ECONOMIC BURDEN AND COST-EFFECTIVENESS OF MODERATE TO SEVERE PSORIASIS TREATMENT IN ASIAN REGION: A SYSTEMATIC REVIEW

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Abstract

Psoriasis poses a significant economic burden. A systematic review of psoriasis treatments cost and effectiveness has been performed extensively in the United States (US) and Europe, but such review is limited in Asia. This review aims to analyze all previous literature on the cost and effectiveness of systemic and biological treatment for moderate to severe psoriasis. Cost of illness and cost-effectiveness studies that examined the economic burden, cost, and effectiveness of psoriasis treatments (systemic and biological) in Asian region from 2010 to 2020 were published in English language. All costs were converted into 2020 US Dollar. All COIs included found that direct medical costs were greater than indirect costs. Adalimumab, ustekinumab, risankizumab, secukinumab 150 mg were cost-effective treatments and of the lowest cost per PASI-75/PASI1 and/or QALY. When comparing the different treatments, topical and systemic psoriasis treatments were observed to be the most cost-effective compared with other modalities. Given the tremendous economic effects of psoriasis on patients and hospitals, economic analysis, clinicians, and policymakers should consider cost and effectiveness evidence, as this systematic literature review was conducted to analyze previous documentation regarding the cost and effectiveness of systemics and biologics in Asian countries.

Keywords: Psoriasis**,** Cost-effectiveness**,** Economic evaluation**,** Cost of illness**,** Moderate to severe psoriasis.

1. Introduction

Psoriasis chronic inflammatory skin disease characterized by thick, red, itchy, painful, and scaly plaques in a particular target region or the entire body (Murage et al., 2018). Psoriasis affects approximately 2–3 percent of the worldwide population (Hayes & Koo, 2010; Spandonaro et al., 2014). In Malaysia, a total of 17,071 psoriasis cases were registered in the Malaysian Psoriasis Registry (MPR) from 1997 to 2016. Psoriasis vulgaris, is the most common type of plaque psoriasis (almost 85% to 90%) (Griffiths & Barker, 2007), which appears as elevated, well-demarcated, erythematous, and oval plaques covered in adherent silvery-white scales (Nestle et al., 2009). Psoriasis does not affect longevity in general, but it has a substantial negative impact on the quality of life comparable to other

chronic diseases, such as ischemic heart disease, diabetes, depression, and cancer. It is often associated with social stigma, loss of self-esteem, pain, discomfort, physical disability, and psychological distress (Hrehorów et al., 2012). Given the significant effect of psoriasis on the quality of life of patients, the World Health Organization (WHO) has acknowledged psoriasis as a severe, non-communicable disease that requires global health care attention (WHO, 2016).

Systemics such as methotrexate, cyclosporine, phototherapy, or biological agents are treatments for moderate to severe psoriasis (Azizam et al., 2019; Rendon & Schakel, 2019). Over the past decades, the introduction of biological agents has remarkably changed the treatment of moderate-to-severe psoriasis and psoriatic arthritis (Amherd-Hoekstra et al., 2010). Today, biologics are considered the most efficient treatment method for patients with ineffective reactions, contraindications, or intolerable adverse effects to conventional systemic medication (Rønholt & Iversen, 2017). The various treatment modalities can be distinguished from their major impact on the total cost. Despite its high efficacy, biologic therapy has high incremental costs, resulting in a significant financial effect (Burgos-Pol et al., 2016; Spandonaro et al., 2014). The need for screening and testing tests prior to identifying any toxicity risks raises the treatment's potential cost for systemic treatment. Meanwhile, phototherapy is especially limited, as it leads to considerable loss of efficiency attributable to patients having to take off days to receive care at the outpatient clinic, which can amount to two or three times a week (Azizam et al., 2019).

A systematic review on the economic burden of psoriasis economic in the US and Europe has been extensively conducted (Brezinski et al., 2015a; Burgos-Pol et al., 2016; Obradors et al., 2013); however, such review are lacking in Asia. Therefore, this systematic literature review was conducted to analyze previous documentation regarding the cost and effectiveness of systemics and biologics in Asian countries.

2. Methodology

2.1 Search Strategy

A systematic review of a literature search on the cost and effectiveness of moderate to severe psoriasis treatment studies was conducted using electronic databases in November 2020, including PubMed, Scopus, Web of Science, and ESCO. The main search keywords used were (psoriasis OR psoriatic) AND (moderate to severe treatment OR biologic treatment OR systemic treatment) AND (cost-effectiveness OR cost-efficacy OR cost of illness OR drug cost OR cost-benefit analysis OR health cost OR indirect cost OR direct cost OR cost analysis OR economic burden OR economic evaluation). The identical search strategy was applied in all databases, where the Boolean search was applied to improve the searching of articles. The search aims to identify all cost-effectiveness studies and cost of illnesses to summarize the economic burden, costs, and cost-effectiveness of psoriasis treatments in Asian countries. The reference lists of relevant articles were analyzed.

2.2 Study Selection

Preferred reporting elements for systematic reviews and meta-analyses (PRISMA-P) were used as review guideline (Fig. 1). This revised protocol is mainly intended for the preparation of systematic reviews and meta-analyses (Moher et al., 2015). The study was chosen based on the inclusion and exclusion criteria of the PICOTS framework, which are population, intervention, comparator, result, timing, and setting; where P: moderate to severe psoriasis patients, I: interventions (biologics and systemic), C: placebo, topical treatment, and O: cost and cost per PASI-75/PASI 1/QALY/ICER. Studies were considered eligible for inclusion in this review if they discussed the efficacy and cost-effectiveness of psoriasis treatments (systemic and biologics) and is published in the English language from the year 2010 until 2020 in the Asian region. The study selection process was divided into three major stages. In the first point, electronic database hits were imported into the reference management software (RefWorks). Following the removal of duplicate citations, the second stage focused on evaluating the remaining studies based on their titles and abstracts. Studies that were indicated as irrelevant to the study subject were excluded. The current analysis contains the complete articles that were retrieved and had met the inclusion requirements. Two reviewers screened the listed abstracts and full texts for eligibility. The first three article screening stages were done independently by two authors (NFR and NAA). A consensus among authors was achieved in the case of any

discrepancy. (NFR and NAA) analyzed and summarized the characteristics of the included studies in table 2 and table 3, respectively.

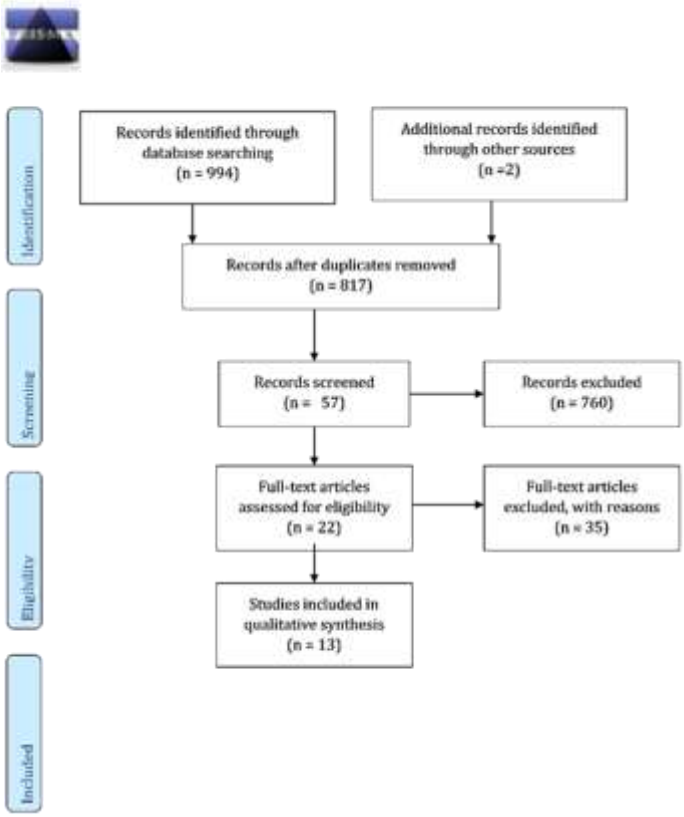

Fig. 1 PRISMA 2009 Flow Diagram

2.3 Data Extraction

The data extraction of this review was based on the Cochrane Handbook for Systematic Reviews of Interventions and the abstract form of the NHS Economic Evaluation Database (Shemilt et al., 2008). For the cost of illness studies, the following items were extracted: setting, time horizon, perspective, type of interventions, and component of costs. As for the cost-effectiveness, the items extracted were settings, treatment options, comparison, and outcome (cost per PASI-75/PASI 1/QALY/ICER). To facilitate the comparison of estimates collected from various studies, all costs were first converted into Malaysia Ringgit (MYR) prior to its conversion into US Dollar (USD) using the exchange rate US = MYR (4.0170) on 31 December 2020 published by the Central Bank of Malaysia (BNM, 2021).

2.4 Quality Assessment

Three structured checklists were used to determine the methodological consistency of the studies. Drummond's checklist, published by the British Medical Journal Working Party, the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) guidelines (Drummond & Jefferson, 1996; Husereau et al., 2013)], and the Joanna Briggs Institute (JBI) Critical Appraisal Tools: Checklist for Economic Evaluation (Gomersall et al., 2015) were used to evaluate all of the studies. Two assessors (NFR and NAA) performed the quality assessment, and uncertainties were resolved by consulting another assessor (AI).

Table 1: Fulfillment of items of quality assessment checklists

	Cost of Illness	Satheendran et al. (2016)	Azizam et al. (2019)	Sruamsiri et al. (2018)	Tang et al. (2013)	Ha et al. (2018)		Cost-effectiveness	Igarashi et al. (2013)	Igarashi et al. (2018)	Imafuku et al. (2017)	Azizam et al. (2019)	Wang et al. (2014)	Takahashi et al. (2017)	Takahashi et al. (2019)	Saeki et al. (2020) Saeki et al. (2020)
JBI's checklist		+	+	+	+	+			+	+	+	+	+	+	+	+
1. Is there a well-defined question?		+	+	+	+	+			+	+	+	+	+	+	+	+
2. Is there comprehensive description of alternatives?		+	+	+	+	+			+	+	+	+	+	+	+	+
3. Are all important and relevant costs and outcomes for each alternative identified?		–	–	–	+	–			+	+	+	+	+	+	+	+
4. Has clinical effectiveness been established?		+	+	+	+	+			+	+	+	+	+	+	+	+
5. Are costs and outcomes measured accurately?		–	–	+	+	–			+	+	+	+	+	+	+	+
6. Are costs and outcomes valued credibly?		–	–	–	+	–			+	+	+	+	+	+	+	+
7. Are costs and outcomes adjusted for differential timing?		N/A	N/A	N/A	N/A	N/A			N/A	+	–	N/A	–	–	–	+
8. Is there an incremental analysis of costs and consequences?		–	–	–	–	–			+	+	+	+	+	–	+	+
9. Were sensitivity analyses conducted to investigate uncertainty in cost estimates or consequences?		–	–	–	–	–			+	+	–	+	–	–	–	+
10. Did study results include all issues of concern to users?		+	+	+	+	+			+	+	+	+	+	+	+	+
11. Are the results generalizable to the setting of interest in the review?		+	+	+	+	+			+	+	+	+	+	+	+	+
Drummond´s checklist																
Study design																
1. The research question is stated.		+	+	+	+	+			+	+	+	+	+	+	+	+
2. The economic importance of the research question is stated.		+	+	+	+	+			+	+	+	+	+	+	+	+
3. The viewpoint(s) of the analysis are clearly stated and justified.		+	+	+	+	+			+	+	+	+	+	+	+	+

4. The rationale for choosing alternative programs or interventions compared is stated.		+	+	+	+	+			+	+	+	+	+	+	+	+
5. The alternatives being compared are clearly described.		+	+	+	+	+			+	+	+	+	+	+	+	+
6. The form of economic evaluation used is stated.		N/A	N/A	N/A	N/A	N/A			+	+	–	+	+	+	+	+
7. The choice of form of economic evaluation is justified in relation to the questions addressed.		N/A	N/A	N/A	N/A	N/A			+	+	+	+	+	+	+	+
Data extraction																
8. Is there an incremental analysis of costs and consequences?		–	–	–	–	–			+	+	+	+	+	–	+	+
9. Were sensitivity analyses conducted to investigate uncertainty in estimates of cost or consequences?		–	–	–	–	–			+	+	–	+	–	–	–	+
10. Did study results include all issues of concern to users?		+	+	+	+	+			+	+	+	+	+	+	+	+
11. Are the results generalizable to the setting of interest in the review?		+	+	+	+	+			+	+	+	+	+	+	+	+
12. Methods to value benefits are stated.		+	+	+	+	N/A			+	+	+	+	+	+	+	+
13. Details of the subjects from whom valuations were obtained were given.		–	–	+	+	N/A			–	+	–	+	–	+	+	+
14. Productivity changes (if included) are reported separately.		N/A	N/A	N/A	N/A	N/A			Nc	+	Nc	Nc	Nc	Nc	Nc	Nc
15. The relevance of productivity changes to the study question is discussed.		N/A	N/A	N/A	+	N/A			Nc	+	Nc	Nc	Nc	Nc	Nc	Nc
16. Quantities of resource use are reported separately from their unit costs.		+	+	+	+	+			–	+	+	–	–	–	–	–
17. Methods for the estimation of quantities and unit costs are described.		–	+	+	+	–			+	+	+	+	+	+	+	+
18. Currency and price data are recorded.		+	+	+	+	+			+	+	+	+	+	+	+	+
19. Details of currency of price adjustments for inflation or currency conversion are given.		–	–	–	–	–			+	–	+	–	+	–	–	–
20. Details of any model used are given.		N/A	N/A	N/A	N/A	N/A			–	+	–	–	–	–	–	+
21. The choice of model used and the key parameters on which it is based are justified.		N/A	N/A	N/A	N/A	N/A			–	+	–	–	–	–	–	+
Analysis and interpretation of results																
22. Time horizon of costs and benefits is stated.		+	+	+	+	–			+	+	+	+	+	+	+	+

23. The discount rate(s) is stated.		N/A	N/A	N/A	N/A	N/A			–	+	–	–	–	–	–	+
24. The choice of discount rate(s) is justified.		N/A	N/A	N/A	N/A	N/A			–	–	–	–	–	–	–	–
25. An explanation is given if costs and benefits are not discounted.		N/A	N/A	N/A	N/A	N/A			–	–	–	+	–	–	–	–
26. Details of statistical tests and confidence intervals are given for stochastic data.		–	–	–	–	–			–	–	+	+	+	–	–	+
27. The approach to sensitivity analysis is given.		–	–	+	–	–			+	+	–	+	–	–	–	+
28. The choice of variables for sensitivity analysis is justified.		–	–	+	–	–			+	+	–	+	–	–	–	+
29. The ranges over which the variables are varied are justified.		+	+	+	–	–			+	+	+	+	+	+	+	+
30. Relevant alternatives are compared.		+	+	+	+	–			+	+	+	+	+	+	+	+
31. Incremental analysis is reported.		–	–	–	–	–			+	+	+	+	+	+	+	+
32. Major outcomes are presented in a disaggregated as well as aggregated form.		+	+	+	+	+			+	+	+	+	+	+	+	+
33. The answer to the study question is given.		+	+	+	+	+			+	+	+	+	+	+	+	+
34. Conclusions follow from the data reported.		+	+	+	+	+			+	+	+	+	+	+	+	+
35. Conclusions are accompanied by the appropriate caveats.		+	+	+	+	+			+	+	+	+	+	+	+	+
Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Guideline																
Title and abstract																
1. Title		–	–	–	–	–			+	+	+	+	+	+	+	+
2. Abstract		+	+	+	+	+			+	+	+	+	+	+	+	+
3. Background and objectives		+	+	+	+	+			+	+	+	+	+	+	+	+
Methods																
4. Target population and subgroups		+	+	+	+	+			+	+	+	+	–	+	+	+
5. Setting and location		–	–	–	–	–			+	+	+	–	+	–	–	–
6. Study perspective		+	+	–	+	+			+	+	+	+	+	+	+	+
7. Comparators		+	+	+	N/A				+	+	+	+	+	+	+	+
8. Time horizon		+	+	+	+	+			+	+	+	+	+	+	+	+
9. Discount rate		N/A	N/A	N/A	N/A	N/A			–	+	–	+	–	–	–	+
10. Choice of health outcomes		–	–	+	–	–			+	+	+	+	+	+	+	+
11a. Measurement of effectiveness (single study-based estimates)		N/A	N/A	N/A	N/A	N/A			N/A	+	N/A	+	N/A	+	+	+
11b. Measurement of effectiveness (synthesis-based estimates)		N/A	N/A	N/A	N/A	N/A			+	N/A	+	N/A	–	N/A	N/A	N/A
12. Measurement and valuation of preference-based outcomes		N/A	N/A	N/A	N/A	N/A			–	+	–	–	–	–	+	–

13a. Estimating resources and costs (single study-based economic evaluation)		N/A	N/A	N/A	N/A	N/A			+	N/A	+	+	+	+	+	N/A
13b. Estimating resources and costs (model-based economic evaluation)		N/A	N/A	N/A	N/A	N/A			N/A	+	N/A	N/A	N/A	N/A	N/A	+
14. Currency, price date, and conversion		+	–	–	–	–			+	+	+	+	+	–	–	+
15. Choice of model		N/A	N/A	N/A	N/A	N/A			N/A	+	N/A	N/A	N/A	N/A	N/A	+
16. Assumptions		–	–	–	–	–			–	+	–	–	–	–	–	+
17. Analytical methods		–	–	–	–	–			–	+	+	+	+	–	–	+
Results																
18. Study parameters		+	+	+	+	+			+	+	+	+	+	+	+	+
19. Incremental costs and outcomes		–	–	–	–	–			+	+	+	+	+	–	+	+
20a. Characterizing uncertainty (single study-based economic evaluation)		N/A	N/A	N/A	N/A	N/A			–	N/A	–	+	–	–	+	N/A
20b. Characterizing uncertainty (model-based economic evaluation)		N/A	N/A	N/A	N/A	N/A			N/A	+	N/A	N/A	–	–	N/A	+
21. Characterizing heterogeneity		–	–	+	–	–			+	–	+	+	–	+	–	–
Discussion																
22. Study findings, limitations, generalizability, and current knowledge		+	+	+	+	+			+	+	+	+	+	+	+	+
Others																
23. Source of funding		+	+	+	+	–			–	+	+	–	–	–	–	+
24. Conflicts of interest		+	–	+	+	+			+	+	+	+	+	+	+	–

(+) Fulfillment of item, ***(–)*** no fulfillment of item, ***N/A*** not applicable.

3. Result

3.1 Studies Selection

The database search identified 994 articles for cost-effectiveness studies, where two (2) articles from other sources were included following discussion among the authors. After the duplicates were removed, 817 potentially eligible articles were screened for their titles and abstracts. Upon screening, 22 articles were qualified for full-text screening. Finally, only 13 articles were qualified for inclusion in the final synthesis based on their inclusion criteria. Five (5) studies discussed the cost of moderate to severe psoriasis treatments and eight (8) articles were studied on the cost-effectiveness of psoriasis. From the total eight (8) studies on cost-effectiveness, two (2) studies employed the Markov model for evaluating the cost-effectiveness, whereas six (6) studies mentioned no specific model for the same purpose. The consensus among authors showed a high level of agreement on the included studies, in which the Kappa score was $K > 0.90$.

3.2 Study Characteristics

The outcomes from this review were stratified into two parts: 1) review from cost of illness studies; and 2) review of the cost-effectiveness analysis studies.

3.2.1 Cost of Illness Study (COI)

This systematic analysis covered five cost of illness studies in total. From the abovementioned total, two studies were conducted in Southeast Asia, which was in Malaysia (Azizam et al., 2019; Tang et al., 2013); whereas two studies were conducted in Eastern Asia: one in Korea and the other in Japan (Ha et al., 2018; Sruamsiri et al., 2018). Meanwhile, one study was conducted in Southern Asia, which was in India (Satheendran et al., 2016). In terms of study design, two studies were prospective (Azizam et al., 2019; Satheendran et al., 2016) and three studies were retrospective (Ha et al., 2018; Sruamsiri et al., 2018; Tang et al., 2013). All studies were conducted in one-year time horizon. Three studies included direct and indirect costs (Azizam et al., 2019; Satheendran et al., 2016; Tang et al., 2013), whereas two studies included only direct cost (Ha et al., 2018; Sruamsiri et al., 2018). Two studies calculated costs from both perspectives: patient and provider (Azizam et al., 2019; Tang et al., 2013), two studies measured costs from the insurance payer's perspective (Ha et al., 2018; Sruamsiri et al., 2018) and, and one study calculated cost from the patient's perspective (Satheendran et al., 2016). With regards to the type of treatment, two studies calculated costs associated with biologics (Azizam et al., 2019; Sruamsiri et al., 2018), three studies measured costs associated with systemic (methotrexate) and phototherapy (psoralen-UVA or PUVA and narrowband UVB) treatments (Azizam et al., 2019; Satheendran et al., 2016; Tang et al., 2013). Meanwhile, one study has not specified any treatment costs (Ha et al., 2018).

Table 2: Cost of Illness

Reference (Year)	Time Horizon and Country	Treatment Option	Analysis Perspective	Included Costs (Description)	Type of Outcome	Result (Cost)	Result (Others)
Satheendran et al. (2016	1 year, India	BATH PUVA MTX	Health care and patient	Direct medical cost (drug) and indirect cost (food, transportation, accommodation)	Cost and treatment	**BATH PUVA** Direct medical cost/patient was $107.13, and the indirect cost was $301.53 **Methotrexate** Direct medical cost/patient was $3.19 and for indirect cost was $57.66	Methotrexate treatment is more effective and cheaper than BATH PUVA.
Sruamsiri et al. (2018	2 year, Japan	ADL, IFX, UST	Not reported from author	Medical cost	Persistent rate, cost, and treatment.	**Total cost per 1 year/follow up (medical cost + outpatient cost and cost of drugs other than BTs)** **Pre-cost (Total patient)** ADL: $7,370 IFX: $9,212 UST: $8,727 **Cost increase (Total patient)** ADL: $14,914 IFX: $23,554 UST: $18,085 **Cost patient (Biologic-naïve and experienced patients) (Persistent group)** ADL Pre-cost: $10,589 Cost increase: $15,573 IFX Pre-cost: $10,298 Cost increase: $21,780 UST Pre-cost: $8,967 Cost increase: $18,812	ADL 33.3% of patients were persistent in the two years of treatment. IFX 30% of patients were persistent in the two years of treatment. UST 78.4% of patients were persistent in the two years of treatment.

						Cost patient **(Biologic-naïve and experienced patients)** **(Non-persistent group)** ADL Pre-cost: $5,770 Cost increase: $14,584 IFX Pre-cost: $8,747 Cost increase: $24,310 UST Pre-cost: $7,835 Cost increase: $17,726 **Outpatient cost post BT initiation one year follow-up.** ADL: $10,444 IFX: $18,987 UST: $19,501 **Inpatient cost** ADL: $921 IFX: $5,828 UST: –$359	

Table 2: Continued

Reference (Year)	Time Horizon and Country	Treatment Option	Analysis Perspective	Included Costs (Description)	Type of Outcome	Result (Cost)	Result (Others)
Azizam et al. (2019	1 year, Malaysia	Topical + Phototherapy Topical + Systemic and Topical + Biologic	Health care and patient	Direct medical cost (drug) and indirect cost (out of pocket, transportation, and loss of productivity)	Cost of illness	**Provider cost:** $1,390/patient **Patient cost:** $542.54/patient **Cost** **Topical + Phototherapy** Provider: $603.66 Patient: $2,230.66 Total: $2,834.32/9 **Topical + Systemic:** Provider: $657.24 Patient: $420.85 Total: $1,078.09/40 **Topical + Biologic** Provider: $8,523.20 Patient: $303.53 Total: $11,357.43/10 **Cost/patient (inpatient)** $275.14 **Cost/patient (outpatient)** $74.19	Not applicable
Tang et al. (2013	1 year, Malaysia	Not applicable, no treatment stated	Health care and patient	Direct cost (medical cost) and indirect cost (transportation, cost other medicine without doctor's prescription)	QoL and cost of illness	**Outpatient management cost** $325.73/patient **Inpatient management cost (Hospitalization)** $92.19/patient **Direct cost:** $248.86 **Indirect cost:** $69.90	Patient had > 10 PASI score and lower quality of life.
Ha et al. (2016	1 year, Korea	Not Applicable	Health care	Psoriasis pre-index period	Health care expenditure and	**Moderate to severe** Pre-index: $88.73/patient	21.2% had moderate to

		(psoriasis compared with other skin disease)		cost and post-index cost. (direct cost)	utilization	Post-index: $135.07/patient **Mild** Pre-index: $21.46/patient Post-index: $23.97/patient **Other skin disease** Pre-index: $69.16/patient Post-index: $104.66/patient	severe psoriasis. Mean health care utilization was 8.97 and 12.71 for pre-index and post-index period, respectively, for moderate to severe psoriasis; and 2.63 and 3.25, respectively, for mild psoriasis.
Azizam et al. (2019	1 year, Malaysia	Topical + Phototherapy Topical + Systemic and Topical + Biologic	Health care and patient	Direct medical cost (drug) and indirect cost (out of pocket, transportation, and loss of productivity)	Cost of illness	**Provider cost:** $1,390/patient **Patient cost:** $542.54/patient **Cost** **Topical + Phototherapy** Provider: $603.66 Patient: $2,230.66 Total: $2,834.32/9 **Topical + Systemic:** Provider: $657.24 Patient: $420.85 Total: $1,078.09/40 **Topical + Biologic** Provider: $8,523.20 Patient: $303.53 Total: $11,357.43/10 **Cost/patient (inpatient)** $275.14 **Cost/patient (outpatient)** $74.19	Not applicable

Table 2: Continued

Reference (Year)	Time Horizon and Country	Treatment Option	Analysis Perspective	Included Costs (Description)	Type of Outcome	Result (Cost)	Result (Others)
Tang et al. (2013	1 year, Malaysia	Not applicable, no treatment stated	Health care and patient	Direct cost (medical cost) and indirect cost (transportation, cost other medicine without doctor's prescription)	QoL and cost of illness	**Outpatient management cost** $325.73/patient **Inpatient management cost (Hospitalization)** $92.19/patient **Direct cost:** $248.86 **Indirect cost:** $69.90	Patient had > 10 PASI score and lower quality of life.
Ha et al. (2016	1 year, Korea	Not Applicable (psoriasis compared with other skin disease)	Health care	Psoriasis pre-index period cost and post-index cost. (direct cost)	Health care expenditure and utilization	**Moderate to severe** Pre-index: $88.73/patient Post-index: $135.07/patient **Mild** Pre-index: $21.46/patient Post-index: $23.97/patient **Other skin disease** Pre-index: $69.16/patient Post-index: $104.66/patient	21.2% had moderate to severe psoriasis. Mean health care utilization was 8.97 and 12.71 for pre-index and post-index period, respectively, for moderate to severe psoriasis; and 2.63 and 3.25, respectively, for mild psoriasis.

Table 2: Continued

Reference (Year)	Time Horizon and Country	Treatment Option	Analysis Perspective	Included Costs (Description)	Type of Outcome	Result (Cost)	Result (Others)
Tang et al. (2013	1 year, Malaysia	Not applicable, no treatment stated	Health care and patient	Direct cost (medical cost) and indirect cost (transportation, cost other medicine without doctor's prescription)	QoL and cost of illness	**Outpatient management cost** $325.73/patient **Inpatient management cost (Hospitalization)** $92.19/patient **Direct cost:** $248.86 **Indirect cost:** $69.90	Patient had > 10 PASI score and lower quality of life.
Ha et al. (2016	1 year, Korea	Not Applicable (psoriasis compared with other skin disease)	Health care	Psoriasis pre-index period cost and post-index cost. (direct cost)	Health care expenditure and utilization	**Moderate to severe** Pre-index: $88.73/patient Post-index: $135.07/patient **Mild** Pre-index: $21.46/patient Post-index: $23.97/patient **Other skin disease** Pre-index: $69.16/patient Post-index: $104.66/patient	21.2% had moderate to severe psoriasis. Mean health care utilization was 8.97 and 12.71 for pre-index and post-index period, respectively, for moderate to severe psoriasis; and 2.63 and 3.25, respectively, for mild psoriasis.

Note. ADA: adalimumab; UST: ustekinumab; IFX: Infliximab; MTX: methotrexate; Pre-index: the index date of patients with psoriasis was the diagnosis date of psoriasis; QoL: quality of life; BT: biologics treatment; currency exchange US Dollar–Malaysian Ringgit: MYR0.2489; Japanese Yen–Malaysian Ringgit: MYR25.672, Indian rupee–MYR: 18.878; Malaysian Ringgit–US Dollar: MYR4.017.

3.2.2 Cost Effectiveness Analysis of Psoriasis Treament

Eight cost-effectiveness analysis (CEA) studies were included in this systematic review (Azizam et al., 2019; Igarashi et al., 2018, 2013; Imafuku et al., 2017; Saeki et al., 2020; Takahashi et al., 2017, 2019; Wang et al., 2014) for cost and effectiveness assessment of psoriasis treatments. Six studies were from Japan, one study from Taiwan, and the other from Malaysia. From the eight studies, five focused on biologics drugs (Igarashi et al., 2018, 2013; Imafuku et al., 2017; Saeki et al., 2020; Wang et al., 2014); two studies on systemic plus topical and biological or systemic alone and biological drugs (Takahashi et al., 2017, 2019) and one study on phototherapy, systemic, and biologic (Azizam et al., 2019). All eight studies were done for a comparative study of treatments. Out of eight cost-effectiveness studies, only five studies reported incremental cost-effectiveness ratio (ICER) results (Azizam et al., 2019; Igarashi et al., 2018; Saeki et al., 2020; Takahashi et al., 2019; Wang et al., 2014). From the aforementioned total studies, one study adopted a short-term time horizon, which was less than one year (Azizam et al., 2019); two studies adopted one-year time horizon (Takahashi et al., 2017, 2019); one study adopted both short-term (less than one year) and long-term (more than one year) time horizon (Imafuku et al., 2017), and two studies adopted two-year time horizon (Igarashi et al., 2013; Wang et al., 2014). Meanwhile, the remaining studies adopted a longer term time horizon, ranging from 5 years (Igarashi et al., 2018) to lifetime (Saeki et al., 2020).

3.2.3 Quality Assessment

Demonstrates the results of the quality assessment see Fig. 2. The mean amount of fulfilled criteria for the cost of illness were 6.6 out of 14 (median 6, range 6–8), 18 out of 35 (median 18, range 15–20), and 9.6 out of 24 (median 9, range 8–11); while for cost-effectiveness, the mean values were 9.63 out of 14 (median 9.6 range 8–11), 25.5 out of 35 (median 24 range 21–32), and 17.75 out of 24 (median 17.5, range 13–22) for Joanna Briggs Institute (JBI) checklist, Drummond's checklist, and the CHEERS guideline, respectively. Studies by [28,29], which adopted the long-term time horizon, had fulfilled most of the criteria of the applicable items. Information on adjustment data, baseline data, data integration, and uncertainty evaluation were the most frequently excluded quality elements from economic analyses Table 1.

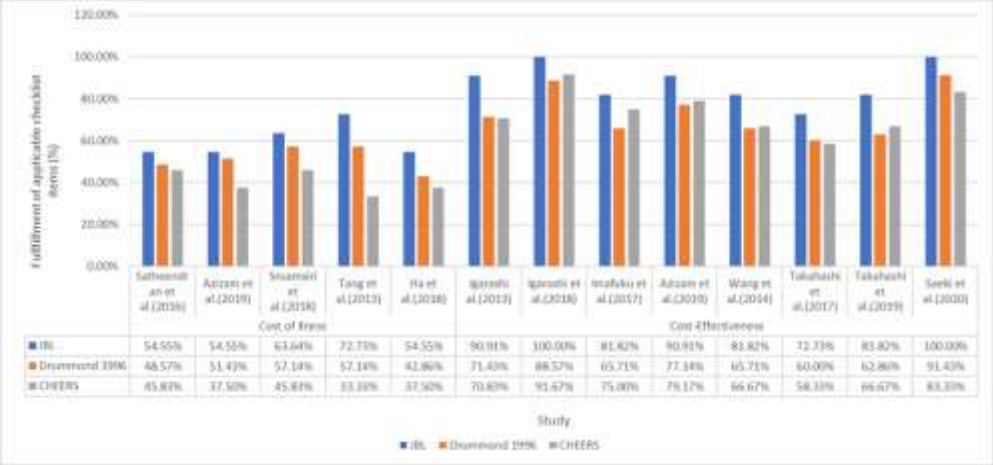

Fig. 2 Studies Checklist Assessment

Table 3: Cost-effectiveness

Reference (Year)	Time Horizon and Country	Treatment Option	Comparison	Cost Outcome (Quantification)	Efficacy Outcome (Quantification)	ICERs
Igarashi et al. (2013)[1]	2 years, Japan	a) ADA The initial dose of 80 mg b) UST 45 mg c) INF	Compare between adalimumab, ustekinumab and infliximab.	**Annual cost per each treatment** Year 1 a) Adalimumab: $23,999 b) Ustekinumab: $38,867 c) Infliximab: $26,664 Year 2 a) Adalimumab: $23,111 b) Ustekinumab: $32,598 c) Infliximab: $23,091 **Base cost-effectiveness/PASI 75** Year 1 a) Adalimumab: $40,471 b) Ustekinumab: $35,970 c) Infliximab: $46,828 Year 2 a) Adalimumab: $38,972 b) Ustekinumab: $31,162 c) Infliximab: $39,275	a) Adalimumab Mean: 59% of patients achieved PASI 75 b) Ustekinumab Mean: 74% of patients achieve PASI 75 c) Infliximab Mean: 83% of patients achieve PASI 75	Not reported from authors

[1] Annual cost for ustekinumab 45 mg is higher than other treatments. However, Ustekinumab 45 mg is more cost-effective than adalimumab and infliximab.

Table 3: Continued

Reference (Year)	Time Horizon and Country	Treatment Option	Comparison	Cost Outcome (Quantification)	Efficacy Outcome (Quantification)	ICERs
Igarashi et al. (2018)[2]	5 years, Japan	a) ADA 40 mg b) UST 45 mg c) SEC 300 mg d) IFX 5 mg	Secukinumab compared with (adalimumab, ustekinumab and infliximab)	**Health care (Total cost)** a) Secukinumab 300 mg $77,105/QALY b) Ustekinumab 45 mg $82,089/QALY c) Adalimumab $60,9845/QALY d) Infliximab $/86,889/QALY **Patient perspective** Monthly & 3 Months a) Secukinumab 300 mg $21,976; $11,235 b) Adalimumab $18,240; $11,209 c) Ustekinumab 45 mg $11,007; $ 11,007 d) Infliximab $14,526; $ 14,526	a) Secukinumab 4.07 QALYs b) Ustekinumab 4.03 QALYs c) Adalimumab 3.87 QALYs d) Infliximab 4.04 QALYs **Patient perspective** 3 Months a) Secukinumab 300 mg $11,235/49% reduction b) Adalimumab $11,209/39% reduction	Secukinumab 300 mg vs. Adalimumab $ 81,622 Secukinumab dominates infliximab and ustekinumab

[2] Secukinumab is more cost-effective compared with infliximab and ustekinumab treatments for both perspectives. Adalimumab has lower cost but the outcome is lower.

Table 3: Continued

Reference (Year)	Time Horizon and Country	Treatment Option	Comparison	Cost Outcome (Quantification)	Efficacy Outcome (Quantification)	ICERs
Imafuku et al. (2017)[3]	1 year, Japan	a) SEK 150 mg and 300 mg b) ADA 40 mg and 80 mg c) UST 45 mg and 90 mg d) IFX 5 mg/kg	Biologics compared with placebo	**Cost/PASI 75** One year a) SEC 150 mg & 300 mg $14,692; $30,925 b) ADA 40 mg & 80 mg $26,804; $41,580 c) UST 45 mg & 90 mg $41,925; $71,450 d) INF $55,575 Short-term a) SEC 150 mg & 300 mg $5,510; $11,597 b) ADA 40 mg & 80 mg $8,935; $12,794 c) UST 45 mg & 90 mg $16,770; $ 28,580 d) INF $ 20,841	**Estimated response rate** a) SEC 150 mg & 300 mg 86.2%; 82.8% b) ADA 40 mg & 80 mg 62.8%; 81% c) UST 45 mg & 90 mg 59.4%; 67.7% d) INF 71.4% **PASI–75 NNT** a) SEC 150 mg & 300 mg 1.29; 1.36 b) ADA 40 mg & 80 mg 1.57; 1.27 c) UST 45 mg & 90 mg 1.97; 1.68 d) INF 2.00	Not reported from authors

[3] Secukinumab and Adalimumab is more cost-effective compared with other treatments option. Total for both doses cost show secukinumab is more cost-effective.

Table 3: Continued

Reference (Year)	Time Horizon and Country	Treatment Option	Comparison	Cost Outcome (Quantification)	Efficacy Outcome (Quantification)	ICERs
Takahashi et al. (2017)[4]	1 year, Japan	a) Topical steroid (TS) b) Topical vitamin D3 (TVD3) c) Topical steroid + topical vitamin D3 (TS+TVD3) d) Calcipotriol/betamethasone dipropionate (C+B) e) Systemic treatment (Cyclosporin) f) Biologics (SEK, UST, and ADA)	This research compares the topical treatment with systemic and biologics.	**Average cost a year** a) TS: $176 (45 patients) b) TVD3: $317 (5 patients) c) TS+TVD3: $284 (25 patients) d) C+B: $336 (45 patients) e) Cyclosporin: $665/year (7 patients) f) Secukinumab: $6,124/year (4patients) g) Ustekinumab: $4,350/year (9 patients) h) Adalimumab: $5,166/year (8 patients) **Cost/1PASI** a) TS: $29 b) TVD3: $39 c) TS+TVD3: $33 d) C+B: $31 e) Cyclosporin: $33 f) Secukinumab: $74 g) Ustekinumab: $48 h) Adalimumab: $56	**Day/1 PASI and PASI 75** a) TS 25.2 days and 0% of patients achieve PASI 75 b) TVD3 40.2 days and 4.4% of patients achieve PASI 75 c) TS+TVD3 23.1 days and 8% of patients achieve PASI 75 d) C+B 20.5% and 33% of patients achieved PASI 75 e) Cyclosporin 9.2 days and 88.8% of patients achieved PASI 75 f) Secukinumab 7.2 days and 100% of patients achieved PASI 75 g) Ustekinumab 8.5 days and 100% of patients achieved PASI 75 h) Adalimumab 8.3 days and 100% of patients achieved PASI 75	Not reported from authors

[4] Ustekinumab is more cost-effective than other biologics for moderate to severe treatment.

Table 3: Continued

Reference (Year)	Time Horizon and Country	Treatment Option	Comparison	Cost Outcome (Quantification)	Efficacy Outcome (Quantification)	ICERs
Takahashi et al. (2019)[5]	1 year, Japan	a) Topical corticosteroid (TC) b) Topical corticosteroid + Topical vitamin D3 (TC + TVD) c) Combine corticosteroid/vitamin D3 (CVD) d) Systemic treatment + topical corticosteroid (S +TC) e) Systemic treatment + topical vitamin D3 (S +TVD) f) Systemic treatment + combine topical + topical corticosteroid/vi	Compared with topical, systemic, and biologics.	**Total cost & Patient payment/year** a) TC $542/year & $141/year b) TC +TVD $498/year & $188/year c) CVD $1,037/year & $268/year d) S + TC $1,828/year & $475/year e) S + TVD $2,465/year & $568/year f) S + CT + TC/VD3 $2,899/year & $915/year g) Biologics $9,583/year & $915/year **Total cost/1 PASI** a) TC $1,489/1 PASI & $33/0.001EQ-5D b) TC +TVD $529/1 PASI & $14/0.001EQ-5D c) CVD $402/1 PASI & $9/0.001EQ-5D d) S + TC $534/1 PASI & $54/0.001EQ-5D e) S + TVD $575/1 PASI & $25/0.001EQ-5D f) S + CT + TC/VD3 $1,381/1 PASI & $96/0.001EQ-5D g) Biologics	a) TC PASI score 4.4 (2.4–7.9) Initial EQ-5D score 0.879 b) TC +TVD PASI score 4.6 (3.2–7.8) Initial EQ-5D score 0.865 c) CVD PASI score 4.8 (1.2–7.8) Initial EQ-5D score 0.826 d) S + TC PASI score 7.3 (4.2–11.8) Initial EQ-5D score 0.844 e) S + TVD PASI score 4.3 (3.5–10.5) Initial EQ-5D score 0.859 f) S + CT + TC/VD3	**a) TC: -** b) TC +TVD $14,365/ 0.893QALY c) CVD $9,930/ 0.951QALY d) S+ TC $70,992/ 0.951QALY e) S+ TVD $39,845/ 0.951QALY f) S + CT +TC/VD3 $33,092/ 0.892QALY g) Biologics $61,739/ 0/983QALY

[5] Topical combine corticosteroid is more cost-effective among other treatments. However, systemic combine treatment more cost-effective for moderate to severe treatment compared with biologics to treat moderate to severe.

		tamin D3 (S + CT + TC/VD) g) Biologics (secukinumab, ustekinumab, brodalumab, ixekizumab, and adalimumab)		$8,156/1 PASI & $266/0.001EQ-5D **Patient cost** a) TC $387/1 PASI & $137/0.001EQ-5D b) TC +TVD $200/1 PASI & $5/0.001EQ-5D c) CVD $103/1 PASI & $2/0.001EQ-5D d) S + TC $139/1 PASI & $14/0.001EQ-5D e) S + TVD $133/1 PASI & $6/0.001EQ-5D f) S + CT + TC/VD3 $436/1 PASI & $30/0.001EQ-5D g) Biologics $2,043/1 PASI & $67/0.001EQ-5D	PASI score 6.6 (4.2–11.8 Initial EQ-5D score 0.841 g) Biologics PASI score 1.6 (0.3–13.7) Initial EQ-5D 0.948	Note: S +TC more expensive cost ICER/QALY
Saeki et al. (2016)[6]	Life-time horizon (100 years), Japan	a) RSK b) ADA c) BDL d) GSK e) IFX f) IKZ g) SEK h) UST	Risankizumab compared with other biologic treatments	**Health care (Direct cost)** a) RSK: $158,310 b) ADA: $116,889 c) BDL: $129,159 d) GSK: $145,540 e) IFX: $123,276 f) IKZ: $124,633 g) SEK: $132,830 h) UST: $141,574 **Societal (Direct and indirect cost**) a) RSK: $247,645 b) ADA: $217,990 c) BDL: $226,927 d) GSK: $239,768 e) IFX: $226,695 f) IKZ: $226,154 g) SEK: $230,880` h) UST: $241,586	**PASI 75 base on meta-analysis** RSK: 89.2% ADA: 69.5% BDL: 88.7% GSK: 86.8% IFX: 80.4% IKZ: 80.4% SEK: 83.1% UST: 70.5% **QALYs** RSK: 1.84 ADA: 1.14 BDL: 1.29 GSK: 1.54 IFX: 0.95 IKZ: 1.06 SEK: 1.29 UST: 1.17	Base case ICER Risankizumab vs. comparator **Health perspective** a) RSK: – b) ADA: $58,930 c) BDL: $52,918 d) GSK: $42,387 e) IFX: $39,392 f) IKZ: $42,783 g) SEK: $45,941

[6] Risanzkizumab is considered cost-effective compared with other treatments for ICER analyses.

				Patient (Co-payment only) a) RSK: $9,614 b) ADA: $9,682 c) BDL: $10,342 d) GSK: $11,904 e) IFX: $8,063 f) IKZ: $8,756 g) SEK: $10,312 h) UST: $6,446		h) UST: $24,687 **Societal** a) RSK: – b) ADA: $42,191 c) BDL: $37,610 d) GSK: $26,148 e) IFX: $23,557 f) IKZ: $27,302 g) SEK: $30,228 h) UST: $8,938 **Patient** a) RSK: – b) ADA: cost-saving c) BDL: cost-saving d) GSK: cost-saving e) IFX: $1,744 f) IKZ: $1,090 g) SEK: cost-saving h) UST: $4,674

Wang et al. (2014)[7]	2 years, Taiwan	a) Etanercept b) Adalimumab c) Ustekinumab	Compare between etanercept, adalimumab and ustekinumab	Not reported by author	PASI75 a) Etanercept: 44% b) Adalimumab: 63% c) Ustekinumab: 64%	YEAR 1 a) Etanercept Base: $39,716 b) Adalimumab Base: $23,715 c) Ustekinumab Base: $26,333 Year 2 a) Etanercept Base: $71,985 b) Adalimumab Base: $62,676 c) Ustekinumab Base: $52,666
Azizam et al. (2019)[8]	6 months, Malaysia	a) Topical Biologic b) Topical Systemic c) Topical phototherapy	Between biologic and systemic	**Total cost** Biologic cost: $108,115 Systemic cost: $74,220 Phototherapy $55,924 **Base case results for cost-effectiveness** Biologic cost: $13,514 Systemic cost: $2,249 Phototherapy: $6,990	PASI 75 Biologic: 67.7% Systemic: 55%	Biologics was dominated by systemic with ICER –$1,356

Note. ICER: Incremental cost-effectiveness ratio; PASI: Psoriasis Area and Severity Index; QALY: Quality adjusted life year; ADA: Adalimumab: UST: Ustekinumab; IFX: Infliximab; SEK: Secukinumab; GSK: Guselkumab; BDL: Brodolumab; IKZ: Ixekizumab; RSK: Risankizumab; currency exchange US dollar- Malaysia: MYR0.2489; Japanese yen– Malaysia: MYR25.672; Malaysia - US dollar: MYR4.017.

[7] Adalimumab and ustekinumab had lower cost compared with etanercept.

[8] Systemic is more cost-effective compared with biologics and phototherapy for moderate to severe treatment.

4.0 Discussion

There is scarce information about the cost-effectiveness analysis (CEA) of psoriasis treatments in Asia, especially in Southeast Asia. This study focuses on reviewing the cost of illness (COIs) and CEA of psoriasis treatments in the Asian region. COIs, economic burden, and CEAs have been comprehensively studied in European countries and United States (Brezinski et al., 2015a; D'Ausilio et al., 2015; D'Souza & Payette, 2015; Feldman et al., 2014; Kersh, Kellen, & Rose, 2016; Küster et al., 2016; Steinke et al., 2013; Vanderpuye-Orgle et al., 2015). However, only five COI studies (Azizam et al., 2019; Ha et al., 2018; Satheendran et al., 2016; Sruamsiri et al., 2018; Tang et al., 2013) and eight CEAs (Azizam et al., 2019; Igarashi et al., 2018, 2013; Imafuku et al., 2017; Saeki et al., 2020; Takahashi et al., 2017, 2019; Wang et al., 2014) studies had met the inclusion criteria. This work anticipates more CEA and COI studies to be done, as psoriasis has a significant impact on a person's quality of life and financial status. Chronic skin diseases, such as psoriasis, have been shown to affect patients' quality of life, social relationships, psychological status, and daily activities. The deterioration in quality of life experienced by psoriasis patients is more severe than other skin diseases (Grozdev et al., 2011; Thorleifsdottir et al., 2017; Yang & Yang, 2015). According to a study conducted by (Leovigildo et al., 2016), about 43% of patients were unable to work due to the disease affecting the motivation, self-confidence, and mood of patients, which in turn, affect their social activities, educational development, and work performance.

Findings from COI studies showed variation in terms of economic burden or costs associated with psoriasis management in Asian countries. In India, the range of total cost per patient was $60.85/patient (methotrexate) to $408.66/patient (Bath PUVA) (Satheendran et al., 2016). Meanwhile, in Japan, the total cost ranged from $7,370.00 to $9,212.00, where the cost had increased more than double between $14,914.00–$23,554.00 after post biological therapy (BT) initiation of psoriasis treatment. The cost of managing psoriasis in persistent and non-persistent groups ranged between $10,298.00–$21,780.00 and $5,770.00–$24,310.00, respectively (Sruamsiri et al., 2018); this result was consistent with the study conducted in Germany (Mahlich et al., 2019). In Malaysia, the average cost for the management of psoriasis was $1,932.54/patient. Biologic yielded the highest average cost and overall cost, which was $1,135.74/patient and $11,357.43/10, respectively, in comparison with other treatments (Azizam et al., 2019). Moreover, in Korea, the cost of psoriasis management for pre-index ranged from $21.46/patient to $88.73/patient, whereas for post-index, it ranged from $23.97/patient to $135.07/patient. The cost of managing psoriasis was greater than that of other skin diseases in Korea (Ha et al., 2018). It is relevant because psoriasis disease is associated with other commodities disease and different levels of score that contribute to the cost increase in managing psoriasis.

Psoriasis causes a great financial burden from many perspectives. Four out of five COI were calculated costs from the perspective of provider and patient, and a COI measured costs from a provider/health care system perspective (Azizam et al., 2019; Satheendran et al., 2016; Sruamsiri et al., 2018; Tang et al., 2013). Out of four articles that evaluated both of the abovementioned perspectives, only 75% of the studies considered direct and indirect medical costs, such as patient's transportation, accommodation, food, and loss of productivity (Azizam, et al., 2019; Satheendran et al., 2016; Tang et al., 2013). In India, the direct cost of managing psoriasis ranged from a direct cost versus an indirect cost, which revealed $3.19 versus $57.66 (methotrexate) to $107.13 versus $301.53 (PUVA) per patient (Satheendran et al., 2016). Meanwhile, in Malaysia, the direct cost (provider) and indirect cost (patient) ranged from $603.66–$8,523.20 and $303.53–$2,230.66, respectively. The indirect cost was lowest for biological treatment but greater for phototherapy treatment (Azizam et al., 2019). One study in Malaysia calculated the direct and indirect costs, which ranged from $248.86 to $69.90 (Tang et al., 2013). The direct medical cost had taken into account both perspectives (provider and patient) in a study in Japan (Sruamsiri et al., 2018). All COIs included demonstrated higher direct medical costs than indirect costs. This is consistent with a systematic review analysis of the economic burden in the US (Brezinski et al., 2015b). Next, in terms of outpatient and inpatient management costs, the outpatient cost of psoriasis in Malaysia was $325.73/patient, while the inpatient cost was $92.19/patient (Tang et al., 2013). Another study conducted in Malaysia showed an outpatient cost was lower than inpatient cost, where the former cost $74.19/patient and the latter at $275.14/patient (Azizam et al., 2019). In Japan, cost of outpatient versus inpatient ranged from $10,444.00 to $19,501.00 versus $359.00 to $5,828.00 (Sruamsiri et al., 2018).

Studies of CEAs in Asian countries showed varying results regarding the most cost-effective treatments in treating psoriasis. In a Taiwanese setting, adalimumab and ustekinumab are the most cost-effective treatment (Wang et al., 2014). Results on the most cost-effective treatment varied significantly between the CEA studies conducted in a

Japanese setting. It was observed that Risankizumab (Saeki et al., 2020), adalimumab 40 mg/80 mg, secukinumab 150 mg/300 mg (Igarashi et al., 2018; Imafuku et al., 2017), ustekinumab, combined corticosteroid and active vitamin D3 topical, and topical steroid were the most cost-effective treatments for psoriasis patients in a Japanese setting (Igarashi et al., 2013; Takahashi et al., 2017, 2019). In Malaysia, topical and systemic appeared to be the most effective treatments for moderate to severe psoriasis, compared with other modalities (Azizam et al., 2019).

The horizon identified in various studies differs. Approximately 30% of CEAs of psoriasis treatments (Imafuku et al., 2017; Takahashi et al., 2017, 2019) adopted a time horizon of 1 year, 2 years (Igarashi et al., 2013; Wang et al., 2014)**,** 5 years (Igarashi et al., 2018), even lifetime (Saeki et al., 2020). Since psoriasis is a chronic condition, patients with this disease will require care for the rest of his life. As a result, the perfect scenario for evaluating it would be measuring its cost-effectiveness over a prolonged period of time. Although a long-time horizon is ideal, the data associated with long-term experience with numerous psoriasis interventions is mainly limited. Therefore, some studies have adopted a time horizon of 3 years, which is considered feasible in the real world (Riveros, Ziegelmann, & Correr, 2014).

The majority of the CEA studies (Azizam et al., 2019; Igarashi et al., 2013; Imafuku et al., 2017; Saeki et al., 2020; Takahashi et al., 2017, 2019; Wang et al., 2014) employ Psoriasis Area Severity Index (PASI) score as an outcome; this is supported by the available evidences (Ahn et al.,2013; Alfageme Roldán et al., 2016; Baker et al., 2013; Cohen et al., 2012; Mrowietz et al., 2011; Riveros et al., 2014). In a cost-effectiveness study of psoriasis treatment using Quality-Adjusted Life-Year (QALY) as a measure of effectiveness, the response of PASI and Dermatology Life Quality Index (DLQI) had to be converted into a utility form by a EuroQol-5D instrument (EQ-5D) before it was used to measure QALY. However, evidence suggests that EQ-5D scores show a weak to a moderate relationship with DLQI and PASI scores (Blome et al., 2013; Norlin, 2013). Thus, applying utility values to PASI and DLQI responses resulted in high bias (Riveros et al., 2014). Moreover, in testing the effectiveness of psoriasis treatment, PASI is considered the gold standard, as its score meets the methodological criteria of validity (Bronsard et al., 2010; Hägg et al., 2017). More patients with moderate to severe psoriasis can achieve better outcomes when PASI is used for measuring the effectiveness of the psoriasis treatment.

More than 60% of CEAs had compared the cost-effectiveness among biologic agents. This is relevant because biological treatment is the best treatment for moderate to severe psoriasis treatments at this time, and it has been proven to be effective and capable of improving the quality of life of patients. Thus, cost-effectiveness studies are very important to justify the use of biologics in their respective countries. Nevertheless, this review was subjected to several limitations. First, the findings from this review cannot be generalized to all Asian countries, as only a few studies were included in this work. Furthermore, some important parameters and sensitivity analyses were not reported. Additionally, a variation method used in calculating cost-effectiveness may lead to different results.

5.0 Conclusion

Treatment modalities have a significant impact on the overall cost and quality of life of patients. Biological treatment is the most effective treatment, in which it is deemed to be able to eliminate the symptoms of psoriasis in a short time, as well as reduce the length of stay in hospital. However, the extremely high cost of medication limits its use in many health care settings. Systemic treatment is also an effective treatment for moderate to severe cases. Nevertheless, various screening tests and monitoring need to be performed to identify the side effects, thereby increasing the overall cost of treatment. On the other hand, phototherapy affects productivity and causes patients to lose income because patients are often required to take a time off to seek treatment at the clinic (two or three times a week). Given the huge economic burden caused by psoriasis on patients and providers, the health economists, clinicians, and policymakers should consider the cost and effectiveness that are in line with the patients' values and characteristics in resource allocation for psoriasis management.

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