

Challenges in Economic Evaluation of Psoriatic Arthritis

Psoriatic arthritis (PsA) is a heterogeneous chronic inflammatory disorder of the peripheral joints, peripheral entheses, synovial sheaths of tendons, and spine associated with psoriasis. PsA is characterized by different clinical phenotypes and its course is variable¹. Patients can also have gut² and eye involvement³. In addition, patients with PsA or psoriasis have increased frequency of insulin resistance, obesity, type 2 diabetes, metabolic syndrome, hypertension, hyperlipidemia, and cardiovascular disease compared with the general population⁴. Recently, a new designation has been proposed with the aim to cover all these clinical situations: psoriatic disease⁵.

In the past, PsA was considered a rare and mild disease. The prevalence of psoriasis in the general population is currently estimated to be around 2%–3%, with one-third of patients developing associated musculoskeletal manifestations. In the last 20 years, evidence has been gathered demonstrating that PsA is destructive and deforming in 40%–60% of patients, with joint damage emerging in the first years of the disease course⁶. It is believed that around 20% of patients with PsA develop a serious destructive disease. Patients with PsA suffer from functional impairment, decreased quality of life (QOL), and psychosocial disability, and have a significant increase in mortality versus the general population^{7,8}.

Therapies for PsA have been inadequate until recently. Nonsteroidal antiinflammatory drugs are useful in improving symptoms but have no effect on the progression of radiographic joint damage. Local corticosteroid injections may be of great aid in patients with persistent mono- or oligoarthritis but use of systemic glucocorticoid treatment is not supported by evidence. Traditional disease-modifying antirheumatic drugs (DMARD), which are the second-line treatment, are employed in PsA to control symptoms, but there is no evidence that they slow the progression of structural joint damage.

The introduction of tumor necrosis factor- α (TNF- α) blocking agents has transformed the management of PsA. These drugs minimize signs and symptoms of inflammation, increase functional capacity and QOL, and decrease the progression rate of structural damage in peripheral joints^{9–11}.

However, TNF- α blockers are very expensive and not directly accessible to all patients, depending on either a national health system or private insurance.

Illness costs in PsA were high even without these drugs and not much more different from those in other chronic inflammatory rheumatic diseases. Huscher and coworkers compared indirect and direct costs of illness in rheumatoid arthritis (RA), ankylosing spondylitis (AS), systemic lupus erythematosus (SLE), and PsA by evaluating the effect of disease duration, self-assessed health status, functional status, and demographic markers on the different cost domains¹². The authors utilized data from a large number of patients aged < 65 years from the National Database of the German Collaborative Arthritis Centres. Mean direct costs were €4737 per year in RA, €3676 in AS, €3191 in SLE, and €3156 in PsA. Taking into account indirect costs applying the human capital approach, total costs increased to €15,637 in RA, €13,513 in AS, €14,411 in SLE, and €11,075 in PsA while with the friction cost approach values were €7899, €7204, €6518, and €5570, respectively. Costs were strongly associated with functional status and disease duration. The authors concluded that costs were high in all 4 diseases and chiefly determined by functional capacity. In the Psoriatic Arthritis Cost Evaluation (PACE), an Italian cost-of-illness study on TNF- α inhibitors in patients with PsA with poor response to traditional DMARD, the cost per patient of PsA treatment for society in the 6 months prior to the start of anti-TNF- α therapy was €1519.17¹³. This value corresponds to the approximate computation of probable cost per year of €3100, which differs from the total cost of €11,075 found by Huscher, *et al* in Germany¹². The higher functional status and the shorter disease duration in the Italian study together with different types of costs may account for the differences. A recent study from Hungary ascertained total costs for PsA as €5574/patient/year¹⁴. Mean direct medical costs accounted for €1876, direct non-medical costs for €794, and indirect costs for €2904.

Costs are also high for patients with only skin lesions^{15–17}. In 2006, Javitz and coworkers evaluated the direct cost of medical care for psoriasis and PsA in US adults utilizing a limited societal perspective¹⁵. Indirect

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and intangible costs were not taken into account. Direct medical costs (outpatient and office procedures, outpatient and physician office visits, prescription medications, over-the-counter medications and hospitalizations) were acquired from privately and publicly accessible databases and from the literature. An estimation of annual costs was applied to the US population in 1997 based on 1997 dollars. The total cost for about 1.4 million patients with psoriasis or PsA was \$649.6 million. Outpatient physician visits accounted for \$86.6 million, dermatologic prescription drugs for \$147.9, photochemotherapy for \$27.4, over-the-counter medications for \$357.2, and hospitalizations for \$30.5 million. Total annual costs were about \$452 per person with clinically significant psoriasis or almost \$718 per person with clinically significant and active psoriasis. The total annual cost in the above study¹⁵ was less than the cost of \$1.09 billion and \$4.32 billion found earlier by Kraning and Odland¹⁶ and Krueger, *et al*¹⁷, respectively. The major reason for these differences was the lower number of hospitalization days compared with the previous years due to availability of better drugs for improving symptoms and to higher use of day-treatment clinics. Ackermann and Kavanaugh in their review of the economic burden of PsA emphasized the main weaknesses of this study¹⁵: the lack of assessment of indirect costs and the absence of separate rates for PsA in the cost evaluation¹⁸. Actually, indirect costs are very high in PsA, especially as a result of productivity losses due to sick leave and extensive work disability.

In this issue of *The Journal*, Zhu and coworkers report the results of their study on direct and indirect costs of PsA in Hong Kong¹⁹. The average annual direct and indirect costs were \$4141 and \$3127 (2006 US dollars), respectively. They found that pain and function were significantly associated with costs and suggest that treatments to reduce pain and restore function are highly likely to reduce costs incurred by patients with PsA. However, no patient participating in the study was treated with TNF- α blockers since these drugs are not within the Hong Kong government's reimbursement system, and patients have to pay for treatment themselves.

The study by Zhu and colleagues raises a question: should a public health system reimburse anti-TNF- α therapy to reduce the costs of treatment of PsA? In other words, are anti-TNF- α inhibitors cost-effective? The cost-effectiveness studies on anti-TNF- α blocking agents in PsA performed so far have demonstrated that these drugs are cost-effective for both the cutaneous and musculoskeletal manifestations of psoriatic disease²⁰⁻²⁵. Most of these studies were carried out using data obtained from published international clinical trials²⁰⁻²⁴ and one was performed in a clinical practice setting¹³. In the PACE study, 107 patients from 9 Italian rheumatology centers, with different forms of PsA that responded inadequately to conventional treatment, were given anti-TNF- α agents, mainly etanercept¹³. Cost

(expressed in 2007 Euros) and utility (measured using EuroQOL) before and after start of TNF- α therapy were evaluated to estimate the incremental quality-adjusted life year (QALY) gained and calculate a cost-effectiveness acceptability curve. The study was performed from the viewpoint of the community, the largest entity that can have a point of view, and which includes the Italian third-party payer (the National Health System), patients, and their families. After 12 months of anti-TNF- α therapy, there was a significant escalation of direct costs due to the increased drug cost of anti-TNF- α agents, which was only partially compensated by the reduction of indirect costs. In the last 6 of 12 months of anti-TNF- α therapy, direct costs increased by €5052, the cost for the Italian National Health System by €5044, and the social cost by €4638. However, a gain of 0.12 QALY produced a cost per QALY gained of €40,876 for the Italian National Health System and of €37,591 for society. The acceptability curve demonstrated that there would be a 97% likelihood that anti-TNF- α therapy would be valued as cost-effective at the willingness-to-pay threshold of €60,000 per QALY gained suggested for Italy. One of the values of the Italian study was the demonstration that anti-TNF- α therapy is cost-effective in the short term in clinical practice.

In conclusion, the study by Zhu, *et al*¹⁹ underlines that the socioeconomic burden of PsA is considerable and is not different from that of RA and AS. Anti-TNF- α agents, which are more expensive than conventional drugs, reduce disease activity and improve function and QOL and are, therefore, able to reduce direct and indirect costs due to PsA. Recent studies have shown their cost-effectiveness. It is desirable that other pharmacoeconomic studies be performed on these drugs in the near future. However, it is essential that these agents be less costly. The expected introduction of other biologic drugs together with the influence of market forces could lower their costs.

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