

Effectiveness of the Healthy Skin Clinic – a randomized clinical trial of nurse-led patient counselling in hand eczema

Annette Møllerup¹, Niels K. Veien² and Jeanne D. Johansen¹

¹Department of Dermato-Allergology, National Allergy Research Centre, Copenhagen University Hospital Gentofte, Niels Andersens Vej 65, 2900, Hellerup, Denmark and ²The Dermatology Clinic, Fyrkildevvej 7, 9220, Aalborg Øst, Denmark

doi:10.1111/cod.12243

Summary

Background. Hand eczema is a common disease, and continuous preventive skin protection and skin care must be adopted to prevent a chronic course. Hand eczema is not a uniform disease, and counselling must therefore be individually tailored.

Objectives. To evaluate the effectiveness of a nurse-led counselling programme, the Healthy Skin Clinic, emphasizing the patient's self-management, resources, and risks.

Patients and methods. Patients (n = 306) referred for diagnostic work-up and treatment of hand eczema were randomized and allocated either to the programme or to usual care. The primary outcome was clinical disease severity at follow-up. Secondary outcomes were quality of life, burden of disease, skin protective behaviours, and self-reported medication adherence.

Results. Patients in the intervention group had greater reductions in clinical severity and reported more beneficial behavioural changes at follow-up than those in the usual-care group. This was especially true of patients who were treated solely with topical corticosteroids and who had a primarily exogenous aetiology of hand eczema. However, the effect was very dependent on baseline disease severity. No differences in quality of life or burden of disease were found between the two groups.

Conclusion. A tailored nurse-led programme of skin protection counselling may be recommended as an essential part of hand eczema treatment.

Key words: chronic hand eczema; contact dermatitis; effectiveness; HECSI; interdisciplinary prevention; nurse-led counselling intervention; self-care.

Hand eczema is common in the general Danish population, with a 1-year prevalence of 10–14% (1, 2). Exposures to allergens and/or irritants in the environment are known factors in causing hand eczema. Endogenous

factors, such as atopic dermatitis and mutations of the filaggrin genes, may contribute to an individual's susceptibility. Hand eczema often becomes chronic, either with continuous symptoms or as intermittent eczematous eruptions. The treatment and prevention of relapses begins with determining the aetiology so that, if possible, the causative agent(s) can be removed (3, 4). Although not causal, aggravating exposures in everyday life need to be identified, and continuous preventive skin protection and skin care must be adopted by the individual (5). However, many patients find it difficult to apply protective strategies in everyday life, and state that the need for a constant focus on prevention is draining (6).

Hand eczema is often work-related, and most research focuses on secondary prevention within specific high-risk

Correspondence: Annette Møllerup, Department of Dermato-Allergology, National Allergy Research Centre, Copenhagen University Hospital Gentofte, Niels Andersens Vej 65, 2900 Hellerup, Denmark. Tel: +45 39 77 73 02; Fax: +45 39 77 71 18. E-mail: annette.mollerup@regionh.dk

Funding: The work was supported by grants from Trygfonden and Aage Bangs Fund.

Conflict of interests: The authors declare that they have no competing interests.

Accepted for publication 11 March 2014

occupations, as shown in several recent interventional studies (7–9). Less is known about the group of hand eczema patients referred for dermatological treatment at either specialized centres in hospitals or at private dermatology practices. In a prospective, multicentre study of 799 patients, Hald et al. described the clinical severity and prognosis of hand eczema, and found that a poorer prognosis correlated with the patient being an unskilled worker, having severe hand eczema at the first consultation, having symptoms such as fissures and scaling as an indication of chronic disease (10), and having a delayed course (11).

Recent evidence from The Netherlands suggests that an integrated care programme is superior to usual dermatological care (12). The programme combined all-ergo-dermatological evaluation and standardized topical treatment with nurse-led counselling on medication adherence, hygiene, skin care, and skin protection. An occupational physician was involved in cases of work-related eczema. Inclusion in the programme reduced clinical severity significantly as compared with usual care in a trial with 26 weeks of follow-up (12). However, after 12 months of follow-up, there was no statistical difference between the groups, and the programme was found not to be cost-effective (13).

A multidisciplinary approach to the prevention and treatment of hand eczema with large-scale campaigns and skin protection seminars is available in Germany (14). In cases of severe occupational hand eczema, a tertiary individual prevention (TIP) programme is offered. The TIP programme involves 2–3 weeks of inpatient dermatological diagnostic work-up and treatment, intensive counselling, and the possible involvement of an occupational physician. Local dermatologists perform follow-up after discharge, and the patient remains off work for 6 weeks, allowing full skin barrier recovery (15).

Differences between healthcare systems make it difficult to transfer the German model to Denmark, where hand eczema is almost exclusively treated in an outpatient setting. It may, however, be relevant to implement the educational features in the TIP programme. Hand eczema is not a uniform disease (16), so counselling on skin protection and skin care needs to be individually tailored. This current study examined the effectiveness of individual, nurse-led counselling, focusing on self-management, as compared with usual care, that is, information from the dermatologist, including hand-outs. We hypothesized that the counselling programme would result in a better prognosis as regards clinical severity, motivation for medication adherence, and quality of life. Finally, on the basis of recent findings (17), we expected different benefits of the intervention between men and women.

Patients and Methods

We conducted a prospective, dual-setting study comprising a cohort of patients ($n = 306$) referred for diagnostic work-up and treatment of hand eczema. The settings were an outpatient clinic in Gentofte, a metropolitan university hospital, and a large private dermatology clinic in Aalborg in the northern region of Denmark. The patients in the study population were consecutively enrolled from May 2011 to April 2012 (Aalborg, October 2011 to April 2012). The Danish Data Protection Agency and the Ethics Committee of the Capital Region (H-2-2011-007) both approved the conduct of the study.

To enhance the external validity of the study, we used only a few inclusion criteria (18). Eligible patients (referred because of hand eczema, aged between 18 and 70 years, and capable of replying to questionnaires in Danish) were invited to participate. The hand eczema diagnosis was confirmed at the first medical consultation, after which the clinical severity of the patient's hand eczema was assessed by use of the Hand Eczema Severity Index (HECSI) (19). On the basis of block-wise randomization according to setting and sex, the patients were allocated to either the usual-care group or to the group testing the intervention, named the Healthy Skin Clinic (18). Randomization was individual, and was performed centrally at the National Allergy Research Centre with a computer-generated algorithm unknown to the investigator. Baseline assessment of the HECSI was carried out prior to randomization by a member of an intervention team of four qualified nurses and the first author.

Outcome variables

The primary outcome variable was the change in HECSI score from baseline to follow-up. The HECSI is a detailed scoring system whereby eczema intensity is evaluated according to the presence of six symptoms on a scale from 0 (not present) to 3. The extent of the eczema is evaluated for five areas on a scale from 0 (no areas involved) to 4 (total area involved). The total index score, with a range from 0 to 360, is then found by multiplying the intensity and the extent (19). No minimum disease severity was required for inclusion in the study.

The secondary outcome variables were the changes in disease-related quality of life, in perceived burden of disease, and in self-reported medication adherence. Quality of life was measured with the Dermatology Life Quality Index (DLQI) (20). Summation of 10 item scores gives a total score of 0–30, with higher scores indicating poorer quality of life. The DLQI was supplemented with ratings of itching, scratching and fatigue on a scale from

0 (not present) to 10 (excessive) adopted by the Impact of Chronic Skin Disease on Daily Life (21). Also, the patient's perceived burden of disease was measured on a scale from 0 (no eczema) to 10 (excessive eczema), both at baseline and at follow-up. Medication adherence was measured with the Danish version of the Medication Adherence Report Scale (DMARS-4), which has been validated in cancer pain patients (22). This generic four-item scale covers whether respondents avoid, forget, alter or discontinue the prescribed medication. Measurement is on a five-point Likert scale with a total range from 4 to 20. A higher score indicates higher adherence. Data on the patients' use of dermatologically indicated systemic medication were obtained from registers run by the Danish Medicines Agency.

The trial flow

The principal investigator, that is, the first author, led the intervention team of nurses who assessed clinical severity both at inclusion and at follow-up, and counselled the patients in the intervention group according to protocol (18). Allocation for clinical assessments and/or for counselling was random. Hence, the participant could be included by one team member, could be counselled by another team member, and could have the follow-up outcome assessed by a third team member. The team members had the same training in the use of the HECSI, and inter-rater variability was evaluated by occasional checks, where patients were scored by two different assessors. In total, 7 patients were doubly assessed, and the intra-class correlation coefficients for absolute agreement for total HECSI scores was 0.78 (*F*-test with true value: $p=0.016$). A high level of team communication was ensured in order to provide commonality of the intervention.

When included in the trial, the patient was given a baseline questionnaire. Besides the secondary outcome variables, the questionnaire covered exposures and aggravating factors as addressed by items from NOSQ-2002 (23), and measurement of self-rated health with the generic Health Status Questionnaire, Short Form (SF-36). Additional self-constructed items were included in the questionnaire, which was pilot tested by 14 previous hand eczema patients. In the trial, one reminder including a new questionnaire was sent to non-responders after 2–3 weeks.

Immediately after randomization, counselling for general skin protection and skin care (24) was given to the patients in the intervention group. Further, more individualized counselling was offered in timely relation to the next medical consultation, after which the

aetiology of the eczema was confirmed. To the patients allocated to the usual-care group, a DVD with a 14-min information video about hand eczema was handed out as a supplement to the oral and written information given by the dermatologist. A follow-up questionnaire was administered to participating patients from both groups after 6 months. Patients allocated to the usual-care group were offered counselling according to the Healthy Skin Clinic at follow-up.

Some patients had previously been tested for contact allergy, and were not tested in this course of work-up and treatment, but the majority were diagnosed and had patch tests and/or prick tests performed according to their patterns of exposures. Patients treated in the hospital setting were tested for filaggrin mutations when appropriate. According to hand eczema guidelines, the first treatment choice comprises topical steroids (3). Other treatment options differed between settings; for example, Grenz ray therapy was offered only in the Aalborg clinic. This treatment, as well as potassium permanganate baths and ultraviolet B/TLO1 light therapy, was included with the use of systemic medication in a dichotomous variable labelled 'intensified treatment'.

The Healthy Skin Clinic intervention

The central point of the intervention was the nurse-led counselling consultation. In short, the Healthy Skin Clinic was founded on three concurrent elements. First, a skin profile generated by responses from the baseline questionnaire described each patient's susceptibility, knowledge, co-morbidities, social support, and known allergies and suspected aggravating factors. The purpose of this profile was to focus on the relevant areas for individual counselling. Second, a patient self-management book was offered on a secure website with information, educational videos, and tools for self-monitoring. Patients who did not use the internet were given a folder containing almost the same features. Third, support for self-management was offered in the form of *ad hoc* communication and networking. The patients could make contact with either the intervention team of nurses or with other trial participants by use of the website. A further description of the intervention can be found elsewhere (18).

Sample size estimation

A decrease in HECSI score from a mean of 19.9 to a mean of 11.2 at 6 months of follow-up after the treatment of hand eczema has previously been reported (10). The study did not report the standard deviations (SDs) of the

mean values, and a histogram indicated that the HECSI scores were not normally distributed. Nevertheless, the context of that study appeared to be similar to ours. Thus, we used these values to estimate the development in the usual-care group, and expected a difference at follow-up of 30% in favour of the intervention. Sample size calculation based on the following values with assumed SDs – usual-care group mean HECSI score of 11.2 (SD 9.0), intervention group mean HECSI score of 7.7 (SD 6.0), alpha error level of 5%, and beta error level at 90% – resulted in a need for 82 participants in each group (25). This figure corresponds to other suggestions of a minimum of 60–80 participants being needed in each group in interventional studies targeting changes in health behaviour (26, 27). With consideration of potential dropouts in a highly heterogeneous sample, we determined that the inclusion of 150 patients in each intervention arm would be sufficient.

Statistical analysis

Data were entered and analysed with IBM SPSS™ STATISTICS version 19.0 for Windows™. Group comparisons of categorical data were performed with chi-square tests. Disease severity as expressed by the HECSI had a positively skewed distribution. Also, a Bland–Altman plot showed increased variance of the Δ HECSI measures (baseline HECSI score minus follow-up HECSI score) at increasing HECSI values. After square-root transformation, the data graphically showed a sufficiently normal distribution to allow multiple linear regression analyses (Shapiro–Wilk test: usual-care group, $p=0.82$; intervention group, $p=0.09$). The DLQI score also turned out to be non-normally distributed, and transformations did not resolve this issue. Accordingly, when comparing the HECSI and the DLQI scores between groups, we used the median values and non-parametric statistical tests. All p -values presented are two-sided, with a significance level of 0.05.

Results

Throughout the 1-year period of inclusion, a total of 389 patients were invited to participate in the trial, and 306 patients consented. These patients were consecutively enrolled as shown by the trial flow chart (Fig. 1). In total, data of 292 patients were analysed for the purpose of this study.

Most patients attended consultations twice (44.6%), followed by patients attending three times, throughout the follow-up period (23.5%). Some patients only attended medical consultations once, and then failed to continue testing procedures and subsequent treatment adjustments

(11.9%). The follow-up session was scheduled after 26 weeks (mean 28.7, minimum–maximum 24–49). There was an average response time of 16 days (minimum–maximum 0–79) for the self-administered baseline questionnaire.

The patients had an age range of 18–69 years. One hundred and three were male, and 189 were female. No significant differences in sex, age, history of atopic dermatitis or other possible prognostic factors were found between the groups at baseline (Table 1).

We found only minor differences between the usual-care group and the intervention group in prescribed medication. Register data from the Danish Medicines Agency on redeemed prescriptions within the period May 2010 to December 2012 were available for 271 (92.8%) patients. These data were categorized into four groups: (a) topical corticosteroids (+/– other); (b) antibiotics (topical or systemic); (c) systemic treatment (azathioprine and acitretin); and (d) topical calcineurin inhibitors (tacrolimus and pimecrolimus). Throughout the follow-up period, almost all patients were prescribed topical corticosteroids (263/271; 97.0%), but no significant differences in prescribed medication between the groups were found. The distribution within groups of the variable intensified treatment, as a compound of on-site treatment and systemic medication, is shown in Table 1.

Dropout analysis

At the end of the trial, we analysed differences in age and sex among the following four groups: (a) did not want to participate ($n=83$); (b) excluded/consent withdrawn ($n=14$); (c) lost to follow-up ($n=38$); and (d) full data on primary outcome ($n=254$). An ANOVA analysis and *post hoc* analysis (Games–Howell) with multiple comparisons showed significant differences between groups according to age. The patients in group (c) who were lost to follow-up were significantly younger (mean age of 33.0 years) than the patients in group (d), who had a mean age of 40.8 years ($p < 0.001$). No other significant differences between the groups were found, including the sex distribution among the four groups (Pearson χ^2 -test: $p=0.41$).

Dropout analysis was also performed regarding the patients enrolled in the trial. In the usual-care group, the patients who completed the trial had a mean age of 42 years, and those who were lost to follow-up had a mean age of 34.5 years (heterogeneity of variance, Games–Howell test, $p=0.007$). In the intervention group, both the patients who completed the trial (mean age of 39.5 years) and the patients who were excluded (mean age of 45.8 years) were significantly older than the

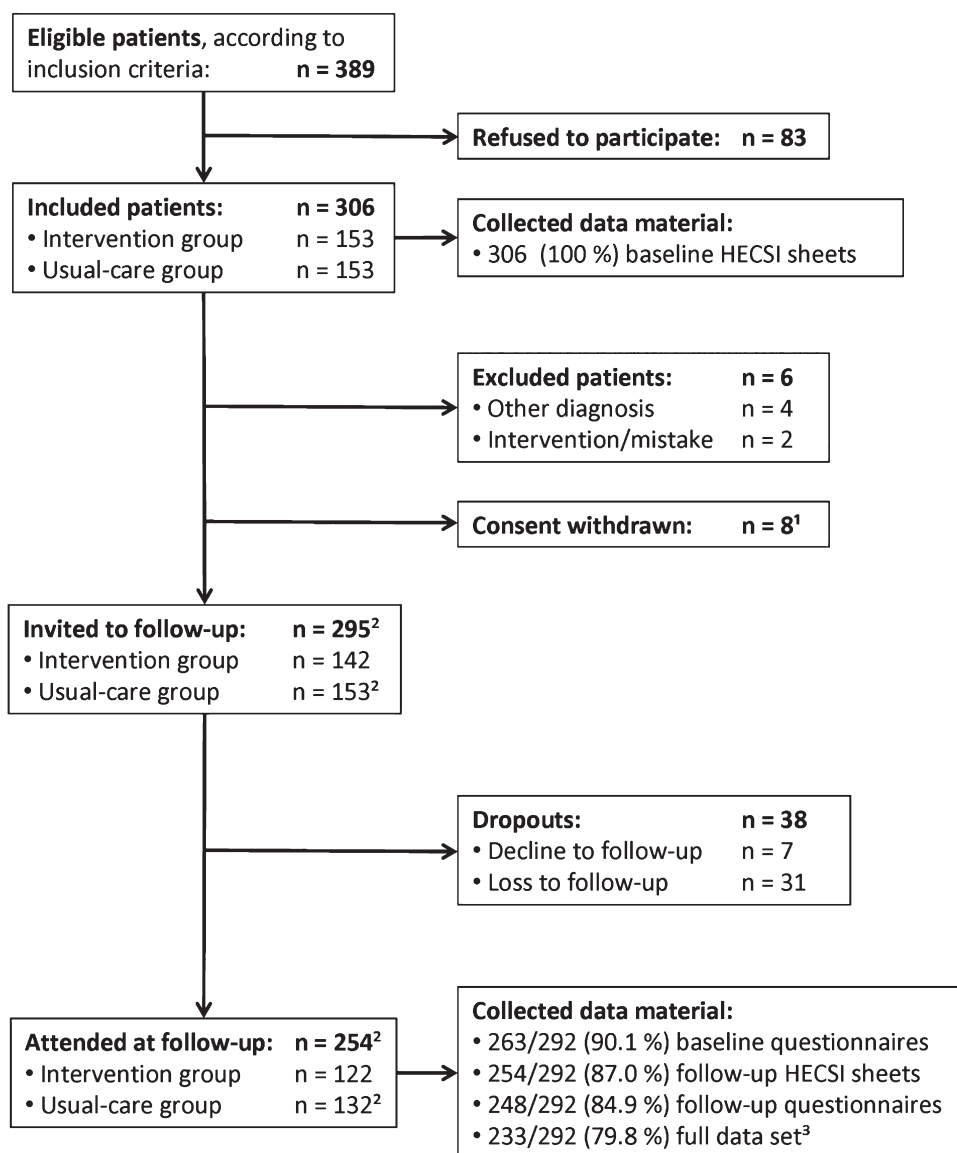


Fig. 1. Trial flow chart. ¹Eight patients from the intervention group withdrew their consent to participate in the study. ²Two patients from the usual-care group who were given the intervention by mistake were invited to follow-up to be offered the full counselling programme. One patient from the usual-care group had other diagnoses that were not clarified until after the patient had been invited to follow-up. Data of all three were then excluded from further analysis, and they are also excluded from this flowchart. ³The full data set consists of both baseline and follow-up Hand Eczema Severity Index (HECSI) sheets, and both baseline and follow-up questionnaires.

patients who were lost to follow-up (mean age of 32 years) (homogeneity of variance, Tukey test, $p = 0.048$ and $p = 0.017$, respectively). We also analysed differences in the HECSI score at baseline among the three groups. A Kruskal–Wallis analysis of the baseline HECSI score showed equal disease severity in the patients who completed the trial and the patients who were excluded or who were lost to follow-up (usual-care group, χ^2 -test 1.55, $p = 0.46$; intervention group, χ^2 -test 3.23, $p = 0.20$).

In the enrolment phase, the majority of those who did not want to participate argued that their decisions were based on lack of time or energy, for example because of co-morbidity. The same arguments were used by the 8 patients, all allocated to the intervention group, who withdrew from the trial. Three of the 4 patients who were excluded because of other diagnoses (palmoplantar pustulosis and psoriasis) were also from the intervention group.

Table 1. Characteristics of the patient cohort (n = 292)

		Intervention, n (%)	Usual care, n (%)	p-value ^a
Total study population		142	150	–
Setting	Hospital	92	96	–
	Clinic	50	54	–
Sex	Female	90 (63)	99 (66)	–
	Male	52 (37)	51 (34)	–
Atopic dermatitis	Yes	45 (32)	36 (24)	0.14
	No	97 (68)	114 (76)	–
Occupational disease ^b (n = 288)	Yes	62 (44)	80 (54)	0.10
	No	78 (56)	68 (46)	–
Age groups (years)	18–29	47 (33)	33 (22)	0.06 ^c
	30–39	27 (19)	35 (23)	–
	40–49	37 (26)	38 (25)	–
	50–59	20 (14)	28 (19)	–
	60–70	11 (8)	16 (11)	–
Severity groups, quartiles at baseline	HECSI < 20	33 (23)	37 (25)	0.71 ^c
	HECSI 20–43	39 (28)	36 (24)	–
	HECSI 43–76	30 (21)	43 (29)	–
	HECSI > 76	40 (28)	34 (22)	–
Intensified treatment ^d	Yes	65 (46)	53 (35)	0.07
	No	77 (54)	97 (65)	–
Included according to season	May–September	33 (23)	31 (21)	0.59
	October–April	109 (77)	119 (79)	–
Self-reported seasonal variation ^e (n = 257)	Yes	52 (41)	49 (37)	0.53
	No	74 (59)	82 (63)	–
Positive patch test ^e (n = 257)	Yes	52 (41)	66 (50)	0.14
	No	74 (59)	65 (50)	–
Hand eczema before adulthood ^e (n = 252)	Yes	24 (20)	26 (20)	0.99
	No	97 (80)	105 (80)	–

HECSI, Hand Eczema Severity Index.

Data relate to the entire study population (n = 292) unless stated otherwise.

^aPearson χ^2 -test unless stated otherwise.^bData from clinical database.^cLinear-by-linear.^dCompound variable of on-site treatment and systemic medication.^eQuestionnaire data.**Clinical severity of hand eczema**

Table 2 shows the clinical severity in the two groups. The median HECSI score in the overall cohort of patients at baseline was 43.0 (minimum–maximum 0–260; n = 292). At 6 months of follow-up, the median HECSI score had decreased to 24.0 (minimum–maximum 0–236; n = 254). Both groups improved significantly throughout the 6 months (Wilcoxon signed rank test: usual-care group, $p < 0.001$; intervention group, $p < 0.001$). The intervention group had a larger improvement (median Δ HECSI = –16.0) than the usual-care group (median Δ HECSI = –8.5). This result showed a trend towards a statistically significant difference (Mann–Whitney U -test: $p = 0.08$).

We then computed improvement as a dichotomous variable, simply defined as an individual Δ HECSI of < 0 . Significantly more patients (74.3%; 81/109) who had received intensified treatment than patients (61.4%; 89/145) who had not been prescribed this treatment improved (Pearson χ^2 : $p = 0.03$). The progress in disease severity was also analysed separately according to settings. At baseline, only minor differences in clinical disease severity appeared between the two settings. The Aalborg clinic had a median HECSI score of 46.5, and the Gentofte hospital had a median HECSI score of 40.0 (Mann–Whitney U -test: $p = 0.53$). However, 77 of 104 (74.0%) patients in the Aalborg clinic and 41 of 188 (21.8%) patients in the hospital setting were prescribed intensified treatment [Pearson χ^2 : $p < 0.001$,

Table 2. Hand Eczema Severity Index (HECSI) values at baseline (T_0), at follow-up (T_1), and as Δ -scores

	Intervention group			Usual-care group			Between groups <i>p</i> -value ^c
	Median ^a (IQR)	<i>p</i> -value ^b	n	Median ^a (IQR)	<i>p</i> -value ^b	n	
(a) Overall cohort							
T ₀ -HECSI	42 (20–82)	–	142	44 (20–72)	–	150	0.49
T ₁ -HECSI	24 (12–46)	–	122	25 (10–45)	–	132	–
ΔHECSI	– 16 (– 49 to 5)	< 0.001	–	– 9 (– 33 to 6)	< 0.001	–	0.08
(b) Hospital							
T ₀ -HECSI	42 (20–91)	–	92	38 (18–64)	–	96	0.14
T ₁ -HECSI	25 (11–46)	–	78	23 (10–57)	–	85	–
ΔHECSI	– 16 (– 47 to 3)	< 0.001	–	– 5 (– 27 to 11)	0.05	–	0.01
(c) Clinic							
T ₀ -HECSI	41 (20–71)	–	50	49 (27–81)	–	54	0.32
T ₁ -HECSI	21 (12–46)	–	44	27 (11–40)	–	47	–
ΔHECSI	– 16 (– 50 to 6)	0.005	–	– 20 (– 50 to – 1)	< 0.001	–	0.62

IQR, interquartile range.

Negative Δ -scores indicate improvement at follow-up.

Bold type indicates significance.

^aMedians and IQRs are rounded values.

^bWilcoxon's signed rank test for differences within groups.

^cMann–Whitney U -test for differences between groups.

odds ratio (OR) 10.2]. No significant differences between the intervention arms were found in the private clinic, but, in the hospital setting, disease severity in the intervention group was reduced significantly more than in the usual-care group (Table 2).

We then performed a multiple linear regression analysis to predict Δ HECSI (square-root-transformed data) with the covariates age, baseline severity, intervention arm, atopic dermatitis, and intensified treatment (Table 3a). This regression model explained 28% of the variability in disease severity outcome (adjusted $R^2 = 0.278$). The analysis showed that higher age was predictive of increased disease severity at follow-up ($p = 0.005$), but the effect was marginal (0.038 on the square-root-transformed HECSI scale per year). Baseline HECSI scores alone predicted disease severity much more profoundly, as one unit higher severity predicted an improvement of half a unit. Atopic dermatitis and intensified treatment did not add statistically significantly to the prediction, and nor did the intervention add to the prediction of outcome at follow-up. As Table 3b shows, we found a highly significant interaction between baseline severity and intensified treatment ($p < 0.001$).

Figure 2 shows that the intervention had different effects in the subgroups of patients, whether or not these received intensified treatment (Fig. 2).

We then stratified for this variable, and performed further analysis in the subcohort of patients ($n = 145$) who had not received this treatment. These analyses showed significantly greater improvement in the

HECSI in the intervention group than in the usual-care group (Table 4). The intervention impacted on different subgroups in various ways. We found significant differences between the intervention group and the usual-care group among patients without atopic dermatitis and among patients who had no self-reported seasonal variation in their hand eczema. Otherwise, no differences between the intervention arms were found (Table 4).

Effects on quality of life and burden of disease

Table 5a shows the results according to quality of life. The DLQI was measured both at baseline and at follow-up as an assessment of the impact within the past week. The usual-care group and the intervention group had equal overall DLQI scores at baseline. Both groups improved significantly throughout the course of the trial, but no differences were found between the groups at follow-up.

In both the questionnaire at baseline and that at follow-up, the patients rated how much their hand eczema had impacted on their life, both as current burden of disease (Table 5b), and within the past 4 weeks related to itching, scratching, and fatigue (data not shown). All of these subjective outcome variables were measured on a visual analogue scale from 0 to 10. Both groups showed similar patterns of significant improvement in all variables during the trial with no differences between the groups. At the face-to-face follow-up session, a third global assessment

Table 3. Summary of (a) multiple regression analysis and (b) univariate analysis of variance test of the interaction variable baseline Hand Eczema Severity Index (HECSI) $\times$ intensified treatment (BS HECSI $\times$ treatment)

(a) Variables	<i>B</i>	95% CI of <i>B</i>	<i>SE_B</i>	β	<i>p</i> -value
Intercept	0.506	–	0.647	–	–
Atopic dermatitis	0.548	– 0.224 to 1.319	0.392	0.084	0.163
Age	0.038	0.012–0.064	0.013	0.177	0.005
Baseline HECSI	– 0.540	– 0.657 to – 0.423	0.060	– 0.548	< 0.001
Intervention arm	– 0.133	– 0.758 to 0.491	0.317	– 0.023	0.674
Intensified treatment	– 0.186	– 0.858 to 0.486	0.341	– 0.032	0.586
(b) Interaction variable	<i>F</i> (d.f.)	<i>p</i> -value			
BS HECSI $\times$ treatment	48.658 (2)	< 0.001			

Bold type indicates significance.

B, unstandardized regression coefficient; CI, confidence interval; *SE_B*, standard error of the coefficient; β , standardized coefficient; *F*, *F*-test; d.f., degrees of freedom.

Table 4. Subgroup analysis of Δ HECSI scores in patients not given intensified therapy (*n* = 145)

Δ HECSI scores	Intervention group		Usual-care group		Between groups <i>p</i> -value ^b
	Median ^a (IQR)	<i>n</i>	Median ^a (IQR)	<i>n</i>	
Overall subcohort	– 9 (– 32 to 6)	63	– 3 (– 19 to 10)	82	0.037
No atopic dermatitis	– 15 (– 37 to 6)	48	0 (– 26 to 11)	60	0.034
Atopic dermatitis	– 8 (– 18 to 7)	15	– 6 (– 15 to 11)	22	0.65
< 40 years	– 12 (– 26 to 7)	31	– 6 (– 18 to 7)	35	0.25
$\geq$ 40 years	– 9 (– 37 to 5)	32	– 2 (– 27 to 17)	47	0.07
No occupational disease	– 19 (– 51 to – 5)	23	– 4 (– 30 to 11)	29	0.10
Occupational disease	– 9 (– 26 to 7)	39	– 3 (– 19 to 14)	52	0.17
No seasonal variation ^c	– 20 (– 37 to 8)	27	– 4 (– 20 to 10)	47	0.016
Seasonal variation	– 5 (– 18 to 8)	29	– 2 (– 27 to 20)	28	0.87
No positive patch test	– 11 (– 32 to 6)	38	– 4 (– 29 to 17)	32	0.13
Positive patch test	– 8 (– 51 to 7)	22	– 4 (– 19 to 9)	44	0.27

Bold type indicates significance.

HECSI, Hand Eczema Severity Index; IQR, interquartile range.

Negative Δ -scores indicate improvement at follow-up.

^aMedians and IQRs are rounded values.

^bMann–Whitney *U*-test of differences between groups.

^cSeasonal variation is self-reported (data from questionnaire).

of current eczema was performed immediately before the HECSI scoring. This was a means to address a potential lag effect resulting from response-related delays because of the self-administered questionnaires. The global assessments in both groups correlated significantly by ranks with the concurrent HECSI scores ($p < 0.001$), but we did not find any differences between the groups (intervention group, Spearman $r = 0.65$; usual-care group, Spearman $r = 0.63$).

We did not find any sex differences for the primary outcome in the trial. Men had a higher HECSI score at baseline (median of 47.0) than women (median of 39.0), but this difference was not significant ($p = 0.16$). Accordingly, men improved slightly more than women

(medians of – 16.0 and – 11.0 for men and women, respectively), although this difference was not significant. However, differences between the two sexes were found in the measurements of quality of life. Significant differences were found at baseline, when women had a median DLQI score of 6.0, and men had a median DLQI score of 4.0 (Mann–Whitney *U*-test: $p < 0.001$). Both sexes had a significantly improved quality of life during the trial, as shown by the Wilcoxon signed rank test ($p < 0.001$ for women, and $p = 0.003$ for men), but women had a larger improvement than men. At follow-up, women had a median Δ DLQI of – 3.0, and men had a median Δ DLQI of – 1.0, and this difference was statistically significant (Mann–Whitney *U*-test: $p = 0.004$).

Table 5. Subjective outcome measurements at baseline (T_0), at follow-up (T_1), and as Δ -values

	Intervention group		Usual-care group		Between groups <i>p</i> -value ^a
	Median (IQR)	n	Median (IQR)	n	
(a) DLQI (possible score 0–30; a higher score indicates higher impairment within the past week)					
T ₀ -DLQI	5 (3–8)	123	5 (2–9)	128	0.71
T ₁ -DLQI	3 (1–6)	114	2 (1–6)	117	–
ΔDLQI	– 1 ^b (– 4 to 0)	105	– 2 ^b (– 4 to 0)	111	0.35
(b) Current burden of disease (possible score 0–10; a higher score indicates a higher burden)					
T ₀ -VAS	5 (3–7)	126	5 (3–7)	132	0.49
T ₁ -VAS	3 (2–5)	117	3 (2–6)	128	–
ΔVAS	– 1 ^b (– 3 to 1)	109	– 1 ^b (– 4 to 1)	120	0.42

DLQI, Dermatology Life Quality Index; IQR, interquartile range; VAS, visual analogue scale.

Values are presented as rounded median values and IQRs.

Negative Δ -scores indicate improvement at follow-up.

^aIndependent Mann–Whitney U -test for differences between groups.

^b $p < 0.05$ by Wilcoxon's signed rank test for differences within groups.

Medication adherence and skin protective behaviour

Overall, the groups had equally high self-reported medication adherence at baseline, with the intervention group and usual-care group having mean DMARS-4 sum scores of 17.5 and 16.9, respectively. DMARS-4 scores did not change throughout the trial in any of the groups, and accordingly no difference was found between the groups at follow-up.

The patients were asked about their daily number of handwashes, both at work and in leisure time. This variable was dichotomized into < 10 times daily and > 10 times daily, at work or in leisure time. At baseline, no differences between the usual-care group and the intervention group were found, which was also the case at follow-up for work-related handwashing. However, at follow-up, fewer patients in the intervention group than in the usual-care group reported handwashing > 10 times daily in leisure time (Table 6). Also, the pattern of daily emollient use changed. No differences between the groups were found at baseline, but, at follow-up, significantly more patients in the intervention group than in the usual-care group reported daily use of emollients, with an OR of 2.15 (Table 6).

Discussion

We have presented an overview of findings from a randomized trial on a cohort of hand eczema patients from two clinical settings. A package of education, counselling and self-monitoring features was compiled to form the Healthy Skin Clinic intervention, with the aim of supporting self-management of hand eczema.

In general, the patients in the trial showed improved disease severity, whether or not they received the

intervention. We found an overall tendency ($p = 0.08$) for there to be a larger improvement in the HECSI score in the patients who were offered the Healthy Skin Clinic intervention than in the patients allocated to the usual-care group. In the hospital setting, which provided the majority of participants, the difference in Δ HECSI was statistically significant, whereas no differences were found in the private clinic. Different treatment options may account for these inconsistent findings. On-site treatment was much more common in the private clinic (given predominantly as Grenz ray therapy) than in the hospital setting (OR 16.9, 95% confidence interval 9.3–30.8, $p < 0.001$). We found that on-site treatment and additional systemic medication, that is, intensified treatment, were positively associated with improvements in disease severity. It is plausible that the effects of this treatment diluted the impact of an intervention based on the patients' self-management.

On the other hand, disease severity at baseline turned out to be the explanatory variable that was most likely to predict the severity outcome at follow-up. A square-root transformation of the HECSI scores was successful in establishing a normal distribution of data. However, it could not entirely reverse the disproportionate association of baseline and Δ -values of HECSI, which could be found by use of the Bland–Altman plot. This means that the progress in disease severity was dependent on the values at baseline, and higher values at baseline were likely to result in a better prognosis. This could be partly explained by the 'regression-to-the-mean' phenomenon, because of potential measurement errors (28). The inter-rater reliability showed a satisfactory intra-class correlation coefficient ($r = 0.78$), which was similar to that in the HECSI validation study (19). However, the occasional

Table 6. Self-reported handwashing (risk behaviour) and emollient use (protective behaviour)

	Intervention, n (%)	Usual care, n (%)	OR	95% CI	p-value ^a
(a) Behaviour at baseline					
Handwashing > 10 times daily					
At work	32/113 (28.3)	37/120 (30.8)	0.89	0.50–1.56	0.67
In leisure time	11/124 (8.9)	16/127 (12.6)	0.68	0.30–1.52	0.34
Daily use of emollients	104/126 (82.5)	102/129 (79.1)	1.25	0.67–2.34	0.48
(b) Behaviour at follow-up					
Handwashing > 10 times daily					
At work	32/111 (28.8)	38/115 (33.0)	0.82	0.47–1.45	0.49
In leisure time	5/119 (4.2)	23/123 (18.7)	0.19	0.07–0.52	< 0.001
Daily use of emollients	103/119 (86.6)	96/128 (75.0)	2.15	1.11–4.16	0.022

Bold type indicates significance.

CI, confidence interval; OR, odds ratio.

^aPearson's χ^2 -test for differences between groups.

performed checks related by chance to patients with HECSI-scores lower than 56. In the original validation study of the HECSI, increased inter-observer variation was found for patients obtaining higher total scores as compared with patients with lower scores (19). The exponential nature of the HECSI scale itself may increase the possibility of measurement errors.

Some relevant findings are in support of the Healthy Skin Clinic having a possible effect on hand eczema prognosis. The results from the subgroup analysis suggest that the intervention may have impacted on the group of patients in whom endogenous factors were not preponderant, that is, those without seasonal fluctuation or atopic dermatitis. Also, in the overall cohort, the patients in the intervention group reported significantly less risky behaviour, that is, handwashing > 10 times daily in leisure time, and more protective behaviour, that is, daily emollient use at follow-up, than those in the usual-care group, although no differences were present at baseline. This finding suggests that the intervention was effective in changing behaviour, which is consistent with other recent studies of skin care education interventions (8). This behavioural change may contribute to a better long-term prognosis, as frequent handwashing is strongly associated with the development and persistence of hand eczema (29, 30). The frequency of handwashing at work did not change throughout the follow-up period, which is not surprising, as this behavioural element may be under strict regulation by people other than the patient.

The DLQI scores were rather low at baseline, with median values of 5 in the two intervention arms. We did not obtain baseline outcome measurements other than the HECSI at the inclusion point. The patients were handed a questionnaire and asked to return it within a week, but, in several cases, a reminder had to be administered. The same administration mode was applied

to the questionnaires at follow-up. Fluctuations in disease activity or the initiation of adequate treatment may have caused a lag effect, which presumably could introduce a bias into the findings. We have recently reported findings from the same cohort showing that women were generally far more affected by their hand eczema than men, and this was also true after adjustment for disease severity (17). However, in this follow-up study, we found that women had more improvement in quality of life than did men, although they did not show a corresponding improvement in their clinical severity. This emphasizes the complexity of quality of life measurements. The DLQI has recently been found to be the severity assessment method that is least correlated with other severity scores of hand eczema (HECSI, Physician Global Assessment, and a Clinical Photo Guide), and it has been suggested that the DLQI lacks specificity with regard to hand eczema assessment, because it has been developed to evaluate skin diseases in general (31).

We did not find any beneficial development in medication adherence in either group during the trial. We addressed the issue of adherence as an element in the skin profile, because research suggests that adherence might be improved merely by communication with the patient concerning this issue (32). Medication adherence at baseline was rather high, so it is likely that the scale of DMARS-4 reaches a ceiling, making improvements difficult to measure. It is plausible that the 38 patients who were lost to follow-up would have reported lower medication adherence, and hence a more balanced distribution would have been seen, if they had returned the questionnaires. However, when self-reporting, patients arguably overestimate adherence (33), which could cause a social desirability bias. It has therefore been recommended simply to ask 'What did you put on your skin yesterday' to assess patterns of medication

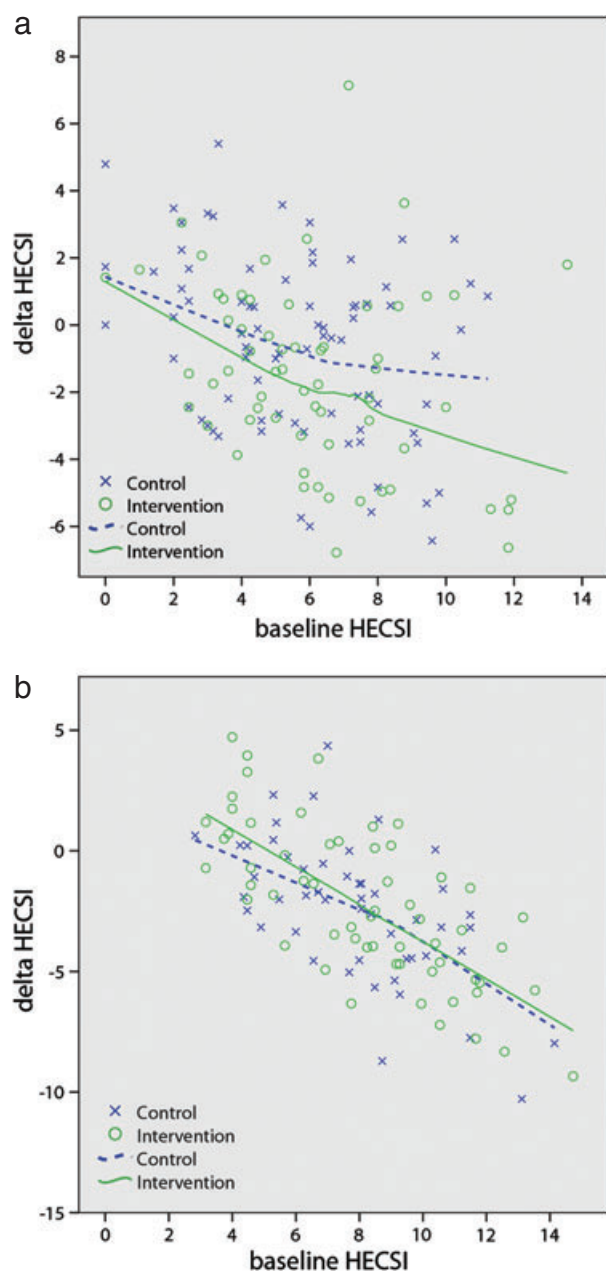


Fig. 2. Association between baseline values of HECSI and Δ HECSI (square-root-transformed data) in subgroups of (a) patients who did not have intensified treatment and (b) patients who had intensified treatment during the trial. HECSI, Hand Eczema Severity Index; negative Δ -scores represent improvement from baseline to follow-up; intensified treatment, compound variable of on-site treatment and systemic medication. The lowest baseline HECSI value (square-root-transformed) in the group of patients who had intensified treatment was 2.83, so this is the starting point of the lines in (b).

adherence, and hence to address recent behaviour instead of intended behaviour (34).

Strengths and limitations of the study

This trial was ambitious, and tried to balance a randomized controlled design with a complex intervention focusing on clinical relevance. Hence, some methodological flaws were exposed. A piloting feasibility study could potentially have provided knowledge on important contextual and processual factors, which then could have been responded to (35).

First, we deliberately included patients on the basis of wide criteria and at two different settings, to enhance generalizability, but this resulted in a cohort that was even more heterogeneous than anticipated. This was especially critical in relation to the prescription of intensified treatment. These potent choices of therapy possibly diluted the more tardy and subtle effects of an intervention based on counselling, self-monitoring, and self-management.

Second, the time lags of HECSI assessments and questionnaires made it difficult to validate the clinical findings with supplemental subjective measurements. In addition, the clinical outcome measurements were not blinded, which could result in an observer bias. However, the HECSI scores at baseline were obtained prior to randomization. The data sheets were then removed from the participants' data files to make the subsequent outcome assessment as blinded as possible. The assessors at follow-up were randomly allocated to the patient in question, so, in many cases, they had not previously met the patient and did not have knowledge of the baseline scores. There were no between-group differences in the ranked correlations between the patients' global assessments and the HECSI scores. Thus, systematic overestimation of Δ HECSI in the intervention group appears to be unlikely. However, the HECSI scale itself has some drawbacks related to the mathematical properties of data distribution that challenge outcome measurement.

Third, the controllability of the intervention may be questioned. We did not require the patients in the intervention group to fully comply with the intentional self-monitoring features or with the other elements in the Healthy Skin Intervention. However, only patients from the intervention group withdrew from the trial, which is in line with the previous findings of constant prevention being experienced as tiresome (6). We deliberately chose a realistic design in which the intervention was intended to supplement the medical treatment, facilitating subsequent implementation. As a minimum, all of the patients in the intervention group were given general

counselling on skin protection and skin care, but, to some extent, this might also have been offered by the dermatologist to the patients in the usual-care group. Thus, we cannot rule out a potential contamination bias. Moreover, many of the participants were repeat patients, and had therefore previously been treated at a private dermatology practice, where they could have been informed about skin protection. These factors would most likely lead to an underestimation of the effects found in the trial.

Conclusion

This trial shows that patients with hand eczema constitute a complex, heterogeneous group, and that the confounders are many and sometimes unavoidable. Considering the multidimensional intervention, other methods could be suitable for evaluating effectiveness. Prospective cohort studies may be more feasible than randomized trials, because the latter require delicate balancing between restricted patient selection and issues of external validity. As suggested by Upshur et al., no single research method is applicable in all circumstances (36). Evaluation of the intervention could also pertain to the impact that it may have in terms of increased knowledge, awareness, motivation, and confidence. Hence, a forthcoming explorative study using qualitative methodology is considered to be relevant.

We found that patients who were offered the intervention improved more than those in the usual-care group. This was especially true in the subgroups of patients not

given intensified therapy and with a primarily exogenous aetiology of hand eczema. Moreover, beneficial behavioural changes were seen only in the intervention group. On the other hand, the results, were to a large extent, dependent on disease severity at baseline, and we could not show any clear-cut effect of the intervention when performing a multiple linear regression. Nevertheless, although the intervention has not been economically evaluated, tailored nurse counselling on skin protection and skin care based on the everyday risks and resources of the patient can be recommended as an essential part of hand eczema treatment.

Acknowledgements

The Dermatology Clinic (Henrik Sølvsten, Hans B. Lomholt, Anne T. Funding, and Grete Laurberg), Aalborg and the Department of Dermato-Allergology, Copenhagen University Hospital, Gentofte are gratefully acknowledged. We thank the nurses Gitte Harboe, Nina Jørgensen, Anne Marie Topp and Vivi Just for their participation in developing the Healthy Skin Clinic intervention, and as members of the intervention team during the trial. Lene Theil Skovgaard, associate professor at the University of Copenhagen, is acknowledged for valuable statistical assistance. Swen Malte John, Britta Wulfhorst and colleagues at the Department of Dermatology, Environmental Medicine and Health Theory, University of Osnabrück, Germany are acknowledged for inspiration in the development of the intervention. The study was funded by Trygfonden, Denmark. Financial support was also received from Aage Bang's Foundation.

References

- 1 Thyssen J P, Johansen J D, Linneberg A, Menné T. The epidemiology of hand eczema in the general population – prevalence and main findings. *Contact Dermatitis* 2010; **62**: 75–87.
- 2 Hald M, Berg N D, Elberling J, Johansen J D. Medical consultations in relation to severity of hand eczema in the general population. *Br J Dermatol* 2008; **158**: 773–777.
- 3 Menné T, Johansen J D, Sommerlund M, Veien N K. Hand eczema guidelines based on the Danish guidelines for the diagnosis and treatment of hand eczema. *Contact Dermatitis* 2011; **65**: 3–12.
- 4 Coenraads P J. Hand eczema. *N Engl J Med* 2012; **367**: 1829–1837.
- 5 Veien N K, Hattel T, Laurberg G. Hand eczema: causes, course, and prognosis I. *Contact Dermatitis* 2008; **58**: 330–334.
- 6 Mollerup A, Johansen J D, Thing L F. Knowledge, attitudes and behaviour in everyday life with chronic hand eczema: a qualitative study. *Br J Dermatol* 2013; **169**: 1056–1065.
- 7 Bregnhøj A, Menné T, Johansen J D, Søsted H. Prevention of hand eczema among Danish hairdressing apprentices: an intervention study. *Occup Environ Med* 2012; **69**: 310–316.
- 8 Ibler K S, Jemec G B, Diepgen T L et al. Skin care education and individual counselling versus treatment as usual in healthcare workers with hand eczema: randomised clinical trial. *BMJ* 2012; **345**: e7822.
- 9 Wilke A, Gediga G, Schlesinger T, John S M, Wulfhorst B. Sustainability of interdisciplinary secondary prevention in patients with occupational hand eczema: a 5-year follow-up survey. *Contact Dermatitis* 2012; **67**: 208–216.
- 10 Hald M, Agner T, Blands J et al. Clinical severity and prognosis of hand eczema. *Br J Dermatol* 2009; **160**: 1229–1236.
- 11 Hald M, Agner T, Blands J, Johansen J D. Delay in medical attention to hand eczema: a follow-up study. *Br J Dermatol* 2009; **161**: 1294–1300.
- 12 van Gils R F, Boot C R, Knol D L et al. The effectiveness of integrated care for patients with hand eczema: results of a randomized, controlled trial. *Contact Dermatitis* 2012; **66**: 197–204.
- 13 van Gils R F, Bosmans J E, Boot C R et al. Economic evaluation of an integrated care programme for patients with hand dermatitis. *Contact Dermatitis* 2013; **69**: 144–152.
- 14 Wulfhorst B, Bock M, Skudlik C, Wigger-Alberti W, John S M. Prevention of hand eczema: gloves, barrier creams and

- workers' education. In: *Contact Dermatitis*, 5th edition, Johansen J D, Frosch P, Lepoittevin J-P (eds): Berlin, Heidelberg, Springer-Verlag, 2011: pp. 985–1016.
- 15 Skudlik C, Weisshaar E, Scheidt R et al. First results from the multicentre study rehabilitation of occupational skin diseases – optimization and quality assurance of inpatient management (ROQ). *Contact Dermatitis* 2012; **66**: 140–147.
 - 16 Diepgen T L, Agner T, Aberer W et al. Management of chronic hand eczema. *Contact Dermatitis* 2007; **57**: 203–210.
 - 17 Mollerup A, Veien N K, Johansen J D. An analysis of sex differences in patients with hand eczema – everyday exposures, severity and consequences. *Contact Dermatitis* 2014; doi: 10.1111/cod.12206 (Epub ahead of print).
 - 18 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.
 - 19 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.
 - 20 Basra M K, Fenech R, Gatt R M, Salek M S, Finlay A Y. The Dermatology Life Quality Index 1994–2007: a comprehensive review of validation data and clinical results. *Br J Dermatol* 2008; **159**: 997–1035.
 - 21 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.
 - 22 Jacobsen R, Moldrup C, Christrup L, Sjøgren P, Hansen O B. The Danish version of the Medication Adherence Report Scale: preliminary validation in cancer pain patients. *Pain Pract* 2009; **9**: 1–7.
 - 23 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.
 - 24 Agner T, Held E. Skin protection programmes. *Contact Dermatitis* 2002; **47**: 253–256.
 - 25 DSS Research – Knowledge Center 2013. Available at: <https://www.dssresearch.com/knowledgecenter/toolkitcalculators/samplecalculators.aspx>.
 - 26 Haynes R B, Ackloo E, Sahota N, McDonald H P, Yao X. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 2008(); CD000011.
 - 27 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*: Newcastle, University of Newcastle, Centre for Health Sciences Research, 2004.
 - 28 Kirkwood B R, Sterne J A C. *Medical Statistics*, 2nd edition: Oxford, Blackwell Science Ltd, 2003.
 - 29 Ibler K S, Jemec G B, Agner T. Exposures related to hand eczema: a study of healthcare workers. *Contact Dermatitis* 2012; **66**: 247–253.
 - 30 Meding B, Lindahl G, Alderling M, Wrangsjö K, Anveden B I. Is skin exposure to water mainly occupational or nonoccupational? A population-based study. *Br J Dermatol* 2013; **168**: 1281–1286.
 - 31 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.
 - 32 Hodari K T, Nanton J R, Carroll C L, Feldman S R, Balkrishnan R. Adherence in dermatology: a review of the last 20 years. *J Dermatol Treat* 2006; **17**: 136–142.
 - 33 Carroll C L, Feldman S R, Camacho F T, Manuel J C, Balkrishnan R. Adherence to topical therapy decreases during the course of an 8-week psoriasis clinical trial: commonly used methods of measuring adherence to topical therapy overestimate actual use. *J Am Acad Dermatol* 2004; **51**: 212–216.
 - 34 Feldman S R, Horn E J, Balkrishnan R et al. Psoriasis: improving adherence to topical therapy. *J Am Acad Dermatol* 2008; **59**: 1009–1016.
 - 35 Campbell N C, Murray E, Darbyshire J et al. Designing and evaluating complex interventions to improve health care. *BMJ* 2007; **334**: 455–459.
 - 36 Upshur R E, VanDenKerkhof E G, Goel V. Meaning and measurement: an inclusive model of evidence in health care. *J Eval Clin Pract* 2001; **7**: 91–96.