

# Psoriasis as a multisystem disease - cost of illness analysis

Inna Popova<sup>1</sup>, Maria Kamusheva<sup>2\*</sup>, Iva Miteva<sup>3</sup>, Guenka Petrova<sup>2</sup> and Lubka Miteva<sup>1</sup>

<sup>1</sup>Department of Dermatology, Medical University of Sofia, Bulgaria

<sup>2</sup>Faculty of Pharmacy, Medical University of Sofia, Bulgaria

<sup>3</sup>Faculty of Public health, Medical University of Sofia, Bulgaria

## Abstract

**Introduction:** Psoriasis is a chronic disease consuming many medical and non-medical resources, which should be evaluated for every healthcare system.

**Goal:** The goal of the current study is to determine the financial burden of psoriasis and its concomitant diseases in Bulgaria for hospitalized patients with psoriasis.

**Materials and methods:** A retrospective study among Bulgarian patients with psoriasis is conducted in the clinic of dermatology diseases of University hospital "Alexandrovska" in Sofia for the period 2014-2015. The medical dossiers of hospitalized psoriatic patients were reviewed and information regarding several patients' characteristics was analyzed. Bottom up approach was applied in order to calculate the costs associated with treatment of psoriasis and concomitant diseases.

**Results:** The total number of included patients in the survey was 246, 106 out of them were hospitalized in 2014, and 140 - in 2015. The average monthly pharmacotherapy costs for treatment of one patient with psoriasis in hospital are higher in 2015 than in 2014 - 35 BGN and 33 BGN, respectively. The average costs for pharmacotherapy of the concomitant diseases per patient are almost equally paid from the National health insurance fund (20.53 BGN) and the patient (23.10 BGN). The share of direct medical costs per patient is 58% (12% for ambulatory therapy (medications and phototherapy) and 46% in hospital settings (medications, medical care, and laboratory test), 42% - indirect costs. As the age increases, the number of concomitant diseases also increases among the patients with psoriasis. Statistical significant more men ( $p=0.04$ ) suffer from psoriasis and ischemic cardiac disease.

**Conclusion:** Psoriasis is a multisystem disease with significant financial burden for Bulgarian healthcare system as a result of the costs for treatment of the concomitant diseases, hospitalization costs and phototherapy.

## Introduction

Psoriasis is a chronic autoimmune disease, which consumes significant part of healthcare resources due to the significantly high pharmacotherapy costs for the main and for the concomitant diseases [1-3]. According to current evidence there is supposed association between psoriasis and arthritis, depression, inflammatory bowel disease and cardiovascular diseases [4,5]. At the same time, several other comorbid conditions have been proposed as related to the chronic inflammatory status of psoriasis [6-8]. Understanding the impact of these conditions on the health care consumption should lead to better management of the disease [9]. Systematic review of published studies on the costs associated with managing and treating psoriasis and psoriatic arthritis in 5 European countries gives us a reason to conclude that both diseases have significant economic burden [10]. Presence of comorbid conditions in psoriatic patients has important implications for clinical management and might lead to significant economic burden. Quality of life, direct health care expenditures and pharmacokinetics of the therapies are impacted by existing comorbid conditions [4].

Due to the growing number of new psoriasis therapies applying for reimbursement by National Health system and limited budget, it is crucial to determine the financial burden of psoriasis and concomitant diseases in this patient population.

## Goal

The goal of the current study is to estimate the financial burden of psoriasis and concomitant diseases for hospitalized psoriatic patients

in Bulgaria. The study is intended to present the direct and indirect cost of psoriasis therapy at hospital settings as well as the financial burden associated with psoriasis concomitant diseases.

## Materials and methods

### Design of the study

Retrospective study among Bulgarian psoriatic patients admitted in the dermatology clinic of University hospital "Alexandrovska" in Sofia, Bulgaria was conducted over the period 2014-2015. This is the biggest university hospital and the referee national clinic for psoriasis in the country. The medical files of hospitalized psoriatic patients admitted during 2014 and 2015 were reviewed and representative sample of 246 patients was created by selecting every 3<sup>rd</sup> file. The number of selected hospitalized patients for 2014 is 106, for 2015 is 140 (~ 30% from the admitted patients for each year). All patients from the sample were hospitalized for 10 days, which defines the number of the days out of work. Information regarding different patients' characteristics was collected such as gender, age, professional status, symptoms, duration of the disease (in years), risk factors for hospitalization, current psoriatic treatment during the hospital stay, relapses, concomitant diseases,

**Correspondence to:** Maria Kamusheva, Dunav 2 str., Sofia, Bulgaria, Tel: +359 2 9236 584, E-mail: maria.kamusheva@yahoo.com

**Key words:** psoriasis, economic burden, concomitant diseases, costs of illness

**Received:** March 22, 2017; **Accepted:** September 27, 2017; **Published:** September 30, 2017

diagnostic and therapeutic procedures conducted in the hospital. As relapse was defined the deterioration of PASI score despite ongoing treatment or after treatment discontinuation. The presence of a relapse is at the discretion of the treating physician in patients who achieve at least 50% improvement in PASI score during psoriatic treatment or so-called treatment success. Additionally, information about the prescribed ambulatory psoriatic treatment after hospital discharge that usually covers one month period was collected.

### Cost of illness calculation

**Direct medical costs:** “Bottom-up” approach was applied in order to calculate the direct medical costs – hospital and ambulatory per patient per month.

The hospital costs consist of cost of hospital stay, pharmacotherapy of psoriasis and concomitant diseases, procedures, and patients' charges. Ambulatory costs include cost of ambulatory pharmacotherapy of psoriasis and concomitant diseases after hospital discharge, and additional procedures.

Costs of hospital procedures (e.g. phototherapy, biochemical tests, hospital stay etc.) were taken from the National Health Insurance Fund (NHIF) tariffs. Information about wholesaler price for the medicinal products used in hospitals, including Value Added Tax (VAT), was taken from Positive drug list (PDL). Cost of hospital pharmacotherapy was calculated based on applied therapeutic schemes by multiplying prescribed quantities and unit price.

Ambulatory costs for psoriasis were calculated for medicines, based on their retail prices in the PDL, and for additional phototherapy based on NHIF tariff.

Cost of concomitant diseases was calculated using the retail prices (for partially reimbursed medicinal products (MPs)) or wholesaler price (for fully reimbursed MPs) from the PDL.

**Indirect costs:** Indirect costs during the hospital stay for each year were calculated as productivity losses using the formula:

$$[(\text{Number of patients} \times \text{number of days out of work}) \times (\text{GDP per capita for the year of observation} / \text{number of working days for the year of observation})]$$

GDP per capita for 2014 was 10 757.07 BGN, and for 2015r. – 11 148.23BGN.

All costs are presented in BGN at the ex-change rate of 1 Euro=1.958 BGN.

### Statistical analysis

Descriptive statistics, frequency distributions through Kruskal-Wallis tests and correlation analysis are applied.

## Results

### Patients' characteristics

A total number of 246 hospitalized patients were included in the analysis, and out of them 106 were admitted in 2014 and 140 in 2015 (30% from the admitted patients for each year).

Distribution of the patients according to their age, gender, % affected body surface, professional status is presented separately and is summarized for both years (2014 and 2015) – (1). The men prevail for the analyzed period – 60.38% and 62.86% for 2014 and 2015, respectively. The highest is the share of patients in the group 61 - 70

years of age (26.4%), followed by age group 51-60 years – near 20%. 41% of the patients have affected body surface between 30 and 40% and only 2% - over 80%. Family history was present in 19% and relapse – in around 81%. More than half of the patients with psoriasis have concomitant diseases- 146 out of 246. 37 (in 2014) and 42 (in 2015) patients have more than 1 concomitant disease.

The average body surface area by psoriasis did not differ statistically between men and women.

The percentage of patients with family history of psoriasis is approximately 81%. The applied Chi-squared test showed a statistical difference between the percentages of psoriatic patients with relapse ( $p=0.04$ ) in the groups of patients with and without family history (91% and 79%, respectively). The relative risk for relapse in the group with family history in comparison with the control group (without family history) is  $RR=1.16$  ( $p=0.009$ ). This means that patients with family history possess a risk for relapse 1.16 times greater among the psoriasis patients without family history (1).

16 out of 246 patients were reported risk factors for hospitalization. The main provoking risk factor for hospitalization is the intake of various medications, weather conditions, stress, concomitant disease, chemical agents, and tattoos. Stress is with the highest impact, followed by intake of medications (1).

Hypertension and psoriatic arthritis are the most common concomitant diseases, reported by 146 patients (2).

Statistically significant difference was established for the absolute share of men (70.8%) and women (29.2%) with ischemic heart disease ( $p=0.04$ ). Men with psoriatic arthritis are more than women with the same disease ( $p=0.04$ ) – 69% vs. 31%.

Psoriatic patients with hypertension, diabetes, heart diseases also reported the existence of additional diseases such as hepatic diseases, prostatitis, varicose, endocrine and nephrology diseases, COPD etc. (2).

### Pharmacotherapy of psoriasis

Different topical medications, as unguents, creams, oils: salicylic oil, cold cream, antipsoriatic masts, prepared on individual patients' prescription are widely used but their cost account for small amount due to the inclusion of only substances costs (3).

Antihistamines (in approximately 85% of the patients) and antibiotics (in approximately 64%) are some of the most often prescribed readymade medicinal products for hospitalized psoriatic patients (4).

### Pharmacotherapy for concomitant diseases

For the therapy of the concomitant diseases, the highest is the share of patients on beta-blockers, ACE-inhibitors, AT1 blockers, diuretics and Ca-blockers as one of the most prescribed medications for treatment of concomitant diseases (5).

### Costs of psoriasis

**Direct costs, associated with hospital treatment of psoriasis:** The average monthly costs for psoriatic pharmacotherapy in hospital for 2015 increased in comparison to 2014 – approximately 35 BGN and 33 BGN, respectively. The average monthly cost for both years is equal to 32.90 BGN.

The dermatology clinic receives on total 480 BGN per patients, according to the NHIF tariff for diagnosis „Severe forms of psoriasis

**Table 1.** Patients' characteristics

Characteristics	2014		2015		Total	
	Subgroup	Distribution (N)/{%}	Subgroup	Distribution (N)/{%}	Subgroup	Distribution (N)/{%}
Gender	Man	64 {60.38%}	Man	88 {62.86%}	Man	152 {61.79%}
	Woman	42 {39.62%}	Woman	52 {37.14%}	Woman	94 {38.21%}
	Total	106	Total	140	Total	246
Age (years)	<30	16 {15.24%}	<30	21 {14.89%}	<30	37 {15.04%}
	31<X*<40	13 {12.38%}	31<X<40	16 {11.35%}	31<X<40	29 {11.79%}
	41<X<50	13 {12.38%}	41<X<50	27 {19.15%}	41<X<50	40 {16.26%}
	51<X<60	23 {21.90%}	51<X<60	27 {19.15%}	51<X<60	50 {20.33%}
	61<X<70	30 {28.57%}	61<X<70	34 {24.28%}	61<X<70	65 {26.42%}
	>71	10 {9.52%}	>71	15 {10.64%}	>71	25 {10.04%}
Affected body surface (%)	<40	49 {47.11%}	<40	52 {37.14%}	<40	101 {40.89%}
	41<X*<50	26 {25%}	41<X<50	28 {20%}	41<X<50	54 {21.86%}
	51<X<60	21 {20.19%}	51<X<60	16 {11.43%}	51<X<60	37 {14.98%}
	61<X<70	5 {4.8%}	61<X<70	20 {14.29%}	61<X<70	25 {10.12%}
	71<X<80	0 {0%}	71<X<80	21 {15%}	71<X<80	21 {8.50%}
	>80	3 {2.88%}	>80	3 {2.14%}	>80	6 {2.42%}
Missing data	2	Missing data	2	Missing data	2	
Duration of the disease	<=10 years	58 {56.31%}	<=10 years	82 {59.85%}	<=10 years	141 {57.08%}
	>10 years	45 {43.69%}	>10 years	55 {40.15%}	>10 years	100 {40.49%}
	Missing data		Missing data		Missing data	5
Relapse	Yes	86 {81.9%}	Yes	113 {80.71%}	Yes	200 {80.97%}
	No	19 {18.1%}	No	27 {19.15%}	No	46 {18.62%}
Family history	Yes	20	Yes	27	Yes	47 {19%}
	No	85	No	112	No	198 {80%}
	Missing data		Missing data		Missing data	1
Professional status	Employee	32	Employee	56	Employee	88 {35.77%}
	Unemployed	28	Unemployed	23	Unemployed	51 {20.73%}
	Retiree	44	Retiree	57	Retiree	101 {41.06%}
	Student	0	Student	4	Student	4 {1.63%}
	Missing data		Missing data		Missing data	2
Patients with concomitant diseases	Yes	66	Yes	79	Yes	146
	No	39	No	61	No	100
Number of concomitant diseases	1	30	1	37	1	67
	>1	37	>1	42	>1	79

\*X – parameter

**Table 2.** Presence of diseases from various systems in observed patients with psoriasis

Disease/ICD	Number of patients with 1 diagnosis	Patients reported more than 1 disease
arthropathic psoriasis/L40.50	10	19
Ischemic heart disease/ I25.9	5	19
Heart failure/I50	3	10
Hypertensive heart disease/I11	13	52
Essential hypertension/I10	7	27
Diabetes/E10; E11	1	20
Depression/F31	1	3
Obesity/E66		5
Other	27	53

– ordinary, arthropathic, pustular and erythrodermic“ and it covers pharmacotherapy cost, 10 phototherapy procedures, microbiologic testing as well as biopsy .

Total pharmacotherapy cost, paid by the hospital budget as part of the hospital charges, consist 6.85%, and for phototherapy – 16.6%. The costs for laboratory and microbiology tests constitute approximately 21%, and the main cost drivers is the hospital stay, medical supplies, staff and others expenditures account for 56%. (6)

There is no statistically significant relationship between the costs for hospital treatment, genders (p=0.83) and age (p=0.53). The cost paid by NHIF and by the patient in respect with their gender (p=0.12 и p=0.88) and age (p=0.53 and p=0.21) is not correlated. This means that the age and gender did not influence the cost of therapy.

After the discharge, patients usually have to receive 10 additional phototherapy procedures (80 BGN) paid by the NHIF.

**Table 3.** Topical medicines on individual prescriptions and their cost

	Components	Price (BGN)	Fulfilled prescriptions n (%)
Salicylic unguent	Ac. Salicylici 5,0 Olei Ricini q.s. Vaselini ad 100,00 M.f. ung. D.S. topical application	7,20	139 (56,28%)
	Ditranoli 0,25 Ac. Salicylici 5,0 Vaselini 100,0 M.f. ung. D.S. topical application	9,54	68 (27,53%)
Cold cream	Aq. Calcis 40,0 Lanolini Vaselini aa 10,0 M.f. cream D.S. topical application	4,80	188 (76,11%)
Salicylic oil	Acidi salicylici 5,0 Olei Ricini Olei Helianthi aa 50,0 M.D.S topical application	1,10	53 (21,46%)

**Direct medical costs for treatment of concomitant diseases:** Pharmacotherapy costs for concomitant diseases were calculated for 82 out of 246 patients due to missing data. The pharmacotherapy costs per month for 1 patient, paid by NHIF, are lower than the same, paid by the patient, for both years (7).

**Table 4.** Pharmacotherapy of the psoriasis

Pharmacological group	INN	Formulation	Treated patients – n (%)
<b>Antihistamines</b>	Chloropyramine	Amp	209 (84.62%)
	Promethazine	Amp	3 (1.21%)
	Chlorpromazine		1 (0.4%)
<b>NSAIDs</b>	Diclofenac	Amp	2 (0.81%)
<b>Analgesics</b>	Metamizole	Amp	1 (0.4%)
<b>Antifungal</b>	Bifonazole	Cream	8 (3.24%)
<b>Cephalosporin antibiotic</b>	Ceftriaxon	fl.	159 (64.37%)
<b>Antihypertensive</b>	Clonidine	Amp	1 (0.4%)
<b>Corticosteroids</b>	Clobetasol	cream/ung	42 (17%)
	Methylprednisolone	Amp	2 (0.81%)
<b>Corticosteroids + antibiotic</b>	Betamethasone+gentamycin	cr/ung	15 (6.07%)
	Flumetasone / Neomycin	cr/ung	5 (2.02%)
	Flumetasone / Clioquinol	cr/ung	16 (6.48%)
<b>Corticosteroids+ keratolytic</b>	betamethasone / sal. Acid	cr/ung	2 (0.81%)
	Flumetasone /Salicylic acid	cr/ung	10 (4.05%)
<b>Antibiotic</b>	Gentamycine	cream	3 (1.21%)
<b>Antiseptic</b>	Argentum nitricum	Sol	1 (0.4%)
<b>Vitamins</b>	Vit.B12	Amp	9 (3.64%)
<b>Antimetabolite drugs</b>	Methotrexate	tabl.	14 (5.67%)

**Table 5.** Ambulatory therapy for concomitant diseases

Pharmacological group	INN	Treated patients n (%)
<b>ANTIHYPERTENSIVE</b>		
<i>Beta-blockers</i>	Metoprolol, Bisoprolol	23 (28.05%)
<i>ACE-inhibitors</i>	Perindopril, Enalapril, Berlipril, Lisinopril	9 (11%)
<i>ATI-blockers</i>	Telmisartan, Losartan, Valsartan	13 (15.85%)
<i>Diuretics</i>	Hydrochlorothiazide, Indapamide, Furosemide, Spironolactone	12 (14.63%)
<i>Ca-blockers</i>	Amlodipine, Verapamil, Lercanidipine	17 (20.73%)
<i>Other antihypertensive MPs</i>	Moxonidine, Clonidine, Ivabradine	12 (14.63%)
<i>Anticoagulants/ antithrombotic agents</i>	Clopidogrel, Aspirin 100mg	8 (9.8%)
<i>Antiarrhythmic</i>	Propafenone	1 (1.2%)
<i>Antihyperlipidemic</i>	Simvastatin	1 (1.2%)
<i>Vasodilators</i>	Nicergoline, Vinpocetine, Pentoxifylline	3 (3.6%)
<i>Antidiabetics</i>		
<i>Biguanid</i>	Metformin	8 (9.8%)
<i>Sulphonylureas</i>	Glimepiride, Gliclazide	2 (2.4%)
<i>Insulins</i>	Mixtard, Humulin, Actrapid, Humalog, Lantus	5 (6%)
<i>Antimetabolite</i>	Methotrexate	3 (3.6%)
<i>Antidepressants</i>	Amitriptiline, Trazodone	2 (2.4%)
<i>NSAIDs</i>	Diclofenac	1 (1.2%)
<i>Anti-gout agents</i>	Allopurinol	2 (2.4%)
<i>Antibacterial agents</i>	Chlornitromycin, Ciprofloxacin	2 (2.4%)
<i>Thyroid hormones</i>	Levothyroxine	3
<i>Hepatoprotectors</i>	Ademethionine, Ursodeoxycholic acid	2 (2.4%)
<i>Bronchodilators</i>	Salbutamol, Budesonide+Formoterol, Theophylline	2 (2.4%)
<i>Gastroprotectors</i>	Famotidine	1 (1.2%)

**Table 6.** Distribution of costs for hospital treatment paid for 1 patient with psoriasis

Resources	Cost/patient (BGN)
<b>Phototherapy (10 procedures)</b>	80
<b>Microbiologic testing</b>	20
<b>Biopsy</b>	80
<b>Medications</b>	32.90
<b>Hospital stay and administrative cost</b>	267.10
<b>Total</b>	480

**Table 7.** The average pharmacotherapy costs/patient for treatment of concomitant diseases

Average costs/ month/ patient	2014	2015	Average
<i>Pharmacotherapy of the concomitant diseases, paid by NHIF</i>	15,70 BGN (SD=28,63)	26,02 BGN (SD=48,20)	20,79 BGN (SD=40,76)
<i>Pharmacotherapy of the concomitant diseases, paid by the patient</i>	19,41 BGN (SD=19,27)	26,34 BGN (SD=29,70)	23,38 BGN (SD=26,21)

The share of average costs for pharmacotherapy of concomitant diseases is almost equal between NHIF (20.53 BGN) and the patient (23.10 BGN). The hospital costs for concomitant diseases, paid by NHIF and patients did not differ statistically:  $p=0.83$ ;  $p=0.88$  and  $p=0.12$  (respectively). Hospital costs are the highest costs (7).

Other medical costs related to concomitant diseases are the visits to general practitioners constituting of 17.50 BGN per patient per month, paid by the NHIF and 2.60 BGN co-paid by the patients.

The costs of concomitant diseases therapy logically are increasing with the increase in their number per patient and the differences are statistically significant ( $p=0.023$ ). In case of 5 diseases the average pharmacotherapy cost is approximately 145 BGN per month, in case of 4 or 3 – 51.30 BGN and 23.53 BGN, and with 1 disease – 17.88 BGN. The average pharmacotherapy cost for treatment of 1 concomitant disease is 17.88 BGN and it is lower than treatment cost for 2 or more diseases - 29.44 BGN ( $p=0.01$ ).

**Indirect costs:** Using the formula described in the methodology we calculated the indirect costs due to productivity losses which totally amount to 61 934, 61 BGN (442,39 per patient) for 2015 and 45 428,26 BGN (428,57 per patient) for 2014.

Among total costs is evident that the hospitalizations costs are leading, followed by indirect costs and costs of concomitant diseases at the ambulatory level.

The share of indirect costs from the total costs is approximately 42% (3).

### Statistical correlation among the observed parameters

Chi-squared test showed statistically significant correlation ( $p<0.0001$ ) between both type of psoriatic pharmacotherapy costs (hospital and ambulatory) with contingency coefficient = 0.811. The higher the costs paid by NHIF, the higher the pharmacotherapy costs paid by the patients.

Strong statistically significant linear correlation was observed between the costs for concomitant diseases paid by NHIF and by the patients ( $p<0.0001$ ), Spearman coefficient= 0,947, CI = 95% (0.917, 0.966).

Statistically significant correlation ( $p=0.0095$ ) exists between the age and number of the concomitant diseases. Higher number of concomitant diseases is observed with increase of the patients' age. The linear trend is statistically significant ( $p=0.0035$ ) for the frequency distributions of concomitant diseases in all age groups: with increasing of the age, the number of patients with concomitant diseases also increases.

### Discussion

The current study reveals that more than half of the hospitalized patients with psoriasis (59%) have at least one concomitant disease. This is in aligning with previous researches showed that the number of the patients with at least one concomitant disease was 51% [11]. The most frequent comorbidities were hypertension, diabetes mellitus, and hypertonic heart disease and those with depression and obesity, which confirms already the results by studies conducted in Bulgaria and Germany [12-14].

The psoriatic pharmacotherapy administered in hospital is in accordance with the available consensus and guidelines for treatment of psoriasis [15,16]. During the study period the biological therapy for

psoriasis was just introduced for reimbursement. Therefore the current study could be considered as base case analysis of the hospital therapy of psoriasis before the introduction of the biological therapy and as such it should be important to replicate the study later on to see any possible changes in the findings after the introduction of these drugs.

The current study determines only the costs for treatment of psoriasis in hospital as well as the indirect costs. Monthly indirect nonmedical costs generated due to patients' absence from work, are relatively close to the hospital cost. Most of the published studies in Spain and Germany compare the hospital and ambulatory costs for psoriasis patients and conclude that the hospital costs exceed the ambulatory costs for psoriasis. Additional studies for Bulgarian patients with psoriasis should be conducted in order to reveal the correlation between different types of costs [17,18]. Our study reveals that the indirect costs due to lost productivity exceed the direct ones for concomitant diseases which is in contrast with other studies [19-23], but in accordance with others [24]. This fact could be explained with the short period of cost calculation.

The average monthly pharmacotherapy costs for concomitant disease per patient in ambulatory practice are higher (around 43 BGN) in comparison with the average pharmacotherapy costs for psoriasis in hospital. The financial burden is greater for the patients than for NHIF.

Logically, the presence of more concomitant diseases leads to higher total costs, paid by NHIF and patient, which is statistical significant. Increasing of patients' age correlates with the number of comorbid conditions among patients with psoriasis. Higher number of men ( $p=0.04$ ) suffer simultaneously from psoriasis and ischemic heart disease, while women suffer mostly from psoriasis and arthropatic psoriasis.

### Conclusions

Psoriasis is a multisystem disease with significant financial burden for Bulgarian healthcare system because of relatively high costs for treatment of the concomitant diseases, hospitalization costs and phototherapy. Indirect costs increase the total financial burden as they constitute a significant part of the total costs paid by the society for one patient with psoriasis. Improvement of the hospital care for psoriatic patients in Bulgaria could bring initially additional financial burden, but could reduce the levels of further hospitalizations and could alter the significant impact of indirect costs due to hospitalization which will lead to a reduction in overall costs in the future.

### Declaration of funding

Publication of the current study was financially supported by Novartis Bulgaria.

### Declaration of financial/other relationships

The authors declare that they have no conflicting interests regarding the submitted work.

### References

1. Cheng J, Feldman SR (2014) The cost of biologics for psoriasis is increasing. *Drugs Context* 3: 212266. [[Crossref](#)]
2. Beye V, Wolverson SE (2010) Recent Trends in Systemic Psoriasis Treatment Costs. *Arch Dermatol* 146: 46-54. [[Crossref](#)]
3. Svedbom A, Dalén J, Mamolo C, Cappelleri JC, Mallbris L, et al. (2016) Economic Burden of Psoriasis and Potential Cost Offsets with Biologic Treatment: A Swedish Register Analysis. *Acta Derm Venereol* 96: 651-657. [[Crossref](#)]



4. Oliveira Mde F, Rocha Bde O, Duarte GV (2015) Psoriasis: classical and emerging comorbidities. *An Bras Dermatol* 90: 9-20. [[Crossref](#)]
5. Gelfand JM, Troxel AB, Lewis JD, Kurd SK, Shin DB, et al. (2007) The risk of mortality in patients with psoriasis: results from a population-based study. *Arch Dermatol* 143: 1493-1499. [[Crossref](#)]
6. De Simone C, Guerriero C, Giampetruzzi AR, Costantini M, Di Gregorio F, et al. (2003) Achilles tendinitis in psoriasis: Clinical and sonographic findings. *J Am Acad Dermatol* 49:217-222. [[Crossref](#)]
7. Zhang C, Zhu KJ, Zheng HF, Cui Y, Zhou FS, et al. (2011) The effect of overweight and obesity on psoriasis patients in Chinese Han population: a hospital-based study. *J Eur Acad Dermatol Venereol* 25:87-91. [[Crossref](#)]
8. Ni C1, Chiu MW1 (2014) Psoriasis and comorbidities: links and risks. *Clin Cosmet Investig Dermatol* 7: 119-132. [[Crossref](#)]
9. Mease P, Goffe BS (2005) Diagnosis and treatment of psoriatic arthritis. *J Am Acad Dermatol* 52: 1-19. [[Crossref](#)]
10. Burgos-Pol R, Martínez-Sesmero JM, Ventura-Cerdá JM, Elías I, Caloto MT, et al. (2016) The Cost of Psoriasis and Psoriatic Arthritis in 5 European Countries: A Systematic Review. *Actas Dermosifiliogr* 107: 577-590. [[Crossref](#)]
11. Kimball AB, Guérin A, Tsaneva M, Yu AP, Wu EQ, et al. (2011) Economic burden of comorbidities in patients with psoriasis is substantial. *J Eur Acad Dermatol Venereol* 25: 157-163. [[Crossref](#)]
12. Augstin M, Hossa E, Batiea SF, Moffetet EW, Jurutka PW, et al. (2014) Regulation of late cornified envelope genes relevant to psoriasis risk by plant-derived cyaniding. *J Dtsch Dermatol Ges* 12: 48-57. [[Crossref](#)]
13. Dantzer R, O'Connor JC, Freund GG, Johnson RW, Kelley KW (2008) From inflammation to sickness and depression: when the immune system subjugates the brain. *Nat Rev Neurosci* 9: 46-56. [[Crossref](#)]
14. Gospodinov D (2012) Psoriasis – Clinical and epidemiological analysis, comorbidities and quality of life. PhD thesis (in Bulgarian).
15. Kadurina M (2013) Treatments guideline for psoriasis with biological products – Bulgarian dermatology society, 15-39 (in Bulgarian).
16. Grozdev I (2013) Treatment consensus for psoriasis treatment in Bulgaria (in Bulgarian).
17. Marinov L, Savova A, Nikolova I, Petrova G (2013) A literature review of the pharmacotherapy and cost of illness of psoriasis and psoriatic arthritis. *Medical review* 49: 39-44.
18. Steinke SI, Peitsch WK, Ludwig A, Goebeler M (2013) Cost-of-illness in psoriasis: comparing inpatient and outpatient therapy. *PLoS One* 8: e78152. [[Crossref](#)]
19. Berger K, Ehlken B, Kugland B, Augustin M (2005) Cost-of-illness in patients with moderate and severe chronic psoriasis vulgaris in Germany. *J Dtsch Dermatol Ges* 3: 511-518. [[Crossref](#)]
20. Jacobs P, Bissonnette R, Guenther LC (2011) Socioeconomic burden of immune-mediated inflammatory diseases—focusing on work productivity and disability. *J Rheumatol Suppl* 88: 55-61. [[Crossref](#)]
21. Kvamme MK, Lie E, Kvien TK, Kristiansen IS (2012) Two-year direct and indirect costs for patients with inflammatory rheumatic joint diseases: data from real-life follow-up of patients in the NOR-DMARD registry. *Rheumatology (Oxford)* 51: 1618-1627. [[Crossref](#)]
22. Schmitt JM, Ford DE (2006) Work limitations and productivity loss are associated with health-related quality of life but not with clinical severity in patients with psoriasis. *Dermatology* 213: 102-110. [[Crossref](#)]
23. Schultz AB, Chen CY, Edington DW (2009) The cost and impact of health conditions on presenteeism to employers: a review of the literature. *Pharmacoeconomics* 27: 365-378. [[Crossref](#)]
24. Colombo GL, Altomare GF, Peris K, Martini P, Quarta G, et al. (2008) Moderate and Severe Plaque Psoriasis: Cost of Illness Study in Italy. *Ther Clin Risk Manag* 4: 559-568. [[Crossref](#)]