ORIGINAL ARTICLE

Body mass index in patients with moderate-to-severe psoriasis in Spain and its impact as an independent risk factor for therapy withdrawal: results of the Biobadaderm Registry

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Abstract

Background There are few data on the prevalence of obesity in the general psoriasis population and on the real impact of obesity on the management of psoriasis patients in the clinical setting.

Objectives To evaluate the prevalence of overweight and obesity in patients with moderate-to-severe psoriasis compared to the general population and to assess the relationship between Body Mass Index (BMI) and the risk of discontinuing treatment.

Methods Patients registered on Biobadaderm, a prospective registry, were grouped according the different categories of BMI and compared to the general Spanish population. Drug survival was analysed considering only drug withdrawal due to lack of effectiveness, remission and adverse events.

Results A total of 1162 moderate-to-severe psoriasis patients on systemic conventional or biological treatment were recruited. The prevalence of obesity was found to be significantly higher in psoriasis patients than in the general Spanish population ($P < 0.001$). In multivariate analysis a 5-unit increase in BMI, similar to a change in BMI category from normal weight to overweight and from overweight to obesity, was associated with a 12% increased risk of discontinuing therapy due to lack of effectiveness (HR 1.12, 95% CI: 1.01–1.24) and with a 17% increased risk of having an adverse event (HR 1.17, 95% CI: 1.02–1.36), both independently of the drug used.

Conclusions Patients with moderate-to-severe psoriasis had a higher prevalence of obesity than the general population. Increased BMI was associated with an increased risk of treatment discontinuation due to lack of effectiveness and a higher risk of adverse events.

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Conflicts of interest

Dr Carrascosa served as a consultant and participated in speakers' bureaus for Abbott Laboratories, Janssen Pharmaceuticals Inc, MSD, and Pfizer-Wyeth. Dr Garcia-Doval received a travel grant for a congress from Merck/Schering-Plough Pharmaceuticals. Dr Carretero served as a consultant for Abbott Laboratories, Janssen-Cilag Pty Limited, MSD,

and Pfizer Inc; gave expert testimony for Abbott Laboratories, MSD, and Pfizer Inc; received grants from Abbott Laboratories, Janssen Pharmaceuticals Inc, MSD, and Pfizer Inc and equipment from MSD and Pfizer Inc. Dr Vanaclocha participated in speakers' bureaus for Abbott Laboratories, Pfizer Inc, MSD, and Janssen Pharmaceuticals Inc. Dr Daudén served as a consultant for Abbott Laboratories, Amgen, Astellas, Celgene, Centocor Ortho Biotech Inc, Galderma, Glaxo, Jannsenn-Cilag, Leo Pharma, MSD, Novartis, and Pfizer Inc; received honoraria form Abbott Laboratories, Amgen, Celgene, Janssen-Cilag Pty Ltd, Leo Pharma, MSD, Novartis, and Pfizer Inc; participated in speakers' bureaus for Abbott Laboratories, Janssen Pharmaceuticals Inc, MSD, and Pfizer Inc; and received grants from Abbott Laboratories, Janssen Pharmaceuticals Inc, MSD, and Pfizer Inc. Dr Herrera-Ceballos served as a consultant and participated in speakers' bureaus for Abbott Laboratories, Janssen Pharmaceuticals Inc, MSD, and Pfizer-Wyett. Dr De la Cueva acted as a consultant for Janssen-Cilag, Abbott, MSD, Pfizer, Leo-Pharma and Novartis. Dr Belinchón acted as a consultant for Abbott Laboratories, Janssen Pharmaceuticals Inc, MSD, and Pfizer-Wyeth. Dr Sánchez-Carazo acted as a consultant for Abbott Laboratories, Janssen Pharmaceuticals Inc, MSD, and Pfizer-Wyeth. Dr Alsina gave expert testimony for Abbott Laboratories and Merck/Schering-Plough. Dr López-Estebaranz served as a consultant for Abbott Laboratories, Janssen Pharmaceuticals Inc, MSD, and Pfizer-Wyeth and participated in speakers' bureaus for Abbott Laboratories, Janssen Pharmaceuticals Inc, MSD, and Pfizer-Wyeth. Dr Ferrán acted as a consultant for Abbott Laboratories, Janssen Pharmaceuticals Inc, MSD, and Pfizer-Wyeth; participated in speakers' bureaus for Janssen Pharmaceuticals Inc and MSD; and received grants from Serono. Dr Rivera participated in speakers' bureaus for Abbott Laboratories, Janssen Pharmaceuticals Inc, MSD, and Pfizer-Wyeth. Dr Ferrandiz served as a consultant for Abbott Laboratories, Janssen Pharmaceuticals Inc, and Almirall SA; received honoraria from Abbott Laboratories, Almirall SA, Janssen Pharmaceuticals Inc, and Pfizer Inc; participated in a speaker's bureau for Abbott Laboratories, Almirall SA, and Janssen Pharmaceuticals Inc and received grants from Abbott Laboratories. The remaining authors declare no conflicts of interest.

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Introduction

Psoriasis is an inflammatory immune-mediated chronic skin disease that affects approximately 1–3% of the adult population.[1] Recent evidence suggests a relationship between psoriasis and risk factors for cardiovascular disease, including obesity and metabolic syndrome.[2,3]

Obesity is defined according to body mass index (BMI). People can be classified according to the BMI as being of normal weight (BMI < 25), overweight (BMI 25–29.9) and obese (BMI > 30).[4]

The relationship between psoriasis and obesity is not clear. Adipose tissue is considered as an active endocrine organ capable of releasing proinflammatory cytokines, which could explain the increased risk of psoriasis in obese patients.[5] Some authors, however, have suggested that psoriasis may promote obesity as a result of the patients' lifestyle (sedentary, alcohol, etc.). Whichever is true, obesity may condition the response to therapy.[6]

Biological therapy nowadays represents an undoubted improvement in the management of moderate-to-severe psoriasis, even when several conventional therapies have previously failed. However, the economic burden associated with biological therapy is extremely high.[7] Thus, it appears to be important to know if the higher prevalence of obesity in our psoriasis population might condition its effectiveness and safety and, in the same way, its costs.

Despite this debate, there are very few data on the prevalence of obesity in the general psoriasis population or on the impact on the management of obese psoriasis patients in the clinical setting.

Biobadaderm (The Spanish Registry of Adverse Events Associated with Biological Therapy in Dermatology) is a prospective registry of patients with psoriasis treated with systemic agents. The main objective of this registry was to assess the risk of adverse events related to biological therapy in patients with moderate-to-severe disease intended to be representative of real use of systemic drugs.[8]

Using Biobadaderm data, we designed a study with two objectives. The first was to evaluate the prevalence of overweight and obesity in Spanish patients with moderate-to-severe psoriasis compared to the general population. Secondly,

we aimed to assess the relationship between BMI and the risk of discontinuing treatment due to lack of effectiveness, clinical remission and adverse events (using treatment survival in obese patients as a proxy measure for effectiveness). We also wanted to test if the effect of increased BMI on these outcomes was similar in patients receiving biologics and classic systemic therapy.

Methods

Population

We used data from the Biobadaderm database. The BIOBADADERM registry (Spanish Registry of Adverse Events from Biological Therapy in Dermatological Diseases) began in 2008 and continues to this day. All patients registered up to November 2011 have been recruited in this study. In the 13 participating centres, all consecutive patients receiving treatment with biological drugs were included in the registry. It has a control arm consisting of moderate-to-severe psoriasis patients receiving conventional systemic drugs. This is a prospective inception cohort and its methodology has been previously described.[8] Less than 1% of the patients refused to participate. Quality control for Biobadaderm data include continuous online monitoring of all data and yearly *in situ* monitoring of a random sample.

The prevalence of overweight in the general population was obtained from National Statistics Institute (INE) data (2009 study data by age and gender.[8]) Analyses were restricted to subjects aged over 18.

Variables evaluated

BMI was calculated as weight in kilograms divided by subject height in metres squared, at the time of their entry into the Biobadaderm cohort. Three different categories were defined as follows: BMI < 25 (normal weight), BMI 25–29.9 (overweight) and BMI > 30 (obese). We compared the percentages of each group (normal weight, overweight and obese) with respect to the general Spanish population. Drug survival was analysed using the first cycle of treatment for each patient. First day of drug administration was considered as the starting date and last administration as the end of the therapy. Treatments were considered discontinued when at least two consecutive administrations were missed. Patients were followed up until the drug was withdrawn or they were censored.

As there may have been many different reasons for discontinuing the drug, analysis was restricted to withdrawals due to: (i) lack of effectiveness; (ii) remission; and (iii) adverse events leading to drug withdrawal. As no strict effectiveness criteria have been defined by Biobadaderm, lack of effectiveness was considered when effectiveness did not fulfil expectations of the physician and/or the patient after the induction therapy or was lost after an initial improvement. Discontinuation was considered to be due to an adverse event when this was stated by the treating physician.[8] Adverse events included in Biobadaderm are serious adverse events and other events that require withdrawal of treatment or non-scheduled medical care, including changes in the disease.[8]

Statistical analysis

We compared the prevalence of different categories of BMI (normal weight, overweight and obese) with data from the general Spanish population (chi-squared test) and the mean BMI of patients with psoriasis treated with conventional systemic drugs as well as each biological agent individually (Student's *t*-test). For each category of BMI, the incidence rate for the outcome was described. Different survival curves were compared by using the log-rank test, stratified by drugs, after checking that the curves did not cross each other. As there were some signs of confounding by drug, a log-rank test stratified by drug between BMI categories was used. Multivariate analysis was performed by Cox regression to minimize the effect of confounding variables and to check the effect of BMI adjusted for age and drugs. For the multivariate analysis, only the first cycle of treatment was included for each patient to avoid the effect of clustered measures by the patient. To evaluate possible confounding factors, the effect of BMI was considered before and after introducing them in the model, and the confounder was kept in the model if there was a change in the coefficient of BMI greater than 10%. Interaction was evaluated using likelihood ratio test of the models with and without the interaction term.

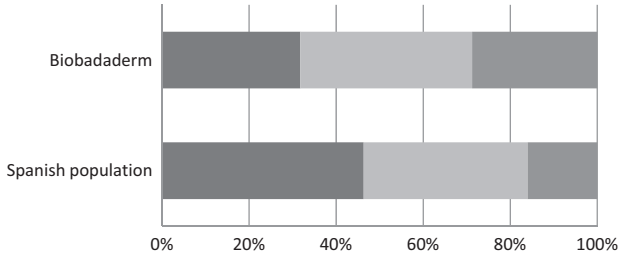
Results

Prevalence of overweight/obesity

A total of 1162 moderate-to-severe psoriasis patients on systemic conventional or biological treatment were recruited. Of these, 31.73% were of normal weight, 39.50% overweight and the remaining 28.74% classified as obese. The prevalence of obesity was found to be significantly higher in the psoriasis population (29%) than in the general Spanish population (16%) ($P < 0.001$)[9]. No differences were found regarding the prevalence of overweight (Fig. 1).[9]

Association between drugs and BMI

No significant differences were found when comparing the overall percentage of patients receiving biologics or conventional therapy for the different categories of BMI ($P = 0.58$). No differences were found in mean BMI between patients treated with biologics (mean BMI: 27.9) or conventional therapy (mean BMI: 27.8) (Student's *t*-test, $P = 0.29$). However, patients receiving infliximab (mean BMI: 29.1; $P = 0.006$), efalizumab (mean BMI: 28.9; $P = 0.02$) and ustekinumab (mean BMI: 28.8; $P = 0.02$) had a significantly higher BMI than patients on conventional systemic treatment (mean BMI 27.8).



	Spanish population	Biobadaderm
Normal	16347600	369
Overweight	13282300	459
Obesity	5645700	334

Figure 1 Comparisonbetweenpsoriaticpopulation (Biobadaderm) and general population (Instituto Nacional de Estadística)9.

Therapy survival

The most common cause for discontinuing biological therapy was lack of effectiveness (182 withdrawals per 1000 person-years), followed by remission (86 per 1000 person-years) and, less frequently, adverse events (54 per 1000 person-years). Rates of drug withdrawal for classic drugs were 128 per 1000 person-years due to lack of effectiveness, 160 per 1000 person-years due to remission and 105 per 1000 person-years due to adverse events. All differences in rates between classic therapy and biologics are statistically significant, but larger for discontinuation due to remission and adverse events (Table 1).

On univariate analysis discontinuation of therapy due to lack of effectiveness was statistically related to BMI for biologics (Table 1). A 5-unit increase in BMI was associated with a 14% increased risk of stopping therapy due to lack of effectiveness (RR 1.14, 95%CI: 0.99–1.31). Drug survival curves showed a trend (log-rank test, $P = 0.03$) to lower survival the higher the BMI category (log-rank test for trend, $P = 0.04$). We could not detect a crude effect of BMI on patients receiving classic systemic therapy.

On univariate analysis discontinuation of therapy due to remission was not related to BMI (Table 2).

A crude association was also found between the risk of adverse events conditioning the maintenance of treatment (drug survival) and BMI for biologics (Table 3). As described above, every 5-unit increase in BMI (i.e a change similar to that associated with BMI category change from normal weight to overweight and from overweight to obese) was associated with a crude 41% increased risk of having an adverse event (AE) as defined in Biobadaderm (RR 1.41, 95%CI: 1.09–1.81) (Table 3). There were also significant differences at the limit of statistical significance in the survival curves of the drug (log-rank test, $P = 0.05$) with a trend to lower survival, the higher the BMI category (log-rank test for trend, $P = 0.018$). There was no detectable crude effect of BMI in the risk of adverse events on patients receiving classic systemic therapy (RR1.12, 95%CI 0.88-1.43).

Multivariate analysis

A multivariate analysis was performed to discard the effect of some confounding factors, particularly the drug chosen. The results of the multivariate analysis models are shown in Table 4.

After adjustment for the drug used, the hazard related to withdrawal for remission was not associated with BMI. In contrast, a 5-unit increase in BMI was associated with an increase in 12% in the hazard of discontinuation due to lack of effectiveness and a 17% increase in the hazard of discontinuation due to

Table 1 Discontinuation of the drug due to lack of effectiveness. Univariate analysis. First cycle of therapy for every patient

Category	Number of treatment cycles	Withdrawals due to lack of effectiveness	Patient-years	Rate of withdrawals due to lack of effectiveness		Survival of the drug up to lack of effectiveness	
				Incidence rate (1000 person-years)	RR associated with a 5-unit increase in BMI (95%CI)	Log-Rank Test of differences in survival (*P* value)	Log-Rank Test for trend associated with ordered BMI group (*P* value)
Biologics							
All patients with biologic therapy	626	180	987	182			
Normal weight	202	56	343	163	1.14 (0.99-1.31)*	**0.03***	**0.04***
Over-weight	239	59	383	154			
Obese	185	65	261	249			
Classic systemic drugs							
All patients with classic systemic therapy	536	86	674	128			
Normal weight	167	23	206	111	0.99 (0.90-1.39)	0.30	0.14
Overweight	220	34	280	121			
Obese	149	29	187	154			

*Stratified by drug

Table 2 Discontinuation of the drug due to remission. Univariate analysis. First cycle of therapy for every patient

Category	Number of treatment cycles	Withdrawals due to remission	Patient-years	Rate of drug withdrawal due to remission		Survival of the drug up to the remission	
				Incidence rate (1000 person-years)	RR associated with a 5-unit increase in BMI (95%CI)	Log-Rank test of differences of survival (*P* value)	Log-Rank Test for trend associated with ordered BMI group (*P* value)
Biologics							
All patients with biologic therapy	626	85	987	86			
Normal weight	202	25	343	72	1.13 (0.93-1.40)*	0.23*	0.99*
Overweight	239	41	383	107			
Obese	185	19	261	72			
Classic systemic therapy							
All patients with classic systemic therapy	536	108	674	160			
Normal weight	167	39	206	189	0.97 (0.80-1.19)	0.60	0.45
Overweight	220	41	280	146			
Obese	149	28	187	149			

*Stratified by drug

d. se- u- ug r- d- d- he t- t- of ct fe- ef- ng i- d- n- n- u- o- f- n- o- c- he t- of tly n- e- d- n- e- p- e- d- n- i- ts, n- e- e- v- e- se er- v- d- a-

Table 3 Discontinuations due to adverse events (AE). Univariate analysis. First cycle of therapy for every patient

Category	Number of treatment cycles	Withdrawals due to adverse events	Patient-years	Rate of withdrawals due to adverse events		Drug survival up to adverse events	
				Rate (per 1000 person-years)	RR associated with 5-unit increase in BMI (95%CI)	Log-Rank test of differences in survival (*P* value)	Log-Rank Test for trend associated with ordered BMI group (*P* value)
Biologics							
All patients on biologic therapy	626	53	987	54			
Normal weight	202	12	343	35	**1.41(1.09-1.81)***	0.05*	**0.018***
Overweight	239	20	383	52			
Obese	185	21	261	80			
Classic systemic therapy							
All patients with classic systemic therapy	536	71	674	105			
Normal weight	167	18	206	87	1.12 (0.88-1.43)	0.45	0.57
Overweight	220	34	280	121			
Obese	149	19	187	101			

*Stratified by drug

T- he asso- cia- tion fou- nd in in the the uni- vari- ate analy- yses bet- ween BMI and risk of with- dra- wal was as a resu- lt of AE was part- ly due to con- fou- nd- ing by drug used. Wh- en the drug was used in the mo- del, the incl- uded

Table 4 Multivariate analysis. First cycle of therapy for each patient

	Hazard ratio per 5 BMI units in all patients (95% CI)	Likelihood ratio test for interaction between BMI and therapy group (biologics/classic therapy), *P* value†
Discontinuation due to lack of effectiveness	**1.12 (1.01–1.24)**	0.75
Discontinuation due to remission	1.05 (0.92–1.20)*	0.19
Discontinuation due to adverse event	**1.17 (1.02–1.36)***	0.30

*Adjusted for drug.

†This *P* value tests the hypothesis of a different effect of BMI in both therapy groups (classic drugs and biologics). As none is significant, we did not detect a different effect of BMI in therapy groups, and we can use the result in all patients as the most appropriate hazard ratio.

effect of BMI decreased (a 5-unit increase in BMI increased the hazard ratio by 41% in the univariate analysis, but after adjusting for age in the multivariate analysis, the increased risk was only 17%).

All tests for drug group-BMI interaction were not significant, meaning that we could not detect a difference in the effect of BMI between patients receiving biologics and classic drugs.

Discussion

In this prospective study, we observed that Spanish patients with moderate-to-severe psoriasis had a higher prevalence of obesity than the general Spanish population despite similarity in the prevalence of overweight. In addition, increased BMI was associated with an increased risk of treatment discontinuation due to lack of effectiveness and a higher risk of adverse events, also affecting survival of the drug.

Biobadaderm is a prospective and presumably representative registry of the psoriasis population being treated with systemic therapy in Spain.[8] Participating centres are distributed all over Spain and recruit patients from their own area. Data such as height and weight are routinely registered at the beginning of the study when the patient is enrolled in the registry. Thus, weight cannot be primarily conditioned by the therapy of choice. However, as patients may be drug-naïve or may come from switching to another therapy, effects from previous therapy on weight cannot be ruled out. According to the results of our study, one in every three moderate-to-severe psoriasis patients was obese, with a prevalence almost twice that expected with respect to the general population (INE)[9], in coherence with other epidemiological studies.[10]

The association between psoriasis and obesity has been reported in different population-based studies. Lindegård first described this association in a study of 159 200 Swedish citizens over a 10-year period.[11] Obesity was one of the multiple independent associations with psoriasis found by Neimann *et al.* in a population of 120 000 individuals with mild and severe psoriasis.[12] In a recent review and meta-analysis of observational studies, Amstrong *et al.* found the pooled odds ratio (OR) for obesity among patients with psoriasis to be 1.66 (95% confidence interval (CI) 1.46–1.89) compared with those without psoriasis, after evaluating 16 observational studies with a total of 2.1 million study participants including 201831 patients with psoriasis-[13]

Overweight and obesity have also been found to have a higher prevalence in patients with psoriasis by different authors.[14] An increasing number of studies have been recently published lighting the rationale of the link between psoriasis and obesity.[15–17]

The second main objective of our work was to evaluate the impact of overweight/obesity in the risk of discontinuing the therapy.

There are several reasons underlying the discontinuation of a therapy in the clinical setting. Gianecki *et al.* found loss of efficacy to be the main reason for discontinuing biological treatments, followed by adverse events.[18]. Consistently, in our series, lack of effectiveness was the most common cause for withdrawal of biologics, followed by remission and adverse events. Regarding classic systemic therapy, remission was the most common cause of withdrawal, followed by lack of effectiveness and adverse events. These data might reflect differences in the profile of the patients treated with each type of drug in terms of severity, other patient characteristics associated with therapy selection or even discrepancy regarding the expected results with the drug used. However, these differences have been taken into account in multivariable analysis adjusted for drug used, and its results show an increased risk of therapy withdrawal due to lack of effectiveness in all types of therapy.

After controlling for the confounding effects that affect the crude rates, and with the increased power associated with multivariate analysis, we have shown that a 5-unit increase in BMI (similar to a change in BMI category from normal weight to overweight and from overweight to obesity) was associated with a 12% increased risk of discontinuing therapy due to lack of effectiveness (HR 1.12, 95% CI: 1.01–1.24) and with a 17% increased risk of having an adverse event (HR 1.17, 95% CI: 1.02–1.36), both independently of the drug used. We did not find a difference in these effects between patients on classic and biological therapy.

There is increasing evidence to suggest that bodyweight and body mass index may influence the outcome of short-term ther-

apy in patients with moderate-to-severe psoriasis. Naldi found Psoriasis Area Severity Index (PASI) 75 response rate in a cohort of psoriatic patients treated with systemic therapy to be reduced in obese patients compared to those with normal weight, both in systemic conventional or biologic therapy.[19]

There appears to be at least two main reasons for obese patients to respond less or easily lose efficacy with time. One of them is the impact of weight on pharmacokinetics, which has been found to be a main factor conditioning drug clearance, which may also reduce the drug′s availability and could have a potential impact in the clinical outcome.[20]

The feasibility of adjusting some biological drugs to weight may explain why infliximab and ustekinumab were more frequently considered by dermatologists as the first drug of choice for obese patients in our series.

Moreover, the proinflammatory cytokines released from abdominal fat are thought to compete with those from psoriasis skin, reducing the drug molecules available for neutralizing skin inflammation.[21]

Interestingly, Naldi *et al.* found that patients with BMI > 30 had a response rate (PASI-75) about 30% lower than the rate observed in lighter people, both in classic and biologic therapy. Thus, interactions due to co-occurrence of obesity and psoriasis could influence the prospects of response of any therapy independently of its mechanism of action.

Higher weight was also associated with an increased risk of developing adverse events conditioning the discontinuation of the therapy, both for classic drugs and biologics, although the crude results were non-significant for classic drugs, probably as a result of lower statistical power and confounding. An increased number of adverse events does not necessarily mean that they could be attributable to the therapy, but to the obesity itself. Thus, the relationship between obesity and discontinuation due to adverse events could be explained by the fact that obesity has been considered as a risk factor for infections, cancer or cardiovascular diseases, and may be other causes of drug discontinuation.[22]

More difficult to assess is discontinuation due to remission, as this concept has not been standardized. However, we were not able to find any relationship between discontinuation due to remission and the different categories of BMI.

Of course, our study had to deal with limitations. The assessment of the reasons for discontinuation is subject to a degree of subjectivity that could lead to measurement bias. Although reference measurement parameters, e.g. PASI, body surface area, psoriasis global assesment, are commonly used to evaluate efficacy, a significant heterogeneity between centres can be expected in relation to the patient profile and physician experience. However, all doctors participating in Biobadaderm belong to the Spanish Academy of Dermatology and Venereology Psoriasis Group, in which guidelines define efficacy as PASI 75 at the end of the induction period established for each drug.[23] This bias is unlikely to exert any effect on adverse events, as objective criteria, reinforced by training participants, were used in Biobadaderm.[24]

It is also possible that the associations found were influenced by the effect of confounding variables like the drug used, the age when the patient was recruited or baseline differences that are likely to be more pronounced between patients on classic therapy and biologics. In fact, higher rates of remission and adverse events have been found in patients on classic therapy. However, we have controlled for the effect of these potential confounders using stratification and multivariate analysis. The drug used (or factors associated with drug selection) produced confounding and had to be kept in some of the final models, but after multivariable analysis, the independent effect of BMI remained.

We can conclude that obesity in the moderate-to-severe psoriasis population should be a priority target in the management of the disease, as it is very prevalent and is associated with a worsened therapeutic outcome. On one hand, patients with moderate-to-severe psoriasis in our area have a significantly higher prevalence of obesity than the average for the general population. On the other, the increased prevalence of obesity in these patients will not only have a potentially negative impact on the course of their skin disease and general health, but may also influence the therapeutic outcome.

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References

1 Ferrándiz C, Bordas X, García-Patos V *et al.* Prevalence of psoriasis in Spain (Epiderma Project: phase I). *J Eur Acad Dermatol Venereol* 2001; **15**: 20–23.
2 Sterry W, Strober BE, Menter A. International Psoriasis Council. Obesity in psoriasis: the metabolic, clinical and therapeutic implications. Report of an interdisciplinary conference and review. *Br J Dermatol* 2007; **157**: 649–655.
3 Naldi L, Chatenoud L, Linder D *et al.* Cigarette smoking, body mass index, and stressful life events as risk factors for psoriasis: results from an Italian case-control study. *J Invest Dermatol* 2005; **125**: 61–67.
4 WHO. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. WHO Technical Report Series 854. Geneva: World Health Organization [WWW document] 1995. URL: http://whqlibdoc.who.int/trs/WHO TRS 854.pdf (last accessed: January 2013).
5 Ronti T, Lupattelli G, Mannarino E. The endocrine function of adipose tissue: an update. *Clin Endocrinol (Oxf)* 2006; **64**: 355–365.

6 Setty AR, Curhan G, Choi HK. Obesity, waist circumference, weight change, and the risk of psoriasis in women: Nurses Health Study II. *Arch Intern Med* 2007; **167**: 1670–1675.
7 Ferrándiz C, García A, Blasco AJ *et al.* Cost-efficacy of adalimumab, etanercept, infliximab and ustekinumab for moderate-to-severe plaque psoriasis. *J Eur Acad Dermatol Venereol* 2012; **26**: 768–777.
8 Rivera R, García-Doval I, Carretero G *et al.* miembros del grupo BIOBADADERM. BIOBADADERM, the Spanish Registry of Adverse Events Associated with Biological Drugs in Dermatology: first report. *Actas Dermosifiliogr* 2011; **102**: 132–141.
9 National Health Survey (Encuesta nacional de salud). Instituto Nacional de Estadística URL: http://www.ine.es/jaxi/menu.do?type=pcaxis&path=%2Ft15%2Fp419&file=inebase&L=0 (last accessed: January 2013).
10 Aranceta J, Pérez Rodrigo C, Foz Sala M et al. Grupo Colaborativo para el estudio DORICA fase 2. Tables of coronary risk evaluation adapted to the Spanish population: the DORICA study. *Med Clin (Barc)* 2004; **123**:686–691.
11 Lindegård B. Diseases associated with psoriasis in a general population of 159,200 middle-aged, urban, native Swedes. *Dermatologica* 1986; **172**: 298–304.
12 Neimann AL, Shin DB, Wang X *et al.* Prevalence of cardiovascular risk factors in patients with psoriasis. *J Am Acad Dermatol* 2006; **55**: 829–835.
13 Armstrong AW, Harskamp CT, Armstrong EJ. The association between psoriasis and obesity: a systematic review and meta-analysis of observational studies. *Nutr Diabetes* 2012 Dec; **3**(2): e54. doi:10.1038/nutd.2012.26.
14 Puig L. Obesity and psoriasis: body weight and body mass index influence the response to biological treatment. *J Eur Acad Dermatol Venereol* 2011; **25**: 1007–1011.
15 Johnston A, Arnadottir S, Gudjonsson JE *et al.* Obesity in psoriasis: leptin and resistin as mediators of cutaneous inflammation. *Br J Dermatol* 2008; **159**: 342–350.
16 Gerdes S, Rostami-Yazdi M, Mrowietz U. Adipokines and psoriasis. *Exp Dermatol* 2011; **20**: 81–87.
17 Hayes J, Koo J. Psoriasis: depression, anxiety, smoking, and drinking habits. *Dermatol Ther* 2010; **23**: 174–180.
18 Gniadecki R, Kragballe K, Dam TN *et al.* Comparison of drug survival rates for adalimumab, etanercept and infliximab in patients with psoriasis vulgaris. *Br J Dermatol* 2011; **164**: 1091–1096.
19 Naldi L, Addis A, Chimenti S *et al.* Impact of body mass index and obesity on clinical response to systemic treatment for psoriasis. Evidence from the Psocare project. *Dermatology* 2008; **217**: 365–373.
20 Zhu Y, Hu C, Lu M *et al.* Population pharmacokinetic modeling of ustekinumab, a human monoclonal antibody targeting IL-12/23p40, in patients with moderate to severe plaque psoriasis. *J Clin Pharmacol* 2009; **49**: 162–175.
21 Romaní J, Caixàs A, Carrascosa JM *et al.* Effect of narrowband ultraviolet B therapy on inflammatory markers and body fat composition in moderate to severe psoriasis. *Br J Dermatol* 2012; **166**: 1237–1244.
22 Loef M, Walach H. The combined effects of healthy lifestyle behaviors on all cause mortality: A systematic review and meta-analysis. *Prev Med* 2012; **55**: 163–170.
23 Puig L, Carrascosa JM. Daudén E et al Grupo Español de Psoriasis de la Academia Española de Dermatología y Venereología. Spanish evidence-based guidelines on the treatment of moderate-to-severe psoriasis with biologic agents. *Actas Dermosifiliogr* 2009; **100**: 386–413.
24 Garcia-Doval I, Carretero G, Vanaclocha F *et al.* Risk of serious adverse events associated with biologic and non-biologic psoriasis systemic therapy: patients ineligible vs eligible for randomized controlled trials. *Arch Dermatol* 2012; **148**: 463–470.

