



# SIGNS domain: Measuring responsiveness & MCID of TIS

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# Aim

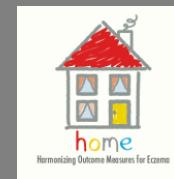
To demonstrate  
the responsiveness and minimal clinically  
important difference  
of  
“Three Item Severity” (TIS) score



Earlier:

## EASI, (objective) SCORAD and POEM

Ref: EASI, (objective) SCORAD and POEM for atopic eczema: responsiveness and minimal clinically important difference. M.E. Schram, Ph. I. Spuls, M.M.G. Leeflang, R. Lindeboom, J.D. Bos, J. Schmitt. *Allergy* 2012; 67: 99-106



# Three Item Severity scale

Sumscore of:

- Erythema (0-3)
- Oedema (0-3)
- Excoriations (0-3)
  
- At a representative lesion



# Data from three trials

- MAcAD: methotrexate versus azathioprine in adult patients with atopic eczema (M.E. Schram/Ph.I. Spuls)
- PROVE: cyclosporin versus prednisolone in adult patients with atopic eczema (J. Schmitt)
- SWET: softened water versus non-softened water on severity of eczema in children (K. Thomas)



# Responsiveness

- Synonym: sensitivity to change
- Definition: the ability of an outcome measure to detect change over time
- How was it measured:
  - Global: correlation with reference test
  - Receiver operating characteristics (ROC)/Area Under the Curve (AUC)

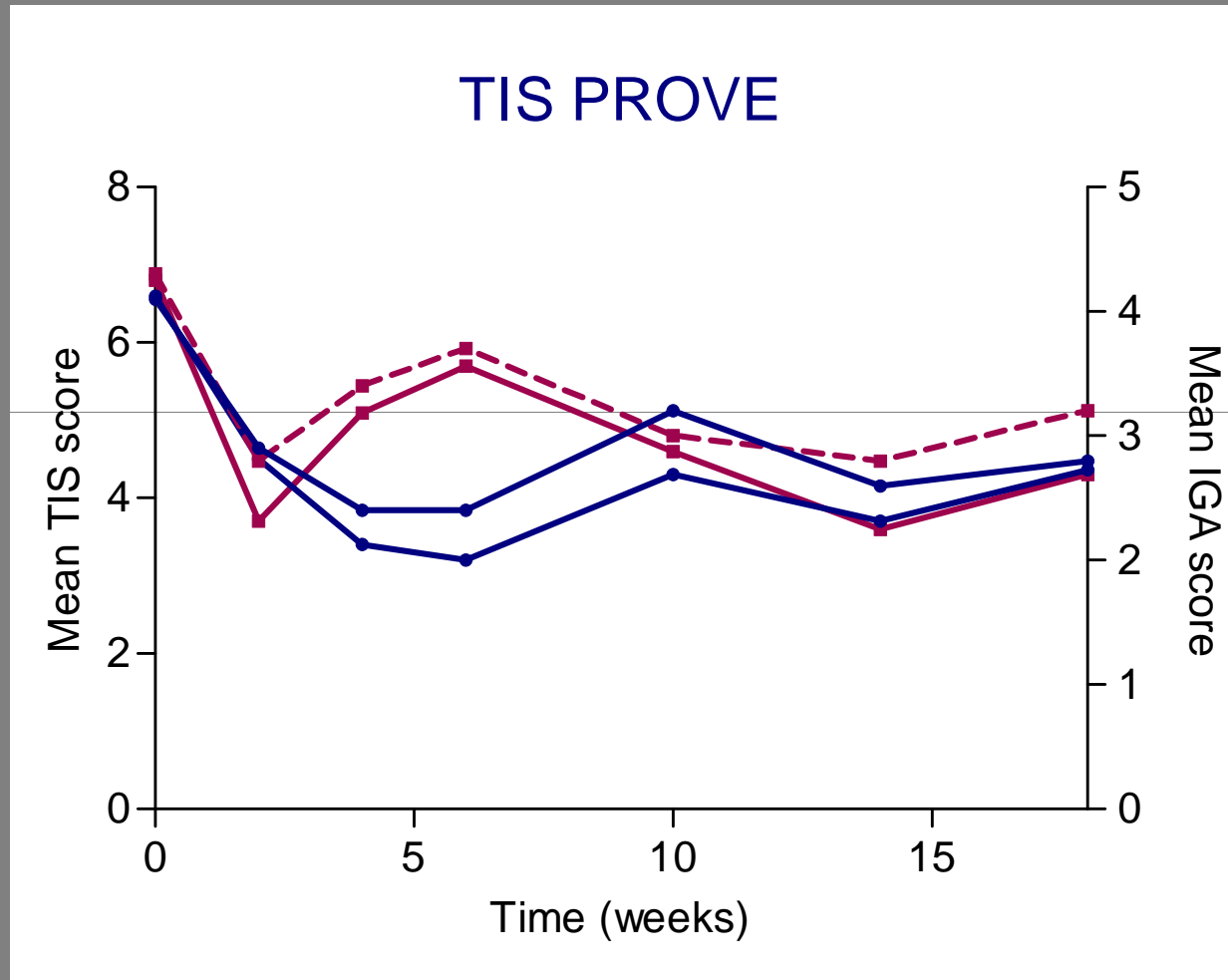


# Reference test

- How to decide if a patient has changed in disease severity or not?
- Preferably: transitional scale
- MAcAD & PROVE: Investigator global assessment (0-5)
- SWET: Bother score (0-10)

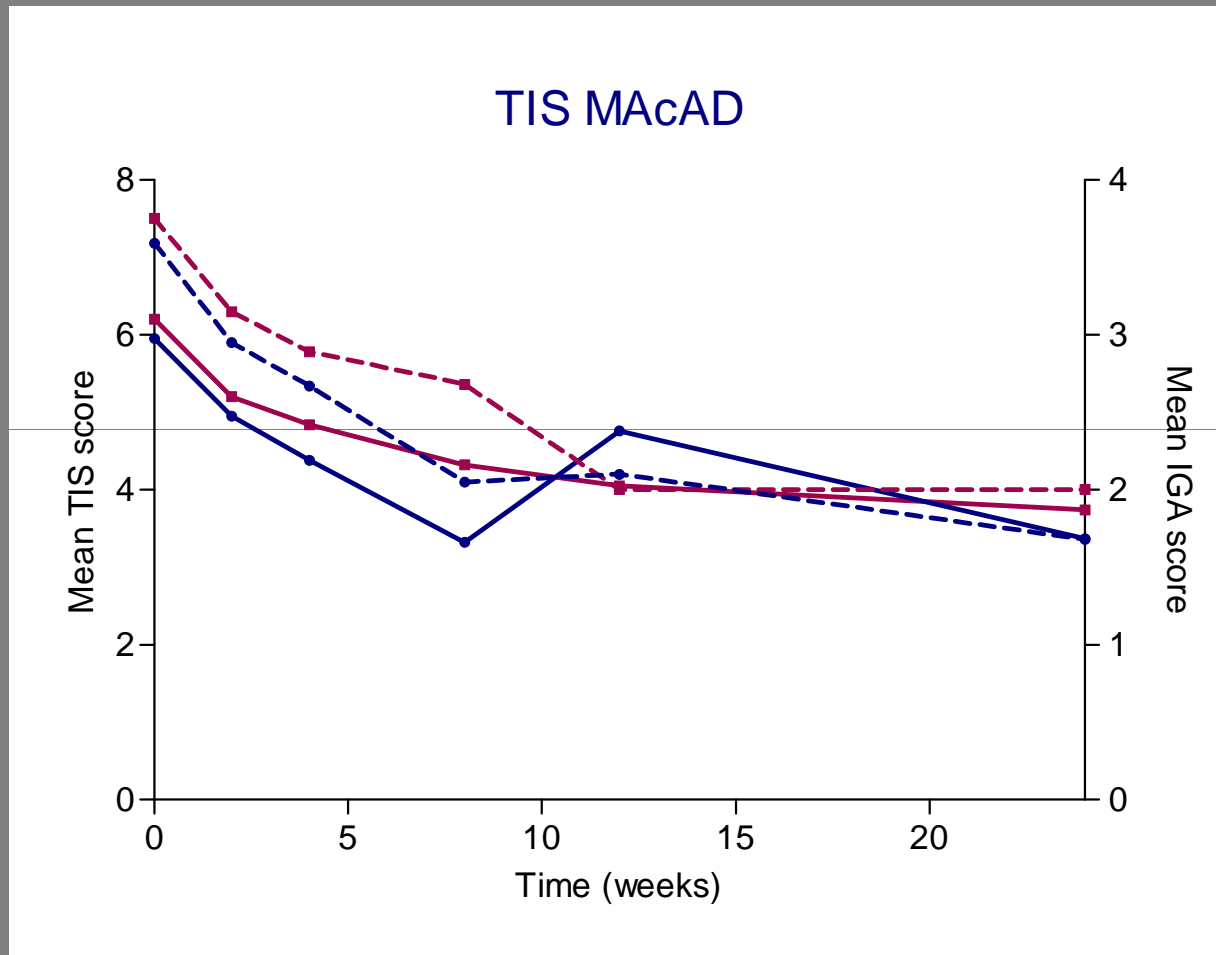


# Global responsiveness - PROVE

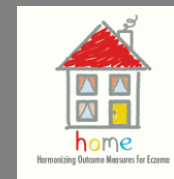




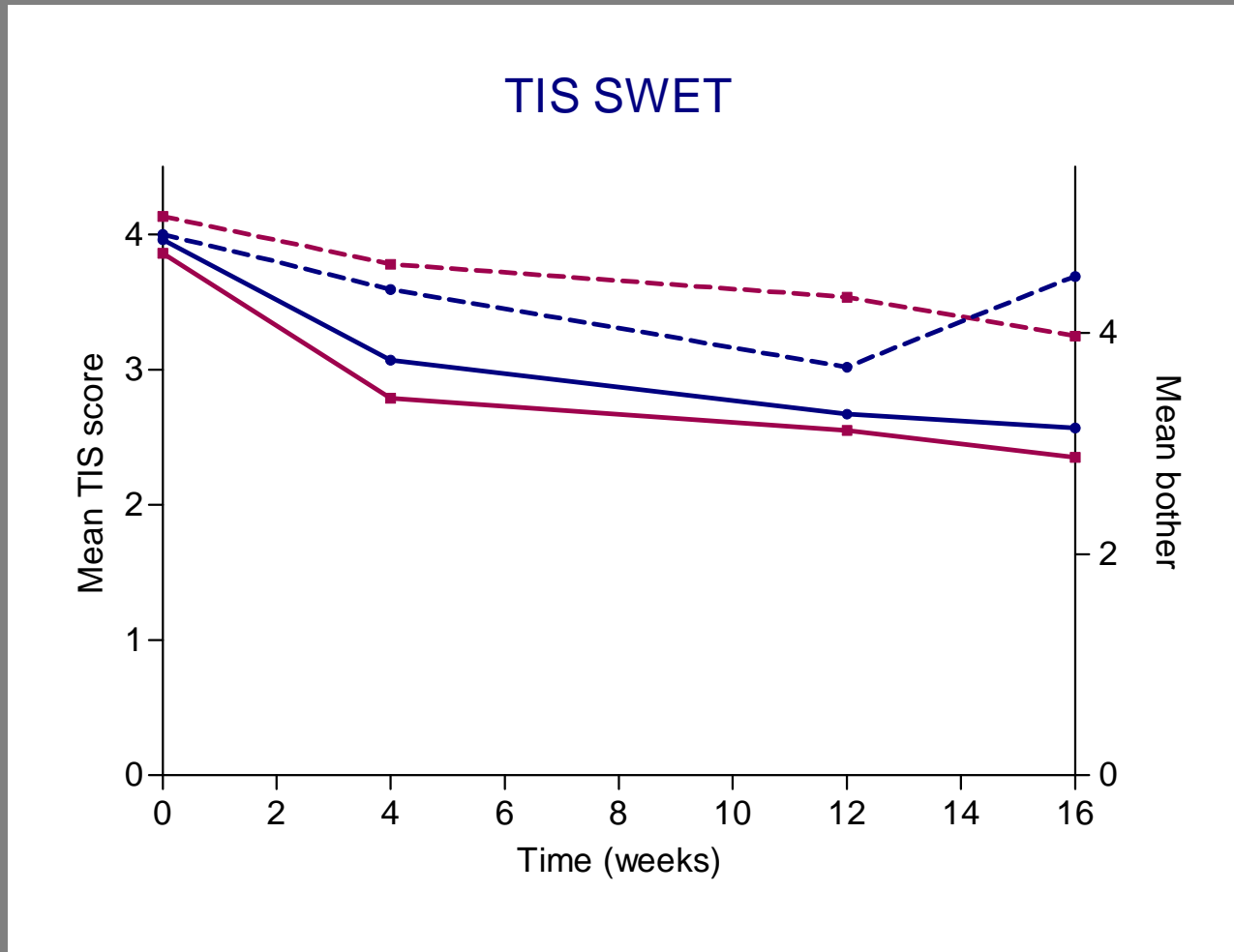
# Global responsiveness - MAcAD



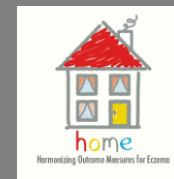
- MAcAD MTX TIS
- MAcAD AZA TIS
- MAcAD MTX IGA
- MAcAD AZA IGA



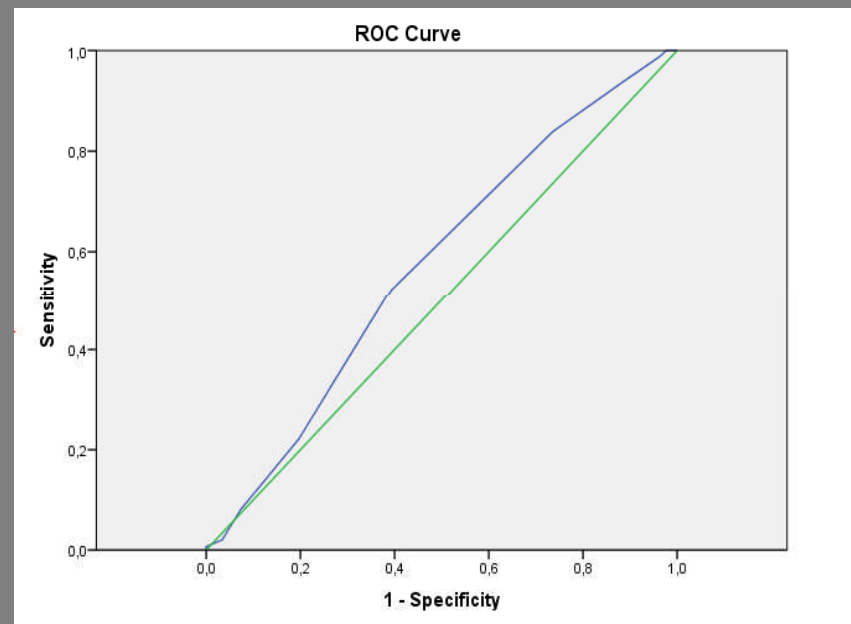
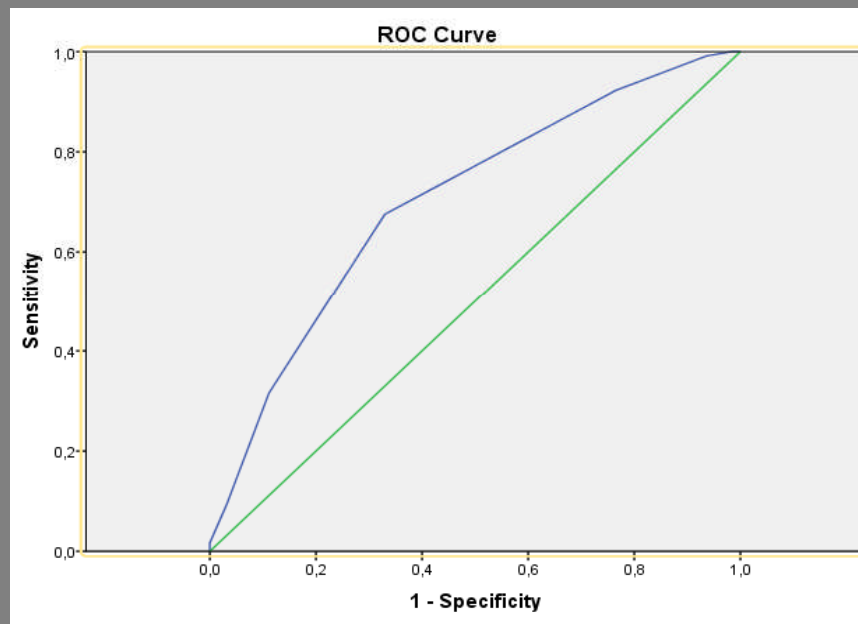
# Global responsiveness - SWET



- SWET A TISS
- SWET B TISS
- - SWET A Bother
- - SWET B Bother



# Responsiveness ROC – MAcAD/PROVE & SWET



# Responsiveness ROC – MAcAD/PROVE & SWET

	AUC	95% CI	Cut-off	Sensitivity%*	Specificity%*
SCORAD	0.70	0.61 - 0.78	4.05	64.7	64.2
Objective SCORAD	0.73	0.70 - 0.77	6.45	54.8	78.8
EASI	0.67	0.60 - 0.76	2.75	73.8	57.4
POEM	0.67	0.59 - 0.75	1.50	62.1	66.1
<b>TIS</b>					
<b>MAcAD/PROVE</b>	<b>0.71</b>	<b>0.64 - 0.76</b>	<b>0.5</b>	<b>67.5</b>	<b>67.0</b>
<b>SWET</b>	<b>0.57</b>	<b>0.51 - 0.63</b>	<b>0.5</b>	<b>52.3</b>	<b>61.7</b>

AUC; area under the curve, CI; confidence interval.

\*Sensitivity and specificity reflect the highest correct classification for the cut-off value.



# Minimal clinically important difference

- Definition: the smallest change in an outcome measure that represents a clinically relevant difference in disease status
- How was it calculated:
  - Longitudinal: absolute changes within individuals
  - Sensitivity analyses: Cut-off point ROC
  - Brent & Altman (B&A) analyses/ Limits of agreement

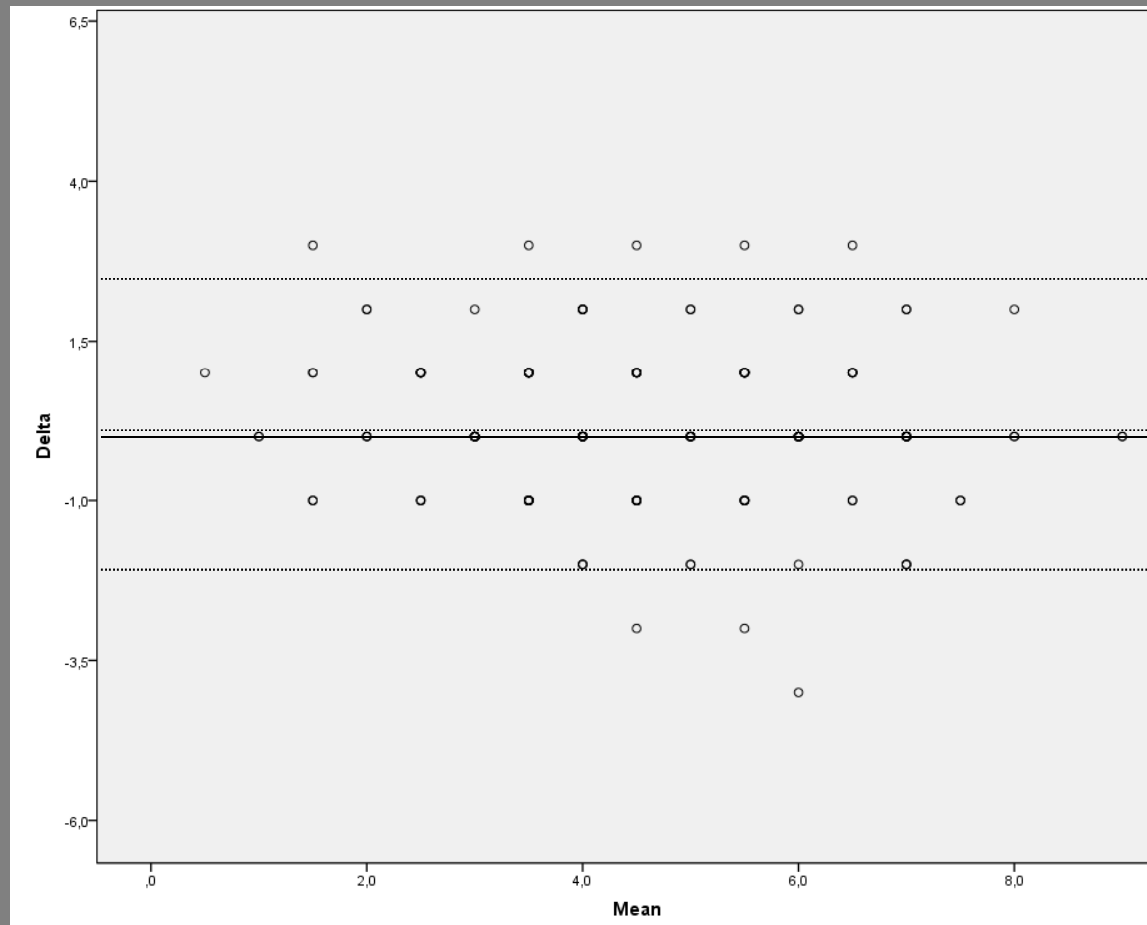


# Longitudinal - MCID

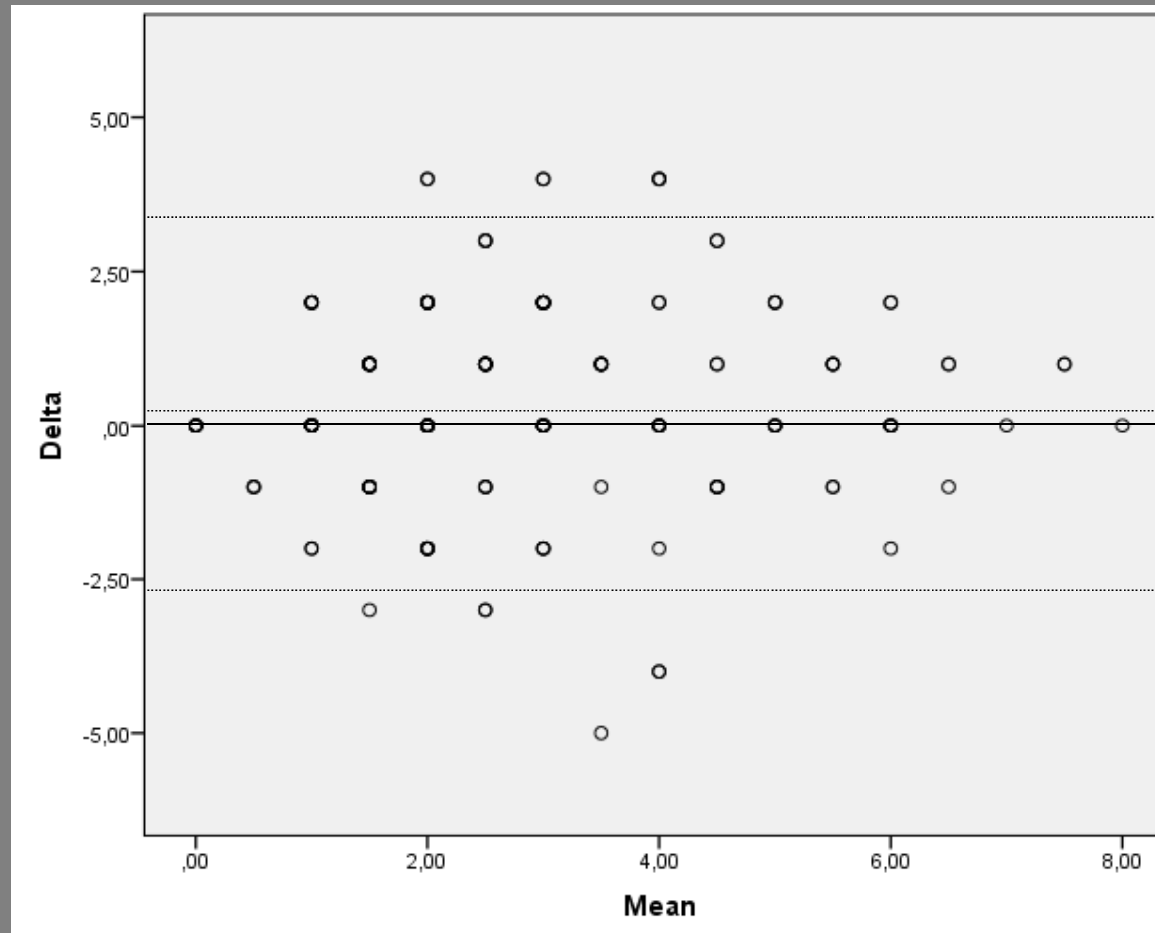
Outcome measure	RCT	Anchor (IGA)	N of obs.	Mean difference	Min.	Max.	SD
TIS	MAcAD & PROVE	5 -> 4	8	1.25	0	2	0.71
		4 -> 3	48	1.06	-1	4	1.17
		3 -> 2	43	0.91	-2	3	1.04
		2 -> 1	17	1.00	-1	4	1.46
		1 -> 0	1	2.00	-	-	-
		<b>TOTAL</b>	<b>117</b>	<b>1.02</b>	<b>-2</b>	<b>4</b>	<b>1.14</b>
Outcome measure	RCT	Anchor (Bother score)	N of obs.	Mean difference	Min.	Max.	SD
TIS	SWET	9 -> 8	9	0.78	0	1	0.44
		8 -> 7	4	0.75	0	2	0.96
		7 -> 6	16	0.87	-2	4	1.63
		6 -> 5	24	0.63	-3	3	1.50
		5 -> 4	24	0.58	-3	3	1.47
		4 -> 3	25	0.52	-2	5	1.71
		3 -> 2	27	0.33	-2	2	1.00
		2 -> 1	14	1.07	-1	3	1.14
		1 -> 0	6	0.33	-3	5	1.35
		<b>TOTAL</b>	<b>149</b>	<b>0.62</b>	<b>-3</b>	<b>5</b>	<b>1.354</b>



# B&A – MAcAD & Prove



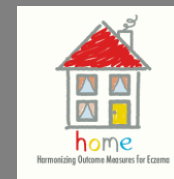
# B&A – SWET





# Overview of results

- Responsibility:
  - AUC 0.71 (95% CI 0.64-0.76) in MAcAD and PROVE data,
  - AUC 0.57 (85% CI 0.51-0.63) in SWET data
- MCID:
  - MAcAD/ PROVE: 1.02 (SD 1.21)
  - SWET: 0.62 (SD 1.36)



# Discussion

- We did not use a transitional scale
- The IGA was not performed in the SWET
- TIS was calculated from SCORAD scores used in the MAcAD & PROVE
  
- Nevertheless, the TIS does seem fairly responsive
  
- Does anybody have usable trial data?



# Aknowledgement

HOME

Phyllis Spuls  
Kim Thomas  
Jochen Schmitt

