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Chronic hand eczema: A prevalent disease in the general population associated with reduced quality of life and poor overall health measures

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Abstract

Background: The impact of hand eczema (HE) on Health-Related Quality of Life (HRQoL) has only been sparsely studied in a general population setting, and never by use of the disease specific Quality Of Life in Hand eczema Questionnaire (QOLHEQ).

Objectives: To examine the HRQoL of unselected individuals with HE using the QOLHEQ. Further, to provide prevalence estimates of severe and chronic HE (CHE), and to contrast overall health related outcomes between individuals with and without HE.

Methods: In this nationwide, cross-sectional study a questionnaire covering questions on HE related outcomes, and overall health was sent to a random sample of 100 000 Danish adults via a secure digital mailbox, linked to their unique civil registration numbers. Data on demographic characteristics were retrieved from the civil registration system. Individuals reporting HE, further answered the QOLHEQ and other disease specific questions.

Results: The response rate was 42.7% ($n = 42\,691$). Total estimates of lifetime, 1-year and point prevalences of HE were 24.4%, 13.3% and 5.8%. Of individuals reporting a 1-year prevalence, 35.1% reported moderate–severe disease and 82.6% CHE. Individuals with HE were more likely to report less good or poor overall health, and sick leave (any reason), compared to those without. In the 2176 (92.5%) with current HE who completed the QOLHEQ, median QOLHEQ scores corresponded to a moderate impairment of the symptoms and treatment and prevention domains and a slight impairment overall and for the emotions and functioning domains. Factors that were strongly associated with moderate to severe HRQoL impairment included severe, chronic and occupational HE as well as female sex.

Conclusions: HE is highly prevalent, bears a considerable burden on society and significantly affects the lives of impacted individuals. Our findings indicate a necessity for targeted prevention aimed at high-risk groups, and support and treatment for those most affected.

KEYWORDS
atopic dermatitis, contact allergy, epidemiology, hand eczema, prevalence, quality of life

1 | INTRODUCTION

Hand eczema (HE) is an inflammatory, often itchy and painful skin condition that affects nearly 10% of European adults annually.[1,2] While several studies have investigated the health related quality of life (HRQoL) in selected HE populations (e.g., patients in hospitals[3–6] or various occupational groups[7–9]), the impact of HE on HRQoL has only been sparsely studied in general population settings. General population studies provide a more comprehensive and generalizable understanding of the impact of HE on affected individuals and society as a whole. These studies include the substantial number of individuals with HE who have not sought medical attention or who may not be employed in specific occupations.[10,11] In 1990, Meding and Swanbeck reported that more than 80% of unselected individuals with HE had experienced negative psychosocial interference because of their HE.[12] Additionally, two other Swedish studies from 2009 and 2011 found that unselected individuals with HE had consistently lower HRQoL, as measured by the generic instruments EuroQol 5-D and Short Form 36, than individuals without.[13,14] However, these more general QoL instruments have shortcomings, when addressing QoL impact of a localised disease on an important skin site, as HE. For this reason, The Quality Of Life in Hand Eczema Questionnaire (QOLHEQ), a disease specific measurement instrument constructed and used to measure the HRQoL in individuals with HE, was recently developed.[15] This questionnaire has been validated in several countries, including Denmark.[15–19] However, no studies have yet employed the QOLHEQ in a general population setting.

In this nationwide study, we examine the HRQoL of more than 2000 unselected individuals with HE using the QOLHEQ. We contrast overall health perception and sick leave prevalence between individuals with and without HE. Additionally, we provide updated estimates of HE prevalence, including prevalence of chronic and severe disease, within a large general population sample.

2 | METHODS

The study was a cross-sectional survey conducted from May through June 2021. In Denmark all 5.8 million inhabitants have a unique civil registration number. A secure, digital mailbox (eBoks) linked to the civil registration number has been mandatory for all Danish citizens older than 15 years since 2014 (with exemption granted in exceptional cases).[20] eBoks, mainly used for public authority communication, can also facilitate web-based scientific study invitations, provided that researchers obtain prior permissions from relevant authorities.

A sample of 100 000 individuals, aged 18–75 years with Danish citizenship and birthplace, was drawn randomly from the Civil Registration System. Data retrieved from the Civil Registration System included sex, age and municipality of residence. Research Electronic Data Capture (REDCap)[21] was used to construct and send the questionnaire and to collect and store the data.

An invitation to participate in the study was sent to the participants' eBoks in mid-May 2021 and a single reminder was sent to non-responders 2 weeks later. The subject of the questionnaire was stated as to characterise prevalence, causes and consequences of various skin exposures and eczema/rash in Denmark. It was highlighted that participation was voluntary and that all responses were needed, regardless of the participants having (a history of) eczema/rash or not.

The study was approved by the Danish Data Protection Agency (P-2020-558) and the Danish Health Data Authority (FSEID-00005217).

2.1 | Questionnaire

The questionnaire covered questions on overall health, socioeconomic status, use of health care services, smoking, comorbidities and self-reported prevalences of HE, contact allergy and atopic dermatitis. Participants reporting any prevalence of HE further answered HE specific questions (by use of branching logic). The questions used were from the Nordic Occupational Skin Questionnaire (NOSQ-2002),[22] the Health 2006 survey[11] and other HE specific validated instruments with some being added/modified. The prevalence of HE was assessed based on answers to the questions 'have you ever had HE' (lifetime prevalence), and (if yes) 'have you had HE within the past 12 months' (1-year prevalence), further (if yes) 'do you currently have HE?' (point prevalence). The questions used to assess the point and 1-year prevalence have been previously validated.[23–25] The QOLHEQ was answered by participants reporting a point prevalence of HE. The instrument contained 30 questions/items grouped in four domains/subscales: symptoms, emotions, functioning and treatment and prevention. Individuals were asked how often they had been bothered by the skin condition on their hands in various situations during the past 7 days. The severity of HE was assessed by the validated photographic guide[26] and a visual analogue scale (VAS). Chronic HE (CHE) was defined as disease duration >3 months or ≥2 relapses of HE within the last 12 months.[27] The prevalence of atopic dermatitis was assessed using the question 'has a doctor ever told you, or your parents, that you have/had atopic eczema (childhood eczema, asthmatic eczema)?', modified from Silverberg et al.[28] Contact allergy was determined by affirmative answers to the questions 'Have you ever been tested for allergy by use of a patch test on your back?', and (if yes) 'Did the patch test reveal any allergies?'. These questions were introduced by a photo of an individual being patch tested accompanied by a layman description of the procedure.

2.2 | Geography

Based on Official Municipality Keys, responders and non-responders were grouped according to the five Danish Municipality groups (Capital, Metropolitan, Provincial, Commuter and Rural Municipalities). These groups are used to analyse geographical differences in Denmark and are based both on the number of inhabitants in the largest city in the municipality and the accessibility to jobs, Figure S1.

2.3 | Statistical analysis

Prior to conducting the study, a sample size of 33 670 participants was estimated. Considering a response rate of 35%, 100 000 individuals were contacted, Appendix S1.

Characteristics of subjects were presented as numbers and proportions (%) for categorical variables and comparisons between group proportions were analysed using Chi square tests. Continuous variables were found to be not normally distributed. Given the large sample size, and with the aim to provide a more comprehensive interpretation of group differences, both median (interquartile range [IQR]) and mean (standard deviation [SD]) values were reported. Accordingly, comparisons between groups for continuous endpoints were performed by use of both non-parametric (Mann Whitney *U* tests and Kruskal–Wallis tests) and parametric methods (*t* tests and ANOVA tests). All endpoints were calculated excluding missing answers (see Appendix S1 for missing data). QOLHEQ scores were calculated by use of the SPSS-syntax downloaded from the official QOLHEQ website.[29] Univariate and multivariable binary logistic regression models were used to examine factors associated with less good-poor overall self-reported health ratings, sick leave for more than 7 days the past year, annual household income <600 000 DKK, and moderate–severe HRQoL impairment. Crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were reported. Statistical analysis was performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA).

2.4 | Interpretability of QOLHEQ scores

Interpretability of QOLHEQ scores was based on the international severity bands proposed by Oosterhaven et al.,[30] as a Danish interpretability study has yet to be performed. The bands for total scores, evaluated via anchor questions for HRQoL, are: 'not at all' (0–10), 'slightly' (11–39), 'moderately' (40–61), 'strongly' (62–86) and 'very strongly impaired' (≥87).[30]

3 | RESULTS

The response rate was 42.7% ($n = 42\,691$) after one reminder. The response rate increased with age, and non-responders were more likely to be males ($P < 0.001$). The response rates ranged from 41.0% (Capital Municipalities) to 44.6% (Commuter Municipalities, Table S1). Table 1 shows characteristics of individuals responding to the question on the lifetime prevalence of HE (40908) stratified by sex. The total lifetime, 1-year, and point prevalences were 24.4%, 13.3% and 5.8%, respectively. The 1-year prevalence of CHE was 11.0%, accounting for 82.6% of all individuals reporting a 1-year prevalence of HE. This high prevalence was mainly explained by individuals reporting ≥2 eruptions of HE (total 1-year prevalence 9.7%) and to a lesser degree by individuals reporting disease duration >3 months within the last year (total 1-year prevalence 5.0%). All prevalence estimates were significantly higher among females than males. For individuals reporting a 1-year prevalence of HE, the average severity of HE in the past year as assessed by the photoguide was mild in 64.9%, moderate in 28.8%, severe in 4.7% and very severe in 1.6% with no significant differences between males and females ($p = 0.174$). Similarly, the estimates for severity of current HE did not differ significantly between sex (Table 1). Females reported higher severity scores of HE at worst an averagely the last year on a VAS compared with males, whereas the estimates for current HE were comparable (Table 1). The proportion of individuals reporting moderate to very severe HE (averagely the past year assessed by the photoguide) stratified by municipality group is shown in Figure 1. Of individuals with current HE, 35.3% reported moderate to very strong HRQoL impairment, as assessed by the QOLHEQ, with higher estimates of moderate and strong impairment among females than males, Table 1.

3.1 | Health related outcomes in individuals with and without hand eczema

Table 2 shows comparisons between individuals with HE the past year and those without, in terms of their overall health rating, sick leave (>7 days for any reason the past year), general practitioner consultations (for any reason the past year), and symptoms of sleep disturbance and pruritus (the past 48 h). Individuals with HE had significantly lower overall health ratings, greater variability in the number of general practitioner consultations (median [IQR] 2.0 [3.0] vs. 2.0 [2.0], $p < 0.001$), and higher prevalences of sick leave compared to those without HE (27.5% vs. 20.6%, $p < 0.001$, Table 2). The median number of weeks of sick leave (of those reporting sick leave for any reason) was comparable between the two groups. Individuals with HE reported higher levels of pruritus compared to those without, whereas no difference in sleep disturbance was found between the two groups (Table 2).

Self-reported health and sick leave outcomes of individuals with HE in the past year compared to those without were further examined in logistic regression analyses including both unadjusted and adjusted models (Table 3). In all models, including the fully controlled models (adjusted for age, sex, atopic dermatitis, annual household income, daily smoking and municipality group), individuals with HE were more likely to report less good-poor overall health (aOR 1.45, 95% CI

TABLE 1 Characteristics of responders.

	Total population ($n = 40\,908$)	Females ($n = 23\,289$)	Males ($n = 17\,619$)	*p*-Value
Age, years				
Median (IQR)	54.5 (25)	53.4 (26)	55.9 (23)	**<0.001**
Mean (SD)	51.7 (16.1)	50.6 (16.2)	53.1 (15.8)	**<0.001**
Age, range, *n* (%)				**<0.001**
18–34 years	8059 (19.7)	5050 (21.7)	3009 (17.1)	
35–54 years	12 919 (31.6)	7511 (32.3)	5408 (30.7)	
≥55 years	19 930 (48.7)	10 728 (46.1)	9202 (52.2)	
Atopic dermatitis, *n* (%)[1]	3590 (8.8)	2701 (12.0)	889 (5.2)	**<0.001**
Asthma, *n* (%)[a]	5662 (13.8)	3454 (15.3)	2208 (12.9)	**<0.001**
Allergic rhinitis, *n* (%)[a]	8618 (21.1)	5243 (23.3)	3376 (19.7)	**<0.001**
Prevalence of HE, *n* (% [95% CI])				
Lifetime prevalence	9973 (24.4 [24.0–24.8])	6662 (28.6 [28.0–29.2])	3311 (18.8 [18.2–19.4])	**<0.001**
1-year prevalence	5424 (13.3 [12.9–13.6])	3688 (15.8 [15.4–16.3])	1736 (9.9 [9.4–10.3])	**<0.001**
1-year prevalence of CHE	4482 (11.0 [10.7–11.3])	3093 (13.3 [12.8–13.7])	1389 (7.9 [7.5–8.3])	**<0.001**
Point prevalence	2353 (5.8 [5.5–6.0])	1498 (6.4 [6.1–6.8])	855 (4.9 [4.5–5.2])	**<0.001**
Duration of HE in the last year, *n* (%)[b]				
>3 months	2047 (5.0)	1306 (5.6)	741 (4.2)	**<0.001**
Number of eruptions of HE in the last year, *n* (%)[c]				
≥2	4162 (9.7)	2906 (12.0)	1256 (6.8)	**<0.001**
Severity of HE, photoguide, *n* (%)				
At worst (ever)[b]				0.355
Mild	2587 (48.2)	1737 (47.5)	850 (49.7)	
Moderate	1926 (35.9)	1329 (36.3)	597 (34.4)	
Severe	620 (11.4)	435 (11.9)	185 (10.8)	
Very severe	237 (4.4)	158 (4.3)	79 (4.6)	
Averagely (past year)[b]				0.174
Mild	3465 (64.9)	2373 (64.3)	1096 (63.1)	
Moderate	1536 (28.8)	1052 (28.5)	486 (28.0)	
Severe	252 (4.7)	160 (4.3)	92 (5.3)	
Very severe	86 (1.6)	52 (1.4)	34 (2.0)	
At present[c]				1
Mild	1615 (68.6)	1066 (71.2)	549 (64.2)	
Moderate	541 (23.0)	331 (22.1)	210 (24.6)	
Severe	116 (4.9)	57 (3.8)	59 (6.9)	
Very severe	51 (2.2)	30 (2.0)	21 (2.5)	
VAS score, range 0–10				
At worst (ever)[b]				
Median (IQR)	4.9 (4.3)	5.0 (4.4)	3.9 (4.1)	**<0.001**
Mean (SD)	4.8 (2.5)	5.0 (2.5)	4.5 (2.5)	**<0.001**
Averagely (past year)[b]				
Median (IQR)	2.7 (2.8)	2.7 (2.9)	2.6 (2.6)	**0.005**
Mean (SD)	3.3 (2.0)	3.3 (2.0)	3.2 (2.0)	**0.022**
At present[c]				
Median (IQR)	2.5 (2.5)	2.5 (2.4)	2.5 (2.6)	0.764
Mean (SD)	3.1 (2.0)	3.1 (2.0)	3.1 (2.1)	0.821

TABLE 1 (Continued)

	Total population ($n = 40\,908$)	Females ($n = 23\,289$)	Males ($n = 17\,619$)	p-Value
HRQoL impairment, n (%)[c,d]				**<0.001**
None	182 (8.4)	88 (6.3)	94 (12.1)	**<0.05**
Slight	1227 (56.4)	728 (52.1)	499 (64.1)	**<0.05**
Moderate	556 (25.6)	422 (30.2)	134 (17.2)	**<0.05**
Strong	180 (8.3)	138 (9.9)	42 (5.4)	**<0.05**
Very strong	31 (1.4)	21 (1.5)	10 (1.3)	ns

Note: Overall differences between proportions were calculated by use of Chi square tests. Pairwise Z-tests with the outcome of significance (or not) at the $p < 0.05$ level were used for post-hoc comparisons. All endpoints were calculated excluding missing answers. Data on missing answers are found in Appendix S1. Bold values denote significance at the $p < 0.05$ level.

Abbreviations: CHE, chronic hand eczema; CI, confidence interval; HE, hand eczema; HRQoL, health related quality of life; IQR, interquartile range; ns, not significant; VAS, visual analogue scale.

[a]Lifetime prevalence of a physician diagnosis.

[b]Calculated as n/n individuals reporting a 1-year prevalence of HE.

[c]Calculated as n/n individuals reporting a point prevalence of HE.

[d]HRQoL was assessed by the Quality of life in Hand Eczema Questionnaire (QOLHEQ).

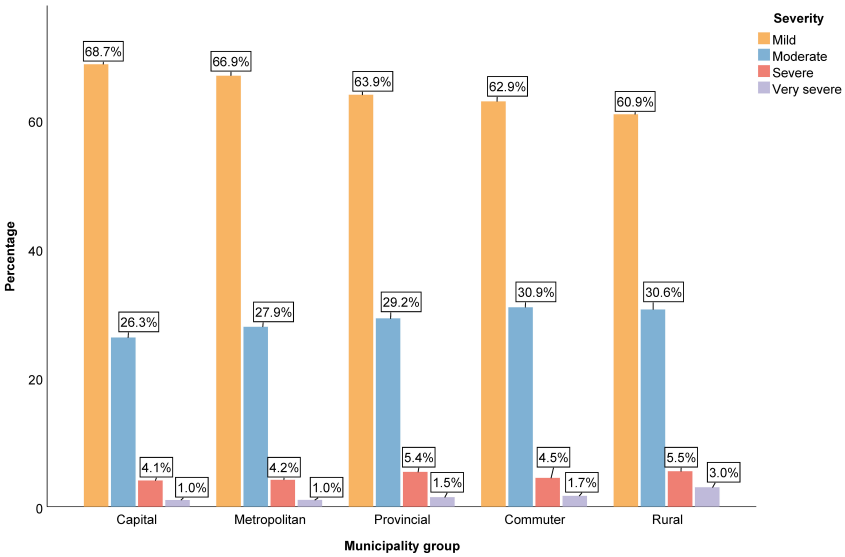

FIGURE 1 Self-reported severity of hand eczema (averagely the past year) as assessed by the photographic guide stratified by municipality group. Individuals reporting a 1-year prevalence of hand eczema ($n = 5345$) were included in analysis, missing answers $n = 79$.

[1.32–1.60]) and sick leave for more than 7 days the last year (aOR 1.28, 95% CI [1.28–1.38]) compared to individuals without. Lastly, we also examined self-reported annual household income (<600 000 DKK as compared to ≥600 000) in individuals with HE as compared to those without. No significant associations between annual household income and HE were found (Table 3).

3.2 | HRQoL in individuals with HE

The QOLHEQ was completed by 92.5% (2176/2353) of individuals reporting a point prevalence of HE. Table 4 displays median QOLHEQ scores, both overall and for each domain, stratified by demographic characteristics. Median (IQR) QOLHEQ scores were 31 (27) (total), 11.0 (7) (symptoms), 7.0 (9) (emotions), 3.0 (7) (functioning) and 10.0 (7) (treatment and prevention) for all individuals with current HE. This corresponds to a slight HRQoL impairment both overall and for the emotions and functioning domains, and a moderate impairment of the symptoms and treatment and prevention domains. Females had significantly higher scores than males across all domains and younger age (18–34 years) was associated with decreased HRQoL in all domains except for the treatment and prevention domain. A significant difference between QOLHEQ scores according to municipality group was found for the symptoms domain. Post-hoc tests revealed significantly higher scores for the rural population compared to the capital ($p = 0.003$), whereas no difference was found between any other municipality groups (Table 4). The corresponding analyses for mean QOLHEQ scores are shown in Table S2.

3.3 | Factors associated with moderate to very strong HRQoL impairment

We further examined factors associated with moderate to very strong HRQoL impairment as compared to no to slight impairment

TABLE 2 Self-reported overall health, sick leave and medical attention seeking behaviour in individuals with and without hand eczema in the general population.

	Hand eczema (last year)	No hand eczema (last year)	*p*-Value
Overall health rating, n/ntotal (%) 'How do you think your health is, all in all?'			**<0.001**[a]
Excellent	472/4844 (9.7)	4159/34236 (12.1)	**<0.05**
Very good	1771/4844 (36.6)	13.238/34236 (38.7)	**<0.05**
Good	1789/4844 (36.9)	12.655/34236 (37.0)	ns
Less good	674/4844 (13.9)	35.52/34236 (10.4)	**<0.05**
Poor	138/4844 (2.8)	632/34236 (1.6)	**<0.05**
Sick leave for any reason (last year), *n*/*n* total (%)[b]			
Yes	1251/4553 (27.5)	6613/32038 (20.6)	**<0.001**
Weeks of sick leave (last year)			
Median (IQR)	3.0 (7.7)	3.0 (7.7)	0.197
Mean (SD)	9.8 (14.8)	9.6 (14.9)	0.617
Number of GP consultations for any reason (last year)			
Median (IQR)	2.0 (3.0)	2.0 (2.0)	**<0.001**
Mean (SD) nHE = 4834, nNoHE = 34 062	3.13 (3.8)	2.6 (3.2)	**<0.001**
Sleep NRS (range 0–10)[c]			
Median (IQR)	2.0 (5)	2.0 (5)	0.070
Mean (SD)	2.6 (2.7)	2.6 (2.7)	0.408
nHE = 4915, nNoHE = 34 717			
Pruritus NRS (range 0–10)[d]			
Median (IQR)	1.0 (3)	0.0 (1)	**<0.001**
Mean (SD)	2.1 (2.5)	1.0 (1.9)	**<0.001**
nHE = 4915, nNoHE = 34 653			

Note: All endpoints were calculated excluding missing answers. Data on missing answers are found in Appendix S1. Bold values denote significance at the $p < 0.05$ level.

Abbreviations: GP, general practitioner; HE, hand eczema; IQR, interquartile range; ns, not significant.

[a]Overall difference between proportions of 'overall health rating' was calculated by use of Chi square tests. Post-hoc pairwise Z-tests with the outcome of significance (or not) at the $p < 0.05$ level was then performed.

[b]Sick leave (any reason) for more than 1 week the past year.

[c]Numeric rating scale (NRS) of self-reported sleep quality the past 48 h where 0 indicates no difficulty in sleeping and 10 indicates inability to sleep.

[d]NRS of self-reported itch the past 48 h where 0 indicates absence of itch and 10 intolerable itching.

TABLE 3 Associations between hand eczema and less good to poor overall health ratings and, sick leave for any reason the past year and annual household income.

	n	Crude OR (95% CI)	*n*	Model 1[a] OR (95% CI)	*n*	Model 2[b] OR (95% CI)
Less good to poor overall health rating						
Hand eczema the last year	4834	**1.45 (1.33–1.57)**	4834	**1.50 (1.38–1.64)**	3994	**1.45 (1.32–1.60)**
No hand eczema the last year	34 173	1	34 173	1	28 002	1
Sick leave >7 days for any reason the last year						
Hand eczema the last year	4553	**1.46 (1.36–1.56)**	4548	**1.28 (1.18–1.37)**	3793	**1.28 (1.18–1.38)**
No hand eczema the last year	32 038	1	31 983	1	26 471	1
Annual household income <600 000 DKK (<80.567 EUR)						
Hand eczema the last year	4013	1.02 (0.95–1.09)	4006	0.97 (0.90–1.04)	4002	0.99 (0.92–1.06)
No hand eczema the last year	28 184	1	28 131	1	28 053	1

Note: Binary logistic regression analyses, presented as odds ratios (ORs) with 95% confidence intervals (CIs), with the outcomes less good to poor compared with good to excellent self-reported overall health rating, sick leave (any reason) for more than 7 days the past year as compared to no sick leave for more than 7 days the past year and annual household income <600 000 DKK as compared to ≥600 000 DKK. Bold values mark significance at the $p < 0.05$ level. Data on missing answers are found in Appendix S1. 5852 individuals reported that they did not wish to disclose their household income and were excluded from model 2 analyses and all analyses on annual household income.

[a]Ajusted for age, sex and atopic dermatitis.

[b]Adjusted for age, sex atopic dermatitis, annual household income, daily smoking and municipality group.

TABLE 4 Quality of Life in Hand Eczema Questionnaire (QOLHEQ) scores of individuals in the general population with self-reported current hand eczema.

	Total, median (IQR) (range 0–117)	Symptoms, median (IQR) (range 0–27)	Emotions, median (IQR) (range 0–31)	Functioning, median (IQR) (range 0–32)	Treatment and prevention, median (IQR) (range 0–27)
Point prevalence of HE					
All, $n = 2176$	31.0 (27)	11.0 (7)	7.0 (9)	3.0 (7)	10.0 (7)
Sex					
Females, $n = 1397$	35.0 (29)	12.0 (7)	8.0 (9)	4.0 (8)	10.0 (8)
Males, $n = 779$	26.0 (23)	10.0 (6)	6.0 (8)	2.0 (7)	8.0 (8)
p-Value	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**
Age group					
18–34 years, $n = 565$	36.0 (27)	12.0 (7)	9.0 (10)	4.0 (7)	10.0 (7)
35–54 years, $n = 778$	30.0 (28)	11.0 (8)	7.0 (9)	3.0 (8)	9.0 (8)
≥55 years, $n = 833$	31.0 (26)	11.0 (7)	6.0 (8)	3.0 (8)	10.0 (8)
p-Value[a]	**<0.001**	**0.002**	**<0.001**	**0.005**	0.41
Municipality					
Capital, $n = 570$	32.0 (26)	11.0 (7)	7.0 (8)	4.0 (7)	9.0 (7)
Metropolitan, $n = 305$	30.0 (28)	11.0 (6)	7.0 (9)	3.0 (6)	9.0 (8)
Provincial, $n = 489$	33.0 (30)	11.0 (7)	7.0 (9)	3.5 (8)	10.0 (9)
Commuter, $n = 393$	32.0 (26)	11.0 (6)	7.0 (9)	3.0 (8)	10.0 (7)
Rural, $n = 419$	33.0 (29)	12.0 (7)	7.0 (9)	3.0 (8)	10.0 (8)
p-Value[b]	0.583	**0.038**	0.6	0.763	0.717

Note: Differences between group medians were calculated by use of Kruskal–Wallis (>2 groups) and Mann Whitney U (2 groups) tests. Bold values denote significance at the $p < 0.05$ level.

Abbreviations: HE, hand eczema; IQR, interquartile range.

[a]Post-hoc analyses age group (years): Total score: 18–34 versus 35–54, $p < 0.001$, 18–34 versus ≥55, $p < 0.001$. Symptoms: 18–34 versus 35–54, $p = 0.003$; 18–34 versus ≥55, $p = 0.001$. Emotions: 18–34 versus 35–54, $p < 0.001$; 18–34 versus ≥55, $p < 0.001$. Functions: 18–34 versus 35–54, $p = 0.011$; 18–34 versus ≥55, $p = 0.002$.

[b]Post-hoc analyses Municipality: Symptoms: Rural versus Capital, $p = 0.003$. No significant difference between the remainder of groups.

(total QOLHEQ score ≥ 40 vs. <40, respectively) in individuals with current HE, Table 5. In the univariate analysis, factors significantly associated with moderate-very strong impairment included female sex, atopic dermatitis, duration of HE >3 months, ≥2 eruptions, daily smoking, contact allergy, moderate-very severe HE, HE being notified as occupational and annual household income <600 000 DKK. A decreased likelihood was associated with older age-groups as compared to individuals <35 years. All these factors remained significantly associated with moderate-very strong HRQoL impairment after adjusting for age, sex and atopic dermatitis (model 2), with severe-very severe HE showing the strongest association (aOR 10.08, 95% CI [6.69–15.17]). After additionally adjusting for severity of HE (model 3), the significant association between lower annual household income and HRQoL impairment disappeared, whereas previously significant associations remained. In the fully controlled model, the highest aORs were found for HE being notified as occupational (3.10, 95% CI [2.18–4.39]), duration of HE >3 months (3.00, 95% CI [2.33–3.80]), and female sex (2.76, 95% CI [2.20–3.47]). Factors that were not significantly associated with HRQoL impairment included municipality group and HE being acknowledged as occupational (of notified cases).

4 | DISCUSSION

This nationwide, general population study demonstrates that HE is highly prevalent, bearing a considerable burden on society and significantly affecting the lives of impacted individuals.

We found estimates of total point, 1-year, and lifetime prevalences of HE to be 5.8%, 13.3% and 24.4% respectively, all with higher estimates among females than males. Although a nationwide study on HE prevalence in adults has not previously been performed in Denmark, earlier reports from smaller study populations centred mostly around Copenhagen are comparable.[11,31–35] Around one third of individuals with HE suffered from moderate-very severe disease which is in line with previous reports.[11,36]

We found a high 1-year CHE prevalence (11%, 82.6% of those with HE the last year), based on the definition of HE lasting over 3 months or recurring twice or more within a year. This was primarily driven by individuals reporting multiple eruptions rather than durations exceeding 3 months. The prevalence of CHE by this definition has so far only been reported in one Dutch study,[36] where 63.9% reporting a 1-year prevalence of HE had CHE. This difference could be explained by a general difference in CHE prevalence or by study

TABLE 5 Demographic and self-reported characteristics associated with moderate to very strong HRQoL impairment among individuals with self-reported current hand eczema in the general population.

	Crude OR (95% CI)	Model 1[a] OR (95% CI)	Model 2[b] OR (95% CI)
Age group, years, $n = 2176$			
<35, $n = 565$	1	1	1
35–54, $n = 778$	**0.74 (0.60–0.93)**	**0.76 (0.60–0.96)**	**0.73 (0.57–0.94)**
≥55, $n = 833$	**0.66 (0.53–0.83)**	0.80 (0.63–1.02)	**0.70 (0.54–0.91)**
Sex, $n = 2176$			
Females, $n = 1397$	**2.27 (1.86–2.76)**	**2.22 (1.81–2.73)**	**2.76 (2.20–3.47)**
Males, $n = 779$	1	1	1
Atopic dermatitis[c], $n = 2059$			
Yes, $n = 726$	**1.67 (1.38–2.03)**	**1.42 (1.16–1.75)**	**1.56 (1.26–1.95)**
No, $n = 1333$	1	1	1
Duration of HE in the last year, $n = 2157$			
>3 months, $n = 1496$	**3.24 (2.60–4.04)**	**3.55 (2.80–4.91)**	**3.00 (2.33–3.80)**
≤3 months, $n = 661$	1	1	1
Number HE eruptions in the last year, $n = 2022$			
≥2, $n = 1803$	**2.14 (1.53–3.00)**	**2.00 (1.37–2.78)**	**1.83 (1.15–2.91)**
<2, $n = 219$	1	1	1
Smoking (daily), $n = 2021$			
Yes, $n = 539$	**1.62 (1.27–2.08)**	**1.71 (1.33–2.20)**	**1.45 (1.10–1.91)**
No, $n = 1714$	1	1	1
Contact allergy (of $n = 822$ patch tested individuals)			
Yes, $n = 539$	**1.44 (1.08–1.93)**	**1.45 (1.07–1.96)**	**1.68 (1.21–2.33)**
No, $n = 283$	1	1	1
Severity of HE at present[d], $n = 2163$			
Severe-very severe, $n = 148$	**6.78 (4.67–9.85)**	**10.08 (6.69–15.17)**	-
Moderate, $n = 500$	**2.99 (2.42–3.68)**	**3.48 (2.77–4.37)**	-
Mild, $n = 1515$	1	1	-
HE notified as occupational, $n = 2144$			
Yes, $n = 184$	**3.83 (2.79–5.26)**	**3.81 (2.73–5.32)**	**3.10 (2.18–4.39)**
No, $n = 1960$	1	1	1
HE acknowledged as occupational (of $n = 182$ notified cases)			
Yes, $n = 133$	1.10 (0.56–2.17)	1.03 (0.51–2.11)	0.96 (0.45–2.06)
No, $n = 49$	1	1	1
Annual household income, $n = 1688$			
<600 000 DKK (<80.567 EUR), $n = 921$	**1.37 (1.12–1.68)**	**1.26 (1.02–1.57)**	1.23 (0.98–1.55)
≥600 000 DKK (≥80.567 EUR), $n = 767$	1	1	1
Municipality, $n = 2176$			
Capital, $n = 570$	1	1	1
Metropolitan, $n = 305$	0.90 (0.67–1.20)	0.83 (0.60–1.13)	0.75 (0.54–1.05)
Provincial, $n = 489$	1.12 (0.87–1.43)	1.13 (0.87–1.48)	1.07 (0.81–1.42)
Commuter, $n = 393$	0.85 (0.64–1.11)	0.94 (0.71–1.26)	0.83 (0.61–1.13)
Rural, $n = 419$	1.11 (0.86–1.44)	1.12 (0.90–1.58)	1.05 (0.78–1.41)

Note: Univariate and multivariable binary logistic regression analyses with the outcome odds ratio (OR) with 95% confidence intervals (CIs). Individuals reporting a point prevalence of HE with total quality of life in hand eczema questionnaire (QOLHEQ) scores ≥40 (moderate-very strong health related quality of life (HRQoL) impairment) were compared to those with scores <40 (minimal-slight HRQoL impairment). Bold values denote significance at the $P < 0.05$ level. Data on missing answers are found in Appendix S1.

[a]Model 1: Adjusted for age, sex, and atopic dermatitis.

[b]Model 2: Adjusted for age, sex, atopic dermatitis and average severity of HE in the past year.

[c]Lifetime prevalence of physician diagnosed atopic dermatitis.

[d]Assessed by the photographic guide.

heterogeneity. CHE, a focus for therapeutic interventions and a criterion for inclusion in clinical HE studies, require accurate epidemiological data for resource allocation.[37,38] However, CHE assessment lacks standardisation, in particular, the definition of an eruption of HE, it's minimum duration and symptom free period between eruptions, remain unclear. We recommend including standardised CHE questions in future HE guidelines[39] and NOSQ-2002 revisions.[22]

Individuals with HE reported poorer health outcomes compared to individuals without, including lower overall health ratings, and more sick leave for any reason the past year. Our results are in line with those of Moberg et al.[13] and Bingefors et al.[14] who reported lower HRQoL ratings in individuals with HE compared to those without, although they employed different instruments. We used a generic single question evaluation of responders' overall health perception ('How do you think your health is, all in all?'). This is a well-validated and widely used method in public health surveys and has been linked to various health outcomes including increased mortality.[40,41] However, self-reported health is a subjective measure that may be influenced by factors such as culture and education, which were not taken into consideration in our comparisons.[40] According to a recent review on the economic burden of CHE, studies have reported high prevalences of sick leave because of HE.[42] To our knowledge, no studies have yet compared self-reported sick leave prevalences between unselected individuals with HE and those without. Our results indicate an increased healthcare utilisation and economic burden of the disease at the population level.

The HRQoL in all individuals with current HE as assessed by the QOLHEQ was slightly impaired overall with moderate impairment of the symptoms and treatment and prevention domains.

Not surprisingly, the factor most strongly associated with moderate to very strong HRQoL impairment was self-reported severe HE and when further adjusting for severity of HE; HE duration, HE being notified as occupational, and female sex showed the strongest associations with HRQoL impairment. In addition, multiple eruptions of HE, young age, atopic dermatitis, smoking and contact allergy were also associated with decreased HRQoL. These insights could guide targeted interventions, particularly for severe, chronic and occupational HE.

Individuals with current HE in rural areas reported significantly higher symptom scores (dryness, fissuring, etc.) than those from capital areas. However, no significant differences in overall QOLHEQ scores or HRQoL impairment risk were observed between municipality groups. The higher symptom impairment in the rural population aligns with more rural residents reporting moderate to severe HE. Yet, this did not translate to overall greater HRQoL impairment. An explanation for this finding could be a modifying effect of area of residence on the relationship between HE disease severity and HRQoL as proposed by Nørreslet et al.[9]

The QOLHEQ has not previously been studied in a general population setting, and our results thus cannot be compared to similar populations but can serve as a future reference for studies to come. Our large case population (2353 with current HE) and the 92% QOLHEQ completion rate enabled meaningful group comparisons. Self-reported HE point prevalence, previously validated with moderate sensitivity (70.3%–73.0%) and high specificity (99%–99.8%),[24,25] aligns with clinically determined prevalence in a recent meta-analysis (3.5% vs. 4.0%).[1] Thus, despite a risk of potential misclassification, self-reported current HE is a reliable measure of true HE prevalence.

Most prior general population HE studies have smaller samples and mainly characterise individuals reporting a 1-year HE prevalence, reflecting HE's seasonal fluctuations.[1] However, the QOLHEQ is validated only for current HE cases. For broader application of QOLHEQ, a modified version addressing average annual HE impact, rather than the past week, might be beneficial.

The response rate of 42% is comparable to similar more recent studies in Denmark and neighbouring countries.[43,44] Importantly, our sample size of 100 000 individuals was calculated based on an estimated response rate of 35%. Non-response analysis considered sex, age, and municipality group, but lacked information on HE prevalence in non-responders, potentially introducing selection bias. The study was conducted in early summer 2021 after the third COVID-19 wave. At this time, Danish society had almost completely reopened (excluding night clubs), but it remains possible that our prevalence results were inflated by increased hand hygiene practices.

5 | CONCLUSION

In conclusion, HE is highly prevalent in the Danish general population with the majority suffering from CHE and one third from moderate-very severe disease. Individuals with HE report poorer overall health ratings and higher prevalences of sick leave than those without. Factors that show the strongest association with impaired HRQoL among those with HE include female sex, severe, chronic and occupational HE.

Our findings indicate unmet treatment needs and the necessity for providing targeted support for high-risk individuals.

AUTHOR CONTRIBUTIONS

Anna Sophie Quaade: Conceptualization; methodology; visualization; writing – review and editing; writing – original draft; funding acquisition; investigation; formal analysis; project administration; data curation. **Farzad Alinaghi:** Writing – review and editing; formal analysis; data curation; investigation; methodology. **Jojo Biel-Nielsen Dietz:** Writing – review and editing; data curation; formal analysis. **Christina Yndal Erichsen:** Writing – review and editing; formal analysis; data curation. **Jeanne Duus Johansen:** Conceptualization; funding acquisition; writing – review and editing; supervision; methodology.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The study was approved by the Danish Data Protection Agency (P-2020-558) and the Danish Health Data Authority (FSEID-00005217).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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