

A long-term follow-up study of the Hand Eczema Trial (HET): a randomized clinical trial of a secondary preventive programme introduced to Danish healthcare workers

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Summary

Background. Preventive skin care programmes have shown beneficial effects on the prevalence and severity of hand eczema, but most trials only report short-term outcomes. One such trial was the randomized Hand Eczema Trial (HET, 2009) investigating the effects of a secondary prevention programme in healthcare workers. Positive results have been reported at 5-month follow-up.

Objectives. To examine the long-term (42–47 months) effects of the HET.

Methods. The present study was a follow-up questionnaire study on the effect of the intervention. Outcomes were the presence and severity of hand eczema, health-related quality of life (HR-QoL), skin protective behaviour, and knowledge of skin protection. A supplementary outcome was general improvement/worsening of hand eczema.

Results. Comparison of the outcomes at follow-up showed no marked differences between the two groups. General improvement was reported by 70% in the intervention group and by 54% in the control group ($p = 0.25$). A small, statistically significant improvement was found regarding HR-QoL in the intervention group only ($p = 0.015$).

Conclusions. The impact of an intervention that is effective after 5 months is attenuated over time, with no long-term effect on the outcomes examined. We suggest that skin care education should be repeated at regular intervals.

Key words: hand dermatitis; hand eczema; long-term follow-up; occupational hand dermatitis; occupational skin disease; prevention programme; randomized clinical trial; secondary prevention programme.

Hand eczema (HE) is the predominant occupational skin disease in many European countries (1). In Denmark, it accounts for approximately one-third of all notified work-related diseases (2). The impact of HE includes loss

of productivity and high socio-economic costs for society (3, 4). Individual patients experience both impaired health-related quality of life (HR-QoL) and cumulative life course impairment (5–7). The prognosis is variable. One study reported remission of occupational HE in 40% of patients after 7–14 years (8), whereas ongoing occupational HE was reported in > 70% after 12 years by another study (9). In principle, these studies both agree with the general international finding that HE often has a chronic course (10–13).

Recently, it was reported that healthcare workers (HCWs) accounted for 26% of the recognized cases of

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occupational contact dermatitis in Denmark (14). HCWs have an increased risk of developing irritant HE, owing to repeated exposure to irritants such as water and detergents, and occlusion resulting from the use of protective gloves. They also have an increased risk of developing allergic HE, due to exposure to allergens such as rubber additives (from rubber gloves), biocides, and other relevant allergens (15, 16). The prevalence of HE in HCWs in Denmark was recently reported to be 21%, which is comparable to the 12–55% range found in other countries (17–21).

Primary, secondary and tertiary preventive programmes have been designed to reduce the prevalence and severity of HE (22). In a recent systematic review, moderate evidence for the effectiveness of prevention programmes was found, but long-term results on the effects of prevention programmes remain limited (23).

The Hand Eczema Trial (HET) from 2009 was a randomized, observer-blinded trial investigating the effects of a secondary prevention programme in Danish HCWs with HE, and clearly showed the positive effect of intervention at follow-up after 5 months regarding severity of HE, HR-QoL, and skin protective behaviour (24). The aim of the present study was to evaluate the effect of the intervention after 42–47 months.

Materials and Methods

Hand Eczema Trial

The HET was initiated in 2009 as a randomized clinical trial measuring the effects of a secondary preventive HE programme among 255 HCWs with HE. The HET cohort was recruited from a survey exploring the prevalence of HE and risk factors associated with the development of HE among HCWs employed at three Danish hospitals ($n = 3181$) (24). The HET cohort was randomized into an intervention group ($n = 123$) and a control group ($n = 132$), with stratification being performed according to hospital, profession and disease severity measured by use of the Hand Eczema Severity Index (HECSI) score (25). The intervention consisted of a single consultation (duration of 20–30 min) with a trained dermatologist who educated the participants individually in skin protective behaviour, and afforded individual counselling based on work and home-related exposures, and allergy, which had been diagnosed by the use of patch tests and prick tests. The primary outcome of the HET was defined as the difference in HECSI score between entry and follow-up. The secondary outcomes were the differences in HR-QoL, assessed by use of the Dermatology Life Quality Index (DLQI), self-reported disease severity (by use of a validated photographic guide), skin protective behaviour

(measured by numbers of daily hand washings and hand disinfections, use of protective gloves at work, and use of moisturizers at work and at home), and knowledge of skin protection at entry as compared with follow-up. The follow-up time was 5 months. The trial ended in December 2010. No intervention was given to the control group, and both groups received 'treatment as usual', defined as the standard practice for general practitioners in Denmark according to the national guidelines from the Danish Health Authority.

Long-term follow-up

In January 2014, an electronic follow-up questionnaire was distributed by email to the HET cohort ($n = 255$). Those who had not responded within 2 weeks received a second copy of the questionnaire by email, and those who had not responded within 3 weeks received a paper version of the questionnaire at their home address. The questionnaire was a short version of the HET questionnaire, which, in turn, was a modified version of the previously validated Nordic Occupational Skin Questionnaire (NOSQ 2002, long version) (26). It contained items measuring the following outcomes: self-reported prevalence and severity of HE, HR-QoL, skin protective behaviour, and knowledge of HE and skin care. The follow-up time varied from 42 to 47 months, owing to differences in the time of enrolment in the HET.

Outcome assessment

The following outcomes were considered:

- (1) The prevalence of HE was assessed according to the proportion providing an affirmative answer to the question 'Have you had hand eczema since the end of HET in 2010'.
- (2) The self-reported severity of HE was measured by use of a validated photographic guide (the same as that used in the HET) presenting four different clinical severity levels (mild = 1, moderate = 2, severe = 3, very severe = 4) of HE (27).
- (3) The DLQI was applied to assess quality of life in the past 7 days. The DLQI ranges from 0 (no impact on quality of life) to 30 (highest negative impact on quality of life).
- (4) Knowledge of HE was measured by use of a multiple-choice test consisting of four questions regarding the aetiology of HE, skin protective behaviour, risk factors regarding the development of HE, and treatment of HE. The same questions were used in the HET.

Concerning behavioural outcomes, the following items were addressed:

- (1) Work-related skin protective behaviour was assessed by measuring the self-reported numbers of daily instances of hand disinfections, hand washes, and applications of moisturizer, as well as daily wearing (in hours) of protective gloves at work.
- (2) Home-related skin protective behaviour was measured according to the self-reported numbers of daily hand washes and moisturizer applications after work.

Statistical analyses

For descriptive analyses of the cohort, non-parametric statistics were used, and χ^2 tests were used to analyse associations between outcomes and the groups. Paired samples *t*-tests within the groups were used to analyse differences in outcomes from $t=0$ months to the mean follow-up time, 45 months, and the difference between the groups at long-term follow-up was analysed with an independent samples *t*-test. All analyses were carried out with IBM SPSS (SPSS, Armonk, NY, USA) (release 20).

Results

The overall response at follow-up was 72% ($n=184$); 85% (105/122) in the intervention group, and 60% (79/132) in the control group. Table 1 shows the demographic data of the participants at follow-up. No differences between the intervention group and the control group were found with respect to sex distribution, age, or present/previous atopic eczema.

Eruptions of HE during the last 30 months – since the end of the HET – were reported by 78% of participants in the intervention group and by 80% of those in the control group ($p=0.25$). Table 2 shows the change in outcomes from $t=0$ months to the mean follow-up time of 45 months. Both the intervention group and the control group improved statistically significantly in self-reported severity as measured by use of the photographic guide, with small differences of 0.44 and 0.30 points, respectively (intervention group, $p<0.01$; control group, $p=0.004$) (paired samples *t*-test). The intervention group also showed a statistically significant improvement in the DLQI score, with a difference of 0.781 DLQI points ($p=0.015$), whereas the control group did not ($p=0.23$). No statistically significant change was found with respect to knowledge of HE ($p=0.87$, intervention group; $p=0.36$, control group).

Table 1. Demographic data

Demographic factors	Intervention group, $n=105$	Control group, $n=79$	p -value
Male	5	9	–
Female	100	70	–
Age (years), mean (SD)	45 (9.6)	45 (9.5)	0.50
Atopy*, no. (%)	27 (26)	28 (35)	0.27

SD, standard deviation.

*Atopy was defined according to the UK Working Party's Diagnostic Criteria for Atopic Dermatitis.

With regard to skin protective measures at work (numbers of disinfections, hand washes, and moisturizer applications, and hours using protective gloves) and at home (number of hand washes and number of moisturizer applications), no differences were seen within or between the two groups at long-term follow-up (Table 3).

The participants were asked to report whether, in general, they experienced improvement, worsening or no change of their HE since their participation in the HET. General improvement was reported by 70% (74/105) of the intervention group and by 54% (43/79) of the control group ($p=0.25$). Furthermore, the participants were asked whether they had consulted their private practitioner or dermatologist because of HE since the HET. This was reported by 12% of the intervention group and by 14% of the control group ($p=0.88$). Only 1 participant (from the control group) reported having sick leave from work since the HET.

Discussion

The present long-term follow-up study of a secondary prevention programme in HCWs with HE found no significant differences between the intervention group and the control group at a mean follow-up of 45 months with respect to self-reported severity, HR-QoL, skin protective behaviour, or knowledge of HE prevention. The study indicates that the effect of an intervention shown to be effective after 5 months decreases over time. An overall statistically significant improvement in self-reported severity of HE was seen in both the intervention group and the control group. This was self-reported and assessed by use of a photographic guide intended to measure the severity 'in general' at the time of follow-up.

In the intervention group, the DLQI showed a statistically significant improvement, suggesting a positive long-term effect of the intervention. However, the difference in the DLQI was small (0.78 DLQI points) and below the minimal clinically important difference for the DLQI

Table 2. Change in outcomes from $t = 0$ months to a mean follow-up time of 45 months (42–47 months) (paired sample t -test and independent samples t -test as appropriate)

	Intervention group			Control group			Difference between groups	
	$t = 0$	$t = 45$	p-value	$t = 0$	$t = 35$	p-value	$t = 35$	p-value, two-tailed
	months	months		months	months		months (95%CI)	
Photographic guide (range 0–4)	1.74	1.30	0.440 (0.287–0.593)	1.67	1.37	0.300 (0.100–0.500)	0.08 (–0.274 to 0.114)	0.42
DLQI (range 0–10)	2.83	2.05	0.781 (0.153–1.509)	2.92	2.37	0.547 (–0.354 to 1.448)	–2.294 (–1.139 to 0.550)	0.49
Knowledge (range 0–10)	9.50	9.52	–0.019 (–0.264 to 0.225)	9.55	9.44	0.115 (–0.134 to 0.364)	0.093 (–0.160 to 0.347)	0.47

CI, confidence interval; DLQI, Dermatology Life Quality Index.

Table 3. Behavioural outcomes at a mean follow-up time of 45 months (42–47 months)

	Intervention group, n = 105	Control group, n = 79
Work-related outcomes		
Disinfections: mean number per day at work (median)	15–20 (> 20)	15–20 (> 20)
Hand washes: mean number per day (median)	6–10 (6–10)	6–10 (6–10)
Moisturizer: mean number per day at work (median)	1–2 (1–2)	1–2 (1–2)
Protective gloves: mean hours per day at work (median)	0.5–2 (0.5–2)	0.5–2 (0.5–2)
Home-related outcomes		
Hand washes: mean number per day (median)	6–10 (6–10)	6–10 (6–10)
Moisturizer: mean number per day (median)	1–2 (1–2)	1–2 (1–2)

(28). The continued positive effects on the DLQI and the significant improvement in self-reported severity of HE in both groups may be interpreted as reflecting an increased focus on skin care and prevention after participation in the HET. They may also be explained by the Hawthorne effect, that is, a change in behaviour resulting from awareness of being observed as a part of a study (29). Unfortunately, the follow-up study did not include a HECSI score of the participants, which may have been a more sensitive tool for identifying differences in severity between the two groups.

The level of knowledge of HE was high at the start of the HET in both groups, and did not improve further in either group. This may imply that the questions used to evaluate knowledge were not adequate to elucidate differences. The preventive measures at work did not change in either of the groups. Both groups reported the same ranges of numbers of hand washes (6–10 per day), hand disinfections (15–20 times per day) and applications of moisturizers (1–2 times per day) at work. The numbers of hand washes and hand disinfections may reflect the lowest possible measures required to conform with the hygiene standards in hospital settings, or the inherent conflict between skin protective measures and the general hygiene measures required by the job.

Behavioural habits and exposures are important factors in patients with HE. Long-term changes in detrimental habits may be difficult after just one educational session. This was shown in patients with cutaneous melanoma. In the first year after receiving the diagnosis of cutaneous malignant melanoma, the patients reduced their sun exposure significantly, according to

the advice given to them. However, after 3 years, they increased their sun exposure again to higher levels than their matched and healthy controls (30, 31). Therefore, repeated information/education is necessary to remind the patients of the importance of behavioural changes.

Other RCTs have evaluated the effects of secondary prevention in patients with HE, although often not on a long-term basis (32–34). Two German studies evaluated the long-term effects of a secondary interdisciplinary prevention programme in geriatric nurses (6 years of follow-up) and hairdressers (5 and 10 years of follow-up) (35, 36). In both studies, the interventions were more complex than those in the HET, in that they comprised four visits during a period of 6 months, including dermatological and health educational interventions (arranged individually or in seminars) and, for the hairdressers, also a work consultation (36). The outcomes were self-reported, and focused on job continuation (35, 36) and skin changes (35). In the study of geriatric nurses, the outcomes indicated long-term effects of the intervention; however, only a few results showed statistical significance. For hairdressers, there was a higher rate of participants in the intervention group remaining at work after 5 years, and, after 10 years, a stabilization of the effects was found (36).

The strength of this study is that it provides long-term follow-up data on a randomized intervention study. Similar publications are quite rare, in spite of their obvious importance for the evaluation of existing, or the planning of future, intervention programmes. The overall response was 72.9%, and the participation was higher in the intervention group than in the control group (85% versus 60%). However, the absolute numbers were low, with a total of 255 respondents.

It would have further strengthened the study if participants had been re-examined clinically and a HECSI score had been provided. Due to logistical and practical circumstances, this was not possible, but the same validated questions regarding the severity and presence of HE were used, and a similar approach has been used in the few other long-term follow-up studies available.

Conclusion

The present study indicates that the long-term effect of secondary prevention of HE in HCWs is limited. Documented positive effects found after 5 months decrease over time, and are not significant after a mean follow-up time of 45 months (range 42–47 months). As HE is a chronic disease, our data strongly suggest the need to provide repeated information and education to patients with HE.

References

- Diepgen T L. Occupational skin-disease data in Europe. *Int Arch Occup Environ Health* 2003; **76**: 331–338.
- The National Board of Industrial Injuries in Denmark. Available at: www.ask.dk
- Diepgen T L, Scheidt R, Weisshaar E et al. Cost of illness from occupational hand eczema in Germany. *Contact Dermatitis* 2013; **69**: 99–106.
- Mascaro J M, Querol I, Lindner L et al. Costs of patients with occupational severe chronic hand eczema refractory to topical corticosteroids for employer's mutual insurance companies in Spain. *Value Health* 2009; **12**: A453–A454.
- 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.
- Cvetkovski R, Zachariae R, Jensen H et al. Quality of life and depression in a population of occupational hand eczema patients. *Contact Dermatitis* 2006; **54**: 106–111.
- Ibler K S, Jemec G B. Cumulative life course impairment in other chronic or recurrent dermatologic diseases. *Curr Probl Dermatol* 2013; **44**: 130–136.
- Mäliköinen T, Alanko K, Jolanki R et al. Long-term follow-up study of occupational hand eczema. *Br J Dermatol* 2010; **163**: 999–1006.
- Meding B, Lantto R, Lindahl G et al. Occupational skin disease in Sweden – a 12-year follow-up. *Contact Dermatitis* 2005; **53**: 308–313.
- Nethercott J R, Holness D L. Disease outcome in workers with occupational skin disease. *J Am Acad Dermatol* 1994; **30**: 569–574.
- Susitaival P, Hannuksela M. The 12-year prognosis of hand dermatosis in 896 Finnish farmers. *Contact Dermatitis* 1995; **32**: 233–237.
- Chia S E, Goh C L. Prognosis of occupational dermatitis in Singapore workers. *Am J Contact Dermat* 1991; **2**: 105–109.
- Gooskens V H, Nater J P, Coenraads P J. Skin diseases and working disability in the Netherlands. II. Catamnestic study in 3 groups of patients with occupational contact eczema. *Berufsdermatosen* 1977; **25**: 163–173.
- Carøe T, Ebbeløj N, Agner T A. Survey of exposures related to recognized occupational contact dermatitis in Denmark in 2010. *Contact Dermatitis* 2014; **70**: 56–62.
- Clayton T H, Wilkinson S M. Contact dermatoses in healthcare workers: reduction in type I latex allergy in a UK centre. *Clin Exp Dermatol* 2005; **30**: 221–225.
- Nettis E, Colanardi M C, Soccio A L et al. Occupational irritant and allergic contact dermatitis among healthcare workers. *Contact Dermatitis* 2002; **46**: 101–107.
- Ibler K I, Jemec G B, Flyvholm M A et al. Hand eczema: prevalence and risk factors of hand eczema in a population of 2274 healthcare workers. *Contact Dermatitis* 2012; **67**: 200–207.
- Lampel H P, Patel N, Boyse K et al. Prevalence of hand dermatitis in inpatient nurses at a United States hospital. *Dermatitis* 2007; **18**: 140–142.
- Lan C C, Feng W W, Lu Y W et al. Hand eczema among university hospital nursing staff: identification of high-risk

- sector and impact on quality of life. *Contact Dermatitis* 2008; **59**: 301–306.
- 20 Stutz N, Becker D, Jappe U et al. Nurses' perceptions of the benefits and adverse effects of hand disinfection: alcohol-based hand rubs vs. hygienic hand washing: a multicentre questionnaire study with additional patch testing by the German Contact Dermatitis Research Group. *Br J Dermatol* 2009; **160**: 565–572.
 - 21 Smith D R, Adachi Y, Mihashi M et al. Hand dermatitis risk factors among clinical nurses in Japan. *Clin Nurs Res* 2006; **15**: 197–208.
 - 22 Seyfarth F, Schliemann S, Antonov D, Elsner P. Teaching interventions in contact dermatitis. *Dermatitis* 2011; **22**: 8–15.
 - 23 van Gils R F, Boot C R, van Gils P F et al. Effectiveness of prevention programmes for hand dermatitis: a systematic review of the literature. *Contact Dermatitis* 2011; **64**: 63–72.
 - 24 Ibler K I, Jemec G B, Diepgen T L et al. Skin care education and individual counseling versus treatment as usual in healthcare workers with hand eczema: a randomized clinical trial. *BMJ* 2012; **345**: e7822.
 - 25 Held E, Skoet R, Johansen J D, Agner T. The hand eczema severity index (HECSI): a scoring system for clinical assessment of hand eczema. *Br J Dermatol* 2005; **152**: 302–307.
 - 26 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.
 - 27 Coenraads P J, van der Walle H, Thestrup-Pedersen K et al. Construction and validation of a photographic guide for assessing severity of chronic hand dermatitis. *Br J Dermatol* 2005; **152**: 296–301.
 - 28 Basra M K, Salek M S, Camilleri L et al. Determining the minimal clinically important difference and responsiveness of the Dermatology Life Quality Index (DLQI): further data. *Dermatology* 2015; **230**: 27–33.
 - 29 Hagel S, Reischke J, Kesselmeier M et al. Quantifying the Hawthorne effect in hand hygiene compliance through comparing direct observation with automated hand hygiene monitoring. *Infect Control Hosp Epidemiol* 2015; **36**: 957–962.
 - 30 Idorn L W, Datta P, Heydenreich J et al. A 3-year follow-up of sun behavior in patients with cutaneous malignant melanoma. *JAMA Dermatol* 2014; **150**: 163–168.
 - 31 Idorn L W, Datta P, Heydenreich J et al. Sun behavior after cutaneous malignant melanoma: a study based on ultraviolet radiation measurements and sun diary data. *Br J Dermatol* 2013; **168**: 367–373.
 - 32 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.
 - 33 van Gils R F, Boot C R L, 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.
 - 34 Schürer N Y, Klippel U, Schwanitz H J. Secondary individual prevention of hand dermatitis in geriatric nurses. *Int Arch Occup Environ Health* 2005; **78**: 149–157.
 - 35 Wilke A, Gediga K, Weinhöppel U et al. Long-term effectiveness of secondary prevention in geriatric nurses with occupational hand eczema: the challenge of a controlled study design. *Contact Dermatitis* 2012; **66**: 79–86.
 - 36 Wulffhorst B, Bock M, Gediga G et al. Sustainability of an interdisciplinary secondary prevention program for hairdressers. *Int Arch Occup Environ Health* 2010; **83**: 165–171.