Psoriasis is one of the commonest skin disorder seen in dermatological clinical practice. Prevalence is up to 2% of the population\textsuperscript{1} throughout the world.\textsuperscript{27} Psoriasis is characterized by hyper proliferation and abnormal differentiation of epidermal keratinocytes, lymphocyte infiltration consisting mostly of T lymphocytes and various endothelial vascular changes in the dermis such as angiogenesis, dilatation and high endothelial venule formation.\textsuperscript{28}

Psoriasis is a complex disease in which there are erythematous, sharply demarcating papules and rounded plaques covered by silvery scales. Psoriasis is an immune mediated genetically determined common disorder which affects skin, nails, and joints has various systemic associations. It is a chronic condition of the skin which causes disfiguration, inflammation and proliferation, which has a significant influence of both genetic and environment. The distinguishing lesions involve red, scaly, sharply demarcated, indurated plaques, present particularly over extensor surfaces and scalp. The duration of the disease, the periodicity of flares and extent is different in different individuals.\textsuperscript{29}
EPIDEMIOLOGY:

**Incidence and prevalence:** The prevalence of psoriasis is different in various parts of the world. Most of the recent research show that the range extends from about 0.5% to close to 2.5%.

**Age of onset:**

Psoriasis can present at any age and can appear just after birth or in old age. A bimodal age of onset has been described with 2 peaks, an early one and a late one at after 40 years of age. Patients with family history of psoriasis tend to have an earlier age of onset.

**Familial occurrence:**

A high familial occurrence of psoriasis suggests that genetic factors play a role in its etiology. Psoriasis occurs with increased frequency in some families.
**Trigger factors:**

A wide variety of stimuli may facilitate the conversion from the pre-psoriatic state to overt psoriasis. These agents can induce psoriasis denovo in previously unaffected individuals or may precipitate psoriatic flares in remission.\(^\text{21}\)

a. Infections: Infections, primarily the bacterial infections, can induce psoriasis. Provoking infections have been observed in up to 45% of psoriatic patients. The most common infections are the streptococcal infections, especially pharyngitis is observed.

b. Trauma: Wounding the skin causes keratinocytes to release cytokines and growth factors capable of influencing epidermal proliferation and recruiting immune cells.\(^\text{21}\)

c. Endocrinal factors: Studies suggest that remission of psoriasis can occur during pregnancy but there is exacerbation during post-partum period.

d. Metabolic disorders: Hypocalcemia and dialysis also precipitate psoriasis.

e. Drugs: various drugs known to exacerbate psoriasis are lithium, Beta-blockers, antimalarials, NSAID’s.

f. Stress can exacerbate psoriasis. Psychogenic stress is a well-established systemic triggering factor in psoriasis.\(^\text{31}\) It has been associated with initial presentation of the disease as well as flares of pre-existing psoriasis. Exacerbations of psoriasis usually occur a few weeks to months after the stressful event.
g. Alcohol consumption, smoking and obesity: Obesity, increased alcohol consumption and an increased incidence of smoking have all been associated with psoriasis.\textsuperscript{32}

**Treatment of psoriasis:**
Every patient with psoriasis presents with a series of issues which are different for different individuals. Hence, the treatment for these patients depends upon age, sex, occupation, personality, general health, and the type, extent, duration and natural history of the disease.

The treatment modalities include coal tar, topical steroids, oral methotrexate, retinoids, cyclosporine, UVB phototherapy, photochemotherapy (PUVA) and the new agents like the biologicals. The trend in psoriasis therapy is based on the severity the treatment is decided.

**Psoriasis treatments**
Topical agents: Emollients, Anthralin, Topical Corticosetroids, Keratolytics like Salicylic acid, Tars, Topical retinoids like Tazarotene, synthetic form of Vitamin D like Calcipotriene

Phototherapy: UVB, Narrow Band UVB, Bath PUVA, Climatotherapy

Systemic therapy: Methotrexate, Retinoids, Cyclosporine, Azathioprine, Hydroxyurea, Mycophenolate mofetil

Biologicals: Secukinumab, Etanercept, Infliximab, Interleukin-10
Topical therapy

Corticosteroids

Since the introduction of corticosteroids, these have been the mainstay in treating all grades of psoriasis. It is used commonly due to its immunosuppressive, anti-inflammatory and antiproliferative properties, which make this class of drugs a useful therapy for this immune-mediated disease. The corticosteroids with low potency are predominantly suggested to apply on the face, groin, axillary areas, while high-potency corticosteroids are frequently used as primary therapy on all other areas in adults. There are superpotent corticosteroids which are used for cutaneous plaques or lesions on the palms, soles and also the scalp. It is available in various forms like lotions, solutions, creams, emollients, ointments, gels, and sprays. They are used in combination with the other agents.

Due to the severe side effect profile, the use of topical corticosteroids are limited or usually only continued for a very short period of time. These topical agents that have medium-potency and the ones that are highly potent can cause hypothalamic-pituitary-adrenal axis suppression.
With the use of topical corticosteroids there is skin atrophy which is seen, if these are used in excessive quantities, for long periods or on steroid-sensitive areas. There is purple striae which is seen on the skin and it is irreversible. However, tachyphylaxis is the biggest threat of them all and in order to avert these side effects of superpotent corticosteroids, Katz et al\textsuperscript{33} had industrialized a regimen in which a superpotent corticosteroid, betamethasone dipropionate is used as an optimized base, which was applied 3 times over a 24-hour period each week. This regimen has been called "weekend therapy" or "pulse therapy".

**Topical vitamin D analogs**

Calcipotriene is a synthetic analogue of Vitamin D3. This is shown to slow down the skin cell growth and remove the scales. Certain clinical trials showed a superior activity by calcipotriol when the comparison was made between calcipotriol and anthralin. It was preferred by patients because it did not stain to the extent of anthralin and was less irritating. This group of agents may not be as effective as the superpotent topical corticosteroids, but studies which compared a combination of both calcipotriene and superpotent corticosteroids have established superiority over either agent alone.\textsuperscript{34} Studies have shown that the addition of calcipotriene ointment to a regimen of superpotent corticosteroids can increase the duration of remission of psoriasis.\textsuperscript{35}
With the success of the halobetasol and calcipotriene regimen, attempts were made to examine the compatibility of both medications when they are combined, particularly since the calcipotriene molecule is easily destabilized. The combination of calcipotriene with other therapeutic modalities has also benefited patients. The common side effects of calcipotriene treatment include itching, rash, skin thinning and burning.

**Retinoids**

A vitamin A derivative, Tazarotene is a topical retinoid used to slow skin cell growth. Tazarotene gel is one of the most recently approved topical therapies for psoriasis. It is available in 0.05% and 0.1% gels, and a cream formulation has also been developed. Like calcipotriene, with its use the side effects of corticosteroids including atrophy, tachyphylaxis, and rebound effects are not seen. It has been shown that when this drug is used as a sole agent, patients have experienced irritation at the site of application. This retinoid dermatitis is worse with the 0.1% formulation, although the latter formulation is more effective than the 0.05% gel. The combination of tazarotene with topical corticosteroids has been studied for the purpose of avoiding retinoid dermatitis.

The most common side effects are skin irritation and dry skin and increased susceptibility to sunburn. While using tazarotene it is advised to use a sunscreen and wear sun-protective clothing. If you experience discomfort, burning, itching or stinging, check with your doctor.
Anthralin and tars

Since the 20th century topical anthralin has proven to be an effective treatment for psoriasis. The mechanism of action of anthralin in psoriasis is not very well understood, but it partly has to do with the anti-inflammatory effects and normalization of keratinocyte differentiation. Due to the availability of better drugs like the topical vitamin D analogues, the use of anthralin has been drastically reduced due to its side effect profile of causing irritation and staining of the skin. 36

Psoralen photochemotherapy:

Psoralen photochemotherapy (PUVA) is the combination of psoralens (P) and long-wave ultra violet radiation (UVA). This UVA radiation has a major impact on the mid and deep dermal components. So the therapeutic effect of the combination of both the agents brings about the therapeutic effect which cannot be seen when they are used individually. Due to the phototoxic reaction induced by the drug, there is remission of the disease seen. 19 UVA light aids in the activation of chemicals called as Psoralens. Psoralens are phototoxic compounds that can interact with various components of cells and cause the inhibition of DNA replication and in turn there is cell cycle arrest. 37
PSORALEN

The drug: Psoralens is obtained from *Ammi majus*, a particular kind of plant that grows in the Nile valley and babachee found in India, also called *Psoralea carylifoliae*. They are also found in large number of other plants such as limes, celery and cloves.\(^{21}\)

Chemistry: Psoralen are naturally occurring furocoumarins. The psoralen have also been synthetically produced, the best known is 4,5,8-trimethyl psoralen (TMP) which is shown to be less phototoxic after oral administration and is also used in the treatment of vitiligo. Methoxsalen 8-MOP is the most commonly used agent used for the treatment of psoriasis which is obtained from both plant and synthetic sources.\(^{21}\) Currently 8-MOP and 5-MOP (bergapten) are prescribed. There are newer psoralens under research like 5-methoxypsoralen, 3-carbothoxypsoralen and angelicin.\(^{19}\)
Pharmacology:

The oral preparations like 8-methoxypsoralen and 5-methoxypsoralens are available as crystals, micronized crystals or solubilized psoralens in gel matrix. The advantage of liquid preparations is that a higher and more reproducible peak plasma levels can be obtained than the crystalline preparations. When taken orally, methoxsalen (8-MOP) gets absorbed from the gastrointestinal tract and is distributed to all organs of the body. But if psoralen is not combined with the UV radiation the photochemical binding does not occur and will lead to rapid excretion. Extensive photosensitivity is seen in the first hour after the dose and it reaches a peak at about 2 hours and the effect wanes off after about 8 hrs.\textsuperscript{38}

When applied locally, 8-MOP rapidly penetrates skin and can be detected in urine after 4 hrs. The plasma concentration of TMP after bath treatment is approximately 1% of that obtained after oral ingestion. The equilibrium uptake of methoxsalen into psoriatic plaques has been shown to be twofold greater than for normal stratum corneum.\textsuperscript{38}
Mechanism of action:

The reaction of the skin to UVA (320-400 nm) radiation is evidently improved by the ingestion of methoxsalen. The exact mechanism by which 8-MOP produces its cutaneous photosensitivity is not known but following are the postulated mechanism by which it acts. All molecules are characterized by a particular absorption spectrum. The absorption spectrum of small molecules is narrow whereas of large molecules such as DNA, the absorption spectrum is very broad because of the variety of atoms and bonds contained within such a molecule. The photobiological effects of exposure to non-ionizing radiation involve the initial essential step of absorption of photons by molecules called ‘chromophore’. Once a photon is absorbed by a molecule, the energy is transferred to molecule which goes in for excited state. This absorbed energy can initiate a photochemical reaction. Psoralens as a monotherapy have no therapeutic benefit unless combined with long wave radiation in 320-400 nm range (UVA).
Methods of administration:

Psoralen can be applied topically to the localized lesions followed by UVA irradiation or delivered in bath water for generalized lesions followed by irradiation. Psoralens interact with UV radiation in UVA range. The therapeutic action spectrum of PUVA has been found to peak in the 320-335 nm wavelength range.²¹

Recommended dose of topical psoralen for PUVA

Lotion containing 0.1% to 1% 8-MOP is used. Vanishing cream consisting of 0.001% or 0.1% trimethoxsalen (TMP) can be applied over lesion.

Recommended dose for bathwater PUVA

Bath solution is prepared by adding 37.5 ml of 8-MOP in 100L of water in a bath tub, resulting in a final concentration of 3.75 mg/L. As differences in water temperature can alter the absorption kinetics of psoralens and thereby the minimal phototoxic dose (MPD), bath temperature should remain constant from treatment to treatment in order to reduce the risk of burning or under treatment. A temperature of 37.8°C appears optimal and is comfortable for the patient.⁴⁰
**Methotrexate (MTX)**

The anti-inflammatory, anti-proliferative and immunosuppressive properties makes methotrexate the drug of choice in psoriasis. This drug brings about its action by inhibiting dihydrofolate reductase (DHFR). This leads to the inhibition of the activity of thymidylate synthase which is an essential constituent for the synthesis of purines and pyrimidines, in turn important for the synthesis of DNA. The interference in that pathway is known to take place during the S-phase of the cell cycle, which causes the inhibition of growth and cell death (apoptosis) which is why it is helpful in psoriasis. By inhibiting DNA synthesis, MTX limits epithelial hyperplasia, reinforces the apoptosis of activated T cells, and inhibits the chemotaxis of neutrophils. The exact mechanism of action of MTX in psoriasis vulgaris still remains unclear. 41

**Dosing:** Methotrexate is administered as a weekly single oral dose. Doses are reduced to the lowest possible amount of drug needed to achieve adequate control of psoriasis with concomitant topical therapy.

**Duration of Dosing:**
- Treatment can be continued for as long as is necessary provided there are no meaningful signs of liver or bone marrow toxicity with adequate monitoring. Folic acid supplementation 1-5mg daily by mouth, except for the day of methotrexate dosing, reduces the frequency of side effects
Living with Psoriasis:

There is a lot of misunderstanding among general population which leads to discrimination and people keep away from patients, fearing the transmission of the disease. Psoriasis is a non-infectious condition and does not spread from person to person. It is also important to know that the discrimination and isolation of the infected persons carry a stigma and suffer humiliation leading to psychological depression, than physical morbidity. There is a need to remove myths regarding psoriasis from the community and the patient as well. Public attitude has to be changed from fear and hatred to sympathetic and sharing, this change in attitude can only happen through continuous education to the family, relatives and friends of these patients. The patients are supposed to be educated thoroughly regarding disease treatments and lifestyles which mend the humanistic aspect for the patients and it will also remove the apprehension and fear from the patient’s mind leading to improvement in QOL of the patients. The different instruments developed on validity to evaluate QOL are available through various web sources for utilization. The QOL instruments are generally of two types like generic and disease specific. These questionnaires cover varied aspects of a patient’s life like the symptoms, emotional facets, day to day activities, and impact on work, effect on personal relationships and also on the adverse effects of the treatment. The generic questionnaires focus on overall QOL whereas disease specific are designed to evaluate the QOL of patients in a particular condition.
PASI SCORE:

The clinical assessment of psoriasis is performed by clinicians using Psoriasis Area Severity Index (PASI). The locations of affected area are, the head (h), upper limb (u), trunk (t) and lower limbs (l), are independently recorded by using these parameters, erythema, induration and desquamation, each of which is classified on a severity scale of 0 to 4, where 0 = nil, 1 = mild, 2 = moderate, 3 = severe and 4 = very severe. The percentage association can be calculated as: 1 = less than 10% area; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; and 6 = more than 90%. The changes in the PASI score are reflective of effectiveness of a particular clinical intervention and an easy way to follow the prognosis of psoriasis. The humanistic outcomes are mainly mirrored by the PASI score hence this outcome in patients with psoriasis can be assessed using various instruments. The merits and demerits along with limitations are summarized in the table (1).
Table 1: Merits and demerits of various Instruments

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Merits</th>
<th>Demerits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psoriasis Index of Quality of Life (PSORIQoL)</td>
<td>Centered on concept and gauging the influence of the disease on QoI</td>
<td>25 questions not patient compliant</td>
</tr>
<tr>
<td>Psoriasis Life Stress Inventory (PLSI)</td>
<td>measure of the daily disturbances of psychosocial stress related to day to day activities</td>
<td>Focus is on the stress linked with psoriasis</td>
</tr>
<tr>
<td>Psoriasis Disability Index (PDI)</td>
<td>Reports self-reported disability wherein the focus is on everyday activities, occupation, relationships, and treatment effects.</td>
<td>Can be biased as its self-reported</td>
</tr>
<tr>
<td>Psoriasis Area and Severity Index (PASI) and Simplified PASI (SAPASI)</td>
<td>Gives an satisfactory depiction of the impact of the disease on patients’ QoL</td>
<td>The impact of psoriasis on patients’ QoL is not measured directly</td>
</tr>
<tr>
<td>Dermatology Life Quality Index (DLQI)</td>
<td>All the indications and emotional state, daily activities, work and school, personal relationships treatment is assessed</td>
<td>Self-reported</td>
</tr>
<tr>
<td>Short Form 36 (SF-36)</td>
<td>Covers all the aspects and the impact of psoriasis</td>
<td>36 items- can be too lengthy hence not patient compliant</td>
</tr>
<tr>
<td>EuroQoL 5D (EQ-5D)</td>
<td>Valuation of consequences associated to health conditions or their treatment</td>
<td>May not be sufficient to assess all the aspects</td>
</tr>
</tbody>
</table>
Psoriasis and Unemployment

People with psoriasis have to cope with not just the chronic illness on a day to day basis but also the effect psoriasis has indirectly on work related issues. For patients who are employed their occupation provides them with not just the financial assistance but also a basis of social support, individuality, and significance in life. These patients always have this constant fear and uncertainty about the extent of effect psoriasis will have at their economic and occupational end. Some of the patients who have the options to take benefits stating their ill health choose to voluntarily leave the work front, while some others remain employed depending on the financial and societal issues they are facing in their personal front. These patients do face problems due to factors associated with psoriasis like stress, external appearances, if the job involves continuous exposure to sun, medication schedules and side effects, and frequent appointments with doctors. Studies have shown that the extent of reporting symptoms like depression, anxiety, social isolation, and low self-esteem have been observed more in unemployed than employed individuals. Suicide, attempted suicides are multifaceted clinical matters connected with conditions like psoriasis. Suicide in personnel with psoriasis has been stated in most scenarios to be related with an associated psychiatric disorder.
Social Sustenance
There is an improvement in the quality of life seen which has been associated with demographic features such as male gender, individuals who are younger, higher socioeconomic status, and employment. Furthermore, patients who have been put on regimens which has lower number of pills, patients who are adherent to therapy have better QOL following the treatment has shown to improve QOL. Many people existing with psoriasis find it challenging to do their daily tasks of living, or involve in modest to energetic physical activities, or participate in a lively social life along with the management of psoriasis.45–47

Stigmatization
Studies have shown that psoriasis patients experience significant stigmatization than do other patients, and that these experiences that they have, facilitate a connection between the disease severity and the QOL measured on patients. Psychosocial intervention tolls would help in the betterment of these patients. 48
DERMATOLOGY LIFE QUALITY INDEX (DLQI)

Studies have shown that several questionnaires have been used to measure HRQOL in patients with psoriasis, including generic instruments, generic instruments for dermatology and disease-specific questionnaires. Report provides extensive support for the reliability, validity, and responsiveness of the DLQI questionnaire.\(^\text{17}\)

The Dermatology Life Quality Index questionnaire is designed for use in adults who are over the age of 16. It is self-explanatory and was handed to the patient who was asked to fill it out with detailed explanation. It could be usually completed in one or two minutes. The DLQI was used to assist the clinical consultation, evaluation and clinical decision making process.

The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired. The DLQI can also be expressed as a percentage of the maximum possible score of 30.

Meaning of DLQI Scores

0-1 = no effect at all on patient’s life
2-5 = small effect on patient’s life
6-10 = moderate effect on patient’s life
11-20 = very large effect on patient’s life
21-30 = extremely large effect on patient’s life
Pharmacoeconomics

Pharmacoeconomics helps in quantifying and comparing the costs and consequences of treatment to the healthcare systems and to the society. The pharmacoeconomic evaluation perspective is of significance as the results will depend on the perspective selected. The healthcare costs are categorized into direct medical, direct nonmedical, indirect nonmedical, intangible, opportunity, and incremental costs. In order to apply this, an economic evaluation is required which can compare the healthcare options. This includes analyses like cost of illness, cost-minimization, cost-benefit, cost-effectiveness, and cost-utility analyses. These analyses help in comparing the different treatment option available for a particular disease and the outcome is measured in monetary units. They change the method of measurement of outcomes and expression of results depending on the parameters available. These pharmacoeconomic methods can be applied for effective formulary management, individual patient treatment, medication policy determination, and resource allocation.

For healthcare professionals the major challenge is to provide quality patient care while assuring an efficient use of resources. Keeping these aspects in mind and the rising concerns about increase in medication costs and consistent need to decrease pharmacy expenditures clinicians/prescribers, pharmacists, and other healthcare professionals, pharmacoeconomics, or the discipline of placing a value on drug therapy has evolved to answer that question.
Clinicians have come up with various approaches which can help in containing costs of the treatment. But, most of these approaches emphasizes primarily on the least expensive alternative instead of the alternative that represents the best value for the money. The services provided these days by professionals should demonstrate pharmacoeconomic value that is, a balance of economic, humanistic, and clinical outcomes. Pharmacoeconomics can provide the systematic means for this quantification.

**Economic Evaluation Methods**

The two distinguishing characteristics to be considered for economic evaluation are:

1. If two alternatives can be compared?
2. Examination of costs and alternatives available

Pharmacoeconomic evaluations can be either partial or full economic evaluations.

Partial economic evaluations involve assessment of outcomes and of resources disbursed and in turn they require a minimum of time and effort. If only the consequences or only the costs of a program, service, or treatment are described, the evaluation illustrates an outcome or cost description. Another way of evaluation is a cost analysis that can compare the costs of two or more alternatives without regard to outcome.
There are many extensive economic evaluations which include cost of illness, cost-benefit, cost-effectiveness, and cost-utility analyses. Every analysis can be used to compare competing programs or treatment alternatives. The methods measure costs in a similar way (in rupees) and are different in measuring the outcomes. Although a full economic evaluation generally provides higher quality and more useful information, the time, resources, and effort employed are also great. Thus healthcare practitioners and clinicians also find it necessary to employ various partial economic evaluations.\(^{50}\)

**Cost-of-Illness Evaluation**

A cost-of-illness (COI) evaluation recognizes and evaluates the comprehensive cost of a particular disease for a specific population.\(^{51}\) This assessment process is frequently referred to as burden of illness and involves measuring the direct and indirect costs attributable to a specific disease. By successfully identifying the direct and indirect costs of an illness, one can determine the relative value of a treatment or prevention strategy. For example, by determining the cost of a particular disease to society, the cost of a prevention strategy could be subtracted from this to yield the benefit of implementing this strategy nationwide. COI evaluation is not used to compare competing treatment alternatives but to provide an estimation of the financial burden of a disease. Thus the value of prevention and treatment strategies can be measured against this illness cost.\(^{52}\)
Cost-Effectiveness Analysis

Cost-effectiveness analysis (CEA) is a method used to measure the health benefits and resources used by contending healthcare programs so that policymakers can choose among them.\textsuperscript{53} CEA involves comparing programs or treatment alternatives with different safety and efficacy profiles. Cost is measured in dollars, and outcomes are measured in terms of obtaining a specific therapeutic outcome. These outcomes are often expressed in physical units, natural units, or nondollar units (e.g., lives saved, cases cured, life expectancy, or drop in blood pressure).\textsuperscript{54-55}

The results of CEA are also expressed as a ratio—either as an average cost-effectiveness ratio (ACER) or as an incremental cost-effectiveness ratio (ICER). An ACER represents the total cost of a program or treatment alternative divided by its clinical outcome to yield a ratio representing the dollar cost per specific clinical outcome gained, independent of comparators. This allows the costs and outcomes to be reduced to a single value to allow for comparison. Using this ratio, the clinician would choose the alternative with the least cost per outcome gained.\textsuperscript{56} The most cost-effective alternative is not always the least costly alternative for obtaining a specific therapeutic objective. In this regard, cost-effectiveness need not be cost reduction but rather cost optimization.\textsuperscript{57}
Incremental CEA can be used to determine the additional cost and effectiveness gained when one treatment alternative is compared with the next best treatment alternative.\textsuperscript{58} Thus, instead of comparing the ACERs of each treatment alternative, the additional cost that a treatment alternative imposes over another treatment is compared with the additional effect, benefit, or outcome it provides.

CEA is particularly useful in balancing cost with patient outcome, determining which treatment alternatives represent the best health outcome per dollar spent, and deciding when it is appropriate to measure outcome in terms of obtaining a specific therapeutic objective. In addition, CEA can provide valuable data to support drug policy, formulary management, and individual patient treatment decisions. Globally, CEA is being used to set public policies regarding the use of pharmaceutical products (national formularies) in countries such as Australia,\textsuperscript{59} New Zealand, and Canada.\textsuperscript{60} These countries, along with others, including Spain, the United Kingdom, Italy, and the United States, even have their own guidelines for conducting research.\textsuperscript{61}
Humanistic Evaluation Methods

Pharmacoeconomic evaluations also may focus on humanistic concerns. Methods for evaluating the impact of disease and treatment of disease on a patient's HRQOL, patient preferences, and patient satisfaction are all growing in popularity and application to pharmacotherapy decisions. These methods also can assist clinicians in quantifying the value of pharmaceuticals.

HRQOL has been defined as the assessment of the functional effects of illness and its consequent therapy as perceived by the patient. These effects often are displayed as physical, emotional, and social effects on the patient. Measurement of HRQOL usually is achieved through the use of patient-completed questionnaires. Many questionnaires are available, and most are either disease-specific or generic measures of health status.

Selecting the most cost-effective drugs for an organizational formulary is important. However, it is equally important to determine the most appropriate way to use and prescribe these agents. Hence, developing and implementing appropriate-use guidelines or policies based on sound pharmacoeconomic data can have a great impact on influencing prescribing patterns. Further, implementing sound drug-use guidelines/policies will ensure the most appropriate and cost-effective use of pharmaceutical agents throughout the healthcare system.
The application of pharmacoeconomics also can be useful for making a decision about an individual patient's therapy. Evaluating the impact a drug has on a patient's HRQOL can be useful when deciding between two agents for customizing a patient's pharmacotherapy. Although this can be one of the most difficult applications of pharmacoeconomics, it is also one of the most important.

**Pharmacoeconomic Models**

Studies that *model* the economic impact of a pharmaceutical product or service on a defined population are increasing in popularity. Modeling studies use existing clinical and/or epidemiologic data to project future outcomes.\(^{63}\) Use of economic models can provide support for various clinical decisions, especially those which are time-contingent.\(^{64}\) Identifying assumptions regarding the treatment alternatives being compared, the patient outcomes under study, and the probability of those outcomes occurring can provide the basis for an economic simulation to assist in the medication decision-making process.
Pharmacoeconomic models are often broadly defined to include decision analysis, Markov models, multivariate regression analysis, and basic spreadsheet analyses. Because the development and use of pharmacoeconomic models is so prevalent today, a study examined the perceived value and understanding of pharmacoeconomic models by decision makers in managed care organizations (MCOs). Overall, these models did affect healthcare policy decision making, with 19 of 20 respondents relating at least one experience in which a model played a role in optimizing the formulary position of a drug. Furthermore, no single model format was regarded as the most effective type, although many respondents claimed that simple spreadsheet models were the most effective, followed by well-designed, scientifically rigorous regression models.
Typically, economic modeling in today’s practice settings employs clinical decision analysis, which has been defined as an explicit, quantitative, and prescriptive approach to choosing among alternative outcomes.\textsuperscript{66,67} The tool used in decision analysis is a decision tree. A decision tree provides a framework to display graphically primary variables, including treatment options, outcomes associated with those treatment options, and probabilities of the outcomes. The researcher can then algebraically reduce all these factors into a single value, allowing for comparison. This simple decision-analysis approach is well-suited for comparisons of treatment alternatives with relatively immediate consequences, using simple decision trees for various reasons, including time-dependent clinical outcomes, and thus may require alternate modeling techniques.