Burden of Disease in Patients with Chronic Hand Eczema: Systematic Literature Reviews of Healthcare Resource Use and Health-Related Quality of Life

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Introduction

- Chronic Hand Eczema (CHE) is a fluctuating, multifactorial inflammatory skin disease that affects the hands and the wrists, with itch and pain being two of the most common and burdensome symptoms.[1-3]
- Patients with CHE experience clinical, occupational, social, and psychological burden, and the disease imposes a considerable economic burden.

Methods

- Two systematic literature reviews (SLRs) on HCRU and HRQoL were conducted using gold-standard methods,[4-6] aligned with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[7]
- Electronic databases (Embase, Medline, Cochrane Library, National Health Service Economic Evaluation, and Health Technology Assessment) were reviewed, and supplemented by congress abstracts and grey literature searches (HCRU: August 2023; HRQoL: October 2023).
- Eligibility criteria were defined using the PICO framework (**Table 1**). Records were independently assessed by two reviewers, and discrepancies were solved by consensus or arbitered by a third reviewer.
- All extractions were performed by one reviewer and quality checked by a second reviewer. Cost data were inflated to a common price year (2022) and converted to euros.

Aim and objectives

To systematically identify and summarise evidence on the burden of CHE for patient, regardless of severity, specifically considering:

- Healthcare resource use (HCRU) evidence
- Health-related quality of life (HRQoL) evidence, as well as patient-reported outcomes data

Table 1. PICO criteria

Population	Adults (≥ 18 years old) with Chronic Hand Eczema [a]	
Interventions & comparators	Any/no interventions or comparators	
Outcomes	**HCRU** • Any direct costs, e.g. treatment costs, unit costs • Any indirect costs, e.g. employment, lifestyle changes • Resource use, e.g. hospitalisation, clinic visits, healthcare contact	**HRQoL** • Preference-based multi-attribute utility values • Direct utility elicitation tools • Generic health related quality of life questionnaires • Mapping algorithms, between disease-specific outcomes and any utility measure. • Disease- or dermatology-specific HRQoL measures • Psychological measures
Geographical limit	Studies conducted in countries other than Asia and Africa	
Timespan	2018 – August 2023	2000 – October 2023

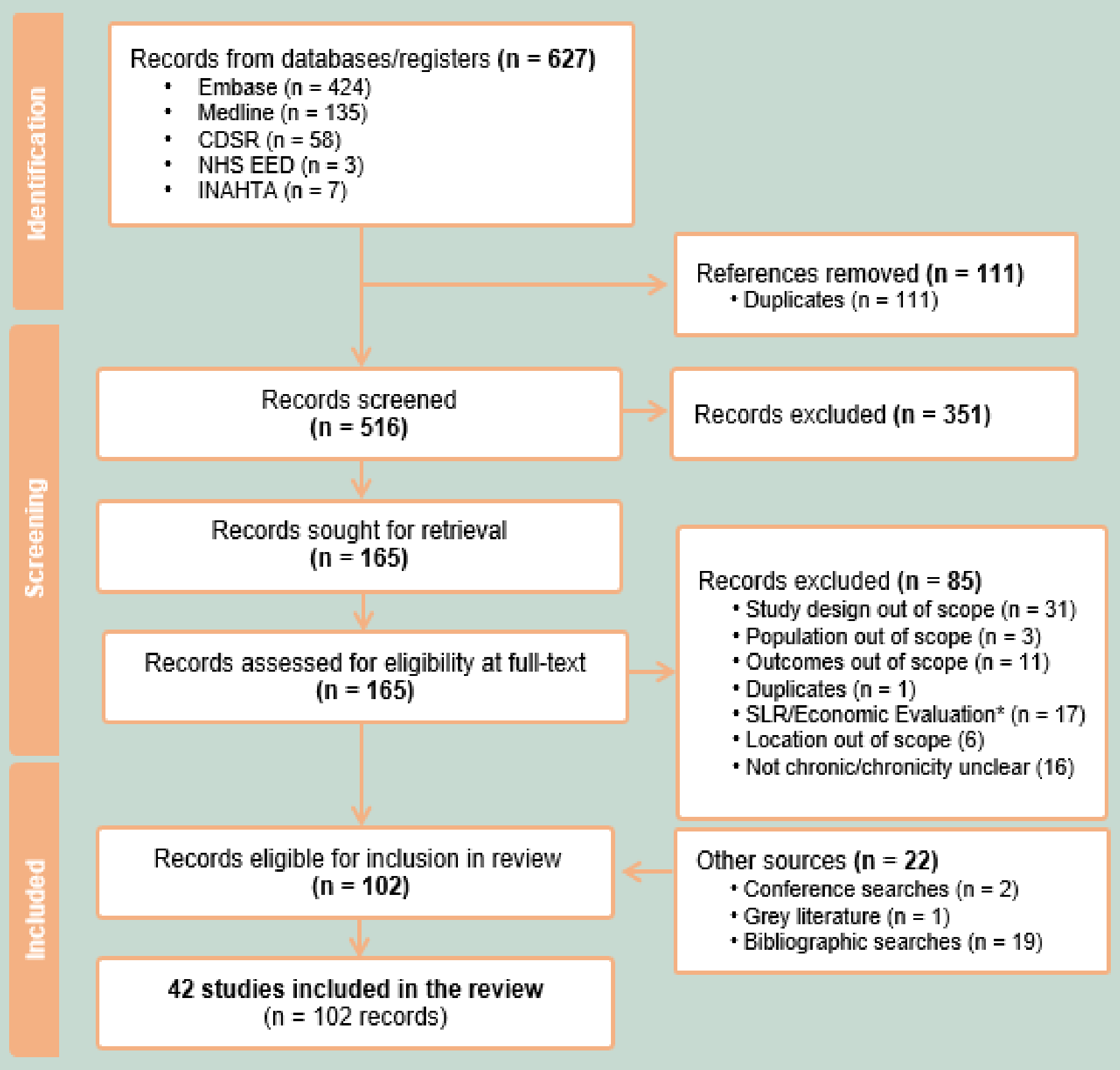
[a] Studies in which the chronicity was not explicitly reported were eligible if the duration of CHE was reported to be longer than 3 months or patients experienced two or more recurrences in the previous 12-months.[8]

Results

HCRU evidence

- Forty-two studies provided HCRU data (**Figure 1**). Only four studies were conducted outside Europe.
- Eight studies conducted in four countries (Germany, Italy, the Netherlands, US) reported cost of disease data across distinct healthcare systems and patient management protocols.[9-16]
- Total annual societal costs per patient ranged from €1,346 to €11,445 (**Figure 2**), comprised of direct costs spanning €460 to €4,304 and indirect costs from €134 to €5,845.
- In all studies except one, indirect costs referred to loss of productivity. One study also reported 1-year out-of-pocket costs per patient in addition to loss of productivity under indirect costs.[12]

Figure 1. PRISMA flowchart (HCRU SLR)



Records from databases/registers **(n = 627)**
- Embase (n = 424)
- Medline (n = 135)
- CDSR (n = 58)
- NHS EED (n = 3)
- INAHTA (n = 7)

References removed **(n = 111)**
- Duplicates (n = 111)

Records screened **(n = 516)**

Records excluded **(n = 351)**

Records sought for retrieval **(n = 165)**

Records assessed for eligibility at full-text **(n = 165)**

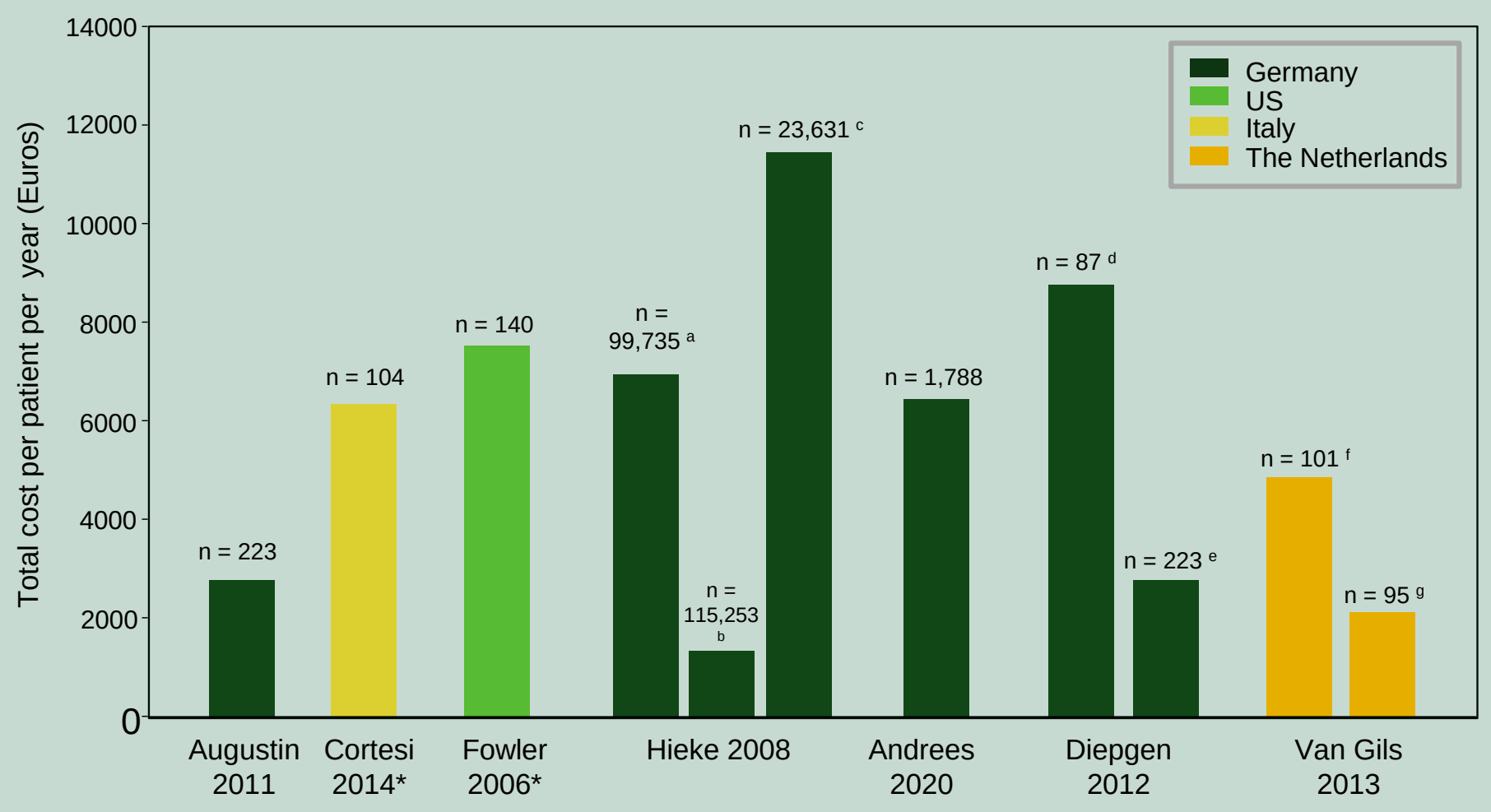
Records excluded **(n = 85)**
- Study design out of scope (n = 31)
- Population out of scope (n = 3)
- Outcomes out of scope (n = 11)
- Duplicates (n = 1)
- SLR/Economic Evaluation* (n = 17)
- Location out of scope (6)
- Not chronic/chronicity unclear (16)

Records eligible for inclusion in review **(n = 102)**

Other sources **(n = 22)**
- Conference searches (n = 2)
- Grey literature (n = 1)
- Bibliographic searches (n = 19)

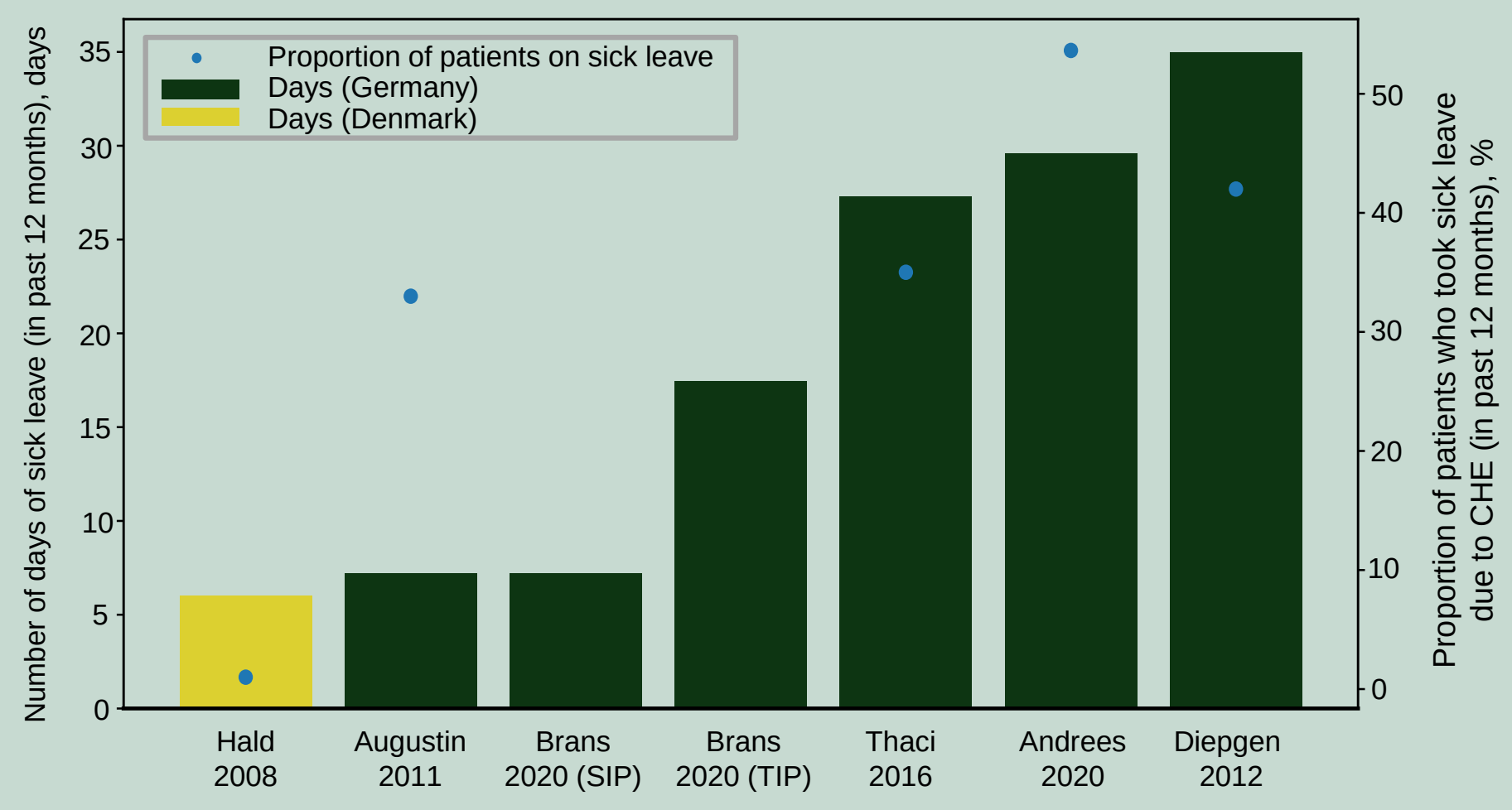
42 studies included in the review
(n = 102 records)

Figure 2. Total cost per patient per year (All cost inflated to common price year = 2022, in Euros)



[a] Full-time workers not covered by German Statutory Accident Insurance (DGUV) [b] Non-workers not covered by DGUV [c] DGUV patients [d] Occupational health insurance [e] Statutory health insurance [f] Integrated care [g] Usual care *Cost data for Fowler 2006 and Cortesi 2014 were reported per month and converted to annual cost for consistency.

Figure 3. Sick leave in the past 12 months (Days and proportion of patients)



Abbreviations: SIP, secondary individual prevention program; TIP, tertiary individual prevention program.

- Forty studies reported data on resource use, most of which were conducted in Europe (**Table 2**). There was high heterogeneity on how data were reported, both regarding its definition but also the temporal window considered. For instance, hospitalisations were reported as proportion of patients who had ever received inpatient care,[17] mean days of hospitalisation per patient-month,[9] or number of days spent in hospital during the last hospitalisation.[13]

Table 2. Number of studies reporting data on resource use

	Europe	North America
Hospitalisations	3	1
Consultations	16	2
Tests & treatments	9	2
Work impairment & missed work time	30	2

- Six studies reported sick leave due to CHE in the past 12 months, including both the proportion of patients who took sick leave as well as the number of days of work.[13, 16, 18-21] Across studies, approximately one third of patients took sick leave in the previous 12 months due to CHE (average 18.5 days; **Figure 3**).

Key messages

HCRU SLR

- Substantial impact of CHE on health care costs and resource utilisation.
- Data are likely not representative of the entire population of patients with CHE, as they are often sourced from populations who 'opt in' to research or are covered by specific insurance.
- Data around cost of illness are limited and extrapolation of results to other countries (than Germany, Italy, The Netherlands, US) may result in inaccuracies.

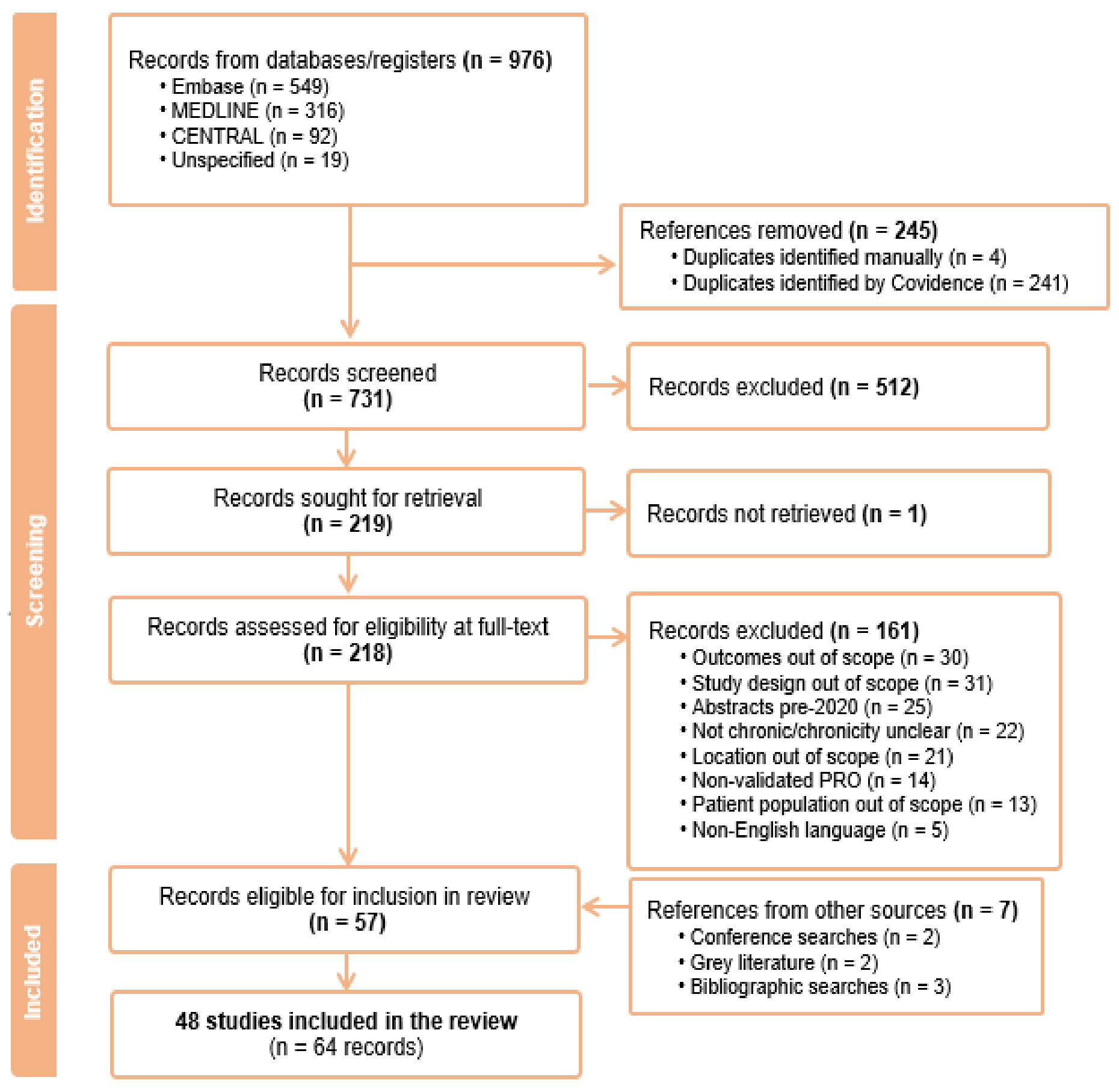
HRQoL SLR

- Patients with CHE have an impaired HRQoL, which is further worsened as the severity of their condition increases.
- Regardless of the severity of their condition or the assessment tool used, patients with CHE consistently reported that their HRQoL was affected (moderate to very large effect on the patients HRQoL as measured by DLQI).
- Heterogeneity across studies was observed in terms of study design, population and measures reported, making synthesis challenging.
- One European study reported that patients with CHE were more likely to self-report clinically significant depression and anxiety compared to other dermatological conditions, except for leg ulcers (for depression) and psoriasis (for anxiety).
- Few studies used a specific hand eczema quality of life assessment tool; therefore, the impact of CHE on patients' quality of life may not have been fully captured.

HRQoL evidence

- Forty-eight studies reported HRQoL and utility data for patients with CHE (**Figure 4**). Most studies were conducted in Germany (n = 22).
- Utility was reported in eight studies using the EQ-5D, primarily informed by patients.[1, 9, 22-27] One study also included utility for healthcare professionals.[25] EQ-5D is a standardised questionnaire that measures HRQoL, which covers five domains (i.e. mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). Additionally, one study employed the time-trade-off (TTO) method for utility assessment.[22] No caregiver utilities were reported.
- Utility values for patients, measured by EQ-5D, decreased with increasing disease severity (mild: 0.81 to 0.97; mild to moderate: 0.76; moderate: 0.71; severe: 0.5 to 0.8; **Figure 5**). Two studies did not specify CHE severity, with patient utilities ranging from 0.74 to 0.84.

Figure 4. PRISMA flowchart (HRQoL SLR)



Records from databases/registers **(n = 976)**
- Embase (n = 549)
- MEDLINE (n = 316)
- CENTRAL (n = 92)
- Unspecified (n = 19)

References removed **(n = 245)**
- Duplicates identified manually (n = 4)
- Duplicates identified by Covidence (n = 241)

Records screened **(n = 731)**

Records excluded **(n = 512)**

Records sought for retrieval **(n = 219)**

Records not retrieved **(n = 1)**

Records assessed for eligibility at full-text **(n = 218)**

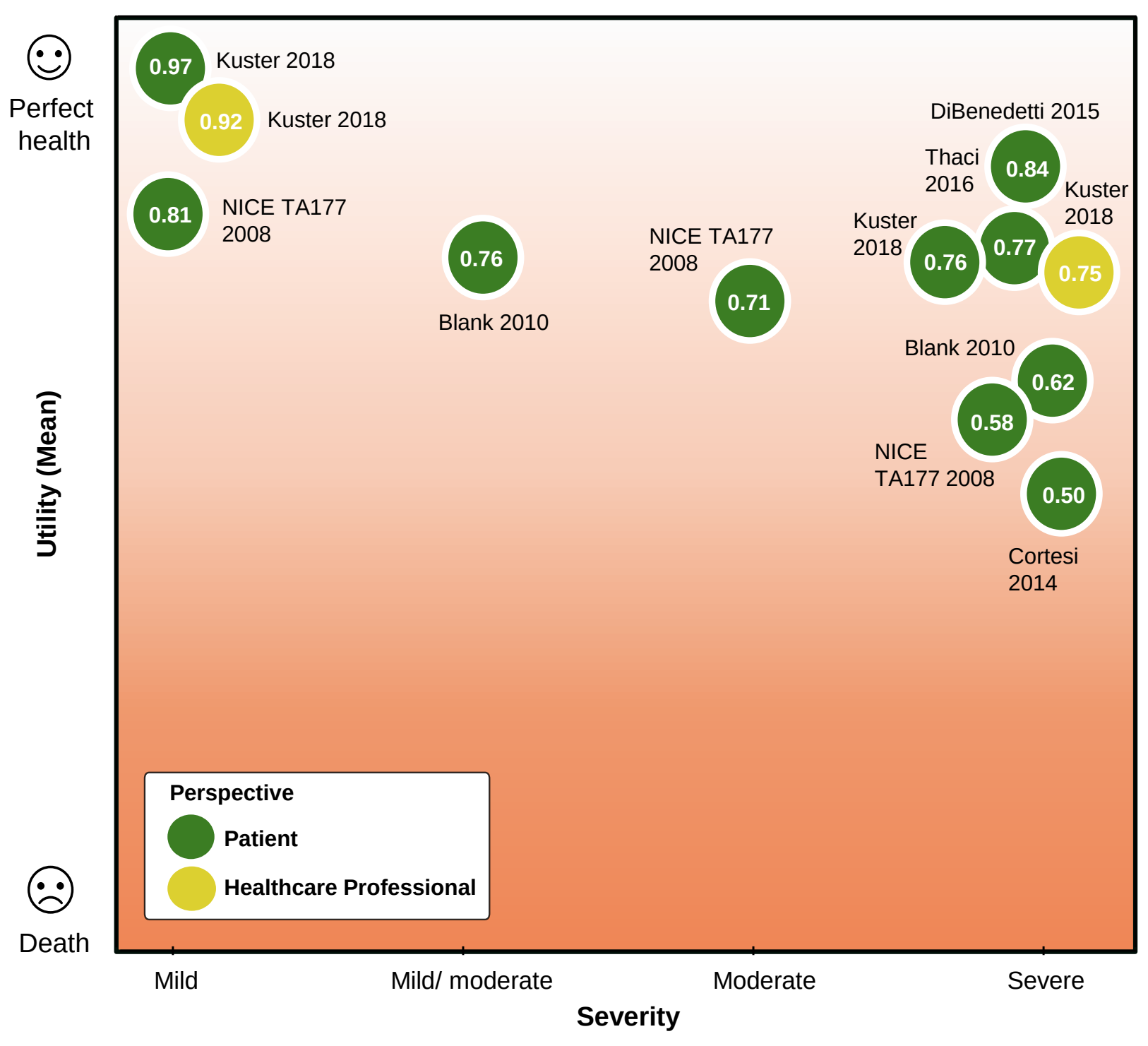
Records excluded **(n = 161)**
- Outcomes out of scope (n = 30)
- Study design out of scope (n = 31)
- Abstracts pre-2020 (n = 25)
- Not chronic/chronicity unclear (n = 22)
- Location out of scope (n = 21)
- Non-validated PRO (n = 14)
- Patient population out of scope (n = 13)
- Non-English language (n = 5)

Records eligible for inclusion in review **(n = 57)**

References from other sources **(n = 7)**
- Conference searches (n = 2)
- Grey literature (n = 2)
- Bibliographic searches (n = 3)

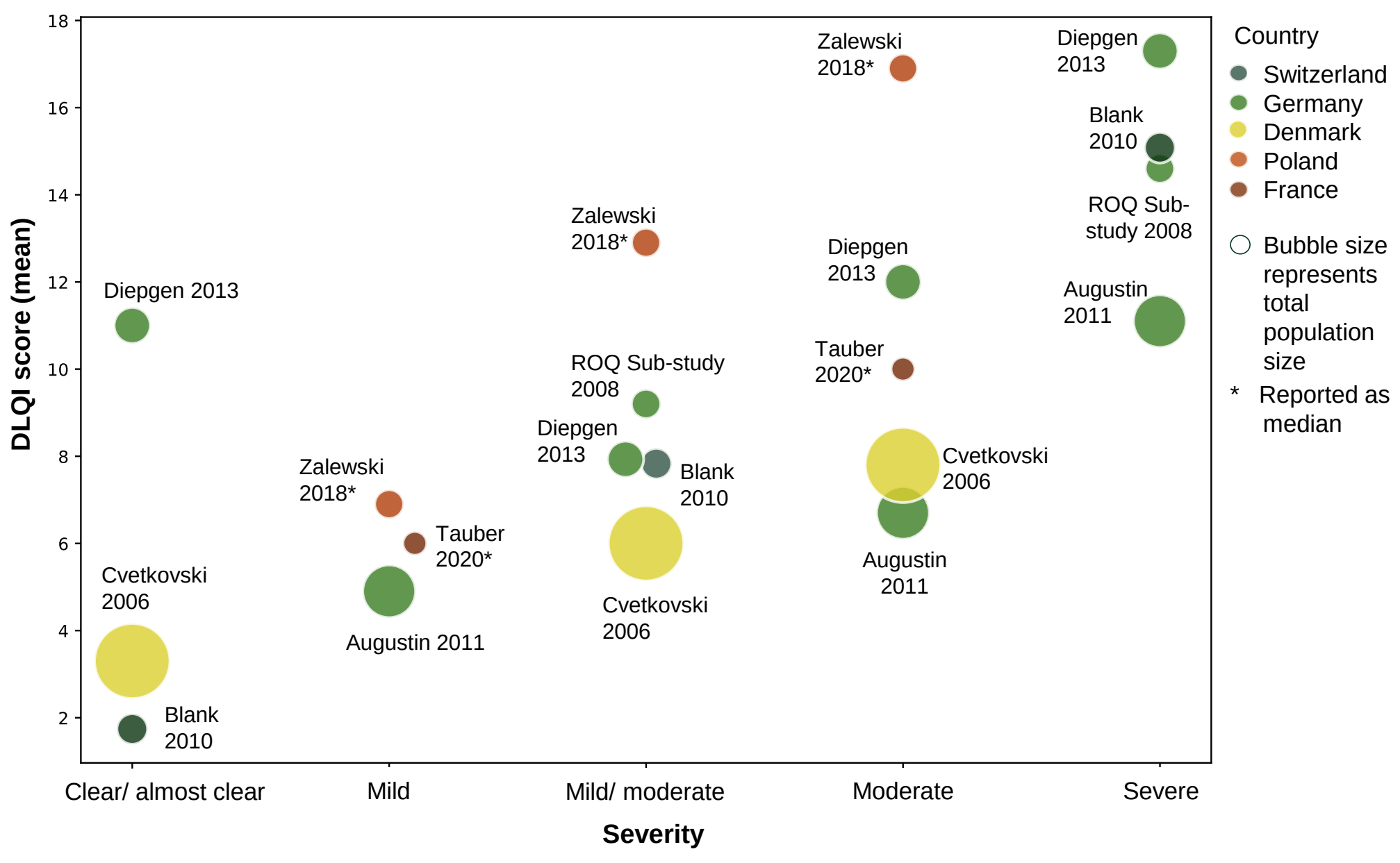
48 studies included in the review
(n = 64 records)

Figure 5. Mean utility value at baseline by severity



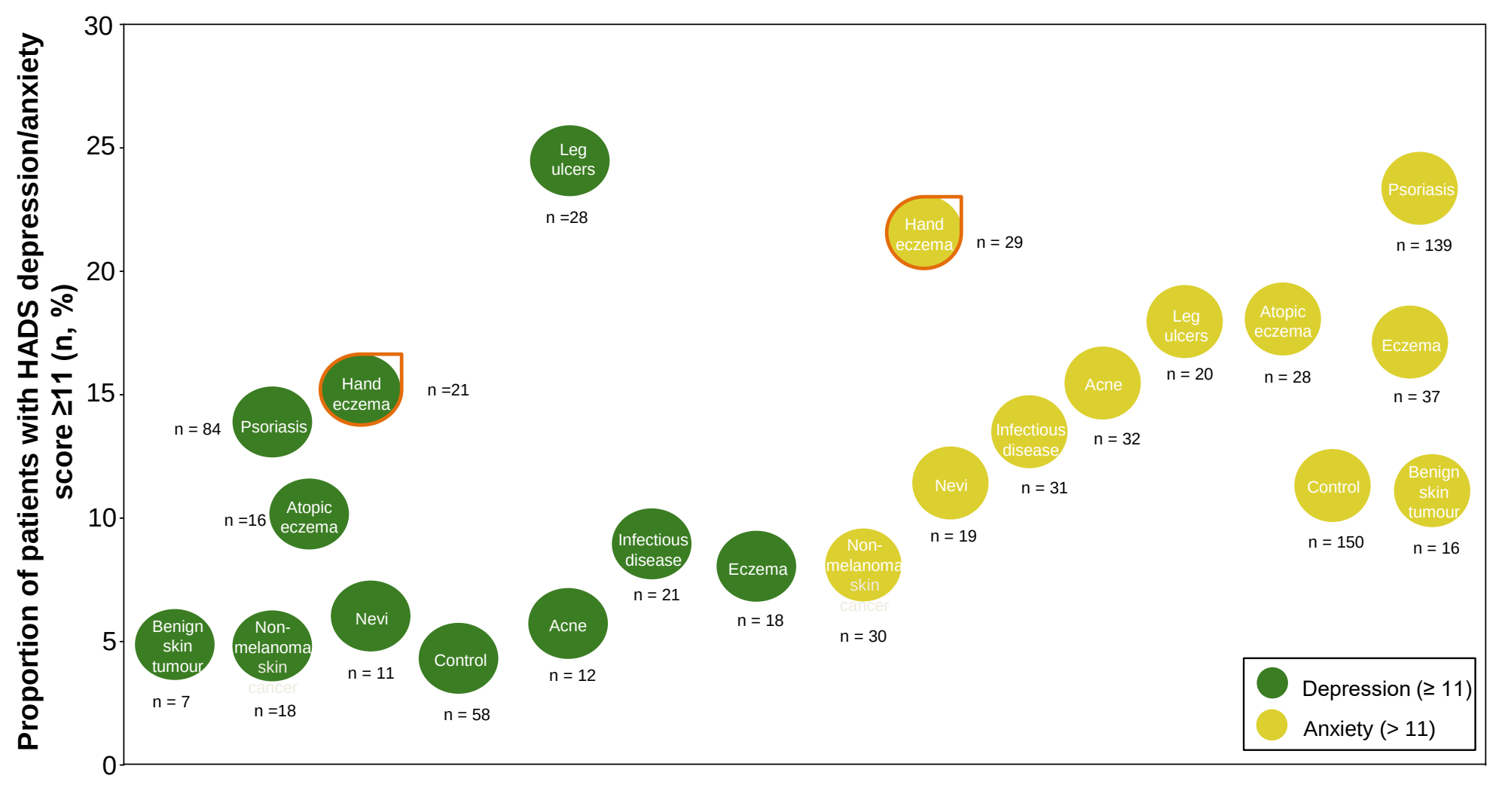
- The Dermatology Life Quality Index (DLQI) was the most used tool to measure HRQoL (n = 33 studies), followed by Quality of Life in Hand Eczema Questionnaire (QOLHEQ) and EQ-5D VAS (n = 6 studies each).
- DLQI is a widely used tool to assess the impact of skin conditions on patients' quality of life. It consists of 10 items with scores ranging from 0 to 30; with higher scores indicate greater impairment associated with the skin condition.[28] Seven studies reported DLQI data stratified for CHE severity, which indicated that patients' quality of life worsened further as the severity of the disease increased (mean DLQI score: mild CHE 4.9 to 7.9; moderate CHE: 6.7 to 12; severe CHE 11.1 to 17.3; **Figure 6**).[2, 13, 23, 29-32]

Figure 6. Mean DLQI score at baseline by severity



- Psychological measures were inconsistently reported (7 studies reporting using 7 different questionnaires). The most used patient-reported outcome measure was the Hospital Anxiety and Depression Scale (HADS; 5 European studies).
- One study conducted in 13 European countries showed that patients with CHE had higher HADS scores compared to healthy controls, with this difference being particularly significant in female patients.[33] Approximately one-sixth and one-fifth of patients with CHE reported symptom levels that reached the clinical case thresholds for anxiety and depression (≥ 11), respectively, and were more likely to self-report clinically significant depression and anxiety compared to other dermatological conditions, except for leg ulcers (for depression) and psoriasis (for anxiety; **Figure 7**).

Figure 7. Proportion of patients with common skin diseases with HADS depression and anxiety clinical case[33]



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Disclosures

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