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INVESTIGATIVE REPORT

A Higher Score on the Dermatology Life Quality Index, Being on Systemic Treatment and Having a Diagnosis of Psoriatic Arthritis is Associated with Increased Costs in Patients with Plaque Psoriasis

Mats EKELUND1, Lotus MALLBRIS2, Susanne QVITZAU3 and Berndt STENBERG4

1Department of Health Economics, Pfizer AB, 2Pfizer Speciality Care, Medical Affairs Europe, Inflammation, Sollentuna, Sweden, 3Medical Department, Pfizer AS, Copenhagen, Denmark, and 4Department of Public Health and Clinical Medicine, Epidemiology and Dermatology & Venereology, Umeå University, Umeå, Sweden

The aim of this study was to examine the relationship between measures of disease severity and costs from a societal perspective in patients with plaque psoriasis. Dermatologists in Sweden recruited 443 consecutive patients who had had no biological treatment during the past 12 months. Following a Psoriasis Area and Severity Index (PASI) assessment, subjects completed self-assessments on health status/quality of life and a healthcare resource utilization/work status questionnaire. The costs of healthcare resources and sick-leave due to plaque psoriasis were estimated and related to the subject’s health status. A patient’s Dermatology Life Quality Index (DLQI) and being on systemic therapy, or having diagnosis of psoriatic arthritis, appeared to be more strongly associated with direct and indirect costs than did their PASI. The cost of biological therapy should be considered from the perspective of the already high costs of patients with high DLQI undergoing traditional systemic treatment.

Key words: costs; DLQI; cost-of-illness; psoriasis, Sweden.

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Psoriasis is a common skin disease that has a considerable impact on patients’ quality of life (QoL) (1–6). Biological agents have proved effective in patients with moderate to severe plaque psoriasis who have not responded to systemic treatment. However, biological agents are expensive, and it is desirable to target their use to patients with high potential for improvements in quality of life and reductions in disease-related cost. While quality of life can be measured through self-administered questionnaires, it has not been established which measurements of disease severity/symptoms and signs correlate best with costs of illness (7–10).

The aim of this study was to estimate and compare the relationship between different measures of disease severity, co-morbidity in terms of joint involvement and treatment mode (systemic vs. non-systemic), and direct and indirect costs relating to plaque psoriasis in Swedish patients with no ongoing biological treatment.

MATERIALS AND METHODS

Design

This was a multicentre, observational, retrospective cost-of-illness study of both direct and indirect costs in patients with plaque psoriasis in a dermatology clinic setting. Approximately 450 subjects were to participate in this survey. The aim was to recruit 150 subjects with Psoriasis Area and Severity Index (PASI) <8, 150 subjects with PASI 8–12, and 150 subjects with PASI >12. The following tests and procedures were performed and data collected at the visit:

- PASI performed by the physician (11).
- Patient’s description of the extent of psoriasis when the disease was at its worst during the previous 2 years (12).
- Dermatology Life Quality Index (DLQI) (13).
- Involvement of joints (yes/no) and a drawing to indicate which joints are affected and a patient assessment of joint pain on a scale of 0–1.
- Patient’s nail psoriasis assessment (yes/no) and reported number of fingers/toes affected.
- Patient questionnaire on healthcare resource utilization (HCRU) and work status. The patient estimated the quantities of healthcare consumption/absence from work due to psoriasis/psoriatic arthritis during the past 12 months for pre-specified items.

Recruitment

The survey involved 443 consecutive subjects with plaque psoriasis. Subjects were enrolled (June 2008–January 2010) at dermatology units at 10 hospitals in Sweden (referral patients) and at outpatient centres of the Swedish Psoriasis Association in Stockholm, Sweden (both referral and self-referral patients). These centres (14) provide consultation with specialized dermatologists and are integrated in the public healthcare system as contracted healthcare providers. Approval was obtained from the ethics committee, and the ethical rules for the pharmaceutical industry (a local guideline) for this type of survey were followed.

Inclusion/exclusion criteria

Inclusion criteria were: age ≥ 18 years old and diagnosed with plaque psoriasis for at least one year. Exclusion criteria were: subjects who had been treated with biological drugs within the past 12 months. Written informed consent was obtained from all subjects before their enrolment.
Subjects participating in the study were examined by a physician who determined their PASI. The questionnaire covered background demographic factors (age, sex and work status), healthcare resource utilization and sick leave. In addition, patients were asked whether they had hand and foot psoriasis and the number of nails affected. On a sketch they indicated how much of their body was affected when their psoriasis was at its worst during the past 2 years. The body was divided into 3 parts, the upper extremities, head and trunk, and lower extremities. Scoring ranged from 0 (0% of the area in one of the regions affected by psoriasis) to 6 (90–100% of the area in one of the regions affected). The head and trunk together and the lower extremities each represented 40% of the body area. Upper extremities represented 20% of the body area. The scoring for the latter was multiplied by 0.5 and the total score index therefore ranged from 0 to 15 (12). The patient’s quality of life was assessed with the DLQI.

Costing

The cost of psoriasis was calculated with a 1-year socio-economic perspective, using the prevalence approach (costs incurred in a given time-period, regardless of disease onset). Costs of healthcare resource utilization and productivity losses were identified through the patient questionnaire, and transformed into costs using standard health-economic valuation methods in line with the recommendations of the Swedish Pharmaceutical Benefits Board (15). Missing values on cost items in the patient questionnaire were conservatively set at zero.

The Pharmacy Retail Prices (AUP) was used for medicine costs, and a standard schedule of fees for outpatient and inpatient care was extracted from the official price list in the south of Sweden (16).

For climate care, phototherapy and Bucky treatment, costing data were derived from public contracts in the south of Sweden, as fees and remuneration are determined through procurement processes (17, 18). Travel costs were based on the deductible tax amounts for using a private car to travel to work (19). Indirect costs were estimated using the human capital approach. The cost of lost production was estimated as the mean employer cost of 1 h of work, as estimated by Folkhälsoinstitutet (the Swedish National Institute of Public Health) (20). One day of sick leave was set to 8 h of lost work for full-time employees and a healthcare visit was set to 4 h of lost production.

Statistical analysis

Statistical analyses were performed by the Pharma Consulting Group AB. The analysis was descriptive in nature, and the primary and secondary objectives focused on measuring the relationship between costs and clinical measures of morbidity/severity. Four main categories were used for the descriptive analysis, mean cost per cost category in patients with:

- PASI < 8, 8 ≤ PASI ≤ 12 and PASI > 12
- DLQI < 5, 5 ≤ DLQI < 10 and DLQI ≥ 10
- DLQI < 5, 5 ≤ DLQI < 10 and DLQI ≥ 10 with and without systemic treatment
- DLQI < 5, 5 ≤ DLQI < 10 and DLQI ≥ 10 with and without diagnosis of psoriatic arthritis

In addition to these analyses, the mean cost for each PASI and DLQI category was further subdivided into the extent of disease at its worst as reported by the patient. The underlying hypothesis was that there is a positive relationship between costs of psoriasis and morbidity/severity of disease. The Kruskal-Wallis test was chosen because the cost variables do not meet the assumption of a normal distribution. Based on data from Sohn et al. (21), it was conjectured that a sample size of approximately 450 patients (150 in each PASI group) could detect a true difference in population means of 2,300 EUR, with a power of 0.80 and type I error probability of 0.05, assuming a standard deviation (SD) of approximately 6,700 EUR. All statistical analysis was performed using SAS (SAS Institute Inc., Cary, NC, USA) version 9.2.

In addition to the statistical analysis based on stratifications, regression analysis was used to explore associations between other measures of disease severity/co-morbidities and costs.

RESULTS

Study population

A total of 443 patients were enrolled in the study. Of these, 153 patients were enrolled in the PASI group < 8, 128 in the PASI group 8 ≤ PASI ≤ 12 and 162 in the PASI group > 12. Mean (median) PASI in the 3 groups were 4.45 (4.80), 9.73 (9.8) and 17.07 (15.55), respectively. The mean age of all enrolled patients was 51.5 years, with similar mean ages between PASI groups. Men were in the majority among the patients enrolled (68.3%). In patients with a PASI ≥ 8, men constituted more than 71.7%, compared with 56.9% in the group with the lowest PASI score.

The mean DLQI score among all patients was 9.3 (SD 6.8). The mean DLQI score in the lowest PASI group (PASI < 8) was 7.8. The mean DLQI score increased to 9.1 in the second PASI group (8 ≤ PASI ≤ 12) and reached 10.9 in the group with a PASI > 12.

Approximately one-quarter of patients reported diagnoses of psoriatic arthritis, and approximately half of the patients reported pain in 3 or more joints. There were no major differences between PASI groups in terms of diagnosis of psoriatic arthritis or experience of joint pain. Approximately half of the patients had nail psoriasis, with little difference between PASI groups. Of all patients, 27.5% received systemic therapy, and of patients with a PASI > 12, 22.8% received systemic therapy. There were small differences in employment status between PASI groups. This result remained the same after stratification by gender (see Table I).

Resource utilization and sick leave

Mean total costs in all patients were 3,399 EUR, with a SD of 5,758 EUR. The 3 cost components associated with the highest costs were lost production (1,230 EUR), medicine costs (713 EUR) and phototherapy (470 EUR). These costs constituted 71% of the total mean costs. Differences in costs between PASI groups were small and not statistically significant (see Fig. S1; available from: http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1591).

Mean total costs for patients with higher DLQI tended to be higher. For patients with DLQI < 5, mean total costs were small and not statistically significant (see Fig. S1; available from: http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1591).
costs were 2,204 EUR. For patients with 5 ≤ DLQI < 10, mean total costs were 2,647 EUR, and for patients with DLQI ≥ 10 the corresponding costs were 5,016 EUR. There was a statistically significant (p < 0.05) difference between DLQI categories for physician visits, tar, medicine costs, moisturizers, other costs and lost production. Lost production, medicine costs and costs of moisturizers were the main components behind differences in mean costs between patients with DLQI ≥ 10 and patients with lower DLQI scores. For total costs there was a statistically significant difference between DLQI categories (p < 0.001) (see Table II).

Psoriatic arthritis was associated with higher mean yearly costs when stratifying for DLQI. The mean yearly cost was approximately twice as high for patients reporting a diagnosis of psoriatic arthritis. Lost production was the most important factor behind increased mean yearly costs (see Table SI; available from: http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1591). Stratifying for DLQI, patients on systemic treatment had higher total mean yearly costs compared with patients not on systemic treatment. For each DLQI category, the mean yearly costs were approximately twice as high for patients on systemic therapy. Lost production followed by medicine costs (topical treatment) and costs of moisturizers were the main causes of cost differences. Systemic therapy therefore seemed to be an add-on to topical treatment rather than a substitute. Patients on systemic treatment with DLQI ≥ 10 had an mean yearly cost of 8,007 EUR. See Fig. S2 (available from: http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1591).

Regression analysis

Regression analysis was performed to explore which disease severity/morbidity measures, controlling for demographic variables, reached significance with regard to costs. A linear model using the following variables was performed: DLQI (continuous), PASI score (continuous), a dummy variable for diagnosis of psoriatic arthritis, a dummy variable for pain in at least 3 joints, the index value describing psoriasis at its worst during the past 2 years (continuous), a dummy

| Table I. Demographics and clinical features of study population |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Enrolled       | PASI < 8 n = 153 | 8 ≤ PASI ≤ 12 n = 128 | PASI > 12 n = 162 | All n = 443     |
| Age, mean (SD) | 52.7 (14.5)      | 50.7 (14.7)      | 51.1 (13.5)      | 51.5 (14.2)     |
| Missing, n     | 5                             | 2                             | 3                             | 10                             |
| Gender, male, n (%) | 87 (56.9) | 91 (71.1)       | 124 (76.5)       | 302 (68.2)       |
| Missing, n     | 0                             | 1                             | 0                             | 1                             |
| PASI score, mean (SD) [median] | 4.5 (2.0) [4.8] | 9.7 (1.2) [9.8] | 17.1 (4.9) [15.6] | 10.6 (6.3) [10.0] |
| DLQI, mean (SD) [median] | 7.8 (6.6) [6.0] | 9.1 (6.8) [8.0] | 10.9 (6.8) [10.0] | 9.3 (6.8) [8.0] |
| Missing, n     | 5                             | 4                             | 9                             | 425                             |
| Diagnosed with psoriatic arthritis, n (%) | 36 (23.5) | 30 (23.4)       | 44 (27.2)       | 110 (24.8)       |
| Patients having pain in at least 3 joints, n (%) | 69 (45.1) | 55 (43.0)       | 69 (42.6)       | 193 (43.6)       |
| Nail psoriasis, n (%) | 468 (44.4) | 69 (53.9)       | 96 (59.3)       | 233 (52.6)       |
| Systemic treatment, n (%) | 47 (30.7) | 38 (29.7)       | 37 (22.8)       | 122 (27.5)       |
| Employed, n (%) | 95 (62.1) | 76 (59.4)       | 109 (67.3)      | 280 (63.2)       |
| Missing, n     | 8                             | 4                             | 4                             | 16                             |

PASI: Psoriasis Area and Severity Index; SD: standard deviation; DLQI: Dermatology Life Quality Index.

| Table II. Costs (EUR) per Dermatology Life Quality Index (DLQI) group |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| DLQI <5 n = 132 | 5 ≤ DLQI <10 n = 118 | DLQI ≥ 10 n = 175 |
| Physician visits | 209.6 (187.2) | 209.7 (143.4) | 345.1 (390.7) | 0.0001 |
| Inpatient care | 49.1 (397.3) | 68.6 (383.3) | 172.2 (751.5) | 0.154 |
| Blood samples | 102.6 (270.5) | 105.6 (235.0) | 115.9 (249.4) | 0.518 |
| Phototherapy | 473.0 (687.9) | 454.5 (691.8) | 499.3 (782.2) | 0.735 |
| Bucky X-ray | 1.7 (10.0) | 1.4 (12.0) | 0.7 (9.6) | 0.625 |
| Sun trip | 53.5 (432.9) | 119.7 (641.6) | 121.1 (644.2) | 0.551 |
| Transportation | 122.5 (229.2) | 73.2 (171.4) | 101.6 (175.9) | 0.143 |
| Tar | 0.7 (5.4) | 1.7 (8.2) | 5.0 (31.9) | 0.026 |
| Medicine costs | 493.9 (1,305.7) | 533.3 (806.1) | 1,050.0 (1,729.5) | <0.0001 |
| Moisturizers | 85.4 (135.2) | 109.1 (201.6) | 341.3 (2,496.2) | 0.0014 |
| Other costs | 54.5 (307.6) | 76.5 (346.8) | 206.7 (402.2) | <0.0001 |
| Lost production | 558.1 (1,853.7) | 893.4 (2,622.7) | 2,056.3 (6,546.3) | 0.0023 |
| Total costs | 2,203.9 (3,047.1) | 2,646.1 (3,562.9) | 5,015.1 (8,000.5) | <0.0001 |
variable for the being on systemic therapy a dummy variable for toe-nail psoriasis, a dummy variable for finger-nail psoriasis, a variable for age (continuous), a dummy variable for gender, and a dummy variable for whether the patient was a member of the psoriasis association.

The variables reaching statistical significance in this model at the 0.05 level were: DLQI, diagnosis of psoriatic arthritis, pain in at least 3 joints, the index value describing psoriasis at its worst during the past 2 years, and being on systemic treatment. Interestingly, the $p$-value for the PASI score was not statistically significant ($p = 0.41$).

For the variables tested in the model above, a simplified model was designed based on only 3 variables: DLQI, diagnosis of psoriatic arthritis, and being on systemic treatment.

Although the explained variance is low in the simplified model, it shows the additive effect of diagnosis of psoriatic arthritis and being on systemic therapy on the total costs for patients at a certain DLQI level (see Table III).

**DISCUSSION**

In this study we found that the DLQI is more strongly related to costs than is the PASI. In fact, the relationship between a patient’s PASI and costs was not apparent in the regression analysis. In contrast, patients with higher DLQI have higher costs associated with their plaque psoriasis compared with patients with less impairment. We also found that presence of joint involvement and being on systemic therapy are additional factors correlating with a patient’s cost of illness. The most important factor behind higher costs for patients with high DLQI, systemic treatment and joint involvement was increased costs of sick leave.

This study used self-reported healthcare resource utilization and sick leave data. The recall period for these data was one year. This recall time was chosen in order to avoid seasonal factors that can affect these data was one year. This recall time was chosen in order to avoid seasonal factors that can affect utilization and sick leave data. The recall period for the data was increased costs of sick leave.

High DLQI, systemic treatment and joint involvement are important factors behind higher costs for patients with plaque psoriasis. These seasonal factors may be especially accentuated in Sweden, where the amount of sunlight varies considerably between summer and winter. It should be noted that having a 1-year recall period may come at the cost of precision (22). There are also limitations in using self-reported health resource utilization data, as they may imperfectly reflect actual utilization (23). While acknowledging the limitations of self-reported data, we do not see how these limitations would affect the relative strengths of the relationships between the costs of illness and disease measures.

Subjects were consecutively recruited to the study, but there was no record of the number or characteristics of patients declining participation. Therefore, we do not know how well the participating patients represent the mean patient in his/her respective PASI category. Men were in the majority in our study group. This is probably not because men have a greater severity of psoriasis than women, but a reflection of previous findings that men tend more often to seek specialized care (24).

One possible explanation for the lack of correlation between a patient’s PASI and their cost of illness may be that the PASI measured disease severity at study inclusion, while the cost of illness reflected the costs from study inclusion to one year prior to the start of the study. Furthermore, the point estimate of the PASI may be a measure of the efficacy of the patient’s treatment at the time rather than the severity of the underlying disease. The patient’s experience of a change in his/her disease may prompt the visit to the clinic. In this case, the point estimate of the PASI is less informative about the underlying disease. In order to control for underlying disease, we explored the relationship between the rating of the psoriasis when it was at its worst during the past 2 years and costs. In regression analysis we found that this measure correlated better than PASI but worse than DLQI.

Considering the results of the present analysis from the perspective of earlier cost-of-illness studies, we found studies that seemed to establish a more pronounced relationship between disease severity, measured as skin area affected, and the cost of illness. Navarini et al. (25) estimated substantial differences in yearly healthcare costs between patients categorized as mild, moderate and severe. However, these differences were caused mainly by differences in the use of biological drugs. In our study, the use of biological drugs was an exclusion criterion that makes comparisons difficult. Colombo et al. (7) compared the costs of patients having a PASI >20 with patients having a PASI ≤20, and found that costs among patients with a PASI >20 were twice as high. Differences were mainly due to hospitalization and indirect costs.

Sato et al. (10) examined healthcare resource utilization, employment disadvantages and DLQI. As in our study, they found that a higher DLQI was associated with higher disease-related costs. In line with our findings, Ghatnekar et al. (9) found that patients on syste-

| Variable | Df | Parameter estimate | Standard Error | t-value | Pr > |t| |
|----------|----|-------------------|----------------|---------|------|---|
| Intercept | 1 | 245.1 | 576.7 | 0.0486 | 0.777 |
| dlqi_tot | 1 | 227.2 | 45.1 | 5.083 | <0.0001 |
| dum_psor | 1 | 1,980.8 | 686.5 | 3.345 | 0.00049 |
| systemic | 1 | 2,451.3 | 684.0 | 3.578 | <0.0001 |

$dlqi$ tot: continuous variable for DLQI score; dum_psor: dummy variable for diagnosis of psoriatic arthritis; systemic: dummy variable for the patient being on systemic therapy.

Societal cost factors in patients with plaque psoriasis
mic therapy had higher productivity losses than patients on topical therapy or phototherapy, and Kimball et al. (8) found that psoriatic arthritis was associated with incremental costs for patients with psoriasis.

In conclusion, the results of this study suggest that important cost drivers in patients with plaque psoriasis are: a patient’s DLQI; having a diagnosis of psoriatic arthritis; and being on systemic treatment. The patient’s own assessment of body surface area at its worst during the past 2 years correlated more with a patient’s mean PASI at the time of study inclusion, but less than the patient’s DLQI. The high cost of biological agents should be considered from the perspective that candidates for biological therapy (i.e. patients on systemic therapy with high DLQI) already incur substantial costs due to their plaque psoriasis.

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Conflicts of interest. ME, LM and SQ are employees of Pfizer. BS declares no conflict of interest.

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