



Humanistic and Economic Impact of Moderate to Severe Plaque Psoriasis in Brazil

Nilcéia Lopes · Leticia L. S. Dias · Luna Azulay-Abulafia ·
Luiza K. M. Oyafuso · Maria Victoria Suarez · Lincoln Fabricio ·
Clarice Marie Kobata · Tania Cestari · Bernardo Gontijo ·
Cid Y. Sabbag · João R. Antonio · Ricardo Romiti · Patricia C. Pertel

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ABSTRACT

Introduction: Psoriasis is an immune-mediated, chronic, inflammatory disease, which has a substantial humanistic and economic burden. This study aimed to assess the impact of this disease on health-related quality of life (HRQoL), work productivity, and direct and indirect costs from a societal perspective among Brazilian patients.

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N. Lopes (✉) · P. C. Pertel
Novartis Biociências S.A., São Paulo, Brazil
e-mail: nilceia.lopez@novartis.com

L. L. S. Dias
ANOVA Consultoria em Saúde, Rio de Janeiro, Brazil

L. Azulay-Abulafia
Instituto de Dermatologia e Estética do Brasil Ltda.,
Rio de Janeiro, Brazil

L. K. M. Oyafuso
Faculdade de Medicina do ABC, Santo André, Brazil

M. V. Suarez
Hospital do Servidor Público Municipal, São Paulo,
Brazil

Methods: This is a cross-sectional, observational, multicenter study, enrolling patients with moderate to severe plaque psoriasis according to physician evaluation. Data collection was performed from December 2015 to November 2016 through face-to-face interviews using a structured questionnaire and five standardized patient-reported outcomes instruments. Direct costs were estimated by multiplying the amount of resources used (12-month recall period) by the corresponding unit cost. Indirect costs were grouped in two time horizons: annual costs (income reduction and absenteeism) and lifetime costs (demission and early retirement).

Results: A total of 188 patients with moderate to severe plaque psoriasis were included, with mean age of 48.0 (SD 13.1). “Anxiety and depression” and “pain and discomfort” were the

L. Fabricio
Hospital Universitário Evangélico de Curitiba,
Curitiba, Brazil

C. M. Kobata
Irmandade da Santa Casa de Misericórdia de São
Paulo, São Paulo, Brazil

T. Cestari
Hospital de Clínicas de Porto Alegre, Porto Alegre,
Brazil

B. Gontijo
Universidade Federal de Minas Gerais, Belo
Horizonte, Brazil

most impaired dimensions, according to the EuroQol Five-Dimension-Three-Level (EQ-5D-3L). The highest effect was found for “symptoms and feelings” [mean (SD) 2.4 (1.7)] Dermatology Life Quality Index (DLQI) subscale. Psoriatic arthritis (PsA) presence and biologic-naïve status were associated with worse HRQoL. Presenteeism was more frequent than absenteeism, according to the Work Productivity and Activity Impairment questionnaire-General Health (WPAI-GH) [17.4% vs. 6.3%], while physical demands and time management were the most affected Work Limitations Questionnaire (WLQ) subscales [means (SD) 23.5 (28.5) and 17.7 (24.9), respectively]. The estimated annual cost per patient was USD 4034. Direct medical costs accounted for 87.7% of this estimate, direct non-medical costs for 2.4%, and indirect costs for 9.9%.

Conclusions: Results evidenced that moderate to severe plaque psoriasis imposes substantial costs to society. Our data showed that this disease negatively affects both work productivity and HRQoL of Brazilian patients. Subgroups with PsA and biologic-naïve patients presented lower HRQoL, showing the impact of this comorbidity and the relevance of biologics in psoriasis treatment.

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Keywords: Cost of illness; Dermatology; Productivity; Psoriasis; Quality of Life

INTRODUCTION

Psoriasis is an immune-mediated, chronic, inflammatory disease, which usually affects skin but also can affect joints and nails [1–3].

C. Y. Sabbag
CEPIC, Centro Paulista de Investigação Clínica e
Serviços Médicos Ltda., São Paulo, Brazil

J. R. Antonio
Fundação Faculdade Regional de Medicina de São
José do Rio Preto, São José do Rio Preto, Brazil

R. Romiti
Hospital das Clínicas da Faculdade de Medicina da
Universidade de São Paulo, São Paulo, Brazil

Worldwide estimates of the prevalence of psoriasis range from 0.51% to 11.43% in adults and from 0% to 1.37% in children [4]. In Brazil, its prevalence is estimated at 1.31% [5]. The disease may present several forms of clinical manifestation with plaque psoriasis, or psoriasis vulgaris, the most frequent of them, accounting for about 90% of cases [2].

Psoriasis treatment includes topical therapy (corticosteroids, vitamin D₃ analogs), phototherapy, conventional systemic drugs (acitretin, methotrexate, or cyclosporine), biologics, over-the-counter medications, and complementary or alternative therapies [6]. About 70% and 80% of patients have mild psoriasis that can be controlled using topical therapies alone [2]. A combination of phototherapy and systemic therapy is needed for patients with moderate to severe disease. Biologics are generally used after phototherapy and when conventional systemic therapies have failed, i.e., either they were not tolerated or were contraindicated [2].

Psoriasis has been associated with substantial humanistic burden, markedly an adverse impact on a patient’s quality of life [7]. In particular, patients with moderate to severe plaque psoriasis have been consistently described as having physical discomfort, impaired emotional functioning, negative body image and self-image, as well as limitations in daily activities and social interaction [7]. Furthermore, several important diseases occur more often in patients with psoriasis than expected on the basis of their respective prevalence in the general population [2], with special relevance to psoriatic arthritis (PsA), Crohn’s disease, cancer (lymphoma and skin cancer), depression, non-alcoholic fatty liver disease, metabolic syndrome, and cardiovascular disorders [2].

Psoriasis also leads to an economic burden for the patients, their families, the health system, and society in general [6, 8–10]. As a chronic disease that runs throughout adulthood and the economically productive time of life, it demands not only costs directly related to its diagnosis and treatment but also societal costs, such as loss of productivity [8]. Studies have shown that patients with moderate to severe psoriasis present productivity losses, comprising

absenteeism, presenteeism, early retirement, changes of occupation, and work adaptations [6, 9, 10].

To our knowledge, to date there are few published studies that assessed the humanistic and/or economic impact of psoriasis in Brazil [11, 12]. Hence, this study aimed to assess the impact of moderate to severe plaque psoriasis on health-related quality of life (HRQoL), work productivity, and direct and indirect costs from the societal perspective among Brazilian patients.

METHODS

Study Design and Eligibility Criteria

This was a cross-sectional, observational, multicenter study performed in ten dermatology medical centers specialized in the treatment of psoriasis in southern and southeastern regions of Brazil. Patients attending routine follow-up visits were consecutively invited to participate in the study. Eligible patients were those able to provide informed consent and to understand and communicate with the investigator, aged at least 18 years old, and with diagnosis of moderate to severe plaque psoriasis according to physician evaluation. Patients who had been enrolled in clinical trials 12 months prior to study enrollment were excluded.

Data Collection

Eligible patients were invited to a face-to-face interview, conducted by a trained healthcare provider. Before the interview, patients received the required information about the study protocol and those who agreed to participate have read and signed the Informed Consent Form. During the interview, the following standardized patient-reported outcomes were used for data collection: Dermatology Life Quality Index questionnaire (DLQI), EuroQol Five-Dimension-Three-Level (EQ-5D-3L), The Hospital Anxiety and Depression Scale (HADS), Work Productivity and Activity Impairment questionnaire-General Health (WPAI-GH), and Work

Limitations Questionnaire (WLQ). In addition, patients answered one questionnaire specifically developed for the study about variables concerning sociodemographic aspects, lifestyle behaviors, clinical characteristics, and health resource utilization/costs. Data collection was performed between December 2015 and November 2016.

HRQoL

HRQoL data were obtained through DLQI and EQ-5D-3L questionnaires. DLQI is composed of ten questions concerning patients' perception of the impact of skin disease on different aspects of their HRQoL over the last week. Those questions can be categorized (and analyzed) under six subscales as follows: symptoms and feelings, daily activities, leisure, work or school, personal relationships, and treatment. Each question is scored on a 0–3 Likert scale that demonstrates the impact of psoriasis on each subscale: "Not at all/Not relevant", score = 0; "A little", score = 1; "A lot", score = 2; "Very much", score = 3. The summed DLQI score ranges between 0 and 30 and they are categorized as follows: 0–1 = no effect at all on the subject's life; 2–5 = small effect on the subject's life; 6–10 = moderate effect on the subject's life; 11–20 = very large effect on the subject's life; and 21–30 = extremely large effect on the subject's life [11, 13, 14].

EQ-5D-3L is a generic instrument to evaluate quality of life, analyzing the impact of health conditions through five domains (mobility, personal care, general activities, pain/discomfort, and anxiety/depression). For each domain, the patient uses his/her perception for classification into the following levels: no problems, some problems, or extreme problems [15, 16]. Each of the health states is converted into a utility score between 0 and 1 (representing a scale between death = 0 and perfect health = 1), using the UK algorithm [17]. EQ-5D-3L also contains a visual analogue scale (EQ-VAS) which records the patient's self-reported health status from 0 (worst imaginable) to 100 (best imaginable) [15, 16].

DLQI and EQ-5D-3L data were presented for total sample and also for subgroups of patients according to the use of biologic drugs in the last 12 months (biologic-experienced—patients who reported the use of biologic drugs vs. biologic-naïve patients—patients who did not report the use of biologic drugs) and the diagnosis of PsA.

Presence of Depression and Anxiety

The HADS was used to evaluate the presence of depression and anxiety symptoms. This questionnaire includes 14 items, with scores ranging from 0 to 21. Responses are categorized concerning the levels of observed symptomatology, for both subscales, as follows: normal (0–7 points), mild (8–10 points), moderate (11–14 points), and severe (15–21 points) [18–21].

Productivity Losses

Productivity losses were assessed by using the WPAI-GH and the WLQ instruments.

WPAI-GH was developed to evaluate the impact of health problems on the subject's productivity, in paid or unpaid activities, in the last 7 days [22, 23]. This questionnaire contains six questions that can afford four scores expressed in percentages: percentage of working time missed due to the disease (absenteeism); percentage of impairment during work due to the disease (presenteeism); general percentage of impairment score during work due to the disease (absenteeism and presenteeism); and percentage of daily activity impairment due to the disease [24, 26]. High scores indicate greater disease impact on productivity [22, 23]. Only patients with current professional activity were assessed for absenteeism, presenteeism, and overall work impairment. All patients were assessed for daily activity impairment.

WLQ evaluates lost productivity through the proportion of time affected by work limitations due to the disease (both presenteeism and absenteeism) in the last 2 weeks [25, 26]. This instrument comprises 25 items, grouped in four subscales: time management (five items addressing difficulty handling time and

scheduling demands); physical demands (six items about a person's ability to perform work tasks that involve bodily strength, movement, endurance, coordination, and flexibility); mental/interpersonal demands (nine items: six items pertain to difficulty performing cognitive job tasks and/or tasks involving the processing of sensory information and three items address challenges in interacting with people at work); and output demands (five items concerning decrements in a person's ability to meet demands for quantity, quality, and timeliness of completed work) [25, 26].

Responses for each item are categorized using a 5-point Likert scale that examines the proportion of time with difficulty: "none of the time (0%)", score = 0; "a slight bit of the time", score = 1; "some of the time (50%)", score = 2; "most of the time", score = 3; "all of the time (100%)", score = 4; plus a "does not apply to my job" option (treated as missing, no score). The physical demands subscale has reverse instruction and examines the proportion of time without difficulty [26]. The mean value of each dimension is scored separately and converted into a 0–100 scale, in which higher scores represent larger limitations [25]. A conversion table for the WLQ Productivity Loss index was used to calculate the productivity impact of health-related work limitations either in terms of percentage decrease in productivity (compared to healthy individuals) or as a percentage increase in work hours needed to compensate for loss of productivity [26].

Resource Utilization and Costs

During the interview, patients reported their health-related resource utilization (in terms of frequency of use of selected medical resources: outpatient visits, lab tests, treatments for psoriasis, inpatient admissions, etc.), considering a 12-month recall period. Direct costs (medical and non-medical) related to disease management were estimated by multiplying the amount of resources used by the corresponding unit cost.

Indirect costs (those related to productivity losses) were grouped in two time horizons: (1)

Table 1 Sources of unit costs of resources and equations of costs data transformation

Resource consumed	Source of unit cost	Price query date (month/year)	Mathematical equation for cost calculation
Direct medical costs			
Drugs ^a	1st choice: BPS—the latest lowest price for public purchase 2nd choice: CMED–PMVG	Feb/2017	Cost = frequency (daily) × duration (days) × unit cost
Hospitalizations	SIH-SUS	Feb/2017	Cost = amount of resource consumed × unit cost
Emergency room visits	SIGTAP	Feb/2017	Cost = amount of resource consumed × unit cost
Outpatients visits	SIGTAP	Feb/2017	Cost = amount of resource consumed × unit cost
Phototherapy	SIGTAP	Feb/2017	Cost = amount of resource consumed × unit cost
Tests	SIGTAP	Feb/2017	Cost = amount of resource consumed × unit cost
Alternative therapies	Patient report	Dec/2015–Nov/2016	Costs reported by patient
Direct non-medical costs			
Transportation	Patient report	Dec/2015–Nov/2016	Costs reported by patient
Food	Patient report	Dec/2015–Nov/2016	Costs reported by patient
Other non-medical resources	Patient report	Dec/2015–Nov/2016	Costs reported by patient
Indirect costs			
Annual costs			
Income reduction	Patient report	Dec/2015–Nov/2016	(Month of patient's inclusion in the study date – month of permanent income reduction) × income reduction value reported by patient
Absenteeism	IBGE—the mean salary of the economically active Brazilian population	Mar/2017	Days absent from work × (mean monthly wage of economic active Brazilian population/30 days)

Table 1 continued

Resource consumed	Source of unit cost	Price query date (month/year)	Mathematical equation for cost calculation
Lifetime costs			
Demission	IBGE—the mean salary of the economically active Brazilian population	Mar/2017	Unemployment time (in months) × mean monthly wage of economic active Brazilian population
Early retirement ^b	Ministry of Social Security—the mean salary of retired Brazilian population	Mar/2017	(Regular retirement age – patient's age at retirement moment) (in years) × (mean annual retirement wage by age for the most recent year available in Social Security Ministry)

BPS Health Prices Database, *CMED* Medication Market Regulation Chamber, *IBGE* Brazilian Institute of Geography and Statistics, *PMVG* maximum selling price to government, *SIGTAP* System List of Procedures Management, Medicines, Prosthetics and Orthotics, and Specialty Materials—OPM of Unified Health System, *SIH-SUS* Hospital Information System of Unified Health System, *SUS* Unified Health System

^a Firstly we consulted the most recommended database to collect the unit price; when the information was not available, we searched in the second choice database. If patient reported the use of half bottle of a particular medicine, we attributed the price of the entire bottle

^b Regular retirement age was represented by the old-age pension in Brazil, which is 65 for men and 60 for women

annual costs: related to the occurrence of health events in which disease impaired the patient's work productivity during a particular period of time (income reduction and absenteeism); (2) lifetime costs: occurrence of health events in which disease impaired the patient's work productivity during their lives (demission and early retirement).

Sources of unit costs and equations of costs calculations are described in Table 1. All data were collected in Brazilian real (BRL) and converted to United States dollar (USD), using the exchange rate from 08/Mar/2017—1 USD = 3.15 BRL.

Sample Size Calculation

The sample size was estimated on the basis of the impact of moderate to severe psoriasis on the patient's HRQoL by using the DLQI

questionnaire. A descriptive approach was used, once there is no hypothesis to be tested.

Considering a standard deviation equal to 6.9, based on previous studies which evaluated the impact of psoriasis on patients' quality of life using the DLQI questionnaire [6, 27], and considering an acceptable error of 1.0 point, 188 patients would be necessary to achieve a robust estimation of the population mean (95% confidence interval, level of significance 0.05).

Statistical Analysis

Data obtained were tested for normal distribution using Shapiro–Wilk and Kolmogorov–Smirnov tests. To compare means, the variables with normal distribution were analyzed by the Student's *t* test, and those with non-normal distribution were analyzed by Mann–Whitney nonparametric test. To assess

possible differences between frequencies of categorical variables, the chi-square test was used. In 2 × 2 cross-tables, the expected values smaller than 5 may affect an approximation of the chi-square; in this case Fisher’s exact test was used. Stata MP 12® and R Project 3.1.2©statistical software were used, assuming a significance level of 5%.

Compliance with Ethics Guidelines

The research was reviewed and approved by independent ethics committees of each participating research site (see supplementary material). The master ethics committee was at the Hospital do Servidor Público Municipal—SP (the research site was the Hospital do Servidor Público Municipal, São Paulo; approval number 1,317,851). All procedures are in accordance with the ethical standards of the ethical standards of the institutional and national research committee and with the Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all patients for being included in the study.

RESULTS

Sociodemographic Aspects, Lifestyle Behaviors, and Clinical Characteristics

This study included 188 patients with moderate to severe plaque psoriasis and the mean age at study visit was 48 years. Most of them were female, Caucasian/white, and married/stable union.

Among patients who smoke/drink or quit smoking/drinking, the majority of them reported that disease had no impact on these behaviors; the most frequent answers were “My smoking habits changed for another reason” and “I’ve kept my alcohol consumption”.

Regarding clinical characteristics, mean age at diagnosis was 33 years, with mean time between first symptoms and medical diagnosis of 2.1 (SD 3.9) years. The most frequent comorbidities were hypertension, dyslipidemia, PsA, obesity, anxiety, diabetes mellitus and

Table 2 Sociodemographic aspects, lifestyle behaviors and clinical characteristics

Characteristics	Number	Percentage
Sociodemographic characteristics (<i>n</i> = 188)		
Age (mean/SD—years)	48	13.1
Gender		
Male	90	47.9
Female	98	52.1
Race		
Caucasian/white	41	68.6
	129	
Brown		21.8
Black	13	6.9
Oriental	4	2.1
Other ^a	1	0.5
Educational level		
Incomplete elementary school	25	13.3
Complete elementary school	20	10.6
Incomplete high school	15	8.0
Complete high school	64	34.0
Incomplete graduation	21	11.2
Complete graduation	30	16.0
Post-graduation	13	6.9
NI	–	–
Marital status		
Single	46	24.5
Married/stable union	116	61.7
Separated/divorced	20	10.6
Widow	6	3.2
Employment status		
Autonomous worker	33	17.6
Employed	71	37.7
Unemployed	23	12.2
Retired	30	16.0
Retired and employed	3	1.6

Table 2 continued

Characteristics	Number	Percentage
Retired and autonomous worker	5	2.6
Student	2	1.0
Housewife	12	6.4
Pensioner	2	1.1
Leave of absence	5	2.7
Others ^b	2	1.1
Monthly individual income USD		
≤ 250.34	37	19.7
250.35–500.69	46	24.5
500.70–751.03	38	20.2
751.04–1251.71	34	18.1
1251.72–2503.42	22	11.7
2503.43–5006.83	6	3.2
≥ 5006.84	1	0.5
NI	4	2.1
Monthly household income USD		
≤ 250.34	3	1.6
250.35–500.69	25	13.3
500.70–751.03	32	17.0
751.04–1251.71	60	31.9
1251.72–2503.42	40	21.3
2503.43–5006.83	18	9.6
≥ 5006.84	6	3.2
NI	4	2.1
Lifestyle behaviors (<i>n</i> = 188)		
Smoking status		
Nonsmokers	103	54.8
Current smokers	32	17.0
Past smokers	51	27.1
NI	2	1.1
Alcohol consumption		
Nondrinkers	68	36.2

Table 2 continued

Characteristics	Number	Percentage
Current drinkers	76	40.4
Past drinkers	40	21.3
NI	4	2.1
Clinical characteristics		
Age at diagnosis (mean/SD— years) (<i>n</i> = 186)	33	16.0
Time between first symptoms and diagnosis (mean/SD— years) (<i>n</i> = 176)	2.1	3.9
Daily time for psoriasis care (mean/SD—min) (<i>n</i> = 174)	40.7	40.7
Disease activity (0–10) (<i>n</i> = 188)		
Itching (mean/SD)	3.4	3.3
Pain (mean/SD)	2.4	3.1
Plaques/lesions (mean/SD)	1.5	2.7
Pharmacological treatment (<i>n</i> = 187)		
Topical therapy	61	32.6
Conventional systemic drugs	5	2.7
Biologics	2	1.1
Topical therapy + conventional systemic drugs	64	34.2
Topical therapy + biologics	23	12.3
Conventional systemic drugs + biologics	1	0.5
Topical therapy + conventional systemic drugs + biologics	31	16.6
Comorbidities (frequency ≥15%) (<i>n</i> = 145)		
Hypertension	67	46.2
Dyslipidemia	57	39.3
PsA	45	31.0
Obesity	38	26.2
Anxiety	37	25.5
Diabetes mellitus	33	22.8

Table 2 continued

Characteristics	Number	Percentage
Depression	24	16.6

NI not informed, SD standard deviation, USD United States dollar, PsA psoriatic arthritis

^a Patient reported race as dark skinned

^b Subjects with sporadic jobs, without current professional activity

depression. Conventional systemic drugs and biologics were reported to be used by approximately 54% and 30% of patients, respectively.

Details on sociodemographic aspects, lifestyle behaviors and clinical characteristics are shown in Table 2.

HRQoL

All patients answered the DLQI ($n = 188$) and 76.4% reported some impact of psoriasis on HRQoL. Moderate to extremely large impairment of psoriasis on HRQoL was reported by 68.8% of patients. The highest effect was found for “symptoms and feelings” [mean (SD) 2.4 (1.7)] and the lowest in “work or school” [mean

(SD) 0.4 (0.8)] DLQI subscales. The mean DLQI score was 7.2 (SD 6.8) (Table 3).

According to the use of biologics, 42.2% ($n = 24/57$) of patients who experienced treatment with biologics presented no disease effect on HRQoL, compared to 19.8% ($n = 26/133$) of biologic-naïve patients ($p = 0.014$). The highest effect was found for the “symptoms and feelings” DLQI subscale [biologic-experienced mean (SD) 2.0 (1.8); biologic-naïve mean (SD) 2.5 (1.7)], with a statistically significant difference between both groups ($p = 0.017$) (Table 3).

The subgroup of psoriasis patients with PsA concomitantly presented a worse HRQoL when compared with the subgroup of patients without this comorbidity, with a statistically significant difference in the DLQI scores [PsA patients mean (SD) ($n = 45$) 9.4 (7.6); non-PsA patients mean (SD) ($n = 143$) 6.5 (6.4); $p = 0.026$].

The EQ-5D-3L obtained valid responses for 176 patients (93.6%). Mean EQ-5D-3L index was 0.70 (SD 0.27), with “anxiety and depression” and “pain and discomfort” as the most impaired domains (Fig. 1 and Table 4). Overall score of EQ-5D VAS was 68.7 (SD 22.3). Biologic-experienced patients presented numerically higher EQ-5D-3L index compared to biologic-

Table 3 DLQI subscales ($n = 188$)

DLQI subscales	Overall sample ($n = 188$)		Biologic-experienced ($n = 57$)		Biologic-naïve ($n = 131$)		<i>p</i> value ^a
	Mean	SD	Mean	SD	Mean	SD	
Symptoms and feelings	2.4	1.7	2.0	1.8	2.5	1.7	0.017
Daily activities	1.8	1.9	1.6	1.9	1.8	1.8	0.210
Leisure	1.3	1.7	1.3	1.6	1.3	1.7	0.797
Personal relationships	0.9	1.4	0.9	1.5	0.9	1.4	0.530
Work or school	0.4	0.8	0.3	0.7	0.4	0.8	0.453
Treatment	0.5	0.8	0.4	0.8	0.5	0.8	0.391
DLQI score	7.2	6.8	6.4	7.2	7.5	6.6	0.093

Score maximum for each DLQI subscale: symptoms and feelings (max = 6); daily activities (max = 6); leisure (max = 6); work or school (max = 3); and treatment (max = 3). DLQI score: 0–1 = no effect at all on subject’s life; 2–5 = small effect on subject’s life; 6–10 = moderate effect on subject’s life; 11–20 = very large effect on subjects’ life; and 21–30 = extremely large effect on subject’s life

DLQI Dermatology Life Quality Index

^a Biologic-experienced vs. biologic-naïve: Mann–Whitney nonparametric tests

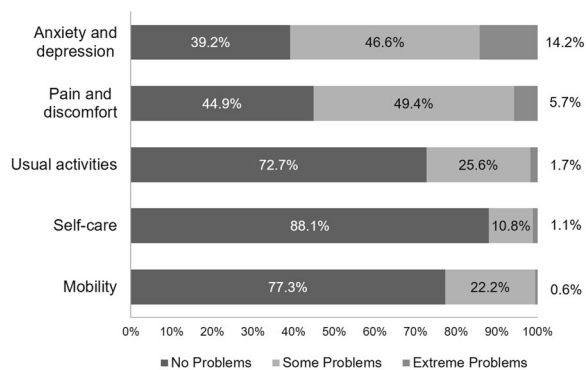


Fig. 1 EuroQoL Five-Dimension-Three-Level (EQ-5D-3L) results ($n = 176$)

Table 4 EQ-5D-3L index

	EQ-5D-3L index ^a		p value ^b
	Mean	SD	
Overall population ($n = 176$)	0.70	0.27	–
Biologic-experienced ($n = 54$)	0.76	0.23	0.089
Biologic-naïve ($n = 122$)	0.67	0.28	
Psoriasis patients with PsA concomitantly ($n = 43$)	0.64	0.27	0.007
Psoriasis patients without PsA concomitantly ($n = 133$)	0.72	0.27	

PsA psoriatic arthritis

^a 0 (worst health status) to 1 (best health status)

^b Mann–Whitney nonparametric tests

naïve patients, although without statistical significance [means (SD) 0.76 (0.23) vs. 0.67 (0.28), respectively; $p = 0.089$]. Exposure to biologic treatment was not associated with statistically significant differences in the proportion of problems in the EQ-5D-3L dimensions, but only biologic-naïve patients were reported to have extreme problems in “usual activities”, “self-care”, and “mobility” (Fig. 2). In addition, biologic-experienced patients showed better results in EQ-VAS overall score than biologic-naïve patients [means (SD) 73.4 (17.5) vs. 66.6 (23.9), $p = 0.150$].

Presence of Depression and Anxiety

Specifically regarding anxiety and depression, all patients completed the HADS questionnaire ($n = 188$). Anxiety mean score was 8.1 (SD 4.6), and 96 patients (51%) presented anxiety symptoms. Depression symptoms were reported by 27.1% of patients and the mean score was 5.3 (SD 4.1). In terms of severity, frequencies of normal, mild, moderate, and severe symptoms were 49.0%, 18.6%, 23.4%, and 9.0% for anxiety and 72.9%, 15.4%, 9.0%, and 2.7% for depression, respectively.

Productivity Losses

The mean daily activity impairment was 25.7% (SD 29.5). Work impairment was more attributable to presenteeism [mean (SD) 17.4%

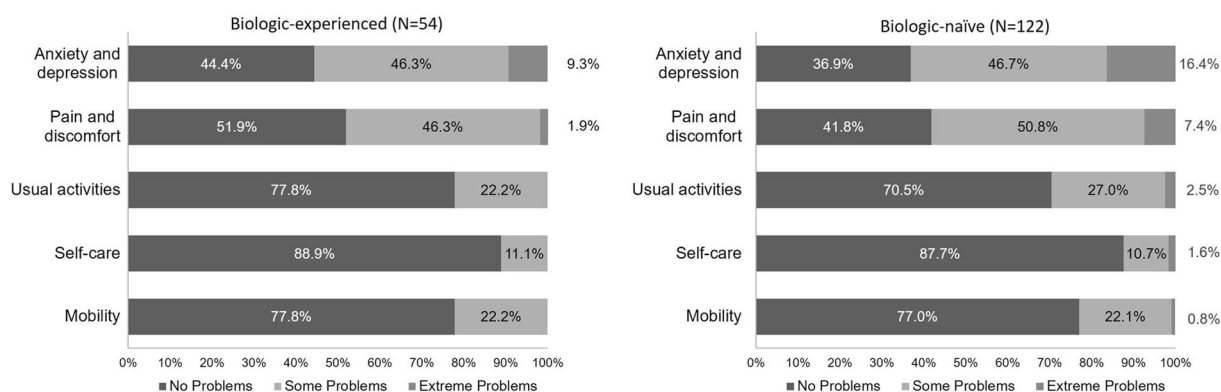


Fig. 2 EQ-5D-3L dimensions, according to the use of biologics ($n = 176$). p values (chi-square test): anxiety and depression = 0.435; pain and discomfort = 0.284; usual activities = 0.414; self-care = 0.823; mobility = 0.915

Table 5 Impairment on productivity among sample according to the WPAI-GH and WLQ instruments

Productivity scores		Mean	SD
WPAI-GH scores ^a (<i>n</i> = 188)	% Working time missed—absenteeism (<i>n</i> = 106)	6.3	13.8
	% Impairment during work—presenteeism (<i>n</i> = 105)	17.4	25.5
	% Overall work impairment—absenteeism and presenteeism (<i>n</i> = 105)	5.4	10.3
	% Daily activity impairment (<i>n</i> = 187)	25.7	29.5
WLQ demands ^b (<i>n</i> = 112)	Time management—%, range 0–100 (<i>n</i> = 106)	17.7	24.9
	Physical demands—%, range 0–100 (<i>n</i> = 111)	23.5	28.5
	Mental-interpersonal demands—%, range 0–100 (<i>n</i> = 110)	16.6	22.4
	Output demands—%, range 0–100 (<i>n</i> = 111)	14.8	22.4
	WLQ Productivity Loss Index (<i>n</i> = 105)	4.7	5.4

Questionnaire—General Health

SD standard deviation, WLQ Work Limitations Questionnaire, WPAI-GH Work Productivity and Activity Impairment

^a In the past 7 days

^b % of time affected by work limitations in the last 2 weeks

(5.5%)] than to absenteeism [mean (SD) 6.3% (13.8%)]. Considering WLQ answers (*n* = 112), physical and time demands were the most affected subscales [means (SD) 23.5 (28.5) and 17.7 (24.9), respectively]. The mean WLQ index was 4.7 (SD 5.4), which means that patients in this sample would need to increase approximately 5% in work hours to compensate for productivity losses (compared to healthy population) (Table 5).

Health Resources Utilization and Costs

The estimated total annual costs of moderate to severe psoriasis were USD 758,467, with a mean of USD 4034 per patient (Table 6). Direct medical costs accounted for the highest proportion of the total costs (87.7%), followed by indirect costs (9.9%) and direct non-medical costs (2.4%).

Direct annual medical costs summed USD 665,167 (USD 3538 per patient), drug therapy being responsible for 97.6% of those costs. Regarding frequency of utilization, drug therapy and outpatient visits were the most consumed direct medical resources (99.5% and 96.3%, respectively). The majority (99.4%) of patients reported having visited physicians and

22.1% other healthcare providers. Dermatologist was the most frequent outpatient visit (98.9%; *n* = 178/180) among physicians, with a mean of 5.4 visits per year per patient; while psychologist was the most frequent (42.5%; *n* = 17/40) outpatient visit among other healthcare providers. Despite the high frequency of outpatient visits, this resource accounted for only 0.7% of total medical direct costs.

Direct non-medical costs were USD 122 per patient (total costs of USD 18,350—2.4%), transportation accounting for 70.5% of the costs, summing USD 12,929 (USD 87 per patient). In terms of frequency of utilization, transportation and food expenses were the non-medical resources reported by the most of patients (78.7% and 75.5%, respectively).

Costs per patient segmented by direct medical costs, direct non-medical costs, and indirect costs are shown in Table 6. Costs related to lifetime productivity loss were not included in the figure, as they are not calculated on a yearly basis. However, lifetime productivity losses for the sample summed USD 649,691 (considering demission—USD 131,428 and early retirement—USD 518,263).

Table 6 Costs

Resources	Patient		Cost (USD)			Cost (%)
	N	%	Per patient		Total	
			Mean	SD		
Annual direct medical costs ^a						
Drug treatment	187	99.5	3474	9764	649,693	97.6
Phototherapy	42	22.3	40	35	1641	0.3
Alternative therapies	16	8.5	169	193	2697	0.3
Test	159	84.6	35	39.1	5646	0.8
Hospitalizations	4	2.1	131	10	524	0.2
Outpatient visits	181	96.3	26	27	4803	0.7
Emergency visits	14	7.4	11	16	162	0.1
Total	188	100.0	3538	9644	665,167	100.0
Annual direct non-medical costs ^a						
Transportation	148	78.7	87	105	12,929	70.5
Food	142	75.5	37	77	5221	28.5
Other non-medical resources	5	2.7	50	68	200	1.0
Total	150	79.8	122	155	18,350	100.0
Annual indirect costs						
Income reduction	14	7.4	1647	2788	23,061	30.8
Absenteeism	46	24.5	1128	1807	51,889	69.2
Total	51	27.1	1470	2931	74,950	100.0
Lifetime indirect costs						
Demission	10	5.3	13,143	14,393	131,428	–
Early retirement	7	3.7	74,037	29,194	518,263	–

SD standard deviation

^a Resources utilization in the last 12 months reported by patients

DISCUSSION

In order to assess the impact of moderate to severe plaque psoriasis on HRQoL and its associated costs among Brazilian patients, this study interviewed 188 patients from ten dermatology medical centers specialized in the treatment of psoriasis in southern and southeastern regions of Brazil.

Our findings from the EQ-5D-3L instrument are consistent with other psoriasis studies as reported by Møller et al. in their systematic review to understand the disutility of patients with plaque psoriasis [28]. They included 12 studies, nine of which evaluated patients with moderate to severe plaque psoriasis; EQ-5D utility index scores ranged from 0.52 (SD 0.39) to 0.9 (SD 0.1), corroborating our findings [mean (SD) 0.70 (0.27)]. Moreover, considering the use of previous biologic agents, biologic-

experienced patients had a slightly higher score than biologic-naïve patients; however, no statistical significance was found [means (SD) 0.76 (0.23) vs. 0.67 (0.28), respectively; $p = 0.089$]. Comparing with the Brazilian general population, our psoriasis patients showed a worse HRQoL in terms of EQ-VAS results (means 82.1 vs. 68.7, respectively) [29].

DLQI mean score [mean (SD) 7.2 (6.8)] is also in line to what has been observed in other international studies [30–33]. It is important to note that according to the defined classes of DLQI (0–1, no effect; 2–5, slight effect; 6–10, moderate effect; 11–20, very large effect; 21–30, extremely large effect), the impact of moderate to severe psoriasis on patients' quality of life was on average moderate. Meyer et al., who performed a cross-sectional study with 590 French patients with psoriasis, found a mean DLQI score of 8.5 for patients with severe psoriasis and 6.4 for patients with mild psoriasis ($p = 0.002$) [34]. Another study that included 100 patients from Serbia, 40% with severe and 25% with moderate psoriasis, found a mean DLQI score of 10.5 (SD 7.2) [31]. Similarly, the highest effect was found for “symptoms and feelings”, endorsing that emotional aspects play an important role in the quality of life of psoriasis patients, since skin is responsible in large part for an individual's presentation [30, 31, 34].

This study also pointed out that biologic-naïve patients show a reduced quality of life as compared to biologic-experienced patients. However, the difference among groups was not statistically significant, which may be justified by the sample size in each group. Furthermore, in agreement with overall sample, the highest effect was found for “symptoms and feelings” in both subgroups of patients (biologic-experienced and biologic-naïve), with the patients treated with biologics presenting significant lower values as compared to biologic-naïve patients, reinforcing the importance of biologics in the reduction of the emotional impact of psoriasis. In fact, the use of biologics has been associated with the reduction of DLQI score and, consequently, with the improvement in patients' quality of life [35].

PsA was reported as comorbidity by approximately one-third of the sample, in accordance with international studies that have shown a range between 6% and 41% [36–38]. In agreement with international literature [36, 37], the subgroup of PsA patients presented reduced HRQoL when compared with patients without this comorbidity, highlighting the relevance of this comorbidity in the course of psoriasis [38].

According to the HADS questionnaire, patients presented a higher frequency of symptoms of anxiety than depression (51% vs. 27%, respectively). Moreover, the prevalence of anxiety found in these psoriasis patients was higher than in the Brazilian general population. A study conducted in a primary care setting in Brazil observed that the prevalence of anxiety using the HADS questionnaire ranged from 35.4% to 43.0% in four state capitals (Rio de Janeiro, São Paulo, Fortaleza, and Porto Alegre) [39]. In our study, anxiety and depression were also reported as comorbidities by 25.5% and 16.6% of patients, respectively; these values were lower than those found by using the HADS instrument, which may indicate an underdiagnoses of these conditions among this psoriasis sample.

The total annual cost of this psoriasis cohort was estimated at USD 4034 per patient (USD 758,467 for total sample). This data is consistent with the results found in a systematic review of psoriasis costs among five European countries (Germany, Spain, France, Italy, and the UK), which showed that the total annual cost per patient ranged from USD 2077 to USD 13,132 [40]. Although it is important to consider the differences in methodologies when comparing costs with other studies, the cited systematic review reported that the majority of included studies used a methodological approach similar to ours. In this systematic review direct costs accounted for the greatest part of the total cost [40], like in our study.

A high proportion of direct costs in the total cost was also observed in studies performed in Canada [6], Hungary [32], and the USA [41]. Additionally, as has been previously observed [42], despite the high utilization of conventional systemic drugs and topical therapies, considered less expensive treatment, drug

treatment was the main healthcare cost driver; whereas emergency visits and hospitalizations accounted for the minor proportions of costs. Some authors argue that the introduction of biologics imposed an economic burden on treatment costs; on the other hand, they seem to have led to a reduction of inpatient admissions; thus they might have a cost-saving effect despite their high unit prices [40, 42, 43]. Driessen et al. conducted a study to assess the economic impact of psoriasis before and after the introduction of biologics. Although a significant increase in total costs was described, a significant decrease in direct costs related to day-care admission was also observed [43]. In the present study, a comparison of costs before and after introduction of biologics was not planned, making it unfeasible to perform this type of analysis.

Transportation was the most cost-consuming direct non-medical resource (70.5% of total direct non-medical costs). This is explained by the utilization of treatments that demand a commute to health services for administration, such as phototherapy and some biologics [30].

Indirect costs accounted for approximately 10% of the total annual costs. These costs have not been frequently recognized by payers; however, according to Boccuzzi, payers should always look beyond the direct costs to measure the total impact of a disease on society [44].

The burden of psoriasis on a patient's professional life has already been shown in different populations. Psoriasis affects patients' productivity, work capacity, absenteeism, and job maintenance [8–10]. In fact, many patients need to change their job area, responsibilities, and even professions because of prejudice related to psoriasis [10]. In agreement with previous data [12, 45], we observed that presenteeism contributes more to productivity loss than absenteeism. Presenteeism also appeared to be relevant in the study performed by DiBona-ventura et al. who assessed the work productivity associated with experiencing psoriasis vs. not experiencing psoriasis, along with varying levels of psoriasis severity, by using the Brazil National Health and Wellness Survey [12]. They found high rates of presenteeism in the population with moderate (23.3%) and severe

psoriasis (45.5%) in comparison with mild psoriasis (21.4%), suggesting an economic burden [12]. However, our methodology did not include costs related to presenteeism in the total annual costs. Nevertheless, our study outlined that psoriasis can lead to demission and early retirement, the latter mostly driving lifetime costs.

The main limitations of this study are related to generalization of results because it has included patients treated in specialized psoriasis centers of treatment from south and southeast regions of Brazil and data may not be fully representative of all levels of assistance and may not represent all geographic regions of the country. In addition, the study focused on patients actively seeking care or referred by their primary care medical service provider and may not be extended to those in the general population who are untreated.

Despite these limitations, our study addressed both the humanistic and economic impact of moderate to severe plaque psoriasis in a sample of Brazilian patients, being able to give a comprehensive overview of the disease burden for patients, their families, the healthcare system, and society.

CONCLUSIONS

This study represents an effort to estimate the economic burden of moderate to severe plaque psoriasis in Brazil in a real-world setting and it provides valuable health economic information to healthcare decision makers for the determination of resource allocation.

The results evidenced that moderate to severe plaque psoriasis imposes substantial costs to society. Our data showed that this disease negatively affects both work productivity and HRQoL of Brazilian patients. Subgroups with PsA and biologic-naïve patients presented lower HRQoL, showing the impact of this comorbidity and the relevance of biologics in psoriasis treatment.

Emotional aspect was the most impaired domain in both specific and general HRQoL instruments, accompanied by high prevalence of anxiety symptoms in HADS analysis. These

findings highlight the importance of mental health in psoriasis patients and the need for investment in a proper and comprehensive treatment.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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