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The Use of Global Assessments in Atopic Dermatitis Research- A Systematic Review of Randomized Controlled Trials

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Overview

- Introduction

- Results of systematic review

- Two examples

- Questions for group

Introduction

- Global severity measures are often used in dermatologic research

- Not based on numerical scoring

- They are intended to provide a clinically meaningful snapshot of disease severity easily understandable to physicians and patients

- The type of scales used and implementation methods vary between studies, however

Problems with Global Assessments

- Not standardized in studies of atopic dermatitis

- Instructions have evolved over time

- While not a HOME core outcome, IGA used as the reference point for validation studies

- Basis for FDA approval for new medications in AD

Influence of Pimecrolimus Cream 1% on Different Morphological Signs of Eczema in Infants with Atopic Dermatitis

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Table 2. Investigators' Global Assessment

Dermatology, 2004

0	clear	no inflammatory signs of AD
1	almost clear	just perceptible erythema and just perceptible papulation/infiltration
2	mild disease	mild erythema and mild papulation/infiltration
3	moderate disease	moderate erythema and moderate papulation/infiltration
4	severe disease	severe erythema and severe papulation/infiltration
5	very severe disease	severe erythema and severe papulation/infiltration with oozing/crusting

Tacrolimus Ointment 0.03% Is Safe and Effective for the Treatment of Mild to Moderate Atopic Dermatitis in Pediatric Patients: Results From a Randomized, Double-Blind, Vehicle-Controlled Study

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Pediatrics, 2005

TABLE 1.   IGADA

Is the IGA an average of sign scores or a measure of global severity?

	assessment scores* of 1 in ≥3 signs and symptoms of AD
Moderate	Majority of affected areas have individual assessment scores* of 2 in ≥3 signs and symptoms of AD
Severe	Majority of affected areas have individual assessment scores* of 3 in ≥3 signs and symptoms of AD
Very severe	All of affected areas have individual assessment scores* of 3 in ≥3 signs and symptoms of AD

* Individual assessment scores are defined in Table 2.

Objectives

- To review the frequency of use, implementation, and analysis of global severity outcome measures in randomized trials in atopic dermatitis

- Long-term goal is to standardize and better-validate the measure for future studies

Search Methods

- Searched all RCTs published since 2000 using the GREAT database

- GREAT database includes all published RCTs on atopic dermatitis (Nottingham)

- Included all RCTs with a global severity score

Outcomes

- Type of scale- dynamic or static
- Scale size (levels)
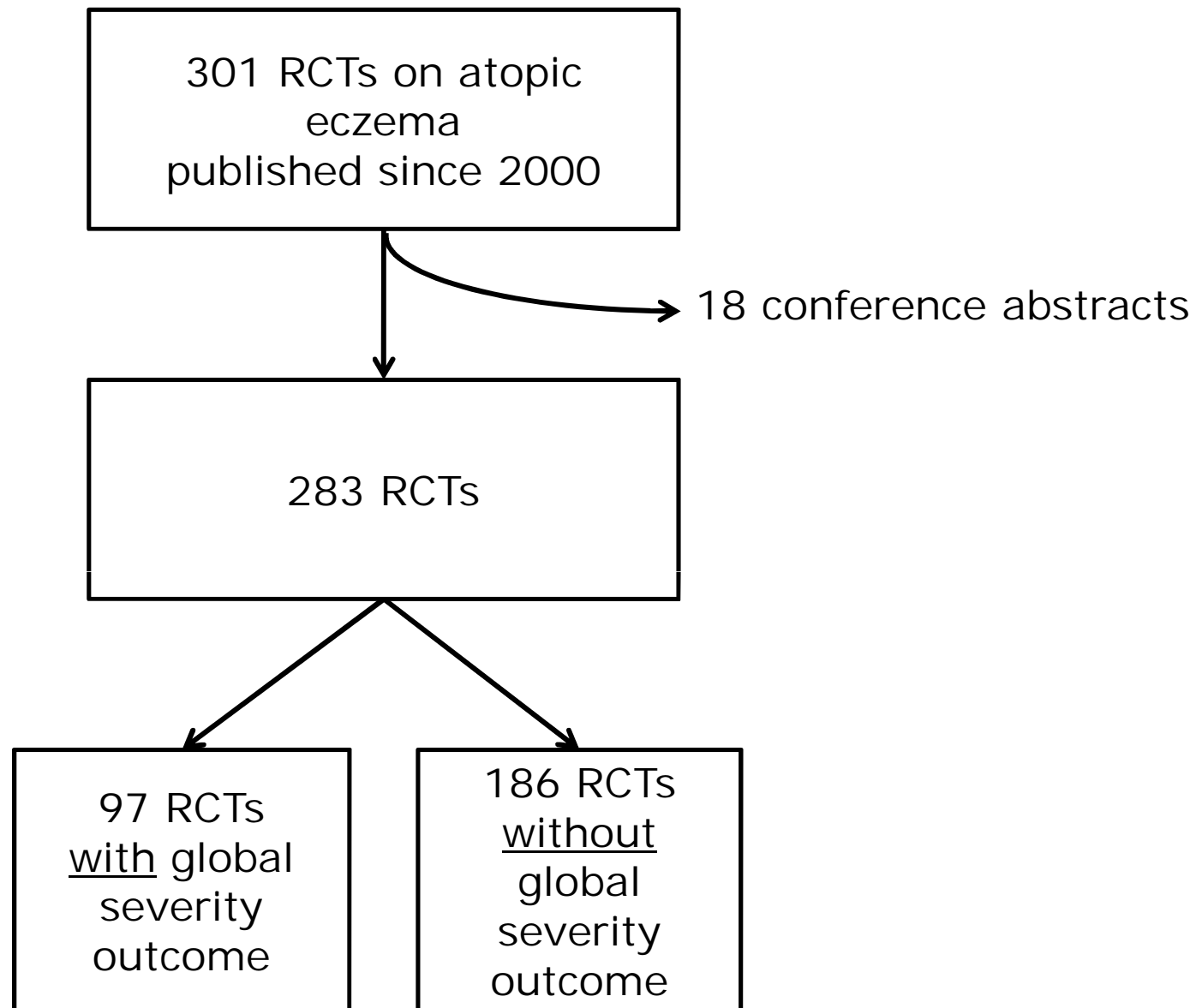- Instructions for use
- Analytic methods

Figure 1. Flow diagram

Who uses a Global Severity Measure?

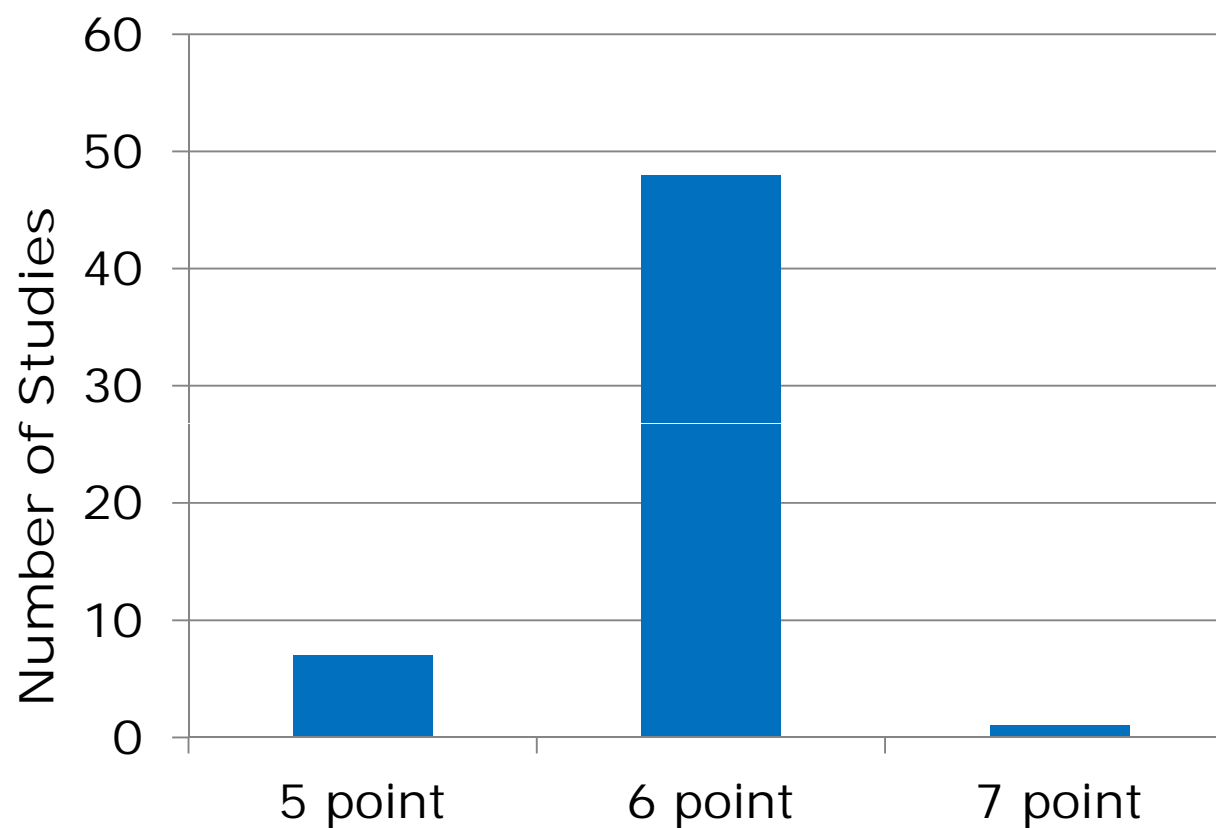| Area	IGA	No IGA	Total
USA, Canada	41 (77%)	12 (23%)	53
Europe	48 (30%)	112 (70%)	159
Other	8 (11%)	62 (89%)	70
Total			283

Global Severity Scale Names

IGA-Severity (9)	IGA-Improvement (21)
Investigator Global Assessment	Investigator Global Assessment
Investigator Global AD Assessment	Investigator Global Assessment of improvement
Investigator Assessment	Investigator Global Assessment of clinical response
Investigator Global Severity Scores	Investigator Global Assessment of global response
Investigator efficacy assessment	Investigator Assessment of the efficacy
Physicians Global Assessment	Investigator-assessed Global change
Physicians Global Evaluation	Investigator assessed overall efficacy
Physicians Static Global Assessment	Investigator's overall Assessment
Global Severity Score	Overall assessment of efficacy
	Assessment of overall treatment response
	General improvement scores
	Global Assessment
	Global Assessment of effectiveness
	Global Assessment of treatment success
	Global dermatological assessment
	Global Evaluation
	Physicians Global Assessment
	Physicians Global Assessment of clinical response
	Physicians Assessment of global response
	Physicians Global Evaluation
	Physicians Global Evaluation of clinical response

AD Global Severity Measure Characteristics (n=97 RCTs)

- Dynamic scale in 38 RCTs (39%)

- Static scale in 60 RCTs (62%)

- Instructions for use in 26 trials (27%)

- Primary outcome in 29 trials (30%)

- Analysis of outcome varied- proportion of treatment success, mean change

Static Global Assessments (n=60)

Clear, Almost Clear, Mild, Moderate, Severe, Very Severe

Definition of Success (n=44)

Score	Number (%)
0-1	31 (70%)
0-2	5 (11%)
0-3	1 (2%)
Other	7 (16%)

Conclusions

- Global assessments are use commonly in AD trials from North America, less so in other countries

- 30% of studies used IGA as primary outcome

- Size of scale varies

- Instructions regarding implementation rarely described and vary

- Standardization needed

Case 1

16 yo with atopic dermatitis

Lesions cover 70% of body

Itching is severe, and trouble sleeping

What is the global severity?

0-clear
1-Almost clear
2-Mild
3-Moderate
4-Severe
5-Very Severe

Using standard instructions:

The total body surface area is 70%.

IGA Score	Clinical Description
0 – Clear	No inflammatory signs of AD
1 – Almost Clear	Just percep. erythema and papulation
2 –Mild	Mild erythema and papulation
3 – Moderate	Moderate erythema and papulation
4 – Severe	Severe erythema papulation
5 – Very Severe	Severe erythema papulation with oozing/crusting

Case 2

6 month baby with AD

Lesions on face only

Symptoms very mild, no effect on sleep

What is the global severity?

0-clear
1-Almost clear
2-Mild
3-Moderate
4-Severe
5-Very Severe

Using standard instructions, please determine the IGA.

The total body surface area is 2%.

IGA Score	Clinical Description
0 – Clear	No inflammatory signs of AD
1 – Almost Clear	Just percep. erythema and papulation
2 –Mild	Mild erythema and papulation
3 – Moderate	Moderate erythema and papulation
4 – Severe	Severe erythema papulation
5 – Very Severe	Severe erythema papulation with oozing/crusting

Questions

- What should the scale size for IGA be?
  - Include almost clear and very severe?

- How should the instrument be implemented?
  - Use as a gestalt assessment? Should itch, QOL, etc be factored in?
  - Current instructions based on sign scores only. Is this OK?

- Should BSA be used to help determine this measure?
  - Studies in psoriasis show it already is (Ellis, 2004)
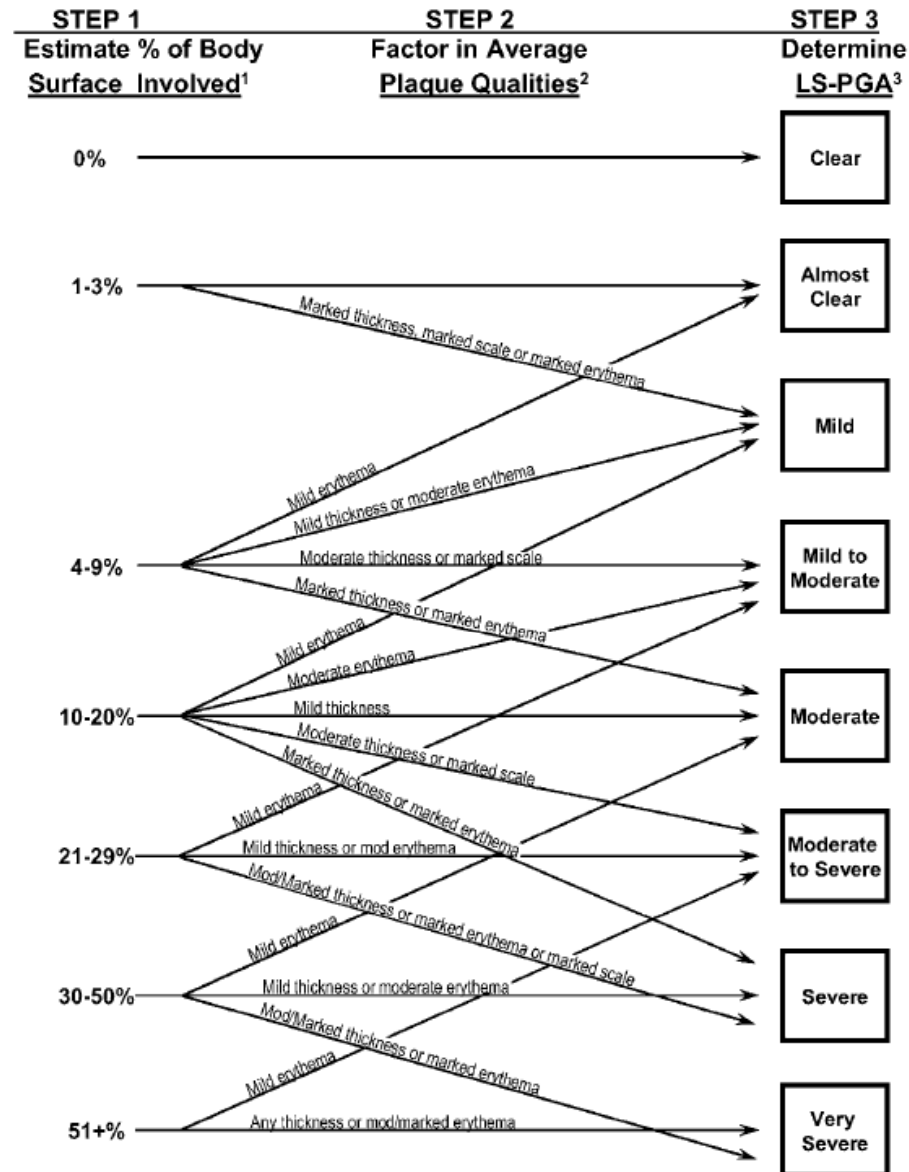
Does Body Surface Area Determine AD Severity?

- 50 children with AD (Manzoni, 2012)
  - BSA correlates with CDLQI (r=.428, P<0.001)

- 180 patients with AD aged 1-67 (Charman, 2005)
  - BSA correlates with degree of bother (r=0.44, P<0.001)
  - Higher adjusted r^2, than edema or erythema
  - Did not add anything to a model with signs

Options for Moving Forward

- Algorithmic approach (e.g. Lattice PGA)

Lattice System Physician's Global Assessment (LS-PGA)

Clinical Research Version

STEP 1	STEP 2	STEP 3
Estimate % of Body Surface Involved[1]	Factor in Average Plaque Qualities[2]	Determine LS-PGA[3]

When the individual plaque qualities are used in the lattice, the most severe score that results is the final LS-PGA.

Options for Moving Forward

- Algorithmic approach (e.g. Lattice PGA)

- New numerical composite index incorporating scoring system, itch, QOL

- Keep as is, but provide some agreed-upon standardized guidance

Example Guidance
Severe Disease

- In general, patients with severe disease have:

  BSA of >10%

  EASI of >18

  Deep or bright red erythema, very edematous lesions with widespread, often deep excoriation

  Quality of life is severely affected

  VAS scores are often > 6cm (1-10 scale)

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OREGON CLINICAL
+ TRANSLATIONAL
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Thank you!

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