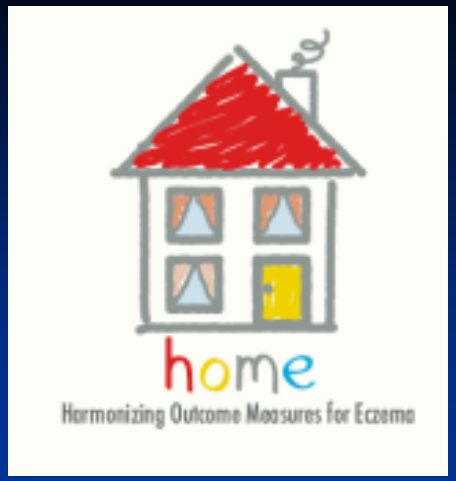
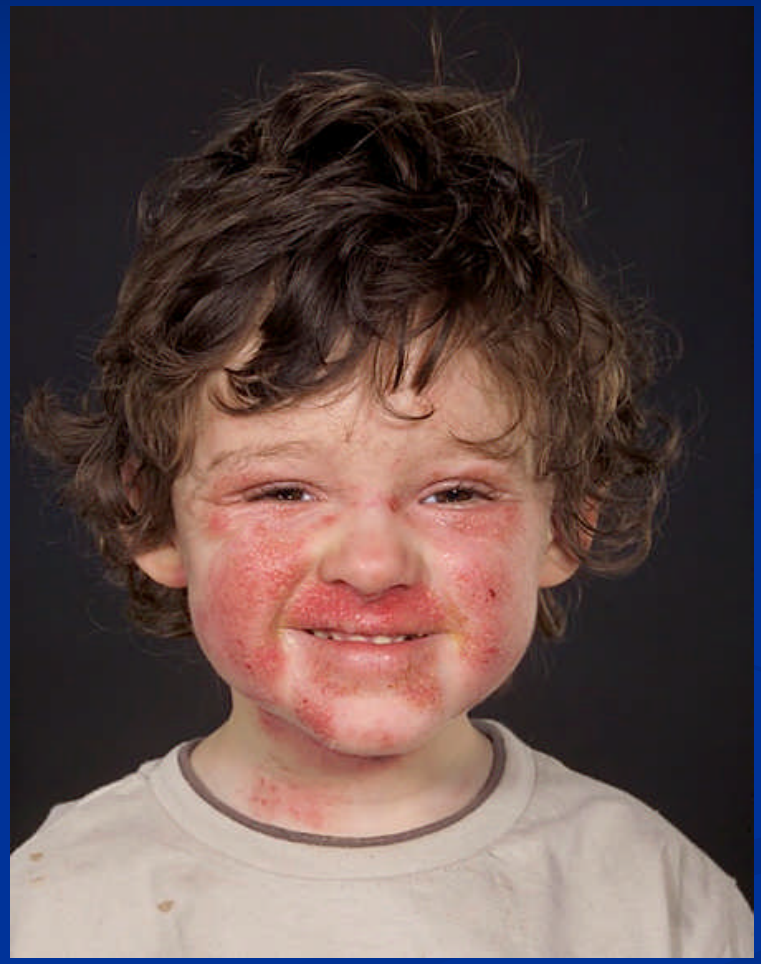


No place like HOME
(Harmonising Outcome Measures for Eczema)

Hywel Williams

Universities of Nottingham

The problem



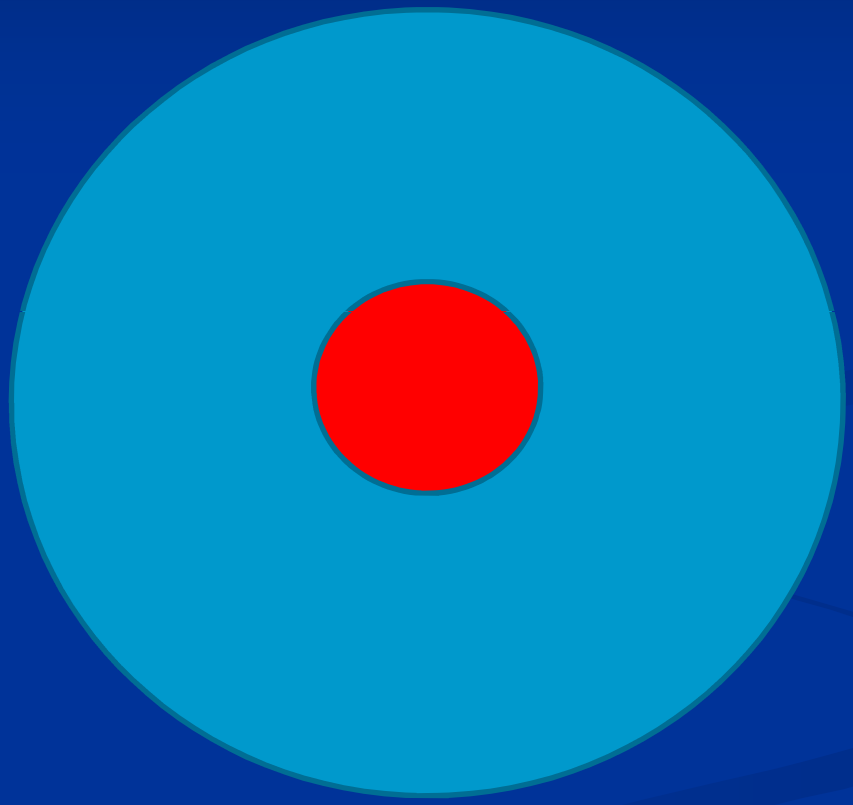
Outcome measures for AD – a real mess

- Too many – at least 20 named scales
- Many not tested at all (Charman C et al *JID* 2003; 120:932–941)
- Some are only partly tested (validity, repeatability, sensitivity change, consistency, interpretability)
- Some that are tested do not pass the tests

Schmitt J, Langan S, Williams HC. What are the best outcome measurements for atopic eczema? A systematic review JACI 2007;120:1389-98.


What's all the FSSS about?
Take it EASI
TIS a right mess
Me too!
Meet my SIS
My name is ADAM
SCORAD scores again
SASSAD rules OK
Give me a POEM
ADASI tonight?
IGADA bad headache
THE TOWER OF BABEL.

What we need: *core* outcomes sets (COS) used in all trials

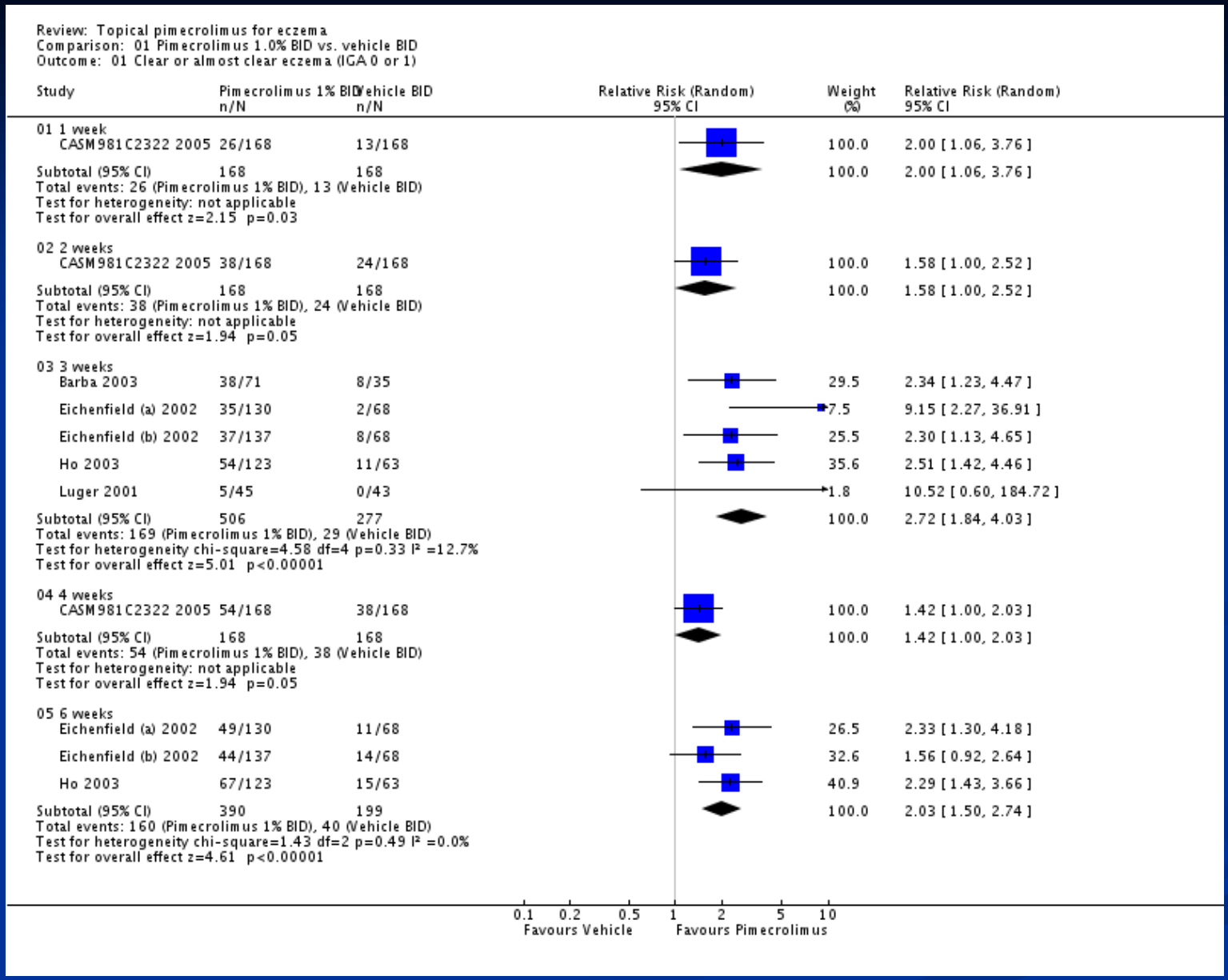


What are core outcome sets?

- Minimum set for all clinical trials
- Typically an efficacy and harm measure
- Need to be relevant to patients
- Relevant to those making decisions about health care
- May be different for clinical trials and routine care
- Need to be valid, repeatable, sensitive to change, easy to use

Why core outcomes?

- Easier to compare, contrast and synthesise results
- Reduces risk of inappropriate outcomes
- Reduces risk of selective reporting outcome bias



Ashcroft DM, Chen L-C, Garside R, Stein K, Williams HC. Topical pimecrolimus for eczema. *Cochrane Database of Systematic Reviews* 2007, Issue 4.

Selective reporting outcome bias

- Viljanen et al randomised 230 infants with AD and cow's milk allergy to *Lacto rham* GG, or mix of four probiotics or inert cellulose and concluded

"Treatment with LGG may alleviate atopic dermatitis symptoms in IgE-sensitised infants but not in non-IgE sensitised infants"

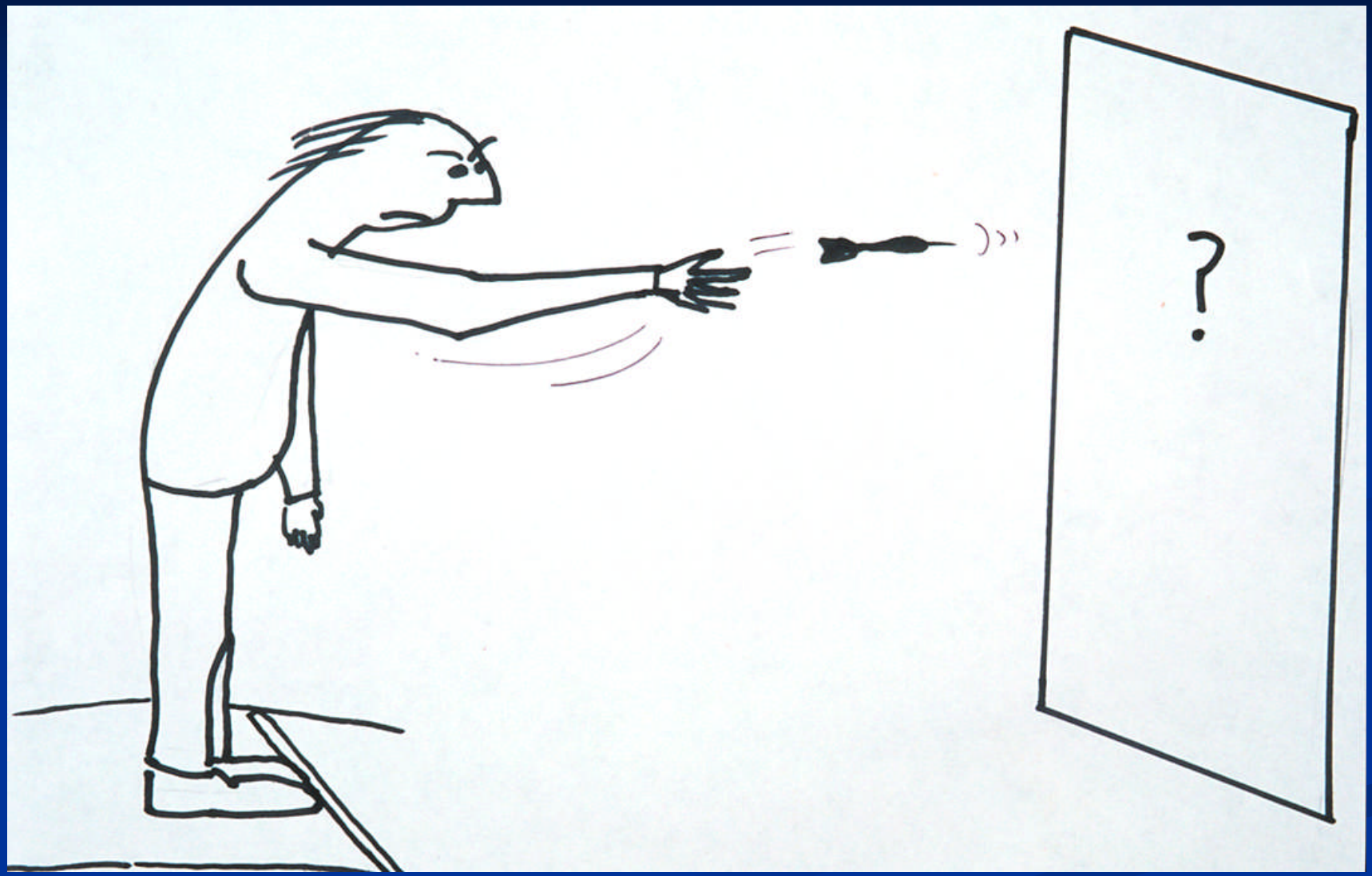
Viljanen et al Allergy 2005;60:494-500

But if you read the paper…

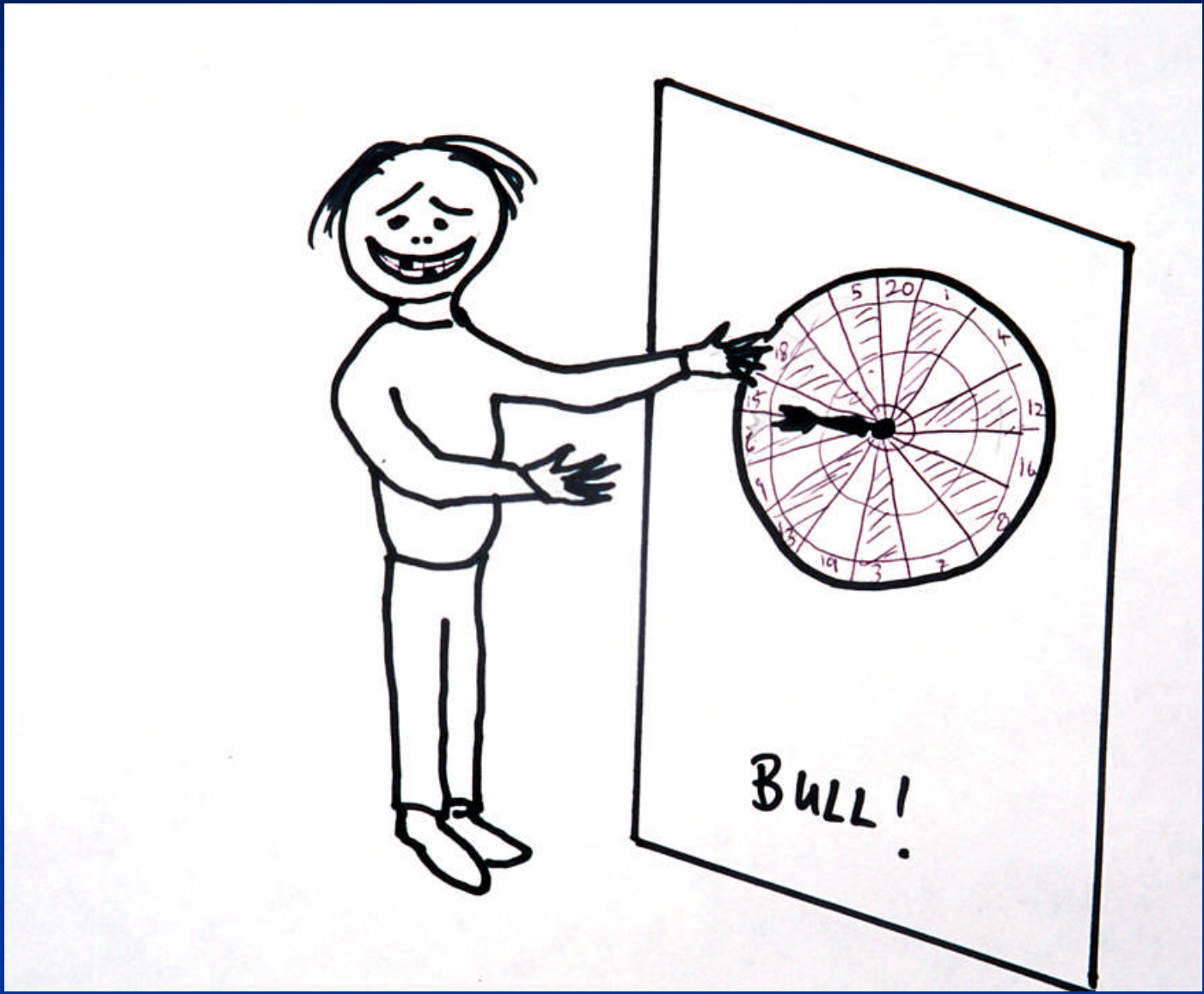
- Viljanen – main analysis for primary outcome not significant.
- Instead, they emphasised exploratory analysis in a subgroup 4 weeks after main assessment
- It's a bit like….

Williams HC. Two "positive studies of probiotics for atopic dermatitis – or are they? Arch Dermatol 2006;142:1201-3

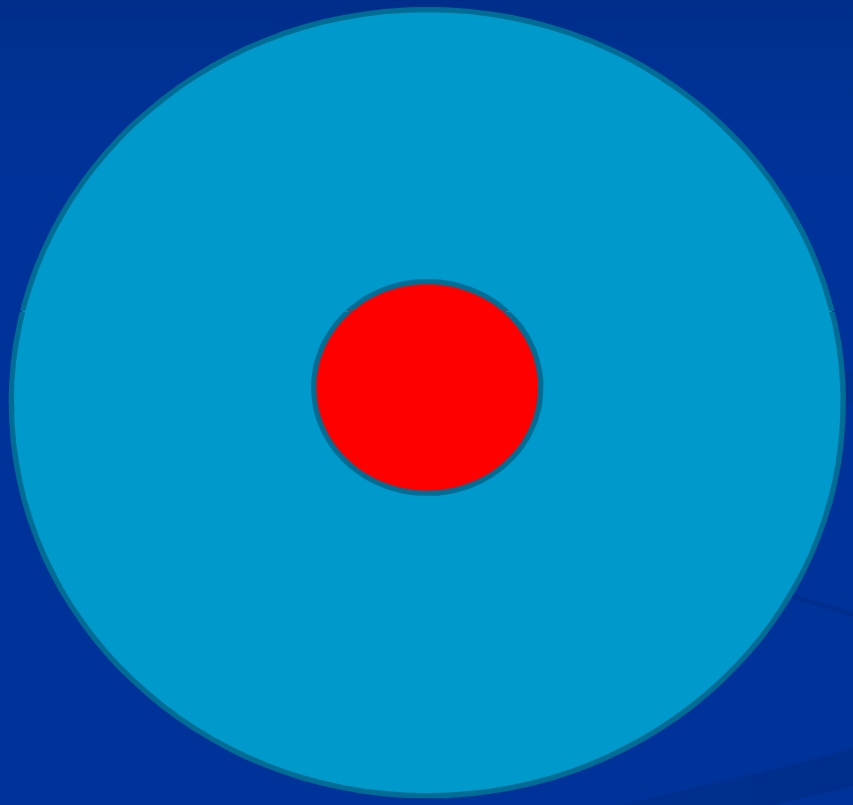
Throwing a dart



Then drawing the dartboard



Core outcome sets are just a *minimum* set



ie does not stop you from adding all sorts of other things that are needed

What is happening elsewhere?

- OMERACT http://www.omeract.org/
- Pain – IMMPACT: www.immpact.com
- COMET initiative: Core Outcome Measures in Effectiveness Trials

http://www.comet-initiative.org/

Tugwell P BM et al. OMERACT: An initiative to improve outcome measurement in rheumatology. Trials. 2007;8(38).
Clarke M. Standardising Outcomes in Paediatric Clinical Trials. PLoS Medicine / Public Library of Science. 2008;5(4):e102.

The world of medicine is moving on – what about atopic dermatitis?

HOME I – Munich 2009

- *Is there enough interest, enthusiasm and commitment to sort our core outcomes for atopic eczema/atopic dermatitis?* - YES

- Are you willing to set aside your preferences/prejudices/allegiances to work as a group? - YES

Our Delphi exercise

- Delphic oracle's skills of foresight and interpretation
- Consensus method frequently applied in outcomes research e.g. OMERACT group
- Structured iterative group process
  - Round 1: Assessment of problem by each participant.
  - Round 2+: Participants receive standardised feedback on own previous response and the groups previous response. Each participant is asked to assess problem again in light of this information.

Loughlin KG, Moore LF; *J Med Educ.* 1979

Delphi consensus panel

- Multi-professional collaboration involving the views of different stakeholder groups
  - Consumers: Members of eczema self help groups (n=6)
  - Clinical experts: Major interest in eczema; scientific advisory board ISAD Kyoto 2008; scientific committee IDEA Nottingham 2008
  - Representatives of regulatory agencies: EMEA, FDA
  - Journal editors: JACI, JID, Arch Dermatol, JAAD, Brit J Dermatol, Acta Derm Venereol, JEADV, JDDG
- Exclusion criteria
  - Involvement in development of named outcome measure for eczema
  - Affiliation with pharmaceutical industry

Delphi questionnaire

- Background information provided, problem addressed

- Indication of the importance of outcome domains for eczema on a 9-point Likert scale (rounds 1 and 2)
- Scores 1-3: domain is not important
- Scores 4-6: equivocal
- Scores 7-9: domain is important

- Final round: Explicit question on whether or not to include outcome domain into the core set

- 2 different contexts / settings
- Clinical trials
- Record keeping in daily practice

Domains vs. outcome measures

- Domains are:
  - Signs
  - Symptoms
  - Quality of life
  - Safety
  - ....
- Outcome measures (or “instruments”) for the domain “signs” include:
  - SCORAD
  - EASI
  - SASSAD
  - etc etc

Outcome domains to be considered

Domains identified by SR:

- Clinical signs (physician/patient)
- Symptoms
- Disease extent
- Course of disease
- Global disease severity (physician/patient)

Additional domains (panel)

- Involvement of visible areas
- Treatment utilisation

Additional domains

- General quality of life
- Dermatology-specific quality of life
- Control of disease flares (short term/long term)
- Time to/ duration of remission
- Health utilities
- Work/school limitations
- Consequences of pruritus
- Cost-effectiveness
- Direct / indirect cost
- Work productivity loss
- Compliance

Definition of consensus

- *A priori* defined in study protocol

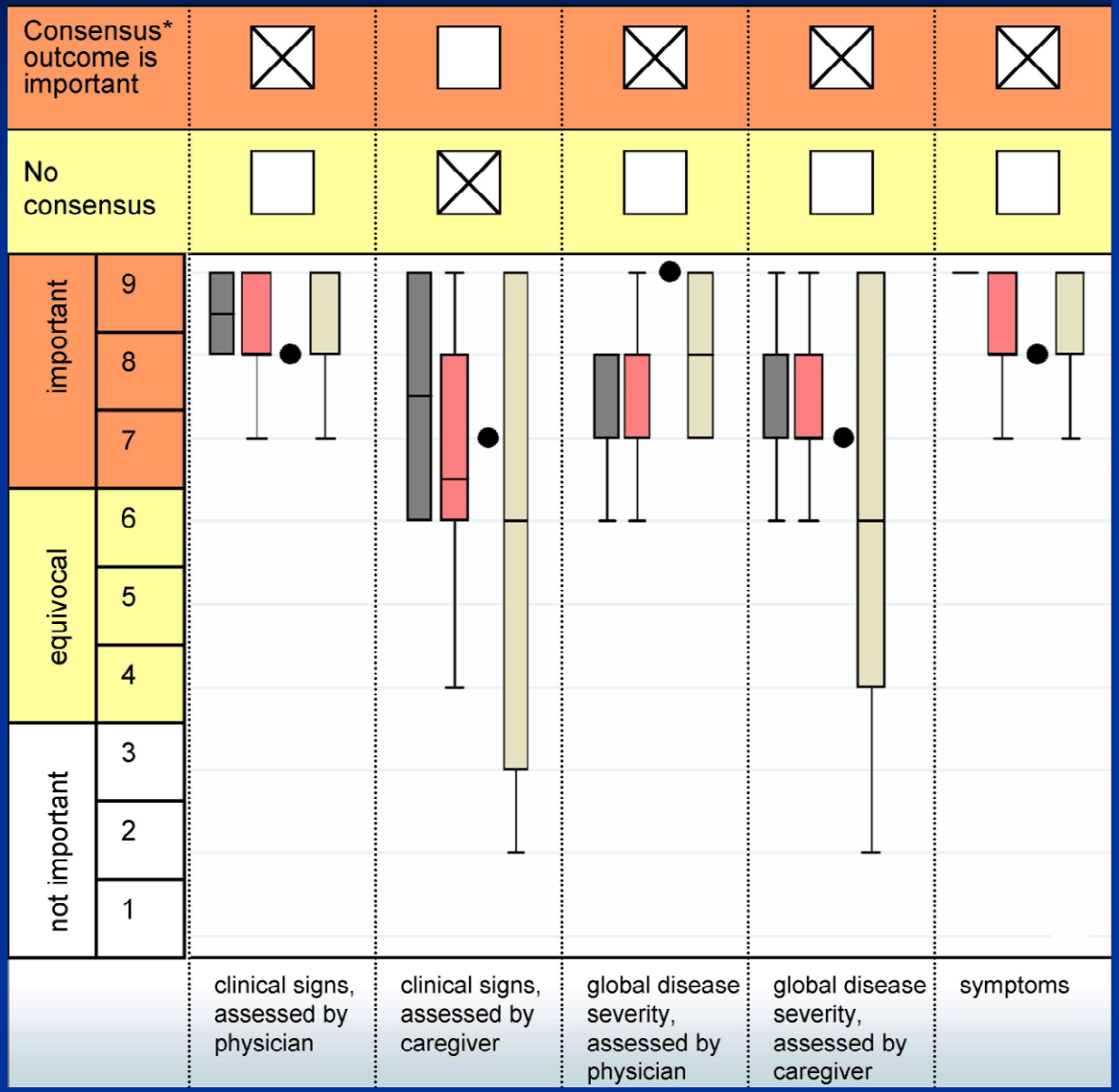
- INCLUSION OF DOMAIN INTO CORE SET

  ≥ 60% of all members of at least three stakeholder groups *including consumers* recommended including a domain in the core set of outcomes.

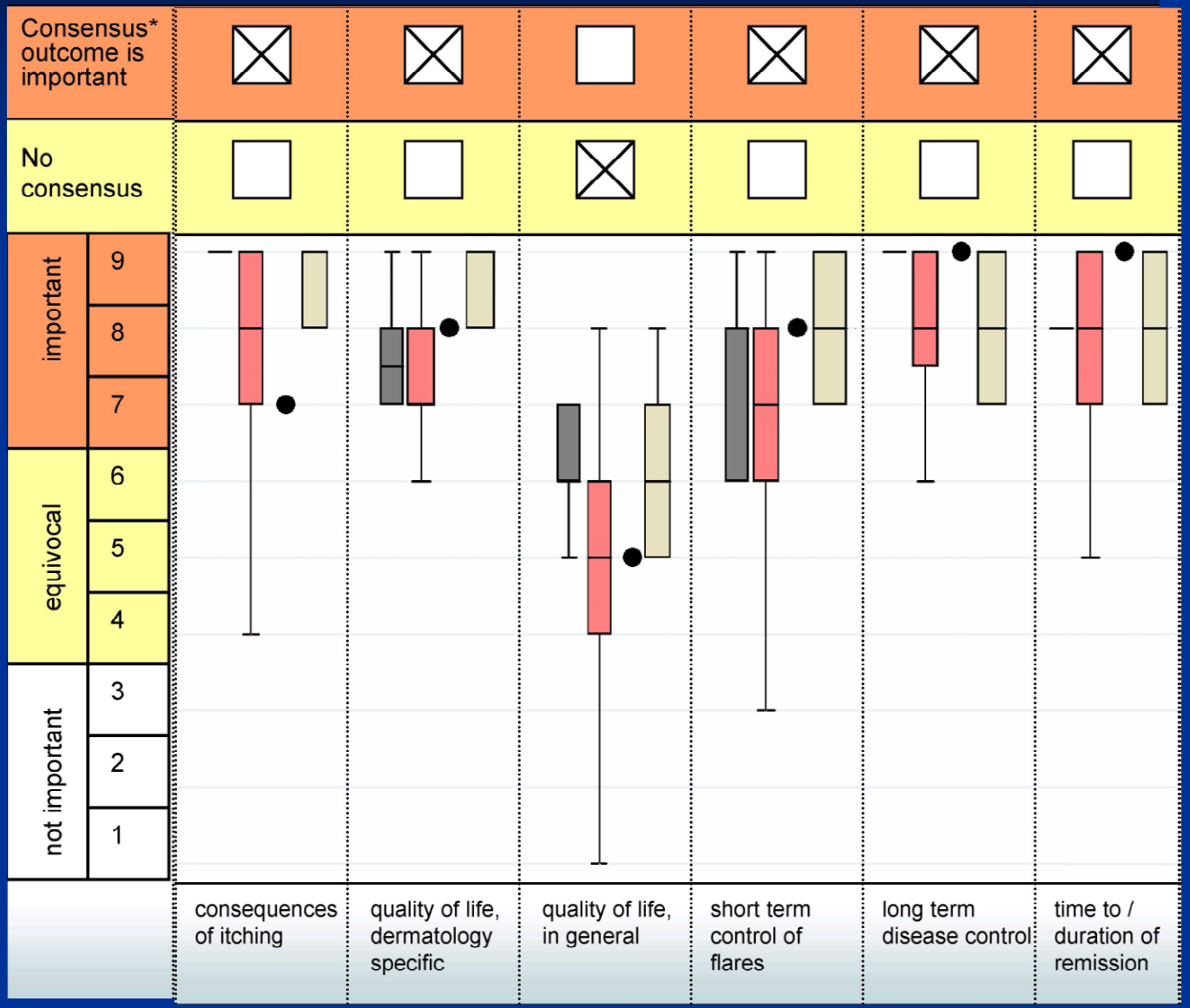
Results

- Main effect of feedback process was reduction of variability in scores assigned to each domain
- Little change in the median score of each domain
- Great variety of domains was considered important by the panel
- Median number of different domains to be included in the core set: 3

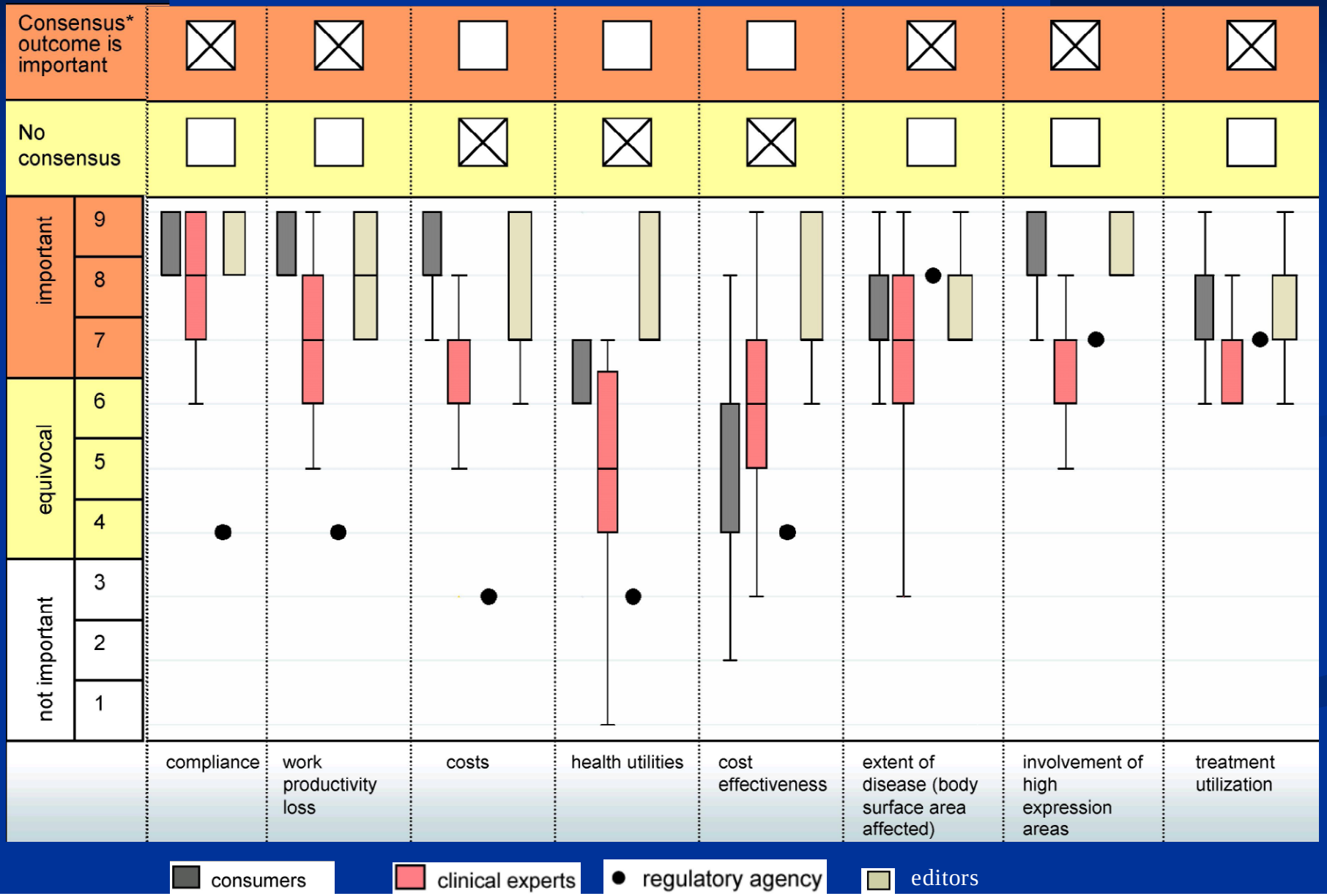
Results rounds 1 and 2: importance of outcome domains: clinical trials



Results rounds 1 and 2: importance of outcome domains: clinical trials



Results rounds 1 and 2: importance of outcome domains: clinical trials



Summary: Important domains for clinical trials

- Clinical signs, assessed by physician
- Global disease severity, assessed by patient
- Global disease severity, assessed by physician
- Symptoms
- Consequences of pruritus
- Short term control of flares
- Long-term disease control
- Time to / duration of remission
- Quality of life, specific
- Compliance
- Extent of disease
- Involvement of high expression areas
- Treatment utilization
- Work productivity loss

Results round 3:
Core set of outcome domains: Clinical trials

Outcome domain	Proportion recommending including outcome domain into the **CORE SET** of outcomes for eczema that should be routinely assessed **in every CLINICAL TRIAL** on eczema?				Consensus to include domain into core set		
	Consumers (n=6)	Experts (n=29)	Agency (n=1)	Editors (n=7)	YES	Un-clear	NO
Clinical signs (physician)	100%	100%	100%	100%	●		
Clinical signs (patient)	17%	21%	0%	0%			●
Investigator global assessment	33%	59%	0%	57%			●
Patient global assessment of	17%	34%	0%	29%			●
Symptoms	83%	76%	0%	57%	●		
Quality of life (specific)	33%	72%	100%	86%		●	
Quality of life (general)	17%	3%	0%	0%			●
Short term control of flares	33%	7%	0%	0%			●
Long term control of flares	67%	62%	100%	43%	●		
Cost	17%	3%	0%	0%			●
Overall extent of disease	17%	21%	0%	14%			●
Involvement of high expr. areas	17%	7%	0%	14%			●
Treatment utilization	17%	31%	0%	14%			●

Summary: Important domains for recordkeeping

- Clinical signs, assessed by physician
- Global disease severity, assessed by patient
- Global disease severity, assessed by physician
- Symptoms
- Consequences of pruritus
- Long-term disease control
- Time to / duration of remission
- Extent of disease
- Involvement of high expression areas
- Work productivity loss

Results round 3:
Core set of outcome domains: Recordkeeping

Outcome domain	Proportion recommending including outcome domain into the **CORE SET** of outcomes for eczema that should be routinely assessed in **DAILY PRACTICE, i.e. to be used AT EVERY PHYSICIAN VISIT**				Consensus to include domain into core set		
	Consumers (n=6)	Experts (n=29)	Reg. agency (n=1)	Editors (n=7)	YES	Un-clear	NO
Clinical signs (physician)	83%	34%	0%	43%		●	
Clinical signs (patient)	33%	14%	0%	0%			●
Investigator global assessment	17%	66%	100%	71%		●	
Patient global assessment	50%	28%	0%	43%		●	
Symptoms	100%	83%	0%	86%	●		
Consequences of itching	67%	17%	0%	0%		●	
Quality of life (specific)	17%	10%	0%	0%			●
Quality of life (general)	0%	7%	0%	0%			●
Short term control of flares	33%	14%	100%	0%			●
Long term control of flares	67%	41%	100%	29%		●	
Compliance	33%	31%	0%	0%			●
Work/school limitations	17%	14%	0%	0%			●
Overall extent of disease	17%	21%	0%	29%			●
Involvement of high expr. areas	17%	17%	0%	14%			●
Treatment utilization	0%	34%	100%	14%			●

Preliminary core set of outcome domains

Clinical trials

- Measurement of eczema symptoms
- Physician-assessed clinical signs using a score
- Measurement for long term control of flares

Recordkeeping in daily practice

- Measurement of eczema symptoms

Aims of HOME II
Amsterdam 2011

- To develop a collaborative working community
- To establish consensus on which domains should be measured in all eczema trials (and clinical record keeping)
- To identify topics for further research

Process of HOME II

- 43 people came from around the world
- Included 4 consumers
- Presentations, discussions and key pad voting
- Consensus rules – if less than 30% disagree

Results from HOME II

Refined core set of domains to include:

- Symptoms
- Clinical signs using a score
- Long term control of flares
- Quality of life

Result of HOME II:
Future working groups

- Four working groups on identifying best instruments for:
  1. Symptoms
  2. Signs
  3. QoL
  4. long-term control

- And maybe others according to interest

Philosophy of HOME

- Working together
- Respecting all stakeholder viewpoints
- Putting prejudices and allegiances aside in order to achieve the greater good for patient care
- Evidence-based and evidence-generating
- Pragmatic
- To have fun
- HOME III - San Diego 6-7th April 2013

HOME Executive Board

Hywel Williams	UK
Jochen Schmitt	Germany
Masutaka Furue	Japan
Magdalene Dohil	USA
Eric Simpson	USA
Phyllis Spuls	Netherlands

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Elizabeth Hoff	USA
Hidehisa Saeki	Japan
Kefei Kang	China
Kam-Ium Ellis Hon	Hong Kong
John Masenga	Africa
Dedee Murrell	Australia

How can the SID help?

- Join us – professionals and patients
- Avoid duplication of effort
- Help us to engage with regulators
- HOME is international


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TIS a right mess
Me too!
Meet my SIS
My name is ADAM
SCORAD scores again
SASSAD rules OK
Give me a POEM
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THE TOWER OF BABEL.

Why do it?