**Supplemental data.**

**Table S1.** **Search strategy for MEDLINE performed December 20, 2016.\***

|  |  |  |
| --- | --- | --- |
| **Search** | **Query** | **No. of records found** |
| #1 | dermatitis, atopic[MeSH Terms] OR ‘atopic dermatitis’[tiab] OR ‘atopic eczema’[tiab] OR ‘infantile eczema’[tiab] OR ‘pediatric eczema’[tiab] | 22,798 |
| #2 | quality of life OR utility OR disutility OR activities of daily living OR patient burden OR patient-reported outcome OR PRO OR patient satisfaction OR patient preference OR patient withdrawal OR functioning OR symptom burden OR caregiver | 1,010,135 |
| #3 | #1 AND #2 | 1610 |
| #4 | costs OR cost analysis OR cost-benefit analysis OR cost benefit OR budget impact OR health care costs OR healthcare costs OR cost of illness OR employer health cost OR health expenditures OR healthcare utilization OR economic burden OR absenteeism OR presenteeism OR productivity | 813,655 |
| #5 | #1 AND #4 | 440 |
| #6 | #3 OR #5 | 1230a |

Abbreviations. MeSH, Medical Subject Heading; PRO, patient-reported outcome; tiab, title/abstract.

\*Search limitations/filters applied to search 6 included date range = past 20 years; language = English; no animal studies; no narrative reviews.

**Table S2. Search strategy for EMBASE performed December 20, 2016.\***

|  |  |  |
| --- | --- | --- |
| **Search** | **Query** | **No. of records found** |
| #1 | 'atopic dermatitis'/exp OR 'atopic dermatitis' OR 'atopic eczema':ab,ti OR 'infantile eczema':ab,ti OR 'pediatric eczema':ab,ti | 37,117 |
| #2 | 'quality of life'/exp OR 'quality of life' OR utility OR disutility OR 'activities of daily living'/exp OR 'activities of daily living' OR 'patient burden' OR 'patient reported outcomes'/exp OR 'patient reported outcomes' OR PRO OR 'patient satisfaction'/exp OR 'patient satisfaction' OR 'patient preference'/exp OR 'patient preference' OR 'patient withdrawal' OR functioning OR 'symptom burden'/exp OR 'symptom burden' OR 'caregiver'/exp OR caregiver | 1,197,099 |
| #3 | #1 AND #2 | 3077 |
| #4 | costs OR 'cost analysis'/exp OR 'cost analysis' OR 'cost benefit analysis'/exp OR 'cost benefit analysis' OR 'cost benefit'/exp OR 'cost benefit' OR 'budget impact' OR 'health care costs'/exp OR 'health care costs' OR 'healthcare costs' OR 'cost of illness'/exp OR 'cost of illness' OR 'employer health cost' OR 'health expenditures'/exp OR 'health expenditures' OR 'healthcare utilization'/exp OR 'healthcare utilization' OR 'economic burden'/exp OR 'economic burden' OR 'absenteeism'/exp OR absenteeism OR 'presenteeism'/exp OR presenteeism OR 'productivity'/exp OR productivity | 548,089 |
| #5 | #1 AND #4 | 672 |
| #6 | #3 OR #5 | 1,804a |

Abbreviations. ab.ti, abstract title; exp, explode; PRO, patient-reported outcome.

\*Search limitations/filters applied to search #6 included date range = past 20 years; language = English; human studies; no narrative reviews.

**Table S3. Search strategy for the Cochrane Library performed December 20, 2016.\***

|  |  |  |
| --- | --- | --- |
| **Search** | **Query** | **No. of records found** |
| #1 | MeSH descriptor: [Dermatitis, Atopic] explode all trees | 1,134 |
| #2 | ‘atopic dermatitis’ or ‘atopic eczema’ or ‘infantile eczema’ or ‘pediatric eczema’:ti,ab,kw (word variations have been searched) | 2,320 |
| #3 | #1 OR #2 | 2,452 |
| #4 | quality of life or utility or disutility or activities of daily living or patient burden or patient-reported outcome or PRO or patient satisfaction or patient preference or patient withdrawal or functioning or symptom burden or caregiver:ti,ab,kw (word variations have been searched) | 194,076 |
| #5 | #3 AND #4 | 471 |
| #6 | costs or cost analysis or cost-benefit analysis or cost benefit or budget impact or health care costs or healthcare costs or cost of illness or employer health cost or health expenditures or healthcare utilization or economic burden or absenteeism or presenteeism or productivity:ti,ab,kw (word variations have been searched) | 53,651 |
| #7 | #3 AND #6 | 79 |
| #8 | #5 OR #7 | 514 |
| #9 | #8 Publication year 1996-2016 | 463 |

Abbreviations. MeSH, Medical Subject Heading; PRO, patient-reported outcome; ti,ab,kw, title, abstract, keyword.

\*Search limitations/filters applied included date range = past 20 years.

**Table S4. Inclusion and exclusion criteria.**

|  |  |  |
| --- | --- | --- |
|  | **Inclusion criteria** | **Exclusion criteria** |
| Population | Studies of at least 25\* patients of any age with mild or moderate AD† | Studies of fewer than 25\* patients with mild or moderate AD or studies evaluating only patients with severe AD |
| Interventions/comparators | * Crisaborole
* TCIs
* TCS
* Phototherapy
* Systemic therapy
 | Studies without at least 1 of these interventions if interventions are disclosed (studies that do not specify interventions are included) |
| Outcomes | * Economic outcomes (direct and indirect costs, economic analyses)
* PROs (HRQoL, caregiver burden)
 | Studies that do not report data for at least 1 of these outcomes |
| Study design | * Phase 2, 3, or 4 randomized controlled trials
* Open-label trials; pragmatic trials
* Single-arm trials
* Prospective observational studies
* Retrospective observational studies and database studies
* Registries and surveys
* Case studies, reports, or series
* Meta-analyses and systematic literature reviews‡
* Health economic studies
* Conference abstracts
* Dissertations
 | * Phase 1 clinical trials
* Pharmacokinetic/pharmacodynamics studies
* Preclinical or animal studies
* Guidelines
* Editorials, letters, or commentaries
* Narrative literature reviews
 |

Abbreviations. AD, atopic dermatitis; HRQoL, health-related quality of life; PRO, patient-reported outcome; TCI, topical calcineurin inhibitor; TCS, topical corticosteroid.

\*Sample size was tracked during screening.

†Although the primary focus was mild, mild to moderate, or moderate AD, studies that did not specify AD severity or studies of populations with mixed AD severity without appropriately stratified data were tracked separately during screening.

‡Reference lists from these types of studies were evaluated for potential additional studies for inclusion in the systematic literature review.

**Table S5.** **QoL instruments used by studies in the systematic review.**

| **Name** | **Abbreviation** | **Reference** | **Type** | **Brief summary and domains** | **Score range** | **Recall period** |
| --- | --- | --- | --- | --- | --- | --- |
| Atopic Dermatitis Impact Scale | ADIS | Torrelo A et al. Eur J Dermatol2012;22:97-105 | Disease specific | Clinicians were asked about the following: * Severity of AD symptoms (3 items)
* AD affectation: sleep disturbances (2 items), school/professional fulfillment (4 items), and emotional disturbances (10 items)
* Attitude toward AD flares and topical pharmacologic treatment (4 items)
* Overall satisfaction with topical pharmacologic treatment (1 item, visual analog scale [VAS])
* Perceived benefits of topical pharmacologic treatment for flares (6 items)

Patients were asked about the following:* Attitude toward medical recommendations (hygienic and preventive strategies, 4 items)
* Satisfaction with medical recommendations for AD management and control (1 item, VAS)
* Satisfaction with the information given by their specialist (1 item, VAS)
* Feelings before the next flare (5 items)
 | 0 (minimum impact) to 10 (maximum impact) | Not specified |
| Children’s Dermatology Life Quality Index | CDLQI | Lewis-Jones MS, Finlay AY. Br J Dermatol 1995;132;942-9 | Dermatology specific | 10 questions covering* Symptoms/feelings
* Leisure
* School/holidays
* Personal relationships
* Sleep
* Treatment
 | 0 (no effect) to 30 (large effect) | 1 week |
| Dermatology Life Quality Index  | DLQI | Finlay AY, Khan GK. Clin Exp Dermatol 1994;19;210-6 | Dermatology specific | 10 questions covering* Symptoms/feelings
* Daily activities
* Leisure
* Work/school
* Personal relationships
* Treatment
 | 0 (no effect) to 30 (large effect) | 1 week |
| Dermatology-specific Quality of Life  | DSQL | Anderson RT, Rajagopalan R.J Am Acad Dermatol 1997;37:41-50 | Dermatology specific | 52 questions over 7 domains:* Physical symptoms
* Daily activities
* Social activities
* Work/school experiences
* Self-perception
* SF-36 vitality subscale
* SF-36 mental subscale
 | 0 (no limitation) to 10 (extreme limitation) | 1 month |
| EuroQoL 5 Dimensions  | EQ-5D | EuroQoL Group.Health Policy1990;16:199-208 | General | 5 dimensions* Mobility
* Self-care
* Usual activities
* Pain/discomfort
* Anxiety/depression
 | 0 to 1 with 0 being full health | Status at time of completion |
| Infant’s Dermatitis Quality of Life Index  | IDQoL | Lewis-Jones MS et al. Br J Dermatol 2001;144:104-10 | Dermatology | 10 questions covering* Symptoms/feelings
* Leisure
* Family activities
* Personal relationships
* Sleep
* Treatment
 | 0 (no effect) to 30 (large effect) | 1 week |
| 12-Item Short-Form Health Survey  | SF-12 | Ware J Jr et al. Med Care 1996;34:220-33www.sf-36.org | General | 12 questions across 8 domains* Physical functioning
* Role-physical
* Bodily pain
* General health
* Vitality
* Social functioning
* Role-emotional
* Mental health
 | 0–100; lower scores have worse QoL | Standard: 4 weeksacute: 1 week |
| 36-Item Short-Form Health Survey | SF-36 | Ware JE Jr, Sherbourne CD. Med Care 1992;30:473-83McHorney CA et al. Med Care 1993;31:247-63www.sf-36.org | General | 36 questions across 8 domains* Physical functioning
* Role-physical problem
* Bodily pain
* General health
* Vitality
* Social functioning
* Role-emotional
* Mental health
 | 0–100; lower scores have worse QoL | Standard: 4 weeksacute: 1 week |
| Skindex-16  | None | Chren MM et al. J Cutan Med Surg 2001;5:105-10 | Dermatology-specific | 16 questions across 3 domains:* Emotions
* Functioning
* Symptoms
 | 0 (never bothered) to 100 (always bothered) | 1 week |

Abbreviations. AD, atopic dermatitis; QoL, quality of life.

**Table S4.** **Instruments to assess atopic dermatitis severity**

| **Name** | **Abbreviation** | **Reference** | **Brief summary and domains** | **Score range** |
| --- | --- | --- | --- | --- |
| Eczema Area and Severity Index | EASI | Hanifin JM et al. Exp Dermatol 2001;10:11-8 | * For age >8 years
* Domains: erythema, induration/papulation, excoriation, and lichenification
	+ Scored 0 (none) to 3 (severe)
* Locations: head and neck, trunk, upper extremities, lower extremities
	+ Extent of involvement scored as: 0 = none; 1 = <10%; 2 = <10%–29%; 3 = 30%–49%; 4 = <50%–69%; 5 = <70%–89%; 6 = >90%–100%
* Each location scored
 | 0–72, tallied as sum of below valuesHead/neck: (Erythema+Induration/papulation+ Excoriation+Lichenification)×Area×0.1Upper limbs: (Erythema+Induration/papulation+ Excoriation+Lichenification)×Area×0.2Trunk: (Erythema+Induration/papulation+ Excoriation+Lichenification)×Area×0.3Lower limbs:(Erythema+Induration/papulation+ Excoriation+Lichenification)×Area×0.4 |
| Investigator’s Global Assessment | IGA | Futamura M et al. J Am Acad Dermatol 2016;74:288-94  | * Multiple options; broadly defined as overall evaluation of AD severity using an ordinal scale or an ordered categorical variable that was scored using points by an investigator or a physician
* FDA recommends IGA as primary end point for AD clinical trials
 | Depends on specific scale used |
| Nottingham Eczema Severity Score | NESS | Emerson RM, Charman CR, Williams HC. Br J Dermatol 2000;142:288-97 | * Specific to children
* Domains: clinical course, disease intensity, and extent of BSA involvement
* Graded from 1–5
 | Ranges from 3 to 15; sum of grades from clinical course + disease intensity + extent of BSA involvement |
| Rajka and Langeland | R&L | Rajka G, Langeland T. Acta Derm Venereol (Stockh) 1989;69 (suppl 144):13-4 | * 3 domains: extent (childhood/adult and infant), course, and intensity
* Grades from 1–3
 | Sum scores for 3 domains; ranges from 3 (mild) to 9 (severe) |
| Severity Scoring of Atopic Dermatitis | SCORAD | European Task Force on Atopic Dermatitis. Dermatology. 1993;186:23-31 | * Extent range from 0%–100%
* 6 intensity domains: erythema, edema/papulation, oozing/crusts, excoriations, lichenification, dryness ranged from 0 (absent) to 3 (severe)
* 2 subjective domains: pruritus, sleep loss graded using a VAS of 0–10
 | Range 0–103. Consists of Extent/5 + (7 × Intensity)/2 + Subjective  |
| Six Area, Six Sign Atopic Dermatitis | SASSAD | Berth-Jones J. Br J Dermatol 1996;135(suppl 48):25-30 | * 6 signs: erythema, exudation, excoriation, dryness, cracking, and lichenification
* 6 sites: arms, hands, legs, feet, head and neck, and trunk
* Scored on scale of 0 (absent) to 3 (severe)
 | 0–108 |
| Patient-Oriented Eczema Measure | POEM | Charman CR et al. Arch Dermatol 2004;140:1513-9 | * Domains related to symptoms: itching, sleep disturbance, bleeding, weeping/oozing of the skin, dryness/roughness of the skin, flaking of the skin, and cracking of the skin
* Responses to 7 questions regarding symptoms scored as follows: 0 = no days; 1 = 1–2 days; 2 = 3–4 days; 3 = 5–6 days; 4 = every day
 | 0–28; total of scores from 7 symptom questions |

Abbreviations. AD, atopic dermatitis; FDA, US Food and Drug Administration.