

Response shift in severity assessment of hand eczema with visual analogue scales

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Summary

Background. Hand eczema is a common and fluctuating disease. Visual analogue scales (VASs) are used to assess disease severity, both currently and when at its worst. However, such patient-reported outcomes may be at risk of being flawed owing to recall bias or response shifts.

Objective. To explore whether the current state of hand eczema severity affects the recollection of the eczema when at its worst, thus resulting in a response shift.

Methods. We utilized a dataset from a recent clinical trial examining nurse counselling of hand eczema patients. The patients assessed the disease severity currently (VAS_{now}) and when at its worst (VAS_{worst}), both at baseline and at a 6-month follow-up.

Results. The patients who reported improvement during the course were generally more likely to downwardly adjust their assessment of VAS_{worst} than patients reporting unchanged or worsened severity (odds ratio 1.94, $p = 0.017$). No other determinants were found.

Conclusion. Patients may downwardly adjust their assessment of worst-ever disease severity according to the assessment of present disease severity. Regular photographic documentation of the hand eczema along with the patient's self-monitoring of symptoms as part of the treatment course could perhaps counteract this tendency for there to be severity habituation.

Key words: disease severity assessment; hand eczema treatment; patient-reported outcomes; recall bias; response shift; visual analogue scales.

Hand eczema is a common, often chronic, disease. The hands are our primary tools in many work-related and everyday life tasks. Moreover, the hands constitute a prominent element of our social lives, because their use is naturally embedded in greetings and gestures.

Consequently, hand eczema has been found to impair the quality of life with a magnitude similar to that of asthma and psoriasis (1).

Disease-specific patient-reported outcome instruments have been lacking in hand eczema. Most recently, the Quality of Life in Hand Eczema Questionnaire has been introduced, but up to now this has only been validated in its German version (2). Otherwise, dermatology-specific instruments such as the Dermatology Life Quality Index (DLQI) (3) and the Impact of Skin Diseases on Daily Life (ISDL) (4), along with generic instruments such as the EQ-5D (5), have been used to obtain patient-reported outcomes in clinical hand eczema trials. The ISDL and the EQ-5D both include visual analogue scales (VASs). In the ISDL, these scales are used to rate itching, pain and fatigue

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within the past 4 weeks as compared with worst-ever assessments. In the EQ-5D, the VAS scale is used to score the present health state as compared with best and worst imaginable health.

A screening tool, the Nordic Occupational Skin Questionnaire (NOSQ), also includes VASs (6). In the NOSQ, the person is asked to rate the eczema both as a current assessment and as a recollection of the eczema when at its worst. This latter assessment is relevant because hand eczema is known to fluctuate in time and severity. However, information obtained from questionnaires is always considered to be at risk of being affected by recall bias.

Recall bias has traditionally been said to occur when accuracy of recall regarding prior exposures is different for certain people. This means that selected groups may report harmful exposures more frequently than other groups. This is especially likely in case-control studies, where such exposures can be linked to the outcome that actually led to the status of being a case (7). Another phenomenon that may give rise to questions of validity in health-related quality of life evaluations is the so-called response shift. This phenomenon covers the possibility that changes in one's understanding or perception of the quality of life construct may occur between assessments (8). The response shift is arguably a natural part of a process of adaptation to and coping with a chronic illness. However, in clinical interventional trials, a response shift may potentially cause bias when pre-intervention and post-intervention assessments are compared.

The above-mentioned definition of response shift (8) does not completely cover the question of whether a worst-ever subjective assessment of health may be influenced by the current health state of the individual. Referring to the NOSQ items, it may be that people change their recollection of the eczema at its worst according to their assessment of the current eczema severity. In principle, the 'worst-ever' assessment is an absolute value, which can only increase at a later point of time but never become lower. This present study aimed to explore whether response shifts are present in patient-reported outcomes of hand eczema severity as measured by VAS at worst and VAS currently. The study was nested in a clinical randomized trial of nurse counselling as part of the hand eczema treatment (9).

Materials and Methods

The study cohort comprised Danish patients aged between 18 and 70 years who were referred for treatment

either at a dermatological outpatient unit or in a private dermatology clinic. Approval of the study was obtained from the Danish Data Protection Agency. In total, 306 individuals were consecutively included in the aforementioned clinical trial, where the primary outcome variable was the Hand Eczema Severity Index (HECSI) (10) at follow-up as compared with the baseline scores. Findings from that trial with regard to sex differences and to the effectiveness of the intervention have previously been reported elsewhere (11, 12).

Self-administered questionnaires at baseline and at 6-month follow-up were used to obtain the patient-reported outcomes. Among others, these were the quality of life, by use of the DLQI, and disease severity, by use of a VAS both as a worst-ever assessment (VAS_{worst}) and as a current rating (VAS_{now}). The VAS items were presented similarly to NOSQ item D₁₂ (6), with horizontal axes and the anchor points 0–5–10. The value '0' was defined as 'no eczema', and the value '10' was defined as 'extremely bad eczema'. The actual wording in Danish was similar to the NOSQ-Danish version. Only data from patients who replied adequately to the items in question and who returned both questionnaires were considered to be eligible for the purpose of this present study of potential response shift. Inadequacy was defined as someone rating VAS_{worst} lower than VAS_{now} at the same time point, or as the response shift in some extreme cases, for example a change in VAS_{worst} from 9–10 at baseline to 0.5–1 at follow-up. Such inconsistencies were considered to be related to either misinterpretation of the item or lack of accuracy when responding, and these cases were excluded from further analyses.

Sample size estimation and statistical analysis

Sample size calculation had been performed according to the HECSI outcome as part of the overall clinical trial (9). However, general estimations of sample size requirements when examining health behaviour and quality of life refer to minima of 80 participants in comparison groups (13). Hence, the number of patients included for this present study should be adequate.

The data were entered and analysed with the use of IBM SPSSTM Statistics version 19.0 for WindowsTM. The data were non-normally distributed, and non-parametric statistical methods were used. Paired analyses (Wilcoxon signed rank test) were used to examine the intra-individual differences in scores between baseline and follow-up. Delta values of both current and worst-ever VAS assessments were calculated by subtracting the follow-up scores from the baseline scores. Both delta values were then dichotomized to identify: (i) participants

who scored lower in current severity at follow-up than at baseline as an indication of improvement; and (ii) participants who scored lower in worst-ever severity at follow-up than at baseline as an indication of response shift (and hence labelled 'response shifters').

Categorical data were analysed with crosstabs and chi-square test, and with logistic regression. Univariate analysis was performed to test the differences in worst-ever responses between groups of patients who reported improvement ($\Delta\text{VAS}_{\text{now}} > 0$) and patients who reported no change or deterioration ($\Delta\text{VAS}_{\text{now}} \leq 0$). Differences between groups were analysed with the Mann–Whitney *U*-test. A two-sided *p*-value of <0.05 was considered to be statistically significant.

Results

In total, data from 224 of the 306 patients from the interventional study were used in this study of possible response shift. Table 1 shows the summary statistics of the VAS_{now} and $\text{VAS}_{\text{worst}}$ both at baseline and at follow-up. There was an overall decrease in self-assessed disease severity within the 6-month follow-up period. The median VAS_{now} at baseline was 4.5, as compared with a median of 3.0 at follow-up ($p < 0.001$). We also found that the median $\text{VAS}_{\text{worst}}$ of 8.0 was significantly lower at follow-up than the baseline median $\text{VAS}_{\text{worst}}$ of 8.5. We used paired statistical tests to ensure that this was not a finding related to different distributions of data within the cohort.

Accordingly, a group of patients rated $\text{VAS}_{\text{worst}}$ as being lower at follow-up than at baseline, and this change in assessment was significant. We then investigated whether the level of VAS_{now} influenced the individual ratings of $\text{VAS}_{\text{worst}}$. For this purpose, we computed a binary variable that divided the cohort according to whether the patient's VAS_{now} was improved or unchanged/worsened. In total, 137 of 224 (61.2%) rated VAS_{now} lower at follow-up, that is, they improved, whereas 87 of 224 (38.8%) reported unchanged or worsened disease severity at follow-up. Moreover, we computed a binary variable that indicated whether the rating of $\text{VAS}_{\text{worst}}$ had changed at 6-month follow-up. In total, 114 of 224 (50.9%) rated $\text{VAS}_{\text{worst}}$ as unchanged, or higher, at follow-up. In contrast, 110 of 224 (49.1%) rated $\text{VAS}_{\text{worst}}$ as lower at follow-up than at baseline, indicating a response shift.

The ratings of VAS_{now} appeared to influence the ratings of $\text{VAS}_{\text{worst}}$ (Table 2). In the group who reported an improvement in self-assessed disease severity, the patients were more likely to report a lower $\text{VAS}_{\text{worst}}$ at follow-up than at baseline. In general, it seemed that,

Table 1. Comparison of self-assessed disease severity at baseline and at follow-up ($n = 224$)

	Baseline	Follow-up	<i>p</i>
VAS_{now}			
Mean (SD)	4.71 (2.62)	3.52 (2.60)	$<0.001^a$
Median	4.50	3.00	$<0.001^b$
25th percentile	2.50	1.50	–
75th percentile	7.00	5.50	–
$\text{VAS}_{\text{worst}}$			
Mean (SD)	8.29 (1.50)	7.99 (1.72)	0.001 ^a
Median	8.50	8.00	0.001 ^b
25th percentile	7.50	7.05	–
75th percentile	9.50	9.50	–

SD, standard deviation; VAS, visual analogue scale; VAS_{now} , self-assessed severity at present; $\text{VAS}_{\text{worst}}$, self-assessed severity at worst; the possible range of VAS is 0 (no eczema) to 10 (extremely bad eczema).

^aPaired-samples *t*-test.

^bRelated-samples Wilcoxon signed rank test.

over time, the $\text{VAS}_{\text{worst}}$ was downwardly adjusted among those patients who experienced an improvement in their disease severity. A Mann–Whitney *U*-test confirmed the significant differences in $\Delta\text{VAS}_{\text{worst}}$ between the groups of unchanged/worsened ($\Delta\text{VAS}_{\text{now}} \leq 0$) and improved ($\Delta\text{VAS}_{\text{now}} > 0$) status at follow-up ($p = 0.020$).

We then analysed whether particular subgroups were overrepresented among the response shifters. Table 3 shows the results from univariate analyses according to binary variables such as sex, occupational disease, history of atopic dermatitis, age above or below 40 years, treatment in addition to topical steroids, self-reported seasonal variation, comorbidity of chronic diseases, median baseline HECSI, ΔHECSI (follow-up HECSI minus baseline HECSI), and ΔDLQI (follow-up DLQI minus baseline DLQI). Among the determinants, the baseline clinical severity assessed by the HECSI score was borderline significant. The group of patients with the most severe disease tended to be more likely to downwardly adjust their perception of $\text{VAS}_{\text{worst}}$ than the group of patients with the least severe disease (odds ratio 1.66; $p = 0.061$). In contrast, there was no difference in the number of response shifters between the patients with clinical improvement and the patients who had unchanged or worsened clinical severity at follow-up, as assessed by the ΔHECSI . Also, possible improvement in the DLQI throughout the course of the study was not associated with a higher number of response shifters.

The $\Delta\text{VAS}_{\text{now}}$ correlated significantly with both the ΔHECSI and the ΔDLQI (Spearman's rho 0.475 and 0.470, respectively, both $p < 0.01$; data not shown).

Table 2. Frequencies of response shifters (lowered VAS_{worst} at follow-up) according to Δ VAS_{now}

	VAS _{worst} , n (%)		OR (95% CI)	<i>p</i> ^a	Total n
	Unchanged or higher	Lower			
VAS _{now}					
Unchanged or worsened	53 (60.9)	34 (39.1)	–	–	87
Improved	61 (44.5)	76 (55.5)	1.94 (1.12–3.36)	0.017	137
Total n	114	110	–	–	224

CI, confidence interval; OR, odds ratio; VAS, visual analogue scale; VAS_{now}, self-assessed severity at present; VAS_{worst}, self-assessed severity at worst; the possible range of VAS is 0 (no eczema) to 10 (extremely bad eczema).

^aPearson chi-square.

Table 3. Frequencies of response shifters according to subgroups

Determining variable	No. of response shifters (%)	OR (95% CI)	<i>p</i>
Sex			
Female	71/145 (49.0)	Ref.	
Male	39/79 (49.4)	1.02 (0.59–1.76)	0.954
Occupational disease ^a (n = 223)			
No	57/111 (51.4)	Ref.	
Yes	53/112 (47.3)	0.85 (0.50–1.44)	0.547
Atopic dermatitis ^a			
No	81/165 (49.1)	Ref.	
Yes	29/59 (49.2)	1.00 (0.55–1.82)	0.994
Age (years)			
<40	45/103 (43.7)	Ref.	
≥40	65/121 (53.7)	1.50 (0.88–2.54)	0.135
Seasonal variation ^b (n = 221)			
Yes	40/91 (44.0)	Ref.	
No	67/130 (51.5)	1.36 (0.79–2.32)	0.267
Chronic comorbidity ^b (n = 221)			
No	69/141 (48.9)	Ref.	
Yes	38/80 (47.5)	0.94 (0.55–1.64)	0.837
Baseline HECSI (median)			
<41	47/110 (42.7)	Ref.	
≥41	63/114 (55.3)	1.66 (0.98–2.81)	0.061
Δ HECSI (n = 221)			
Unchanged/worsened	32/73 (43.8)	Ref.	
Improved	76/148 (51.4)	1.35 (0.77–2.38)	0.293
Baseline DLQI (n = 215) (median)			
<5	53/96 (55.2)	Ref.	
≥5	53/119 (44.5)	0.65 (0.38–1.20)	0.120
Δ DLQI (n = 206)			
Unchanged/worsened	30/68 (44.1)	Ref.	
Improved	72/138 (52.2)	1.38 (0.77–2.48)	0.277

CI, confidence interval; DLQI, Dermatology Life Quality Index; HECSI, Hand Eczema Severity Index; OR, odds ratio.

Number of patients = 224, unless stated otherwise.

^aData on occupational disease and atopic dermatitis were obtained from a clinical database.

^bData on seasonal variation and chronic comorbidity are from questionnaires.

Discussion

In this article, we have presented findings from a small study nested in a large clinical trial of counselling of patients with hand eczema. In general, the patients rated

their disease severity lower at follow-up than at baseline, and this was expected, given that the patients had received treatment and counselling. It was more surprising that the patients also generally rated their worst-ever disease

severity lower at follow-up than at baseline. We found that patients who, within a 6-month time frame, experienced improvement in their condition, as assessed by the VAS_{now} , were more likely to downwardly adjust their ratings of VAS_{worst} than those patients whose self-assessed disease severity was unchanged or even worsened. No other determinants could be significantly linked to this phenomenon of response shift, as shown in Table 3. An interpretation of these findings is that how one recollects the worst-case severity of hand eczema depends on the present state of disease severity. We have not been able to find other studies that have reported on such inconsistencies, although the VAS instrument has been, and still is, widely used.

Mainly, the VASs have been used as pain measurement instruments, and in this respect issues of non-linearity have been raised. A recent study explored the internal construct validity and responsiveness of the pain VAS (14). The pain VAS was found to be a valid instrument for measuring pain at one point in time. However, when responsiveness was investigated, the pain VAS's sensitivity to change varied across the scale. The authors concluded that, in VAS measurement, the VAS data must be transformed by Rasch analysis. Otherwise, non-parametric statistics must be used, as was the case in our study.

Hand eczema is a fluctuating disease, as is confirmed by the differences in VAS_{now} and VAS_{worst} both at baseline and at follow-up. This also explains why the 1-year prevalence of the disease is more frequently used than the point-prevalence in epidemiological studies. We have been able to identify only one study within dermatology that has reported on self-assessments according to most active and least active disease. Persons with other chronic dermatological conditions, such as psoriasis and atopic dermatitis, may experience equally dynamic disease patterns. A Swedish study compared a subjective measure of disease severity in psoriasis and atopic dermatitis with common generic and dermatology-specific quality of life instruments (15). The subjective measure of disease severity comprised assessments of the activity at the time of the survey, but also how the respondent felt at times of most active disease and at times of least active disease. All three measurements were on a horizontal VAS with two anchors. This study found that patients with atopic dermatitis felt worse when their disease was most active and felt better when it was least active than the psoriatic patients. The study did not report on associations between the actual disease severity and the worst–best assessments (15).

The median difference in ΔVAS_{worst} in the present study decreased from 8.5 at baseline to 8.0 at follow-up. This was a statistically significant difference, but it

could be questioned whether the difference is of clinical relevance. The response shift would probably not be enough to prompt a change in either the Physical Global Assessment (PGA) or the Clinical Photo Guide when evaluating hand eczema severity (16). The follow-up period of 6 months was rather short, and also the median VAS_{now} only decreased from 4.5 at baseline to 3.0 at the second rating. More importantly and clinically relevant, the potential severity habituation underlying a response shift may adversely affect the maintenance of preventive behaviour.

The assessments of HECSI and DLQI could be considered as external criteria in our study. The ΔVAS_{now} correlated significantly with both the $\Delta HECSI$ and the $\Delta DLQI$, although the correlations were only moderate. The HECSI assessments and the VAS_{now} ratings were not performed at exactly the same time point. The questionnaires used for the ratings of VAS_{now} and VAS_{worst} were self-administered, with an occasional delay in response. The VAS ratings and the DLQI items were, however, parts of the same questionnaires. A recent study compared four severity assessment methods for hand eczema, and found the DLQI to be the instrument that was least correlated with the other methods. In line with other studies, it was suggested that the DLQI lacks specificity because it was developed to evaluate skin diseases in general (16).

Our study may have other limitations besides the non-concurrency of questionnaire data and assessments of clinical severity. When data of ΔVAS_{now} and ΔVAS_{worst} are dichotomized into categories of improved or unchanged/worsened and higher/unchanged or lowered, respectively, equal weights are given to a ΔVAS of 0.1 and to a ΔVAS of 4. However, this may relate similarly to both comparison groups, so we do not consider this to constitute a risk of bias. The use of paired statistics strengthens the conclusions that VAS_{worst} ratings are adjusted according to the current state of disease severity, but more research in this field is needed.

In conclusion, we found that patients who experienced an improvement in hand eczema disease severity within 6 months downwardly adjusted their assessment of worst-ever disease severity. Given the fluctuating nature of hand eczema, it is advisable for clinicians and researchers to ask about the worst-case severity in addition to the present state. However, we need to consider the possibility that the worst-case severity may, in reality, be higher than reported by the patient in the present encounter. Hand eczema being a visible disease, regular photographic documentation of the hand eczema, performed either by the patient or as part of the treatment

course, could perhaps counteract this tendency to severity habituation. As the degree of itching and pain are not visible, clinicians can also encourage their patients to use a log to regularly register the symptoms. The possibility of VAS_{worst} response shifts is also relevant when this type of data is used for research or as part of regularly conducted screenings for occupational hand eczema. Presumably, the findings of a VAS_{worst} response shift may be applicable to other fields within health science.

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References

- 1 Cvetkovski R S, Zachariae R, Jensen H, Olsen J, Johansen J D, Agner T. Quality of life and depression in a population of occupational hand eczema patients. *Contact Dermatitis* 2006; **54**: 106–111.
- 2 Ofenloch R F, Weisshaar E, Dumke A K, Molin S, Diepgen T L, Apfelbacher C. The Quality of Life in Hand Eczema Questionnaire (QOLHEQ): validation of the German version of a new disease-specific measure of quality of life for patients with hand eczema. *Br J Dermatol* 2014; **171**: 304–312.
- 3 Finlay A Y, Khan G K. Dermatology Life Quality Index (DLQI) – a simple practical measure for routine clinical use. *Clin Exp Dermatol* 1994; **19**: 210–216.
- 4 Evers A W, Duller P, van de Kerkhof P C et al. The Impact of Chronic Skin Disease on Daily Life (ISDL): a generic and dermatology-specific health instrument. *Br J Dermatol* 2008; **158**: 101–108.
- 5 Lindberg M, Bingefors K, Meding B, Berg M. Hand eczema and health-related quality of life; a comparison of EQ-5D and the Dermatology Life Quality Index (DLQI) in relation to the Hand Eczema Extent Score (HEES). *Contact Dermatitis* 2013; **69**: 138–143.
- 6 Susitaival P, Flyvholm M A, Meding B et al. Nordic Occupational Skin Questionnaire (NOSQ-2002): a new tool for surveying occupational skin diseases and exposure. *Contact Dermatitis* 2003; **49**: 70–76.
- 7 Altman D G. *Practical Statistics for Medical Research*, 1st edition: London, Chapman & Hall, 1999.
- 8 McPhail S, Beller E, Haines T. Reference bias: presentation of extreme health states prior to EQ-VAS improves health-related quality of life scores. A randomised cross-over trial. *Health Qual Life Outcomes* 2010; **8**: 146.
- 9 Mollerup A, Veien N K, Johansen J D. Chronic hand eczema – self-management and prognosis: a study protocol for a randomised clinical trial. *BMC Dermatol* 2012; **12**: 6.
- 10 Held E, Skoet R, Johansen J D, Agner T. The hand eczema severity index (HECSI): a scoring system for clinical assessment of hand eczema. A study of inter- and intraobserver reliability. *Br J Dermatol* 2005; **152**: 302–307.
- 11 Mollerup A, Veien N K, Johansen J D. An analysis of gender differences in patients with hand eczema – everyday exposures, severity, and consequences. *Contact Dermatitis* 2014; **71**: 21–30.
- 12 Mollerup A, Veien N K, Johansen J D. Effectiveness of the Healthy Skin Clinic – a randomized clinical trial of nurse-led patient counselling in hand eczema. *Contact Dermatitis* 2014; **71**: 202–214.
- 13 Francis J J, Eccles M P, Johnston M et al. *Constructing Questionnaires Based on the Theory of Planned Behaviour. A Manual for Health Services Researchers*: UK: Newcastle, Centre for Health Sciences Research, University of Newcastle, 2004.
- 14 Kersten P, White P J, Tennant A. Is the pain visual analogue scale linear and responsive to change? An exploration using Rasch analysis. *PLoS One* 2014; **9**: e99485.
- 15 Lundberg L, Johannesson M, Silverdahl M, Hermansson C, Lindberg M. Health-related quality of life in patients with psoriasis and atopic dermatitis measured with SF-36, DLQI and a subjective measure of disease activity. *Acta Derm Venereol* 2000; **80**: 430–434.
- 16 Agner T, Jungersted J M, Coenraads P J, Diepgen T. Comparison of four methods for assessment of severity of hand eczema. *Contact Dermatitis* 2013; **69**: 107–111.