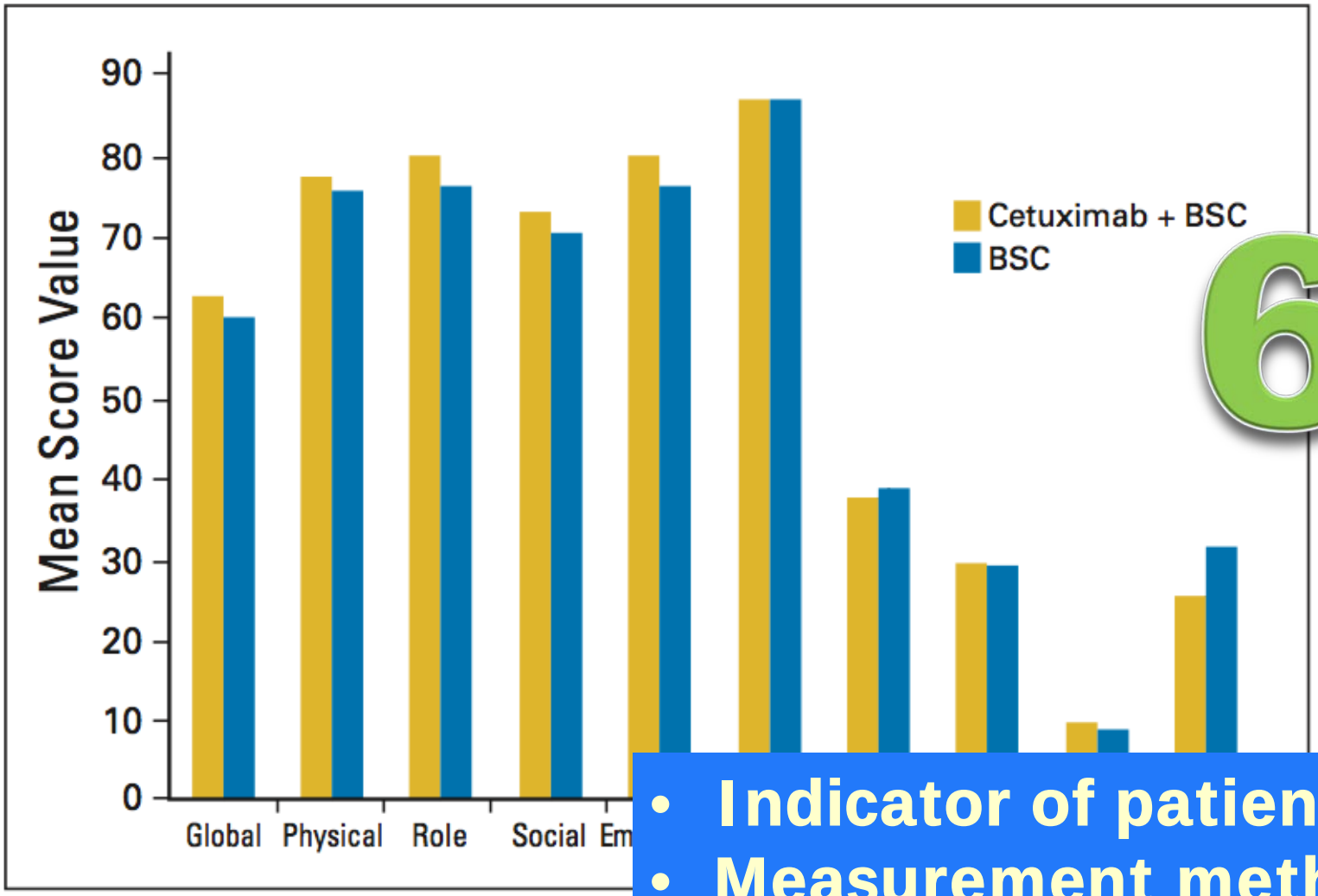


Fig 1. Mean health-related quality-
differences were seen between arms
items of dyspnea, sleep disturbance, c

60

- Indicator of patient status
- Measurement method is less famili
- Measurement scale is less familiar
- Clinical interpretation challenging

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

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?

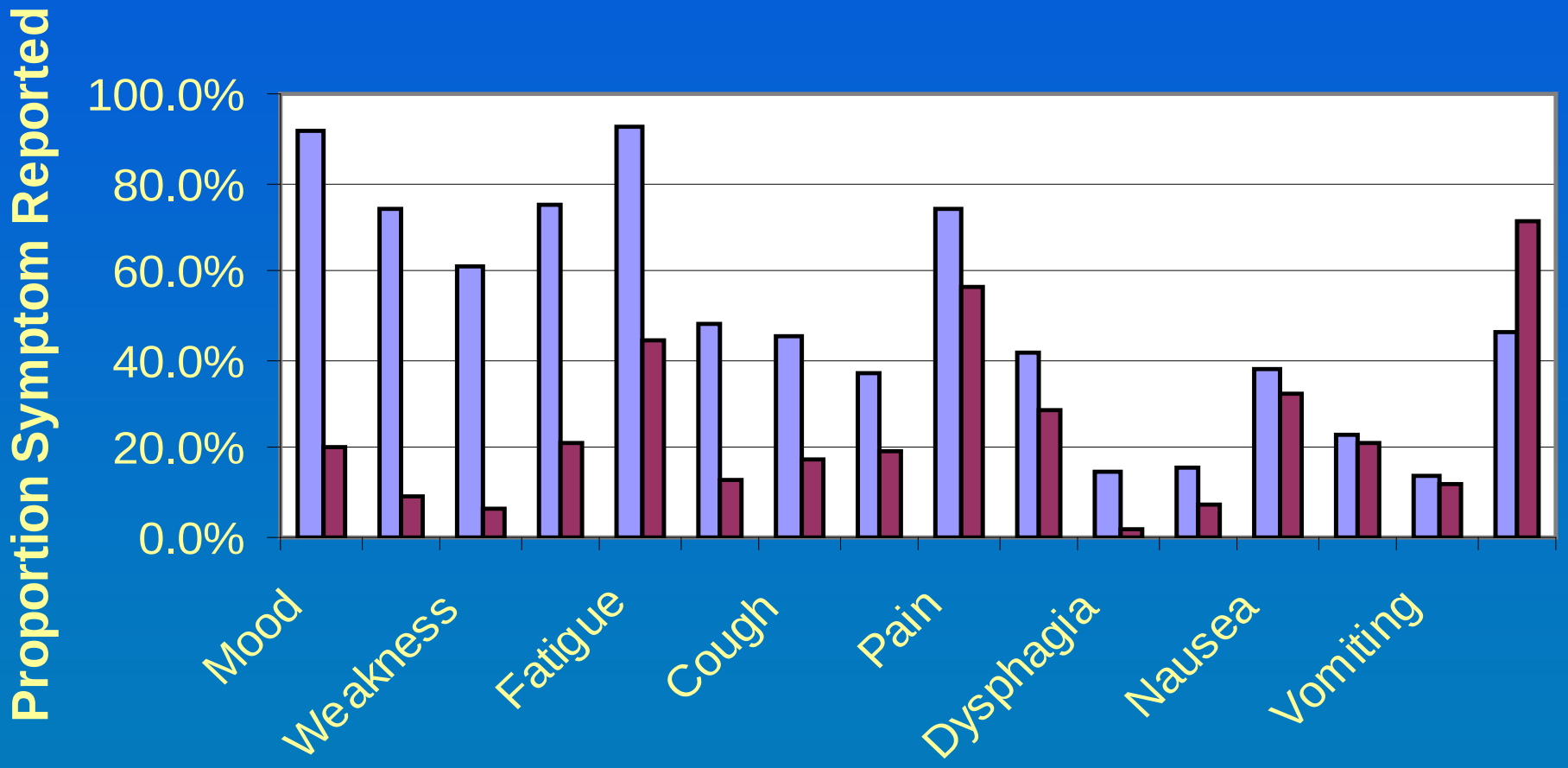
1 2 3 4 5 6 7

Very poor Excellent

HQL Measurement and Epidemiology

Quality of Life Data		Toxicity Data / Performance Status	
Self-reported	Response-shift?	HCP / RA-reported	Rater issues?
Multi-dimensional	Correct dimensions?	Tabulated items	Sufficient?
More complex / Unfamiliar		Less complex / More familiar	

HRQL vs. Toxicity



Savage et al, ASCO 2005

Measuring QOL

HQL Measurement and Epidemiology

ARTICLE

The European Organization for Research and Treatment of Cancer QLQ-C30: A Quality-of-Life Instrument for Use in International Clinical Trials in Oncology

*Neil K. Aaronson, Sam Ahmedzai, Bengt Bergman, Monika Bullinger, Ann Cull, Nicole J. Duez, Antonio Filiberti, Henning Flechtner, Stewart B. Fleishman, Johanna C. J. M. de Haes, Stein Kaasa, Marianne Klee, David Osoba, Darius Razavi, Peter B. Rofe, Simon Schraub, Kommer Sneeuw, Marianne Sullivan, Fumikazu Takeda for the European Organization for Research and Treatment of Cancer Study Group on Quality of Life**

Aaronson, JNCI 1993

	Items*
Functioning scales‡	
Physical	1-5
Role	6, 7
Cognitive	20, 25
Emotional	21-24
Social	26, 27
Global quality of life	29, 30
Symptom scales and/or items§	
Fatigue	10, 12, 18
Nausea and vomiting	14, 15
Pain	9, 19
Dyspnea	8
Sleep disturbance	11
Appetite loss	13
Constipation	16
Diarrhea	17
Financial impact	28

- **Do you have any trouble doing strenuous activities like carrying a heavy shopping...**
- **Do you have any trouble taking a long walk**
- **Do you have to stay in bed or a chair for most of the day**

	Items*
Functioning scales‡	
Physical	1-5
Role	6, 7
Cognitive	20, 25
Emotional	21-24
Social	26, 27
Global quality of life	29, 30
Symptom scales and/or items§	
Fatigue	10, 12, 18
Nausea and vomiting	14, 15
Pain	9, 19
Dyspnea	8
Sleep disturbance	11
Appetite loss	13
Constipation	16
Diarrhea	17
Financial impact	28

- **Do you have any trouble concentrating on things, like reading a newspaper or watching television?**

- **Have you had difficulty remembering things?**

	Items*
Functioning scales‡	
Physical	1-5
Role	6, 7
Cognitive	20, 25
Emotional	21-24
Social	26, 27
Global quality of life	29, 30
Symptom scales and/or items§	
Fatigue	10, 12, 18
Nausea and vomiting	14, 15
Pain	9, 19
Dyspnea	8
Sleep disturbance	11
Appetite loss	13
Constipation	16
Diarrhea	17
Financial impact	28

•Has your physical condition or medical treatments interfered with your family life?

•Has your physical condition or medical treatments interfered with your social activities?

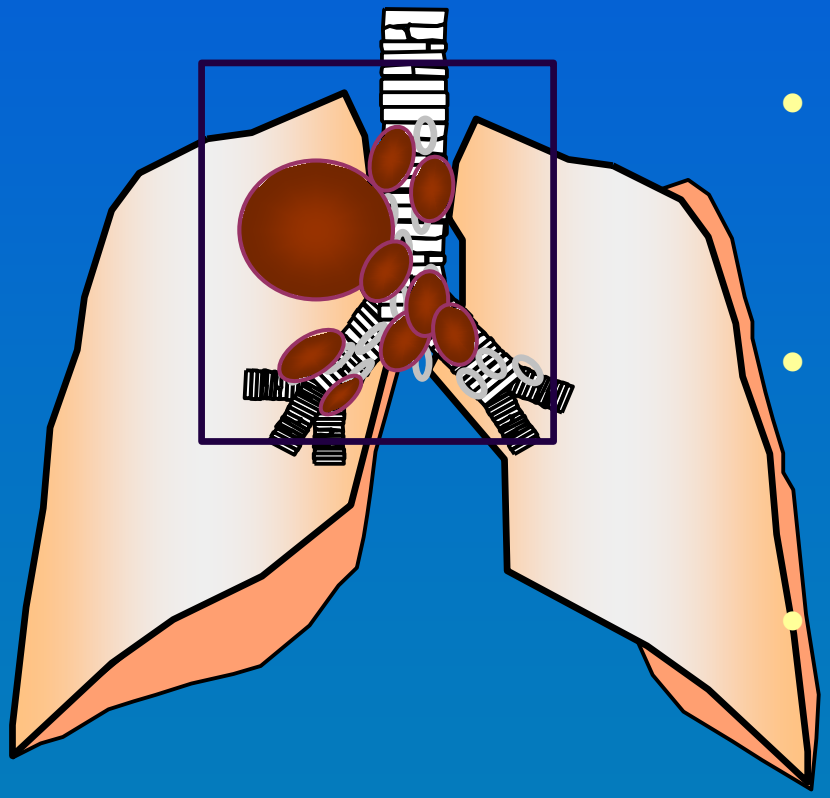
HQL Measurement and Epidemiology

- **Reliability: Does the questionnaire produce reproducible results?**
  - **Internal – e.g. Chronbach's alpha**
  - **Test-retest – repeatability**
  - **Longer questionnaires generally with higher reliability**
- **Validity: Does the questionnaire *really* measure QOL?**
  - **Face / Content**
  - **Construct**

Why QOL is important

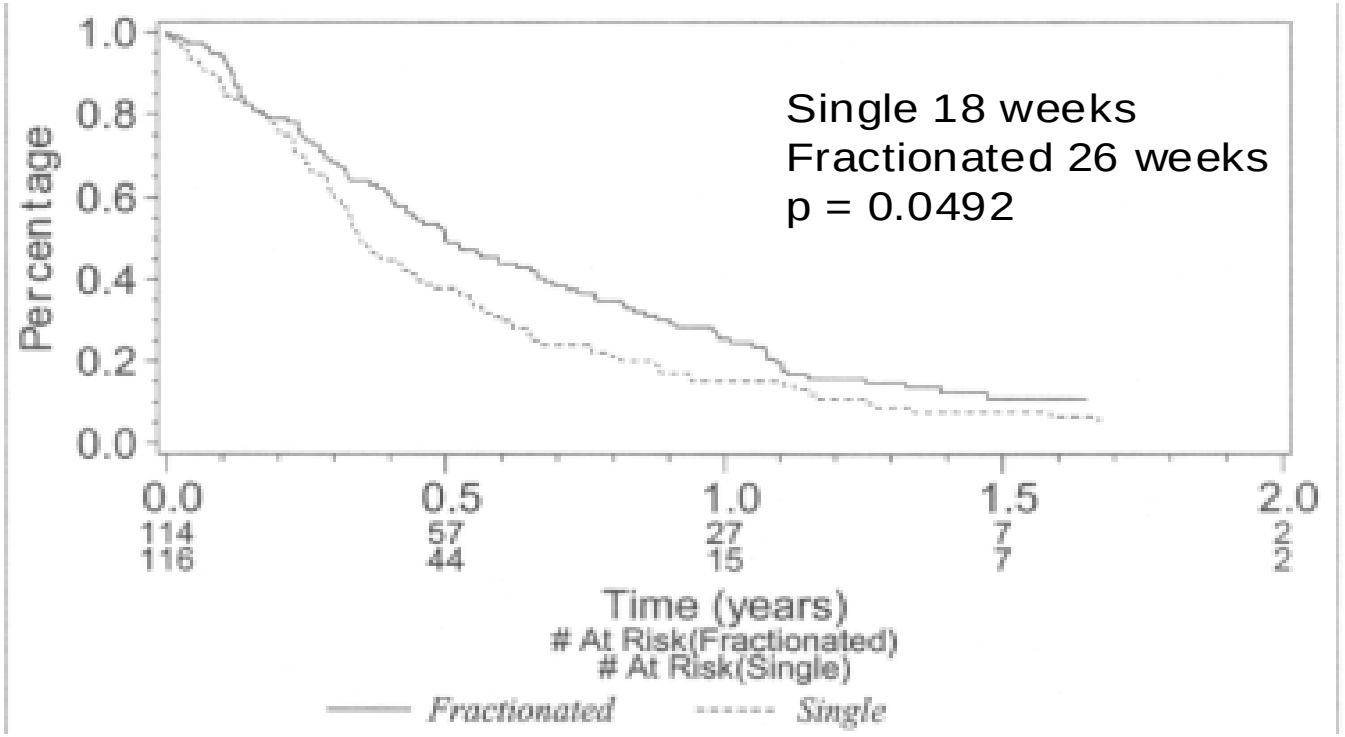
- Different treatments have similar survival
- Treatment improves survival but has severe side effects
- Treatment has no effect on survival but may improve QOL
- Cure is not possible
- Chronic diseases with high survival rates

Clinical Example: Symptomatic Locally Advanced NSCLC (SC.15)

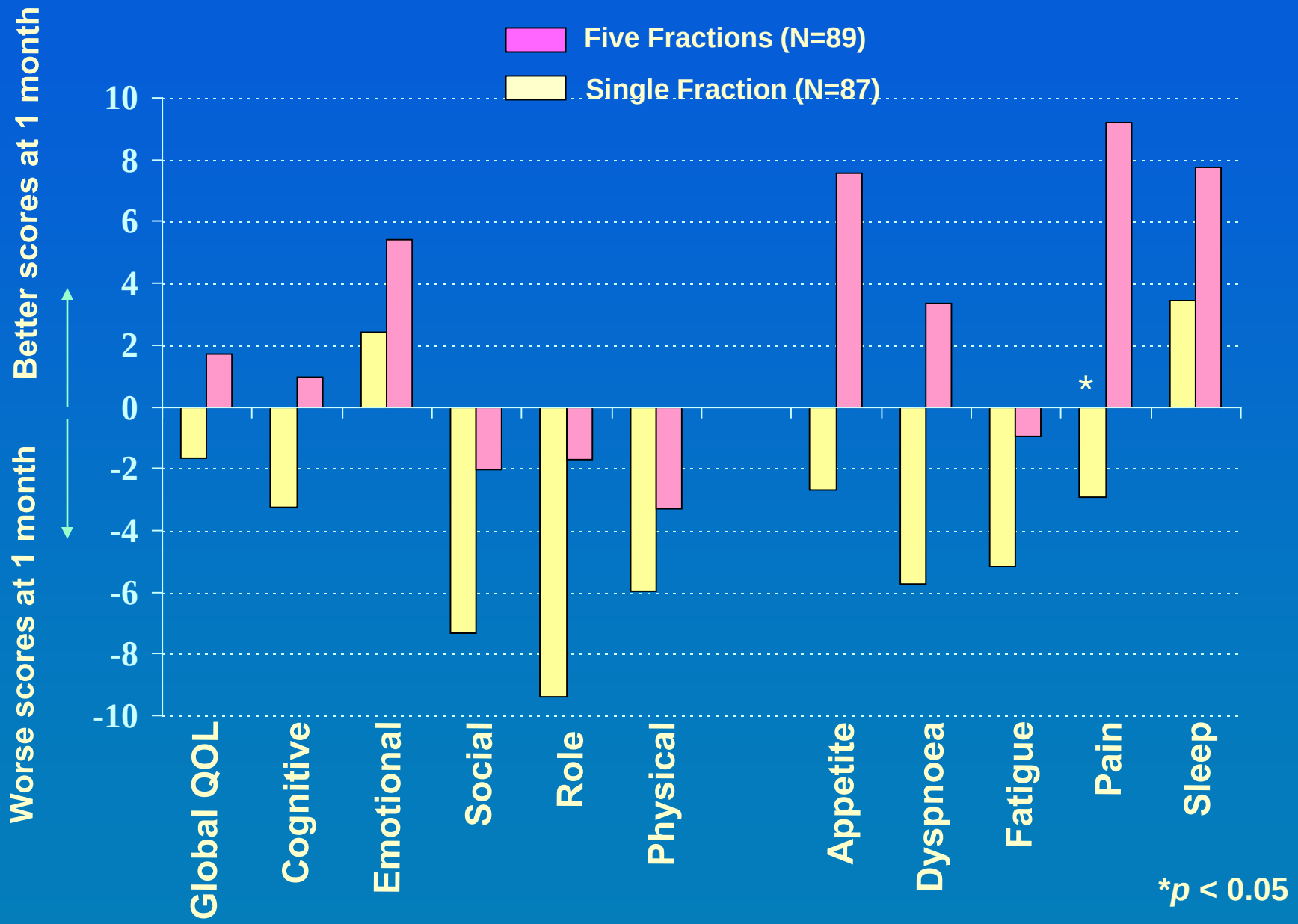


- Disease too extensive for curative therapy
- With or without metastases beyond the thorax
- 2000 cGy in 5 fractions *vs* 1000 cGy in 1 fraction

Survival according to treatment

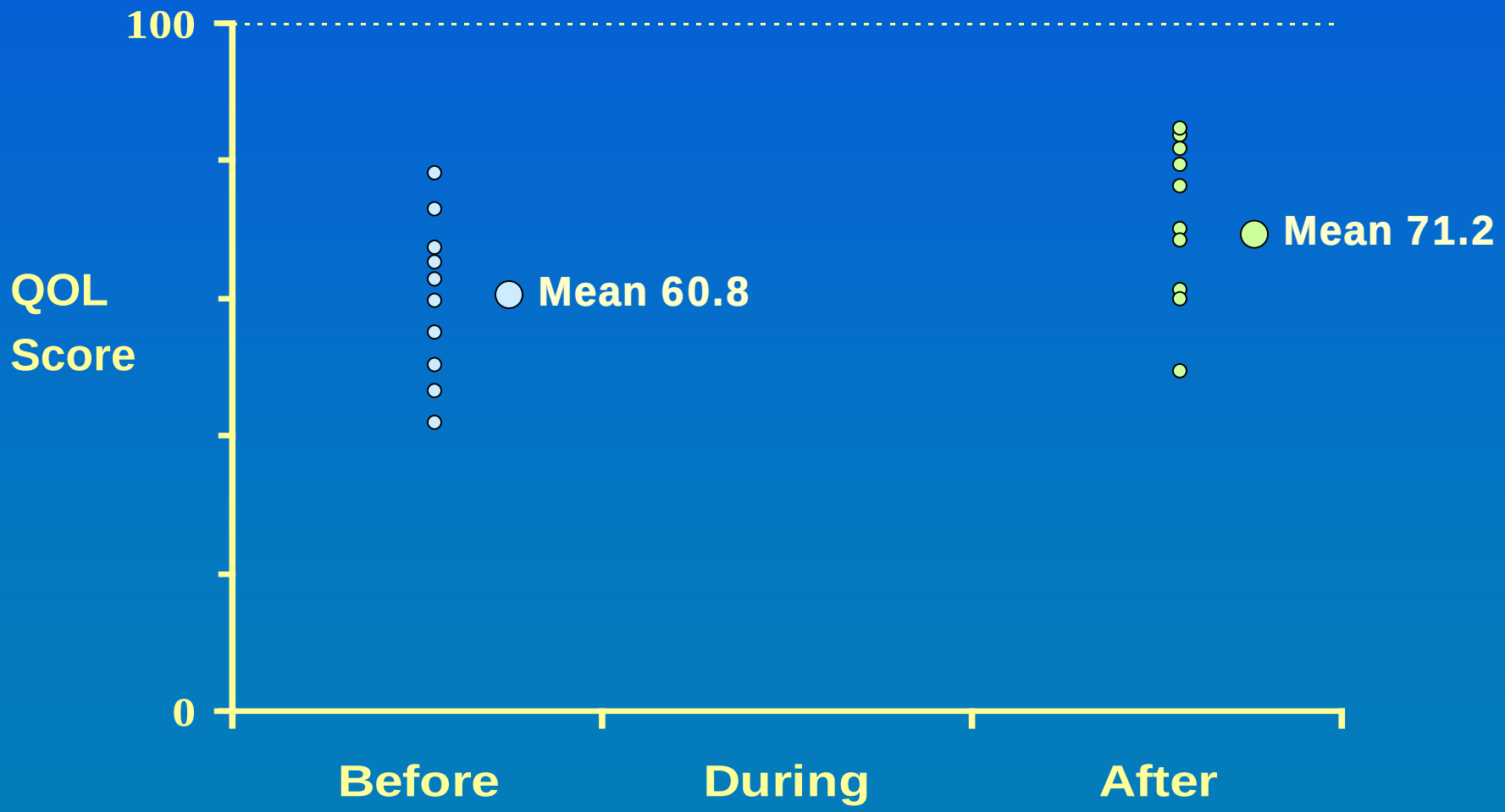


QLQ-C30 Change Scores (Baseline score to 5 weeks)

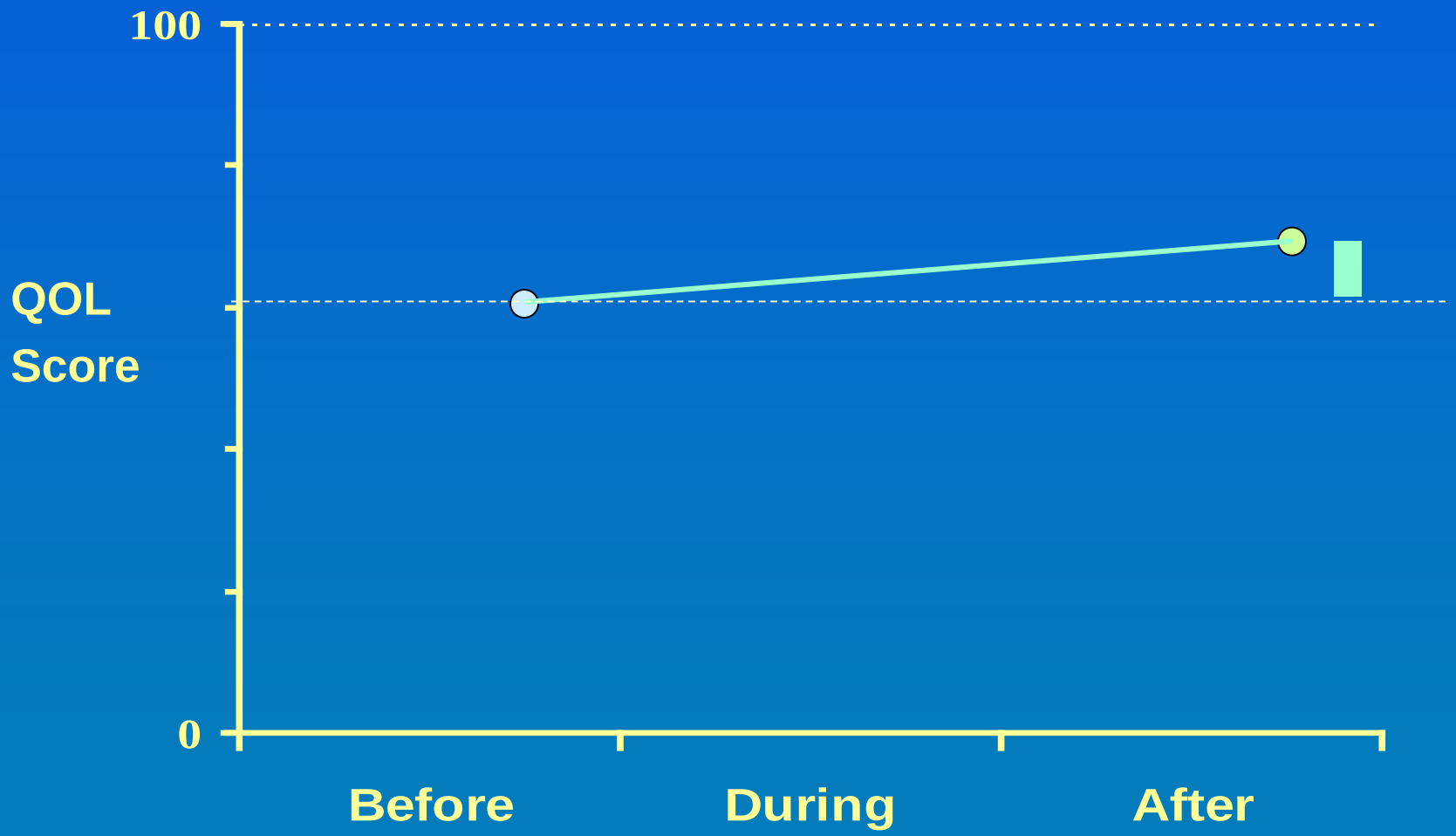


*$p < 0.05$

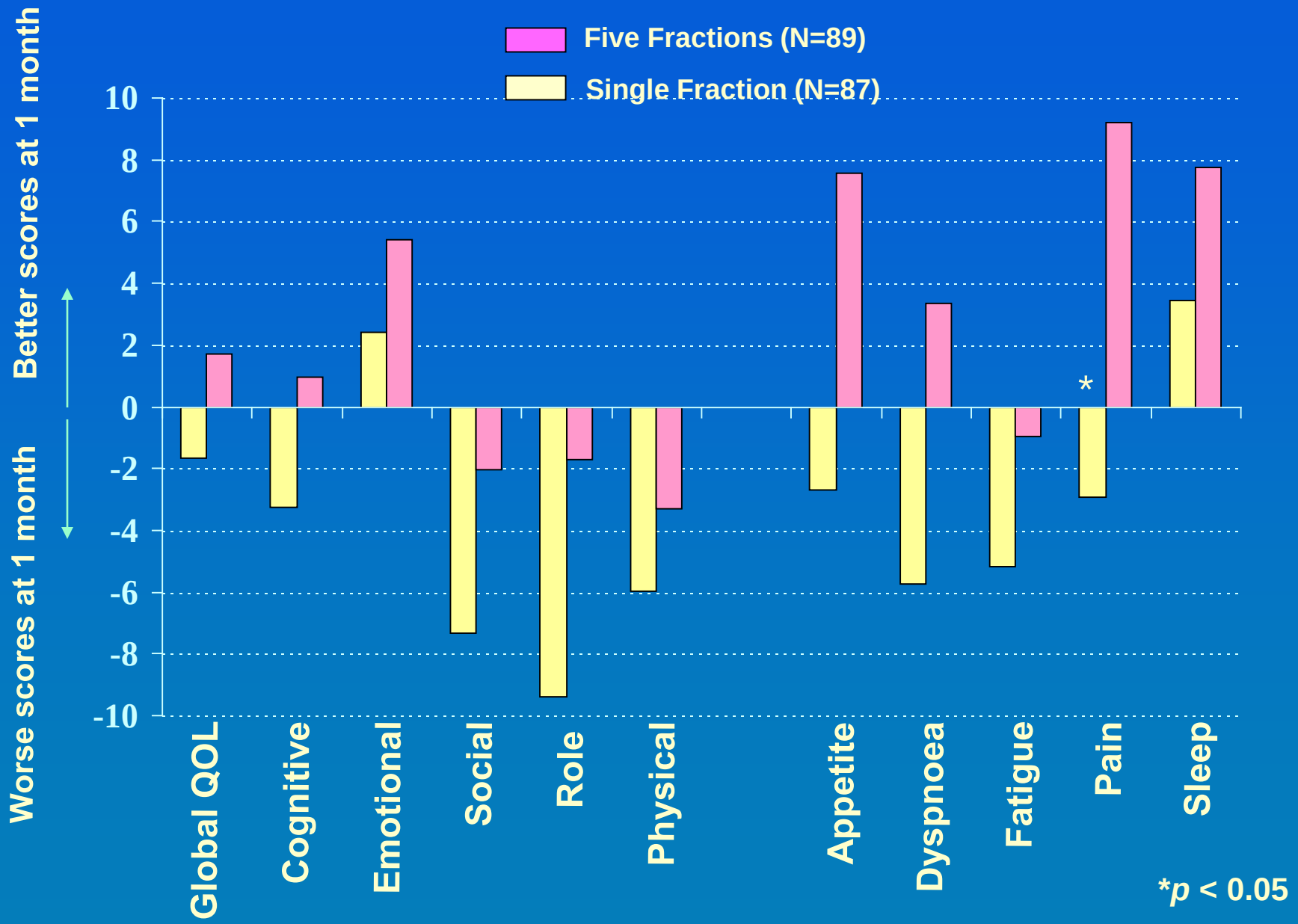
Treatment Intent: Improve QOL



Treatment Intent: Improve QOL

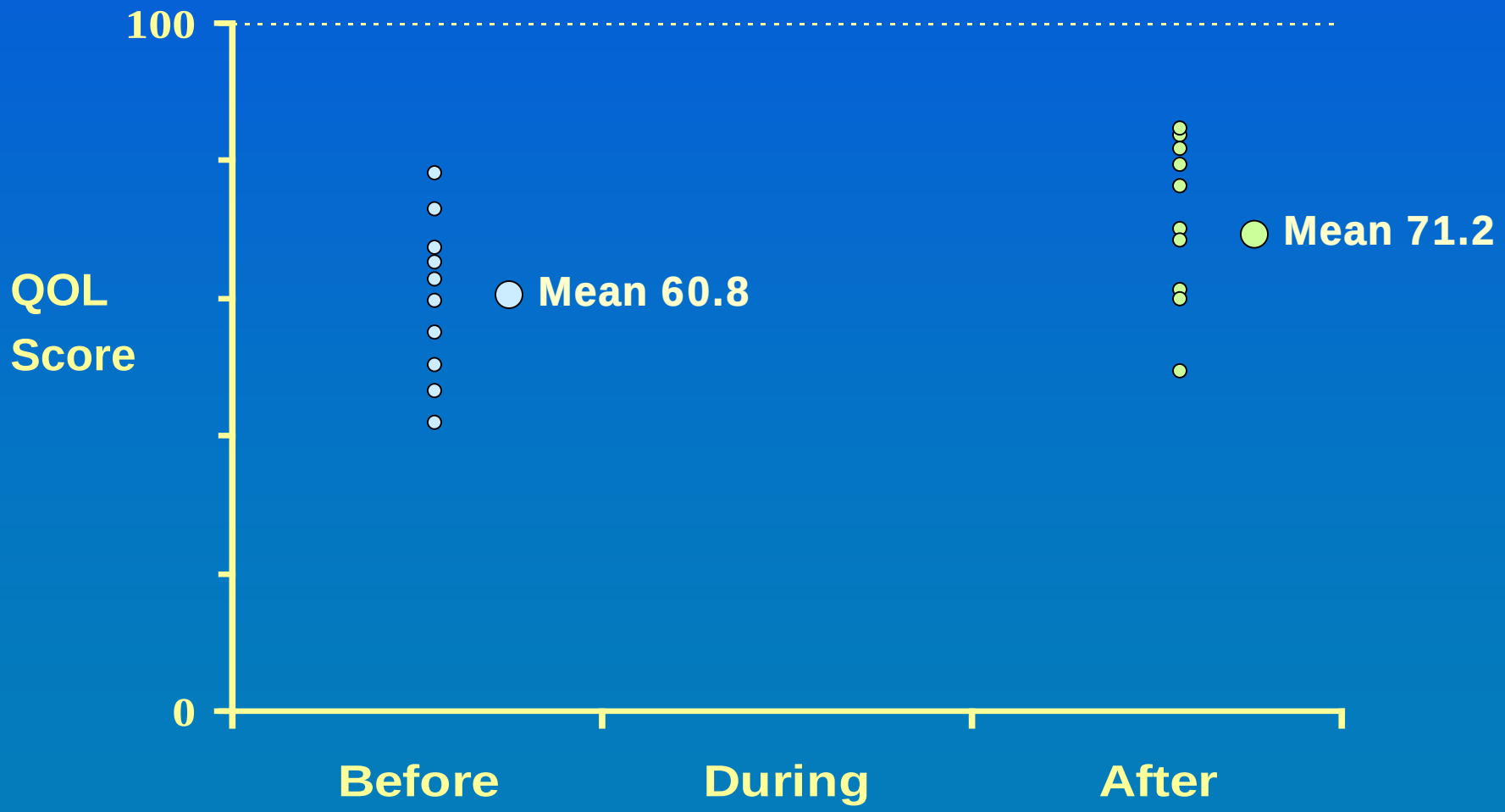


QLQ-C30 Change Scores (Baseline score to 5 weeks)

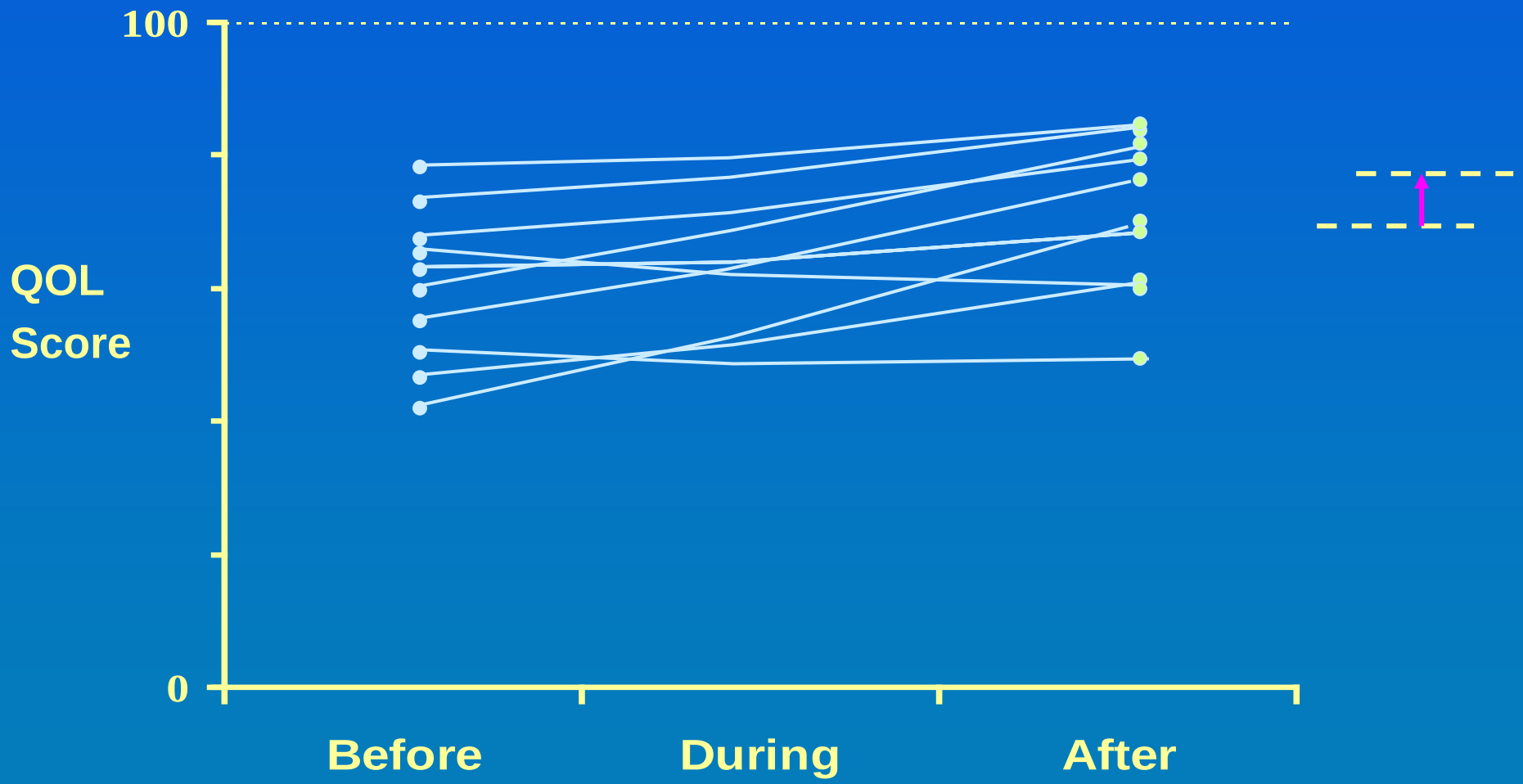


*$p < 0.05$

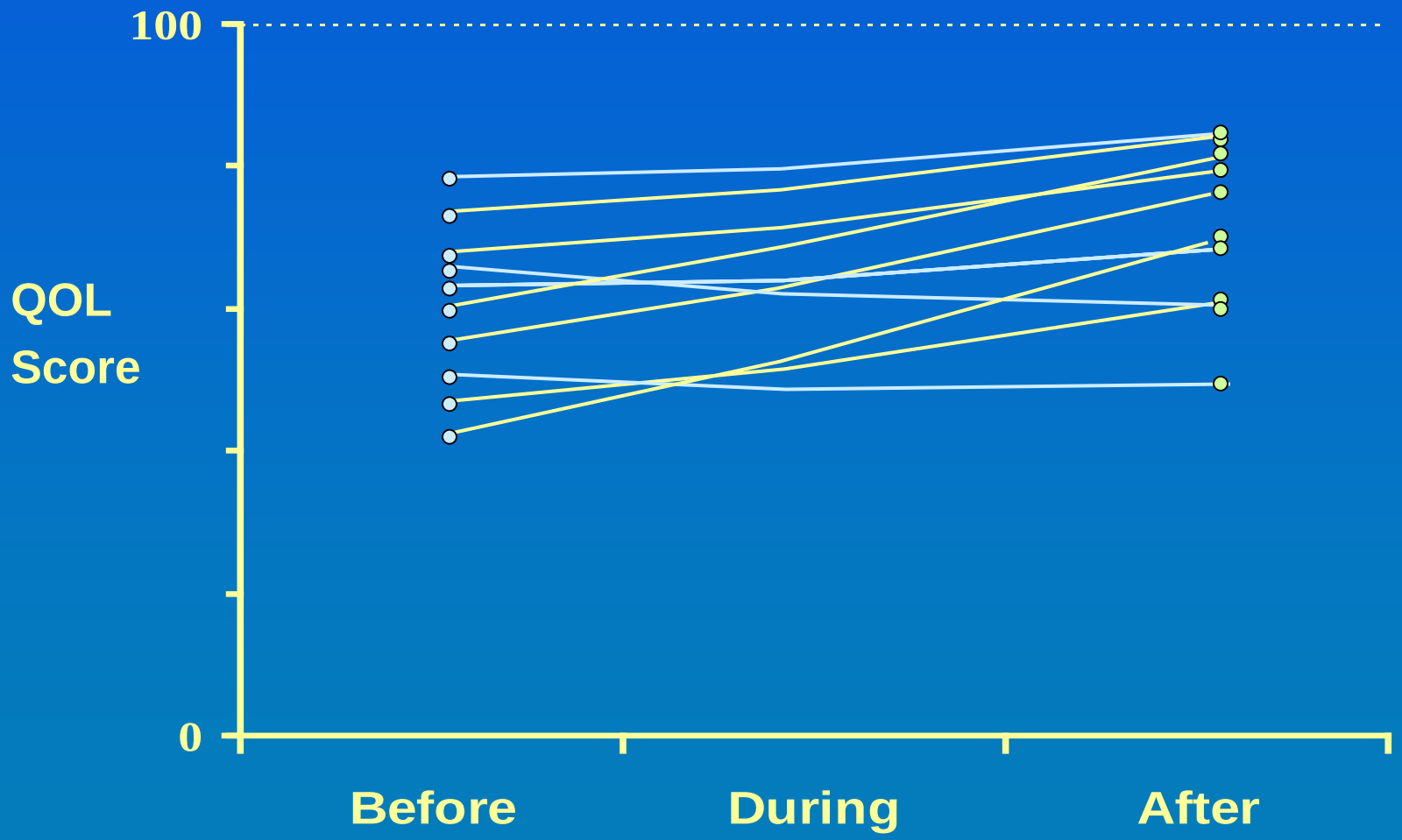
Treatment Intent: Improve QOL



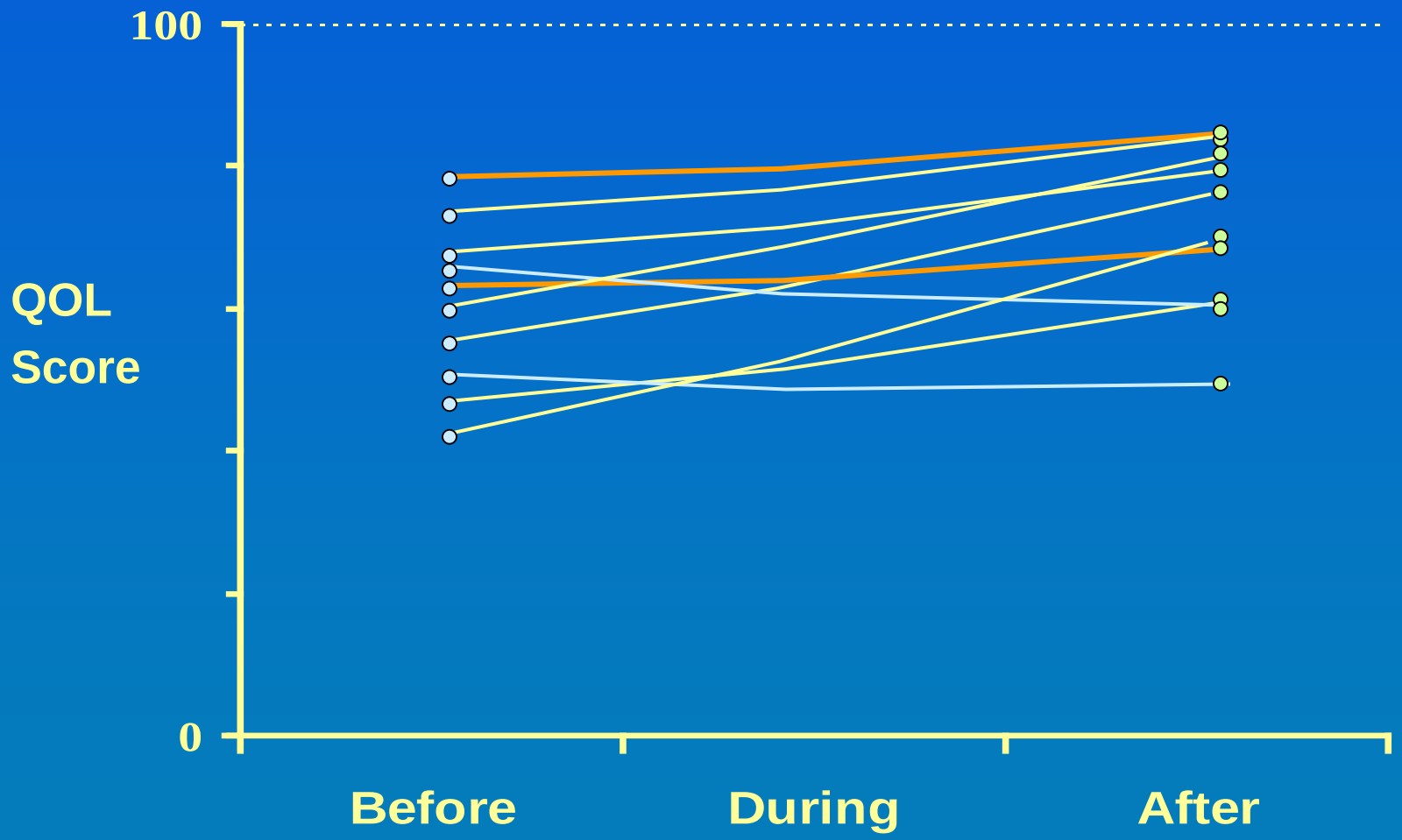
Treatment Intent: Improve QOL



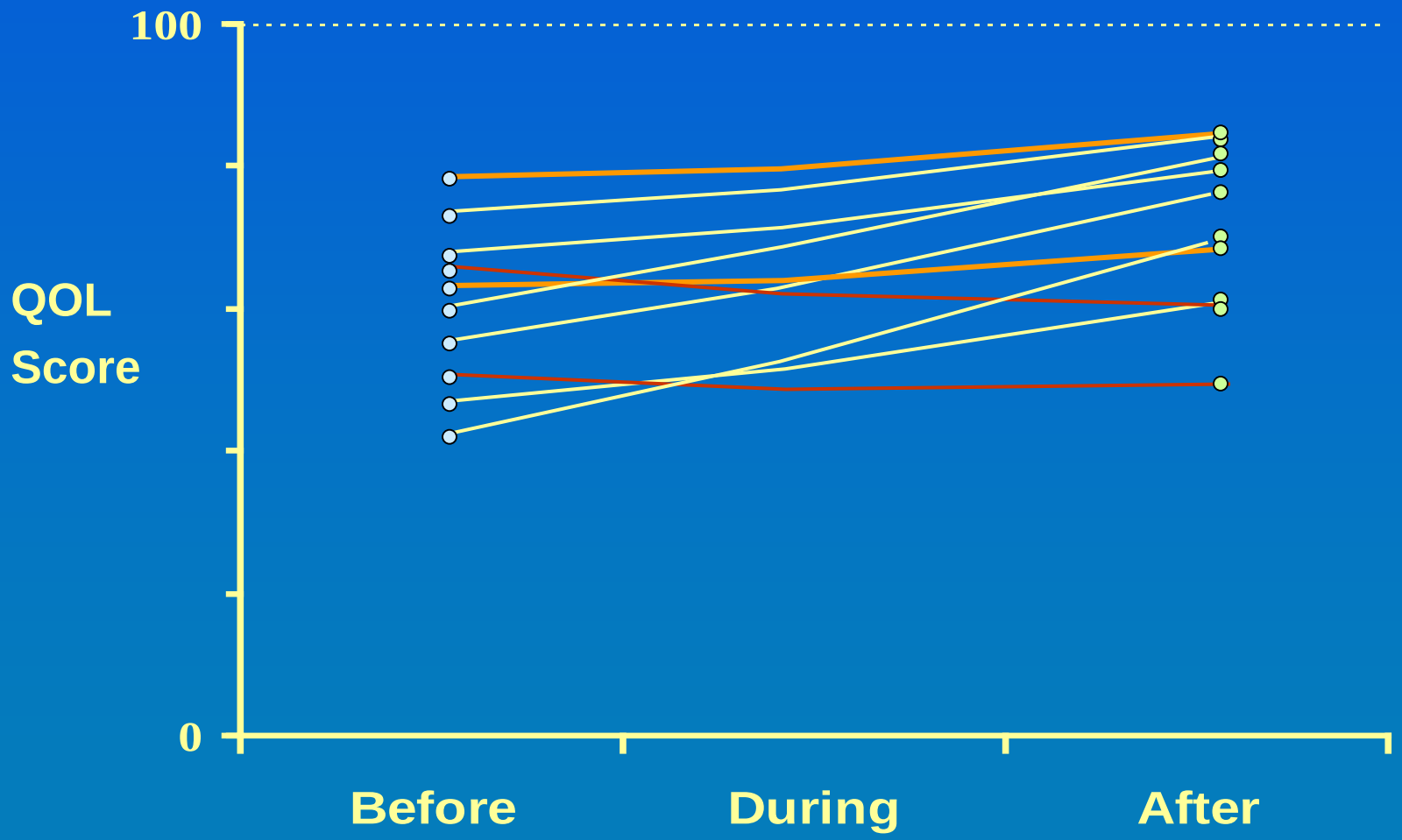
Treatment Intent: Improve QOL



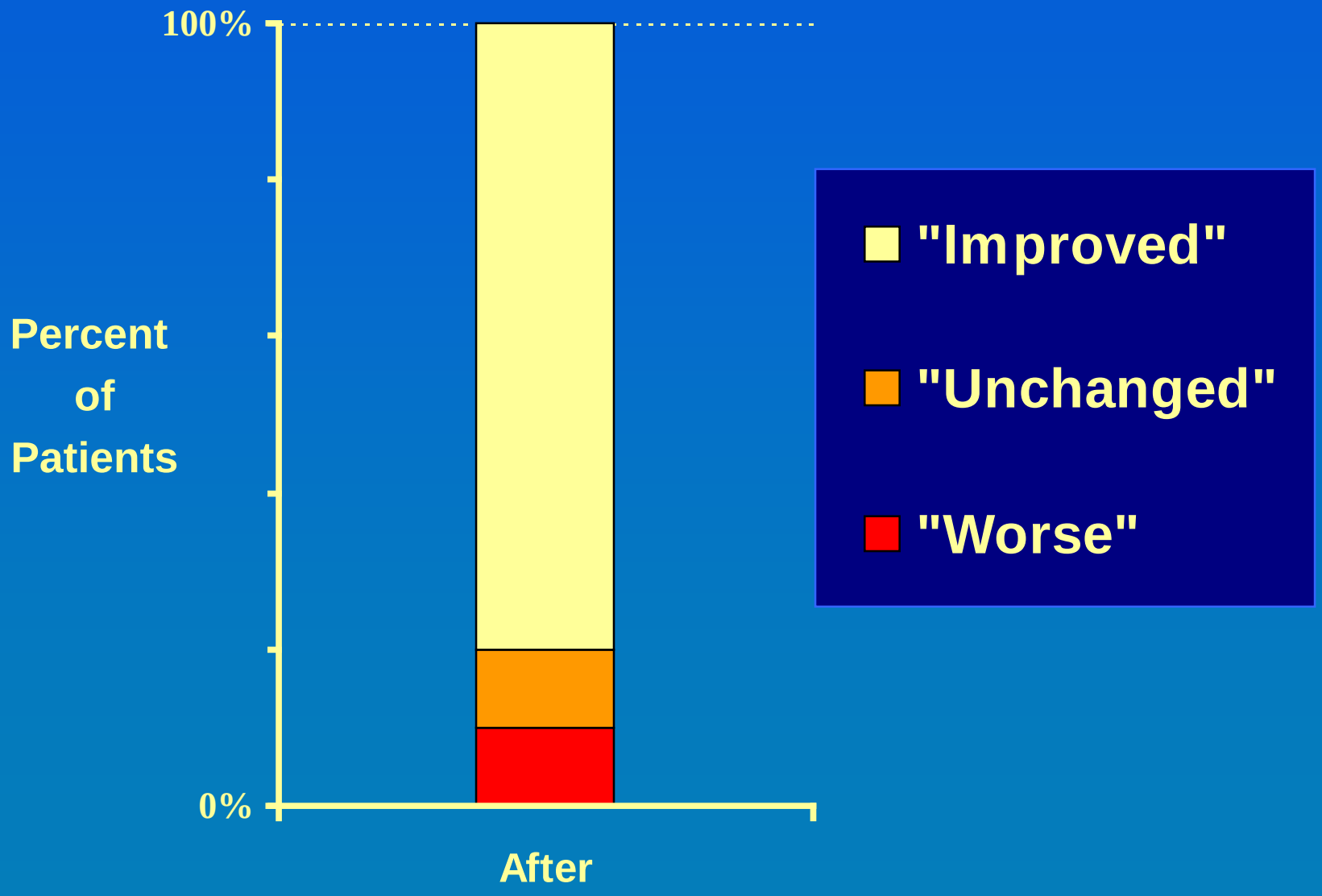
Treatment Intent: Improve QOL



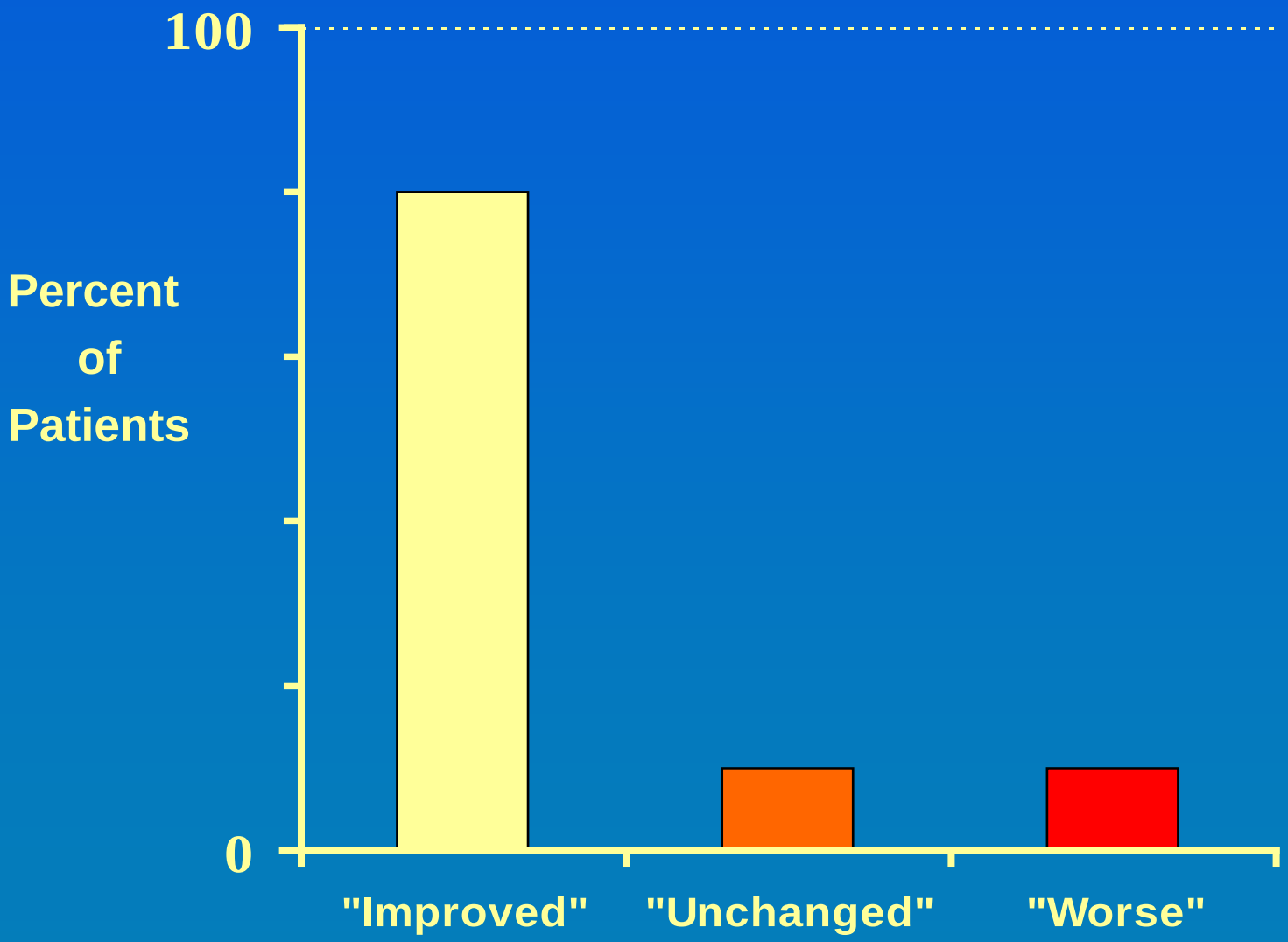
Treatment Intent: Improve QOL



Treatment Intent: Improve QOL



Treatment Intent: Improve QOL



MEDICAL CARE
Volume 41, Number 5, pp 582–592

Point/Counterpoint

Interpretation of Changes in Health-related Quality of Life

The Remarkable Universality of Half a Standard Deviation

GEOFFREY R. NORMAN, PHD,* JEFF A. SLOAN, PHD,† AND KATHLEEN W. WYRWICH, PHD‡

BACKGROUND. A number of studies have computed the minimally important difference (MID) for health-related quality of life instruments.

OBJECTIVE. To determine whether there is consistency in the magnitude of MID estimates from different instruments.

METHODS. We conducted a systematic review of the literature to identify studies that computed an MID and contained sufficient information to compute an effect size (ES). Thirty-eight studies fulfilled the criteria, resulting in 62 ESs.

RESULTS. For all but 6 studies, the MID estimates were close to one half a SD (mean = 0.495, SD = 0.155). There was no consistent relationship with factors such as disease-specific or generic instrument or the number of response options. Negative changes were not associated with larger ESs. Population-based estimation procedures and brief follow-up were associated with smaller ESs, and acute conditions with larger ESs. An explanation for this consistency is that research in psychology has shown that the limit of people's ability to discriminate over a wide range of tasks is approximately 1 part in 7, which is very close to half a SD.

CONCLUSION. In most circumstances, the threshold of discrimination for changes in health-related quality of life for chronic diseases appears to be approximately half a SD.

Key words: Quality of life; threshold; interpretation; MID; effect size. (Med Care 2003; 41:582–592)

Interpreting the Significance of Changes in Health-Related Quality-of-Life Scores

By David Osoba, George Rodrigues, James Myles, Benny Zee, and Joseph Pater

Purpose: To determine the significance to patients of changes in health-related quality-of-life (HLQ) scores assessed by the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ-C30).

Patients and Methods: A subjective significance questionnaire (SSQ), which asks patients about perceived changes in physical, emotional, and social functioning and in global quality of life (global QL) and the QLQ-C30 were completed by patients who received chemotherapy for either breast cancer or small-cell lung cancer (SCLC). In the SSQ, patients rated their perception of change since the last time they completed the QLQ-C30 using a 7-category scale that ranged from "much worse" through "no change" to "much better." For each category of change in the SSQ, the corresponding differences were calculated in QLQ-C30 mean scores and effect sizes were determined.

Results: For patients who indicated "no change" in the SSQ, the mean change in scores in the corresponding QLQ-C30 domains was not significantly different from 0. For patients who indicated "a little" change either for better or for worse, the mean change in scores was about 5 to 10; for "moderate" change, about 10 to 20; and for "very much" change, greater than 20. Effect sizes increased in concordance with increasing changes in SSQ ratings and QLQ-C30 scores.

Conclusion: The significance of changes in QLQ-C30 scores can be interpreted in terms of small, moderate, or large changes in quality of life as reported by patients in the SSQ. The magnitude of these changes also can be used to calculate the sample sizes required to detect a specified change in clinical trials.

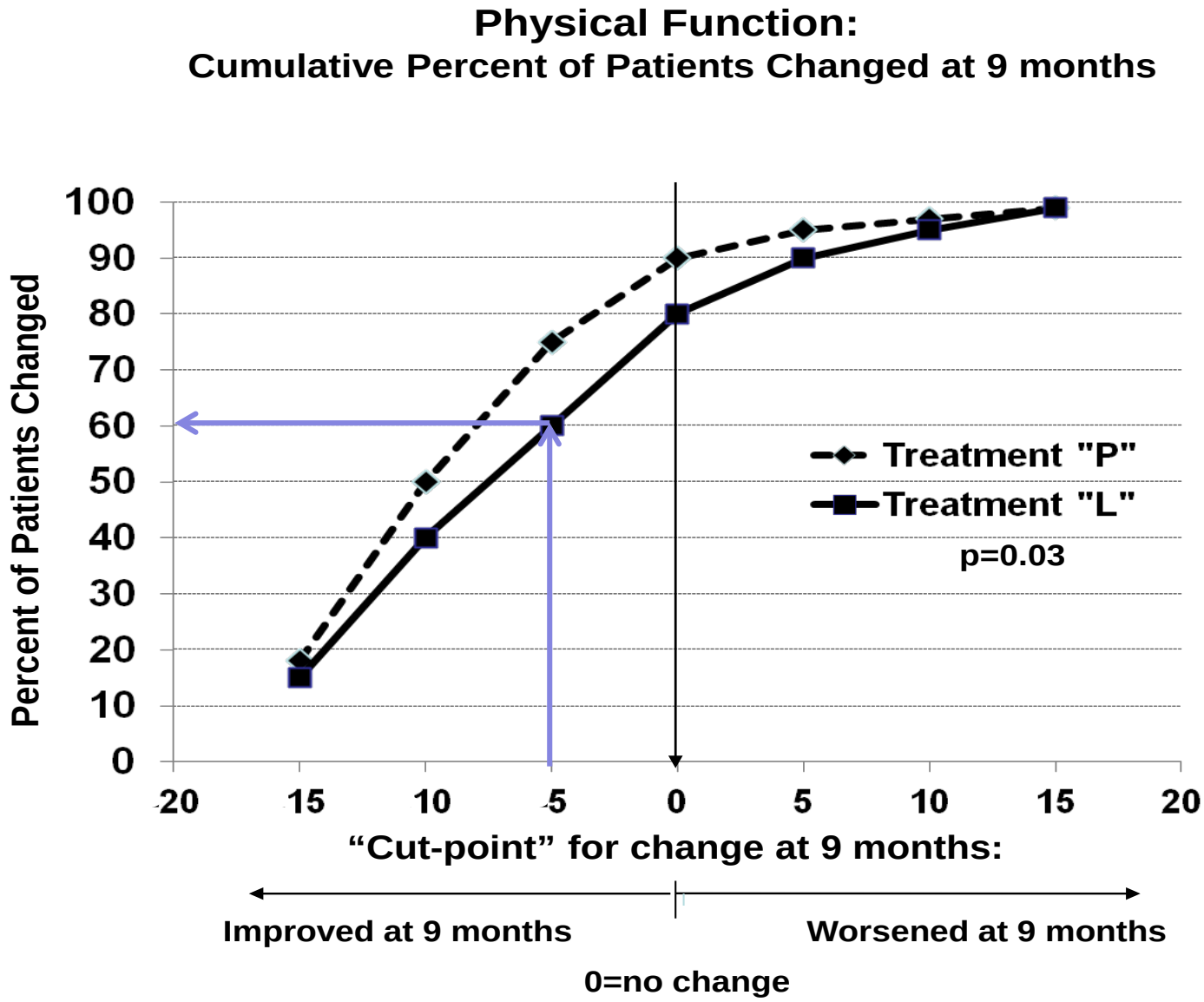
J Clin Oncol 16:139-144.

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

Cumulative Distribution Function

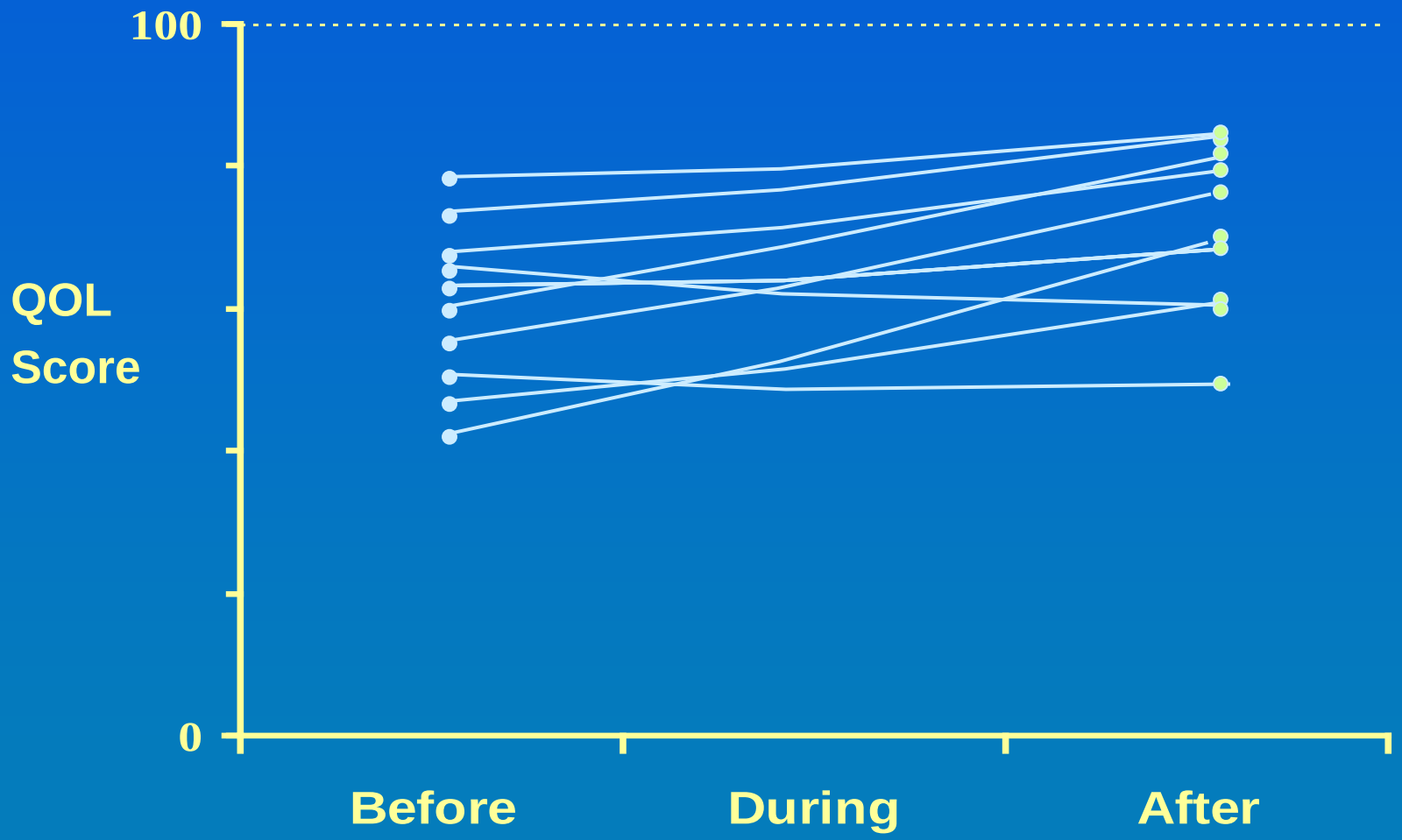


Some Concerns….

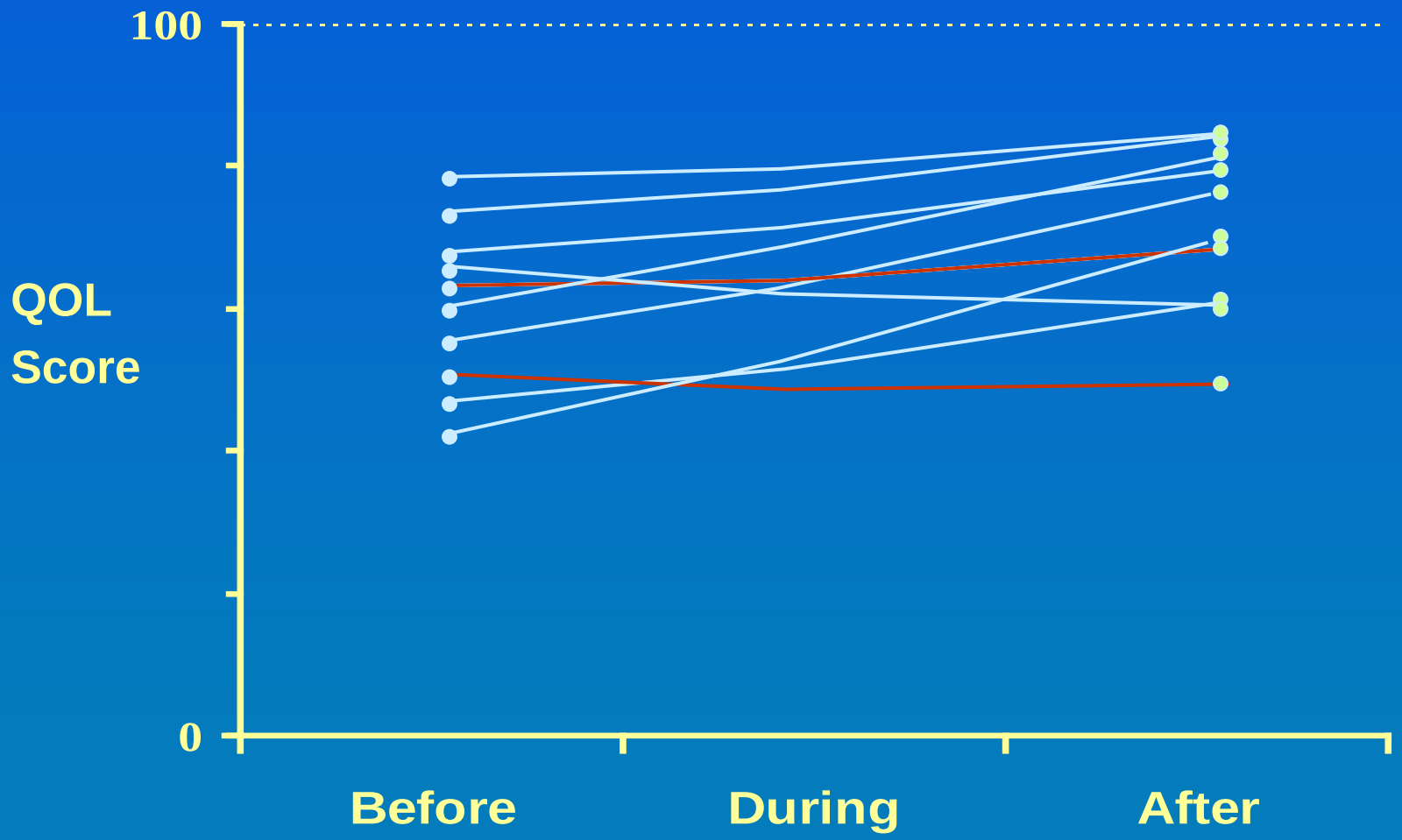
- The biggest problem with analyzing QOL information from clinical trials is **missing data**
  - are pts whose QOL data are missing different from pts supplying QOL data?
  - Or is QOL data missing because pts are sicker that those providing info?

- Analysis can try to account for missing data but it is best trying to prevent missing data

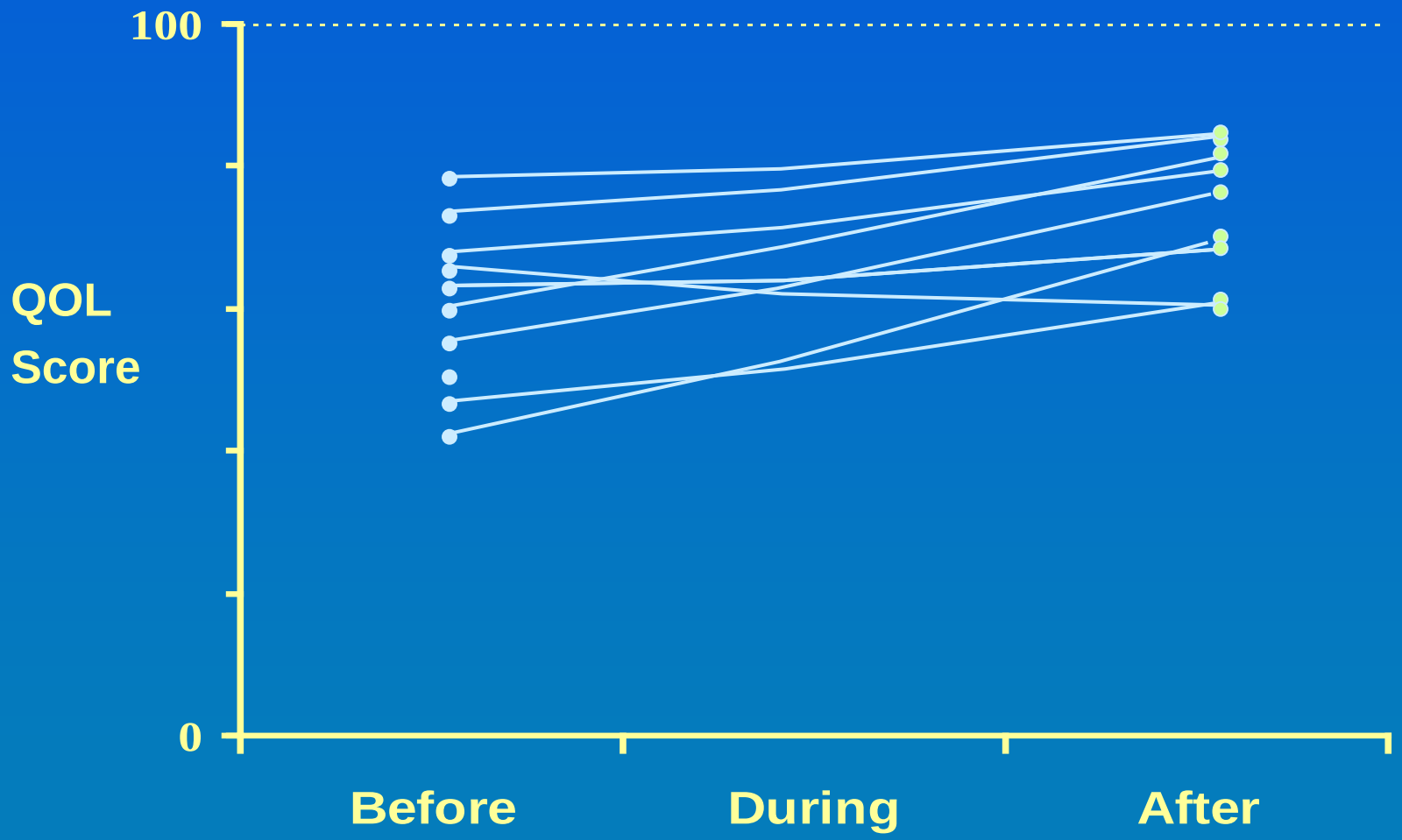
Treatment Intent: Improve QOL



Treatment Intent: Improve QOL



Treatment Intent: Improve QOL



Expert Consensus Panel

1. What are the characteristics of the population of interest?
2. Is the QOL questionnaire relevant, reliable, valid, and responsive to change?
3. Are the timing and frequency of assessment adequate?
4. Is the study adequately powered?
5. How are multiple QOL outcomes addressed in the analyses?
6. How are multiple time points handled?
7. Can alternative explanations account for observed scores?
8. Are missing data handled adequately?
9. Is an observed survival difference accounted for?
10. Was response shift (change in patient's perspective of QOL) taken into account?
11. Is clinical significance addressed?

Spranger et al, Mayo Clin Proc, 2002; 77: 561-571

Review

For reprint orders, please contact reprints@expert-reviews.com

EXPERT REVIEWS

Added value of health-related quality of life measurement in cancer clinical trials: the experience of the NCIC CTG

Expert Rev. Pharmacoeconomics Outcomes Res. 10(2), 119–128 (2010)

Heather-Jane Au†, Jolie Ringash, Michael Brundage, Michael Palmer, Harriet Richardson and Ralph M Meyer; on behalf of the NCIC CTG Quality of Life Committee

†*Author for correspondence*

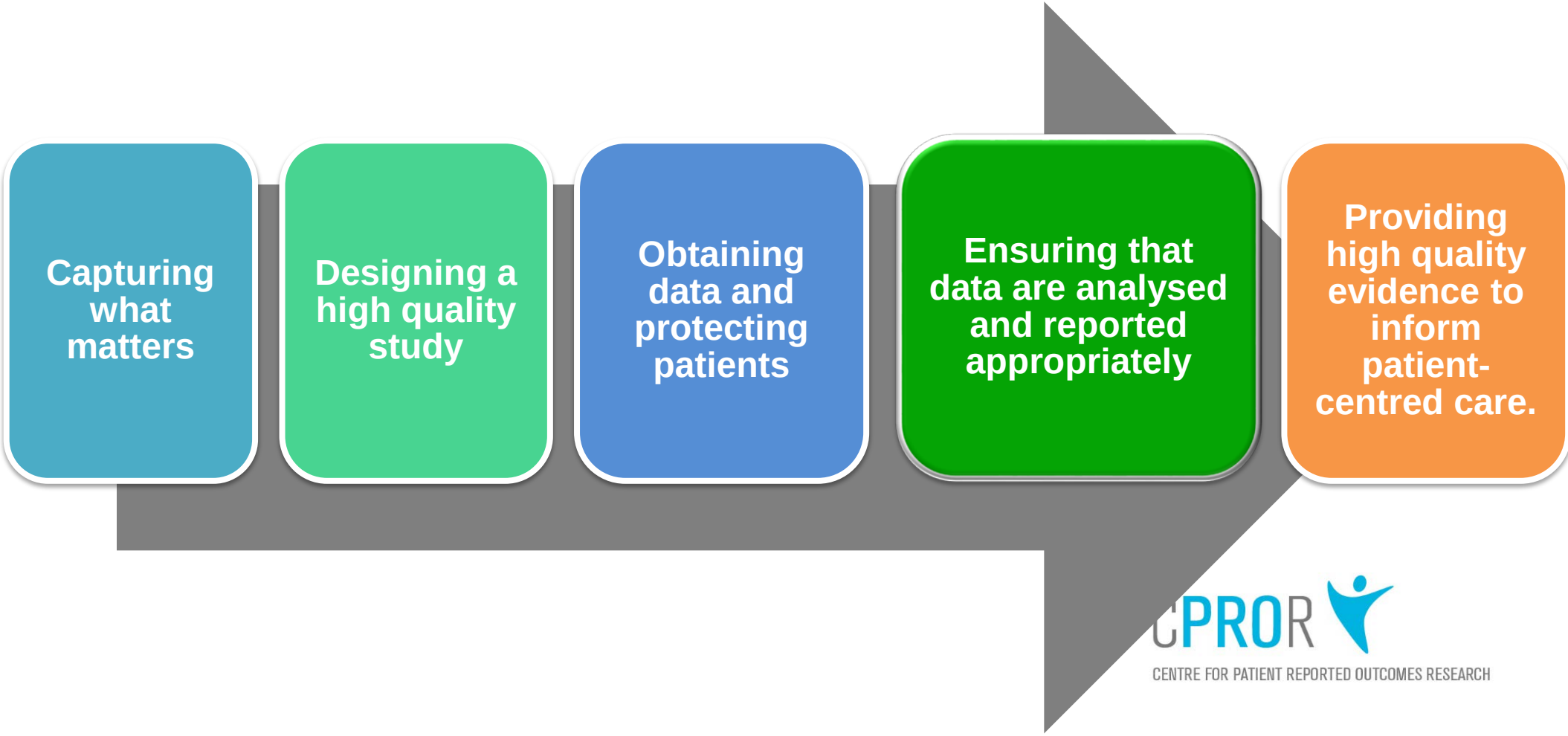
Health-related quality-of-life (HRQoL) data are often included in Phase III clinical trials. We evaluate and classify the value added to Phase III trials by HRQoL outcomes, through a review of the National Cancer Institute of Canada Clinical Trials Group clinical trials experience within various cancer patient populations. HRQoL may add value in a variety of ways, including the provision of data that may contrast with or may support the primary study outcome; or that assess a unique perspective or subgroup, not addressed by the primary outcome. Thus, HRQoL data may change the study's interpretation. Even in situations where HRQoL measurement does not alter the clinical interpretation of a trial, important methodologic advances can be made. A classification of the added value of HRQoL information is provided, which may assist in choosing trials for which measurement of HRQoL outcomes will be beneficial.

Critical appraisal is a systematic process used to identify the strengths and weaknesses of a research article in order to assess the usefulness and validity of research findings.

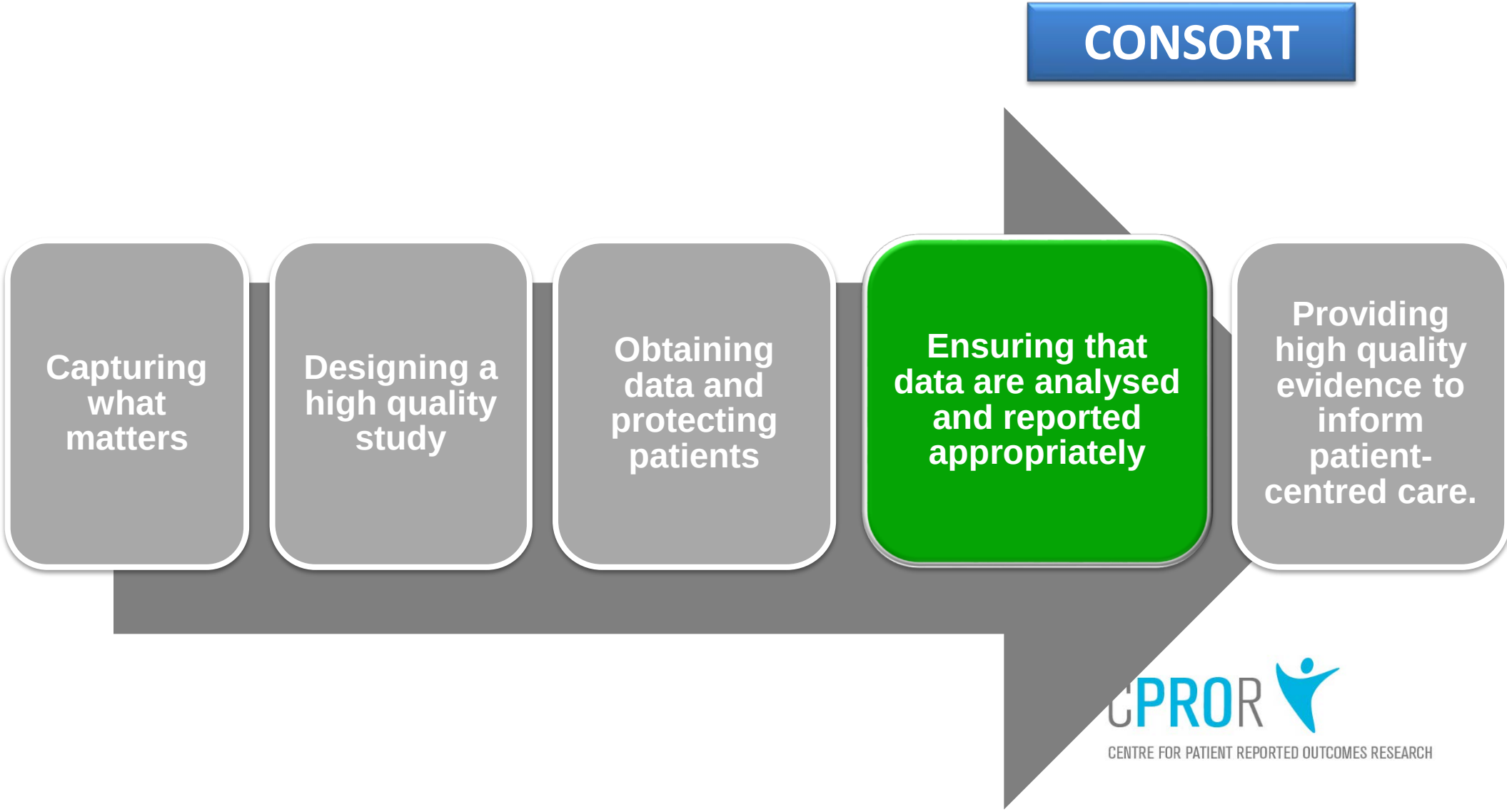
National Cancer Institute of Canada
Institut national du cancer du Canada

Clinical Trials Group
Groupe des essais cliniques

Minimising waste and maximising benefits…..



CPROR
CENTRE FOR PATIENT REPORTED OUTCOMES RESEARCH


CONSORT
Capturing what matters
Designing a high quality study
Obtaining data and protecting patients
Ensuring that data are analysed and reported appropriately
Providing high quality evidence to inform patient-centred care.
CPROR
CENTRE FOR PATIENT REPORTED OUTCOMES RESEARCH

SPECIAL COMMUNICATION

Reporting of Patient-Reported Outcomes in Randomized Trials

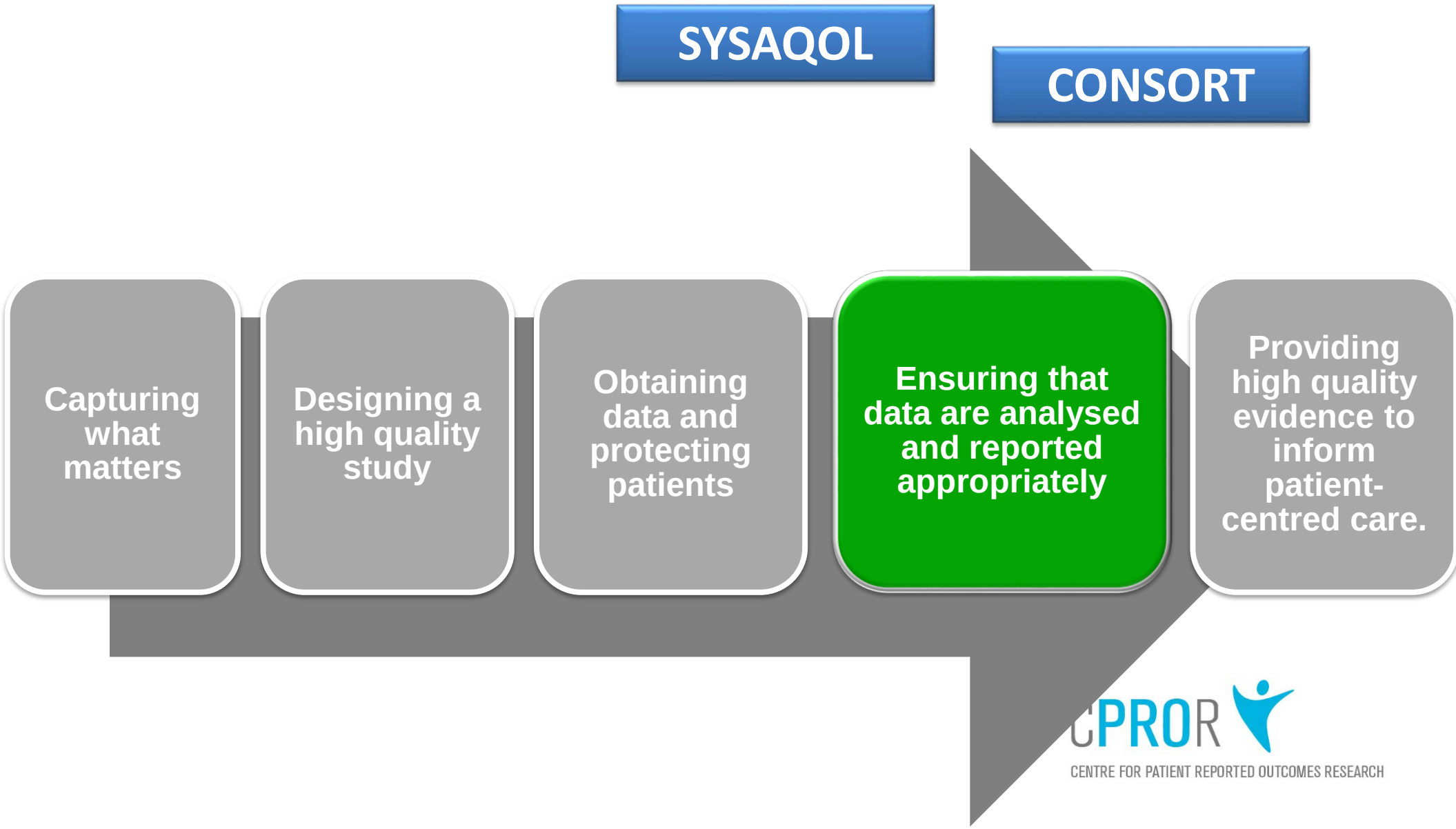
The CONSORT PRO Extension

Melanie Calvert, PhD
Jane Blazeby, MD
Douglas G. Altman, DSc
Dennis A. Revicki, PhD
David Moher, PhD
Michael D. Brundage, MD
for the CONSORT PRO Group

The CONSORT (Consolidated Standards of Reporting Trials) Statement aims to improve the reporting of randomized controlled trials (RCTs); however, it lacks guidance on the reporting of patient-reported outcomes (PROs), which are often inadequately reported in trials, thus limiting the value of these data. In this article, we describe the development of the CONSORT PRO extension based on the methodological framework for guideline development proposed by the Enhancing the Quality and Transparency of Health Research (EQUATOR) Network. Five CONSORT PRO checklist items are recom-

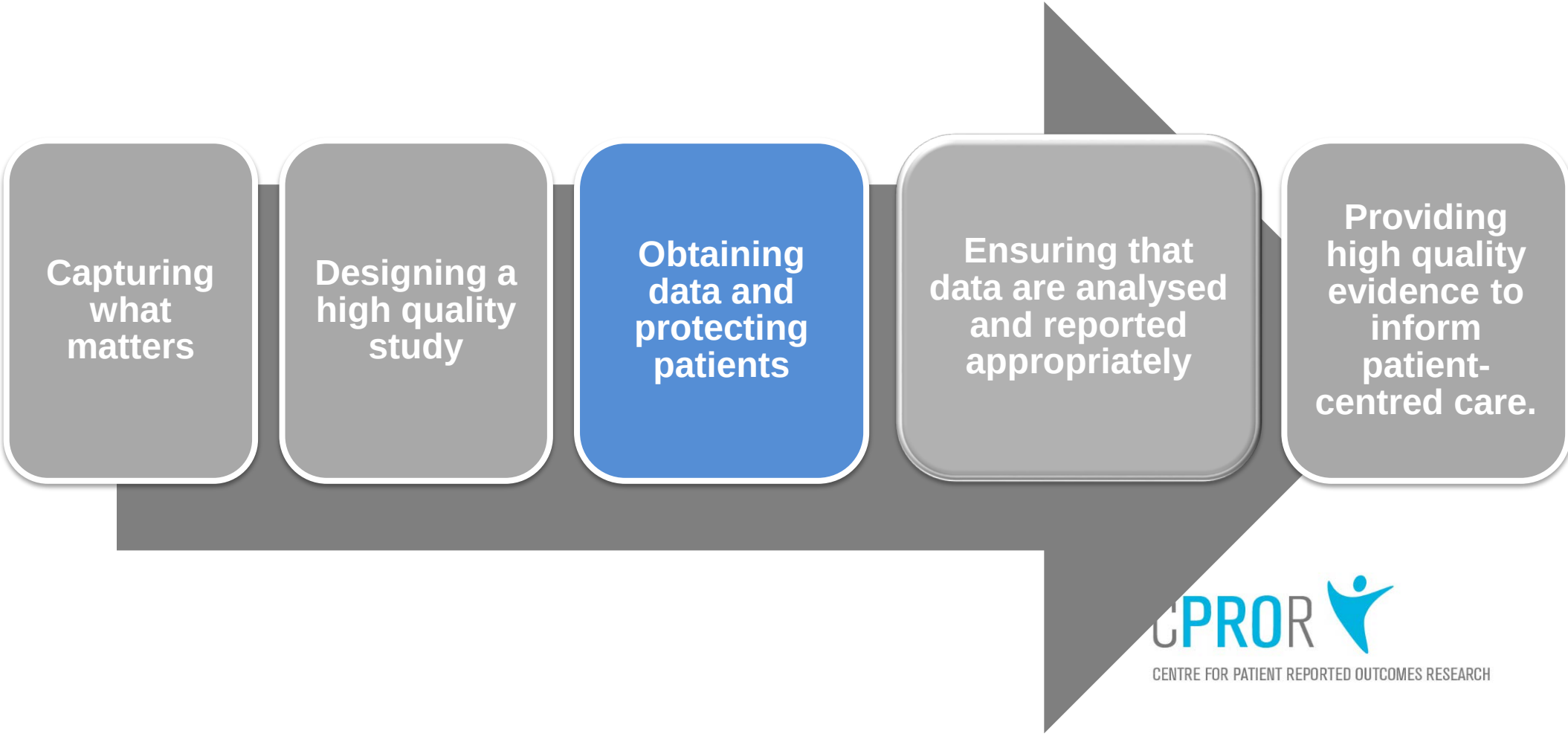
JAMA. 2013;309(8):814-822

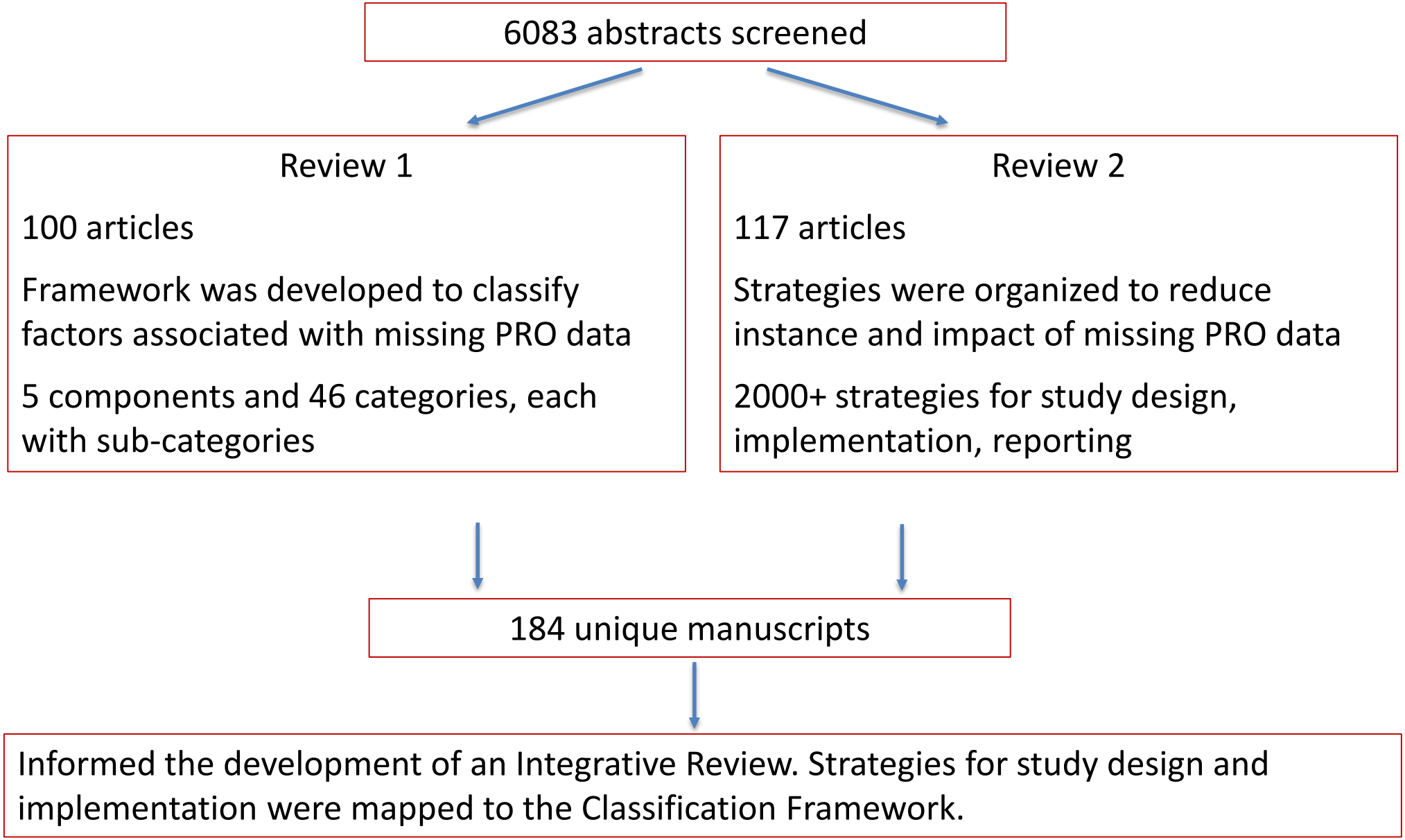
	Original Consort Statement	Consort PRO Extension
2a	Scientific background and explanation of rationale	
2b	Specific objectives or hypotheses	P2b: The PRO hypothesis should be stated and relevant domains identified, if applicable
6a	Completely defined prespecified primary and secondary outcome measures, including how and when they were assessed	P6a: Evidence of PRO instrument validity and reliability should be provided or cited if available including the person completing the PRO and methods of data collection (paper, telephone, electronic, other)
12a	Statistical methods used to compare groups for primary and secondary outcomes	P12a: Statistical approaches for dealing with missing data are explicitly stated
20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	P20/21 PRO–specific limitations and implications for generalizability and clinical practice
21	Generalizability (external validity, applicability) of the trial findings	
22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	PRO data should be interpreted in relation to clinical outcomes including survival data, where relevant


SYSAQOL
CONSORT
Capturing what matters
Designing a high quality study
Obtaining data and protecting patients
Ensuring that data are analysed and reported appropriately
Providing high quality evidence to inform patient-centred care.
CPROR
CENTRE FOR PATIENT REPORTED OUTCOMES RESEARCH

What is SISAQOL

- Setting International Standards in Analyzing Patient-Reported Outcomes and Quality of Life Endpoints Data
- International
- Multi-stakeholder
- Shared interest in improving the standards of PRO analysis in cancer RCTs in order to improve patient outcomes


Capturing what matters
Designing a high quality study
Obtaining data and protecting patients
Ensuring that data are analysed and reported appropriately
Providing high quality evidence to inform patient-centred care.
CPROR
CENTRE FOR PATIENT REPORTED OUTCOMES RESEARCH


6083 abstracts screened
Review 1
100 articles
Framework was developed to classify factors associated with missing PRO data
5 components and 46 categories, each with sub-categories
Review 2
117 articles
Strategies were organized to reduce instance and impact of missing PRO data
2000+ strategies for study design, implementation, reporting
184 unique manuscripts
Informed the development of an Integrative Review. Strategies for study design and implementation were mapped to the Classification Framework.

Clinical Trials 2018;15(1):95-106

Article

CLINICAL TRIALS

Clinical Trials
2018, Vol. 15(1) 95–106

DOI: 10.1177/1740774517741113
journals.sagepub.com/home/ctj
SAGE

A systematic review and development of a classification framework for factors associated with missing patient-reported outcome data

Michael J Palmer[1,2], Rebecca Mercieca-Bebber[3,4,5], Madeleine King[3,4], Melanie Calvert[5,6], Harriet Richardson[1,2] and Michael Brundage[1,2]

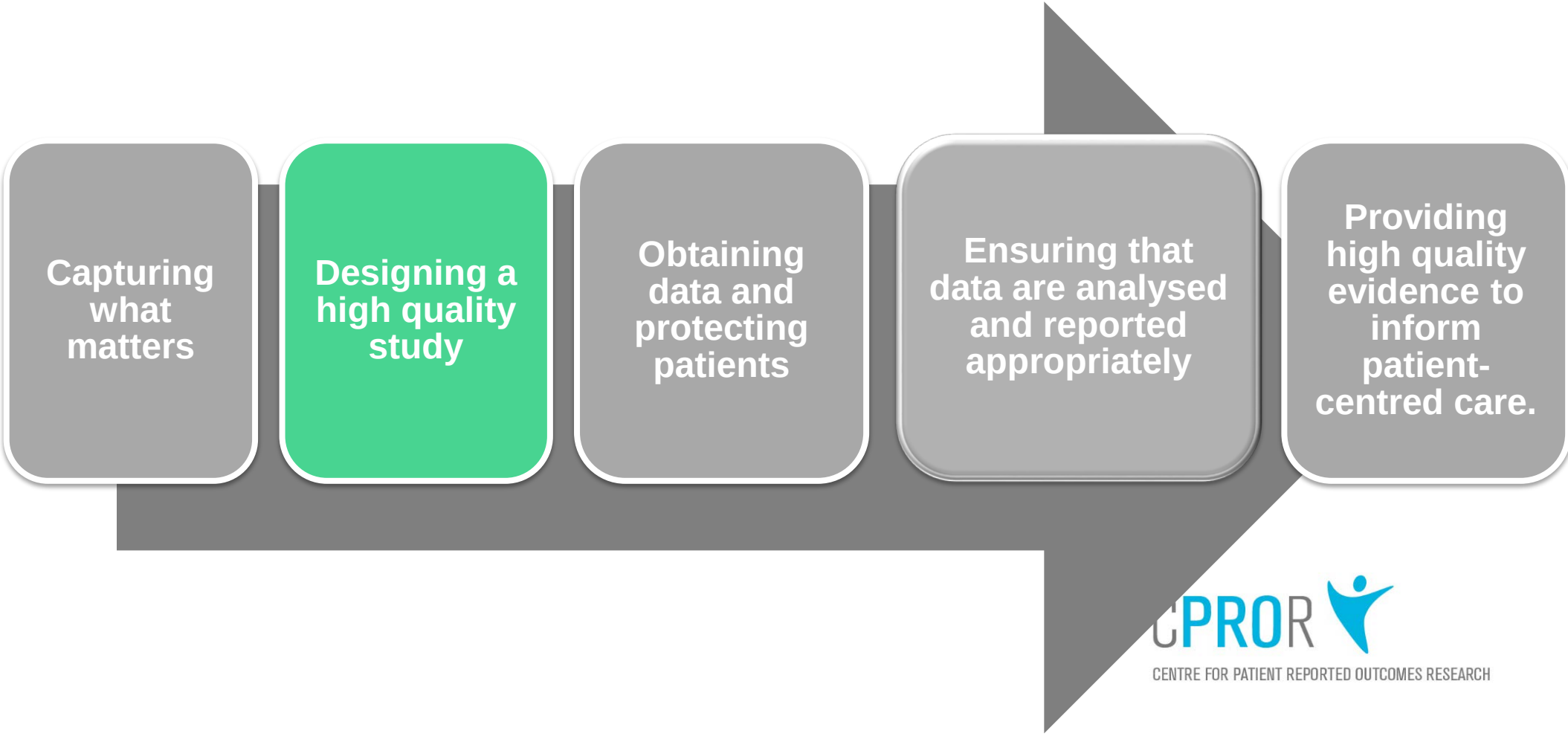
http://bmjopen.bmj.com/content/6/6/e010938

Open Access Research

BMJ Open

Design, implementation and reporting strategies to reduce the instance and impact of missing patient-reported outcome (PRO) data: a systematic review

Rebecca Mercieca-Bebber,[1,2] Michael J Palmer,[3] Michael Brundage,[3] Melanie Calvert,[4] Martin R Stockler,[1,5] Madeleine T King[1,2]


Capturing what matters
Designing a high quality study
Obtaining data and protecting patients
Ensuring that data are analysed and reported appropriately
Providing high quality evidence to inform patient-centred care.
CPROR
CENTRE FOR PATIENT REPORTED OUTCOMES RESEARCH

Funded by WE ARE MACMILLAN. CANCER SUPPORT

UNIVERSITY OF BIRMINGHAM | CPROR
CENTRE FOR PATIENT REPORTED OUTCOMES RESEARCH

Systematic evaluation of Patient-Reported Outcome protocol content and reporting in cancer trials - EPiC

Dr Derek Kyte, PhD

Centre for Patient-Reported Outcomes Research (CPROR)
University of Birmingham d.g.kyte@bham.ac.uk

NCRI Psychosocial Oncology & Survivorship Clinical Studies Group

On behalf of the EPiC study group: Derek Kyte, Ameeta Retzer, Khaled Ahmed, Thomas Keeley, Jo Armes, Julia M Brown, Lynn Calman, Anna Gavin, Adam W Glaser, Diana M Greenfield, Anne Lanceley, Rachel M Taylor, Galina Velikova, Michael Brundage, Fabio Efficace, Rebecca Mercieca-Bebber, Madeleine T King, Grace Turner, Melanie Calvert.

NCRI National Cancer Research Institute
The University Of Sheffield.
UNIVERSITY OF LEEDS
Queen's University
THE UNIVERSITY OF SYDNEY
UNIVERSITY OF SURREY
UCL
QUEEN'S UNIVERSITY BELFAST
fondazione GIMEMA
UNIVERSITY OF Southampton

Funded by WE ARE MACMILLAN. CANCER SUPPORT

UNIVERSITY OF BIRMINGHAM | CPROR
CENTRE FOR PATIENT REPORTED OUTCOMES RESEARCH

Objective: review the rigour with which PROs are incorporated into cancer clinical trials

NHS National Institute for Health Research

METHODS

- Systematic evaluation of 1,141 cancer trials on the NIHR Portfolio 2001-2014. Excluding non-randomised trials or those that terminated early.

We reviewed:

1. PRO protocol content

3. Availability of PRO trial results

5. Quality of PRO reporting

CHECKLISTS	
GENERAL	**PRO-SPECIFIC**
SPIRIT 2013	PRO CHECKLIST
CONSORT 2010	CONSORT PRO

Funded by WE ARE MACMILLAN. CANCER SUPPORT

UNIVERSITY OF BIRMINGHAM | CPROR
CENTRE FOR PATIENT REPORTED OUTCOMES RESEARCH

EPiC Study Results - PRO protocol content

- Trial protocols (n=101) included a mean of 32/51 (range 11–43, SD 6) SPIRIT 2013 recommendations
- 10/33 (range 2–19, SD 4) PRO protocol checklist items.

Funded by WE ARE MACMILLAN. CANCER SUPPORT

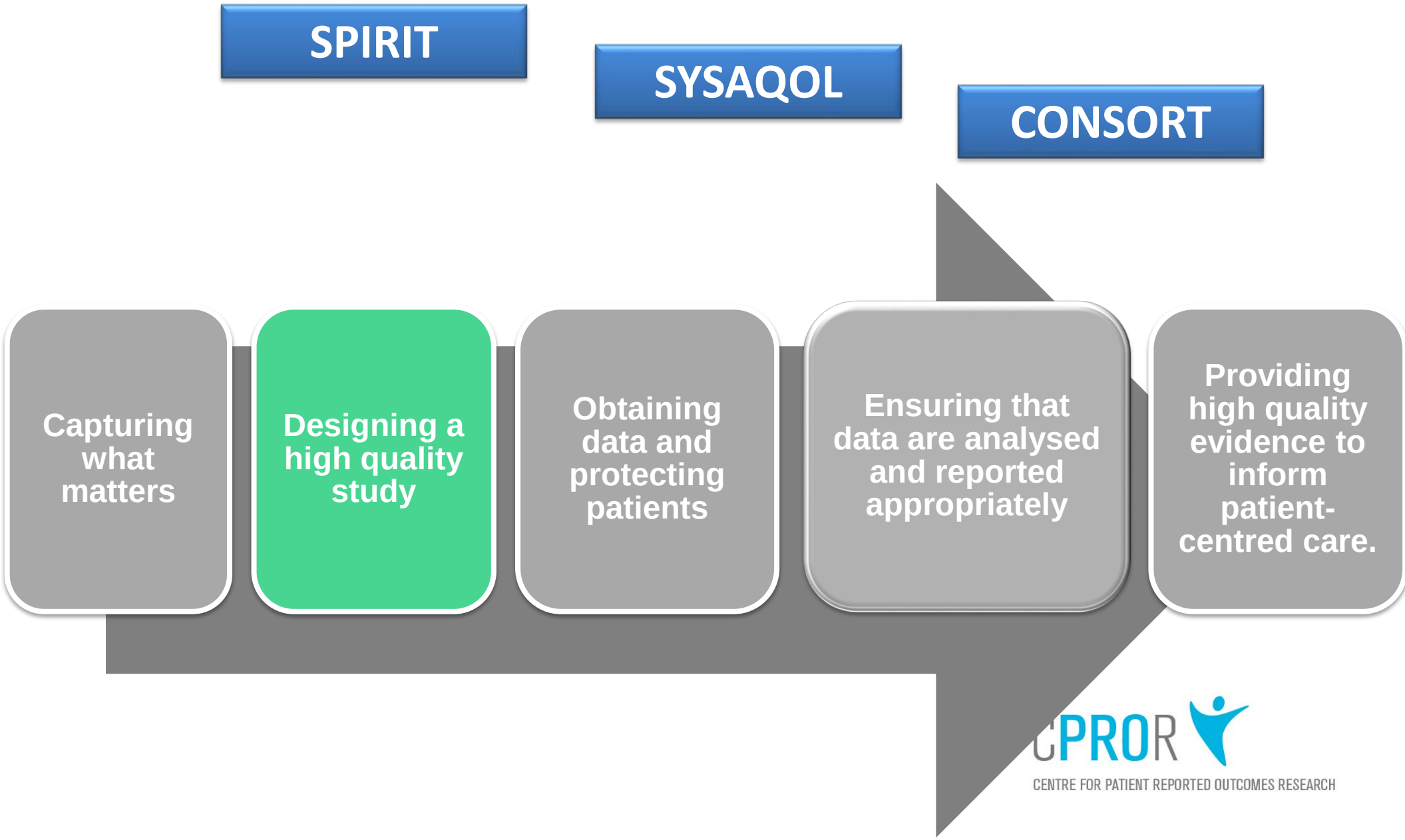
UNIVERSITY OF BIRMINGHAM | CPROR
CENTRE FOR PATIENT REPORTED OUTCOMES RESEARCH

EPiC Study Results - PRO protocol content

Recommended Protocol Item	Protocol Coverage
Detail regarding the rationale for PRO collection	missing in 68%
Description of PRO-specific objectives	missing in 83%
Justification of the choice of PRO instrument with regard to the study hypothesis	missing in 66%
Questionnaire measurement properties	missing in 49%
Information regarding PRO data collection plans	missing in 41%
Methods to reduce avoidable missing PRO data	missing in 61%

Funded by WE ARE MACMILLAN. CANCER SUPPORT

UNIVERSITY OF BIRMINGHAM | CPROR
CENTRE FOR PATIENT REPORTED OUTCOMES RESEARCH


SPIRIT
SYSAQOL
CONSORT
Capturing what matters
Designing a high quality study
Obtaining data and protecting patients
Ensuring that data are analysed and reported appropriately
Providing high quality evidence to inform patient-centred care.
CPROR
CENTRE FOR PATIENT REPORTED OUTCOMES RESEARCH

Top Ten Examples

“Added Value”

10. HRQL results of interest for descriptive purposes

- Head and neck cancer patients
- Women five-years post breast cancer treatment

“Added Value”

9. HRQL as a prognostic factor

- Repeatedly illustrated in multiple study contexts
- Stratification / statistical adjustment

“Added Value”

8. HRQL in Phase I/II trials

- Detect toxicity or response
- Estimate effect size for phase III
- “Pick the winner”

“Added Value”

7. HRQL results that support primary outcome

- Palliative chest radiotherapy for locally advanced lung cancer
- Improvement in nausea and vomiting with effective anti-emetics

“Added Value”

6. HRQL results that “conflict” with primary outcome

- Pre-operative vs. post-operative radiotherapy for limb soft-tissue sarcoma

- Wound healing – post-op favoured
- Long-term functioning – pre-op favoured

“Added Value”

5. Quantification of treatment-related toxicity

- Adjuvant chemotherapy for early-stage lung cancer

  - Significant survival difference
  - Some impact of treatment on HRQL
  - Recovery of HRQL after treatment

“Added Value”

4. Demonstration of reduced treatment-related toxicity

   - Palliative chemotherapy for advanced-stage lung cancer

     - No significant difference in global HRQL
     - Differences seen in treatment tolerance

“Added Value”

3. Measurement of response to treatment

- **Mitoxantrone and prednisone for patients with metastatic prostate cancer**
  - **No significant survival difference**
  - **improved symptoms and HRQL**

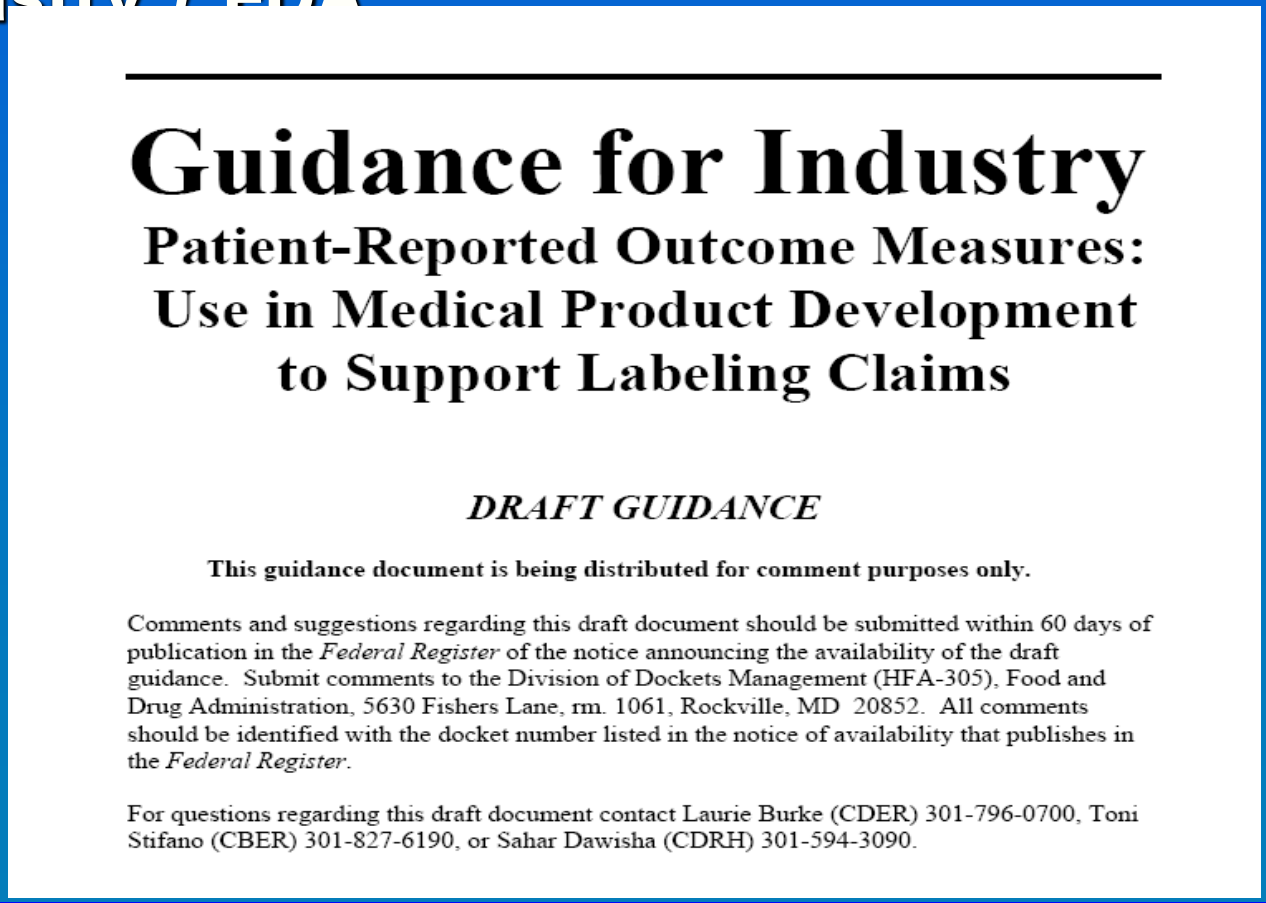
“Added Value”

2. Industry / FDA

- Claims for new drug labelling

“Added Value”

2. Industry / FDA

- 

Guidance for Industry

Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

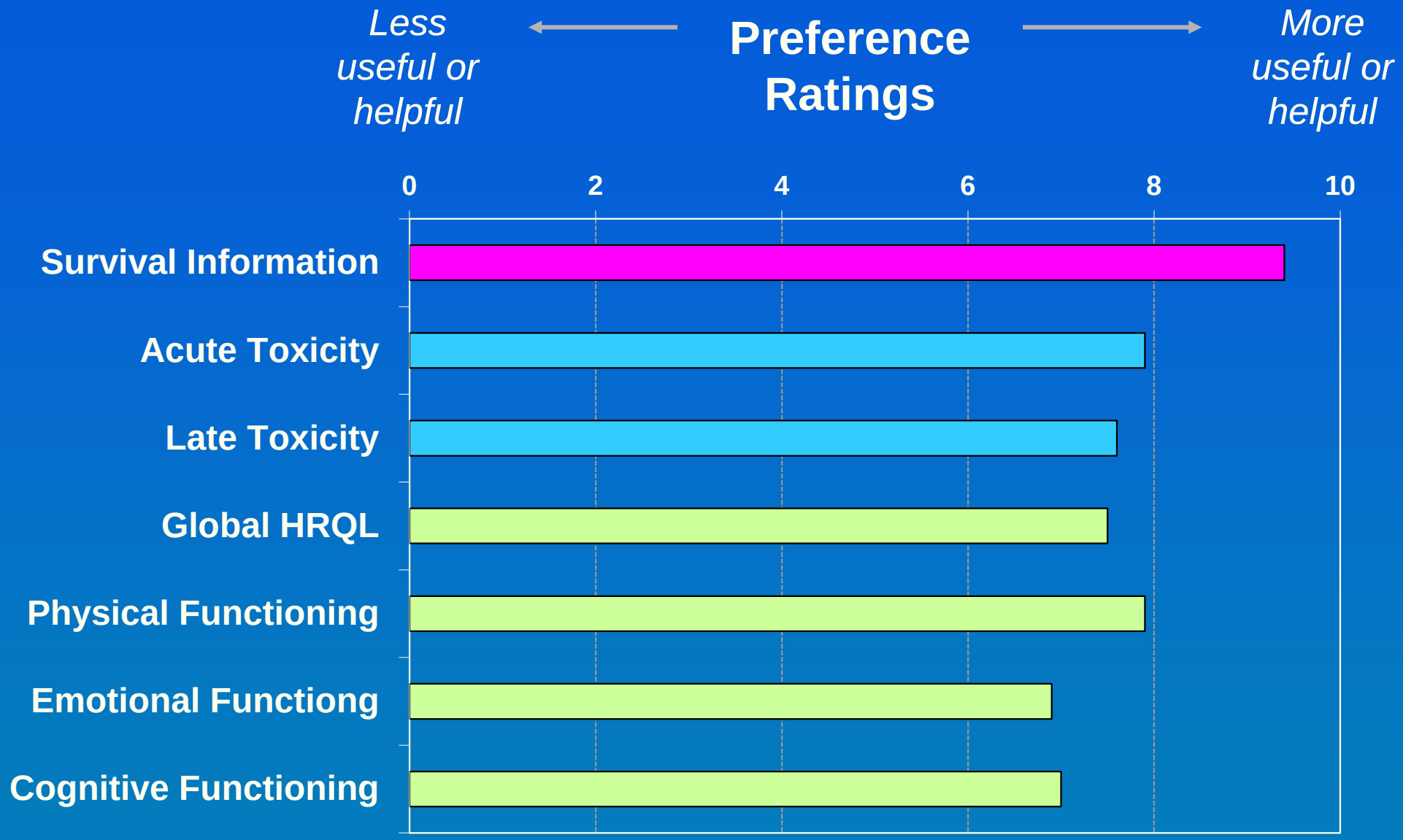
Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact Laurie Burke (CDER) 301-796-0700, Toni Stifano (CBER) 301-827-6190, or Sahar Dawisha (CDRH) 301-594-3090.

“Added Value”

1. **Patient Preferences**

   - **Medical decision making**
   - **Other elements of patient education**



Brundage et al, ISOQOL 2005

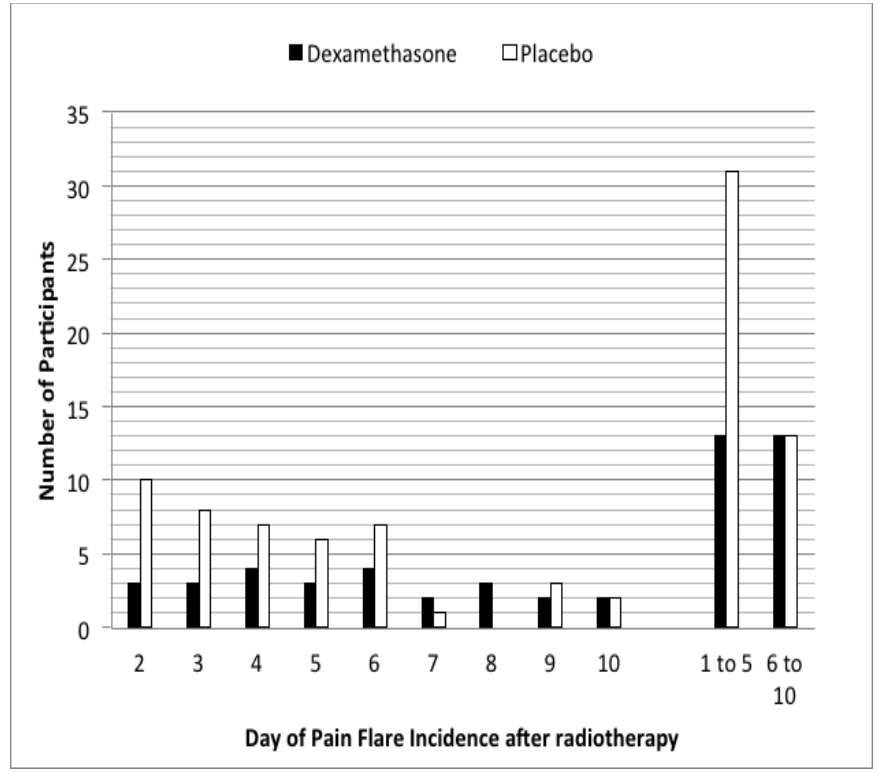
Some High-Impact Trials

- **CE.6** - Temozolomide and Short-Course Radiation in the Treatment of Glioblastoma Multiforme in Elderly Patients **J Clin Oncol**
- **MA.17R** - Extending Aromatase-Inhibitor Adjuvant Therapy to 10 Years. **N Engl J Med**
- **MA.20** - Regional Nodal Irradiation in Early-Stage Breast Cancer. **N Engl J Med**
- **HD.6** - ABVD Alone versus Radiation-Based Therapy in Limited-Stage Hodgkin's Lymphoma **N Engl J Med**
- **SC.23** - Dexamethasone in the prophylaxis of radiation-induced pain flare after palliative radiotherapy for bone metastases **Lancet Oncol**
- **PR.7** - Intermittent Androgen Suppression for Rising PSA Level after Radiotherapy. **N Engl J Med**

Some High-Impact Trials

- **MA.17R** - Extending Aromatase-Inhibitor Adjuvant Therapy to 10 Years.
  N Engl J Med

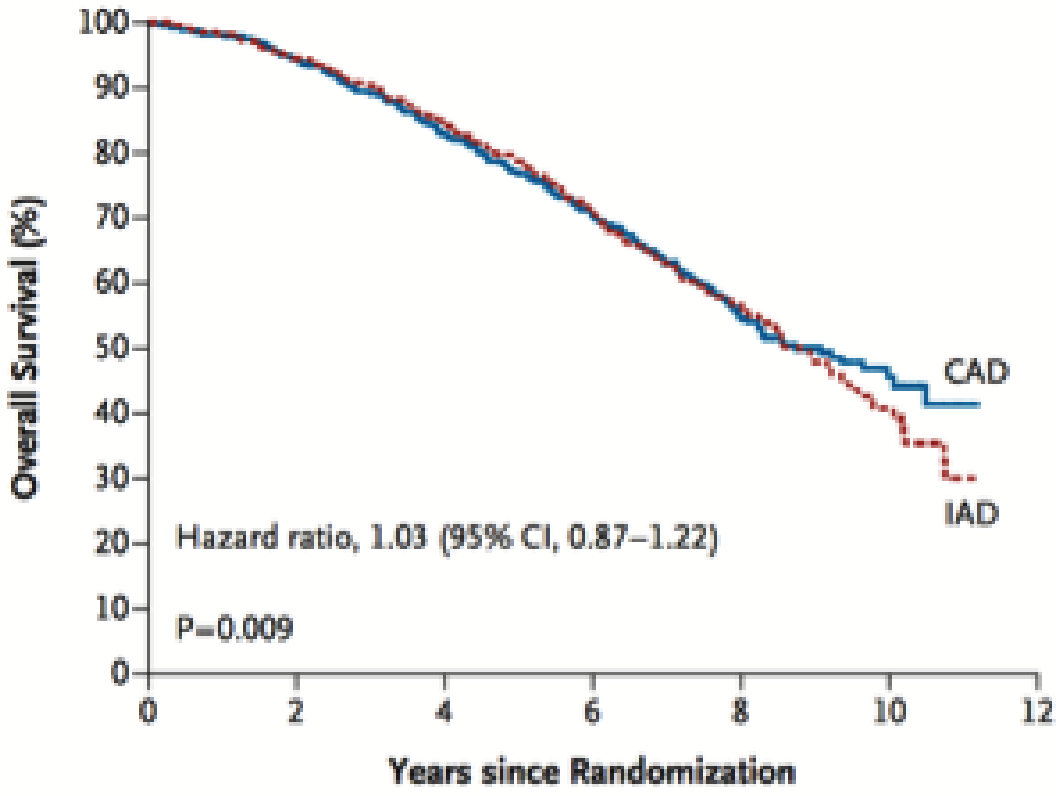
Some High-Impact Trials



- **SC.23 -** Dexamethasone in the prophylaxis of radiation-induced pain flare after palliative radiotherapy for bone metastases **Lancet Oncol**

Some High-Impact Trials

- **PR.7** - Intermittent Androgen Suppression for Rising PSA Level after Radiotherapy. **N Engl J Med**



No. at Risk							
CAD	696	652	561	319	125	35	0
IAD	690	651	571	327	140	34	0

Figure 1. Overall Survival in the Intention-to-Treat Population.

Key Quality of Life (QOL) Findings:

Intermittent therapy resulted in significantly better QOL regarding:

- Hot flashes ($p<0.001$),
- Urinary symptoms ($p<0.006$)
- Desire for sexual activity ($p<0.001$)

Trend toward improved physical functioning and less fatigue ($p=0.07$).

Time for Questions....Over to you!