Review Article

Quality Added Life Years: A Tool for Biologics and Biosimilars Marketing

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ABSTRACT

Definition of quality of life has been much debated about, and continues to be blurred. The four approaches which have been identified for their contribution in measuring and evaluating the health level in a given population are epidemiological or biomedical approach, functional/dysfunctional approach, cultural approach and economic approach. The health-related quality of life, is a value which is assigned to duration of life modified by impairments, functional states, perceptions and social opportunities that are influenced by disease, injury, treatment or policy. Biologics and biosimilars are a class of medications which do not tend to follow the norms of the economics of small molecules and chemical drugs. Bevacizumab is used for metastatic colorectal cancer (mCRC), and the chemotherapy regimens for this cancer have been well established. Bevacizumab has high acquisition costs and its economic value has been questioned in recent pharmacoeconomic studies. In the case of diabetes, QALY is derived from utilities and these are important in terms of decisions regarding reimbursement policies, insurance policies and cost-effectiveness. In addition to concerns regarding costs associated with cancer and diabetes, targeted immunomodulators and other drugs associated with treatment are also a concern because of rising prices in recent years. QALY can be a tool that can help marketers add more value to their marketing strategies and communications in these therapy areas.

Key words: quality of life, biologics, biosimilars, medications, marketing.

INTRODUCTION

Definition of quality of life has been much debated about, and continues to be blurred. However, the definition of health coined by WHO in the year 1958, throws light on the definition of quality of life as "Physical, mental and the social well-being and not merely the absence of disease and infirmity." This definition was criticised due to the unmeasurable concept that it is, which eventually led the quality of life researchers to devise methods of measuring health in all the three dimensions of physical, mental and the social well-being. For the measurement of health status, various techniques have been applied by sociologists, psychologists, statisticians, epidemiologists and economists. The four approaches which have been identified for their contribution in measuring and evaluating the health level in a given population are epidemiological or biomedical approach, functional/dysfunctional approach, cultural approach and economic approach.

The epidemiological or biomedical approach defines health as a biological phenomenon. It involves classification of diseases into categories depending on the symptoms of each disease and considers factors like the hospital discharges as units of medical system output.

The functional/dysfunctional approach is normally considered as an extension of the biomedical approach as it focuses on measuring the impact of biological conditions or dysfunctional states of health. (e.g.: inability to walk, dress etc).

The cultural approach is a further extension of the first two approaches and associates the above described conditions with the "stigma" that the society generally associates with "deviant" behaviour. This approach adds a new dimension to the definition of illness considering how the society perceives a person to be ill or not regardless of the biomedical and dysfunctional acknowledgement. (e.g. Inability to socially move around in the society)

The economic approach considers the measurement of health status by considering the concept of utility. The concept of utility encompasses ethical beliefs, norms and value judgements concerning the identification and assessment of medical needs. [1]

The health-related quality of life, is a value which is assigned to duration of life modified by impairments, functional states, perceptions and social opportunities that are influenced by disease, injury, treatment or policy. The concept of measuring health related concept of life started in the 1970s with researchers putting forward various platforms like questionnaires and indexes for measuring the health-related quality of life in different diseases like Alzheimer's, Asthma, Arthritis, Cancer and Diabetes. The instruments used to measure the ability of people to function in their everyday life were essentially categorised as follows:

Generic instruments

These are designed to measure the health status of a given population across different socio-economic conditions and are applicable across a wide range of disease conditions. Examples of such generic instruments include Sickness Impact profile and Nottingham Heath Profile.

Disease specific instruments

These are designed to assess the health status of a specific population groups, or people in specific diagnostic categories. These instruments are capable of assessing the changes in health conditions with respect to the different stages of a specific disease. Examples of such instruments include Asthma Quality of Life Questionnaire, and Inflammatory Bowel Disease Questionnaire directed at Asthma and Inflammatory Bowel Disease respectively. [2]

Quality added life years (QALY)

QALY is an utility measurement, which captures both the quality and quantity of life. Life expectancy is the most widely accepted form of estimating the quantity of life. The Quality of life is more difficult to measure as it embraces a larger spectrum of health dimensions dealing with the physical, emotional and social aspects of well being. The mathematical expression of QALY is as follows:

$U \{Q, L\} = a L' U(Q)$…………….(1)

Where,

a: constant

r: a parameter which measures the individual's attitude to risk (risk lover, risk neutral, risk averter)

U(Q): describes the quality of health or quality of a given level of health status adjusted over a range of values from 0 to 100. 0 expresses worst possible level of health while 100 expresses best imaginable level of health.

The main objective of QALYs is to calculate an algorithm for assessing the relative benefits of alternative treatments.

Usually, allocation of limited health care resources is done on the basis of QALY by analysing out of the patient pool, which patient will be maximum benefitted by the treatment as understood by QALY. [1] At the individual level, this is generally expressed as maximum QALYs per unit of cost. QALYs are then further used for calculation for Cost Utility ratio using the expression number 2.

$Cost\ utility\ ratio: Cost(A) - Cost(B) \div QALYs(A) - QALYs(B)$ ……………..(2)

Where, A and B are two therapies in comparison for a particular disease. [3]
Biologics and biosimilars are a class of medications which do not tend to follow the norms of the economics of small molecules and chemical drugs. While the difference in cost of a small molecule innovator and generic is almost as much as 80% of the price associated with the innovator, it does not stand true for biologics and biosimilars. [4] Biosimilars are similar to the innovator biologic and not exactly the same due to the complex structure of proteins and biologic molecules. This complexity makes the process of manufacture of a biosimilar as expensive as a biologic which makes playing the price game difficult. This paper explores the possibility of use of QALY as a tool to justify the value proposition of a biosimilar which can rationalise the costs associated with the therapy with particular attention to three diseases namely, cancer, diabetes and rheumatoid arthritis. [5]

QALY for biologics and biosimilars in cancer

Affordability of premium priced biologics and biosimilars has been a matter of concern since their introduction. It is estimated that only 0.05% of the entire population of India can afford the high priced biologics and biosimilars. Owing to the complexity of the molecule, the preparation of biosimilars is equally resource investing as a biologic which doesn't provide a significant price margin to play. Essentially, this ends up in biosimilars being priced at a minimum of 80% of the price of the innovator biologic. Adding to this, almost one third of the Indian pharmaceutical industry is under price control. Given their high price, cancer drugs are likely to be affected by such policies in the future. This acts as a big deterrent for the multinationals who wish to introduce highly effective biologics and biosimilars in the Indian market. To address such issues, new drug pricing strategies are needed to ensure the commercial viability of highly innovative therapies. [6]

Value based pricing and outcome-based pricing are examples of strategy which can help justify the price of a innovative therapy in terms of the value and outcome that it provides to the life of the patient. Value based pricing when combined with pharmacoeconomic modelling techniques like QALY can help in determining the costs and consequences of new therapies relative to the standard care. However, one problem associated with the use of QALY is setting the threshold value of the country. WHO has provided a solution by adjusting such parameters with the country's GDP to establish the thresholds of economic value. This acts as a guide for foreign MNCs wanting to launch innovative therapies in India as the price set would be in harmony with the purchasing power parity of the population. This would ultimately lead to wealthier nations paying more for the therapies while the developing ones pay a comparatively lesser amount. [6] George Dranitaris et al in their work have proven the successful use of parameters like QALY for the value-based pricing of bevacizumab for improved patient access. [7]

Bevacizumab is used for metastatic colorectal cancer (mCRC), and the chemotherapy regimens for this cancer have been well established. Bevacizumab has high acquisition costs and its economic value has been questioned in recent pharmacoeconomic studies. Clinical studies have proven irinotecan and oxaliplatin to be the first and second line of treatment for mCRC. In addition to this, the protocol also established the need to introduce a anti-vascular endothelial growth factor (VEGF) like bevacizumab at some point of time. Though all the three molecules are available in India, their accessibility is limited due to their high price. The Canadian guidelines for economic evaluations and the panel on cost effectiveness in health and medicine of the United States suggested that the treatment preferences should be measured using a population of general public who will be potential future patients. Keeping this in mind, their study was directed

towards the general public. It has also been proven in previous economic study that a patient surrogate group consisting of nurses is most simulating with the patient population and doesn't affect the findings of the cost-utility studies. In their interviews with the participants, bevacizumab was addressed as "new drug". The respondents were then asked how many months of "optimal health" they considered being equivalent to the time spent in each of the less than optimal health states described in the model. These measures were then used to weigh each branch of the model by the quality of life experienced by a patient living through that time period.

The clinical, economic and interview data was all then combined to calculate the cost utility ratio with the primary objective of estimating a suitable price per dose of bevacizumab. The target benchmark used was a price of US$9300 per QALY gained which is three times the Indian per capita GDP. The base case analysis suggested a price of US$98 per QALY gained which also takes into account the per capita income of the population of the country. The price of the drug is likely to reach $253 per month if the survival benefit is to reach 6 months. Most new medicines have not been able to provide a survival benefit of more than 3 months. The amount of QALY added by bevacizumab becomes a value proposition justifying the pricing of the drug. [7]

The survival benefit of extra 3 months demonstrated by bevacizumab becomes a point of differentiation of major companies having bevacizumab in the product portfolio. QALY can aid in proving the value provided by a biosimilar in terms of the outcomes produced. The latest development in anti-cancer therapy is the CAR-T cell therapy being investigated for launch by Novartis in India. QALY as a parameter has the potential of convincing the physicians, insurance companies and payers on the price of the therapy. Thus, QALY not only helps in deciding the price of anti-cancer medications, but also, proves

the value proposition which further helps in the value-based and outcome based pricing of biosimilars and biologics launched in India. The amount of life added to the patient along with the quality of the life can be useful dimensions for marketing of biologics and biosimilars.

QALY for biologics and biosimilars in Diabetes

In India, diabetes has considered as a major health care problem with an estimated 66.8 million people suffering from the condition, representing the largest number of any country in the world. The healthcare sector and economy in India has greatly affected by the rising burden of diabetes. The goal of healthcare experts in India is to transform India into a diabetes care capital in the world. In 2000, India topped the world with 31.7million people with diabetes mellitus followed by China and United States in second and third place respectively. According to the study done by Wild et. al., the maximum increase in the prevalence of diabetes mellitus India is predicted with a huge increase globally from 171 million in 2000 to 366 million in 2030. [8]

India currently faces an uncertainty about future in relation to the potential burden that diabetes may impose on the country. To make evidence-based health decisions, it is very important to conduct studies focusing on economic evaluations. Consequently, also offer the best risk and cost-effective treatment choice along with better quality of life for diabetic patients. [9]

The use of one or other value-based tools in a particular situation is decided by the attributes of the different methods. Quality- adjusted life years (QALY) are health outcome measures that are attained when utility scores are combined with survival times. Health utility scores may vary by geographic conditions and can be affected by variables like prevalent cultural norms. In type 2 diabetes, weight loss is an important therapeutic intervention. In the case of diabetes, QALY is derived from such utilities and these are important in

terms of decisions regarding reimbursement policies, insurance policies and cost-effectiveness. [10]

Non-parametric boots trapping strategy was used in stimulation to construct confident intervals around the data. The incremental cost effectiveness ratio (ICER) per quality adjusted life year (QALY) was calculated in the respective currency and as a fraction of the gross domestic product (GDP) per capita for each country. ICER reveal the cost per unit of benefit from changing from one treatment to another treatment depending on various aspects. Cost effectiveness of the treatment is already setup as per the requirement by WHO Choosing Interventions that are cost effective (CHOICE) programme threshold based on GDP per capita. [11] A health technology is defined as cost effective if incremental cost per incremental QALY gained falls between the range of 1.0- and 3.0-times GDP per capita, highly cost effective if incremental QALY gains are less than 1.0 GDP per capita and dominant (cost saving) if cost per QALY gained are less than 0.00 based on the studies performed by Gupta et al., reduction on 30 years incidence of diabetes related complications was observed. The relative risks such as the risk of myocardial infarction were taken in consideration and observed a reduction in it by 19%. Whereas the risk of dialysis was projected to fall by 64% in India. On the basis of all this data and evidences the estimation for QALY gained was drawn as 4.75 for India. The increase in total current costs that would help in delivering an ICER of 3.0 GDP/QALY was estimated to be 252% for India. [12]

In the study conducted by Berhanu et al, the main objective was to evaluate the costs associated with the use of long-acting insulin analogues (LAIAs) compared with non-LAIA agents, including human insulin, oral antidiabetic drugs, and other injectable therapies, in the treatment of patients with type 1 diabetes (T1D) or type 2 diabetes (T2D). they identified patients using LAIAs had higher drug costs than those using OADs and NPH but had neutral or reduced total and diabetes-related costs compared with patients using non-LAIAs. Use of LAIA pen-delivery systems may lead to improved adherence and reduction in costs. Patients receiving insulin glargine demonstrated higher adherence and persistence than patients on insulin detemir. Insulin Glargine found to be dominant to $26,179/QALY than its competitor. On the other hand insulin detemir was found to be dominant to $3951/QALY than its competitor i.e.insuline glargine only. Glargine consistently less costly (annual savings per patient of $195-$778; >$70 million 10-year total cost savings. Also when detemer treatment is compared with NOH treatment. Economic models suggest that LAIAs are more cost-effective than NPH for T1D; for T2D, insulin glargine is more costly than NPH but less so than insulin detemir. [13]

Diabetes is considered as chronic disease due to major complications associated with it such as renal dysfunction, neuropathy, retinopathy, lever dysfunction, diabetic foot, etc. due to all these complications associated with diabetes, the treatment of diabetes become costlier in total. These costs are not only financial but also affecting directly or indirectly, to the individual or to the whole family of the individual. Studies done till the date in India shows that the economic burden of diabetes care on families of the diabetic patients is raising rapidly. 85-95% of the total treatment cost should paid by individuals suffering from diabetes and their family from household income. Taking into consideration that people diagnosed with diabetes can have significantly higher healthcare requirements and expenditures than in the absence of diabetes, the growing prevalence of diabetes will tremendous future challenges for low to middle income countries. In this context, an intervention that can deliver increased life expectancy of more than 1 year with reduced incidence of diabetes related complications and delayed

onset of these would appear attractive to patients as well as practitioners. [14]

QALY for biologics and biosimilars in rheumatoid arthritis

Despite advances in treatment, RA remains a remarkably complex disease to diagnose and manage. There are multiple phenotypic and genotypic variations in the pathogenesis of the disease that affect both the course of RA and the outcome of therapy. Some patients may have milder disease that never progresses to significant joint damage or functional impairment regardless of treatment received, while others experience a highly aggressive course that may require multiple attempts at treatment before the disease is brought under control. Similarly, both initial response to a given treatment and the durability of that response may vary even within phenotypically-similar populations; some individuals may have initial response with a short-lived remission, others may have a more robust initial and subsequent response, and still others may have inadequate response to many Targeted Immunomodulators before finding an appropriate treatment. In addition to concerns regarding costs associated with dose increases, TIMs have also received considerable attention for rising prices in recent years. The MRP for the two TIMs with the leading market share in RA, adalimumab and etanercept, have risen 70-80% in the last three years. [15] These prices do not consider discounts, rebates, or payment assistance programs provided by manufacturers. However, even after discounts and rebates, TIM costs remain substantial. The institute for clinical and economic review, New England developed a model to determine the long-term cost effectiveness of TIMs used in rheumatoid arthritis with the primary outcomes being discounted lifetime total payer costs, life years, quality adjusted life years (QALY) and incremental cost effectiveness ratio.

The base case results reflected that the treatment with TIMs significantly increased the QALY over the lifetime horizon. Using this base case model, they could successfully apply a value-based pricing for their two investigational drugs as compared to their other counterparts.

A significant study undertaken by Bin Wu et al used QALY to understand the incremental costs and additional quality of life added of the 7 competing therapies used for the treatment of rheumatoid arthritis. When comparing the cost of therapy of tDMARDS vs the biologicals, it was observed that the drug costs contributed to just 40% of the overall cost of treatment while in biologicals they contributed to 90% of the associated costs. The cost-effective frontier that they developed showed the most efficient strategy to be that with infliximab with an ICER of $26562.4 followed by infliximab + rituximab, adalimumab + rituximab and etanercept + rituximab with ICER of $32034.3, $121,344.4 and $581,525.9. Though the costs associated with the biologicals and biosimilars are higher as compared to the costs associated with the traditional DMARD therapy, the incremental life years added and quality of the life was much higher than that of the traditional therapies. [16]

Given the multiple options available for the management of rheumatoid arthritis, QALY can help in driving the physician's decision towards a suitable therapy (class choice and brand choice). Another factor which is very significant in justifying the use of QALY is the genetic predisposition of the individual which gives a better QALY with one therapy over the other. [17]

Conclusion- a 360-degree view of QALY for marketers

Cancer, diabetes and rheumatoid arthritis are lifetime conditions which has immense psychological trauma not just for the patient but also for the caregivers and family members. The above examples of QALY in three major diseases converge towards the ability of QALY in establishing the value of a therapy which ultimately helps in outcome-based models of pricing. [18] A lot of factors account a Healthcare

professional's decision of prescribing a particular biologic or biosimilar, of which cost continues to be major concern. A value-based pricing approach for such molecules appears to be a silver lining for pharma players. Selling of expensive biologics and biosimilars involves a lot of stakes especially since the costs associated with the manufacture and development of such molecules continues to be high. QALY as a metric can be subsequently utilised for pitching the value proposition of biosimilars and establishing the cost effectiveness of biologics and biosimilars.

The primitive use of QALY in understanding the cost effectiveness of therapy has already been understood. What additionally can be leveraged upon is the use of this metric in different parts of the product lifecycle for customised marketing communication at different touch points depending on the stakeholders involved. While in the development and approval phase QALY can be used for establishing the efficacy of the therapy, in the commercialization phase, QALY can be used as a tool by the marketers to differentiate with the other biosimilars available and as a tool for negotiation with the insurance companies in order to obtain an insurance coverage especially for the innovator biologics.

An important aspect of acceptance of a biosimilar amongst the physician's include establishing the similarity of the biosimilar with respect to the reference biologic available. Amongst the different components of the totality of evidence, QALY can also be incorporated eventually. One of the prime factors in driving a prescription is the value that the physician sees in the molecule/therapy. Providing physicians with economic data helps in making them understand how the care provided by one company differs from the other. In conclusion, when combined with other marketing tools of patient support and patient assistance programs, QALY can help in establishing the value proposition of biologics and biosimilars. Wherever there are options available to reach the same therapeutic objective, QALY stands out as a science-based point-of-differentiation which can help drive physician's prescription.

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