

**Sigtuna, Sweden**

**March 2nd, 2004**

***Educational Program on  
Patient-Reported Outcomes  
(PROs)  
in Clinical Trials***

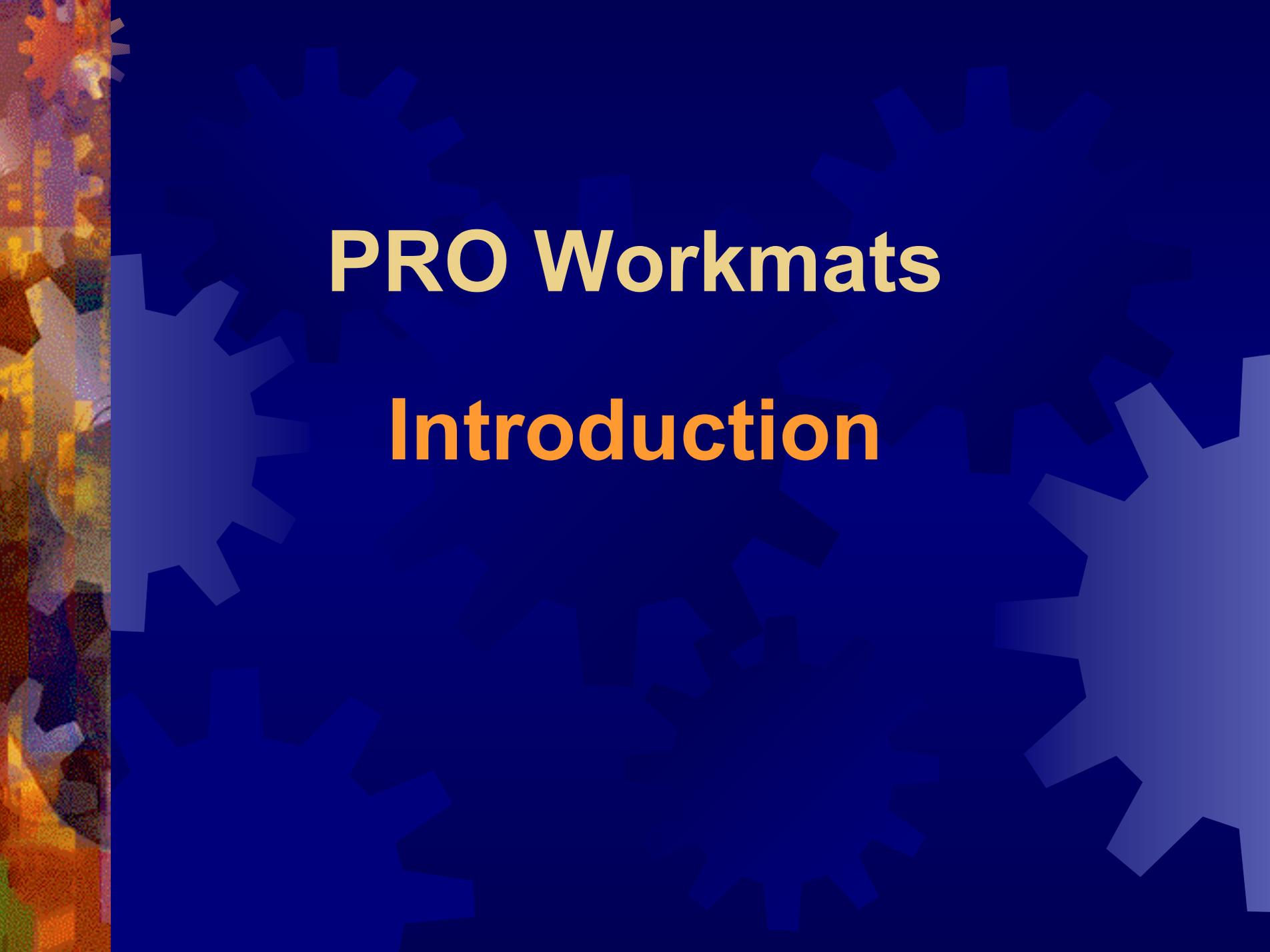
**Facilitators**

**Olivier Chassany and Catherine Acquadro**

# AGENDA

Tuesday 2 March 2004 – 15:15 – 18:00

Time	Content	Speakers
<b>15:15 – 15:30</b>	<b>Introduction</b>	Catherine Acquadro & Olivier Chassany
<b>15:30 – 16:30</b>	<b>Interactive session on Workmat 2: <i>“Deciding which PRO to assess the impact of disease and treatment”</i></b>	Catherine Acquadro & Olivier Chassany
<b>16:30 – 18:00</b>	<b>Interactive session on Workmat 5: <i>“Choosing an appropriate existing measure”</i></b>	Catherine Acquadro & Olivier Chassany



# PRO Workmats

## Introduction

# Background

- **1st version** developed by Adelphi and Mapi Values in 1995 on model from airline industry
- **Adaptation** and development for a Program on HRQL/PRO in Clinical Trials in 2002, collaboration between:
  - ✓ **Mapi Research Institute, Lyon, France**  
*Juliette Longin, PhD*
  - ✓ **The ERIQA Group**  
*Olivier Chassany, MD, PhD*
  - ✓ **and the Cochrane HRQL Methods Group**  
*Catherine, Acquadro, MD and  
CRB Joyce, PhD, FBPsS  
Donald L. Patrick, MSPH, PhD*

# Method: workmats

- **Interactive learning method**
- **Participants**
  - ✓ Small *group discussions* and interactions
  - ✓ To understand the new information
  - ✓ To complete the assignments through group discussions
  - ✓ Group answers have to be discussed by all the members of the group to reach a consensus

# Method: workmats

- **Workmats**

- ✓ Large worksheets
- ✓ Contain concise information: background
- ✓ Present various assignments

- **Participants' Workbook**

- ✓ Reference source
- ✓ Additional information on PRO
- ✓ Notepad

# Method: workmats

Each workmat consists of 3 parts

- **Part 1: a brief background introducing the theme**
- **Part 2: the objectives of the assignments to achieve**
- **Part 3: the assignments to be completed through group discussions, enabling participants to arrive at a joint conclusion**

# Content

<b>Workmat</b>	<b>Content</b>
<b>1</b>	<b>How do disease and treatment impact upon a patient – from the patient’s perspective?</b>
<b>2</b>	<b>Deciding which PRO to assess the impact of disease and treatment</b>
<b>3</b>	<b>How is a new PRO questionnaire developed? 1st Steps: Development of items and item reduction</b>
<b>4</b>	<b>How is a new PRO questionnaire developed? 2nd Steps: Psychometric validation and cultural adaptation</b>
<b>5</b>	<b>Choosing an appropriate existing measure</b>
<b>6</b>	<b>Analysis of PRO data</b>
<b>7</b>	<b>Presentation and interpretation of PRO included in clinical trials</b>

# Objectives

- **To help** pharmaceutical companies, reviewers, and investigators of clinical trials acquire the skills needed to assess PRO included in regulatory files and publications
- **To facilitate decisions** made by health authorities and health-care providers
- **To facilitate dialogue** between regulators, members of pharmaceutical companies, and health-care providers through the same training

# Pilot training: 2002

<b>Tests</b>	<b>Speakers</b>
<b>Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS)</b> , May 15, 2002; Paris, France	Catherine Acquadro, MD; Olivier Chassany, MD, PhD; Juliette Longin, PhD
<b>Food and Drug Administration (FDA)</b> , May 23, 2002; Washington, D.C., USA	Catherine Acquadro, MD; Olivier Chassany, MD, PhD; Bruce Crawford, MA, MPH; Patrick Marquis, MD, MBA
<b>International Cochrane Colloquium</b> , July 31 to August 3, 2002 Stavanger, Norway	Catherine Acquadro, MD; Olivier Chassany, MD, PhD; Elaine McColl, Msc; Donald L. Patrick, MSPH, PhD



**Finalization of workmats**

# 2003 Sessions

## Health Authorities / Congresses

- **24/01: AFSSAPS**, Faculté Lariboisière, Paris, France
- **08/04: ANAES** , Paris, France
- **27/04: DIA** « Assessing Treatment Impact Using PROs : Challenges in Study Design, Conduct and Analysis », Arlington, Virginia, USA
- **23/05: INAMI**, Brussels, Belgium

**→ 55 persons trained on PRO/HRQL**

## WORKMAT 2:

Deciding which PRO to assess the impact of disease and treatment

### Objective

- ✓ To define the relevant PRO, domains and items depending on the conditions studied

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

### BACKGROUND

When deciding which Patient-Reported Outcomes (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 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 interviews with patients suffering from osteoarthritis. Review the patients' 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 PATIENTS INTERVIEWS (collection)

"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 diapers, 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. Sometimes I think I should be taking another treatment. 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 in to 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 symptoms summarized [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 and Symptoms	Aspects of life affected	Type of PRO (See table 1)
Degeneration of the cartilage that lines the joints.  <u>Symptoms:</u> pain/tenderness, swelling, creaking, stiffening of affected joints, weakness and shrinkage of surrounding muscles due to lack of use (because of pain), enlarged and distorted joints		

#### ASSIGNMENT

2

### Impact of osteoarthritis and treatment 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 the most relevant PRO to each comment.

Verbatim comments	Type of PRO (See table 1)

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?

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

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**Table 1: Examples of concepts used in**

### Patient-Reported Outcomes

Type of PRO	Concepts	Attributes
Health-Related Quality of Life (HRQL)	HRQL is multidimensional and represents the patient's evaluation of a health condition and its treatment on daily life: physical function, psychological function, social function, role, function, emotional function, well-being, vitality, etc.	Frequency, impact, intensity, severity, bothersomeness
Symptoms	Reports of physical and psychological symptoms or sensations not directly observable, 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

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

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

### BACKGROUND

When deciding which Patient-Reported Outcomes (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 table 1, assign each of the life aspects affected by the condition to an appropriate PRO.

#### ASSIGNMENT

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#### Choosing a relevant PRO

From the description of osteoarthritis symptoms summarized 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 and Symptoms	Aspects of life affected	Type of PRO (See table 1)
Degeneration of the cartilage that lines the joints.  <u>Symptoms:</u> pain/tenderness, swelling, creaking, stiffening of affected joints, weakness and shrinkage of surrounding muscles due to lack of use (because of pain), enlarged and distorted joints		

**Table 1: Examples of concepts used in Patient-Reported Outcomes**

Type of PRO	Concepts	Attributes
<b>Health-Related Quality of Life (HRQL)</b>	HRQL is multidimensional and represents the patient's evaluation of a health condition and its treatment on daily life: physical function, psychological function, social function, role, function, emotional function, well-being, vitality, etc.	Frequency, impact, intensity, severity, bothersomeness
<b>Symptoms</b>	Reports of physical and psychological symptoms or sensations not directly observable, e.g., energy and fatigue, nausea, irritability	Frequency, severity, bothersomeness
<b>Functional Status</b>		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	
<b>Perceptions</b>		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	
<b>Advantage/Opportunity</b>	Perceptions of stigma or reports of discrimination because of health condition	Frequency, impact
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<b>Treatment adherence</b>	Reports or observations of actual use of treatments	Frequency

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



# Workmat 2

## Learning points

- ✓ The relative burden of disease and treatment on population can be measured through PRO
- ✓ The concept used in PRO cover a broad span from symptoms to quality of life and functional status
- ✓ The patient plays an important part in the development of a questionnaire

# WORKMAT 5:

## Choosing an appropriate existing measure

### Objectives

- ✓ To explore the process for selecting an appropriate PRO 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 a PRO instrument
- ✓ To identify and evaluate established questionnaires for use in a specific patient group

# 5- CHOOSING AN APPROPRIATE EXISTING MEASURE

**10 Questions to ask yourself prior to searching for a PRO instrument**

## BACKGROUND

The development of a new instrument requires an investment of both time and resources. Most frequently, disease-specific instruments are developed to measure concepts not covered by existing instruments. Decisions about whether to invest time and resources into the development of a new instrument depend on the importance of the outcome in the drug development process, the availability of existing instruments to assess the relevant outcomes for the drug and disease indication, and the commitment of the developer. The development of a new Patient-Reported Outcomes (PRO) instrument requires about two years of effort and several studies to pilot test the instrument and to evaluate its psychometric characteristics.

The effect of treatment or intervention on a patient's perspective is a balance between the safety, efficacy, and convenience of the treatment in question vs. the impact of the disease itself. The first step in developing a measurement strategy is to develop a hypothesis for the domains which may benefit from treatment. In order to avoid biasing the instrument in favor of a preferred hypothesis, a specific clinical research scenario must be used.

These assignments will provide you with criteria to help you evaluate whether an appropriate patient's perspective measure already exists for a particular clinical trial.

## ASSIGNMENT 1

### Developing hypotheses

Read the following research scenario and discuss the main clinical effects of treatment. Write in the table what you consider to be the most important PRO and any additional ones that might be affected by the treatment.

Clinical Research Scenario	a. List up to 5 of the most important PRO.	b. Describe how each of these might be affected by the treatment.
<p><b>Comparative trial of anti-inflammatory treatment in patients with mild to moderate osteoarthritis.</b></p> <p><b>Background:</b> Osteoarthritis, generally described as joint pain, is a common disease in the elderly population. The main symptom is pain, which may arise from the affected joint, surrounding bone, or inflammation. The pain is characteristically worse at the end of the day and accompanied with stiffness after inactivity and limitation of joint movement. In the absence of specific agents that might prevent or reverse osteoarthritis, treatment is symptomatic and directed primarily towards pain control and increased mobility.</p> <p><b>Purpose:</b> to evaluate the effects of two different forms of non-steroidal anti-inflammatory drugs (NSAIDs) in patients suffering from mild to moderate osteoarthritis. In order to aid the decision and policy making on the appropriate use of resources in treating osteoarthritis, it is important that the results can be interpreted in the context of a wider population.</p> <p><b>Setting:</b> This multinational clinical trial has been designed to compare the safety and efficacy of two NSAIDs in patients between 45 and 65 years of age. Although Drug A has been shown to be effective in treating osteoarthritis, it has a high incidence of gastrointestinal side effects. Drug B is a new enteric coated tablet, which should reduce the incidence and severity of these side effects, and it is expected to have at a minimum, equal efficacy. Three hundred patients will be recruited into the study from primary care centers in the USA, Canada, the UK, and Scandinavia.</p> <p><b>Design:</b> After a two-week washout period, patients will be randomly assigned to receive either Drug A or B for a six-week treatment period. The primary endpoints are pain and mobility which will be assessed at weekly intervals. The measure of the impact of the treatment on a patient's life is considered to be a secondary endpoint.</p>		
	<p><b>c. Which PRO subscales do you expect to respond (i.e. what are your hypothesis)?</b></p>	
	<p><b>d. The scheme below shows the study design. Mark the points in the study in relation to the primary endpoints where PRO should be measured with an arrow.</b></p>	

Questions:	Potential Responses:
1) What is the purpose of your study?	Clinical trial; epidemiological; needs assessment; caregiver burden
2) What is the population to be studied?	Disease, conditions, ethnic or cultural group, gender, age, socioeconomic status
3) What are the scales most relevant to that population?	Generic, disease-specific, condition-specific; adult vs. child
4) Who is the appropriate respondent?	Adult patient; adult proxy caregiver; child; parent of child; primary caregiver of child other than parent; inpatient/outpatient
5) What is the optimal mode of administration?	Interview (face to face/phone); self-report (home (mail-out/mail-back); clinic, trial laboratory); computer-assisted
6) What is the background of the majority of respondents?	Reading/comprehension level, language, gender, age, culture, education of respondents
7) What is the appropriate instrument length?	Must be sufficiently long to be scientifically robust, yet short enough to be practical in the 'real world'; smaller samples need a greater number of items per scale; larger samples need a lesser amount of items per scale
8) How will you define a meaningful difference? What is a meaningful difference?	Statistically significant vs. clinically relevant vs. socially meaningful
9) Which subscales do you expect to respond?	All hypotheses should be pre-specified in the protocol. Answer will be dependent on the population being studied and will influence the type of measurement tool to use
10) What is the extent of time between administrations?	Answer will affect recall periods and expectations for meaningful differences

## ASSIGNMENT 2

### Designing an instrument using existing PRO measures; research scenario for osteoarthritis

a) For the questionnaires below, and referring to the table on the right and the document "Criteria for evaluating PRO instrument", check those properties that match the hypotheses and description of the trial in Assignment 1.

Instruments	Arthritis Impact Measurement Scales (AIMS 2)	Check	WOMAC Osteoarthritis Index (WOMAC)	Check	Health Assessment Questionnaire (HAQ)	Check	SF-36	Check	Psychological General Well Being Index (PGWB)	Check
Number of items	78		24		20		36		22	
Purpose	To assess health outcomes among persons 18 years and older with arthritis.		To assess health outcomes in clinical trials of patients 55 years and older with osteoarthritis of the hip or knee		To assess disability and pain associated with arthritis		To express health outcomes from a wide range of interventions on a common scale in persons aged 18 years and older		To assess self-reported well being and distress in the community from ages 25-74 years	
Concepts measured	Mobility level (5) Walking and bending (5) Hand & finger function (5) Arm function (5) Self-care tasks (4) Household tasks (4) Social activity (5) Support from family & friends (4) Arthritis pain (5) Work (5) Level of tension (5) Mood (5) Overall concepts (21)		Pain (5) Physical Function (17) Stiffness (2)		Dressing (2) Eating (2) Walking discomfort (2) Hygiene (3) Reach (2) Arising (2) Grip (3) Activities (4)		Mental Health (5) General health perceptions (6) Pain (2) Physical functioning (10) Role limitations (7) Social functioning (2) Vitality (4)		Positive well-being (4) Depression (3) Anxiety (5) Vitality (4) Health perceptions (3) Self-control (3)	
Development language	English (US)		English (US)		English (US)		English (US)		English (US)	
Applications	Clinical use (juvenile version available)		Clinical and research use		Clinical and research use		Clinical and research use		Clinical and research use	
Language adaptations	Chinese, Dutch, French, Greek, Hebrew, Italian, Japanese, Norwegian, Portuguese for Brazil, Russian, Spanish, Swedish		Afrikaans, Arabic for Egypt, Bulgarian, Croatian, Czech, Danish, Dutch, English for Australia, Canada, UK (US), Estonian, Finnish, French, Greek, Hebrew, Italian, Japanese, Mandarin for China, Norwegian, Polish, Portuguese, Russian, Spanish, Swedish, Turkish + 39 other languages		Afrikaans for South Africa, Arabic, Chinese, Croatian, Czech, Danish, Dutch, English (UK), Finnish, French, French Canadian, German, Greek, Hebrew, Hungarian, Italian, Japanese, Korean, Norwegian, Polish, Portuguese, Romanian, Russian, Serbian, Slovenian, Spanish, Swedish, Turkish + 19 other languages.		Afrikaans, Chinese for Taiwan, Danish, Dutch, English for Australia / New Zealand, UK), Finnish, French (France, Canada), German, Hebrew, Hungarian, Italian, Japanese, Korean, Norwegian, Polish, Portuguese, Romanian, Russian, Serbian, Slovenian, Spanish, Swedish, Turkish + 38 other languages		Afrikaans, Catalan, Czech, Danish, Dutch, English (for Australia, Canada, Ireland, UK), Finnish, French, German, Greek, Hebrew, Hungarian, Italian, Japanese, Korean, Latvian, Norwegian, Polish, Portuguese, Slovak, Slovenian, Spanish, Swedish + 23 other languages.	
Reliability	Internal consistency high for all measures		Good test-retest correlation (apart from stiffness scale)		High test-retest correlation and internal consistency		Assessed in more than 10,000 patients and 2,000 non-patients		Good internal consistency and test-retest reliability in a variety of general and mental health populations	
Validity	Good correlation with traditional rheumatology measures		Some correlation with other scales		Good correlation between scores and observer ratings		Construct validity established by comparison of patients and healthy populations		Validity assessed using standard psychological tests (e.g., MMPI for depression)	
Responsiveness	Able to detect changes		Unknown		Able to detect changes but not superior to other instruments (e.g., AIMS)		Able to detect changes		Unknown	
Interpretability	Arthritis data available, used as 'gold standard' in arthritis		Good correlation with clinical indices of arthritis severity but no large surveys documenting norms or benchmarks		Norms and arthritis benchmarks available for comparison		Norms and benchmark data available for comparison		US norms are available	
Scoring	Scores for individual concepts can be summed up to provide an overall score		Concept scores obtained by summing up all scores within a scale, no overall score		4-point scale to measure ability to perform task, overall scores for physical disability and physical discomfort, no system to value tradeoffs		Single score per concept after appropriate transformation of response (0-100); profile option; physical and mental summary score option		Total score obtained from summing up individual item responses	
Burden	Self-administered ; 20 minutes		Self- or interviewer-administered		Interviewer- or self- or telephone administered; 5-8 minutes		Self- or interviewer- or telephone-administered; computerized administration is also available; 5-10 minutes		Self-administered, self response only; 8-15 minutes	
Recall periods	Past month		48 hours		Past week		Time reference 4 weeks (acute version available)		Time reference is last 4 weeks	

b) What would be your preferred instrument for measuring PRO?

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c) Give the reasons for your choice

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## ASSIGNMENTS

### Assignment 1:

The relevance of PRO as an outcome of treatment intervention depends not only on the impact of the disease and population but also on the clinical and psychological impact of the treatment in question including any side effects. In this assignment, you will consider a clinical research scenario and try to find a net balance of the effects on a patient's life between improved clinical parameters and adverse effects of treatment. Study the research scenario for osteoarthritis and answer the questions to help you define a suitable measurement approach.

### Assignment 2:

Data on the attributes of some existing scales for osteoarthritis are provided in the table.

- Start by taking the list of PRO domains from Assignment 1 that you identified as being the important outcome measures for the clinical research scenario. Indicate the extent to which each of these instruments covers these domains by marking the relevant properties.
- Review the "10 Questions to ask yourself" and tables 3.1 & 3.2 provided in the Workbook . Now describe which of the instruments you would choose for this research scenario. Would you add any additional instruments or modules?
- Give the reasons for your choice(s).

# 5- CHOOSING AN APPROPRIATE EXISTING MEASURE

## 10 Questions to ask yourself prior to searching for a PRO instrument

### BACKGROUND

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Questions:	Potential Responses:
1) What is the purpose of your study?	Clinical trial; epidemiological; needs assessment; caregiver burden
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9) Which subscales do you expect to respond?	All hypotheses should be pre-specified in the protocol. Answer will be dependent on the population being studied and will influence the type of measurement tool to use
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# 5- CHOOSING AN APPROPRIATE EXISTING MEASURE

## 10 Questions to ask yourself prior to searching for a PRO instrument

### BACKGROUND

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Questions:	Potential Responses:
1) What is the purpose of your study?	Clinical trial; epidemiological; needs assessment; caregiver burden
2) What is the population to be studied?	Disease, conditions, ethnic or cultural group, gender, age, socioeconomic status
3) What are the scales most relevant to that population?	Generic, disease-specific, condition-specific, adult vs. child
4) Who is the appropriate respondent?	Adult patient; adult proxy caregiver; child; parent of child; primary caregiver of child other than parent; inpatient/outpatient
5) What is the optimal mode of administration?	Interview (face to face/phone); self-report (home (mail-out/mail-back); clinic, trial laboratory); computer-assisted
6) What is the background of the majority of respondents?	Reading/comprehension level, language, gender, age, culture, education
7) What is the appropriate instrument length?	Must be sufficiently long to be scientifically robust, yet short enough to be practical in the "real world"; smaller samples need a greater number of items per scale; larger samples need a lesser amount of items per scale
8) How will you define a meaningful difference?	Statistically significant vs. clinically relevant vs. socially meaningful
9) Which subscales do you expect to respond?	All hypotheses should be pre-specified in the protocol. Answer will be dependent on the population being studied and will influence the type of measurement tool to use
10) What is the extent of time between administrations?	Answer will affect recall periods and expectations for meaningful differences

### ASSIGNMENT

## 2

### Designing an instrument using existing PRO measures; research scenario for osteoarthritis

a) For the questionnaires below, and referring to the table on the right and the document "Criteria for evaluating PRO instrument", check those properties that match the hypotheses and description of the trial in Assignment 1.

Instruments	Arthritis Impact Measurement Scales (AIMS 2)	Check	WOMAC Osteoarthritis Index (WOMAC)	Check	Health Assessment Questionnaire (HAQ)	Check	SF-36	Check	Psychological General Well Being Index (PGWB)	Check
Number of items	78		24		20		36		22	
Purpose	To assess health outcomes among persons 18 years and older with arthritis		To assess health outcomes in clinical trials of patients 55 years and older with osteoarthritis of the hip or knee		To assess disability and pain associated with arthritis		To express health outcomes from a wide range of interventions on a common scale in persons aged 18 years and older		To assess self-reported well being and distress in the community from ages 25-74 years	
Concepts measured	Mobility level (5) Walking and bending (5) Hand & finger function (5) Arm function (5) Self-care tasks (4) Household tasks (4) Social activity (5) Support from family & friends (4) Arthritis pain (5) Work (5) Level of tension (5) Mood (5) Overall concepts (21)		Pain (5) Physical function (17) Stiffness (2)		Dressing (2) Eating (2) Walking discomfort (2) Hygiene (3) Reach (2) Arising (2) Grip (3) Activities (4)		Mental Health (5) General health perceptions (6) Pain (2) Physical functioning (10) Role limitations (7) Social functioning (2) Vitality (4)		Positive well-being (4) Depression (3) Anxiety (5) Vitality (4) Health perceptions (3) Self-control (3)	
Development language	English (US)		English (US)		English (US)		English (US)		English (US)	
Applications	Clinical use (juvenile version available)		Clinical and research use		Clinical and research use		Clinical and research use		Clinical and research use	
Language adaptations	Chinese, Dutch, French, Greek, Hebrew, Italian, Japanese, Norwegian, Portuguese for Brazil, Russian, Spanish, Swedish		Afrikaans, Arabic for Egypt, Bulgarian, Croatian, Czech, Danish, Dutch, English (for Australia Canada, UK, US), Estonian, Finnish, French, Greek, Hebrew, Italian, Japanese, Mandarin for China, Norwegian, Polish, Portuguese, Russian, Spanish, Swedish, Turkish + 39 other languages		Afrikaans, Chinese for Taiwan, Danish, Dutch, English (for Australia, New Zealand, UK), Finnish, French (for France, Canada), German, Hebrew, Hungarian, Italian, Japanese, Korean, Norwegian, Polish, Portuguese, Romanian, Russian, Serbian, Slovenian, Spanish, Swedish, Turkish + 10 other languages.		Afrikaans, Chinese for Taiwan, Danish, Dutch, English (for Australia, New Zealand, UK), Finnish, French (for France, Canada), German, Hebrew, Hungarian, Italian, Japanese, Korean, Norwegian, Polish, Portuguese, Romanian, Russian, Serbian, Slovenian, Spanish, Swedish, Turkish + 38 other languages		Afrikaans, Catalan, Czech, Danish, Dutch, English (for Australia, Canada, Ireland, UK), Finnish, French, German, Greek, Hebrew, Hungarian, Italian, Japanese, Korean, Latvian, Norwegian, Polish, Portuguese, Slovak, Slovenian, Spanish, Swedish + 23 other languages.	
Reliability	Internal consistency high for all measures		Good test-retest correlation (apart from stiffness scale)		High test-retest correlation and internal consistency		Assessed in more than 10,000 patients and 2,000 non-patients		Good internal consistency and test-retest reliability in a variety of general and mental health populations	
Validity	Good correlation with traditional rheumatology measures		Some correlation with other scales		Good correlation between scores and observer ratings		Construct validity established by comparison of patients and healthy populations		Validity assessed using standard psychological tests (e.g., MMPI for depression)	
Responsiveness	Able to detect changes		Unknown		Able to detect changes but not superior to other instruments (e.g., AIMS)		Able to detect changes		Unknown	
Interpretability	Arthritis data available, used as "gold standard" in arthritis		Good correlation with clinical indices of arthritis severity but no large surveys documenting norms or benchmarks		Norms and arthritis benchmarks available for comparison		Norms and benchmark data available for comparison		US norms are available	
Scoring	Scores for individual concepts can be summed up to provide an overall score		Concept scores obtained by summing up all scores within a scale; no overall score		4-point scale to measure ability to perform task; overall scores for physical disability and physical discomfort; no system to value tradeoffs		Single score per concept after appropriate transformation of response (0-100); profile option; physical and mental summary score option		Total score obtained from summing up individual item responses	
Burden	Self-administered; 20 minutes		Self- or interviewer-administered		Interviewer- or self- or telephone administered; 5-8 minutes		Self- or interviewer- or telephone administered; computerized administration is also available; 5-10 minutes		Self-administered, self response only; 8-15 minutes	
Recall periods	Past month		48 hours		Past week		Time reference 4 weeks (acute version available)		Time reference is last 4 weeks	

b) What would be your preferred instrument for measuring PRO?

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c) Give the reasons for your choice

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### ASSIGNMENTS

#### Assignment 2:

Data on the attributes of some existing scales for osteoarthritis are provided in the table.

a) Start by taking the list of PRO domains from Assignment 1 that you identified as being the important outcome measures for the clinical research scenario. Indicate the extent to which each of these instruments covers these domains by marking the relevant properties.

b) Review the "10 Questions to ask yourself" and tables 3.1 & 3.2 Provided in the Workbook. Now describe which of the instruments you would choose for this research scenario. Would you add any additional instruments or modules?

c) Give the reasons for your choice(s).

# Workmat 5

## Learning points

- ✓ The first step is to ask yourself Key Questions
- ✓ The selection of a PRO instrument or the choice of domains (in the case of HRQL) is influenced by many factors, among them the severity and nature of the disease, the expected benefits and side effects of treatment, the evidence of its psychometric properties, its availability in the targeted languages