Formation sur la Qualité de Vie liée à la Santé dans les Essais Cliniques

Educational Program on Health-Related Quality of Life (HRQL) in Clinical Trials

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ANAES - Kremlin-Bicètre

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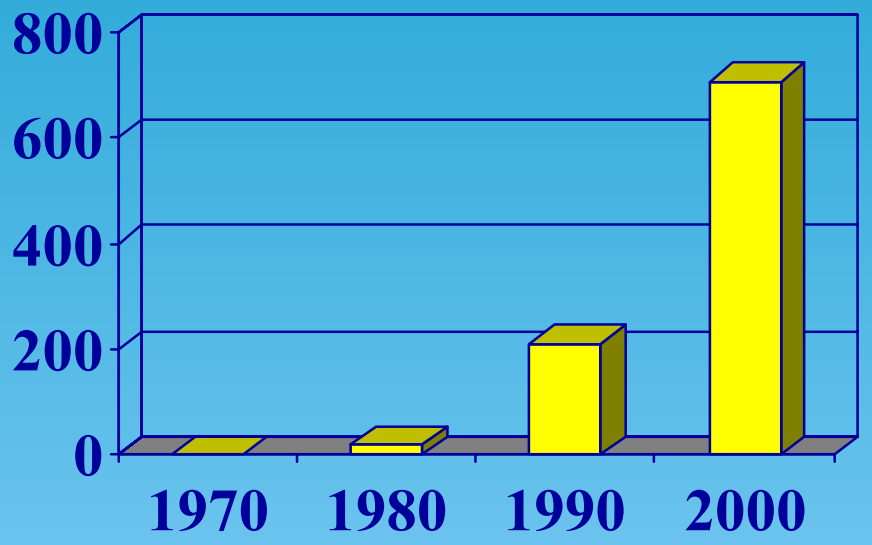
Evolution of HRQL assessment in clinical trials since 1966

- **Literature search (Medline)**

"Quality of Life" matched with "Clinical Trials":

Results: number of references

- 1966 to 1970: 0
- 1966 to 1980: 20
- 1966 to 1990: 210
- 1966 to 2000: 708



Considerable increase of HRQL assessment in clinical trials

Cochrane Health-Related Quality of Life Methods Group

Objective:

- To advise Cochrane reviewers about when and how to incorporate HRQL data into systematic reviews of health care interventions

- Convenors: Catherine Acquadro, MD
  Prof. Dick Joyce, PhD, FBPsS
  Prof. Donald L. Patrick, MSPH, PhD
- Coordinator: Lucile Lapalus (llapalus@mapi.fr)
- Active members : 37 from 12 countries

Objectives

- To help reviewers of clinical trials to acquire the skills needed to assess HRQL outcomes included in regulatory files and publications
- To facilitate decisions made by Health Authorities and health care providers

Presentation of the Workmats (1/2)

- **Workmats :**
  - large worksheets
  - contain concise information: background
  - present various assignments
- **Workbook :**
  - reference source
  - additional information on HRQL

2- DECIDING WHICH PRO TO ASSESS THE IMPACT OF DISEASE AND TREATMENT

HRQL Methods Group

BACKGROUND

When deciding which PRO to assess the impact of disease and treatment, it is always necessary to start with interviews from patients who experience the condition and treatment of interest.

Deciding how to present and group the items gleaned from the interviews can be a challenge and is not without controversy in terms of the best methods to employ.

The following assignments will help you understand the issues related to this process.

ASSIGNMENTS

Assignment 1:

From the description of osteoarthritis provided, and referring to the examples of PRO provided in the table 1, assign each of the life aspects affected by the condition to an appropriate PRO.

Assignment 2:

You are provided with the transcript from an interview with a patient suffering from osteoarthritis. Review the patient comments and select some that you consider to be representative of the impact of the condition. Write comments verbatim in the table and, referring again to the examples, assign relevant PRO to each comment. Compare the list of PRO with those from Assignment 1. How do they differ? Describe any additional PRO you have identified and how they may be affected by treatment.

OSTEOARTHRITIS PATIENT INTERVIEW

"When I'm in acute pain, I can't move. I put my mattress on the floor and lie down. If I have to go somewhere in the house, I crawl around on all fours. The pain wakes me up at night; once or twice a night, often more. I often can't sleep at night — I try to lie on my back, on the right, the left...try everything. Sometimes you get very depressed — you can get angry. Your moods change easily and I can be aggressive and bad tempered. I avoid anything that involves my fingers — can't do a lot of jobs to help with the children, changing nappies, carrying them. Before I was very active. I went dancing and bowling. Now I struggle to do the garden. It's also had an influence on my sex life. I'm often in a bad mood and moaning, and sometimes just can't be bothered. My children have difficulty in understanding too — sometimes I'm unbearable, don't want to speak, feel like doing nothing. It affects me emotionally as I'd like to go out and do things but I can't. I used to see my friends from the bowling club. Now, I don't see them any more. You don't feel that you are any good in company. You don't feel like socializing when you're in pain. Sometimes I forget to take my treatment because it upsets my stomach. I know I can't do the job I used to do — it hurts me too much — I can't lift heavy things or stand up for too long...in the future I suppose I'll have to find some other work. Not being able to work affects the family financially, but the most important thing is to fight and get on with your life. I don't want to be a burden on other people and I feel frustrated by my lack of independence, but I'm determined not to give into it and let it ruin my life. I guess it's something you just have to learn to live with; there's no treatment."

ASSIGNMENT 1

Choosing a relevant PRO

From the description of osteoarthritis summarised below, list with your own words the aspects of life affected by osteoarthritis. Then, define which PRO are affected using the list from Table 1 as a guide.

Osteoarthritis Clinical Signs & Symptoms	Aspects of life affected	PRO
Degeneration of the cartilage that lines the joints. Symptoms: pain/tenderness, swelling, creaking, stiffening of affected joints, weakness & shrinkage of surrounding muscles due to lack of use (because of pain), enlarged & distorted joints.		

ASSIGNMENT 2

Impact of Osteoarthritis on Patients' Lives

a) From the transcript provided in the lower left corner of this Workmat, transfer what you consider to be the most relevant patient comments to the table verbatim and assign relevant PRO to each comment.

Verbatim comments	PRO

b) Did the patient information identify any important additional PRO to those you identified in Assignment 1? Make a mark next to those that were additional. Why do you think that you missed these?

c) Were there any patient comments that you could not assign to a PRO? Describe any below.

Table 1: Concepts used in Patient-Reported Outcomes

Concepts	Domains	Attributes
Symptoms	Reports of physical and psychological symptoms or sensations not directly observate, e.g. energy and fatigue, nausea, irritability	Frequency, severity, bothersomeness
Functional Status		Frequency, difficulty, severity, ability, with help
Physical	Functional limitations and activity restrictions, e.g., self-care, walking, mobility, sleep, sexual	
Psychological	Positive or negative affect and cognitive, e.g. anger, alertness, self-esteem, sense of well-being, distress	
Social	Limitations in work or school, participation in community	
Perceptions		Frequency, severity/intensity, satisfaction
Global	General ratings of health and quality of life, e.g., satisfaction or overall well-being	
Worries and Concerns	About health, finances, future	
Advantage/Opportunity	Perceptions of stigma or reports of discrimination because of health condition	Frequency, impact
Treatment Satisfaction	Evaluations of treatments	Frequency, intensity
Treatment adherence	Reports or observations of actual use of treatments	Frequency
Health-Related Quality of Life (HRQL)	HRQL is multi-dimensional and represents the patient's evaluation of health condition and its treatment on daily life: physical function, psychological function, social function, role, function, emotional function, well-being, vitality,...	Frequency, impact, intensity, severity, bothersomeness

Adapted from Patrick DL, Chiang YP (2000) Measurement of health outcomes in treatment effectiveness evaluations: conceptual and methodological challenges. Med care 38 (Suppl): II 14-25

Presentation of the Workmats (2/2)

- Interactive learning method
- Participants
  - Small group discussions and interactions
  - To understand the new information
  - To complete the assignments through group discussions (writing material)
  - Group answers have to be discussed by all the groups to reach a consensus

Content

Workmats	Content
1	How do disease and treatment affect Health-Related Quality of Life (HRQL)?
2	Deciding which domains to include in a HRQL instrument
3	How is new HRQL questionnaire developed? 1st step: Development of items and item reduction
4	Choosing an appropriate existing HRQL measure
5	Analysis of HRQL data
6	Presentation and interpretation of HRQL outcomes included in clinical trials?

WORKMAT 1

How do disease and treatment affect HRQL?

WORKMAT 1 : (10h00 – 10h30)

- **Learning objectives**
  - **To identify the impact of health conditions and treatment on HRQL**
  - **To distinguish the different ways diseases and treatment can affect HRQL**
  - **To create an awareness that treatments can affect HRQL**

WORKMAT 1

- **Learning points**
  - Diseases and treatments can affect a person's quality of life in different ways
  - HRQL is multidimensional and subjective

WORKMAT 2

Deciding which domains to include in HRQL instrument

WORKMAT 2 : (10h45 – 11h15)

- **Learning objective**
  - **To define the relevant HRQL domains depending on the conditions studied**

WORKMAT 2

- **Learning points**
  - The relative burden of disease and treatment on population can be measured through HRQL domains
  - At a minimum, HRQL consists of physical, psychological, and social domains
  - The patient plays an important part in the development of a questionnaire

WORKMAT 3

How is a new HRQL questionnaire developed?

1st step: Development of items and item reduction

WORKMAT 3 : (11h30 – 12h15)

- **Learning objective**
  - **To describe the process of HRQL instrument development**

WORKMAT 3

- **Learning points**
  - Instrument development is a rigorous scientific process
  - There is no single *right* way to develop an instrument although best practices are available for the steps in the process
  - The instrument should have empirical evidence of validity

Pause Repas: 12h30 – 14h00

Some definitions

- **Psychometrics:** Techniques by which we evaluate the quality of an instrument.
- **Test-retest Reliability (reproducibility):** Degree to which an instrument gives similar scores on repeated administrations in identical conditions to respondents who are assumed to be stable with respect to the domains being assessed. It is often based on the intra-class correlation coefficient (ordinal numbers); a reliability coefficient greater than 0.70 is considered as acceptable for group comparisons.
- **Responsiveness:** Ability of an instrument to detect small but important changes over time (delta change from baseline in a group of patients) or differences between treatment groups at a specified time. Responsiveness may be approached by capacity of the instrument to discriminate between clinically meaningful groups at a single time point (i.e., known groups validity), but this is not always proof that the instrument will be sensitive to HRQL change over time or to differences between treatment groups. Satisfactory effect size = 0.40 on most subscales (> 50%).
- **Validity:** Degree to which an instrument measures what it is intended to measure.Validating a health measure is the process of accumulating different kinds of evidence to determine the most appropriate interpretations of a health score. “Valid for what?”

WORKMAT 4

Choosing an appropriate existing HRQL measure

WORKMAT 4 : (14h00 – 14h45)

- **Learning objectives**
  - To explore the process for selecting an appropriate health status instrument for use in a specific clinical trial scenario
  - To examine the trade-offs in the selection process
  - To review the criteria necessary for appropriately evaluating an HRQL instrument
  - To identify and evaluate established questionnaires for use in a specific patient group

WORKMAT 4

- **Learning points**
  - **The first step is to ask yourself Key Questions**
  - **The choice of domains and the selection of an HRQL instrument is influenced by severity and nature of the disease and the expected benefits and side effects of treatment**

WORKMAT 5

Analysis of HRQL data

WORKMAT 5 : (15h00 – 15h45)

- **Learning objectives**
  - **To identify the issues and potential problems in designing a statistical analysis plan for HRQL data**
  - **To understand the different methods of treating missing data**
  - **To gain the knowledge and skills needed to analyze differences in HRQL outcomes between two or more treatments**

WORKMAT 5

- **Learning points**
  - To pre-specify hypotheses and to establish a rigorous analysis plan with a special focus on multiple test and missing data
  - The type of missing data should be specified (missing items / missing questionnaires)

WORKMAT 6

Presentation and interpretation of HRQL outcomes included in clinical trials

WORKMAT 6 : (16h00 – 16h45)

- **Learning objective**
  - **To critically evaluate published literature describing HRQL surveys**
  - **To interpret HRQL data that are reported in the published literature**

WORKMAT 6

- **Learning points**
  - There are several ways to interpret; all have advantages and disadvantages : Effect Size (ES), Minimal Clinically Important Difference (MCID), Number of Patients to Treat (NNT)
  - As the experience of interpreting HRQL outcomes is minor, raw HRQL scores may be difficult to interpret at the moment
  - Attempts to interpret HRQL scores in different ways are recommended
  - Though the evaluating techniques for HRQL data analysis are still in development, they are valuable nevertheless

Conclusion & questions