A multinational assessment of work-related productivity loss and indirect costs from a survey of patients with psoriasis*

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Summary

Background Total work productivity loss (WPL) and associated indirect costs contribute to the economic burden of psoriasis.

Objectives To estimate total WPL and related indirect costs, and identify predictors of WPL associated with psoriasis severity in France, Germany, Spain, the U.K. and Italy (EU5) and the U.S.A.

Methods Data from the 2015 Adelphi Real World Psoriasis Disease Specific Programme, analysed for absenteeism, presenteeism and total WPL, were quantified (0–100%) from participants who completed the Work Productivity and Activity Impairment (WPAI) instrument. These measures were converted to indirect costs using the human capital method. Univariate and multivariate statistical analyses controlling for patient demographic and clinical characteristics were conducted.

Results Of the 936 respondents (29.6% U.S.A., 70.4% EU5) who completed the WPAI, 32.6%, 40.7% and 26.6% had mild [body surface area (BSA) 0–2%], moderate (BSA 3–10%) and severe (BSA > 10%) psoriasis, respectively. Average age, Dermatology Life Quality Index (DLQI) score and BSA were, respectively, 42.4 years, 5.1 and 9.6%; and 37.2% of respondents were female. Mean percentages of total WPL for respondents with mild, moderate and severe psoriasis were 10.1%, 18.9% and 29.4%, respectively. Presenteeism contributed considerably more to total WPL than did absenteeism across all countries and disease severity classes. Mean annual indirect costs per patient due to WPL ranged from 3742 U.S. dollars in Spain to 9591 U.S. dollars in the U.S.A. Multivariate regression showed that a one-unit increase in DLQI score increases total WPL by 1.8% (P < 0.001).

Conclusions WPL increased progressively with increasing DLQI scores and BSA, confirming the relationship between psoriasis severity and its economic burden.

What’s already known about this topic?

• The economic burden of psoriasis is exceptionally high given the high prevalence and lifelong nature of the condition.
• Several studies have attempted to assess the overall economic burden of psoriasis but there is a lack of comparative data from different countries, and issues around inconsistent methodologies, including statistical analyses.
• Total work productivity loss (WPL) and associated indirect costs are believed to contribute to the economic burden of psoriasis.
Psoriasis is a chronic inflammatory disease predominantly affecting the skin and associated with comorbidities such as psoriatic arthritis, which leads to joint deformations and disability. Psoriasis is characterized by erythematous, scaly plaques that itch and bleed.1 In addition to the physical burden, which can be extremely painful, psoriasis can have a profound negative impact on psychosocial well-being and social stigma.2,3 Psoriasis affects millions of individuals globally, regardless of sex and across all ages. Prevalence ranges from 0.09% to 11.4% globally, with at least 100 million individuals affected worldwide.3 The World Health Assembly acknowledges that many people suffer needlessly from psoriasis because of incorrect or delayed diagnosis, inadequate treatment options and insufficient access to care.3

Several studies have reported on the overall economic burden of psoriasis, which can be exceptionally high given the high prevalence and lifelong nature of the disease.4–6 A recent systematic review estimated that the annual total cost of psoriasis in the U.S.A. amounted to approximately 112 billion U.S. dollars in 2013. It concluded that patients with psoriasis would pay a once-per-lifetime intangible cost of 11 498 U.S. dollars for relief of physical signs and symptoms, and emotional health. Indirect psoriasis costs constituted a significant proportion of overall costs, ranging from 23.9 to 35.4 billion U.S. dollars.5

Indirect costs can be associated with unemployment and productivity loss. Quality of life and work productivity data from the National Psoriasis Foundation Survey highlighted that among unemployed patients with psoriasis or psoriatic arthritis, 92% cited their condition as the sole reason for not working. Additionally, 12% of patients were unemployed and 11% reported working part time. Among working respondents, 49% of patients reported missing work regularly because of psoriasis.2

Despite these findings, there are a number of gaps in the literature when considering the impact of psoriasis on patients’ work productivity and related economic burden. Where data exist, studies tend to be from the U.S.A., with a notable lack of comparative data from other countries. Issues around inconsistent methodologies, including statistical analyses, were identified across studies. As most work productivity instruments focus on those who are working and/or studying, they do not capture data from those not working, which may underestimate the impact of bringing patients back into the workforce. Such data gaps limit efforts to fully understand the economic burden of psoriasis and its impact on work productivity.6–11

This study contributes to the evidence on the economic burden of psoriasis. It addresses some of these gaps and inconsistencies by measuring total work productivity loss (WPL) and indirect costs using the same methodology and at the same point in time in six countries: France, Germany, Spain, Italy and the U.K. (EU5), and the U.S.A. It also aims to identify predictors of total WPL associated with severity of psoriasis across these countries.

Patients and methods

This study was designed and conducted with consideration of the Standards for Reporting Qualitative Research.12 A complete description of the survey methods was previously published.13–15 Data were collected in line with European Pharmaceutical Market Research Association guidelines16 and did not require ethics committee approval. The survey was performed in full accordance with the U.S. Health Insurance Portability and Accountability Act 1996,17 and Health Information Technology for Economic and Clinical Health Act legislation.18 Patients provided informed consent for use of their de-identified, anonymized and aggregated data for research purposes and publication in scientific journals.

Adelphi Real World Psoriasis Disease Specific Programme

Data were drawn from the Adelphi Real World Psoriasis Disease Specific Programme (DSP), which involved a retrospective, cross-sectional survey of U.S. and EU5 patients with psoriasis treated by a dermatologist between January and March 2015. The DSP provides impartial observations of real-world clinical practice from a physician and matched patient viewpoint. It evaluates the impact of psoriasis in areas such as health-related quality of life (HRQoL) and work productivity through data collection and analyses in multiple locations.

Dermatologists provided data for 10 consecutive consultation patients (> 18 years of age) with a confirmed diagnosis of psoriasis and at least one of the following criteria: currently receiving or ever having received an oral retinoid, immunosuppressant or biologic; or ever having physician-reported moderate/severe psoriasis; or ever having a physician-reported body surface area (BSA) > 10% affected by psoriasis. Each physician captured patient demographics,
socioeconomic status, clinical severity and treatment satisfaction traits.

Patients were invited to voluntarily complete a form incorporating the three-level version of the EuroQol five-dimensional questionnaire (EQ-5D-3L), the Dermatology Life Quality Index (DLQI) and the Work Productivity and Activity Impairment Questionnaire (WPAI).

The DLQI consists of 10 questions covering six domains, giving an overall response range of 0–30, where lower scores represent better HRQoL. WPAI consists of six questions designed to assess the impact of their condition on their ability to work and perform regular activities. Assessment of the validity and reproducibility of the WPAI was previously published. The Charlson comorbidity index predicts the one-year mortality for a patient who may have a range of comorbid conditions.

**Data analysis**

Comparisons of patient demographics, socioeconomic traits, disease severity, HRQoL and treatment patterns across countries were made using standard descriptive statistics. We defined mild, moderate and severe psoriasis as BSA affected of 0–2%, 3–10%, and >10%, respectively. Absenteeism was defined as the percentage of time missed from work due to psoriasis calculated for the prior 7 days. Presenteeism, which is the percentage of reduced productivity due to psoriasis while at work, was calculated for the prior 7 days using a scale of 0–10. Total WPL, defined as the percentage of total reduced productivity due to psoriasis, was calculated by combining absenteeism and presenteeism data.

Absenteeism, presenteeism and total WPL were quantified (0–100%) for DSP participants completing the WPAI instrument. Qualitative comparisons across the U.S. and EU5 population norms of absenteeism, presenteeism and total WPL were conducted.

**Calculation of indirect costs**

Indirect costs due to lost productivity were derived from absenteeism, presenteeism and total WPL using the human capital method, utilizing 2015 gross domestic product (GDP) per capita estimates for all countries. All costs were calculated in 2015 U.S. dollars.

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**Figure 1** Sample flow diagram indicating how patients were selected for inclusion in the analysis. PSC, patient self-completed; GDP, gross domestic product; DEU, Germany; ESP, Spain; FRA, France; ITA, Italy. [Colour figure can be viewed at wileyonlinelibrary.com]
For each respondent, absenteeism and presenteeism data were used to calculate the number of hours for which psoriasis impaired work productivity. This was used along with the patient’s estimated hourly pay rate to calculate lost productivity due to overall work impairment because of psoriasis during the past year. Results were expressed as proportion of the 2015 GDP per capita.

Statistical analysis

Univariate and multivariate statistical analyses were conducted to control for patient demographic and clinical characteristics. To estimate the multivariate relationship between patient characteristics including HRQoL, absenteeism, presenteeism and total WPL, generalized linear models were applied with a logit link function and binomial distribution family (e.g. fractional logit model).30,33

Results

Demographic and clinical characteristics

From 3897 identified patient files, 936 patients \( \geq 18 \) years of age with positive reported work hours completed the WPAI (Fig. 1), including 277 patients (29-6%) from the U.S.A. and 659 patients (70-4%) from EU5 (Table 1).

Mean patient age across all countries was 42-4 years and 37-2% of patients were female, with the U.S.A. having the highest proportion (42-6%). In the pooled sample, 92.6% of patients were white, with lower proportions in the U.K. and U.S.A. (78.8% and 86-6%, respectively) than in Italy and France (98-6% and 97-3%, respectively, \( P < 0.001 \)).

Mean BSA of psoriasis involvement was 9.6%. Spain, Italy and the U.K. had the highest proportions of patients with mild disease, whereas the U.S.A. and Germany had the highest proportions of patients with moderate disease (\( P < 0.001 \)). Mean DLQI score was 5-1, with patients from Germany having the highest and patients from Italy having the lowest mean DLQI score (6-1 and 3-3, respectively, \( P < 0.001 \)).

There were notable differences between countries in body mass index (P < 0.001, Table 1), therapy type, days on prescription and BSA prior to receiving current therapy (P < 0.001, Table 2).

Analysis by severity of psoriasis

In the pooled analysis, the average hours of total WPL (as a percentage of work hours) for patients with mild, moderate and severe psoriasis were 10-1% \( [95\% \text{ confidence interval (CI)} 8-4–11.8] \), 18-9% \( [95\% \text{ CI} 16-9–20.8] \) and 29-4% \( [95\% \text{ CI} 26-5–32-4] \), respectively. Presenteeism contributed to the most total WPL, with a relatively low contribution from absenteeism across all severity levels (Fig. 2a).

Average indirect costs associated with total WPL for patients with mild, moderate and severe psoriasis were 3592 U.S. dollars.

Table 1: Patient demographic by country

| Country | Sample size, n | Age (years), mean (95% CI) | Female, % | White, % | Other autoimmune disease, % | BMI, \( < 25 \), % | Other comorbidity score, mean (95% CI) |
|---------|----------------|--------------------------|-----------|----------|---------------------------|----------------|--------------------------------------|
| U.S.A.  | 150            | 46 (4-8.5-4.4)           | 54 (4-8.5-4.4) | 5-1 (4.8-4.4) | 110 (11.8) | 110 (11.8) |              |
| U.K.   | 43 (4-8.5-4.4) | 5-1 (4-8.5-4.4)          | 54 (4-8.5-4.4) | 5-1 (4.8-4.4) | 110 (11.8) | 110 (11.8) |              |
| DEU    | 43 (4-8.5-4.4) | 5-1 (4.8-4.4)            | 54 (4-8.5-4.4) | 5-1 (4.8-4.4) | 110 (11.8) | 110 (11.8) |              |
| ESP    | 43 (4-8.5-4.4) | 5-1 (4.8-4.4)            | 54 (4-8.5-4.4) | 5-1 (4-8.5-4.4) | 110 (11.8) | 110 (11.8) |              |
| ITA    | 43 (4-8.5-4.4) | 5-1 (4.8-4.4)            | 54 (4-8.5-4.4) | 5-1 (4-8.5-4.4) | 110 (11.8) | 110 (11.8) |              |

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Table 2. Patient clinical characteristics by country

|                          | Pooled | U.S.A. | U.K. | DEU | ESP | FRA | ITA | P-value |
|--------------------------|--------|--------|------|-----|-----|-----|-----|---------|
| Sample size, n           | 936    | 277    | 29   | 185 | 157 | 150 | 138 |         |
| Body surface area, n (%) |        |        |      |     |     |     |     | < 0.001d |
| Mild (0–2%)              | 305    | 64     | 13   | 43  | 70  | 52  | 63  |         |
| Moderate (3–10%)         | 381    | 120    | 10   | 76  | 63  | 57  | 55  |         |
| Severe (>10%)            | 249    | 93     | 6    | 66  | 23  | 41  | 20  |         |
| DIQI score, mean (% CI)  | 5.1    | 5.4    | 3.8  | 6.1 | 4.4 | 5.8 | 3.3 | < 0.001e |
| Therapy type, n (%)      |        |        |      |     |     |     |     |         |
| Biologic                 | 431    | 146    | 11   | 58  | 76  | 61  | 79  | < 0.001d |
| Systemic                 | 384    | 96     | 16   | 62  | 75  | 78  | 57  |         |
| Topical or phototherapy  | 115    | 32     | 2    | 64  | 5   | 10  | 2   |         |
| None                     | 6      | 3      | 0    | 1   | 1   | 1   | 0   |         |
| BSA prior to current treatment, n (%) |        |        |      |     |     |     |     |         |
| Quartile 1 (0–10%)       | 237    | 81     | 10   | 40  | 43  | 32  | 31  | < 0.001d |
| Quartile 2 (11–20%)      | 353    | 100    | 7    | 88  | 55  | 58  | 45  |         |
| Quartile 3 (21–30%)      | 175    | 49     | 0    | 28  | 29  | 31  | 38  |         |
| Quartile 4 (31–90%)      | 164    | 47     | 9    | 27  | 29  | 28  | 24  |         |
| Not reported             | 7      | 0      | 0    | 2   | 1   | 1   | 0   |         |
| Days on prescription, n (%) |        |        |      |     |     |     |     | < 0.001d |
| Quartile 1 (0–5 days)    | 207    | 61     | 6    | 23  | 38  | 51  | 28  |         |
| Quartile 2 (6–12 days)   | 263    | 69     | 5    | 46  | 58  | 31  | 54  |         |
| Quartile 3 (13–18 days)  | 126    | 41     | 4    | 25  | 22  | 17  | 17  |         |
| Quartile 4 (19–168 days) | 194    | 63     | 5    | 21  | 30  | 38  | 37  |         |
| Not reported             | 146    | 43     | 9    | 70  | 9   | 13  | 2   |         |

DEU, Germany; ESP, Spain; FRA, France; ITA, Italy; DIQI, Dermatology Life Quality Index; CI, confidence interval; BSA, body surface area. *The U.S. population has 30 apremilast users, which is 100% of the apremilast-user population in the pooled sample. **Biologic: using any biological therapy from adalimumab, etanercept, infliximab, ustekinumab or golimumab; systemic therapy, no biologic and using any systemic therapy from methotrexate, ciclosporin, acitretin, apremilast, fumarate or other; topical or phototherapy: no biological or systemic therapy and using any phototherapy/topical therapy from topical steroid, topical nonsteroid, phototherapy, systemic steroid or local injected corticosteroid. †Days on prescription for biological systemic or nonbiological systemic therapies only. £Pearson’s χ² test. ‡One-way ANOVA.
dollars (95% CI 2806–4378), 7478 U.S. dollars (95% CI 6575–8382) and 12 194 U.S. dollars (95% CI 10 886–13 501), respectively. Again, presenteeism contributed the most to indirect costs associated with total WPL (Fig. 2b).

Analysis by country

Mean percentage of work hours lost per patient relative to total WPL was highest in Italy (25–0%, 95% CI 21.8–28.2) and lowest in the U.K. (12.7%, 95% CI 5.7–19.8). The highest mean percentage of work hours lost due to absenteeism was in Germany (5.8%, 95% CI 3.7–8.0) and due to presenteeism in Italy [(22.5%, 95% CI 19.3–25.6) (Fig. 3a).

Mean annual indirect costs due to WPL per patient were highest in the U.S.A. (9591 U.S. dollars, 95% CI 8407–10 775), reflecting a particularly high contribution from presenteeism (9173 U.S. dollars, 95% CI 8063–10 283).

Presenteeism costs constituted the majority of costs in all countries (> 85%), with average absenteeism costs generally being < 1000 U.S. dollars per patient. Germany was the exception, as mean costs due to absenteeism were higher at 3281 U.S. dollars (95% CI 1936–4626), representing 35% of total WPL costs. The lowest mean costs due to total WPL were in Spain (3742 U.S. dollars, 95% CI 3036–4449) (Fig. 3b).

Predictors of total work productivity loss

The summary analysis in Table 3 demonstrates that severe psoriasis was associated with 3.9% and 9.1% greater WPL than

Figure 2. Percentage of work hours lost and annual indirect costs per patient due to absenteeism, presenteeism and total work productivity loss (WPL) by severity of psoriasis. (a) Percentage of work hours lost due to absenteeism and presenteeism and total WPL by severity of psoriasis for the pooled respondents; (b) annual indirect costs per patient associated with absenteeism, presenteeism and total WPL by severity of psoriasis for the pooled respondents. Pooled analysis of 936 respondents, where 32.6%, 40.7% and 26.6% of all respondents had psoriasis severities defined as mild body surface area (BSA) (0–2%), moderate BSA (3–10%) and severe BSA (>10%), respectively. Error bars indicate 95% confidence interval. USD, U.S. dollars. [Colour figure can be viewed at wileyonlinelibrary.com]
moderate and mild disease, respectively ($P = 0.001$). Appendix S1 contains full results of the multivariate analysis (see Supporting Information).

Having another autoimmune disease in addition to psoriasis (e.g. Crohn disease, rheumatoid arthritis, lupus) was associated with 11.0% higher total WPL than not having another autoimmune disease ($P < 0.001$). Being a patient in Italy was associated with a total WPL 15.5% higher than being a patient in the U.S.A. ($P < 0.001$).

Figure 4 illustrates the impact of increasing DLQI score on each outcome. In particular, a one-unit increase in the DLQI score increased total WPL by 1.8% ($P < 0.001$). This further demonstrates the important contribution of presenteeism to total WPL, given the strong linear relationship between these parameters.

**Discussion**

This study addresses a research gap on the economic burden of psoriasis by providing intercountry comparative data on total WPL and associated costs. Results demonstrate that WPL is a major contributor to indirect costs related to psoriasis. After controlling for patient demographic and clinical characteristics, disease severity and HRQoL were correlated with WPL.

Information on WPL directly relating to psoriasis and its associated indirect cost estimates is limited. Some studies estimated productivity losses due to any health problems, which may have overestimated the contribution of psoriasis in costs associated with WPL.34 Furthermore, the value of other studies directly assessing lost productivity due to psoriasis may be
limited given low patient numbers and considerable variability in methodology and subsequent results.\textsuperscript{35,36}

A study evaluating the economic burden of moderate-to-severe plaque psoriasis among Canadian adults reported mean lost productivity costs of \(3442\) Canadian dollars per patient, which accounted for 43\% of the mean annual costs of psoriasis.\textsuperscript{37} In a Finnish study, psoriasis accounted for 38\% of the total lost productivity costs, with other medical reasons contributing 62\%. One-fifth of patients reported absenteeism due to psoriasis and one-third of patients worked despite their psoriasis.\textsuperscript{6}

Our study converts work loss due to WPL into indirect costs, which provides an important insight into differentiating the potential financial impact of absenteeism from that of presenteeism. Prior work suggests limitations regarding the conversion of presenteeism into lost productivity.\textsuperscript{38} However, research in this area continues to evolve and our study, with its robust methodology across countries, improves upon prior work.

This study contributes to the evidence on the economic burden of psoriasis by measuring total WPL and related indirect costs using the same methodology at the same time point in six countries. In addition, it provides insight into predictors of WPL associated with psoriasis severity. We compared factors such as patient demographics, socioeconomic traits, disease severity, HRQoL and treatment patterns across countries, all of which showed to have an important influence on WPL and related indirect costs among patients with psoriasis.\textsuperscript{1,2,8,11,39,40} Our study showed that on average the proportion of work hours lost due to total WPL is about 30\% in patients with severe psoriasis. Furthermore, we found that total WPL increases progressively with severity of disease that was translated to increases in indirect costs. Presenteeism contributes considerably more than absenteeism to total WPL and associated costs across all levels of disease severity and all countries studied.

This finding is consistent with growing evidence regarding the importance of presenteeism related to other conditions. One study suggested that presenteeism accounts for up to 87\% of costs related to WPL in patients with arthritic pain and 74\% in patients with back pain.\textsuperscript{41} Another study suggested that presenteeism accounts for 68\% of the cost of health-related lost productive time in obese employees.\textsuperscript{42} Furthermore, in a cross-sectional study of U.S. patients with rheumatoid arthritis, the contribution of presenteeism to total lost productivity costs was approximately 70\%.\textsuperscript{43}

Our study provides important insights into differences across countries, with Italy demonstrating the greatest loss of work hours due to total WPL. The U.S.A. had the highest annual mean indirect costs associated with WPL, which reflects the higher GDP per capita in the U.S.A. These high costs in the U.S.A. were noted, despite the corresponding figures for mean percentage of work hours lost per patient being lower compared with Germany and Italy, possibly reflecting potential differences in clinical treatment practices between countries. Some differences in WPL and economic impact may reflect the variation in the proportion of patients with severe psoriasis and societal differences between countries, as well as the relative contribution of absenteeism vs. presenteeism across countries. In this regard, absenteeism contributed more to total WPL in Germany than in other countries.

The DSP survey was an observational design to provide a holistic benchmark of the psoriasis patient population. The DSP may underestimate the WPL because it does not consider patients who might become employed if their psoriasis were less severe/better controlled. Although physicians are requested to collect data on a series of consecutive patients to avoid selection bias, in the absence of true randomization, this process is contingent on reporting by the participating physician. Physician selection bias may also introduce potential limitations, as the physicians surveyed provide a pragmatic sample and may not be completely representative of the overall population of physicians treating psoriasis.

This study consisted of patients who have had moderate-to-severe psoriasis at some point in their disease history, that is patients who would have potentially been eligible at some stage of their disease.
point to receive biological medication. Patients who have been assessed by their physician as ever having only mild psoriasis were excluded from the sample. Therefore, this study can be generalized in the population who have at some point been moderate/severe, including those patients who might be assessed currently with mild disease but who have previously

Figure 4 Predicted mean absenteeism, presenteeism and total work productivity loss relative to Dermatology Life Quality Index (DLQI) score. Impact of increasing DLQI score on predicted mean absenteeism (a), presenteeism (b) and total work productivity loss (c). Error bars indicate standard error of the mean. DLQI, Dermatology Life Quality Index.
had a history of moderate-to-severe psoriasis. Further research would be needed to assess differences in subgroups of patients with mild disease, comparing any differences in patients who currently have mild psoriasis but who have a history of severe disease compared with those who only ever had mild psoriasis.

This study enhances our understanding of intercountry differences in patient characteristics by surveying patients in a similar time frame. However, these intercountry comparisons need to be interpreted in light of differences in healthcare and social security systems; particularly regarding the U.S.A., where private insurance is much more common than in the EU. Further detailed research is needed on a country level to assess the relative societal burden of psoriasis in different countries, as fundamental differences in provision of health and social care could result in different policy measures for treating patients. Finally, our comparisons between patient groups considered general morbidity as captured within the Charlson comorbidity index. Other factors not captured within this index may also result in differences in disease burden and cost. This, too, is an area for future research.

The human capital method used to estimate productivity costs assumes that companies employ personnel until the marginal value of a worker’s productivity equals the marginal costs of labour, or the worker’s wage. However, in the real world an absent worker may be replaced on an interim basis or permanently, often by a less suitable employee, thus incurring recruitment and training costs, while still generating some productivity. These factors are not considered in the human capital method.\(^4^\)\(^4\) However, given that in our study absenteeism was not a large contributor to total WPL, the impact of absenteeism in the real world should be relatively small. It should also be considered that applying the same GDP per capita to all patients within a country does not reflect variations within that country such as income distribution. Finally, the economic impact of patients who are unemployed due to their psoriasis is not accounted for in our analysis. This may lead to an underestimation of the potential for improvement in WPL if the burden of psoriasis was decreased by treatments. In addition, because by design only patients in employment were included, the authors are not able to quantify the costs of patients who were unemployed because of psoriasis; again, this is an area for further investigation.

Lastly, due to the small sample size in some countries (i.e. the U.K.), the recommendations and conclusions drawn from our study have to be interpreted with caution and carefully considered before generalizing to other populations/countries.

In conclusion, this study contributes to our understanding of the global economic burden of psoriasis by demonstrating that WPL correlates with severity of psoriasis and HRQoL in the employed population. It also provides an important insight into predictors of total WPL associated with psoriasis in six countries. Consequently, therapies that effectively treat psoriasis and improve HRQoL are likely to have a positive impact on WPL and hence the considerable economic burden of psoriasis.

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Additional Supporting Information may be found in the online version of this article at the publisher’s website:

Appendix S1 Predictors of total work productivity loss as assessed by multivariate analysis.

Powerpoint S1 Journal Club Slide Set.