Occupational hand eczema

- a survey and identification of prognostic risk factors

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Study II Cvetkovski RS, Rothman KJ, Olsen J, Mathiesen B, Iversen L, Johansen JD, Agner T. Relation between diagnoses on severity, sick leave and loss of job among patients with occupational hand eczema. British Journal of Dermatology 2005. 152: 93-8.

Study III Cvetkovski RS, Jensen H, Olsen J, Johansen JD, Agner T. Relation between patients and physicians severity assessment of occupational hand eczema. British Journal of Dermatology. In press.

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Preface

This thesis is based on dermato-epidemiological studies performed at the Department of Dermatology, Gentofte Hospital, University of Copenhagen, Denmark and the Department of Epidemiology and Preventive Medicine, Boston Medical Centre, Boston, MA, USA during the period from 2001-2005.

The studies comprise extensive work; too much for one person alone. Thus, I am very grateful to all my co-workers: Tove, Jørn, Jeanne, Bobby, Bent and Lars, and their fruitful discussions and comments on the results. I owe special thanks to Henrik Jensen for data management and statistical advice and sincere thanks to Professor Kenneth Jay Rothman, Department of Epidemiology and Preventive Medicine, Boston Medical Centre, Boston, MA, USA for inviting me to visit Boston as a fellow resident. Moreover I am very grateful for Tove Agner's never ending confidence and belief in my research skills and for giving me the opportunity to work closely with her through the years. I also thank Professor Torkil Menné for always having his door open to me ready to discuss results from my study. The value of Torkil's immense clinical and experimental knowledge in the field of contact dermatitis is priceless. I thank Elisabeth Held for reading this manuscript and for providing good comments and discussions on our mutual field of interest, hand eczema. I also thank Tonny Karlsmark for giving me the opportunity to finish the last studies on time. Last, but not least I wish to thank my husband Nikola, my family and friends for their endless support when times were tough.

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Rikke Skøt Cvetkovski
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List of abbreviations

ACD = allergic contact dermatitis
AD = atopic dermatitis
BDI-II = Beck Depression Inventory
CI = confidence interval
CU = contact urticaria
DLQI = Dermatology Life Quality Index
DNBII = Danish National Board of Industrial Injuries
ICD = irritant contact dermatitis
NOACD = non-occupational allergic contact dermatitis
NPV = negative predictive value
OHE = occupational hand eczema
POR = posterior odds ratio
PP = prevalence proportion
PPV = positive predictive value
PR = prevalence ratio
RR = risk ratio
SD = standard deviation
SES = socioeconomic status
SF-36 = Short Form 36
ROC = receiver operating characteristics
VAS = visual analogue scale

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1. Introduction

Despite governmental attempts to reduce exposure to harmful occupational allergens, the number of new occupational hand eczema (OHE) cases in Denmark has remained almost unchanged since the mid-1990s [1]. Complications and consequences of occupational contact dermatitis include chronic severe eczema, prolonged sick leave and unemployment [2-7]. To reduce the number of new OHE cases in the future, it is important that detailed information is available about high-risk factors and occupations so that preventive actions can be targeted in the most cost-effective direction.

2. Background

Incidence of occupational hand eczema

Occupational hand eczema (OHE) is the most frequently recognised occupational disease in Denmark, with an incidence rate of approximately 30.6 per 100.000 workers in 2002 [1]. The Danish rate is slightly higher than the rate reported from the UK in 2000, which was 12.9 per 100.000 workers [8] and also higher than the recently reported Australian incidence rate of 20.5 per 100.000 workers [9] but lower than that reported in 1999 from the USA (46 per 100.000 workers) [10] and Germany from 2001 (68 per 100.000 workers) [11]. National registries are, however, not directly comparable, due to differences in the sample population, definitions of diagnosis, clinical examination and differences in notification procedures [2;8;12;13].

Diagnoses

The most common type of OHE is irritant contact dermatitis (ICD), followed by allergic contact dermatitis (ACD) and contact urticaria (CU) [13]. It is not possible to differentiate between the different types of OHE by clinical patterns [14-16]. Although a clinical presentation with vesicles may indicate ACD, and a dry and scaly appearance may lead to the suspicion of ICD, these clinical signs may be misleading and patch testing is an essential part of the investigation of OHE. Previous studies have not identified any strong prognostic predictors of a poor prognosis of hand eczema according to diagnoses, although the presence of atopic dermatitis (AD) [17-20] or ACD [4;20-22] has been related to a more severe outcome.
Conversely some studies report that ACD has a favourable prognosis compared with irritant contact dermatitis (ICD) [23;24] and others do not find any significant difference between different diagnoses [18].

Disease duration and severity

Hand eczema has been reported to be a long-lasting disease and a recent Swedish study reported that 66% of 868 hand eczema patients after 15 years of follow-up still have periodical hand eczema [25]. Other studies report ongoing symptoms from 33% to 82% after 1-8 years of follow-up but comparison across studies is difficult due to different study designs and different lenghts of follow-up [5;18;23;26]. Overall improvement of hand eczema was found to be between 70% to 78% [5;18;23;26] although a small study of patients with ACD from epoxy resin reported an overall improvement of 100% during 2 years of follow-up [27].

Age and sex

OHE may occur at any age, but peaks among young female workers [11-13] and is thereby different from other conventional occupational disorders such as low back pain, where the age of onset is relatively higher and with a more equal distribution between sexes [28]. The sex difference in the prevalence of hand eczema is generally thought to be caused by different exposures rather than an increased susceptibility of female skin. Women are traditionally more exposed to wet work than men and many jobs involving extensive wet work, e.g. hairdressing, health care, catering and cleaning are predominantly occupied by women. Generally, women report more frequent hand washing per day compared with men [29;30], and the extent of domestic irritant skin exposure such as cooking and child care still exceeds the extent of male exposure. No sex-related difference in skin susceptibility to irritants has been reported from experimental studies [31] and a recent population-based twin study confirmed that sex was not an independent risk factor of hand eczema [32]. The prognosis of OHE has been reported to be worse for older age groups [23] but contradictory findings have been published [20;21;26].

Socioeconomic status

Poor socioeconomic status has been shown to affect outcome adversely in many chronic disorders [33-40] but valid data are lacking for OHE patients. A Swedish study of 3500 dentists, with a response rate of 88%, suggests that these patients with high socioeconomic status have a favourable prognosis [41] . The study, however, included only dentists and no control group, which makes it difficult to draw any strong conclusions.

Affiliation to the labour market

It has been well documented that hand eczema causes prolonged sick leave. The median total sick leave due to hand eczema of 868 hand eczema patients during 15 years of follow-up in a prospective Swedish study by Meding et al. was 38 weeks [25]. In Australia, a retrospective study of 583 OHE cases reported that 61% had taken sick leave due to OHE and 6.5% had taken sick leave longer than 12 months continuously during follow-up time, which was between 6 months and 8 years [5]. In USA, a survey from 1993 showed that 14% of all registered cases resulted in more than 10 days sick leave and 6% in more than 20 days during one year [2]. Predictors of prolonged sick leave are limited but AD, ACD, age above 45 years and time of exposure have been suggested [4;42;43]. Data concerning unemployment are limited but an English study reported that 7% of all cases were unemployed due to their OHE after one year of follow-up [4].

Quality of life (QoL)

Some studies have indicated that OHE has impact on QoL, but the studies are few and relatively small [22;23;44-49]. Women appear in several studies to be more impaired [3;23] but contradictory findings have been published [46;47]. A 15-year follow-up study of 868 hand eczema patients reported that 72% had impaired psychosocial functions [25] and an Australian study reported that 60% of men and 73% of women experienced OHE interfering with leisure activities, sexual activities and social life in general [5]. Patients with ACD have been reported to benefit from an early confirmed diagnosis by patch testing which has resulted in greater improvement of QoL [45;48-50].

Depression

Other studies have suggested that patients with contact dermatitis may experience depressive symptoms [51;52]. A Finnish study of monozygotic and dizygotic twins also suggests a modest association between AD and depressive symptoms [53]. It is possible that the presence of a depression may have serious implications for OHE patients, e.g. premature discontinuation of treatment, which may be part of the explanation why so many patients become chronic cases but valid data are currently not available.

3. Aims

1. To characterize OHE in Denmark with regard to prevalences among sex, age, diagnostic and subdiagnostic groups, socioeconomic status and various occupations.

2. To identify high-risk occupations.

3. To evaluate and compare the severity and consequences of OHE in different diagnostic and subdiagnostic groups at baseline.

4. To evaluate the relation between self-rated severity and severity assessment based on standardized medical certificates issued by dermatologists.

5. To estimate the extent of impairment of QoL among OHE patients at baseline and follow-up.

6. To determine the frequency and severity of depression among OHE patients in relation to demographic and disease-specific data.

7. To identify prognostic risk factors for OHE patients with regard to aggravated or persistently severe OHE, prolonged sick leave and loss of job after 12 months' follow-up.

4. Subjects and methods

Study definitions

Occupational hand eczema	An inflammatory skin response caused or aggravated by occupational exposure and located on the hands
Occupational allergic contact dermatitis	Documented contact dermatitis on the hands and a positive patch test result relevant to an occupational exposure.
Occupational irritant contact dermatitis	Documented contact dermatitis on the hands and relevant occupational exposure to irritant(s). Negative patch test result to occupational exposures.
Occupational contact urticaria	Documented contact dermatitis on the hands, relevant occupational exposure and/or positive skin prick test.
Non-occupational allergic contact dermatitis	A positive patch test result for a non-occupational exposure. Non-occupational contact allergy may be of present or past relevance.
Atopic dermatitis	Documented past or current flexural dermatitis or atopic dermatitis diagnosed by a dermatologist.
Disease duration	The time from onset of symptoms until recognition from the Danish National Board of Industrial Injuries
Prolonged sick leave	More than 5 weeks sick leave due to occupational hand eczema in the past 12 months

Study population and study design

The study was designed as a prospective cohort study with a one-year follow-up period. The study population was identified on a weekly basis from the Danish National Board of Industrial Injuries (DNBII) in the period October 2001 to November 2002 (58 weeks) and comprised all new cases of recognized OHE, who were 18 years old or above.

The Danish National Board of Industrial Injuries Registry

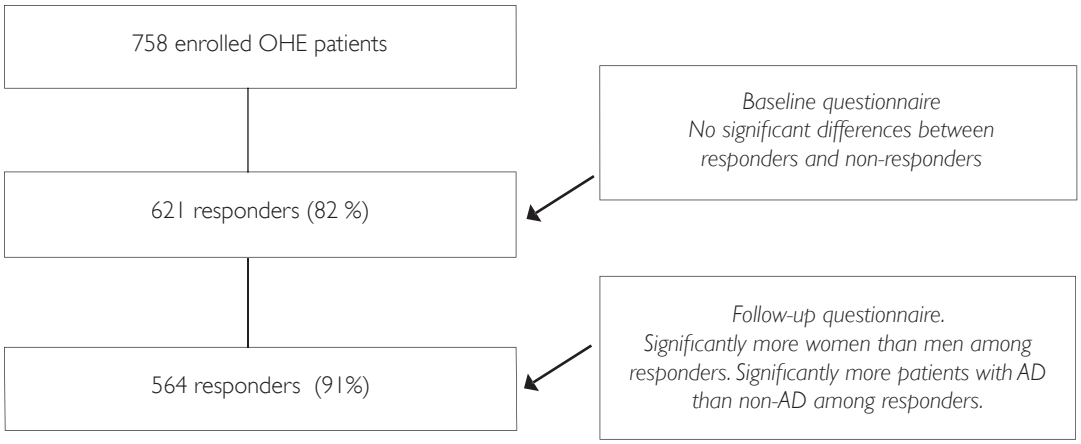
The registry comprises all notified and recognised cases of occupational diseases in Denmark. Danish physicians are legally obliged to notify the registry all suspected or known occupational diseases. Before recognition of a case with OHE, each notified case is examined by a dermatologist and a patch test performed. A case can be recognised with or without payment of economic compensation, which is paid only if a permanent injury persists. Compensation, in Denmark, is paid independently of the current work situation.
A reduction in earning capacity will lead to additional economic compensation. The registry provided demographic and disease-specific data for the study such as age, sex, diagnosis, subdiagnosis, occupation and DNBII-rated disease severity.

The questionnaire

To supplement the information from the DNBII registry we used a postal questionnaire. The questionnaire was administered by post 1-2 weeks after registration of a case in the DNBII. A reminder was posted after 2 weeks, and after an additional period of 2 weeks, non-responders received a reminder telephone call. The questionnaire comprised items with regard to disease duration, self-rated severity, current occupation, sick leave, job change, loss of job, a dermatology-specific QoL questionnaire (DLQI) and a standardized screening instrument of the presence or absence of depression (BDI-II). One year after the baseline questionnaire was returned, a similar follow-up questionnaire was posted to all responders.

Prior to the study, the questionnaire was evaluated and revised on the basis of structured interviews with hand eczema outpatients from the Department of Dermatology, Gentofte Hospital, and then re-evaluated in a test/re-test pilot study with 78 participants. In the pilot study, all items were considered to be relevant and easy to comprehend by the participants and the questionnaire was considered to be functioning well and to have satisfactory validity, reliability and response rate.

Flowchart



Classification of diagnoses

The classification was based on the clinical examination by a dermatologist of each patient. All patients were patch testet with the European Standard Series as a minimum and skin prick tested if considered relevant. Specific occupations or specific exposures were supplemented with additional tests with relevant allergens e.g. patch test series for hairdressers, bakers, dentists, rubber gloves etc [54] or skin prick test with latex (natural rubber gloves), food series (e.g. chefs, bakers). Patients were categorized into only one of five main diagnostic groups: (1) occupational ACD; (2) occupational ICD; (3) occupational CU; (4) occupational ACD + occupational ICD and (5) occupational ICD + occupational CU. All patients were also categorized into subdiagnostic groups by the presence or absence of AD and by the presence or absence of non-occupational allergic contact dermatitis (NOACD).

Socioeconomic status

Socioeconomic status (SES) was measured using the standardized socioeconomic classification system: Socio97, 1st edition 1997, which is a classification system based upon educational requirements and managerial responsibilities of the job. In the analysis we used 4 categories of SES as follows:
(1) high/medium level (2) basic level (3) lowest level (4) students/trainees.

Severity assessment

Severity assessment is needed for rutine clinical care, in research and when compensation in case of OHE is a concern. Ideally, dermatologists examine all diseased persons according to a standardised procedure model. Such models have recently become available [55;56]. Questionnaires with self-rated assessment of severity may be the only other option, but the validity needs to be defined and scrutinised. The presence of hand eczema may influence the life situation of the patient in different ways, depending on age, sex, socioeconomic status and mental health, and a strong correlation between self-rated and physician-rated severity of a disease is not given a priori [57].

Severity assessment was performed both by the DNBII and by the patients themselves in the questionnaire. Each recognised case of OHE was examined by a dermatologist, who issued a standardized medical certificate. The severity assessment in the DNBII registry was based on this medical certificate, which comprised information on morphology and extension of the eczema, as well as the frequency of eruptions. All patients were categorized into levels of severity by the DNBII based on the medical certificate (Table 1).

Table 1.
Severity assessment of OHE by the DNBII based on medical certificate from dermatologists.

Disease relapse	1-2 times/year	3-4 times/year	> 4 times/year
Intensity of skin response*			
No	1	2	3
Mild	4	5	6
Moderate	7	8	9
Severe	10	11	12

*At the time of severity assessment. Comprises: vesicles, fissures, oedema, erythema, hyperkeratosis, scaling.
1= no or minimal eczema, 2-7= mild- moderate eczema, 8-12= severe eczema. DNBII = Danish National Board of Industrial Injuries.

The DNBII severity assessment was considered as "gold standard" in study III. All participants were asked to grade severity of their OHE on a visual analogue scale (VAS) from 0-10. The exact wording of the question was:
How would you grade your occupational hand eczema on a scale from 0-10 during the past 12 months? Where 0 means no eczema and 10 means extremely severe eczema.

Occupations

Wet work is traditionally defined as "skin exposure to liquids longer than 2 hours per day, or use of occlusive gloves longer than 2 hours per day, or very frequent washing of the hands (> 20 times/day or fewer if cleaning procedure is more aggressive)" [58]. Wet occupations in this study comprised the following occupations: health-care workers, cleaners, hairdressers, dental surgery assistants, laboratory technicians and doctors, dentists and veterinarians.
Food-related occupations were defined as: bakers, kitchen workers/chefs and butchers.
Other occupations were defined as: factory workers, manual workers, machinists, construction workers, cashiers, carpenters, printers, office workers, other tradespeople (mixed group of different trade occupations, each with a prevalence below 3%) and mixed occupations.

Affiliation to the labour market

The participants were asked whether they had taken any sick leave due to their OHE during the past 12 months. If the answer was "yes", they were asked for how long, and then asked to summarize all episodes of sick leave into one of the following fixed answer categories: < 1 week, 1-2 weeks, 3-5 weeks or more than 5 weeks. The participants were also asked whether they had changed or lost their job during the past 12 months due to OHE.

Quality of Life and the Dermatology Life Quality Index (DLQI)

Since the mid-1990s it has generally become accepted that "objective improvement" is no longer sufficient to measure outcomes of the disease. For example, a recent UK parliamentary report recommends that the government should take properly assessed QoL fully into account in all health-policy developments [57;59] . A clinical trial, for example, should also quantify patient centred outcomes along with safety, adverse effects, and costs. Quality of life measures may be global (SF-36), dermatology specific (DLQI) or disease specific (Psoriasis disability Index) [60;61]. In Study IV and V we used the dermatology specific QoL questionnaire DLQI. The DLQI is a 10-item questionnaire measuring QoL in patients with skin disease [62]. The 10 items cover 6 aspects of daily life experienced during the past week: (i) symptoms and feelings (items 1, 2), (ii) daily activities (items 3, 4), (iii) leisure (items 5, 6), (iv) work and school (item 7), (v) personal relationships (items 8, 9) and (vi) treatment (item 10). Each item is assigned a score of 0 ("not at all") to 3 ("very much"). The DLQI total scores are calculated by summing the score of each question, resulting in a maximum of 30 and a minimum of 0. The higher the score the greater the impairment of QoL. In study IV and V we dicotomised the total DLQI score into high QoL (score 0-10) and low QoL (score 11-30) according to a previous report [57].

Beck Depression Inventory II

The BDI-II is a 21-item questionnaire measuring depressive symptoms during the past 2 weeks [64]. Each item is assigned a score of 0-3, with 3 indicating the most severe symptoms. A cumulative score is obtained by adding the scores of the individual items. The responders are classified as: (1) score 0-13 = minimal depression, (2) score 14-19 = mild depression, (3) score 20-28 = moderatedepression and (4) score 29-63 = severe depression. In study IV and V we dicotomised the BDI-II score into minimal to mild depressive symptoms (0-19) and moderate to severe depressive symptoms (20-63). Clustering of depressive symptoms was further examined using the specific somatic and cognitive-affective symptom dimensions described by Beck et al. [64]

5. Results and discussion

Basic demographics of the study population are shown in Table 2.

Table 2.
Basic demographics of the study population

Patients enrolled	758
Female/male ratio	1.8
Median age	34.0 years
Mean age	35.6 years
Median disease duration	2.0 years
Socioeconomic status*	
Students/trainees	135 (17.9%)
Employee high/medium level	93 (12.3%)
Employee basic level	329 (43.4%)
Employee lowest level	196 (25.9%)

*5 missing values

Study I

Estimation of prevalences and incidences

The distribution of the different diagnoses and subdiagnoses is given in Table 3. ICD was the most frequent diagnosis for both men (59.7%) and women (63.1%), which confirms earlier results of ICD as a major source of occupational contact dermatitis [65].
The prevalence of AD in this study was similar to that in the general population [66]:16.4%, but was considered low compared with previous studies of hand eczema patients [32;66] .

Table 3.
The distribution of OHE diagnoses and subdiagnoses by sex

Diagnosis	Men (%)	Women (%)	Total (%)
ICD	160 (59.7)	309 (63.1)	469 (61.9)
ACD	72 (26.9)	89 (18.2)	161 (21.2)
CU	9 (3.4)	27 (5.5)	36 (4.8)
ICD + ACD	20 (7.5)	51 (10.4)	71 (9.4)
ICD + CU	7 (2.6)	14 (2.9)	21 (2.8)
AD			
No	234 (87.3)	400 (81.6)	634 (83.6)
Yes	34 (12.7)	90 (18.4)	124 (16.4)
NOACD			
No	227 (84.7)	293 (59.8)	520 (68.6)
Yes	41 (15.3)	197 (40.2)	238 (31.4)

ICD = irritant contact dermatitis, ACD = allergic contact dermatitis, CU = contact urticaria, AD = atopic dermatitis, NOACD = non-occupational allergic contact dermatitis

High-risk occupations

The overall quantitatively dominant occupation in the study population was healthcare workers which comprised 21.4% of the entire study population. With respect to exposures, a marked difference between sexes was observed: 59% of all women were occupied in wet occupations compared with 8.5% of all men. It is, however, important to differentiate between the quantitatively dominant occupations and the relative risk of acquiring OHE in various occupations.

Table 4 shows the top 10 incidence rates across different occupations and a different picture emerges with food-related occupations (bakers) with the highest risk of OHE. The ranking of incidence rates, with hairdressers and food-related occupations in the top 5 list, are similar to those found in Saarland in Germany [11] and in a previous Danish study [13]. The incidence rates in food-related occupations are lower compared with previous Swedish findings [67] but slightly higher than incidence rates reported from an English study of a food manufacturing company [68]. The higher rates among food-handling occupations may be due to the extensive exposure to both food and water, and frequent hand washing. It may also be possible that the pick-up rates of skin conditions are higher in food-related occupations than for other industries since intact skin on exposed hands is a prerequisite for working in a food-handling capacity, which in part may explain the remarkably higher incidence rates.

Table 4.
The frequency and prevalence proportion of OHE according to occupation and estimated incidence rates per 1000 person-years

Occupation	N (%)	No. of employees in Denmark	Person-years (58 weeks)	Estimated rates (cases per 1000 person-years)
Bakers	34 (5.5)	3643	4063	8.37
Hairdressers	35 (5.6)	5591	6236	5.61
Dental surgery assistants	20 (3.2)	4290	4785	4.18
Kitchen workers/ chefs	70 (11.3)	19.213	21.430	3.27
Butchers	11 (1.8)	4682	5222	2.11
Health-care workers	133 (21.4)	174.950	195.131	0.68
Cleaners	50 (8.1)	77.774	86.747	0.58
Doctors,dentists, veterinarians	7 (1.3)	16.600	18.515	0.38
Carpenters	8 (1.3)	40.652	45.343	0.18
Cashiers	14 (2.3)	84.110	93.815	0.15

Allergens and irritants

Contact allergy (NOACD) in general was more frequent among women, while contact allergy with occupational relevance was more frequent among men. There were only minor differences in type of allergens between sexes.
The most frequent allergens for men were: rubber additives, chromate, nickel and epoxy, whereas for women it was, rubber additives, biocides, nickel and dyes/bleaching agents (Table 5), which is consistent with the results of a Finnish study [69]. Irritants showed considerable sex difference. The most frequent irritants for men were: oils and food while it was water/soap and gloves for women (Table 5). The group of patients with NOACD was comprised predominantly of women allergic to nickel.

Table 5.
Occupational allergic and irritant contact dermatitis stratified by sex and exposure

Allergen*	Exposure	Men (%) n = 268	Women (%) n = 490	Total (%) n =758
Rubber additives	Gloves (56), other (7)	18 (6.7)	44 (9.0)	62 (8.2)
Biocides	Cleansing agents (8), oil (8), moisturizers (6), other (21)	11 (4.1)	31 (6.3)	42 (5.5)
Nickel/cobalt	Metal production (13), tools (13), keys (5), other (10)	14 (5.2)	24 (4.9)	38 (5.0)
Chromium	Leather (9), oil (5), cement (4), other (4)	18 (6.7)	2 (0.4)	20 (2.6)
Dyes, bleaching agents	PPD (12), ammonium persulfate (4), toluen-ediamine (2), glycerol monothioglycolate (2), nitroparaphenylenediamine (1), contra colour (1)	2 (0.7)	17 (3.5)	19 (2.5)
Epoxy	Windmills (8), paint (6), glue (2), other (1)	13 (4.9)	3 (0.6)	16 (2.1)
Food allergens**	Spices (4), flour (3), other (6)	8 (3.0)	4 (0.8)	12 (1.6)
Fragrance	Cleansing agents (4), cosmetics (6), other (2)	0 (0.0)	11 (2.2)	11 (1.2)
Acrylic resins	Glue (3), fillings (4), other (3)	5 (1.9)	5 (1.0)	10 (1.3)
Plants	Teak (4), other (3)	4 (1.5)	3 (0.6)	7 (0.9)
Colophony	Tape (2), other (5)	2 (0.7)	4 (0.8)	6 (0.8)
Other	NS	14 (5.2)	12 (2.4)	26 (3.4)
Irritants*	Exposure			
Wet work	Water, soap	34 (12.7)	292 (59.6)	326 (43.0)
Food	Flour (27), fish (7), vegetables (18), fruit (3), meat (11), other (24)	38 (14.2)	52 (10.6)	90 (11.9)
Gloves	NS	8 (3.0)	72 (14.7)	80 (10.6)
Oils	NS	73 (27.2)	5 (1.0)	78 (10.3)
Mechanical irritation	Paper (11), metal (8), wood (4), other (24)	32 (11.9)	15 (3.1)	47 (6.2)
Other	NS	16 (6.0)	14 (2.9)	30 (4.0)
Disinfectants	NS	1 (0.4)	4 (0.8)	5 (0.7)
Physical conditions	NS	1 (0.4)	0 (0.0)	1 (0.1)

* It is possible to have more than one exposure, ** only type IV allergic reactions are given, NS = not specified.

Study II

Severity and diagnosis at baseline

Study II revealed a substantially greater severity among patients with ICD and patients with AD than for any other diagnosis or subdiagnosis (Table 6). Combined diagnoses including ICD had an increased risk of severity similar to that of ICD alone. These results are in contrast to several comparable studies that report ACD to be more strongly associated with severe hand eczema[2;4;21;22]. However, in a recent Dutch study, ICD was found to have a poor prognosis, which supports our findings [24]. The reason why the course of illness for patients with occupational ACD is more moderate than for patients with ICD may be that they can more readily identify and avoid the cause of their eczema. We found no indication of an additive effect of having more than a single diagnosis or contact allergy to more than one allergen, a result which is confirmed in a recent Swedish study by Meding et al [20].

Sick leave

Fifty-seven per cent of the study population reported sick leave due to OHE during the past 12 months and 20% reported prolonged sick leave at baseline. Severe OHE as well as AD were moderately associated with prolonged sick leave, which is consistent with previous literature [70;71]. Women had a higher proportion than men of prolonged sick leave in all agegroups, except for the oldest agegroup (age above 50 years). The differences between women and men were, however, only modest (Table 6). These findings may reflect sex-related delay in seeking and/or complying with treatment, which support earlier findings for other skin diseases [72;73]. Women have also been reported to be more distressed by their hand eczema than men, which may lead to more frequent sick leave [74].

Loss of job

Of the 612 responders to this item, 23% reported job-loss at baseline due to their OHE during the past 12 months. The only strong association with loss of job was food-related occupations (Table 6). However, CU was associated with a protective effect against job loss.

In conclusion, having a diagnosis of occupational ICD had the greatest effect on the overall severity of OHE compared with all other included diagnoses and subdiagnoses. Patients with AD had a poor prognosis with a relatively high-risk of severe OHE and prolonged sick leave. The only notable association with loss of job was with food-related occupations.

Table 6.
Prevalence ratios (PR's) and 95% robust confidence intervals (CI) for age, sex, diagnostic and subdiagnostic groups, severity and occupation in 3 separate multivariable Poisson regression models with severity, sick leave and loss of job as response variables respectively.

Variable	Severity of OHE (mild-severe) PR (95%-CI) Reference: no/minimal	Prolonged sick leave* PR (95%-CI) Reference: 0-5 weeks	Loss of job** PR (95%-CI) Reference: no loss of job
Age in years			
18-24	1	1	1
25-29	1.12 (0.94- 1.33)	1.15 (0.70 – 1.87)	0.85 (0.53 – 1.35)
30-39	1.11 (0.94 – 1.31)	0.97 (0.62 – 1.53)	1.12 (0.76 – 1.65)
40-49	1.19 (0.99 – 1.43)	0.97 0.56 – 1.67)	1.06 (0.34 – 1.16)
50+	**1.40 (1.19 – 1.65)**	0.64 (0.33 –1.25)	0.63 (0.34 – 1.16)
Sex			
Men	1	1	1
Women	1.00 (0.87 – 1.15)	1.25 (0.82 – 1.90)	1.33 (0.91 – 1.92)
Diagnosis			
ACD	1	1	1
ICD	**1.58 (1.32 – 1.90)**	0.93 (0.49 – 1.77)	0.79 (0.55 – 1.13)
CU	0.79 (0.48 – 1.30)	0.29 (0.07 – 1.22)	**0.20 (0.05 – 0.77)**
ICD + ACD	**1.71 (1.38 – 2.11)**	0.93 (0.49 – 1.77)	0.76 (0.43 – 1.34)
ICD + CU	**1.52 (1.07 – 2.16)**	1.62 (0.77 – 3.43)	0.97 (0.48 – 1.94)
AD			
No	1	1	1
Yes	**1.22 (1.08 – 1.39)**	**1.66 (1.12 – 2.46)**	1.34 (0.93 – 1.93)
NOACD			
No	1	1	1
Yes	0.99 (0.89 – 1.11)	1.18 (0.82 – 1.68)	1.25 (0.92 – 1.70)
Severity			
No/minimal	-	1	1
Mild/moderate eczema	-	0.97 (0.64 – 1.47)	0.82 (0.59 – 1.13)
Severe eczema	-	**1.61 (1.02 – 2.54)**	0.78 (0.50 – 1.22)
Occupation			
Wet	1	1	1
Food	1.05 (0.90 – 1.22)	1.41 (0.91 – 2.17)	**1.96 (1.36 – 2.83)**
Other	1.04 (0.91 – 1.20)	0.95 (0.62 – 1.46)	1.15 (0.79 – 1.69)

*Prolonged sick leave= more than 5 weeks' sick leave due to occupational hand eczema during the past 12 months. ** Loss of job due to occupational hand eczema during the past 12 months. OHE = occupational hand eczema, ACD = allergic contact dermatitis, ICD = irritant contact dermatitis, CU = contact urticaria, AD = atopic dermatitis, NOACD = non-occupational allergic contact dermatitis. Bold indicates statistical significance at 5% level.

Study III

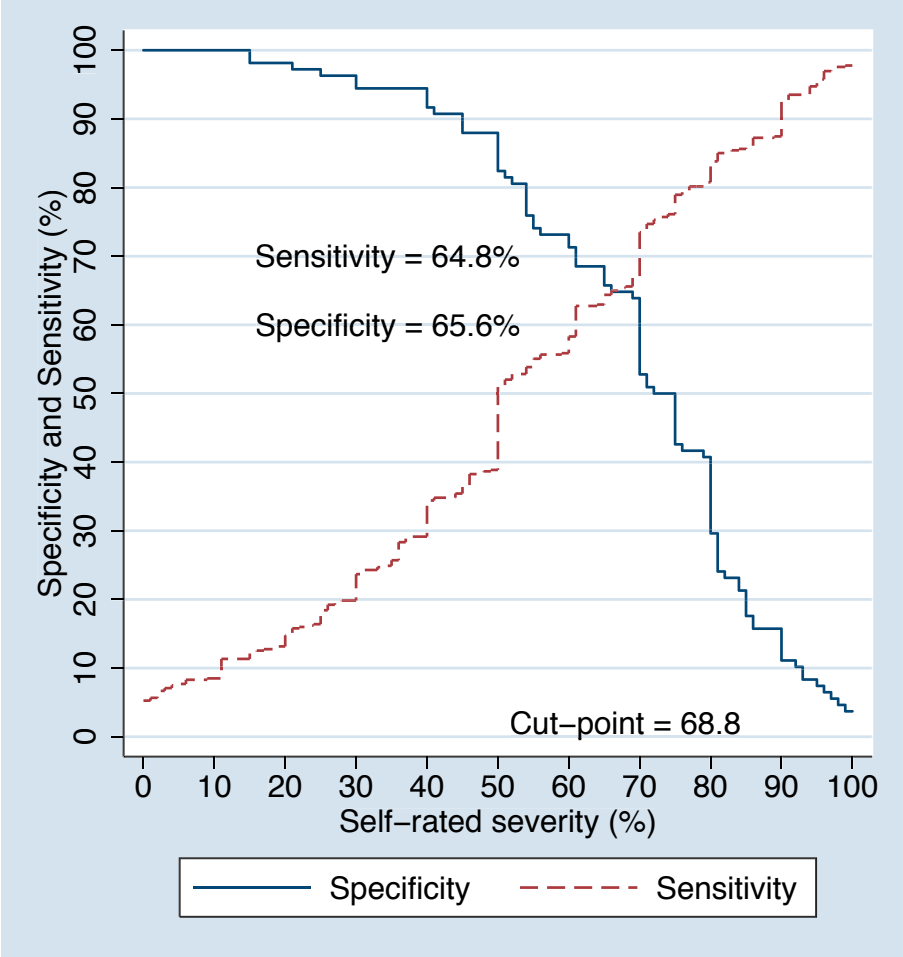
Severity assessment of OHE is important not only in clinical settings but also in research. Self-administered questionnaires may be an attractive tool to assess severity, mainly due to the cost-efficiency compared with expensive clinical examinations.
The objective of Study III was to evaluate the relation between self-rated severity and severity assessment based on standardized medical certificates issued by dermatologists. The relation between the two methods is illustrated by a receiver operating characteristic (ROC) analysis (Figure 1.) The sensitivity in this study comprises the proportion of self-rated severe cases among DNBII-rated severe cases and the specificity the proportion of self-rated non-severe cases among DNBII-rated non-severe cases (Table 7). The cut point on the VAS with the highest sensitivity and specificity was 68.8% (Fig 1). The proportion of severe cases was significantly higher among patients' assessments compared with the rating by the DNBII. 17.9% were categorised as severe cases by the DNBII, while 39.9% of patients had assessed themselves as severe. The sensitivity and specificity were 64.8% and 65.6% respectively (Table 7). The positive predictive value (PPV) was 29.2% and the negative predictive value (NPV) was 89.5% (Table 7). Age, sex, socioeconomic status and type of diagnosis did not appear to have any important influence on the sensitivity, specificity, PPV or NPV. In conclusion, the low positive predictive value suggests major differences in the criteria for self-rated severity versus DNBII-rated severity and it is recommended that researchers include ratings from both patients and physicians in future investigations of severity.

Table 7.
The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), prevalences of severe (score 8-12) OHE cases and self-rated severe OHE cases (VAS cut-point = 68.8) and the crude posterior odds ratio (POR).

Sensitivity	70/ (38+70) = 64.8%	The proportion of self-rated severe cases among DNBII-rated severe cases
Specificity	324/ (324+170) = 65.6%	The proportion of self-rated non-severe cases among DNBII-rated non-severe cases
PPV	70/ (70+170) = 29.2%	The proportion of DNBII-rated severe cases among self-rated severe cases
NPV	324/ (38+324) = 89.5%	The proportion of DNBII-rated non-severe cases among self-rated non-severe cases
Prevalence of severe DNBII-rated cases	108/602 = 17.9%	
Prevalence of severe self-rated cases	240/602 = 39.9%	
Crude POR (95%-confidence interval)	3.5 (2.3 – 5.4)	

DNBII = Danish National Board of Industrial Injuries. VAS = visual analogue scale

Figure 1.
Sensitivity and specificity against self-rated severity. The identification of cut-point.



Study IV

Quality of life (QoL)

The mean total sum scores at baseline showed little variation in QoL impairment among subgroups and we found a mean total score of 5.5, which is in accordance with earlier findings [44;51;62;75]. The mean total DLQI score increased with increasing severity, as seen in other skin diseases [76], and a mean DLQI score for severe OHE cases was 7.8. These findings rank the disease below AD and psoriasis [48;62;77]. We found strong associations between mild to moderate OHE, severe OHE and low QoL at baseline compared with cases classified with no or minimal OHE (Table 8). Furthermore, the risk of low QoL at baseline was 2 times higher among patients with lower socioeconomic status, which has not previously been reported (Table 8). Depressive symptoms were also strongly associated with low QoL (PR = 3.8; 95% CI (2.5 – 5.6), which confirms earlier results [51]. Grob et al. reported in a recent paper that patients with CU have a high risk of low QoL [78].

Our results do not support this finding. We found no significant associations between low QoL and sex, age, diagnoses, disease duration or occupations (Table 8). We found only a modest overall improvement in QoI from baseline to follow-up (86% had high QoL at baseline and 89% had unchanged high QoL or improved QoL after 12 months of follow-up). We found no large differences in QoL changes between severity strata (Table 9).

Regarding the 6 DLQI category scores we found that the 2 categories "work/school" together with "symptoms and feelings" were the most severely affected at baseline compared with the other category groups (Figure 2), which is in accordance with previous findings [79]. We found no significant differences between men and women for any of the 6 different categories, which also support earlier findings [25;47].

Figure 2. Mean DLQI score at baseline by categories and sex

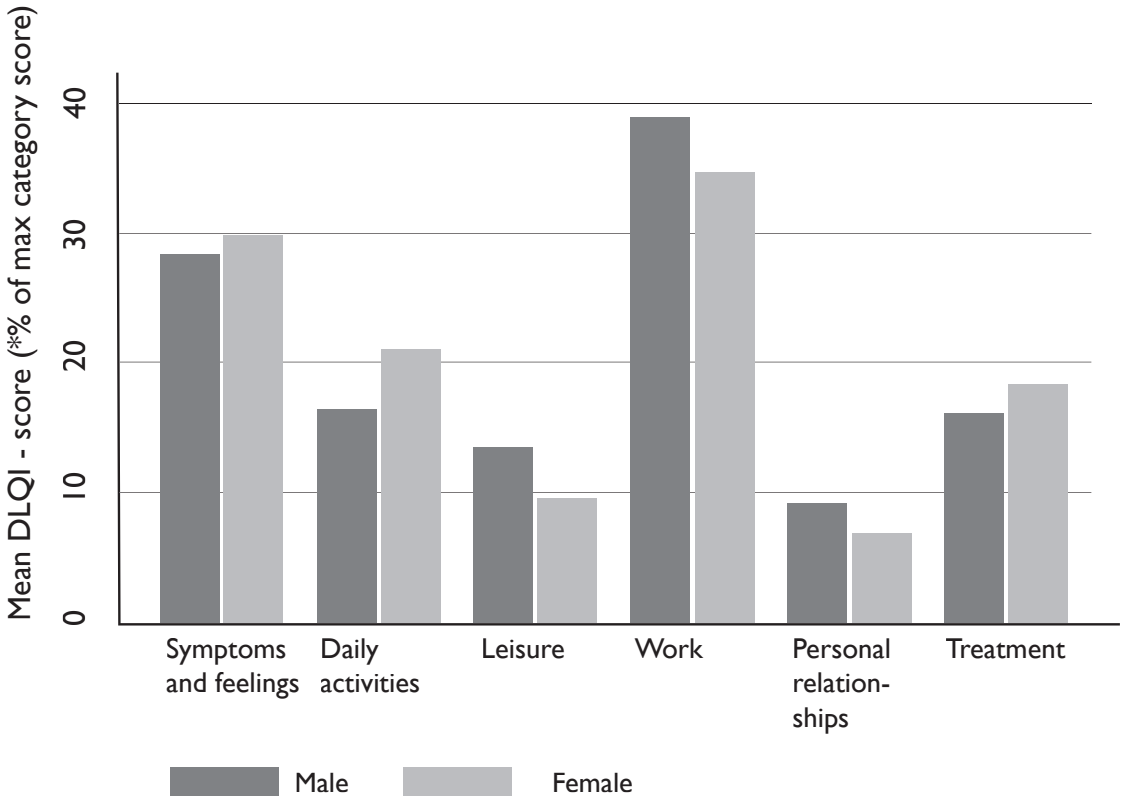


Table 8.
Frequencies and prevalences for high (total DLQI score 0-10) and low QoL (total DLQI score 11-30) and moderate to severe depression (total BDI-II score 20-63) and minimal to mild depression (total BDI-II score 0-19). Two multivariable Poisson regression models were performed with low QoL and moderate/severe depressive symptoms as response variables respectively.

	*Quality of life			**Depressive symptoms		
Variable	High (%)	Low (%)	PR (95%-CI)	Minimal/mild (%)	Moderate/ severe (%)	PR (95%-CI)
Sex						
Men	173 (83.6)	34 (16.4)	1	197 (94.3)	12 (5.7)	1
Women	350 (86.2)	56 (13.8)	0.9 (0.6 – 1.5)	364 (89.9)	41 (10.1)	1.8 (0.8 – 4.0)
Age (years)						
18-24	115 (87.1)	17 (12.9)	1	126 (95.5)	6 (4.6)	1
25-29	90 (85.7)	15 (14.3)	0.9 (0.5 – 1.8)	97 (91.5)	9 (8.5)	2.0 (0.8 – 5.1)
30-39	154 (85.6)	26 (14.4)	1.1 (0.5 – 2.2)	158 (88.3)	21 (11.7)	**2.4 (1.0 – 5.4)**
40-49	83 (84.7)	15 (15.3)	1.1 (0.5 – 2.2)	88 (89.8)	10 (10.2)	1.7 (0.6 – 4.8)
50+	81 (82.7)	17 (17.4)	1.1 (0.5 – 2.2)	92 (92.9)	7 (7.1)	1.0 (0.3 – 3.2)
SES						
Students/ trainees	102 (90.3)	11 (9.7)	1	104 (92.0)	9 (8.0)	1
High/medium level	79 (92.9)	6 (7.1)	0.9 (0.3 – 2.5)	82 (97.6)	2 (2.4)	0.3 (0.1 – 1.2)
Basic level	213 (81.6)	48 (18.4)	**2.0 (1.0 – 3.9)**	238 (90.5)	25 (9.5)	1.0 (0.4 – 2.3)
Lowest level	125 (83.9)	24 (16.1)	1.9 (0.9 – 4.0)	132 (88.6)	17 (11.4)	1.2 (0.5 – 2.7)
Diagnosis						
ACD	112 (86.8)	17 (13.2)	1	121 (93.1)	9 (6.9)	1
ICD	320 (83.6)	63 (16.5)	1.0 (0.6 – 1.8)	351 (91.4)	33 (8.6)	1.4 (0.6 – 3.1)
CU	28 (96.6)	1 (3.5)	0.4 (0.1 – 2.0)	27 (96.4)	1 (3.6)	0.6 (0.1 – 3.4)
ICD+ACD	48 (87.3)	7 (12.7)	0.5 (0.2 – 1.2)	46 (83.6)	9 (16.4)	2.1 (0.8 – 5.4)
ICD+CU	15 (88.2)	2 (11.8)	0.8 (0.3 – 2.5)	16 (94.1)	1 (5.9)	1.2 (0.2 – 9.1)

*8 missing variables to this item. **7 missing variables to this item. SES = socioeconomic status, ACD = allergic contact dermatitis, ICD = irritant contact dermatitis, CU = contact urticaria, DNBII = Danish National Board of Industrial Injuries, QoL = quality of life, DLQI = dermatology life quality index, BDI-II = Beck's depression inventory II, CI = confidence intervals, PR = prevalence proportion. Bold indicates statitistical significance at 5% level.

Table 8 continues next page

Table 8 continued

	*Quality of life			**Depressive symptoms		
Variable	High (%)	Low (%)	PR (95%-CI)	Minimal/mild (%)	Moderate/ severe (%)	PR (95%-CI)
AD						
No	436 (85.7)	73 (14.3)	1	464 (91.0)	46 (9.0)	1
Yes	87 (83.7)	17 (16.4)	1.4 (0.8 – 2.5)	97 (93.3)	7 (6.7)	0.7 (0.3 – 1.5)
NOACD						
No	364 (84.9)	65 (15.2)	1	400 (93.2)	29 (6.8)	1
Yes	159 (86.4)	25 (13.6)	0.7 (0.4 – 1.1)	161 (87.0)	24 (13.0)	1.6 (0.9 – 2.6)
Severity (DNBII)						
No/minimal	181 (94.8)	10 (5.2)	1	176 (92.2)	15 (7.9)	1
Mild/moderate	257 (82.6)	54 (17.4)	**3.5 (1.8 – 7.0)**	289 (92.6)	23 (7.4)	0.6 (0.3 – 1.2)
Severe	85 (76.6)	26 (23.4)	**3.7 (1.7 – 7.7)**	96 (86.5)	15 (13.5)	0.8 (0.4 – 1.7)
Duration (years)						
0 to <2	80 (88.9)	10 (11.1)	1	85 (94.4)	5 (5.6)	1
2 to <3	120 (90.9)	12 (9.1)	0.8 (0.4 – 1.7)	122 (92.4)	10 (7.6)	1.7 (0.7 – 4.4)
3 to <6	142 (81.1)	33 (18.9)	1.7 (0.9 – 3.2)	161 (92.0)	14 (8.0)	1.5 (0.6 – 3.9)
6 to 51	161 (85.2)	28 (14.8)	1.4 (0.7 – 2.6)	171 (90.0)	19 (10.0)	1.6 (0.7 – 4.0)
Occupation						
Wet	220 (86.6)	34 (13.4)	1	228 (90.1)	25 (9.9)	1
Food	96 (84.2)	18 (15.8)	1.0 (0.6 – 1.7)	106 (92.2)	9 (7.8)	0.8 (0.4 – 1.6)
Other	207 (84.5)	38 (15.5)	1.0 (0.6 – 1.6)	227 (92.3)	19 (7.7)	0.7 (0.4 – 1.5)
High QoI	-	-	-	492 (94.3)	30 (5.8)	1
Low QoL	-	-	-	67 (74.4)	23 (25.6)	**4.5 (2.6 – 7.9)**
Depression						
Minimal to mild	452 (89.5)	53 (10.5)	1	-	-	-
Moderate to severe	70 (65.4)	37 (34.6)	**3.8 (2.5 – 5.6)**	-	-	-

*8 missing variables to this item. **7 missing variables to this item. SES = socioeconomic status, ACD = allergic contact dermatitis, ICD = irritant contact dermatitis, CU = contact urticaria, DNBII = Danish National Board of Industrial Injuries, QoL = quality of life, DLQI = dermatology life quality index, BDI-II = Beck's depression inventory II, CI = confidence intervals, PR = prevalence proportion. Bold indicates statitistical significance at 5% level.

Table 9.
Mean DLQI and changes in quality of life (QoL) during 12 months of follow-up by severity at baseline.

	Mean DLQI at baseline	High QoL at baseline(0-10)	Low QoI at baseline (11-30)	Persistently high QoL or improved QoL after 12 months	Persistently low QoL or aggravated QoL after 12 months
Follow-up* responders	5.5	463 (86.2%)	74 (13.8%)	475 (88.5%)	62 (11.6%)
Severity**					
No/minimal	3.3	149 (94.3%)	9 (5.7%)	150 (94.9%)	8 (5.1%)
Mild/moderate	6.0	238 (83.8%)	46 (16.2%)	251 (88.4%)	33 (11.6%)
Severe	7.8	76 (80.0%)	19 (20.0%)	74 (77.9%)	21 (22.1%)

*27 missing variables to this item in the follow-up questionnaire.
**Severity rated by The Danish National Board of Industrial Injuries at baseline. DLQI = Dermatology Life Quality Index. High QoL = DLQI total score (0-10), low QoL = DLQI total score (11-30).

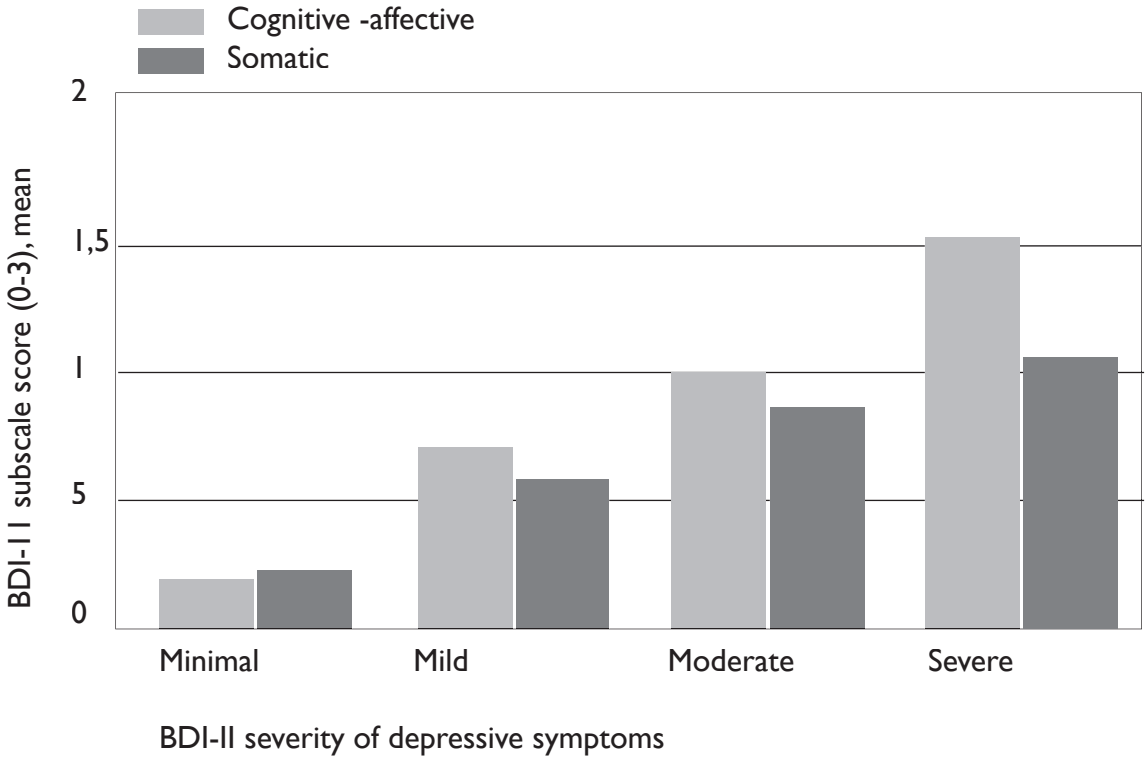
Depression

A total of 9% of the study population at baseline and at 12 months of follow-up showed signs of moderate to severe depression, which is similar to that we would expect in the general population [51] (Table 10). The mean total BDI-II score was estimated to 7.1 (range 0 – 41; SD = 7.4). We found significantly more depressed patients among patients aged between 30 to 39 years (Table 8) and low QoL appeared to be strongly associated with high BDI-II score (PR = 4.5; CI (2.6 – 7.9)), which support earlier findings [51]. We found no significant associations between high BDI-II score and sex, socioeconomic status, diagnoses, severity or disease duration. As shown in Figure 3, the proportion of cognitive/affective depressive symptoms at baseline relative to somatic symptoms was considerably higher among those patients who were classified as depressed (mildly to severely) than those who were classified as not depressed or minimally depressed. Cognitive-affective symptoms are symptoms that are usually expected in patients with a clinical diagnosis of a major depression. We had expected a higher proportion of somatic symptoms in our study, because, in many cases, OHE is predominantly a chronic somatic illness.

Table 10.
Frequency and proportion of occupational hand eczema patients by level of depression at baseline and at 12 months follow-up.

Level of depression	Frequency (%) at baseline	Frequency (%) at follow-up
No/minimal	470 (83)	453 (80)
Mild	46 (8)	60 (11)
Moderate	32 (6)	42 (8)
Severe	14 (3)	8 (1)
Missing values	2 (0.4)	1 (0.2)
Total	564	564

Figure 3.
Mean Beck Depression Iventory (BDI-II) cognitive-affective versus somatic subscale scores among OHE patients at baseline.



Study V

Improvement of, aggravation of, or persistent OHE

During the 12 months of follow-up, 25% of all OHE patients had persistently severe or aggravated disease, 41% had improved and 34% had unchanged mild to moderate disease. The proportion of improved cases is lower than that reported in a recent Swedish study, where Meding and colleagues reported a proportion of improvement of 74% during 15 years of follow-up in a cohort of hand eczema 25, which probably is due to the differences in the length of follow-up.

Age, sex, socioeconomic status and prognosis

Age less than 25 years old was found to be a significant protective factor against a poor prognosis, which supports earlier findings [23] but contradicts others [20]. As in previous studies, we found no effect of sex on the prognosis [20;80,] although contradictory findings have been published [23;25;81]. Poor socioeconomic status has been shown to affect outcome adversely in many chronic disorders [35-40]. We found that the prognosis of OHE in terms of aggravated or persistently severe disease was superior for patients with high/medium socioeconomic status at baseline with only 15% who had aggravated or persistently severe OHE compared with 27%-28% in the patients with lower socioeconomic status. The association was, however, not statistically significant (Table 11, Table 12).

Diagnoses and prognosis

After 1-year of follow-up we found that patients with AD had a 1.5 higher risk of aggravation or persistently severe OHE compared with patients without AD, which is consistent with previous findings [18;20;80;82]. The prognosis has been reported worse for ACD than ICD in earlier papers [3;20;21;81;83;84] but our results do not support this. In study II we found that ICD patients at baseline had a higher proportion of severe OHE than ACD patients: however at 1-year follow-up we could no longer detect any significant differences between the two diagnostic groups.
Chromium has previously been associated with a poor prognosis [18;83;85;86] but our findings could not confirm this. We found that only 12% of chromium positive patients had aggravated or persistently severe OHE after 12 months of follow-up. In a study from 1975, Fregert [21] reported that the prognosis was especially poor in women with nickel allergy. Since 1991, Danish legislation, has led to a reduction of nickel exposure, which may be one of the reasons why we found no association between occupational or non-occupational nickel allergy and aggravation or persistently severe OHE after 12 months of follow-up.

Table 11.
Frequencies and prevalence proportions of changes in self-rated severity* of OHE after 12 months follow-up, by sex, age, socioeconomic status, diagnoses, occupation, job change and depression.

Variable	No change in severity from baseline to follow-up (%)			Aggravation (%)	Improvement (%)	
	No/ minimal	Mild/ moderate	Severe			*Aggravation or persistent severe OHE*
Age (years) men						
18 - 24	7 (20.0)	7 (20.0)	2 (5.7)	5 (14.3)	14 (40.0)	*20.0 %*
25 – 29	3 (10.0)	5 (16.7)	8 (26.7)	4 (13.3)	10 (33.3)	*40.0 %*
30 - 39	6 (15.0)	10 (25.0)	6 (15.0)	5 (12.5)	13 (32.5)	*27.5 %*
40 – 49	3 (10.7)	5 (17.9)	6 (21.4)	3 (10.7)	11 (39.3)	*32.1 %*
50 +	3 (7.5)	5 (12.5)	5 (12.5)	4 (10.0)	23 (57.5)	*22.5 %*
Age (years) women						
18 - 24	8 (9.9)	17 (21.0)	8 (9.9)	11 (13.6)	37 (45.7)	*23.5 %*
25 – 29	6 (10.7)	11 (19.6)	10 (17.9)	7 (12.5)	22 (39.3)	*30.4 %*
30 - 39	23 (19.5)	20 (17.0)	18 (15.3)	11 (9.3)	46 (39.0)	*24.6 %*
40 – 49	10 (15.6)	16 (25.0)	6 (6.3)	4 (6.3)	28 (43.8)	*12.6 %*
50 +	9 (18.8)	10 (20.8)	7 (14.6)	7 (14.6)	15 (31.3)	*29.2 %*
SES1						
Students, trainees	16 (15.7)	13 (12.8)	14 (13.7)	14 (13.7)	45 (44.1)	*27.4 %*
Employee high and medium level	18 (22.5)	17 (21.3)	8 (10.0)	4 (5.0)	33 (41.3)	*15.0 %*
Employee basic level	26 (11.7)	51 (22.9)	36 (16.1)	24 (10.8)	86 (38.6)	*26.9 %*
Employee lowest level	18 (13.7)	25 (19.1)	18 (13.7)	19 (14.5)	51 (38.9)	*28.2 %*

Table 11 continues next page

Table 11 continued

Variable	No change in severity from baseline to follow-up (%)			Aggravation (%)	Improvement (%)	
	No/ minimal	Mild/ moderate	Severe			*Aggravation or persistent severe OH*
Diagnosis						
ACD	22 (20.0)	17 (15.5)	13 (11.8)	15 (13.6)	43 (39.1)	*25.4%*
ICD	36 (10.8)	67 (20.1)	50 (15.0)	38 (11.4)	142 (42.6)	*26.4 %*
CU	10 (35.7)	5 (17.9)	1 (3.6)	2 (7.1)	10 (35.7)	*10.7 %*
ICD + ACD	7 (13.5)	15 (28.9)	7 (13.5)	3 (5.8)	20 (38.5)	*19.3 %*
ICD + CU	3 (17.7)	2 (11.8)	5 (29.4)	3 (17.7)	4 (23.5)	*47.1 %*
AD						
No	71 (16.1)	85 (19.3)	60 (13.6)	46 (10.4)	179 (40.6)	*24.0 %*
Yes	7 (7.1)	21 (21.2)	16 (16.2)	15 (15.2)	40 (40.0)	*31.4 %*
Occupation at baseline2						
Butchers	2 (22.2)	2 (22.2)	3 (33.3)	1 (11.1)	1 (11.1)	*44.4 %*
Kitchen workers/chefs	10 (16.9)	9 (15.3)	14 (23.7)	8 (13.6)	18 (30.5)	*37.3 %*
Hairdressers	3 (10.0)	7 (23.3)	6 (20.0)	5 (16.7)	9 (30.0)	*36.7 %*
Factory worker	9 (17.0)	9 (17.0)	8 (15.1)	7 (13.2)	20 (37.7)	*28.3 %*
Bakers	5 (20.0)	3 (12.0)	2 (8.0)	5 (20.0)	10 (40.0)	*28.0 %*
Mixed occupations	5 (12.8)	5 (12.8)	5 (12.8)	5 (12.8)	19 (48.7)	*25.6 %*
Other tradesmen	5 (10.6)	12 (25.5)	7 (14.9)	5 (10.6)	18 (38.3)	*25.5 %*
Carpenters	1 (12.5)	0 (0.0)	1 (12.5)	1 (12.5)	5 (62.5)	*25.0 %*
Printers	1 (12.5)	1 (12.5)	1 (12.5)	1 (12.5)	4 (50.0)	*25.0 %*
Machinists	0 (0.0)	3 (25.0)	2 (16.7)	1 (8.3)	6 (50.0)	*25.0 %*
Depression						
Minimal to mild	74 (15.0)	99 (20.0)	66 (13.4)	56 (11.3)	199 (40.3)	*24.7%*
Moderate to severe	4 (8.9)	7 (15.6)	10 (22.2)	5 (11.1)	19 (42.2)	*33.3%*
Job change						
No	34 (13.3)	55 (21.5)	32 (12.5)	24 (9.4)	111 (43.4)	*21.9%*
Yes	41 (17.3)	44 (18.6)	37 (15.6)	26 (11.0)	89 (37.6)	*26.6%*
Total	14.5%	19.7%	14.1%	11.3%	40.5%	*25.4%*

Sick leave, job change and loss of job

As seen in Table 12 prolonged sick leave was significantly associated with a) having occupational CU, b) age above 25 years (with statistical significance for the age group 40 to 49 years) and c) being categorized as having severe OHE at baseline by the DNBII. Self-rated severity produced similar associations to those based upon DNBII-rated severity. Severe impairment of QoL at baseline was also strongly associated with the risk of prolonged sick leave during follow-up. It may therefore be advisable to allow future patients to complete the DLQI questionnaire in the waiting room before a dermatology consultation, since a low DLQI score is such a strong predictor of prolonged sick leave the following year. We found a favourable prognosis for patients with high/medium socioeconomic status (no patients with prolonged sick leave or loss of job in this group), which is in accordance with previous findings among dentists in Sweden [41;87] and the results indicate that lower socioeconomic status is an important risk factor of both prolonged sick leave and loss of job.

We found no association between sex and prolonged sick leave, which supports earlier findings [25], neither did we find any large associations between prolonged sick leave and AD, NOACD, disease duration, occupation or the presence of moderate to severe depression.

Our results support previous reports of age as a risk factor for prolonged sick leave [4]. We could not corroborate earlier findings that patients with ACD have a higher risk of prolonged sick leave [3;4;43]. Occupational CU appeared to be associated with a high risk of prolonged sick leave after 12 months of follow-up, which may be due to strict hygiene regulations in food-related occupations (food-related occupations have traditionally many patients with CU). In Study II we found a protective effect of having CU and loss of job.

After 12 months of follow-up we were not able to detect any difference between the different diagnostic groups. As seen in Table 12 strong associations were found between having severe OHE (RR = 14.0) at baseline and loss of job after 12 months of follow-up. Almost 48% of the study population reported job change during the 12 months of follow-up, which is considerably higher compared to the study by Meding et al [25], who found that only 3% of the study population had changed their job during 15 years of follow-up. Job change in our study was associated with younger age groups and lower socioeconomic status.

Table 12.
Risk ratios (RR) and 95% robust confidence intervals for selected variables in 3 separate multivariable Poisson regression models with severity, sick leave and loss of job after 12 months follow-up as response variables respectively. Unemployed, early retirement and other pensions are omitted from the analyses of prolonged sick leave and loss of job.

Variable	Aggravation or persistent severe OHE after 1-year follow-up. RR (95%-CI)	Prolonged sick leave after 1-year follow-up RR (95%-CI)	Loss of job after 1-year follow-up RR (95%-CI)
Age (years)			
18-24	1	1	1
25-29	**1.94 (1.2 – 3.2)**	1.04 (0.2 – 7.2)	3.06 (0.3 – 31.8)
30-39	**1.77 (1.1 – 2.9)**	2.44 (0.6 – 9.7)	7.78 (0.9 – 69.2)
40-49	1.46 (0.8 – 2.6)	**5.28 (1.4 – 20.7)**	4.14 (0.4 – 45.7)
50+	**1.81 (1.0 – 3.2)**	1.44 (0.2 – 9.6)	5.95 (0.5 – 66.6)
Sex			
Men	1	1	1
Women	0.93 (0.6 – 1.4)	0.97 (0.3 – 3.4)	1.10 (0.4 – 2.9)
Diagnoses			
ACD	1	1	1
ICD	0.96 (0.6 – 1.4)	2.90 (0.6 – 13.4)	1.14 (0.4 – 3.4)
CU	0.38 (0.1 – 1.2)	**16.4 (1.2 – 224.1)**	2.14 (0.1 – 31.4)
ACD+ICD	0.63 (0.3 – 1.2)	3.50 (0.6 – 20.5)	2.56 (0.6 – 11.6)
ICD+CU	1.61 (0.9 – 3.0)	3.95 (0.6 – 26.4)	NA
AD			
No	1	1	1
Yes	**1.53 (1.1 – 2.2)**	0.58 (0.2 – 1.8)	1.12 (0.2 – 5.3)

ACD = allergic contact dermatitis, ICD = irritant contact dermatitis, CU = contact urticaria, AD = atopic dermatitis, SES = socio-economic status, NA = not applicable, * Rated by The Danish National Board of Industrial Injuries at baseline. Bold indicates statistical significance at 5% level.

Table 12 continues next page

Table 12 continued

Variable	Aggravation or persistent severe OHE after 1-year follow-up. RR (95%-CI)	Prolonged sick leave after 1-year follow-up RR (95%-CI)	Loss of job after 1-year follow-up RR (95%-CI)
SES			
Lowest level	1	1	1
Basic level	1.01 (0.7 – 1.4)	2.53 (0.7 – 9.2)	2.82 (0.6 – 12.4)
High/medium level	0.56 (0.3 – 1.0)	NA	NA
Students/trainees	0.96 (0.6 – 1.5)	2.60 (0.62 – 10.9)	1.74 (0.2 – 12.6)
Depression			
Minimal to mild	1	1	1
Moderate to severe	1.4 (0.9 – 2.2)	1.46 (0.4 – 5.3)	2.72 (0.7 – 10.0)
DLQI			
High QoL	-	1	1
Low QoL	-	**4.62 (1.6 – 13.7)**	2.6 (0.9 – 7.3)
Severity*			
No/minimal	-	1	1
Mild/moderate	-	1.69 (0.4 – 6.7)	4.52 (0.5 – 37.5)
Severe	-	**5.29 (1.6 – 17.7)**	**14.0 (1.9 – 102.9)**

ACD = allergic contact dermatitis, ICD = irritant contact dermatitis, CU = contact urticaria, AD = atopic dermatitis, SES = socio-economic status, NA = not applicable, * Rated by The Danish National Board of Industrial Injuries at baseline. Bold indicates statistical significance at 5% level.

6. Bias

Selection

Potential sources of bias in this study arise from selective referral and losses to follow-up. The number of notified and thereby recognized cases may not necessarily reflect the true number of patients with OHE, because mild cases with short disease duration may be missed. Nevertheless, the proportion of mild cases in our study was high (more than 30%), which argues against a major underestimation of very mild cases. There is no reason to believe that the type of diagnosis should be related to notification or recognition of OHE and thereby cause any systematic error.

The "healthy worker effect" is another potential bias in this study and arise when people in certain occupations are healthier than general. The "healthy worker" may present a false good image of high-risk occupations because all "weak workers" have already left the particular occupation.

Drop-out analysis

There were no appreciable differences in age, sex, diagnosis, socioeconomic status or severity at baseline between those who returned both questionnaires and those who were lost to follow-up, except a significantly higher proportion of female responders and a significantly higher proportion of patients with AD at follow-up (Table 13).

Table 13.
Drop-out analysis

	Baseline			Follow-up		
Variable	Responders	Non-responders	P-value1	Responders	Non-responders	P-value1
Sex			0.20			**<0.001**
Men	213	55		178	35	
Women	408	82		386	22	
Age (years)			0.57			0.31
18-24	132	23		122	10	
25-29	106	28		92	14	
30-39	183	43		164	19	
40-49	98	24		93	5	
50+	102	18		93	9	
SES			0.05			0.21
Students/trainees	113	22		106	7	
High/medium level	85	8		81	4	
Basic level	264	65		236	28	
Lowest level	154	42		137	17	
Diagnosis			0.95			0.10
ACD	131	30		117	14	
ICD	388	81		347	41	
CU	29	7		28	1	
ICD+ACD	56	15		55	1	
ICD+CU	17	4		17	0	
Severity			0.06			0.27
No/minimal	194	55		173	21	
Mild/moderate	314	66		291	23	
Severe	113	16		100	13	
AD			0.69			**0.04**
No	517	116		464	53	
Yes	104	21		100	4	
NOACD			0.10			0.34
No	434	86		391	43	
Yes	187	51		173	14	

1 Chi-square test for equality between subgroups. SES = socioeconomic status, ACD = allergic contact dermatitis, ICD = irritant contact dermatitis, CU = contact urticaria, AD = atopic dermatitis, NOACD = non-occupational allergic contact dermatitis

Misclassification

All patients were patch tested with standard methods. We know that exposure in the working environment changes constantly. New allergens are introduced all the time and some may have been missed in this study, since patch testing is not always sufficiently up to date to detect these. It is therefore possible that occupational allergies were overlooked or misclassified, but it is unlikely that this omission would have caused any systematic error.

Recall bias

In the questionnaires the patients were asked to summarize all episodes of sick leave during the past 12 months and to assess the time of onset of their disease. It is possible that patients with severe OHE would be more aware of these facts and cause a systematic error in the analysis. This would probably tend to overestimate our associations with sick leave and disease durations for severe OHE.

Overall evaluation of the quality of the study

The relatively large sample size combined with high response rates in the questionnaires and no major systematic misclassification enhances the quality of the study and its conclusions.

7. Prevention

Prevention of new cases of OHE is needed because of its potentially serious consequences such as long-lasting disabling disease course, prolonged sick leave and potential unemployment. These consequences are distressing for the individual and expensive for society [13;43]. It is not only necessary that new cases are prevented. Previously diagnosed cases should also be prevented from progressing into a chronic disabling disease course. Several prevention strategies may be approached such as education and counselling of high-risk patient groups e.g. patients with AD, patients occupied in food-related and wet occupations, trainees [88;89] and patients with lower socioeconomic status. Regulation of threshold values for harmful allergens [83;90;91] and education of skin protection for workers in high-risk occupations [92-96] are also preventive methods of high value. It is, however, important that education and counselling are performed by professionals and updated career counsellors [97].

8. Future studies

1. Additional valuable and confirmative information regarding affiliation to the labour market and chronic OHE could be provided with further follow-up studies of this cohort after 10-15 years.

2. Intervention studies which test the longterm effect of skin protection programmes/skin policies in food-related and wet occupations, may reduce the number of new OHE cases in high-risk occupations.

3. The effect of educational programmes on career counsellors, trainees and patients with lower socioeconomic status should be tested as well as the effect of modified duty position instead of job change.

9. Summary and conclusions

Despite governmental attempts to reduce exposure to harmful occupational allergens, the number of new occupational hand eczema cases in Denmark has remained almost unchanged since the mid-1990s.
Complications and consequences of occupational contact dermatitis include chronic severe eczema, prolonged sick leave and unemployment. To reduce the number of new OHE cases in the future, it is important that detailed information is available about high-risk factors and occupations so that preventive actions can be targeted in the most cost-effective direction.

The aim of the study was to identify high-risk patient groups and prognostic risk factors for severe eczema, prolonged sick leave and loss of job. Furthermore we estimated the relation between self-rated and physician-rated severity, the extent of impairment in quality of life and the prevalence and severity of depressive symptoms among occupational hand eczema patients.

From October 2001 to November 2002 we included all new recognized occupational hand eczema cases in Denmark from the Danish National Board of Industrial Injuries Registry. Data from the registry were supplemented from two postal questionnaires, one at baseline and one after 12 months follow-up. The main results were as follows:

- A total of 758 OHE cases were recognized from the DNBII during the study period (58 weeks). The mean age was 35.6 years and the female/male ratio 1.8.

- The most common type of OHE was irritant contact dermatitis (62%) in both men and women followed by allergic contact dermatitis (21%), the combination of irritant and allergic contact dermatitis (9%), contact urticaria (5%) and the combination of irritant contact dermatitis and contact urticaria (3%). The prevalence of atopic dermatitis (16%) was similar to that of the general population but lower than expected in a hand eczema population.

- The overall incidence rate of OHE was estimated to be 30.6 per 100.000 workers but with large variance between different occupations. The highest incidence rates were found among bakers, hairdressers, dental surgery assistants and kitchen workers/chefs. The quantitatively dominating occupation was healthcare workers and comprised more than 21% of the entire study population.

- The Danish National Board of Industrial Injuries categorized almost 18% as severe OHE cases, while 40% of the patients had assessed themselves as severe. The sensitivity and specificity of selfrated severity were 65% and 66%, respectively. The positive predictive value was 29% and the negative predictive value 90%, which suggests major differences in the 2 rating methods. It is therefore recommended that both ratings are included in future research.

- The mean total DLQI score was estimated to 5.5 for all OHE patients and 7.8 for severe OHE cases. This ranks the disease slightly below AD and psoriasis in impairment of QoL. Severe cases and lower socioeconomic status were strongly associated with low QoL. Only a modest improvement was found from baseline to follow-up.

- A total of 9% of the study population at baseline and after 12 months of follow-up showed signs of moderate to severe depressive symptoms, which is similar to the general population. Low QoL and patients aged between 30-39 years were statistically associated with moderate to severe depressive symptoms.

- During the 12 months of follow-up, 25% of all OHE patients had persistently severe or aggravated disease, 41% had improved and 34% had unchanged mild to moderate disease.

- Patients with AD had a 1.2 times higher risk of severe OHE at baseline and a 1.5 times higher risk of aggravation or persistently severe OHE after 12 months of follow-up.

- Patients aged 50 years or above had a 1.4 times higher risk of severe OHE at baseline than patients aged 18-25. Patients aged above 25 years had almost a 2 times higher risk of aggravation or persistently severe OHE after 12 months of follow-up than patients aged 18-25 years.

- Patients with ICD had a 1.6 times higher risk of severe OHE at baseline compared with other diagnostic groups. After 12 months of follow-up no associations were found between the different diagnostic groups.

- At baseline, 20% reported prolonged sick leave (> 5 weeks) and 23% reported loss of job due to hand eczema during the past 12 months.

- Severe OHE and AD were associated with prolonged sick leave at baseline. After 12 months of follow-up severe OHE cases at baseline had a 5 times higher risk of prolonged sick leave than cases categorized with no/minimal OHE. Previously prolonged sick leave, age above 25 years and patients with CU were also associated with prolonged sick leave after 12 months of follow-up. Patients with high/medium socio-economic status had no reports of prolonged sick leave during follow-up. Low QoL at baseline was a strong predictor of prolonged sick leave after 12 months of follow-up.

- Having a food-related occupation was associated with a 2 times higher risk of loss of job than wet occupations at baseline. After 12 months of follow-up the strongest predictor of loss of job was severe OHE at baseline (RR = 14.0). Patients with high/medium socioeconomic status had no reports of loss of job during the follow-up time.

- Sex, ACD, ICD, NOACD, disease duration, occupation and moderate to severe depression were not associated with aggravation of or persistently severe OHE, prolonged sick leave or loss of job after 12 months of follow-up.

From a public health viewpoint this thesis shows the substantive burden associated with occupational hand eczema. Further research is, however, required to establish the relevance of other factors which may further add to the burden of OHE. From a clinical point of view this thesis gives the clinician opportunities to quickly identify high-risk patient groups that may need additional medical attention and care. Concepts such as socioeconomic status and quality of life assessments may reinforce current views on integrating psychosocial aspects into clinical care.

10. Summary in Danish (Dansk resumé)

Arbejdsbetinget håndeksem er den hyppigst anerkendte arbejdsbetingede sygdom i Danmark. I dette studie fandt vi en incidensrate på 30.6 pr. 100.000 fuldtidsarbejdere, hvilket vil sige en næsten uændret rate gennem de seneste 10 år. Komplikationerne til sygdommen er kronisk svære eksemforandringer, langvarigt sygefravær og manglende tilknytning til arbejdsmarkedet. Information om risikofaktorer og risikoerhverv er nødvendig for at kunne tilrettelægge en effektiv forebyggende indsats. Afhandlingens formål har været at identificere højrisikogrupper og prognostiske risikofaktorer for svært kronisk eksem, langvarig sygemelding og manglende tilknytning til arbejdsmarkedet. Herudover er der foretaget en sammenligning mellem selvvurderet og lægevurderet sværhedsgrad af håndeksem, ligesom en vurdering af livskvalitet og depressive symptomer er foretaget. Fra oktober 2001 til november 2002 (58 uger) blev 758 patienter med anerkendt arbejdsbetinget håndeksem inkluderet. Data blev indhentet dels fra Arbejdskadestyrelsens register og dels fra to spørgeskemaer udsendt ved baseline og efter 12 måneders follow-up.
De væsentligste resultater var følgende:

Risikoerhverv med højeste rate af arbejdsbetinget håndeksem, var bagere, frisører, tandklinik assistenter, kokke og køkkenmedhjælpere.
Den kvantitativt største gruppe var sundhedsarbejdere (21% af populationen).
I modsætning til en række andre arbejdsbetingede sygdomme, rammer håndeksem som hovedregel yngre personer og gennemsnitsalderen i studiepopulationen var også lav: 35,4 år. Heraf var ca. 2/3 kvinder. Irritativt kontakteksem var den hyppigst forekommende håndeksem diagnose hos både mænd og kvinder (62%), efterfulgt af allergisk kontakteksem (21%) og kontakt urticaria (5%). Prævalensen af patienter med atopisk eksem var 16%. Divergensen mellem patienters og lægers vurdering af eksemsværhedsgrad var stor. 18% blev læge-vurderet som svære eksemer, mens 40% af patienterne selv vurderede deres eksem som svært. Det anbefales derfor, at man i fremtidige studier inddrager begge vurderinger for at få et mere nuanceret indtryk af sværhedsgraden af arbejdsbetinget eksem.

14% af studie populationen havde moderat til svær påvirkning af deres livskvalitet ved baseline og kun en mindre andel forbedrede deres livskvalitet efter 12 måneders follow-up (ca. 2-3%). Lav livskvalitet var associeret til lav socialklasse, depression og moderat/svært eksem. Prævalensen af moderate til svære depressoner var 9% og svarer til prævalensen i normalbefolkningen.

De sociale og samfundsmæssige konsekvenser af sygdommen er markante. 19% af de undersøgte havde haft sygefravær mere end 5 uger på et år ved baseline. I løbet af 12 måneders follow-up havde 48% skiftet arbejde mindst én gang. 23% af studiepopulationen rapporterede, at de var blevet afskediget p.g.a. deres håndeksem i året op til anerkendelsen og yderligere 4% i løbet af 12 måneders follow-up. 25% af studiepopulationen havde fortsat svært eksem eller forværring efter 12 måneders follow-up, 41% var blevet bedre og 34% var uændret milde til moderate. Patienter med atopisk eksem og patienter over 25 år klarede sig markant dårligere end andre patientgrupper både ved baseline og efter 12 måneders follow-up.

Hvis man havde fået vurderet svært håndeksem ved indgangen i studiet, fandt vi en 5 gange så stor risiko for at få langvarigt sygefravær det kommende år og en 14 gange så stor risiko for at miste sit job, som hvis man var vurderet til at have ingen eller minimalt eksem. Patienter, der havde lav livskvalitet ved baseline, havde en 5 gange så stor risiko for at få langvarigt sygefravær sammenlignet med patienter med høj livskvalitet. Patienter fra de øverste socialklasser havde intet langvarigt sygefravær og ingen havde mistet deres job, hvilket adskilte dem markant fra de laveste socialklasser.

Resultaterne fra afhandlingen vil kunne bidrage til en fokuseret forebyggelsesindsats mod arbejdsbetinget håndeksem i fremtiden.

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Quality of life and depression in a population of occupational hand eczema patients

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Running head: QoL, depression and occupational hand eczema

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Summary

Background

Occupational hand eczema (OHE) is the most frequently recognised occupational disease in Denmark and despite governmental attempts to reduce exposures to harmful occupational allergens the number of recognized chronic cases has remained almost unchanged during the past decade. Some studies have indicated that OHE not only cause skin problems but also has considerable impact on quality of life (QoL) and may lead to depressions.

Objective

The aims of the study were to estimate risk factors for low QoL and to determine the frequency and severity of depression among OHE patients in relation to demographic data, diagnosis, disease duration and socioeconomic status. Furthermore, we aimed to estimate the overall changes in QoL and depression after 12 months of follow up.

Patients and methods

The study population, 758 patients, comprised all new recognized cases from the Danish National Board of Industrial Injuries Registry between October 2001 and November 2002. Data on demographics, severity, socioeconomic status and diagnoses were obtained from the registry. All patients received a questionnaire package by mail, which included screening instruments to measure QoL and depressive symptoms. A similar follow up questionnaire was mailed to each responder after one year. The response rate was 82% at baseline and 91% at follow up, respectively.

Results and conclusions

The mean Dermatology Life Quality Index total score was 5.5 and 7.8 for severe OHE cases, which rank the disease just below atopic dermatitis and psoriasis in impairment of QoL. Severe OHE cases and lower socioeconomic status were associated with low QoL. The prevalence of moderate to severe depression were 9% at baseline and 12 months later, which is similar to what is found for the general population. Only minor changes in QoL and depressive symptoms were found after 12 months of follow up.

Key words: Health-related quality of life - occupational skin disease – psychosocial factors – socioeconomic status

Introduction

Occupational hand eczema (OHE) is the most frequently recognised occupational disease in Denmark with an incidence rate of approximately 0.32 per 1000 person-years (800 new cases/2.5 mill. workers per year [1]. This incidence rate is higher than the incidence rate in United Kingdom [2] but slightly lower than what has been reported in Germany [3] and USA [4]. National registries are, however, not directly comparable, due to differences in the sample population, definitions of diagnosis, clinical examination and differences in notification procedures.

Despite governmental attempts to reduce exposures to harmful occupational allergens, the number of new OHE cases in Denmark has remained almost unchanged during the past decade [1]. Complications and consequences of occupational contact dermatitis include chronic severe eczema, prolonged sick leave and unemployment [5-8]. Some studies have also indicated that OHE has impact on quality of life (QoL), but these studies are few and relatively small [9-12]. Other studies suggest that patients with contact dermatitis may experience more depressive symptoms than healthy controls [13;14]. It is possible that the presence of a depression may have serious implications for OHE patients, e.g. premature discontinuation of treatment or lack of compliance, which in part may explain why so many patients become chronic cases.

The aims of the present study were to estimate the extent of impairment in QoL and potential risk factors of low QoL. We also aimed to determine the frequency and severity of depressive symptoms among OHE patients in relation to demographic data, diagnosis, disease duration and socioeconomic status and to study the overall changes in QoL and depressive symptoms after 12 months follow up.

Material and methods

Patients

Patients were identified from the Danish National Board of Industrial Injuries (DNBII) Registry. The study population comprised all new recognised cases between October 2001 and November 2002, 18 years of age or older. Basic demographics as well as DNBII-rated severity [7], socioeconomic status and diagnoses were obtained from the registry. All patients received a questionnaire package by mail that included screening instruments measuring depressive symptoms and perceived impairment of QoL. One year after the baseline questionnaire was returned, a similar follow up questionnaire was mailed to each responder.

Classification of diagnoses

The classification of diagnosis was based on the clinical examination by a dermatologist, including patch test and when relevant skin prick test. All patients were patch tested with the European Standard series as a minimum. If indicated, additional testing were performed as for e.g. hairdressers, dentists, bakers etc. All patients were categorized into five main diagnostic groups: (1) occupational irritant contact dermatitis (ICD); (2) occupational allergic contact dermatitis (ACD); (3) occupational contact urticaria (CU); (4) ICD + ACD and (5); ICD + CU. The patients were also categorized into sub diagnostic groups by the presence or absence of atopic dermatitis (AD) and by the presence or absence of non-occupational allergic contact dermatitis (NOACD). AD was in this study defined as past flexural eczema or currently diagnosed AD by a dermatologist. NOACD was defined as a positive patch test result for a non-occupational exposure.

Socioeconomic status

We used the socioeconomic classification system: Socio97, 1st edition 1997, Statistics Denmark, which is a system based upon educational requirements and managerial job responsibilities. In the analysis we used 4 categories of socioeconomic status as follows: 1) students and trainees 2) high/medium level 3) basic level and 4) lowest level.

The questionnaires.

All responders were asked to complete the Dermatology Life Quality Index (DLQI) [15;16] and the Beck Depression Inventory (BDI-II) [17]. The DLQI is a 10-item questionnaire measuring QoL in patients with skin disease. The 10 items cover 6 aspects of daily life experienced during the past week: (i) symptoms and feelings (items 1, 2), (ii) daily activities (items 3, 4), (iii) leisure (items 5, 6), (iv) work and school (item 7), (v) personal relationships (items 8, 9) and (vi) treatment (item 10). Each item is assigned a score of 0 ("not at all") to 3 ("very much). The DLQI total scores are calculated by summing the score of each question, resulting in a maximum of 30 and a minimum of 0. The higher the score, the greater the impairment of QoL. The scores can be expressed as absolute or percentages scores.

The BDI-II is a 21-item questionnaire measuring depressive symptoms during the past 2 weeks. Each item is assigned a score of 0-3, with 3 indicating the most severe symptoms. A cumulative score is obtained by adding the scores of the individual items. The responders are classified as: (i) No or minimal depression (score 0-13), (ii) Mild depression (score 14-19), (iii) Moderate depression (score 20-28) and (iv) Severe depression (score 29-63).

The patients were also asked to answer a number of questions concerning self-rated disease severity, disease duration and current work status.
Details about this part of the questionnaire have been reported elsewhere [7;18].

Statistics

All analyses were performed in STATA version 8.2 (Stata Corp., College Station, TX, U.S.A.). We dichotomized the DLQI total score into high QoL (score 0-10) and low QoL (score >11) [19] as well as depressive symptoms in low (BDI-II total score 0-19) and high (BDI-II total score 20-63). To identify potential predictors for low QoL and high depressive symptoms, we performed two Poisson regression models [20].

Results

Demographics

The study population comprised 268 males and 490 females at recruitment. At baseline 213 males and 408 females (response rate = 82 %) returned the questionnaire. A total of 564 responded to the follow up questionnaire (response rate = 91%). Significantly fewer males (83.6%) responded at follow up than females (94.6%) ($p<0.001$). No other variable but gender showed any large difference between responders and non-responders [18]. Mean age at baseline was 35.8 years.

Quality of Life

The mean total sum scores at baseline showed little variation in QoL impairment across subgroups and we found a mean total DLQI score of 5.5 (range: 0-26; SD = 4.8). It should, however, be noted that 31% of all patients were categorized with no or minimal severity. Regarding the 6 DLQI category scores based on the 10 DLQI items, we found that the categories "work/school" together with "symptoms and feelings" were the most severely affected at baseline compared with the other category groups ("daily activities", "leisure", "personal relationships" and "treatment").

We found no significant differences between males and females for any of the 6 different score categories. We found strong associations between mild to moderate OHE (PR = 3.5; 95% CI (1.8 – 7.0) and severe OHE cases (PR = 3.7; 95% CI (1.7 – 7.7) and low QoL at baseline compared with patients with no to minimal OHE (Table 1). Furthermore, the risk of low QoL at baseline was 2 times higher among patients with lower socioeconomic status (Table 1). Also depression was strongly associated with low QoL (PR = 3.8; 95% CI (2.5 – 5.6). We found no significant associations between low QoL and sex, age, different diagnostic groups, disease duration or occupations. The mean total DLQI scores increased with increasing severity as seen in Table 2. We only found a modest overall improvement in QoL from baseline to follow up (86% had high QoL at baseline and 89% had persistently high or improved QoL after 12 months follow up). We found no large differences in QoL changes between severity strata (Table 2).

Depression

A total of 9% of the study population at baseline and at 12 months follow up showed signs of moderate to severe depression (Table 3). We found a mean BDI-II total score at baseline at 7.1 (range 0-41; SD = 7.4). We found significantly more depressed patients among patients aged between 30 to 39 years (Table 1). Low QoL appeared to be strongly associated with high BDI-II score (PR = 4.5; CI (2.6 – 7.9)). We found no significant associations between high BDI-II score and sex, socioeconomic status, diagnoses, severity or disease duration.

Discussion

Low QoL scores in patients with contact dermatitis have been reported previously and our study support these findings [8-13;15;21-26]. A mean DLQI at 7.8 for severe OHE patients is in accordance with earlier findings and rank the disease just below AD and psoriasis [15;21;24;27]. Not surprisingly, we found strong associations between high degree of severity and low QoL. We also found that patients with lower socioeconomic status reported substantially lower QoL compared with patients with high/medium socioeconomic status, which has not previously been published. One explanation may be that patients with higher socioeconomic status perform better in avoiding direct causes of their disease [28-30] or comply better with treatment and medical consultations. We suggest that increased health education coordinated with intensified medical care should be provided to patients who are socially and economically disadvantaged.

A recent Swedish study on hand eczema and QoL found that more females reported impairment of daily activities than males after 15 years of follow up [8], but our findings did not support this. In agreement with other studies, no significant associations were found between impairment in QoL and age, sex, diagnoses, disease duration or occupations [9;10;12;24]. Patients with ACD have been reported to improve in QoL after patch test in several publications [11;24;25], but due to the data source in this study, we were not able to verify that. It is a general assumption that QoL may be significantly impaired during the process of workers compensation. If so, one would expect QoL to increase once the disease has been acknowledged as an occupational disease by the DNBII. The slight improvement of DLQI after 12 months of follow up did not fulfil this expectation and indicate that the time after recognition of OHE also may cause difficulties in many aspects of daily life.

It is important to acknowledge that QoL questionnaires do not measure all aspects of QoL. QoL is a multidimensional concept with individual meaning to each patient. This complexity can of course not be captured in one score value. Furthermore, the DLQI has only 2 questions that indirectly refers to employment issues. A disease-specific QoL questionnaire targeted OHE patients would ideally include more questions about work-related impairment of both physical functioning and interaction with colleagues [31].
It is therefore possible that our associations with QoL would be different if we had access to a disease-specific QoL questionnaire.

The distribution of depressive symptoms in our cohort was similar to what we would expect in the general population [13]. The high proportion of depressive symptoms among patients aged 30-39 years, as compared to older as well as younger patients, may be due to an incidental statistical finding.

Conclusions

We estimated a mean DLQI total score at 5.5 for all OHE patients and 7.8 for severe OHE patients, which rank the disease just below AD and psoriasis in impairment of QoL. As expected, moderate to severe OHE cases were associated with impaired QoL but as something new we found lower socioeconomic status strongly associated with low QoL. With respect to depression we found prevalences similar to the general population. Only minor changes in QoL and depressive symptoms were found after 12 of months follow up.

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Table 1.
Frequencies, prevalences and prevalence proportions (PR's) for high (total DLQI score 0-10) and low QoL (total DLQI score 11-30) and high (total BDI-II score 20-63) and low (total BDI-II score 0-19) depressive symptoms.

	Quality of life			Depressive symptoms		
Variable	High (%)	Low (%)	PR	Low (%)	High (%)	PR (95%-CI)
Sex						
Males	173 (83.6)	34 (16.4)	1	197 (94.3)	12 (5.7)	1
Females	350 (86.2)	56 (13.8)	0.9 (0.6 – 1.5)	364 (89.9)	41 (10.1)	1.8 (0.8 – 4.0)
Age (years)						
18-24	115 (87.1)	17 (12.9)	1	126 (95.5)	6 (4.6)	1
25-29	90 (85.7)	15 (14.3)	0.9 (0.5 – 1.8)	97 (91.5)	9 (8.5)	2.0 (0.8 – 5.1)
30-39	154 (85.6)	26 (14.4)	1.1 (0.5 – 2.2)	158 (88.3)	21 (11.7)	**2.4 (1.0 – 5.4)**
40-49	83 (84.7)	15 (15.3)	1.1 (0.5 – 2.2)	88 (89.8)	10 (10.2)	1.7 (0.6 – 4.8)
50+	81 (82.7)	17 (17.4)	1.1 (0.5 – 2.2)	92 (92.9)	7 (7.1)	1.0 (0.3 – 3.2)
SES						
Students/trainees	102 (90.3)	11 (9.7)	1	104 (92.0)	9 (8.0)	1
High/medium level	79 (92.9)	6 (7.1)	0.9 (0.3 – 2.5)	82 (97.6)	2 (2.4)	0.3 (0.1 – 1.2)
Basic level	213 (81.6)	48 (18.4)	**2.0 (1.0 – 3.9)**	238 (90.5)	25 (9.5)	1.0 (0.4 – 2.3)
Lowest level	125 (83.9)	24 (16.1)	1.9 (0.9 – 4.0)	132 (88.6)	17 (11.4)	1.2 (0.5 – 2.7)
Diagnosis						
ACD	112 (86.8)	17 (13.2)	1	121 (93.1)	9 (6.9)	1
ICD	320 (83.6)	63 (16.5)	1.0 (0.6 – 1.8)	351 (91.4)	33 (8.6)	1.4 (0.6 – 3.1)
CU	28 (96.6)	1 (3.5)	0.4 (0.1 – 2.0)	27 (96.4)	1 (3.6)	0.6 (0.1 – 3.4)
ICD+ACD	48 (87.3)	7 (12.7)	0.5 (0.2 – 1.2)	46 (83.6)	9 (16.4)	2.1 (0.8 – 5.4)
ICD+CU	15 (88.2)	2 (11.8)	0.8 (0.3 – 2.5)	16 (94.1)	1 (5.9)	1.2 (0.2 – 9.1)

SES = socioeconomic status, ACD = allergic contact dermatitis, ICD = irritant contact dermatitis, CU = contact urticaria, DNBII = Danish National Board of Industrial Injuries, QoL = quality of life, DLQI = dermatology life quality index, BDI-II = Beck's depression inventory II, CI = confidence intervals.

Table 1 continues next page

Table 1 continued

	Quality of life			Depressive symptoms		
Variable	High (%)	Low (%)	PR	Low (%)	High (%)	PR (95%-CI)
AD						
No	436 (85.7)	73 (14.3)	1	464 (91.0)	46 (9.0)	1
Yes	87 (83.7)	17 (16.4)	1.4 (0.8 – 2.5)	97 (93.3)	7 (6.7)	0.7 (0.3 – 1.5)
NOACD						
No	364 (84.9)	65 (15.2)	1	400 (93.2)	29 (6.8)	1
Yes	159 (86.4)	25 (13.6)	0.7 (0.4 – 1.1)	161 (87.0)	24 (13.0)	1.6 (0.9 – 2.6)
Severity (DNBII)						
No/minimal	181 (94.8)	10 (5.2)	1	176 (92.2)	15 (7.9)	1
Mild/moderate	257 (82.6)	54 (17.4)	**3.5 (1.8 – 7.0)**	289 (92.6)	23 (7.4)	0.6 (0.3 – 1.2)
Severe	85 (76.6)	26 (23.4)	**3.7 (1.7 – 7.7)**	96 (86.5)	15 (13.5)	0.8 (0.4 – 1.7)
Duration (years)						
0 to <2	80 (88.9)	10 (11.1)	1	85 (94.4)	5 (5.6)	1
2 to <3	120 (90.9)	12 (9.1)	0.8 (0.4 – 1.7)	122 (92.4)	10 (7.6)	1.7 (0.7 – 4.4)
3 to <6	142 (81.1)	33 (18.9)	1.7 (0.9 – 3.2)	161 (92.0)	14 (8.0)	1.5 (0.6 – 3.9)
6 to 51	161 (85.2)	28 (14.8)	1.4 (0.7 – 2.6)	171 (90.0)	19 (10.0)	1.6 (0.7 – 4.0)
Occupation						
Wet	220 (86.6)	34 (13.4)	1	228 (90.1)	25 (9.9)	1
Food	96 (84.2)	18 (15.8)	1.0 (0.6 – 1.7)	106 (92.2)	9 (7.8)	0.8 (0.4 – 1.6)
Other	207 (84.5)	38 (15.5)	1.0 (0.6 – 1.6)	227 (92.3)	19 (7.7)	0.7 (0.4 – 1.5)
High QoI	-	-	-	492 (94.3)	30 (5.8)	1
Low QoL	-	-	-	67 (74.4)	23 (25.6)	**4.5 (2.6 – 7.9)**
Low depression	452 (89.5)	53 (10.5)	1	-	-	-
High depression	70 (65.4)	37 (34.6)	**3.8 (2.5 – 5.6)**	-	-	-

SES = socioeconomic status, ACD = allergic contact dermatitis, ICD = irritant contact dermatitis, CU = contact urticaria, DNBII = Danish National Board of Industrial Injuries, QoL = quality of life, DLQI = dermatology life quality index, BDI-II = Beck's depression inventory II, CI = confidence intervals.

Table 2. Mean DLQI and changes in quality of life (QoL) during 12 months of follow up, in the total study population and by severity at baseline.

	Mean DLQI at baseline	High QoL at baseline (0-10)	Low QoI at baseline (11-30)	Persistently high QoL or improved QoL after 1 year	Persistently low QoL or after 1 year
Total study population	5.5	463 (86.2%)	74 (13.8%)	475 (88.5%)	62 (11.6%)
Severity*					
No/minimal	3.3	149 (94.3%)	9 (5.7%)	150 (94.9%)	8 (5.1%)
Mild/moderate	6.0	238 (83.8%)	46 (16.2%)	251 (88.4%)	33 (11.6%)
Severe	7.8	76 (80.0%)	19 (20.0%)	74 (77.9%)	21 (22.1%)

*Severity rated by The Danish National Board of Industrial Injuries at baseline. DLQI = Dermatology Life Quality Index. High QoL = DLQI total score (0-10), low QoL = DLQI total score (11-30).

Table 3. Frequency and proportion of occupational hand eczema patients by level of depression at baseline and at 1-year follow up.

Level of depression	Frequency (%) at baseline	Frequency (%) at
follow up		
No/minimal	470 (83)	453 (80)
Mild	46 (8)	60 (11)
Moderate	32 (6)	42 (8)
Severe	14 (3)	8 (1)
Missing values	2 (0.4)	1 (0.2)
Total	564	564

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Prognosis of occupational hand eczema - a follow up study.

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Key words: depression - health-related quality of life – occupational skin disease - predictor – socioeconomic status

It is hereby stated that the data in this manuscript is original and this paper is not under consideration elsewhere. None of its contents have been previously published. All authors have read and approved all versions of the manuscript, its contents and its submission to Archives of Dermatology. It is also herby stated that I, Dr. Rikke Cvetkovski have full access to all the data in the study and I take responsibility for the integrity of the data and the accuracy of the data analysis. Neither me nor my co-workers have any finansial interests in this manuscript. All persons who have made substantial contributions to the work reported, but who are not authors, are named in the ackowledgement and have given me their written permission to be named.

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Abstract

Objective

To identify prognostic risk factors for occupational hand eczema (OHE) patients.

Design

The study was designed as a cohort study with one year follow up.

Setting

All new cases (758) of recognized OHE were identified from the Danish National Board of Industrial Injuries Registry in the period October 2001 – November 2002. All participants received a questionnaire with questions about self-rated severity, sick leave, loss of job, depression and health-related quality of life. One year after the questionnaire was returned, all responders (621 cases) received a follow up questionnaire and 564 patients returned the follow up questionnaire (91%).

Main outcome measures

Persistently severe or aggravated cases, prolonged sick leave and loss of job after 1-year follow up.

Results and conclusions

During the 12 months of follow up, 25% of all OHE patients had persistently severe or aggravated disease, 41% had improved and 34% had unchanged mild to moderate disease. Patients with atopic dermatitis fared badly compared with other patients. Patients aged less than 25 years fared clearly better than older age groups. Furthermore, severe OHE, age 40 years or above and severe impairment of QoL at baseline appear to be important predictors of prolonged sick leave and unemployment. This study also indicates that patients with lower socioeconomic status are a vulnerable subgroup, with high risk of prolonged sick leave, job change and loss of job. Contact allergy on the other hand was not found to be a risk factor of a poor prognosis.

Background

Occupational hand eczema (OHE) has become a disease of increasing importance during the past decades because of its serious consequences such as frequent eruptions and risk of prolonged sick leave[1-7]. Previous studies also indicate that OHE has an appreciable impact on quality of life (QoL) although the number of publications are limited [8-10]. The magnitude of the problem is supported by the fact that OHE is the most frequently recognized occupational disease in Denmark and many Western countries [11;12]. OHE may occur at any age, but is most common among young female workers [11-14].

Previous studies have not identified any strong prognostic predictors of a poor prognosis, although the presence of atopic dermatitis (AD) or allergic contact dermatitis (ACD) has been related to more severe outcome [10;15-17] . It has been suggested that patients with contact dermatitis may experience depressive symptoms [18-20] .

So far, there is no data on the possible associations between depression and the prognosis of OHE patients available. Poor socio-economic status has been shown to affect outcome adversely in many chronic disorders [21-28] but no current data is available for OHE patients. The aim of this study was to identify risk factors for a poor prognosis defined as persistent severe or aggravated OHE, prolonged sick leave and loss of job due to OHE in the year following recognition by the Danish National Board of Industrial Injuries (DNBII).

Setting

The study population and study design

The cohort comprised all new cases of recognized OHE who were 18 years old or more of age at the time of registration at the DNBII registry from October 2001 to November 2002 (58 weeks). Our clinical observations suggest that patients are especially vulnerable at an early stage of the disease. We therefore decided to evaluate the prognosis already after one year of follow up.

Data on diagnosis and sub-diagnosis of OHE, severity assessment of OHE and socioeconomic status for each person enrolled were registered. Socioeconomic status was measured using the socioeconomic classification system: Socio97, 1st edition 1997, Statistics Denmark, which is a system based upon educational requirements and managerial responsibilities in the job. In the analysis we used 4 categories of socioeconomic status.

To supplement the information from the DNBII we used two postal questionnaires. The baseline questionnaire was mailed within 1-2 weeks of case registration. The follow up questionnaire was mailed one year after the baseline questionnaire had been returned.

Classification of diagnoses and subdiagnoses

The classification of diagnosis was based on the clinical examination by a dermatologist of each patient, including patch test and skin prick test. All patients were patch testet with the European Standard Series as a minimum. Specific occupations or specific exposures were given additional tests with relevant allergens such as patch test series for hairdressers, bakers, dentists, rubber gloves, plastic exposure. [29]. All patients were categorized into only one of five main diagnostic groups: (i) occupational irritant contact dermatitis (ICD); (ii) occupational allergic contact dermatitis (ACD); (iii) occupational contact urticaria (CU); (iv) ICD + ACD and (v); ICD + CU. Patients with occupational hyperkeratotic or frictional hand ezcema cases were classified as ICD.

The patients were also categorized into subdiagnostic groups by the presence or absence of atopic dermatitis (AD) and by the presence or absence of non-occupational allergic contact dermatitis (NOACD). AD was in this study defined as past flexural eczema or currently diagnosed AD by a dermatologist. NOACD was defined as a positive patch test result for a non-occupational exposure.

Questionnaires

Severity, sick leave and loss of job

Severity was assessed both by the DNBII and by the patients. The DNBII severity assessment was based on medical certificates from dermatologists. This severity assessment was based on the intensity of the skin response as well as the frequency of eruptions and extension on the hands [30]. We categorized the DNBII severity assessment into 3 groups: (i) No/minimal OHE, (ii) mild/moderate OHE and (iii) severe OHE.

All patients were asked to rate their disease severity on a 100 mm visual analogue scale (VAS).

The exact wording of the question was: *How would you grade your occupational hand eczema on a scale from 0-10 during the past 12 months? 0 meaning no eczema and 10 meaning extremely severe eczema.* The participants were also asked whether or not they had taken any sick leave due to their OHE during the past 12 months. If the answer was "yes", they were asked for how long, and then asked to summarize all episodes of sick leave into one of the following fixed answering categories: < 1 week, 1-2 weeks, 3-5 weeks or more than 5 weeks. The participants were also asked, whether they had lost their job during the past 12 months due to their OHE.

Depression and health-related quality of life

All participants were asked to complete the Beck Depression Inventory (BDI-II) [31] and the Dermatology Life Quality Index (DLQI) [32]. The BDI-II is a 21-questionnaire measuring depressive symptoms experienced during the past 2 weeks. Each item is assigned a score of 0-3, with 3 indicating the most severe symptoms. A cumulative score is determined by adding the scores of the individual items. The responders are grouped based on their

BDI-II total scores using the following classification: (i) No or minimal depression (score 0-13), (ii) Mild depression (score 14-19), (iii) Moderate depression (score 20-28) and (iv) Severe depression (score 29-63).

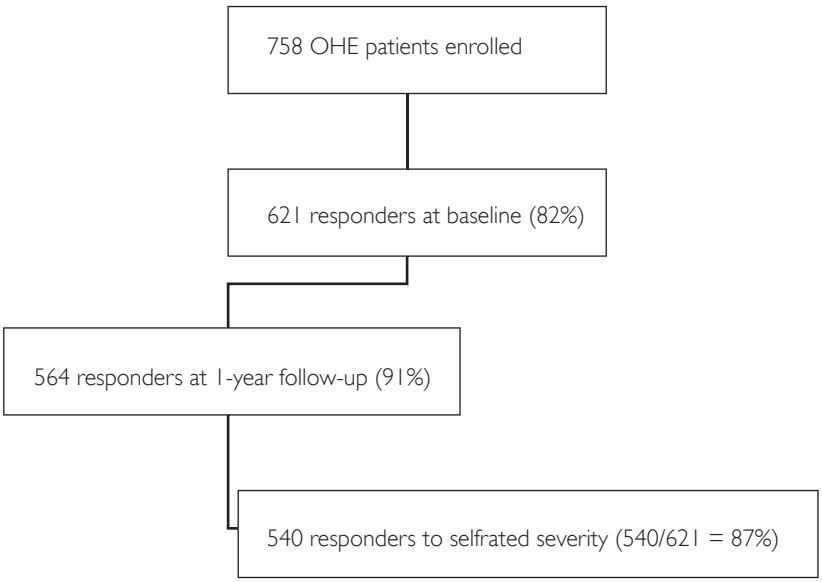
The DLQI is a 10-item questionnaire measuring QoL in skin disease [32;33]. The 10 items covers 6 aspects of daily life experienced during the past week: (i) symptoms and feelings (items 1,2), (ii) daily activities (items 3,4), (iii) leisure (items 5,6), (iv) work and school (item 7), (v) personal relationships (items 8,9) and (vi) treatment (item 10). Each item is assigned a score of 0 ("not at all") to 3 ("very much). The DLQI total scores are calculated by summing the score of each question, resulting in a maximum of 30 and a minimum of 0. The higher the score the greater the impairment of QoL. The scores can be expressed as absolute or percentages scores.

Main outcome measures

Definitions of prolonged sick leave and a poor prognosis

Sick leave due to OHE more than 5 weeks the past 12 months was considered as prolonged sick leave. If a patient was categorized as having prolonged sick leave at baseline it was classified as previous prolonged sick leave in the following analyses. Changes in severity after one year of follow up were categorized as: aggravation, no change or improvement of OHE. If a patient had severe OHE at baseline and did not improve in one year we classified this patient with a poor prognosis. Thus a poor prognosis was defined as either aggravated or persistent severe OHE.

Flowchart



A total of 758 patients met the inclusion criteria. A baseline questionnaire was mailed to all participants 1-2 weeks after registration of a case. One year after we received the questionnaire, a follow up questionnaire was mailed to all responders. 564 persons returned the follow up questionnaire and 540 completed the item with regard to self-rated severity.

Analytic methods

All analyses were performed in STATA version 8.2 (Stata Corp., College Station, TX, U.S.A.). The VAS-scores were transformed from mm to percentage e.g. 64mm = 64%. The VAS-scores were then divided into 3 equal sized groups as follows: (i) No/minimal OHE (< 33.3%), (ii) Mild to moderate OHE (33.3% - 66.6%) and (iii) Severe OHE (66.6%-100%). DLQI total scores at baseline were dichotomized into high QoL (DLQI total score 0-10) and low QoL (DLQI total score 11-30) [34]. We dichotomized depression status into minimal to mild depressive symptoms (BDI-II score 0-19) and moderate to severe depressive symptoms (score 20-63).

We measured prevalence proportions among patients for basic characteristics and risk ratios (RRs) for comparison of a poor prognosis across different variables, such as age, sex, diagnoses, socioeconomic status, disease duration and occupation. We also measured RRs for those taking or not taking sick leave and for those who lost their job during follow up. We estimated RRs from Poisson regression models with robust variance estimators [35]. Unemployed, early retired and other pensioned were omitted from the analyses with prolonged sick leave and loss of job.

Results

The DNBII registry had data on 758 eligible patients. The proportion lost to follow-up was 18.1% at recruitment and 13.0 % at follow-up. We found no large differences in age, sex, socioeconomic status, diagnoses or severity between responders and non-responders at baseline [13]. More females (n= 386; 94.6 % of female responders at baseline) than males (n=178; 83.6% of male responders at baseline) returned the follow-up questionnaire. We found no major difference between responders and non-responders at follow up with regards to age, severity, socioeconomic status or diagnosis (ACD, ICD, CU, ICD+ACD, ICD +CU). Severity was rated by 540 patients in both questionnaires and the Poisson regression model is based on these 540 responders. As for the items regarding sick leave and loss of job there were small differences in the number of responders and non-responders, e.g. some responders answered the item regarding sick leave and not the item regarding loss of job and vice versa.

The overall improvement was 41% but for butchers it was 11% and for doctors, dentists and veterinarians it was 67%. The overall proportion of persistently severe or aggravated symptoms were 25%, also with broad differences between subgroups e.g hairdressers 37% and for doctors, dentists and veterinarians 0% (Table 1). The most severely affected subgroups were butchers, kitchen workers/cooks, hairdressers and patients aged 40-49 years. As seen in Table 1, the proportion of improved cases were similar among cases who reported job change during 12 months follow up and those who reported no job change. Chromium positive patients also did not show any signs of a poor prognosis. Only 12% of chromium positive patients had aggravated or persistently severe disease (data not shown). We found no statistically significant association between a poor prognosis and sex, ACD, ICD, CU, NOACD, disease duration, occupation or socioeconomic status,

although a slight tendency towards a protective effect of high/medium socioeconomic status was found. Almost 48% of the study population reported job change during the 12 months of follow up. Job change was associated with younger age groups (52% of those who reported job change were below 25 years of age) and lower socioeconomic status (57% from the lowest level reported job change compared with 24% from the highest level). As seen in Table 3 prolonged sick leave was significantly associated with a) having occupational CU, b) age above 25 years (with statistically significance for the age group 40 to 49 years) and c) being categorized as having severe OHE at baseline by the DNBII. Self-rated severity produced similar associations as those based upon DNBII-rated severity (data not shown). Severe impairment of QoL at baseline as well as previously reports of prolonged sick leave were strongly associated with the risk of prolonged sick leave during follow up. We found a favorable prognosis for patients with high/medium socioeconomic status (no patients with prolonged sick leave in this group). We found no important associations between prolonged sick leave and age, ACD, ICD, AD, NOACD, disease duration, occupation or the presence of depression.

As seen in Table 4 strong associations were found between having severe OHE (RR = 14.0, 95%-CI 1.9 – 102.9) at baseline and loss of job during the follow up. Again, we found a favorable prognosis for patients with high/medium socioeconomic status (no patients with loss of job in this group).

Discussion

We found an overall improvement of OHE after one year follow up as expected due to "regression towards the mean" [36;37]. However, we found large variability among different sub-groups, which can not entirely be explained by this phenomenon. Almost 41% of the study population reported improvement during 12 months follow up, which is lower than what was reported in a resent Swedish study with 15 years of follow up in a cohort of occupational and non-occupational hand eczema [7]. Meding and colleagues reported that 74% improved during the 15 years of follow up.

Poor prognosis and age, sex and socio-economic status

Age less than 25 years old was found to be a significant protective factor against a poor prognosis, which supports earlier findings [8]. As in previous studies we found no effect of sex on the prognosis [17;38] although contradictory findings have been published [7;8;39]. Poor socioeconomic status has been shown to affect outcome adversely in many chronic disorders [23-28]. We found that the prognosis of OHE in terms of aggravated or persistently severe disease, was clearly better for patients with high/medium socioeconomic status at baseline after one year, but the association was not statistically significant.

Poor prognosis and diagnoses

After 1-year follow up we found that patients with AD had a 1.5 higher risk of aggravation

or persistently severe OHE compared with patients without AD, which is consistent with previous findings [17;30;38;40]. The prognosis has been reported worse for ACD than ICD in earlier papers [17;39;41-44] but our results does not support this. We have previously reported that ICD patients at baseline had a higher proportion of severe OHE than ACD patients [30], however at 1-year follow up we could no longer detect any significant differences between the two diagnostic groups. Chromium has previously been associated with a poor prognosis [40;43;45;46] but our findings could not confirm that, but the number of chromium positive patients were relatively small in the present study. In a study from 1975 Fregert [41] reported that the prognosis was especially poor in women with nickel allergy. Danish legislation, since 1991, has led to a reduction of nickel exposure, which may be one of the reasons why we found no association between NOACD and a poor prognosis. The NOACD subgroup in our study consisted predominantly of females with non-occupational nickel allergy [13].

Sick leave, job change and loss of job

Our results support previous reports of age as a risk factor for prolonged sick leave [3]. For patients with high or medium socioeconomic status there were no reports of taking prolonged sick leave or loss of job at all. This tendency is in accordance with earlier studies among dentists in Sweden [47;48] and the results indicate that lower socioeconomic status is an important risk factor of prolonged sick leave and loss of job. Not surprisingly we found that severe OHE cases at baseline had a significantly higher risk of taking sick leave in the year following recognition than mild cases, which support results from previous studies [30]. Severe OHE cases were, however also at considerably higher risk of losing their job during follow up time, which to the best of our knowledge, has not previously been reported. Independently of OHE severity, severe impairment of QoL at baseline was a strong predictor of prolonged sick leave, which underline the importance of measuring the patients' perceived health-related QoL. We found no significant associations between prolonged sick leave and the presence of depression.

We could also not corroborate earlier findings that patients with ACD have a higher risk of prolonged sick leave [3;30;42]. Occupational CU appeared to be associated with a high risk of prolonged sick leave, which may be related to strict hygiene regulations in food-related occupations but most likely due to chance We found no association between sex and prolonged sick leave, which support earlier findings [7]. Almost 50% of the study population had changed their job during the 12 months of follow up, which is high compared to the study by Meding et al [7]. She found that only 3% of the study population had changed their job during 15 years of follw up, indicating that change of job occur at an early stage of OHE. In our study we found no significant improvement of the disease after the change of job, which is in line with the findings of Meding et al [7]. She found that many patients change jobs from low-risk jobs to high-risk jobs. Patients with high/medium socioeconomic status in our study had a tendency to change job less often than patients with lower socioeconomic status., which may indicate that job modification is easier for this group.

Bias

Potential sources of bias in this study arise from selective referral and losses to follow up. The number of notified and thereby recognized cases does not necessarily reflect the true number of patients with OHE, because mild cases with short disease duration may be missed, although we had more than 30% mild cases in the cohort. It is important to note that there were no appreciable differences in age, sex, diagnosis, socioeconomic status or severity at baseline between those who returned both questionnaires and those who were lost to follow up, except a high proportion of male non-responders at follow up. Our information on job changes and changes in disease status do not include information on the time of change. Conclusions about job change and prognosis should therefore be made with caution.

Conclusions

Predictive factors could be used by clinicians to guide to treatment and to select early risk management strategies. In order to avoid prolonged sick leave that may lead to social and economic deroute, physicians must try to identify subgroups of patients who are in greater risk of a poor outcome than others. We identified patients with AD as a prognostic risk factor of either persistently severe or aggravated disease, which support earlier findings. Furthermore we found that patients aged less than 25 years and high/medium socioeconomic status compared with older age groups and low socioeconomic status fared clearly better with regards to prolonged sick leave and loss of job. This indicates that socioeconomic status may have a place in the currently rather limited number of reliable prognostic factors in early OHE. Also not previously reported, we found that severe OHE and severe impairment of QoL at baseline were strong prognostic predictors of prolonged sick leave. This indicates that QoL and standardized severity assessment may be valuable tools in order to identify patients in high risk of prolonged sick leave and unemployment.

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Legends

Table 1.
Frequencies and prevalence proportions of changes in self-rated severity of OHE after one-year follow-up by sex, age, socio-economic status, diagnosis, atopic dermatitis and occupation.

Table 2.
Effects of selected variables (age, sex, socio-economic status, diagnoses and atopic dermatitis) on aggravation or persistent severe occupational hand eczema after one year of follow up in a Poisson regression model with 95%- robust confidence intervals.

Table 3.
Frequencies, proportions and risk ratios (RRs) with 95% robust confidence intervals in a Poisson regression model for prolonged sick leave after 1-year follow up for workers diagnosed with OHE by age, sex , socioeconomic status, diagnosis, sub-diagnosis, severity, disease duration, occupation, depression and impaired quality of life (QoL). Unemployed, early retired and other pensioned are omitted from the analysis.

Table 4.
Frequencies, proportions and risk ratios (RRs) with 95% robust confidence intervals in a Poisson regression model for loss of job after 1-year follow up for workers diagnosed with OHE by age, sex , socioeconomic status, diagnosis, sub-diagnosis, severity, disease duration, occupation, depression and impaired quality of life (QoL). Unemployed, early retired and other pensioned are omitted from the analysis.

Table 1.

Variable	No change in severity from baseline to follow up (%)			Aggravation (%)	Improvement (%)	
	No/minimal	Mild/moderate	Severe			*Aggravation or persistent severe OHE*
Age (years) males						
18 - 24	7 (20.0)	7 (20.0)	2 (5.7)	5 (14.3)	14 (40.0)	*20.0 %*
25 – 29	3 (10.0)	5 (16.7)	8 (26.7)	4 (13.3)	10 (33.3)	*40.0 %*
30 - 39	6 (15.0)	10 (25.0)	6 (15.0)	5 (12.5)	13 (32.5)	*27.5 %*
40 – 49	3 (10.7)	5 (17.9)	6 (21.4)	3 (10.7)	11 (39.3)	*32.1 %*
50 +	3 (7.5)	5 (12.5)	5 (12.5)	4 (10.0)	23 (57.5)	*22.5 %*
Age (years) females						
18 - 24	8 (9.9)	17 (21.0)	8 (9.9)	11 (13.6)	37 (45.7)	*23.5 %*
25 – 29	6 (10.7)	11 (19.6)	10 (17.9)	7 (12.5)	22 (39.3)	*30.4 %*
30 - 39	23 (19.5)	20 (17.0)	18 (15.3)	11 (9.3)	46 (39.0)	*24.6 %*
40 – 49	10 (15.6)	16 (25.0)	6 (6.3)	4 (6.3)	28 (43.8)	*12.6 %*
50 +	9 (18.8)	10 (20.8)	7 (14.6)	7 (14.6)	15 (31.3)	*29.2 %*
SES[1]						
Students, trainees	16 (15.7)	13 (12.8)	14 (13.7)	14 (13.7)	45 (44.1)	*27.4 %*
Employee high and medium level	18 (22.5)	17 (21.3)	8 (10.0)	4 (5.0)	33 (41.3)	*15.0 %*
Employee basic level	26 (11.7)	51 (22.9)	36 (16.1)	24 (10.8)	86 (38.6)	*26.9 %*
Employee lowest level	18 (13.7)	25 (19.1)	18 (13.7)	19 (14.5)	51 (38.9)	*28.2 %*
Diagnosis						
ACD	22 (20.0)	17 (15.5)	13 (11.8)	15 (13.6)	43 (39.1)	*25.4%*
ICD	36 (10.8)	67 (20.1)	50 (15.0)	38 (11.4)	142 (42.6)	*26.4 %*
CU	10 (35.7)	5 (17.9)	1 (3.6)	2 (7.1)	10 (35.7)	*10.7 %*
ICD + ACD	7 (13.5)	15 (28.9)	7 (13.5)	3 (5.8)	20 (38.5)	*19.3 %*
ICD + CU	3 (17.7)	2 (11.8)	5 (29.4)	3 (17.7)	4 (23.5)	*47.1 %*
AD						
No	71 (16.1)	85 (19.3)	60 (13.6)	46 (10.4)	179 (40.6)	*24.0 %*
Yes	7 (7.1)	21 (21.2)	16 (16.2)	15 (15.2)	40 (40.0)	*31.4 %*

SES = socio-economic status. [1] 4 missing values. ICD = occupational irritant contact dermatitis, ACD = occupational allergic contact dermatitis, CU = occupational contact urticaria, AD = atopic dermatitis. [2] Top 10 list of occupations with poor outcome.

Table 1 continues next page

Table 1 continued

Variable	No change in severity from baseline to follow up (%)			Aggravation (%)	Improvement (%)	
	No/minimal	Mild/moderate	Severe			*Aggravation or persistent severe OHE*
Occupation at baseline2						
Butchers	2 (22.2)	2 (22.2)	3 (33.3)	1 (11.1)	1 (11.1)	*44.4 %*
Kitchen workers/cooks	10 (16.9)	9 (15.3)	14 (23.7)	8 (13.6)	18 (30.5)	*37.3 %*
Hairdressers	3 (10.0)	7 (23.3)	6 (20.0)	5 (16.7)	9 (30.0)	*36.7 %*
Factory worker	9 (17.0)	9 (17.0)	8 (15.1)	7 (13.2)	20 (37.7)	*28.3 %*
Bakers	5 (20.0)	3 (12.0)	2 (8.0)	5 (20.0)	10 (40.0)	*28.0 %*
Mixed occupations	5 (12.8)	5 (12.8)	5 (12.8)	5 (12.8)	19 (48.7)	*25.6 %*
Other tradesmen	5 (10.6)	12 (25.5)	7 (14.9)	5 (10.6)	18 (38.3)	*25.5 %*
Carpenters	1 (12.5)	0 (0.0)	1 (12.5)	1 (12.5)	5 (62.5)	*25.0 %*
Printers	1 (12.5)	1 (12.5)	1 (12.5)	1 (12.5)	4 (50.0)	*25.0 %*
Machinists	0 (0.0)	3 (25.0)	2 (16.7)	1 (8.3)	6 (50.0)	*25.0 %*
Depression						
Minimal to mild	74 (15.0)	99 (20.0)	66 (13.4)	56 (11.3)	199 (40.3)	*24.7%*
Moderate to severe	4 (8.9)	7 (15.6)	10 (22.2)	5 (11.1)	19 (42.2)	*33.3%*
Job change						
No	34 (13.3)	55 (21.5)	32 (12.5)	24 (9.4)	111 (43.4)	*21.9%*
Yes	41 (17.3)	44 (18.6)	37 (15.6)	26 (11.0)	89 (37.6)	*26.6%*
Total	14.5%	19.7%	14.1%	11.3%	40.5%	*25.4%*

SES = socio-economic status. [1] 4 missing values. ICD = occupational irritant contact dermatitis, ACD = occupational allergic contact dermatitis, CU = occupational contact urticaria, AD = atopic dermatitis. [2] Top 10 list of occupations with poor outcome.

Table 2.

Variable	Aggravation or persistant severe OHE after 1-year follow up.
Risk Ratio (95%-CI)	
Age (years)	
18-24	1
25-29	**1.94 (1.2 – 3.2)**
30-39	**1.77 (1.1 – 2.9)**
40-49	1.46 (0.8 – 2.6)
50+	1.81 (1.0 – 3.2)
Sex	
Males	1
Females	0.93 (0.6 – 1.4)
Diagnoses	
ACD	1
ICD	0.96 (0.6 – 1.4)
CU	0.38 (0.1 – 1.2)
ACD+ICD	0.63 (0.3 – 1.2)
ICD+CU	1.61 (0.9 – 3.0)
AD	
No	1
Yes	**1.53 (1.1 – 2.2)**
SES	
Lowest level	1
Basic level	1.01 (0.7 – 1.4)
High/medium level	0.56 (0.3 – 1.0)
Students/trainees	0.96 (0.6 – 1.5)
Depression	
Minimal to mild	1
Moderate to severe	1.4 (0.9 – 2.2)

ACD = allergic contact dermatitis, ICD = irritant contact dermatitis, CU = contact urticaria, AD = atopic dermatitis, SES = socio-economic status

Table 3.

Variable	Prolonged sick leave after 1-year follow up (%)	Total n	Prolonged sick leave at 1-year follow up
RR (95%-CI)			
Males	9 (5.8)	155	1
Females	17 (5.2)	325	0.97 (0.3 – 3.4)
Age (years)			
18-24	3 (2.8)	107	1
25-29	2 (2.7)	74	1.04 (0.2 – 7.2)
30-39	10 (6.9)	144	2.44 (0.6 – 9.7)
40-49	8 (10.0)	80	**5.28 (1.4 – 20.7)**
50+	3 (4.0)	75	1.44 (0.2 – 9.6)
SES*			
Lowest level	4 (3.4)	117	1
Basic level	16 (8.0)	200	2.53 (0.7 – 9.2)
High/medium level	0 (0.0)	72	NA
Students/trainees	6 (6.7)	89	2.60 (0.62 – 10.9)
Diagnoses			
ACD	3 (2.9)	102	1
ICD	16 (5.4)	297	2.90 (0.6 – 13.4)
CU	2 (8.3)	24	**16.4 (1.2 – 224.1)**
ICD +ACD	3 (6.8)	44	3.50 (0.6 – 20.5)
ICD +CU	2 (15.4)	13	3.95 (0.6 – 26.4)
AD			
No	24 (6.0)	400	1
Yes	2 (2.5)	80	0.58 (0.2 – 1.8)
NOACD			
No	18 (5.3)	338	1
Yes	8 (5.6)	142	0.73 (0.2 – 2.4)
Severity (DNBII-rated)**			
None/minimal OHE	3 (2.1)	144	1
Mild/moderate OHE	12 (5.7)	257	1.69 (0.4 – 6.7)
Severe OHE	11 (13.9)	79	**5.29 (1.6 – 17.7)**

*SES = socio-economic status, **severity assessment by the DNBII at baseline [30] DNBII= Danish National Board of Industrial Injuries, NA = not applicable, ICD= occupational irritant contact dermatitis, ACD= occupational allergic contact dermatitis, CU = occupational contact urticaria, AD= atopic dermatitis, DLQI = Dermatology Life Quality Index, QoL = quality of life

Table 3 continues next page

Table 3 continued

Variable	Prolonged sick leave after 1-year follow up (%)	Total n	Prolonged sick leave at 1-year follow up RR (95%-CI)
Duration (years)			
0-1	3 (4.3)	70	1
2	6 (5.9)	102	1.56 (0.3 – 7.0)
3-5	7 (5.1)	137	0.73 (0.2 – 3.1)
6-51	8 (5.4)	149	0.66 (0.2 – 2.3)
Previous prolonged sick leave	14 (18.2)	77	**5.2 (2.0 – 13.6)**
Occupation			
Wet	9 (4.4)	207	1
Food	7 (8.8)	80	1.60 (0.6 – 4.4)
Other	10 (5.2)	193	1.18 (0.4 – 3.6)
Depression			
Minimal to mild	20 (4.5)	444	1
Moderate to severe	6 (17.7)	34	1.46 (0.4 – 5.3)
DLQI			
High QoL	16 (3.8)	421	1
Low QoL	10 (17.9)	56	**4.62 (1.6 – 13.7)**

*SES = socio-economic status, **severity assessment by the DNBII at baseline 30 DNBII= Danish National Board of Industrial Injuries, NA = not applicable, ICD= occupational irritant contact dermatitis, ACD= occupational allergic contact dermatitis, CU = occupational contact urticaria, AD= atopic dermatitis, DLQI = Dermatology Life Quality Index, QoL = quality of life

Table 4.

Variable	Loss of job after 1-year follow up (%)	N	Loss of job at 1-year follow up RR (95%-CI)
Males	7 (4.5)	156	1
Females	13 (4.0)	324	1.10 (0.4 – 2.9)
Age (years)			
18-24	1 (0.9)	108	1
25-29	2 (2.7)	75	3.06 (0.3 – 31.8)
30-39	9 (6.3)	143	7.78 (0.9 – 69.2)
40-49	3 (3.8)	80	4.14 (0.4 – 45.7)
50+	5 (6.7)	74	5.95 (0.5 – 66.6)
SES*			
Lowest level	4 (3.4)	118	1
Basic level	14 (7.0)	200	2.82 (0.6 – 12.4)
High/medium level	0 (0.0)	70	NA
Students/trainees	2 (2.2)	90	1.74 (0.2 – 12.6)
Diagnoses			
ACD	4 (3.9)	102	1
ICD	12 (4.0)	296	1.14 (0.4 – 3.4)
CU	1 (4.2)	24	2.14 (0.1 – 31.4)
ICD +ACD	3 (6.7)	45	2.56 (0.6 – 11.6)
ICD +CU	0 (0.0)	13	NA
AD			
No	18 (4.5)	400	1
Yes	2 (2.5)	80	1.12 (0.2 – 5.3)
NOACD			
No	14 (4.1)	339	1
Yes	6 (4.3)	141	0.94 (0.3 – 2.7)
Severity (DNBII-rated)**			
None/minimal OHE	2 (1.4)	144	1
Mild/moderate OHE	10 (3.9)	256	4.52 (0.5 – 37.5)
Severe OHE	8 (10.0)	80	**14.0 (1.9 – 102.9)**

* SES = socio-economic status, **severity assessment by the DNBII at baseline [30] DNBII= Danish National Board of Industrial Injuries, NA = not applicable, ICD= occupational irritant contact dermatitis, ACD= occupational allergic contact dermatitis, CU = occupational contact urticaria, AD= atopic dermatitis, DLQI = Dermatology Life Quality Index, QoL = quality of life

Table 4 continued

Variable	Loss of job after 1-year follow up (%)	N	Loss of job at 1-year follow up RR (95%-CI)
Duration (years)			
0-1	2 (2.9)	69	1
2	5 (5.0)	101	1.89 (0.3 – 11.6)
3-5	6 (4.4)	138	1.84 (0.4 – 8.7)
6-51	5 (3.4)	149	0.94 (0.2 – 4.9)
Occupation			
Wet	8 (3.9)	205	1
Food	3 (3.7)	81	0.64 (0.1 – 3.3)
Other	9 (4.6)	194	0.75 (0.3 – 2.1)
Depression			
Minimal to mild	15 (3.4)	444	1
Moderate to severe	5 (14.7)	34	2.72 (0.7 – 10.0)
DLQI impaiment			
High QoL	13 (3.1)	420	1
Low QoL	7 (12.3)	57	2.6 (0.9 – 7.3)

* SES = socio-economic status, **severity assessment by the DNBII at baseline [30] DNBII= Danish National Board of Industrial Injuries, NA = not applicable, ICD= occupational irritant contact dermatitis, ACD= occupational allergic contact dermatitis, CU = occupational contact urticaria, AD= atopic dermatitis, DLQI = Dermatology Life Quality Index, QoL = quality of life