

# Quality of Life in Disease Understanding

Bruce Crawford, MA, MPH  
Mapi Values  
Medical Interpreters and Translators Association (MITA)  
19 October 2005

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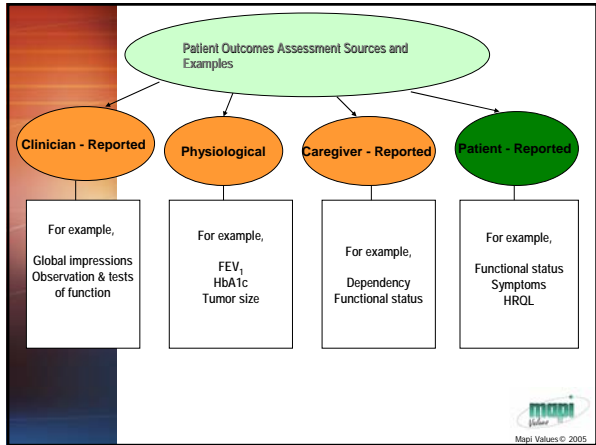
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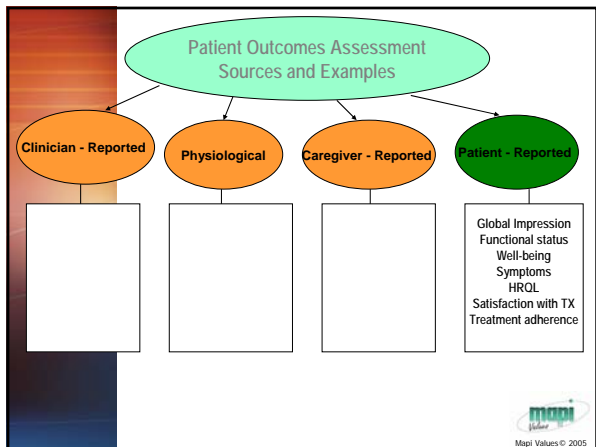
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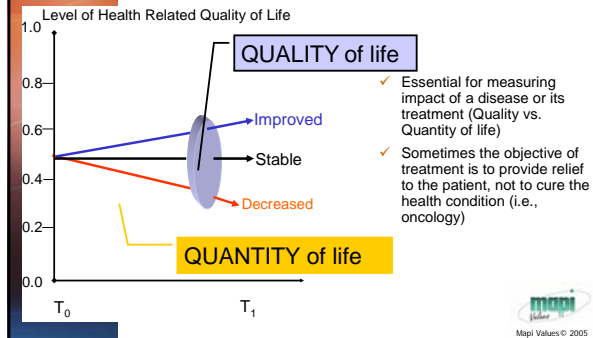
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## Why Measure Subjective Outcomes?




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## The Patient's Perspective is ...

- ✓ A **unique** indicator of the impact of disease
- ✓ **Essential** for evaluating treatment efficacy
- ✓ **Useful** for interpreting clinical outcomes
- ✓ A **key** element in treatment **decision-making**




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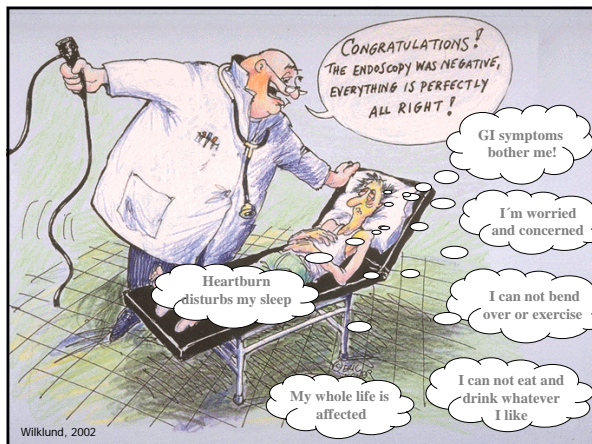
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### Health-Related Quality of Life

- ✓ Represents the patient's *evaluation* of the impact of a health condition and its treatment on relevant aspects of life
  - The evaluative component can be measured by
    - *severity*
    - *bothersomeness*
    - *importance or*
    - *satisfaction*



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### Health-Related Quality of Life

- ✓ Represents the patient's evaluation of the impact of a health condition and its treatment on *relevant aspects* of life
  - The relevant aspects of life are measured as domains, e.g.,
    - *physical*
    - *psychological*
    - *social*
    - *symptoms*



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### Health-Related Quality of Life

- ✓ Represents the patient's evaluation of the impact of a health condition and its treatment on *relevant aspects* of life
  - Domains are selected to be relevant to patients and their significant others, e.g.,
    - *focus groups*
    - *cognitive interviews*
    - *literature reviews*



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## PROs Supplement Traditional Indicators

- ✓ PROs and traditional markers of disease activity are related, but not perfectly correlated
  - daily functioning & FEV-1
    - $r = 0.10$  to  $0.30$
    - shared variance = 9%
- ✓ Thus, the two indicators are complementary



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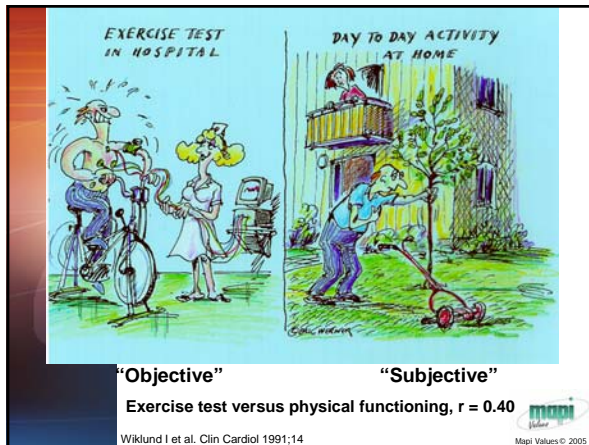
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Wiklund I et al. Clin Cardiol 1991;14



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## QOL Provides Supplemental Information

- ✓ Quality of life assessment of patients in extremity sarcoma clinical trials
- ✓ Sugarbaker et al. Surgery 1982: 91:17



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## Sugarbaker et al. Surgery 1982

- ✓ Research Question: How does QOL compare for Amputation+ Chemo vs limb-sparing surgery+Chemo+ RT for soft tissue sarcoma?
- ✓ Design: RCT
- ✓ Measures: PAIS, SIP, Bethel Function, Katz ADL
- ✓ Subjects: 26 with soft tissue sarcoma, age < 21
- ✓ Results: QOL results similar with trends favoring amputation
- ✓ Conclusion: The limb sparing regimen did not provide better QOL




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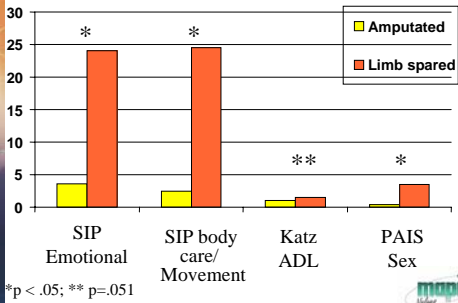
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## QOL Scores (higher = worse) for Patients with Extremity Sarcoma




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## Impact of Rhinitis on Children



"This is when I feel better and I can go out and play with friends."  
(This picture was drawn using a pink marker)



"This is when I don't feel good and my eyes don't look good. Those are drops that someone put in my eye."

(This picture was drawn by the same child who drew the picture on the left. Before she began drawing it, she put down the pink marker and picked up a black one.)




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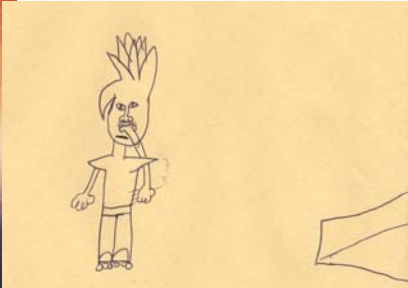
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### Impact of Rhinitis on Children



This child's nose gets "sniffly" when he rollerblades and the "sniffly" nose makes him lose his attention and wipe out (*slang for fall down*).




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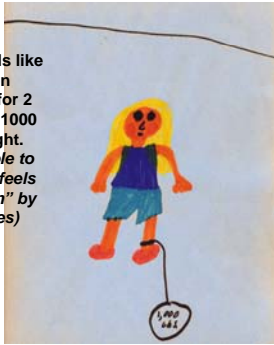

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### Impact of Rhinitis on Children

This child feels like she's been underwater for 2 hours with a 1000 pound weight. (She is unable to breathe and feels "pulled down" by her allergies)


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### Measuring Satisfaction

"Satisfaction is an emotive evaluation, a pleasant feeling caused by the fulfilment of expectations" (Oliver 1997)

Global	<ul style="list-style-type: none"> <li>Willingness to continue</li> <li>Overall satisfaction</li> </ul>
Psychological Burden	<ul style="list-style-type: none"> <li>Feeling in control</li> <li>Stress due to treatment</li> </ul>
Treatment Attributes	<ul style="list-style-type: none"> <li>Packaging</li> <li>Ease of use</li> <li>Cost</li> <li>etc.</li> </ul>
Efficacy	<ul style="list-style-type: none"> <li>Perception of how well the medication works</li> </ul>
Side Effects	<ul style="list-style-type: none"> <li>Bothersomeness of medication side effects</li> </ul>
Convenience	<ul style="list-style-type: none"> <li>Ease/convenience of taking medication as prescribed</li> <li>Interference with daily activities/life</li> </ul>




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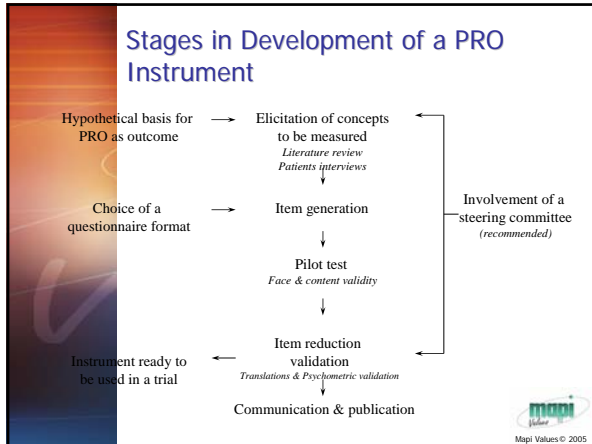
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### Conceptualizing the Development: The Conceptual Model/Framework

- ✓ Schematic detailing how the variables will interact
- ✓ Start with a literature review and overall objectives
  - Distorted joints may be important for satisfaction in RA, but not when you are measuring functioning
- ✓ Helps you focus your research and avoid adding other comments by the patient
  - Your focused research will end up as a shotgun approach

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### Assessing the Impact of Disease and Treatment

- ✓ OA clinical signs and symptoms
  - Pain/tenderness
  - Swelling and creaking
  - Stiffening of affected joints
  - Weakness and shrinkage of surrounding muscles due to lack of use
  - Enlarged and distorted joints
- ✓ What is the impact on patient HRQOL?

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### Assessing the Impact of Disease and Treatment

- ✓ OA patient quotations
  - "When I'm in acute pain I can't move"
  - "The pain wakes me up at night"
  - "Sometimes you get very depressed / you can get angry"
  - "It's also had an influence on my sex life"
  - "Your moods change easily and I can be aggressive and bad tempered"
  - "You don't feel like socializing when you are in pain"
  - "I can't do the job I used to do"



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### Questionnaire Choice

- ✓ Patient's perspective is essential
  - Item generation must be from the patient not the clinician to be acceptable in the scientific community
- ✓ Must be in lay terms
  - Lower reading level important



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### Cross-cultural issues



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**Comparability and Cultural Understanding**

- ✓ Cross cultural research often involves a difficult but important choice between sacrificing cultural understanding and sacrificing comparability
- ✓ Language is not just a way to speak, it shapes the way we process information



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**Comparability and Cultural Understanding**

- ✓ Cultures create words to reflect new experiences, so those experiences can be shared
- ✓ Different languages are not just different sets of words, they are reflections of specific experiences



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**Comparability and Cultural Understanding**

- ✓ A more literal and unadapted translation:
  - Less relevant to a second culture
  - Tend to uncover cultural differences
    - Complicated
    - Implications that render the translations unusable
- ✓ The more culturally equivalent a concept is:
  - More relevant the translations will be to their respective cultures
  - Less likely to find cultural differences



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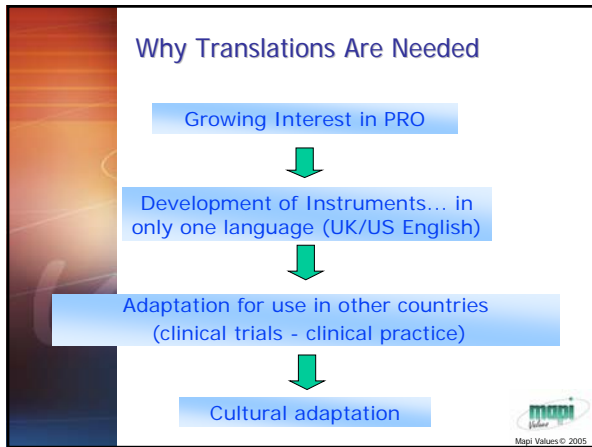
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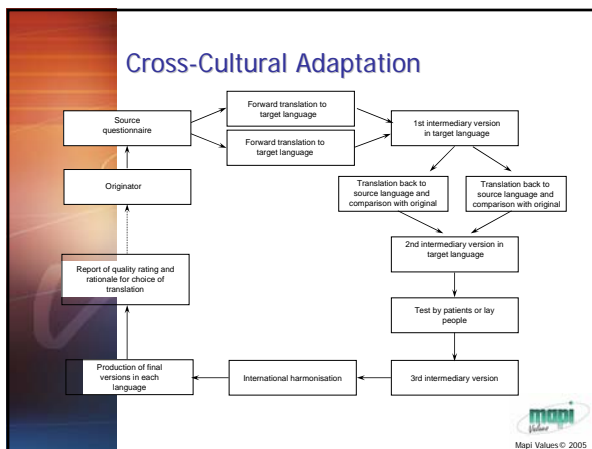
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### For a Translated Questionnaire

- ✓ Conceptual equivalence
  - See linguistic validation process
- ✓ Psychometric equivalence
  - Performance of the translated version = original
  - If there are differences in concepts, they will perform differently



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### Translation Issues – Example

Dutch → French

**Disease area : Chronic Bronchitis**

Original	Fietsen (to cycle)
Problem	What does "to cycle" stand for?
1st French version	Marcher sur une longue distance ou faire du vélo (To walk a long distance or to cycle)
Contact with author	Concept : an activity requiring moderate physical effort
2nd French version	Marcher sur une longue distance ou monter une côte (to walk a long distance or walk up a hill)
Patient test	The 2 notions cannot be associated
Final French version	Marcher d'un pas alerte (To walk at a quick pace)



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### Translation Issues – Example

Swedish → English (UK) → For use in the US

**Disease area: Angina Pectoris**

Original	En kortare promenad (ungefär 2 km) A short walk (about 2 km)
Final UK version	Short walk (about a mile)
Test on American population	One mile is not a short walk
Problem	What is important?"1 mile" or "short walk"?
Contact with author	Concept : short walk
Final American version	Short walk (several blocks)



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## Translation Issues – Example

**Pathology: Allergies**

Original	how much did allergies affect your productivity <u>while you were working</u> ?
Problem	Japan: Productivity not commonly used for human beings - using "amount of work" may be interpreted as "work load"
Alternatives	Effectiveness was used

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## Example: WPAI-AS (Q4)

During the past seven days, how much did allergies affect your productivity while you were working? Think about days you were limited in the amount or kind of work you could do, days you accomplished less than you would like, or days you could not do your work as carefully as usual. If allergies affected your work only a little, choose a low number. Choose a high number if allergies affected your work a great deal. (Circle a number.)

Allergies had no effect on my work 0 1 2 3 4 5 6 7 8 9 10 Allergies completely prevented me from working

CIRCLE A NUMBER

過去7日間、仕事をすると、アレルギーがどれくらい効率に影響を及ぼしましたか？仕事の量や内容が制限されたり、したいと思った仕事が達成できなかったり、普段通り注意深く仕事ができなかったりした日の事などを思い出してください。仕事へのアレルギーの影響が少しかつた場合は番号の低いものを、ひどかった場合は、番号の高いものをお選びください。(番号を○で囲む。)

アレルギーは仕事に影響を及ぼさなかった。 0 1 2 3 4 5 6 7 8 9 10 アレルギーは完全に仕事の妨げになった。

番号を○で囲む。

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## Measuring What You *Really* Want

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**Self-reported Data**

- ✓ Four tasks to answering a question
  - Interpret/understand the question
  - Retrieve the information
  - Formulate the information into an integrated judgment
  - Give the response



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**Where's the problem?**

- ✓ How often have you been depressed and anxious?
  - All of the time, most of the time, some of the time, none of the time
- ✓ How convenient is it for you to take the medication?
  - Very convenient, Somewhat convenient, Not convenient



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**First problem: How often have you been depressed and anxious?**

- ✓ Anxious and depressed when?
  - today or this week or the last month?
- ✓ I was anxious, but not depressed
  - how do I respond?
- ✓ I'm feeling kind of down, but I'm not clinically depressed or anything, so 'none of the time'
  - end up missing a lower end of the depressed scale



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**Second problem: How convenient is it for you to take the medication?**

- ✓ I take my medication whenever I please, so it's very convenient
  - but my Dr tells me to take it at lunchtime, that's really inconvenient.
- ✓ Bias toward a convenience response
  - no option for really inconvenient



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**Understand the Question**

- ✓ In the past 4 weeks, has your health affected your work productivity?

  
**Ambiguous?**

- ✓ Relative concept: current self vs. usual self or current self vs. coworker



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**Retrieve the Information**

- ✓ What affects recall accuracy?
  - Elapsed time
    - Telescoping
  - Salience of the event
    - Feedback of productivity by employer
  - Emotion surrounding memory
    - Pleasant/positive events remembered better
  - Mental state of the respondent
- ✓ Sensitivity of the question
  - Threatening question
  - Confidentiality



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## RUD Questionnaire – Three Questions

On a typical care day since the last visit, how much time per day did you spend assisting the patient with such tasks as...ADL, supervising, assisting..

|\_|\_| hours per day

Since the last visit, how many days did you spend providing these services to the patient? \_\_\_\_\_ days



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## Results from the RUD

### Results

ADL		Assistance		Supervision	
Days	Hours	Days	Hours	Days	Hours
30	8	30	8	30	10
30	24	30	24	30	24
7	24	7	24	7	24



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## Problems with the Results

- ✓ First caregiver: Number of hours per day when totaled = 26. Should the total add to 24? Is there double counting?
- ✓ Second caregiver: Number of hours per day when totaled = 72. This may be realistic, but should this total to 24 hours maximum?
- ✓ Third caregiver: answered 7 days. The last visit was one month ago. Is the response based on a week?



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**Linguistic Validation Conclusion**

- ✓ Complex process
- ✓ Multiple steps and quality control
- ✓ Inappropriate to literally translate
  - It's the concepts that are important!
- ✓ The goal is to obtain conceptual equivalence



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**Analysis of PROs**



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**What do I need to know to analyze results?**

- ✓ What are the PRO hypotheses?
- ✓ What type of questionnaires did we choose?
  - What are the scoring methods?
  - Are there reference scores available to help in interpretation?
- ✓ Is the questionnaire psychometrically valid in our clinical trial population?
- ✓ What type of missing data do we have (by treatment)?
  - How will we handle missing data?
- ✓ How are we controlling for multiple endpoints/tests?
- ✓ What were the clinical results?
  - Do your results make sense in line with clinical findings?



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### Main Issues to consider

- ✓ Pre-analysis
  - Get scoring documentation ASAP
  - Write analysis plan
- ✓ Issues to consider
  - Power calculations
  - Treatment of missing data
  - Multiple testing
  - Pooled analysis - international studies



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### Analyses to include

- ✓ PRO psychometrics: baseline; responsiveness
- ✓ PRO Descriptive statistics, all timepoints
- ✓ PRO patient population
- ✓ Missing data for PROs (item/scale/questionnaire)
- ✓ Change Scores over time by treatment group; total
  - Adjust for multiple testing or select apriori hypotheses
- ✓ Effect sizes, statistical values, p-values, standard deviations, confidence intervals



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### Power Calculations

- ✓ Difficult to calculate prior to study start
  - Often do not have appropriate information
    - Standard Deviations; expected point differences or definitions of clinically meaningful differences
- ✓ Prior to study
  - Use best available as approximation
    - published literature
    - validation studies
- ✓ During analysis
  - Re-calculate once you get your data in
    - Report



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## International Instruments – Psychometric Validation is Needed

- ✓ Confirmation versus original
- ✓ Stability of constructs after translation
  - Does the instrument maintain its measurement characteristics in a new situation (country/language)?
  - “Consistency” of scale performances
  - Structural equivalence
- ✓ Be aware of copyright issues



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## RHINOCONJUNCTIVITIS QUALITY OF LIFE QUESTIONNAIRE (RQLQ)

SELF-ADMINISTERED (SELF-ADMINISTERED) .....VERSION

© 1996  
DOL TECHNOLOGIES LTD.




N.B. THE ORDER OF THE QUESTIONS HAS BEEN CHANGED FROM THE ORIGINAL 1996 VERSION

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WWW: http://www.fhs.mcmaster.ca/hrqol/qolinfo.htm

This translation has been made possible through a grant from  
Translated by MAPI RESEARCH INSTITUTE  
Senior translator

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MAY 1998



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## Psychometric Analysis

- ✓ **Acceptability** missing data  
descriptive statistics
- ✓ **Scaling assumption** item-item correlations  
item-scale correlations  
factorial/multitrait analysis
- ✓ **Reliability** reproducibility  
internal consistency (Cronbach's alpha)
- ✓ **Validity** content validity  
criterion/construct validity  
clinical validity
- ✓ **Sensitivity** discriminative power  
responsiveness over time



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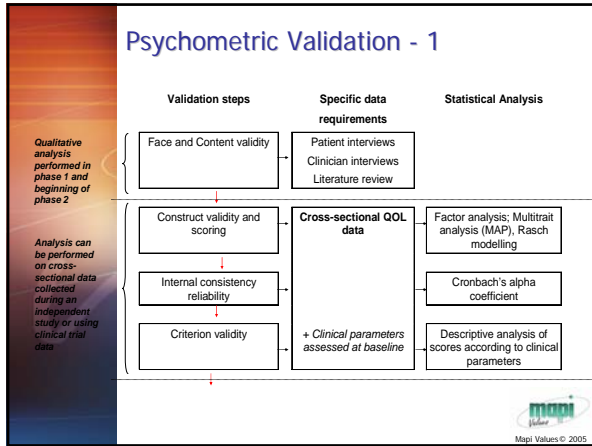
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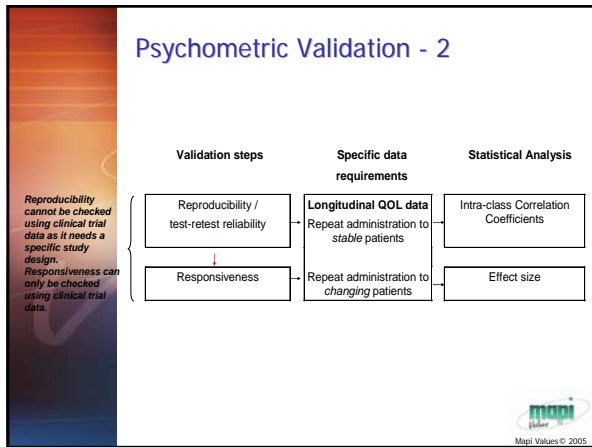
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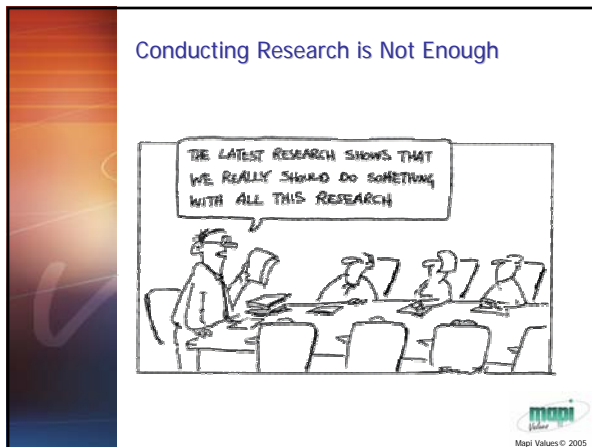
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**To Be Used in Clinical Practice, Physicians Need Education**

Sure, "how to use" is easy, but the "why" still confuses me.

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**Example of Questionnaire Validation**

アレルギー (アレルギー) 70-86, 2005(年誌)

**第3編 アレルギー性鼻炎・結膜炎 QOL 調査票 (RQLQ)**  
日本語版およびアレルギーによる作業能率の低下、活動性障害調査票 (WPAIAS) 日本語版の開発

日本臨床アレルギー学会, Mapi Value 社, McMaster 大学臨床免疫学教授, Aventis Pharmaceuticals

奥田 聡<sup>1)</sup> Bruce Crawford<sup>2)</sup> Elizabeth Juniper<sup>3)</sup> Michael J. Leahy<sup>4)</sup>

**Key words:** RQLQ, WPAIAS, QOL, Allergic rhinitis, allergic conjunctivitis

アレルギー性鼻炎 (AR) は慢性の疾患で生命を脅かすほどではないが、患者の QOL に悪影響を及ぼし、生活の作業能率を低下させる<sup>1)</sup>。QOL および生活の作業能率の影響を評価するためには、2つの調査票が開発された: RQLQ (Rhinocconjunctivitis Quality of Life Questionnaire) と WPAIAS (Work Productivity and Activity Impairment Questionnaire) の日本語版である (付 3, 付 4)。オリジナルの調査票は英語版 (RQLQ は J. Juniper, WPAIAS は M.C. Leahy により開発された) で実証的妥当性、再現性、必要性<sup>2)</sup> に関して計量心理学的に有効性が証明されている。日本語で検証するために、オランダ語版の調査票から

研究目的

RQLQ および WPAIAS は Mapi Research 社によって日本語に翻訳された (付 1, 付 2)。JCP アロジェト社 (日本臨床アレルギー学会専門会社) に依頼し季節性アレルギー性鼻炎 (SAR) 200 例を募集した。この中から、後述の症状合計スコア (TSS) 12 点以上のものを選出した。試験者は JCP 所属の医師と JCP 診療所で選出した。その際、試験は Day 0 (試験日) の夜明け前 (起床) を作成した。試験者に対しては、Day 0 の QOL 調査票の記入、および 1 週間後の再来院まで試験日の記録を依頼した。

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**Japanese QOL Label Claim – Humalog®**

【臨床成績】

項目	試験群	対照群
HbA1c (%)	7.2	7.5
空腹血糖 (mmol/L)	5.8	6.2
2 時間血糖 (mmol/L)	8.5	9.2
血糖変動係数 (%)	28.5	32.1

【重要文脈及び文脈請求】

この製品は、糖尿病患者の血糖コントロールを改善し、QOL を向上させるために設計されています。臨床試験の結果は、この製品が対照群と比較して、血糖コントロールを改善し、QOL を向上させることを示しています。

QOL

Label claim may help influence prescribing decisions

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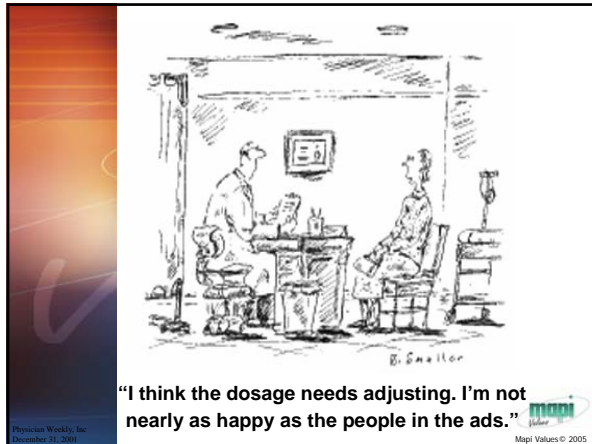
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### Conclusions

- ✓ PROs are providing a greater level of information on the patient's health
- ✓ Appropriate translations will improve the performance of the questionnaire
  - Don't let physicians translate themselves and provide to patients
  - Validity issues and copyright laws
- ✓ Psychometric validation will ensure the acceptance of the translated instrument and their results
- ✓ Good communication is important to disseminate data and improve patient health

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## QUESTIONS AND DISCUSSION

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**Contact Details**

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