Systematic Review of Cost-Effectiveness Analyses of Treatments for Psoriasis

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Abstract

Objectives: To systematically review the current literature on cost-effectiveness analysis (CEA) of existing treatment options for psoriasis, assess the quality of these studies, and summarize the evidence on the drivers of cost-effectiveness.

Methods: A literature search using Medical Subject Headings and keywords was performed in the databases, MEDLINE, EMBASE, NHS EED and HTA; the CEA Registry was searched using keywords only. All references within the relevant review articles were examined manually. Two researchers independently determined the final articles and a third researcher resolved any discrepancies. We evaluated study quality in terms of the study perspective, effectiveness measures, cost measures, economic model, and time horizon. Any sensitivity analyses conducted in the studies were examined to identify the drivers of cost-effectiveness, which are any variables leading to changes in the study conclusions.

Results: Fifty-three articles were included in our final review: about 70% did not consider costs related to adverse events; approximately one-quarter used Quality-Adjusted Life Years; 34% were short-term analyses with a time horizon under one year. Thirty-eight studies conducted a sensitivity analysis, in 18 of which could have a potential impact on the final cost-effectiveness results due to uncertain variables. The key drivers of cost-effectiveness included the costs related to the treatment, efficacy, utility values, and hospitalization for non-responders.

Conclusions: High quality cost-effectiveness studies are required to facilitate resource allocation decision-making. To improve study quality, future research should provide evidence on the long-

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term experience with psoriasis treatments and resolve the uncertainty associated with key s of cost-effectiveness.

Key Points for Decision Makers

- Most cost-effectiveness analyses of psoriasis treatments are of low quality, with short time horizons, non-comparable effectiveness measures, incomplete cost measures, or no sensitivity analysis.
- Cost related to treatment, hospitalization for non-responders, efficacy, and utility values are the key drivers of cost-effectiveness of psoriasis treatments.
- Future studies are required to provide evidence on the long-term experience with psoriasis treatments and resolve the uncertainty associated with key drivers of cost-effectiveness.

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1. Introduction

Psoriasis is a common, chronic inflammatory disease of the skin. The prevalence of psoriasis in adults varies from 0.91% (United States) to 8.5% (Norway) and its incidence varies from 78.9/100,000 person-years (United States) to 230/100,000 person-years (Italy) [1]. Psoriasis has a major impact on patients' physical and mental function, as well as their quality of life [2]. Furthermore, psoriasis is associated with increased health care resource use and costs [3].

Psoriasis mostly affects Caucasians [4], typically with onset between the ages of 15 and 30 years and with comparable frequency among males and females [5]. Despite a wide range of treatment options, including topical therapy, phototherapy, traditional systemic therapy, and biologic agents, psoriasis remains incurable, with relapses and remissions [6]. First-line therapies, conventionally prescribed for mild psoriasis, are topical agents such as emollients, tar, steroids, and vitamin D analogues. Second-line therapies, conventionally prescribed for moderate-to-severe psoriasis, include phototherapy and traditional systemic agents such as Methotrexate, Cyclosporine, and Acitretin. Patients who fail to achieve response with, or are ineligible for, both first- and second-line therapies are prescribed biologic agents (such as Etanercept, Infliximab, Ustekinumab, Adalimumab), which were introduced in 2003 [6–8].

Cost-effectiveness analysis (CEA) is widely used to assist decision makers to select the most appropriate treatments within constrained health care system budgets. A great number of CEAs on the various treatments of psoriasis have been published in the medical literature in recent years. To ensure resource allocation decisions are informed by high quality evidence, it is critical to assess these economic evaluations. While several systematic reviews have been conducted on

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previously published CEAs [9,10], their focus has been on only biologic therapies [9] or subsequent treatments after failure of the first biologic [10]. There has been no comprehensive assessment of the quality of these CEAs and key drivers of cost-effectiveness (i.e., variables leading to changes in study conclusions) have not been identified. This study systematically reviewed all CEAs of psoriasis treatments, examined the quality of these studies, and summarized the evidence on drivers of cost-effectiveness.

2. Methods

2.1. Literature Search

A systematic literature search using the databases MEDLINE, EMBASE, NHS EED and HTA (produced by the University of York Centre for Reviews and Dissemination), and the CEA Registry was performed to identify all CEAs of psoriasis treatments until November 13, 2013. The NHS EED search filter [11] was applied to identify all economic evaluations in MEDLINE and EMBASE (Appendix-I). The keywords and Medical Subject Headings (MeSH) for psoriasis were used to capture relevant economic evaluations in all databases except the CEA Registry, in which only keywords were used. In addition, we manually examined all references within the relevant review articles to identify potentially overlooked studies. Although no language exclusions were applied, only those published in English were included in the final review.

2.2 Eligibility Criteria

Study inclusion was determined by two researchers independently (NI and CM). During the first stage, titles and abstracts of all articles identified by the literature search were screened. Articles were excluded if the study was not about psoriasis (psoriatic arthritis was excluded), psoriasis

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treatment, or economic evaluation, or if they were conference abstracts, letters/editorials, conference reports, errata, or book chapters. Next, the full texts of all articles deemed eligible from the previous stage were reviewed to further confirm their eligibility. At this stage, the exclusion criteria were burden of illness studies, cost analyses, study types other than economic evaluations, review articles, editorials or reports, or articles not written in English. Any discrepancies between the two reviewers were resolved by consensus with input from a third reviewer (WZ).

2.3. Data Extraction and Qualitative Synthesis

For each study included in the final review, data were extracted into a table. The information extracted included authors, country, study year, comparators, population characteristics, study design, time horizon, perspective, data sources, effectiveness, cost, sensitivity analysis, and conclusions. A qualitative synthesis was performed and the studies were summarized according to different treatment types.

2.3.1. Quality Assessment

The quality of the cost-effectiveness studies was first independently assessed by two reviewers (NI and CM) using the Quality of Health Economic Studies (QHES) instrument developed by Chiou *et al*. [12]. This scheme took into consideration Drummond's Checklist and the US Public Health Service Panel on Cost-Effectiveness in Health and Medicine. Although there are other instruments that can evaluate the quality of health economic studies, such as the British Medical Journal checklist [13], the Canadian Guidelines [14], and the Journal of the American Medical Association (JAMA) user's guide [15,16], the QHES instrument was used because it is the only

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validated instrument [17]. Consisting of 16 questions, this instrument was designed to quickly assess the common types of health economic evaluations including cost-effectiveness and cost-utility analyses [18]. For each question, a rating of "yes" or "no" was assigned by the two reviewers independently. Once again, the two reviewers discussed the discrepancies until consensus was reached with input from WZ. Data were presented as the proportion of articles reporting each of the 16 items. Furthermore, we evaluated the quality in terms of the study perspective, effectiveness measures and their data source, cost measures, economic model, and time horizon.

2.3.2. Sensitivity Analysis and Drivers of Cost-effectiveness

For each article included in the final review, we examined whether a sensitivity analysis was executed. Sensitivity analysis in CEAs is key to identifying the drivers of cost-effectiveness, as it identifies which variables may potentially change study conclusions. If a sensitivity analysis was conducted, we captured what uncertain parameter estimates were considered, their impact on the study conclusions, and what drivers of cost-effectiveness were identified.

3. Results

3.1. Literature Search

The literature search identified 2,617 abstracts: 695 from MEDLINE, 1,787 from EMBASE, 120 from NHS EED and HTA, 15 from CEA Registry, and 10 from the hand search of the references from relevant review articles (Figure 1). After the initial screening of all titles and abstracts, 500 articles were selected for full-text review. A total of 53 articles were included in the final review

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after excluding burden of illness and cost analysis studies, non-economic evaluation studies, reviews, editorials, reports, non-English studies, and non-downloadable articles.

Most of the studies included in the review were from North America [19–40] and Europe [41–67], with one multisite study across North America and Europe [68] and one each from India [69], Israel [70], and Japan [71]. More than three-quarters (77.8%) of the studies were published after 2003, in the post-biologic era.

3.2. Quality Assessment

The majority of the studies reported objectives, sources of variable estimates, methodology of data abstraction, measurement of costs, and primary outcome measures (Table 1). However, approximately 40% of the studies only estimated the cost-effectiveness ratios (e.g., cost per responder) for each treatment option but did not undertake an incremental analysis of the treatment alternatives. About 60% of the CEA studies applied a time horizon that was truncated, meaning they did not allow time for all relevant and important outcomes to be observed. For example, discontinuation or failure of treatment, potential adverse events, or hospitalization over time were often excluded as they were not likely to occur within the short time horizon adapted for the CEA. The measurement of costs was not appropriate in approximately 40% of the studies, either because they considered only the costs of the specific treatment options or because they disregarded the costs related to adverse events (please see Section 3.3.3). More than 30% did not explicitly mention the source of funding for their study and approximately one in four studies discussed potential biases.

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3.3. Synthesis of CEA Studies

Data on CEAs extracted from the selected studies are summarized in Table 2. About one-third (n = 17) of the studies compared the cost-effectiveness of biologic therapies while only about a quarter (n = 13) were on topical therapies only. A little over one-third (n = 18) compared therapies from more than one group of psoriasis treatment modalities described above.

3.3.1. Perspective

More than half of studies (n = 29) employed a health system perspective (including the government, national health system, third-party payer, insurer, or managed care perspective). Nine (9) studies applied a broader societal perspective and 14 studies did not explicitly state the considered perspective.

3.3.2. Effectiveness

The effectiveness measures used in the various analyses included the Psoriasis Area and Severity Index (PASI) (n = 26), disease/therapy-free days/years (n = 7), and others such as clearing/success rates (n = 4). The Quality-Adjusted Life Years (QALY) gained was estimated and used in about a quarter (n = 14) of the studies reviewed. Another study conducted a CEA using utilities assessed by a visual analog scale and a cost-benefit analysis using the willingness-to-pay method. Efficacy evidence was estimated by a systematic review of the literature, which includes meta-analyses, in 32 of the studies.

3.3.3. Cost

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The costs considered in the analyses were medication (including phototherapy, as applicable) costs only (n = 9), direct health care costs without considering adverse events (n = 19), direct costs including the costs of adverse events (n = 13), direct and indirect (for example, absenteeism/unemployment) costs (n = 6), and direct and indirect costs plus the costs of adverse events (n = 6). In terms of the indirect costs, only one article took account of presenteeism, which is reduced productivity while working due to health problems.

3.3.4. Economic Model and Time Horizon

Decision analytic and Markov models were used in 13 and 12 of the studies respectively. Four studies used the "York" model developed by Woolacott *et al*. [67]; 9 studies used trial-based analysis, and 7 studies did not specify using any models. The CEA studies also varied in time horizon: less than 1 year in 18 studies, between 1 and 3 years in 25 studies, and more than 3 years in 7 studies.

3.3.5. Final Decisions

The study design, analytic methods, and comparators used were diverse across the studies; therefore determining a single conclusion based on these findings is difficult. Despite these variations, some of the agents that were found to be cost-effective were Adalimumab (n = 7), Methotrexate (n = 6), Infliximab (n = 5), Etanercept (n = 5), Ustekinumab (n = 4), Calcipotriol (n = 3), Cyclosporine (n = 2), Phototherapy (n = 2), and fixed combination of Calcipotriol/Betamethasone (n = 2).

3.4. Drivers of Cost-effectiveness

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A total of 38 studies conducted sensitivity analyses (Table 3). Among them, 25 studies conducted one-way and/or two-way sensitivity analysis to measure the impact on final outcomes when one variable or two variables (simultaneously) were changed while all other variables were held constant. One study conducted a multi-way sensitivity analysis only, by simultaneously changing multiple variables. The remaining 12 studies conducted probabilistic sensitivity analysis, either alone or with one-way, two-way, or multi-way sensitivity analysis. The most common uncertain variables considered for the analysis were cost and efficacy of the treatment. We found that in 20 studies, the uncertainty analyses had no impact on the final conclusions of the study whereas in the other 14 studies, the cost-effectiveness conclusions were definitely affected. In the remaining 4 studies, the authors either did not clearly state the threshold for final cost-effectiveness decision or present the impact results of sensitivity analyses. In these studies, there is a potential impact of uncertain variables on the cost-effectiveness conclusions.

According to the 18 studies where we found a definite impact or a potential impact of uncertain variables on the final conclusions, the key drivers included: (1) the costs of the medication or phototherapy itself, or related factors such as dosage, treatment-free response period, average wholesale price, and weight [21,22,24,27,34,43,46,50,51,71]; (2) the overall costs including medication, physician, and laboratory costs [34,61]; (3) efficacies including PASI response rate, Dermatology Life Quality Index response rate, and clearing rate [23,26,27,34,43,46,59,61]; (4) utility values, which comprised of those for different disease severity levels or PASI response health states, baseline utility values, and utility ratings for the side effects or being on waiting list [22,26,51,57,67]; (5) hospitalization assumptions for non-responders [24,62,67]; (6) others including lost productivity while hospitalized [62] and different time horizons [40].

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4. Discussion

This is the first article that searched for and reviewed the available CEA studies for all treatment options in psoriasis. We focused on assessing the quality of these studies and identifying the drivers of cost-effectiveness instead of the actual cost-effectiveness outcomes. We conclude the CEA studies of high quality should apply a reasonably long time horizon, adopt a valid and comparable effectiveness measure, consider all cost items relevant to the study perspective, and conduct a sensitivity analysis to assess the uncertainty around parameter estimates. We found only a small number of the studies met these rigorous standards [22,35,40,43,51,53,56–59,62,67].

Over 30% of CEAs of psoriasis treatments adopted a time horizon of less than one year, despite the fact that psoriasis is a chronic disease with negative impacts on health and quality of life. Although a long time horizon is preferred, information related to the long-term experience with various psoriasis treatments is largely lacking [10,67]. This includes the annual drop-out rates from therapy, the 'remission' period assumed between spells of intermittent treatment, the efficacy of subsequent lines of treatment, the cost and incidence of adverse events, and the risk of hospitalization [10,67].

A great number of these CEAs evaluated the cost per responder and the PASI was often used to identify treatment response. Regardless of its limitations [72] and other recommendations on alternative weighting in scoring [73], the PASI has been found to be reliable and valid [74]. Some researchers proposed using an alternative scoring system called the Psoriasis Assessment Severity Score (PASS) as it is more sensitive than the PASI [75]; however, the US Food and

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Drug Administration (FDA) requires PASI scores to be reported upon evaluating efficacy of new therapeutic modalities of psoriasis [76]. While PASI-75 (a 75% reduction in the PASI score) is the current benchmark in reporting the primary endpoints of psoriasis trials, PASI-50 (a 50% reduction) has also been found to be a clinically significant endpoint [77]. A variety of cut-offs have been used in the reviewed studies (PASI-50, PASI-75, and PASI-90). However, having only a disease-specific outcome such as cost per PASI-75 responder in CEAs, we could not determine the cost-effectiveness of an intervention due to the lack of a commonly accepted threshold or compare the cost-effectiveness results to cost-effectiveness found in other diseases. QALY has been widely used and identified as the most important effectiveness measure to employ in CEAs over the last decade or so [78]. The National Health Service in England and Wales uses QALY as the principal measure of health outcome as recommended by the National Institute of Health and Clinical Excellence [78], though we found that about three-quarters of the studies reviewed did not use this measurement.

When estimating direct health care costs, potential adverse events were often ignored. Only one study considered adverse events as well as the impact of treatment on work productivity including absenteeism and presenteeism. Previous studies [79,80] have found that having psoriasis was associated with substantial work productivity loss in terms of both absenteeism and presenteeism. Furthermore, indirect costs due to productivity loss could exceed the direct health care costs of psoriasis treatments. It was suggested that future effectiveness and cost-effectiveness studies on new psoriasis treatments should take into account the new interventions' impact on patient productivity and the corresponding economic burden [79,80]. Both absenteeism and presenteeism were ignored in most of the CEA studies. The omission is

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primarily due to the lack of empirical data on the work productivity impact of treatment. Future studies should incorporate the work productivity measure into the cost-effectiveness study model.

Sensitivity analysis was conducted in 38 studies. In over half of these studies, we did not find any impact of the uncertain parameter estimates of interest on the final conclusions. For the studies where we found an impact, the costs related to the treatment, treatment efficacy, utility values, and hospitalization for non-responders were the key drivers for the cost-effectiveness conclusions. Our findings may be subject to publication bias because studies may not be published if their results were highly sensitive to the uncertain parameter estimates.

One limitation of our review is that we may have missed a few CEA studies. Several CEAs were conducted directly by manufacturers [67,81–83] but the details were not published in literature; therefore they were not accessible as our search was restricted to literature publications only. In addition, we limited the final review to studies in English. Furthermore, there were 2 articles that could not be downloaded because they were studies from the early 1990s. Despite these drawbacks, we included the majority of CEA studies in literature, which enabled us to evaluate the overall quality and identify key drivers of cost-effectiveness.

In conclusion, high quality cost-effectiveness studies are needed to inform resource use decision-making for psoriasis treatments. To improve the quality, further studies should be conducted to provide evidence related to the long-term experience with different treatments and to address the uncertainty associated with the key drivers of cost-effectiveness.

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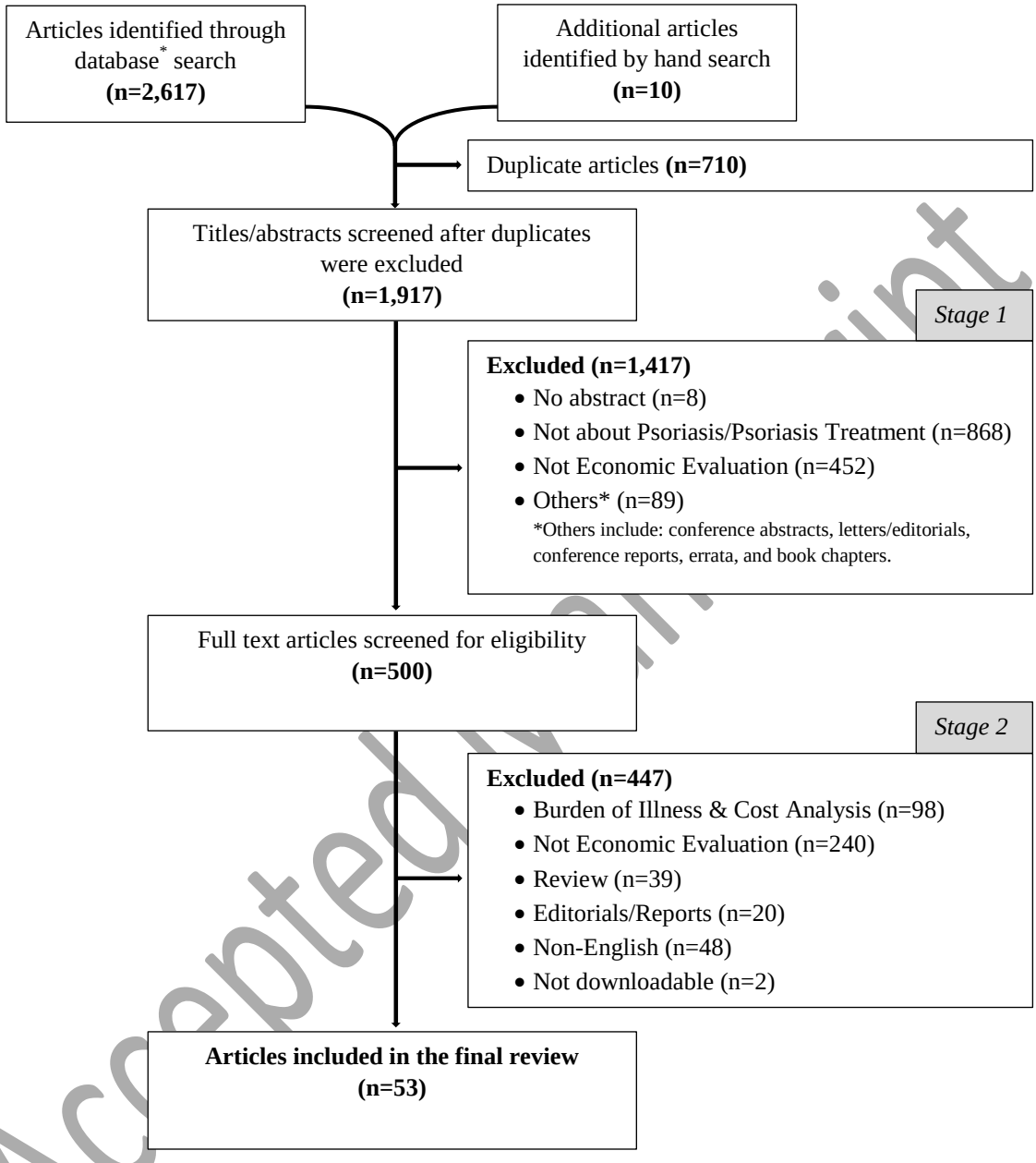

Figure 1: PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) flowchart of inclusion and exclusion of articles in the review.

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Table 1: Proportion of articles reporting each of the items* of Quality of Health Economic Studies instrument

Item	Description	N (%)
1.	Was the study objective presented in a clear, specific, and measurable manner?	52 (98.1)
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	39 (73.6)
3.	Were variable estimates used in the analysis from the best available source (i.e. Randomized Control Trial-Best, Expert Opinion-Worst)?	52 (98.1)
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	NA
5.	Was uncertainty handled by: 1) statistical analysis to address random events; 2) sensitivity analysis to cover a range of assumptions?	38 (71.7)
6.	Was incremental analysis performed between alternatives of resources and costs?	33 (62.3)
7.	Was the methodology for data abstraction (including value health states and other benefits) stated?	53 (100.0)
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3-5%) and justification given for the discount rate?	22 (41.5)
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	33 (62.3)
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and were the major short term, long term and negative outcomes included?	52 (98.1)
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	49 (92.5)
12.	Were the economic model (including structure) study methods and analysis, and the components of the numerator and denominator displayed in a clear transparent manner?	44 (83.0)
13.	Were the choice of economic model, main assumptions and limitations of the study stated and justified?	48 (90.6)
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	13 (24.5)

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15.	Were the conclusions/recommendations of the study justified and based on the study results?	53 (100.0)
16.	Was there a statement disclosing the source of funding for the study?	36 (67.9)

NA=Not applicable (in all but 5 of the articles reviewed).

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Table 2: Summary of Economic Analyses

Author(s), Study Year; Location; Cost Year; Currency	Economic question(s) addressed	Comparators	Perspectives	Patient characteristics	Time horizon	Sources of effectiveness evidence	Cost components considered	Final decisions
TOPICAL								
Ashcroft *et al*., 2000; UK; 2000; £ **[48]**	Cost-effectiveness of topical calcipotriol and short-contact dithranol	Calcipotriol vs. Dithranol	UK National Health Service	Mild-to-moderate psoriasis	12 weeks up to 1 year	Degree of improvement in psoriasis as judged by the patient	Drug costs	Short-contact Dithranol as first line treatment may help contain costs and improve outcomes in terms of more durable remission following treatment
Augustin *et al*., 2007; Germany; 2006(?); € **[49]**	Cost-effectiveness of fix Calcipotriol/Betamethasone combination compared to a morning/evening non-fix Calcipotriol/Betamethasone combination	Fix Calcipotriol/Betamethasone combination vs. a morning/evening non-fix Calcipotriol/Betamethasone combination	German Societal Perspectives	Mild-to-moderate psoriasis	48 weeks	DCD (disease controlled days); patient's assessment of change from baseline following a 6-point scale (clearance, marked, moderate or slight improvement, no change, worsening)	Medication unit costs; adverse events; UVB rescue therapy per session and visit	Fix Calcipotriol/Betamethasone combination is more cost-effective than a non-fix morning/evening combination
Augustin *et al*., 2009; Germany; 2007(?); € **[50]**	Evaluate and compare effectiveness and cost of various topical psoriasis therapies	A compound product containing Calcipotriol/Betamethasone, given once daily for 4 weeks, followed by daily Calcipotriol for 4 more weeks; (2) Tacalcitol, given once daily for 8 weeks; (3) Separate administration in the morning/evening of Calcipotriol and Betamethasone, twice daily, for 8 weeks	Not mentioned	Mild-to-moderate psoriasis	48 weeks	DCD (disease controlled days)	Drug costs; costs related to adverse effects; UVB phototherapy	Fix Calcipotriol/Betamethasone combination is a more cost-effective treatment than a treatment with the single agents or Tacalcitol monotherapy
Bergstrom *et al*., 2003; USA; NR; USD **[25]**	To test whether or not different formulations of the same medication—topical clobetasol propionate—would affect measurable outcomes	Clobetasol foam to affected skin and scalp vs. clobetasol cream to the skin and clobetasol solution to the scalp	Not mentioned	Moderate-to-severe psoriasis	2 weeks	1-point change in PASI score	Drug costs	No significant difference in cost was appreciated between foam and cream/solution over the period after controlling for body surface area
Bottomley *et al*., 2007; UK; 2006-2007; £ **[51]**	Cost-effectiveness of Calcipotriol/Betamethasone dipropionate in the initial treatment of moderate severity plaque psoriasis	Multiple treatment sequence*	National Health Service in Scotland	Moderate-to-severe psoriasis	1 year	QALY	Drug costs; GP consultation; specialist outpatient consultant consultation; specialist outpatient nurse consultation; nurse-led phototherapy course	With reduced costs and superior outcomes, the TCF (two compound formulation) 'dominated' the other treatments since the latter were associated with higher cost and lower utility or QALY gain
Colombo *et al*., 2012; Italy; 2012; € **[44]**	Cost-effectiveness of a gel containing calcipotriol and betamethasone dipropionate vs. the ointment formulation	Calcipotriol and Betamethasone dipropionate vs. the ointment formulation	Italian National Healthcare System as a third-party	Mild-to-moderate psoriasis	1 year	PASI-75	Costs of medication; fees for specialist and GP visits	The gel strategy appears to be favorable from the pharmacoeconomic point of view than the ointment formulation

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Author(s), Study Year; Location; Cost Year; Currency	Economic question(s) addressed	Comparators	Perspectives	Patient characteristics	Time horizon	Sources of effectiveness evidence	Cost components considered	Final decisions
			payer					
Devaux *et al*., 2012; France; 2010; € **[66]**	Cost-efficacy of vitamin D analogues plus topical steroids (VDS) vs. vitamin D analogues alone (VD)	Vitamin D analogues plus topical steroids (VDS) vs. vitamin D analogues alone (VD)	Not mentioned	Not mentioned	4 weeks	PASI-90 (Treatment success), and PASI-75 (Satisfactory response)	Drug costs	The cost/efficacy ratio was evaluated as 1.2–1.8 times higher for VDS than for VD
Harrington, 1995; UK; 1994 (NHS cost); £ **[45]**	Cost-effectiveness of calcipotriol ointment and "short-contact" dithranol regimen	Calcipotriol ointment twice daily for 8 weeks vs. dithranol once daily	Not mentioned	Mild-to-moderate psoriasis	8 weeks	Own outcome criteria from a scale of 1 to 4[†]	Drug costs	Calcipotriol should be used in any national treatment program for mild-to-moderate psoriasis over dithranol
Marchetti *et al*., 1998; USA; 1997; USD **[31]**	Cost-effectiveness analysis of topical therapies for patients with mild-to-moderate stable plaque psoriasis	Tazarotene 0.1%, Tazarotene 0.05%, Fluocinonide, and Calcipotriene	Third-party payer	Mild-to-moderate psoriasis	1 year	Disease-Free Days	Costs for physician visits, drug acquisition, laboratory testing, and adverse events management	Tazarotene 0.1% was the most cost-effective option
Oh *et al*., 1997; Canada; 1995; CAD **[22]**	Determine cost-effectiveness of calcipotriol compared with medium- to high-potency steroids in the management of psoriasis of limited extent that had previously been treated with betamethasone-17-valerate, 0.1%	Calcipotriene (CP), Betamethasone dipropionate (BD), Betamethasone valerate (BV), Fluocinonide (F)	Government payer perspective	Mild-to-moderate psoriasis	1 year	QALY	Costs of physician visits, laboratory tests, UVB therapy; the cost of PUVA therapy (including costs of psoralen tablets, physician fees, laboratory tests, and facilities fees to provide PUVA therapy;'; costs associated with failures and relapses (i.e., additional treatments, visits, and tests)	Calcipotriene is cost-effective alternative to medium- to high-potency corticosteroids, both as second-line therapy to Betamethasone valerate (BV) or when failure is with BV
Papp *et al*., 2012; Belgium, Denmark, Finland, France, Germany, Norway, Portugal, Sweden, and Switzerland; NR; Respective local currency **[64]**	Cost-effectiveness evaluation of Clobetasol Propionate Shampoo (CPS) maintenance in patients with moderate scalp psoriasis	Bemethson ointment Betnovat emulsion/solution, Diprolene cream, Celestan V ointment, Clarelux foam, Ecural solution Elucon solution + bucky Elucon solution, Diprosalic lotion/ Psodermil solution, Elocom solution, Dermovate sol/ Dermoval sol, Daivonex solution, Dovobet-Daivobet lotion/Xamiol gel, Vehicle, No further treatment, Maintenance CPS, Acute CPS	Payer perspective	Moderate-to-severe psoriasis	24 weeks	Disease-Free Days	Cost of physician visits and cost of interventions	Clobetasol propionate shampoo (CPS) is cost-effective in maintaining the success achieved
Peeters *et al*., 2005; France, Germany, Spain and UK; 2004; € **[65]**	Cost-effectiveness of once-daily treatment with Calcipotriol/Betamethasone Dipropionate followed by Calcipotriol alone compared with Tacalcitol in the treatment of psoriasis vulgaris	Daivobet/Daivonex, and Tacalcitol	French societal perspective	Mean PASI score ≈10; Mean age≈51 years	8 weeks	PASI-75	Drug costs, hospital stays, days of hospital attendance, physician visits, lab tests, and costs of adverse events	Calcipotriol/Betamethasone is more effective and less costly than Tacalcitol

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Author(s), Study Year; Location; Cost Year; Currency	Economic question(s) addressed	Comparators	Perspectives	Patient characteristics	Time horizon	Sources of effectiveness evidence	Cost components considered	Final decisions
Sawyer *et al*., 2013; UK; 2011; £ **[60]**	Cost-effectiveness and optimal treatment sequence for psoriasis of the trunk, limbs and scalp	Various combination of treatment sequence	UK National Health Service perspective	Patients with psoriasis of the trunk, limbs and scalp	1 year; extended to 3 and 10 years	QALY	Costs of topical agents, primary and secondary care visits and second-line therapies for treatment failures	Potent corticosteroids, used alone or in combination with vitamin D, are the most cost-effective treatment for patients with psoriasis of the trunk and limbs. Potent or very potent corticosteroids are the most cost-effective treatment for patients with scalp psoriasis.
PHOTOTHERAPY								
Aggarwal *et al*., 2013; India; NR; USD **[69]**	Compare efficacy and cost-effectiveness of PUVA vs. PUVAsol in chronic plaque psoriasis	PUVA vs. PUVAsol	Patient's and hospital's perspective	Moderate-to-severe psoriasis	12 weeks	Percentage of improvement in PASI	Costs of drugs, payment for phototherapy; consultation fee; transportation or travel cost; wages or salary lost; equipment cost; overhead costs; salaries of doctors and other staff	PUVAsol had a clinical efficacy comparable with PUVA and favourable cost-effectiveness ratio
Koek *et al*., 2010; Netherlands; 2003; € **[58]**	Costs and cost-effectiveness of phototherapy with UVB light provided at home compared with outpatient ultraviolet B phototherapy	Home vs. outpatient UVB phototherapy	Societal perspective	Mild-to-severe psoriasis	17.6 weeks (mean duration at the end of phototherapy); 68.4 weeks (mean duration one year after the end of phototherapy	QALY	Outpatient phototherapy; consultation with dermatologist, and GP; medication travelling costs; parking costs for visits to hospital; parking costs for visits to GP; absence from paid work; reduced productivity while at paid work; absence from unpaid work; side effects (that did not vary across groups)	Home UVB phototherapy is not more expensive than phototherapy in an outpatient setting and proved to be cost effective
Snellman *et al*., 1998; Spain (Finnish Patients); 1988-90; FIM **[63]**	Cost-effectiveness of heliotherapy	Time; before and after Heliotherapy	Not mentioned	Moderate-to-severe psoriasis	1 year before and after a 4-week treatment	Difference in mean Psoriasis Severity Index (PSI) ‡	Ward treatment, phototherapy in outpatient clinics, lab X-ray, physician consultations, medication at home, trips for treatments, self-arranged sun-bathing holidays, productivity loss due to absenteeism and unpaid help	The cost of heliotherapy exceeded manifold the mean monthly cost of conventional psoriasis therapy. There was no overall savings using heliotherapy in moderate to moderately severe psoriasis; it saved costs only in severe psoriasis that required expensive medication.
SYSTEMICS								

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Author(s), Study Year; Location; Cost Year; Currency	Economic question(s) addressed	Comparators	Perspectives	Patient characteristics	Time horizon	Sources of effectiveness evidence	Cost components considered	Final decisions
TRADITIONAL SYSTEMICS								
Ellis *et al*., 2002; USA; 1999; USD **[27]**	Cost-effectiveness for treating psoriasis using two strategies: one consisted principally of methotrexate and the other was principally a rotational schedule of modified cyclosporine with methotrexate.	Methotrexate-based vs. cyclosporine-methotrexate rotation treatment strategies	Payers' perspective	Moderate-to-severe psoriasis	10 years	Years clear of psoriasis	Acquisition of medications, laboratory and physician fees, and costs of treating side effects	$2700 per incremental year clear of psoriasis with the cyclosporine strategy
Hakkaart-van Roijen *et al*., 2001; Canada, Spain, Turkey, UK; 1997; USD **[68]**	The cost-effectiveness of tapered versus abrupt discontinuation of oral cyclosporine micro-emulsion for the treatment of psoriasis	Tapered versus abrupt discontinuation of oral cyclosporine	Societal perspective	Patients with chronic plaque psoriasis inadequately controlled with topical treatment	1 year	Number of systemic therapy-free days (STFDs)	Costs of medication; visits to the dermatologist; laboratory tests; costs of lost production due to illness and/or its treatment costs; adverse events (did not vary across groups)	Tapering cyclosporine was more cost effective than abruptly stopping cyclosporine
BIOLOGICS								
Ahn *et al*., 2013; USA; 2010; USD **[23]**	Determine and compare the cost-effectiveness of biologics with regard to cost per patient achieving DLQI MID, and cost per patient achieving PASI-75	Adalimumab, Alefacept, Etanercept, Infliximab, Ustekinumab; placebo	Third-party payer	Moderate-to-severe psoriasis	12 weeks; modeled for annual cost-effectiveness analysis as well	PASI and DLQI MID	Drug costs; physician visits; lab tests; intravenous infusion procedures	Intravenous infliximab 3 mg/kg was the most cost-effective biologic agent with respect to both the cost per patient achieving PASI-75 and the cost per patient achieving a DLQI MID
Anis *et al*., 2011; USA; 2007; USD **[24]**	Economic evaluation of biologics for moderate to severe psoriasis	Adalimumab, Etanercept, Infliximab, Alefacept, Efalizumab	Not mentioned	Patients who failed conventional therapies	Not clear; annualized results reported	QALY	Drug and related costs; hospitalization costs; productivity cost; justified for not using the cost of adverse events	Optimal sequence in prescribing biologics will be: Adalimumab→ Etanercept→ Infliximab→ Efalizumab→ Alefacept
Blasco *et al*., 2009; Spain; 2008; € **[41]**	Estimate the cost/efficacy ratios of Adalimumab, Etanercept, Infliximab, and Efalizumab in the management of moderate to severe psoriasis	Adalimumab, Infliximab, Etanercept, Efalizumab	Spanish National Health System payer perspective	Moderate-to-severe psoriasis	10-24 weeks	PASI-75	Drug cost only	The most efficient biologic agent in terms of the cost/efficacy ratio was Adalimumab
de Portu *et al*., 2010; Italy; 2008; € **[46]**	Cost-effectiveness analysis of Infliximab compared with other anti-TNF-α agents for the treatment of psoriasis in Italy	(1) After 24 weeks: Infliximab (5 mg/kg), Etanercept (25 or 50 mg biw, 50 mg weekly, step down), Adalimumab (40 eow); (2) After 48-50 weeks: Infliximab (5 mg/kg), Etanercept (50 mg biw, step down), Adalimumab (40 mg eow)	Italian health-care system (third party payer)	Moderate-to-severe psoriasis	24 weeks, and 48-50 weeks (based on RCTs)	PASI-75	Direct medical costs with specific reference to the cost of therapy	Infliximab seems to be cost-effective in the therapy of psoriasis
Ferrandiz *et al*., 2012; Spain;	Cost-efficacy of Adalimumab, Etanercept,	Adalimumab, Etanercept, Infliximab and Ustekinumab	Spanish National	Moderate-to-severe psoriasis	24 weeks	PASI-75	Only drug cost	Adalimumab was the most cost-efficient

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Author(s), Study Year; Location; Cost Year; Currency	Economic question(s) addressed	Comparators	Perspectives	Patient characteristics	Time horizon	Sources of effectiveness evidence	Cost components considered	Final decisions
2010; € **[52]**	Infliximab and Ustekinumab for moderate-to-severe plaque psoriasis		Health System payer perspective					
Greiner & Braathen, 2009; Switzerland; 2006; CHF **[54]**	Cost-effectiveness of biologics for moderate-to-severe psoriasis	Infliximab, Etanercept, Adalimumab, Efalizumab, Alefacept	Swiss healthcare system	Moderate-to-severe psoriasis	36 weeks	PASI-50, PASI-75, and PASI-90	Drug acquisition costs (i.e. medication, administration, and monitoring) and costs incurred by adverse events	Infliximab and Adalimumab generated the lowest ICERs at 36 weeks
Igarashi *et al*., 2013; Japan; NR; USD **[71]**	Cost-efficacy comparison of biologics for patients with moderate to severe psoriasis	Adalimumab, Infliximab, Ustekinumab	Japanese National Health Insurance (NHI)	Moderate-to-severe psoriasis	2 years	PASI-75	Drug costs	Ustekinumab was more cost-efficient than Adalimumab or Infliximab
Liu *et al*., 2012; USA; 2011; USD **[29]**	Cost per responder associated with biologic therapies	Adalimumab 40 mg eow, Etanercept 50 mg BIW, Ustekinumab 45 mg, Ustekinumab 90 mg, Infliximab 5 mg/kg	Not mentioned	Moderate-to-severe psoriasis	52 weeks	PASI-75 and PASI-90	Drug acquisition and administration costs	3-month cost per responder was lowest for Adalimumab
Martin *et al*., 2011; USA; NR; USD **[32]**	Cost-effectiveness analysis of Ustekinumab and Etanercept	Ustekinumab and Etanercept	Not mentioned	Moderate-to-severe psoriasis	16 weeks	PASI-75	Drug costs	The cost per responder was lower for Ustekinumab than for Etanercept
Menter & Baker, 2005; USA; 2003; USD **[21]**	Cost-efficacy of Alefacept, Efalizumab, or Etanercept for plaque psoriasis	1) Alefacept 15 mg IM weekly for two 12-week courses; 2) Efalizumab 1 mg/kg SC weekly; 3) Etanercept 50 mg SC twice weekly for 12 weeks followed by a maintenance dose of 50 mg weekly	Managed care perspective	Moderate-to-severe psoriasis	18 months	PASI-75	Drug costs, IM/SC injection fees, office visit fees, costs for laboratory monitoring; costs incurred due to adverse events	Cost-efficacy of Alefacept, Efalizumab and Etanercept was comparable
Nelson *et al*., 2006; USA; 2004; USD **[33]**	Cost-effectiveness of biologics in the treatment of psoriasis	Alefacept, Efalizumab, Etanercept, Infliximab, and Adalimumab	Not mentioned	Severe psoriasis	12 weeks	PASI-75 and Mean DLQI improvement	Drug cost; costs of the physician visits; required laboratory testing, and infusions	Adalimumab and Infliximab appear to be the most cost-effective biologic agents
Nelson *et al*., 2008; USA; 2006; USD **[34]**	Cost-effectiveness of biologic treatments for psoriasis	Adalimumab, Alefacept, Efalizumab, Etanercept, Infliximab	Third-party payer	Mean age range: 43-47 years; predominantly male; mean baseline PASI Score: 14.2-23.4	12 weeks	PASI-75 and DLQI MID	Costs of drug, lab, physician, and infusion; justification given for not using long-term adverse effects	Etanercept at a dose of 25 mg administered subcutaneously once weekly was the most cost-effective agent in cost per patient achieving DLQI MID; Infliximab IV at a dose of 3 mg/kg was the most cost-effective agent in terms of cost per patient achieving PASI-75 improvement
Pan *et al*., 2011; Canada; NR; CAD **[35]**	Cost-effectiveness of Ustekinumab and Etanercept in patients with moderate-to-severe plaque psoriasis	Ustekinumab vs. Etanercept	Ontario Ministry of Health	Moderate-to-severe psoriasis	12 weeks (extended to 10 years)	QALY	Drug cost; monitoring cost; outpatient visits	Ustekinumab dominated Etanercept because of lower costs and higher utility values

Author(s), Study Year; Location; Cost Year; Currency	Economic question(s) addressed	Comparators	Perspectives	Patient characteristics	Time horizon	Sources of effectiveness evidence	Cost components considered	Final decisions
Poulin *et al*., 2009; Canada; 2009; CAD **[37]**	Cost-effectiveness of biologics in the treatment of psoriasis	Adalimumab, Ustekinumab, Infliximab, Etanercept, Efalizumab, Alefacept	Not mentioned	Moderate-to-severe psoriasis	1 year	PASI-75	Drug costs	Adalimumab is the most cost-effective
Schmitt-Rau *et al*., 2010; Germany; 2009; € **[61]**	Cost-effectiveness of biological therapy in remission induction of moderate to severe plaque psoriasis	Adalimumab, Etanercept, Infliximab, and Ustekinumab	German third-party payer's perspective	Moderate-to-severe psoriasis	12 weeks	PASI-75	Drug costs; cost of physician visits; laboratory and monitoring costs, and costs of chest X-rays	Infliximab at a dose of 3 mg/kg was the most cost-effective agent. However, marked overlap of cost-effectiveness ratios was observed in sensitivity analysis
Villacorta *et al*., 2013; USA; 2011; USD **[40]**	Cost-effectiveness of Ustekinumab compared with Etanercept	Ustekinumab vs. Etanercept	US societal perspective	Moderate-to-severe psoriasis	12 weeks (extended to 3 years)	QALY	Direct cost; physician visit; costs for receiving subcutaneous injections at the physician's office; traveling, waiting, and actually receiving treatment at the physician's office	Ustekinumab 45 mg is the most cost-effective compared to Etanercept 50 mg therapy
Woolacott *et al*., 2006; UK; 2004-05; £ **[67]**	Cost-effectiveness of Etanercept and Efalizumab	Etanercept, Efalizumab, and Supportive Care	Not mentioned	Moderate-to-severe psoriasis	10 years	QALY	Cost of drugs and of their administration and monitoring, and the cost of outpatient visits and of inpatient stays; justification given for not using cost of adverse events	Both Etanercept and Efalizumab could be cost-effective depending on patient characteristics and the threshold the NHS is willing to pay per QALY
MIXED								
Chen *et al*., 1998; USA; NR; USD **[26]**	Cost-effectiveness of Methotrexate vs. Goeckerman therapy for Psoriasis	Methotrexate vs. Goeckerman therapy	US societal perspective	Mild-to-moderate psoriasis	52 weeks	Clearing rates; Utility assessed by willingness-to-pay or visual analog scale	Costs for supplies, laboratory tests, and medications; physician fees and hospital fees	Mixed findings: in severe psoriasis, only methotrexate demonstrates a net benefit. Both therapies were cost-effective compared with no therapy. Liquid methotrexate should be chosen over the tablet form since it was cheaper and had the same outcome. Goeckerman was cost-effective against liquid methotrexate in severe, but not in mild or moderate psoriasis
Colombo *et al*., 2009; Italy; 2008; € **[43]**	Cost-effectiveness of intermittent therapy with Etanercept in comparison with non-systemic therapy	Etanercept vs. non-systemic therapy	Italian National Health Service's perspective	Moderate-to-severe psoriasis	10 years	QALY	Hospitalization; day-hospital admissions; specialist medical examinations; laboratory tests and instrumental investigations; costs of	Intermittent Etanercept is a cost-effective therapeutic option compared with non-systemic therapy

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Author(s), Study Year; Location; Cost Year; Currency	Economic question(s) addressed	Comparators	Perspectives	Patient characteristics	Time horizon	Sources of effectiveness evidence	Cost components considered	Final decisions
							phototherapy or drug therapies	
de Argila *et al*., 2007; Spain; 2002/2004; € **[42]**	Cost-effectiveness analysis comparing methotrexate to PUVA for moderate to severe chronic plaque psoriasis	Methotrexate vs. PUVA	Societal (direct + indirect costs) and Public Health Service of Extremadura (direct costs only)	Moderate-to-severe psoriasis	1 year	PASI-50	Drug costs; physician visits; costs of PUVA sessions; follow-up tests; treatment to adverse reactions; costs of transport and lost working time	PUVA more cost-effective than with methotrexate. However, indirect costs (borne by patients in the Spanish Health System), are higher for PUVA therapy, a fact that raises an issue of equity
Feldman *et al*., 2003; USA; 2002; USD **[28]**	Cost-effectiveness of psoriasis therapy	Methotrexate, UVB, PUVA, Acitretin, Cyclosporine, Etanercept, Infliximab, Alefacept	Third-party payer	Moderate-to-severe psoriasis	1 year	PASI-75	Drug costs; costs of office visits during treatment; lab works	Methotrexate was the most cost-effective
Freeman *et al*., 2011; UK; 2008-09; £ **[53]**	Cost-effectiveness of psoriasis therapy in UK	Topical, phototherapy, systemic and biologics	Primary care perspective	Moderate-to-severe psoriasis	2 years	QALY	Drug costs; GP consultation fees	Calcipotriol b.d. as first line and Steroid as second line, AND Calcipotriol b.d. as first line and Two-compound formulation (TCF) are both cost-effective
Hankin *et al*., 2005; USA; 2004; USD **[20]**	Cost-effectiveness of phototherapy, oral systemic agents, and biologics	Biologics vs. oral systemic medications vs. phototherapy	US managed health care systems	Moderate-to-severe psoriasis	1 year	PASI-50 and PASI-75	Costs for medication or phototherapy; treatment administration; monitoring for potential treatment-related adverse events, and treatment of adverse events	Oral systemic medications, UV therapy, and UV therapy combined with Acitretin appear to be the most cost-effective therapies
Hankin *et al*., 2010; USA; 2008; USD **[19]**	Cost-effectiveness of treatments for moderate to severe psoriasis	Biologics vs. oral systemic medications vs. phototherapy	US managed health care systems	Moderate-to-severe psoriasis	1 year	PASI-75	Drug wholesale acquisition cost; administration of IV infusion or phototherapy; Alefacept IM injection and Infliximab IV infusion (where applicable)	Methotrexate was the most cost-effective
Hartman *et al*., 2002; Netherlands; 1998; € **[55]**	Cost-effectiveness analysis of a psoriasis care instruction programme with dithranol compared with UVB phototherapy and inpatient dithranol treatment	Psoriasis care instruction programme with dithranol vs. UVB phototherapy and inpatient dithranol treatment	Societal perspective	Moderate-to-severe psoriasis	1 year	PASI-90, and the number of clearance-days	Drug costs; hospital stay; use of the UVB unit including time of nurse; use of the day-care unit including time of nurse; dermatologist fee; nurse fee; outpatients visits dermatologist fee; GP fee; outpatients visits other specialists fee; absence from paid	UVB was most cost-effective

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Author(s), Study Year; Location; Cost Year; Currency	Economic question(s) addressed	Comparators	Perspectives	Patient characteristics	Time horizon	Sources of effectiveness evidence	Cost components considered	Final decisions
							work; travelling costs	
Heinen-Kammerer *et al*., 2007; Germany; NR; € **[56]**	Cost-effectiveness of psoriasis therapy with Etanercept in comparison to non-systemic therapy	Etanercept vs. non-systemic therapy	Perspectives of health insurance	Moderate-to-severe psoriasis	10 years	QALY	Drug costs; physician's fee; costs of side effects	Etanercept is a cost-effective measure within the German healthcare system
Knight *et al*., 2012; Sweden; 2008; Swedish kronor/€ **[57]**	Cost-effectiveness of treatment with Etanercept for psoriasis	Non-systemic therapy, Etanercept 50 mg once weekly, intermittent, and Adalimumab 40 mg every other week	Swedish societal perspective	Moderate-to-severe psoriasis	10 years	QALY	Drug cost; resource cost (administration as an outpatient visit); cost per initial treatment; cost per re-treatment following interruption; hospitalisation cost; cost of absenteeism, and cost of unemployment, due to psoriasis	Once-weekly Etanercept 50 mg, used intermittently, is a cost-effective treatment compared with Adalimumab and non-systemic standard of care
Lloyd *et al*., 2009; UK; 2006; £ **[59]**	Economic evaluation of Etanercept in the management of chronic plaque psoriasis	Etanercept 50 mg biw, Etanercept 25 mg biw, and no systemic therapy	UK National Health Service	Moderate-to-severe psoriasis	12 weeks (extended to 10 years)	QALY	Drug costs; costs of initial outpatient and follow-up outpatient visits; costs of adverse events, and inpatient days	Etanercept 50 mg biw is cost effective in the UK
Marchetti *et al*., 2005; USA; 2003; USD **[30]**	Cost-effectiveness of second line therapies of psoriasis	Calcipotriene + Corticosteroid (betamethasone), ICI (triamcinolone acetonide), Excimer Laser, UVB, PUVA (UVA + methoxsalen capsules), Anthralin + Corticosteroid (clobetasol), Tazarotene + Corticosteroid (clobetasol)	Payer's perspective	Mild-to-moderate psoriasis	1 year	Treatment-free day, and remission day	Drug costs; costs of office visits during treatment and during remission; costs of management of adverse events	Addition of the 308-nm excimer laser to the rotational mix of treatments is expected to add incremental clinical benefit for patients without incremental cost for payers
Pearce *et al*., 2006; USA; 2003; USD **[36]**	Cost-effectiveness and cost of treatment failures associated with systemic psoriasis therapies	Acitretin, Alefacept, Cyclosporine, Efalizumab, Etanercept, Infliximab, Methotrexate, NB-UVB, and PUVA	Not mentioned	Moderate-to-severe psoriasis	12 weeks	PASI-75	Physician office visits; nursing visits; and laboratory costs	Methotrexate appears to be the most cost-effective agent
Shani *et al*., 1999; Israel; NR; USD **[70]**	Cost-effectiveness of Dead-Sea Climatotherapy versus other modalities of treatment for psoriasis	Topical, phototherapy and systemic	Not mentioned	Severe psoriasis	4-24 weeks	Combined score from (1) percentage of patients cleared, (2) length of treatment, (3) mean remission, and (4) annual cost	Direct (round-trip flight, roundtrip transfer to the hotel, hotel accommodation, medical treatment, and solarium fee), and indirect costs (loss of productivity during the 4-week treatment plus 2-day flights, and treatment of possible side-effects, and the remission time)	Climatotherapy leads as the most cost-effective
Sizto *et al*., 2009; UK;	Economic evaluation of systemic therapies for	Methotrexate, Cyclosporine, Supportive care, Etanercept 25	UK National Health Service	Moderate-to-severe psoriasis	Not clear; annualized	QALY	Drug and associated monitoring and	Methotrexate and cyclosporine are cost

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Author(s), Study Year; Location; Cost Year; Currency	Economic question(s) addressed	Comparators	Perspectives	Patient characteristics	Time horizon	Sources of effectiveness evidence	Cost components considered	Final decisions
2005/2006; £ **[62]**	moderate to severe psoriasis	mg intermittently, Etanercept 50 mg intermittently, Efalizumab, Adalimumab, Etanercept, Infliximab	perspective		estimates presented		administration costs; cost of hospitalizations; cost of productivity considered in sensitivity analysis; justified for not using cost of adverse effect	effective but require monitoring for toxicities. Of the biologics, Adalimumab was the most cost effective
Staidle *et al*., 2011; USA; 2010; USD **[38]**	Cost-effectiveness of severe psoriasis therapy	Acitretin, Alefacept, Adalimumab, Cyclosporine (5 mg/kg/day), Etanercept Infliximab, PUVA, Methotrexate, NB-UVB, Home NB-UVB, Ustekinumab	Third-party payers	Moderate-to-severe psoriasis	1 year	PASI-75 and DLQI MID	Costs of medication; office visits; laboratory tests and monitoring procedures	Phototherapies and methotrexate are the most cost-effective options
Stern, 1988; USA; NR; USD **[39]**	Cost-effectiveness of topical tar therapy in psoriasis	Topical tar vs. UVB	Not mentioned	Not mentioned	Not mentioned	Cost to clearing (no PASI or DLQI)	Direct cost; transportation, parking, days of work lost, leisure days lost	Tar is NOT a cost-effective option compared to UVB
Vano-Galvan *et al*., 2012; Spain; NR; € **[47]**	Evaluate efficiency of home-based phototherapy with narrow-band UVB radiation compared with biologic drugs for the treatment of psoriasis	Home phototherapy vs. biologics (Etanercept, Adalimumab, Infliximab)	Payer's perspective	Moderate-to-severe psoriasis; n=12	16 weeks	PASI-75	Drug cost; consultation fees; screening tests; costs of phototherapy (costs of unit, delivery and collection of the unit, consultations, tests) as applicable	Home-based phototherapy with narrow-band UVB radiation was cost-effective compared with biologic drugs

* (1) TCF (Two Compound Formulation), first-choice, once daily for 4 weeks; followed by TCF, second-choice, once daily for 4 weeks; (2) Calcipotriol, first choice, once daily for 4 weeks; followed by potent steroid (BDP), second-choice, daily for 4 weeks; (3) Calcipotriol, first-choice, twice daily for 4 weeks; followed by potent steroid (BDP), second-choice, daily for 4 weeks; (4) Potent steroid (BDP), first-choice, daily for 4 weeks; followed by calcipotriol, second-choice, once daily for 4 weeks; (5) Concurrent calcipotriol, first-choice, once daily (morning) and potent steroid (BDP) once daily (evening) for 4 weeks; followed by the same regimen, second-choice, for a further 4 weeks

† (1) Satisfactory response: overall clinical response of "cleared" or "marked improvement" by both the investigator and the patient, and the cosmetic acceptability of treatment rated as "excellent" or "good" by the patient; (2) Very satisfactory response: criteria for a "satisfactory response" with addition that no lesional or perilesional irritation was experienced by the patient; (3) Satisfied patient: "satisfactory response" with exception that only the patient's overall clinical response was evaluated; (4) Very satisfied patient: "satisfied patient" but who also experienced no lesional or perilesional irritation whilst using treatment.

‡ Degree of psoriasis was estimated separately for head (h), body (b), upper limb (u) and lower limb (l) for scaling (S), thickness (T) and area (A) of skin involvement. Scaling and thickness were scored from 0 to 3 (0: no signs, 1: slight involvement, 2: moderate involvement, 3: severe involvement) and skin involvement area was scored as percentage of the body area in question. The PSI was calculated as: $0.1 * \{[0.1A_h(S_h + T_h)] + [0.35A_b(S_b + T_b)] + 0.2A_u(S_u + T_u)] + [0.35A_l(S_l + T_l)]\}$. The constants in the brackets represent the share of head, body, upper limbs and lower limbs in the total body area; the PSI can range from 0 to 60.

NR= Not Reported; USD= United States Dollar; CAD= Canadian Dollar; £= British Pound Sterling; €= Euro; FIM= Finnish Markka; CHF= Swiss Franc; NHS= National Health Service; QALY= Quality-Adjusted Life Years; PASI= Psoriasis Area Severity Index; HRQOL= Health-Related Quality of Life; DLQI= Dermatology Life Quality Index; MID= Minimally Important Difference; UVB= Ultraviolet-B; NB-UBV= Narrow-band UVB; PUVA= Psoralen + Ultraviolet A (UVA) Phototherapy; PUVAsol= Psoralen + natural sunlight; ICI= Intralesional Corticosteroid Injections; b.d.= Twice Daily; eow= Every Other Week; BIW= Twice weekly; IM= Intramuscular; SC= Subcutaneous; IV= Intravenous.

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Table 3: Summary of Sensitivity Analyses and Cost Drivers

Author(s), year	Sensitivity analysis	Impact on conclusions	Key drivers	Uncertain parameter estimates	Detailed impact of uncertainty	Details of sensitivity analysis
TOPICAL						
Ashcroft *et al*., 2000 **[48]**	One-way	No		Cost and efficacy	Success rate, drug cost per patient and doses affected the ICERs but not the cost-effectiveness conclusions.	The success rate of calcipotriol was 0.784 (instead of 0.608 in the baseline case) and the success rate of dithranol was 0.542 (instead of 0.496 in the baseline case). Different average drug costs per patient for calcipotriol and dithranol and different dose for dithranol
Augustin *et al*., 2007 **[49]**	One-way	No		Compliance with non-fix combination and effectiveness of the fix combination	No impact on final conclusions: The fix combination either dominated the non-fix combination or was more cost effective treatment.	The patients' compliance remained as observed within the studies, i.e. with transition probabilities as taken from the trials (maximum compliance of non-fix combination). The effectiveness of the fix combination of calcipotriol/betamethasone varied by ± 10%.
Augustin *et al*., 2009 **[50]**	One-way	Yes	Cost of tacalcitol	Patient compliance, effectiveness of the compound calcipotriol/ betamethasone product, cost of calcipotriol and tacalcitol	Compliance did not change the superiority of compound product. A 10% reduction in effectiveness of compound product did not change its cost-effectiveness status. The robustness of the model presented here was also supported by further sensitivity analyses. Treatment with the compound product was more cost-effective than tacalcitol therapy; only at € 0.23/g or less did tacalcitol monotherapy become equally or more cost effective. Compared with calcipotriol, the compound product remained more cost effective even if calcipotriol was free.	It assumed a maximum compliance for all treatment arms. The effectiveness of the compound calcipotriol/ betamethasone product varied by ± 10%. The costs of calcipotriol and tacalcitol were adjusted until the cost-effectiveness of morning/evening administration of calcipotriol and betamethasone or tacalcitol therapy was equal to that of the compound calcipotriol/ betamethasone product.
Bottomley *et al*., 2007 **[51]**	One-way	Yes	Cost of phototherapy, TCF at maximal possible dose, baseline utility and utility on the waiting list	Costs of phototherapy, amount of the TCF of calcipotriol and betamethasone dipropionate used (cost), baseline utility, utility on waiting list, PASI-75 per treatment option, utility gain magnitude with response and non-response, response to phototherapy, relapse rate of the comparators, duration of waiting list, topical prescribed while awaiting phototherapy, use of potent steroid other than the least costly and most commonly used namely betnovate	The cost of phototherapy, cost of TCF (assuming maximum possible use of drug), baseline utility and utility on the waiting list had the most notable influence on the model results. The variations of other parameters did not alter the conclusions.	Alternative values or plausible limits or 95% confidence interval values
Colombo *et al*., 2012 **[44]**	One-way	No		Cost of dovobet gel	No impact on the conclusions: Gel is better than ointment.	The cost of dovobet gel varied from €0.65 to €0.69.
Marchetti *et al*., 1998 **[31]**	One-way	No		Drug acquisition cost, medical care cost, efficacy, length of treatment	The rank order was stable: A large change would be necessary for tazarotene 0.1% to lose its first	The analysis assessed the degree of change needed to indicate a change to the next rank-ordered therapy.

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Author(s), year	Sensitivity analysis	Impact on conclusions	Key drivers	Uncertain parameter estimates	Detailed impact of uncertainty	Details of sensitivity analysis
					rank and 0.05% to lose its second rank; Unrealistic levels would be needed to improve calcipotriene's ranking.	
Oh *et al*., 1997 **[22]**	One-way	Yes	Cost and amount of calcipotriol and utility ratings of the side effects of fluocinonide	Success rate, cost and amount of calcipotriol used, utility ratings of the side effects of fluocinonide	The analysis was sensitive to changes in the cost and amount of Calcipotriol: Calcipotriol which was cost effective at the base case could become dominant over fluocinonide and betamethasone dipropionate. The analysis was sensitive to changes in utility ratings of the side effects of fluocinonide: Fluocinonide could become the dominant strategy. Variations in the values of other parameters did not affect the study conclusions.	Values of parameters varied by confidence intervals in the meta-analyses or a range derived from panel discussions. The mean initial usage of calcipotriol 30.6 g per week was used rather than the panel's baseline estimate of 45 g per week. The decrement in health status associated with fluocinonide approached that of calcipotriol (i.e., 0.02).
Papp *et al*., 2012 **[64]**	Probabilistic sensitivity analysis	No		Cost and efficacy	The deterministic model was stable and not sensitive to the uncertainties in application.	Simulations for probabilistic sensitivity analysis
Peeters *et al*., 2005 **[65]**	One-way	No		Cost and study follow-up completion	No impact was found on the conclusions.	Apply the non-observed period the mean cost assessed on the same treatment group for patients who completed the study follow-up, adjusted to the time left to spend until day 56. Cost-effectiveness was estimated only for patients who completed the study follow-up, defined as patients for whom medical resource data were captured for 8 weeks.
Sawyer *et al*., 2013 **[60]**	One-way and probabilistic sensitivity analysis	No		Clinical effectiveness, reduced adherence, early vs. late response, utilities, topical use, acquisition cost, referral, time horizon	For Trunk/limbs psoriasis only, base-case conclusions within the framework of the restricted-comparator scenario were insensitive to changes in efficacy, adherence, cost and time horizon; To be a cost-effective first-line treatment option, threshold analyses showed that the unit cost of TCF product would need to drop by 55–70% given perfect adherence and by 20–50% given reduced adherence. For scalp psoriasis, the conclusions of were insensitive to changes in key parameters of efficacy, adherence, cost and time horizon; A threshold analysis showed that only given a 60–70% discount would TCF product represent a more cost effective first-line treatment than potent corticosteroids alone.	Scenario analyses and a series of one-way sensitivity analyses were performed to assess how changes in one or more parameters might change the conclusions of the analysis. Simulations for probabilistic sensitivity analysis
PHOTOTHERAPY						
Koek *et al*., 2010 **[58]**	One-way, two-way, and probabilistic sensitivity analysis	No		Utility values, including costs of work absenteeism, both treatment costs using invoice prices	Identical results using the SF-6D were found. Mean costs for home phototherapy became lower than the costs for outpatient phototherapy. Combined with the gain in QALYs for home phototherapy, the alternative calculation of costs would produce dominated strategy. Overall, the conclusions did not change, i.e., the home therapy was more cost effective.	QALYs were calculated from SF-6D utilities instead of EQ-5D utilities. The costs of absence from paid work and unpaid work were calculated. The treatment costs for both interventions were calculated using invoice prices. Bootstrap resampling for probabilistic sensitivity analysis

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Author(s), year	Sensitivity analysis	Impact on conclusions	Key drivers	Uncertain parameter estimates	Detailed impact of uncertainty	Details of sensitivity analysis
SYSTEMICS						
TRADITIONAL SYSTEMICS						
Ellis *et al*., 2002 **[27]**	One-way	Potential impact depending on the threshold chosen	Relative efficacy of cyclosporine and methotrexate (clearing rate) and cost of cyclosporine	Relative effectiveness of methotrexate and cyclosporine at producing improvement and clearance, cost, rates of side effects	The relative efficacy of cyclosporine and methotrexate (i.e., the clearing rate) and the cost of cyclosporine were the only two variables that had a significant impact on the results.	The relative effectiveness of cyclosporine to produce a year of clear skin varied over a range from approximately 1 time to 20 times as effective as methotrexate. Costs varied over a wide range for a number of inputs.
Hakkaart-van Roijen *et al*., 2001 **[68]**	Multi-way and probabilistic sensitivity analysis	No		Clinical practice, healthcare system, unit costs, efficacy, climate	No indication was found that the conclusions differ substantially between countries.	Cost varied because tapered discontinuation was less expensive than abrupt discontinuation and efficacy varied because tapered discontinuation produced more systemic therapy-free days on average than abrupt discontinuation. Bootstrap resampling for probabilistic sensitivity analysis
BIOLOGICS						
Ahn *et al*., 2013 **[23]**	One-way and two-way	Yes	DLQI and PASI-75	Cost and efficacy	In a one-way analysis, the cost-effectiveness was sensitive to variations in average wholesale price and the percentage of patients achieving PASI-75 or DLQI at a level of ± 5 % and 10%. Variation of the average wholesale price resulted in a respective ± 5 % change in the cost-effectiveness ratio in all cases, and therefore, did not affect which agents were most cost effective. The cost-effectiveness varied by efficacy.	Vary the efficacies of the therapies as measured by DLQI and PASI-75 improvement and the total cost of treatment by ± 5% and ± 10% while holding all other values at their 'best estimate' or baseline value. Extreme case scenarios, both best and worst case: the lowest cost and highest clinical efficacy vs. the highest cost and lowest efficacy
Anis *et al*., 2011 **[24]**	One-way and probabilistic sensitivity analysis	Yes	Frequency of hospitalization for non-responders, weight and waste of excess drug, average wholesale price and dosage	Frequency and length of hospitalization for non-responders, weight and waste of excess drug, utility weight, drug cost, dosages	Rate of hospitalizations and assumptions regarding weight and waste of excess drug were found to be influential parameters: Changing the percentages of patients who were assumed to be hospitalized was influential to the ICERs; Changing the average length of stay from 17 to 19.5 days did not noticeably affect the results; Lowering the average patient weight from that reported in the clinical trials of adalimumab (i.e. 93 kg) to that reported in trials of infliximab (90 kg) did not affect the most cost-effective sequence of treatments. Only when the average weight was assumed to have been 90 kg and when excess drug was assumed to have been shared among patients did infliximab advance to the second treatment in the sequence. However, the rest of the sequence remained similar to the base case. Using average wholesale price instead of weighted average costs increased all costs and, in turn, increased all ICERs. Including dosages other than those recommended in product labels changed the sequence of treatments due to the differences in the drug costs.	The study adjusted the length of stay to a greater estimate (19.5 days) and explored the scenarios where 0% and 100% of non-responders were hospitalized. The assumptions on different weight (93kg to 90kg), excess wastage vs. no excess wastage assumptions, UK weights for utility, average wholesale price and including dosages other than recommended

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Author(s), year	Sensitivity analysis	Impact on conclusions	Key drivers	Uncertain parameter estimates	Detailed impact of uncertainty	Details of sensitivity analysis
Blasco *et al*., 2009 **[41]**	Two-way	No		Cost and efficacy of biologic agents	The ratio varied by both efficacy and cost but the sensitivity analysis confirmed the robustness of these figures and the conclusions did not change.	Baseline scenario, best-case scenario, worse-case scenario: cost for weight-dependent dosing and efficacy 95% confidence interval upper and lower limits
de Portu *et al*., 2010 **[46]**	One-way and two-way	Potential impact depending on the threshold chosen	Price of infliximab, cost and efficacy (PASI-75) of all treatments	Price of infliximab, cost and efficacy	ICERs were quite sensitive to price variations of infliximab and best case and worse case scenarios.	The wholesale price of infliximab varied by ± 10%. The best and the worst possible scenarios: the lowest cost and highest efficacy vs. the highest cost and lowest efficacy
Ferrandiz *et al*., 2012 **[52]**	Two-way	No		Cost and efficacy	The advantage of adalimumab was methodologically robust because it was the most cost efficient in the three scenarios.	Base case and the most and least favourable scenarios for each treatment: For infliximab, the most favourable and least favourable estimates were calculated using the 95% confidence intervals for the difference in weight between subjects with and without psoriasis. When drug was given in a single dose (e.g. adalimumab, etanercept, ustekinumab), the costs for the three scenarios were the same. The most and least favourable estimates of incremental efficacy were calculated using the upper and lower limits of the 95% confidence intervals, respectively.
Greiner & Braathen, 2009 **[54]**	One-way	No		Cost and efficacy	The variation of total treatment costs had a strong impact, changing the response rates of the initial treatment had a moderate impact, while varying the response rates of the treatment change had a relatively small impact on the ICERs at 36 weeks. However, these analyses did not substantially affect the outcomes of the cost-effectiveness model and confirmed the robustness of the model in all cases, with lowest ICERs for infliximab and adalimumab followed by higher ratios in the ranking efalizumab, etanercept, and alefacept.	Sensitivity analyses comprised a 25% and a 50% reduction of PASI-75 response for the treatment change of non-responders and the variation of total treatment costs as well as of the response rates for the initial therapies by ± 25%.
Igarashi *et al*., 2013 **[71]**	One-way	Yes	Drug costs estimated by the number of gender-specific vials necessary for infliximab	Non-weight-based efficacy for ustekinumab, drug costs estimated by the number of gender-specific vials necessary for infliximab	The sensitivity analysis with non-weighted ustekinumab 45 mg was comparable with the base case analysis, which confirmed that ustekinumab 45 mg remained the lowest cost per responder. The cost per responder for infliximab decreased due to the reduction of the annual drug cost and showed better cost efficacy than adalimumab for Year 2.	Efficacy for ustekinumab 45 mg was changed to non-weight-based PASI-75 response rate. Drug cost for infliximab was changed based on assumptions that male patients used four vials and female patients used three vials.
Martin *et al*., 2011 **[32]**	One-way	No		Time horizons, PASI-90 response rates, weights impact on ustekinumab cost	All sensitivity analyses had no impact on conclusions: The cost per responder for ustekinumab remained lower than that for etanercept.	For the week-52 analysis, PASI-75 response rates were carried forward from week 12 to week 52 for both ustekinumab and etanercept. The cost per responder at week 16 was evaluated using PASI-90 response rates. Alternate weight distributions (proportion of patients > 100 kg) were analyzed for ustekinumab.
Menter and	One-way	Potential	Median treatment-free response	Median treatment-free response	A shorter period adversely affected cost-efficacy,	> 7 months treatment-free response period for

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Author(s), year	Sensitivity analysis	Impact on conclusions	Key drivers	Uncertain parameter estimates	Detailed impact of uncertainty	Details of sensitivity analysis
Baker, 2005 **[21]**		impact (the impact results not shown)	period for alefacept and etanercept high-dose period	period for alefacept, etanercept high-dose period, duration of efalizumab therapy	whereas longer off-treatment response periods enhanced the cost-efficacy of alefacept. If the etanercept high-dose (50 mg) period was extended beyond 13 weeks, the cost-efficacy of etanercept decreased. Cost efficacy decreased with a longer duration of efalizumab therapy.	alefacept, >12 weeks of the higher doses of etanercept therapy, longer duration of efalizumab therapy
Nelson *et al*., 2008 **[34]**	One-way and two-way	Yes	Average wholesale price, costs and efficacies (DLQI and PASI-75)	Efficacies of the therapies: both DLQI and PASI-75, average wholesale price of medications, total physician costs, total lab costs	The cost-effectiveness ratios were sensitive to variations in average wholesale price and DLQI and PASI-75 efficacies at a level of ± 5% in the one-way sensitivity analysis. In analysis of extreme scenarios, significant overlap in multiple agents was observed at the 5% variance level. There was significant overlap in the cost-effectiveness ratios of all of the agents (DLQI) or multiple agents (PAIS-75) at 10% variance level.	The variables were varied by factors of ± 5% and ± 10%. Best-case and worst-case scenarios: the lowest cost and highest efficacy vs. the highest cost and lowest efficacy
Pan *et al*., 2011 **[35]**	One-way and probabilistic sensitivity analysis	No		Discount rate, time horizon, discontinuation rate, utility values for PASI scores	Sensitivity analyses did not affect the conclusions: Discontinuation rate had no effect on the model outcomes. Reducing the model's time horizon to 2 or 5 years did not change the ultimate outcome of ustekinumab dominating etanercept. Similarly, changing the discount rates did not change the outcome. The utility gain with ustekinumab versus etanercept was greater with this parameter change and thus ustekinumab remained dominant.	Discontinuation rate varied between 0 and 90%. Time horizons were reduced to 2 or 5 years. Discount rates were 0% and 3%. The utility values derived directly from EQ-5D scores from a different source were used. Simulations for probabilistic sensitivity analysis
Schmitt-Rau *et al*., 2010 **[61]**	One-way and two-way	Yes	Cost and efficacy (PASI-75)	Cost and efficacy	Cost-effectiveness ratios were sensitive to variation of both, the PASI-75 efficacy parameter and the cost in the one-way sensitivity analysis at a level of 5%. Especially varying PASI-75 efficacy led to a marked effect. This effect was most distinct in the agents showing 'low' efficacy. Cost-effectiveness ratios of the 'high-efficacy' drugs such as infliximab 5 mg/kg were barely influenced. Marked overlap of cost-effectiveness ratios was observed when cost and efficacy were varied at a 5% level in the extreme-scenario analysis, indicating differences observed may not be true differences.	One-way sensitivity analysis and extreme scenario analysis: here all variables were varied simultaneously to determine a 'best-case scenario' and a 'worst-case scenario'. PASI-75 improvement and pharmacy retail price were varied by a factor of ± 5%. This factor was chosen on the basis of the 95% confidence intervals of the pooled efficacy data from the randomized controlled trials.
Villacorta *et al*., 2013 **[40]**	One-way and probabilistic sensitivity analysis	Yes	Time horizon	Utility values, self-administration of etanercept 50 mg, discontinuation rate, drug price, time horizon, mortality, PASI-50 response rate for ustekinumab 90 mg, healthcare costs for patients in the PASI<50 health state, lost time for ustekinumab and etanercept treatments, hourly compensation, discount rate, starting doses of	These results were robust to sensitivity analyses with few exceptions: only when 100% patients administer etanercept 50 mg, ustekinumab 45 mg did not dominate etanercept 50 mg but was cost-effective; ustekinumab 45 and 90 mg were not cost effective for up to a 12-week time horizon compared with etanercept 25mg weekly and 50mg weekly.	A probabilistic sensitivity analysis explored the base-case model uncertainty with simulations.

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Author(s), year	Sensitivity analysis	Impact on conclusions	Key drivers	Uncertain parameter estimates	Detailed impact of uncertainty	Details of sensitivity analysis
				etanercept		
Woolacott *et al*., 2006 **[67]**	Probabilistic sensitivity analysis for four different scenarios	Yes	Baseline utility value assessed by baseline DLQI and hospitalization for non-responders	Baseline utility value assessed by baseline DLQI, hospitalization for non-responders	The ICERs of biologicals decreased when assuming the fourth quartile DLQI at baseline or 21-day hospitalization for non-responders, separately or altogether. When combining the two assumptions, the ICERs of biologicals were the lowest indicating they enter a cost-effective sequence at the lowest threshold.	Scenario I: fourth quartile DLQI at baseline and no hospitalization for non-responders; Scenario II: any DLQI at baseline, 21 days inpatient hospitalization when not responding to therapy; Scenario III, fourth quartile DLQI at baseline and 21 inpatient days; Scenario IV: comparison of biologicals with other systemic therapies (any DLQI at baseline and 21 inpatient days); Simulations for probabilistic sensitivity analysis
MIXED						
Chen *et al*., 1998 **[26]**	One-way	Yes	Methotrexate efficacy (clearing rate) and utilities at different severity levels	Efficacy of both Goeckerman and methotrexate, their costs, and utilities	Goeckerman efficacy did not alter its ICER to no therapy but slightly changed the ICER to methotrexate. Methotrexate efficacy did not alter its ICER to no therapy but ICER of Goeckerman to methotrexate was sensitive to methotrexate efficacy. ICERs were sensitive to variations in utilities at different severity levels.	Base case, best case and worst case scenarios: the best plausible assumption vs. the worst plausible assumption
Colombo *et al*., 2009 **[43]**	One-way	Potential impact depending on the threshold chosen	Cost of etanercept and efficacy (PASI) of etanercept	Cost of etanercept, cost of basal treatment, cost of hospitalization, efficacy and discounting rate	Cost of etanercept had more impacts on ICERs. ICERs did not differ significantly from the values obtained in the base case, in both groups of disease severity when cost of basal treatment and hospitalization cost changed. Changes in efficacy moved the ICER by 3% to 12%.	All estimates varied by ± 20%.
Feldman *et al*., 2003 **[28]**	One-way	No		Doses, modalities, efficacy	Methotrexate remained the least costly/treatment success when a range of efficacies was considered. UVB and PUVA had similar costs; Cyclosporine was more than phototherapy but less than biologicals; Acitretin and infliximab at 5mg/kg dose had similar costs when sensitivities were considered. All of other biologicals had comparable costs, remaining much more costly than any of the other treatments.	Costs varied by a range of doses (etanercept at 25 or 50 mg twice-weekly, infliximab at 5 and 10 mg/kg) and modalities (alefacept intramuscularly or intravenously). High and low efficacies were plugged into the model and were reported as negative and positive error bars respectively for each treatment.
Freeman *et al*., 2011 **[53]**	Multi-way	No		Choice of topical treatments in the reference pathway and all four treatment pathways, percentage of patients progressing through each treatment pathway, the magnitude of efficacy or costs and the option to include a new (or not commonly used) topical	Changing the reference pathway to potent steroid (first-line) and calcipotriol twice daily (second-line) had negligible impact on the results.	For example, it switched the reference pathway (now TCF first- and second-line) and treatment pathway 1 (now calcipotriol twice daily (first-line) and potent steroid (second-line) and assumed that treatment pathways 1, 2, 3 and 4 typically had 45%, 25%, 25% and 5% patients, respectively.
Hartman *et al*., 2002 **[55]**	One-way and probabilistic sensitivity analysis	No		Price of the hourly wage for a dermatologist, cost price per visit to the UVB, the cost price for short contact treatment, price for stay in hospital, number of clearance days	The impact of changes in cost prices on the mean total cost per patient was limited.	The price of the hourly wage for a dermatologist, the cost price per visit to the UVB, the cost price for short contact treatment, and the price for stay in hospital were varied; Charges, calculated costs in a teaching hospital, and the calculated costs in a

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Author(s), year	Sensitivity analysis	Impact on conclusions	Key drivers	Uncertain parameter estimates	Detailed impact of uncertainty	Details of sensitivity analysis
						general hospital were used; The lowest and the highest values of these three prices were included in the sensitivity analysis. Bootstrap resampling for probabilistic sensitivity analysis
Heinen-Kammerer *et al*., 2007 **[56]**	One-way	No		Cost of basal treatment, cost of etanercept, probability of a hospital stay	It was shown that with increasing costs of basal treatment, the incremental costs of etanercept treatment declined. Altogether, the model proved to be relatively stable. The assumed hospital costs had the greatest influence on results. By reducing the probability of a hospital stay by 30 %, the costs per QALY rose only moderately by 24,036 €/QALY. Overall, the conclusions remained.	Treatment costs for basal treatment varied between €20 and €120 per cycle.
Knight *et al*., 2012 **[57]**	One-way and probabilistic sensitivity analysis	Yes	Utilities for the PASI-75 health state and the PASI-50–74 health state	Discount rates for cost and health effects, resource costs, hospitalization costs, indirect cost, efficacy rates, utility values	Altering the discounting rates affected the ICERs but not the conclusions. One-way sensitivity analysis of the resource and indirect costs had little effect on the ICERs. This was also true of the efficacy rates. Altering the utility values for the PASI-75 health state and the PASI-50–74 health state had the largest effect on the deterministic results.	Alter discounting rates between 0% and 5%. All resource costs, hospitalization costs and cost due to loss of working hours (indirect costs) varied within a range of ± 25% from the base-case value. Alter the utility values for the PASI-75 health state to its 95% credible interval of 0.986 and reduce the utility for the PASI-50–74 health state to its 5% credible interval value of 0.751.
Lloyd *et al*., 2009 **[59]**	One-way and probabilistic sensitivity analysis	Yes	Response rate achieved in re-treatment	Baseline PASI and DLQI scores, the treatment-free period between cycles of therapy, the percentage of the response achieved on re-treatment, the number of hospital days for patients who did not respond to treatment, the number of outpatient visits required per cycle of treatment, the duration of therapy before treatment interruption, discounting rates	The cost-effectiveness of both etanercept regimens was sensitive to the assumed requirement for hospitalization in untreated individuals and to the response rate achieved in re-treatment. The analysis was found to be less sensitive to the frequency of clinic visits required for monitoring or to the method of discounting applied to future costs and benefits.	Each variable varied within a range of values. Bootstrap resampling for probabilistic sensitivity analysis
Pearce *et al*., 2006 **[36]**	One-way	No		Efficacy	No impact was found on the conclusions.	The efficacies of the agents varied by a factor of ± 5%.
Sizto *et al*., 2009 **[62]**	One-way and probabilistic sensitivity analysis	Yes	Hospitalization days for non-responders and lost productivity while hospitalized	Hospitalization days for non-responders, disutility on intermittent therapy, dosage of cyclosporine, continuous cyclosporine use, dosage of etanercept, utility values, PASI-50 response, weight, lost productivity while hospitalized, proportion of non-responders hospitalized	Changing the number of days hospitalized owing to nonresponse to treatment had an important effect: It increased the cost-effectiveness of all treatments when the number of days was increased from 21 (base case) to 39 and all treatments were considered cost effective at £30 000 threshold; When it was assumed that non-responders did not require hospitalizations, the ICERs of methotrexate and cyclosporine became positive. Including the costs of lost productivity during hospitalization increased the cost-effectiveness of all treatments because of the avoidance of this added cost to society and all treatments except infliximab were considered cost	Uncertainty was assessed using both a one-way sensitivity analysis where key parameters are sequentially changed to alternative plausible values and a probabilistic sensitivity analysis. Simulations for probabilistic sensitivity analysis

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Author(s), year	Sensitivity analysis	Impact on conclusions	Key drivers	Uncertain parameter estimates	Detailed impact of uncertainty	Details of sensitivity analysis
					effective at the threshold. The variance of other variables did not change the conclusions.	
Vano-Galvan *et al*., 2012 **[47]**	Two-way	No		Cost and efficacy	The robustness of our results was demonstrated by the sensitivity analysis, which showed home phototherapy to be more cost-effective than biologic therapy in all 3 scenarios.	Base case, best case and worst case scenarios: a 15% variation in the critical variables of effectiveness and cost

Note: Blank cells indicate 'not applicable'.
ICER: Incremental Cost-Effectiveness Ratio; TCF: Two Compound Formulation; SF-6D: Short Form-6D; EQ-5D: EuroQol-5D; QALYs: Quality-Adjusted Life Years; PASI: Psoriasis Area Severity Index; DLQI: Dermatology Life Quality Index; UVB: Ultraviolet-B; PUVA: Psoralen + Ultraviolet A (UVA) Phototherapy

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