



**PhD thesis**

# Hand eczema

Self-management and prognosis

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Hospital**



**NATIONAL ALLERGY RESEARCH CENTRE**



Hand eczema  
Self-management and prognosis

This PhD study is the product of scientific work conducted at



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## 1 INTRODUCTION

Bernardino Ramazzini (1633-1714), known as the father of occupational medicine, wrote this passage about bakers' and millers' diseases in his book 'De Morbis Artificum' (1):

*“Now and then I have noticed that bakers have swollen, aching hands. Everyone in this trade gets rough hands by kneading the dough. A baker just has to show his hands to reveal his trade. No other tradesman has similar hands. Avicenna says: ‘work affects any part of the body’ and this is confirmed in other occupations. A wash in leach, in strong white wine and the likes may be useful.”*

Treatment with leach and wine may not meet modern times' criteria of evidence-based medicine but Ramazzini's notion about possible detrimental effects of work still holds true. The hands are our primary tool in everyday activities and sometimes the skin of our hands becomes sick due to environmental exposures. The result may be contact dermatitis on the hands.

### 1.1 Definition and epidemiology of hand eczema

Hand eczema is an inflammatory disease characterised by erythema, vesicles and oedema in the acute phase while infiltration, scaling, hyperkeratosis, and fissures may be seen in chronic eczema (2). Some subtypes of hand eczema present with only one morph like hyperkeratotic palmar eczema, but in general, hand eczema is a polymorphous condition (Figure 1) (2). Itch is, although not visible, a common, severe symptom and the individual may experience pain in case of fissures or scaling. Hand eczema can be accompanied by contact urticaria due to penetration of proteins through the damaged skin barrier. This manifests itself as a prompt reaction of itching and stinging immediately after contact to e.g. fruits, vegetables or raw fish. Moreover secondary infections with pathogen bacteria, e.g. *staphylococcus aureas*, can complicate the course of disease.

In surveys of the general population, the one year prevalence of hand eczema was found to be 10-14%, the point prevalence of hand eczema around 4% and the lifetime prevalence around 15% (3;4). Hence hand eczema is a common condition and a major contributor to occupational diseases. More women than men have hand eczema, at a ratio of 2:1 (4), which supposedly relates to exposure patterns rather than to individual susceptibility (5). A Swedish study has estimated the highest incidence to be among young women (aged 20-29 years old) with 11.4 cases/1000 person-years (6). This is twice as high as the general median incidence rate of 5.5 cases/1000 person-years reported in a recent review (4).

### 1.2 Aetiology of hand eczema

Hand eczema is a complex disease. The three major aetiological types are allergic contact dermatitis, irritant contact dermatitis and atopic dermatitis. In cohort studies, allergic contact dermatitis has been reported to account for 17.2-24.2% and irritant contact dermatitis for 33-38.2% of hand eczema cases (7;8). Irritant contact dermatitis is often caused by wet work, but

detergents, oils, acids/alkalis and organic solvents are also known to be common irritants (9). Hand eczema as a manifestation of atopic dermatitis was ascribed to 16-19.3% of the patients while 12-21.5% of the patients were diagnosed with undetermined causes in the studies (7;8). The same distribution of main aetiological groups has roughly been found in epidemiological studies. In a substantial population survey in Sweden, more than 1000 individuals were examined by a dermatologist including patch testing and exposure analysis (10). Irritant contact dermatitis was the most common type of hand eczema (35%), followed by atopic hand eczema (22%) and allergic contact dermatitis (19%) (10). However, a certain overlap of the aetiology appears. A study of aetiologically defined subtypes of hand eczema reported 15.2% of the patients having combined allergic and irritant contact dermatitis and 7.8% of the patients having a combination of atopic dermatitis and irritant contact dermatitis (n = 319) (11). In any case, when hand eczema is present this means that the normal skin barrier is insufficient and irritants, in general, may then be considered as aggravating factors (7). Seasonal variation may also be an exogenous co-factor, promoted by the low humidity in frosty weather at wintertime.



**Figure 1:** Different symptoms and localisation of eczema: a) erythema, b) scaling and fissure, c) oedema and erythema, d) scaling, e) vesicles, oedema and scaling, f) vesicles and scaling (images from patients included in the thesis)

Hand eczema may be associated to certain lifestyle factors, yet evidence is sparse. A Swedish cross-sectional survey analysed lifestyle data among 27,793 individuals who had responded to a question about past-year hand eczema. Comparisons were made between those who reported hand eczema within the recent year (7.9% and 11.5%, men and women respectively) and those who did not. Hand eczema was more common in individuals who reported stress, obesity and smoking, and less common among those who reported high physical exercise. The association between alcohol intake and hand eczema was only marginal (12).

Research of hand eczema has within recent years focused increasingly on endogenous factors which may contribute to an individual susceptibility. Among these are filaggrin mutations (13). Filaggrin is a specific protein in the stratum corneum layer of the epidermis and contributes to two important barrier functions. It binds to and condenses the keratin cytoskeleton, thus preventing water loss and the entrance of foreign substances through the large surface area of the skin. Moreover, the protein is degraded to hygroscopic amino acids, resulting in a natural moisturising factor (13;14). Around 10% of the Danish population have filaggrin loss-of-function mutations, but in individuals with severe atopic dermatitis this percentage may be as high as 50% (15). Filaggrin loss-of-function mutations have been shown to increase the risk of hand eczema in individuals with atopic dermatitis. It can also be associated to earlier onset and longer persistence of hand eczema (16).

Another endogenous factor which contributes largely to hand eczema is a history or presence of atopic dermatitis. Hand eczema as a manifestation of atopic dermatitis is by no means a new discovery. In a 1952 study of 150 hand eczema cases, 12 patients were primarily diagnosed with atopic eczema. In all cases, three or more other etiological factors were considered to interplay with the primary diagnosis (17). Thus, the complexity of hand eczema has been acknowledged for many years.

All co-factors need not be present at the same time in this possible interplay of endogenous and environmental contributors. Each of them can be defined as a sufficient cause, although not a necessary cause, of the hand eczema disease (18). However, they may also all contribute to hand eczema as predisposing, exposing, aggravating or persisting factors.

### **1.3 Prognosis and consequences of hand eczema**

Hand eczema can be difficult to cure and often becomes a long-term condition. It may begin as an acute eczema and then develop into a more constant dermatitis with acute eczematous eruptions occurring in a dynamic pattern (2). As part of obtaining the medical history of the individual patient it is therefore recommended to include information about the course, i.e. whether it is acute, chronic, intermittent and/or cyclic (2). Hand eczema has been shown to have a rather poor prognosis in clinical practice. Two-thirds of patients with hand eczema reported persistent or intermittent eczema after five years in a Danish longitudinal single-site study of a well-described cohort (19). This figure equates with the self-reported persistence of hand eczema disease also found in general population studies. A Swedish questionnaire follow-up survey of individuals previously identified as having hand eczema (20) showed that 66% reported episodes of eczema throughout the 15 year period. Consequences to this long-lasting condition were both occupational and psychosocial. One of twenty reported long sick-leave periods, change of occupation, or early retirement due to hand eczema. Of those individuals with hand eczema within the recent year, as many as 96% reported some kind of impaired social life related to the disease (20).

Hand eczema has been reported to have a profound effect on the individual's quality of life. In a large population survey, hand eczema was found to have an impact of a similar magnitude as psoriasis and asthma on quality of life. The use of a short, generic quality of life measurement tool, the EQ-5D, made this comparison between different diseases possible. The impact on quality of life was irrespective of age, but women reported more problems in the dimensions of 'usual activities' and 'anxiety/depression' as compared to men (21). More recently, another large population study confirmed that hand eczema was associated to lower scores of quality of life using the generic Health Status Questionnaire, Short-Form-36 (SF-36) (22). Female gender and self-assessed higher severity predicted more impaired quality of life. The latter findings are in agreement with a cohort study of patients with hand eczema using the Dermatology Life Quality Index (DLQI) as a measurement (23). No gender differences for dermatology-specific quality of life were found in a previous multi-centre study, but a statistically significant positive correlation between clinically assessed severity and DLQI was reported (24).

No commonly accepted definition of chronic hand eczema has been published. One definition is an eczema which persists for more than three months or which re-occurs twice or more within a 12 months period in spite of adequate dermatological treatment (25). Many patients consulting a dermatologist have hand eczema that matches this definition. Hald et al. did follow-up on a Danish cohort of 333 patients who consulted a dermatologist for the first time ever because of hand eczema (26). This study reported a median patient-delay (the interval from onset of symptoms until seeing a general practitioner) of three months. An additional healthcare-delay (the interval from the first consultation at the general practitioner until seeing a dermatologist) with a median of three months was found. A longer patient-delay was found to be a risk factor for a poor prognosis (26). From a traditional biomedical viewpoint, the above-mentioned definition of chronic hand eczema presupposes a satisfactory patient compliance in order to "achieve an adequate dermatological treatment". In the next section patient compliance in general dermatology is addressed under the subheading 'medication adherence', which is a more contemporary term.

## **1.4 Medication adherence in dermatology**

Several studies have examined patient compliance with dermatologic treatment with reference to the degree to which the patient's behaviour corresponds with the recommendations of the health care provider. The term 'medication adherence' has replaced the term 'compliance' in order to acknowledge the shared decision-making ideally incorporated into any medical treatment (27). Both terms are also used in the negative senses, i.e. phrased as noncompliance or nonadherence (27;28). A recent study found that 30.7% of patients with dermatological diseases did not collect their prescribed medication; patients with psoriasis were the least adherent (28). This is in agreement with previous findings estimating that reduced adherence to dermatological treatment can be seen in 34-45% of patients (29). Usually noncompliance is stipulated when less than 80% of the prescribed medication is used. Although this is difficult to measure in dermatology, where topical treatment is widely used, attempts have been made. A

small study monitored adherence of patients with psoriasis (n=30) and found that the number of treatment gaps increased throughout the 8-week trial and weekend days were overrepresented in treatment gaps (30).

Hand eczema is by no means a uniform disease (31). In treatment and subsequent prevention of relapses it is essential to determine the aetiology to remove the causative agent(s), if possible (2;32). Moreover it is pivotal to identify potential aggravating factors in everyday life, which may not be directly associated to the aetiology, but nevertheless contribute to a poorer prognosis (7). Medication adherence is then considered a concept too simplistic to embrace the many behavioural changes in everyday life that may be necessary when one has hand eczema.

### **1.5 Self-management in chronic illness**

Self-management is a term frequently used when referring to chronic diseases. However it is seldom defined. It has been argued that, on average, a chronically ill individual receives direct care from health care professionals in only two of 8,758 hours each year (33). The individual is then left almost constantly to self-management when dichotomising disease management into direct (or managed care) and self-managed care. Although hand eczema is common, evidence of everyday life with the disease is sparse. In recent reviews of treatment and management of chronic hand eczema only a little attention is drawn to the individual's self-management (25;31;34). As an example, the use of education and non-pharmacological methods only account for approximately 1.3% of the total text in a review considered to be extensive and comprehensive in the description of treatment options in cases non-respondent to topical corticosteroids (34). Much of the available evidence of self-management relates to diabetes, which is suggested as the prototype for chronic disease management due to the continual requirement of patient judgment about medication treatment (35). With hand eczema, however, one cannot monitor the disease and adjust the treatment by regular measurement of biomarkers, because the diagnosis is based upon clinical symptoms. Moreover the aggravating factors in everyday life may be unavoidable.

There is no 'gold standard' definition of self-management (36). The kinship of self-management to other concepts like medication adherence, health literacy, patient education, shared decision-making, empowerment, patient activation, patient autonomy, consumerism and coping creates a blurred terminological landscape when reviewing the literature. Previously, the Danish National Board of Health attempted to clarify the various concepts within health care in a description of modifying and facilitating relations (37). A diagram involving 40 interrelated health concepts depicts to a great extent the complexity of modern health care (Appendix A).

Self-management, or self-care, is attributed different meaning depending on the perspective from which the concept is seen (38). In the seventies, self-management was viewed within a political context, as a response to medicalization in, for example, women giving birth. Some authors argued then that self-management would be less threatening to health service professionals if it were part of wellness and health promotion (39;40). Self-management, at

present, is discussed as requiring evaluation of cost-effectiveness through randomised clinical trials, or as a means to reducing the costs of an overburdened health care system (41). Self-management appears to be inherently linked to nursing, as a demarcation of professional boundaries. The general theory *Self-care deficit theory of nursing*, advanced by Orem, describes what nursing is and what it should be (42;43), with levels of supportive care relating to self-care presented on a spectrum of care (42;44).

Most authors refer to self-management as a kind of behaviour or set of actions which can be normatively evaluated. The patient's capability for self-management can then be quantified and evaluated as good or poor (45-48). Self-help, self-care and self-management are similar labels but the definitions differ in the range of inclusiveness i.e. the individual and/or the family (49;50). Although the terms are often used interchangeably, some authors differentiate between self-care and self-management. Hence, the former represents tasks performed by healthy individuals to prevent the onset of illness, whereas the latter refers to day-to-day actions to control or reduce the impact of disease on physical health status (51). Other conceptualisations appear to be interventional, i.e. may be more correctly termed self-management support. Referring to The Expert Patients Programme in UK it is obvious that the sentence "*Self-management has been available in England since the 1990's ....*" attributes such meaning to the term (52).

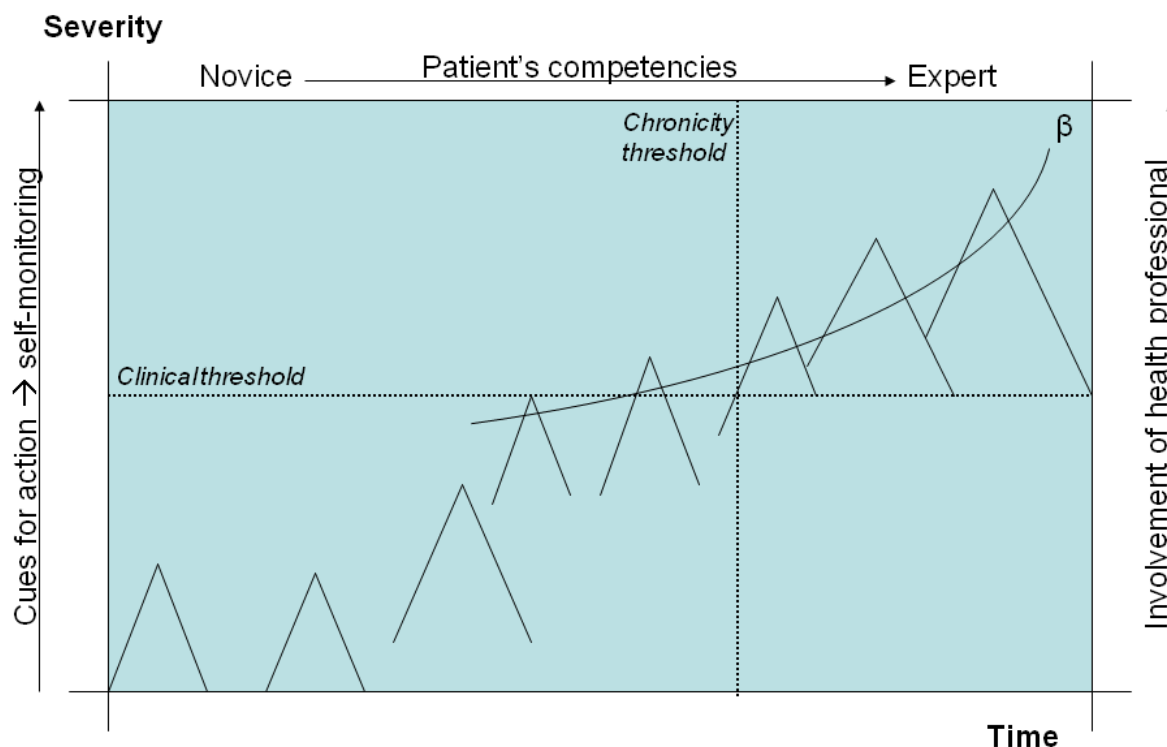
Self-management as behaviour may not be recognised as already taking place from these perspectives. Self-management has, however, always existed in one way or another and most patients, historically, have self-managed their diseases without intervention from a professional health care system. Hence, disease self-management cannot be divorced from life self-management (53). This thesis also posits self-management to be *lived* rather than *used* as an integrated part of the individual's life. It is a contextual and fluent product of cognitive ability, habits, social support, preferences and values.

## 1.6 Self-management in hand eczema

"*The Dynamics and Management of Self-Induced Eruptions*" from 1961 by Obermayer appears to be the first PubMed-indexed publication which addresses self-management related to dermatological diseases. Obermayer argued that "*His weapon is the building of her ego by expressing confidence in her ability to help herself*" (54). This perspective actually appears to be rather modern as it acknowledges that psychological factors also play a significant role in the treatment of dermatological patients. However, in hand eczema, it is also relevant to consider specific important characteristics of the disease which may relate to the fluctuation of symptoms.

Many courses of chronic hand eczema proceed similarly in activity patterns, regardless of aetiology. Asymptomatic phases can be interrupted by recurrent eczema. The skin needs a long restitution period in order to regain strength and homeostasis after an eruption, although this is difficult with the hands being our primary tool both on and off work. The eruptions may become

more frequent and severe, in time leading to impaired healing capacity and more permanent alterations of the skin. To depict this dynamics, the following model was designed for this study (Figure 2).



**Figure 2:** Conceptualisation of self-management in chronic hand eczema. The figure, inspired by Malten (55) and Dreyfus (56), displays a theoretical model of the individual's adaptation to chronic hand eczema.

The model was inspired by the hypothesis of how the most abundant subtype of hand eczema, irritant contact dermatitis, theoretically emerges through repeated exposure of the skin. In a substantial publication, Malten argued that when the skin is exposed to irritants so frequently that complete recovery from one stimulus is not achieved before another irritant stimulus causes an effect, a threshold may be exceeded with the clinical disease being 'the tip of the iceberg' (55). This visualisation of a comprehensive pathway of disease served as inspiration to illustrate a course of chronic hand eczema in a conceptual model. The model shows how hand eczema undergoes changes in disease severity and how the individual may adapt to the chronic course of disease.

In the model the three leftmost peaks represent episodes of impaired skin which are within subclinical levels of severity and are only detectable by use of bioengineering methods, such as the measurement of transepidermal water loss (TEWL) or the skin surface pH (57). The *Clinical threshold* refers to skin changes becoming visible. Thus, the remaining five peaks are eczematous eruptions diagnosed clinically. The *Chronicity threshold* represents the transition from acute to chronic disease, where the skin does not recover completely between eruptions. Above the curved line  $\beta$  are the peaks of eruptions which require medical treatment, e.g. by the

prescription of topical corticosteroids. Below  $\beta$  are phases which possibly do not have any involvement from the health care system. Hence, larger parts of the course may be managed by the individual solely expressing the pivotal role of self-management.

The interior part of the model displays the dynamics inherent in chronic hand eczema per se. The exterior of the frame then illustrates how the individual may respond to the disease within three dimensions. Firstly, cues for action may become more evident as the symptoms become graver due to more severe hand eczema. This relates to self-monitoring of the disease. Secondly, the time dimension in a chronic course may alter the individual's ability to cope with and act upon new symptoms of the disease, e.g. the start-up of topical corticosteroid treatment when new vesicles occur. Both the skills to perform an activity, and the ability to assess whether the activity is necessary, are involved, which is broadly covered by the term 'patient's competencies' (58). Thirdly, recurrent symptoms may bring forward more involvement from the health care professionals. The three dimensions of self-monitoring, patient competencies and the patient-provider relationship are elaborated in the following section.

### **1.6.1 Self-monitoring**

A prodromal phase may precede the onset of actual clinical symptoms of hand eczema. The individual has to act as first responder to objective changes of the skin or subjective symptoms like itching and evaluate whether the symptoms are severe enough to consult a dermatologist or to recommence medication. This awareness needs to be continuous in order to prevent flare-ups of the eczema. One has to acknowledge that the dispositions to new eruptions are still there, even though the symptoms may be absent. This may be challenging as, arguably, self-regulation is not pursued unless benefits are perceived e.g. by improved health (51).

Evidence of eczema self-monitoring is sparse. A study of topical treatment for atopic dermatitis used daily records of self-observed erythema and pruritus from patients in order to evaluate the safety and efficacy of the prescribed treatment (59). Otherwise, skin self-examination is more frequently used to prevent skin cancer and it has been found to decrease mortality from melanoma by 63% in a selective group of high-risk patients (60). Around half of the individuals in a population survey with an average risk of skin cancer performed skin self-examination at least once in the past year. Female gender, education beyond high school, and age more than 25 years correlated to higher frequencies of self-examination (60). These studies did not report of possible healthy adherer effects (61). The individual performing more frequent skin self-examination may also perform other beneficial behaviours like more adequate skin protection.

The benefit of early detection of a potentially lethal disease like skin cancer may be valued higher as compared to chronic hand eczema, although hand eczema can affect everyday life more persistently. A certain adaptation to hand eczema may also occur, whereby the perception of the normal skin changes as one gets used to even small alterations. This could increase the threshold of when to respond, due to a habituation of the symptoms, i.e. the responsiveness to



a repeated stimulation diminishes. The use of baseline photographic documentation could potentially avert this problem.

### 1.6.2 Patient's competencies

The recurrent eruptions can be viewed as a series of experiences, all of which may add to the individual's knowledge about the eczema. Experience also forms our attitudes, in the way that Perloff defines attitudes as *"a learned, global evaluation of an object (person, place or issue) that influences thought and action"* (62). Thus, the lived experience merely of having chronic eczema provides insight which can lead to higher abilities managing the disease. Knowledge obtained through everyday life may be tacit. Experiences of different exposures that aggravate the condition can be committed to memory by reflection and brought to use when necessary. The health care provider may facilitate the explication of this tacit knowledge by asking reflective questions during the consultations or by offering tools for self-monitoring. The development in skills is displayed in the model (Figure 2), referring to the theory of competencies as ladder-built (56;63). While competencies develop, a more intuitive, reflective practical knowledge gradually replaces actions relying on principles and guidelines (56;63).

In a study of occupational contact dermatitis only one third of 222 workers were able to identify correctly their diagnosis of either allergic contact dermatitis or irritant contact dermatitis (64). Those individuals who knew correctly of their diagnosis were less likely to report current dermatitis at the time of the trial than those who were not aware of the causes of the disease. Thus it was concluded that more attention to the patient's education, also regarding the causes of their disease, could improve the prognosis (64). In many cases, exposure in the workplace is complex and involves several irritants and allergens at the same time (65). Long and complicated names of ingredients on the labels of products like cosmetics are widely used and add to this complexity (66). Still, a great deal of the knowledge which is most essential for everyday life is of a more practical nature. The formulation of 10 widely used recommendations have primarily been directed towards workers in wet-work occupations (65;67), but they are also highly applicable in our everyday lifestyles (Box 1).

1. Wash your hands in lukewarm water. Rinse and dry your hands thoroughly after washing
2. Use protective gloves when starting wet-work tasks
3. Protective gloves should be used when necessary but for as short a time as possible
4. Protective gloves should be intact and clean and dry inside
5. When protective gloves are used for more than 10 minutes, cotton gloves should be worn underneath
6. Do not wear finger rings at work
7. Avoid frequent hand wash unless the hands are visibly dirty. Instead use disinfectants based on alcohol. (disinfectant should be used according to the recommendations for the workplace)
8. Apply moisturizers on your hands during the working day and/or after work. Select a lipid-rich moisturizer free from fragrances and with preservatives having the lowest allergen potential
9. Moisturizers should be applied all over the hands including the webs, fingertips and back of the hand
10. Take care also when doing domestic work, use protective gloves for dish washing and insulating gloves in the winter

**Box 1:** 10 recommendations as part of skin protection programmes (65;67)

It has recently been examined in a Danish questionnaire survey of 410 patients with occupational hand eczema if these recommendations are widely known (68). The overall percentage of correct answers was 73% and the study showed that men and, in general, patients older than 50 years, had significantly lower number of correct answers. Although more than 80% of the respondents stated that they had previously been given information concerning their hand eczema, only seven patients answered all 13 questions correct. It was concluded that information of skin protection and skin care should be offered to all patient groups, and repeatedly (68). However there is a step from information to learning. Learning needs to be translated into habits for newly adopted competencies to develop into sustainable behaviours. This process may rely upon how compatible the habit is with one's daily routine (69).

### 1.6.3 The patient-provider relationship

The age span in hand eczema can range from preschool infants to elderly individuals. Thus, some people are affected by the disease for a large part of their life. The individual then meets several health care providers, e.g. dermatologists, nurses or occupational advisors, all of whom may differ in their views about prevention, as well as their attitudes towards disease self-management. The health care system has undergone many changes within recent years and the roles of the individual and the professional(s) involved have changed as well. Hand eczema seldom acquires in-patient hospitalisation, thus having the predisposition of being managed in a genuine partnership between the individual and the health care providers. The remains of paternalism from the health care professionals are also being challenged by increasingly informed patients; some even refer to patients as consumers (70).

The patient-provider relationship in hand eczema disease has not been widely explored. In an interview study of patients or parents of juvenile patients with atopic dermatitis, it was concluded that people preferred to consult a patient-centred medical expert with good communication skills, who is able to inform, advise and support on issues of managing the disease, although on the surface, they appeared to be 'reflective consumers' by being active, critical and informed (71). Atopic dermatitis and chronic hand eczema often constitute the same disease patterns and the aforementioned findings may not be contradictory per se. The role and responsibility of the individual change according to the dynamic and the complexity of the chronic course, as illustrated in figure 2. The patient's perceptions are not static, but develop under the constant influence of experiences related to health. These perceptions can be in accordance with the perceptions of the health care provider or they can be very different (72).

Both shared decision-making and patient-centred care are newly developed concepts. Already twenty years ago Lunde emphasised that doctors need to know of and discuss the patient's views on equal terms with the medical views if the principle of patient autonomy is to be respected (72). However, recent research shows that the ideal and the reality of shared decision-making are difficultly balanced. Shared decision-making has been investigated by field observation of consultations within heart rehabilitation and arthritis treatment, (73). The power

relations between patient and health care professional were challenged when patients actively engaged in the decision-making process, and this could be perceived as interference of a societal context of presumed human equality. The patient's lived experience could be subject of the consultation, but only as an appendix, since it was not integrated as a serious parameter in the choice of treatment (73). The health care system appears to be governing in a new manner, but the application of joint management may be difficult within existing institutions and cultures. Thus, more research into how we may best support self-management of the patients with hand eczema, within this institutional frame, is needed.

### **1.7 Workers/patients' education in hand eczema**

Some professionals, e.g. hairdressers, run a high risk of hand eczema due to excessive exposure to irritants and allergens (74). Thus, the higher prevalence of hand eczema in certain professions is relevant to employers as well as to educational institutions. Educational interventions based upon the ten recommendations (Box 1) have been shown to be effective both in groups of gut cleaners and workers in the dairy industry (75;76). Recently, the introduction of such simple skin protection programmes has proven effective in a controlled clinical trial of hairdressing apprentices and a randomised clinical trial of health care workers (77;78).

Most research tends to focus on primary or secondary prevention within specific high-risk professions. Less is known of counselling and self-management support of the patients treated in either specialised centres or by private dermatologists. An integrated care programme has recently been evaluated in a Dutch multi-centre study (79). The programme combined dermatological work-up and standardised topical treatment with nurse-led counselling on medication adherence, hygiene, skin care, and skin protection. The programme significantly improved the clinical severity at six months follow-up compared to usual care in the cohort of 196 patients. However, there was no statistical difference between the groups after 12 months and the programme was not found to be cost-effective (80). Complex interventions which combine educational programmes and dermatological treatment have also been developed in Germany. These interdisciplinary prevention programmes have been shown to be effective in hairdressers with the effects also being durable in follow-up studies after five and ten years (81). Moreover, the programmes have been widely implemented as tertiary individual prevention (TIP), which involves 2-3 weeks of in-patient hospitalisation and, in total, of six weeks of sick leave to allow for full skin barrier recovery (82;83).

The German model involves only occupational hand eczema and, although successful, because of contextual differences between countries, it is difficult to apply this model to the Danish health care system, where hand eczema is treated in an out-patient setting. In particular, the 'window of opportunity' in the individual courses of treatment differs between the two health care systems. A typical Danish outpatient may have 2-3 medical consultations each of 10-15 minutes duration. In case of patch-testing, this may be supplemented by short sessions with a nurse or

bio-analyst. Nonetheless, some of the educational features of the TIP-programme could be transferable in Danish ambulatory and clinic care.

In a systematic review, patient education in chronic skin diseases was examined and, according to criteria (randomised controlled trials of patient education in skin diseases, with quality of life as an outcome variable), only studies of atopic dermatitis and psoriasis (n = 10) were included (84). Half of the studies reported improvements in quality of life and in three of the studies the disease severity improved. The span of interventions ranged from 15 minutes education sessions with a medical student to four months periods involving as many consultations by a nurse as necessary (84). As part of patient education strategies in general dermatology, both videotaped and computer-assisted methods have been suggested to increase the patient's information recall, although the face-to-face communication is considered the key component to patient education (85). An online video educational tool was superior to a written pamphlet in a randomised trial of adults with atopic dermatitis. The information was identical, but the video group of patients improved significantly more than the pamphlet group in both eczema severity and knowledge of the disease (86).

Computer-assisted methods used interactively could be a way to compensate for shortened hospital stays. E-health, defined as information and communication technology applications in direct patient care, has been examined in randomised clinical trials mainly of patients with diabetes but also with atopic dermatitis and other chronic illnesses. Small-to-moderate positive effects on primary health outcomes have been reported and it has been suggested as a promising tool (87). The usability of an Online Patient Book<sup>®</sup>, a Web 2.0 health informatics tool has recently been explored in a Danish cohort of men undergoing surgery for prostate cancer. The tool was found to support the men in being active partners in their own course of treatment and care (88). Such tools may also be cost-effective, as reported from studies of a Dutch web-based eczema portal. This portal combines e-consulting with monitoring and self-management training for patients and parents of children with atopic dermatitis (89).

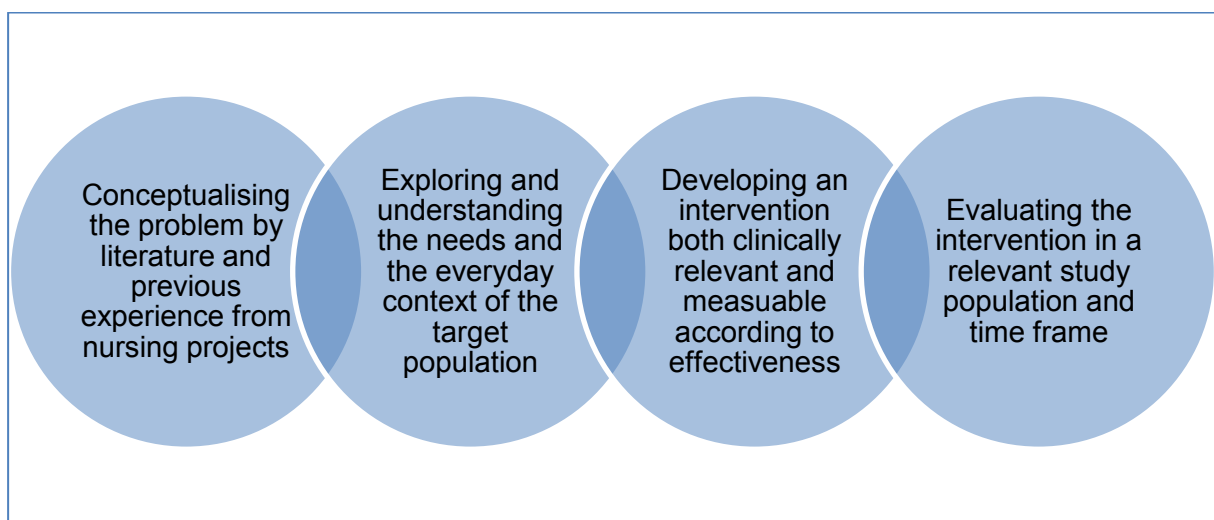
In health promotion targeted interventions refer to the use of *“a single intervention approach for a defined population subgroup that takes into account characteristics shared by the subgroup's members”* (90). Conversely, tailored interventions are directed toward individuals, not groups, and they are based on measured intra-individual differences. The two approaches can be combined with careful consideration to how to benefit most from each (90). Tailored health communication has been found to improve health behaviours and outcomes as regards nutrition, physical activity and health risk reduction, while online tailored communication has been suggested to facilitate better care and more efficient health care services (91). Five strategies have been presented to enhance cultural appropriateness whether interventions are targeted or tailored. Among these are *constituent-involving strategies* which draw directly on the experience of members of the target group (90). Focus groups can be a means of learning more about the target group (92), including barriers and facilitators of behaviour (93), to develop a relevant and more effective self-management support intervention.

## 2 AIMS OF THE STUDIES

Skin protection programmes have proved effective in primary and secondary prevention interventions. However, these studies are likely to include rather homogeneous cohorts of people as they target populations of individuals with occupational hand eczema. Hand eczema in the general population is known to have a poor prognosis. This may relate to the complexity of everyday life with aggravating tasks that cannot be avoided. Little is known about how people with hand eczema self-manage or whether tailored counselling effectively can support their self-management.

The aims of this thesis were

- To explore the barriers and needs in self-management of hand eczema in the context of everyday life (Manuscript I)
- Based on these findings, to develop an intervention programme of nurse-led counselling to support self-management of patients with hand eczema (94)
- To characterise a cohort of patients referred to hand eczema treatment and explore commonalities and differences between genders (Manuscript II)
- To evaluate if a nurse-led counselling programme supports self-management in patients, leading to a better prognosis for hand eczema (Manuscript III)



**Figure 3:** Overall phases of the thesis. Although presented linearly, the phases have partly overlapped, in a back-and-forth process.

### 3 PATIENTS AND METHODS

In this thesis a mixed-methods design has been used and three papers are presented. An overview of the three paper's different designs, methods and participants is presented in table 1. The study protocol of the clinical trial has previously been published (94).

**Table 1:** Overview of the design, methods and participants in the papers I-III

	Paper I	Paper II	Paper III
<b>Aim</b>	To explore the knowledge, attitudes and everyday life behaviours of patients with chronic hand eczema in order to generate insights about barriers in self-management	To gain insight into the common features and differences between men and women with hand eczema	To evaluate the effectiveness of a nurse-led counselling programme, The Healthy Skin Clinic, in hand eczema
<b>Design</b>	Qualitative exploratory study	Prospective cohort study	Clinical controlled trial with block-wise randomisation according to sex & setting
<b>Methods for data collection</b>	Purposeful sampling based on representativeness of target population	Consecutive enrolment of patients in dermatological treatment at Gentofte University Hospital and Dermatology Clinic Nord in Aalborg	Consecutive enrolment of patients in dermatological treatment at Gentofte University Hospital and Dermatology Clinic Nord in Aalborg
<b>Instruments</b>	Semi-structured interviews in gender-segmented focus groups	HECSI DLQI VAS of current disease NOSQ-2002 DMARS-4	HECSI DLQI VAS of current disease NOSQ-2002 DMARS-4
<b>Methods for analyses</b>	Content analysis according to a template of concepts, categories and codes	Descriptive and predictive statistics (chi square tests, t-test, logistic regression and ANCOVA-test)	Descriptive and predictive statistics (chi square tests, multiple linear regression and ANCOVA-test)
<b>Participants</b>	Twelve women and eleven men participated in four focus groups	An unselected cohort of 294 individuals with hand eczema (190 female, 104 male)	An unselected cohort of 292 individuals with hand eczema (189 female, 103 male)

HECSI, Hand Eczema Severity Index; DLQI, Dermatology Life Quality Index (permission granted); VAS, Visual Analogue Scale; NOSQ-2002, Nordic Occupational Skin Questionnaire; DMARS-4, Danish Medication Adherence Report Scale

### 3.1 The Healthy Skin Clinic Intervention

Founded on a review of the literature, a counselling programme was developed. The programme was entitled 'The Healthy Skin Clinic' and was a package of counselling and supportive elements. A key feature of the programme was a nurse consultation focusing at an individual level on skin protection and skin care. The patients were offered user access to a newly designed website; [www.hudrask.dk](http://www.hudrask.dk), to facilitate further support. "Hudrask" means "Healthy Skin" in Danish. The site comprised an individually processed profile of risks and resources, a log to self-monitor the eczema, information material including newly produced educational videos, quizzes, and a formula to contact the intervention team of nurses, as well as a dialogue forum in which to communicate with other users of the site. The few patients allocated to the intervention group who did not use the internet were given a folder with pamphlets and prints designed for a self-monitoring log. In this section some of the different elements in the Healthy Skin Clinic Intervention are elaborated, including the underlying rationales. Appendix B provides a more in-depth insight into the development process of the website from the initial list of requirements, to mock-ups and additional materials. The appendix also shows some screenshots, although not translated to English, from the website to give a more comprehensive picture of the intervention.

More attention has been given within the last ten years to how patients are informed as part of their dermatological treatment. Yet, how to counsel patients on skin protection and skin care has not been a standardised part of Danish guidelines. Traditionally, interest in skin care and personal hygiene is part of the nursing curriculum and practice and this was also the point of departure in the development process. Prior to this thesis, the nursing staff at Gentofte Hospital had for some years discussed, how they independently counselled patients with hand eczema. Instructions had been made of how and which information about skin care could be given. This counselling was allocated to selected patients based on the dermatologist's opinion. Moreover, the effectiveness of this practice had never been evaluated.

Interventions to increase medication adherence, and thus indirectly the patient's self-management, are most effective when intervening in several dimensions (27;95). The decision to develop a self-management support programme as a multimodal intervention was substantiated by results from a series of focus group interviews. The findings from these interviews are described in the manuscript (Paper I). Additionally, the participants were in favour of a website featuring a virtual patient dialogue forum and the possibility of ad hoc communication with the health providers. When developed, the website was then piloted by nine of the interviewees. They found the site easy to grasp and the information material suitable both in content and form. The website was then launched at the initiation of the randomised controlled trial. The nurses who pioneered the nursing instructions of skin care were enrolled as members of the intervention team in the clinical trial. They also actively took part in the formulation of the teaching materials in the intervention.

The website [www.hudrask.dk](http://www.hudrask.dk) had two parallel interfaces. The patients could communicate with each other in the patient dialogue forum but at the same time each patient had an individual user interface, which was highly secured. Thus, the patient had the possibility to safely and asynchronously communicate with members of the intervention team by using a contact formula at the top of the site. Specific questions or comments could then be directed to the nurses. The intervention team did not monitor each user on a regular basis. Nor did the nurses initiate communication with the patient because the overall focus of the intervention was the patient's self-management. Thus, the patients assessed if renewed contact to the health care professionals could be of use at any given time in the course. The patients did, however, receive biweekly emails reminding them that they could use the website and, if desired, initiate communication with the team as part of the project.

The name of the programme, The Healthy Skin Clinic, was chosen because this term focused upon health promotion rather than on the disease per se. A dichotomous perspective of being either sick or healthy does not fit a course of hand eczema. As illustrated in the model of chronic hand eczema (Figure 2), the course of disease involves both health promotion, from a perspective of salutogenesis, and tertiary prevention related to pathogenesis (96). The former is the process of people being enabled to increase control over, and to improve their health. The latter activities, arguably, emanate from the health sector and deal with identifiable risk factors and risk behaviours (97). The interface between health promotion and disease prevention is not clearly delimited, as several terms, e.g. rehabilitation, include both concepts (37). Still, a salutogenetic perspective allows one to address the entirety of the individual's biography and not only to focus upon his or her disease (98), which seemed to be of particular relevance in this complex disease with its individual-environment interplay.

### 3.1.1 Tailoring the intervention by use of a SKIN-profile

The pivot of the intervention was the nurse-led counselling which occurred immediately after the first medical consultation and the subsequent enrolment of the patient in the trial. This involved a dialogue of how the 10 recommendations (Box 1) were applicable in the everyday life of the patient. In order to tailor the counselling, a subsequent nurse consultation was offered in timely relation to the next medical appointment. An individual profile of resources and risks, the SKIN-profile, was developed in the lag time between consultations. The SKIN-profile was a way to visualise for both the patient and the nurse which specific focal areas in the individual course would be most relevant during this second session. The SKIN is short for susceptibility, competence (in Danish *kompetence*), individual factors and necessary precautions.

The profile was generated by some of the patients' answers from the baseline questionnaire. These answers were converted into a percentual scale by use of a matrix. For example the General Self-Efficacy Scale (99;100), in conjunction with the Danish Medication Report Scale (101), generated the competence dimension. General Self-Efficacy is the belief in one's competence to cope with a broad range of stressful or challenging demands. The scale then is



an instrument that addresses self-efficacy as a concept related to personality traits. It is suggested to be useful when studying behaviour of patients who have to adjust their lives to multiple demands because of their chronic illness (100). The Danish Medication Report Scale (DMARS-4) is a generic four-item scale, validated in Denmark in a group of cancer patients (101). An example of the SKIN-profile as it appeared on the website is shown in Appendix B.

### **3.1.2 Promoting self-monitoring by use of a log**

The self-monitoring module was invented in both an electronic form and as a paper sheet, the latter as part of the folder given to patients without access to the internet. In the website version it was possible for the intervention team to look at each patient's individual log. Each registration in the log consisted of a date and a subjective assessment of severity on a scale from 0-10. Furthermore, the patients were encouraged also to note which symptoms they had at the time and maybe reflections on which internal or external factors could account for any changes in the condition. A small electronic programme was developed in which the localisation of the eczema could be displayed by ticking the areas on a set of four hands similar to the sketches in the paper sheets. Finally, the patients had the possibility of uploading a photo of their eczema. Each registration could then be retrieved at a later point by the patient (and the team) and shown in detail. The electronic self-monitoring module is presented in screenshots in the Appendix B.

## 4 OVERVIEW OF THE STUDIES

This PhD thesis is based on the following manuscripts:

- I. **Mollerup A**, Johansen JD, Thing LF. Knowledge, attitudes and behaviour in everyday life with chronic hand eczema: a qualitative study. *Br J Dermatol* 2013;169(5):1056-65.
- II. **Mollerup A**, Veien NK, Johansen JD. An analysis of gender differences in patients with hand eczema – everyday exposures, severity and consequences. *Contact Dermatitis* 2014; accepted for publication (2013; submitted).
- III. **Mollerup A**, Veien NK, Johansen JD. Effectiveness of the Healthy Skin Clinic – A randomised clinical trial of nurse-led patient counselling in hand eczema. *Contact Dermatitis* 2014; accepted for publication (2013; submitted).

## 4.1 Manuscript I

**Mollerup A**, Johansen JD, Thing LF. Knowledge, attitudes and behaviour in everyday life with chronic hand eczema: a qualitative study. *British Journal of Dermatology* 2013; 169(5):1056-65.

# Knowledge, attitudes and behaviour in everyday life with chronic hand eczema: a qualitative study

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## Summary

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**Background** Chronic hand eczema is a common disease that may impact quality of life and have occupational and social consequences. Self-management is pivotal, both in handling acute eruptions and avoiding relapses. However, little is known about how people with hand eczema self-manage and integrate their disease into everyday life.

**Objectives** To explore the knowledge, attitudes and everyday life behaviours of patients with chronic hand eczema in order to generate insights about barriers in self-management.

**Methods** Qualitative, semistructured, focus group interviews were carried out. Twenty-three people with hand eczema participated in the four group sessions. The content of the interviews was analysed according to a template of concepts, categories and codes.

**Results** Patients felt they lacked knowledge about the causes of eczema and how best to manage it. They perceived it as a complex condition, yet only simple solutions were offered. The patients found it difficult to apply preventive strategies in everyday life. They wanted to take an active role in their course of illness, but experienced barriers such as discomfort from emollient treatment or feelings of stigmatization. The patients stated that the need to focus constantly on prevention was energy-consuming.

**Conclusion** Self-management support in chronic hand eczema needs to be individualized in order to provide specific knowledge relevant to the patient, so that the patient has realistic expectations concerning the course of disease and can adopt new habits that minimize effort in preventive behaviour.

### What's already known about this topic?

- Chronic hand eczema requires self-initiated topical treatment and continuous preventive behaviour.
- Medication adherence to dermatological treatment is considered low.

### What does this study add?

- Everyday life with hand eczema is complex, but patients perceive that they are offered only simple solutions.
- The barriers to preventive behaviour involve treatment-related discomfort and social considerations.
- Self-management support must focus on people's knowledge, attitudes and behaviour with the aim of integrating preventive behaviour through habits.

Hand eczema is a common inflammatory disease affecting 10–14% of the Danish population annually.<sup>1,2</sup> In addition to clinical symptoms, it often involves itching and pain, which diminish quality of life.<sup>3,4</sup> Symptoms have been shown to persist 15 years after onset, with negative psychosocial consequences, such as long-term sick leave, change of occupation or early retirement.<sup>5,6</sup>

Typically, hand eczema is a dynamic process<sup>4,7</sup> where self-management is imperative, both for handling acute eruptions and avoiding relapses. However, little attention has been given to long-term self-management of the disease in recent reviews.<sup>7,8</sup>

The onset of chronic illness has been described as a ‘biographical disruption’,<sup>9</sup> where individuals actively attempt to adapt to the required treatment regimen.<sup>9,10</sup> Medication adherence is considered low within dermatology.<sup>11,12</sup> However, chronic hand eczema requires a wider perspective than that of medication adherence alone. Adequate treatment and subsequent prevention of relapses begins with determining the aetiology to remove the causative agent(s), if possible.<sup>4,13</sup> Moreover, it is important to identify aggravating exposures<sup>14</sup> and to offer health education and support with consideration for the illness beliefs and self-management ability of the affected person.<sup>15</sup>

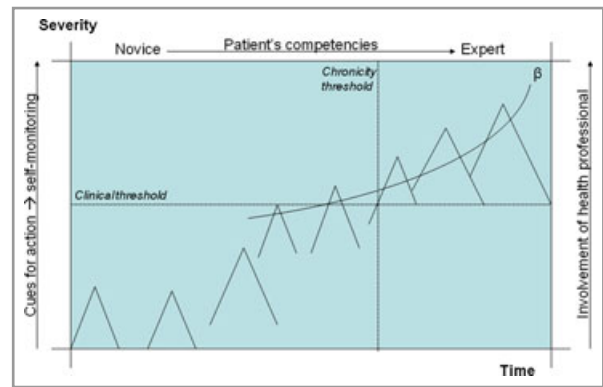
Two recent studies have explored perceived needs and how chronic psoriasis is self-managed. Both studies highlight the patients’ views of living with a complex and challenging disease and their experiences of lacking knowledge and support from the healthcare system.<sup>16,17</sup> Also, patients’ views on care and treatment of psoriasis and atopic eczema suggest different attitudes between men and women towards the use of emollients, and a need for individually designed information.<sup>18</sup> No similar studies have been identified for chronic hand eczema.

Just as hand eczema is not a uniform entity,<sup>7</sup> neither is self-managing the illness, which cannot be separated from life self-management.<sup>10,19</sup> Understanding how people integrate their eczema into everyday life is important if the healthcare system is to support self-management according to perceived needs and problems. The aim of this qualitative study was to explore knowledge, attitudes and behaviour in the everyday lives of people with chronic hand eczema and, in particular, to investigate perceived barriers in self-management of hand eczema.

## Methods

### Design and methodological considerations

The design of this study is qualitative with data generated from focus group interviews. A qualitative content analysis was performed with a deductive approach by use of a template.<sup>20,21</sup> In the literature there is no commonly accepted definition of self-management in relation to fluctuating diseases with potentially chronic courses, such as hand eczema. In order to clarify the researchers’ preconceptions and guide the analysis, self-management was conceptualized by construction



**Fig 1.** Conceptualization of self-management in chronic hand eczema. The figure displays a theoretical model of the individual’s adaptation to chronic hand eczema, inspired by Malten<sup>22</sup> and Dreyfus.<sup>23</sup> Throughout the course of disease, cues for action become more evident; health professional involvement increases and the individual’s competencies develop. Clinical threshold, clinically visible skin changes; chronicity threshold, transition of acute to chronic disease; peaks, eruptions of eczema;  $\beta$ , shifts between active disease and recovery phases.

of a model comprising the disease’s characteristics and the individual’s adaptation to disease (Fig. 1).

Inspiration for the model came from Malten’s ‘Thoughts on irritant contact dermatitis’<sup>22</sup> and Dreyfus’s model of adult skill acquisition.<sup>23</sup> Theoretically, adaptation to an everyday life with hand eczema involves development in self-monitoring and potential interaction with health professionals throughout the course of disease. The recurrence of eruptions can be viewed as a series of experiences, all of which may add to the patient’s knowledge about his or her eczema, thus the patient’s competencies develop. We explored these competencies, broadly defined as the skills of performing an activity and the ability to assess whether the activity is necessary. This definition involves the dimensions of knowledge, attitudes and actual behaviour.<sup>24,25</sup>

The population of patients with hand eczema is very heterogeneous, with a large variety of experiences. Focus group interviews are especially suitable when seeking breadth in the inquiry.<sup>20,26,27</sup> The setting was an outpatient clinic at the Department of Dermato-allergology, Gentofte Hospital, University of Copenhagen, Denmark. Purposeful sampling<sup>20,26,27</sup> secured a wide representation of age, gender, hand eczema history and occupation. All participants were ethnically Danish. Hand eczema is often occupational, thus participants were aged between 18 and 65 years.

### Recruitment to focus groups

Eligible participants were found among current patients. Twenty-six individuals consented to participate, of which three later withdrew (Table 1). The groups were formed based on date of consent and they were stratified by sex, as men and women are exposed in diverse ways. Moreover,

Table 1 Focus group compositions

Focus group <sup>a</sup>	Name	Age (years)	Occupation	Aetiology of HE
1	Eric	43	Skilled metal worker, self-employed as a baker 3 years ago	A/I
	Michael	45	Industrial operator	Single A
	David	49	Engineer, sales representative	Indeterminate A
	Bob	64	Architect, recently took early retirement	Multiple A
	Paul	65	Dentist, recently took early retirement	Multiple A
2	Maria	21	Hairdresser	I
	Brigitte	39	Healthcare assistant	AD/multiple A/I
	Kirsten	40	Skilled electrician, now employed as a janitor	Single A
	Susanne	44	Healthcare assistant, on sick leave for 18 months, then terminated	I
	Annette	48	Food package industry, currently on sick leave, mostly due to depression	AD/multiple A/I
3	Ingrid	64	Accountant, secretary	Single A
	Kevin	25	Skilled and employed as a painter	A/I
	Peter	30	Medical doctor	AD/multiple A/I
	Jacob	32	Window cleaner	AD/multiple A/I
	Frank	39	Skilled and employed as a mechanic	Single A/I
4	Hugo	56	Skilled and employed as a painter	Single A/I
	Alexander	58	Laboratory technician	Indeterminate A
	Anne	24	Previously in the food industry, now studying pedagogy	Multiple A/I
	Sandra	30	Ex-hairdresser, now studying to qualify for office work	AD/I
	Betty	55	Independent child-minder of three preschool children	I
	Anita	60	Child care, office work, recently took early retirement	A/I
	Marianne	61	Clerical work in a bank, canteen work, took early retirement 8 years ago	A/I
	Lilly	62	Previously postal delivery, currently secretarial office work	A/I

A, allergic; AD, atopic dermatitis; HE, hand eczema; I, irritative. The names are pseudonyms to secure participants' anonymity. <sup>a</sup>Focus groups 1 and 3 were male; groups 2 and 4 were female.

gender may play a discriminative role in self-management.<sup>28</sup> Participant compatibility promotes group interaction and cohesiveness through a higher level of trust and confidence.<sup>20</sup>

Sessions were held at the National Allergy Research Centre, situated in a noninstitutionalized apartment.<sup>29</sup> The constructed model (Fig. 1) guided the development of a semistructured topic guide (Table 2). The interviews were moderated by the first author with relevant detours allowed. The participants were encouraged to elaborate, and frequently asked each other

to clarify and further describe experiences. A project nurse was responsible for audio recording and time schedule. The average duration of the focus groups was 2 h.

**Data collection and analysis**

Data collection and transcription were iterative. The first author transcribed the interviews while reflecting upon her moderating role and the feasibility of the topic guide. Qualitative

Table 2 Topic guide for focus group interviews

Opening question	Please, describe to us a typical day where you become aware of an eczematous eruption?
Self-monitoring	How is the dynamics of your hand eczema? Is it constantly present or does it fluctuate? How is your awareness of potential eczema in the absence of actual eczematous activity? Do you sometimes forget what your normal skin looks like?
Everyday experiences of self-management	How does hand eczema affect your everyday life? Restraints and limitations? Which precautions do you take to prevent further deterioration or relapse? How has your everyday life changed because of hand eczema?
Knowledge of disease prevention and treatment	How do you act in case of an eruption? Do you get the feeling of becoming more knowledgeable throughout the course of disease? What do you do to become more knowledgeable?
Controlling the eczema	What could be beneficial to you so that you could better manage and control your eczema? How can we as healthcare professionals best support you?
Involvement of healthcare professionals	How do you experience the relationship with your dermatologist? Have you at any point consulted providers of complementary and alternative medicine?
Closing question	Do you have any eye-opening experiences about self-managing hand eczema which you could pass on to others?

content analysis was performed through a deductive approach using a template<sup>20,21</sup> in which the relationship between codes, and later categories and themes, was organized. The researchers' preconceptions were explicated by the aforementioned conceptualization of self-management (Fig. 1) and were logically acknowledged as *a priori* themes in the template.<sup>20</sup> The first interview then further informed the template's development. Table 3 shows the transformation of key concepts into constituents, dimensions, themes, categories and *in vivo* codes in the analysis.

Potentially, template analysis limits interpretation of data. Thus, important themes may be overlooked.<sup>20,30</sup> This issue was addressed by accepting the initial template as preliminary, including a few tentative codes to be altered in later stages of analysis.<sup>20,21</sup> The first author did the coding, after which subsequent analysis was performed through an iterative team process to achieve consensus about the interpretation of the findings. Manual coding was chosen because of the size of the material, to facilitate a more comprehensive analysis of the interviews, and to promote engagement with the transcripts on an interpretive level. Codes were merged into superior codes and categories by writing labels on Post-it notes; a wall was then used for creating a mind map of interrelations. Finally, codes were organized in a matrix referring to line numbers in the transcripts to establish an identification path for ongoing examination of contextual congruence.

## Results

The dialogues proceeded freely, although each group had participants with modest contributions. Wording of the interviews varied between individual descriptions of phenomena and discussions. The analysis generated three key themes: (i) knowledge – application in everyday life; (ii) attitudes towards prevention – formed by experiences; and (iii) behaviour – balancing the effort.

### Knowledge: application in everyday life

Participants viewed treatment and prevention as highly complex, based on personal experience and impressions from medical consultations. Some perceived being given different explanations and recommendations, and the diagnosis was widely believed to be ascertained with difficulty. Acknowledging the necessity of exposure avoidance, participants used metaphors such as 'it's like a jungle' to describe the information grey zone they found themselves in. Overall, participants expressed ambivalence. Although hand eczema is complex, simple solutions are offered; the simplicity of using emollients as preventive measures, apparently contradicted the complexity (Table 4).

Participants had knowledge about their conditions, especially aetiological and deteriorating factors. However, some tended to generalize, reflecting on whether they shared similar allergies with others, although they had previously tested negative (Table 4). One participant had systematically created

an Excel file cataloguing ingredients in various emollients. The recurrence of certain lipids in the long list created a pattern of recognition, leading to an assumption of intolerance, although no tests had confirmed this.

Participants expressed knowledge of skin protection and skin care. They all had experience of using protective gloves or emollients. However, applying this knowledge to behaviour met with internal barriers like habits (Table 4). Some participants engaged in the new preventive regimen while attempting to carry on with habitual leisure activities. Others tried to develop beneficial habits through innovative solutions (Table 4).

More knowledge was actively pursued, and it was widely acknowledged that individual insight increased over time. However, 'not knowing enough' was an overall mantra. The participants felt they lacked knowledge and tended to focus on the causality of (their) eczema. Several expressed the opinion that research into causality was far more interesting and needed than research into treatment. They also referred to hand eczema as a problem, solvable by use of test schedules, rather than a long-lasting condition. The perceived knowledge gap also related to medical consultations, where 'trial-and-error' was experienced (Table 4).

### Attitudes towards prevention: formed by experiences

Participants discussed what caused their eczema. Some had had eczema since childhood, which impacted their career choices. For others, the eczema could be ascribed to known exposures, such as nickel, but they failed to understand why the disease did not necessarily improve by avoiding the relevant allergen. Therefore many reflected upon other potential causes not yet identified, and various illness beliefs were presented (Table 5). Some suspected that red wine, alcohol or certain foods had aggravating effects, although only a few participants had been diagnosed with food allergies.

Some patients experienced discomfort when following preventive regimens, such as using protective gloves or emollients. The recommended use of cotton gloves underneath protective gloves was felt to diminish hand dexterity, which is important to bakers, for example. Several described emollient regimens as unfeasible because of greasy and slippery hands, while another participant felt that the effects of emollients gradually diminished. To some, the creams seemed to provoke rather than prevent eczema. The profound discomfort of using creams then hampered their intention of continuous preventive behaviour (Table 5).

Many participants felt stigmatized by the visible disease, referring to the stress of socializing during times of severe eczema with fissures or infection. Wearing cotton clothes was also perceived as stigmatizing, because it drew more attention to the hands. Interestingly, fear of stigmatization sometimes led to career choices that were against medical advice and at first appeared irrational (Table 5).

Several codes were merged into a category labelled 'external barriers to protective behaviour'. Business confidentiality

**Table 3** The deductive approach of template analysis applied for this study, including description of key concepts, constituents and definitions as *a priori* themes, which steered the data analysis. Examples of *in vivo* codes, categories and final themes generated from the analysis complete the template

Theoretical concepts		Empirical data			
Key concept	Constituents and clinical significance	Dimensions and definitions	Themes	Categories	Codes
Self-management in a course of hand eczema involves dynamic adaptation to disease and development of competencies	Competencies: in addition to skills of performing an activity, also the ability to assess whether the activity needs to take place; hence, this involves knowledge, attitudes, and behaviour <sup>24,25</sup>	Knowledge  Attitude: a learned, global evaluation of an object (person, place or issue) that influences thought and action <sup>39</sup>  Behaviour	Applying knowledge in everyday life  Attitudes towards prevention formed by experiences  Balancing the effort in behaviour	Paradox of complexity and simplicity	Simple solutions Grey zone of knowledge 'Like a jungle'
				Generalization	'Your allergy could be my allergy'
				Beliefs about illness and causality  Barriers to preventive behaviour	Accumulated dose Degraded immune system Lack of vitamins and minerals  Side-effects and bodily discomfort Stigmatization
				Time-consuming and energy-draining Maintaining control	Shopping is troublesome  'All or nothing' Consistence Compensating after failing
Deductive		→	→	→	Inductive



Table 4 Key theme (i): knowledge – application in everyday life

Category	Context	Data extracts
Paradox of complexity and simplicity	The simplicity of emollient therapy could be experienced as contrasting to the expertise presumed to be in the healthcare system, as stated by Betty:	'She [the general practitioner] made an acute referral and then I came to the professor, and she looked at me and said: 'You need to have Vaseline.' Then I thought, well, do you have to be a professor to say that you need to have [laughing] Vaseline?'
Generalization	David reflected on whether he had the same allergies as other group members:	'You mentioned something about working in the garden and colophony and such, which I have also suspected. At some point in time, I'll make an experiment with colophony to see if anything reacts, right. Because if I'm only handling wood and such occasionally, then I may not notice if an eruption occurs and maybe it erupts after 5–6 h and then I don't know what it is.'
Habits and limits of time and foresight as internal barriers	Michael referred to situations where habits and limited time take over:	'All of a sudden you find yourself in a situation... say, this spring, we had rented a house in Sweden for the Whitsun holidays. And when we were about to leave, you have to clean the house, and just by routine you grab some soap, put your hands in it and it wasn't until we were all done that I came to think about it; this wasn't such a smart move, right.'
Innovative solutions	When performing leisure activities, one participant had attempted to knit while wearing cotton gloves. Others referred to the sewing of 'cotton socks' to protect from potential harmful hand grips on the bicycle, a bun recipe with the dough being mixed and kneaded within a plastic bag, or using the mobile phone to memorize emollient usage like Kevin:	'Well, not everyone feels like this, right. I think it's a habit, but with the mobile phone you can set more than one alarm. I have begun to set it thrice a day. At least in the evening, because then the phone hoots even if you have gone to bed. Well – put on the cream and the gloves.'
Lack of knowledge	While discussing the level of knowledge within the field of hand eczema, Paul argued:	'What puzzles me is the lack of better diagnosis in this; that is, better science. I think this 'trial and error' is a very primitive form of medicine [...] Quite simply, I ask for something more radical. And in a way, a more accessible medicament [...] We're talking about the largest organ in the human body [...] This is a bit poor considering where we ought to be.'

within the chemical industry, and poor legal regulations, were mentioned as external obstacles to prevention. For example, the allowed use of numerous synonyms for chemicals created confusion: 'I have a list of 50 different names of formaldehydes. It's extremely difficult and you can't remember them all. They can do what they like. That's so frustrating because then you, as a consumer, cannot avoid the stuff' (Bob). Work obligations and consideration for family or colleagues sometimes outweighed consistent protective behaviour (Table 5).

Moreover, exposures occurred because of others' behaviours. In spite of relevant precautions at work, one participant had an eruption, interpreted as work-related, from touching a door handle where a colleague could have left residue of the allergen. 'One can't control other people's actions [...] no matter how many labels you read [...]' (Michael).

Overall, participants wanted an active role in their course of illness. Yet they felt restrained from acting due to lack of knowledge or struggling to navigate in a world of 'a million different chemicals'.

### Behaviour: balancing the effort

Some participants systematically tried to avoid potential allergens in products, comparing this process to the work of a detective. They emphasized the need to use thorough, problem-solving methods. Self-examination of exposures was partly motivated by the urge to be active and use one's influence wherever possible, e.g. the rationale of avoiding specific foods because one has a skin disease (Table 6).

Overall, participants felt a constant obligation to focus on their disease. Always being alert so as to avoid exposures, or remembering to use gloves or emollients, was perceived as highly energy-consuming (Table 6). An 'all or nothing' attitude towards prevention was expressed, which could be followed by guilt or compensating actions when failing. The need to maintain control led to the formulation of rules to be followed rigorously, such as hand washing always followed by the use of emollients. Occasionally, 'forbidden acts' resulted from the need to get unavoidable things done, followed by attempts to compensate. Relinquishing daily activi-

Table 5 Key theme (ii): attitudes towards prevention – formed by experiences

Category	Context	Data extracts
Illness beliefs	Eric's reflections on the onset of a nickel eczema appearing after he had stopped working with metal:	'It began with these small blisters, but then I know that my eczema is due to nickel. I'm skilled as a metal worker and I've been working with this since I was 16 years old. Then I stopped 3 years ago because we bought a bakery. So now I'm a baker, and that's when it began. When I was working with metal, I didn't have anything. It's a bit amazing.'
Side-effects and bodily discomfort	Maria described how using emollients could be experienced as provoking the eczema:	'Sometimes when it's bad and I put on my cream, it becomes...even if there's no water in the cream, it still feels dank and provocative in a way, so it only gets worse. So mostly, actually, I only put on the cream when my hands are not so bad. Because when they're itchy and have blisters and all that, I just think it gets worse when I put on the cream.'
	Kirsten described bodily discomfort almost as if the hands had a will of their own, when she referred to situations of going to the drugstore saying:	'My hands are like this.' 'Well, try this and try that.' 'But it should be without perfume and not have too many ingredients.' 'Yes, well, we have this one and this one.' I go there and buy 3–4 creams, right. Then I come home and as soon as I open it and put it on, my hands just go 'wash it off.'
Stigmatization as internal barrier to preventive behaviour or as a prompt to go against medical advice	David referred to situations where preventive behaviour conflicted with his work as a sales representative:	'Well, someone is sitting on the opposite side of the table; thinking 'he's wearing gloves – this might be contagious,' right. So they focus on that instead of the product you're trying to sell, right.'
	Brigitte had deliberately chosen her current profession against medical advice, using these arguments:	'Well, you learn to live with it, because as I said, I went from office work to healthcare assistant again because I thought: 'Why not just go ahead and do it?' Because there, wearing gloves might be more accepted than if you're sitting in an office where you get all these... well, people who don't know about these things, and all the stupid questions. As a healthcare assistant, you're just being normal and hygienic, whereas in an office, it's ... 'Why are you sitting here when it's 30 degrees outside?' Frankly, all those stupid questions. I've said to myself that these hands are not going to restrain me and what I want to do in my work life.'
External barriers to protective behaviour	Job obligations and consideration to others interfered with a consistent 24/7/365 preventive behaviour. Eric argued:	'Well, sometimes you're in a rush, right. It's no good if the other guy at the table has to wait because you need an extra 5 min in order to find some gloves.'

ties or hobbies because of hand eczema was seen by some as inevitable, a condition of life. Others adjusted their activity levels to the condition by diminishing the length and extent of exposure. Also, more subtle changes to everyday behaviour were implemented (Table 6).

Remaining true to oneself while consistently maintaining a preventive regimen was difficult. One participant experienced improvement in her eczema in vacations at her parents' home when relieved from domestic activities. Her parents yelled 'Stop' when she approached the kitchen sink. However, she did not feel she could transfer this task delegation to her domestic situation with her spouse, because she was not the type to 'just let it be, although she ought to' (Anne). Others expressed feelings of indolence. The constant need for prevention led to frustration that one was different from others. This could lead to calculated risk-taking (Table 6).

## Discussion

The current study is among the first to explore the everyday life competencies of patients with chronic hand eczema. Hand

eczema affects many facets of life, as the hands are a primary tool for performing everyday tasks. In group interviews, the 23 participants described the profound impact of the disease itself but also addressed the consequences of continuous treatment and prevention.

The frequently mentioned knowledge gap could be interpreted as frustration with the difficulty of identifying a potential allergen, leading to lack of predictability. Many experienced fluctuations in disease severity and had become aware over time of contributing factors. To some, however, it remained unclear what provoked a sudden relapse, or whether a relevant allergen had not been identified. Allergic contact dermatitis per se is a specific disease caused by an allergen triggering the immune system. However, because almost everyone with damaged skin experiences deterioration when exposed to irritants, the mechanism of cause and effect becomes unclear. Combating an intangible enemy may lead to further psychological strain.<sup>31</sup> Tending to generalize extensively, participants questioned whether they had certain allergies although they had already tested negative. This indicates that information about disease specificity is not fully compre-

Table 6 Key theme (iii): behaviour – balancing the effort

Category	Context	Data extracts
Focusing on where to have influence	David reflected upon domestic effects when suddenly deciding to avoid pork because of others who did not tolerate meat from pigs. Although referring to himself as hysterical, he also gave interesting reasons:	'Well, this is where I can control it myself. Because what is present in the air and all that...I can put on some gloves when I use solvents and things like that. But I cannot control what's in the air.'
Time-consuming and energy-draining	A common thing such as shopping may be troublesome in the case of severe allergies, as stated by Jacob:  Betty referred to always thinking about using your own remedies:	'Well, the worst to me is when you're buying soaps and all those kind of things, where you have to look at the back of the can all the time and look out for things that you can't tolerate. And then when you come home and look carefully, you find out that there's something in it anyway. So you can't use it. Then you have to go to the shop and return it. You spend a lot of time looking at this card [CAVE card] and the can to see if the product contains this or that.'  'You have to think about things all the time. You have to remember your detergents, your gloves and your personal creams, and remember... I really had to learn this in the beginning, right? Remember not to use what was there. 'No, no, you shouldn't use this, you must use your own.' Not just throwing yourself into all those things, that really took a lot of effort at first...'
'All or nothing'; consistency and forbidden acts	Annette referred to compensating acts after performing a forbidden activity:  Talking about subtle changes that were consistently implemented into everyday life behaviour, Bob referred to the reading of magazines:	'Yeah, but if you're alone, and you have to do some things, then you just do them, right? Then it hurts afterwards. So, you have to do it. And then you put on layers and layers and layers of cream.'  'But you don't hold them [magazines] in your hands while reading. You lay them on the table and then you flick through the pages. Well, that's what I did back then in the early 80s when this colophony problem was diagnosed. Since then, I haven't had a piece of paper in my hands like you used to do back then [...] because I know very well that the thin skin between my fingers, that would go wrong.'
(Self) image of an indolent person	Reluctantly feeling indolent as a person was experienced by Marianne:	'Sometimes you feel lazy, right? Because you don't do the many activities that you previously did. I mean, sometimes you just feel: 'Well, now I just sit here.' It's a bit boring, I think. There are many things which you have to give up. That is, I liked knitting and I liked to cook and make pickles and jam. I was very, you know, active with my hands. I don't bother to do these things anymore because it's far too troublesome.'
Frustration about the constant need for prevention may lead to cheating	Feeling different from others could lead to episodes where risks were calculated and acted upon, as stated by Sandra:	'I just think, if you're aware of what will happen, then you can cheat, right? I mean, because you think that it's troublesome or annoying or simply because you would like to be like... [Marianne added: 'Like everyone else']... Yes, it was difficult for me to say, but yes.'

hended, resulting in an overemphasis upon risks and a concern about global potential exposure.

The simultaneous complexity and simplicity was perceived as a paradox, possibly contributing to assumption-based conclusions. The findings in this study confirm that patients generally perceive medical knowledge as unsatisfactory to explain their disease.<sup>10</sup> The individual struggles to repair the biological disruption and establish an acceptable and legitimate place for the new life condition.<sup>9,10</sup>

The participants' intentions of preventive behaviour met unwitting barriers such as habits and limits in foresight. Our hands are natural elements in our socialization. Thorough, continuous preventive behaviour challenges our social embedding and how we view ourselves, as Moberg also found when studying life with eczema.<sup>32</sup> The need to protect the hands interferes with many social situations, if the individual cannot

participate equally in everyday tasks. This disruption of reciprocity<sup>9</sup> and resultant stigmatization was also expressed by the participants in our study. The sustainability of a preventive regimen involving visible skin protection and discomforting emollient usage becomes subject to a cost-benefit analysis. Without any clear-cut rewards, the outcome can be equated with the Sisyphus syndrome also described in psoriasis treatment.<sup>10</sup>

Failing led to feelings of guilt, which then increased the strain, bringing further attention to the condition. The participants perceived continuous prevention as energy consuming and burdensome. Although some maintained a sustainable regimen, for example by using active memorization, others were very focused on bodily signals, such as discomfort from emollients, thus hindering the regimen. Negative outcome expectancies associated with emollient usage have been

reported elsewhere.<sup>31</sup> In the dissertation 'Living with eczema', Moberg uses (with reference to the philosopher Drew Leder) the term 'the dys-appearing body', a reference to how the body in illness becomes an object of attention and thematization.<sup>32</sup> This interferes with the usual 'taken-for-granted' body, which facilitates social interaction.<sup>33</sup>

This study highlights three focal points, which may inform clinical practice. Firstly, the individual needs specific, targeted information and sufficient support in sorting this information according to relevance. Secondly, the complexity of living with hand eczema in everyday life requires the individual's acceptance of hand eczema as fluctuating and involving uncertainty. Thirdly, with relevant knowledge and acceptance the effort of preventive behaviour may be more balanced and less resource demanding. Habits are shortcuts to the brain,<sup>34,35</sup> so much more focus on helping the patient adopt new habits is required.

The barriers for the individual may be extremely difficult to overcome.<sup>31</sup> Steps have been taken to rethink the healthcare system's traditional approach of 'rational communication and compliance'<sup>10</sup> and to acknowledge the significance of self-management. Current studies from Holland and Germany confirm this approach by showing interesting results through more interdisciplinary tertiary prevention of hand eczema.<sup>36,37</sup> The findings from our study have contributed to a self-management support intervention programme, which is currently being evaluated.<sup>38</sup>

This study was limited to four focus groups comprising patients in the same hospital setting. This may potentially impact transferability of the findings. However, the participants were representative of the heterogeneous population of patients with hand eczema in terms of sex, age and professional background. Subtype and history of disease also varied, adding to a broadening of the findings, although allergic contact dermatitis was over-represented. Vivid group interaction and rich interview data further strengthen the study's conclusions.

The deliberate gender segmentation prompted remarks from participants who wondered if men and women respond differently. Perhaps additional gender-mixed focus groups would have enlightened this perspective. This question underlines the social constructivist perspective of qualitative interviews with researchers being shareholders in generating the findings.

In conclusion, treatment and support for self-management need to be individualized for patients with chronic hand eczema. This involves providing knowledge that is specific and relevant to the patient, as well as helping the patient develop realistic expectations concerning the course of disease and adopt new habits that minimize effort in preventive behaviour.

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## 4.2 Manuscript II

**Mollerup A**, Veien NK, Johansen JD. An analysis of gender differences in patients with hand eczema – everyday exposures, severity and consequences. *Contact Dermatitis* 2014; accepted for publication (2013 submitted).

**1. Title:**

An analysis of gender differences in patients with hand eczema – everyday exposures, severity and consequences

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The authors declare that they have no competing interests.

**6. Author contributions:**

AM and JDJ are responsible for the overall design of the trial and the implementation at Gentofte. AM and NKV implemented the trial at the Aalborg setting. AM is the principal investigator. AM drafted the manuscript, which was reviewed by NKV and JDJ. All authors have approved the final manuscript.

**7. Running head:**

Gender differences in hand eczema.

## Abstract

### Background

Hand eczema is often related to high-risk occupations and aggravating exposures in everyday life. The disease is twice as frequent in women as in men partly due to diverse exposure patterns. Other gender differences may be relevant to consider in treatment and prevention.

### Objectives

To gain insight into the common features and differences between men and women with hand eczema.

### Methods

Clinical disease severity of patients (n = 306) attending dermatological treatment at two settings was assessed by the Hand Eczema Severity Index (HECSI). Self-reported medication adherence, aggravating factors, hand eczema-related consequences and quality of life was obtained from a questionnaire.

### Results

Men and women had equal clinical severity of disease with an overall median HECSI of 43. Self-reported medication adherence was equal between genders but patients older than 40 years reported higher adherence. The impact of disease was larger in women than in men. Women reported significantly more aggravating factors and sick leave. Also women had a more impaired quality of life than men at equal disease severity and this could be associated to the higher number of aggravating factors.

### Conclusion

Gender differences in hand eczema need to be considered in the dermatological treatment and counselling of patients.



## Introduction

Hand eczema has a one-year prevalence in the Danish population of 10-14 % (1;2). Hand eczema has a multi-factorial aetiology, wide variations in morphology and is often accompanied by itching and pain (3). Successful disease management involves removal of the cause(s) if possible (3;4). Often, many factors aggravate the eczema regardless of the specific cause. These exposures in everyday life need to be identified and continuous skin protection and skin care adopted by the individual (5).

Hand eczema is twice as frequent in women as in men (1). This supposedly relates to exposure patterns rather than individual susceptibility (6). A higher prevalence of atopic dermatitis among women may also contribute (1). The disease severity is not necessarily higher among women (7). On the contrary the severity was higher among men in a multicentre study of hand eczema patients (8). In this study no gender differences in dermatology specific quality of life was seen. In other studies more impaired quality of life among women than men has been reported (9;10).

Hand eczema is often related to high-risk occupations. However, in research only little attention is drawn to the fact that the labour market is highly gender segmented. In a recent study of occupational contact dermatitis, the absolute highest ranking of female risk professions, i.e. hairdressers, was not even among the top 10 risk occupations among men (11).

Also self-management of hand eczema may be influenced by gender. A cross-sectional survey found that more women than men sought medical attention because of their hand eczema (2). In general, gender has been found to influence health maintenance behaviour like everyday activities to protect and improve health (12). Presumably, women also have higher medication adherence (13). In contact dermatitis, women have been found to be more frequent users of conventional medicine (14) as well as complementary and alternative medicine (15). Conversely, a Swedish study suggests that among patients with psoriasis or atopic dermatitis men are offered more advanced therapy than women in spite of similar disease severity (16).

Hand eczema often becomes chronic and results in lower quality of life, sick leave, job rotation or early retirement (8;17;18). Recent evidence from Holland and Germany suggests that integrated care programmes, although expensive, are superior to usual dermatological care (19-22). As part of a clinical trial (23), we explored some aspects of hand eczema from a gender perspective, focusing on exposures, severity and consequences, as well as medication adherence and treatment in a cohort of patients. The aim was to gain insight into gender differences which need to be considered in treatment and counselling of patients with hand eczema.

## Materials and Methods

We conducted a prospective dual-setting study comprising a cohort of patients (n=306) referred to treatment at either an outpatient care clinic in Gentofte Hospital, University of Copenhagen (a tertiary referral centre), or at a private dermatology practice in the northern region of Denmark (a secondary referral centre). Approval of the study was obtained by the Danish Data Protection Agency and the Ethics Committee of the Capital Region (H-2-2011-007).

Eligible patients (referred because of hand eczema, aged between 18-70 years, capable of replying to questionnaires in Danish) were enrolled consecutively to the study. The majority of patients were diagnosed and tested according to their patterns of exposure and they were prescribed topical and/or other treatment. Some conditional differences between the two settings appeared. Only patients treated in the

hospital were tested for filaggrin-mutations (24) when appropriate and Grenz Ray Therapy was only offered in the private practice.

#### *Assessment of the clinical severity of hand eczema*

At the first medical consultation, the principal investigator or one of four specially trained nurses assessed the clinical severity of hand eczema by use of the Hand Eczema Severity Index (HECSI) (25). The HECSI evaluates the presence of clinical symptoms and the area involved. The deduced total index score has a range from 0-360. No minimum disease severity was required in the study.

#### *Demographics, susceptibility and dermatological treatment*

Demographic variables, history of atopic dermatitis, data of filaggrin-mutations, and information of prescribed treatment were obtained from the medical files. Prescribed treatment such as Grenz Ray Therapy, UVB/TL01 light therapy or potassium-permanganate baths was computed to a variable labelled 'on-site treatment'. These treatments were given as managed care as opposed to topical steroid treatment or systemic pharmaceuticals administered by the patient.

#### *Self-reported data of medication adherence, exposures, consequences and quality of life*

A questionnaire was handed to the participants at time for inclusion. One reminder including a new questionnaire was sent to non-responders after 2-3 weeks. The overall response rate was 90% (women: 174/190; men: 91/104).

Data of self-reported medication adherence were obtained by the Danish version of the Medication Adherence Report Scale (DMARS-4), which has been validated in cancer pain patients. The generic scaled covers whether respondents avoid, forget, alter or discontinue the prescribed medication. Measurement of the four items is on a 5-point Likert scale (26).

Information of exposures and aggravating factors were obtained by modified items from the Nordic Occupational Skin Questionnaire (NOSQ-2002) (27). We asked the patients which factors both work-related and in leisure time were aggravating to their eczema. In contrast to NOSQ-2002 (questions F3) we merged some factors in order to give way for hand sweating and physical friction. Also, we addressed eczema on hands or wrists as one entity, and the patients could report every aggravating factor. The questionnaire also addressed frequency of symptoms during the past year, burden of eczema disease measured on a VAS-scale from 0 (no eczema) to 10 (excessive eczema) and possible occupational component.

The questionnaire included the widely used Dermatology Life Quality Index (DLQI) (28;29). This was supplemented by items of the degree (from 0-10) of itching, scratching and fatigue within the last four weeks. These questions were from the Impact of Chronic Skin Disease on Daily Life (ISDL), which so far has been validated in patients with atopic dermatitis and psoriasis (30). Additional items from NOSQ-2002 (questions C1) gave data about consequences of the disease (27).

#### *Sample size estimation*

Sample size calculation was performed as part of the overall clinical trial and had estimated a group-size need of 87 to detect a difference of 30% in HECSI between two groups (23). General estimations of sample size requirements when examining health behaviour and quality of life refer to minimums of 60-71 participants in groups of comparison (31;32).

### Statistical analysis

Using IBM SPSS Statistics version 19.0 for Windows, categorical data were analysed by chi-square test and logistic regression. The HECSI-values were tested according to the normal distribution and turned out no-normal. However, after square-root transformation the data showed satisfactory normal distribution (Shapiro-Wilk's test:  $p = 0.073$  for women and  $p = 0.985$  for men). DLQI also turned out to be not-normally distributed. Accordingly, when comparing HECSI and DLQI between groups we used the median value and Mann-Whitney U-test. All p-values presented are two-sided and in bold if significant with a significance level of 0.05.

### Results

A total of 389 patients were eligible according to the inclusion criteria and 306 individuals consented. No differences as regards age and gender distribution were found between the non-participants and the included patients. A few patients ( $n=4$ ) had their diagnosis changed to psoriasis and eight patients withdrew their consent. Hence, a total of 294 patients were included of whom the hospital provided 190 patients and the private practice provided 104 patients. The patients had an age range of 18-69 years. One hundred and four were male and 190 were female.

A third of the women (65/190) had a history or current atopic dermatitis compared to only fifteen percent (16/104) of the male patients ( $p < 0.001$ ). A tendency of more women than men having mutation(s) in the filaggrin-genes was found with 12/47 tested women having a mutation compared to only 1/19 of the men (Fisher's Exact Test,  $p = 0.088$ ). Around sixty percent reported habitually having dry skin with no gender differences. We found no statistically significant gender differences in onset, previous history or frequency of hand eczema.

### Disease severity

Analyses of the clinical disease severity revealed only small differences in HECSI between men and women (table 1).

**Table 1:** Clinical and subjective disease severity between groups of gender

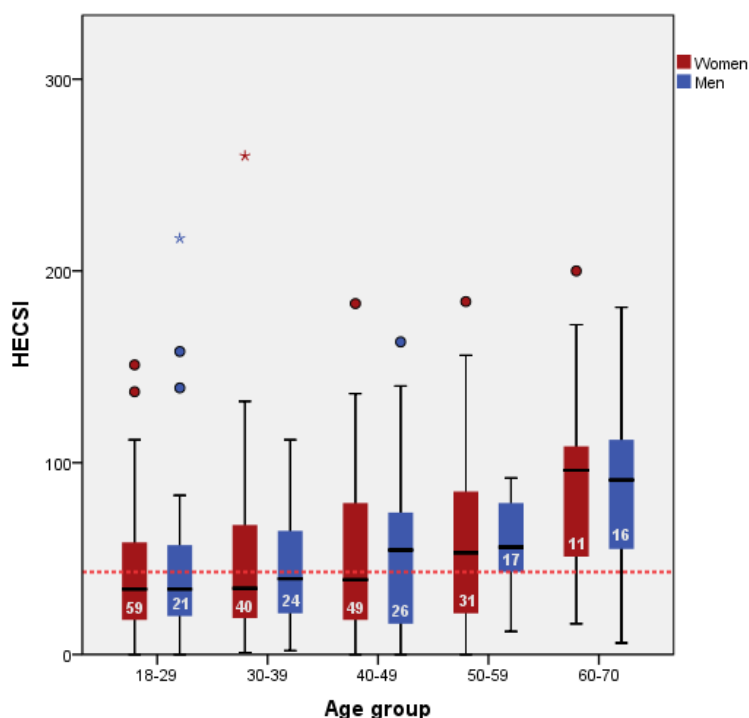
	Women	n	Men	n	p-value
<b>HECSI, median (IQR)</b>	39.0 (18.0-72.5)	190	46.0 (23.0-81.25)	104	0.161
<b>Clinical symptoms<sup>1</sup></b>	17.0 (9.0-26.0)	190	19.0 (12.0-27.0)	104	0.194
<b>Extent (area)<sup>2</sup></b>	8.0 (4.0-11.0)	190	8.0 (5.0-12.0)	104	0.669

VAS from 0-10, mean (SD)	Women	n	Men	n	p-value
<b>Worst case eczema</b>	8.48 (1.57)	172	7.97 (1.48)	90	<b>0.012<sup>3</sup></b>
<b>Itch within 4 weeks</b>	5.82 (2.76)	174	4.15 (2.80)	91	<b>&lt; 0.001</b>
<b>Scratching within 4 weeks</b>	5.19 (2.88)	172	4.31 (2.91)	91	<b>0.014</b>
<b>Fatigue within 4 weeks</b>	3.18 (3.16)	170	1.94 (2.37)	90	<b>0.004</b>

VAS, Visual Analogue Scale where zero equates no eczema or no complaints, and 10 equates worst case eczema or excessive complaints, HECSI-values presented as medians and inter quartile range (IQR), other values presented as means and standard deviation (SD) as regards intelligibility, Mann-Whitney U-test independent groups were used because of non-normal data unless otherwise stated, <sup>1</sup>Possible range 0-90, <sup>2</sup>Possible range 0-20, <sup>3</sup>t-test independent groups

In an analysis of trends, we found an increase in clinical severity related to higher age both among women (p-value = 0.003) and men (p-value < 0.001) as measured by Linear-by-Linear association. Fig 1 shows the age-related distribution of HECSI (n = 294).

**Figure 1:** Clinical severity (HECSI) according to gender and age groups (n = 294). Plot shows median (horizontal, dotted line), inter quartile range (box) and range of values (whiskers), number in boxes equate number of patients within age groups, dots and stars represents individual outliers in the study population



The worst-case burden of disease measured on a scale from 0 to 10 was different between genders. Moreover, women reported significantly more eczema-related itching, scratching and fatigue within the last four weeks compared to men (Table 1).

More women (49.1%) than men (17.6%) reported itching or stinging immediately after handling foods as indication of secondary contact urticaria. This difference was highly significant (OR 5.69; 95% CI 2.98-10.86; p < 0.001).

#### *Exposures and aggravating factors*

The patients were asked whether they experienced improvement when absent from work. We found no gender differences as 44.3% of the women and 47.4% of the men reported an occupational relation (n = 236).

Overall, women reported more aggravating factors than men, with a median number of 4 and 3 respectively (Mann-Whitney U-test: p < 0.001, n = 260). Table 2 shows the gender differences in factors reported as aggravating.

**Table 2:** Self-reported aggravating factors of hand eczema with number (percentage) of patients answering ‘yes’ to factor in question

<b>What are the most important influences<sup>1</sup> on or off work that aggravate your eczema?</b>	<b>Men n (%)</b>	<b>Women n (%)</b>	<b>Odds Ratio<sup>2</sup> (95% CI)</b>	<b>p-value<sup>2</sup></b>
Soap, hygiene products	41 (46.1)	106 (61.6)	1.88 (1.12-3.16)	<b>0.017</b>
Detergents and laundry products	32 (36.0)	110 (64.0)	3.16 (1.85-5.37)	<b>&lt; 0.001</b>
Handling of food	15 (16.9)	82 (47.7)	4.50 (2.39-8.44)	<b>&lt; 0.001</b>
Wet hands/handwashing	50 (56.2)	141 (82.0)	3.55 (2.00-6.28)	<b>&lt; 0.001</b>
Protective gloves	20 (22.5)	64 (37.2)	2.04 (1.14-3.67)	<b>0.017</b>
Sweaty hands	14 (15.7)	45 (26.2)	1.90 (0.98-3.69)	0.059
Physical friction	25 (28.1)	42 (24.4)	0.83 (0.46-1.48)	0.520
Machine maintenance, oils	28 (31.5)	2 (1.2)	0.03 (0.01-0.11)	<b>&lt; 0.001</b>
Construction work, painting etc.	20 (22.5)	16 (9.3)	0.35 (0.17-0.72)	<b>0.004</b>
Gardening, handling plants	18 (20.2)	49 (28.5)	1.57 (0.85-2.90)	0.149
Infections (colds, flu, fever)	2 (2.2)	12 (7.0)	3.26 (0.71-14.91)	0.127
Moods, stress, hormonal changes	14 (15.9)	51 (29.7)	2.23 (1.15-4.30)	<b>0.017</b>
<b>Total number of item respondents</b>	<b>89</b>	<b>172</b>		

<sup>1</sup>Patients were encouraged to tick off several factors, item was modified according to NOSQ-2002 question F3 (27),

<sup>2</sup>Logistic regression

We also asked the patients about their daily handwashing and use of emollients. Women reported significantly higher frequencies of handwashing both at work and in leisure time (Table 3). Also emollient usage differed with 89.5% of the women reporting daily use compared to 64% of the men (OR 4.79; 95% CI 2.48-9.25;  $p < 0.001$ ;  $n = 257$ ).

**Table 3:** Patterns of daily handwashing

<b>Total</b>	<b>How many times do you wash your hands during work?</b>				<b>p-value<sup>1</sup></b>
	0-5/day	6-10/day	11-20/day	> 20/day	
Women (n = 153)	59 (38.6)	37 (24.2)	22 (14.4)	35 (22.9)	<b>&lt; 0.001</b>
Men (n = 80)	49 (61.3)	19 (23.8)	4 (5.0)	8 (10.0)	
	<b>How many times do you wash your hands during leisure time?</b>				
	0-5/day	6-10/day	11-20/day	> 20/day	
Women (n = 165)	60 (36.4)	86 (52.1)	15 (9.1)	4 (2.4)	<b>&lt; 0.018</b>
Men (n = 88)	47 (53.4)	33 (37.5)	8 (9.1)	0 (0.0)	

<sup>1</sup>  $\chi^2$ -test Linear-by-Linear Association

### *Treatment and medication adherence*

In the trial, 102/294 patients (34.7%) were prescribed on-site treatment with no gender differences of the frequencies. We then analysed the association of prescribed on-site treatment according to quartile-based severity groups. Compared to having a mild hand eczema (HECSI <20), patients with a moderate-severe eczema (HECSI 43-75) were prescribed on-site treatment twice as often (OR=2.11; 95% CI 1.09-4.09;

$p=0.027$ ) and patients having a severe hand eczema ( $\text{HECSI}>76$ ) were prescribed on-site treatment seven times as often ( $\text{OR} = 7.15$ ; 95% CI 3.10-16.49;  $p < 0.001$ ).

Overall, the cohort had an equally high self-reported medication adherence ( $n = 260$ ) with a mean sum-score of 17.3 among women and 17.4 among men (score range from 4-20). The sum-score was dichotomised into low (4-15) and high (16-20) adherence. In a logistic regression with imputation of dichotomised age ( $\pm 40$  years), patients older than 40 years reported high medication adherence compared to younger patients with an OR of 3.29 (95% CI 1.77-6.11;  $p < 0.001$ ).

#### *Consequences of hand eczema and quality of life*

Thirty-six (24.5%) of 147 women reported eczema-related sick leave within the last 12 months. This was a significantly higher proportion compared to 9/84 (10.7%) of the men ( $\text{OR} 2.70$ ; 95% CI 1.23-5.94;  $p = 0.013$ ). In a logistic regression the number of aggravating factors were predictive of sick leave among women ( $p = 0.001$ ) but not among men ( $p = 0.315$ ). We also addressed the necessity of using protective gloves; changes in work tasks; change of job; difficulties in getting a job; experiences of colleagues' negative attitudes; effect upon occupational choice; decrease of income; job loss; retirement or other consequences. There was a tendency towards that more women (77.8%) than men (68.1%) reported overall consequences related to their hand eczema (Pearsons  $\chi^2$ ,  $p = 0.088$ ).

In analyses of DLQI, we found a much more impaired quality of life with a mean of 7.38 (SD 6.11) among women compared to a mean of 4.49 (SD 3.76) among men ( $p < 0.001$ ). The only subscale without gender differences was that of impact on leisure activities (Table 4).

**Table 4:** Analyses of the DLQI-subscores according to gender differences

Subscale (possible score)	Women		Men		p-value <sup>2</sup>
	mean <sup>1</sup>	no patients	mean <sup>1</sup>	no patients	
Symptoms/feelings (0-6)	2.77	171	2.09	90	<b>0.001</b>
Daily activity (0-6)	1.32	172	0.58	90	<b>&lt; 0.001</b>
Leisure (0-6)	0.81	169	0.55	88	0.107
Work and School (0-3)	0.98	171	0.66	90	<b>0.012</b>
Personal relationships (0-6)	1.00	173	0.53	90	<b>0.01</b>
Treatment (0-3)	0.70	172	0.29	91	<b>&lt; 0.001</b>

<sup>1</sup>The values are presented as means because these are most descriptive of the gender differences, given the limited space. However analyses were done as crosstabs of ordinal scales; <sup>2</sup> $\chi^2$ -test Linear-by-Linear Association

A linear regression of clinical severity measured by HECSI and the overall DLQI established that the level of HECSI could statistically significantly predict DLQI for both genders (fig 2a). The results of this regression are shown in Table 5a. The HECSI accounted for 36.0% and 16.7% of the explained variability in DLQI for women and men respectively.

DLQI measures the effect of disease within the past week. However, the questionnaire was self-administered with some delay in response; hence a lag effect could bias the association of HECSI and DLQI. Although men tended towards later responses than women (mean of 18.7 and 14.9 days respectively), this difference was not statistically significant (t-test,  $p = 0.102$ ). In the questionnaire the participants assessed the current burden of their hand eczema on a scale from 0-10. The participants

presumably filled out the whole questionnaire within a time frame of one day, thus to address potential lag effect a linear regression of current burden of eczema and DLQI was performed (fig 2b).

**Table 5:** Linear regression analyses within gender groups of (a) HECSI and DLQI; (b) current burden of disease (VAS) and DLQI and (c) test of differences in regression slopes between gender groups

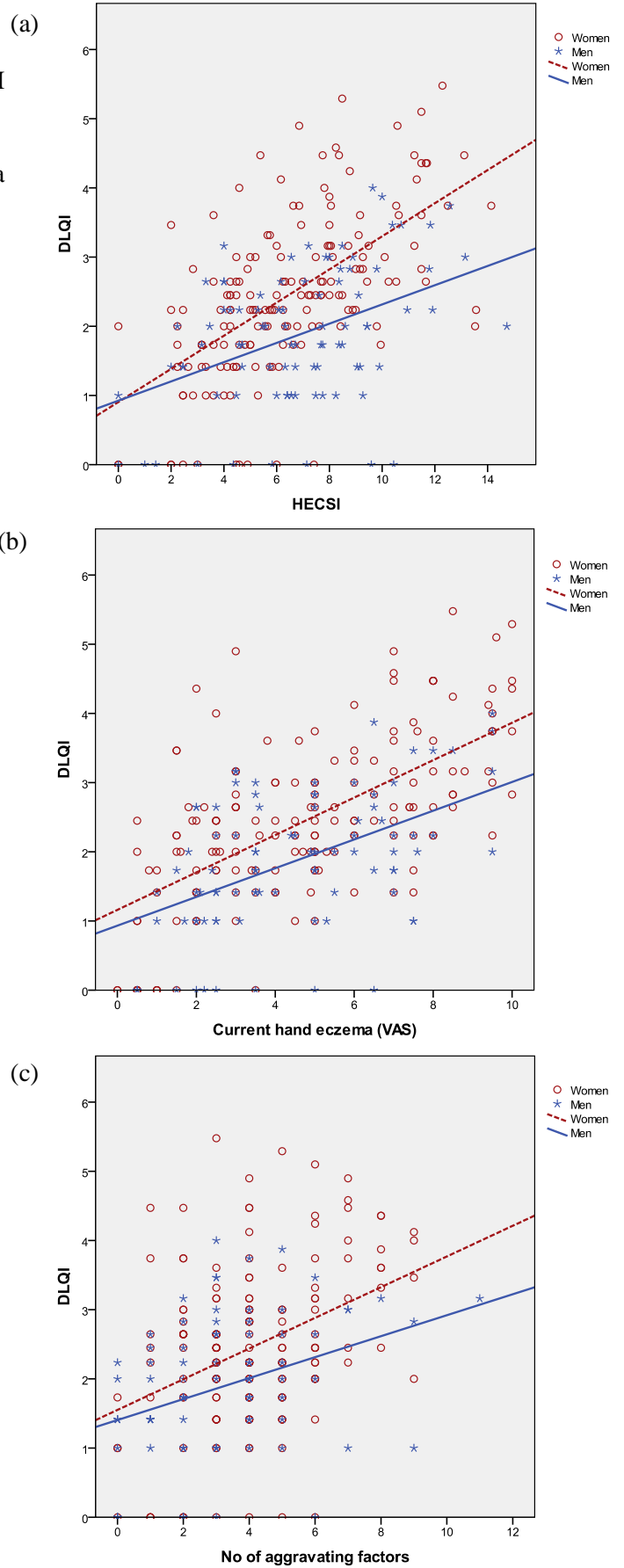
	$\beta$ (95% CI)	Adjusted $R^2$	F (df)	p-value <sup>1</sup>
<b>(a) HECSI and DLQI</b>				
Women (n = 166)	0.24 (0.19-0.29)	0.36	93.94 (1, 164)	< 0.001
Men (n = 87)	0.14 (0.07-0.20)	0.17	18.24 (1, 85)	< 0.001
<b>(b) VAS and DLQI</b>				
Women (n = 163)	0.27 (0.22-0.32)	0.40	107.55 (1, 161)	< 0.001
Men (n = 86)	0.21 (0.13-0.29)	0.23	26.38 (1, 84)	< 0.001
<b>(c) Aggravating factors and DLQI</b>				
Women (n = 165)	0.22 (0.14-0.31)	0.14	26.57 (1,163)	< 0.001
Men (n = 84)	0.15 (0.06-0.24)	0.11	11.50 (1,82)	0.001
	F (df)	p-value <sup>2</sup>	F (df)	p-value <sup>3</sup>
<b>(d) ANCOVA tests</b>				
Gender*HECSI interaction	5.89 (1)	0.016		
HECSI & DLQI (gender-adj)			28.23 (1)	< 0.001
Gender*VAS interaction	1.64 (1)	0.202		
VAS & DLQI (gender-adj)			18.63 (1)	< 0.001
Gender*aggravators interaction	1.18 (1)	0.279		
Aggravators & DLQI (gender-adj)			7.86 (1)	0.005

Data of HECSI and DLQI were square root-transformed;  $\beta$  slope of regression; (df) degrees of freedom; <sup>1</sup> test of null hypothesis within groups; <sup>2</sup> test of homogeneity of slopes by use of interaction variable; <sup>3</sup> test of null hypothesis between gender groups

This analysis showed similarly to the analysis of HECSI and DLQI that the level of current burden of eczema could significantly predict DLQI for both genders. The results of these analyses are shown in Table 5b. The current burden of eczema accounted for 39.7% and 23.0% of the explained variability in DLQI for women and men respectively. The same pattern was found when evaluating the predictive effect of the number of aggravating factors (Table 5c).

An analysis of covariance (ANCOVA) (33) is presented in Table 5d. By use of the interaction variables, the analyses showed that both the disease severity and the number of aggravating factors impacted DLQI statistically significantly higher in women compared to men. The impact increased related to severity. We could not calculate effect sizes or interpret the regression equation with confidence intervals because square root-transformed data do not allow back-transformation (33).

**Figure 2:** Linear regression of  
 (a) clinical severity measured by HECSI and DLQI  
 (b) current burden of disease (VAS) and DLQI  
 (c) number of aggravating factors and DLQI  
 HECSI and DLQI are square root-transformed data





## Discussion

Our study examined, and found, some gender differences in a cohort referred to dermatological treatment because of hand eczema. We obtained both objective (HECSI and on-site treatment) and subjective data (burden of disease, aggravating factors, medication adherence and consequences including quality of life). The gender distribution in the study population was representative of the well-known gender ratio of 2:1 with a predominance of women.

### *Gender commonalities of clinical disease severity, treatment and medication adherence*

The overall clinical disease severity in the cohort with a median of 43.0 was high compared to other studies as for example the mean HECSI of 19.9 in the study of Hald et al.(7) or the median HECSI of 17.0 reported in a multicentre study by Agner et al. (8). However our findings equate the baseline HECSI-values with reported means of 43.9 and 36.5 in a recent intervention study (19). We consecutively included patients throughout one year but most patients were included from October to April. This could give a relative increase in the overall severity of the cohort but it should not affect between-differences in the groups of men and women.

In contrast to previous findings (8) we found no differences in HECSI between women and men. Women had a marginally lower disease severity but also they appeared to have more variability of severity than men. Disease severity increased according to higher age in both groups which has been found previously (8).

Our findings do not confirm that men are given managed treatment more often than women. On the contrary we found that the HECSI-scores could predict the prescription of managed treatment. This opposes previous findings that significantly more men than women received UV treatment for psoriasis or eczema. The Laundry Bag Project's study (16) had a retrospective design and assumed a similar disease severity whereas we directly could impute a clinical severity measurement in a logistic regression.

Although women presumably adhere to prescribed medication more than men our results did not support this. Overall, our cohort reported a rather high medication adherence. DMARS-4 is only validated in Denmark in cancer pain patients who reported a similar high score (26). However our finding that self-reported high adherence was related to higher age is consistent with previous studies of topical therapy of psoriasis (13).

### *Gender differences as regards exposures and aggravating factors*

The analyses of self-reported exposures and aggravating factors revealed many gender differences. Although these factors do not explicit the occurrence of exposures, they may be interpreted as conditions in everyday life that need to be addressed in the treatment of hand eczema. Some of the factors mentioned relate typically to one gender mostly like the maintenance of machines or hormonal changes but the differences also indicate the gendered segmentation of both work-related and leisure-related tasks. More women than men work within "wet-work" occupations (34). This could explain the differences in some of the aggravating factors (Table 2) and the work-related patterns of daily handwashing (Table 3). However, women also reported more frequent handwashing during leisure time consistent with other studies (35).

Based upon questionnaire data, we do not know why these significant behavioural differences are present. Perhaps the threshold of perceived filthy hands lowers when one is used to comply with high hygienic standards at work. We actually found, that those patients who reported handwashing > 10 times/day at work were more likely to also report handwashing > 10 times/day privately with an OR of 2.46: Pearsons  $\chi^2$ ,  $p = 0.047$ . Ibler et al. found frequent handwashing to be the most important behavioural risk factor for

hand eczema in a survey of healthcare workers (36). However, this pattern would possibly be the same in both genders and even within the same job women are found to be more exposed to water than men (35). Perhaps some of these behavioural differences are founded as gender-conditioned habits in childhood and may only be reversed by deliberately addressing the issue in the course of treatment. This area needs further research.

We found that more women than men reported daily use of emollients. This may contribute to the women in general having a non-significant but lower clinical disease severity than men in spite of more aggravating factors.

#### *Gender differences in subjective disease severity, consequences and quality of life*

We found statistically significant gender differences with women having a higher mean score of worst-case burden of eczema. The degree of itch and eczema-related fatigue possibly contributes as women also reported significant more itching and fatigue than men. The results are in agreement with a recent study of patients with chronic pruritus. This study reported gender differences of localisation and quality of itch as well as influencing factors with women having an overall higher mean VAS of itch (37) as did another recent study (38).

We found a very large gender disparity of DLQI with a mean of 7.38 among women (previously clinically interpreted as a moderate effect) and 4.49 among men (a small effect) (39). The latter value is unexpectedly low also compared to other studies (8;37). Disease severity and DLQI have previously been found to correlate moderately in patients with occupational contact dermatitis (38;40). In our study we found gender differences in quality of life associated to hand eczema severity. The two linear regressions in fig 2(a) and fig 2(b) demonstrate directly that women have a more impaired quality of life than men at equal hand eczema severity whether this severity is objectively assessed or self-reported. An explanation could be that women find it more difficult to perform protective behaviour and risk avoidance given the differences in aggravating factors as indicated by fig 2(c). In everyday life with hand eczema patients find it very tiresome to deal with the preventive regimen (41). Also women with hand eczema have been found to have a higher level of anxiety than men (38) and this may decrease the individual's coping ability.

More women than men reported sick leave within the recent year and the number of aggravating factors could predict sick leave among women but not among men. The prevalence of sick leave may be directly associated to the extent of exposures at work as an unavoidable consequence, if temporary changes of occupational tasks are not possible. General gender differences in sick leave frequencies may also contribute but these are complex and beyond the scope of this study.

#### *Strengths and weaknesses of the study*

Our study has some limitations. We included patients consecutively at two very different settings both in terms of regions and placing within healthcare. The patients who consented to participate are a selected group who may differentiate from non-participants especially according to the self-reported data. As always in questionnaire data recall bias may be influential to the results. Moreover the questionnaire was administered as part of a clinical trial and patients may have over-reported good behaviour i.e. a social desirability bias. However we had clinical severity data of all participants as well as data of susceptibility and prescribed treatment. Also our study population is representative of the general population having hand eczema according to gender and age distribution. Our cohort of patients was highly heterogeneous also in disease severity and comprised hand eczema both related and unrelated to occupation.

### *Conclusion*

Although on the surface disease severity was equal among genders, hand eczema impacted women much more profoundly according to sick leave and quality of life. The quality of life could be linked directly to both disease severity and number of aggravating factors and this comprehensive overview has to the best of our knowledge not been reported elsewhere. Gender differences need to be considered in dermatological treatment of hand eczema patients especially in the counselling of ongoing preventive behaviour. The findings emphasises the necessity of addressing the everyday exposures and habits as part of a tailored patient counselling programme.

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### **4.3 Manuscript III**

**Mollerup A**, Veien NK, Johansen JD. Effectiveness of the Healthy Skin Clinic - A randomised clinical trial of a nurse-led patient counselling in hand eczema. *Contact Dermatitis* 2014; accepted for publication (2013; submitted).

**1. Title:**

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

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**5. Disclosures:**

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The authors declare that they have no competing interests.

**6. Author contributions:**

AM and JDJ are responsible for the overall design of the trial and the implementation at Gentofte. AM and NKV implemented the trial at the Aalborg setting. AM is the principal investigator. AM drafted the manuscript, which was reviewed by NKV and JDJ. All authors have approved the final manuscript.

**7. Running head:**

The Healthy Skin Clinic in hand eczema



## Abstract

### Background

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

### Objectives

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

### Patients and methods

Patients (n = 306) referred to diagnostic work-up and treatment of hand eczema at two settings were randomised and allocated either to the programme or to receive usual care. Primary outcome was clinical disease severity at follow-up compared with severity at inclusion into the study. Secondary outcomes were quality of life, burden of disease, skin protective behaviours and self-reported medication adherence.

### Results

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

### Conclusion

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

### Key words

Chronic hand eczema

Self-care

Nurse-led counselling intervention

Contact dermatitis

Effectiveness

Interdisciplinary prevention

HECSI

## Introduction

Hand eczema is common in the general Danish population with a one-year prevalence of 10-14% (1;2). Exposures to allergens and/or irritants in the environment are known factors in causing hand eczema. Endogenous factors like atopic dermatitis and mutations of the filaggrin-genes may contribute to an individual susceptibility. Hand eczema often becomes chronic either with continuous symptoms or as intermittent eczematous eruptions. Treatment and prevention of relapses begins with determining the aetiology to, if possible, remove the causative agent(s) (3;4). Although not causal, aggravating exposures in everyday life need to be identified and continuous preventive skin protection and skin care must be adopted by the individual (5). However, many patients find it difficult to apply protective strategies in everyday life and state that the necessity of constant focus on prevention is draining (6).

Hand eczema is often work-related and most research focuses on secondary prevention within specific high-risk occupations as shown in several recent interventional studies (7-9). Less is known of the group of hand eczema patients referred to dermatological treatment at either specialised centres in hospitals or at private practices of dermatology. In a prospective, multi-centre study of 799 patients, Hald et al. described clinical severity and prognosis of hand eczema and found that a poorer prognosis correlated to being an unskilled worker, to having severe hand eczema at the first consultation, to having symptoms like fissures and scaling as an indication of chronic disease (10) and to having a delayed course (11).

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

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

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

## Patients and Methods

We conducted a prospective dual-setting study comprising a cohort of patients (n=306) referred for diagnostic work-up and treatment of hand eczema. The settings were an out-patient clinic in Gentofte, a

metropolitan university hospital and a large private dermatology clinic in Aalborg in the northern region of Denmark. The patients in the study population were consecutively enrolled May 2011-April 2012 (Aalborg October 2011-April 2012). The Danish Data Protection Agency and the Ethics Committee of Capital Region (H-2-2011-007) both approved conduct of the study.

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

#### *Outcome variables*

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

The secondary outcome variables were the change in the disease-related quality of life, in the perceived burden of disease and in the self-reported medication adherence. Quality of life was measured by the dermatology life quality index (DLQI) (20). Summation of ten item-scores gives a total score of 0 to 30 with higher scores indicating poorer quality of life. The DLQI was supplemented by ratings of itching, scratching and fatigue on a scale from 0 (not present) to 10 (excessive) adopted by the Impact of Chronic Skin Disease on Daily Life (ISDL) (21). Also, the patient's perceived burden of disease was measured on a scale from 0 (no eczema) to 10 (excessive eczema) both at baseline and at follow-up. Medication adherence was measured by the Danish version of the Medication Adherence Report Scale (DMARS-4), which has been validated in cancer pain patients (22). This generic four-item scale covers whether respondents avoid, forget, alter or discontinue the prescribed medication. Measurement is on a five-point Likert scale with a total range from 4-20. Higher score indicates higher adherence. Data about the patients' use of dermatological indicated systemic medication were obtained from registers run by the Danish Medicines Agency.

#### *The trial flow*

The principal investigator, i.e. the first author, led the intervention team of nurses who assessed the clinical severity both at inclusion and at follow-up, and counselled the patients in the intervention group according to protocol (18). Allocation to do clinical assessments and/or the counselling was random. Hence the participant could be included by one team member, could be counselled by another, and could have the follow-up outcome assessed by a third member of the team. The team members had the same training in the use of HECSI and inter-rater variability was evaluated by occasional checks where patients were scored by two different assessors. In total seven patients were doubly assessed and the intraclass correlation coefficients for absolute agreement for total HECSI-scores was 0.78 (F-test with true value; p

= 0.016). A high level of team communication was conducted in order to provide commonality of the intervention.

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

Immediately after randomisation, counselling of general skin protection and skin care (24) was given to the patients in the intervention group. A second more individualised counselling was offered in timely relation to the next medical consultation after which the aetiology of the eczema was confirmed. To the patients allocated to the usual care group, a DVD with a 14 minutes information video about hand eczema was handed out as supplementary to the oral and written information given by the dermatologist. A follow-up questionnaire was administered to participating patients from both groups after six months. Patients allocated to the usual care group were offered counselling according to the Healthy Skin Clinic at follow-up.

Some patients had previously been tested for contact allergy and were not tested in this course of work-up and treatment, but the majority were diagnosed and had patch tests and/or prick tests according to their patterns of exposures. Patients treated in the hospital setting were tested for filaggrin-mutations when appropriate. According to hand eczema guidelines first choice of treatment is topical steroids (3). Other treatment options differed between settings i.e. Grenz Ray Therapy was only offered in the Aalborg clinic. This treatment as well as potassium-permanganate baths and UVB/TL01-light therapy was computed with the use of systemic medication into a dichotomous variable labelled 'intensified treatment'.

#### *The 'Healthy Skin Clinic'-intervention*

The central point in the intervention was the nurse-led counselling consultation. In short the Healthy Skin Clinic was founded upon three concurrent elements. Firstly, a SKIN-profile generated by responses from the baseline questionnaire described each patient's susceptibility, knowledge, co-morbidity, social support as well as known allergies and suspected aggravating factors. The purpose of this profile was to focus on the relevant areas for the individual counselling. Secondly, a patient self-management book was offered in terms of a secure website with information, educational videos, and tools for self-monitoring. Patients who did not use the Internet were handed over a folder containing almost the same features. Thirdly, support to self-management was offered as the possibility of ad hoc communication and networking. The patients could facilitate contact to either the intervention team of nurses or to other trial participants by use of the website. Further description of the intervention can be found elsewhere (18).

#### *Sample size estimation*

A decrease in HECSI from a mean of 19.9 to a mean of 11.2 at six months follow-up after treatment of hand eczema has previously been reported (10). The study did not report the standard deviations of the mean values and a histogram indicated that the HECSI-values were not normally distributed. Still, the context of that study appeared to be similar to ours. Thus we used these values to estimate the development in the usual care group and expected a difference at follow-up of 30% in favour of the intervention. Sample size calculation based upon the following values with assumed standard deviations:

usual care group mean-HECSI 11.2 (SD 9.0), intervention group mean-HECSI 7.7 (SD 6.0), alpha error level at 5% and a beta error level at 90% brought forward a need of 82 participants in each group (25). This figure corresponds to other suggestions of a minimum of 60-80 participants in each group in interventional studies targeting changes in health behaviour (26;27). With consideration to potential dropouts in a highly heterogeneous sample we assessed that inclusion of 150 patients in each intervention arm would be sufficient.

#### *Statistical analysis*

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

#### **Results**

Throughout the one year period of inclusion a total of 389 patients were invited to participate in the trial and 306 patients consented. These patients were consecutively enrolled as shown by the trial flow chart (Fig 1). In total, data of 292 patients were analysed for the purpose of this study. Most patients attended at consultations twice (44.6%) followed by patients attending thrice throughout the follow-up period (23.5%). Some patients only attended at medical consultations once and then failed to continue testing procedures and subsequent treatment adjustments (11.9%). The follow-up session was scheduled after 26 weeks (mean 28.7, min-max: 24-49). There was an average response time of 16 days (min-max: 0-79) for the self-administered baseline questionnaire.

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

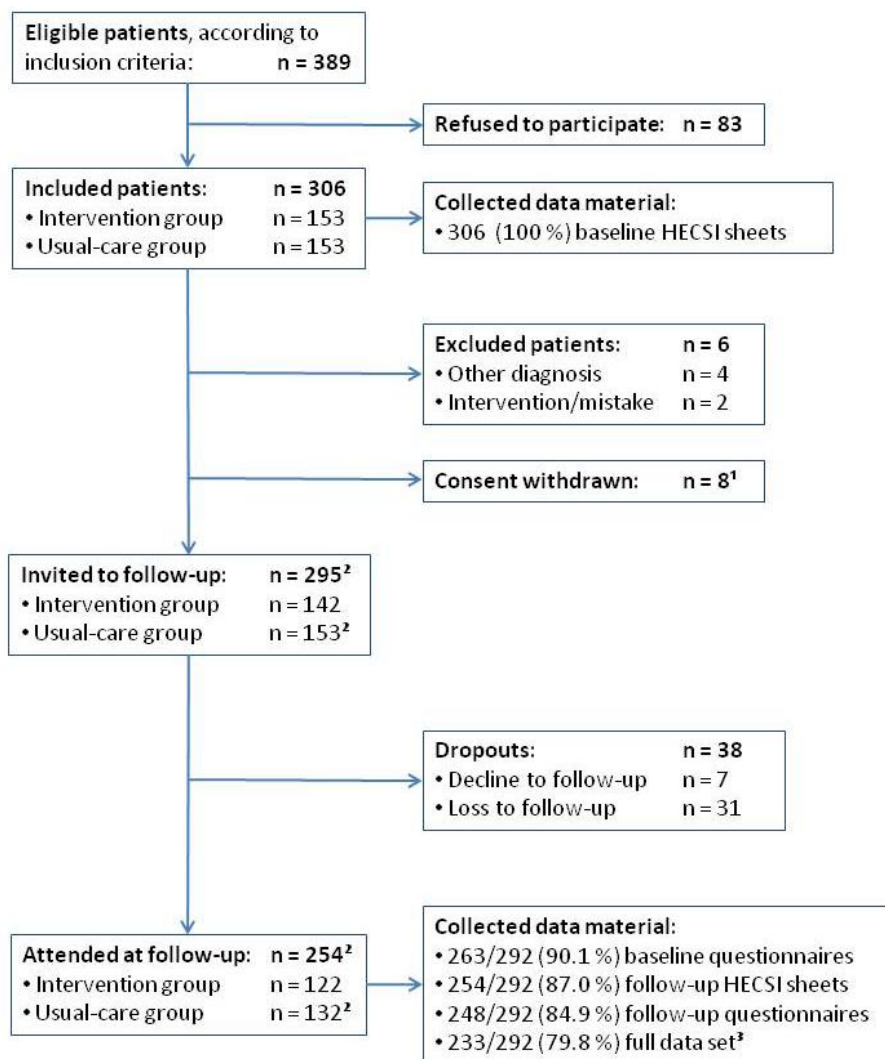
We found only minor differences between the usual care group and the intervention group in prescribed medication. Register data from the Danish Medicines Agency of redeemed prescriptions within the period May 2010 to December 2012 were available for 271 (92.8%) patients. These data were categorised into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

#### *Dropout analysis*

At the end of the trial we analysed differences of age and sex among the following four groups: (a) did not want to participate ( $n = 83$ ); (b) excluded/consent withdrawn ( $n = 14$ ); (c) lost-to-follow-up ( $n=38$ ); and (d) full data of primary outcome ( $n=254$ ). An ANOVA-analysis and post hoc analysis (Games-

Howell) with multiple comparisons showed significant differences between groups according to age. The patients in group (c) who were lost-to-follow-up were significantly younger (mean age of 33.0 years) compared to the patients in group (d) who had a mean age of 40.8 years ( $p < 0.001$ ). No other significant differences between the groups were found nor when comparing the sex distribution among the four groups (Pearson  $\chi^2$ -test;  $p = 0.41$ ).

**Figure 1:** Trial flow chart



<sup>1</sup>Eight patients from the intervention group withdrew their consent to participate in the study. <sup>2</sup>Two patients from the usual-care group who were given the intervention by mistake, were invited to follow-up to be offered the full counselling program. One patient from the usual-care group had other diagnosis which were not clarified until after invited to follow-up. Data of all three were then excluded from further analysis, also in this flowchart. <sup>3</sup>Full data set consists of both baseline and followup HECSI-sheets, and both baseline and followup questionnaires

Dropout analysis was also performed as regards the patients enrolled in the trial. The usual care group: the patients who completed the trial had a mean age of 42 compared to the lost-to-follow-up with a mean age of 34.5 (heterogeneity of variance, Games-Howell test  $p = 0.007$ ). The intervention group: compared to the patients who were lost-to-follow-up (mean age of 32) both the patients who completed (mean age

of 39.5) and the patients who were excluded (mean age of 45.8) were significantly older (homogeneity of variance, Tukey test  $p = 0.048$  and  $p = 0.017$  respectively). Also we analysed differences of HECSI at baseline among the three groups. A Kruskal-Wallis analysis of baseline HECSI showed equal disease severity between the completing patients compared to patients who were excluded or who were lost-to-follow-up (usual care group:  $\chi^2$ -test 1.55,  $p = 0.46$ , intervention group:  $\chi^2$ -test 3.23,  $p = 0.20$ ). In the enrolment phase the majority of those who did not want to participate argued that their decisions were based upon lack of time or energy e.g. due to co-morbidity. The same arguments were used by the eight patients, all allocated to the intervention group, who withdrew from the trial. Three of the four patients who were excluded due to other diagnosis (*pustolosis palmoplantaris*, *psoriasis*) were also from the intervention group.

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

**Table 1:** Characteristics of the patient cohort (n = 292). Values are expressed as number of patients (%). HECSI, Hand Eczema Severity Index. Data relate to entire study population (n=292) unless stated otherwise.

<sup>a</sup>Pearson  $\chi^2$ -test unless stated otherwise, <sup>b</sup>Linear-by-Linear, <sup>c</sup>Data from clinical database, <sup>d</sup>Compound variable of on-site treatment and systemic medication, <sup>e</sup>Questionnaire data

### Clinical severity of hand eczema

Table 2 shows the clinical severity in the two groups. The median HECSI in the overall cohort of patients at baseline was 43.0 (min-max: 0-260; n = 292). At six months follow-up the median HECSI had

decreased to 24.0 (min-max: 0-236; n = 254). Both groups improved significantly throughout six months (Wilcoxon Signed Rank Test, usual care group:  $p < 0.001$ ; intervention group:  $p < 0.001$ ). The intervention group had a larger improvement (median  $\Delta$ HECSI = -16.0) than the usual care group (median  $\Delta$ HECSI = -8.5). This result showed a tendency toward a statistically significant difference (Mann-Whitney U-test:  $p = 0.08$ ).

**Table 2:** Values of HECSI at baseline ( $T_0$ ), at follow-up ( $T_1$ ) and as  $\Delta$ -scores

	Intervention group			Usual care group			Between groups
	median <sup>a</sup> (IQR)	p-value <sup>b</sup>	n	median <sup>a</sup> (IQR)	p-value <sup>b</sup>	n	p-value <sup>c</sup>
<b>(a) Overall cohort</b>							
$T_0$ -HECSI	42 (20;82)		142	44 (20;72)		150	0.49
$T_1$ -HECSI	24 (12;46)		122	25 (10;45)		132	
$\Delta$ HECSI	-16 (-49;5)	<b>&lt; 0.001</b>		-9 (-33;6)	<b>&lt; 0.001</b>		0.08
<b>(b) The hospital</b>							
$T_0$ -HECSI	42 (20;91)		92	38 (18;64)		96	0.14
$T_1$ -HECSI	25 (11;46)		78	23 (10;57)		85	
$\Delta$ HECSI	-16 (-47;3)	<b>&lt; 0.001</b>		-5 (-27;11)	0.05		<b>0.01</b>
<b>(c) The clinic</b>							
$T_0$ -HECSI	41 (20;71)		50	49 (27;81)		54	0.32
$T_1$ -HECSI	21 (12;46)		44	27 (11;40)		47	
$\Delta$ HECSI	-16 (-50;6)	<b>0.005</b>		-20 (-50;-1)	<b>&lt; 0.001</b>		0.62

HECSI, Hand Eczema Severity Index, negative  $\Delta$ -scores indicate improvement at follow-up.

<sup>a</sup>Medians and Inter Quartile Range are rounded values; <sup>b</sup>Wilcoxon's Signed Rank Test for differences within groups;

<sup>c</sup>Mann-Whitney U-test for differences between groups

We then computed improvement as a dichotomous variable simply defined as the individual  $\Delta$ HECSI  $<$  zero. Significantly more patients (74.3%; 81/109) who had received intensified treatment improved compared to patients (61.4%; 89/145) who had not been prescribed this treatment (Pearson  $\chi^2$ :  $p = 0.03$ ). The progress in disease severity was also analysed separately according to settings. At baseline, only minor differences in clinical disease severity appeared between the two settings. The Aalborg clinic had a median HECSI of 46.5 compared to the Gentofte hospital setting with a median HECSI of 40.0 (Mann-Whitney U-test:  $p = 0.53$ ). Still, 77/104 (74.0%) of the patients in the Aalborg clinic was prescribed intensified treatment in comparison to 41/188 (21.8%) in the hospital setting (Pearson  $\chi^2$ :  $p < 0.001$ , OR 10.2). No significant differences between the intervention arms were found in the private clinic, but in the hospital setting disease severity in the intervention group were reduced significantly more than in the usual care group (Table 2).

We then performed a multiple linear regression analysis to predict  $\Delta$ -HECSI (square rooted-transformed data) with the covariates age, baseline severity, intervention arm, atopic dermatitis, and intensified treatment (Table 3a). This regression model was explicative of 28% of the variability in disease severity outcome (adjusted  $R^2$  0.278). The analysis showed that higher age was predictive of increased disease severity at follow-up ( $p = 0.005$ ), but the effect was marginal (0.038 on the square rooted HECSI-scale per year). Baseline HECSI-values per se predicted the disease severity much more profoundly as one unit's higher severity predicted an improvement of half a unit. Atopic dermatitis and intensified treatment



did not add statistically significantly to the prediction. Nor did the intervention add to the prediction of outcome at follow-up. As Table 3(b) shows, we found a highly significant interaction variable between the baseline severity and intensified treatment ( $p < 0.001$ ).

**Table 3:** Summary of (a) Multiple Regression Analysis, (b) Univariate Analysis of Variance test of the interaction variable baseline HECSI\*intensified treatment (BS HECSI\*treat)

(a) Variables	<i>B</i>	95% CI of <i>B</i>	<i>SE<sub>B</sub></i>	$\beta$	p-value
Intercept	0.506		0.647		
Atopisk dermatitis	0.548	-0.224,1.319	0.392	0.084	0.163
Age	0.038	0.012,0.064	0.013	0.177	<b>0.005</b>
Baseline HECSI	-0.540	-0.657,-0.423	0.060	-0.548	<b>&lt; 0.001</b>
Intervention arm	-0.133	-0.758,0.491	0.317	-0.023	0.674
Intensified treatment	-0.186	-0.858,0.486	0.341	-0.032	0.586

(b) Interaction variable	F (df)	p-value
BS HECSI*treat	48.658 (2)	<b>&lt; 0.001</b>

HECSI, Hand Eczema Severity Index; *B*, unstandardized regression coefficient; CI, confidence interval; *SE<sub>B</sub>*, standard error of the coefficient;  $\beta$ , standardized coefficient; F, F-test; df, degrees of freedom

Figure 2 indicates that the intervention had different effects in the subgroups of patients whether these had intensified treatment or not (Fig 2). We then stratified for this variable and did further analysis in the sub cohort of patients ( $n = 145$ ) who had not received this treatment. These analyses showed significantly larger improvement in HECSI in the intervention group compared to the usual care group (Table 4). The intervention impacted different subgroups in various ways. We found significant differences between the intervention group and the usual care group among patients without atopic dermatitis and among patients who had no self-reported seasonal variation of their hand eczema. Otherwise no differences between the intervention arms were found (Table 4).

**Table 4:** Subgroup analysis of  $\Delta$ HECSI-scores in patients not treated by intensified therapy ( $n = 145$ )

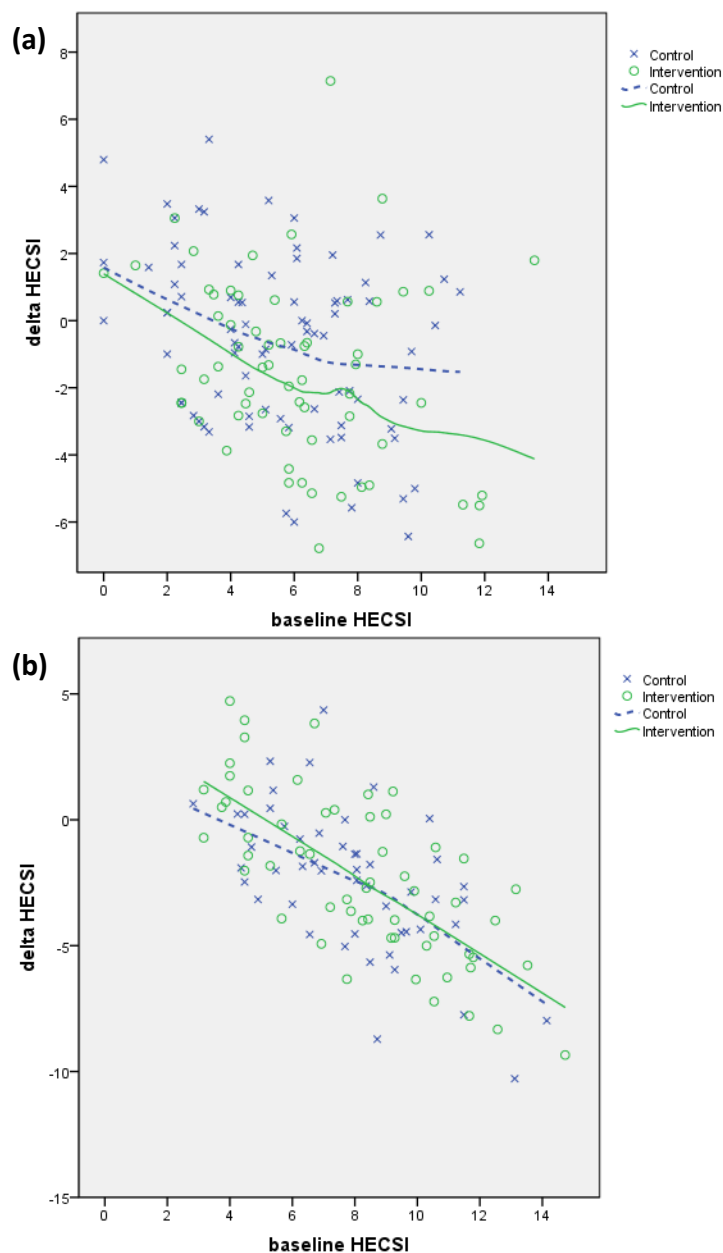
$\Delta$ HECSI-scores	Intervention group		Usual care group		Between groups
	Median <sup>a</sup> (IQR)	n	Median <sup>a</sup> (IQR)	n	p-value <sup>b</sup>
Overall sub cohort	-9 (-32;6)	63	-3 (-19;10)	82	<b>0.037</b>
No atopic dermatitis	-15 (-37;6)	48	0 (-26;11)	60	<b>0.034</b>
Atopic dermatitis	-8 (-18;7)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

HECSI, Hand Eczema Severity Index; negative  $\Delta$ -scores indicate improvement at follow-up.

<sup>a</sup>Medians and Inter Quartile Range are rounded values; <sup>b</sup>Mann-Whitney U-test of differences between groups,

<sup>c</sup>Seasonal variation is self-reported (data from questionnaire)

**Fig 2:** Association between baseline values of HECSI and  $\Delta$ HECSI (square root-transformed data) in subgroups of (a) patients who did not have intensified treatment and (b) patients who had intensified treatment during the trial



HECSI, Hand Eczema Severity Index; negative  $\Delta$ -scores equate improvement from baseline to follow-up; intensified treatment, compound variable of onsite-treatment and systemic medication.

Lowest baseline HECSI (square rooted) in the group of patients who had intensified treatment was 2.83 thus this is the starting point of the lines in figure 2(b)

#### *Effects on quality of life and burden of disease*

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

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

**Table 5:** Subjective outcome measurements of (a) DLQI and (b) VAS at baseline ( $T_0$ ), follow-up ( $T_1$ ) and  $\Delta$ -values

	Intervention group		Usual care group		Between groups
	median (IQR)	n	median (IQR)	n	p-value <sup>b</sup>
<b>(a) DLQI (possible score 0-30; higher score indicate higher impairment within past week)</b>					
$T_0$ -DLQI	5 (3;8)	123	5 (2;9)	128	0.71
$T_1$ -DLQI	3 (1;6)	114	2 (1;6)	117	
$\Delta$ DLQI	-1 <sup>a</sup> (-4;0)	105	-2 <sup>a</sup> (-4;0)	111	0.35
<b>(b) Current burden of disease (possible score 0-10; higher score indicate higher burden)</b>					
$T_0$ -VAS	5 (3;7)	126	5 (3;7)	132	0.49
$T_1$ -VAS	3 (2;5)	117	3 (2;6)	128	
$\Delta$ VAS	-1 <sup>a</sup> (-3;1)	109	-1 <sup>a</sup> (-4;1)	120	0.42

DLQI, Dermatology Life Quality Index, VAS, Visual Analogue Scale, values are presented as rounded median values and Inter Quartile Range. Negative  $\Delta$ -scores indicate improvement at follow-up.

<sup>a</sup> $p < 0.05$  by Wilcoxon Signed Rank Test for differences within groups, <sup>b</sup>Independent Mann-Whitney U-test for differences between groups

We did not find any gender differences of the primary outcome in the trial. Men had a higher HECSI at baseline (median of 47.0) than women with a median of 39.0 but this difference was not significant ( $p = 0.16$ ). Accordingly men improved slightly more than women (a median of  $-16.0$  compared to a median of  $-11.0$ , men and women respectively), although this was not significant. However, differences between the two genders were found in the measurements of quality of life. Significant differences were found at baseline where women had a median DLQI of 6.0 compared to a median DLQI of 4.0 among men (Mann-Whitney U-test;  $p < 0.001$ ). Both genders improved quality of life significantly during the trial as shown by the Wilcoxon Signed Rank Test ( $p < 0.001$  for women and  $p = 0.003$  for men), but women had a larger improvement than men. At follow-up women had a median  $\Delta$ -DLQI of  $-3.0$  compared to the median  $\Delta$ -DLQI of  $-1.0$  among men and this difference was statistically significant (Mann-Whitney U-test;  $p = 0.004$ ).

#### *Medication adherence and skin protective behaviour*

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

The patients were asked about their daily number of handwashing both at work and privately. This variable was dichotomised into  $< 10$  times/daily and  $> 10$  times daily at work or in leisure time. At baseline no differences between the usual care group and the intervention group were found which was

consistent at follow-up in the case of work-related handwashing. However at follow-up, fewer patients in the intervention group reported handwashing > 10 times daily privately compared to the patients in the usual care group (Table 6). Also the pattern of daily emollient use changed. No differences between the groups were found at baseline but at follow-up significantly more patients in the intervention group reported daily use of emollients compared to the usual care group with an odds ratio of 2.15 (Table 6).

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

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

<sup>a</sup>Odds Ratio; <sup>b</sup>Confidence Interval; <sup>c</sup>Pearsons  $\chi^2$ -test for differences between groups

## Discussion

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

In general the patients in the trial improved in disease severity whether they received the intervention or not. We found an overall tendency ( $p = 0.08$ ) towards larger improvement of HECSI in the group of patients who were offered the Healthy Skin Clinic intervention compared to the patients allocated to the usual care group. In the hospital setting, which provided the majority of participants, the difference in  $\Delta$ HECSI was statistical significant whereas no differences were found in the private clinic. Different treatment options may account for these inconsistent findings. On-site treatment was much more abundant in the private clinic (given predominantly as Grenz Ray therapy) compared to the hospital setting (OR = 16.9, 95% CI 9.3-30.8,  $p < 0.001$ ). We found that on-site treatment and additional systemic medication, i.e. intensified treatment, were positively associated to improvement in disease severity. It is plausible that the effects of this treatment diluted the impact of an intervention based upon the patients' self-management.

On the other hand the disease severity at baseline turned out to be the explanatory variable most likely to predict the severity outcome at follow-up. A square root transformation of the HECSI-values was successful as to establish a normal distribution of data. However it could not entirely reverse the disproportional association of baseline and  $\Delta$ -values of HECSI which could be found by the Bland-Altman plot. This means that the progress in disease severity was dependent on the values at baseline and higher values at baseline were likely to bring about a better prognosis. This could partly be explained by

the ‘regression-to-the-mean’-phenomenon because of potential measurement errors (28). The interrater-reliability showed a satisfactory intraclass correlation coefficient ( $r = 0.78$ ) similar to that in the HECSI validation study (19). However the occasional performed checks related by chance to patients where the highest assessed HECSI-score was 56. In the original validation study of HECSI an increased inter-observer variation was found for patients obtaining higher total scores compared to patients with lower scores (19). The exponential nature of the HECSI-scale per se may enhance possible measurement errors.

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

The DLQI-scores were rather low at baseline with median values of 5 in the two intervention arms. We did not obtain other baseline outcome measurements than HECSI at the inclusion point. The patients were handed a questionnaire and asked to return it within a week, but in several cases a reminder had to be administered. The same administration mode was applied to the questionnaires at follow-up. Fluctuations of disease activity or the initiation of adequate treatment may have caused a lag effect which presumably could introduce a bias in the findings. We have recently reported findings from the same cohort showing that women generally were far more impacted by their hand eczema than men also when adjusted for disease severity (17). However in this follow-up study we found that women improved more in quality of life than did men, although they did not show a corresponding improvement of their clinical severity. This emphasises the complexity of quality of life measurements. The DLQI has recently been found to be the severity assessment method least correlated to other severity scores of hand eczema (HECSI, Physician Global Assessment and a Clinical Photo Guide) and it is suggested that DLQI lacks specificity with regard to hand eczema assessment because it has been developed to evaluate skin diseases in general (31).

We did not find any beneficial development in medication adherence in either group during the trial. We addressed the issue of adherence as an element in the SKIN-profile because research suggests that adherence might improve merely by communicating this issue with the patient (32). Medication adherence at baseline was rather high thus it is likely that the scale of DMARS-4 reaches a ceiling effect by which improvements are difficultly measured. It is plausible that the 38 patients who were lost-to-follow-up would have reported lower medication adherence hence a more balanced distribution had been present, if they had returned the questionnaires. Still when self-reporting, patients arguably overestimate adherence (33) which could cause a social desirability bias. It has therefore been recommended simply to ask “What did you put on your skin yesterday” to assess patterns of medication adherence hence to address recent behaviour instead of intended behaviour (34).

### *Strengths and limitations of the study*

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

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

Secondly, the timely incoherence of HECSI-assessments and questionnaires made it difficult to validate the clinical findings by supplements of subjective measurements. In addition the clinical outcome measurements were not blinded which could promote an observer bias. However, the HECSI-scores at baseline were performed prior to randomisation. The data sheets were then removed from the participants' data files to make the subsequent outcome assessment as blinded as possible. The assessors at follow-up were randomly allocated to the patient in question thus in many cases they had not previously met the patient nor had knowledge of the baseline scores. We asked the patients to do a global assessment (by VAS 0-10) of their current eczema immediately before the follow-up HECSI scoring. When analysing the intervention group and the usual care group separately, we did not find any differences between the groups in the ranked correlations of HECSI and patients' assessment (intervention group: Spearman  $r = 0.65$  versus the control group: Spearman  $r = 0.63$ , both groups:  $p < 0.001$ ). Thus the possibility of a systematic overestimation of the  $\Delta$ HECSI-scores in the intervention group appears to be unlikely. Still, the HECSI-scale itself has some drawbacks related to mathematical properties of data distribution which challenge outcome measurement.

Thirdly, controllability of the intervention may be questioned. We did not require that the patients in the intervention group should fully comply with the intentional self-monitoring features or with the other elements in the Healthy Skin Intervention. Still, only patients from the intervention group withdrew from the trial which is in line with the previous findings of constant prevention experienced as tiresome (6). We deliberately chose a realistic design where the intervention was to supplement the medical treatment thus easily promoting a subsequent implementation. As a minimum all the patients in the intervention group were given the general counselling of skin protection and skin care but to some extent this may also have been offered by the dermatologist to the patients in the usual care group. Thus we cannot rule out a potential contamination bias. Moreover many of the participants were repeat patients thus had previously been treated at a private dermatology practice where they could have been informed of skin protection. These factors most likely would lead to an underestimation of the effects found in the trial.

### *Conclusion*

This trial demonstrates that patients with hand eczema are a complex, heterogeneous group and that the confounders are many and sometimes unavoidable. Considering the multidimensional intervention, other methods could be suitable in evaluating the effectiveness. As suggested by Upshur et al. no single research method is applicable in all circumstances (36). Evaluation of the intervention could also pertain to the impact it may have in terms of increased knowledge, awareness, motivation and confidence. Hence a forthcoming explorative study using qualitative methodology is considered relevant.

We found that patients who were offered the intervention improved more than the usual care group. This held especially true in the subgroups of patients not treated by intensified therapy and with a primarily exogenous aetiology of the hand eczema. Moreover, beneficial behavioural changes were only seen in the intervention group. On the other hand, the results were to a large extent dependent on disease severity at baseline and we could not demonstrate any clear-cut effect of the intervention when performing a multiple linear regression. Still, although the intervention has not been economically evaluated, a tailored nurse counselling of skin protection and skin care based on the everyday risks and resources of the patient can be recommended as an essential part of hand eczema treatment.

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## 5 CONSIDERATIONS ON METHODOLOGY AND VALIDITY

This section presents some analytical steps and considerations which have not yet been presented or were only briefly touched upon in the manuscripts. The triangulation of both qualitative and quantitative methodology in the thesis may increase the understanding of complex phenomena (102), like self-management. Qualitative and quantitative strategies are complementary and the same scientific standards can then be applied to either one (102).

Based on the premise that the researcher is an active part of the research process (93), reflexivity is a positioning which should be deliberately pursued (102). In the thesis, the model of hand eczema (Figure 2) established a meta-position and brought to the fore the author's preconception. In the qualitative trial, the model is also a prerequisite to grasping internal validity like the linkage from self-management to the interview guide. External validity involved strategic sampling allowing a wide representation of the population of people with hand eczema (Paper I). Transferability then is analytic-based relating to the contextual similarities between settings (103). In the clinical trial, internal validity was pursued by choosing a relevant design and by using relevant validated measurements whenever possible. Also, randomisation and the deliberately wide inclusion criteria were considered to enhance generalisability of the findings. The hypotheses presented in the sub-studies were the anchors that systematised data analysis.

### 5.1 The qualitative study

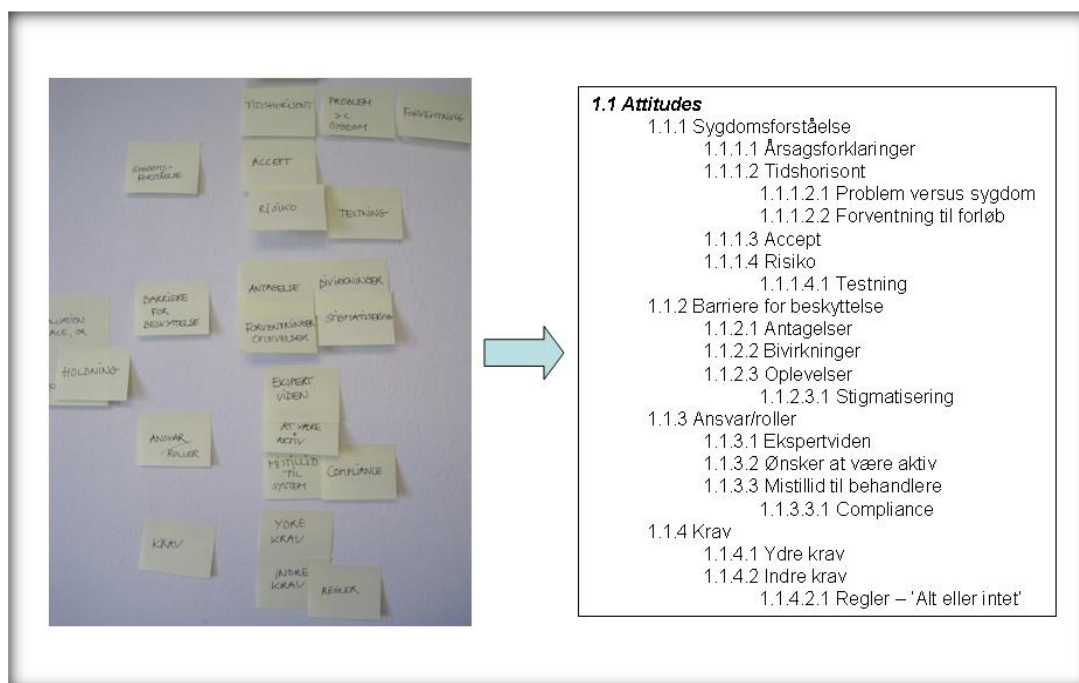
#### 5.1.1 Sampling, transcription style and the process of template analysis

In the qualitative study sampling was done strategically and pragmatically. The strategic approach implies that some criteria were set for the characteristics of the participants. Primarily, the aim was for the study population to mirror the target population, and this was accomplished. Pragmatism was essential by accepting that timely limitations of the study affected the gathering of data. Eventually, this led to the planning and completion of four focus groups with the segregating factor being gender. The term 'theoretical saturation of data' is used in qualitative research and means that sampling needs to continue to the point of redundancy (93). Although this criterion was not deliberately used in the present study, several experiences and descriptions of the struggles in everyday life with hand eczema were common across the groups.

Transcription of the interviews' audio recordings was done by the author with minor secretarial assistance, as regards the fourth interview. Transcription per se is the first step of the analysing process (103) and has been referred to as 'frozen interpretive constructs' (93). The study's interest was on meanings and perceptions of the participants, more than on how they interacted and conversed this meaning within the group. Hence the transcription style tended mostly towards de-naturalism within the continuum of transcription style (103;104).

Using computer software in the data analysis may distance the researcher from the data (105) and was abandoned because the process of forming an overview of the expressed meaning

was felt to be impeded. In the manuscript (Paper I) the template analysis process is described. In more detail, coding was performed directly on the printed transcripts. Further analysing steps involved arranging Post-it notes on a wall as a low-practical, but also very flexible, approach (Figure 4). Each code from the transcripts was written on a Post-it note and then these were categorised. In the interpretive phase themes were formulated which were discussed by the research team. As aforementioned, the analysing point of departure was the model (Figure 2).



**Figure 4:** Template analysing step by use of Post-its on a wall

### 5.1.2 Strengths and weaknesses of focus groups

Focus groups are considered a valuable technique that often promote unanticipated findings (93). *“The group effect”*, the participants’ interaction, adds to what is arguably the real strength of the focus groups. The participants both query each other and explain themselves, thus providing insights into complex behaviours and motivations (92). The data generated by focus group interviews are likely to be more complex because this *“querying and explaining”* in the group are promoted by a contextual preconception of the participants (106). Focus groups are also considered valuable in exploring experiences of symptoms from a patient’s perspective (107). A disadvantage of data collection by use of focus groups may be the fear of self-disclosure, because of the group interaction. Thus some topics may be unacceptable for discussion (92). On the other hand, depending on the composition of the group, sometimes less inhibited group members may break the ice for other participants (108).

The abovementioned strengths and weaknesses of focus groups are also closely related to the moderator and his/her skills in facilitating an atmosphere that allows for social interaction in the group, whereby the participants address each other on the basis of their experiences (106).

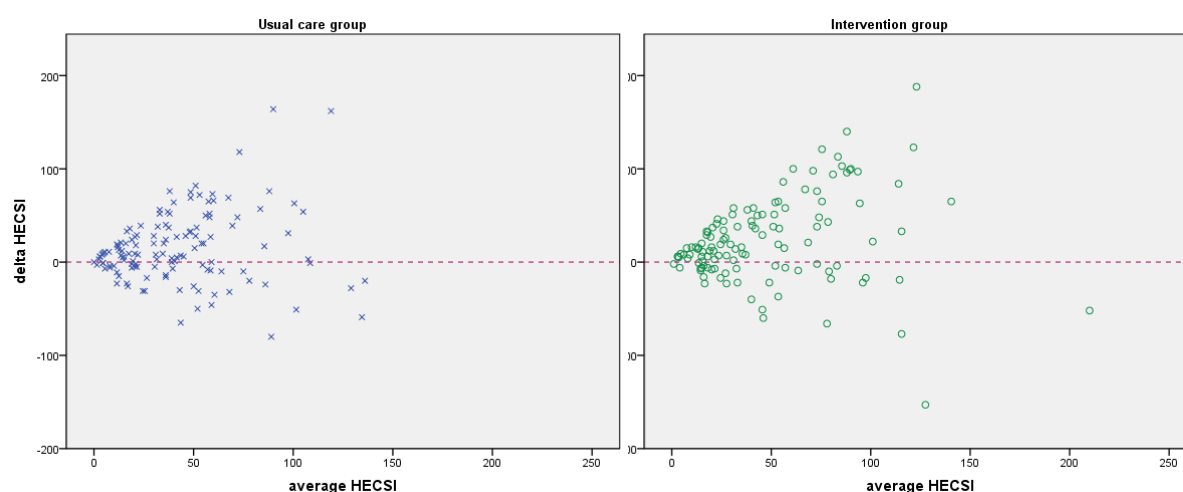
## 5.2 The clinical trial

The plan for the two sub-studies of the clinical trial, Papers II and III, involves various data collection methods. Data has been gathered both as clinical assessments, as questionnaire data, as information from the medical files and as register data retrieved from both a clinical database and the Danish Medicines Agency. In this section some reflections of reliability and validity of the clinical trial are presented which have only been briefly addressed in the papers.

A total of 306 patients were enrolled in the trial and their disease severity was assessed by the HECSI-score. Hereof were four patients who were later excluded because they had a final diagnosis of *psoriasis* or *pustolosis palmoplantaris*. According to the protocol, one of the inclusion criteria was the clinical diagnosis of hand eczema given by the dermatologist. Although a few patients at inclusion did not present any manifest symptoms they were still included if given this diagnosis. Moreover, it was assumed that the majority of patients had been symptomatic for several months prior to this referral, as both patient-delay and health care system-delay has previously been reported (26).

The effectiveness-trial (Paper III) suggests that the Healthy Skin Clinic Intervention contributed to a better prognosis of the intervention group compared to the usual care group but the findings were not consistent in the entire cohort and the degree of effect could not be calculated. The biological variation of the hand eczema disease measured by HECSI was immense both as regards the severity at baseline and the development during the trial. An exploratory variable that was very predictive of the prognosis at follow-up was the baseline HECSI-score. A Bland-Altman plot shows the association of the average HECSI  $[(\text{baseline} + \text{follow-up})/2]$  to the delta HECSI (baseline minus follow-up) (Figure 5). The increased variance at higher severity scores makes it relevant to examine the mathematical properties of the scale and ask if the same cut-off scores of HECSI as regards improvement are applicable to all patients in follow-up trials of hand eczema.

**Figure 5:** Bland-Altman plots (109) showing an increase in variance at higher severity scores



### 5.2.1 Clinical assessments by use of HECSI

A recent review has identified as much as 45 different methods to quantify hand eczema (110) and there is no consensus of which measurement to use. The ideal scoring system is accurate and is differentiated in a way as to avoid overlaps of severity categories. Moreover, it mirrors the variety of morphology and does not combine subjective complaints and clinical signs (110). To date the only measurement which is validated according to both inter- and intraobserver reliability is the Hand Eczema Severity Index (HECSI) (110;111). In the HECSI, the hand eczema intensity is clinically evaluated by the presence of symptoms and the extent by the affected area (Table 2). The total score is calculated by multiplying the intensity and the extent (111).

The potential range of a total score of 0-360 appears to grasp the variation between the patients much better than other clinical severity measurements, e.g. the Osnabrück Hand Eczema Score (OHSE) with a range of 0-18 (112), or the five-item photographic guide used for patients' self-evaluation (113;114). However, this may also promote a cohort effect whereby comparison between studies is challenged. Recent studies have reported very different values of severity. In two secondary prevention-trials, HECSI at baseline had means of approximately 3-6 and 9 respectively (78;115); and these were logically lower mean severity scores than a more recent trial within a tertiary setting that reported means of 36-44 (79), as well as the present trial. However, the latter two trials have a much higher severity than the mean of 19.9 that was reported in the study which founded sample size estimation in this current thesis (116). This is remarkable considering that all of these studies involved individuals already affected by disease and referred to work-up and treatment. Because the Hald-study was descriptive (116), it may be that the time point for scoring was not as strict as in our study. Thus, in some cases, the assessments have been done after some time of treatment.

	Fingertips		Fingers		Back of hands		Palms		Wrists	
<b>Erythema</b>	0-3		0-3		0-3		0-3		0-3	
<b>Infiltration</b>	0-3		0-3		0-3		0-3		0-3	
<b>Vesicles</b>	0-3		0-3		0-3		0-3		0-3	
<b>Fissures</b>	0-3		0-3		0-3		0-3		0-3	
<b>Scaling</b>	0-3		0-3		0-3		0-3		0-3	
<b>Oedema</b>	0-3		0-3		0-3		0-3		0-3	
<b>SUM within area</b>	0-18		0-18		0-18		0-18		0-18	
<b>Area</b>	0-4		0-4		0-4		0-4		0-4	
<b>SUM x area</b>	0-72	+	0-72	+	0-72	+	0-72	+	0-72	

**Table 2:** Measurements of HECSI and potential scores, lowest score is zero, highest score is 360

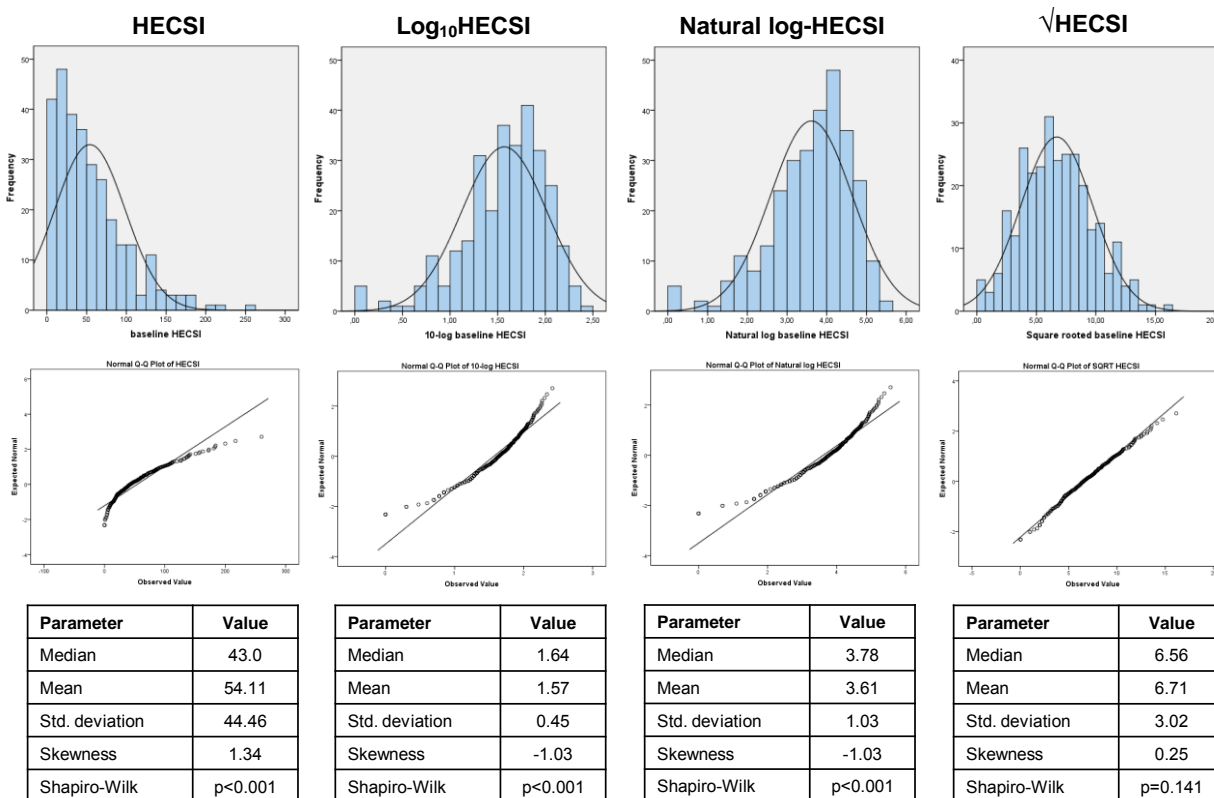
In the aforementioned Hald-study the cohort of patients was subdivided into three groups of equal size. These groups were labelled as mild, moderate and severe cases based upon the following cut-off scores of baseline disease severity, measured by HECSI: mild (score 0-11), moderate (score 12-27) and severe (score  $\geq 28$ ). Improvement was then evaluated by whether the patients were categorised in a different group at follow-up compared to baseline (116). Application of these cut-off scores to the current trial would suggest that approximately two-thirds of the patients should be referred to as severe cases, because of a much higher general severity. Moreover, if a patient changed from a baseline HECSI-score of 200 to a follow-up score of 30, this would not be labelled as an improved case according to this approach. A more disperse system, based on percentiles, could be considered relevant. Improvement could thus be defined as moving from  $\geq$  one percentile towards zero from baseline to follow-up. Likewise, the courses of disease could be categorised as unchanged or aggravated. Although this categorisation is likely to diminish the variability and the effects of outliers, it would, however, still be applicable to only this cohort. The mode was not used in the thesis, but it did contribute to illustrate some methodological drawbacks of using the HECSI-score as an outcome variable, as discussed in more detail below.

Besides considerable variation in reported disease severity, the distribution of data when using HECSI may be challenging. Although not always brought forward, the HECSI-scores often distribute non-normally. In response to this, one study has performed both parametric and non-parametric statistical analyses (78), while another log-transformed the data but did further analysis by use of severity groups, as aforementioned (116). As part of the analysis process in this thesis a critical glance at the HECSI-scale was performed.

A Gaussian distribution, i.e. the normal distribution, is characterised by data being distributed symmetrically and bell-shaped around the mean, which equates to the median value of the variable. Moreover, the 67<sup>th</sup> and the 95<sup>th</sup> percentiles equal one and two standard deviations, respectively. Also descriptive of normality is a skewness of zero, referring to symmetry, whereas an asymmetrical distribution may have a positive skewness, i.e. a value  $>$  zero. An assumed normality gives way to further statistical analysis like linear and multiple linear regression analysis. In case of non-normally distributed data, often a transformation of data to another measurement scale may overcome the problems. Transformation of data may also reduce the influence of outliers. Which type of transformation is most relevant depends on the presented distribution. However the most commonly used is the logarithmic transformation, which is also the only transformation that allows back-transformation (109). It is not possible to take the logarithms of a value of zero. Thus, when computing these new variables in the thesis, the formula used was:  $\text{Log}_{10}(\text{HECSI}+1)$  or natural log ( $\text{HECSI}+1$ ).

In the thesis the distributions of HECSI were examined within relevant groups based on gender, setting, and intervention arm. Figure 6 shows the distribution of the overall cohort as regards both the raw data and the data when transformed either by logarithms or by square roots. Both by the Shapiro-Wilk's test of normality and graphically by depiction of histograms and Q-Q plots,

the raw HECSI-distribution appears non-normal. However, when transforming the data by logarithms, whether these were  $\text{Log}_{10}$  or the natural log, the distribution of data became negatively skewed. The square root transformation is less dramatic than taking logs (109) and was clearly the best choice for this set of data. Still, the transformation by square roots could not eliminate all outlying values and non-parametric statistical tests, based on ranks, were then primarily used in the data analyses.



**Figure 6:** Distribution of data in the thesis, according to HECSI and when HECSI is transformed by  $\text{Log}_{10}$ , natural log or square roots.

The systematic scoring approach and multitude of the HECSI has most recently been criticised of being too laborious for use in a clinical practise. Moreover, issues of redundancy in some of the items have been raised. As a response, a simplified score of only three symptoms i.e. induration, fissuring and scaling has been suggested (117). However, this may compromise the accuracy of the assessments and underestimate the severity of certain hand eczema subtypes for example those with vesicles. Roughly half of the patients in the Hald-study presented vesicles among the morphological signs at baseline (116), and in a recent classification study 210 of 508 (41.3%) had a vesicular subtype of hand eczema with either rare or recurrent eruptions (8). Data of the individual morphology-scores as part of the HECSI-assessments in the present thesis have not yet been examined, but clearly a considerable proportion of the patients in the cohort presented with these symptoms. Given that this scoring system is considered to be of practical relevance and, at the same time, to compromise between accuracy



and user friendliness (110), other modifications of the HECSI-scale may be more suitable for example by acknowledging the mathematical properties.

### 5.2.2 Introducing the $\sqrt{\text{HECSI}}$

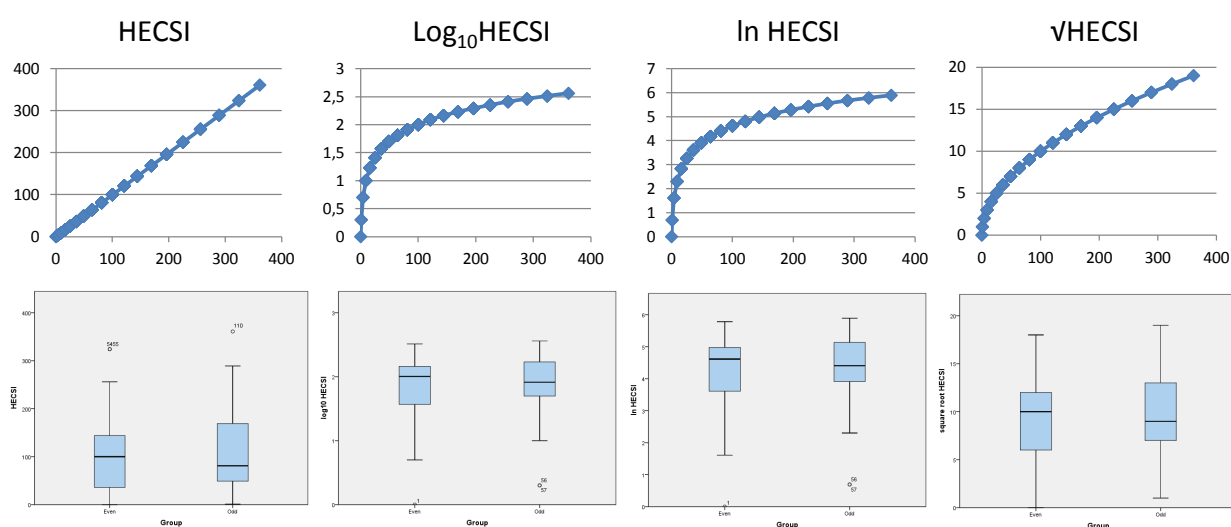
Most patients in the original validation study had a HECSI-score below 100 points and the interobserver variation increased for patients obtaining higher total scores. Neither the distribution of the data nor any banding in severity groups were discussed in the publication (111). Among the lessons learned from the clinical trial for this thesis were that the total HECSI-scale is deduced in a way that fits with a square root distribution. We performed a small methodological study to fully explore this.

A dummy cohort of 110 HECSI-scores, which were normally distributed when square root-transformed across the entire scale from 0-360, was produced. Since the transformation of data by use of logarithms requires addition of 1 to the score of zero, the entire scale was extended to a maximum of 361. This number is also the square value of 19, thus the 110 HECSI-scores conveniently were all square numbers from 0-19. Then the data of this dummy cohort were transformed and the derived distributions were viewed graphically (Figure 7), numerically, and by Shapiro-Wilk's test of normality (Table 3). The dummy cohort was also divided into two subgroups to detect within the four distributions if the reduced sample sizes brought forward any outliers (Figure 7). This division was done as regards even and odd values of the HECSI-score.

Parameter	HECSI	$\log_{10}$ HECSI	$\ln$ HECSI	$\sqrt{\text{HECSI}}$
Median	90.5	1.95	4.51	9.5
Mean	108.5	1.85	4.25	9.5
Std deviation	84.3	0.50	1.16	4.3
Variance	7113.7	0.25	1.35	18.4
Skewness	0.880	-1.328	-1.328	0
Shapiro-Wilk's test	$p < 0.005$	$p < 0.005$	$p < 0.005$	$p = 0.422$

**Table 3:** Summary statistics of raw HECSI,  $\log_{10}$  and natural log-transformed HECSI and  $\sqrt{\text{HECSI}}$  in the dummy cohort ( $n = 110$ )

Table 3 shows that only the  $\sqrt{\text{HECSI}}$  has an insignificant Shapiro-Wilk's test and also the skewness is zero, both of which equate to a normal distribution. Scale performance as regards the ability to differentiate between the scores can be viewed in Figure 7. The upper row shows that at a cut-off at 100, the raw HECSI-scale roughly uses one fourth of the range from 0-360 to cover values  $\leq 100$ . Conversely, the log-transformed distributions use 80% of the range of 0-5.89 and 0-2.56, respectively, and this allows only very little differentiation between higher scores. The  $\sqrt{\text{HECSI}}$ -scale is divided into approximately two with values from 0-100 equating 0-10 and the remaining values equating to 11-19. The lower row of Figure 7 shows that only the  $\sqrt{\text{HECSI}}$ -scale has the ability to embrace every score of the two subsamples. This indicates that the  $\sqrt{\text{HECSI}}$ -scale is less prone to smaller sample sizes and large biological variation as compared to the three other distributions.



**Figure 7:** The upper row shows associations of raw and transformed HECSI-scores and the lower row shows statistic summaries. Box-plots of subsamples show medians (black horizontal lines within boxes); inter quartile range (box) and range of values (whiskers); dots represent individual outliers in dummy cohort; ln, natural logarithm

Consistent transformation may promote a more relevant operationalization of the measurement scale, in two ways. Firstly, the square root-transformation solves the issues of non-normal distributions, thus allows sample size estimation and regression analyses, both of which rely on parametric statistics.

Secondly, a transformed scale promotes the more obvious decisions of cut-off scores and between-cohort comparisons. The accuracy of the raw HECSI-scoring procedure is warranted in any clinical trial. However, the raw HECSI-scale may be more directly applicable to studies of secondary prevention where the general severity is likely to be low compared to heterogeneous study populations of patients from the clinical practice. In a clinical trial the minimal clinically relevant difference (MIREDIFF) between pre- and post-measurements could be set at two (units), as an example. In the group of less affected patients this could be an improvement from 5 to 3 on the  $\sqrt{\text{HECSI}}$ -scale, equivalent to an improvement from 25 to 9 on the raw scale. In the higher end, an improvement from 15 to 13 would equate to an improvement from 225 to 169 on the raw scale. The  $\sqrt{\text{HECSI}}$ -scale would then counteract the exponential character of the HECSI-scale, per se, and oppose the problem of increasing variance at higher severity, which was displayed by the Bland-Altman plot (Figure 5). Intuitively, this may also provide a better way to build consensus of relevant banding according to severity groups.

To summarise, the face validity of the scale appears to be higher with a  $\sqrt{\text{HECSI}}$ -range from 0-19 compared to a HECSI-range from 0-360. A reasonable operationalisation could be to use the raw score in studies that expect values from 0-100 (e.g. within secondary prevention) and the  $\sqrt{\text{HECSI}}$ -scale in studies of expected higher severity.

### 5.2.3 Questionnaire data

From the outset, it was intended that data of secondary outcome variables should be collected at exact time of inclusion. This would favour the simultaneous collection of data and promote a high response rate. However, it was considered to be too inconvenient to the patients if they should engage in a face-to-face interview immediately after a medical consultation and potentially prior to the nurse counselling. Hence, the baseline questionnaire was handed to the patient when enrolled in the trial, along with a pre-paid envelope. This did, however, affect the response rate of the questionnaires at baseline, although approximately 90% of the patients still responded to the baseline questionnaire.

In questionnaire studies social desirability bias may be present, whereby the respondents adjust their answers to what they expect to be the preferred one. As with the clinical assessment the triangulation of both subjective and objective data minimise the risk of exaggerating the findings in the trial by giving too much weight to one single data source. Also recall bias can be a problem when using subjective data. This means that selective groups may report, for example, harmful exposures more frequently than other groups would. However this is more likely in case-control studies where such exposures can be linked to the outcome that led to the status of being a case (109).

The trial protocol describes the planned collection of data as regards self-rated health status (94). These data were obtained by use of the generic Health Status Questionnaire, Short Form (SF-36), a well-validated and frequently-used research tool (118). This was licensed through [www.qualitymetric.com](http://www.qualitymetric.com). The patients' responses to some of the items were used directly when generating the SKIN-profile. As regards self-reported medication adherence, we used the DMARS-4 scale. In the data analyses we found no differences between genders (Paper II) and no differences between the intervention group and the usual care group (Paper III). The findings were discussed, but they were not presented in the papers. Hence, they are detailed in a table in Appendix C.

At follow-up the patients were asked to rate themselves according to symptom recognition, initiation of topical treatment, knowledge of allergens/irritants, and possible change of habits due to the eczema. This was a self-constructed ten-item scale and the results are presented in Appendix C. Ideally, the same data would have been collected at baseline. Thus, it would be possible to detect if any differences during the trial could be attributed to the intervention. This was abandoned because just by asking, for example, about change of habits could induce a change hereof. This was not warranted amongst the patients in the usual care group. Although the scale is not validated, it has brought forward findings that may be reliable. Statistically significant differences between men and women occurred with women clearly scoring themselves higher according to most items. Women reported a higher preventive behaviour compared to men in terms of using protective gloves, and women reported more change of habit in regards to hand eczema. According to knowledge of self-medication and knowledge of the hand eczema's aetiology, women also scored themselves significantly higher.

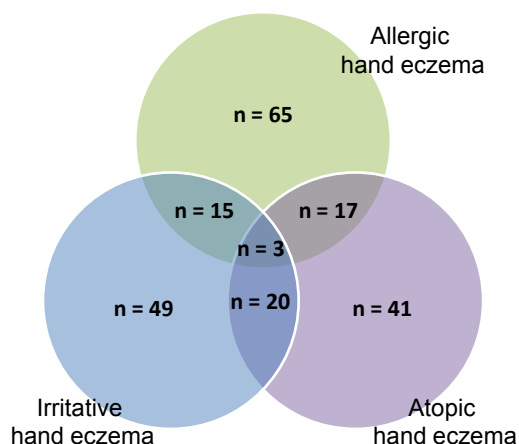
The content of the ten items was inspired by the model of chronic hand eczema (Figure 2) and was discussed with an expert within the field. Hence, the content validity may be acceptable. However the face validity and the construct validity were not explored. As these items were only a part of the follow-up questionnaire, they were not pre- or pilot-tested. Issues of reliability, e.g. by use of test-retests of the same individuals, are therefore also indefinite. To some extent, the validity of the scale may be proven by examination of the answers, according to other items in questionnaires. For example, it is likely that this scale correlates to the General Self-Efficacy Scale, but this has not been explored at part of the thesis. Also, the behavioural item about using gloves may be directly linked to other questions of the use of gloves. Construct validity can be examined by comparing groups with expected differences, such as the two genders.

#### 5.2.4 Data from medical files and clinical databases

The MOAHLFA-index is a means to describe departmental characteristics and these data are registered in a clinical database, as part of the diagnostic work-up of allergy testing. The data comprised in the index are *Male*, *Occupational dermatitis*, *Atopic dermatitis*, *Hand-Leg-Face dermatitis*, *Age > 40 years*. Information about occupational disease and of history of atopic dermatitis was obtained either through this database or by a thorough review of all the patients' medical files. Data of atopic dermatitis were thus based on the clinicians' diagnosis and registration rather than, for example, the U.K. diagnostic criteria, which were designed for clinical and epidemiological studies. The clinical diagnosis made by an experienced dermatologist is considered to be gold standard (119). However, all clinical databases and medical files rely on the validity of the data entered and misclassification may occur. Presumably, this would relate to all subgroups, i.e. groups of genders and to both intervention arms. Thus, it was not likely to be a bias in the studies.

The clinical database comprised data of 88% of the included patients (257/292), i.e. those who had been allergy tested either as an event in the current course of treatment or previously. Aetiological diagnoses were attributed to a total of 210 patients, either as an individual diagnosis of irritant contact dermatitis, allergic contact dermatitis or atopic dermatitis or a combination thereof. A non-specific diagnosis of *dermatitis* was registered among the remainders. Although not representative of the entire cohort, the distribution of aetiology is displayed by a Venn-diagram (Figure 8). This distribution is not entirely in accordance with the general population-based distribution of aetiology, where irritant contact dermatitis is suggested as the most abundant type (4;10). Even when considering the patients in the cohort who are not registered by diagnosis in the database, as many as 100 of 292 patients (34.2 %) have been positively identified as having allergic hand eczema, either as a stand-alone diagnosis or in combination. The majority of patients in the Gentofte setting had consulted a private dermatology practice prior to the current course of diagnostic work-up and treatment. This means that the patients in this setting presumably had hand eczema of such a complexity that referral to a specialised unit was appropriate. The diagnosis of contact allergies is depending on the scale of the exposure assessment (120). Thus, a certain cohort-effect may account for

these numbers. However, the distribution corresponds to a cross-sectional, multi-centre study that reported a percentage of 37.6 (120 of 319 patients) having allergic contact dermatitis (11).



**Figure 8:** Distribution of aetiology of the cohort (n = 210), based on information from clinical database

Although the individual counselling of patients in the intervention group also attempted to address the aetiology of the eczema, in some cases it was not always feasible, either due to insufficient documentation in the medical files or because the patients only attended the first medical consultation and never got tested at all. Retrospectively, a more systematic approach in the data collection phase, including deliberately asking the dermatologist concerned about the diagnosis in each case would have been advisable. This could have contributed to a more comprehensive understanding of the findings from the effectiveness study of the intervention.

### 5.2.5 Considerations of appropriate design

Validity issues of the primary outcome measurement also relate to the fact, that the observer was not blinded to the patient's trial status at follow-up. Clinical trials should uphold the maximum possible degree of blindness (109). It was not feasible to blind the patient to his or her assignment to either the intervention group or the usual care group. Nor could the intervention team of nurses be blinded. To enhance rigour of the trial it would have been advisable to overcome the logistical problems of having one designated, trained observer perform the outcome assessment both at baseline and at follow-up. On the other hand, the randomness that was inherent in having a team of five assessors could compensate for this potential observer bias. Moreover the extensive range, per se, of the HECSI-scale may encourage more systematisation in the scoring procedure, with less focus on the status of the patient. The correlation of HECSI and the concurrent self-assessed burden of disease, measured on a scale from 0-10 at follow-up, also showed no difference between the intervention group and the usual care group (Paper III). This triangulation of data then indicates that no systematic observer bias was present.

The design of the clinical trial may be questioned. The intervention was directed towards the patient and no changes in attitudes or behaviour were intended, nor warranted, among the medical and nursing staff. This was part of the protocol, as a means to delimit contamination bias, whereby the patients in the usual care group could be given counselling almost analogous to that given to the intervention group (121;122). Also, directing the intervention towards the patient could possibly minimise setting-induced effects, thus promoting generalisability of the findings. The risk of contamination bias could have been avoided by conducting a before-after trial. This means that we could have prospectively gathered data of hand eczema patients within a reasonable timeframe, after which the Healthy Skin Clinic intervention could have been clinically implemented. After the implementation, another collection of data could have been performed and a comparative analysis of the data before and after the implementation could have been carried out. However, it is likely that this methodological approach would have given rise to unexpected differences between the before-after study populations, which then could have biased the findings.

It is suggested that clinicians should not renounce randomised trials, even though blinding, for example, is considered unfeasible, as these trials may still be the most reliable way to compare the effectiveness of different treatments (123). Cluster-randomisation is increasingly used to evaluate health service interventions (124). If randomisation had been applied to the settings, rather than at an individual level, this could overcome the risk of contamination of the usual care group. However, this design would possibly bring forward several setting-specific baseline characteristics which should be accounted for in the data analysis. It would require several settings and a certain amount of inter-variability could be expected. In a large cohort study of 799 participants by Hald et al. (116) the patients were included consecutively from nine dermatological clinics in Denmark. Within the same timeframe these clinics provided from 18 to 184 participants, which suggest that the size and organisation of the clinics differed. Although not considered relevant in the Hald-study, which was descriptive (116), it would possibly have some effect on an interventional study.

## 6 GENERAL DISCUSSION

This section includes a general discussion of the overall thesis, including the three manuscripts I-III. The findings confirm the complexity of hand eczema referring to the patients' experiences, the clinical courses, and the field of research. With the patients' everyday lives and self-management as the pivot, the thesis shows that hand eczema is a disease with far-reaching consequences to the individual. The thesis also shows that an individually tailored counselling programme may be helpful in supporting the self-management of the patients.

### 6.1 Everyday life with hand eczema

The prefatory aim of this thesis was to explore patients' self-management in everyday life with hand eczema. This insight could then qualify the development of a nurse-led counselling intervention to support self-management of the disease. Conducting four focus group interviews brought forward paradoxes of complexity and simplicity, as well as the need to focus on habits as a means to integrate the disease in everyday life (Paper I).

Among the 23 participants in the interviews there was consensus that hand eczema had a profound impact in everyday life. Most participants knew of the recommended protective regimen (Box 1), but they faced both internal and external barriers in acting out the behaviour. At the same time, a general lack of knowledge was expressed, in reference to both those affected by hand eczema and the health professionals. This knowledge gap was also interpreted to as a lack of control, because of the unpredictability of the course of disease. At the same time, it conveyed a mismatch between the patients' expectations of, and the actual limitations of, treatment. Expectations of treatment change at different points in an illness trajectory. At some point, the needs are more instrumental, e.g. information from tests and treatment, while at other times more affective needs may be in the foreground (125). Aggravating factors in everyday life can lead to persistence of hand eczema although the primary aetiological factor has been removed. This may inspire a search for other causes of the disease, as expressed in the tendency to adopt the allergies of peer participants in the focus groups. When chronically ill, the search for the cause of illness is also a search for its meaning (125;126).

The participants in the focus groups intended to act with consideration of their hand eczema. However, the barriers in everyday life were perceived as many and difficult to overcome. These barriers comprised both internal barriers, like habits or striving to remain true to oneself, and external barriers like job obligations and consideration for others. The constant focus on prevention was felt as tiresome and, in many cases, unrewarding, much like the Sisyphus syndrome (125). Previously, the process of integration of chronic illness into everyday life has been defined as *"a complex person-environment interaction whereby new life experiences, i.e. transitions, illness, and self-management, are assimilated into the self and activities of daily living resulting in an overall life balance"* (127). In a qualitative study of individuals with different chronic diseases, this was found to be a nonlinear and unpredictable process where *"living a*

*life*” and *“living an illness”* should co-exist. This involves behavioural work, psychological work, and social or vocational work, but as well considerable existential work (127).

Consider a woman who experiences daily itching because of her hand eczema. She may have several allergies and pays constant attention in order to avoid exposures. Her condition may be aggravated by everyday tasks like doing the dishes, doing the laundry, cooking, changing diapers for her toddler, and so on. She may have given up sports because sweating provokes her itching. At social events she cannot offer to assist with the clean-up. She attempts to consistently protect her hands by using gloves when she touches items which presumably comprise the allergens. At the same time, she feels stigmatised by other persons’ glances at, or remarks about, her use of gloves. To avoid this stigmatisation she makes a career change from a low-risk occupation to a profession where glove use is customary and even mandatory on a regular basis. However this may also forward an additional risk factor for the persistence of her eczema, and it is clearly against medical advice. Is this woman then nonadherent in her course of disease? Does she show poor self-management?

Bury has previously argued, that it is necessary to re-think the traditional medical belief in rational communication of information and compliance in chronic illness (125). Chronic illness is a disruption of the person’s biography and this also includes disruptions of social interaction (126). Many people may face winter-related dryness of the hands or brief impairment of the skin related to a single occasion of exposure. Acknowledgement and legitimacy of a chronic illness can be particularly problematic if the symptoms coincide with what is widely experienced (126). In a study of hand eczema and quality of life, Moberg et al. suggest that people without hand eczema underestimate the impact of the condition and this constitutes a problem in everyday life for the individuals with hand eczema (21). Even within clinical dermatology this may be the case. Patient satisfaction and agreement between clinical severity and quality of life has previously been examined among 396 dermatological outpatients (128). Around 40% of the patients in the study had impaired quality of life but were assessed by their dermatologists as not having clinically severe diseases. Patient satisfaction was lower in this group as compared to the group with agreement between patient-dermatologist, or the group where the clinical severity was rated worse than the symptoms. The authors then suggested that the dermatologists demonstrated more concern for the patients with clinically more severe disease (128). Hand eczema is acknowledged by many as a natural consequence of a specific occupation. Thus, it is largely underreported (129). Accordingly, many people may not view hand eczema as a disease at all, although occupational contact dermatitis alone is a societal burden with an estimated annual cost in Denmark of more than 100 million Euros (130).

The thesis’ definitory point of departure with self-management being *“lived”* rather than *“used”* (p. 6) is in agreement with a previous qualitative study of chronic illness (131). This study explored the meaning of self-management among individuals living with arthritis. The participants identified self-management as a process of bringing order into their lives. Thus, it fluctuated according to new challenges in life or illness. Self-management of chronic illness was



then more than “*doing*”, but was also entwined with “*being*” and “*becoming*”. The meaning of self-management for the people living with arthritis involved finding ways to live everyday life optimally (131). The biographical disruption in becoming chronically ill also involves a disruption of taken-for-granted assumptions and behaviours (126). How to maintain normal activities become subject to deliberate consciousness, which may be so frustrating and tiring that people would rather give them up (126). This was also the finding from participants in the focus groups in the thesis. Chronic illness then leads to perceived losses and limitations (127). To one individual with hand eczema, how to continue doing needlework as a hobby may be the most important, while another may feel economically threatened because of the incapacity to work. To others, being able to bathe their child, and not always leaving this to the co-parent, may be pivotal. In many cases, the individual needs to prioritise among the everyday tasks in order to minimise aggravation of the hand eczema. A realistic goal may not involve being unwavering avoidant, but rather the incorporation of beneficial habits one at a time. This implies balancing dependence on and independence from family and friends (127), but foremost it may require reflective processes of everyday life up to now. A self-management support programme, when tailored, may possibly incorporate the everyday life of the patient without being judgmental about the patient’s behavioural performance. The overall findings from the four focus group interviews in the thesis led to the conclusion that self-management support for the patient with chronic hand eczema needs to be individualised (Paper I). This individualisation involves the provision of knowledge, specific and relevant to the patient, but also the assistance in sorting the information. It also implies helping the patient to develop realistic expectations as regards the course of disease. Ultimately, counselling needs to focus on the adoption of new habits in order to minimise the effort in preventive behaviour.

The focus groups were deliberately gender-segmented to facilitate participant compatibility and thereby group interaction. The significance of gender per se was not an issue neither in the conduct of the interviews or in the analysis of the data. Nevertheless, promoted by the absence of the other sex, some of the participants wondered if men and women differ in facing everyday life with hand eczema. And they do indeed. The next section discusses the many gender differences, but also some commonalities, as characteristics of the cohort at baseline in the clinical trial.

## 6.2 A gendered perspective of hand eczema

Sixty years ago hand eczema was described as perhaps the most confusing syndrome in the field of dermatology (17). As a mirror of the overall population having hand eczema, the cohort in the clinical trial turned out to be of high heterogeneity. The first analytical step then was to describe the characteristics of the cohort. The known gender ratio in hand eczema found in population studies was almost replicated in our cohort with the inclusion of 190 women and 104 men in the data analysis. Previous studies suggest that this prevalence ratio relates to differences in exposures as the most affected occupations are typical female occupations (132). However, hand eczema is often the “*tip of the iceberg*”, the sum of several exposing and

aggravating factors (7;19;55), which makes it relevant to examine gender differences as regards non-occupational conditions as well. Comprising both patients with occupational and non-occupational originated disease, this cohort offered an opportunity for gaining a comprehensive overview of hand eczema.

The finding that men and women in our cohort had similar clinical disease severity assessed by the HECSI-score opposes a previous multicentre study which found a statistically significant higher severity in men (24). Nonetheless, our results correspond to those reported in other Danish studies (7;116). What really showed large gender disparity in our study were the impact and consequences of hand eczema. At equal clinical severity women experienced a significantly lower dermatology-specific quality of life as compared to men (Paper II). At the same time, women reported more everyday exposures and aggravating factors, such as more handwashing, than men did. The number of aggravating factors could directly predict a lower quality of life in a regression analysis, which may confirm our findings in the qualitative study (Paper I) that participants perceived it as very tiresome to avoid exposure and to constantly focus on prevention. This clearly demonstrates the complex interplay in hand eczema between the individual and the environment.

The reporting of aggravating factors does not equate to an exposure per se. Yet, the questions of aggravating factors involve largely ordinary everyday tasks like the handling of food, hygiene products and gardening. Biology may influence our perception of bodily phenomena, like the reported gender differences in chronic pruritus (133), and biology partly constitutes our personalities. It may be that women have higher self-awareness than men. Thus, the higher reported everyday exposures and aggravating factors could be subject to a reporting bias. More likely though, these differences depict that gender roles still play a significant part in our modern cultures. A quite recent Swedish study of young adults suggested that over a follow-up period of 13 years, the significant risk factors for hand eczema changed from endogenous to exogenous factors (134). Handwashing was a significant exogenous risk factor of reporting hand eczema at present. Moreover, the study reported that among individuals with hand eczema, women spent significantly more time doing household activities as compared to men (134). This gendered distribution of domestic work has also been reported elsewhere (135). Danish society presents one of the world's most even occupational frequencies between genders (2010: men 76.5%, women 72.4%) (136). Still, the choices of professions, including those likely to expose one to hand eczema, are segmented according to gender (137). Targeted preventive interventions may be beneficial in specific occupations. Tailored programmes are, nevertheless, needed in order to embrace private exposures as well. Such an approach implies a dialogue with the patient, one that very specifically addresses the everyday exposures and habits, as well as bringing forward alternatives.

The clinical trial of the thesis aimed to evaluate the effectiveness of such a tailored intervention, the Healthy Skin Clinic. Block-wise randomisation secured an even distribution as regards gender and setting of patients allocated to the usual care group and to the intervention group.

### 6.3 Does tailored patient counselling in hand eczema work?

This thesis has hitherto emphasised the complexity of everyday life with hand eczema which makes terms like, and measurements of, patient compliance inappropriate. However, like other health care interventions, tailored patient counselling programmes are subjected to 'cost-benefit' thinking. The randomised controlled trial has been amplified as the gold standard in evidence-based medicine. Thence, it follows that the Healthy Skin Clinic-intervention was evaluated according to this standard.

A key principle in controlled trials is that the cause-and-effect relationship is best shown by eliminating all other possible reasons behind the effect. This was not achieved in our clinical trial, where an unexpectedly high number of patients received intensified treatment (Paper III). We did analysis of groups stratified for treatment and found that the intervention group improved more than the usual care group, but only in the strata where no intensified treatment was given. A recent Dutch randomised controlled trial evaluated an integrated care programme and found it to be superior to usual care at six months follow-up. This trial had deliberately excluded patients who were on systemic treatment affecting hand eczema and possibly also those who received phototherapy. Hence, the patients in this study were more selected than our cohort. Similarly to our study, the Dutch trial found that improvement was more easily achieved amongst the patients having high baseline HECSI scores (79). Nonetheless, this apparently did not relate to the between-group baseline differences where the intervention group had a mean HECSI of 43.9 compared to the mean HECSI of 36.5 in usual care group. The study did not report on the distribution or transformation of HECSI, although the HECSI-distribution obviously was non-normal (79). A subsequent follow-up study found no differences between the intervention group and the usual care group after 12 months (80). We chose a waiting list design for our trial. Thus, the patients in the usual care group were offered the Healthy Skin Clinic Intervention at follow-up. We are therefore not able to evaluate more long-term effects of the intervention.

Our intervention had no impact on clinical severity in the group of patients who were treated intensively (Paper III). One might argue, then, that more intensified treatment would be relevant, because this was more effective. On the other hand, relevant behavioural changes were achieved in the intervention group, but not in the usual care group. Fewer patients from the intervention group as compared to the usual care group had risk behaviour at follow-up as regards private-time handwashing, and the reverse pattern was found according to beneficial emollient use. If converted to sustainable new habits, this behaviour may be conducive to the prevention of relapse. Conversely, radiation therapy and medication only target the symptoms and not the contributing factors.

The patients in our trial had a generally high disease severity, which affected their quality of life. The median reported number of aggravating factors was four and three for women and men respectively (Paper II). Almost 80% of the women reported overall consequences followed by 68% of the men. Thus, in many cases the patients had disease courses of high complexity. It is

likely that the counselling intervention was too modest by offering 1-2 short, face-to-face consultations with a nurse, supplemented with access to a website. In comparison, a habit reversal training intervention has previously been described. This programme was used as an adjunct to medical treatment for patients with different pruritic skin conditions. To oppose the itch-scratch cycle the programme involved four sessions with a psychiatrist and a dermatology nurse prior to a final follow-up visit (138). The successful German TIP-programme also allocates far more resources in the educational and psychological aspects of hand eczema treatment (81-83). We aimed to supplement our few consultations with the newly developed website. The patients allocated to the intervention group used this website very differently and some did not use it at all. Clearly, this novel approach needs to be evaluated also by the use of qualitative methods.

Both the health care professionals and the patients may need time to become accustomed to the usage of new information technologies in health care. Nevertheless, previous research indicates that Internet-based education may be advantageous in increasing patients' cognitive empowerment. A Finnish study compared Internet-based education to face-to-face education conducted by a nurse (139). The outcome variables were measurements of both knowledge and the perceived sufficiency of knowledge. The study reported that in some aspects the Internet-based education actually surpassed the face-to-face education. This arguably could relate to an overload of information at the face-to-face session whereas the patients testing the Internet-based education used the website several times, and for longer time periods (139). The study comprised preoperative education to patients prior to ambulatory orthopaedic surgery and the focus was only on cognitive empowerment. Patients with hand eczema are likely to also benefit on a cognitive level from a similar website e.g. [www.hudrask.dk](http://www.hudrask.dk) introduced in our trial. However, integration of chronic illness in everyday life is not only related to cognition, as this process has been suggested to involve both psychological and existential work (127). It may be equally important to make way for motivational and emotional support in a face-to-face encounter. Therefore, the two very different approaches should be complementary and not an either-or strategy.

The eight patients who withdrew from our trial were all from the intervention group. These patients did not differ from the other patients in disease severity. We did not explicitly require a certain amount of active participation in the trial. Those, who withdrew, argued that their decisions were based on lack of time and energy, which may confirm the previous findings that maintaining a consistent focus on prevention can be tiresome (Paper I).

A recent health technology assessment examined the effectiveness of the widely used Stanford Chronic Disease Self-Management Program and found statistically significant, yet clinically minimal improvements across a number of measures. However, all the findings had low to very low quality of evidence (140). In our trial, we could not demonstrate a substantial effect of our intervention as the clinical severity was not improved in the entire cohort. However it is important to stress that although an effect is not found, it may still be present.

## **7 CONCLUSION**

Much research in hand eczema, at the present, relates to genetics and individual susceptibility in order to identify predisposing factors. This thesis focuses on the everyday life when having hand eczema, including everyday exposures, self-management and prevention of relapse. As regards the aims of the thesis, the conclusions are as follows:

- Everyday life with hand eczema is complex, but patients perceive being offered only simple solutions. Perceived lack of knowledge may also be interpreted as lack of control. Among the barriers to applying preventive behaviour in everyday life are treatment-related discomfort and social considerations (Paper I)
- The constant focus on skin protection is tiresome and adopting new habits may minimise the effort in preventive behaviour. Treatment and support for self-management need to be tailored, including the provision of knowledge that is specific and relevant to the patient, as well as helping the patient develop realistic expectations concerning the course of disease (Paper I)
- While on the surface men and women may have equal clinical severity of hand eczema, the impact of disease is considerably larger on women than on men. Women experience more impaired quality of life than men do at equal disease severity, whether this severity is objectively assessed or self-reported (Paper II)
- Women report significantly more aggravating factors that may be difficultly avoided in everyday life than do men. The number of aggravating factors can predict the quality of life to a larger extent in women as compared to men (Paper II)
- Patients, counselled by a tailored nurse-led programme, including a new website, as an adjunct to usual care, had larger clinical improvement at six months follow-up compared to patients who had usual care information by the dermatologist. The programme was especially beneficial in patients who were treated solely with topical corticosteroids and who had a primarily exogenous aetiology of eczema. The effect was widely dependent on the baseline disease severity (Paper III)
- Beneficial behavioural changes were only seen in the group who were counselled according to the tailored nurse-led programme. No differences in quality of life and burden of disease were found between intervention arms (Paper III)
- The gold standard of hand eczema severity measurement, i.e. the HECSI-scale, has considerable methodological flaws, which can best be rectified by a square root-transformation (Paper III)

## **8 PERSPECTIVES AND FUTURE STUDIES**

This thesis contributes with new and valuable insight about everyday life with hand eczema from the patient's perspective. Only a few qualitative studies in hand eczema have been performed, although the disease is common. Qualitative studies are important as they may give us an understanding of complex phenomena like human behaviour.

Based on the findings in the thesis, it is recommended that a nurse-led tailored counselling focusing on the individual's everyday life exposures and resources is offered at an early stage of the treatment course. This should involve a concrete dialogue of how to apply skin protection and skin care (Box 1) into everyday life, both on and off work.

In continuation of the findings from this thesis, qualitative research could contribute with more knowledge about the individuals' possible habituation to the symptoms. As a triangulation of methods, a further comparative analysis of the patients' self-monitoring and the HECSI-scores at follow-up in this thesis would give insight into which symptoms are most often overlooked by the patient as compared to the clinical assessments. This analysis may also bring evidence of the interplay of objective and subjective symptoms and their individual contribution to the overall global burden of disease.

The gender differences in hand eczema may be constituted by both nature and nurture. Men and women presumably do not differ in skin susceptibility. On the other hand, we are largely influenced by our societal context. More research in how we culturally form our gendered habits in childhood, like the habits related to handwashing, could be relevant. We found that patients who reported a high number of daily handwashing at work were also more likely to report a high number of daily handwashing privately (Paper II). Hence, it would be relevant to explore if there is a subjective threshold of perceived filthy hands.

As regards the gender disparity in reporting aggravating factors, more research in everyday exposures and how people rearrange their everyday life would be relevant. That is, which tasks may be delegated to the spouse or other family members, and how do people prioritise when they delegate. This could possibly qualify our patient counselling.

Some innovations have been tested as part of this thesis i.e. the SKIN-profile, the self-monitoring log and the website as a whole. It is important that such new features, as elements in the patient counselling, are evaluated by the target population. Thus both focus group interviews and individual interviews with some of the patients enrolled in the trial can give valuable evidence of the feasibility of such an approach. The SKIN-profile may be evaluated as regards predictive value by comparative analysis of the individual profile and the inter-related outcome. Also future studies are warranted of how to best make use of the new information technologies both in the course of treatment but also as an aid in the self-managing of hand eczema.

More research of the fluctuation in disease and long-term prognosis of hand eczema are needed with the aim of identifying the windows of opportunity for prevention. This would imply the set-up of large prospective cohorts of patients preferably enrolled already by the general practitioner and then monitored when shifted between health care sectors. The self-monitoring log may act as the patient's tool of communication when referred from the general practitioner to the dermatologist and further on to the specialised hospital unit. More research is needed to determine if the log is a feasible instrument.

A consensus of how to assess and interpret the clinical severity of hand eczema would be beneficial. This thesis has introduced the  $\sqrt{\text{HECSI}}$  as a valuable instrument that may be relevant and valid especially in heterogeneous study populations. Futures studies may determine whether a banding of the  $\sqrt{\text{HECSI}}$  according to severity categories is clinically relevant.

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## 10 SUMMARIES

### 10.1 Summary in English

Hand eczema is a common disease which often has a chronic course. Dermatological treatment involves thorough exposure analysis and frequently the use of topical corticosteroid medication. However, to prevent relapse and a potential chronic course the individual needs to adapt to a consistent behaviour of skin protection and skin care. The patient's self-management is then the pivot in the course of disease but the evidence of how individuals self-manage everyday life with hand eczema is sparse.

The aims of this thesis were firstly to explore the perceived barriers and needs in self-managing hand eczema in everyday life, and secondly, based on these findings, to develop and evaluate an intervention of a tailored, nurse-led counselling. The thesis then consists of a qualitative study part and a study part using quantitative methodology in terms of a clinical randomised controlled trial. The study populations in both studies were Danish individuals referred to dermatological treatment of hand eczema.

The qualitative study part involved four focus group interviews with 23 individuals having hand eczema. Template analysis was performed and among the findings were that the participants felt a lack of knowledge about the causes of eczema and how best to manage it. They perceived hand eczema to be complex, but felt that only simple solutions were offered. Both internal and external barriers made it difficult to apply preventive strategies in everyday life and the constant need to focus on prevention was experienced as tiresome. The participants expressed that a more flexible and needs-based communication with the health providers could be helpful. Furthermore, the interaction with peers in the groups was appreciated.

Founded on the findings from the qualitative study and review of the literature a counselling programme was developed. This programme was entitled 'The Healthy Skin Clinic' and was a package of counselling and supportive elements. A key feature of the programme was a nurse consultation focusing at an individual level on skin protection and skin care. To facilitate further support, the patient was offered user access to a newly designed website, [www.hudrask.dk](http://www.hudrask.dk). The site comprised an individually processed profile of risks and resources, a log to self-monitor the eczema, information material including newly produced educational videos, quizzes, and a formula to contact the intervention team of nurses as well as a dialogue forum in which to communicate with other users of the site.

The Healthy Skin Clinic-programme was evaluated in a clinical trial with inclusion of 306 patients referred to dermatological treatment in Copenhagen University Hospital Gentofte or in the Dermatology Clinic Nord in Aalborg. Block-wise randomisation secured an even distribution according to gender and setting of patients allocated to the usual care group and to the intervention group. Data of outcome variables were obtained both at baseline and at follow-up

after six months. The patients in the usual care group were offered the Healthy Skin Clinic-programme at follow-up.

The first analytical step was to describe the characteristics of the cohort and by doing so, several important gender differences were found. Men and women had equal clinical severity of hand eczema, but the impact of disease was considerably larger on women as compared to men. Women reported significantly more aggravating factors and sick leave. Also women had a more impaired quality of life than men had at equal disease severity, whether this severity was objectively assessed or self-reported. No gender differences in prescribed treatment were found. Self-reported medication adherence was similar between genders, but among the patients older than 40 years, more reported higher adherence.

In the study of intervention effectiveness more patients in the intervention group compared to the usual care group reported behaviour of skin protection and skin care in terms of lowered number of handwashing and more frequent daily users of emollients. Also, the patients in the intervention group improved more in clinical severity, measured by the Hand Eczema Severity Index (HECSI), as compared to the patients in the usual care group. However, these results were only statistically significant among the patients who were treated with topical corticosteroids only. The intervention did not affect the participants' quality of life as evaluated by the Dermatology Life Quality Index (DLQI). Several important factors account for the results. An unexpectedly large proportion of the patients were given radiation therapy or systemic medication. These choices of treatment are potent and possibly diluted the counselling effects which may be more tardily and subtle. Although not statistically significant at baseline, differences of clinical severity between the two groups also became influential as a higher baseline disease severity was a highly significant predictor of improved outcome.

In the data analysis of the primary outcome some constitutional drawbacks of the HECSI-scale became apparent. The scale itself promotes an exponential and skewed distribution which is compromising to the statistical analyses. By use of a dummy cohort, a simulation study showed that the HECSI-scale preferably, and as an obvious choice, should be transformed to a square rooted scale. The  $\sqrt{\text{HECSI}}$ -scale has better statistical properties and offers a measurement which built on the accuracy of the raw HECSI-scale but at the same time is independent of specific cohort-effects and easy to interpret.

This thesis presents relevant findings from research in patientology and an ambitious clinical intervention. In the dermatological treatment and prevention of hand eczema an individual counselling is recommended with a relevant focus on gender differences and more emphasis on sustainable habit breaking. Complex interventions such as counselling programmes are difficultly evaluated by randomised controlled trials. They need to be viewed as multidimensional entities requiring also other evaluation approaches, including qualitative inquiries.

## 10.2 Resumé på dansk

Håndeksem er en hyppig, og ofte kronisk, sygdom. Dermatologisk udredning og behandling involverer en grundig eksponeringsanalyse og jævnligt medicin i form af topikale kortikosteroider. Det er imidlertid nødvendigt, at man vedvarende beskytter og plejer sin hud hvis man har håndeksem for at forebygge tilbagefald og et muligt kronisk forløb. Patientens egenomsorg er derved omdrejningspunktet i sygdomsforløbet, men der findes kun lidt forskning om, hvordan mennesker håndterer et hverdagsliv med håndeksem.

Formålet med denne afhandling var først at undersøge de oplevede barrierer og behov ved at udøve egenomsorg for håndeksem i hverdagslivet. På baggrund af den opnåede indsigt var formålet dernæst at udvikle og evaluere en individualiseret vejledning givet af en sygeplejerske. Afhandlingen består derved af en kvalitativ del og en del, der anvender kvantitativ metodik i form af et klinisk kontrolleret randomiseret studie. I begge dele var studiepopulationerne personer i Danmark, der var henvist til dermatologisk behandling for håndeksem.

Den kvalitative del af afhandlingen involverede fire fokusgruppeinterviews med 23 personer, der havde håndeksem. Data blev analyseret med brug af en template. Vi fandt, at deltagerne oplevede manglende viden omkring årsager til eksem og hvordan man bedst kan integrere det i hverdagen. Det blev oplevet som svært at indføre præventive strategier i hverdagslivet og det konstante behov for at fokusere på forebyggelse blev oplevet som trættende. Deltagerne udtrykte, at en mere fleksibel og behovsstyret kommunikation med sundhedspersonale kunne være til gavn. Derudover blev det påskønnet at møde andre personer med håndeksem.

Et vejledningsprogram blev udviklet på baggrund af fundene fra det kvalitative studie og gennemgang af litteraturen på området. Programmet fik navnet 'HudRask' og var en pakke af vejledende og støttende elementer. Et hovedelement i programmet var en konsultation med en sygeplejerske, hvor der blev fokuseret på individuel beskyttelse og pleje af huden. Patienten blev tilbudt brugeradgang til en nyudviklet hjemmeside, [www.hudrask.dk](http://www.hudrask.dk) til at facilitere yderligere støtte. Sitet indeholdt en individuelt udarbejdet ressource- og risikoprofil, et logbogsmodul til selvmonitorering af eksem, informationsmateriale herunder nyproducerede pædagogiske videos og quizzer. Desuden var der en kontaktformular med mulighed for at tage kontakt til interventionsteamet af sygeplejersker og et dialogforum til kommunikation mellem brugere af sitet.

HudRask-programmet blev evalueret i et klinisk studie med inklusion af 306 patienter, der var henvist til dermatologisk behandling ved København Universitets Hospital Gentofte eller ved Hudklinik Nord i Aalborg. Blokrandomisering sikrede en ligelig fordeling i forhold til køn og setting og allokerede patienterne til enten vanlig information eller til interventionsgruppen. Data for effektvariable blev indsamlet både ved baseline og ved follow-up efter seks måneder. Patienterne, der havde fået vanlig information i projektet, blev tilbudt HudRask-vejledningen ved follow-up.

Det første analytiske skridt var at beskrive karakteristika af kohorten og derved blev flere betydende kønsforskelle fundet. Mænd og kvinder havde lige stor klinisk sværhedsgrad af håndeksem, men eksemet påvirkede kvinder betydeligt mere end mænd. Kvinder rapporterede signifikant flere forværende faktorer og sygefravær. Sammenlignet med mænd, havde kvinder også mere nedsat livskvalitet ved samme sygdomssværhedsgrad, uanset om denne var objektivt bedømt eller selv vurderet. Der blev ikke fundet kønsforskelle i behandlingsniveau. Den selvrapporterede kompliance til behandling var ens mellem mænd og kvinder, men i gruppen af patienter over 40 år rapporterede flere en høj compliance til behandling sammenlignet med yngre patienter.

Patienterne i interventionsgruppen havde større forbedring af håndeksemets kliniske sværhedsgrad, bedømt ved Hand Eczema Severity Index (HECSI), sammenlignet med patienterne i gruppen, der fik vanlig information. Dette gjaldt dog kun for de patienter, der udelukkende blev behandlet med topikale kortikosteroider. Samlet set var der ved follow-up forskel mellem grupperne i den rapporterede adfærd relateret til hudbeskyttelse og hudpleje. Der var således i interventionsgruppen en øgning af patienter, der rapporterede daglig brug af fugtighedscreme og et fald i patienter, der havde hyppig håndvask i fritiden sammenlignet med gruppen af patienter, der modtog vanlig information. Interventionen påvirkede ikke deltagernes livskvalitet evalueret ved Dermatology Life Quality Index (DLQI). Flere væsentlige faktorer kan være årsag til disse samlede resultater. Et uforudset stort antal patienter fik intensiveret behandling i form af røntgenbehandling og/eller systemisk medicinsk behandling. Disse behandlingsformer er potente og udtyndede sandsynligvis effekten af vejledning, som formodentlig er mere diskret og forsinket. En høj klinisk sværhedsgrad ved baseline var desuden en højst signifikant prædikator for forbedring i løbet af follow-up perioden.

I dataanalysen blev nogle indlejrede svagheder ved HECSI-skalaen tydelige. Skalaen frembringer i sig selv en eksponentiel og skæv fordeling, som kompromitterer de statistiske analyser. Ved hjælp af en dummy kohorte viste et simulationsstudie, at HECSI-skalaen helt oplagt burde blive transformeret ved brug af kvadratrodd.  $\sqrt{\text{HECSI}}$ -skalaen har bedre statistiske egenskaber og giver et måleredskab, der bygger på nøjagtigheden af HECSI-skalaen, men som samtidig er lettere at fortolke uafhængigt af den specifikke kohorte.

Samlet set bidrager denne afhandling med relevante fund fra forskning i patientologi og en ambitiøs klinisk intervention. I den dermatologiske behandling og forebyggelse af håndeksem anbefales en individualiseret vejledning med et relevant fokus på kønsforskelle og med vægt på vaner og vedvarende adfærdændringer. Vejledningsprogrammer er dog komplekse interventioner, som er vanskelige at evaluere gennem randomiserede kontrollerede studier. Snarere må de vurderes som flerdimensionale størrelser, der også fordrer andre evalueringsformer herunder kvalitativ metode.

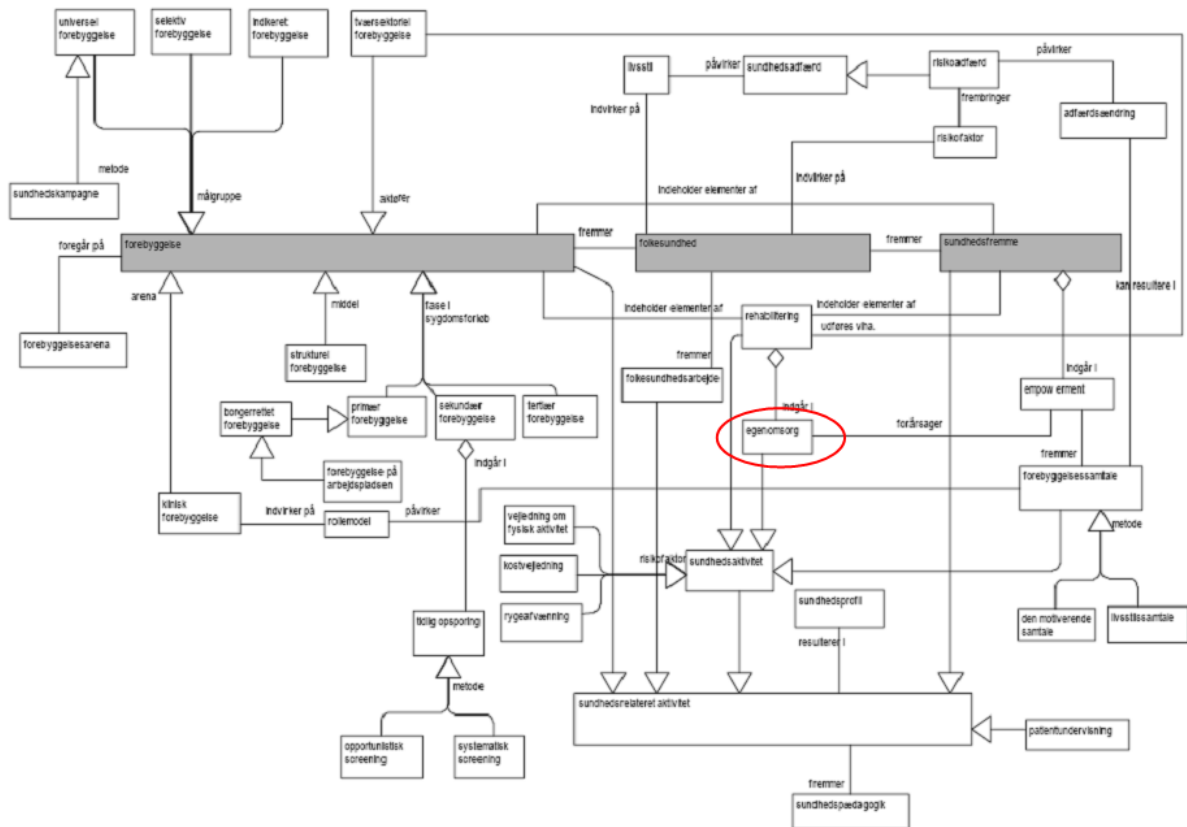
## **11 APPENDICES**

This section conveys the following appendices:

- A. Diagram of interrelated health care concepts
- B. The process of developing the website [www.hudrask.dk](http://www.hudrask.dk)
- C. Additional tables of self-reported data at baseline and at follow-up

## App A Interrelated health care concepts

Terminology of prevention, health promotion and public health presented by the Danish Board of Health (37)



The arrows indicate mediators and facilitators between concepts. The concept self-care or self-management is marked by the red circle.

## App B The website development process

Founded on the literature review and the findings from the focus groups, The Healthy Skin Clinic counselling programme was developed. The process of developing [www.hudrask.dk](http://www.hudrask.dk) as an element of the Healthy Skin Clinic involved firstly the formulation of specific requirements which were preferable as features of the site. This was done both in wording and graphically by a mock-up, generated by power point. Then offers from two relevant IT-companies were obtained of which the company Langtved Data A/S was chosen. As part of the contracting phase, meetings were held with the Danish Data Protection Agency to clarify the needed level of security.

Hereafter the actual process of development began in cooperation between the project manager (the author), the IT-company and the web designer Christina Rosendal. The intervention team of nurses took part by formulating much of the text in the patient information sites.

The four educational videos were inspired by study visits to the Institute for Interdisciplinary Dermatological Prevention and Rehabilitation at the University of Osnabrück, Germany. Manuscripts and ideas were created by Gitte Harboe and the author. The videos were produced by Aske Haslund Fabech assisted by Marcus Elskær Mollerup.

**Figure 9:** Still-photo from a video about the use of disinfectants instead of handwashing.

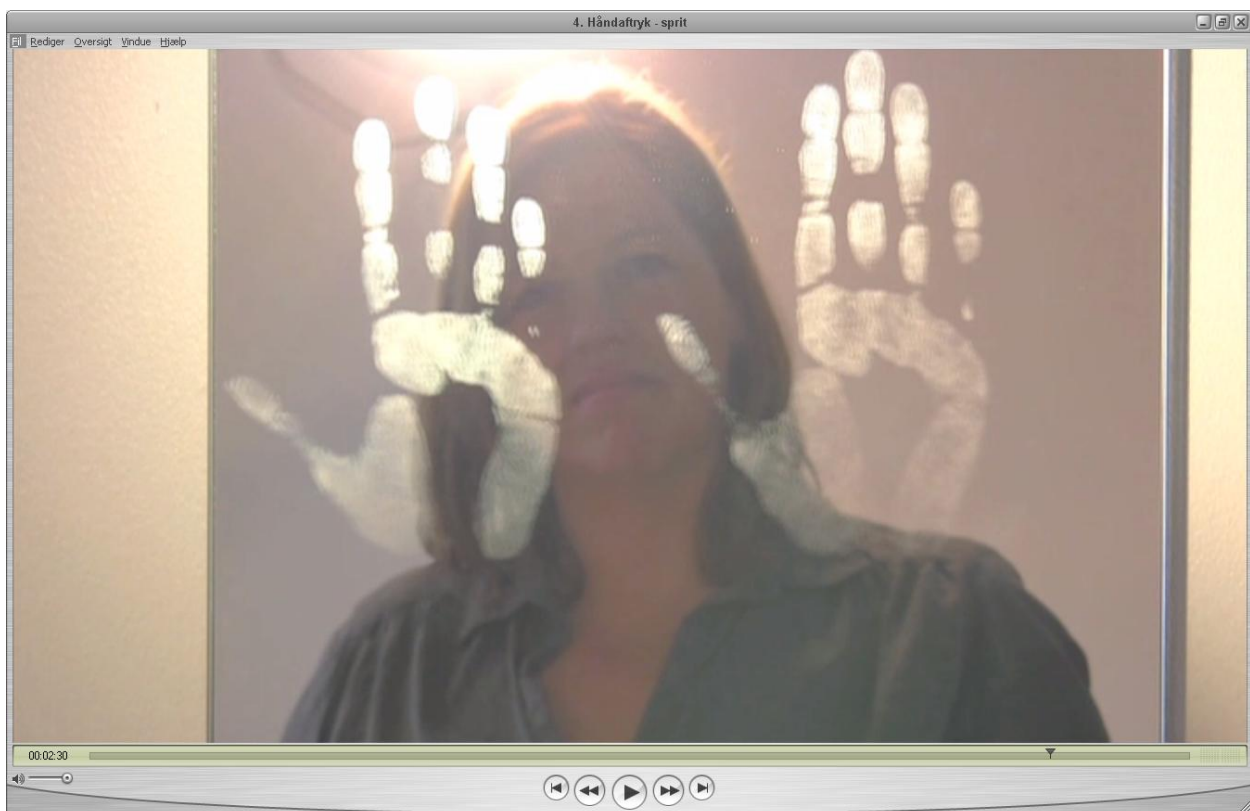




Figure 10: From mock-up (upper figure) to final layout of website (lower figure)

Some screenshots are presented in this next section to illustrate the different features of the website. Some aiding functions were applied to the website like the possibility of enhancing the script size or the linkage to a loud-reading tool on a governmental website, free of charge, as an aid to people with dyslexic problems. The large red compartment was used for instructions when relevant to the current site or to link to other parts of the website. The yellow “Post-it” was used to bring forward one-liners and short messages partly conveyed from the participants in the focus group interviews as a way to facilitate reflections of everyday life behaviour of the patients. Finally to the right are presented the logo with the hand and the label Healthy Skin Clinic (in Danish: HUDRASK). The individual user name is shown just above this logo. Each user was given a user name, i.e. K052-I, to secure anonymity.

The website comprised five main menus with the first from the left being the individual SKIN-profile. As aforementioned, this profile was generated from the individual responses to the baseline questionnaire. The profile aimed to focus the counselling session. Figure 11 shows an example of a SKIN-profile as it was displayed in the website. Internal links to the information sites, which were considered most relevant to the individual patient, were imputed below the individual SKIN-profile to tailor the information individually to the patient (not shown on the figure).

**Figure 11:** Screenshot from www.hudrask showing a SKIN-profile

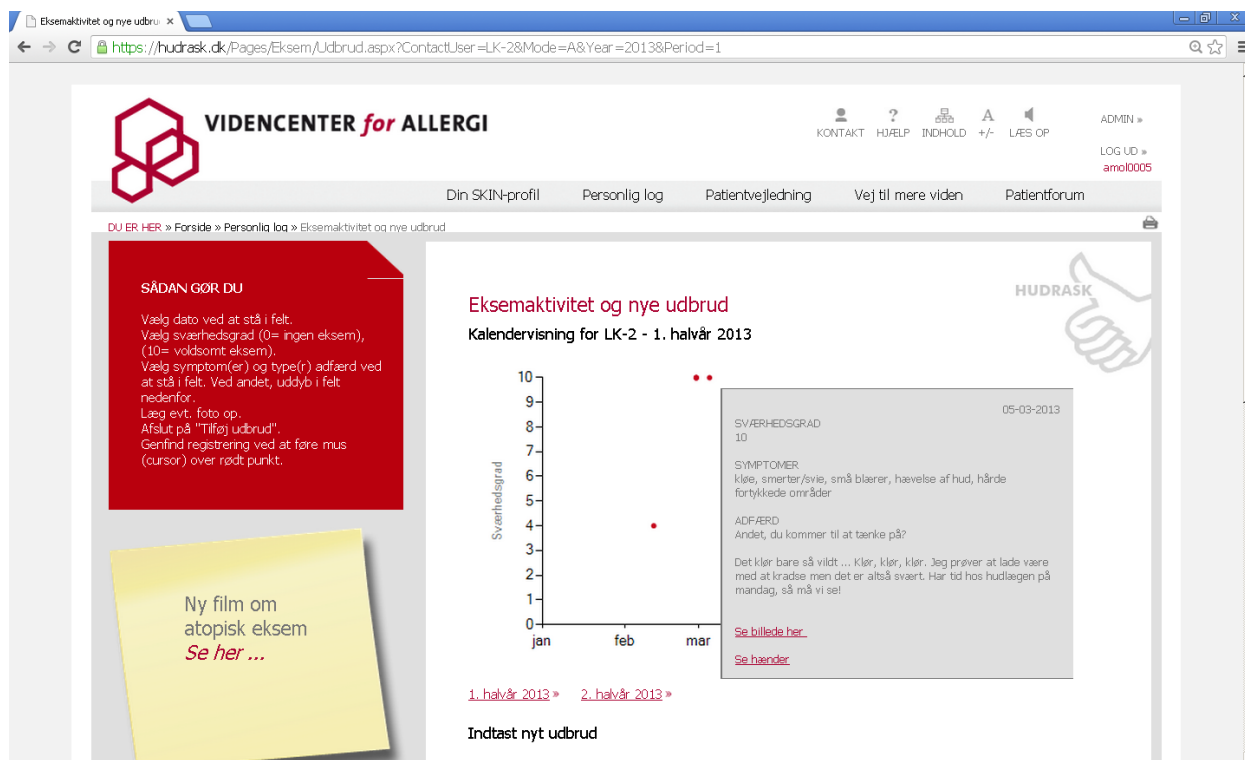
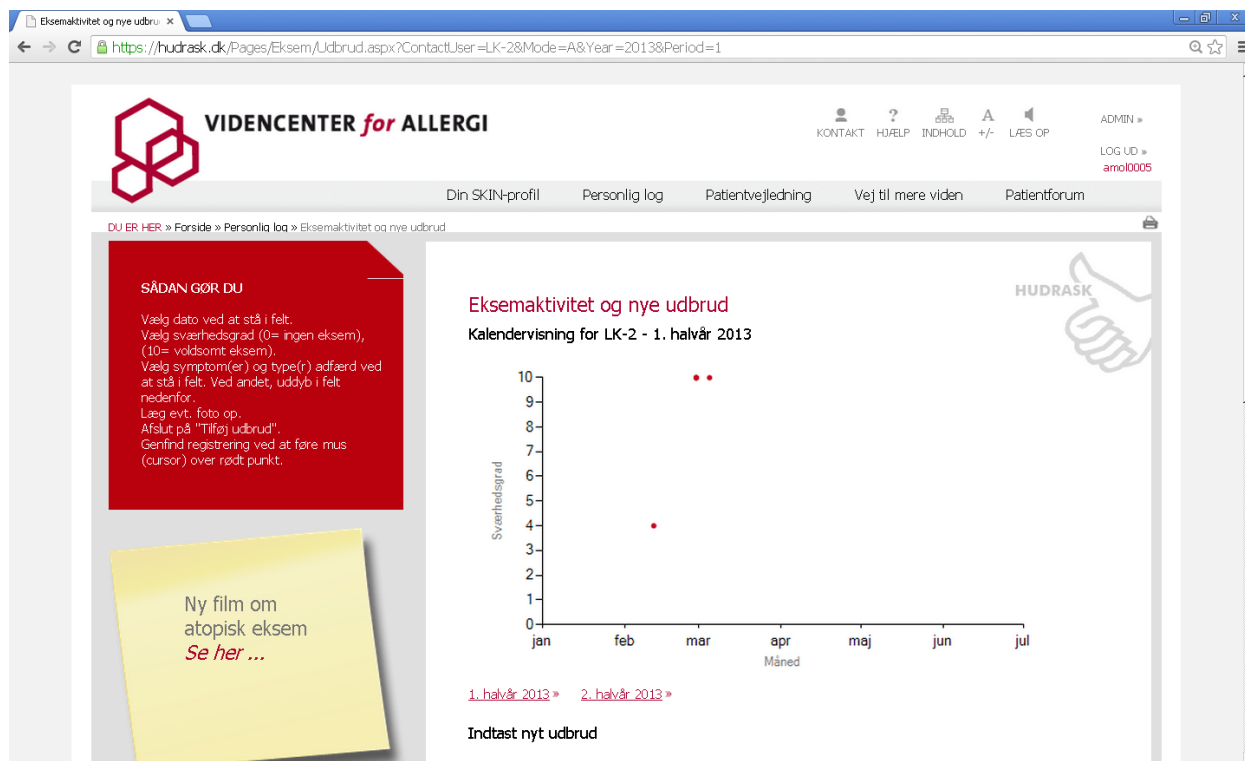
The screenshot shows a web browser window displaying the website 'VIDENCENTER for ALLERGI'. The page title is 'Hvordan er min SKIN-profil'. The navigation menu includes 'Din SKIN-profil', 'Personlig log', 'Patientvejledning', 'Vej til mere viden', and 'Patientforum'. The user is logged in as 'amo10005'. The main content area is divided into three sections:

- SÅDAN LÆSES SKIN-PROFIL:** A red box containing instructions on how to read the SKIN-profile, mentioning resources, loadings, and social networks.
- Hvordan er min SKIN-profil:** A central section with text explaining the profile's components: RESSOURCER (resources), BELASTNINGER (loadings), and SÅRBARHED (sensitivity). It includes a diagram showing the relationship between these factors and a hand icon labeled 'HUDRASK'.
- Post-it note:** A yellow sticky note with the text: 'Din daglige mælk bør være fedtfattig. Det gælder ikke for din daglige fugtighedscreme!'.

At the bottom of the page, there are three links: 'Hvad er SKIN-profil Kompetence', 'Hvordan ser min SKIN-profil ud? Individuelle faktorer', and 'Sårbarhed Nørdyrligne hensyn'.

The second main menu was the self-monitoring module, the personal log. A subpage of this menu offered room for personal thoughts not visible to even the intervention team.

**Figure 12:** (a) Screenshot from [www.hudrask.dk](http://www.hudrask.dk) showing the self-monitoring log (upper figure) and (b) details of a specific registration (lower figure)



The third main menu was a folder of the various patient information sheets. Nineteen subpages offered information including visual elements and relevant links.

**Figure 13:** Information sites of corticosteroid treatment (upper figure) and what fissures are and how to deal with them (lower figure)

**VIDENCENTER for ALLERGI**

KONTAKT HJÆLP INDHOLD +/- LÆS OP ADMIN »  
LOG UD » amol0005

Din SKIN-profil Personlig log Patientvejledning Vej til mere viden Patientforum

DU ER HER » Forside » Patientvejledning » Hormoncremer ved håndseksem (binyrebarkhormon)

**SNUP EN 6'ER**  
Hvor lang tid er det yderste hudlag, barrierelaget, normalt om at forny sig?  
a) 24 timer?  
b) 28 dage?  
c) 6 måneder?  
VÆR MED: [test\\_din\\_viden](#)

Brug evt. mindre fed creme flere gange i løbet af dagen – og en fed salve til natten!

**Hormoncremer ved håndseksem (binyrebarkhormon)**

**Hvad er hormoncreme?**  
Det aktive stof i hormoncremer er binyrebarkhormon, som er rørt op i creme eller salve. Hormoncreme kaldes også binyrebarkhormoncreme, steroidcreme eller kortisoncreme.  
Hormoncremernes virkning er velkendt. De har været anvendt i mere end 50 år til behandling af forskellige hudsygdomme.  
Hormoncremer dæmper irritation, rødme og kløe i huden. De er derfor effektive ved eksemssygdomme.

HUDRASK

Derموvat® 0,05% creme  
Dinoderm®  
Elocon® 0,1% Kream/Creme/Krem  
Fucidin®  
Elocon® 0,1% Kream/Creme/Krem  
Dinoderm®  
Elocon® 0,1% Kream/Creme/Krem  
Fucidin®  
Elocon® 0,1% Kream/Creme/Krem

**VIDENCENTER for ALLERGI**

KONTAKT HJÆLP INDHOLD +/- LÆS OP ADMIN »  
LOG UD » amol0005

Din SKIN-profil Personlig log Patientvejledning Vej til mere viden Patientforum

DU ER HER » Forside » Patientvejledning » Revner (fissurer) i huden ved håndseksem

**SNUP EN 6'ER**  
Hvor lang tid er det yderste hudlag, barrierelaget, normalt om at forny sig?  
a) 24 timer?  
b) 28 dage?  
c) 6 måneder?  
VÆR MED: [test\\_din\\_viden](#)

Brug alarmen på mobilen til at huske dig på at indsmøre dine hænder med creme i løbet af dagen.

**Revner (fissurer) i huden ved håndseksem**

**Hvad er fissurer?**  
Fissurer er revner, der kan komme i den tørre og fortykkede hud ved håndseksem. De kan være generende f.eks. ved kontakt til håndsprit, citrusfrugter m.m.  
Fissurerne kan være meget ømme og smertefulde f.eks. ved berøring. Det kan være vanskeligt at bruge hænderne, og hos enkelte kan det endvidere være svært at passe sit arbejde.

HUDRASK

Close-up photograph of a hand showing deep fissures in the skin between the fingers.

Four videos were produced to the website as an alternative didactic means to support the educational messages (Figures 9 and 14). These films were of 3-4 minutes duration and covered topics like the use of disinfectants instead of handwashing and how emollients are helpful in hand eczema prevention by adding a layer to protect from harmful exposures. The videos also presented information of the structure of the skin to the patients as shown in the Figure 14. Additional videos of how to perform nickel spot tests or patch tests and how to read labels of ingredients in cosmetic products were available by external links to the website of The Danish National Allergy Research Centre.

**Figure 14:** Newly produced film supplemented the educational material on the website

The screenshot shows a web browser window displaying the 'VIDENCENTER for ALLERGI' website. The browser's address bar shows the URL: [https://hudrask.dk/Pages/Other/Video.aspx?video=Haandaftryk\\_haandvask.flv&keepBackLink=true](https://hudrask.dk/Pages/Other/Video.aspx?video=Haandaftryk_haandvask.flv&keepBackLink=true). The website header features the logo 'VIDENCENTER for ALLERGI' and navigation links: 'KONTAKT', 'HJÆLP', 'INDHOLD', 'LÆS OP', and 'ADMIN'. A user is logged in as 'amo1005'. The main content area is titled 'Film' and displays a video player showing a cross-section of skin with numbered labels 2 and 4. Below the video player, there are links for 'Se film om:' including 'Hvad er nikkelallergi', 'Lappeprøven - Hvordan foregår den', and 'Nikkelallergi - hvad gør man ved det'. On the left sidebar, there is a red box with the text 'SNUP EN 6'ER' and a quiz question: 'Hvor lang tid er det yderste hudlag, barrierelaget, normalt om at forny sig?' with options a) 24 timer?, b) 28 dage?, and c) 6 måneder?. Below this is a yellow sticky note that says 'FOREBYG MED FUGTIGHEDSCREME!'.

The fourth main menu was “*Ways to increase your knowledge*” which consisted of several links to other relevant websites and a site with a collection of frequently asked questions (FAQ). The latter is shown in Figure 15. Another element in this fourth main menu was the quiz-module, shown in Figure 16, which was offered as an educational but also humorous element of the site. In total, 36 questions were formulated within six categories: 1) skin anatomy and physiology, 2) skin care, 3) hygiene, 4) skin protection and gloves, 5) aetiology and epidemiology of hand eczema; and 6) general and behaviour related questions. The questions ran in independent loops within each category which secured a variation of six-item quizzes to be prompted. Each topic in question was further elaborated when the correct answers were generated at the end of the quiz.

Figure 15: Frequently asked questions (FAQ) as part of the fourth main menu

**VIDENCENTER for ALLERGI**

KONTAKT HJÆLP INDHOLD +/- LÆS OP ADMIN »  
LOG UD » am010005

Din SKIN-profil Personlig log Patientvejledning Vej til mere viden Patientforum

DU ER HER » Forside » Vej til mere viden » FAQ

**F.A.Q.**  
Er en forkortelse for Frequently Asked Questions, altså hyppigt stillede spørgsmål.  
På denne side kan man finde svar på spørgsmål, som kan være af interesse for alle med håndeksem.

*Anvend handsker så længe det er nødvendigt, men så kort som muligt!*

**F.A.Q.**

**AFTRAPNING AF HORMONCREMER: Hvorfor er det vigtigt at trappe ud af hormoncremer, hvis man har brugt dem gennem længere tid?**  
Huden vænner sig til det aktive hormon i cremen. Hvis man holder for pludseligt op med behandlingen, kan eksemet blusse op igen. Man bør aftale med sin læge/hudlæge, hvordan aftrapningen kan foregå. Læs mere om behandling med hormoncremer under menuen 'Patientvejledning'.

**HORMONCREMER OG FUGTIGHEDSCREMER: Når jeg har smurt mit eksem med hormoncreme, hvornår må jeg så bruge fugtighedscreme?**  
Der bør gå mindst en halv time, før man smører sig med (fed) fugtighedscreme, når man har smurt hormoncreme på eksemområder. Læs mere om hormoncremer og om fugtighedscremer under 'Patientvejledning'.

**HORMONCREMER OG HÅNDVASK: Når jeg har smurt med hormoncreme, hvornår må jeg så vaske mine hænder?**  
Forsøg at undgå at vaske hænder i den første times tid, efter at eksemområder er smurt med hormoncremer. Læs mere om hormoncremer og om fugtighedscremer under 'Patientvejledning'.

**HÅNDEKSEM OG FØDEVARER: Når mit eksem blusser op, kan det så være forskellige madvarer, der har betydning for eksemet?**

Figure 16: The quiz module as part of the fourth main menu

**VIDENCENTER for ALLERGI**

KONTAKT HJÆLP INDHOLD +/- LÆS OP ADMIN »  
LOG UD » am010005

Din SKIN-profil Personlig log Patientvejledning Vej til mere viden Patientforum

DU ER HER » Forside » Vej til mere viden » Snupe en 6'er

**EN KORREKT HÅNDVASK TAGER 1 MINUT**  
Bruger du så lang tid på at vaske dine hænder?  
Hvis ikke, så slider du måske unødigt meget på huden samtidig med at hænderne ikke bliver tilstrækkeligt rene.  
Se [film om håndvask](#) med vand og sæbe

*Brug evt. mindre fed creme flere gange i løbet af dagen - og en fed salve til natten!*

**Snupe en 6'er**

**Hvad er filaggrin?**

- a) Et protein i hudens yderste lag, der er vigtig for barrierefunktionen?
- b) En særlig form for finsk mandehumor?
- c) En variation af filigran-guldsmedekunst?

**Skal man altid bruge samme fugtighedscreme**

- a) Nej det er fint at bruge en creme i løbet af dagen og en anden når man er hjemme
- b) Ja så kan huden bedst finde ud af det
- c) Nej for så bliver du allergisk over for den

**Hvor mange gange kan man vaske hænder med sæbe, før huden er affedt?**

- a) En gang?
- b) 20 gange? Jo mere man vasker hænder, jo hurtigere danner man fedt.
- c) Uendeligt, huden danner fedt uafbrudt.

**Hvilken handske skal man vælge, hvis man har håndeksem?**

- a) Den der bedst skjuler eksemet
- b) Den der er tykkest
- c) Den der beskytter mod det arbejde man udfører

The final main menu of the website comprised the patients' virtual dialogue forum (Figure 17). The users of the site could initiate a thread of communication by inserting a subheading and an additional comment or question. The patients were cautioned as to how much personal information they would share with other users when they were introduced to the website. Otherwise a high level of security including a three-item security log-in module, the so called NemID system, was applied to the site as a requirement from the Danish Data Protection Agency.

Figure 17: The patient dialogue forum

The screenshot displays the 'VIDENCENTER for ALLERGI' website interface. The top navigation bar includes links for 'KONTAKT', 'HJÆLP', 'INDHOLD', and 'LÆS OP'. A user is logged in as 'am010005'. The main content area features a red box with the heading 'BRUG HINANDENS ERFARINGER' (Use each other's experiences) and a yellow sticky note that says 'Husk, at engangshandsker er til én gangs brug!' (Remember, disposable gloves are for one-time use!). The forum thread is titled 'arbejdsrelateret eksem' and contains the following comments:

- Comment 1:** "Jeg har til bider været rigtig glad for at tage en antihistamin om aftenen - det virker som om det tager kløen indenfra :-)" (I have been really happy to take an antihistamine in the evening - it seems to take the itch from the inside :-). Date: 07-07-2011 09:39:19.
- Comment 2:** "Ligger med isposer på hænderne om natten :( . Men det er utroligt hvor hurtigt kløen forsvinder med kulde." (I lie with ice packs on my hands at night :( . But it's incredible how fast the itch disappears with cold. Date: 16-10-2011 16:37:58).
- Comment 3:** "Ligger med bomuldshandsker om natten, da det tager lidt af smerten." (I lie with cotton gloves at night, as it takes a bit of the pain. Date: 08-03-2012 23:24:15).
- Comment 4:** "Jeg påfører altid crem på en ekstra gang inden jeg skal sove med bomuldshandsker, dette lindrer det hele natten igennem." (I always apply cream one extra time before I go to bed with cotton gloves, this soothes it all night long. Date: 20-06-2011 09:31:31).

## App C Additional tables

**Table 4:** Danish Medication Adherence Report Scale at baseline, at follow-up and as delta-values in groups of (a) genders and (b) intervention arms

(a) How often do you have the following experiences? (1: very often, 5: never)	Women			Men			p-value <sup>2</sup> Δ DMARS
	T <sub>0</sub> DMARS-4	T <sub>1</sub> DMARS-4	n <sup>1</sup>	T <sub>0</sub> DMARS-4	T <sub>1</sub> DMARS-4	n <sup>1</sup>	
Some people try to avoid taking prescribed medication. Do you?	4.2 (1.0)	4.3 (0.9)	157	4.4 (1.0)	4.3 (1.0)	88	
Some people forget to take/use their medication. Do you?	4.0 (0.9)	4.2 (0.8)	158	4.0 (0.8)	3.9 (0.9)	88	
Some people decide to miss out on a dose or to alter the dose. Do you?	4.6 (0.8)	4.6 (0.8)	157	4.6 (0.6)	4.5 (0.8)	88	
Some people stops taking prescribed medication when symptoms are fewer. Do you?	4.3 (0.9)	4.3 (1.0)	157	4.2 (0.9)	4.1 (1.1)	87	
<b>DMARS-4 sum-score</b>	17.2 (2.6)	17.4 (2.5)	155	17.2 (2.6)	16.7 (2.8)	87	0.08

(b) How often do you have the following experiences? (1: very often, 5: never)	Intervention group			Usual care group			p-value <sup>2</sup> Δ DMARS
	T <sub>0</sub> DMARS-4	T <sub>1</sub> DMARS-4	n <sup>1</sup>	T <sub>0</sub> DMARS-4	T <sub>1</sub> DMARS-4	n <sup>1</sup>	
Some people try to avoid taking prescribed medication. Do you?	4.3 (1.0)	4.3 (0.9)	118	4.3 (1.0)	4.4 (0.9)	127	
Some people forget to take/use their medication. Do you?	4.1 (0.9)	4.1 (0.8)	118	4.0 (0.8)	4.0 (0.9)	128	
Some people decide to miss out on a dose or to alter the dose. Do you?	4.7 (0.6)	4.6 (0.8)	118	4.5 (0.8)	4.5 (0.9)	127	
Some people stops taking prescribed medication when symptoms are fewer. Do you?	4.3 (0.9)	4.3 (1.0)	117	4.2 (1.0)	4.2 (1.0)	127	
<b>DMARS-4 sum-score</b>	17.5 (2.4)	17.2 (2.6)	117	16.9 (2.7)	17.1 (2.7)	125	0.86

<sup>1</sup>n is number of patients within groups who answered these questions in the follow-up questionnaire; hence a Δ-score of DMARS-4 could be calculated, <sup>2</sup>Independent-Samples Mann-Whitney U Test for differences in sum-score between groups

Data presented as means and SD's as regards intelligibility but non-parametric statistical tests were used because of no-normal distributions, higher score indicate a higher level of medication adherence



**Table 5:** Self-management at follow-up in groups of (a) genders and (b) intervention arms

(a): How would you describe yourself according to the following statements? (0: not fit at all, 10: fits perfect)	Women		Men		p-value <sup>1</sup>
	mean (SD)	n	mean (SD)	n	
I can recognise new eruptions or worsening of my hand eczema and respond to this	7.6 (2.5)	157	6.8 (3.0)	90	0.07
I know when to begin using topical steroid at eruptions or worsening of my hand eczema	7.7 (2.6)	150	6.6 (3.0)	89	<b>0.003</b>
I am confident that I can handle my hand eczema in case of eruptions or worsening	7.2 (2.5)	156	6.6 (2.6)	89	0.07
I know when to consult my GP or a dermatologist because of my hand eczema	7.1 (2.9)	156	6.8 (2.8)	89	0.28
I have changed my habits as regards my hand eczema	7.8 (2.8)	156	6.8 (3.0)	89	<b>0.001</b>
I use gloves to protect my skin against allergens and irritants	8.1 (2.6)	156	6.6 (3.2)	90	<b>&lt;0.001</b>
I can take the necessary precautions related to my hand eczema in my leisure time	8.1 (2.1)	156	7.5 (2.3)	90	0.06
I can take the necessary precautions related to my hand eczema while I am at work	7.2 (2.7)	147	7.1 (2.5)	87	0.59
I know my allergies and/or the irritants that cause my hand eczema	5.6 (3.6)	153	4.3 (3.6)	91	<b>0.013</b>
I can control my hand eczema if I try hard enough	5.6 (3.4)	154	5.7 (3.3)	90	0.81
<b>Overall sum-score</b>	<b>72.4 (15.3)</b>	<b>139</b>	<b>65.4 (15.5)</b>	<b>86</b>	<b>0.002</b>

(b): How would you describe yourself according to the following statements? (0: not fit at all, 10: fits perfect)	Intervention group		Usual care group		p-value <sup>1</sup>
	mean (SD)	n	mean (SD)	n	
I can recognise new eruptions or worsening of my hand eczema and respond to this	7.4 (2.7)	119	7.1 (2.7)	126	0.44
I know when to begin using topical steroid at eruptions or worsening of my hand eczema	7.3 (2.8)	113	7.3 (2.8)	124	0.92
I am confident that I can handle my hand eczema in case of eruptions or worsening	7.1 (2.3)	118	6.8 (2.7)	125	0.41
I know when to consult my GP or a dermatologist because of my hand eczema	7.3 (2.6)	118	6.8 (3.1)	125	0.16
I have changed my habits as regards my hand eczema	7.5 (2.7)	118	7.3 (3.2)	125	0.45
I use gloves to protect my skin against allergens and irritants	7.3 (3.1)	119	7.9 (2.7)	125	0.14
I can take the necessary precautions related to my hand eczema in my leisure time	7.9 (2.1)	119	7.8 (2.3)	125	0.82
I can take the necessary precautions related to my hand eczema while I am at work	7.4 (2.4)	116	6.9 (2.9)	117	0.15
I know my allergies and/or the irritants that cause my hand eczema	5.2 (3.5)	118	5.1 (3.8)	124	0.72
I can control my hand eczema if I try hard enough	5.7 (3.4)	119	5.7 (3.3)	123	0.99
<b>Overall sum-score</b>	<b>70.8 (15.2)</b>	<b>111</b>	<b>68.7 (16.2)</b>	<b>113</b>	<b>0.32</b>

GP, general practitioner, SD, standard deviation, <sup>1</sup>Mann-Whitney U-test for differences between groups. Data presented as means and SD's as regards intelligibility but non-parametric statistical tests were used because of no-normal distributions, higher score indicate a higher level of confidence in and actual skin protection behaviour





