Review of Utility Estimates in Atopic Dermatitis

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OBJECTIVES

- To identify and review published utility estimates in atopic dermatitis (AD).
- To catalogue the methods of utility assessment, patient populations studied, and economic evaluations incorporating the utility estimates.

METHODS

- We searched and reviewed the published literature, including health technology assessments (Table 1).

Table 1. Utility Search Terms

Search Terms	Results
1. "1999" [Publication Date]: "3000" [Publication Date] AND "Dermatitis, Atopic" [MeSH] Limits: English	5,205
2. "Quality of Life"[MeSH] OR "standard gamble" OR "time trade off" OR "time trade-off" OR TTO OR EuroQol OR EQ5D OR EQ-5D OR "quality of well being" OR "health utility index" OR "health utilities index" OR HUI OR SF-6D OR QALY OR "Quality adjusted life year" OR "Quality-adjusted life year" OR "Quality adjusted life-year" OR "Quality-adjusted life-year" OR cost-utility OR cost utility OR utility OR utilities Limits: English	112,890
3. "Letter"[Publication Type] OR "Comment"[Publication Type] OR "Editorial"[Publication Type] Limits: English	499,112
1 AND 2 NOT 3	196

RESULTS

Literature Review

- A review of 196 titles and abstracts identified 77 potentially relevant articles.
  - Of those, 12 articles described utility estimation efforts in AD.[1-12]
  - Within those 12 publications, 15 sets of utilities in AD were presented.
    - Garside and colleagues[5] presented three sets of otherwise unpublished utilities for AD. One set was produced by the consultancy MERG (Medical Economics Research Group) and submitted by Novartis as part of their proprietary submission to NICE for pimecrolimus. Two sets were generated by the authors.
    - Poole and colleagues[8] presented two sets of utilities in AD.

Utility Estimates for AD with No Differentiation for Severity

- Two of the publications[1,7] presented only a single estimate of utility in AD, and one[10] presented utility estimates for controlled and uncontrolled AD only, rather than utility estimates varying by disease severity (Table 2).
  - This data limitation may explain why these utility studies have not been used in any economic evaluations of treatments for AD, although the study by Lundberg and colleagues[7] was reviewed briefly by Garside and colleagues[5] as part of their health technology appraisal of topical calcineurin inhibitors (TCIs) in AD.

Table 2. Utility Estimates for AD With No Differentiation by Severity

Reference	Number of Subjects With AD[a]	Data Collection Method and Setting	Measurement Technique	Mean Utility
Chen et al., 2004[1]	5	Interviews Various dermatology clinics in the US	TTO	0.890
Lundberg et al., 1999[7,b]	132	Questionnaire and interviews Dermatology outpatient clinic in Uppsala, Sweden (November 1996-December 1997	TTO SG	0.93 0.98
Schmitt et al., 2008[10]	58 Plus a random sample (n = 139) of the general population in Dresden, Germany	Computer-assisted interviews in Germany	TTO	Population-based utility estimates: Controlled AD: 0.97 Uncontrolled AD: 0.64

SG = standard gamble; TTO = time trade-off; US = United States.

[a] Studies also included patients with other skin diseases.

[b] Mean Dermatology Quality of Life Index (DLQI) score was 7.31, indicating (per Garside et al.[5]) that perhaps the subjects had severe AD.

Utilities Estimated Using Algorithms Applied to Short-Form Health Surveys

- One study by Wollenberg and colleagues [12] described a method of estimating utilities by converting trial-based SF-36 scores, using an established algorithm published by Brazier et al.[13]
  - The study reported only changes in utility, rather than absolute utilities for AD; therefore, this study is not considered further in this discussion.
- In two separate studies, Poole and colleagues[8,9] estimated utilities for AD using a method based on SF-12 responses (Table 3).

Table 3. Utility Estimates Based on Short-Form Health Surveys

Reference	Number of Subjects With AD	Source of Assessment	Measurement Technique	Mean Utility
Poole et al., 2009[8]	257	Screening data for patients with AD enrolled in an RCT[a]	• Applied the response mapping algorithm developed by Gray et al.[14] to predict individual EQ-5D[b] responses from SF-12 responses • Applied Monte Carlo bootstrap simulation, per the recommendation of Gray et al.[14] • Mapped SF-6D scores from SF-36 responses • Applied the UK tariffs for EQ-5D and SF-6D to estimate utilities	**EQ-5D:** Mild (median): 0.848 (IQR 0.704-0.882) Moderate (median): 0.796 (IQR 0.737-0.876) Severe (median): 0.760 (IQR 0.661-0.823) **SF-6D:** Mild (median): 0.800 (IQR 0.734-0.863) Moderate (median): 0.800 (IQR 0.723-0.863) Severe (median): 0.754 (IQR 0.632-0.800)
Poole et al., 2010[9]	926	Baseline data for patients with moderate to severe AD enrolled in an RCT[c]	• Used the response mapping algorithm developed by Gray et al.[14] to predict individual EQ-5D responses from SF-12 responses • Applied the UK tariff for EQ-5D to the predicted EQ-5D responses to estimate utilities • Applied the Monte Carlo bootstrap, per the recommendation of Gray et al.[14]	Moderate: 0.770 (SD +/- 0.157) Severe: 0.665 (SD +/- 0.225)

IQR = interquartile range; RCT = randomized controlled trial; SD = standard deviation.

[a] The study was a 6-month, multicenter, double-blind, phase 3 trial of the efficacy and safety of a tacrolimus ointment regimen compared with a standard corticosteroid ointment regimen in adults with moderate to severe AD (the European Tacrolimus Ointment Study). The study was conducted in 57 centers from 12 European countries from November 2000 to May 2002. Baseline was day 1 of the trial.

[b] EQ-5D = the Euroqol group's health status assessment questionnaire.

[c] The study investigated long-term maintenance treatment with tacrolimus ointment in adults with AD. Following open-label treatment with tacrolimus twice daily for up to 6 weeks, patients were randomized to a double-blind "disease-control period" of 12 months comparing tacrolimus ointment, used twice weekly as maintenance treatment, with an emollient vehicle.

Utility Estimates for AD in Children

- Of the remaining utility studies, two were specific to AD in children[4,11]; although, the estimates produced by Friedman and colleagues[4] have been used in an economic analysis in adults also (Table 4).[2]

Table 4. Utility Estimates for AD in Children

Reference	Number and Description of Subjects	Data Collection Method and Setting	Measurement Technique	Mean Utility
Friedman et al., 2004[4]	3,539 parents of children aged 3 months to 18 years, with 29% of parents having children with a history of AD	Web-based survey in the US asking for parents' assessment of children's AD	VAS[a,b]	Mild: 91[c,d,e] Mild/moderate: 84[c,d,e] Moderate: 73[c,d,e] Moderate/severe: 61[c,d,e] Severe: 49[c,d,e]
Stevens et al., 2005[11]	150 members of the general population	Interviews in the UK	SG	Utility estimates for 16 child-centered health states (reflecting 4 key aspects of AD health in children) ranging from 0.841 (no problems on any of the 4 aspects of health) to 0.356 (problems with all 4 aspects of health)[f]

VAS = visual analog scale.

[a] Reported by the authors on a scale ranging from 0 to 100.

[b] VAS scores typically are converted to utilities using an algorithm that reflects attitudes toward risk (utility score = 1 – [1 – VAS score]$^{\alpha}$, where α reflects attitudes toward risk and $\alpha > 1$ assumes risk aversion[15]); therefore, unconverted VAS scores, such as the ones reported by Friedman et al.,[4] typically are not directly comparable to utility estimates derived via the SG or TTO methods.

[c] Garside and colleagues,[5] in the UK, converted the VAS scores published by Friedman et al.[4] (assuming an α of 2.4) into estimates of utility for 5 levels of severity of AD: mild: 0.9970; mild to moderate: 0.9876; moderate: 0.9571; moderate to severe: 0.8971; and severe: 0.8052.

[d] Coyle and Barbeau,[2] in Canada, converted the VAS scores published by Friedman et al.[4] (assuming an α of 1.95) into estimates of utility for 4 levels of severity of AD, (having ignored Friedman's estimate for mild to moderate AD): Investigator Global Assessment (IGA) 1: 0.99; IGA 2: 0.92; IGA 3: 0.84; IGA 4: 0.74.

[e] Ellis and et al.,[3] in the US, converted the VAS scores published by Friedman et al.[4] (assuming an α of 1.6) into estimates of utility for 4 levels of severity of AD: IGA 0/1: 0.98; IGA 2: 0.95; IGA 3: 0.88; and IGA 4/5: 0.72. (It is unclear how the 5 health states described by Friedman and colleagues[4] were mapped to the 4 levels of severity used by Ellis and colleagues.[3])

[f] Garside et al.[5] converted the estimates eventually published by Stevens et al.[11] into estimates of utility for 3 levels of severity of AD: mild: 0.8625; moderate: 0.69; severe: 0.59.

Utility Estimates in Economic Evaluations

- In addition to the use in economic evaluations of the utilities presented in Table 4 (see footnotes), several economic evaluations generated their own estimates of utility in AD.
- The utility estimates presented by Poole and colleagues[9] were used within that publication to estimate informally the cost-effectiveness of treatment of adults with moderate to severe AD with tacrolimus ointment compared with topical corticosteroids.
- Garside and colleagues[5] used an economic model (referred to as the PenTAG model) to estimate the value of TCIs in children and adults with AD.
  - For children with AD, the authors used the utility estimates eventually published by Stevens and colleagues.[11]
  - For adults with AD, the authors used utility estimates generated from a small study conducted with the Utility Panel.
    - The Utility Panel[16] is a collaborative project in the UK run by PenTAG, the University of Southampton, and the University of Sheffield.
    - The aim of the project is to gather valid UK population-based utility estimates for a variety of diseases for use in economic evaluation.
    - At the time Garside and colleagues' health technology appraisal was published,[5] the Utility Panel included 15 lay people from Exeter, UK, who were trained in the SG method of assessing utilities.
    - Although not explicitly stated, it is implied that the 15 members of this initial panel provided SG estimates of the utility of AD.
- In addition, Garside and colleagues[5] described otherwise unpublished utility estimates outlined by Novartis in their proprietary submission to NICE in support of the health technology appraisal of pimecrolimus.
  - These utility estimates were generated by MERG for Germany and Switzerland using the EQ-5D, with population utility weights estimated from a German sample.
- Garside and colleagues[5] also described the results of a small utility study (N = 4) conducted with members of the Expert Advisory Group (EAG) consulting with the authors on the health technology appraisal of TCIs in AD (Table 5).
  - The authors asked the EAG to estimate the degree of impairment in mild, moderate, and severe AD, respectively, using the EQ-5D descriptive system and using VAS scores.

Table 5. Otherwise Unpublished Utility Estimates Presented by Garside et al.[5]

AD Severity	MERG	Utility Panel	EAG (EQ-5D)	EAG (VAS)
Very mild	0.89	—	—	—
Mild	0.76	0.985	0.691	0.945
Moderate	0.71	0.875	0.689	0.780
Severe	0.60	0.675	– 0.154	0.505

- Hjelmgren and colleagues[6] conducted a cost-effectiveness analysis of tacrolimus ointment versus corticosteroids in patients with moderate to severe AD in Sweden.
  - The efficacy of tacrolimus and corticosteroids was taken from a clinical trial.
  - The utility estimates were gathered from a VAS included in a mail survey in Sweden that produced 248 responses.
  - The health states described in the survey were based on the definitions of improvement included in the clinical trial. The health states, and corresponding utilities, were as follows:
    - Virtually cleared (a 90%-100% improvement from baseline): 0.7960
    - Moderate (30%-89% improvement from baseline): 0.5843
    - Severe, first-line therapy (< 30% improvement from baseline or worsening of symptoms with first-line therapy): 0.4205
    - Severe, second-line therapy (patients who do not respond to first-line treatment and therefore switch to second-line therapy [a mixture of corticosteroids]): 0.3194.

Other Findings

- No studies considered whether AD was affecting particularly sensitive parts of the body (e.g., face).
- The location of AD, as well as AD's effect on sleep, may be important from a quality-of-life standpoint. Two studies[4,11] included sleep as a consideration of severity in their AD health states.
- The health states used as the basis for the utility estimation varied greatly across studies. Only two studies mapped utilities to IGA scores[2,3] (see Table 4), and their methods were unclear.

CONCLUSIONS

- There are several published studies presenting utility estimates in AD; however, they vary greatly in terms of methods employed.
- Economic evaluations in AD, the results of which are sensitive to uncertainty in utility inputs, have relied on various estimates.

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DISCLOSURE

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