EUROPEAN HEALTHCARE FACTS · VOL. 1

Psoriasis Healthcare and Facts in Europe

For decision makers and stakeholders

Matthias Augustin, Marc Alexander Radtke, Jobst Augustin



TABLE OF CONTENTS

1. PREFACE

2. SYNOPSIS

Characteristics of Psoriasis Socio-economical Relevance Treatment Standards

3. CLINICAL PICTURE

	Psoriasis vulgaris	11
	Nail Involvement	12
	Rare Forms of Psoriasis	12
	Psoriasis in Children	13
	Hidden Manifestations	13
	Koebner Phenomenon	14
	Pathogenesis	14
	Psoriatic Arthritis – Joint Involvement	16
	Comorbidities and other Associated Diseases	18
	Classification of Psoriasis according to ICD-10	18
	Degrees of Severity	19
	Measuring Disease Activity and Degrees of Severity – Clinical Scores	19
	BSA – Body Surface Area	19
	PASI – Psoriasis Area and Severity Index	20
	PASI Evaluation	22
	DLQI – Dermatology Life Quality Index	23
	NAPPA – Nail Assessment in Psoriasis and Psoriatic Arthritis	24
•	EPIDEMIOLOGY	25
	Comorbidity and Complications	26
	Comorbidity in Children with Psoriasis	27
		-1
•	DISEASE BURDEN	28
	Quality of Life (QoL) in Psoriasis Patients	28
	Cumulative Life Course Impairment (CLCI)	28
	Additional Strain for Patients with Psoriatic Arthritis	29
	Quality of Life and Patient Needs	30
	Measuring Global Disease Burden in Psoriasis	31
		5

	6.	THERAPEUTIC STRATEGIES	32	
		A Variety of Systemic Drugs Available	33	
	7.	SOCIO-ECONOMIC FACTORS	34	$\rangle >$
		Direct Costs Indirect Costs Health Economic Data for Psoriasis	34 35 36	
/	8.	EUROPEAN HEALTH SYSTEMS	36	
	9.	EUROPEAN DERMATOLOGY SURVEY	44	
7	5	The Survey Survey Methods and Quality Management Bibliographical Research Statistical Analysis Limitations Quality Management Healthcare Expenditures Dermatologists in European Countries Access to Dermatological Care: Waiting Times Drug Prescriptions for Psoriasis Epidemiology and Treatment of Psoriasis in Europe National Guidelines for the Treatment of Psoriasis Publicity of Psoriasis Treatment Guidelines Guideline Content: Definition of Psoriasis Severity Network of European Psoriasis Registries Global Psoriasis Atlas (GPA)	44 44 44 45 45 46 49 51 51 56 57 58 59 60 60 60	
	10.	PERSPECTIVE	61	
	11.	FACTSHEETS	62	
	12.	GLOSSARY	92	
	13.	REFERENCES	94	

2009. Since the clinical guidelines mostly refer to evidence from clinical trials, there is a shortage of evidence on the management of psoriasis in particular treatment situations which have not yet been subject to clinical trials. These "challenging treatment situations beyond guidelines" have at least been assessed by expert consensus. In addition to guideline development, consideration needs to be given on how such guidelines are actually implemented. There is strong evidence that health-related quality of life (HRQoL) in psoriasis treatment – as in other diseases – is associated with the patient's perception of attaining the goals of therapy. For this, a systematic assessment methodology for measuring patient goals and needs in treatment and the degree of goal achievements should be implemented.

125 000 000 PEOPLE WORLDWIDE HAVE PSORIASIS



stigmatization

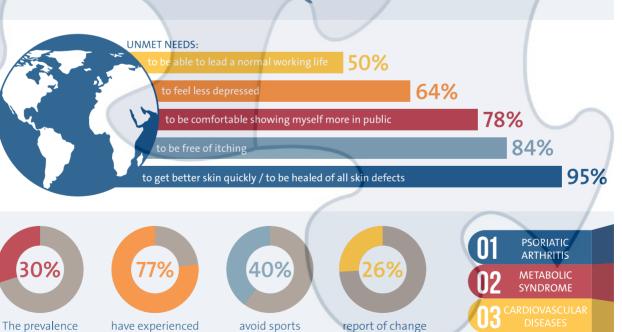


Figure 1. Psoriasis worldwide

of depression in

psoriasis

or discontinuation

of daily activities

TOP 3 COMORBIDITIES

Degrees of Severity

The classification of psoriasis according to ICD-10 does not properly represent the clinically important classification by degree of severity. National as well as international dermatological organizations have therefore come to a consensus regarding the degrees of severity concerning psoriasis [88,89]. These consensus-based classifications however are not used consistently [90]. Most classifications do consider that the degree of psoriasis severity is partly objective, regarding the extent and type of lesions, and partly subjective, considering the experienced disease burden. Therefore, objective measures such as the PASI (Psoriasis Area and Severity Index) as well as subjective measures such as quality of life (e.g. Dermatology Life Quality Index, DLQI) are used as indicators for degrees of severity [91]. According to an internationally common classification method, patients with an affected body surface area (BSA) of more than 10% and/or a PASI score of higher than 10 and/or a DLQI score of higher than 10 can be classified as patients with moderate to severe degrees of psoriasis [92]. Following another classification, PASI scores below 10 is considered as mild, a score of 10 to 20 as moderate and above 20 as severe psoriasis. Further definitions on an international level are at work.

Following an international consensus, therapyrefractive forms of psoriasis are also to be considered as severe, as well as sensitive localizations such as the face, the dorsum of the hand, the scalp, the anogenital area, nail involvement and psoriatic arthritis [93].

Figure 20.

Body scheme indicating several psoriasis lesions of the lower extremity which fit into the area of three palms (in blue), suggesting a body surface area (BSA) of 3 % affected. The area of the right hand in green indicates the practical measure used.

Measuring Disease Activity and Degrees of Severity – Clinical Scores

3% BSA

Although a standardized measurement of psoriasis severity for clinical practice may be theoretically advantageous for patient assessment and therapeutic evaluation, the clinical practice relevance of currently available severity scores is uncertain and an abundant variety of scoring systems is available, especially for psoriasis. The implementation of assessment tools such as the PASI (Psoriasis Area and Severity Index) or the BSA (Body Surface Area) has led to assessment of disease severity in a more objective way. Additionally, a score for the diseasespecific quality of life may be determined. Most frequently, the DLQI is used (additional information regarding quality of life, see specific section).

Moreover, there are scores and measures to determine the severity of specific psoriasis manifestations such as nail involvement, like NAPSI, NAPPA, PSSI or the PGA.

BSA – Body Surface Area

The BSA score indicates the percentage body area affected by psoriasis [94]. To simplify the procedure of measuring, dermatologists use the inside hand surface of the patient as one unit of measurement. The inside of the hand surface makes up to about 1% of the entire body surface area (see Figure 20).

Comorbidity and Complications

In all age groups, comorbidity occurs more frequently in people with psoriasis than in people without, in children and adolescents even twice as often [33,114].

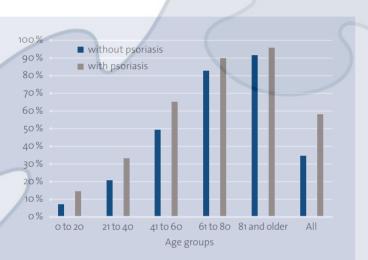


Figure 32. Prevalence of at least one comorbidity (out of 11 single disease, including hypertension, diabetes, depression) in insured persons with psoriasis (n=30,000) vs. persons without psoriasis (n=1,25 million; Augustin 2010 [32]).

It is also well known from several studies that patients with psoriasis carry an increased risk of developing comorbidities related to the metabolic syndrome, which includes arterial hypertension, obesity and abnormalities in lipid and glucose metabolism [110,111]. This association is believed to account at least partially for the higher rate of cardiovascular complications observed among patients with psoriasis and to contribute to the decreased life expectancy observed in patients with severe disease [112]. The exact relationship between cutaneous inflammation and metabolic syndrome is not fully understood [113] but there is evidence that metabolic changes are not exclusively the

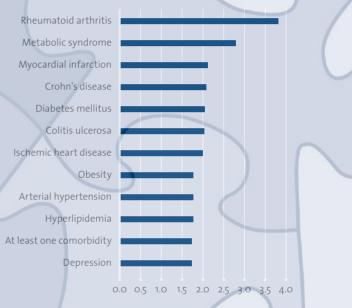


Figure 33. Prevalence rates of comorbidity [32]: Relative frequencies of respective comorbid diseases in psoriasis patients compared to healthy persons (=1). All shown differences were statistically significant.

consequence of long-lasting active skin disease but may in fact precede the first onset of psoriasis [114,115]. Finally, epidemiological as well as genetic studies point to a possible relationship between psoriasis and other immune-mediated inflammatory conditions, including Crohn's disease [116–118]. Most studies on conditions associated with psoriasis, however, have been performed on small and selected samples of patients. Comorbidities may be pathogenically related to psoriasis or may emerge with no recognizable coherence but it is confirmed and widely accepted that cardiovascular diseases and metabolic diseases occur with rates above average.

5. DISEASE BURDEN

Quality of Life (QoL) in Psoriasis Patients

Quality of life is defined as the perceived quality of a person's daily life; it is a multidimensional concept that includes all emotional, social and physical aspects of the individual's life [127]. Numerous studies have shown that the extent of quality of life impairment caused by psoriasis is not proportional to objective measures of disease severity but instead perceived in an individual way [107,128,129].

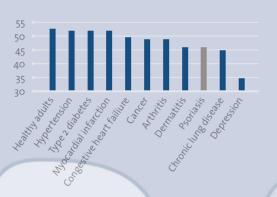


Figure 35. Psychological burden: Comparison of generic health related quality of life with other chronic diseases (measured with SF-36 according to Rapp, 1999 [130]) Psoriasis can affect health-related quality of life to an extent similar to the effects of other chronic diseases such as depression, myocardial infarction, cancer or hypertension [130]. The extent of quality of life burden is highest for patients with psoriasis alongside with atopic dermatitis and urticaria. On average, psoriasis patients show higher levels of psychological and physical strain influencing their quality of life compared to patients affected by other chronic diseases such as diabetes, rheumatism, heart disease or even cancer [131].

Cumulative Life Course Impairment (CLCI)

The concept of cumulative life course impairment (CLCI) describes the life-long interactions between the main factors influencing health-related quality of life in patients with psoriasis, such as stigmatization, physical and psychological comorbidity as well as coping strategies and external factors [132,133]. The effects of these burdens can accumulate over the years lived with the disease and result in irreversible patient strain and in lost opportunities with respect to personal, social and professional life [134,135].

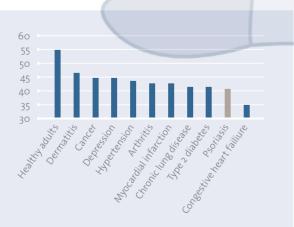


Figure 36. Physical burden: Comparison of generic health related quality of life with other chronic diseases (measured with SF-36 according to Rapp, 1999 [130])

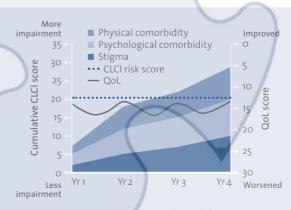


Figure 37. Phenomenon of cumulative life course impairment (CLCI): unmanageable limitations (e. g. limited possibilities regarding work, private life and partnership) add up irreversibly over time [132].

Note: Page 27 not included in the extract.

	Co	sts				Effecti	veness				Mc	odel
Topical Treatment	Direct only	Direct + indirect	QALY	DLQI	DFD/ DCD	SF- 36/6D	Other QoL	EQ-5D	PASI	WTP	Decis. Tree/ DAM	Markov Model
Cost-Effectiveness	11	3	4	1	6	2	0	1	8	0	2	4
Cost-Utility	3	1	4	0	1	2	0	1	1	0	0	2
Cost-Benefit	0	0	0	0	0	0	0	0	0	0	0	0
All publications	14	4	8	1	7	4	0	2	9	0	2	6
	Co	sts				Effecti	veness	-			Mo	odel
Systemic Treatment	Direct only	Direct + indirect	QALY	DLQI	DFD/ DCD	SF- 36/6D	Other QoL	EQ-5D	PASI	WTP	Decis. Tree/ DAM	Markov Model
	Direct	Direct +	QALY 4	DLQI 3	,	SF-	Other	EQ-5D	PASI 17	WTP 1	Decis. Tree/	Markov
Treatment	Direct only	Direct + indirect			DCD	SF- 36/6D	Other QoL	EQ-5D 1 3			Decis. Tree/ DAM	Markov Model
Treatment Cost-Effectiveness	Direct only 15	Direct + indirect 4	4	3	DCD	SF- 36/6D 1	Other QoL 1	1	17	1	Decis. Tree/ DAM 8	Markov Model 2
Treatment Cost-Effectiveness Cost-Utility	Direct only 15 9	Direct + indirect 4 1	4	3	DCD 1 0	SF- 36/6D 1 0	Other QoL 1 O	1	17 8	1 O	Decis. Tree/ DAM 8 1	Markov Model 2 3

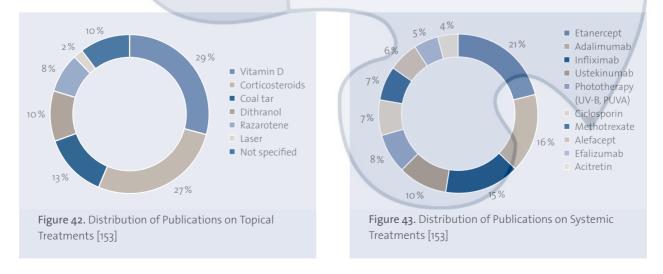
Table 2. Distribution of used costs, effectiveness parameters and model types (n=60 publications) [153]

Indirect Costs

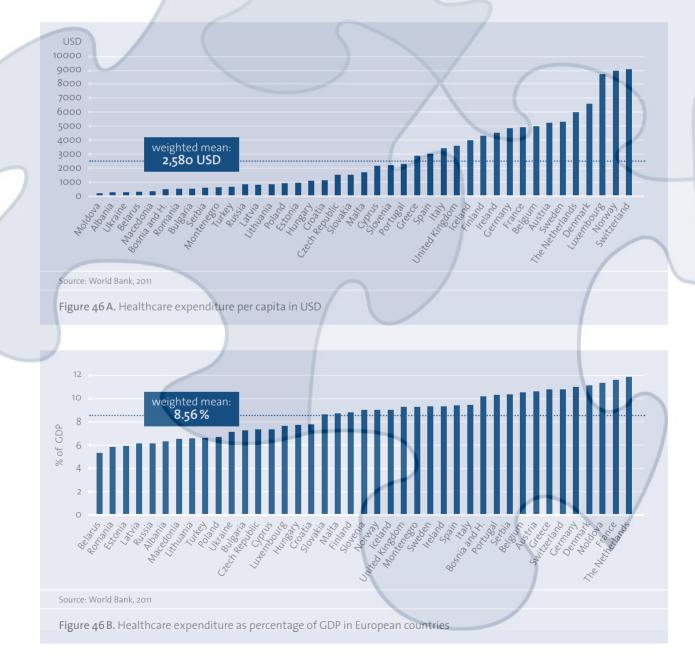
The economic burden of psoriasis in terms of indirect costs is composed by absenteeism (sick leave) and by presentism (reduced productivity at work). Even though there still is a lack of large-scale data on this, several studies indicate that both account for substantial losses of productivity and thus contribute to indirect disease related costs.

Health Economic Data for Psoriasis

A recent systematic review has identified more than 90 studies relating to health economic issues of psoriasis, including about 28 from Europe. The studies refer to cost of illness studies as well as cost-effectiveness studies and relate to all levels of treatments. With respect to the cost-effectivness studies the overall conclusion is that there is a large heterogeneity of study methodologies and a low level of comparability between the studies. Moreover, cost data and cost-effectiveness ratios largely depend on the local healthcare systems. Accordingly, they can only be transferred to other countries in a limited way. Moreover, the cost data for treatments is subject to continues variation related to changing drug prices in most countries. For this, only a few general conclusions can be drawn. An example of current drug costs for psoriasis from Germany 2017 indicates the variability of drug costs. They need to be related to the effectiveness of the treatments used.



A common method to express healthcare expenditures is the normalization on the Gross Domestic Product (GDP). This calculation changed the order of countries compared to absolute expenditures. By this categorization, the Netherlands (11.96%) and France (11.63%) are set at the top of the table. In contrast, states with very low absolute sums of healthcare expenditures but also low GDP now range higher (e.g. Moldova [11.37%], Serbia [10.43%] and Bosnia and Herzegovina [10.21%]). Nevertheless, the bottom of the table is dominated by Eastern European countries and the Balkan states. Data is shown in figure 46 A-D.



Ireland

Turkey Spain Norway Denmar

Portugal Poland

Malta Slovenia The Netherlands

Sweden Finland

Hungary Iceland

Latvia Germany

France Belgium Lithuania

Luxembour Italy Cyprus Slovakia Czech. Rep

Switzerland Estonia

Romania United Kingdom Croatia Serbia Bulgaria

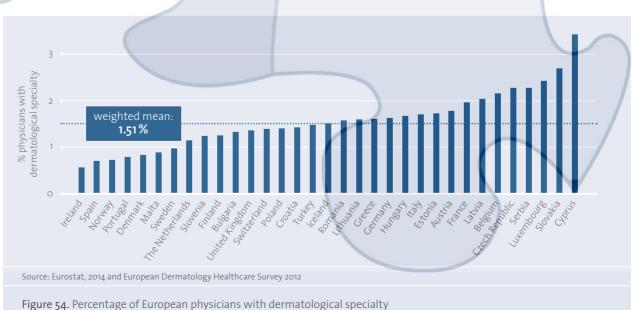
Dermatologists in European Countries

Official data (Eurostat) ranged from 15 dermatologists per 1 million inhabitants in Ireland to 100 in Greece. The survey data provide a similar pattern. The mean was about 50 dermatologists per 1 million inhabitants while some large European countries like Germany, France and Italy indicated 60 to 70 dermatologists per 1 million inhabitants.

Figure 53. Dermatologists per 1 m. persons in the national populations across Europe (average: 45)

Source: Eurostat, 2014

Calculation of the percentage of dermatologists per practicing physicians in total resulted in a mean of 1.51% (± 0.42%-pts. SD) in the 33 countries surveyed, weighted by the number of inhabitants. The crude rate was 1.60% (± 0.65%-pts. SD). Noticibly low numbers were found in Ireland (0.56%), Spain (0.70%) and Portugal (0.79%), whereas the highest percentages were calculated based on the data from Cyprus (3.43%), Slovakia (2.70%) Luxembourg (2.43%). Thus, a sixfold range in dermatological workforce exists within Europe.



Note: Pages 42-48 not included in the extract.

Psoriasis is a frequent reason for consultation of a dermatologist in all countries. In contrast, psoriatic arthritis is treated less frequently by dermatologists in some countries. Especially in Spain and Denmark, psoriatic arthritis patients are mostly treated by rheumatologists.

Psoriatic arthritis

- Always
- Frequently
- Sometimes
- Rarely
- Never
- No data

Figure 69. Treatment of psoriatic arthritis by dermatologists

National Guidelines for the Treatment of Psoriasis

In order to provide a standardized, high-quality treatment of psoriasis, national guidelines on treatment have been introduced in many countries within the

last decade. According to dermatology experts, in 2012 a national guideline for psoriasis existed in 19 of 33 countries (58%).

National psoriasis guidelines available

- Yes
- No
- No data

Figure 70. Availability of national psoriasis guidelines



IRELAND

		Ireland	EU
	Inhabitants	4.6 million	509 million
	Population development	+ 0.3 % per year	+0.21% per year
Socio-demographic features	Structure of population	11.3 % ≥ 65 years	17.4 % ≥ 65 years
	Life expectancy	ø 80 years (♂ 77.6 / ♀ 82.1)	ø 80 years (♂ 76.8 / ♀ 82.5)
	Risk of poverty	29.4%	24.3%
Turnin (GDP total	210.3 billion USD	16.63 trillion USD
Economic	GDP/per capita	45 835 USD	32 677 USD
Health expenditures	Per capita	4 542 USD	3 530 USD
nearthexpenditures	Percentage of GDP	9.4%	10.1%

Main System characterist	ics						
Administration	National Health System						
Financing	Funding predominantly by taxes (78.3% of total expenditures), but marked by high co-p.						
Expenses	Public: 74 %, private OOP payments: 18 %, VHI: 8 %	%					
Coverage and consumer choice	 Out-of-pocket expenditures (18% of expenditures) for GP visits, pharmaceuticals and hospital stays Inequities in access between private and public patients (especially concerning hospit Only one third of the population can access public services free of charge. 						
Providers	- About half private, half public - The number of GPs is relatively low.						
Primary care	GP visit card (owned by about 39 % of the population) for access to primary care (created to boost use of primary healthcare services)						
Specialist care	No data						
Inpatient care							
GP function	No data						
Role of VHI	 51% of the population have voluntary private health insurance (mostly for coverage of out-of-pocket payments required by NHS) accounting for about 8% of total health expenditures. Private market is regulated by risk-equalization scheme balancing differences in risk profiles of insurance subscribers. 						
	Overall population in public system	100 % (automatic coverage)					
	Insured persons with additional insurance 51.2% (complementary schemes)						
Co-payments	 OOP expenditures for GP visits (50-80 EUR pe and hospital stays (66 EUR per day) Co-payments are limited to 90 EUR per month 	r visit), pharmaceuticals (drug payment scheme) for medical card owners					
Dermatological Health ch	aracteristics						
Dermatologists / 1 million Inhabitants	11 Percentage of dermatologis						
Access to secondary care	GP referral financially encouraged Insurance cov outpatient se						

12. GLOSSARY

Term/Abbreviation

Acitretin	Conventional oral antipsoriatic drug belonging to the retinoids
Adalimumab	Biological; TNF antagonist; recombinant human monoclonal anti-TNF antibody
Apremilast	Oral antipsoriatic drug based on phosphodiesterase 4 (PDE4) inhibition
Balneo-phototherapy	Combination of a bath (brine- or psoralen-containing) and UV phototherapy
Biological, Biopharmaceutical	New generation of drug substances that are obtained through biotechnological manufacturing processes; approved for moderate to severe psoriasis in the European Union: adalimumab, etanercept, infliximab, ustekinumab
Biosimilar	Biopharmaceutically manufactured drug copying a biological
Brodalumab	Monoclonal antibody (biological) blocking a distinct receptor (IL-17R)
BSA – Body Surface Area	Score for the assessment of disease severity based on the affected body surface area
CHD – Coronary heart disease	Disease of the coronary arteries
Ciclosporin	Conventional systemic therapeutic agent
CLCI – Cumulative Life Course Impairment	Concept of life-long accumulating disease-related burden that can limit work possibilities, partnership and choices for private life
Colitis ulcerosa	Chronic inflammatory bowel disease
Comorbidity	Accompanying illness or associated disease; common comorbidities of psoriasis vulgaris: psoriatic arthritis, cardiovascular diseases, diabetes, metabolic syndrome, depression, other autoimmune diseases (colitis ulcerosa, Crohn's disease, rheumatoid arthritis)
Conventional systemic therapeutic agents	Systemic treatment; approved for psoriasis vulgaris: fumaric acid esters, methotrexate, ciclosporin A, phototherapy (UV-A, UV-B, Balneo-phototherapy), retinoids
Crohn's disease	Chronic inflammatory bowel disease
CVderm – German Center of Health Services Research	Instituted in October 2005 at the University Medical Center Hamburg-Eppendorf, Hamburg, Germany; tasks of CVderm: basic documentation of health services research on dermatologic and allergic diseases in Germany, initiation of healthcare studies as well as methodological consulting for other research groups
Dimethyl fumarate	Oral antipsoriatic drug belonging to fumaric acid esters
DLQI – Dermatology Life Quality Index	Patient score for the assessment of quality of life
DRG	Diagnosis-related group; system to classify hospital cases
Etanercept	Biological; TNF antagonist; recombinant human TNF receptor fusion protein
FFS	Fee-for-services; payment model where services are unbundled and paid for separately
Fumaric acid ester	Conventional systemic therapeutic agent
GDP	Gross domestic product
GP	Gross profit
GPA – Global Psoriasis Atlas	Global research program since 2017 analyzing the epidemiology, disease burden, costs and healthcare of psoriasis worldwide
Guselkumab	Monoclonal antibody (biological) blocking a distinct cytokine (IL-23/p19)
Incidence	Number of new cases in a population within a defined time period (usually one year), e.g.: number of new cases per 100,000 inhabitants per year
Infliximab	Biological; TNF antagonist; recombinant human monoclonal anti-TNF antibody
lxekizumab	Monoclonal antibody (biological) blocking a distinct cytokine (IL-17)
Juvenile idiopathic arthritis	Chronic inflammatory rheumatic joint disease during childhood (juvenile) with unknown cause (idiopathic)
Koebner phenomenon	Disease-specific skin changes caused by physical, chemical or inflammatory irritation

Definition / Explanation