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Inequalities in access to biological treatments for psoriasis:

Results from the Italian Psocare Registry

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Running head: Inequalities in access to biological treatments in psoriasis.

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Bulleted statements

- **What's already known about this topic?**

  Disparities in healthcare provisions and outcomes have been noted in several medical areas. Little is known about dermatology. Data from Medicare in the United States, indicated financial and racial barriers to receipt of biologic therapies in psoriasis.

- **What does this study add?**

We documented inequalities of drug prescriptions for psoriasis in Italy, with a trend towards a higher frequency of prescription for more expensive biologics in higher socio-economic sectors of the population.

Abstract

Background: Limited evidence is available on the impact of socioeconomic factors in drug prescriptions for psoriasis.

Objectives: To investigate factors influencing prescription of conventional versus biological treatment for psoriatic patients, based on the Psocare registry with a special focus on socioeconomic factors.

Methods: This was a cross-sectional study evaluating the baseline data of patients included in the Italian Psocare Registry. All of the consecutive adult patients with a diagnosis of chronic plaque psoriasis (Ps) or psoriatic arthritis and who were prescribed a systemic treatment for Ps at the participating centres were included in this study. Univariate and multivariate analyses of the baseline factors associated with a biologics prescription were performed.

Results: From September 2005 to September 2009, 12,838 patients were identified. A multivariate analysis revealed that, among other factors, completing a level of education higher than lower secondary school and being employed as a manager or a professional were independent factors associated with a biologics prescription at entry in the registry. Additional analyses on the association between these two variables and a severe Ps condition (i.e., psoriasis area and severity index [PASI] score > 20) revealed a significant increasing trend of severe disease towards lower educational attainment, while

unemployed patients were more likely to have a more severe condition as compared to the other categories of workers.

Conclusions: We documented inequalities of drug prescriptions for Ps in Italy, with a trend towards a higher frequency of prescription for more expensive biologics in higher socio-economic sectors of the population.

INTRODUCTION

Inequalities in health can be defined as unfair systematic differences in the healthcare and the health status among individuals.[1,2] Disparities in healthcare provisions and outcomes (i.e., morbidity and mortality) have been noted, for example, between different social groups, between urban and rural populations and between different geographical areas in the same country.[3,4] Much of these discrepancies cannot be accounted for on biological grounds. Instead, the major part is played by socioeconomic and environmental factors, including lifestyles.

Several treatment options are available for Ps. The annual cost of these treatments shows large variations. In particular, more targeted therapies, including biological agents (such as TNF-alpha-blockers), are very expensive, and their prescription is restricted to patients not responding or having contraindications to less expensive conventional agents.

To date, only two studies from the United States have focused attention on the impact of socioeconomic factors on drug prescriptions in Ps. One study from the Medicare social insurance program documented that people without access to a Medicare Part D low-income subsidy had a much lower chance of having received biologics than those with such an access.[5] Another study limited to a single academic medical centre, documented that

difficulty in obtaining biologics was associated with younger age, lower income level and lack of insurance.[6]

The aim of our study was to investigate the factors influencing the prescription of conventional treatments versus biological treatments for psoriatic patients, based on the PSOCARE registry, with a special focus on socioeconomic factors, which may reflect inequalities in healthcare. The PSOCARE registry systematically recruits all of the patients at the reference centres who are starting a new systemic treatment for Ps in Italy.[7]

METHODS

This was a cross-sectional study evaluating the baseline data of the patients who were included in the Italian Psocare Registry. In this study, 155 dermatology outpatient clinics participated. These clinics were located across Italy and were appointed by the Italian Regional Health Authorities (see Appendix) as reference centres for the treatment of moderate-to-severe Ps. The Italian National Health Service (NHS) was established in 1978 and it is founded on the principles of universal coverage, social financing through the use of general taxation, and non-discriminatory access to the health care services.[8]

The study was conducted according to the Declaration of Helsinki and got the ethics committees approval of the participating centres. The Italian Psocare Registry's goals and methods have been described in detail elsewhere.[7]

The main outcome of this study was to describe the factors associated with the choice of systemic treatment at entry in the registry.

Patients

All consecutive adult patients (aged ≥ 18 years) who were clinically confirmed with a diagnosis of chronic plaque Ps or psoriatic arthritis (PsA) and who were prescribed a new systemic treatment for Ps for the first time in their life at the participating centres were included in this study. To get reimbursement by the NHS, a compulsory registration within the Psocare registry was required for subjects receiving a biological therapy. On the contrary, conventional treatment could also be prescribed outside the registry.

The conventional treatments that were considered included acitretin, cyclosporine, methotrexate and PUVA therapy, while etanercept, infliximab, adalimumab and ustekinumab were considered as biological treatments.

According to the registered indications, only the patients with moderate-to-severe Ps (psoriasis area severity index - PASI > 10) with failure, contraindication or adverse events to conventional systemic agents (e.g., cyclosporine, acitretin, methotrexate and PUVA) were eligible for biological therapy (e.g., infliximab, etanercept and adalimumab). The patients receiving combination treatments or off-label dosages and the patients who had unspecified baseline treatments were excluded from this study. All of the patients gave written informed consent before being included in this study.

Data collection

The study investigators registered the patients on a web-based electronic data collection system endowed with internal quality controls, which also guaranteed confidentiality. The data collected at the baseline included: 1) demographic details and personal habits (e.g., smoking, average alcohol consumption, educational attainment and employment status); 2) a history of current or previous main comorbidities and medications; 3) a dermatological

and family history of Ps and/or PsA; 4) the severity of Ps, any drugs prescribed and the results of the laboratory tests performed before the prescription. The PASI was adopted as the measure of disease severity. In addition the perceived patient's severity was rated between 0 and 10 by using a standard visual analogue scale (VAS). The Charlson comorbidity index (CCI) was also used as a surrogate measure for overall comorbidity.

Statistical analysis

For descriptive purposes, data are presented as means with standard deviations (SDs) or numbers with percentages for the continuous and categorical variables, respectively.

The continuous variables were categorised, for analysis purposes, using clinically meaningful thresholds as cut-offs. A univariate analysis of the baseline factors associated with a biologics prescription was performed by means of a Pearson's χ^2 test. In the case of ordinal data, a Cochran–Armitage test for linear trend was also performed across different levels of variables.

All of the variables with a *p*-value < 0.10 from the univariate analysis were considered for inclusion in the multivariate analysis. A multiple logistic regression with a forward stepwise algorithm selection was used to identify the significant predictors of a biological prescription. The effects of the identified factors were expressed in terms of an odds ratio (OR), along with a 95% confidence interval (CI) and a *p*-value. When required, the effect of interaction between selected variables was tested as well. Multiple logistic regression models were also used to adjust the effects of selected factors on severe Ps conditions (PASI score > 20). Patients with missing data were excluded from the analysis. When planning this study we considered that with 12,838 patients fulfilling inclusion/exclusion criteria at the time of data extraction we could detect OR >1.18 in multiple logistic regression models

(ratio of control and case group of 1.35, proportion of exposure in control group >10%, multiple correlation coefficient <0.3, α=0.05, β=0.2).

In addition, the association among the variables were analysed by means of an artificial adaptive system, the auto semantic connectivity map (AutoCM).[9] AutoCM is a data mining tool based on an artificial neural network (ANN) model that is especially effective at highlighting any patterns and/or systematic relationships and hidden trends among variables. The weights determined by AutoCM are proportional to the strength of the associations across all of the variables. The weights are transformed into distances, and a mathematical filter (i.e., the minimum spanning tree [MST])[10] is applied to the matrix of the distances. A connectivity map is then generated from the MST. In the connectivity map, hubs of variables are detected, and related dependent variables converge to these hubs. The system also provides a quantification of the strength of links among variables by a numerical coefficient ranging from zero, minimum strength, to 1, maximal strength. All of the tests were considered significant at a *p*-value < 0.05. Analyses were performed with SPSS software, version 20 (IBM Corp.) and AutoCM software, version 7 (Semeion).

RESULTS

Overall, from September 2005 to September 2009, 12,838 patients fulfilling the study inclusion criteria were identified. The general characteristics of the patients are reported in Table 1. The mean age was 48.8 ± 14.4 years (mean ± SD), with a male:female ratio of 1.9. The mean BMI was 27.0 ± 4.9 kg/m^2, and the prevalence of smokers and regular drinkers was 40.2% and 35.7% respectively. Most patients were married (70.7%), had attained lower or upper secondary education (33.3% and 38.9% respectively) and worked as employees, craftsmen or skilled workers (32.5%). The mean PASI score was 17.2 ± 10.5, with an average

disease duration of 16.9 ± 13.0 years and a mean CCI of 0.29 ± 0.78. PsA and pustular Ps were present in 24.8% and 2.9% of the patients, respectively. Prescribed drugs at entry in the registry were etanercept (29.0%), cyclosporine (27.3%), acitretin (14.7%), methotrexate (11.7%), infliximab (8.8%), adalimumab (4.9%) and PUVA therapy (3.8%). The overall rate of biological drug prescriptions was 42.5%.

Analysis of variables associated with biological drug prescriptions

All of the factors with a *p*-value <0.10 in the univariate analysis (Table 1) were evaluated for inclusion in the multivariate model. These factors were age, BMI, smoking and drinking habits, marital status, geographical area, educational attainment, present or last occupation, calendar year of first visit, PASI score, patient's perceived severity, disease duration, a history of hypertension, hyperlipemia, chronic liver diseases, neoplasms, the presence of pustular Ps or PsA, the number of previous systemic treatments for Ps, hospital admissions for Ps in the last 5 years and previous clinical remissions for Ps.

A multivariate analysis revealed that an age lower than 60 years, a BMI greater than 25 kg/m^2, an ex-/non-smoker or ex-/non-drinker status, being visited in central/southern Italy, an educational attainment higher than lower secondary school, employment as a manager or a professional, the calendar year of visit (with a significant increasing trend over time), a PASI score greater than 10, a positive history of hypertension or a negative history of neoplasms, the absence of pustular Ps or the presence of PsA, the number of previous systemic treatment for Ps (with a substantial growing trend with increasing numbers) and any hospital admission for Ps in the last 5 years were all associated with biologic prescriptions at entry in the registry. Interestingly, educational attainment showed to be an independent predictive factor, with a clear increasing trend of biological drug prescriptions

towards higher education. This was also confirmed by a higher employment status. Additional analyses on the association between these two variables and a severe Ps condition (PASI score > 20) revealed a significant increasing trend of severe disease towards lower educational attainment, while unemployed patients were more likely to have a more severe condition as compared to other categories of workers, including managers and professionals (Table 2). Furthermore we assessed the interaction between the geographical area and both the employment status and the educational attainment. While the first was not significant the latter was an effect modifier for the prescription of biologicals, with education having more impact on the outcome in the northern area compared to central/southern regions (data not shown).

AutoCM analysis

The Figure shows the map produced by the AutoCM algorithm. The algorithm highlights the main associations between variables in the database, offering a simple graphical way to display their mutual interaction. The resulting map can be divided into three regions. In the first and second regions, at the top and at the bottom, the variables are connected to conventional and biological drug prescriptions, respectively, at entry in the registry. Both of the variables act as main hubs in the system. Being a smoker or a drinker, being 60 years old or more, being overweight or obese, having any history of main comorbidities (except for chronic liver diseases or a short duration of disease) and being fairly naïve to systemic treatments were all factors connected to conventional prescriptions. Unskilled workers and those with primary or lower secondary school degrees were associated, as well, to conventional drug use. These results confirmed those of the main analysis.

Conversely, at the bottom of the map, having severe Ps or mild Ps associated with PsA, being a non-responder to previous systemic treatments or being admitted at a hospital for Ps in the last 5 years were all associated with biological prescriptions. In addition, being a manager or having at least a university degree was confirmed to be associated with biological drug use.

Finally, the middle region of the map captures other less relevant pieces of information, which are common to most of the patients included.

DISCUSSION

Targeted biological therapies have represented a breakthrough in the management of patients with Ps. These drugs are much more expensive than conventional agents, and their use is restricted to patients with contraindications or side effects to these agents. The aim of our study was to investigate the determinants that influenced the prescription of systemic conventional treatments versus biological treatments for moderate-to-severe psoriatic patients based on data from the PSOCARE registry. In our study, less than half of the patients received a biological treatment for their Ps. We documented an increasing trend in the number of prescriptions of biological agents with a higher education and employment status of the patients. Conversely, unemployed patients and patients with lower educational attainment were less likely to receive a prescription of a biological agent. These differences were not accounted for by other factors, such as disease severity or lifestyle issues. As a matter of fact, the unemployed and less educated patients had a higher chance of presenting at the baseline with a more severe cutaneous condition (PASI score >20) as compared to the other patients. A similar result was found in a study of Horn et al.,[11]

where patients with severe psoriasis were more likely to have lower household income, although information on severity and income was self-reported by the patient.

Our results were confirmed in a secondary analysis performed by using ANN systems. The main advantage of this analysis is the possibility of presenting, in a single map, the mutual associations among all the variables in the registry. A possible disadvantage, however, is that the higher complexity of the model, compared to the classical approach used in the main analysis, requires a larger sample size in order to achieve sufficient generalizability of results.

Socio-economic status (SES) is traditionally composed of three dimensions: educational attainment, occupation and household income. Education in combination with occupation are the most frequently used indicators. Household income may be difficult to obtain due to privacy restriction. It has been shown, however, that higher levels of education are associated with better economic outcomes,[12] while the occupational status reflects the educational attainment required to obtain the job and income levels, so that it encompasses both income and educational attainment.[13] In our study, we didn't collect other variables which may contribute to the definition of wealth such as household income, family size, religion and ethnicity.

A significant trend for the penetration of biologicals over time was observed from 2005 to 2009 in our registry, but the increased penetration did not temper the effect of inequalities in biologicals prescription.

The Italian NHS is expected to guarantee uniform care throughout the country. Public healthcare spending, in the last 25 years, has consistently exceeded central government forecasts, and the expectation is that the resources are allocated fairly in a way to warrant equal access to care for all of the individuals registered for it.[14] Even if it is understandable

that the information about new therapies could be more available to those people who are younger, those people with a higher level of education and those with a higher socioeconomic status, it is not expected that those factors could influence prescriptions by treating physicians. It can be also hypothesized that higher socioeconomic status and education might be associated with better patients' negotiation skills or increased empathy from physicians, although further research is needed to clarify these points.

It should be noted that in our study, all of the consecutive patients receiving a first prescription of a new systemic agent and being seen at a network of dermatological centres were enrolled, and a selection bias is unlikely.[15]

Health inequities have been defined as systematic unfair differences in care that is preventable by a reasonable action.[16] Inequalities have been documented in clinical care for selected skin conditions, such as skin cancer and atopic dermatitis.[3,17-23] Two previous experiences from the United States, have documented the impact of socioeconomic factors on drug prescriptions in Ps. One study from the Medicare program showed that people without access to a Medicare Part D low-income subsidy had a 70% lower odds of receiving biologics than those with such an access. A similar low chance was also observed for black patients compared with white patients.[5] Another study limited to a single academic medical centre, documented that difficulty in obtaining biologics was associated with younger age, lower income level and lack of insurance.[6] Interestingly, a study based on data from the PsoReg registry in Sweden, documented that patients with psoriasis had fewer opportunities to access biological medications as they age.[24] The study made adjustment for educational level but not for income.

In agreement with data from the two studies from the United States, we documented disparities of care in Ps in Italy, with the prescription of biological agents being more

frequent in higher socio-economic sectors of the population. We did not assess if a disparity of a prescription translated into differences in the clinical outcome or co-morbidities over time. Such an issue should be considered in future studies.

Ideally, everybody should expect an identical standard of care. The aim of policy for equity is to reduce or eliminate those disparities, which are considered to be both avoidable and unfair.[4] There are some possible actions to reduce inequalities in healthcare provisions for psoriatic patients, including patient education and auditing of clinical decisions. Recently, the American Academy of Dermatology (AAD) created the Access to Dermatologic Care Task Force (ATDCTF) to foster the consciousness of dermatologists about the disparities affecting minority populations because of race or ethnicity, socioeconomic status, geography, gender, age and disability status and to cultivate policies that improve these people's access to dermatological services.[3] Similar actions should be implemented in other countries as well.

To summarise, we documented the inequalities in drug prescriptions for Ps in Italy with a trend towards a higher number of prescriptions for more expensive biologics in higher socio-economic sectors of the population. This is unfair considering that drugs are paid for by the money of the National Health System in which all Italian citizens contribute.

REFERENCES

1. Sauaia A, Dellavalle RP. Health Care Inequities: An Introduction for Dermatology Providers. *Dermatol Clin* 2009; **27**:103-7.
2. Smith GD, Morris JN, Shaw M. The independent inquiry into inequalities in health : Is welcome, but its recommendations are too cautious and vague. *BMJ* 1998; **317**:1465-6.
3. Buster KJ, Stevens EI, Elmets CA. Dermatologic Health Disparities. *Dermatol Clin* 2012; **30**:53-9.

4. Whitehead M. The concepts and principles of equity and health. *Int J Health Serv* 1992; **22**:429-45.
5. Takeshita J, Gelfand JM, Li P, Pinto L, Yu X, Rao P, Viswanathan HN, Doshi JA. Psoriasis in the US Medicare Population: Prevalence, Treatment, and Factors Associated with Biologic Use. *J Invest Dermatol* 2015; **135**:2955-63.
6. Kamangar F, Isip L, Bhutani T, et al. How psoriasis patients perceive, obtain, and use biologic agents: Survey from an academic medical center. J Dermatolog Treat. 2013; **24**:13-24.
7. Gisondi P, Cazzaniga S, Chimenti S, et al. Metabolic abnormalities associated with initiation of systemic treatment for psoriasis: evidence from the Italian Psocare Registry. *J Eur Acad Dermatol Venereol* 2013; **27**:e30-41.
8. The Italian Ministry of Health. Guide to the Italian National Health Service. Available at: http://www.salute.gov.it/portale/temi/p2_6.jsp?lingua=english&id=3879&area=healthcareUE&menu=vuoto (last accessed 12 September 2016).
9. Buscema M, Helgason C, Grossi E. Auto contractive maps, H function and maximally regular graph: theory and applications. Special Session on: Artificial Adaptive Systems in Medicine: applications in the real world. New York, NY: NAFIPS (IEEE), 2008.
10. Kruskal JB. On the shortest spanning subtree of a graph and the traveling salesman problem. *Proceedings Am Math Soc* 1956; **7**:48-50.
11. Horn EJ, Fox KM, Patel V, et al. Association of patient-reported psoriasis severity with income and employment. J Am Acad Dermatol. 2007; **57**:963-71.
12. Ghazi SR, Nawaz K, Shahzad S, et al. Relationship between Parents' Socio-Economic Status and their Children Academic Performance. *International Review of Social Sciences and Humanities* 2013; **5**:58-65.

13. Okioga CK. The Impact of Students' Socio-economic Background on Academic Performance in Universities, a Case of Students in Kisii University College. *American International Journal of Social Science* 2013; **2**:38-46.
14. France G, Taroni F, Donatini A. The Italian health-care system. *Health Econ* 2005; **14**:S187-202.
15. Mrowietz U, Kragballe K, Reich K, et al. Definition of treatment goals for moderate to severe psoriasis: a European consensus. *Arch Dermatol Res* 2001; **303**:1-10.
16. Marmot M, Friel S, Bell R, et al. Closing the gap in a generation: health equity through action on the social determinants of health. *Lancet* 2008; **372**:1661-9.
17. Spears CR, Nolan BV, O'Neill JL, et al. Recruiting underserved populations to dermatologic research: a systematic review. *Int J Dermatol* 2011; **50**:385-95.
18. Buster KJ, You Z, Fouad M, Elmets C. Skin cancer risk perceptions: A comparison across ethnicity, age, education, gender, and income. *J Am Acad Dermatol* 2012; **66**:771-9.
19. Coups EJ, Geller AC, Weinstock MA, et al. Prevalence and Correlates of Skin Cancer Screening among Middle-Aged and Older White Adults in the United States. *Am J Med* 2010; **123**:439-45.
20. Gloster HM, Neal K. Skin cancer in skin of color. *J Am Acad Dermatol* 2006; **55**:741-60.
21. Shaw TE, Currie GP, Koudelka CW, Simpson EL. Eczema Prevalence in the United States: Data from the 2003 National Survey of Children's Health. *J Invest Dermatol* 2011*;* **131**:67-73.
22. Horii KA, Simon SD, Liu DY, Sharma V. Atopic Dermatitis in Children in the United States, 1997–2004: Visit Trends, Patient and Provider Characteristics, and Prescribing Patterns. *Pediatrics* 2007; **120**:e527-34.

23. Linos E, Swetter SM, Cockburn MG, et al. Increasing burden of melanoma in the United States. *J Invest Dermatol* 2009; **129**:1666-74.

24. Geale K , Henriksson M , Schmitt-Egenolf M . Evaluating equality in psoriasis healthcare: a cohort study of the impact of age on prescription of biologics. *Br J Dermatol* 2016; **174**:579-87.

Figure - AutoCM map of selected variables at entry in the registry.

Legend: The map shows the association among the variables and can be divided into three regions: The first region at the top (dotted line) and the second region at the bottom (dashed line) show information connected to conventional and biological drug prescriptions at entry into the registry; the last region in the middle (dash-dotted line) captures other less relevant pieces of information, which are common to most of the patients included. A quantification of the strength of links among variables is also provided as an overlaid numerical coefficient ranging from zero, minimum strength, to 1, maximal strength.

Table 1 – Distribution of selected variables at entry in the Psocare registry and analyses of factors associated with biological drug prescription..

	Distribution N=12,838*	Univariate analysis		Multivariate analysis***	
	n (%)	Biologics n (%)	*P*-value**	OR (95% CI)	*P*-value
Age, yrs *(mean, SD)*	*48.8 (14.4)*				
18–29	1247 (9.7%)	428 (34.3%)	<0.001	1.12 (0.93–1.51)	0.17
30–44	3929 (30.6%)	1748 (44.5%)	(0.14)	1.34 (1.11–1.62)	0.002
45–59	4557 (35.5%)	2181 (47.9%)		1.33 (1.12–1.57)	0.001
≥ 60	3105 (24.2%)	1113 (35.8%)		1	
Gender					
Male	8454 (65.9%)	3626 (42.9%)	0.37		
Female	4384 (34.1%)	1844 (42.1%)			
BMI, kg/m^2 *(mean, SD)*	*27.0 (4.9)*				
<20.0	485 (4.0%)	186 (38.4%)	<0.001	1.00 (0.74–1.34)	0.99
20.0-24.9	3924 (32.2%)	1572 (40.1%)	(<0.001)	1	
25.0-29.9	5088 (41.7%)	2151 (42.3%)		1.15 (1.01–1.32)	0.03
≥30.0	2696 (22.1%)	1253 (46.5%)		1.27 (1.08–1.49)	0.004
Smoking habits					
No/Ex	7480 (59.8%)	3269 (43.7%)	<0.001	1.22 (1.09–1.38)	0.001
Yes	5018 (40.2%)	2019 (40.2%)		1	
Drinker					
No/Ex	7851 (64.3%)	3398 (43.3%)	0.001	1.16 (1.03–1.31)	0.02
Yes, regular	4365 (35.7%)	1753 (40.2%)		1	
Marital status					
Unmarried	2735 (21.6%)	1108 (40.5%)	0.03		
Married/common-law husband/wife	8964 (70.7%)	3878 (43.3%)			
Divorced	567 (4.5%)	247 (43.6%)			
Widowed	407 (3.2%)	158 (38.8%)			
Geographical area of Italy					
Northern	3999 (31.1%)	1342 (33.6%)	<0.001	1	
Central/Southern	8839 (68.9%)	4128 (46.7%)		2.42 (2.13–2.75)	<0.001

	Distribution N=12,838*	Univariate analysis		Multivariate analysis***	
	n (%)	Biologics n (%)	*P*-value**	OR (95% CI)	*P*-value
Educational attainment, yrs *(mean, SD)*	*10.3 (3.9)*				
0–5 (primary)	2023 (16.0%)	717 (35.4%)	<0.001	1	
6–8 (lower secondary)	4214 (33.3%)	1728 (41.0%)	(<0.001)	1.13 (0.94–1.35)	0.19
9–13 (upper secondary)	4926 (38.9%)	2217 (45.0%)		1.35 (1.12–1.62)	0.002
≥ 14 (higher)	1510 (11.9%)	729 (48.3%)		1.36 (1.07–1.72)	0.01
Present or last occupation					
Unskilled workers, farmers	1571 (12.4%)	575 (36.6%)	<0.001	1	
Employees, craftsmen, skilled workers	4115 (32.5%)	1773 (43.1%)		1.13 (0.93–1.36)	0.23
Managers, professionals	1111 (8.8%)	572 (51.5%)		1.40 (1.09–1.81)	0.01
Retired	3212 (25.3%)	1322 (41.2%)		0.90 (0.72–1.11)	0.31
Housewives, unemployed, students, other	2664 (21.0%)	1149 (43.1%)		1.10 (0.89–1.35)	0.38
Calendar year of visit					
2005–2006	5061 (39.4%)	2394 (47.3%)	<0.001	1	
2007	3333 (26.0%)	1253 (37.6%)	(<0.001)	0.84 (0.73–0.96)	0.01
2008	3073 (23.9%)	1198 (39.0%)		1.09 (0.93–1.27)	0.28
2009	1371 (10.7%)	625 (45.6%)		1.86 (1.52–2.27)	<0.001
PASI score *(mean, SD)*	*17.2 (10.5)*				
<10	1729 (18.8%)	642 (37.1%)	<0.001	1	
10–20	4946 (53.7%)	1828 (37.0%)	(<0.001)	1.23 (1.05–1.44)	0.01
> 20	2531 (27.5%)	1326 (52.4%)		1.94 (1.63–2.30)	<0.001
Patient's perceived severity, VAS *(mean, SD)*	*6.6 (2.6)*				
0–4	1899 (19.5%)	783 (41.2%)	<0.001	1	
5–7	3745 (38.5%)	1572 (42.0%)	(<0.001)	1.1 (0.9-1.4)	
8–10	4081 (42.0%)	1899 (46.5%)		1.1 (0.9-1.3)	
Disease duration, yrs *(mean, SD)*	*16.9 (13.0)*				
0–4	2341 (18.9%)	634 (27.1%)	<0.001		
5–14	3757 (30.4%)	1639 (43.6%)	(<0.001)		
15–29	4157 (33.6%)	2050 (49.3%)			

	Distribution N=12,838*	Univariate analysis		Multivariate analysis***	
	n (%)	Biologics n (%)	*P*-value**	OR (95% CI)	*P*-value
≥ 30	2117 (17.1%)	947 (44.7%)			
CCI *(mean, SD)*	*0.29 (0.78)*				
0	10812 (84.2%)	4593 (42.5%)	0.76		
1–2	1369 (10.7%)	596 (43.5%)			
> 2	657 (5.1%)	281 (42.8%)			
History of:					
Diabetes					
No	11946 (93.1%)	5074 (42.5%)	0.26		
Yes	892 (6.9%)	396 (44.4%)			
Arterial hypertension					
No	9706 (75.6%)	4015 (41.4%)	<0.001	1	
Yes	3132 (24.4%)	1455 (46.5%)		1.20 (1.03–1.38)	0.02
Hyperlipaemia					
No	11307 (88.1%)	4754 (42.0%)	<0.001		
Yes	1531 (11.9%)	716 (46.8%)			
Chronic liver diseases					
No	12404 (96.6%)	5264 (42.4%)	0.04		
Yes	434 (3.4%)	206 (47.5%)			
Neoplasms					
No	12620 (98.3%)	5426 (43.0%)	<0.001	4.09 (2.41–6.94)	<0.001
Yes	218 (1.7%)	44 (20.2%)		1	
Pustular Ps					
No	12469 (97.1%)	5361 (43.0%)	<0.001	1.78 (1.25–2.54)	0.001
Yes	369 (2.9%)	109 (29.5%)		1	
PsA					
No	9655 (75.2%)	3159 (32.7%)	<0.001	1	
Yes	3183 (24.8%)	2311 (72.6%)		4.52 (3.94–5.20)	<0.001
No. of previous systemic treatments for Ps *(mean, SD)*	*1.1 (1.2)*				

	Distribution N=12,838*	Univariate analysis		Multivariate analysis***	
	n (%)	Biologics n (%)	*P*-value**	OR (95% CI)	*P*-value
0	5442 (42.4%)	889 (16.3%)	<0.001	1	
1	3238 (25.2%)	1436 (44.3%)	(<0.001)	4.07 (3.53–4.68)	<0.001
2	2530 (19.7%)	1807 (71.4%)		12.46 (10.63–14.60)	<0.001
≥3	1628 (12.7%)	1338 (82.2%)		25.59 (20.73–31.58)	<0.001
Hospital admission for Ps in the last 5 yrs					
No	9030 (70.3%)	3321 (36.8%)	<0.001	1	
Yes	3808 (29.7%)	2149 (56.4%)		1.21 (1.06–1.37)	0.004
Previous clinical remission for Ps					
No	9246 (72.0%)	3708 (40.1%)	<0.001	1.18 (1.04–1.35)	0.01
Yes	3592 (28.0%)	1762 (49.1%)		1	

BMI: body mass index CCI: Charlson comorbidity index CI: confidence interval OR: odds ratio

PASI: psoriasis area severity index PsA: psoriatic arthritis

* Numbers may not add up to the total due to missing data.

** Pearson's χ^2 test. In the case of ordinal data, when the test was significant (p-value ≤ 0.05), a Cochran–Armitage test for linear trend across different levels of variables was also performed.

*** Independent factors selected in multiple logistic regression analysis with forward stepwise selection algorithm.

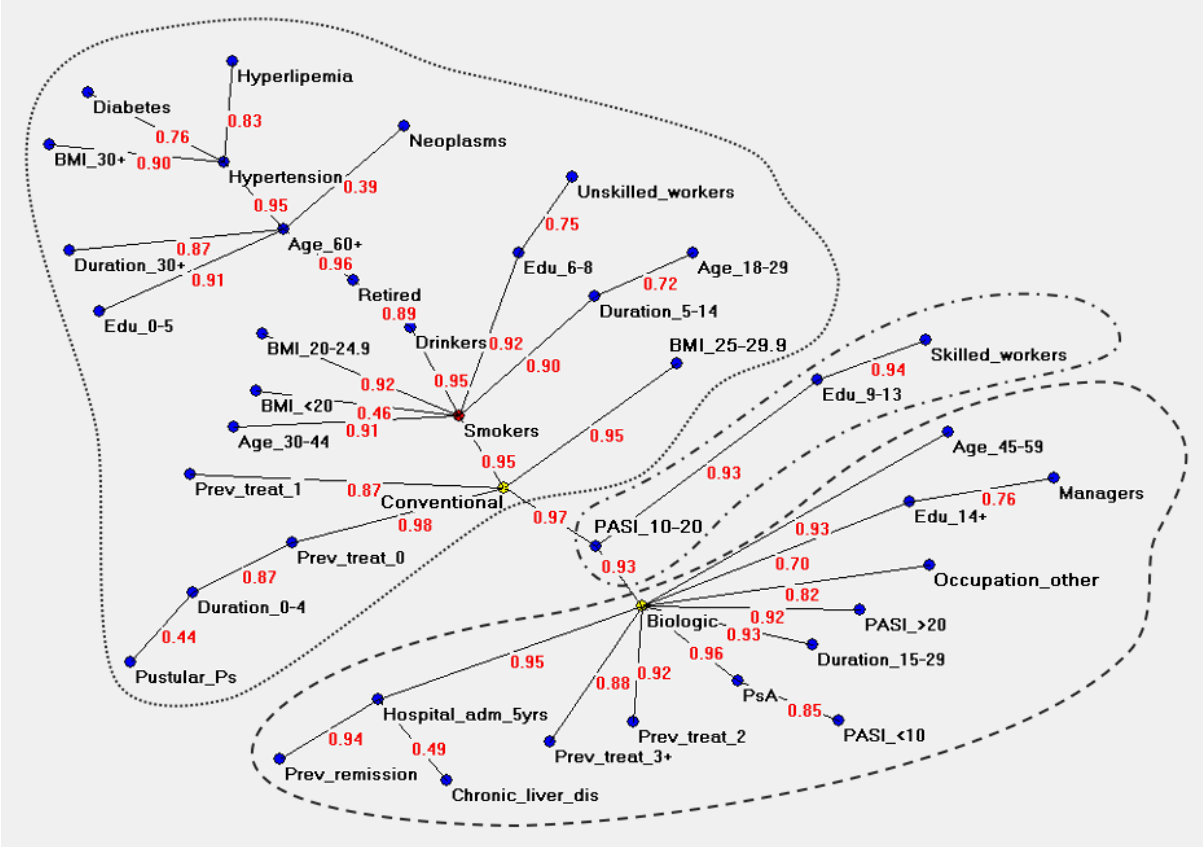
Table 2 – Univariate and multivariate adjusted analyses of association between educational attainment, employment status and severe Ps.

	Univariate analysis		Multivariate analysis**	
	PASI score > 20, N (%)	***P*-value***	**OR (95% CI)**	***P*-value**
Educational attainment, yrs				
0–5 (primary)	467 (31.5%)	< 0.001	1.55 (1.34 –1.79)	< 0.001
6–8 (lower secondary)	869 (28.6%)	(< 0.001)	1.21 (1.09–1.35)	0.001
9+ (upper secondary/university)	1125 (24.7%)		1	
Present or last occupation				
Unskilled workers, farmers	300 (26.5%)	< 0.001	1.02 (0.82–1.26)	0.86
Employees, craftsmen, skilled workers	707 (24.0%)		0.89 (0.74–1.06)	0.19
Managers, professionals	237 (29.3%)		1	
Retired	685 (30.1%)		1.19 (0.98–1.44)	0.07
Housewives, unemployed, students, other	532 (27.8%)		1.35 (1.11–1.66)	0.004

CI: confidence interval OR: odds ratio PASI: psoriasis area severity index

* Pearson's χ^2 test. In the case of ordinal data, when the test was significant (p-value ≤ 0.05), a Cochran–Armitage test for linear trend across different levels of variables was also performed.

** OR as resulted from multiple logistic regression analyses, including terms for age, gender, BMI and number of previous systemic treatments for Ps.



Appendix. The Italian Psocare Centres

U.O.C. Dermatologia e Venereologia Ospedale Generale Regionale F. Miulli, Acquaviva delle Fonti (V. Griseta, A. Miracapillo); S.O.C. Dermatologia SS. Antonio e Biagio e C. Arrigo, Alessandria (M. Azzini, L. Mocci, M. Michelini); U.O. Clinica Dermatologica, Ancona (A. Offidani, L. Bernardini, A. Campanati); U.O. Dermatologia INRCA/IRCCS, Ancona (G. Ricotti, A. Giacchetti); U.O. Dermatologia Ospedale Beauregard, Aosta (M. Norat, F. Gualco); U.O. Dermatologia Ospedale S. Donato, Arezzo (A. Castelli, A. Cuccia, A. Diana); S.O.C. Dermatologia Ospedale di Asti (G. Roncarolo); U.O. Dermatologia Ospedale S. G. Moscati, Avellino (M.A. Belli, M.A. Baldassarre); U.O.C. Dermatologia P.O. Cutroni Zodda, Barcellona (Me.) (G. Santoro); U.O. Dermatologia II Azienda Ospedaliera Policlinico Consorziale, Bari (G.A. Vena, F. Lo Console, R. Filotico, V. Mastrandrea); U.O. Dermatologica Ospedale di Battipaglia (B. Brunetti, F. Musumeci); U.O. di Dermosifilopatia Ospedale S. Martino, Belluno (E. Carrabba, P. Dal Mas, F. Annicchiarico, B. Benvegnù, G. Spaziani); U.O. Dermatologia Azienda Ospedaliera Rummo, Benevento (F. Cusano, S. Saletta Iannazzone); U.O. Dermatologia Ospedale S. Cuore di Gesù Fatebenefratelli, Benevento (A. Galluccio, M. Pezza); USC Dermatologia A.O. Ospedali Riuniti di Bergamo (L. Marchesi, G. Imberti, A. Reseghetti); U.O. Dermatologia Ospedale degli Infermi, Biella (C. Barbera); U.O. di Dermatologia Presidio Ospedaliero Bellaria Maggiore, Bologna (M. Reggiani, A. Lanzoni); U.O. Dermatologia Policlinico S. Orsola Malpighi, Bologna (A. Patrizi, F. Bardazzi, A. Antonucci, S. De Tommaso, R. Balestri); Divisione dermatologica Bolzano, Bolzano (W. Wallnofer, F. Ingannamorte); Divisione Dermatologica, Azienda Spedali Civili di Brescia (P. Calzavara-Pinton, S. Iannazzi, C. Zane, R. Capezzera, S. Bassisi, M.T. Rossi); U.O. complessa di Dermatologia P.O. Perrino, Brindisi (V. Altamura); U.O. Dermatologia Ospedale di Brunico (W. Vigl, C. Nobile); Clinica Dermatologica Università di Cagliari (N. Aste, S. Murgia, C. Mugheddu); U.O. Dermatologia A.O. Ospedale S. Elia, Caltanissetta (G. Scuderi, F. Baglieri, C. Di Dio); U.O. Dermatologia Ospedale B. Eustachio, Camerino (E. Cilioni Grilli); U.O. Dermatologia P.O. Cardarelli, Campobasso (C. Mastronardi, C.P. Agnusdei, A. Antrilli); S.O.C. Dermatologia Ospedale Casale Monferrato (L. Aulisa); U.O. Dermatologia A.O. San Sebastiano, Caserta (U. Raimondo, G. Scotto di Luzio, V.C. Battarra, P. Farro, R. Plaitano); Clinica Dermatologica, Università di Catania A.O. V. Emanuele, Catania (G. Micali, M.L. Musumeci, D. Massimino, M. Li Calzi); U.O. Dermatologia A.O. Garibaldi S. L. Currò A. Tomaselli, Catania (S. La Greca); U.O.C. di Dermatologica A.O. Universitaria V. Emanuele, Catania (M. Pettinato, G. Sapienza); U.O. Dermatolo gia A.O. Pugliese Ciaccio, Catanzaro (G. Valenti, P.F. De Giacomo, D. d'Amico); U.O. Dermatologia Ospedale di Cesena (F. Arcangeli, D. Brunelli, E. Ghetti); Clinica Dermatologica, Università di Chieti (A. Tulli, G. Assi, P. Amerio); U.S. Complessa di Dermosifilopatia Ospedale S. Anna, Como (G. Laria, F. Prestinari); U.O. Dermatologia P.O. Mariano Santo, Cosenza (S. Spadafora, M. Coppola); Istituti Ospitalieri di Cremona Servizio Ospedaliero di Dermatologia, Cremona (G. Caresana, E. Pezzarossa, E. Domaneschi, C. Felisi); U.O. Dermatologia P.O. Crotone (L. Donato); S.O.C. Dermatologia Ospedale Santa Croce e Carle, Cuneo (M. Bertero,

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