Context of Use for COA's

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Context of Use

Context of Use refers to what the Clinical Outcome Assessment is intended to be used for. There are many possible roles

1. Characterizing/choosing the patient population for study: disease definition and character

- Do they have the disease e.g., heart failure, which could be based on biomarkers and symptoms
- Do they have severe enough disease (NYHA classification of CHF)
- Do they have characteristics of particular interest because of the drug's mechanism (negative symptoms in psychosis; relevant aspects of low back pain – chronic pain vs spasm, localized spinal nerve pain; extent and nature of disability in MS; particular features of cognitive impairment.

All this relates to potential enrichment stratification, covariate adjustment, identifying particular features responsive to the treatment.

Context of Use

2. Use as a study endpoint, the measurement that will be compared for treatment and control, either as a change from baseline (usual) or as a distinct variable.

   This is clearly where the greatest interest lies: the COA as the measure of a treatment's effectiveness.

   A question that is always of interest for a multi-component test (multiple questions, multiple tests) is whether the components are separately informative (suicidality question in HamD).

What Makes a COA Attractive?

1. It measures a discrete event of interest. These range from fairly easy/objective to highly subjective. We tend to think of these endpoints as familiar and straightforward, but that is not always so:

- Easy, relatively
  - AMI, stroke, CV death

  [But not so simple; Lipid Research Clinical Trial of cholestyramine had a complex definition of AMI that depended on symptoms and was almost wholly useless. Very good idea to field test]

- Harder
  - Recurrence of depression
  - TIA
  - Need for hospitalization, CV intervention, surgical or medical [Are criteria uniform?]

Attractive endpoints, discrete yes or no. But potentially huge subjectivity, variability by investigator and site, and they get less attention than they deserve.

What Makes a COA Attractive?

2. It measures graded events (virtually all symptoms, functional measures) reliably and consistently.

This is, of course, what we need and where concerns arise

- Clinical and patient globals CAN do this but we are nervous about how they are really done and they don't explain well what the critical components are. If possible, it is good to have well-thought out landmarks, and I've always suspected a bias toward the middle when these are omitted. In general we'd rather use clinical and patient expertise to find out what matters, and construct a scale properly describing what is important. We want the scale to be roughly proportional to severity.

  I worry about variability in physician global quality, not all people running trials are equally thoughtful, attentive, etc.

What Makes a COA Attractive?

2. Graded events (cont)

- We have a bias toward PRO for symptoms, activities (functions) because it's the patient who experiences the symptoms and loss of function.

  PRO's can be designed to be broadly comprehensible to patients and to be consistent over a broad range of patients.

  I think it is important to try to measure current status, not "change from last visit" and get status today, not over a larger period (who recalls?) unless you use diaries (preferably electronic).

What Makes a COA Attractive?

2. Graded events (cont)

- Simplicity helps

How bad is your pain? On a Likert scale seems pretty straightforward, as do somewhat more complex issues, like depression, GI symptoms.

Some measurements like pulmonary function, ETT, seem very close to measuring the symptomatic pulmonary and heart failure measures they are designed to substitute for.

A Well-Established Scale

The Minnesota Living with Heart Failure Scale was developed about 1984 because (I think) NYHA was not considered adequate and, of course, required physician assessment. The current version has 21 questions.

MINNESOTA LIVING WITH HEART FAILURE® QUESTIONNAIRE

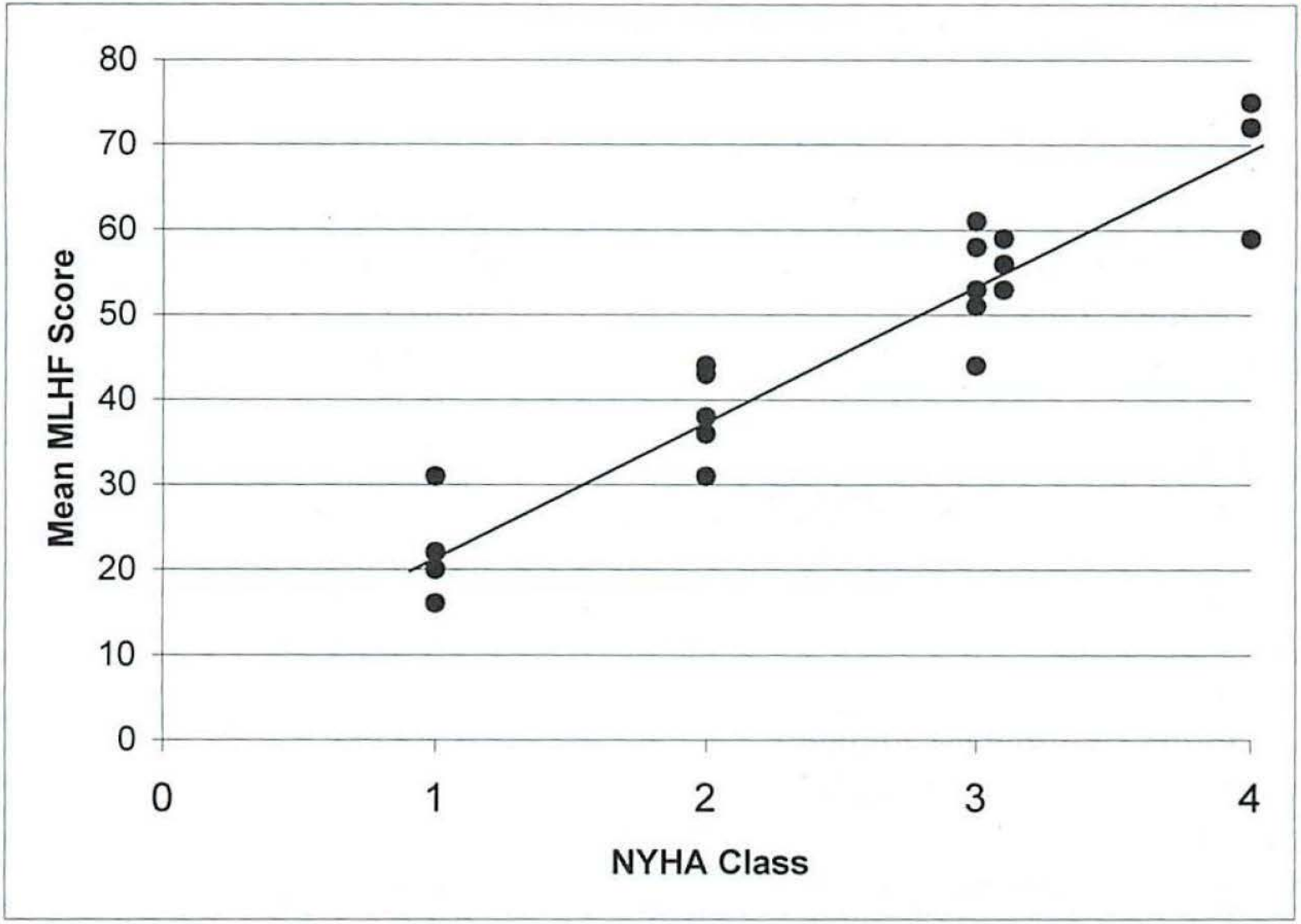
The following questions ask how much your heart failure (heart condition) affected your life during the past month (4 weeks). After each question, circle the 0, 1, 2, 3, 4 or 5 to show how much your life was affected. If a question does not apply to you, circle the 0 after that question.

Did your heart failure prevent you from living as you wanted during the past month (4 weeks) by -	**No**	**Very Little**				**Very Much**
1. causing swelling in your ankles or legs?	0	1	2	3	4	5
2. making you sit or lie down to rest during the day?	0	1	2	3	4	5
3. making your walking about or climbing stairs difficult?	0	1	2	3	4	5
4. making your working around the house or yard difficult?	0	1	2	3	4	5
5. making your going places away from home difficult?	0	1	2	3	4	5
6. making your sleeping well at night difficult?	0	1	2	3	4	5
7. making your relating to or doing things with your friends or family difficult?	0	1	2	3	4	5
8. making your working to earn a living difficult?	0	1	2	3	4	5
9. making your recreational pastimes, sports or hobbies difficult?	0	1	2	3	4	5
10. making your sexual activities difficult?	0	1	2	3	4	5
11. making you eat less of the foods you like?	0	1	2	3	4	5
12. making you short of breath?	0	1	2	3	4	5
13. making you tired, fatigued, or low on energy?	0	1	2	3	4	5
14. making you stay in a hospital?	0	1	2	3	4	5
15. costing you money for medical care?	0	1	2	3	4	5
16. giving you side effects from treatments?	0	1	2	3	4	5
17. making you feel you are a burden to your family or friends?	0	1	2	3	4	5
18. making you feel a loss of self-control in your life?	0	1	2	3	4	5
19. making you worry?	0	1	2	3	4	5
20. making it difficult for you to concentrate or remember things?	0	1	2	3	4	5
21. making you feel depressed?	0	1	2	3	4	5

11/10/04

Living with Heart Failure

Some of this looks a little doubtful; e.g., questions about mental status getting along with people, appetite, and side effects of drugs, seem far less pertinent than questions about how you get around, exercise, and have shortness of breath. So I'd bet you could lose half of the 21 without decreasing its value, as an assessment of CHF severity. Perhaps it's really 2 scales, one of CHF severity, a second of impact on life [But, of course, perhaps they go together] But, despite my complaints, look at its performance compared to NYHA classification (There are many, many, more analyses).


Mean MLHF Score
80
70
60
50
40
30
20
10
0
0
1
2
3
4
NYHA Class

What Makes a COA Attractive?

So what I like to see is

1. Independence from observer competence/effort.

   Clinical Global: depends on who does it
   PRO: designed for all

2. Focus on critical components

   NYHA does; Living with heart failure may have excess attention to less direct consequences of heart failure

3. Not affected by other influences

   Ham-D is affected by everything in the acute setting.
   Recurrence of depression, in contrast, not much influenced.

4. Would be nice if components of a scale were informative.