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REVIEW

A Systematic Literature Review of Economic Evaluations and Cost Studies of the Treatment of Psoriasis, Atopic Dermatitis, and Chronic Urticaria

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ABSTRACT

Introduction: Psoriasis (PSO), atopic dermatitis (AD), and chronic urticaria (CU) are common manifestations of immunological skin and subcutaneous conditions and have been shown to have a substantial impact on the quality of life of patients. The cost of treating those conditions can also be high, as the use of biologic treatments has become more common for moderate to severe patients. In this review, we examine characteristics of economic evaluations and cost studies conducted for the three conditions.

Methods: A literature search was conducted using PubMed, Embase, and the Cochrane Library from January 1, 2016 to October 26, 2020 to identify economic evaluations where the cost of one or more drug treatment was evaluated and cost studies covering any intervention type. Each database was searched using keyword and MeSH terms related to treatment costs (e.g., health care cost, drug cost, etc.) and each condition (e.g., PSO, AD, eczema, CU, etc.).

Results: A total of 123 studies were reviewed, including 104 studies (85%) of PSO (including psoriasis, plaque psoriasis, psoriatic arthritis, and psoriasis vulgaris), 14 studies (11%) of AD, and 5 studies (4%) of CU. Seventy-two studies (59%) reviewed reported the inclusion of biologic treatments, 10 studies (8%) did not include biologic treatments, and 41 studies (33%) did not report whether or not a biologic treatment was included. While nearly all studies (98%) included direct costs, only 22 studies (18%) included indirect costs.

Conclusions: Economic evaluations for AD and CU may be needed in order to better understand the value of new treatments. Moreover, a clearer delineation for biologic treatments and indirect costs (i.e., productivity losses and gains) may be required.

Keywords: Atopic dermatitis; Chronic urticaria; Cost analysis; Economic evaluations; Psoriasis; Psoriatic arthritis; Systematic review; Treatment cost

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Key Summary Points

Why carry out this study?

With the growing use of high-cost biologic treatments for more commonly seen inflammatory skin and subcutaneous conditions such as PSO, AD, and CU, it is important that we can readily address their economic value and cost for patients and payers.

This literature review examines economic evaluations and cost studies conducted for those conditions in recent years to consider how they have been conducted and differences across conditions and types of interventions included.

What was learned from this study?

There have been far fewer economic evaluations and cost studies conducted for AD and CU compared to PSO, and very few economic evaluations for those conditions—possibly due to the more recent introduction of biologic treatments for AD and CU.

Moreover, many studies have not clearly reported about the inclusion of biologic treatments and productivity losses for patients and/or have not clearly shown the impact of their inclusion.

More studies are needed to examine the economic value of treatments for AD and CU, and the effect of the inclusion of biologic treatments and indirect costs (e.g., productivity losses/gains) should be considered.

INTRODUCTION

Psoriasis (PSO), atopic dermatitis (AD), and chronic urticaria (CU) are commonly presenting inflammatory skin and subcutaneous conditions that have been shown to have a substantial impact on the quality of life of patients [1–3]. PSO, AD, and CU are all chronic inflammatory skin diseases with a systemic treatment involving a potentially high socioeconomic impact, and for that reason they have been reviewed together in previous studies [4, 5]. In addition to skin symptoms, PSO can lead to painful joints and swelling (referred to as psoriatic arthritis) [6]. AD, also referred to as eczema, can cause itching, dry scaly skin, and recurrent eczematous patches [7]. CU (or hives) is characterized by swollen red wheals on the skin, itching, and angioedema of lips, eyelids, or throat [8]. These symptoms can lead to major hindrances in the daily lives of patients.

All three of these conditions are commonly treated conditions worldwide. PSO affects approximately 1.5% of the North American population [9]. Moreover, AD is prevalent in approximately 7.2% and 10.7% of adults and children in the United States (US), respectively, and CU has been reported to affect approximately 2–3% of the general population in the US over their lifetimes [10, 11]. In Europe, PSO has been reported to affect 1.92–5.2% of the population [9, 12]. Moreover, AD has been reported to affect 5.8% of men and 9.7% of women in Europe [12]. CU is said to affect 9.2% of the population in Europe [12]. In a study that considered the percentage of patients presenting to a number of hospital dermatology departments and dermatology clinics in Japan with various skin conditions, the prevalence of PSO was 4.4% and AD was one of the most commonly treated dermatological conditions, representing nearly 10% of the patients treated at dermatology departments and clinics in a given year [13]. CU is also relatively common and is said to affect 5.0% of the patients [13]. In short, these conditions affect a substantial number of patients worldwide.

The management of these three conditions has evolved considerably over the past 10 years. This has occurred in parallel with our increasing understanding of their pathogenesis. Biologic treatments, including tumor necrosis factor inhibitors, have been available for PSO since 2003 and offer an effective treatment option for severe PSO [14]. Furthermore, an anti-interleukin-4/13 antibody for AD and an anti-

immunoglobulin E antibody for CU became available in 2017 and 2014, respectively [15, 16]. Whereas biologics have dramatically changed the treatment and management of these three conditions, they tend to be high-cost treatments, which may raise concerns about their relative cost/benefit for patients and healthcare systems. A study conducted in 2013 for the US showed that the direct cost of treatment for PSO may range from 51.7 billion to 63.2 billion US dollars (USD) annually, and that indirect costs (e.g., costs associated with productivity losses) may range from 23.9 billion to 35.4 billion USD annually [17]. A similar study conducted across five of the largest countries in Europe in 2015 that reviewed literature on the cost of treatment for PSO found that treatment costs can be as high as 13,132 USD for PSO and 17,050 USD for psoriatic arthritis per year [18]. The study also found that treatment costs increase with the treatment and management of more severe disease and the use of biologics. In 2015, it was estimated that the treatment of AD costs over 5 billion USD annually in the US [19, 20]. Some more recent studies have also shown that moderate to severe AD patients face substantially higher treatment costs compared to mild patients [21, 22]. Specifically, the emergence of effective but more expensive biologic treatments is likely to have led to (or to lead to) higher costs. A cost analysis conducted in 2008 at the Johns Hopkins University suggested that the treatment of CU consumed a mean of 2047 USD per patient annually [23]. More recent literature on the cost of illness of CU is scarce, but one study in Kuwait found that the use of biologic treatments is associated with an over fourfold increase in annual treatment costs for CU patients [24].

Some previous studies have conducted a systematic review of economic evaluations for PSO or AD, and at least one has reviewed economic evaluations for a broader range of immunological conditions [25–27]. Those studies have shown that many economic evaluations have been conducted for the US and European region, and many have been conducted from the perspective of the payer—i.e., from the perspective of the national health insurance system or another third-party insurer. While the quality of the economic evaluation studies conducted has been reported to be high, a lack of reporting of study characteristics and variability in methods used across studies despite similar therapy areas have been suggested [25, 27, 28]. For example, studies have failed to report the study perspective (e.g., payer perspective, societal perspective), which is an important consideration when determining the types of costs to include in the analysis. Our previous review also showed that among studies that considered indirect costs such as productivity losses experienced by patients and/or their caregivers, many included absenteeism (i.e., costs associated with the loss of productivity while at work due to their condition) and unemployment/early retirement costs [25]. Evidence related to CU, however, is hindered due to a lack of studies in general. A review conducted from January 2000 to December 2012 found only three studies that evaluated treatments for CU from an economic standpoint or considered their utility estimates [29]. More recent reviews have encountered a similar paucity of studies available for CU [29, 30].

This study encompasses a systematic review of literature to understand the economic evidence for PSO, AD, and CU. While the previous study was limited to a review of cost-effectiveness analyses (CEAs) and cost-utility analyses (CUAs), all types of economic evaluations are reviewed for the present study, including cost-effectiveness studies covering drug treatments and economic studies (cost-of-illness studies, budget impact studies, etc.) covering any intervention type. The treatment of inflammatory skin diseases is diverse and not limited to drug therapy. However, for this study, we are particularly concerned about the cost of medical care with expensive biologics, so we have focused only on pharmacotherapy in this study. Differences in the kinds of evaluations conducted and the study characteristics are considered by disease area (condition) and by type of intervention in order to help inform future economic studies of these conditions.

Table 1 Description of key items extracted

Data item	Definition
Type of study design	
Cross-sectional analysis	These were economic evaluations or cost studies conducted using a cross-sectional data source—typically using a prospective survey approach or an online database
Retrospective analysis	These were economic evaluations or cost studies conducted using a retrospective data source—typically using a claims database or medical records
Economic evaluation conducted alongside a clinical trial	These were typically economic evaluations that were conducted as part of a clinical trial. There were often (but not always) randomized trials that compared two or more treatments
Model-based studies/economic evaluation NOT conducted alongside a clinical trial	There were typically model-based studies that were not conducted as part of a clinical trial or a retrospective analysis. In these cases, the study inputs may have been sourced from a literature review, claims database, analysis, online database, etc.
Type of economic evaluation[a]	
Budget impact analysis	An economic evaluation that estimates the financial consequence of an intervention
Cost–benefit analysis	A type of economic evaluation which compares the cost of an intervention to its monetary benefits. The results are typically expressed as an internal rate of return or net present value
Cost-consequence analysis	An economic evaluation that presents costs and outcomes separately and allows the reader to form their own opinion about their relative importance
Cost-effectiveness analysis (CEA)	An economic evaluation that compares the cost and outcomes (effects) of an intervention, typically by expressing them as the cost associated with an incremental improvement in outcome or an incremental cost effectiveness ratio (ICER). For this study, publications that did not use quality-adjusted life years (QALYs) as the outcome measure for the ICER calculation were categorized as CEAs
Cost-utility analysis (CUA)	A cost-effectiveness analysis whereby the outcome (effect) is expressed in terms of QALYs
Cost studies (direct or indirect costs)	Studies that only examine the cost of an intervention and do not consider the relative benefit or outcomes or the budget impact
Study perspective	

Table 1 continued

Data item	Definition
Payer/third-party/healthcare system	The perspective (viewpoint) of the study is from the payer, which is often the national health insurance system or another third-party insurer. The payer perspective may not include the out-of-pocket costs of patients, whereas the healthcare system perspective often includes them
Societal	The perspective (viewpoint) of the study is that of society as a whole, so the indirect costs of an intervention (e.g., productivity costs) are often also included
Patient	The perspective (viewpoint) of the study is that of the patient only, so the payer costs may not be incorporated unless the payer is the patient
Sources of cost information	
Claims database	These are databases that include administrative data on the bills, insurance information, etc. associated with treatment. Examples include the Truven Health Analytics MarketScan Databases and Optum® Clinformatics™
Formulary/government listings	This refers to official reimbursement information available from national, regional, or other payer-level listings that includes the cost of diagnostics, treatment, and other healthcare interventions
Online database	These are online databases/datasets available through government and other sources. Examples include the US Department of Defense's Military Health System database, the Humana research database, and other electronic patient files
Medical records	These are computerized medical databases and other electronic medical records from a specific source
Survey	These are cross-sectional studies conducted as a questionnaire on paper, over the telephone, online, etc. Examples include the US Medical Expenditure Panel Survey (MEPS), the Adelphi Real World Psoriasis Disease Specific Programme, and other ad-hoc studies
Cost elements	
Direct costs	These are direct medical costs associated with treating a condition
Indirect costs	These are costs associated with undergoing treatment for a condition that are not direct treatment costs, such as costs associated with productivity losses or gains
Adverse event costs	These are the costs of treating adverse events associated with treating an underlying condition
Health state costs	These are reported costs associated with a specific level of severity of a condition

Table 1 continued

Data item	Definition
Total costs	These are the total costs of treating a condition, such as the combination of direct and indirect costs. These were typically considered when only the total costs were reported

[a]"Full economic evaluations" are studies that examine the outcomes or budget impact of one or more drug treatment. These include budget impact analyses, cost–benefit analyses, cost-consequence analyses, cost-effectiveness analyses, and cost-utility analyses

METHODS

This review was performed in accordance with recommended international guidelines for the conducting of systematic reviews, including the Centre for Reviews and Dissemination (CRD) guidance [31], the Cochrane Handbook [32], and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [33, 34]. This article provides a review of previously conducted studies and does not involve any new studies with human participants or animals performed by any of the authors.

Search Strategy

A systematic search of three electronic databases was conducted: (1) MEDLINE In-Process (via PubMed.com), (2) MEDLINE and Embase (via Embase.com), and (3) the Cochrane Library (via cochranelibrary.com). Keywords for the searches of the aforementioned databases were identified from the literature for two concepts: (1) type of economic evidence and (2) relevant diseases (or population of interest). The search strategy used for this study is included in Table S1 of the Supplementary Material. We anticipated that many previous studies may not clearly classify inflammatory and autoimmune skin diseases, so we broadly included autoimmune and inflammatory diseases as classified by International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD10) in the early stages of our search, and from there, we used title abstract review screening and full-text screening to exclude articles that were not for the three diseases targeted.

To identify economic evaluations, keywords such as "health care cost," "drug cost," and "economic burden" were included. Moreover, relevant MeSH terms such as "economics," "pharmaceutical," "cost benefit analysis," and "cost of illness" were included. To identify those that include the conditions, keywords such as "psoriasis," "atopic dermatitis," "eczema," and "chronic urticaria" were included. Moreover, relevant MeSH terms such as "psoriasis," "arthritis, psoriatic," "dermatitis, atopic," and "chronic urticaria" were included. Search terms for PSO covered psoriasis, plaque psoriasis, psoriatic arthritis, and/or psoriasis vulgaris. Since methods of analysis and modeling for economic evaluations have evolved a great deal, this review covers publications from 2016 to the present to ensure relevancy to current decision making. Specifically, the search period included all publications available from January 1, 2016 up to October 26, 2020.

In addition to a database search, references cited in each of the included studies and relevant (but not included) systematic reviews were manually searched to identify any additional relevant studies, as recommended by the CRD and Cochrane guidelines [29, 30]. A hand search of select academic, industry, and medical society proceedings from 2018 to 2020 was also conducted to identify any recent publications that may not have been published yet, including those from the International Society for Pharmacoeconomics and Outcomes Research

(ISPOR), the European Association of Hospital Pharmacists, and the Society for Investigative Dermatology. However, only conference publications that included full-text articles (as opposed to abstracts only) were included.

Study Selection

Studies included in the analysis had to be original economic evaluations or cost and resource use studies that fulfilled all of the inclusion criteria and none of the exclusion criteria. An overview of the study inclusion and exclusion criteria is included in Table S2 of the Supplementary Material. Study types reviewed included (1) full economic evaluations such as CEAs, CUAs, cost–benefit analyses (CBAs), and budget impact analyses and (2) other cost and resource use studies such as cost-of-illness studies. As part of the inclusion criteria, the study population had to include adult patients (aged 18 or older) with one or more of the relevant conditions: PSO, AD, and/or CU.

For full economic evaluations, only studies related to a drug treatment were included. Specifically, studies that included any pharmacological therapy were included even if the specific drug name was unclear. However, economic evaluations that described only non-pharmacotherapy, such as phototherapy and testing, were excluded. For other cost and resource use studies, such as cost-of-illness studies and budget impact analyses, there were no limits on the interventions included. After the exclusion of duplicates, a review of the title and abstract for each publication identified was conducted to confirm whether or not they met all of the inclusion criteria and none of the exclusion criteria. Full-text articles were then obtained for records that met the inclusion criteria. Each record was re-evaluated through a full-text review by two independent analysts. Any disagreements about inclusion or exclusion

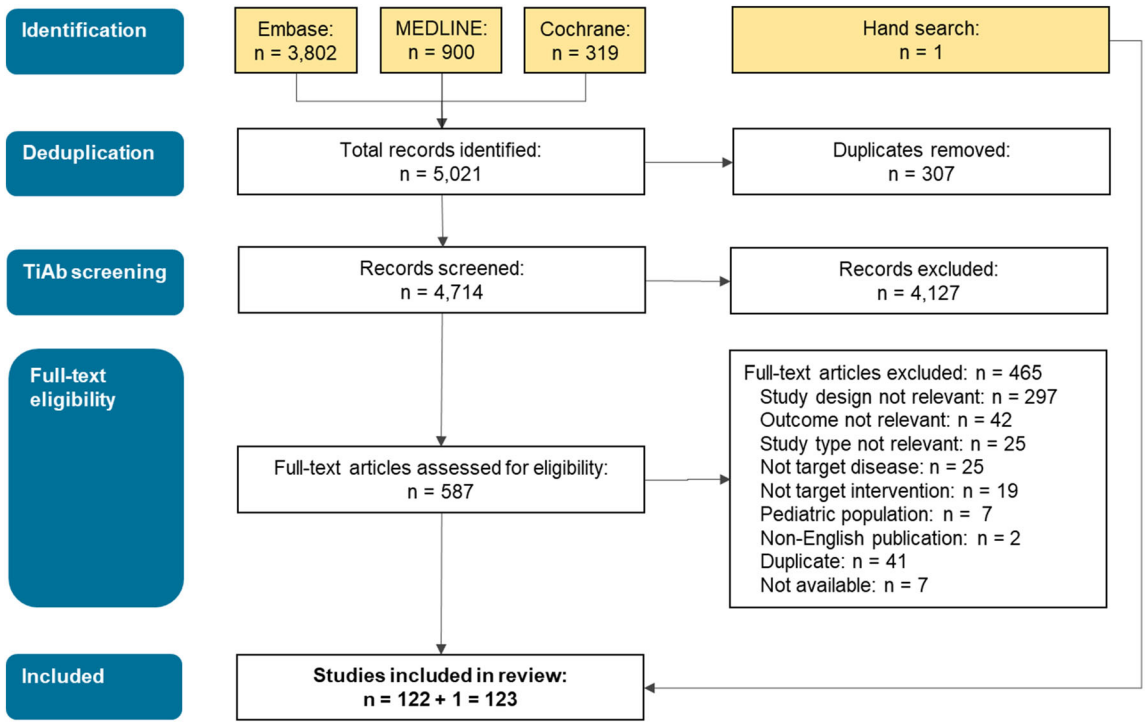

Fig. 1 PRISMA flow diagram

Table 2 Characteristics of the included studies by disease covered and type of intervention

Characteristic	All studies *n* (%)	Disease covered			Type of intervention		
		Psoriasis *n* (%)	Atopic dermatitis *n* (%)	Chronic urticaria *n* (%)	Biologics included *n* (%)	Biologics not included *n* (%)	Not reported/ unknown *n* (%)
Total	123 (100.0%)	104 (100.0%)	14 (100.0%)	5 (100.0%)	72 (100.0%)	10 (100.0%)	41 (100.0%)
Type of intervention							
Biologics included	72 (58.5%)	65 (62.5%)	3 (21.4%)	4 (80.0%)	72 (100.0%)	0 (0.0%)	0 (0.0%)
Biologics not included	10 (8.1%)	9 (8.7%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	10 (100.0%)	0 (0.0%)
Not reported/unknown	41 (33.3%)	30 (28.8%)	10 (71.4%)	1 (20.0%)	0 (0.0%)	0 (0.0%)	41 (100.0%)
Publication year							
2016	17 (13.8%)	15 (14.4%)	0 (0.0%)	2 (40.0%)	9 (12.5%)	2 (20.0%)	6 (14.6%)
2017	17 (13.8%)	15 (14.4%)	1 (7.1%)	1 (20.0%)	10 (13.9%)	1 (10.0%)	6 (14.6%)
2018	35 (28.5%)	29 (27.9%)	5 (35.7%)	1 (20.0%)	21 (29.2%)	3 (30.0%)	11 (26.8%)
2019	25 (20.3%)	20 (19.2%)	5 (35.7%)	0 (0.0%)	12 (16.7%)	1 (10.0%)	12 (29.3%)
2020	29 (23.6%)	25 (24.0%)	3 (21.4%)	1 (20.0%)	20 (27.8%)	3 (30.0%)	6 (14.6%)
Type of study design							
Cross-sectional analysis	10 (8.1%)	5 (4.8%)	5 (35.7%)	0 (0.0%)	1 (1.4%)	0 (0.0%)	9 (22.0%)
Retrospective analysis	65 (52.8%)	55 (52.9%)	7 (50.0%)	3 (60.0%)	30 (41.7%)	4 (40.0%)	31 (75.6%)
Economic evaluation conducted alongside a clinical trial	8 (6.5%)	8 (7.7%)	0 (0.0%)	0 (0.0%)	5 (6.9%)	2 (20.0%)	1 (2.4%)
Model-based studies/economic evaluation not conducted alongside a clinical trial	40 (32.5%)	36 (34.6%)	2 (14.3%)	2 (40.0%)	36 (50.0%)	4 (40.0%)	0 (0.0%)
Type of economic evaluation							
Budget impact analysis	6 (4.9%)	5 (4.8%)	1 (7.1%)	0 (0.0%)	4 (5.6%)	1 (10.0%)	1 (2.4%)
Cost–benefit analysis	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	0 (0.0%)	0 (0.0%)
Cost-consequence analysis	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	0 (0.0%)	0 (0.0%)
Cost-effectiveness analysis	22 (17.9%)	22 (21.2%)	0 (0.0%)	0 (0.0%)	17 (23.6%)	5 (50.0%)	0 (0.0%)

Table 2 continued

Characteristic	All studies *n* (%)	Disease covered			Type of intervention		
		Psoriasis *n* (%)	Atopic dermatitis *n* (%)	Chronic urticaria *n* (%)	Biologics included *n* (%)	Biologics not included *n* (%)	Not reported/unknown *n* (%)
Cost-utility analysis	25 (20.3%)	21 (20.2%)	2 (14.3%)	2 (40.0%)	23 (31.9%)	2 (20.0%)	0 (0.0%)
Both cost-effectiveness and cost-utility analyses	1 (0.08%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)	0 (0.0%)
Cost studies (direct or indirect costs)	67 (54.5%)	53 (51.0%)	11 (78.6%)	3 (60.0%)	26 (36.1%)	1 (10.0%)	40 (97.6%)
Study perspective							
Payer/third-party/healthcare system	46 (37.4%)	41 (39.4%)	4 (28.6%)	1 (20.0%)	34 (47.2%)	4 (40.0%)	8 (19.5%)
Societal	13 (10.6%)	9 (8.7%)	3 (21.4%)	1 (20.0%)	2 (2.8%)	1 (10.0%)	10 (24.4%)
Societal and payer perspective	2 (1.6%)	1 (1.0%)	0 (0.0%)	1 (20.0%)	2 (2.8%)	0 (0.0%)	0 (0.0%)
Patient	1 (0.8%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)
Payer and patient perspective	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	0 (0.0%)	0 (0.0%)
Other	5 (4.1%)	5 (4.8%)	0 (0.0%)	0 (0.0%)	3 (4.2%)	1 (10.0%)	1 (2.4%)
Not reported	55 (44.7%)	47 (45.2%)	6 (42.9%)	2 (40.0%)	30 (41.7%)	4 (40.0%)	21 (51.2%)
Region/country of evaluation							
North/South America	62 (50.4%)	55 (52.9%)	7 (50.0%)	0 (0.0%)	41 (56.9%)	4 (40.0%)	17 (41.5%)
Canada	2 (1.6%)	2 (1.9%)	0 (0.0%)	0 (0.0%)	2 (2.8%)	0 (0.0%)	0 (0.0%)
United States	57 (46.3%)	50 (48.1%)	7 (50.0%)	0 (0.0%)	37 (51.4%)	4 (40.0%)	16 (39.0%)
Other	3 (2.4%)	3 (2.9%)	0 (0.0%)	0 (0.0%)	2 (2.8%)	0 (0.0%)	1 (2.4%)
Europe	45 (36.6%)	39 (37.5%)	4 (28.6%)	2 (40.0%)	23 (31.9%)	3 (30.0%)	19 (46.3%)
Germany	7 (5.7%)	7 (6.7%)	0 (0.0%)	0 (0.0%)	4 (5.6%)	0 (0.0%)	3 (7.3%)
Italy	8 (6.5%)	8 (7.7%)	0 (0.0%)	0 (0.0%)	4 (5.6%)	1 (10.0%)	3 (7.3%)
The Netherlands	4 (3.3%)	2 (1.9%)	1 (7.1%)	1 (20.0%)	2 (2.8%)	1 (10.0%)	1 (2.4%)
Spain	5 (4.1%)	4 (3.8%)	1 (7.1%)	0 (0.0%)	4 (5.6%)	0 (0.0%)	1 (2.4%)
Sweden	4 (3.3%)	4 (3.8%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	1 (10.0%)	2 (4.9%)
United Kingdom	8 (6.5%)	7 (6.7%)	0 (0.0%)	1 (20.0%)	7 (9.7%)	0 (0.0%)	1 (2.4%)
Other	9 (7.3%)	7 (6.7%)	2 (14.3%)	0 (0.0%)	1 (1.4%)	0 (0.0%)	8 (19.5%)

Table 2 continued

Characteristic	All studies	Disease covered			Type of intervention		
	n (%)	Psoriasis *n* (%)	Atopic dermatitis *n* (%)	Chronic urticaria *n* (%)	Biologics included *n* (%)	Biologics not included *n* (%)	Not reported/unknown *n* (%)
Middle East/Asia/Oceania	12 (9.8%)	8 (7.7%)	2 (14.3%)	2 (40.0%)	8 (11.1%)	2 (20.0%)	2 (4.9%)
Japan	7 (5.7%)	5 (4.8%)	1 (7.1%)	1 (20.0%)	6 (8.3%)	0 (0.0%)	1 (2.4%)
Other	5 (4.1%)	3 (2.9%)	1 (7.1%)	1 (20.0%)	2 (2.8%)	2 (20.0%)	1 (2.4%)
Multinational	4 (3.3%)	2 (1.9%)	1 (7.1%)	1 (20.0%)	0 (0.0%)	1 (10.0%)	3 (7.3%)
Study funding source							
Industry funded	103 (83.7%)	89 (85.6%)	11 (78.6%)	3 (60.0%)	61 (84.7%)	8 (80.0%)	34 (82.9%)
Non-industry funded	5 (4.1%)	5 (4.8%)	0 (0.0%)	0 (0.0%)	4 (5.6%)	0 (0.0%)	1 (2.4%)
No funding	4 (3.3%)	2 (1.9%)	1 (7.1%)	1 (20.0%)	2 (2.8%)	0 (0.0%)	2 (4.9%)
Not reported	11 (8.9%)	8 (7.7%)	2 (14.3%)	1 (20.0%)	5 (6.9%)	2 (20.0%)	4 (9.8%)

were resolved through discussion until a consensus was reached, failing which a third reviewer was consulted for a final and irrevocable decision.

Data Extraction

Data from the included studies were extracted by a reviewer into data extraction tables created for this analysis. To identify and rectify any errors in data extraction, a second reviewer checked and validated the outcome data by conducting an independent internal data check once all required data had been collected/extracted. Key data extracted from the publications for analysis included target disease/condition, type of intervention (e.g., biologics included, biologics not included), publication year, type of study design, type of economic evaluation, study perspective, region/country of evaluation, source of funding, cost information included, cost elements reported, source of the cost information, currency used, cost year considered, and key cost drivers. Table 1 provides a description of some of the key items that were extracted from the publications. Moreover, key cost drivers were determined based on information included in each study concerning cost items (e.g., drug acquisition cost, administration cost). Cost items that were shown to have a quantitative relationship with total cost based on the results of sensitivity analyses or that comprised a high proportion of the costs for the study based on a breakdown provided were categorized as key cost drivers.

Data extraction forms were managed in Microsoft Excel version 14.0 (2010). Synthesis of the extracted evidence was qualitative in nature, with numeric data converted to categorical data as necessary. Descriptive statistics (*n* and percentage) were conducted for each condition by type of intervention and/or sources of costs.

Quality Assessment

The reporting quality of studies included in this review was assessed using the Drummond and

Jefferson checklist (also referred to as the BMJ checklist), hereafter referred to as the 'Drummond checklist,' published in 1996 [35]. The Drummond checklist is 36-item checklist that can be used to evaluate economic evaluations based on three general areas: study design; data collection; and analysis and interpretation of results. The checklist has been used extensively and helps ensure the consistency of reporting. Previous reviews have established that the Drummond checklist is a commonly used list for evaluating economic evaluation studies [36, 37].

RESULTS

Studies Identified for Inclusion

The PRISMA flow diagram for the search results is shown in Fig. 1. The search strategy identified 5,021 publications in total. Removal of duplicates resulted in 4714 publications to be screened. Review of titles and abstracts ('TiAb' screening) by two independent reviewers resulted in the exclusion of 4127 publications, with 587 publications remaining for the full-text review to assess for inclusion based on the inclusion and exclusion criteria. Four-hundred fifty-eight publications were excluded because they failed to meet one or more of the inclusion criteria, met one or more of the exclusion criteria, or were identified as a duplicate study during the full-text review. Moreover, the full text could not be retrieved for seven studies. One additional publication was identified through a search of the references cited in the included studies. Ultimately, 123 publications were included in the final analysis.

Details of Studies Included

Diseases Covered

Table 2 provides an overview of the characteristics of the studies included in this analysis. Studies related to PSO comprised the majority of the studies. One hundred-four studies (84.6%) covered PSO, 14 studies (11.4%) covered AD, and 5 studies (4.1%) covered CU.

Type of Intervention

Seventy-two studies (58.5%) were for interventions that included biologics, whereas 41 studies (33.3%) did not report whether biologics were included or not. Among the 104 studies that covered PSO, 65 studies (62.5%) reported that they included biologics. Moreover, among the 5 CU studies included, 4 studies (80.0%) reported that they included biologics. However, only 3 out of 14 studies (21.4%) that covered AD reported that they included biologics.

Publication Year

Eighty-nine studies (72.4%) were published more recently, from 2018 to 2020. In particular, studies related to AD were published more recently (from 2018 to 2020), including 13 out of 14 of the studies included (92.9%). A similar trend was observed for both studies that included biologic interventions and studies that did not, with 73.6% and 70.0% of studies being published from 2018 to 2020, respectively. Only 2 out of 5 studies (40.0%) relating to CU, however, were published from 2018 to 2020.

Type of Study Design

Sixty-five studies (52.8%) were retrospective analyses, 40 studies (32.5%) were model-based studies not conducted alongside a clinical trial, 10 studies (8.1%) were cross-sectional analyses, and 8 studies (6.5%) were conducted alongside a clinical trial. Cross-sectional analyses were more common among studies covering AD (35.7% vs. 4.8% and 0.0% for PSO and CU, respectively). Moreover, model-based studies not conducted alongside a clinical trial were somewhat more common when biologics were included as an intervention (50.0% vs. 40.0% and 0.0% for studies with nonbiologics and those in which the intervention was not reported/unknown, respectively).

Type of Economic Evaluation

About half of the studies included were full economic evaluations, and about half were other cost studies. Specifically, 67 studies (54.5%) were cost studies, 25 studies (20.3%) were CUAs, 22 studies (17.9%) were CEAs, 6 studies (4.9%) were budget impact analyses, 1

study (0.8%) was a cost–benefit analysis, and 1 study (0.8%) was a cost-consequence analysis. One study included both a CEA and CUA. For PSO and CU, 42.3% and 40.0%, respectively, of the studies included were CEA and/or CUAs. However, for studies covering AD, the majority were cost studies, and only 2 out of 14 studies (14.3%) were CUAs. Among the studies reviewed for which biologics were included as an intervention, 40 out of 72 studies (55.6%) were a CEA or CUA, compared to 8 out of 10 studies (80.0%) for those that did not include biologics.

Study Perspective

Forty-six studies (37.4%) were conducted based on the payer/third-party/healthcare system perspective, 13 studies (10.6%) were conducted based on the societal perspective, 2 studies (1.6%) were conducted based on both the societal and payer perspective, and 7 studies (5.7%) were based on another perspective. However, 55 of the studies (44.7%) identified did not report the study perspective. Studies of PSO were somewhat more commonly conducted from the payer/third-party/healthcare system perspective, whereas studies of AD and CU were more commonly conducted from the societal perspective compared to PSO studies.

Region/Country of Evaluation

Sixty-two studies (50.4%) were conducted for North America or South America, with 57 studies (46.3%) conducted for the US. Europe was the next most common region, with 45 studies (36.6%) conducted for a European country, including 8 studies (6.5%) conducted for the United Kingdom (UK), 8 studies (6.5%) for Italy, and 7 studies (5.7%) for Germany. Among studies conducted in the Middle East/Asia/Oceania regions, Japan was the most common country for conducting studies, with 7 studies (5.7%) conducted for Japan. North/South America and Europe were the most commonly included regions/countries for PSO and AD, with over 75% of the studies conducted for those regions. However, only 2 out of 5 studies (40.0%) of CU were conducted for those regions. Studies conducted in the US more commonly reported that they included a biologic treatment.

Study Funding Source

One hundred three studies (83.7%) were sponsored by a company in the healthcare industry, most commonly a pharmaceutical company. Five studies (4.1%) received funding from a non-industry sponsor such as a government agency, 4 studies (3.3%) received no funding, and 11 studies (8.9%) did not report whether they received any funding or not. Sources of funding were relatively similar across conditions and types of intervention.

Details of Cost Information Included

Cost Information Included

Table 3 provides an overview of the cost information included in the economic evaluations and cost studies of this analysis. Seventy-four studies (60.2%) examined costs only, 41 studies (33.3%) examined costs and resource use, 7 studies (5.7%) examined costs, resource use, and the budget impact, and 1 study (0.8%) examined the budget impact only. While 67 out of 104 studies (64.4%) of PSO and 3 out of 5 studies of CU (60.0%) considered costs only, the majority of studies conducted for AD (64.3%) examined both costs and resource use. Among studies that included biologics, 58 out of 72 studies (80.6%) only examined costs. Similarly, among the studies that included nonbiologic interventions, 7 out of 10 studies (70.0%) examined costs only. However, only 9 out of 41 studies (22.0%) for which the intervention (biologics or nonbiologics) was not reported or was unknown included only costs.

Costs Elements Reported

Nearly all studies (97.6%) included direct costs, 22 studies (17.9%) included indirect costs, 19 studies (15.4%) included total costs, 9 studies (7.3%) included adverse event costs, and 2 studies (1.6%) included health state costs. The inclusion of indirect costs was somewhat more common among studies of AD and CU (28.6% vs. 17.9% overall and 60.0% vs. 17.9% overall, respectively). No major differences were

Table 3 Cost information included by disease covered and type of intervention

Characteristics	All studies *n* (%)	Disease covered			Type of intervention		
		Psoriasis *n* (%)	Atopic dermatitis *n* (%)	Chronic urticaria *n* (%)	Biologics included *n* (%)	Biologics not included *n* (%)	Not reported/ unknown *n* (%)
Total	123 (100.0%)	104 (100.0%)	14 (100.0%)	5 (100.0%)	72 (100.0%)	10 (100.0%)	41 (100.0%)
Cost information included							
Budget impact only	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)
Costs only	74 (60.2%)	67 (64.4%)	4 (28.6%)	3 (60.0%)	58 (80.6%)	7 (70.0%)	9 (22.0%)
Costs and resource use	41 (33.3%)	31 (29.8%)	9 (64.3%)	1 (20.0%)	8 (11.1%)	2 (20.0%)	31 (75.6%)
Costs, resource use, and budget impact	7 (5.7%)	5 (4.8%)	1 (7.1%)	1 (20.0%)	6 (8.3%)	1 (10.0%)	0 (0.0%)
Costs elements reported (as reported including duplicates)							
Direct costs	120 (97.6%)	101 (97.1%)	14 (100.0%)	5 (100.0%)	72 (100.0%)	10 (100.0%)	38 (92.7%)
Indirect costs	22 (17.9%)	15 (14.4%)	4 (28.6%)	3 (60.0%)	7 (9.7%)	0 (0.0%)	15 (36.6%)
Adverse event costs	9 (7.3%)	6 (4.9%)	2 (14.3%)	1 (20.0%)	7 (9.7%)	1 (10.0%)	1 (2.4%)
Health state costs	2 (1.6%)	0 (0.0%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.9%)
Total costs	19 (15.4%)	13 (12.5%)	4 (28.6%)	2 (40.0%)	8 (11.1%)	1 (10.0%)	10 (24.4%)
Sources of costs							
Claims database	46 (37.4%)	39 (37.5%)	6 (42.9%)	1 (20.0%)	25 (34.7%)	1 (10.0%)	20 (48.8%)
Formulary/government listings	39 (31.7%)	36 (34.6%)	2 (14.3%)	1 (20.0%)	29 (40.3%)	5 (50.0%)	5 (12.2%)
Online database	26 (21.1%)	23 (22.1%)	1 (7.1%)	2 (40.0%)	14 (19.4%)	4 (40.0%)	8 (19.5%)
Medical records	4 (3.3%)	3 (2,9%)	1 (7.1%)	0 (0.0%)	3 (4.2%)	0 (0.0%)	1 (2.4%)
Survey	8 (6.5%)	3 (2.9%)	4 (28.6%)	1 (20.0%)	1 (1.4%)	0 (0.0%)	7 (17.0%)
Currency used							
British pounds (GBP)	8 (6.5%)	7 (6.7%)	0 (0.0%)	1 (20.0%)	7 (9.7%)	0 (0.0%)	1 (2.4%)
Canadian dollars (CAD)	2 (1.6%)	2 (1.9%)	0 (0.0%)	0 (0.0%)	2 (2.8%)	0 (0.0%)	0 (0.0%)
Euros (EUR)	37 (30.1%)	31 (29.8%)	5 (35.7%)	1 (20.0%)	15 (20.8%)	3 (30.0%)	19 (46.3%)
Japan yen (JPY)	6 (4.9%)	4 (3.8%)	1 (7.1%)	1 (20.0%)	5 (6.9%)	0 (0.0%)	1 (2.4%)
US dollars (USD)	65 (52.8%)	55 (52.9%)	8 (57.1%)	2 (40.0%)	41 (56.9%)	4 (40.0%)	20 (48.8%)
Other currency	5 (4.1%)	5 (4.8%)	0 (0.0%)	0 (0.0%)	2 (2.8%)	3 (30.0%)	0 (0.0%)
Cost year considered							
2010–2012	5 (4.1%)	5 (4.8%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	0 (0.0%)	4 (9.8%)
2013–2015	32 (26.0%)	25 (24.0%)	3 (21.4%)	4 (80.0%)	16 (22.2%)	3 (30.0%)	13 (31.7%)
2016–2018	43 (35.0%)	37 (35.6%)	6 (42.9%)	0 (0.0%)	29 (40.3%)	3 (30.0%)	11 (26.8%)
2019–2021	9 (7.3%)	8 (7.7%)	0 (0.0%)	1 (20.0%)	7 (9.7%)	2 (20.0%)	0 (0.0%)
Not reported	34 (27.6%)	29 (27.9%)	5 (35.7%)	0 (0.0%)	19 (26.4%)	2 (20.0%)	13 (31.7%)

observed between types of intervention in the cost elements reported.

Sources of Costs

A claims database was the source of costs for 46 studies (37.4%), 39 studies (31.7%) sourced costs from formulary/government listings, 26 studies (21.1%) sourced costs from an online database, and 8 studies (6.5%) sourced costs from a survey. A claims database or a survey were the most common sources used for studies related to AD (10 out of 14 studies). Formulary/government listings and an online database were more commonly used as sources of cost information for studies related to PSO compared to studies of AD and CU. Among the studies that included biologics, those that sourced costs from a formulary/government listings were somewhat more common (40.3% vs. 31.7% overall). Among studies that did not include biologics, those that sourced costs from formulary/government listings were also somewhat more common (50.0% vs. 31.7% overall).

Currency Used

Sixty-five studies (52.8%) were based on USDs, despite the fact that 57 studies (46.3%) were conducted for the US. Thirty-seven studies (30.1%) were based on euros (EUR), and 8 studies (6.5%) were conducted based on British pounds, which is consistent with the fact that 45 studies (36.6%) were conducted for a European country. No major differences in the currencies used were observed between conditions or types of intervention, although studies of CU more commonly used a currency other than USD or EUR.

Cost Year Considered

Forty-three studies (35.0%) included costs for a year during 2016–2018 and 32 studies (26.0%) included costs for a year during 2013–2015. Over one-fourth of the studies (27.6%), however, did not report the cost year for the analysis. Nearly all of the studies of CU included costs for a year during 2013–2015, but this may be due to that fact that most of the CU studies included were published between 2016 and 2018, whereas studies of PSO and AD were more commonly published between 2018 and 2020.

Key Cost Drivers and Their Data Sources

Table 4 provides a summary of the key cost drivers—i.e., aspects that trigger higher costs—and the sources of the data. Sixty-seven studies (54.5%) did not report the key cost drivers clearly. Thirty-two studies (26.0%) reported that drug costs were a key cost driver. Outpatient costs were the second most common key cost driver, with 11 out of 123 studies (8.9%) having outpatient costs as a key cost driver. Pharmacy costs were the next most common key cost driver, with 9 out of 123 studies (7.3%) having pharmacy costs as a key cost driver. Drug costs, outpatient costs, and/or pharmacy costs were also the key cost drivers for studies whereby the source of the cost information was claims data, formulary/government listing(s), or online database(s). However, for studies where the source of the cost information was survey data, productivity loss was a key cost driver for 3 out of 11 studies (27.3%), and drug costs were a key cost driver for only 2 out of 11 studies (18.2%). For the 4 studies whereby the source of the cost information was medical records, the key cost driver was not reported.

Quality of Evidence

The quality of the 123 studies included was evaluated using the Drummond checklist. A summary of the evaluation of the studies is shown in Table 5. Moreover, detailed results by condition and by publication are provided in Tables S3 and S4 of the Supplementary Material. Reporting was generally good, with only 8 out of 36 of the checklist items being evaluated as "No" for 50% or more of the studies. In terms of the data collection process, 76.4% of the studies included did not report costs based on productivity changes (item 14), and 74.0% and 58.5% did not report the quantity of resources separately from their unit costs, respectively (item 16 and item 17). Details concerning price adjustments for inflation or currency conversion (item 19) were reported by only 40.7% of

Table 4 Key cost drivers reported and their data sources

Cost drivers	All studies	Sources of cost information (including duplicates)				
		Claims database	Formulary/government listing	Online database	Medical records	Survey
Total, *n* (%)	123 (100.0%)	56 (100.0%)	39 (100.0%)	29 (100.0%)	4 (100.0%)	11 (100.0%)
Drug costs	32 (26.0%)	12 (21.4%)	10 (25.6%)	8 (27.6%)	0 (0.0%)	2 (18.2%)
Hospitalization costs	3 (2.4%)	3 (5.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Inpatient costs	4 (3.3%)	1 (1.8%)	1 (2.6%)	1 (3.4%)	0 (0.0%)	1 (9.1%)
Outpatient costs	11 (8.9%)	9 (16.1%)	0 (0.0%)	2 (6.9%)	0 (0.0%)	0 (0.0%)
Pharmacy costs	9 (7.3%)	8 (14.3%)	0 (0.0%)	1 (3.4%)	0 (0.0%)	0 (0.0%)
Productivity loss	7 (5.7%)	2 (3.8%)	0 (0.0%)	2 (6.9%)	0 (0.0%)	3 (27.3%)
Others	6 (4.9%)	2 (3.8%)	2 (5.1%)	0 (0.0%)	0 (0.0%)	2 (18.2%)
Not reported	67 (54.5%)	19 (33.9%)	26 (66.7%)	15 (51.7%)	4 (100.0%)	3 (27.3%)

Totals may exceed 100% given that some studies included more than one key cost driver

the studies included. For the analysis, 74.0% of the studies included did not clearly state the discount rate used (item 23), and 50.4% did not describe the approach used for the sensitivity analysis if applicable (item 27). Moreover, 52.8% of the studies included did not report an incremental analysis (item 31). However, all of the studies stated the research question, answered the study question, and based their conclusions on the data (items 1, 33, and 34, respectively, in Table 5). The quality of the evaluations and studies included for PSO, AD, and CU was similar (see Table S3 in the Supplementary Material).

DISCUSSION

This review identified 123 unique studies that evaluated one or more treatments for PSO, AD, and CU. The aim of this review was to understand the kind of evaluations conducted and differences by condition and type of intervention included. Our review found that most studies conducted between 2016 and 2020 were for PSO. The reason that more studies were identified for PSO may be because high-cost biologic treatments have been available for PSO since 2003, whereas their availability for AD and CU is more recent (2017 and 2014, respectively). Only 2 studies each of AD and CU were identified that provided a full economic evaluation of treatment. More economic evaluations and cost studies related to AD and CU may be conducted in the future as biologic treatments become more common for those conditions.

Although this review included a large number of cost studies by proportion, previously conducted reviews primarily considered economic evaluations such as CEAs and CUAs and therefore reported a high proportion of CEAs and CUAs and studies involving model-based analyses [29, 30, 38–40]. For those reviews, 62% to 100% of studies included were CEAs or CUAs. For those studies, model-based analyses were commonly used, with some studies reporting that as many as 80–97% of the studies used model-based analyses [25, 38]. However, cost studies that do not explicitly consider the additional benefit of a treatment and

Table 5 Quality assessment using the Drummond checklist

Item		All studies (n = 123)		
		Yes n (%)	No n (%)	Unclear/not applicable n (%)
Study design				
1	Was the research question stated?	123 (100.0%)	0 (0.0%)	0 (0.0%)
2	Was the economic importance of the research question stated?	122 (99.2%)	1 (0.8%)	0 (0.0%)
3	Was/were the viewpoint(s) of the analysis clearly stated and justified?	84 (68.3%)	39 (31.7%)	0 (0.0%)
4	Was a rationale reported for the choice of the alternative programs or interventions compared?	107 (87%)	12 (9.8%)	4 (3.3%)
5	Were the alternatives being compared clearly described?	112 (91.1%)	6 (4.9%)	5 (4.1%)
6	Was the form of economic evaluation stated?	54 (43.9%)	0 (0.0%)	69 (56.1%)
7	Was the choice of form of economic evaluation justified in relation to the questions addressed?	51 (41.5%)	0 (0.0%)	72 (58.5%)
Data collection				
8	Was/were the source(s) of the effectiveness estimates used stated?	50 (40.7%)	3 (2.4%)	70 (56.9%)
9	Were details of the design and results of the effectiveness study given (if based on a single study)?	32 (26.0%)	7 (5.7%)	84 (68.3%)
10	Were details of the methods of synthesis or meta-analysis of estimates given (if based on an overview of a number of effectiveness studies)?	10 (8.1%)	7 (5.7%)	106 (86.2%)
11	Were the primary outcome measures for the economic evaluation clearly stated?	64 (52.0%)	1 (0.8%)	58 (47.2%)
12	Were the methods used to value health states and other benefits stated?	36 (29.3%)	17 (13.8%)	70 (56.9%)
13	Were the details of the subjects from whom valuations were obtained given?	109 (88.6%)	14 (11.4%)	0 (0.0%)
14	Were productivity changes (if included) reported separately?	18 (14.6%)	94 (76.4%)	11 (8.9%)
15	Was the relevance of productivity changes to the study question discussed?	17 (13.8%)	1 (0.8%)	105 (85.4%)
16	Were quantities of resources reported separately from their unit costs?	32 (26.0%)	91 (74.0%)	0 (0.0%)
17	Were the methods used for the estimation of quantities and unit costs described?	41 (33.3%)	72 (58.5%)	10 (8.1%)
18	Were currency and price data recorded?	121 (98.4%)	2 (1.6%)	0 (0.0%)
19	Were details of price adjustments for inflation or currency conversion given?	50 (40.7%)	72 (58.5%)	1 (0.8%)
20	Were details of any model used given?	41 (33.3%)	8 (6.5%)	74 (60.2%)
21	Was there a justification for the choice of the model used and the key parameters on which it was based?	19 (15.4%)	22 (17.9%)	82 (66.7%)
Analysis and interpretation of results				
22	Was the time horizon of cost and benefits stated?	40 (32.5%)	14 (11.4%)	69 (56.1%)
23	Was the discount rate stated?	30 (24.4%)	91 (74.0%)	2 (1.6%)
24	Was the choice of rate justified?	15 (12.2%)	21 (17.1%)	87 (70.7%)
25	Was an explanation given if cost or benefits were not discounted?	5 (4.1%)	56 (45.5%)	62 (50.4%)
26	Were the details of statistical test(s) and confidence intervals given for stochastic data?	77 (62.6%)	46 (37.4%)	0 (0.0%)
27	Was the approach to sensitivity analysis described?	52 (42.3%)	62 (50.4%)	9 (7.3%)

Table 5 continued

Item		All studies (n = 123)		
		Yes*n* (%)	No*n* (%)	Unclear/not applicable*n* (%)
28	Was the choice of variables for sensitivity analysis justified?	23 (18.7%)	40 (32.5%)	60 (48.8%)
29	Were the ranges over which the parameters were varied stated?	43 (35.0%)	41 (33.3%)	39 (31.7%)
30	Were relevant alternatives compared? (That is, were appropriate comparisons made when conducting the incremental analysis?)	100 (81.3%)	13 (10.6%)	10 (8.1%)
31	Was an incremental analysis reported?	55 (44.7%)	65 (52.8%)	3 (2.4%)
32	Were major outcomes presented in a disaggregated as well as aggregated form?	85 (69.1%)	27 (22%)	11 (8.9%)
33	Was the answer to the study question given?	123 (100.0%)	0 (0.0%)	0 (0.0%)
34	Did conclusions follow from the data reported?	123 (100.0%)	0 (0.0%)	0 (0.0%)
35	Were conclusions accompanied by the appropriate caveats?	117 (95.1%)	6 (4.9%)	0 (0.0%)
36	Were the generalizability issues addressed?	61 (49.6%)	62 (50.4%)	0 (0.0%)

Items highlighted in italics are those for which 50% or more of the studies evaluated yielded "No" responses

retrospective analyses are clearly important sources of information on treatment costs for immunological skin disorders such as PSO, AD, and CU, and should be considered for subsequent research. For the present review, cost studies that did not explicitly consider the additional benefit of a new treatment were particularly common for AD, representing 11 out of 14 studies identified.

While over one-third of the studies were conducted from the payer/third-party/health-care system perspective, nearly half of the studies included did not report the study perspective. Some previous reviews have also reported a relatively high proportion of studies that did not report the study perspective [26, 41]. However, for most of the previous reviews identified, the study perspective was reported for nearly all of the studies included [25, 38, 39, 42, 43]. The high number of studies not reporting the study perspective for this review may be due to the inclusion of cost studies that did not consider the additional benefit of the new treatment and may not have been conducted for reimbursement decision making. Lack of information on the study perspective, however, can make it difficult to gauge whether a study has considered all of the relevant costs. Another notable finding was that studies conducted for AD were more commonly conducted from the societal perspective. The reason for this is unclear, but AD may involve more indirect costs for patients in terms of productivity loss, which are often included when the societal perspective is used. In fact, the inclusion of indirect costs was somewhat more common among studies of AD and CU.

While nearly all studies included direct costs, only about 1 out of 5 studies included indirect costs. Again, the inclusion of indirect costs was somewhat more common among studies of AD and CU. Although multiple studies recommend the inclusion of productivity losses/gains in CEA [44–47], a study conducted in 2000 that examined CUAs found that, among 228 studies conducted between 1975 and 1997, only 19 studies (8.3%) included productivity costs [48]. However, that study included a wider range of disease areas and was limited to CUAs.

Most of the studies included were also conducted more recently: between 2018 and 2020, suggesting that more economic evaluations and cost research have been conducted for PSO, AD, and CU in recent years. For previous reviews, when the publication date was reported, such a clear and substantial increase in the number of

studies conducted in recent years was not observed [25, 42]. Nearly two-thirds of the studies included examined costs only. However, studies of AD more commonly considered both costs and resource use. The source of the cost data included was most commonly claims data or formulary/government listings. While some previous reviews have also reported a reliance on administrative claims databases and formulary/government listings for cost data [38, 43], many previous reviews have found a lack of reporting of the source of cost data or have not included the source of cost data as a part of their review. This reduces the reliability and relevancy of those findings [38, 40–42]. As such, the availability of information on the source of cost data for the studies reviewed was quite good for the present review.

Among 82 studies which reported type of intervention, 72 studies included biologics. The inclusion of biologic treatments in a substantial number of studies is consistent with a previous study conducted for PSO [24] and makes sense given that in recent years biologics have become an important and effective part of the standard of care for PSO [49, 50]. A similar trend was observed for CU and AD, although the number of studies was limited. Until recently, dupilumab was the only biologic available for the treatment of AD [51, 52]. However, nemolizumab received marketing approval for AD in Japan in March 2022 and is expected to become available in the near future [53]. Moreover, tralokinumab received approval in the US at the end of 2021 [54]. For AD, orally administered Janus kinase (JAK) inhibitors are also available in many countries and typically involve treatments that are similar to biologic treatments [55–57]. So, future studies that reveal the economic value and cost of treatment of AD may consider the impacts of biologics and similar high-cost treatments such as JAK inhibitors.

Most of the studies included were conducted for the US or a European country—particularly the UK, Italy, or Germany. Other reviews have also found that most studies are conducted for the US and Europe—and that the UK, Italy, and Germany are several European countries that are often included [25, 26, 28, 38, 41]. However, other reviews have normally found a higher proportion of studies to have been conducted in Europe, suggesting that economic evaluations and cost studies of immunological skin conditions may be more commonly conducted for the US compared to other conditions. Consideration of the economic value and cost of treatment in other markets may be needed in light of expanding treatment options. A majority of the studies included were industry-sponsored studies. This is also consistent with findings from previous reviews for skin disorders and other conditions [25–27].

A review of the key cost drivers for the studies included and their data sources suggests that drug costs and, to some extent, outpatient costs and pharmacy costs are important costs drivers for the three diseases. This may be due to a low frequency of hospitalization for PSO, AD, and CU patients. However, at least one previous study has shown that the cost of inpatient care for PSO can be substantial compared to outpatient care when it is required [58]. Overall, the quality of the reporting in the economic evaluations and cost studies reviewed was good, given that only 8 out of 36 of the checklist items were evaluated as "No" for 50% or more of the studies. While some items such as productivity changes, the quantity of resources used separated from the unit costs, the study perspective, and discount rates were often not reported, the study design, data collection, and analysis approach were generally reported well. A lack of reporting of quantities of resource use, the study perspective, and discount rates has been commonly reported for reviews of other therapies as well [26, 38, 41, 42]. A lack of reporting of the source of efficacy data and/or a lack of justification of the choice of model has also been reported for other therapy areas [28, 38, 39, 42], but was not a major issue for the studies in this review. A lack of reporting of dates for the resources used and unit costs has also been reported to be an issue for at least one previous review for another therapy area, but was not a major issue for the studies in this review [42].

Although this study provides a comprehensive review of the characteristics of economic evaluations and cost studies of three key immunological skin disorders, there are some

limitations of the analysis that should be reported. First, while various treatments such as phototherapy have been indicated for these three conditions, this review focused only on pharmacotherapy. Second, studies related to PSO comprised the majority of those reviewed, and the small number of studies related to AD and CU allowed for only a limited comparison between the conditions. Also, this review was conducted using three online databases: MEDLINE, Embase, and the Cochrane Library. Other databases and gray literature sources including any unpublished reports—including those issued through government agencies—were not included in the review, which may have led to the nonidentification of some relevant studies. However, it does not seem likely that the inclusion of more databases would have resulted in a substantially higher number of studies that could have altered the conclusion drawn. Lastly, only economic evaluations and cost studies published after 2016 and up to October 26, 2020 were included in this study. While an expansion of the study period to include publication prior to 2016 might have allowed for more consideration of changes in the characteristics of economic evaluations and cost studies of the three conditions over time, the findings would have been less relevant given the more recent introduction of biologics for AD and UC. Since the JAK inhibitors indicated for AD were approved in the EU [55] and the US [56, 57] after late 2020, updating the study to include relevant publications may be considered in the future.

CONCLUSIONS

The results of this review show that, in recent years, studies related to the economic evaluation and cost of treatment of PSO have been common, and there have been comparatively very few studies of AD and CU—possibly due to the fact that high-cost biologic treatments for AD and CU have only been available since 2017 and 2014, respectively. Also, many studies have not reported or clearly delineated the effect of the inclusion of biologic treatments or the role of a reduction in productivity among patients. Economic evaluations for AD and CU may be needed in order to better estimate the value and cost of new treatments under those conditions, and a clearer delineation between biologic treatments and indirect costs (i.e., productivity losses and gains) in future studies would contribute to a better understanding of their impact on treatment costs.

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