Het PRO-Active model: *Fysieke activiteit vanuit het perspectief van de patiënt*

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Overview of presentation

1. Physical activity: a relevant outcome for patients with COPD
2. Understanding physical activity from the patients’ perspective: the PROactive model
3. Applying the PROactive model in future research and clinical practice

% population engaging in sufficient moderate physical activity: room for improvement

[Graph showing percentage of population engaging in sufficient moderate physical activity]

Poor physical activity as one of the main risk factors of burden of chronic disease 2010

Estimated deaths and disability-adjusted life years attributable to the independent effects of 67 risk factors

DALY = sum of years lived with disability and years of life lost

[Table showing DALYs for various risk factors]

Poor physical activity is estimated to cause 9% of premature mortality worldwide

[Graph showing the impact of poor physical activity on DALYs]

**COPD prevalent condition that is among the 10 leading causes of death worldwide**

COPD ranks second in view of disability adjusted life years (43% increase between 1990 and 2010).

367,785 COPD patients

361,800 COPD patients


**Physical inactivity: a worrisome problem in COPD**

Reduced physical activity increases the risk for hospital (re)admission, morbidity (cardiovascular, diabetes, osteoporosis) and mortality.

Very low: Mainly sitting work, no PA in leisure time
Low: < 2h/week low intensity physical activity
Average: 0.50
High: 1.0

**Health outcomes can be assessed in various ways**

Patient outcome assessment (e.g. physical activity)

Clinician reported

Physical / biomarkers

Observer reported (caregiver)

Patient reported

Example: 6 min walk test
Example: Doubly-labeled water
Example: "my husband can’t do anything anymore"

**Physical activity reported by patients to be most affected by COPD**

The PERCEIVE study (N=1100)

- cannot complete activities I like to do: 54%
- suffer from sleep disturbances: 52%
- less money because of treatment costs: 29%
- lost social contacts: 19%
- lost the "joy of life": 16%
- stopped working/career: 15%
- moved to another location (better air): 13%
Definition of a Patient Reported Outcome (PRO)

“A PRO is any direct report of the status of a patient’s health condition that comes directly from the patient without interpretation of the patient’s response by a clinician or anyone else”

“any outcome directly evaluated by the patient and based on patient’s perception of a disease and its treatment(s)”

“The use of a Patient Reported Outcome instrument is advised when measuring a concept best known by the patient or best measured from the patient’s perspective”


Why do we need patient reported outcome measures (PROMs)?

1) Relevance for drug claims:
- difficult to show superiority of new drugs on hard outcomes
- importance of improvements in quality of life

2) Essential to understand drug effectiveness:
- e.g. Drug is not working: is patient adherent?

3) Key element in treatment decision making:
- e.g. Similar drug, but other side effects: patient’s preference?

4) Unique indicator of disease and treatment impact:
- how many symptoms does patient have and are symptoms improving with treatment?

FDA guidelines on patient reported outcome instrument development

- Identify concepts & develop conceptual framework
- Create the instrument (items, scales, format, pilot)
- Assess measurement properties (Redundancy, revise, MCID, training materials)
- PATIENT INPUT IN EVERY STAGE IS VITAL


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PROactive: a European Public-private consortium to design a PRO instrument on physical activity

Scientific coordinator: Prof. Dr. Thierry Troosters (KU Leuven)

Funded by the Innovative Medicines Initiative Joint Undertaking (IMI JU) # 115011
http://www.proactivecopd.com

Why do existing questionnaires on physical activity not meet the FDA criteria on PRO instruments?

104 PRO instruments:
- 47.1% defined aim
- 37.5% used patients’ input to generate items
- 0% used a conceptual framework

182 domains:
- conceptual confusion
- incomplete assessment

Two conceptual frameworks published, but none suitable

What do we already know about physical activity from qualitative studies? A systematic review

None of the studies addressed experience with physical activity specifically and do not describe population in sufficient detail

One to one interviews
Focus groups

References:
- Gimeno-Santos et al. Health QOL Outcomes 2011, 9:86
Incorporating the patients’ experiences and words to guarantee content validity

Empirical (qualitative research) evidence that demonstrates the items and domains of a PRO instrument are appropriate and comprehensive, relative to its intended measurement concept, population, and use

WHAT?
- Concept & Item content
- Administration & responses
- Frequency & Recall period

WHO?
- Target Population

WHEN?
- Frequency & Recall period

Step 1: determine the heterogeneity of the population under investigation

Consensus based on multi-disciplinary international expert panel meeting

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Quote</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>At least 40% of each gender Medical chart</td>
</tr>
<tr>
<td>Age</td>
<td>At least 30 &lt; 60 years      Medical chart</td>
</tr>
<tr>
<td>Socio-economic class</td>
<td>Min. 20% low + 20% high     Questionnaire</td>
</tr>
<tr>
<td>Smoking status</td>
<td>Ex-smokers + min. 25% current Self-report</td>
</tr>
<tr>
<td>GOLD stage</td>
<td>All stages; 10-20% stage I Lung function</td>
</tr>
<tr>
<td>BODE index</td>
<td>All categories (40% mild) Lung function, 6 minutes walking distance test, MRC dyspnea scale</td>
</tr>
<tr>
<td>Exacerbations</td>
<td>Max. 20% in last 3 months Medical chart + interview</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>Max. 20% Medical chart + interview</td>
</tr>
<tr>
<td>Depression</td>
<td>Max. 10% Hospital Anxiety and Depression Scale</td>
</tr>
<tr>
<td>Long term oxygen use</td>
<td>Max. 10% Medical chart</td>
</tr>
</tbody>
</table>

Full phenotyping of COPD patients participating in qualitative studies

Step 2: qualitative interviews to understand the concept from the patient’s perspective

- One on one interview, followed by focus groups
- Enrolling patients from 4 different European countries from diverse care settings and geographical characteristics
  - Belgium, the Netherlands, United Kingdom (Scotland), Greece

Advantages and disadvantages of focus groups and interviews

<table>
<thead>
<tr>
<th>Focus groups</th>
<th>Interviews</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advantages</td>
<td>Disadvantages</td>
</tr>
<tr>
<td>- Rich sources of data</td>
<td>- Cost more in-depth and detailed information about an individual’s experience</td>
</tr>
<tr>
<td>- Allows to use ideas of others or voice their own ideas</td>
<td>- Can be useful for sensitive topics</td>
</tr>
<tr>
<td>- Participants can compare their experiences with others</td>
<td>- Data can be easier to analyze</td>
</tr>
<tr>
<td>- Able to meet many participants in one interview</td>
<td>- Scheduling can be easier</td>
</tr>
</tbody>
</table>

- Site visit or on-site interview making it easier to access a wide range of other group members
- Interviews need to be highly trained and able to meet the group
- One interview group members can keep time of entire group
- Data taken longer to collect the data
- Limited to one patient’s view at a time, no group interaction
- Interviews need to be trained with excellent group interaction skills
- May be more costly (e.g., travel, nurses’ rental, transcription fees)

Step 3: analysis of interviews & focus groups

- PRO Instrument Review
- Clinical Experts
- Literature
- Interview Guide
- Hypothesized Conceptual Framework
- Relevant Concept C-attributes (e.g., Frequency, Severity)
- Target Product Profile

CODING FRAMEWORK
CODING DICTIONARY

Translations into English
Building Blocks for Analyses
Using Atlas

Using Atlas
Example

Female patient focus group 1, Greece, age 74 years, GOLD stage II

- Breathing difficulties
- Leg problems
- Taking breaks
- Time needed to recover
- Difficulty walking

"So, you are breathing with difficulty and you are fighting to recover from your legs and from your breathing so that you can walk another ten metres. And the same again at the next ten metres. A stop. You can't go any longer."

Conceptual model on how COPD patients experience physical activity

<table>
<thead>
<tr>
<th>Influencing factors</th>
<th>Consequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical activity</td>
<td></td>
</tr>
<tr>
<td>Symptoms during physical activity:</td>
<td></td>
</tr>
<tr>
<td>- Breathing difficulties</td>
<td></td>
</tr>
<tr>
<td>Amount of physical activity:</td>
<td></td>
</tr>
<tr>
<td>- Walking flat or uphill</td>
<td></td>
</tr>
<tr>
<td>- Climbing stairs</td>
<td></td>
</tr>
<tr>
<td>- Carrying things</td>
<td></td>
</tr>
<tr>
<td>- Self-care activities</td>
<td></td>
</tr>
<tr>
<td>- Household chores</td>
<td></td>
</tr>
<tr>
<td>Need for physical adaptations:</td>
<td></td>
</tr>
<tr>
<td>- Paced</td>
<td></td>
</tr>
<tr>
<td>- Rest for a break</td>
<td></td>
</tr>
</tbody>
</table>

From quotes, to codes to themes based on interviews and focus groups

1) Excel file with all quotes extracted per code per patient

<table>
<thead>
<tr>
<th>code</th>
<th>Quotes from one to one interviews</th>
<th>Total quotes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Climbing stairs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P3</td>
<td></td>
<td></td>
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<tr>
<td>P4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2) Excel file indicating how many patients addressed a topic

<table>
<thead>
<tr>
<th>code</th>
<th>% patients interviews</th>
<th>Total quotes</th>
<th>% patients focus groups</th>
<th>Total quotes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pacing, slowing down</td>
<td>87%</td>
<td>71</td>
<td>64%</td>
<td>44</td>
</tr>
<tr>
<td>Need for breaks</td>
<td>83%</td>
<td>73</td>
<td>62%</td>
<td>61</td>
</tr>
<tr>
<td>Breathing techniques</td>
<td>30%</td>
<td>13</td>
<td>27%</td>
<td>27</td>
</tr>
<tr>
<td>Pushing yourself</td>
<td>26%</td>
<td>13</td>
<td>45%</td>
<td>38</td>
</tr>
<tr>
<td>Using Medication</td>
<td>39%</td>
<td>18</td>
<td>42%</td>
<td>39</td>
</tr>
</tbody>
</table>

Themes similar irrespective of age and gender

- self-care
- walking uphill
- walking
- hobbies
- cycling
- climbing stairs
- household chores
- carrying things

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The PROactive model as the basis of a new PRO instrument to measure physical activity in COPD

- Interviews
- Focus groups
- Item generation
- Cognitive debriefings
- Item selection
- Further validation

- Daily PRO instrument
- Clinic visit PRO instrument
- Checking clarity of instructions, items and response options
- Culturally sensitive translations
- Purposive sampling + phenotyping
- Quantitative multicenter study

Response options, recall period and administration mode

- Comprehensive item generation from quotes to capture the physical activity themes outlined in the conceptual framework
- Administration mode: electronically (e-diary)
- Response options: 5 point Likert scales
- Recall period: literature + expert view + patient input:
  - Daily version
  - Clinic visit version with 7 days recall

- Items should be relevant irrespective of country

Item lists translated in a culturally sensitive way & programmed in electronic device (PDA) prior to cognitive debriefings in 4 countries

/References

Keeping track of items, wordings, and scoring options in an item tracking grid

<table>
<thead>
<tr>
<th>Original wording</th>
<th>remarks</th>
<th>Adapted version</th>
</tr>
</thead>
<tbody>
<tr>
<td>How much walking outdoors did you do today? None at all – a little bit – some – a lot – a great deal</td>
<td>Needs more specification in terms of distance or time. Outdoors is confusing; outside is more lay language</td>
<td>How much walking did you do outside today? None at all A little bit (up to 10 minutes in total) Some (up to 30 minutes in total) A lot (up to 1 hour in total) A great deal (more than 1 hour in total)</td>
</tr>
</tbody>
</table>

Culturally sensitive translations

LOPEN

België: gaan, stappen of rennen
Nederland: gaan of stappen

Final item Pool

Amount of physical activity
Symptoms during physical activity
COPD-related symptoms of physical activity
Need for physical adaptations

Why do we need the PROActive patient reported outcome instruments?

1) Relevance for drug claims:
   - difficult to show superiority of new drugs on hard outcomes
   - importance of improvements in PROActive instruments

2) Unique indicator of disease and treatment impact:
   - does rehabilitation also improves daily physical activity?
   - can treatment of depression result in higher physical activity?

3) Key element in treatment decision making:
   - Different drugs might have different effect on PROs:
     e.g. reduced breathlessness vs. Quicker recovery

The future of the PROActive instruments

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