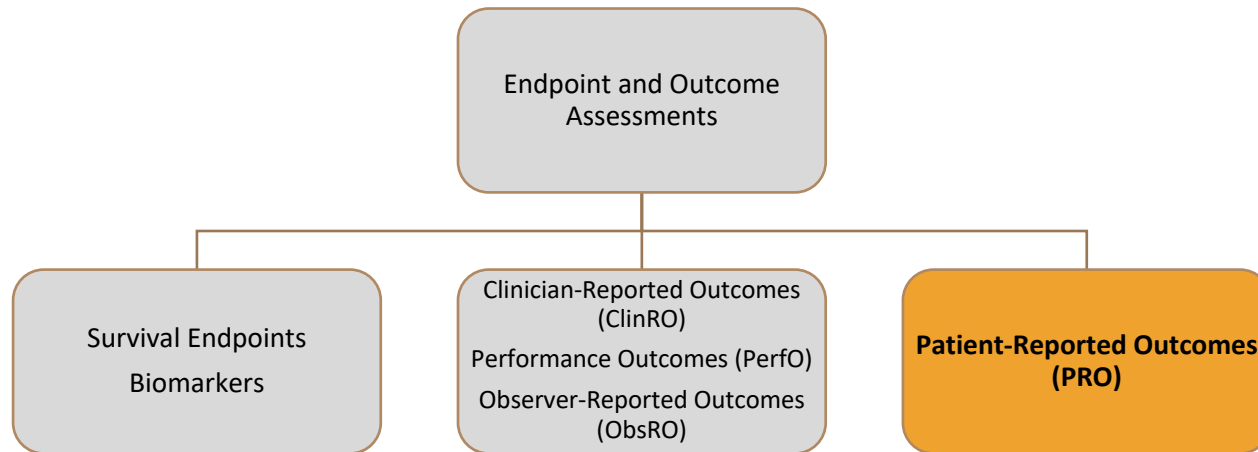


# Going Pro with PROs: Implementation and Analysis of Patient Reported Outcomes

Shilpakala Vasudevan

# Patient Reported Outcomes (PROs)

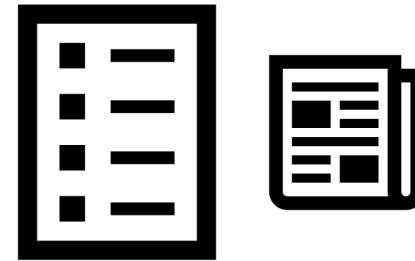


- Directly from the patient
- No interpretation from anyone else
- Measured from patient's perspective



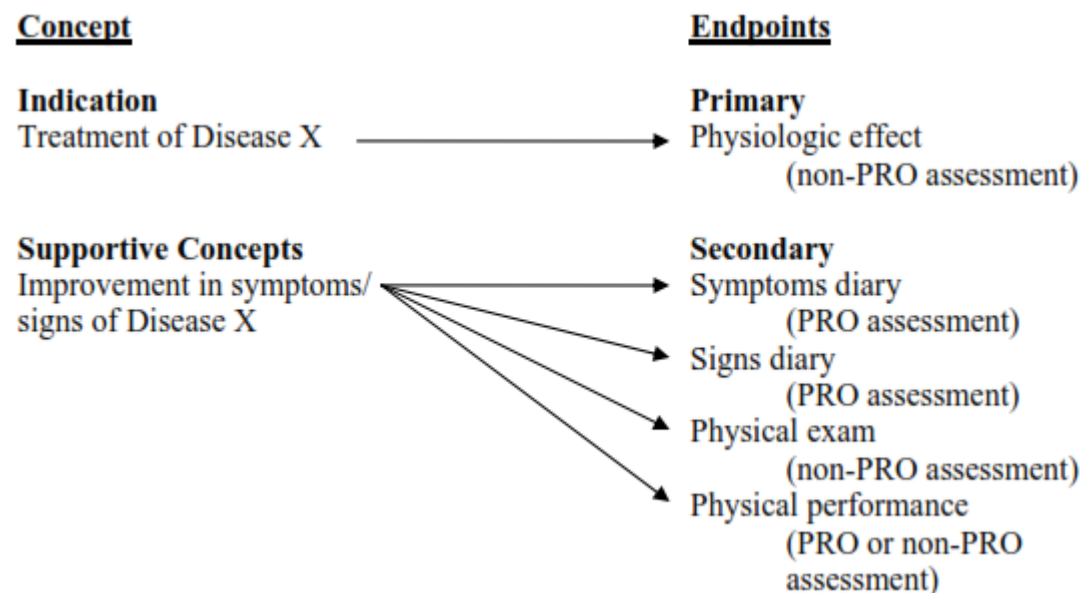
# PRO instruments

- Patient Reported Outcome Measures (PROMs)
- Questionnaires + information/documentation
- Need to have:
  - Validity
  - Reliability
  - Ability to detect change
- Modes of reporting:
  - Electronic based
  - Telephone based
  - Paper based

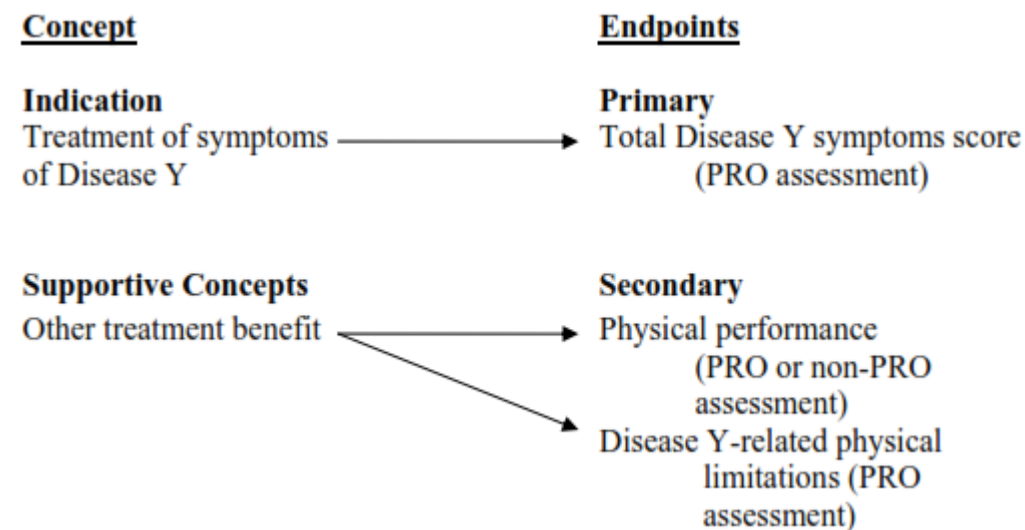


# Endpoint model

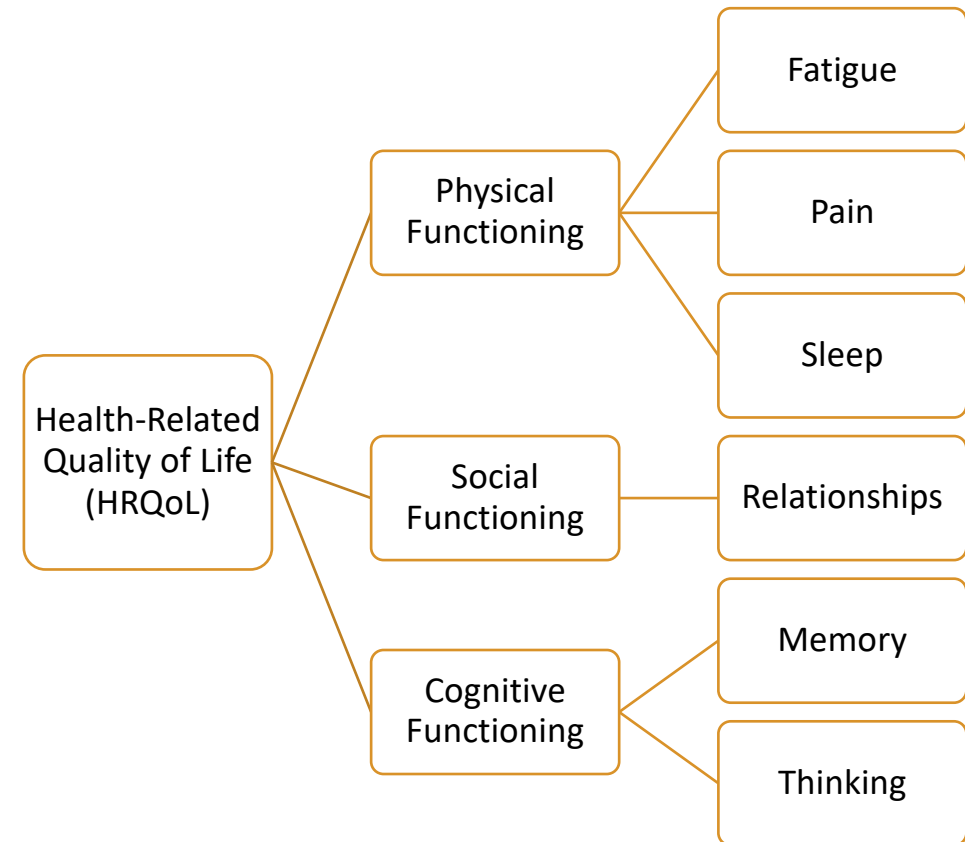
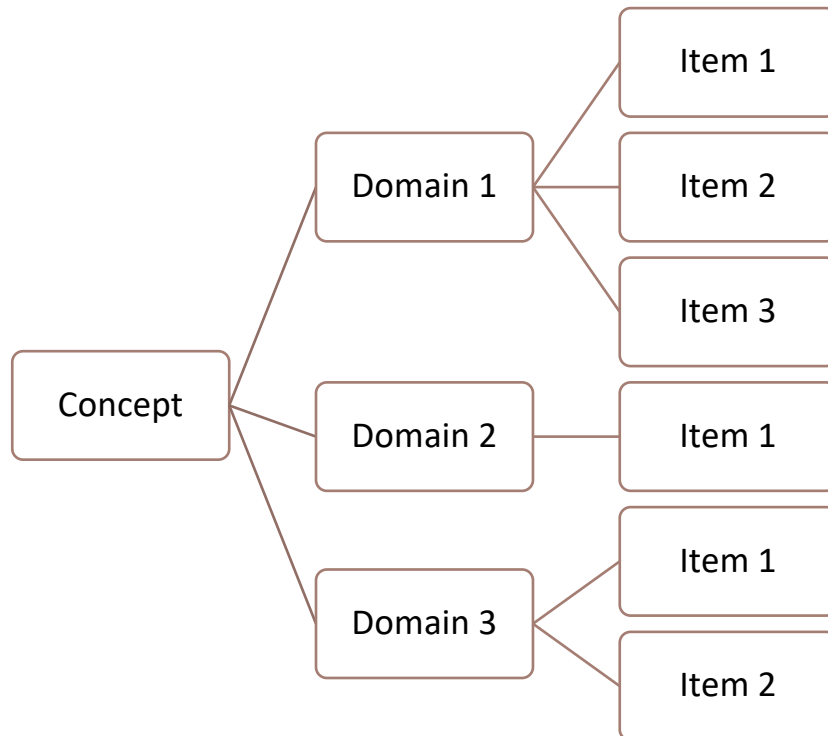
## Secondary endpoints



## Primary and Secondary endpoints



# Conceptual Framework





# Responses in Questionnaire

What is the severity of your pain?

Visual Analog Scale (VAS): 0 \_\_\_\_\_ 100

What is the severity of your pain?

Anchored or Categorized VAS: 0 20 40 60 80 100

What is the severity of your pain?

Likert Scale: ☐ No pain ☐ Moderate pain ☐ Extreme pain

Rating Scale:

How do you rate your pain on scale of 1 (low) to 5 (high)?

☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5

Pictorial Scale:

Rate the severity of your pain

No pain Moderate Extreme

Checklist:

Is your pain severe?

☐ Yes ☐ No

# Questionnaires

## Generic Questionnaires

- EuroQol-5D (EQ-5D)
- 36-Item Short Form Health Survey (SF-36)
- European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30)
- e-Health Impact Questionnaire (eHIQ)
- Health Utilities Index (HUI)

## Disease specific questionnaires

- Musculoskeletal Health Questionnaire (MSK-HQ)
- The Nutrition and Dietetic Patient Outcomes Questionnaires (NDPOQ)
- Diabetes Health Profile (DHP)
- The Myocardial Infarction Dimensional Assessment Scale (MIDAS)
- Functional Assessment of Cancer Therapy (FACT)
- Brief Pain Inventory (BPI)
- Rheumatoid Arthritis Quality of Life (RAQoL)

# EXAMPLE 1: SINGLE ITEM QUESTIONNAIRE

## Eastern Cooperative Oncology Group (ECOG)

### ECOG PERFORMANCE STATUS **QSCAT=ECOG**

#### Grade ECOG

- ☐ 0 Fully active, able to carry on all pre-disease performance without restriction
- ☐ 1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
- ☐ 2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
- ☐ 3 Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
- ☐ 4 Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
- ☐ 5 Dead — **QSORRES when QSTESTCD = ECOG101**

**QSSTRESC/QSSTRESN**



# EXAMPLE 1: SINGLE ITEM QUESTIONNAIRE

## Eastern Cooperative Oncology Group (ECOG)

| usubjid | trt01p      | parcat | Param                   | paramcd | avisit           | adt       | aval | avalc                                  |
|---------|-------------|--------|-------------------------|---------|------------------|-----------|------|----------------------------------------|
| 01-1001 | Treatment A | ECOG   | ECOG Performance Status | ECOG101 | Baseline         | 02JUN2016 | 2    | Ambulatory and capable of all selfcare |
| 01-1001 | Treatment A | ECOG   | ECOG Performance Status | ECOG101 | End of Treatment | 16MAY2017 | 4    | Completely disabled                    |
| 01-1002 | Treatment B | ECOG   | ECOG Performance Status | ECOG101 | Baseline         | 17SEP2012 | 3    | Capable of only limited selfcare       |
| 01-1002 | Treatment B | ECOG   | ECOG Performance Status | ECOG101 | End of Treatment | 09MAY2014 | 5    | Dead                                   |

Summary of ECOG Performance Status, pre and post chemotherapy

|              | Treatment A<br>(N=100) |                    | Treatment B<br>(N=98) |                    | Total<br>(N=198)  |                    |
|--------------|------------------------|--------------------|-----------------------|--------------------|-------------------|--------------------|
|              | Pre-chem<br>n (%)      | Post-chem<br>n (%) | Pre-chem<br>n (%)     | Post-chem<br>n (%) | Pre-chem<br>n (%) | Post-chem<br>n (%) |
| 0            | 0                      | 0                  | 1 ( 1.0)              | 0                  | 1 ( 0.5)          | 0                  |
| 1            | 15 (15.0)              | 10 (10.0)          | 14 (14.3)             | 11 (11.2)          | 29 (14.6)         | 21 (10.6)          |
| 2            | 22 (22.0)              | 19 (19.0)          | 23 (23.5)             | 20 (20.4)          | 45 (22.7)         | 39 (19.7)          |
| 3            | 29 (29.0)              | 31 (31.0)          | 33 (33.7)             | 25 (25.5)          | 62 (31.3)         | 56 (28.3)          |
| 4            | 24 (24.0)              | 27 (27.0)          | 21 (21.4)             | 34 (34.7)          | 45 (22.7)         | 61 (30.8)          |
| 5            | 0                      | 2 ( 2.0)           | 0                     | 1 ( 1.0)           | 0                 | 3 ( 1.5)           |
| Not reported | 10 (10.0)              | 11 (11.0)          | 8 ( 8.2)              | 9 ( 9.2)           | 18 ( 9.1)         | 20 (10.1)          |



## EXAMPLE 2: MULTIPLE ITEM QUESTIONNAIRE

### Fatigue Severity Scale (FSS)

#### Fatigue Severity Scale (FSS)

**QSCAT=FSS**

Please circle the number that indicates your degree of agreement with each statement below, where 1=strongly disagree and 7=strongly agree.

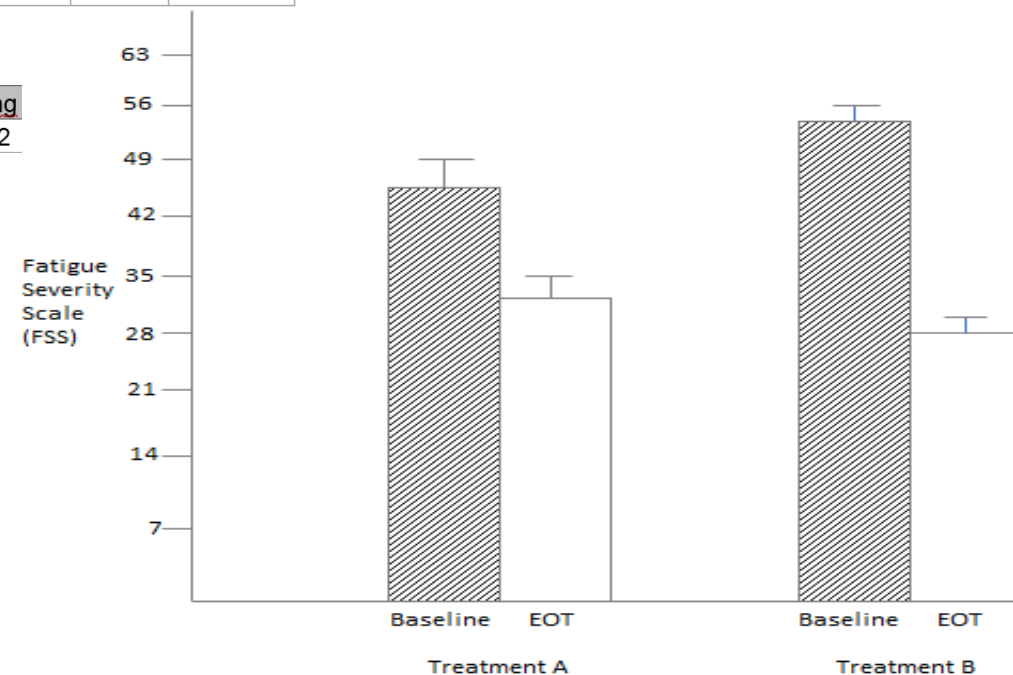
|                                                                              |                         |                   |   |                |                               |   |   |   |
|------------------------------------------------------------------------------|-------------------------|-------------------|---|----------------|-------------------------------|---|---|---|
|                                                                              |                         | Strongly Disagree |   | Strongly Agree |                               |   |   |   |
|                                                                              | <b>QSORRES</b>          |                   |   |                | <b>QSSTRESC/<br/>QSSTRESN</b> |   |   |   |
| 1. My motivation is lower when I am fatigued.                                | <b>QSTESTCD=FSS0101</b> | 1                 | 2 | 3              | 4                             | 5 | 6 | 7 |
| 2. Exercise brings on my fatigue.                                            | <b>QSTESTCD=FSS0102</b> | 1                 | 2 | 3              | 4                             | 5 | 6 | 7 |
| 3. I am easily fatigued.                                                     | <b>QSTESTCD=FSS0103</b> | 1                 | 2 | 3              | 4                             | 5 | 6 | 7 |
| 4. Fatigue interferes with my physical functioning.                          | <b>QSTESTCD=FSS0104</b> | 1                 | 2 | 3              | 4                             | 5 | 6 | 7 |
| 5. Fatigue causes frequent problems for me.                                  | <b>QSTESTCD=FSS0105</b> | 1                 | 2 | 3              | 4                             | 5 | 6 | 7 |
| 6. My fatigue prevents sustained physical functioning.                       | <b>QSTESTCD=FSS0106</b> | 1                 | 2 | 3              | 4                             | 5 | 6 | 7 |
| 7. Fatigue interferes with carrying out certain duties and responsibilities. | <b>QSTESTCD=FSS0107</b> | 1                 | 2 | 3              | 4                             | 5 | 6 | 7 |
| 8. Fatigue is among my three most disabling symptoms.                        | <b>QSTESTCD=FSS0108</b> | 1                 | 2 | 3              | 4                             | 5 | 6 | 7 |
| 9. Fatigue interferes with my work, family, or social life.                  | <b>QSTESTCD=FSS0109</b> | 1                 | 2 | 3              | 4                             | 5 | 6 | 7 |

## EXAMPLE 2: MULTIPLE ITEM QUESTIONNAIRE

### Fatigue Severity Scale (FSS)

| usubjid | trt01p      | parcat | param      | paramcd | avisit           | base | aval | chg |
|---------|-------------|--------|------------|---------|------------------|------|------|-----|
| 02-1011 | Treatment A | FSS    | Motivation | FSS0101 | Baseline         | 6    | 6    |     |
| 02-1011 | Treatment A | FSS    | Motivation | FSS0101 | End of Treatment | 6    | 3    | 3   |
| 02-1011 | Treatment A | FSS    | Exercise   | FSS0102 | Baseline         | 4    | 4    |     |
| 02-1011 | Treatment A | FSS    | Exercise   | FSS0102 | End of Treatment | 4    | 3    | 1   |
| 02-1011 | Treatment A | FSS    | Fatigue    | FSS0103 | Baseline         | 5    | 5    |     |
| 02-1011 | Treatment A | FSS    | Fatigue    | FSS0103 | End of Treatment | 5    | 1    | 4   |

| usubjid | trt01p      | parcat | param                  | paramcd | avisit           | base | aval | chg |
|---------|-------------|--------|------------------------|---------|------------------|------|------|-----|
| 02-1011 | Treatment A | FSS    | Fatigue Severity Scale | FSS     | End of Treatment | 34   | 12   | 22  |



# EXAMPLE 3: MULTIPLE DOMAIN SINGLE ITEM QUESTIONNAIRE

## EuroQol-5 Dimension (EQ-5D)



Under each heading, please check the ONE box that best describes your health TODAY

**Mobility** QSORRES when QSCAT =EQ5D01

I have no problems in walking about ☐

I have some problems in walking about ☐

I am confined to bed ☐

**Self-Care** QSORRES when QSCAT =EQ5D02

I have no problems with self-care ☐

I have some problems washing or dressing myself ☐

I am unable to wash or dress myself ☐

**Usual Activities** (eg, work, study, housework, family or

leisure activities) QSORRES when QSCAT =EQ5D03

I have no problems with performing my usual activities ☐

I have some problems with performing my usual activities ☐

I am unable to perform my usual activities ☐

**Pain/Discomfort** QSORRES when QSCAT =EQ5D04

I have no pain or discomfort ☐

I have moderate pain or discomfort ☐

I have extreme pain or discomfort ☐

**Anxiety/Depression** QSORRES when QSCAT =EQ5D05

I am not anxious or depressed ☐

I am moderately anxious or depressed ☐

I am extremely anxious or depressed ☐

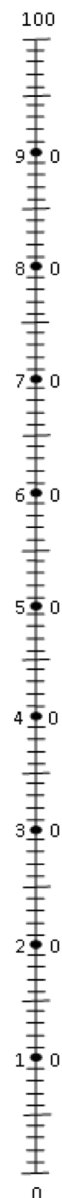
To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

QSTESTCD=EQ5D0106

**Your own  
health state**

Best imaginable  
health state



Worst  
imaginable  
health state



## EXAMPLE 3: MULTIPLE DOMAIN SINGLE ITEM QUESTIONNAIRE

### EuroQol-5 Dimension (EQ-5D)

| Domain             | Raw score | Response           | coefficient |
|--------------------|-----------|--------------------|-------------|
| Mobility           | 1         | No problems        |             |
|                    | 2         | Some problems      | -0.069      |
|                    | 3         | Confined to bed    | -0.314      |
| Self-Care          | 1         | No problems        |             |
|                    | 2         | Some problems      | -0.104      |
|                    | 3         | Unable             | -0.214      |
| Usual Activities   | 1         | No problems        |             |
|                    | 2         | Some problems      | -0.036      |
|                    | 3         | Unable             | -0.094      |
| Pain/Discomfort    | 1         | No pain            |             |
|                    | 2         | Moderate pain      | -0.123      |
|                    | 3         | Extreme pain       | -0.386      |
| Anxiety/Depression | 1         | Not anxious        |             |
|                    | 2         | Moderately anxious | -0.071      |
|                    | 3         | Extremely anxious  | -0.236      |

| usubjid | trt01p      | parcat | param              | paramcd  | aval | avalc             | coefficient |
|---------|-------------|--------|--------------------|----------|------|-------------------|-------------|
| 03-1111 | Treatment A | EQ5D01 | Mobility           | EQ5D0101 | 2    | Some problems     | -0.069      |
| 03-1111 | Treatment A | EQ5D02 | Self-Care          | EQ5D0201 | 2    | Some problems     | -0.104      |
| 03-1111 | Treatment A | EQ5D03 | Usual Activities   | EQ5D0301 | 1    | No problems       |             |
| 03-1111 | Treatment A | EQ5D04 | Pain/Discomfort    | EQ5D0401 | 2    | Moderate pain     | -0.123      |
| 03-1111 | Treatment A | EQ5D05 | Anxiety/Depression | EQ5D0501 | 3    | Extremely anxious | -0.236      |

EQ-5D Health State = 1 – (Coefficient1 + Coefficient2 + Coefficient3 + Coefficient4 + Coefficient5)

$$\text{EQ-5D Health State} = 1 - (0.069 + 0.104 + 0 + 0.123 + 0.236) = 0.468$$

| usubjid | trt01p      | parcat | param        | paramcd  | aval  |
|---------|-------------|--------|--------------|----------|-------|
| 03-1111 | Treatment A | EQ5D   | Health State | EQ5DHLST | 0.468 |



# EXAMPLE 3: MULTIPLE DOMAIN SINGLE ITEM QUESTIONNAIRE

## EuroQol-5 Dimension (EQ-5D)

```
PROC TTEST data=adqs;
  by avisit;
  class trt01p;
  var aval;
run;
```

EQ-5D – Observed Means and Change from Baseline

|                         | Treatment A (N=100) |           |        |             | Treatment B (N= 98) |           |        |             | Treatment A – Treatment B |               |         |
|-------------------------|---------------------|-----------|--------|-------------|---------------------|-----------|--------|-------------|---------------------------|---------------|---------|
|                         | n                   | Mean(Std) | Median | 95% CI      | n                   | Mean(Std) | Median | 95% CI      | Mean                      | 95% CI        | P-Value |
| Mobility                |                     |           |        |             |                     |           |        |             |                           |               |         |
| Observed Value          |                     |           |        |             |                     |           |        |             |                           |               |         |
| Cycle 1 Day1 (Baseline) | 100                 | 0.67      | 0.63   | (0.60,0.74) | 98                  | 0.53      | 0.52   | (0.50,0.56) | -0.12                     | (-0.10,-0.14) | <0.001  |
| Cycle 2 Day1            | 97                  | 0.85      | 0.83   | (0.80,0.90) | 96                  | 0.65      | 0.64   | (0.62,0.68) | -0.17                     | (-0.12,-0.22) | <0.001  |

Note 1: P-values are based on 2-sample t-test

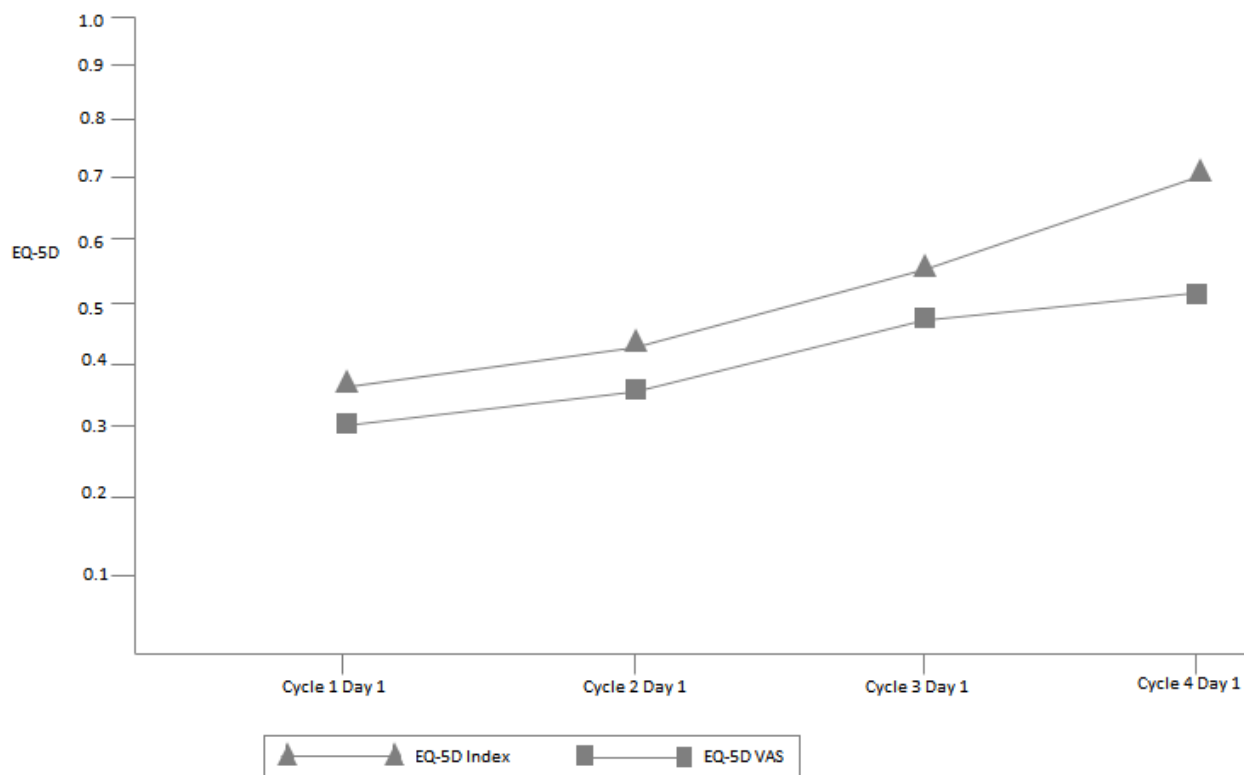
Note 2: Higher scores are associated with better health status and lower scores for worse health.

# EXAMPLE 3: MULTIPLE DOMAIN SINGLE ITEM QUESTIONNAIRE

## EuroQol-5 Dimension (EQ-5D)

### Comparison of EQ-5D Index and EQ-5D VAS/100

|             |    | Treatment A<br>(N=100) |              | Treatment B<br>(N=98) |              |
|-------------|----|------------------------|--------------|-----------------------|--------------|
|             |    | EQ-5D<br>Index         | EQ-5D<br>VAS | EQ-5D<br>Index        | EQ-5D<br>VAS |
| Mean        |    | 0.50                   | 0.48         | 0.69                  | 0.62         |
| SD          |    | 0.22                   | 0.20         | 0.20                  | 0.18         |
| Percentiles | 25 | 0.30                   | 0.33         | 0.55                  | 0.50         |
|             | 50 | 0.47                   | 0.50         | 0.69                  | 0.62         |
|             | 75 | 0.72                   | 0.64         | 0.78                  | 0.73         |
| Min         |    | 0.03                   | 0.07         | 0.04                  | 0.12         |
| Max         |    | 0.67                   | 0.58         | 0.79                  | 0.65         |



# EXAMPLE 4: MULTI DOMAIN MULTI ITEM QUESTIONNAIRE

## a) Functional Assessment of Cancer Therapy: General (FACT-G)

| <u>PHYSICAL WELL-BEING</u>      |                                                                                       | Not at all | A little bit | Some-what | Quite a bit | Very much |
|---------------------------------|---------------------------------------------------------------------------------------|------------|--------------|-----------|-------------|-----------|
| GP1                             | I have a lack of energy .....                                                         | 0          | 1            | 2         | 3           | 4         |
| GP2                             | I have nausea .....                                                                   | 0          | 1            | 2         | 3           | 4         |
| GP3                             | Because of my physical condition, I have trouble meeting the needs of my family ..... | 0          | 1            | 2         | 3           | 4         |
| GP4                             | I have pain .....                                                                     | 0          | 1            | 2         | 3           | 4         |
| GP5                             | I am bothered by side effects of treatment .....                                      | 0          | 1            | 2         | 3           | 4         |
| GP6                             | I feel ill .....                                                                      | 0          | 1            | 2         | 3           | 4         |
| GP7                             | I am forced to spend time in bed .....                                                | 0          | 1            | 2         | 3           | 4         |
| <u>SOCIAL/FAMILY WELL-BEING</u> |                                                                                       | Not at all | A little bit | Some-what | Quite a bit | Very much |
| GS1                             | I feel close to my friends .....                                                      | 0          | 1            | 2         | 3           | 4         |
| GS2                             | I get emotional support from my family .....                                          | 0          | 1            | 2         | 3           | 4         |
| GS3                             | I get support from my friends.....                                                    | 0          | 1            | 2         | 3           | 4         |
| GS4                             | My family has accepted my illness .....                                               | 0          | 1            | 2         | 3           | 4         |
| GS5                             | I am satisfied with family communication about my illness.....                        | 0          | 1            | 2         | 3           | 4         |
| GS6                             | I feel close to my partner (or the person who is my main support) .....               | 0          | 1            | 2         | 3           | 4         |
| <u>EMOTIONAL WELL-BEING</u>     |                                                                                       | Not at all | A little bit | Some-what | Quite a bit | Very much |
| GE1                             | I feel sad .....                                                                      | 0          | 1            | 2         | 3           | 4         |
| GE2                             | I am satisfied with how I am coping with my illness.....                              | 0          | 1            | 2         | 3           | 4         |
| GE3                             | I am losing hope in the fight against my illness.....                                 | 0          | 1            | 2         | 3           | 4         |
| GE4                             | I feel nervous.....                                                                   | 0          | 1            | 2         | 3           | 4         |
| GE5                             | I worry about dying.....                                                              | 0          | 1            | 2         | 3           | 4         |
| GE6                             | I worry that my condition will get worse .....                                        | 0          | 1            | 2         | 3           | 4         |
| <u>FUNCTIONAL WELL-BEING</u>    |                                                                                       | Not at all | A little bit | Some-what | Quite a bit | Very much |
| GF1                             | I am able to work (include work at home) .....                                        | 0          | 1            | 2         | 3           | 4         |
| GF2                             | My work (include work at home) is fulfilling.....                                     | 0          | 1            | 2         | 3           | 4         |
| GF3                             | I am able to enjoy life.....                                                          | 0          | 1            | 2         | 3           | 4         |
| GF4                             | I have accepted my illness.....                                                       | 0          | 1            | 2         | 3           | 4         |
| GF5                             | I am sleeping well .....                                                              | 0          | 1            | 2         | 3           | 4         |
| GF6                             | I am enjoying the things I usually do for fun .....                                   | 0          | 1            | 2         | 3           | 4         |
| GF7                             | I am content with the quality of my life right now.....                               | 0          | 1            | 2         | 3           | 4         |



# EXAMPLE 4: MULTI DOMAIN MULTI ITEM QUESTIONNAIRE

## a) Functional Assessment of Cancer Therapy: General (FACT-G)

|                                            |     |   |   |          |   |            |
|--------------------------------------------|-----|---|---|----------|---|------------|
| <b>EMOTIONAL<br/>WELL-BEING<br/>(EWB)</b>  | GE1 | 4 | - | <u>3</u> | = | <u>1</u>   |
|                                            | GE2 | 0 | + | <u>1</u> | = | <u>1</u>   |
|                                            | GE3 | 4 | - | <u>4</u> | = | <u>0</u>   |
|                                            | GE4 | 4 | - | <u>2</u> | = | <u>2</u>   |
|                                            | GE5 | 4 | - |          | = |            |
|                                            | GE6 | 4 | - | <u>1</u> | = | <u>3</u>   |
| <i>Score range: 0-24</i>                   |     |   |   |          |   |            |
|                                            |     |   |   |          |   |            |
| <i>Sum individual item scores:</i>         |     |   |   |          |   | <u>7</u>   |
| <i>Multiply by 6:</i>                      |     |   |   |          |   | <u>42</u>  |
| <i>Divide by number of items answered:</i> |     |   |   |          |   | <u>8.4</u> |

| usubjid | trt01p      | parcat | param                               | paramcd  | aval | z-score |
|---------|-------------|--------|-------------------------------------|----------|------|---------|
| 04-1001 | Treatment A | FACT03 | I feel sad                          | FACT0301 | 3    | 1       |
| 04-1001 | Treatment A | FACT03 | I am satisfied with coping          | FACT0302 | 1    | 1       |
| 04-1001 | Treatment A | FACT03 | I am losing hope                    | FACT0303 | 4    | 0       |
| 04-1001 | Treatment A | FACT03 | I feel nervous                      | FACT0304 | 2    | 2       |
| 04-1001 | Treatment A | FACT03 | I worry about dying                 | FACT0305 |      |         |
| 04-1001 | Treatment A | FACT03 | I worry my condition will get worse | FACT0305 | 1    | 3       |

FACT0301: 4-3=1    FACT0302: 1    FACT0303: 4-4=0  
 FACT0304: 4-2=2    FACT0305: Missing    FACT0306: 4-1=3

$$\text{FACT03} = (1+1+0+2+3) \times 6 / 5 = 8.4$$

| usubjid | trt01p      | parcat | param                | paramcd | T-score |
|---------|-------------|--------|----------------------|---------|---------|
| 04-1001 | Treatment A | FACT03 | Emotional well-being | FACTSCR | 8.4     |

FACT-G score = Physical T-score + Social T-score + Emotional T-score + Functional T-score

# EXAMPLE 4: MULTI DOMAIN MULTI ITEM QUESTIONNAIRE

## a) Functional Assessment of Cancer Therapy: General (FACT-G)

```
PROC MIXED data=adqs (where=(avisitn > 1 and aval ne .));
by avisitn;
class trt01pn avisitn subjid ;
model aval=trt01pn avisitn trt01pn*avisitn base;
repeated avisitn/type=un subject=subjid r rcorr;
lsmeans trt01pn*avisitn / diff cl;
run;
```

FACT-G– Between Treatment Comparison

|                                                    | Treatment A (N=50) |             | Treatment B (N=47) |             | Treatment A – Treatment B |           |         |
|----------------------------------------------------|--------------------|-------------|--------------------|-------------|---------------------------|-----------|---------|
|                                                    | Estimated Mean     | 95% CI      | Estimated Mean     | 95% CI      | Estimated Mean            | 95% CI    | P-Value |
| Emotional Functioning                              |                    |             |                    |             |                           |           |         |
| Post Baseline Observations:                        |                    |             |                    |             |                           |           |         |
| Cycle 2 Day 1                                      | 78.3               | (65.0,90.0) | 82.1               | (74.6,88.3) |                           |           |         |
| Cycle 3 Day 1                                      | 73.6               | (63.3,82.9) | 77.5               | (68.9,85.8) |                           |           |         |
| Overall Comparisons of Post Baseline Observations: |                    |             |                    |             |                           |           |         |
| Treatment                                          | 75.4               | (62.9,87.1) | 80.3               | (71.8,83.9) | 4.9                       | (3.3,6.5) | 0.04    |
| Time                                               |                    |             |                    |             |                           |           | 0.03    |
| Treat x time interaction                           |                    |             |                    |             |                           |           | 0.036   |

Note: Analysis based on repeated measures mixed effects model with treatment, time, treatment-by-time interaction as fixed effects. P-values are from Type 3 Tests of Fixed Effects.

# EXAMPLE 4: MULTI DOMAIN MULTI ITEM QUESTIONNAIRE

## b) 36-Item Short Form Survey Instrument (SF-36)

21. How much **bodily** pain have you had during the **past 4 weeks**?

- ☐ 1 - None
- ☐ 2 - Very mild
- ☐ 3 - Mild
- ☐ 4 - Moderate
- ☐ 5 - Severe
- ☐ 6 - Very severe

22. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?

- ☐ 1 - Not at all
- ☐ 2 - A little bit
- ☐ 3 - Moderately
- ☐ 4 - Quite a bit
- ☐ 5 - Extremely

How much of the time during the **past 4 weeks**...

|                                                                         | All of<br>the<br>time   | Most<br>of the<br>time  | A good<br>bit of the<br>time | Some<br>of the<br>time  | A little<br>of the<br>time | None<br>of the<br>time  |
|-------------------------------------------------------------------------|-------------------------|-------------------------|------------------------------|-------------------------|----------------------------|-------------------------|
| 23. Did you feel full of pep?                                           | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3      | <input type="radio"/> 4 | <input type="radio"/> 5    | <input type="radio"/> 6 |
| 24. Have you been a very nervous person?                                | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3      | <input type="radio"/> 4 | <input type="radio"/> 5    | <input type="radio"/> 6 |
| 25. Have you felt so down in the dumps that nothing could cheer you up? | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3      | <input type="radio"/> 4 | <input type="radio"/> 5    | <input type="radio"/> 6 |
| 26. Have you felt calm and peaceful?                                    | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3      | <input type="radio"/> 4 | <input type="radio"/> 5    | <input type="radio"/> 6 |
| 27. Did you have a lot of energy?                                       | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3      | <input type="radio"/> 4 | <input type="radio"/> 5    | <input type="radio"/> 6 |
| 28. Have you felt downhearted and blue?                                 | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3      | <input type="radio"/> 4 | <input type="radio"/> 5    | <input type="radio"/> 6 |
| 29. Did you feel worn out?                                              | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3      | <input type="radio"/> 4 | <input type="radio"/> 5    | <input type="radio"/> 6 |
| 30. Have you been a happy person?                                       | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3      | <input type="radio"/> 4 | <input type="radio"/> 5    | <input type="radio"/> 6 |
| 31. Did you feel tired?                                                 | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3      | <input type="radio"/> 4 | <input type="radio"/> 5    | <input type="radio"/> 6 |



# EXAMPLE 4: MULTI DOMAIN MULTI ITEM QUESTIONNAIRE

## b) 36-Item Short Form Survey Instrument (SF-36)

### Step 1: Recoding Items

| Item numbers                    | Change original response category * | To recoded value of: |
|---------------------------------|-------------------------------------|----------------------|
| 1, 2, 20, 22, 34, 36            | 1 →                                 | 100                  |
|                                 | 2 →                                 | 75                   |
|                                 | 3 →                                 | 50                   |
|                                 | 4 →                                 | 25                   |
|                                 | 5 →                                 | 0                    |
| 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 | 1 →                                 | 0                    |
|                                 | 2 →                                 | 50                   |
|                                 | 3 →                                 | 100                  |
| 13, 14, 15, 16, 17, 18, 19      | 1 →                                 | 0                    |
|                                 | 2 →                                 | 100                  |
| 21, 23, 26, 27, 30              | 1 →                                 | 100                  |
|                                 | 2 →                                 | 80                   |
|                                 | 3 →                                 | 60                   |
|                                 | 4 →                                 | 40                   |
|                                 | 5 →                                 | 20                   |
|                                 | 6 →                                 | 0                    |
| 24, 25, 28, 29, 31              | 1 →                                 | 0                    |
|                                 | 2 →                                 | 20                   |
|                                 | 3 →                                 | 40                   |
|                                 | 4 →                                 | 60                   |
|                                 | 5 →                                 | 80                   |
|                                 | 6 →                                 | 100                  |
| 32, 33, 35                      | 1 →                                 | 0                    |
|                                 | 2 →                                 | 25                   |
|                                 | 3 →                                 | 50                   |
|                                 | 4 →                                 | 75                   |
|                                 | 5 →                                 | 100                  |

### Step 2: Averaging Items to Form Scales

| Scale                                      | Number of items | After recoding per Table 1, average the following items |
|--------------------------------------------|-----------------|---------------------------------------------------------|
| Physical functioning                       | 10              | 3 4 5 6 7 8 9 10 11 12                                  |
| Role limitations due to physical health    | 4               | 13 14 15 16                                             |
| Role limitations due to emotional problems | 3               | 17 18 19                                                |
| Energy/fatigue                             | 4               | 23 27 29 31                                             |
| Emotional well-being                       | 5               | 24 25 26 28 30                                          |
| Social functioning                         | 2               | 20 32                                                   |
| Pain                                       | 2               | 21 22                                                   |
| General health                             | 5               | 1 33 34 35 36                                           |

Example: Emotional well-being (24,25,26,28,30):

| Question | Response     | Value |
|----------|--------------|-------|
| 24       | 4            | 60    |
| 25       | 3            | 40    |
| 26       | 3            | 60    |
| 28       | 4            | 60    |
| 30       | 2            | 80    |
| Average  | = 300/5 = 60 |       |

## EXAMPLE 5: TIME TO EVENT FOR QUALITY OF LIFE

### Time to Deterioration (TTD) of quality of life

Time for quality of scores to deteriorate with a minimal clinically important score change, from the baseline score.

| usubjid | param                               | paramcd | randdt    | adt       | aval | cnsr | evntdesc                | cnstdtc              |
|---------|-------------------------------------|---------|-----------|-----------|------|------|-------------------------|----------------------|
| 05-1011 | Time to deterioration of QoL (Days) | TTD     | 10FEB2016 | 07NOV2017 | 637  | 2    | Withdrawal by Subject   | Date of last contact |
| 05-1012 | Time to deterioration of QoL (Days) | TTD     | 25JUN2013 | 28APR2017 | 1404 | 1    | End of study            | Date of last contact |
| 05-1013 | Time to deterioration of QoL (Days) | TTD     | 17SEP2012 | 12JUN2016 | 1365 | 0    | Deterioration           |                      |
| 05-1014 | Time to deterioration of QoL (Days) | TTD     | 09MAY2014 | 01MAY2017 | 1089 | 3    | Subject Discontinuation | Date of last contact |
| 05-1015 | Time to deterioration of QoL (Days) | TTD     | 29JAN2015 | 28FEB2017 | 762  | 0    | Deterioration           |                      |
| 05-1016 | Time to deterioration of QoL (Days) | TTD     | 30OCT2016 | 14JAN2017 | 77   | 4    | Lost to Follow-up       | Date of last contact |

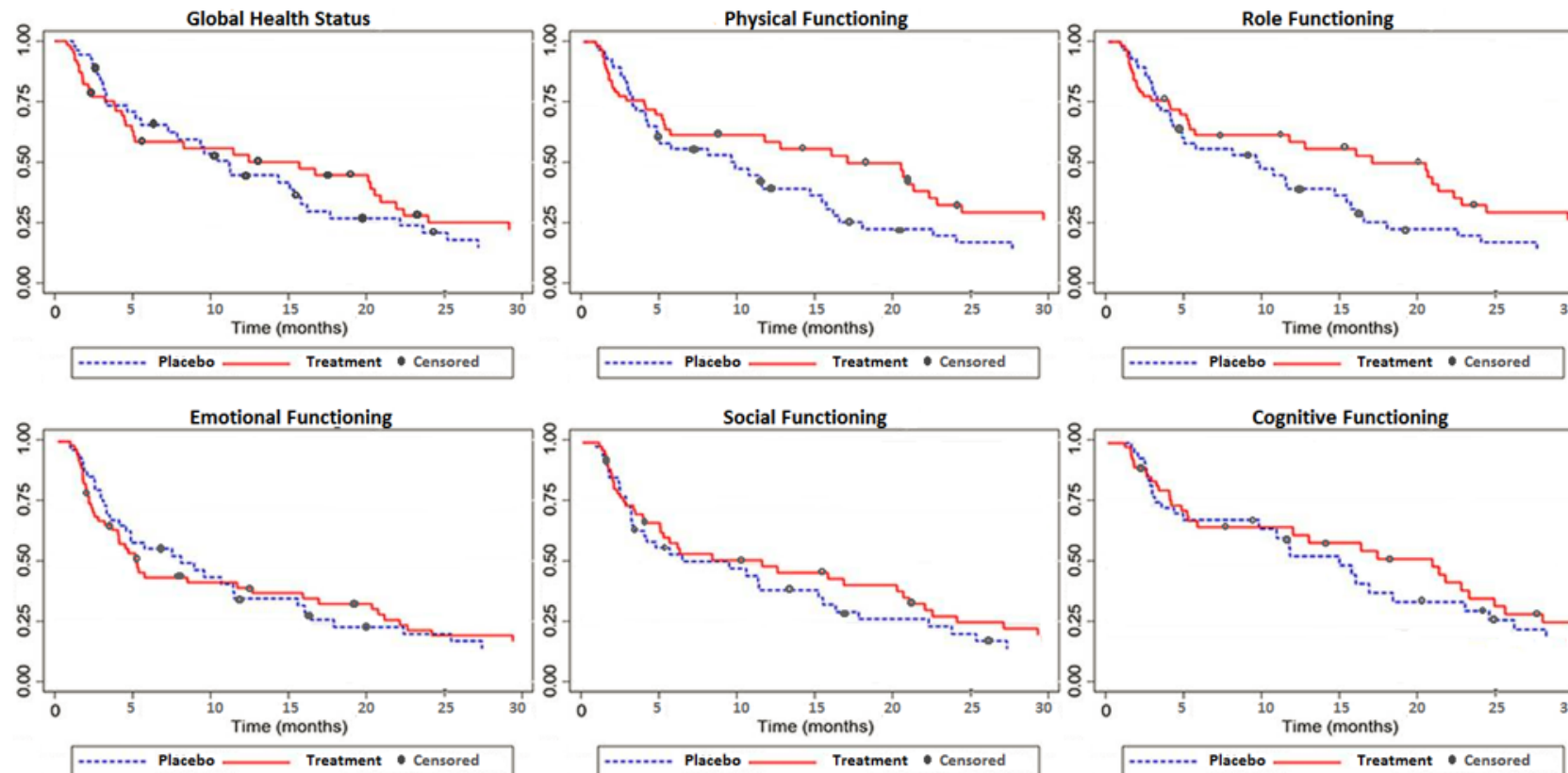


10 points or higher increase in pain for two consecutive cycles.

# EXAMPLE 5: TIME TO EVENT FOR QUALITY OF LIFE

## Time to Deterioration (TTD) of quality of life

```
PROC LIFETEST data=adtte method=km outsurv=dsplot;
  time aval*cnsr(1);
  by trtpn trtp;
run;
```





## EXAMPLE 6: SAFETY PATIENT REPORTED OUTCOMES

### Patient Reported Outcomes-Common Terminology Criteria for Adverse Events (PRO-CTCAE)

|                                                                                          |                                    |                                |                                   |                                   |
|------------------------------------------------------------------------------------------|------------------------------------|--------------------------------|-----------------------------------|-----------------------------------|
| <b>20. PRO-CTCAE™ Symptom Term: Cough</b>                                                |                                    |                                |                                   |                                   |
| a. In the last 7 days, what was the SEVERITY of your COUGH at its WORST?                 |                                    |                                |                                   |                                   |
| <input type="radio"/> None                                                               | <input type="radio"/> Mild         | <input type="radio"/> Moderate | <input type="radio"/> Severe      | <input type="radio"/> Very severe |
| b. In the last 7 days, how much did COUGH INTERFERE with your usual or daily activities? |                                    |                                |                                   |                                   |
| <input type="radio"/> Not at all                                                         | <input type="radio"/> A little bit | <input type="radio"/> Somewhat | <input type="radio"/> Quite a bit | <input type="radio"/> Very much   |

|                                                                                                                           |                            |                                |                              |                                   |
|---------------------------------------------------------------------------------------------------------------------------|----------------------------|--------------------------------|------------------------------|-----------------------------------|
| <b>21. PRO-CTCAE™ Symptom Term: Wheezing</b>                                                                              |                            |                                |                              |                                   |
| a. In the last 7 days, what was the SEVERITY of your WHEEZING (WHISTLING NOISE IN THE CHEST WITH BREATHING) at its WORST? |                            |                                |                              |                                   |
| <input type="radio"/> None                                                                                                | <input type="radio"/> Mild | <input type="radio"/> Moderate | <input type="radio"/> Severe | <input type="radio"/> Very severe |

|                                                                                                        |                                    |                                    |                                   |                                         |
|--------------------------------------------------------------------------------------------------------|------------------------------------|------------------------------------|-----------------------------------|-----------------------------------------|
| <b>22. PRO-CTCAE™ Symptom Term: Swelling</b>                                                           |                                    |                                    |                                   |                                         |
| a. In the last 7 days, how OFTEN did you have ARM OR LEG SWELLING?                                     |                                    |                                    |                                   |                                         |
| <input type="radio"/> Never                                                                            | <input type="radio"/> Rarely       | <input type="radio"/> Occasionally | <input type="radio"/> Frequently  | <input type="radio"/> Almost constantly |
| b. In the last 7 days, what was the SEVERITY of your ARM OR LEG SWELLING at its WORST?                 |                                    |                                    |                                   |                                         |
| <input type="radio"/> None                                                                             | <input type="radio"/> Mild         | <input type="radio"/> Moderate     | <input type="radio"/> Severe      | <input type="radio"/> Very severe       |
| c. In the last 7 days, how much did ARM OR LEG SWELLING INTERFERE with your usual or daily activities? |                                    |                                    |                                   |                                         |
| <input type="radio"/> Not at all                                                                       | <input type="radio"/> A little bit | <input type="radio"/> Somewhat     | <input type="radio"/> Quite a bit | <input type="radio"/> Very much         |

## EXAMPLE 6: SAFETY PATIENT REPORTED OUTCOMES

### Patient Reported Outcomes-Common Terminology Criteria for Adverse Events (PRO-CTCAE)

| usubjid | trt01p      | aereport  | aedecod | aestdt    | aetoxgr | aetoxgrn |
|---------|-------------|-----------|---------|-----------|---------|----------|
| 06-1111 | Treatment A | Clinician | Nausea  | 02MAR2015 | Grade 1 | 1        |
| 06-1111 | Treatment A | Patient   | Nausea  | 24FEB2015 | Grade 3 | 3        |
| 06-1112 | Treatment B | Clinician | Nausea  | 25MAY2016 | Grade 0 | 0        |
| 06-1112 | Treatment B | Patient   | Nausea  | 02MAY2016 | Grade 2 | 2        |

Summary of Any Grade of Adverse Events, Clinician-reported and Patient-reported

|                |                    | Treatment A | Treatment B | p-value |
|----------------|--------------------|-------------|-------------|---------|
|                |                    | (N=100)     | (N=100)     |         |
|                |                    | n (%)       | n (%)       |         |
| Nausea         | Clinician-reported | 20 (20)     | 16 (16)     | 0.22    |
|                | Patient-reported   | 26 (26)     | 22 (22)     | 0.12    |
| Abdominal pain | Clinician-reported | 35 (35)     | 21 (21)     | 0.54    |
|                | Patient-reported   | 42 (42)     | 25 (25)     | 0.33    |
| Cough          | Clinician-reported | 10 (10)     | 0           | 0.15    |
|                | Patient-reported   | 13 (13)     | 9 (9)       | <0.001  |
| Swelling       | Clinician-reported | 22 (22)     | 15 (15)     | 0.32    |
|                | Patient-reported   | 29 (29)     | 17 (17)     | 0.24    |
| Palpitations   | Clinician-reported | 32 (32)     | 28 (28)     | 0.17    |
|                | Patient-reported   | 37 (37)     | 33 (33)     | <0.001  |

Note: p-value from Fisher's exact test, comparing grades between treatments

# Challenges

- Missing data
  - Clear and readable questionnaires
  - Missed visits, Withdrawal from study
  
  - Check percentage of missing data
  - Randomly missing or selective loss of data
  - Imputation
- Recall period



***THANK YOU***