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REVIEW ARTICLE

Economic Burden of Chronic Hand Eczema: A Review

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Abstract
There has been no extensive synthesis of studies evaluating the cost of chronic hand eczema (CHE). This review evaluated the societal costs, healthcare resource utilisation, missed work time and job loss due to CHE. MEDLINE and 16 other databases and websites were searched in October 2020 for studies meeting prespecified inclusion criteria. Studies conducted in Europe, Australia, New Zealand or the Americas were included. Two reviewers independently assessed titles and abstracts, and full-text papers published in English between 2000 and 2020, for relevance. Data extraction was carried out by one reviewer and checked by a second reviewer. All data were based on costs between 2001 and 2013 but have been inflated to 2020 prices and converted to US dollars and Euros. A total of 30 studies (reported in 33 publications) were included in the synthesis. Mean total societal costs per year per patient ranged from $2549 (€1813) to $10,883 (€7738). Pharmacological therapy was, on average, $28.34 (€20.15) per month in Italy and $36.49 (€25.94) per month for emollients in Switzerland. Yearly treatment costs were $599.05 (€425.92) for drugs, including topical corticosteroids, topical calcineurin inhibitors, other topical treatments and oral treatments, and $178.40 for emollients, in Germany. CHE was associated with hospitalisation costs ranging from $81.86 (€58.20) per patient per month (US) to $105.04 (€74.68) per patient per month (Italy) and $639.59 (€454.75) per year (Germany). Up to 57% of patients took sick leave and up to 25% reported job loss/job change due to CHE. This review confirms the significant cost burden of CHE. Given the paucity of studies estimating the monetary costs of absenteeism, presenteeism and job loss associated with CHE, current mean societal costs are likely underestimated. Uncontrolled disease may also lead to increased costs to patients and society.

1 Introduction

Hand eczema (HE), or hand dermatitis, is an inflammatory skin condition that may be chronic in some patients, and its socioeconomic burden is considerable [1]. The severity of HE varies among patients and can lead to significant limitations in earning potential and absenteeism [2–4]. While HE may occur following excessive or prolonged exposure to irritants, allergens, or proteins, individuals with a history of atopic dermatitis (AD) are at increased risk for developing HE [5].

Key Points

The direct and indirect economic costs of chronic hand eczema (CHE) are comparable with other dermatological conditions.

Ongoing development of new therapies means the direct economic burden of CHE may be higher than estimated in this literature review, since some of the included studies are more than 10 years old.

There are few studies of the economic cost burden of absenteeism, presenteeism and job change in CHE.

The societal costs of CHE are likely underestimated.

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HE can range in severity from mild to severe, and the clinical course from acute to chronic [6]. The European Society of Contact Dermatitis Guideline Development Group defines chronic HE (CHE) as the persistence of HE for more than 3 months, or when the condition reoccurs at least twice within 12 months [6]. Management involves different interventions (avoidance, emollients, topical corticosteroids [TCS], phototherapy, oral immunosuppressants, oral retinoids [alitretinoin], gloves) to control the disease and treat the flare-ups [6].

Understanding costs is important to facilitate healthcare resource allocation decisions and to know the extent of cost burdens for patients and payers. CHE impacts patients' ability to function and/or work, therefore it is important to characterize its societal economic burden. The costs of HE have been previously reported by Politiek [1] in a systematic literature review of cost-of-illness studies, but that review did not focus on CHE. This review summarizes the current evidence on the costs of CHE with regard to its costs to society, in terms of economic costs (direct medical costs, direct non-medical costs and indirect costs), healthcare resource utilisation, missed work time and job losses (Table 1).

Table 1 Components of the burden of chronic hand eczema

Economic costs—societal costs
Direct costs
Medical costs
Prescribed treatment costs
Hospital costs
Other costs
Non-medical costs
Non-prescribed treatment costs
Indirect costs
Lost productivity costs
Out-of-pocket costs
Non-economic healthcare resource utilisation costs
Hospitalisations
Consultations
Laboratory evaluation and treatments
Work impairment and missed work time
Absenteeism and presenteeism
Job change

2 Methods of the Review

This review was conducted following Cochrane and Centre for Reviews and Dissemination (CRD) guidance [7, 8] and followed a protocol developed a priori (PROSPERO registration number: CRD42020215195). The protocol provides full details of the review methods employed.

2.1 Eligibility Criteria

Studies of patients of all ages with CHE were eligible for inclusion. Studies in which the definition of 'chronic' was not reported were eligible if the duration of CHE was reported to be longer than 3 months or where patients visited a dermatologist or a hospital. Outcomes of interest included societal costs in general (cost of illness), specific direct medical costs (healthcare related), direct non-medical costs (non-medical economic costs related to the condition) and indirect costs (morbidity, e.g. work productivity), and costs associated with healthcare resource utilisation (resource use, e.g. staff time).

Only studies published in English since 2000 and conducted in Europe, Australia, New Zealand or the Americas were included.

2.2 Searches

MEDLINE, the NHS Economic Evaluations Database (EED), the Cochrane Central Register of Controlled Trials, the Health Technology Assessment (HTA) database, EMBASE, and a range of websites were searched in July 2018 and the searches were updated in October 2020 (Online Resource 1).

2.3 Screening, Data Extraction and Quality Assessment

Results of searches were downloaded in a tagged format and loaded into bibliographic software (EndNote) and deduplicated against one another. Results from resources that did not allow export in a format compatible with EndNote were saved in Microsoft Word or Excel (Microsoft Corporation, Redmond, WA, USA) documents as appropriate and manually deduplicated. A single researcher removed obviously irrelevant records. Two reviewers then independently assessed the remaining titles and abstracts for eligibility followed by an assessment of the full-text papers. Disagreements at each stage were resolved by discussion or the involvement of a third reviewer. One reviewer extracted data, and quality assessed studies (Online Resource 2). A second reviewer checked the data and the study quality. A narrative synthesis of evidence was performed to summarize the findings from the included primary studies.

3 Results

3.1 Included Studies

Thirty studies (33 papers) were eligible (Fig. 1).

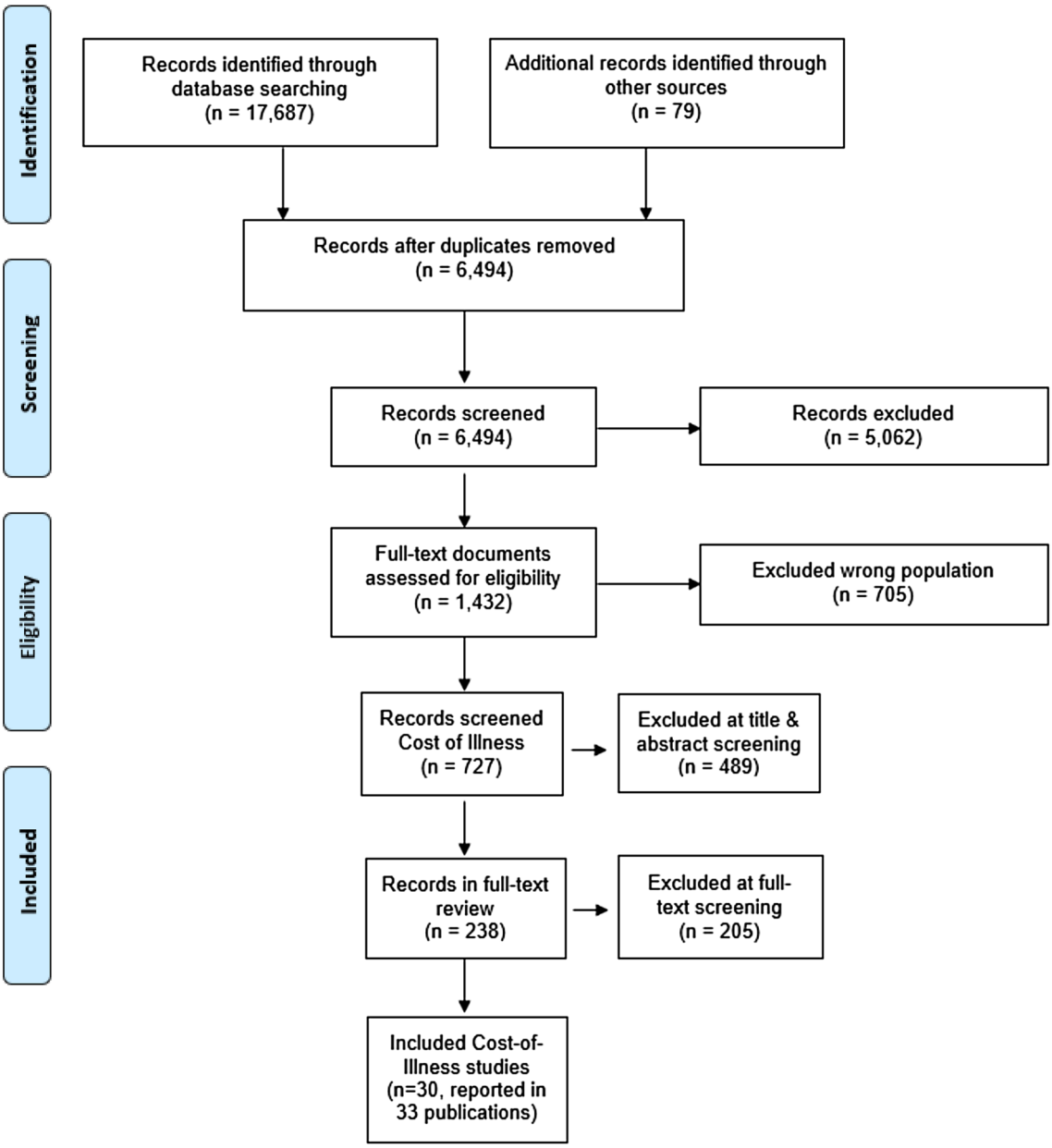

Fig. 1 PRISMA diagram of record selection process. *PRISMA* preferred reporting items for systematic reviews and meta-analyses

3.2 Cost Studies

Costs were converted to 2020 prices using country-specific price indices [9] and converted to US dollars and Euros using Purchasing Power Parities [10].

3.2.1 Direct Costs

Six studies reported direct costs [11–16] for five countries (Tables 2, 3 and 4). In the studies reporting costs of specific treatments, the least costly treatment was emollients ($14.87 per patient per month [pppm] in Germany) and the costliest was alitretinoin (30 mg capsule, $702.44 pppm in Switzerland). Costs were also reported for TCS, ciclosporin, psoralen plus ultraviolet A (PUVA) and azathioprine for various countries, as well as for supportive care and remission (details are reported in Table 2). Overall mean pppm costs were reported for pharmacological therapy in two studies ($28.34 in Italy and $165.02 in the US) and non-pharmacological therapy (e.g. emollients, galenic formulations and ultraviolet irradiation) [$29.21 in Italy].

Table 2 Treatment costs

References	Country	Cost	US$ (2020)	€ (2020)
Cortesi et al. [15]	Italy	Mean per patient-month cost of pharmacological therapy (minimum–maximum)	$28.34 ($0–$144.92)	€20.15 (€0–€103.04)
		Mean per patient-month cost of non-pharmacological therapy, e.g. emollients, galenic formulations, and ultraviolet irradiation (minimum–maximum)	$29.21 ($0–$161.71)	€20.77 (€0–€114.98)
Fowler et al. [16]	USA	Per patient monthly costs (mean ± SE)		
		Prescription drugs	$165.02 (±$8.47)	€117.33 (±€6.02)
		Outpatient services	$255.71 (±$20.02)	€181.81 (±€14.23)
NICE TA177 [12]	UK	Acquisition cost (per cycle of therapy)		
		Alitretinoin	$716.17	€509.20
		Ciclosporin	$307.16	€218.39
		PUVA	$960.14	€682.66
		Azathioprine	$31.34	€22.28
		Refractory costs for alitretinoin, ciclosporin, PUVA, azathioprine (per 4 weeks)	$20.60	€14.65
		Supportive costs (per 4 weeks)		
		Alitretinoin	$101.92	€72.47
		Ciclosporin	$99.88	€71.01
		PUVA	$91.50	€65.06
		Azathioprine	$95.22	€67.70
		Remission costs (4 weeks)		
		Alitretinoin	$9.70	€6.90
		Ciclosporin	$20.60	€14.65
		PUVA	$20.60	€14.65
		Azathioprine	$20.60	€14.65
Blank et al. [11]	Switzerland	Mean cost per month		
		Alitretinoin (30 mg capsules)	$702.44	€499.43
		Emollients	$36.49	€25.94
		Average cost per month		
		Patients taking alitretinoin (30 mg)	$797.72	€567.18
		Patients taking placebo	$75.01	€53.33
		Patients clear or almost clear maintenance	$46.63	€33.15
		Severe non-responders	$191.57	€136.21
Augustin et al. [14]	Germany	Yearly treatment costs		
		Topical corticosteroids	$599.05	€425.92
		Emollients	$178.40	€126.84

PUVA psoralen-ultraviolet A therapy, *SE* standard error

Table 3 Hospital costs

References	Country	Cost	US$ (2020)	€ (2020)
Cortesi et al. [15]	Italy	Mean per patient-month cost of hospitalisation (minimum–maximum)	$105.04 ($0–$1425.97)	€74.68 (€0–€1013.86)
Fowler et al. [16]	US	Mean per patient-month cost of inpatient services (±SE)	$81.86 (±$12.18)	€58.20 (±€8.66)
Augustin et al. [14]	Germany	Yearly inpatient cost	$639.59	€454.75

Three studies reporting hospital costs [14–16] varied in terms of the costs included and how they were estimated. Mean hospitalisation pppm costs ranged from $53.30 in Germany to $105.04 in Italy (Table 3). Four studies reported on other types of costs associated with CHE [11, 13–15], which included costs for tests and pregnancy testing as well as oral contraceptives (Table 4).

Table 4 Other direct costs

References	Country	Cost	US$ (2020)	€ (2020)
Cortesi et al. [15]	Italy	Mean (minimum–maximum) per patient-month cost		
		Medical consultation	$63.96 ($0–$627.03)	€45.48 (€0–€445.82)
		Diagnostic examinations	$30.51 ($0–$240.03)	€21.69 (€0–€170.66)
		Other products (or instruments, such as gloves or gauze bandages, vacuum cleaners, and cosmetic)	$42.37 ($0–$1460.22)	€30.13 (€0–€1038.22)
Blank et al. [11]	Switzerland	Mean cost per month		
		Pregnancy testing + oral contraceptives	$27.37	€19.46
		Dermatologist visits	$39.53	€28.11
		Lipid monitoring tests	$16.22	€11.53
		PUVA/311 nm (topical/oral)	$174.34	€123.96
		Topical corticosteroids total (assumption was that 25% of patients were treated with Class I–III and 75% were treated with Class IV topical corticosteroids)	$29.40	€20.90
		Topical corticosteroids Class I–III	$42.57	€30.27
		Topical corticosteroids Class IV	$25.34	€18.02
van Gils et al. [13]	The Netherlands	Cost per consultation		
		Dermatologist	$117.80	€83.76
		General practitioner	$45.82	€32.58
		Clinical occupational physician	$37.21	€26.46
		Specialized nurse	$97.44	€69.28
		Occupational physician	$37.21	€26.46
		Homeopath	$99.01	€70.40
		Internist	$117.80	€83.76
		Psychologist	$137.49	€97.76
		Light therapy	$77.03	€54.77
		Insurance physician	$70.45	€50.09
		Acupuncture	$73.34	€52.14
Augustin et al. [14]	Germany	Yearly costs		
		Outpatient care	$172.32	€122.52
		Diagnostics	$397.34	€282.51
		UV therapy	$457.14	€325.03

PUVA psoralen-ultraviolet A therapy, *UV* ultraviolet

3.2.2 Indirect Costs

Indirect costs (two studies [14, 15]) reported lost productivity or out-of-pocket costs. Lost productivity costs for CHE ranged from $623.77 per year in Germany ($n = 223$; CHE refractory to potent TCS) [14] to $285.30 pppm in Italy ($n = 104$; severe CHE) [15]. Out-of-pocket costs for CHE were reported in two studies ($335.98 per year in Germany [14] and $63.40 pppm in Italy [15]).

3.2.3 Total Costs

Five studies [13–17] (four countries) reported the total societal cost of CHE (total direct plus indirect costs). The total costs per year per patient with CHE ranged between $2549 and $10,883, based on studies in the US and Europe. The highest estimate was in patients with occupation-related CHE. See Table 5 for the total costs reported by each study. These studies are difficult to synthesise because of differences in national health care systems and patient management protocols.

3.3 Studies Reporting Resource Use

Fifteen studies reported resource use data [4, 11, 14, 15, 19, 21–25, 28–32].

Table 5 Cost of illness of chronic hand eczema

References	Country	Cost	US$ (2020)	€ (2020)
Cortesi et al. [15]	Italy	Mean total costs per patient-month (minimum–maximum)	$652.66 ($53.51–$3595.59)	€464.04 (€38.05–€2556.46)
Fowler et al. [16]	USA	Total direct medical cost per month	$452.05 (SE $32.35)	€321.41 (SE €23.00)
Diepgen et al. [17]	Germany	Total yearly costs		
		SHI patients	$3440.26	€2446.02
		Direct medical costs	$2816.48	€2002.52
		Indirect costs	$623.77	€443.50
		OHI patients	$10,883.20	€7737.96
		Direct medical costs	$5349.57	€3803.54
		Indirect costs	$5532.17	€3933.37
		Non-working SHI patients	$2007.18	€1427.10
		Work-unaffected SHI patients	$2316.87	€1647.29
		Work-impaired SHI patients	$8142.67	€5789.44
		Direct costs	$5115.84	€3637.36
		Indirect costs	$3026.83	€2152.08
		Work disease OHI patients	$12,500.33	€8887.73
		Direct costs	$5349.57	€3803.54
		Indirect costs	$5532.17	€3933.37
Augustin [14]	Germany	Total yearly societal cost per patient	$3440.26	€2446.02
		Direct costs	$2816.48	€2002.52
		Indirect costs	$623.77	€443.50
van Gils [13]	The Netherlands	Mean (SD) cost per year per patient		
		Integrated care—total societal costs	$5838.46 (1290.34)	€4151.15 (917.43)
		Direct costs	$1546.79 (129.74)	€1099.77 (92.25)
		Indirect costs	$4291.67 (1247.77)	€3051.38 (887.16)
		Usual care—total societal costs	$2549.26 (694.33)	€1812.52 (493.67)
		Direct costs	$775.42 (76.02)	€551.32 (54.05)
		Indirect costs	$1773.84 (659.87)	€1261.20 (469.17)

OHI occupational health insurance, *SD* standard deviation, *SE* standard error, *SHI* statutory health insurance

3.3.1 Hospitalisations

Three studies reported hospitalisations [14, 15, 25]. In Italy ($n = 104$), patients spent a mean of 0.2 days (0.0–5.4) in hospital per month and a mean of 0.03 days (0.0–2.1) attending hospital per month [15]. In Germany, 32% (this was how the study described this datum, no further context was provided) of 1148 CHE patients received care as an inpatient [25] and inpatients ($n = 223$) spent 10.6 days (only data provided) in hospital per stay [14].

3.3.2 Consultations

Fourteen studies reported consultations for CHE [4, 11, 14, 15, 19, 21–24, 28–32] (Table 6). Data on primary care visits were reported in different ways. A Finnish study ($n = 1238$ across multiple trials) showed that primary care visit frequency depended on CHE subdiagnosis; approximately 33% visited a doctor more than five times due to their CHE in the past 12 months [24]. Dermatologist/specialist consultations ranged from 0.9 visits per month in Italy to 3.1 visits over a 4-week period in Germany.

3.3.3 Laboratory Evaluation and Treatments

Four studies reported laboratory evaluations and treatments for CHE [11, 14, 15, 23] (Table 7). Resource use data were reported for diagnostic tests, which ranged from 0.6 per month in Italy in severe CHE to 1.7 per 4 weeks in Germany in CHE. Emollient resource use ranged from 1.2 products per month in Italy in severe CHE to 1.3 products per 4 weeks in Germany in CHE. Use of TCS was reported to be 1.1 products per 4 weeks in Germany in CHE. Ultraviolet sessions ranged from 4 per month in Italy in severe CHE to 8.6 per 4 weeks in Germany in CHE. An Italian study reported the use of 1.1 galenic products (not defined) per month

Table 6 Consultations for chronic hand eczema

References	Country	Consultations
Thyssen et al. [24]	Finland	> 5 visits (1982–83) Hand eczema: 34.5% Allergic contact dermatitis: 34.9% Irritant dermatitis: 11.9%
Cortesi et al. [15]	Italy	Mean (minimum–maximum) number of specialist consultations (dermatologist, allergist, occupational physician, immunologist, police doctor) per patient-month: 0.9 (0.0–2.7)
Augustin et al. [14]	Germany	Outpatient care visits in the last 4 weeks: 3.1
Apfelbacher et al. [32]	Germany	After inclusion in the CARPE registry, trend of visits in the past 12 months To the dermatologist: decreased strongly To the general practitioner: decreased strongly
Blank et al. [11]	Switzerland	Dermatologist visits per month: 1
Malkonen et al. [30]	Finland	Consulted a doctor within the last 7 years: 48%
Herschel et al. [19]	Germany	Mean number of physician visits in the past 12 months: 4.0 (SD 5.0) No GP visits in past 12 months: 22% GP care: 21.4% Dermatologist care: 74.9%
Josefson et al. [28]	Sweden	GP visit: 50% ($n = 129$)
Dibenedetti et al. [21]	USA	Time frame in which patients sought medical attention after noticing symptoms of CHE ($n = 163$) Within 6 months: 26% 6 months to 1 year: 34% Type of physician consulted for the first time Primary care physician: 54% Dermatologist: 39%
Meding et al. [4]	Sweden	Visited a doctor ($n = 868$): 33%
Hald et al. [22]	Denmark	Self-reported duration of hand eczema symptoms within the past 12 months in relation to medical consultations ($n = 427$) Not seen by a medical doctor ($n = 138$, missing data $n = 1$) All the time: 3.6% More than half the time: 8.0% Half the time: 5.8% Less than half the time: 63.0% No symptoms: 19.6% Seen by a GP but not a dermatologist ($n = 102$) All the time: 9.8% More than half the time: 12.7% Half the time: 9.8% Less than half the time: 45.1% No symptoms: 22.5% Seen by a GP and a dermatologist ($n = 184$, missing data $n = 2$) All the time: 16.8% More than half the time: 11.4% Half the time: 14.7% Less than half the time: 42.9% No symptoms: 14.1%
Lerbaek et al. [29]	Denmark	($n = 188$) 1 GP visit: 25.3% 2–5 visits: 22.6% > 5 visits: 15.6% Total visits ($n = 186$): 63.4% Multivariate model to predict >1 medical consultation Significant predictors, AD vs. no AD: OR 3.0 (95% CI 1.4–6.4), $p = 0.006$
Petersen et al. [23]	Denmark	Patients who have experienced periods of hand eczema since 2007 ($n = 419$) GP visit: 47% Dermatologist visit: 40% 1 GP visit: 23% > 5 GP visits: 6% 1 dermatologist visit: 14% > 5 dermatologist visits: 13%

Table 6 (continued)

References	Country	Consultations
Steengaard et al. [31]	Denmark	($n = 144$) Visits to dermatologist, total: 35.4% Intervention: 44.0% Control: 26.1%, $p = 0.20$

AD atopic dermatitis, *CHE* chronic hand eczema, *CI* confidence interval, *GP* general practitioner, *OR* odds ratio, *SD* standard deviation

Table 7 Laboratory evaluations and treatments

References	Country	Tests and treatments
Blank et al. [11]	Switzerland	Cost items, per month (used in a cost-effectiveness model) Alitretinoin 30 mg capsules: 28 × 30 mg (one capsule per day) Emollients: 200 g Pregnancy testing + oral contraceptives: 1 test, 21 tablets Lipid monitoring tests: 1 test PUVA/311 nm (topical/oral): 20 cycles per 10 weeks in a 6-month period (3.33 cycles per month) Topical corticosteroids: 60 g
Augustin et al. [14]	Germany	Diagnostics tests in the last 4 weeks: 1.7 Emollient products in the last 4 weeks: 1.3 Topical corticosteroid products in the last 4 weeks: 1.1 UV therapy (including PUVA) sessions in the last 4 weeks: 8.6
Cortesi et al. [15]	Italy	Mean (minimum–maximum) tests and treatments per patient-month Number of diagnostic tests (patch test, prick test, RAST, PRIST, atopy patch test, skin biopsy, test for hives, and immunofluorescence): 0.6 (0.0–2.1) Number of UV: 4.0 (4.0–4.0) Number of emollients: 1.2 (0.5–5.4) Number of galenic products: 1.1 (0.5–2.1) Number of other therapies (e.g. detergents/soaps, antiseptics): 0.8 (0.5–2.1)
Petersen et al. [23]	Denmark	Emollient use: 59% of patients Topical corticosteroid use: 64% of patients Systemic therapy: 7% of patients Phototherapy: 6% of patients

PRIST paper radioimmunosorbent test, *PUVA* psoralen-ultraviolet A therapy, *RAST* radioallergosorbent test, *UV* ultraviolet

and 0.8 other therapies (detergents, soaps and antiseptics) per month in severe CHE. A definition of disease severity was not provided for these studies. One trial of alitretinoin in Germany ($n = 223$) reported that in a 4-week period, patients receiving routine care had a mean of 1.7 diagnostic tests (39% of patients), 1.3 emollient products (91%), 1.1 TCS products (84%) and 8.6 phototherapy sessions (27%) [14].

A hypothetical cost-effectiveness model of alitretinoin in Swiss CHE patients estimated the monthly number of tests and treatments [11]. The cost items included alitretinoin 30 mg (one capsule daily), emollients (200 g), pregnancy testing plus oral contraceptives (one test, 21 tablets), lipid monitoring tests (one test), topical/oral PUVA therapy/311 nm (3.33 cycles per month), and TCS (60 g).

3.3.4 Absenteeism and Presenteeism

Nineteen studies (20 publications) reported the proportion of patients taking sick leave (absenteeism) due to CHE ranged from 1 to 57% [4, 14, 16, 21–27, 29–32, 37–41]. The study period duration, disease severity, and sample sizes varied and these data are therefore difficult to interpret and compare (Table 8).

The study reporting sick leave due to CHE in 57% of patients ($n = 579$) was among patients with occupational HE [27]. There were no major differences between sick leave and different diagnoses of occupational HE, although those with combined diagnoses of occupational contact dermatitis (e.g. irritant and allergic) had a high proportion of prolonged sick leave (more than 5 weeks per year). Prolonged sick leave was reported in 19% of patients, with a higher proportion in food-related occupations (27.2%) compared

Table 8 Work impairment and missed work time

References	Country	Work impairment and missed work time
Agner et al. [18]	Europe	People with hand eczema and subdiagnoses of atopic eczema and allergic contact dermatitis were associated with increased frequency of sick leave: 0.122 ($p = 0.023$) and 0.128 ($p = 0.032$), respectively
Apfelbacher et al. [25]	Germany	Currently unable to work: 21.6% Sick leave in the past 12 months (all patients): 32.7%
Apfelbacher et al. [38]	Germany	Sick leave in past 12 months > 0–2 weeks: 48.6% > 2–6 weeks: 30.5% > 6 weeks: 20.9%
Apfelbacher et al. [32]	Germany	Changed or given up their job because of CHE: 5.4% Sick leave (in the past 12 months): 35.3% Currently unable to work (at baseline): 24.5%
Augustin et al. [14]	Germany	Sick leave in the last year: 33% Average number of days sick leave per year: 7.2 days
Cazzanniga et al. [20]	Germany and Switzerland	CHE in workers in food-handling jobs was strongly associated with the ability to work and sick leave In men, there was a strong association with long duration of hand eczema (> 6 years) and job loss or change
Diepgen et al. [17]	Germany	Patients in employment who had sick leave in the last 12 months: 42% Mean number of days of sick leave: 35 days
Diepgen et al. [39]	Germany	Sick leave due to hand eczema: 28.4% Sick leave for more than 5 consecutive weeks: 12.3%
Herschel et al. [19]	Germany	Unable to work: 24.7% Changed jobs due to disease: 12.6%
Thyssen et al. [24]	Finland	At least 7 days off sick: 6% Change in job due to hand eczema: 3% Receiving sickness pension because of the illness: 2%
Malkonen et al. [30]	Finland	Sick leave in the past 7 years because of hand eczema: 23% Sick leave was associated with age (45 years or older) at the time of diagnosis, but not with sex, diagnosis, atopy, occupation or specific work-related allergies Job loss (unemployment and retirement) due to occupational hand eczema: 25% of patients (most frequent among patients aged 45 years or older, in patients with allergic contact dermatitis, or in food-related occupations)
Fowler et al. [16]	USA	Mean percentage of work time missed: 4.08% (SE ± 11.03) Mean percentage of impairment while working: 26.86% (SE ± 31.39) Percentage of overall work impairment: 29.33% (SE ± 31.73)
Dibenedetti et al. [21]	USA	Missed work or school activities over the previous 3 months: 24% In patients who missed work or school over the previous 3 months: mean days missed: 4.4 (SD 3.3) Changed jobs or left job due to CHE: 4% Short-term disability due to CHE: 6% (3% had applied for workers' compensation)
Josefson et al. [28]	Sweden	Changed job due to hand eczema: 15.5% of women with hand eczema
Meding et al. [4]	Sweden	Median total sick leave time: 38 weeks (range 1–312) At least 7 days (since 1983): 6%
Agner [33]	Denmark	Within the past 5 years Changed profession or were no longer working: 51% Changed profession: 32.6% Outside the labour market: 18.8% (NB: this is not necessarily due to hand eczema) Participants who reported being 'clear' (with regard to hand eczema healing) Changed profession or left the labour market: OR 1.62 (95% CI 1.06–2.47) Stayed in the same profession: OR 2.85 (95% CI 1.83–4.24) [difference is significant] More participants who changed profession or left their profession reported improvement in their hand eczema compared with those who stayed in the same profession: OR 1.91 (95% CI 1.44–2.54) and 1.51 (95% CI 1.09–2.10), respectively Change of profession and being outside the labour market did not significantly influence the number of severe cases at 4- to 5-year follow-up: OR 0.75 (95% CI 0.37–1.55) and 1.61 (95% CI 0.83–3.12), respectively

Table 8 (continued)

References	Country	Work impairment and missed work time
Cvetkovski et al. [27]	Denmark	Sick leave due to occupational hand eczema in the past 12 months: 57% Job loss in the past 12 months: 22.9% More than 5 weeks per year of sick leave (prolonged sick leave): 19.9% Women had more prolonged sick leave than men in all age groups except the oldest group (50 + years) Prolonged sick leave Severe occupational hand eczema: 30% Either moderate or minimal occupational hand eczema: 17.6%
Cvetkovski et al. [46]	Denmark	Multivariate analysis predicting sick leave after 1-year follow-up for workers with occupational hand eczema Significant predictors: aged 40–49 years compared with aged 18–24 years (RR 5.28, 95% CI 1.4–20.7); severe symptoms compared with no/minimal symptoms (RR 5.29, 95% CI 1.6–17.7); previous long-term sick leave compared with no previous long-term sick leave (RR 5.20, 95% CI 2.0–13.6); low quality of life compared with high quality of life (RR 4.62, 95% CI 1.6–13.7) Non-significant predictors (*p*-values NR): sex, socioeconomic status, subdiagnosis, AD, duration of eczema, occupation, depression
Hald et al. [22]	Denmark	CHE (i.e. patients with symptoms about half the time or more, or continuous symptoms the preceding year) Sick leave within the past 12 months: 1% Mean duration of sick leave: 6 days
Lerbaek et al. [29]	Denmark	Changed jobs: 8.5% Sick leave < 1 week: 2.2% 1–2 weeks: 4.3% 3–5 weeks: 2.7% > 6 weeks: 3.2% Total patients reporting sick leave: 12.4% Multivariate predictors of sick leave ever Marginally significant predictors: AD yes vs. no: OR 2.9 (95% CI 1.0–8.1), $p = 0.05$); socioeconomic status (0.05) Non-significant predictors: sex ($p = 0.28$); zygosity of twins ($p = 0.84$); age of onset (0.54); positive patch test ($p = 0.52$)
Hald et al. [40]	Denmark	Patients reporting sick leave at baseline: 9.4% 6-month follow-up (after seeing a dermatologist): 4.1%
Mollerup et al. [41]	Denmark	Sick leave within the last 12 months Women: 24.5% Men: 10.7%
Petersen et al. [23]	Denmark	Sick leave: 8% – most common in women ($p = 0.007$) and associated with severity of hand eczema at baseline ($p = 0.029$) and eczema on body locations other than the hands ($p = 0.005$) Job loss: 5%
Steengaard et al. [31]	Denmark	Sick leave in hairdressing-school participants Intervention (selected teachers underwent a 2-day course in general skin physiology and prevention of hand eczema and allergy): 16.0% Control (traditional training): 8.7%, $p = 0.3$ Those who left their jobs who reported hand eczema as the reason for leaving: 12.5%

Table 8 (continued)

References	Country	Work impairment and missed work time
van der Meer et al. [36]	The Netherlands	Absenteeism A survey of 1178 healthcare professionals revealed that 403 took sick leave. Of those who took sick leave, 1.0% ($n = 4$) was due to hand eczema, for an overall prevalence of 0.3% ($n = 2$) [0.1–0.9%] 3-month prevalence of hand eczema: 1.7% ($n = 2$) [0.4–6.5%] Presenteeism: healthcare professionals for the past 3 months ($n = 116$) (CI) Went to work at least 1 day while having hand eczema: 84% (76–89%) Went to work >30 days while having hand eczema: 22% (13–34%) Went to work on >60 days while having hand eczema: 1.7% (0.4–6.6%) Presenteeism: amount of work performed on work days with HE (scale of 0–10 where 0 is 'could not work' and 10 is 'same as usual') ($n = 98$) Mean: 9.4 (SE 0.1) Median: 10 Score ≤ 5: 3.4% (CI 1.4–8.0%) Score ≤ 9: 25% (CI 18–32%) Presenteeism: quality of work performed on work days with hand eczema (scale of 0 to 10 where 0 is 'worst quality' and 10 is 'same quality as usual') ($n = 98$) Mean: 9.5 (SE 0.1) Median: 10 Score ≤ 5: 2.1% (CI 0.7–6.2%) Score ≤ 9: 26% (CI 17–37%)

AD atopic dermatitis, *CHE* chronic hand eczema, *CI* confidence interval, *NR* not reported, *OR* odds ratio, *RR* risk ratio, *SD* standard deviation, *SE* standard error

with those in wet occupations (20.1%) and other occupations (16.5%).

Two German studies reported an annual mean of 7.2 days ($n = 223$) [14] and 35 days ($n = 199$) [17] of sick leave. The average duration of sick leave per episode due to CHE was 6 days in Denmark ($n = 427$) [22]. A Finnish study ($n = 1238$) reported that 6% of patients reported sick leave lasting at least 7 days in the past 12 months [24].

A study conducted in Germany and Switzerland ($n = 1466$) found that for food handlers, CHE was strongly associated with their ability to work and with taking sick leave [20]. A Danish study ($n = 579$) reported a higher proportion of prolonged sick leave among patients working in food-related occupations (27.2%) compared with those in 'wet' occupations [where workers immerse their hands in liquids] (20.1%) and other occupations (16.5%) [27].

Presenteeism (working while sick) was reported in one study of Dutch healthcare professionals [36] ($n = 1232$). Of those with CHE for the past 3 months ($n = 116$), 84% went to work at least 1 day while having CHE, 22% went to work on more than 30 days while having CHE, and 1.7% went to work on more than 60 days while having CHE. The 'amount of work performed' on workdays while having CHE ($n = 98$) was reported as a mean score of 9.4 (where 0 was 'could not work' and 10 was 'same as usual'). The 'quality of work performed' on workdays with HE ($n = 98$) was reported as 9.5 (where 0 was 'worst quality' and 10 was 'same quality as usual'). The study authors suggested that attending healthcare work despite their CHE may have unfavourable consequences for the patients of these healthcare professionals, such as not following hygiene protocols due to CHE.

3.3.5 Job Change

Eleven studies reported job loss/job change due to CHE [19, 21, 23–25, 27–32], ranging from 3 to 25% (Table 8). Two German studies reported that 22% and 24.5% of patients with CHE were unable to work. One Finnish study ($n = 1238$) reported that 2% of patients received a sickness pension [24], while a Danish study ($n = 50$) reported that 13% of people with CHE who left their jobs reported hand, wrist and forearm eczema as the reason for leaving [31].

One study (three publications) conducted in Denmark reported that of 1496 participants, 32.6% of patients with CHE changed profession and 18.8% were no longer working, however these changes were not necessarily due to CHE [33–35]. More participants who changed profession or left their profession reported improvement in their HE compared with those who stayed in the same profession.

4 Discussion

This review reports the available published current information on the direct and indirect costs of CHE, including 30 studies conducted in Europe, Australia, New Zealand, and the Americas. The annual societal costs per patient of CHE ranged between $2549 (€1813) [30% direct costs, 70% indirect costs] and $10,883 (€7738) [49% direct costs, 51%

indirect costs] in Europe and is reported as $5425 (€3857) per patient in the US. The highest estimate was in patients with occupation-related CHE. Overall, the mean number of consultations per month was as high as 3.1, in part due to patch test visits. However, in most studies it was close to once every 2 months. Most studies reported that more than 20% of participants took sick leave due to CHE; the mean number of days of sick leave ranged from 7.2 to 35 days per year. The effect of CHE on presenteeism is unclear, although widespread. These findings demonstrate that CHE has a significant cost burden, both directly and indirectly through its effect on work productivity.

In comparison with other dermatological conditions, the direct annual costs of psoriasis in the US has been estimated at between $8000 and $9777 (€5688 and €6952) per patient, translating to an annual economic burden to the US of between $59.2 and $72.5 billion (€42.1 and €51.5 billion) [42]. The annual indirect costs per patient have been estimated at between $3695 and $3915 (€2627 and €2783) translating to an annual economic burden of between $27.4 and $40.7 billion (€19.5 and €28.9 billion) [42]. In a German cross-sectional study, the average annual total cost of psoriasis was reported to be $9820 (€6982) per person [43]. An estimate of the annual cost of AD to the US has been reported as $5.92 billion (€4.21 billion) [costs per patient were not reported] [44]. However, because the current costs are typically estimated using an 'average' CHE patient rather than by disease severity, and because patients with CHE may be difficult to identify given the lack of standardisation in the definition of CHE, the true cost for CHE may be higher. Other costs that may not have been factored into the estimates include disability costs associated with CHE.

The available primary studies have shortcomings that may have impacted on the results of this analysis. The previous lack of a standardised definition of CHE and CHE severity hamper a synthesis of the monetary costs attributable to sick leave and job loss associated with CHE. There is no available information on the extent and impact of CHE as a cause of permanent disability or potential additional costs in patients with more severe or uncontrolled disease. Most study patients were often from managed care populations who, for example, had health insurance or represented specific occupational groups. Identifying CHE patients in research and administrative databases is challenging as there is currently no International Classification of Diseases, Ninth/Tenth Revision (ICD-9/10) code for CHE, although the ICD, Eleventh Revision (ICD-11; effective January 2022) may include disease areas not covered by ICD-10, therefore future research may be able to identify patients with CHE. With few treatments indicated for CHE, and that vary across territories, this makes it challenging to identify data linked to specific treatments. Classifying disease severity based on clinical characteristics is also difficult due to the lack of structured data from many existing databases.

The synthesis of data for this review also had limitations. The cost-of-illness studies identified were from a limited number of studies and countries in Europe (Germany, Italy, and The Netherlands) and in the US, which could limit the generalisability of the data. The sample of studies that were included are heterogenous, and the studies' sampling methods and population characteristics may also hamper generalisability. In particular, in many of the resource use studies, the study patients were often from specific populations. Although the economic data were uplifted to current costs, most costs data have come from studies older than 10 years, meaning the data may not reflect current practice.

4.1 Implications for Future Research

Understanding costs is important to inform healthcare resource allocation decisions and to gain insight into the economic burden for patients and payers. More current data would be helpful for economic modelling and for estimating cost of illness. Evaluations should involve longer treatment durations and follow-up periods. Studies on costs and healthcare resource utilization should obtain data for different groups of CHE patients representing a spectrum of regions, disease severity, social health determinants (and other environmental factors) and occupations. Studies of indirect costs should take account of presenteeism, which has not been widely reported to date. Future research needs to continually evaluate the costs associated with existing therapies (such as biologics [45]) and emerging therapies in patients with CHE. For example, while alitretinoin has been approved for severe CHE in regions including the EU, its use in the treatment algorithm from various regions and the associated costs need to be better characterized [6]. Given the recent and ongoing development of newer therapies, the financial burden of CHE may be higher than currently estimated.

5 Conclusions

This review has confirmed that CHE has a significant cost burden. Given the increased risk of CHE in some occupations, it is clear that CHE has a significant economic impact on both patient and society due to job loss and presenteeism, which are insufficiently assessed in the literature. Finally, researchers and clinicians should continually strive to determine the lifetime burden of CHE and develop efficacious and safe therapies to reduce the physical, psychosocial and economic burden to CHE.

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