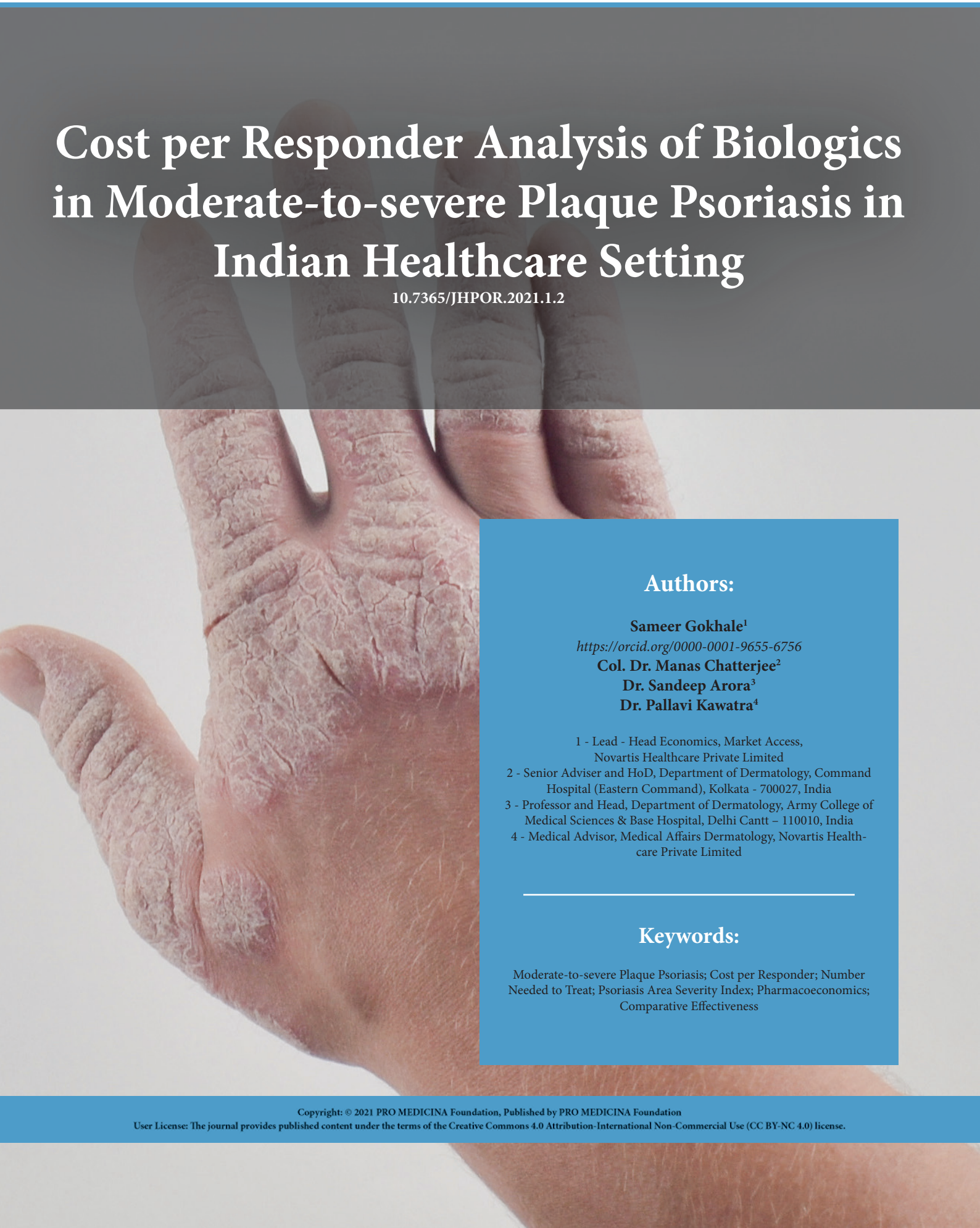
#01/2021
ISSN 2299-1247

JHPOR | Journal of Health Policy & Outcomes Research

Cost per Responder Analysis of Biologics in Moderate-to-severe Plaque Psoriasis in Indian Healthcare Setting

10.7365/JHPOR.2021.1.2



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Keywords:

Moderate-to-severe Plaque Psoriasis; Cost per Responder; Number Needed to Treat; Psoriasis Area Severity Index; Pharmacoeconomics; Comparative Effectiveness

How to cite this article?
Gokhale S., Chatterjee M., Arora S., Kawatra P. Cost per Responder Analysis of Biologics in Moderate-to-severe Plaque Psoriasis in Indian Healthcare Setting J Health Policy Outcomes Res [Internet]. 2021 [cited YYYY Mon DD];1. Available from:https://www.jhpor.com/article/2262-cost-per-responder-analysis-of-biologics-in-moderate-to-severe-plaque-psoriasis-in-indian-healthcare-setting

contributed: 2021-02-02 final review: 2021-03-17 published: 2021-03-22

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Abstract

Background: Moderate-to-severe plaque psoriasis (PsO) affects >8 million Indians and has a detrimental effect on quality of life (QoL). Effective skin clearance can be one of the important factors for improving patient's QoL. Newer biologics offer significant levels of skin clearance eventually improving QoL. However high cost of originator biologics is an impediment and poses a challenge for healthcare stakeholder to choose more efficacious and cost-effective biologic among the available options.

Aims: To estimate the annual cost per responder (CPR) in PsO patients in India based on Psoriasis Area Severity Index (PASI)-75/90 for 52-weeks of treatment and estimate the number needed to treat (NNT).

Methods: CPR has been developed to compare direct medical costs. The tool enables the user to input epidemiology numbers, level of drug usage and allows user to decide the biologic to choose to offer better health outcomes. Efficacy for biologics under evaluation were reported from the network meta-analysis and measured as proportion of patients achieving PASI-75/90 at week-52. NNT to obtain one patient with a PASI-75/90 response was henceforth calculated.

Results: The tool demonstrates CPR and NNT results dynamically with user provided inputs. Additional number of responders who could potentially be treated with the biologic under consideration with the annual cost-savings generated were also presented. This will help users to assess comparative effectiveness of a biologic intervention by combining clinical and economic dimensions.
Conclusion: This CPR tool supports evidence-based decision making for improved health outcomes in the Indian healthcare setting.

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Introduction

Moderate-to-severe plaque psoriasis (PsO) affects more than 8 million Indians.[1] PsO is characterized by erythematous and scaly skin patches that are itchy and painful[2] and has significant detrimental effect on patients quality of life (QoL).[3] PsO is often linked with social stigmatization, loss of self-confidence, physical disability and psychological distress.[4] Effective skin clearance can be one of the important factors for improving PsO patient's QoL.[3, 5] Biologic interventions such as tumor necrosis factor inhibitors (TNFi) have revolutionized PsO treatment with more patients reaching Psoriasis Area Severity Index (PASI)-75. These response rates have now been superseded with achievable responses of PASI-90 and PASI-100 by newer biologics.[6] Achieving PASI-90 and/or PASI-100 response in comparison with PASI-75 by the newer generation biologics has been shown to be associated with improved QoL.[7-9] Currently available TNFi biologics in India include etanercept, infliximab, (innovators and biosimilars) and biosimilars of adalimumab. Secukinumab is a novel biologic agent that specifically targets interleukin-17 (IL-17) that has been approved and has been marketed in India for more than past 4 years.[10, 11]

High cost of originator biologic therapies is an impediment in using them for moderate-to-severe PsO patients who really need them. It is challenging for a healthcare stakeholder (physicians, insurers, and payers) to choose more efficacious and cost-effective biologic therapies among available options in Indian healthcare setting.[6] Comparative effectiveness among available PsO treatments can best be evaluated using head-to-head randomized controlled trials (RCTs). However clinically relevant head-to-head RCTs involving PsO patients are limited. Comparative effectiveness in such cases often relies on network meta-analysis (NMA).[12] NMA can provide relative effectiveness among PsO therapies by using both direct comparisons of treatments within RCTs and indirect comparisons across trials based on a common comparator.[13] Furthermore, cost-effectiveness studies assessing PsO treatment strategies in Indian setting are scarce. This presents an unmet need for healthcare stakeholder's clinical decision-making and an efficient healthcare resource utilization for moderate-to-severe PsO patients. Economic evaluation involving cost per responder (CPR) for biologics and an estimation of number needed to treat (NNT) will address this unmet need and aid an efficient decision-making.

NNT is an epidemiological measure used in communicating the effectiveness of a new healthcare intervention (here biologics treating PsO patients to achieve PASI-75/90 at 52-weeks). It is the number of patients needed to treat to prevent one additional bad outcome (psoriatic ar-

thritis, cardiovascular disease etc.). In an ideal scenario, NNT as one indicates that everyone improves with the new intervention and no one improves with the treatment in comparison. Lower NNT indicates more effective treatment intervention.[14] NNT estimates to achieve one additional responder for a specific PASI level provides a relative measure of clinical efficacy with various biologics of interest. CPR is calculated by dividing annual treatment costs of biologic treatment per PsO patient by the proportion of responders achieving PASI-75/ 90 at week-52 for respective biologic. CPR hence provides a relative measure of average value for different biologics. NNT and CPR analyses provides reliable measures for assessing comparative effectiveness by combining clinical and economic dimensions. These two measures will provide vital information for healthcare stakeholders to make an efficient clinical and economical decision making.[15]

Objective of this manuscript is to estimate and compare the NNT and annual CPR in moderate-to-severe PsO patients based on PASI-75, PASI-90 for 52-weeks of biologic treatments from the Indian healthcare perspective. Secukinumab was compared with available originator TNFis in India, etanercept, adalimumab biosimilar and infliximab.

Materials and Methods

CPR tool was developed to compare direct medical costs such as drug acquisition, administration, and monitoring costs of biologic interventions. Cost of managing adverse events were assumed similar across biologic treatments and hence were not considered for CPR calculations. This enabled users to input epidemiology numbers, and drug usage level. User was also given a choice to select which TNFi can be displaced by secukinumab to offer better health outcomes. Analysis inputs were obtained from published literature, experts' consultation, and local market research. Choice of adding currently available originator biologics for PsO treatment in India with licensed posology was given. Annual drug costs were based on the respective ex-factory prices. The number of doses required for 52 weeks (1 year) of respective treatments were calculated as per the prescribing information (See Table 1). Average annual costs of induction and maintenance costs were considered. Infliximab drug costs were calculated considering an average body weight of 86.6 ± 19.8 kg, based on secukinumab clinical trial. Wastage (i.e. full vials only) were considered to estimate infliximab costs.[16-18]

As illustrated in Figure 1, the user was given an option of inputting the number of PsO patients seen per month along with percentage split between new and maintenance groups. Monthly numbers were converted to annual for calculations. User was asked to input the percentage of patients who were treated with systemic and the percentage of patients treated with biologics.[19] Table 2 presents annual resource utilization costs for available interventions. Utilization of infliximab was significantly higher than other biologics with increased number of physician visits and monitoring tests.

Efficacy of biologic treatment in PsO was based on the percentage improvement from baseline in the PASI score. PASI score; a commonly used tool to assess the severity of PsO, is a weighted measurement of the average redness, thickness and scaliness of psoriasis lesions and body surface area (BSA).[20] PASI-75 which represents an improvement of at least 75% in PASI score from baseline, has been traditionally accepted as a clinically meaningful endpoint for PsO treatment. However, PASI-90 and even PASI-100 is currently considered as a marker for treatment success.[21-23] Efficacy for biologics under evaluation at 16 weeks were reported from the network meta-analysis (NMA)[24] and were measured as proportion of patients achieving PASI-75 and PASI-90 response (See Table 3). We hypothesized that the response rates and NNT values will remain constant over 52 weeks. The CPR was calculated for PASI-75 and PASI-90 responses as the ratio between 52 weeks of annual drug costs for the induction and maintenance year and the percentage of patients achieving each PASI response outcome using the following equation:

$$\textit{Cost per Responder for PASI} - 75 = \frac{(\textit{per unit drug cost of a biologic}) \times (\textit{no. of doses per 52 weeks})}{\textit{percentage of patients with a PASI-75 response at 52 weeks}}$$

$$\textit{Cost per Responder for PASI} - 90 = \frac{(\textit{per unit drug cost of a biologic}) \times (\textit{no. of doses per 52 weeks})}{\textit{percentage of patients with a PASI-90 response at 52 weeks}}$$

The NNT to obtain one patient with a PASI-75, PASI-90 response at 52 weeks was calculated for each biologic intervention using following equations:

$$\textit{NNT-75} = 1 \div \textit{percentage of patients with PASI-75 response}$$

$$\textit{NNT-90} = 1 \div \textit{percentage of patients with PASI-90 response}$$

Additional number of responders who could potentially be treated with secukinumab with the annual cost-savings generated for PASI-75 and PASI-90 outcomes were also presented.

Results

The tool exhibits CPR and NNT results dynamically with user provided inputs for a specific scenario where secuk-

inumab was compared with available TNFis. Bar chart in Figure 2(A) displays annual number of responders with or without secukinumab for PASI-75 and PASI-90 response. Additional number of responders with secukinumab introduction is highlighted at the bottom of the graph. Graph 2(B) compares CPR for various biologic interventions. Costs is presented in Indian rupees (₹). NNTs are also displayed across biologic interventions. Number of secukinumab responders along with CPR are classified into naive and maintenance groups as shown in Figure 2(C). The user will be able to compare NNT and CPR numbers across all the available biologic interventions post providing necessary inputs for calculations. Summary results are presented in Figure 2(D) for scenario in discussion where Secukinumab is compared with anti TNFis.

Discussion

Newer biologics such as secukinumab in Indian healthcare market has marked a paradigm shift in the management of PsO with clear skin being an achievable option. With the inclusion of newer therapies, it is important to assess the value of each therapy. This tool enables users to assess an impact of cost per patient basis on the goal of PASI-75/90 achieved. We believe that such a tool demonstrates comparative effectiveness among available interventions.

Cost of biologic interventions was based on assumption of complete adherence to the indicated dosage by PsO patients during their assessment period. It does not include patient care and indirect costs associated with PsO that might change the treatment. Ex-factory prices were considered for analysis and results may vary depending on application of discounts. Itolizumab was not included in the analysis since its utilization was very low at the time when we conducted this analysis.

There are limitations of this tool that should be acknowledged. The efficacy results were taken from NMA and not from head-to-head RCTs due to non-availability of relevant studies in Indian healthcare setting. NMA approach is recommended by several healthcare authorities and is widely used.[12-13] Another limitation is of long-term (52-weeks) extrapolation of NMA's short-term clinical outcomes at week-16. The tool also assumed that response rates and NNT values would remain constant over 52 weeks. Such assumptions were made to provide data for comparison not limited to the induction period, but extended to a longer time horizon such as 52 weeks. This tool does not take into account cost of managing adverse events. However, adverse events across biologic interventions were generally comparable.[16-17]

This study offers a user-friendly tool for evaluation of comparative efficacy and cost-efficacy of DCGI-approved biologic agents for the treatment of moderate-to-severe PsO, specifically in the Indian patient population. In conclusion, CPR tool can enable better decision making for improved health outcomes in the Indian healthcare system.

Table 1. Dosing and unit prices of biologics for annual PsO treatment in Indian healthcare setting

Biologic	Dosing	Price per Unit (in ₹)	Induction Year		Maintenance Year		Annual Cost (Average of Induction and Maintenance)
			No. of Doses	Cost	No. of Doses	Cost	
Etanercept	50 mg	₹5,990	64	₹383,360	52	₹311,480	₹347,420
Adalimumab	40 mg	₹6,990	28	₹195,720	26	₹181,740	₹188,730
Infliximab	5 mg/ kg	₹15,155	24.8	₹375,844	19.5	₹295,523	₹335,684
Secukinumab	150 mg	₹12,857	32	₹411,424	24	₹308,568	₹359,996

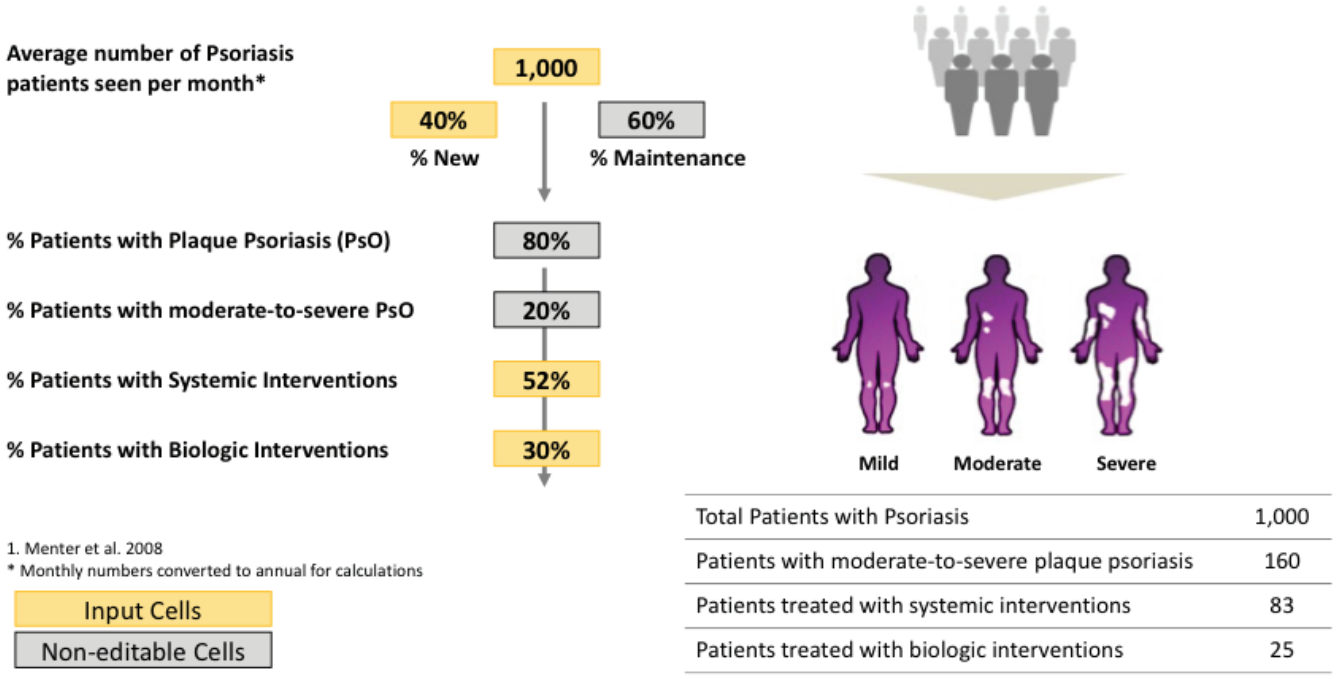
Average body weight of 86.6 ± 19.8 kg was assumed based on global trials (16-18)

Table 2. Annual healthcare resource utilization per biologic intervention in PsO treatment in Indian healthcare setting

Biologic Agent	No. of Annual Physician Visits	Cost per Physician Visit	No. of Annual Monitoring Visits	Cost per Monitoring Visit	Annual Cost of Resource Utilization
Etanercept	4	₹800	4	₹5,000	₹23,200
Adalimumab	4	₹800	4	₹5,000	₹23,200
Infliximab	10.5	₹800	6.5	₹5,000	₹40,900
Secukinumab	4	₹800	4	₹5,000	₹23,200

Table 3. Efficacy of biologic interventions at 16 weeks[24]

Biologic Agent	% Patients PASI ≥75	% Patients PASI ≥90
Etanercept	62.20%	34.30%
Adalimumab	63.80%	35.90%
Infliximab	81.00%	56.50%
Secukinumab	88.70%	69.10%



Total Patients with Psoriasis	1,000
Patients with moderate-to-severe plaque psoriasis	160
Patients treated with systemic interventions	83
Patients treated with biologic interventions	25

Figure 1. Epidemiology inputs for CPR model
Note: This is an illustrative example and all input cells can be changed by user to see dynamic epidemiology numbers

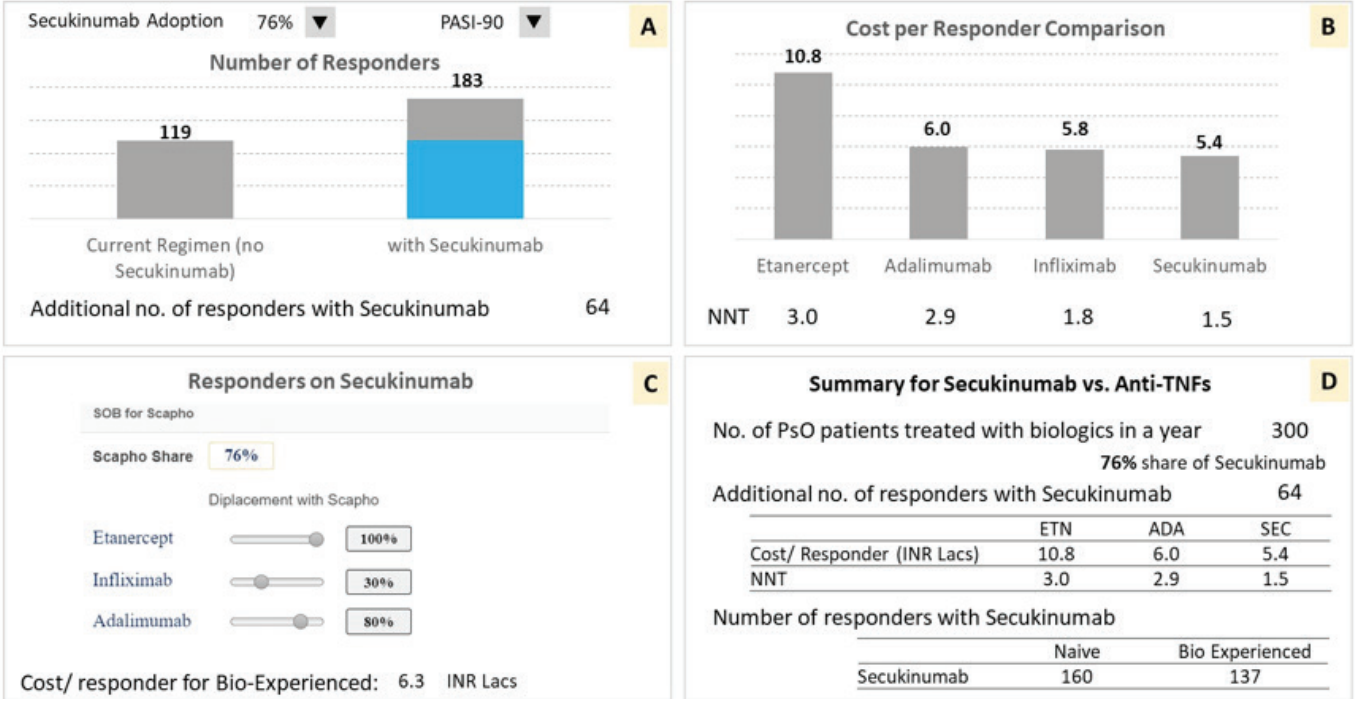


Figure 2. CPR and NNT Results Page (Scenario 1: Secukinumab vs. Anti-TNFs)

Acknowledgement
Authors would like to acknowledge Pankaj Gupta, Sanjay Tilak, Ajay Kapoor, and Sushant Anand employees of Novartis Healthcare Pvt. Ltd. for making substantial conceptual or design contributions for the CPR tool.

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