**Appendix** **Table 1 PICOS summary of eligibility criteria**

|  |  |  |  |
| --- | --- | --- | --- |
| **Review** | **PICOS** | **Inclusion Criteria** | **Exclusion Criteria** |
| **AD** | **Population** | The eligible population will be patients of all ages with mild to severe AD. | Patients with any comorbidity. |
| **Outcomes** | Quality of life and utility data based on EQ-5D, EQ-5D VAS, SF-36 and SF-6D | * Studies not reporting EQ-5D/EQ-5D VAS/SF-36/SF-6D-derived utility index scores at baseline
* Studies reporting SF-36 scores divided in its eight domains and not mean MCS and PCS
 |
| **Study Design** | Quality of life and utility data based on EQ-5D, EQ-5D VAS, SF-36 and SF-6D | Studies focusing on treatment and not reporting utility value at baseline |
| **Limits** | * Full publications from 2000 to date
* English language publications only
* Conference abstracts and presentations from 2016 to date
 | * Studies published before 2000
* Non-English language publications
* Conference papers until 2016
 |
| **CHE** | **Population** | The eligible population was patients of all ages with chronic hand eczema | Patients with any other disease |
| **Outcomes** | * Eligible studies reporting data on at least one of the following outcomes:
* Costs (societal costs, direct and indirect costs)
* Utilities elicitation exercises
* HRQoL, including PROMS
 |  |
| **Study Design** | * Published economic evaluations
* Reviews and HTAs
* Cost of illness studies
* Costs studies
* Reports of disease specific and generic PROMS, including utility studies
 |  |
| **Limits** | * English language publications
* For alitretinoin, tacrolimus and pimecrolimus conference abstracts and presentations of any date.
* For other interventions or topics, studies published as conference presentations or abstracts within the last 3 years only will be eligible
* Economic studies providing costs must have costs from 1998 or later
 | * Non-English language studies
* Studies from Asia or Africa
 |
| **Chronic Diseases** | **Population** | The eligible population will be patients of all ages with chronic conditions. | Patients with any comorbidity. |
| **Outcomes** | Quality of life and utility data based on EQ-5D, EQ-5D VAS, SF-36 and SF-6D | * Reviews not reporting a range of scores for EQ-5D and SF-36
* Studies reporting SF-36 scores divided in its eight domains and not mean MCS and PCS
 |
| **Study Design** | Systematic literature reviews reporting EQ-5D, EQ-5D VAS, SF-36 and SF-6D | * Reviews that did not report directly on primary publications
* Publications focusing on disease treatment
 |
| **Limits** | * Full publications from 2000 to date
* English language publications only for journal articles
* Conference abstracts and presentations from 2016 to date
 | * Studies published before 2000
* Non-English language journal articles
* Studies not reporting EQ-5D/EQ-5D VAS/SF-36/SF-6D-derived utility index scores at baseline
* Publications on the validity of patient reported outcomes
* Discussion papers on HRQoL in various disease areas, not focusing on one disease area
* Conference papers before 2016
* Publications on non-chronic conditions
 |

Abbreviations: AD = atopic dermatitis; CHE = chronic hand eczema; HRQoL = health-related quality of life; HTA = health technology assessment; MCS = mental component score; PCS = physical component score; RROMS = patient reported outcome measures; SF-36 = short form 36 health survey; SF-6D = short form 6 dimensions; VAS = visual analog scale

**Appendix Table 2 Search strategies**

|  |  |  |  |
| --- | --- | --- | --- |
| **Review** | **Databases** | **Dates** | **Search Terms** |
| **AD** | PubmedScienceDirect | **Full publications:** 2000 to June 2019**Conference abstracts:**2016 to June 2019 | (EQ5D OR EQ 5D OR EuroQoL OR SF36 OR SF 36 OR SF6D OR SF 6D) AND (atopic\*); (EQ5D OR EQ 5D OR EuroQoL OR SF36 OR SF 36 OR SF6D OR SF 6D) AND (skin diseas\*);(EQ5D OR EQ 5D OR EuroQoL OR SF36 OR SF 36 OR SF6D OR SF 6D) AND (dermatitis, atopic); and (EQ5D OR EQ 5D OR EuroQoL OR SF36 OR SF 36 OR SF6D OR SF 6D) AND (atopic dermatit\*) |
| **CHE** | MEDLINEEMBASEScHARRHUDHealth Technology Assessment (HTA) database and HTA agency websites | **MEDLINE:** Inception to July 2017**Others:**Inception to July 2018**Conference presentations and abstracts**:Last 3 years | See Table 3 |
| **Chronic Conditions** | PubmedScienceDirect | **Full publications:** 2000 to June 2019**Conference abstracts:**2016 to June 2019 | (EQ5D OR EQ 5D OR EuroQoL OR SF36 OR SF 36 OR SF6D OR SF 6D) AND (review) |

Abbreviations: AD = atopic dermatitis; CHE = chronic hand eczema; SF-36 = short form 36 health survey; SF-6D = short form 6 dimensions; VAS = visual analog scale

**Appendix Table 3 Search terms for chronic hand eczema utilities**

|  |
| --- |
| 1 Skin Diseases, Eczematous/ (66)2 Eczema/ (10338)3 Eczema, Dyshidrotic/ (272)4 exp Dermatitis, Contact/ (32433)5 (eczema$ or dermatos$ or dermatit$).ti,ab,kf. (80815)6 (dyshidro$ or dyshydro$ or dishidro$ or dishydro$ or pulpitis or pulpite).ti,ab,kf. (1697)7 or/1-6 (99041)8 exp Hand/ (80100)9 (hand or hands or palm or palms or palmar or palmoplantar or acra or acral or acras or digit ordigits or finger or fingers or nail or nails).ti,ab,kf. (499470)10 or/8-9 (529329)11 7 and 10 (5938)12 Hand Dermatoses/ (7260)13 or/11-12 (11394)14 Quality-Adjusted Life Years/ (10132)15 (quality adjusted or adjusted life year$).ti,ab,kf. (13402)16 (qaly$ or qald$ or qale$ or qtime$).ti,ab,kf. (8652)17 (illness state$1 or health state$1).ti,ab,kf. (5511)18 (hui or hui1 or hui2 or hui3).ti,ab,kf. (1265)19 (multiattribute$ or multi attribute$).ti,ab,kf. (770)20 (utility adj3 (score$1 or valu$ or health$ or cost$ or measur$ or disease$ or mean or gain orgains or index$)).ti,ab,kf. (12533)21 utilities.ti,ab,kf. (6000)22 (eq-5d or eq5d or eq-5 or eq5 or euro qual or euroqual or euro qual5d or euroqual5d or euro qolor euroqol or euro qol5d or euroqol5d or euro quol or euroquol or euro quol5d or euroquol5d or eur qol or eurqol or eur qol5d or eur qol5d or eur?qul or eur?qul5d or euro$ quality of life or european qol).ti,ab,kf. (8621)23 (euro$ adj3 (5 d or 5d or 5 dimension$ or 5dimension$ or 5 domain$ or 5domain$)).ti,ab,kf. (2974)24 (sf36$ or sf 36$ or sf thirtysix or sf thirty six).ti,ab,kf. (19329)25 (time trade off$1 or time tradeoff$1 or tto or timetradeoff$1).ti,ab,kf. (1653)26 ((qol or hrqol or quality of life).ti,kf. or \*quality of life/) and ((qol or hrqol$ or quality of life) adj2(increas$ or decrease$ or improv$ or declin$ or reduc$ or high$ or low$ or effect or effects or worse or score or scores or change$1 or impact$1 or impacted or deteriorat$)).ab. (29935)27 Cost-Benefit Analysis/ and (cost-effectiveness ratio$ and (perspective$ or life expectanc$)).ti,ab,kf. (2785)28 \*quality of life/ and (quality of life or qol).ti. (46161)29 quality of life/ and ((quality of life or qol) adj3 (improv$ or chang$)).ti,ab,kf. (22360)30 quality of life/ and ((quality of life or qol) adj (score$1 or measure$1)).ti,ab,kf. (9965)31 quality of life/ and health-related quality of life.ti,ab,kf. (26010)32 quality of life/ and ec.fs. (8921)33 quality of life/ and (health adj3 status).ti,ab,kf. (7706)34 (quality of life or qol).ti,ab,kf. and Cost-Benefit Analysis/ (10428)35 Models, Economic/ (8741)36 or/14-35 (137751)37 elicitation$1.ab,kf. or elicit$.ti. or elicit$.ab. /freq=2 (52694)38 13 and (36 or 37) (162)39 exp Animals/ not Humans/ (4458766)40 (news or editorial or case report).pt. or case report.ti. (852598)41 38 not (39 or 40) (148)42 remove duplicates from 41 (148)Key to Ovid symbols and commands$ Unlimited right-hand truncation symbol $N Limited right-hand truncation - restricts the number of characters following the word to N ti,ab,kf Searches are restricted to the Title, Abstract, Keyword Heading Word fieldsadjN Retrieves records that contain terms (in any order) within a specified number (N) of words ofeach other/ Searches are restricted to the Subject Heading fieldexp The subject heading is explodedpt. Search is restricted to the publication type fieldab. /freq=N Search is restricted to records where the terms occur at least N times in the abstract or/1-6 Combines sets 1 to 6 using Boolean OR  |

 Appendix Table 4 Atopic Dermatitis Studies Data Extraction

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study and Country** | **Study type** | **Number of patients** | **Mean age** | **Disease severity** | **Treatment** | **Results by instrument** |
| Eckert et al. 2017[49](#_ENREF_49) | Cross-sectional study | 1047(349 AD) | 41.6 | Mild or moderate/severe |  | SF-36 PCS: 47.6 |
|  | SF-36 MCS: 44.5 |
| USA | SF-6D: 0.67 |
| Holm et al. 2005[71](#_ENREF_71) | Longitudinal study | 131(101 AD) |   |  Moderate |   | SF-36 PCS: 49.3 |
| Denmark | SF-36 MCS: 49.6 |
| Kiebert et al. 2002[48](#_ENREF_48) | Cross-sectional study | 239 | Children: 8.9 Adults: 36  | Mild, moderate, severe |   | SF-36 general PCS: 50.6 |
|  | SF-36 general MCS: 46.2 |
|   | SF-36 PCS: 52.6 mild |
|   | SF-36 MCS: 51.1 mild |
|   | SF-36 PCS: 49.7 moderate |
|  | SF-36 MCS: 43.1 moderate |
|   | SF-36 PCS: 49 severe |
|  USA | SF-36 MCS: 38.5 severe |
| Langenbruch et al. 2014[45](#_ENREF_45) | Non-interventional cross-sectional perspective study | 1678 | 38.4 |  | Emollients, topical corticosteroids, topical calcineurin inhibitor, systemic therapy | EQ-5D VAS: 63.6 |
| Germany |
| Lee et al. 2018[44](#_ENREF_44) | Cross-sectional  | 37578 (677 AD) | Non AD: 45.54AD: 36.1 |   |   | EQ-5D: 0.94 |
| South Korea | EQ-5D VAS: 71.8 |
| Lundberg et al. 2000[47](#_ENREF_47) | Cross-sectional  | 366 (132 AD) | 34.79 |   |   | SF-36 PCS: 46.5 |
| Sweden | SF-36 MCS: 45.4 |
| Nguyen et al. 2019[72](#_ENREF_72) | Cross-sectional  | 430 (120 AD) | 36.5 |   |   | EQ-5D: 0.73 |
| Vietnam |
| Poole et al. 2009[41](#_ENREF_41) | Multicenter, randomized, emollient vehicle-controlled, phase III study | 257 | 28 | Mild, moderate, severe | Twice-weekly tacrolimus ointment or twice-weekly emollient vehicle | EQ-5D: 0.85 mild |
|   | EQ-5D: 0.8 moderate |
|    | EQ-5D: 0.76 severe |
| SF-6D: 0.8 mild  |
|   | SF-6D: 0.8 moderate |
| 13 EU countries | SF-6D: 0.75 severe |
| Poole et al. 2010[42](#_ENREF_42) | Multicenter, double blind, randomized controlled trial phase III | 926 | 32.5 | 57% moderate43% severe  | Tacrolimus ointment or standard corticosteroid regimen applied twice-daily for 6 months | EQ-5D: 0.77 moderate  |
| 12 EU countries | EQ-5D: 0.66 severe |
| Scalone et al. 2006[73](#_ENREF_73) | Retrospective, prevalence-based cost of illness study | 98 |  | Moderate to severe and flare-up |   | EQ-5D VAS: 65 |
| Italy |
| Silverberg et al. 2019[50](#_ENREF_50) | Cross-sectional, population-based studyValidation study | 3495 (602 AD) | 52 |  Mild to severe |   | SF-6D general: 0.69 |
| Silverberg et al. 2019[51](#_ENREF_51) | SF-6D: 0.73 mild |
|  | SF-6D: 0.64 moderate |
| USA | SF-6D: 0.59 severe |
| Simpson et al. 2017[74](#_ENREF_74) | Phase III clinical trials | 1379 | 38.3 | Moderate to severe | Subcutaneous dupilumab 300 mg once weekly, or every 2 weeks vs placebo | EQ-5D: 0.61-0.63 |
| USA |
| Steinke et al. 2014[75](#_ENREF_75)Germany | Non-interventional cross-sectional retrospective cohort study | 1678 | 38.4 |   | Emollients, corticosteroids, climate therapies, antihistaminic drugs, topical tacrolimus, PUVA, fasting therapy | EQ-5D VAS: 72.1  |
| Vietri et al. 2017[43](#_ENREF_43) | Survey-panel-based general health questionnaires(Cross sectional study?) | 548 | 45 | Moderate to severe |   | EQ-5D: 0.79 moderate  |
| UK, Germany, France | EQ-5D: 0.61 severe |
| Vinding et al. 2014[46](#_ENREF_46) | Case-control study | 439(180 AD) | 30-86 |  |   | EQ-5D: 0.84  |
| Denmark | EQ-5D VAS: 76.8 |

Abbreviations: AD = atopic dermatitis; MCS = mental component score; PCS = physical component score; SF-36 = short form 36 health survey; SF-6D = short form 6 dimensions; VAS = visual analog scale

Appendix Table 5 Chronic Hand Eczema Studies Data Extraction

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study and Country** | **Study type** | **Number of patients** | **Mean age** | **Disease severity** | **Treatment** | **Results by instrument** |
| Blank et al. 2010[76](#_ENREF_76) | Markov model |  |  | Mild to moderate CHE | Alitretinoin | EQ-5D: 0.76  |
| Switzerland |
| Cortesi et al. 2014[54](#_ENREF_54) | Cost of illness | 110 | 44.5 |  Severe CHE |   | EQ-5D: 0.50 |
| Italy |
| Di Benedetti et al. 2015[55](#_ENREF_55) | Survey based | 163 | 47.1 | Severe CHE |   | EQ-5D: 0.80 |
| USA | EQ-5D VAS: 74.2 |
| Gola et al. 2013[77](#_ENREF_77)  | Observational | 15 | 44 | Severe CHE | Alitretinoin | EQ-5D VAS: 42 |
| Italy |
| Küster et al. 2018[53](#_ENREF_53)  | Cross-sectional | 158 |  | Mild and severe CHE |   | EQ-5D: 0.92-0.97 mild |
| Germany | EQ-5D: 0.75-0.77 severe |
| NICE TA177, 2008[52](#_ENREF_52) |  |  |  | Moderate and severe CHE |   | EQ-5D: 0.81 mildEQ-5D: 0.71 moderate |
| UK | EQ-5D: 0.58 severe |
| Ofenloch et al. 2014[78](#_ENREF_78) | Validation study | 316 | 46.7 |   |   | EQ-5D: 0.84 |
| Germany |
| Thaci et al. 2016[79](#_ENREF_79) | Observational | 631 |  | Severe CHE | Alitretinoin | EQ-5D: 0.76 |
| Germany | EQ-5D VAS: 53.6 |
| Van Gils et al. 2013[56](#_ENREF_56)  | Economic evaluation | 196 |  | Moderate to severe CHE |  | EQ-5D VAS: 36.4  |
| Netherlands |

Abbreviations: CHE = chronic hand eczema; VAS = visual analog scale

Appendix Table 6 Chronic Condition Reviews Data Extraction

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Review** | **Number of studies** | **Disease** | **Time Frame** | **Results by instrument** |
| Alhaji et al. 2018[62](#_ENREF_62) | 13 | Chronic kidney disease | Apr 2007-Apr 2017 | SF-36 PCS: 38-68.2 SF-36 MCS: 37.5-76.4 |
| Ali et al. 2016[66](#_ENREF_66) | 99 | Psoriasis | Up to Nov 2014 | SF-36 PCS: 32.7-56.2 SF-36 MCS: 35.7-52.4 |
| Beaudet et al. 2014[80](#_ENREF_80) | 19 | Type 2 diabetes | Earliest available-May 2012 | EQ-5D: 0.71-0.94 |
| Buchanan‐Hughes et al. 2019[81](#_ENREF_81) | 26 | Chronic hepatitis C | Earliest available-31 Aug 2017 | EQ-5D: 0.41-0.95  |
| Dyer et al. 2010[60](#_ENREF_60) | 66 | Cardiovascular disease | Jan 1988- Oct 2008 | EQ-5D: 0.24-0.90 EQ-5D VAS: 37-89 |
| Golicki et al. 2016[59](#_ENREF_59) | 15 | Multiple myeloma |   | EQ-5D: 0.17-0.92EQ-5D VAS: 18.7-77.5 |
| Gu et al. 2019[82](#_ENREF_82) | 36 | Systemic Lupus Erythematosus | Up to 15th December 2017 | SF-36 PCS: 45.46-61.44 SF-36 MCS: 51.41-62.12 |
| Harrison et al. 2008[63](#_ENREF_63) | 26 | Rheumatoid arthritis | 1980-mid 2006 | EQ-5D: 0.43-0.75 SF-6D: 0.55-0.70 |
| Honorè et al. 2018[83](#_ENREF_83) | 3 | Autoimmune hepatitis | 2007-2011 | SF-36 PCS: 40.62 SF-36 MCS: 46.43 |
| Hughes et al. 2014[84](#_ENREF_84) | 31 | Breast and prostate cancer |   | EQ-5D: 0.55-0.90 |
| Janssen et al. 2011[85](#_ENREF_85) | 59 | Type 2 diabetes | 1987-2009 | EQ-5D: 0.2-0.76EQ-5D VAS: 45-80 |
| Kennedy-Martin et al. 2015[86](#_ENREF_86) | 12 | Diabetic kidney disease | Jan 2000-Jul 2013 | EQ-5D: 0.33-0.81 |
| Lee et al. 2016[87](#_ENREF_87) |   NR | Heart failure |   | EQ-5D VAS: 63 |
| Li et al. 2018[88](#_ENREF_88) | 7 | Systemic sclerosis | Up to Apr 2017 | SF-36 PCS: 31.20-52.80 SF-36 MCS: 37.40-68.30 |
| Matcham et al. 2014[61](#_ENREF_61) | 31 | Rheumatoid arthritis | 1992-2012 | SF-36 PCS: 22-46.1 SF-36 MCS: 30.3-60.8 |
| McLernon et al. 2008[89](#_ENREF_89) | 30 | Liver disease | 1966-Sep 2006 | EQ-5D: 0.67-0.75 EQ-5D VAS: 57-70 |
| Mlynczak et al. 2016[58](#_ENREF_58" \o "Mlynczak, 2016 #575) | 22 | Lymphomas |   | EQ-5D: 0.37-0.98 |
| Młyńczak et al. 2016[57](#_ENREF_57) | 18 | Leukemia |   | EQ-5D: -0.18-0.98 |
| Pickard et al. 2007[90](#_ENREF_90) | 34 | Cancer | Jan 1988-Jan 2006 | EQ-5D: 0.33-0.93 EQ-5D VAS: 43-84 |
| Poku et al. 2013[91](#_ENREF_91) | 17 | Visual conditions | MEDLINE: 1946-Feb 2012 EMBASE: 1980-2009 Econlit: 1969-2009 CINAHL: 1994-2009 | EQ-5D: 0.65-0.89  |
| Smith et al. 2013[64](#_ENREF_64) | 109 | Cardiovascular diseases | Sep 1992-Sep 2012 | EQ-5D: 0.21-0.88 SF-6D: 0.87-0.88 |
| Thein et al. 2005[92](#_ENREF_92) | 19 | Chronic Hepatitis C | Up to Aug 2003 | EQ-5D: 0.67-0.82 |
| Tosh et al. 2012[93](#_ENREF_93) | 31 | Visual conditions | 2001-2010 | EQ-5D: 0.64-0.89 EQ-5D VAS: 65-74.7 SF-6D: 0.66 |
| Tran et al. 2018[94](#_ENREF_94) | 33 | Melanoma |   | EQ-5D: 0.79-0.86 |
| Yang et al. 2016[95](#_ENREF_95) | 38 | Ankylosing spondylitis | Up to Jan 22nd 2016 | SF-36 PCS: 45.93-58.17SF-36 MCS: 47.49-62.52 |

Abbreviations: MCS = mental component score; PCS = physical component score; SF-36 = short form 36 health survey; SF-6D = short form 6 dimensions; VAS = visual analog scale

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