EXPERT REVIEWS

Health economic issues in psoriasis

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In today's healthcare environment, there is a much greater focus on the costs needed to achieve a given benefit, and this applies as much to dermatology as any other clinical setting. Cost–benefit analyses in medicine provide a basis for comparing options and take into account two important economic principles:

- There is usually a trade-off between costs and benefits
- The notion of value (personal choice)

In medicine, there has been a significant investment in disease research and pharmaceutical development, which has led to the introduction of a relatively large number of new active substances that are clinically more effective and/or safer to use, and this has benefited many patients in a wide range of diseases. However, these newer products are generally more expensive and there is increasing pressure on healthcare resources and/or costs. Indeed, many countries have expressed a concern with regard to the growth in healthcare spending over the last 10 years. Nevertheless, despite an increase in health-related expenses over this period (for example it was between 2 and 5% in Germany), there has not been a significant increase in health costs per year when related to gross national product. This indicates that, in the current economic environment, most countries, such as Germany, can afford the healthcare costs that are being consumed. Interestingly, there is a wide variation between different countries in terms of the percentage of gross national product that is allocated to healthcare delivery, with the USA spending the most (13.9% in 2002; FIGURE 1).

With increased pressure being placed on governmental spending and policy, there is greater pressure to control healthcare spending. The problem is potentially exacerbated by the very success that good healthcare brings, in that individuals are surviving longer and the population of elderly individuals is becoming larger in most developed countries. This drives up demand and increases the pressure on healthcare resource allocation. Management of the demand–allocation equation generally involves state intervention and a level of regulation that stipulates what is and is not acceptable.

In this environment, health economics is a valuable tool since, on the one hand, it can value the input (costs) and, on the other, it can compare outcomes (clinical benefits). An example of this is pharmacoeconomics, which interrogates the value of drug therapy – comparing cost of treatment at the input level and balancing this against efficacy, effectiveness and quality of life [QoL]) and any secondary cost benefits associated with treatment at the output level. This data is becoming a mandatory requirement for many regulatory authorities prior to product approval and endorsement.

In the field of dermatology, we face the challenge of working in this more regulated environment and, to do this, we must understand the language of the policy makers as they relate to our patients. FIGURE 2 highlights some of the health economic issues that are relevant in a cost analysis in patients with psoriasis.

Cost of illness in psoriasis

Our group performed a cost-of-illness study in Germany involving 184 patients with moderate-to-severe plaque psoriasis. The mean total cost for managing each patient is shown in TABLE 1 and these extrapolate out to an average cost of €6709 per year Patients not on systemic therapy had the lowest annual cost (€4088 per year) followed by patients on systemic therapy (€7148 per year), while 'high-need' patients induced the greatest costs (€8831 per year). Not considered in this

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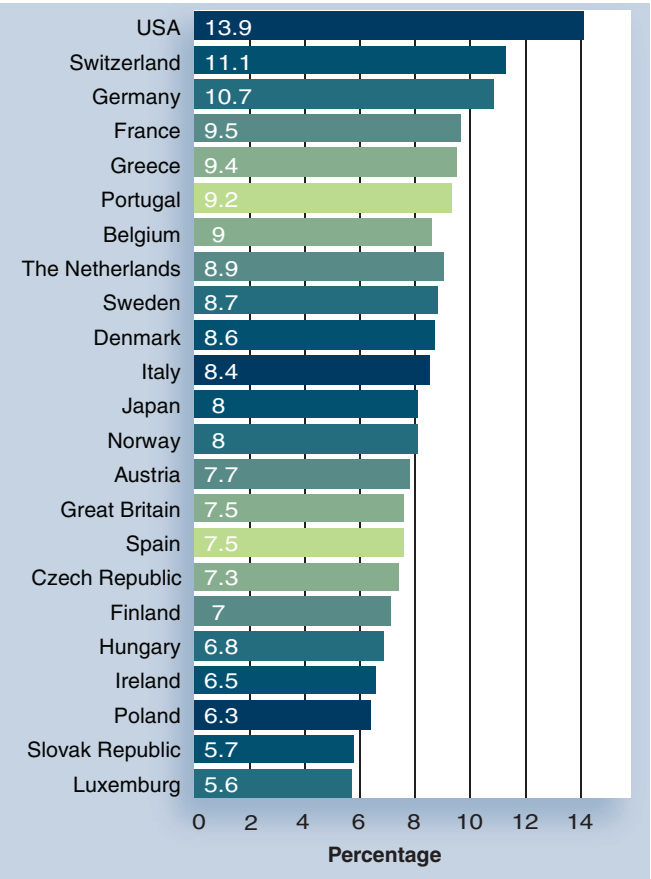

Figure 1. Health expenses as a percentage of gross national product in 2002.

analysis were any costs related to the reduction in QoL associated with the disease and this is an important consideration for many patients with moderate to severe psoriasis. QoL cannot be measured directly in monetary units, and so they are termed intangible costs in economic analyses. Factors affecting QoL include physical, mental and social factors such as itching, pain, depresssion, frustration or stigmatization. There are also treatment-related effects to take into account, such as adverse reactions to therapy, problems with topical treatment, time consumed, treatment in clinic and frequent physician visits. Importantly, if we can reduce the burden associated with psoriasis therapy, this will have two positive effects: first, it will reduce the intangible costs and, second, it should improve treatment compliance. Both will result in a net economic benefit.

Benefits

With respect to benefits to the patient, there are a number of different ways of assessing these, such as improved clinical outcome (reduction in Psoriasis Area and Severity Index [PASI] scores), lower costs and, perhaps most importantly, we have patient-reported outcomes in health. The latter is more difficult to estimate, but we now have tools to assist us in measuring patient benefit in terms of:

- Psychological burden, for example, depression, anxiety and helplessness
- Patient utilities, for example, willingness to pay and trade-offs
- QoL
- Patient-defined benefits (including patient benefit index)

Quality of life is such an important consideration in psoriasis that physicians should try to consider the disease from the patient's perspective and not simply treat the skin lesion. In this regard, the patient is the only person who can provide the relevant information and the introduction of the Dermatology Life Quality Index (DLQI) has greatly facilitated this process; it is one of the key instruments for documenting patient-reported benefits and outcomes. Interestingly, there is not a strong relationship between the severity of psoriasis (as measured by PASI) and the negative impact of the disease on QoL of the patient (as measured by DLQI). This means that, when determining cost–benefit ratios, the PASI should be used as an indicator of clinical outcome related to cost, whereas the DLQI should be used as a measure of QoL outcome related to cost. In a cohort of 1511 representative psoriasis patients in Germany, we found that approximately 35% had severe or very severe disease based on DLQI scores (Figure 3).

Another concept of beenfit assessment developed in the past years is the evaluation of patient-defined benefits. Briefly, patients before treatment are asked to rate their personal treatment goals (structured patient needs questionnaire). After treatment, patients are asked in as far the previously defined goals have been achieved (patient benefit questionnaire). By weighing the outcomes with the patient's preferences, a single

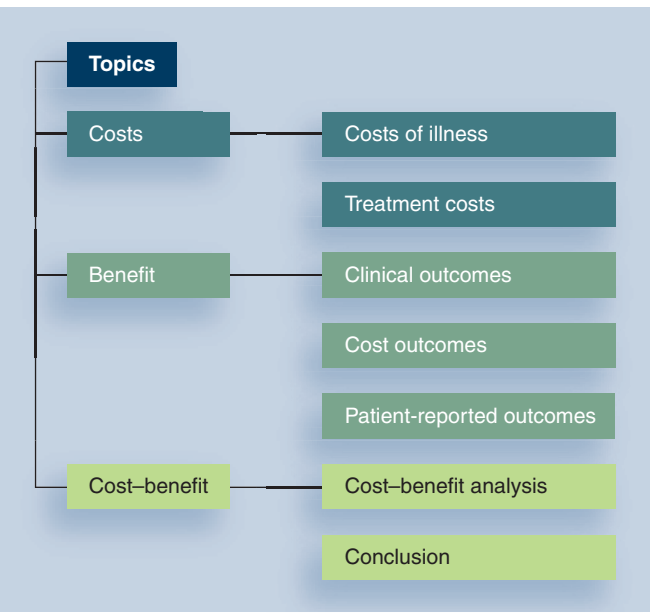

Figure 2. Health economic issues in psoriasis.

Table 1. Mean costs per patient per year in Euros for treating 184 patients with moderate-to-severe psoriasis in Germany.

- Indirect costs: 1.310
- Total: 6.709
- Including:
  - Pat without systemic tx: 4.088
  - Pat with systemic tx: 7.148
  - 'High-need' pat: 8.831

Costs per patient per year in Euros (n = 184).
Reproduced with permission from [6].

outcomes measure, patient benefit index (PBI) is calculated. The distribution of the PBI in a given treatment arm or any other intervention group is a very sensitive indicator of patient-defined benefits [1,2]. the PBI can be used for clinical trials, allocation decision as well as for pharmacoeconomic considerations. Moreover, it permits the monitoring of patients in routine practice (Figure 4).

Cost versus benefit

This is the process of balancing the costs of treatment on the one hand with the benefits of treatment on the other and, in practice, there are three types of analysis:

- Cost versus symptomatic improvement (e.g., PASI), representing a 'cost–effectiveness' analysis
- Cost versus an outcomes cost improvement, representing a 'cost–benefit' analysis
- Cost versus an improvement in QoL (e.g., QUALYS), representing a 'cost–utility' analysis

Cost–effectiveness analysis

Cost–effectiveness analysis is best defined as the cost required to produce a clinical response; in psoriasis, it could be the cost to achieve a 75% reduction in PASI from baseline (PASI-75). An example of a cost–effectiveness study in psoriasis was published by Hankin and colleagues in 2005, in which they assessed the cost–effectiveness of psoriasis treatment from a US perspective [3]. The analysis involved a number of steps, such as evaluating the costs of range of psoriasis treatments in the US, reviewing the clinical literature for the various products to determine improvement in PASI, estimation of the total costs of care and, finally, a cost-effectiveness analysis. The results of this analysis in terms of the costs to achieve PASI-75 are highlighted in Table 2. The analysis confirms the cost–effectiveness of a relatively inexpensive drug, such as methotrexate, but it must be emphasized that the patient groups in these studies were not comparable and drugs such as infliximab were evaluated as second-line therapy in patients with more severe psoriasis.

Cost–benefit analysis

A cost–benefit analysis compares the costs of treatment with outcome benefits measured also in terms of costs. A very simple example of cost–benefit analysis is a comparison of early- and late-intervention in psoriasis as depicted in Figure 5. Early intervention that is able to alter the course of psoriasis may be able to avoid some of the higher costs, which are associated with more severe disease. So, while early intervention may be initially more expensive, if it can avoid some of the higher costs associated with disease progression, it will likely produce a clear cost–benefit.

Cost-utility analysis

Cost utility is used by a number of regulatory authorities in the decision-making process when assessing new drugs. In particular, they use the concept of the quality-adjusted life year (QALY), which is a measure of health (utility) over time. The change in the utility value induced by a new therapy multiplied by the duration of treatment provides the number of QALYs gained. The total cost of treatment divided by this number gives us the cost/QALY and this is used in a number of countries for making reimbursement decisions. Some countries, such as the UK, do this by maintaining cost/QALY league tables that provide an indication of the cost for delivering a health outcome. An example of this in psoriasis was published by NICE in the UK when they calculated

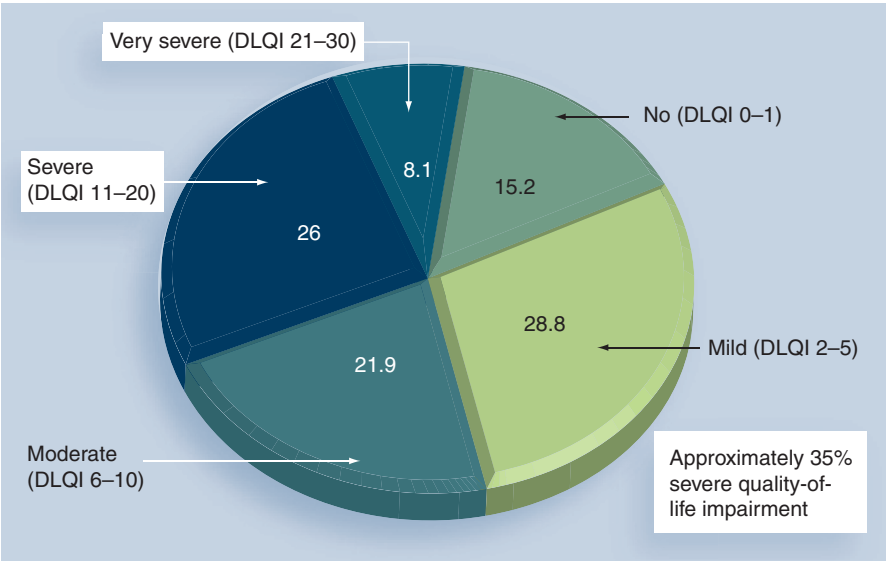

Figure 3. Quality of life in psoriasis. Distribution of disease severity based on DLQI scores in a representative sample of 1511 patients with psoriasis attending German clinics. DLQI: Dermatology Life Quality Index. Reproduced with permission from [4].

Table 2. A cost–effectiveness analysis in moderate-to-severe psoriasis (adapted from Hankin *et al*. 2005).

Treatment	Annualized costs of care ($)					Cost–effectiveness			
	Rx	Del	Mon	AE	Total	PASI %	PSAI1	Cost/year (PASI-50)	Cost/year (PASI-75)
Methotrexate 7.5 mg	595		1188		1783	58.4	31	1526	2290
Methotrexate 15 mg	1190		1188		2378	71.6	33	1660	2491
PUV-A	3737		106	11	3854	92.9	41	2074	3111
	3737		106	11	3854	61.1	63	3154	4731
Broadband UVB + acitretin 25 mg	3792		618	54	4464	80.7	55	2766	4149
Broadband UVB	4600		106	18	4724	83.7	56	2822	4233
	4807		106	18	4931	80.1	62	3078	4617
	4558		106	18	4682	47.0	100	4981	7472
Narrowband UVB	4558		106	18	4682	73.0	64	3207	4811
PUVA + acitretin 20 mg	6773		618	49	7440	97.3	76	3823	5735
Cyclosporine 3 mg/kg	5019		1794	138	6951	52.0	134	6683	10,025
Cyclosporine 1.5 mg/kg	2789		1794	138	4721	33.4	141	7067	10,600
Acitretin 50 mg	12,359		618	83	13,060	60.4	216	10,811	16,217
Infliximab 5 mg/kg	24,898	1422	116		26,436	82.8	319	15,964	23,946
Etanercept 50 mg	21,052	0	106		21,158	64.2	330	16,478	24,717
Efalizumab 1 mg/kg	17,836	0	163		17,999	52.0	346	17,307	25,960
Alefacept 15 mg/M	23,880	806	2412		27,098	45.0	602	30,109	45,163

AE: Adverse effect; Del: Delivery; Mon: Monitoring; PASI%: Adverse percentage change in Psoriasis Area and Severity Index score from baseline to end point; PUVA: Psoralen with UVA; Rx: Therapy.
Data from [3].

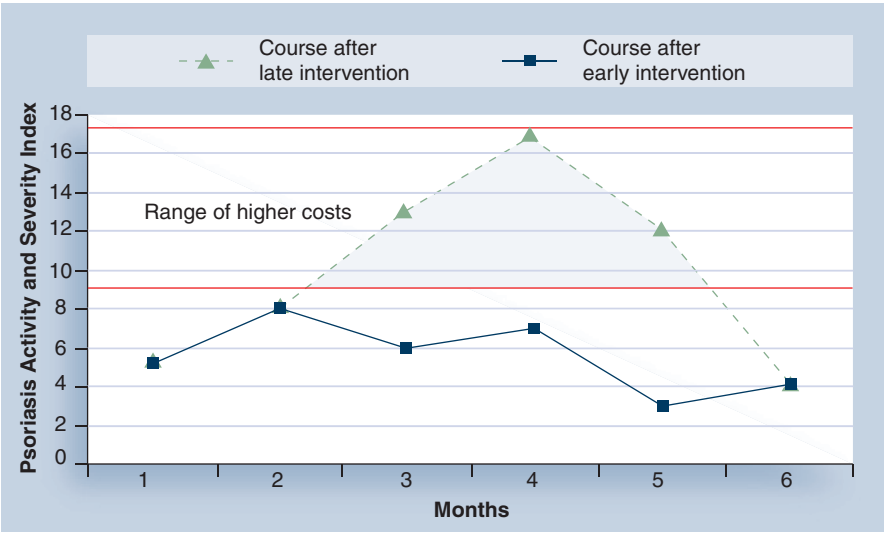

Figure 4. Cost–benefit effects of early intervention in psoriasis. Adapted from [4].

costs/QALY for infliximab (€38,000 for all psoriasis patients) and etanercept (€55,000–80,000 for all patients and €36,000–38,000 for high-need patients).

Are psoriasis patients receiving the level of healthcare they need?

An issue that was raised in a national German study involving a cohort of 1511 representative psoriasis patients was that of undertreatment; particularly in patients with more-severe disease. In total, 19.4% of this German cohort had severe disease and they had a reduced QoL (DLQI 12.5 vs 8.6), had more days off work per year (11.7 vs 3.9) and a greater number required hospital treatment (50 vs 23%) compared with

patients with less-severe disease [4]. Despite these poor results, only 45.4% of patients with severe psoriasis had received systemic therapy.

One question that arises from these data is whether or not these findings are specific to Germany or do they occur elsewhere? While not specifically addressing the problem as it pertains to psoriasis, we can learn from the experience of biologic therapy in rheumatoid arthritis. In 2006, Kobelt carried out an interesting international comparison of the use of biologics for the treatment of rheumatoid arthritis following reimbursement. Uptake (prescription) of the new drugs was fastest in countries such as the USA and Sweden and slowest in Germany [5].

This means that, in some countries, if we want the best treatments for our patients, then we may have to argue strongly for them. To help us in this regard, we will need to be cognizant of the clinical and cost–effectiveness advantages of drugs such as infliximab and, ultimately, it will be value and benefits that will be important rather than cost.

Questions & answers

In the cost–effectiveness study that you reviewed, methotrexate was shown to be very cost-effective compared with the biologics. Should we be using methotrexate more widely?

In countries where there is an underprovision of healthcare and systemic therapy is required, then methotrexate is a good choice. However, the studies reviewed did not include identical groups of patients and, while there are clearly patients who will benefit from methotrexate, there are many who will benefit from biologic therapy. My view is that, in patients with more severe disease, we need to increase the prescription of systemic therapy generally – methotrexate and biologics where appropriate.

What are the key cautions and limitations of the interpretation and use of QALYs?

There are several technical limitations, such as how do you calculate the utilities when there are a number available (they will potentially give you different QALYs for the same drug). Also, QALYs do not take into account the preferences of the individual patient or physician.

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