home
Harmonizing Outcome Measures for Eczema

The HOME story:
Chapter 3

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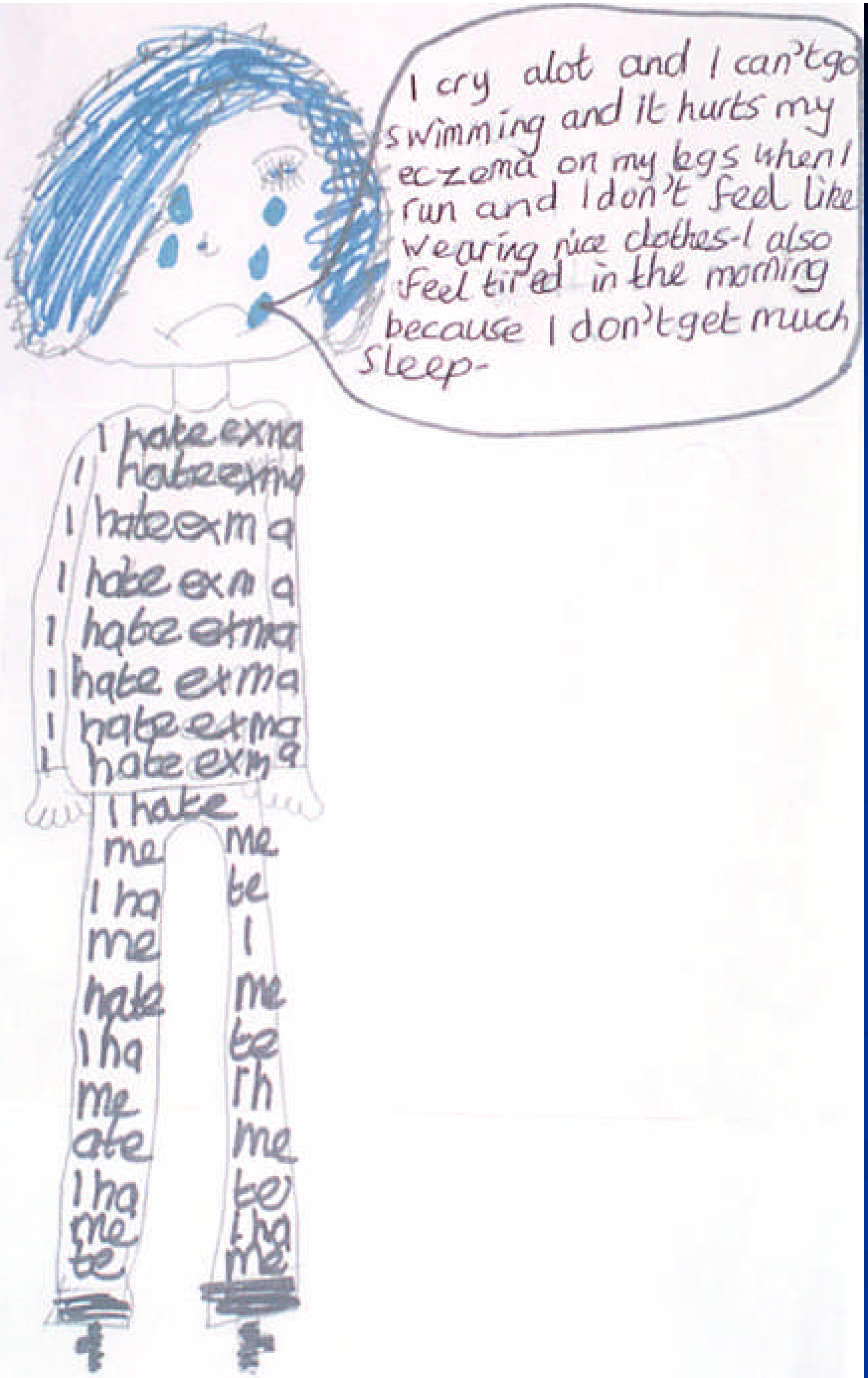
Nottingham

Centre of Evidence Based Dermatology

The problem


I cry alot and I can't go swimming and it hurts my eczema on my legs when I run and I don't feel like wearing nice clothes. I also feel tired in the morning because I don't get much sleep.
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I'm much happier now my eczema's better because I can wear summer clothes and play outside and go swimming

Outcome measures for eczema/atopic dermatitis – a mess

- Too many – over 20 named scales

- Many not tested at all

- Some are only partly tested (validity, repeatability, sensitivity change, consistency, interpretability)

- Some that are tested do not pass the tests

ressly for "Patriarchs and Prophets."

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THE TOWER OF BABEL.

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

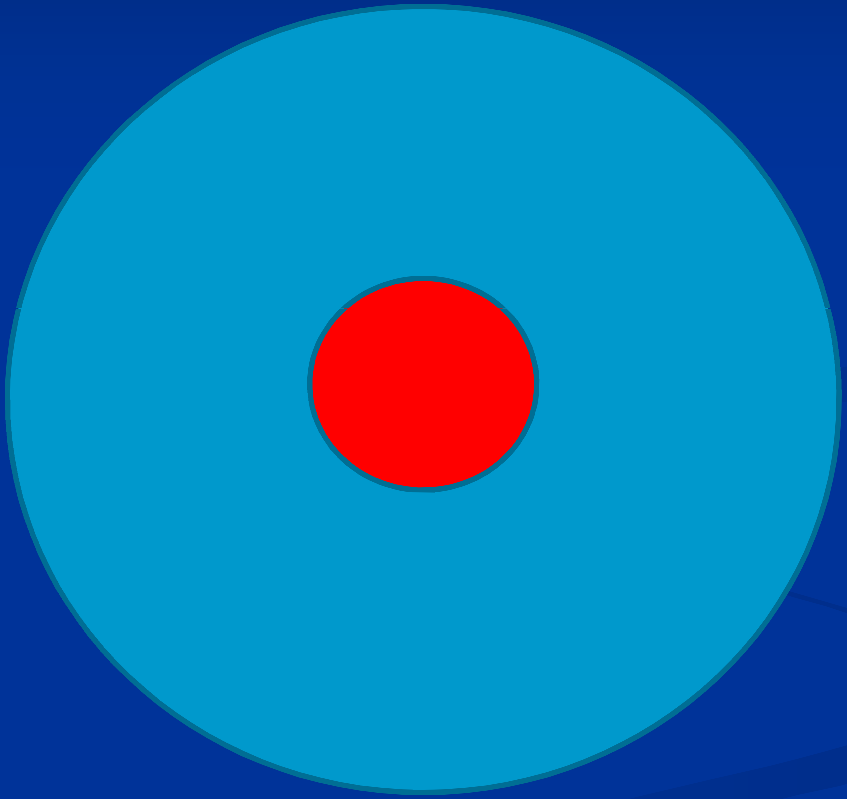
SASSAD rules OK

Give me a POEM

ADASI tonight?

IGADA bad headache

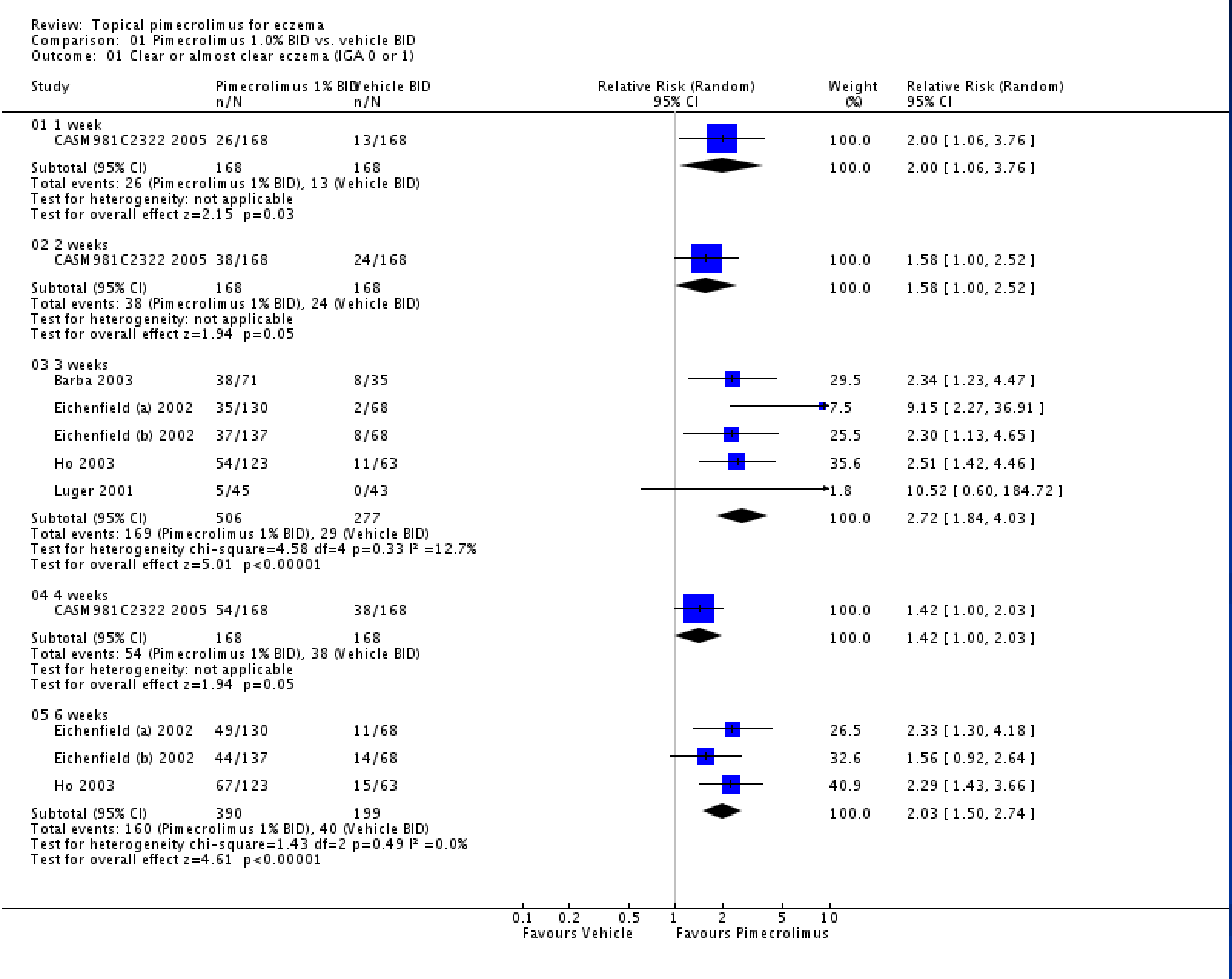
What we need are *core* outcomes that are used in all trials



What are core outcomes?

- Minimum set for all clinical trials
- Need to be relevant to patients
- Relevant to those making decisions about health care
- Maybe different for clinical trials and routine care
- Need to measure what they're supposed to measure, be repeatable, sensitive to change, and be easy to use

Why? - so that we can compare



Review: Topical pimecrolimus for eczema
Comparison: 01 Pimecrolimus 1.0% BID vs. vehicle BID
Outcome: 01 Clear or almost clear eczema (IGA 0 or 1)

Study	Pimecrolimus 1% BID n/N	Vehicle BID n/N	Weight (%)	Relative Risk (Random) 95% CI
01 1 week				
CASM981C2322 2005	26/168	13/168	100.0	2.00 [1.06, 3.76]
Subtotal (95% CI)	168	168	100.0	2.00 [1.06, 3.76]
Total events: 26 (Pimecrolimus 1% BID), 13 (Vehicle BID)				
Test for heterogeneity: not applicable				
Test for overall effect z=2.15 p=0.03				
02 2 weeks				
CASM981C2322 2005	38/168	24/168	100.0	1.58 [1.00, 2.52]
Subtotal (95% CI)	168	168	100.0	1.58 [1.00, 2.52]
Total events: 38 (Pimecrolimus 1% BID), 24 (Vehicle BID)				
Test for heterogeneity: not applicable				
Test for overall effect z=1.94 p=0.05				
03 3 weeks				
Barba 2003	38/71	8/35	29.5	2.34 [1.23, 4.47]
Eichenfield (a) 2002	35/130	2/68	7.5	9.15 [2.27, 36.91]
Eichenfield (b) 2002	37/137	8/68	25.5	2.30 [1.13, 4.65]
Ho 2003	54/123	11/63	35.6	2.51 [1.42, 4.46]
Luger 2001	5/45	0/43	1.8	10.52 [0.60, 184.72]
Subtotal (95% CI)	506	277	100.0	2.72 [1.84, 4.03]
Total events: 169 (Pimecrolimus 1% BID), 29 (Vehicle BID)				
Test for heterogeneity chi-square=4.58 df=4 p=0.33 I² =12.7%				
Test for overall effect z=5.01 p<0.00001				
04 4 weeks				
CASM981C2322 2005	54/168	38/168	100.0	1.42 [1.00, 2.03]
Subtotal (95% CI)	168	168	100.0	1.42 [1.00, 2.03]
Total events: 54 (Pimecrolimus 1% BID), 38 (Vehicle BID)				
Test for heterogeneity: not applicable				
Test for overall effect z=1.94 p=0.05				
05 6 weeks				
Eichenfield (a) 2002	49/130	11/68	26.5	2.33 [1.30, 4.18]
Eichenfield (b) 2002	44/137	14/68	32.6	1.56 [0.92, 2.64]
Ho 2003	67/123	15/63	40.9	2.29 [1.43, 3.66]
Subtotal (95% CI)	390	199	100.0	2.03 [1.50, 2.74]
Total events: 160 (Pimecrolimus 1% BID), 40 (Vehicle BID)				
Test for heterogeneity chi-square=1.43 df=2 p=0.49 I² =0.0%				
Test for overall effect z=4.61 p<0.00001				

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

What is happening elsewhere?

- OMERACT http://www.omeract.org/
- Pain – IMMPACT: www.immpact.com
- COMET initiative: Core Outcome Measures in Effectiveness Trials http://www.liv.ac.uk/nwhtmr/comet/comet.htm

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 eczema?

It all started …. in Munich

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

Then we set about our Delphi exercise

Which involved:

- 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
- 2 different contexts / settings
  - Clinical trials
  - Recordkeeping in daily practice

Delphi questionnaire (cont.)

- How many domains should be included into core sets for clinical trials and for daily recordkeeping?
- What are the top three most important outcome domains for clinical trials and for daily recordkeeping?
- Final round: Explicit question on whether or not to include outcome domain into the core set for clinical trials and for daily recordkeeping
- Feedback: previous rating, group response (median, IQR)
- Three rounds conducted by electronic mail

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 utilization

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

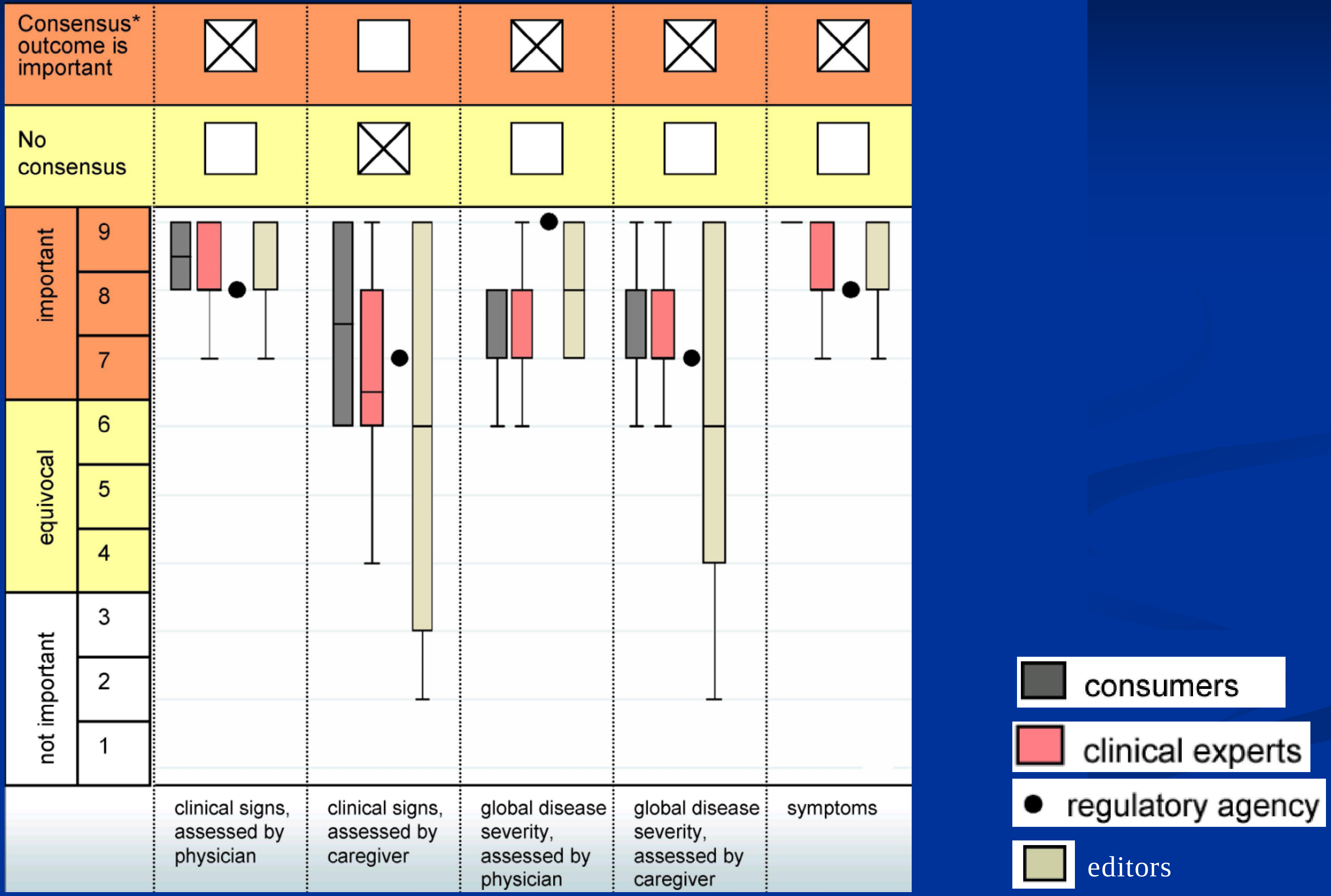
Definition of consensus

- *A priori* defined in study protocol
- INCLUSION OF DOMAIN INTO CORE SET
  $\geq$ 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 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	Unclear	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%			●

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

Schmitt J et al on behalf of (HOME) Delphi panel. Core outcome domains for controlled trials and clinical recordkeeping in eczema: International multi-perspective Delphi consensus process. *J Invest Dermatol* 2011;131:623-30.

Then came Amsterdam: 2011

Aims of HOME II
Amsterdam 2011

- To develop a collaborative working community
- To make decisions on which essential domains need to measured in all eczema trials (and clinical record keeping)
- To make decisions about which tools should be used to measure those essential things
- 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
- Impartial guidance from Maarten Boers
- 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 (Phyllis Spuls leading)
  2. Signs (Jochen Schmitt)
  3. QoL (Magdalene Dohil)
  4. Long-term control (Kim Thomas)

  - And maybe others according to interest

Adoption of the OMERACT filter

Truth, Discrimination and Feasibility

AIM of HOME: To agree a set of core outcome measures for eczema for use in all clinical trials. Ultimately, the aim is to have just *one instrument* per domain for:

1. Signs
2. Symptoms
3. Quality of Life
4. Measure of long term control of flares

	Stage 1 →	Stage 2 →	Stage 3 →	Stage 4 →	Stage 5
Task	Identify all instruments previously used to measure the domain.	Establish the extent and quality of testing of the identified instruments.	Determine which instruments are good enough quality meet the requirements of the OMERACT filter and be shortlisted for further consideration.	Carry out validation studies on shortlisted scales.	Finalise core outcome(s) for domain.
Methodology	Systematic review of outcome instruments used.	Systematic review of validation studies of the long-list of identified instruments. Highlight any gaps in validation.	Apply OMERACT filter; Truth, discrimination and feasibility: **Truth**: *"Is the measure truthful, does it measure what it intends to measure? Is the result unbiased and relevant?"* Consensus discussion and voting on truth: 1. Face validity 2. Content validity 3. Construct validity 4. Criterion validity **Discrimination**: *"Does the measure discriminate between situations that are of interest?"* Consensus discussion and voting on discrimination: 1. Reliability 2. Sensitivity to change **Feasibility**: *"Can the measure be applied easily in it's intended setting, given constraints of time, money, and interpretability?"* Consensus discussion and voting on feasibility: 1. Time taken 2. Cost 3. Interpretability	Consensus discussion and voting to determine what validation studies will be conducted on short-listed instruments. Gaps in testing were highlighted in stage 2 (systematic review). Appropriate methods used to fill the gaps in validation.	Re-apply the OMERACT filter with the results of the completed validation studies. Consensus discussion and voting on core outcome to be recommended.
Output	Long-list of all instruments previously used to measure the domain.	Summary of which instruments have been tested and the quality, extent and results of any testing.	Short-list of potential instruments that meet the requirements of the OMERACT filter.	Short-list of fully tested instruments.	Recommended core outcome(s) for the domain.

And so to HOME III in San Diego

A big thank you to Magdalene Dohil and Larry Eichenfield

Aims of HOME III

- To discuss and interpret new research since HOME II from the four working groups
- To make decisions about which tools should be used to measure the essential four domains
- To prioritise topics for further research

Progress will vary…

Philosophy of HOME

- Working hard 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
- With very little money

home

Harmonizing Outcome Measures for Eczema

International spirit:

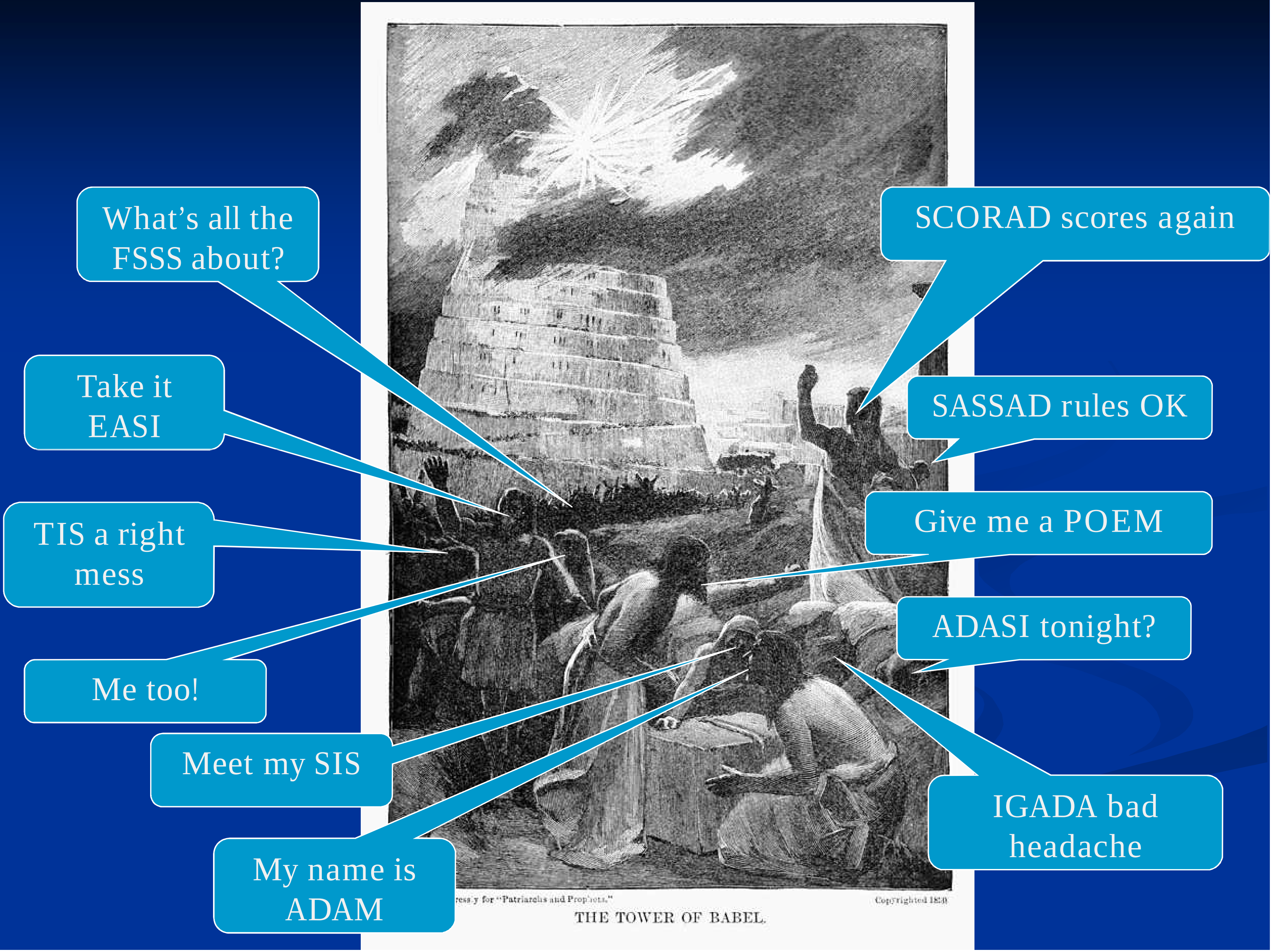
HOME Executive Board		Group lead
Hywel Williams	UK	
Jochen Schmitt	Germany	Signs
Masutaka Furue	Japan	
Magdalene Dohil	USA	Quality of Life
Eric Simpson	USA	
Phyllis Spuls	Netherlands	Symptoms
Kim Thomas	UK	Long term

home

Harmonizing Outcome Measures for Eczema

HOME Scientific Advisory Board

Jon Hanifin (Chair)	USA
Maarten Boers	Netherlands
Uwe Gieler	Germany
Jean-Francois Stalder	France
Carsten Flohr	UK
Christian Apfelbacher	Germany
Amy Paller	USA
Stephan Weidinger	Germany
Sue Lewis-Jones	UK
Mira Pavlovic	France
Gil Yosipovitch	USA
Carolyn Charman	UK
Mary-Margaret Chren	USA
Roberto Takaoka	Brazil
Yukihiro Ohya	Japan
Elizabeth Hoff	USA
Hidehisa Saeki	Japan
Kefei Kang	China
Kam-lum Ellis Hon	Hong Kong
John Masenga	Africa
Dedee Murrell	Australia



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THE TOWER OF BABEL.

Why do it?

The University of Nottingham
UNITED KINGDOM · CHINA · MALAYSIA

Disclaimer

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