

# Long-Term Cost-Effectiveness Analysis of Etanercept and Adalimumab for Plaque Psoriasis not Associated with Arthritis

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## ABSTRACT

**Introduction:** Pharmacoeconomic studies examining the cost-effectiveness of biological agents to treat moderate-to-severe psoriasis in real-life clinical practice are scarce. The aim of this study was to assess the efficiency, in terms of incremental cost-effectiveness, of etanercept and adalimumab in a real clinical setting.

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**Methods:** Direct and indirect costs were assessed from a Spanish societal perspective in a historical hospital cohort of patients with moderate-to-severe psoriasis attending a tertiary referral hospital over a 1-year period. The data examined included drug-related variables, use of health-care resources, transportation and work productivity losses. Effectiveness was measured as the proportion of patients achieving a reduction of at least 75% with respect to the baseline value for the Psoriasis Area Severity Index (PASI 75) during the first 52 weeks of treatment.

**Results:** No statistically significant differences in effectiveness between etanercept ( $n = 135$ ) and adalimumab ( $n = 48$ ) were found (PASI 75 80% vs. 85.7%; RR = 1.07 [0.90, 1.27]; RRA = 5.7 [−8.9, 20.2];  $p = 0.943$ ). There were no significant differences in total cost per patient with etanercept as compared to adalimumab ( $14,843.73 \pm 6,178.98$  € vs.  $15,405.91 \pm 9,106.50$  €;  $p = 0.768$ ).

**Conclusion:** Under conditions of daily clinical practice in our hospital, total health-care costs associated with the treatment of moderate-to-severe psoriasis with etanercept appear to be equivalent to those with adalimumab in the first year of treatment.

**Keywords:** Adalimumab; Etanercept;  
Moderate-to-severe psoriasis;  
Pharmacoeconomic analysis

## INTRODUCTION

Psoriasis is a highly morbid inflammatory disease of variable duration, extent and severity that involves skin and/or joints and which may affect patients' quality of life [1]. Biological drugs such as etanercept and adalimumab have considerably changed the therapeutic approach to this disease and enabled clinical control of a high proportion of patients [2, 3]. However, the substantial economic impact of these therapies on the national health system budget is a potential hindrance to their widespread use. The few cost-effectiveness studies of biological therapies for psoriasis conducted to date have relied largely on clinical trials and have led to similar safety and efficiency results. Most of these studies involved incremental cost-effectiveness analyses of efficacy data obtained from clinical trials and adapted these to the social and economic peculiarities of the national health systems in the USA, Spain, Great Britain, Italy, Switzerland or Sweden, for example [4–10]. Thus, decision tree or hidden Markov models and Monte Carlo simulations were used to assess the cost-effectiveness of drugs such as infliximab [4–8, 10], etanercept [4–10], adalimumab [4–10], efalizumab [4, 6, 7], alefacept [8] and ustekinumab [7]. These studies measured effectiveness as the proportion of patients achieving a reduction of at least 75% with respect to the baseline value for the Psoriasis Area Severity Index (PASI 75) after 12 weeks [4–8, 10], and additionally, after 24 or 48 weeks in some studies [6, 9] with a few studies also linking the results to quality of life

[5, 9, 10]. However, all the studies that assessed the sensitivity of their incremental cost-effectiveness estimates revealed an overlap between the studied drugs [4–7, 11]. This is interesting as it reveals that effectiveness predictions from simulated data lead to similar results for different biological agents.

However, when trying to extrapolate such results into clinical practice, several factors need to be taken into consideration. For instance, clinical trials do not compare therapeutic choices, but rather individual drugs against a placebo. Also, most clinical trials comprise too short time periods to be representative of a disease, such as psoriasis, which has a chronic course that requires long-term treatment and where events occur that are usually not considered in these studies (e.g. suspension of the treatment after a period of sustained efficacy, dose elevations in response to recurrence, or withdrawal due to a lack or loss of efficacy or an adverse reaction). Moreover, the drugs used in clinical trials are administered in strict accordance with the recommendations in their technical sheets, but in clinical practice, there is evidence that physicians tend to manage patients using non-standard dosing patterns, intermediate doses, varying treatment interruption periods and increasing doses based on their own clinical judgement to achieve the therapeutic goal [12]. Based on this, we considered that observational studies providing a more accurate view of the use of biological drugs in clinical practice were required to test the hypothesis that etanercept and adalimumab exhibited no statistically significant differences in long-term cost-effectiveness for the treatment of moderate-to-severe psoriasis in patients naïve to biological treatments [13]. This led us to assess the incremental cost-effectiveness of these drugs as first-choice biological treatments for moderate-

to-severe plaque-type psoriasis using clinical practice data recorded at a reference hospital.

## MATERIALS AND METHODS

### Population and Design

#### *Design*

This was a retrospective, observational, single-centre, pharmacoeconomic study designed to compare the cost-effectiveness of etanercept and adalimumab as first-choice biological therapies in a historical cohort of patients with moderate-to-severe psoriasis. Demographic and clinical information was obtained from patients' clinical histories, accessed via the report manager of the Reina Sofía University Hospital.

#### *Selection Criteria*

Selected patients were caucasian subjects of both sexes, aged 18–75 years and diagnosed with moderate-to-severe plaque-type psoriasis (PASI >10%, Dermatology Life Quality Index >10 and/or body surface area >10%) at least 1 year prior to the commencement of data collection; patients starting etanercept or adalimumab as first biological therapy over the period 2005–2010 and remaining on etanercept for at least 12 weeks and on adalimumab for 16 weeks. Exclusion criteria included the presence of other psoriasis varieties (guttata, inverse, unguet, pustular, erythrodermic) or psoriatic arthritis diagnosed by a rheumatology specialist before or during the study period.

#### *Data Sources*

Treatment effectiveness and regime information was obtained from the patients' digital clinical histories. The cost considered for each drug was the laboratory sale price stated in the Spanish

Catalogue of Pharmaceutical Specialities plus value-added tax [14]. Unit costs per specialist visit, stay costs for the different medical services and day hospital admission costs were obtained from the Reina Sofía University Hospital's economic management database. Diagnostic test costs were obtained from *Boletín Oficial de la Junta de Andalucía (BOJA)*, no. 217, dated 27 October 2005, which was in use by the Hospital Economic Unit at the time of the study to estimate such costs [15]. Work loss times and costs were calculated from the average annual gross salary published by Eurostat to estimate the average salary per worked hour on the assumption of a 40-h working week [16]. Productivity loss costs were calculated in terms of the time spent in transportation and health care in the hospital; an average time of 3.5 h per patient per visit was used for both outpatient visits and day hospital stays. Direct non-health costs incurred in relation to transportation from patients' homes to and from the hospital for each visit were estimated from the average between a taxi fare (lowest minimum fare plus a 1-km ride) and the urban bus fare when the transfer took place in the city, and the average cost of a 1-km ride in a medium-range car when the patient came from a different location [17–19].

The time spent undergoing supplementary tests was not considered since many were performed at health centres near the patients' homes. Also not considered were the time and costs associated with the administration of the drugs, since these were assumed to be essentially identical for both etanercept and adalimumab.

#### *Effectiveness*

Treatment effectiveness was measured as PASI 75, the main parameter of choice for assessing

effectiveness in most clinical trials. Both absolute and incremental effectiveness were determined.

### Costs

Cost analyses included direct costs (drug, health-care resources, transportation) and indirect costs (productivity losses). Total associated costs were calculated by multiplying resource use by the corresponding unit cost. All costs are shown in euros (€) and updated to July 2012.

### *Economic Evaluation Method*

The time frame of the analysis was 1 year. The study was conducted from a Spanish social perspective, which was judged to be the most complete format, as it considered both direct and indirect costs and included a social impact. In this respect, the study departed from the usual, funder's approach.

### Regimes and Monitoring

Incremental cost-effectiveness during the first 52 weeks of treatment was examined. Etanercept for adult treatment is available in subcutaneously administered 25 and 50 mg doses. The recommended dose is usually 25 mg twice a week or 50 mg once a week or, optionally, 50 mg twice a week [20]. The recommended dose for adalimumab is 40 mg administered subcutaneously every second week, starting 1 week after the initial dose [21]. The dose, dosing interval and duration of the treatment regimen for each drug until its indefinite suspension were recorded. Costs associated with adverse reactions were excluded.

### Statistical Analysis

The statistical methods used to describe centrality and dispersion of the data were the

relative frequency (absolute frequency), followed by the minimum and maximum value for categorical variables and the arithmetic mean  $\pm$  standard deviation for quantitative variables. Statistically significant differences between the two treatments were established with the Chi-squared test for categorical variables and the Kruskal–Wallis test for quantitative variables. All computations were performed using different packages of the 'R' statistical software system [22].

## RESULTS

### Demographics and Patient Characteristics

We examined the clinical histories of 1,998 patients with plaque-type psoriasis who visited the Dermatology Service of the Reina Sofía University Hospital over the period 2005–2010. A total of 183 patients starting etanercept ( $n = 135$ ) or adalimumab ( $n = 48$ ) as first-choice biological treatment during this period and complying with the inclusion criteria were selected for the study. The demographics and clinical characteristics of the patients are summarized in Table 1. There were no statistically significant differences between the two drug groups in most of the parameters. The only differences observed were in the frequencies of allergic rhinitis and asthmatic bronchitis (both  $P < 0.001$ , respectively). All other characteristics were similar in both treatment groups; therefore we deemed these differences to be irrelevant when interpreting the results. During the first year, there were 14 dropouts (3: lack of adherence; 7: loss of efficacy; 4 adverse events). Only in four patients (3 in the etanercept group and 1 in the adalimumab group) was the drug withdrawn due to adverse reactions, but the adverse events

**Table 1** Baseline characteristics of the patients in each treatment group

	Etanercept ( <i>n</i> = 135)	Adalimumab ( <i>n</i> = 48)	<i>P</i> value*
Demographic characteristics			
Age (years)	45 (19–78)	42 (18–73)	n.s.
Gender (male/female)	99/52	35/13	n.s.
Body weight (kg)	79 ± 17	82 ± 16	n.s.
Height (cm)	168 ± 8	170 ± 11	n.s.
BMI (kg/m <sup>2</sup> )	28.1 ± 4.5	29.2 ± 9	n.s.
Duration of psoriasis (years)	13.7 (1–59)	15.4 (1–34)	n.s.
Concomitant treatment			
Methotrexate	1 (0.6%)	2 (4.1%)	n.s.
Acitretin	0 (0%)	1 (2%)	n.s.
Ciclosporin	0 (0%)	0 (0%)	n.s.
Phototherapy	0 (0%)	2 (4.1%)	n.s.
Comorbidity			
Smoker/ex-smoker/ non-smoker	8/4/124	6/2/40	n.s.
Hypertension	22 (16.2%)	10 (21%)	n.s.
Diabetes	13 (9.6%)	6 (12.5%)	n.s.
Obesity	43 (32%)	13 (27%)	n.s.
Hyperlipidaemia	13 (9.6%)	6 (12.5%)	n.s.
Cardiovascular disease	7 (5.1%)	3 (7.1%)	n.s.
Chronic renal insufficiency	1 (0.7%)	0 (0%)	n.s.
Epilepsy	1 (0.7%)	0 (0%)	n.s.
Hiatus hernia/ gastroduodenal ulcer	4 (2.8%)	0 (0%)	n.s.
Liver steatosis/chronic liver disease	3 (2.2%)	3 (7.1%)	n.s.
Ulcerous colitis/Crohn's disease	0 (0%)	2 (4.1%)	n.s.
Atrophic chronic ulcer/ pernicious anaemia	2 (1.4%)	0 (0%)	n.s.
Anxiety/depression or schizophrenia	8 (5.9%)	2 (4.1%)	n.s.
Allergic rhinitis/asthmatic bronchitis	11 (8.1%)	0 (0%)	<0.001
Apnoea syndrome/sleep hypopnoea	1 (0.7%)	2 (4.1%)	n.s.
Chronic obstructive pulmonary disease	3 (2.2%)	2 (4.1%)	n.s.
Gout/hyperuricaemia	3 (2.2%)	0 (0%)	n.s.
Hypothyroidism	5 (3.7%)	0 (0%)	n.s.
Glaucoma	1 (0.7%)	0 (0%)	n.s.
Prostatic adenoma	3 (2.2%)	0 (0%)	n.s.
Hodgkin's lymphoma	1 (0.7%)	0 (0%)	n.s.

Values are mean ± SD or median (range)

*BMI* body mass index

\* Chi<sup>2</sup> with Yates correction for categorical variables and Kruskal–Wallis test for quantitative variables

were described accurately in the clinical history of only one of these cases.

## Effectiveness

There were no statistically significant differences in PASI 75 during the first 52 weeks of treatment between etanercept and adalimumab [80.0% vs 85.7%; relative risk (RR) = 1.07 (0.90, 1.27); relative risk aversion (RRA) = 5.7 (−8.9, 20.2); *P* = 0.943]. Therefore, both drugs were deemed similarly effective during the study period.

## Costs

Supplementary Table 1 shows the unit costs of the drugs, health-care resources, transportation and work loss values used in the analysis. The total drug cost for the first year of treatment was €1,893,180.75 for etanercept and €696,404.16 for adalimumab. The cost per patient was thus €14,451.76 ± 5,606.17 for etanercept and €14,508.42 ± 9,072.35 for adalimumab. Table 2 shows that the costs of an internal medicine specialist outpatient and day hospital visits, simple X-rays and dermatology inpatient visits were lower for etanercept as compared to adalimumab (all *P* < 0.05). Nevertheless, there were no significant differences in total health-care resource costs between both treatment groups. When analysing work productivity losses (Table 3) and patients' transportation expenditure (Table 4), a significant increase was found in the cost associated with visits to the internal medicine specialist in the group treated with adalimumab compared with etanercept (all *P* < 0.05). However, these differences did not contribute to the total work productivity losses or patients' transportation costs, which resulted in no statistically different overall costs between

**Table 2** Analysis of costs associated with health-care resource use during the first year of treatment with etanercept and adalimumab

Resource	Etanercept ( <i>n</i> = 135)			Adalimumab ( <i>n</i> = 48)			<i>P</i> * value
	Units	Total cost (€)	Mean cost per patient (€)	Units	Total cost (€)	Mean cost per patient (€)	
Outpatient service							
Dermatology							
First visit	135	5,872.50	43.50 (0)	48	2,088.00	43.50 (0.00)	n.a.
Follow-up visit	1,158	20,612.40	157.89 (55.30)	406	7,442.60	155.11 (58.731)	n.s.
Subtotal	1,293	26,484.90	194.92 (63.61)	454	9,530.60	198.61 (58.71)	n.s.
Rheumatology							
First visit	16	696.00	5.12 (14.07)	10	298.08	6.21 (15.50)	n.s.
Follow-up visit	23	409.40	3.01 (10.29)	20	518.88	10.81 (32.26)	n.s.
Subtotal	39	1,105.40	8.13 (23.16)	30	816.96	17.02 (46.01)	n.s.
Digestive system							
First visit	8	348.00	2.56 (10.27)	6	298.08	6.21 (15.50)	n.s.
Follow-up visit	20	356.00	2.62 (12.36)	13	244.32	5.09 (19.29)	n.s.
Subtotal	28	704.00	5.18 (21.78)	19	542.40	11.30 (31.71)	n.s.
Internal medicine							
First visit	3	130.50	0.96 (6.41)	5	223.68	4.66 (13.70)	0.029
Follow-up visit	4	71.20	0.52 (4.30)	10	182.88	3.81 (14.82)	n.s.
Subtotal	7	201.70	1.48 (10.22)	15	406.56	8.47 (26.73)	0.028
Infectious disease							
First visit	3	130.50	0.96 (6.41)	0	0.00	–	
Follow-up visit	4	71.20	0.52 (4.30)	0	0.00	–	n.a.
Subtotal	7	201.70	1.48 (10.22)	0	0.00	–	n.a.
Emergency visits	10	540.76	3.98 (23.39)	0	0.00	–	n.a.
Radiology							
Simple X-ray	143	1,319.89	9.71 (14.58)	78	791.04	16.48 (17.65)	0.031
CAT	5	523.05	3.85 (23.51)	0	0.00	–	n.a.
NMR	3	682.41	5.02 (33.53)	1	227.47	8.12 (42.99)	n.s.
Ecography	8	295.36	2.17 (9.81)	5	190.08	3.96 (15.37)	n.s.
Subtotal	159	2,820.71	20.74 (51.20)	84	1,208.59	28.56 (48.73)	0.042
Day hospital							
Dermatology	8	1,284.00	9.51 (94.21)	17	2,751.36	57.32 (303.32)	n.s.

**Table 2** continued

Resource	Etanercept ( <i>n</i> = 135)			Adalimumab ( <i>n</i> = 48)			<i>P</i> * value
	Units	Total cost (€)	Mean cost per patient (€)	Units	Total cost (€)	Mean cost per patient (€)	
Rheumatology	3	481.50	3.54 (30.68)	0	0.00	–	n.a.
Infectious diseases	0	–	–	0	0.00	–	n.a.
Subtotal	11	1,765.50	12.98 (97.78)	17	2,751.00	57.32 (303.32)	n.s.
Inpatient service							
Dermatology	0	0	–	27	18,042.72	375.89 (1,989.05)	0.027
Internal medicine	0	0	–	12	5,052.48	105.26 (557)	0.027
Digestive system	0	0	–	0	0.00	–	n.a.
Subtotal	0	0	–	39	23,095.68	481.16 (2,546.04)	0.027
Total health resource cost	1,554	33,825.21	248.90 (148.3)	658	37,144.40	802.45 (2,594.67)	n.s.

*CAT* Computer axial tomography, *n.a.* not applicable, *NMR* nuclear magnetic resonance, *n.s.* not significant

Reported within parentheses are standard deviation values

\* Kruskal–Wallis test for the quantitative variable ‘mean cost per patient’ comparing both drugs

both drugs. Table 5 shows the total cost of each treatment choice. There were no significant differences in total cost per patient with etanercept compared with adalimumab.

### Cost-Effectiveness Analysis

The absence of statistically significant differences in effectiveness between the two treatments excluded a cost-effectiveness analysis, which was replaced with a cost minimization analysis. This included not only drug costs, but also direct costs derived from the use of resources, patients’ transportation and indirect (work productivity loss) costs.

## DISCUSSION

This study approached cost-effectiveness analysis from a novel, broad perspective, in social terms and based on observational data. This strengthens the applicability of its results

to similar populations, as it reduces uncertainty in the decision-making process in clinical practice when using estimates of pharmacoeconomic studies based on clinical trial data.

However, our approach is subject to several methodological limitations that warrant some comment. The single-centre, retrospective design used in this study may have detracted from the representative nature of the results owing to inaccuracies in the patients’ clinical histories. This potential bias, which is inherent in most retrospective work, is a result of the lack of well-defined standards for recording visits and of variability in clinical practice—two distinct features of clinical trial designs. In any case, our results could be validated by a future standardized, multi-centre, prospective study.

One other potential shortcoming of our study was the exclusion of costs arising from the management of adverse reactions to etanercept and adalimumab. The exclusion of

**Table 3** Analysis of total and per-patient costs in relation to work productivity losses during the first year of treatment with etanercept and adalimumab

	Etanercept ( <i>n</i> = 135)			Adalimumab ( <i>n</i> = 48)			<i>P</i> * value
	Units	Total cost (€)	Mean (SD) cost per patient (€)	Units	Total cost (€)	Mean (SD) cost per patient (€)	
Outpatient service							
Dermatology	1,293	48,377.60	369.25 (116.23)	454	17,443.68	363.41 (123.39)	<i>n.s.</i>
Rheumatology	39	1,459.19	10.73 (32.17)	31	1,539.36	32.07 (78.68)	<i>n.s.</i>
Digestive system	28	1,047.62	7.70 (33.81)	20	769.44	16.03 (50.32)	<i>n.s.</i>
Internal medicine	7	261.91	1.93 (13.90)	15	576.96	12.02 (40.79)	0.028
Infectious diseases	7	261.91	1.93 (13.90)	0	–	–	<i>n.s.</i>
Subtotal	1,374	51,408.21	377.95 (149.52)	520	20,329.44	423.53 (189.68)	<i>n.s.</i>
Day hospital							
Dermatology	8	299.32	2.20 (16.27)	17	641.28	13.36 (21.70)	<i>n.s.</i>
Rheumatology	3	112.25	0.83 (7.15)	0	–	–	<i>n.a.</i>
Infectious diseases	0	0.00	–	0	–	–	<i>n.a.</i>
Subtotal	11	411.57	3.03 (22.79)	17	641.28	13.36 (21.70)	<i>n.s.</i>
Total productivity loss	1,385	51,819.78	380.98 (150.76)	537	20,970.72	436.90 (234.85)	<i>n.s.</i>

*SD* standard deviation; *n.a.* not applicable, *n.s.* not significant

\* Kruskal–Wallis test for the quantitative variable ‘mean cost per patient’ comparing both drugs

these costs was dictated by the poor documentation of such reactions in the clinical histories. Based on previous studies and a recent report issued by the United Kingdom’s National Institute for Health and Clinical Excellence, there are no significant differences in adverse reactions between both drugs [23]; therefore, any such differences can be assumed to have led to no additional disparities in cost between the two treatment groups in our study.

Finally, the treatment groups in our study differed markedly in the number of patients, largely as a result of etanercept being made commercially available 1 year earlier than adalimumab. Thus, after the first year, adalimumab played a secondary role and was preserved for use in patients refractory to

etanercept, even though no such application was stated in its technical sheet. Moreover, a large number of patients in the adalimumab group had psoriatic arthritis in addition to plaque psoriasis; therefore, these patients were excluded to avoid biased estimation of the costs associated with the use of health-care resources. Also, alternative biologicals currently in use to treat moderate-to-severe psoriasis in our hospital (e.g. infliximab and ustekinumab) were excluded, since they are administered intravenously and only at the hospital—a marked difference from etanercept and adalimumab. In addition, these alternative biological agents are prescribed mostly for patients with arthritis and/or those selected for rescue with other biologicals. In addition, the use frequency of ustekinumab as a first-choice



**Table 4** Analysis of total and per-patient costs associated with return transportation between patients' homes and the hospital during the first year of treatment with etanercept and adalimumab

	Etanercept ( <i>n</i> = 135)				Adalimumab ( <i>n</i> = 48)				<i>P</i> * value
	Trips	Total distance per patient (km)	Total cost (€)	Mean cost (SD) per patient (€)	Trips	Total distance per patient (km)	Total cost (€)	Mean cost (SD) per patient (€)	
Outpatient service									
Dermatology	2,586	393.08	22,797.30	162.45 (280.92)	906	752.3	2,629.98	54.79 (48.05)	n.s.
Rheumatology	78	9.85	636.67	4.75 (17.23)	61	63.0	1,239.11	25.81 (81.67)	n.s.
Digestive system	56	8.04	502.39	3.75 (22.82)	41	55.9	1,057.82	22.03 (76.44)	n.s.
Internal medicine	14	3.01	173.33	1.29 (10.16)	30	53.1	1,006.82	20.97 (85.88)	0.025
Infectious disease	14	1.85	107.47	0.80 (8.46)	0	–	–	–	n.a.
Subtotal	2,748	415.8	24,217.15	173.04 (292.86)	1,038	924.3	5,933.73	123.61 (215.37)	<0.001
Day hospital									
Dermatology	16	11.14	626.94	4.65 (2.13)	17	77.1	1,691.28	35.22 (1.92)	0.003
Rheumatology	6	4.18	235.10	1.74 (0.94)	0	–	–	–	n.a.
Infectious diseases	0	–	–	–	0	–	–	–	n.a.
Subtotal	22	15.3	862.05	6.39 (2.98)	17	77.1	1,691.28	35.22 (62.7)	n.s.
Total transportation cost	2,77	431.16	25,079.20	179.43 (292.67)	618	1,001.43	7,624.99	158.83 (563.95)	n.s.

SD Standard deviation, *n.a.* not applicable, *n.s.* not significant

\* Kruskal–Wallis test for the quantitative variable 'mean cost per patient' comparing both drugs

biological agent in our patient cohort—probably as a result of its more recent commercialization—was too low to enable its cost analysis during the first year of treatment.

In any case, we believe our analysis is representative of daily clinical practice since it compares two drugs, which jointly accounted for 70.4% of our hospital's expenditure on biologicals for the treatment of psoriasis during the studied period. Based on our results, there are no significant differences in efficiency or total cost per patient when etanercept is compared with adalimumab for moderate-to-severe psoriasis not associated with arthritis. Although the overall analysis showed no differences in direct and indirect costs between both drugs, in the specific sub-analyses, an increase in direct and indirect costs associated with internal medicine outpatient and day hospital visits, and simple X-rays was found in the adalimumab group as compared to the etanercept group. As there

were no differences in the baseline characteristics of patients in each treatment group, a possible explanation is that a selection bias could have been introduced by dermatologists in choosing adalimumab for individuals with non-specific rheumatic symptoms. These symptoms are likely to have motivated the patient to consult the internal medicine specialist. Nevertheless, we know of no data in the clinical history reviewed to support this hypothesis.

In the virtual absence of similar studies, ours can be used as an additional source of information towards placing both etanercept and adalimumab as primary choices for the treatment of plaque-type psoriasis within the scope of the Spanish National Health System. Some design-related factors can alter one's perception of the usefulness of previous studies on this topic. Unlike previous studies, ours provides an approach to a difficult problem that is akin to clinical practice based on real-life

**Table 5** Analysis of direct, indirect, total and per-patient costs associated with the first year of treatment with etanercept and adalimumab

Cost	Etanercept ( <i>n</i> = 135)		Adalimumab ( <i>n</i> = 48)		<i>P</i> * value
	Total cost (€)	Mean (SD) cost per patient (€)	Total cost (€)	Mean (SD) cost per patient (€)	
Drug	1,893,180.75	14,451.76 (5,606.17)	696,404.16	14,508.42 (9,072.35)	n.s.
Health-care resource use	33,825.21	250.55 (147.62)	37,144.40	802.45 (2,594.67)	n.s.
Patient transportation	25,079.20	173.44 (292.67)	7,624.99	158.83 (563.95)	n.s.
Productivity loss	51,819.78	380.98 (156.76)	20,970.72	436.90 (234.85)	n.s.
Total first-year costs	2,003,904.94	14,843.73 (6,178.98)	762,144.27	15,405.91 (9,106.50)	n.s.

*n.s.* Not significant, *SD* standard deviation

Reported within parentheses are standard deviation values

\* Kruskal–Wallis test for the quantitative variable ‘mean cost per patient’ comparing both drugs

use data from a tertiary referral public hospital. First, we chose a period of time for the study to be the first year of treatment with the target drugs. This is very important since, although other studies have tried to predict its long-term course, psoriasis is a chronic disease and differs between patients in natural history and response to treatment, which hinders accurate long-term cost estimations [8, 9]. In the only pharmacoeconomic study of psoriasis reported to date in Spain, Blasco et al. [4] compared the incremental cost-effectiveness per patient of infliximab, etanercept, adalimumab and efalizumab in terms of clinical trial data. They found adalimumab to be the most cost-effective choice, followed by etanercept, efalizumab and infliximab. As noted earlier, however, the corresponding sensitivity analysis revealed a strong overlap between the cost-effectiveness ratios for these drugs. Also, the authors failed to consider the costs involved in hospital resources, transportation and work productivity losses. This precludes accurate interpretation of their results if one considers the significance of all treatment-associated costs in this context. The only study seemingly

considering the costs associated with health-care resource use and work productivity losses was conducted by Sizto et al. [5]. But, in contrast to our study, short-term efficacy was based on relative probabilities of achieving PASI response (50/75/90) in a meta-analysis of trials, not from clinical data source. This authors found that adalimumab was most cost-effective than etanercept, but with confidence intervals overlapping in the sensitive analysis.

There are also some limitations to comparing our results with those of others based on clinical practice owing to differences in study design, variables and objectives. Fonia et al. analysed drug and health-care resource-related costs in a historical cohort of patients with psoriasis seen at a third-level hospital in Great Britain [24] and found the expected increase in costs derived from the introduction of biological agents to be accompanied by a decrease in use of hospital resources by the patients. However, these authors failed to examine costs in terms of the particular drug, which precludes comparison with our results. Subject to similar constraints is the study by Wu et al. [25], who used a USA-based health database to compare the costs of

various treatment modes with etanercept over a period of 12 months, but considered drug-related costs alone. Finally, Fowler et al. [26] compared the direct and indirect incremental costs of health care for 12,280 patients with psoriasis and 36,840 controls in terms of information in a database of 30 insurance companies in the USA. Their study included total treatment cost per patient, but excluded disease severity and the effects of each drug separately, which again precludes comparison with our results.

## CONCLUSION

In summary, our data suggest that etanercept is as cost-effective as adalimumab during the first year of treatment in patients with moderate-to-severe psoriasis not associated with arthritis.

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**Conflict of interest.** Dr. Ruano has received honoraria for lecturing and grants for research from Pfizer, honoraria for lecturing from Janssen-Cilag and other financial benefit from Abbott. Dr. Jiménez-Puya has received honoraria for research, advisory board or lecturing from Abbott and Janssen-Cilag, and honoraria for research or lecturing from Pfizer. Dr. Rodríguez-Martín has received honoraria for consultancy from Pfizer. Dr. Gómez has received honoraria for research from Pfizer and for lecturing from Abbott and Janssen-Cilag. Dr. Vélez has received honoraria for lecturing from Abbott,

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**Compliance with ethics guidelines.** All procedures were performed in accordance with the ethical standards of the responsible committee on human experimentation and with the Declaration of Helsinki of 1975. Informed consent was obtained from all the patients included in the study.

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