# Quality Adjusted Survival Analysis

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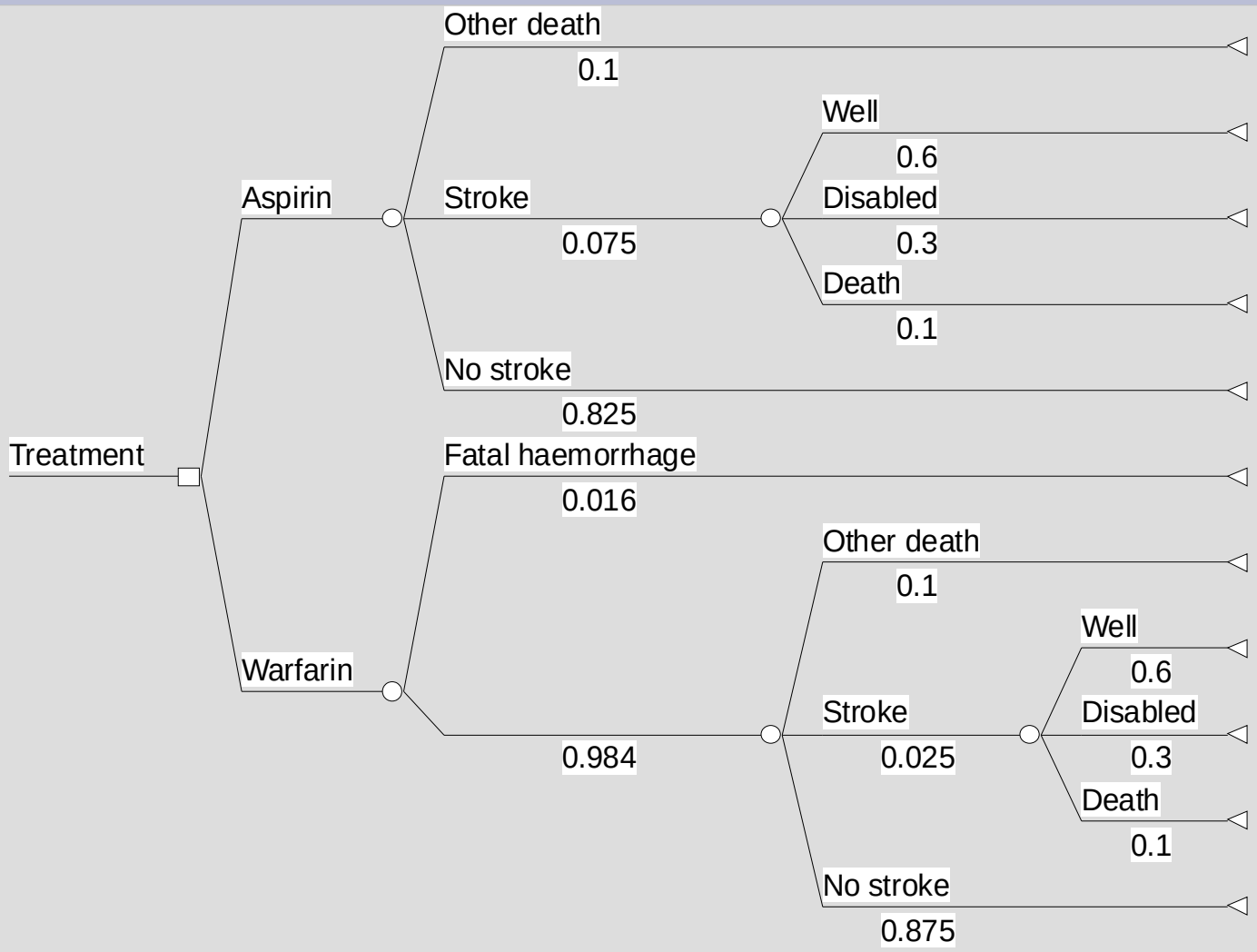
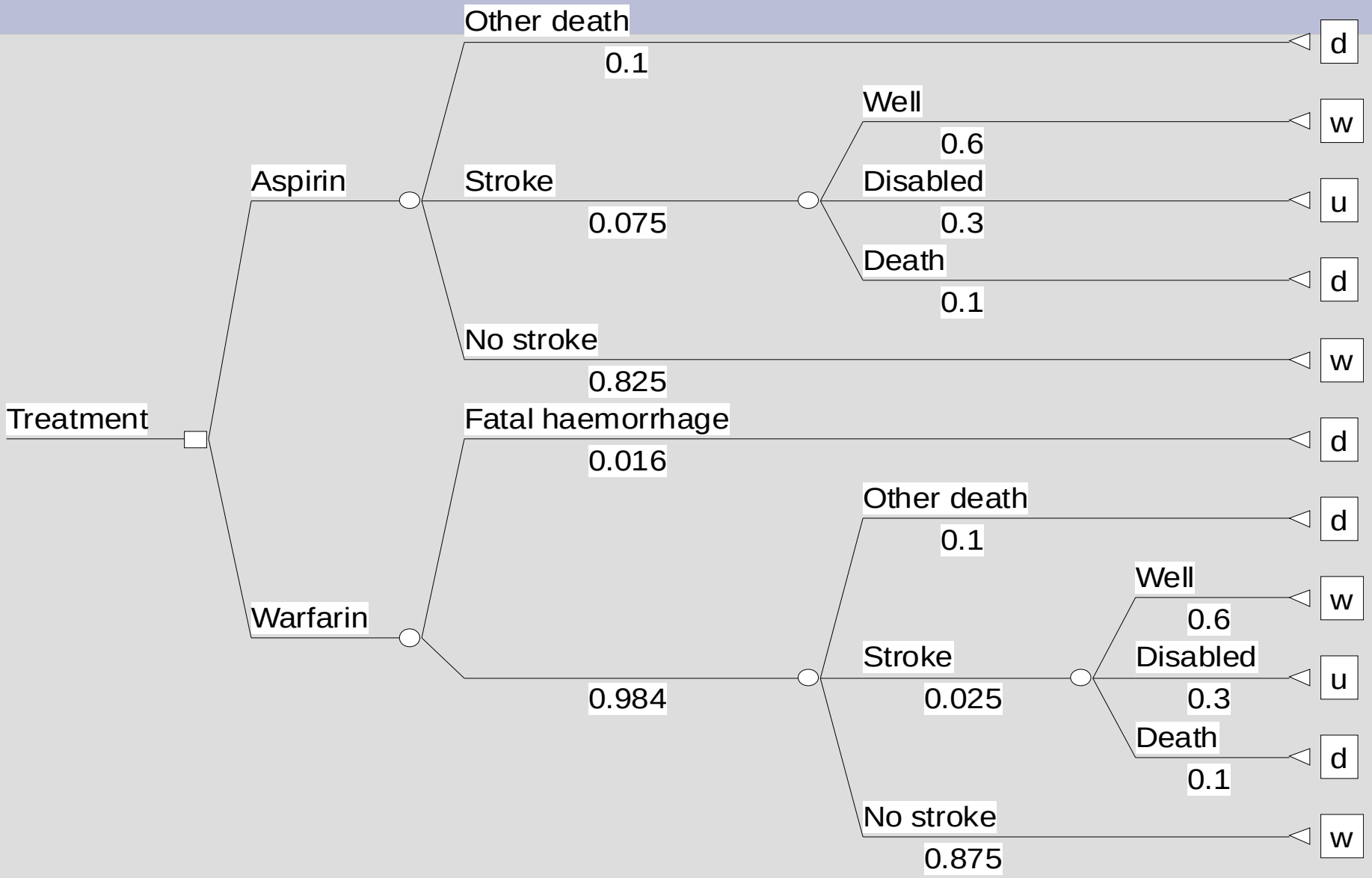
# Quality Adjusted Survival Analysis

- Why QAS?
- What to include in trials to evaluate *quality of life* (QoL)
- Analysis contexts
  - decision trees
  - discrete health states (constant QoL -> QALYs)
  - 'continuous' QoL variation
    - small subgroups with severe outcomes
- Utility based QALYs
  - How to determine utility coefficients/ valuations
  - Statistical methods

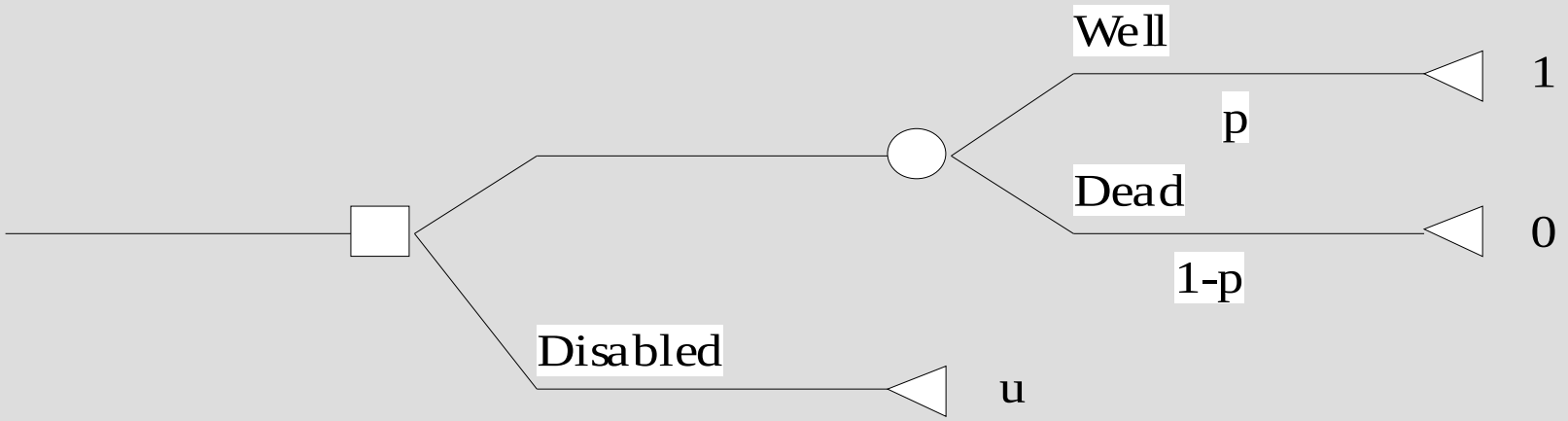
# Ex 1: Warfarin decision tree



# Ex. 1: Valuation of outcomes



# Ex 1: Standard gamble utility assessment




study subject identifies risk of death, 1-p, they would accept to return to good health from their disabled state

utility u follows from p

Valuation perspective:
societal
government / insurer
hospital / physician
patient / past patient

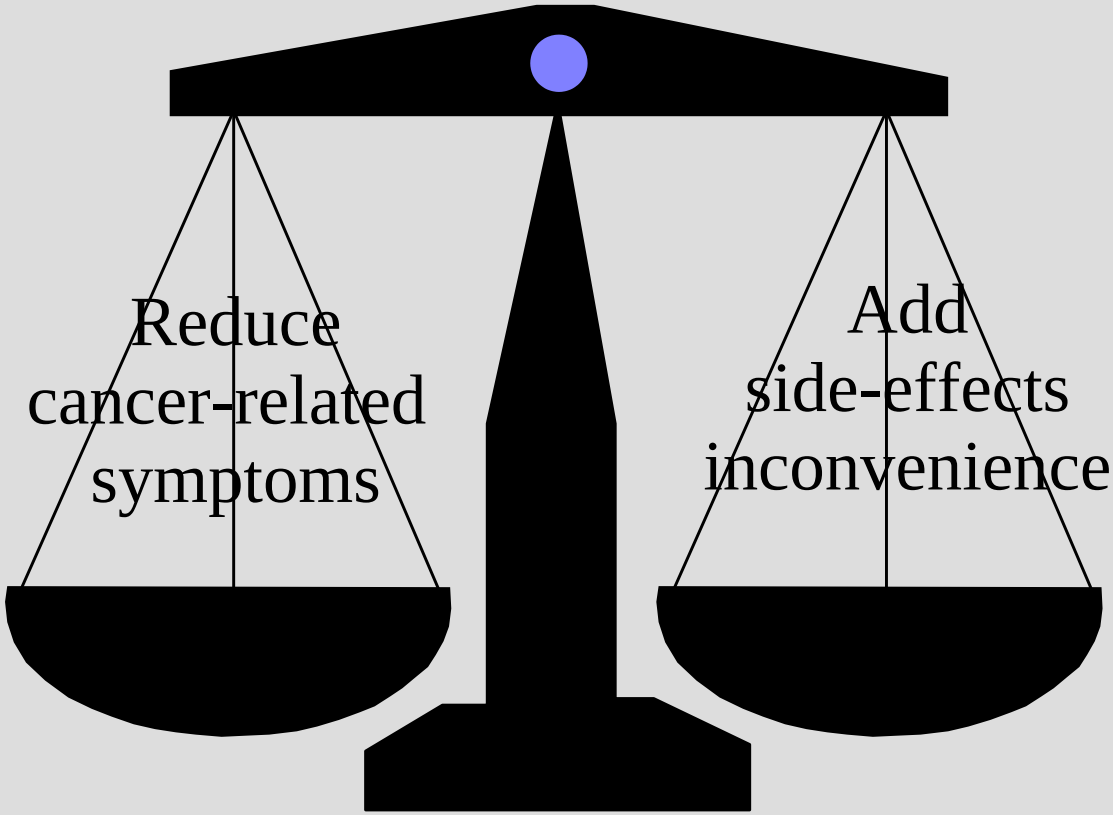
# Ex. 2: Advanced breast cancer (ABC)

# Goals of treatment

The goals of treatment in advanced breast cancer are palliative, ie

To improve length and quality of life without realistic hope of cure

# Effects of chemotherapy on quality of life



# What do we know about palliative chemotherapy in advance breast cancer ?

Stockler, Wilcken, Ghersi, Simes.

The management of advanced breast cancer:

systematic reviews of randomised controlled trials regarding the use of cytotoxic chemotherapy and endocrine therapy.

NHMRC National Breast Cancer Centre 1996

12 questions

65 RCTs

90 comparisons

# Systematic reviews of CT for ABC

Stockler & Wilcken. Cancer Treat Rev 2000

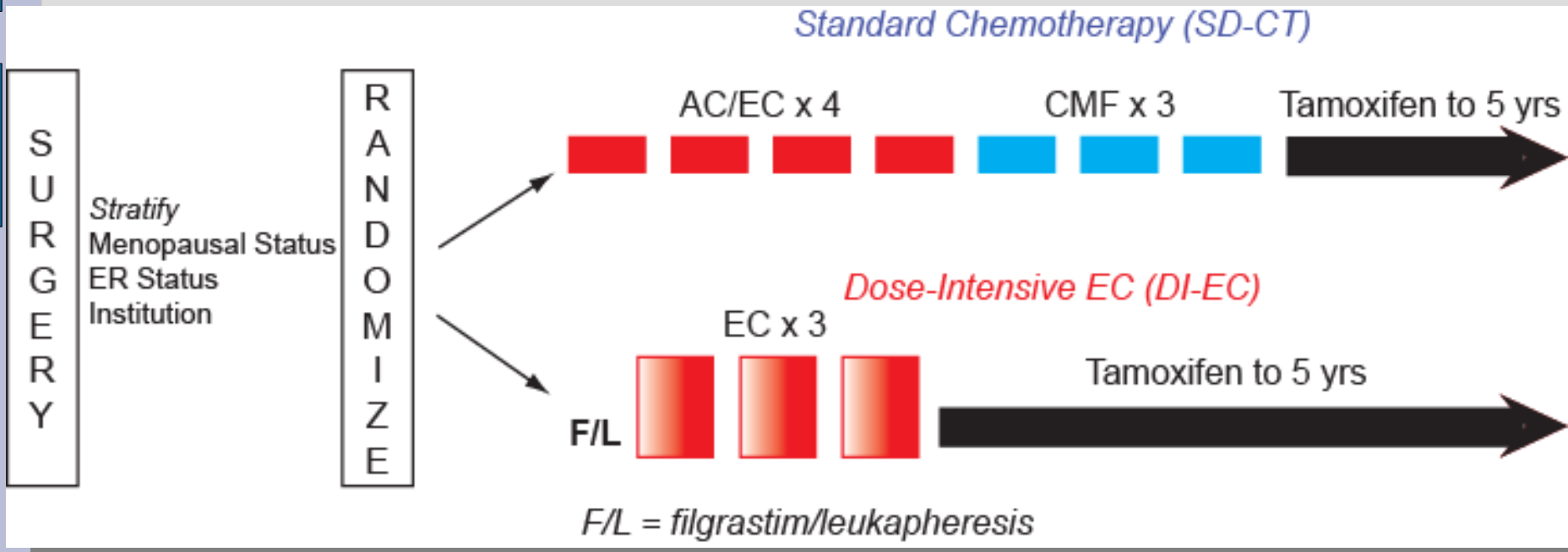
100s of RCTs comparing recipes

no RCTs of chemotherapy vs control

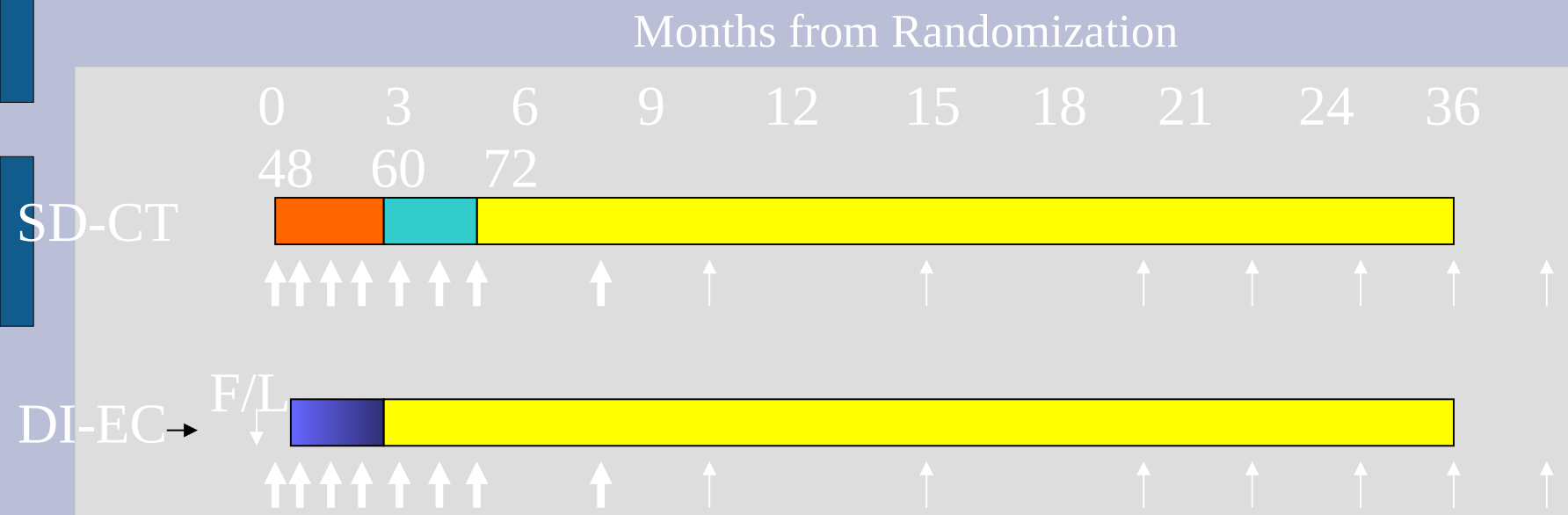
better survival and quality of life with

- more rather than fewer cycles CT Coates ANZBCTG
- standard rather than 1/2 doses of CT Tannock

# IBCSG Trial 15-95



# QL Schema




SD-CT = Standard Dose Chemotherapy

DI-EC = Dose-Intensive Epirubicin and Cyclophosphamide

Tamoxifen

QL Assessment: Core & Module

QL Assessment: Core

F/L Filgrastim/Leukapheresis

# QL Endpoints

| Core Form | Module |
| --- | --- |
| Physical Well-Being | Hair Loss |
| PACIS (Coping) | Numbness |
| Mood | Thought of Actually Having Treatment |
| Appetite | Loss of Sexual Interest/Ability |
| Tiredness | Sore Mouth |
| Nausea/Vomiting | Pain |
| Hot Flushes | Bothered by Treatment Related Difficulties |
| Social Support | Performing Daily Activities |
| Arm Movement | |
| Subjective Health Estimation (SHE) | |

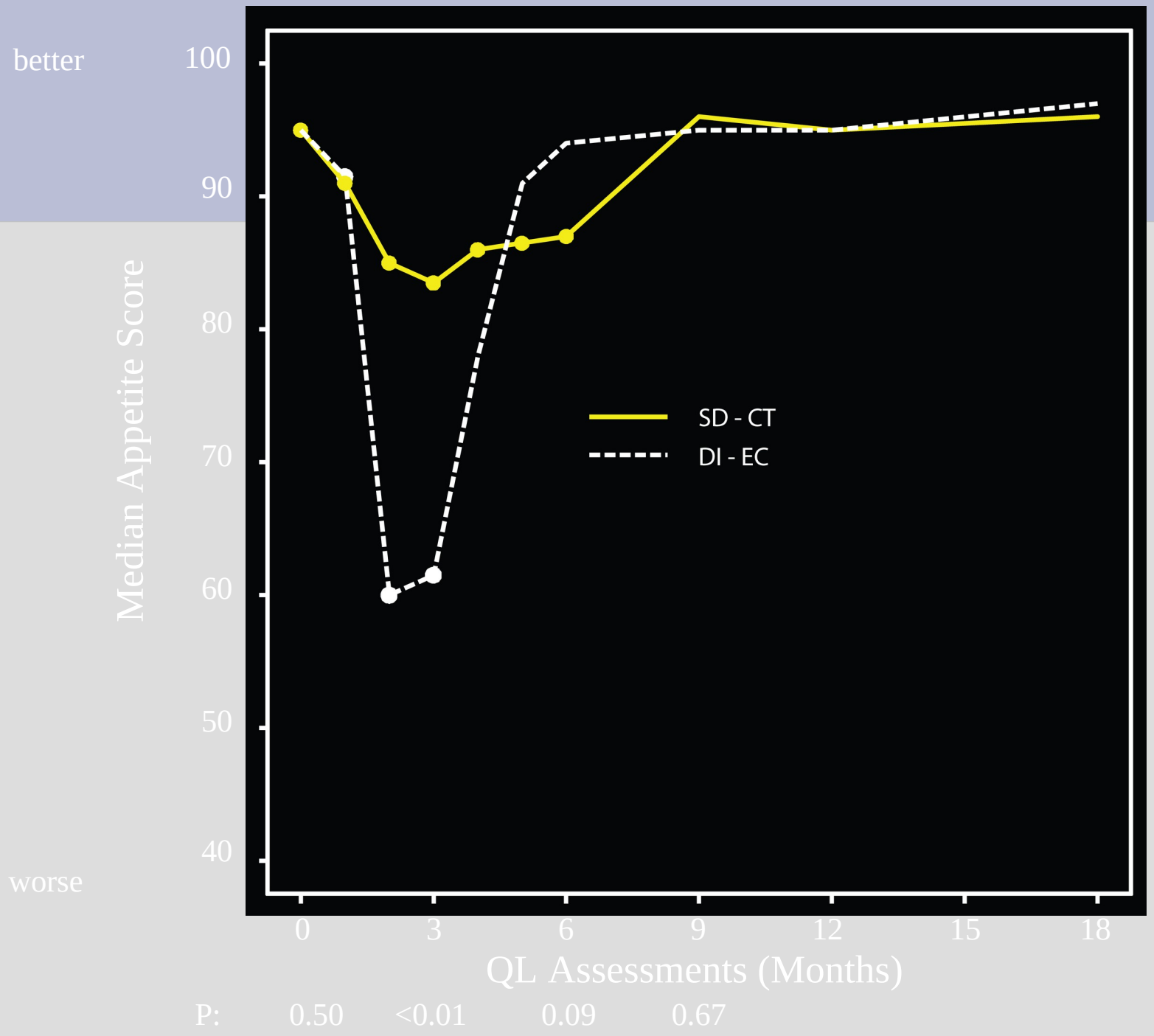
# QL Patient Population

*243 Analyzable Patients*

## QL Form Submission Rates

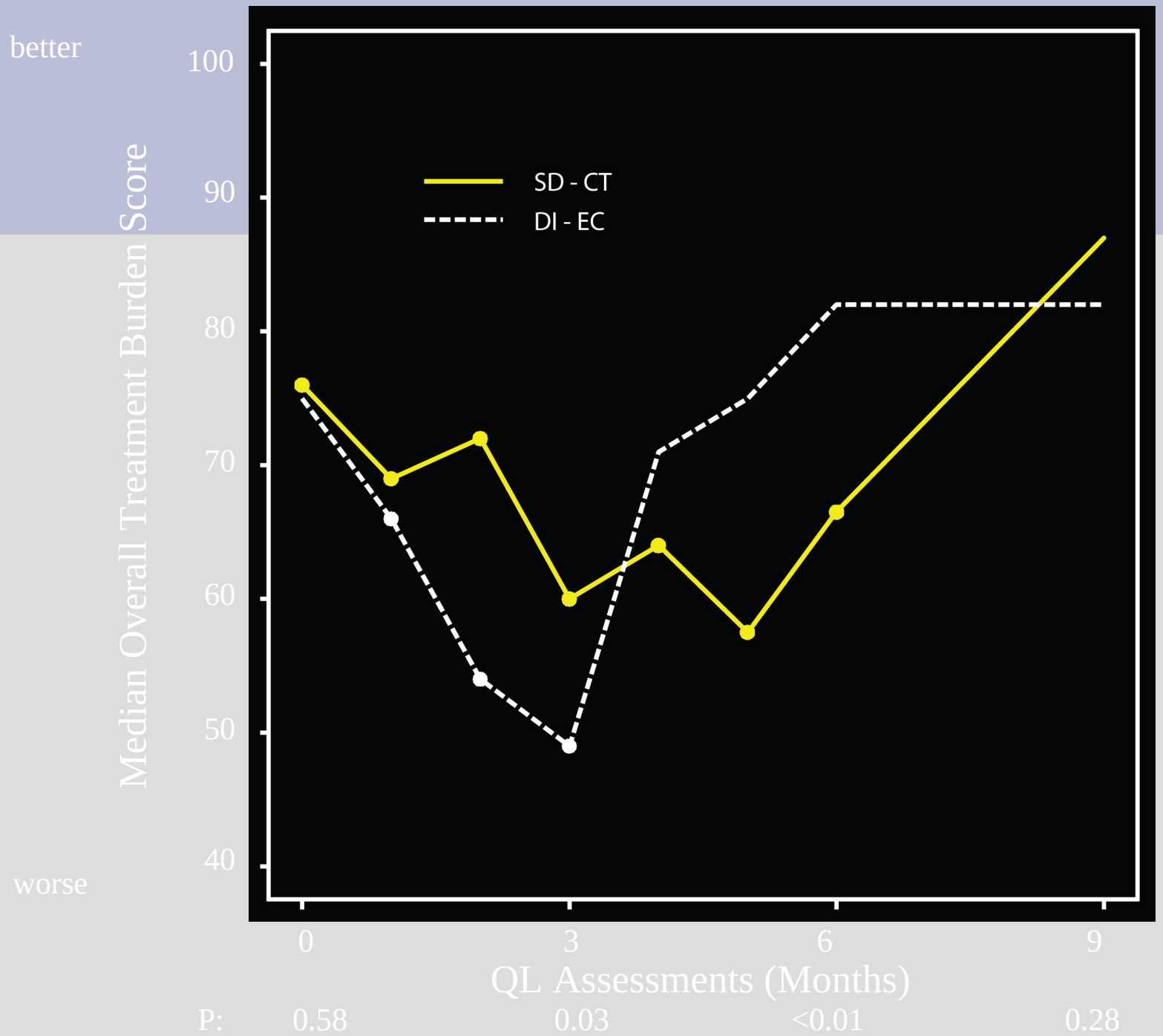
| | |
|---|---|
| Baseline: | 78% (N = 193) |
| Month 3: | 82% |
| Month 6: | 78% |
| Month 9: | 84% |
| Month 12: | 82% |
| Month 18: | 85% (N = 209) |

# Appetite

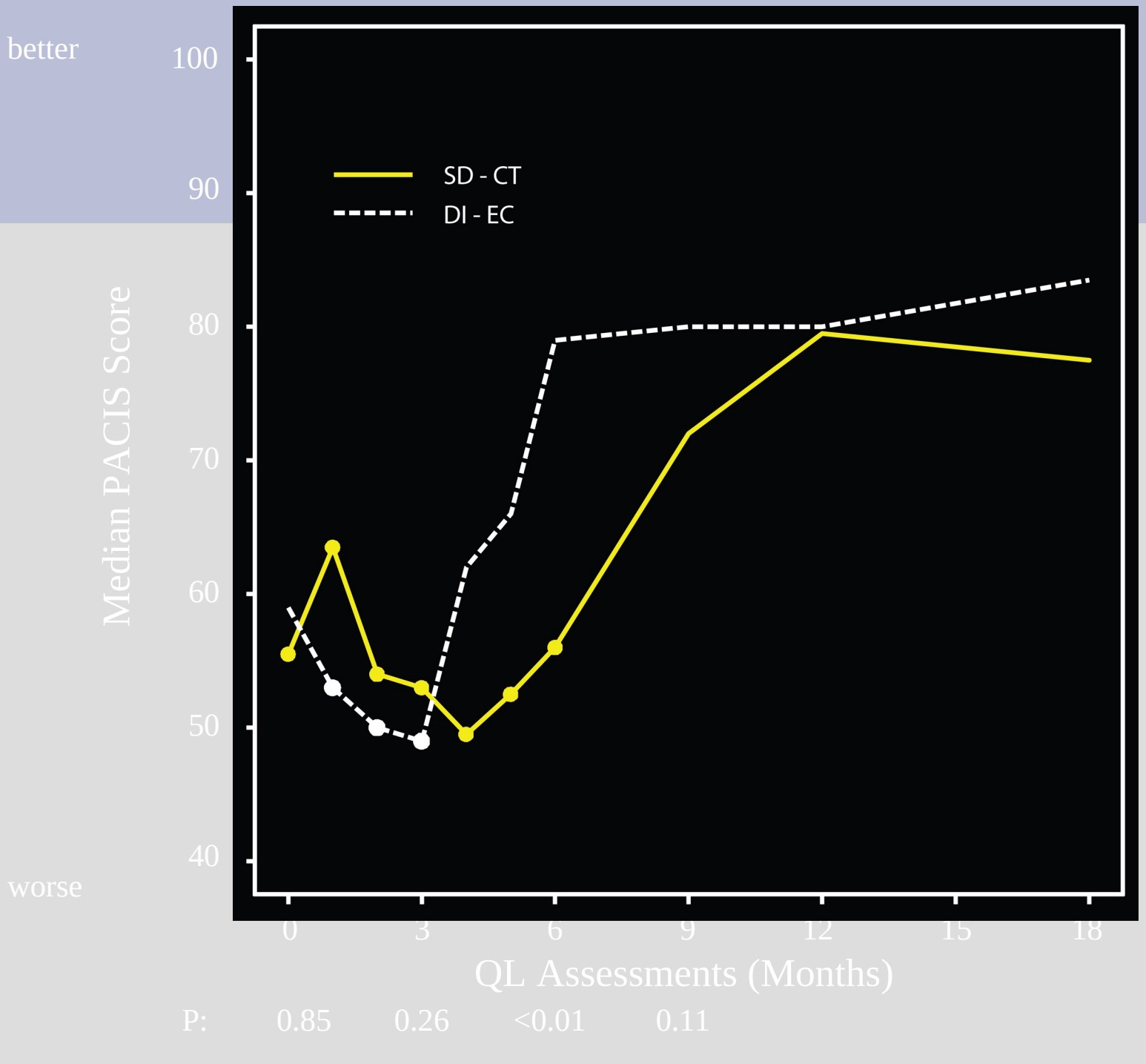



P: 0.50 <0.01 0.09 0.67

# Treatment Burden



# PACIS (Coping)



# *Q-TWiST*

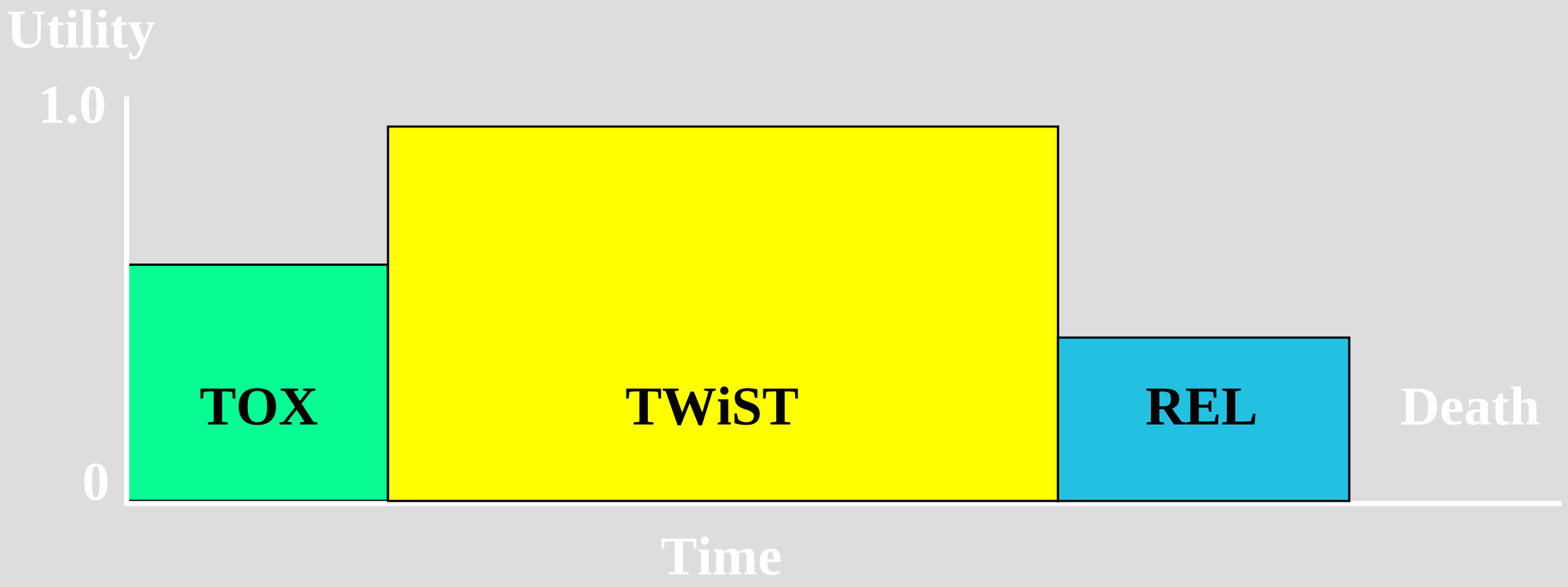
*Quality-adjusted Time Without Symptoms or Toxicity*

Incorporate QL information into survival analysis ?

Evaluate “trade offs” in clinical trials

# *Q-TWiST*

*Quality-adjusted Time Without Symptoms or Toxicity*




$$\text{Q-TWiST} = u_{TOX} \times \text{TOX} + \text{TWiST} + u_{REL} \times \text{REL}$$

# Lumley et al Fig.3, Tbl. I

## MEG 8901 trial in advanced cancer patients

– double blind, placebo controlled, n =240

3 regimens of megestrol acetate usage (“placebo”, “low dose”, “high dose”)

*weight loss, nutrition,* 5 P&B LASA lines to measure QoL.

- GLQ uniscale

Test retest reliabilities of these scales measured in *Coates, Glaziou and McNeil*

Demonstrates *improved precision*

# Lumley et al

## ANZ 8614 trial

Mitozantrone (Mz) vs CMFP chemotherapy

better QoL with Mz (if similar survival)? n=391

five LASA GLQ-8 + five (P&B) LASA scales

2 questions in common from the two instruments (on appetite, nausea-vomiting) omitted from GLQ-8

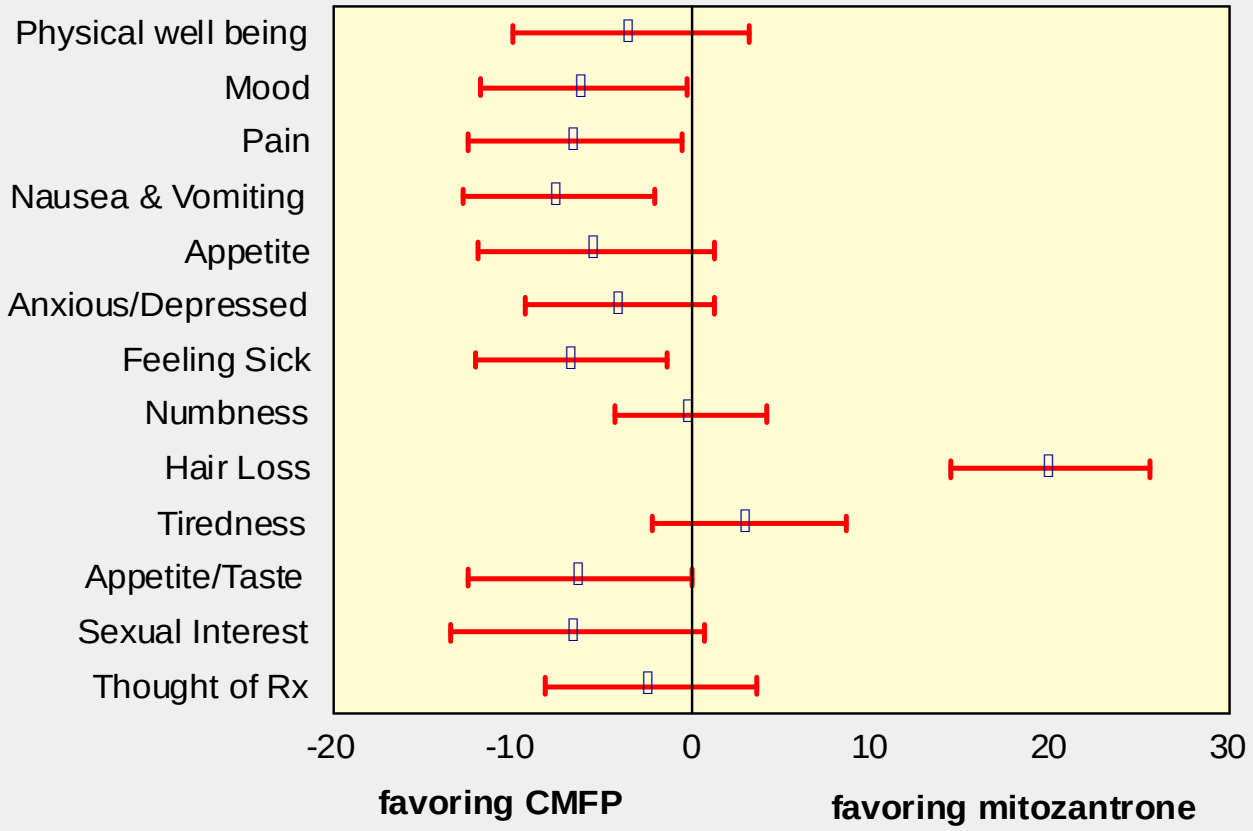
the scale “Sexual interest and ability” omitted (low response rate)

*Spitzer* LASA uniscale measurement of overall QoL

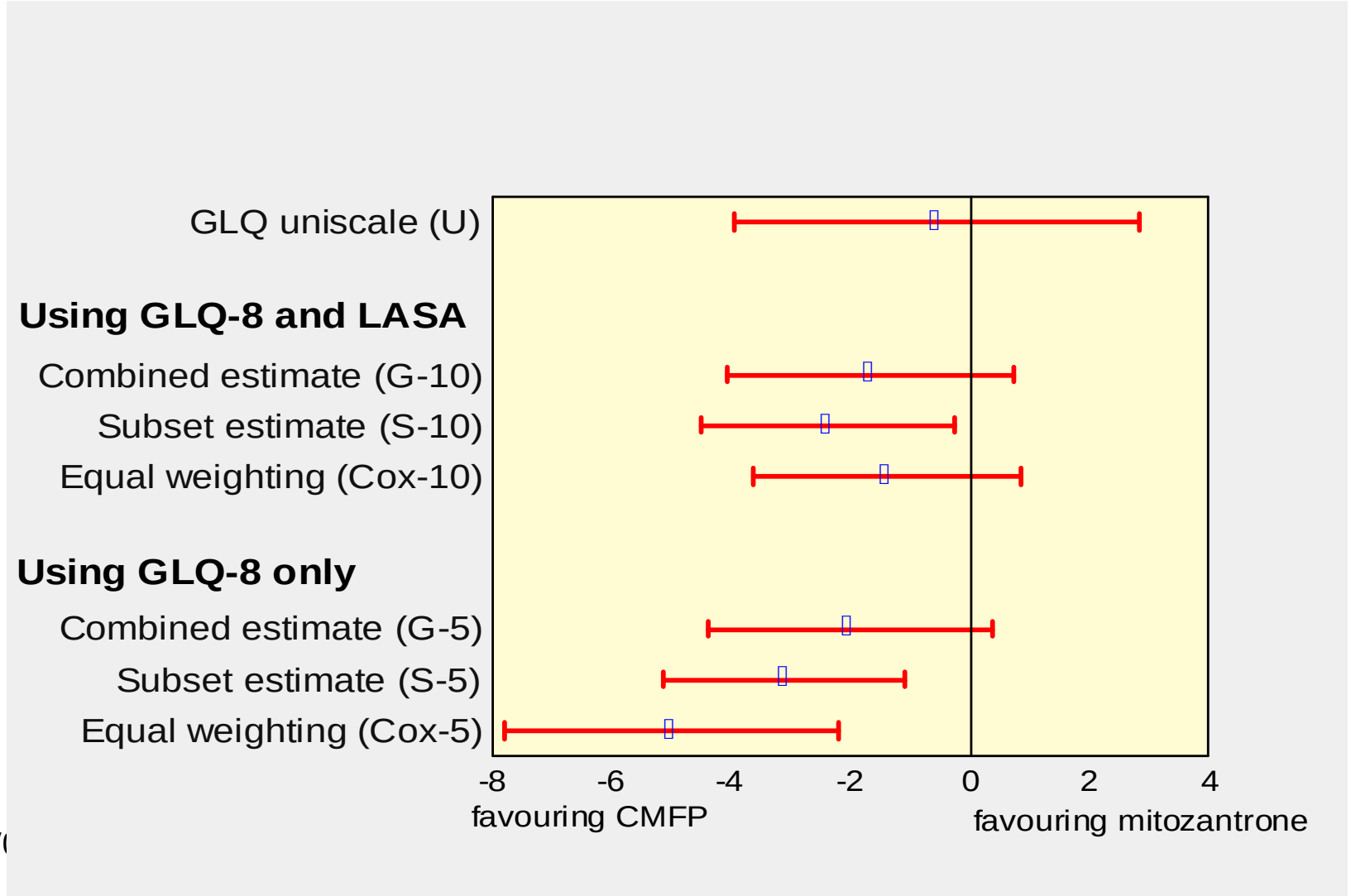
Test retest reliabilities of these scales measured in *Coates, Glaziou, McNeil (1990)*

GLQ-8 around 0.80+, LASA around 0.70+

# ANZ8644 Treatment comparison: QL battery components



# ANZ8644 Treatment comparison: overall QL indices



# Utility and QoL

Methodology for valuing quanity and quality of life

How do we measure the utility of present symptoms or of a health state?

How do we determine which components of QoL are important to an individual patient?

Review two recent papers:

- Lumley, Simes, Gebski, Hudson (2001)
- Martin Glasziou, Simes and Lumley (2000)

# Ex 3: LIPID trial

Background

- Long term intervention with Pravastatin, a cholesterol lowering drug (Simes, NEJM, 1998)
- randomized n=9014 patients with CHD and average cholesterol levels
  - powered to detect reduced mortality outcomes
- Pravastatin in Lipid cohort extension (10 yrs f/u)
  - safety and cost-effectiveness
  - Myocardial infarction (MI) and other CVD events

# Ex 1: LIPID trial (cont.)

Hypothesis: statin will reduce hazards in
- MI incidence and its severity;
- strokes and their severity;
- revascularisation procedures (stent, CABG)
  - health state following revasc
- hospitalisations and associated costs

Analysis of multivariate outcomes?

How do we determine the utility of a health state?

# Value and utility scales (Martin, Lumley, Simes 1996)

Value scales reflect preference for certain or sure outcomes, whereas utility scales reflect strength of preference for uncertain outcomes.

Two broad strategies to combine outcomes, decide trade-offs in QoL:

ask individuals to make a trade-off evaluation;

combine QoL data to form a summary reflecting typical or group preference.

# Time trade-off

If you consider yourself in less than full health, please help us determine how important quality of life versus length of life is to you by answering the following hypothetical question.

Imagine a friend who is expected to live for 15 years with the same quality of life as you have now. Suppose treatment could restore them to full health, but would shorten their life. At most, how much time would you advise giving up out of 15 years?

I would advise giving up at most ____ years and/or _____ months in order to return to full health.

## Time trade offs:

*Top.* Number of years good health judged equivalent to 15 yrs, 10 yrs, 5 yrs survival, with the continuation of present symptoms.

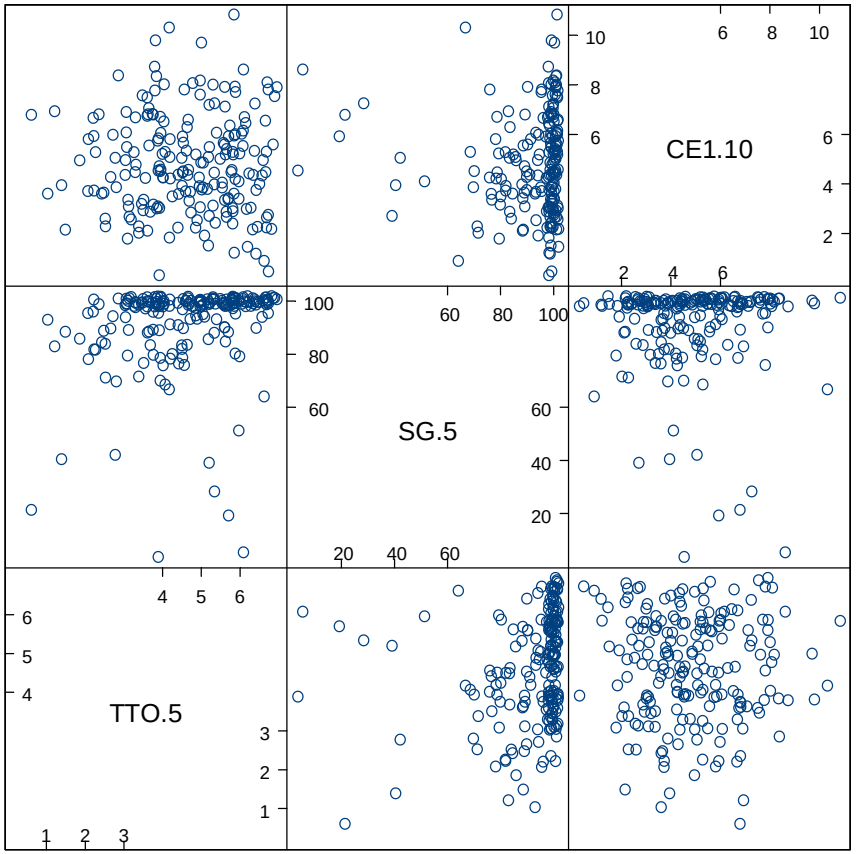
*Bottom.* Number of years of life (as a proportion of the total survival frame) that would be sacrificed for good health.

TTO proportions appear independent of time frame. Any effects small compared to variability between subjects.

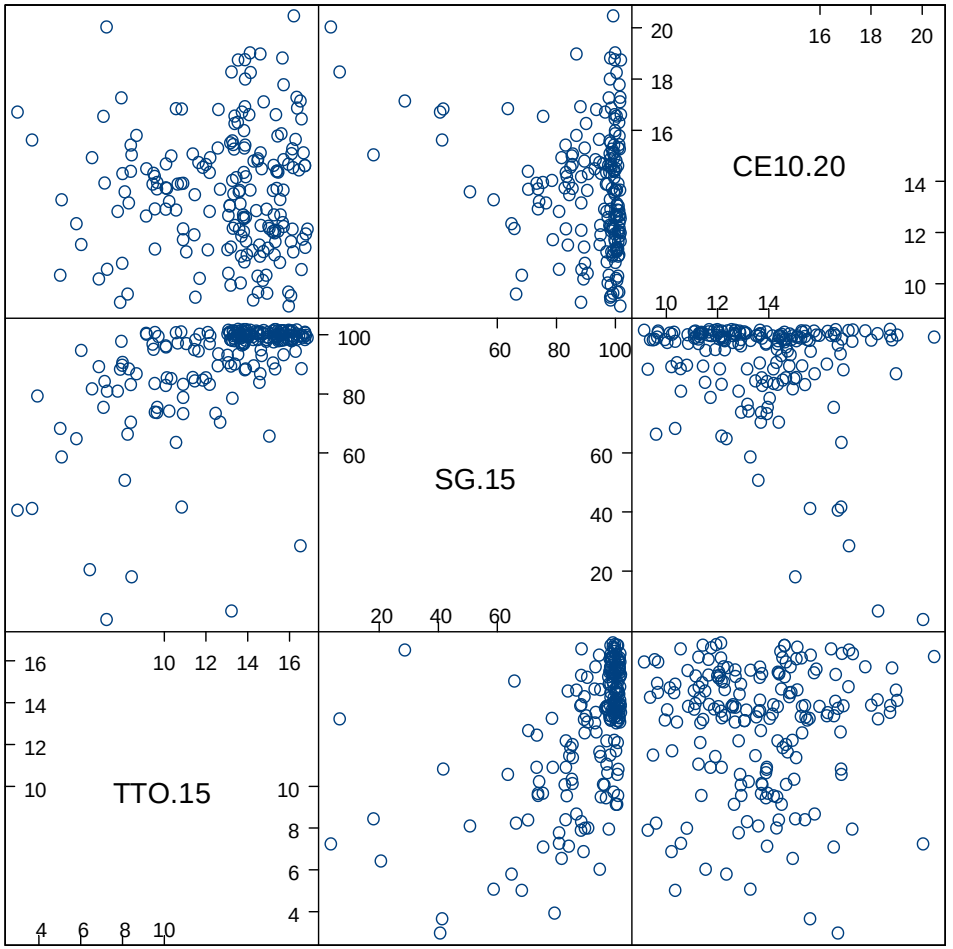
Standard gamble: For the specified survival period, what risk would you accept for a miracle worker with outcome full health (or death) to treat present QoL/ symptoms.

A risk of death equivalent to present QoL is measured.

Standard gamble judgements appear independent of time frame.




Relationships between TTO, SG and CE, early time frames




Relationship for latest time frame

How do we determine which components of QoL are important to an individual patient?

A disadvantage of single-item QoL assessments is that they provide no descriptive information on the components comprising quality of life.

# LASA scale measurement of QoL

# Measuring QoL in Cancer: Scales

Priestman and Baum (1976) introduced use of Linear Analogue Self-Assessment (LASA) scales.

In advanced breast cancer the linear scales recorded responses on
physical well-being,
mood,
pain,
nausea/vomiting,
appetite.

GLQ-8, LASA, chemotherapy toxicity, Coates, Glaziou, McNeil, 1990

QLQ-C30 30 items, cancer specific, multi-dimensional, EORTC

Spitzer 5 items, scored 1-5, Spitzer et al, 1981

Physician rating – incomplete data bias, use these scales?

## (A). L.A.S.A SCALE

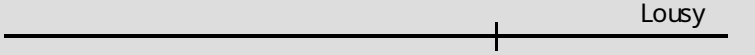
Please mark the scales with a "|" according to how you rate the following aspects overall, for the entire period since your last clinical assessment.

**Example:**

PHYSICAL WELL-BEING:
Good — Lousy

TIREDNESS:
None — A lot

MOOD:
Happy — Miserable



This would indicate considerable tiredness since your last assessment.

PAIN:
None — Severe

NAUSEA & VOMITING:
None — Uncontrollable

APPETITE:
Good — None

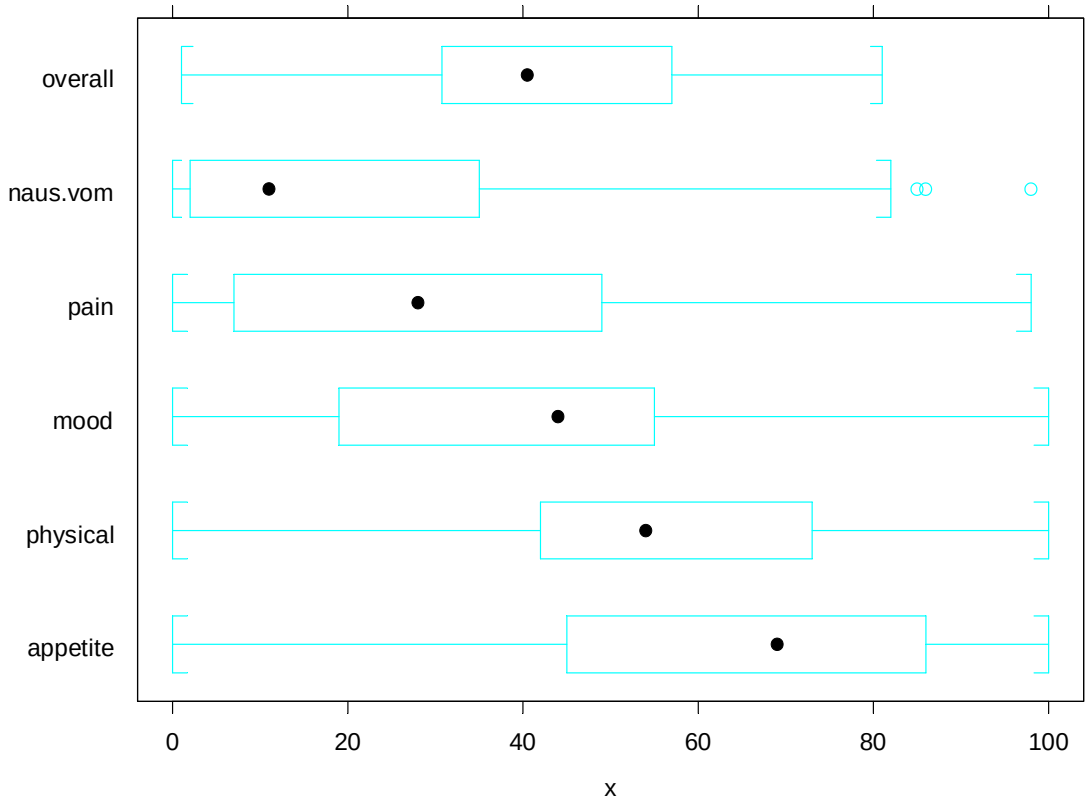
**(B). OVERALL QUALITY OF LIFE (Explanation Below)**

OVERALL LIFE QUALITY

Best Possible — Worst Possible

Quality of life means different things to different people. One person may think physical comfort is most important, and would rate quality of life mainly on the presence or absence of pain. Another person may think that the ability to listen to music is more important than pain, and would rate deafness as a major factor, while others would place more importance on their ability to function normally and independently, or on the presence of supporting relatives or friends.

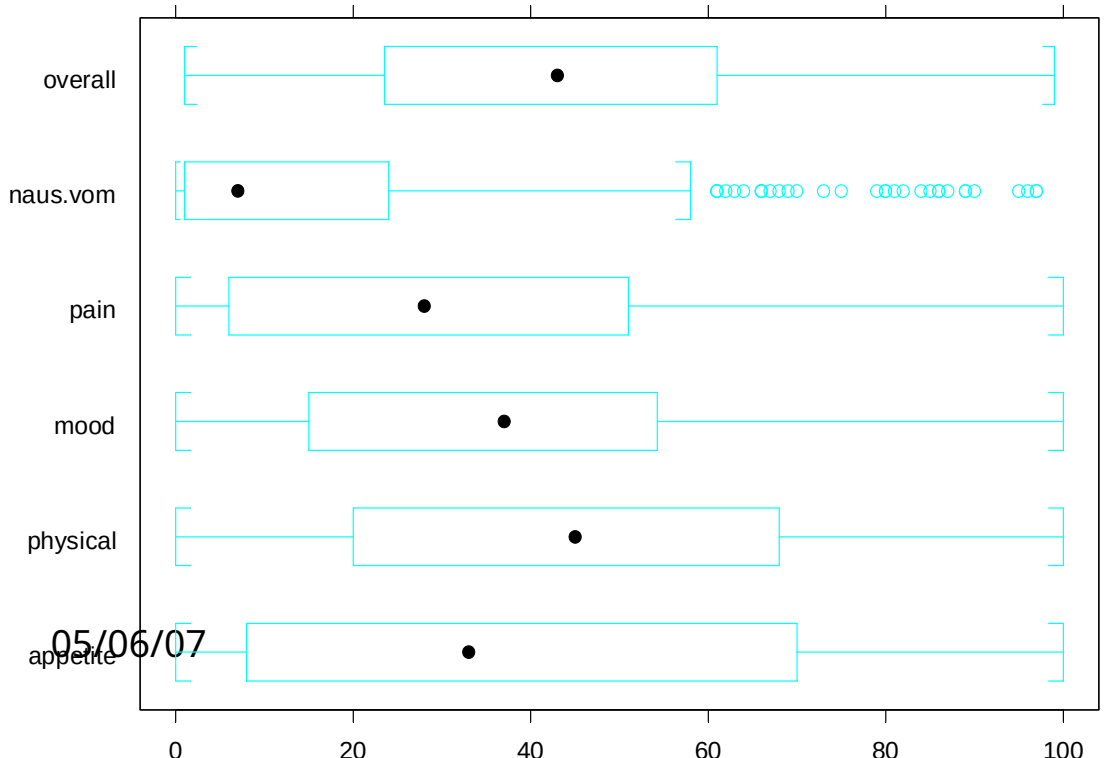
Including all things ~~that are important for you, whether or not they are on the list, please~~ place a mark to indicate your OVERALL quality of life since your last appointment.




ANZ 8614 characteristics:

QoL components and overall:

Baseline




Weeks 1-13

# Comparison of weights in different studies

Table 3: Comparison of weights for the 5 Priestman & Baum LASA scales

| | Weight for | |
|---|---|---|
| | MEG8901 | ANZ8614 |
| physical well-being | 0.332 | 0.238 |
| mood | 0.287 | 0.168 |
| pain | 0.019 | 0.094 |
| nausea & vomiting | 0.008 | 0.116 |
| appetite | 0.044 | 0.064 |

MEG8901 other cancer patients

ANZ8614 advanced breast cancer patients