

# Patient Reported Outcomes

16 December 2013, Nottingham

Esther van Zuuren

Dermatologist, Leiden University Medical Centre  
Netherlands

A Patient Reported Outcome (PRO):

- any aspect of a patient's health status and/or of a patient's treatment, as reported directly by the patient without interpretation of the patient's response by a clinician or anyone else (FDA guidance, Dec 2009) e.g.
  1. Symptoms
  2. Disease severity
  3. Health-Related Quality of Life (HRQoL)
  4. Treatment preferences and treatment satisfaction
  5. Adherence behaviour

Last 15-20 yrs patient's perspective in clinical trials is encouraged

- PROs “Empower patients to make decisions based on their values” and “level the playing field between physician and patient”
- PROs address what matters to patients and their use in clinical trials can provide the information that is critical for decision making in practice guidelines.
- Evidence suggests, however, that reporting of PROs remains sub-optimal across RCTs\*

\*Qual Life Res 2011; 20:653–664

# PROs in 'dermatology' trials

Survey by Townshend AP, Chen CM, Williams HC\*

- To what extent PROs were included in RCTs?
- How prominently and where were they featured in the article?
- Focus on participants assessment of efficacy of the treatment
- Did the assessments correlate with the judgements of the clinicians?
- 125 RCT (1994-2001)

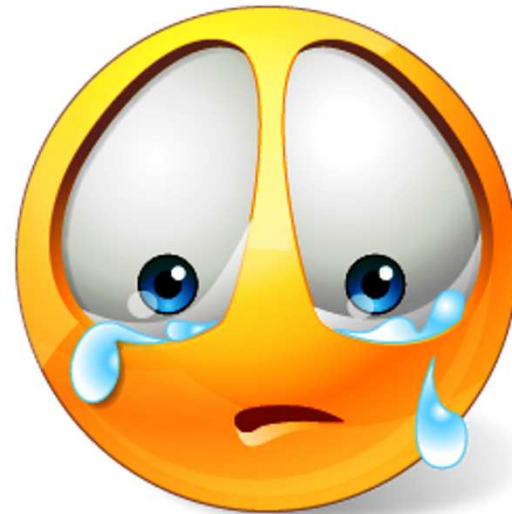
**How prominent are patient-reported outcomes in clinical trials of dermatological treatments?**

## Results

- 25% included some PRO (32 papers)
- 2 papers mentioned PROs in Methods section and did not give any result
- 9/30 presented data on PROs in full, 21 only in figs and graphs
- 29 studies contained both clinicians as participants assessed outcomes, only 5 provided enough information on agreement
- No comparison was possible for measurements of different outcomes, nor when limited data were provided (just P values)

## Conclusion

- PROs in dermatology trials were seen in just  $\frac{1}{4}$  of RCTs
- When included, often poorly and incompletely recorded or not at all



- Conditions in which outcomes are known only to the patients themselves, such as itch intensity and emotions, demand PROs as primary outcomes
- An important early part of the systematic review process is to define and list all patient-important outcomes that are relevant to their question
- The careful prior consideration of all patient-important outcomes and inclusion as a blank row in a 'Summary of findings' table will highlight what is missing in outcome measurement in the eligible randomised trials

# PROs in Cochrane reviews

## Selenium (+LT<sub>4</sub>) compared with placebo (+LT<sub>4</sub>) for participants with Hashimoto's thyroiditis

**Patient or population:** participants with Hashimoto's thyroiditis.

**Settings:** hospital outpatient department.

**Intervention:** selenium (+ levothyroxine)<sup>a</sup>.

**Comparison:** placebo (+ levothyroxine).

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo (+ levothyroxine)	Selenium (+ levothyroxine)				
<b>Change from baseline in health-related quality of life</b>	See comment	See comment	Not estimable	See comment	See comment	Not reported in any study



# PRO Measures (PROMs)

- PROs are most commonly assessed by means of standardized measures or questionnaires (PROMs)
- Disease specific or generic
- Investigators use many instruments to capture PROs, and methods for developing, validating, and analysing PRO data are diverse
- The outcome can be measured in absolute terms (e.g., severity of a symptom, sign, or state of a disease) or as a change from a previous measure

## Generic PROMs (e.g. SF-36)

- applicable to all populations
- measure broad aspects of health
- allow between-population comparisons

## Dermatology specific PROMs (Skindex 17, 29, DLQI)

- applicable in all skin diseases
- allowing for comparisons between skin diseases

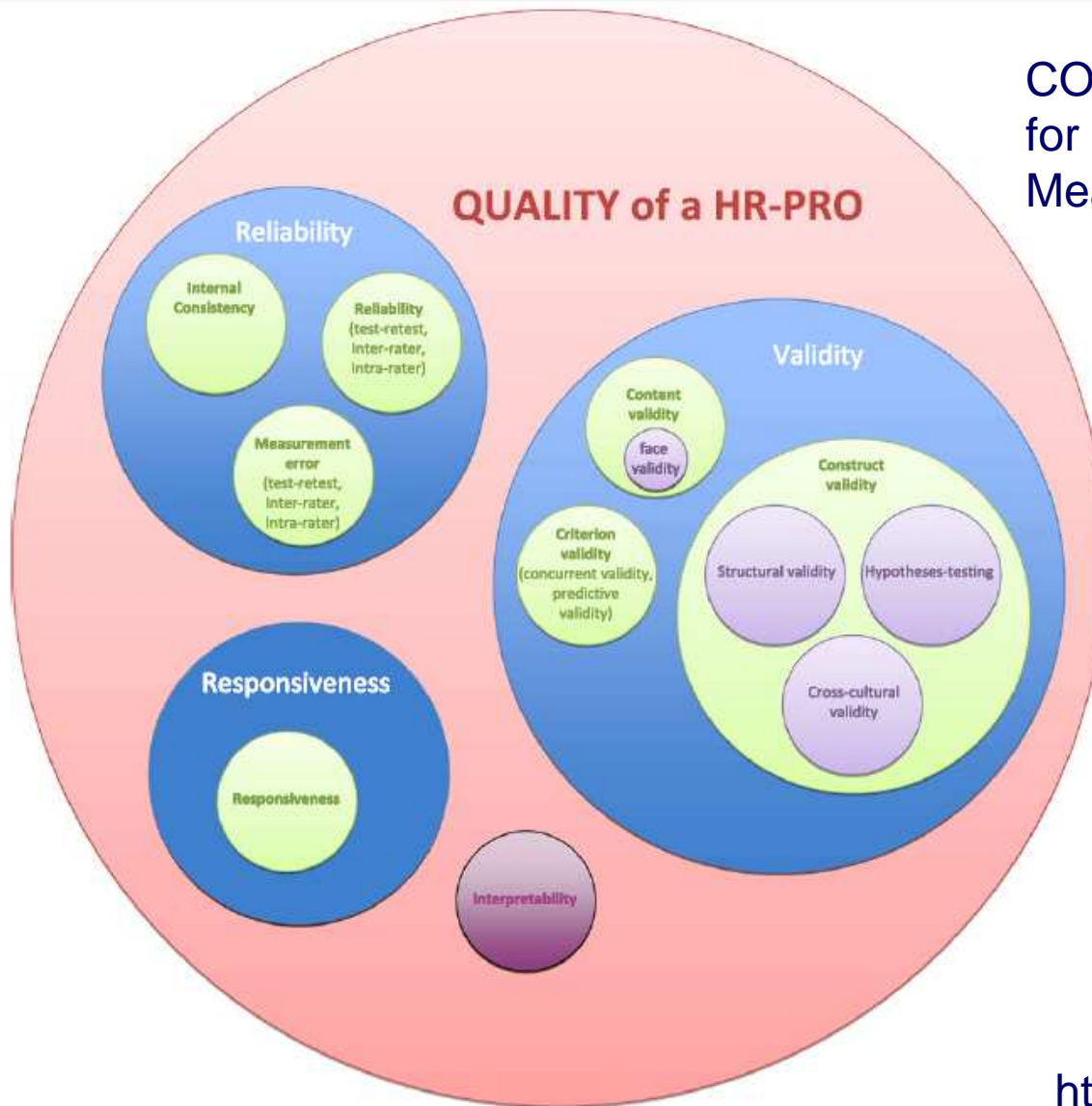
## Disease specific PROMs (PSA, POEM, RosaQoL)

- focus on disease/condition, population, symptom
- limit possible comparisons
- increased responsiveness

# PRO Measures (PROMs)

- Validity: is the instrument measuring what it is intended to measure?
- Review authors should look for, and evaluate the evidence of the validity of PROMs used in their included studies
- Responsiveness: an instrument's ability to detect change over time
- Reliability: the degree to which an instrument can produce consistent results, and consistent results on different occasions, when there is no evidence of change. To what extent are scores true scores?

# PRO Measures (PROMs)



COSMIN

COnsensus-based Standards for the selection of health Measurement INstruments

# Interpreting PROMs

What do differences on the scales mean? What does a decrease of 20 on a score on a questionnaire mean?

Establishing 'interpretability' makes results of PROMs meaningful

Minimal important difference (MID): smallest change in scores that a patient would identify as important and that would result in a change in treatment

Checklist in Chapter 17.6.a authors should consider before incorporating PROs into their reviews and ‘Summary of findings’ tables

1. What were PROs measuring?
<ul style="list-style-type: none"> <li>a. What concepts were the PROs used in the study measuring?</li> <li>b. What rationale (if any) for selection of concepts or constructs did the authors provide?</li> <li>c. Were patients involved in the selection of outcomes measured by the PROs?</li> </ul>
2. Omissions
<ul style="list-style-type: none"> <li>a. Were there any important aspects of health (e.g., symptoms, function, perceptions) or quality of life (e.g. overall evaluation, satisfaction with life) that were omitted in this study from the perspectives of the patient, clinician, significant others, payers, or other administrators and decision makers?</li> </ul>
3. If randomized trials and other studies measured PROs, what were the instruments' measurement strategies?
<ul style="list-style-type: none"> <li>a. Did investigators use instruments that yield a single indicator or index number, a profile, or a battery of instruments?</li> <li>b. If investigators measure PROs, did they use specific or generic measures, or both?</li> <li>c. Who exactly completed the instruments?</li> </ul>
4. Did the instruments work in the way they were supposed to work – validity?
<ul style="list-style-type: none"> <li>a. Had the instruments used been validated previously (provide reference)? Was evidence of prior validation for use in this population presented?</li> <li>b. Were the instruments re-validated in this study?</li> </ul>
5. Did the instruments work in the way they were supposed to work – ability to measure change?
<ul style="list-style-type: none"> <li>a. Are the PROs able to detect change in patient status, even if those changes are small?</li> </ul>
6. Can you make the magnitude of effect (if any) understandable to readers? (You must!)
<ul style="list-style-type: none"> <li>a. Can you provide an estimate of the difference in patients achieving a threshold of function or improvement, and the associated number needed to treat (NNT).</li> </ul>

Lack of 'appropriately assessed' patient-reported outcomes in randomised controlled trials assessing the effectiveness of interventions for rosacea

Esther van Zuuren and  
Zbys Fedorowicz (Bahrain Branch of CC)

Br J Dermatol 2013;168(2):442-4



# Rosacea

- Chronic skin condition affecting the face in mainly fair-skinned people
- Starts 3rd-5th decade in life
- 4 subtypes
  - Subtype 1: erythematotelangiectatic rosacea
  - Subtype 2: papulopustular rosacea
  - Subtype 3: phymatous rosacea
  - Subtype 4: ocular rosacea
- Pathogenesis?: multiple hypotheses
- Therapies?: numerous options....



# Subtypes

Subtype 1



Subtype 2



Subtype 3



Subtype 4



- First Cochrane review 2004
- First update 2005
- Second update 2011

## Primary outcomes:

- QoL and participant-assessed changes in rosacea severity

## Secondary outcomes:

- Physician-assessed changes in rosacea severity (e.g. global evaluation, lesion count), drop-out rates and adverse events

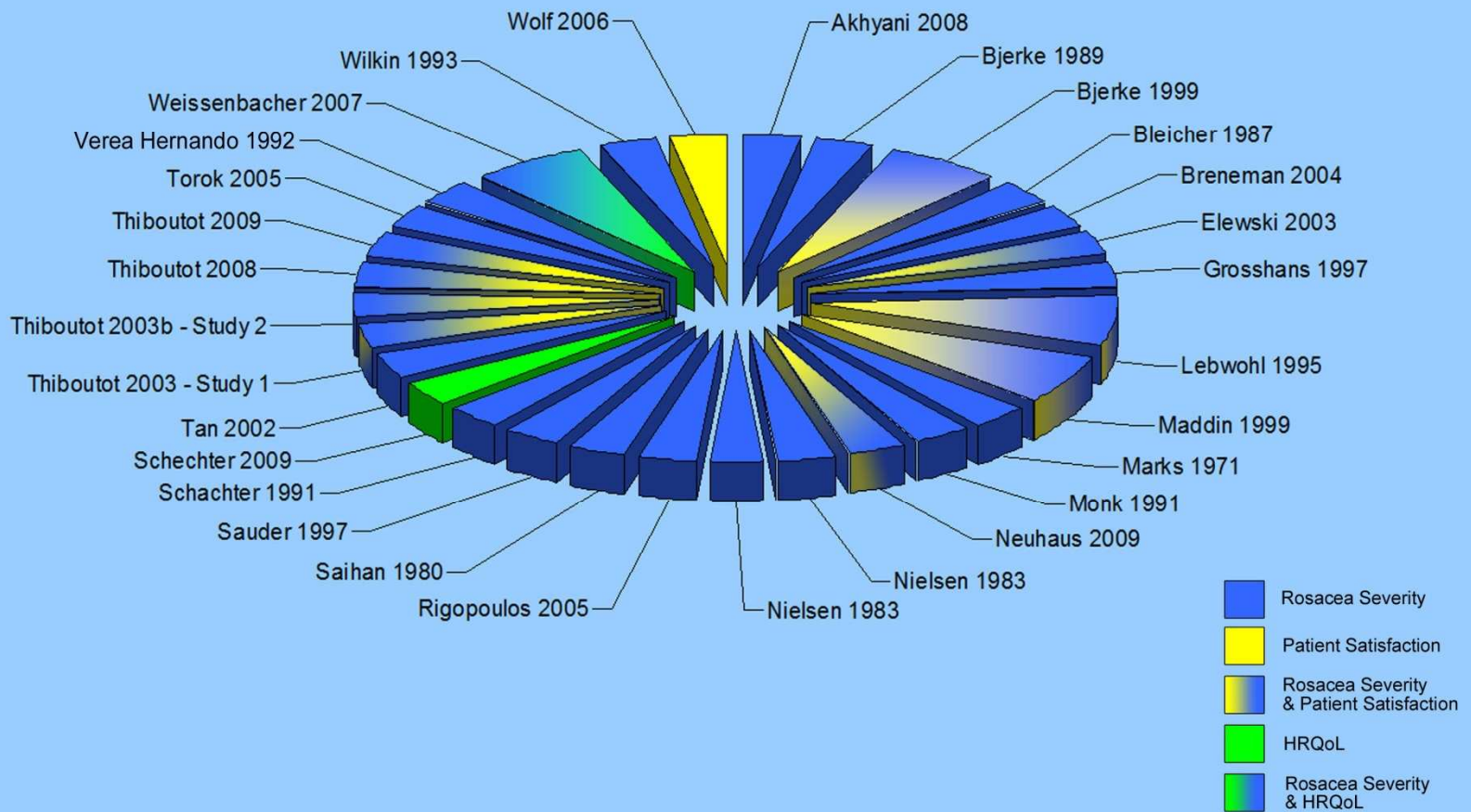
# 58 included studies

Independent evaluation of PROs in 58 studies using the 'Checklist for describing and assessing PROs in Clinical Trials'

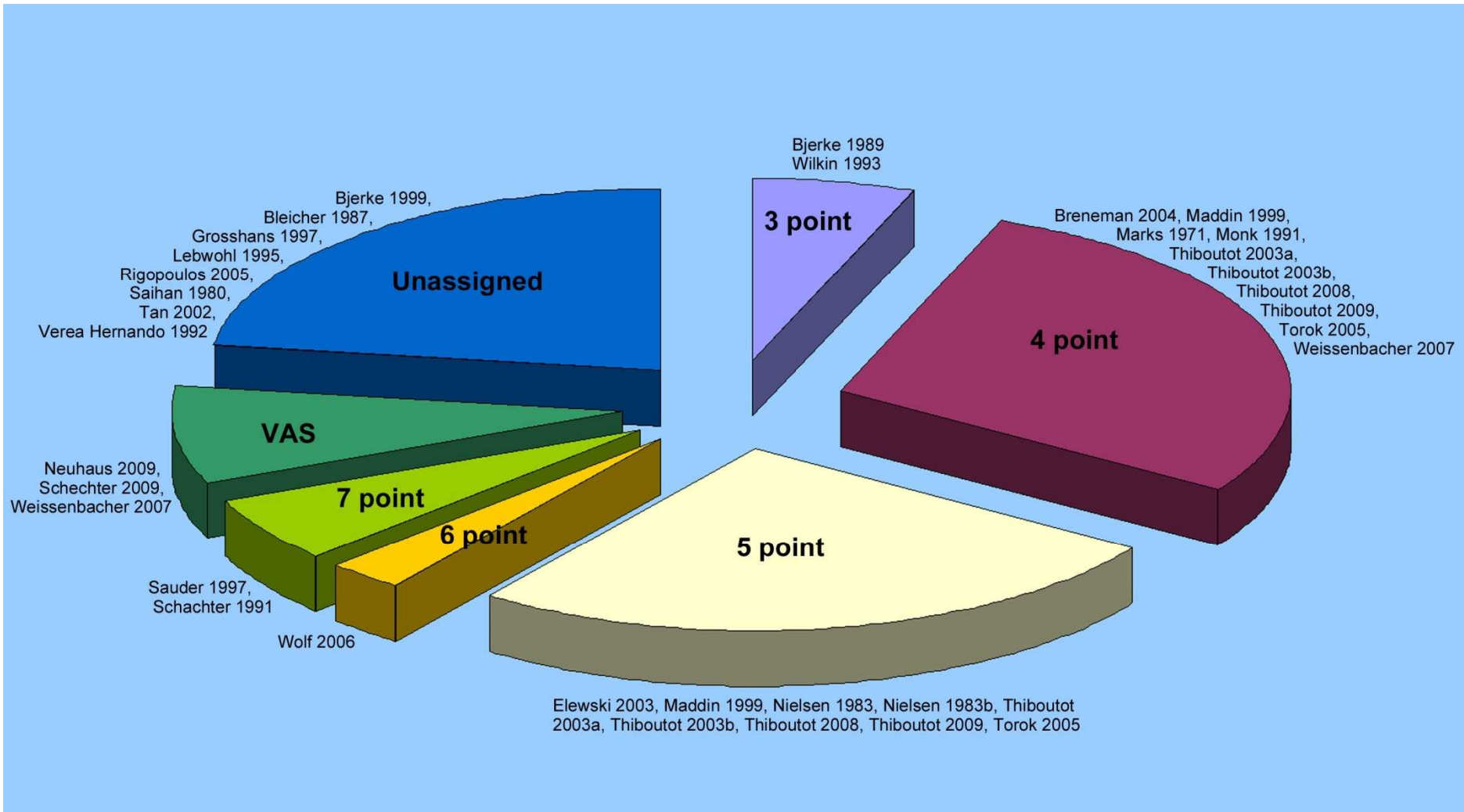
- Which instrument was used to measure the PRO?
- Was the instrument validated? Ref?
- Timing assessments (baseline and follow-up)
- Type of scale used?
- Evidence profile using GRADEpro

- 2/58 reported changes in HRQoL
  - Validated tools, 1 disease specific, 1 generic
- 29/58 reported other PROs
  - Patient's assessment of disease severity (27/58)
  - Patient satisfaction (10/58)
  - None addressed all items in the 'quality checklist'
  - 6 used non validated questionnaires
  - Majority of instruments based on Likert scales
  - 3 utilised VAS scales

### Characteristics of Patient-Reported Outcomes (PROs) in 29 RCTs of interventions for rosacea



# Scales used for patient-reported outcomes





The overall quality of the evidence based on the GRADE profile was moderate to low for participant assessed outcomes

- Based on patients' assessments there is evidence that topical metronidazole (4 studies) and azelaic acid (3 studies) are effective in papulopustular rosacea
- Topical cyclosporin improves QoL of participants with ocular rosacea (1 study), and pulsed dye laser and intense pulsed light therapy reduces erythema & telangiectasia (1 study)

- QoL only assessed in 2 studies
- Other PRO's assessed in 50% of the studies
- Importance of PROs and specifically those used in evaluating the impact of interventions on HRQoL underestimated in most of the included studies
- Majority of assessment tools not validated or method of assessment was unreported
- Introduction of COSMIN (Consensus based Standards for the selection of health Measurement Instruments) criteria is likely to lead to improved rigour in the assessment of PROs



## Conclusion II

- 2007 development of a rosacea-specific validated instrument to assess QoL in rosacea patients (RosaQoL)
- ROSacea International Experts (ROSIE) group emphasizes that aims of therapy should include improvement in QoL!
- Future trials should include PROs
- PROs should be based on participant assessed treatment efficacy utilising validated and reliable instruments & with more emphasis on measuring changes in QoL as a result of the interventions



Questions?