

## Introduction of Pharmaco-economics for non-health economists

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### ABSTRACT

It is becoming increasingly important to examine the relationship between the clinical trial outcomes and the costs of the drugs. Safety, efficacy and quality are no longer enough in a world with scarce resources, where budgets are limited and needs for healthcare are unlimited. Allocate the healthcare budgets to those interventions that offer the most health gain per unit of money became important. The Health Technology Assessment (HTA) helps answer to this question. The HTA approach is a multidisciplinary and comprehensive evaluation methodology that is worldwide increasingly applied in order to support decision makers during the introduction of new health technologies. Given the differences in health care systems and social services among countries, there is a need for country-specific data. The aim of this communication is to introduce health economics (HE) and HTA to non-economist participants.

### INTRODUCTION

HE applies the discipline of economics to the topic of health. In a competitive environment where health resources are finite, HE helps define the differences in value of the new product compared to no treatment or to the other available treatments. Pharmaceutical companies are more and more requested to make this assessment in order to help the decision-makers and the payers to make their decision. In addition, HE evaluation is a key for global reimbursement strategy.

### HOW TO POSITION HE?

The unique link between the clinical trials results, where the stakeholders are the provider, the prescriber and the patients, and the market access hold by the payers is the monetary value. In health care, value is expressed in terms of money and health. The value of money corresponds to the maximum of health gain per unit of money spent. Health care must produce health in the most productive and most efficient way. The decision-makers will pay attention to the effectiveness due to the limitation of the budgets as well as to the financial impact of the product implementation on health care budget, the affordability.

### DISEASE BURDEN

Given the differences in healthcare systems and social services among countries, there is a need for country-specific HTA in terms of evaluating the global burden of disease (GBD). GBD provides a comparable assessment of the frequencies per time unit and geographic entity of the incidence (new cases), the prevalence (existing cases), the morbidity (loss of health due to diseases) and mortality. The GBD is assessed using mainly two different concepts: The disability-adjusted life year or DALY and quality-adjusted life year or QALY. Both DALY and QALY express health in time (life years) and give a weight to years lived with disease. In practice, the difference between a DALY and QALY depends on whether the quality of life is expressed as a loss (DALY) or a gain (QALY). On the other hand, there is a need for country-specific data on economic burden illustrated by the cost of illness measurement to estimate the amount that could be potentially avoided or gained if a disease were to be eradicated or decreases in terms of number of cases by using the new proposed treatment. Due to multiple stakeholders and therefore multiple decision drivers, it is important to specify from which perspective the cost is considered and what are the factors that will drive their decisions. In addition, clinical and economic burden define the direct impact of the new intervention compared with the current situation. For some interventions, the indirect impact is also considered such as the herd effect.

## COST-EFFECTIVENESS

An economic evaluation in health is often called a cost-effectiveness evaluation. “Be cost-effective” does not necessarily mean that the investment leads to cost-saving but rather an additional investment provides additional measurable and acceptable health gain. Therefore, we should take into account the two dimensions: the cost (C) and the health gain (E) and define the correct ratio for the society or the Incremental Cost Effectiveness Ratio (ICER) as  $\Delta C/\Delta E$ . The most commonly used outcome measure for health is QALY, consequently  $ICER = \Delta C/QALY \text{ gained}$ . There is a threshold for each country depending on the societal engagement. In cost-effectiveness Analysis (CEA), a financial value is usually placed on a QALY reflecting what a society can afford to pay for the average QALY as measured by its Gross Domestic Product (GDP) per capita.

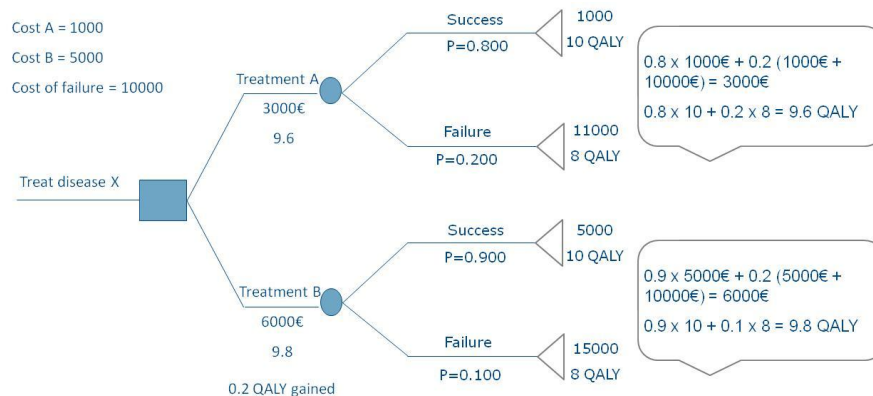
## HEALTH ECONOMICS METHODS

Several methods are currently employed by health economists to model cost-effectiveness. Modeling and simulations can assist decision-makers to carry out the effective delivery of health care services in their countries when only data on efficacy and safety from short-term, randomized clinical trials are available. Two methods are cited here.

### DECISION TREE.

Decision trees are often used for modeling programmes in which the time frame is short and mortality rate does not differ across strategies. Decision trees move from left to right, beginning with a set of initial choices (decision nodes) and ending in a number of outcomes (terminal nodes) with probabilities (Figure 1). The advantage of using this method is that all possible patient pathways are represented. Additional advantages are the relative simplicity in terms of the construction, comprehension and interpretation. Figure 1 shows a comparison between two treatments where results are presented in terms of probability of patient being treated successfully, probability of treatment failure considering the cost, the QALY and the QALY gained. The disadvantage of decision trees relates to the fact that the time component is not represented.

**Figure 1: Example of a decision tree**



$$ICER = (6000€ - 3000€) / (9.8 - 9.6) = 15000€/QALY \text{ gained}$$

### MARKOV MODEL

Markov models have been applied with increasing frequency in published decision analyses. In contrast to the decision tree, in these models, timing of events is important and diseases risks are continuous over time. Different health states of the patient are defined within these models with “transition probability” per cycle between the states. In addition, each model type has strengths and weaknesses that must be considered to appropriately determine which type to select for the decision problem. Therefore, all efforts should be expended to maximize the methodological rigour and robustness of the chosen model.

The models have to be validated in terms of structure, outcomes and robustness.

- Validation of the structure through clinical experts' opinion to confirm that the model's framework created reflect the reality
- Validation of the outcomes: by comparing the assumed versus the real observations
- The robustness of the model could be determined using several available sensitivity analysis tests to measure the sensitivity of the model's outcomes following modifications of the input data. One-way or multi-way sensitivity analysis are used where respectively one or multiple variables varied at the same time within distribution probabilities to evaluate the impact on the base-case scenario. The base-case scenario is defined as the “best guess” data feeding the model.

## CLINICAL TRIALS VERSUS HEALTH ECONOMIC ASSESSMENT

Table below illustrate in brief the differences between clinical trials and health economics in terms of aims, methods and data.

| Clinical Trial:                   | Health Economics Assessment:                                                           |
|-----------------------------------|----------------------------------------------------------------------------------------|
| ✓ Efficacy                        | ✓ Effectiveness                                                                        |
| ✓ Time horizon: short time effect | ✓ Time horizon: long enough to capture all cost and effect associated to the treatment |
| ✓ Multi-country trials            | ✓ Country specific assessment                                                          |
| ✓ Purpose = Authorization         | ✓ Purpose = reimbursement                                                              |
| ✓ Strict protocol instructions    | ✓ "Do what you normally do"                                                            |
| ✓ Protocol induced resource use   | ✓ Real resource use                                                                    |
| ✓ Protocol induced findings       | ✓ Real clinical findings                                                               |

## CONCLUSION

In different countries, companies offering new medicines or new medical technologies are obliged to present an economic evaluation to the authorities in order to provide them with the optimal scenarios or idea of the cost and benefits they could made compare to the current situation. The aim of a good politic in terms of health is not to make economy but to product health in another term to make health gain. A healthy population will be more productive and will consume more and thus contribute to the growth of the welfare and the country's economy.

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