Meditrial
Digital Research Organization

HEOR CRASH COURSE

REAL WORLD APPLICATION IN EARLY DRUG DEVELOPMENT

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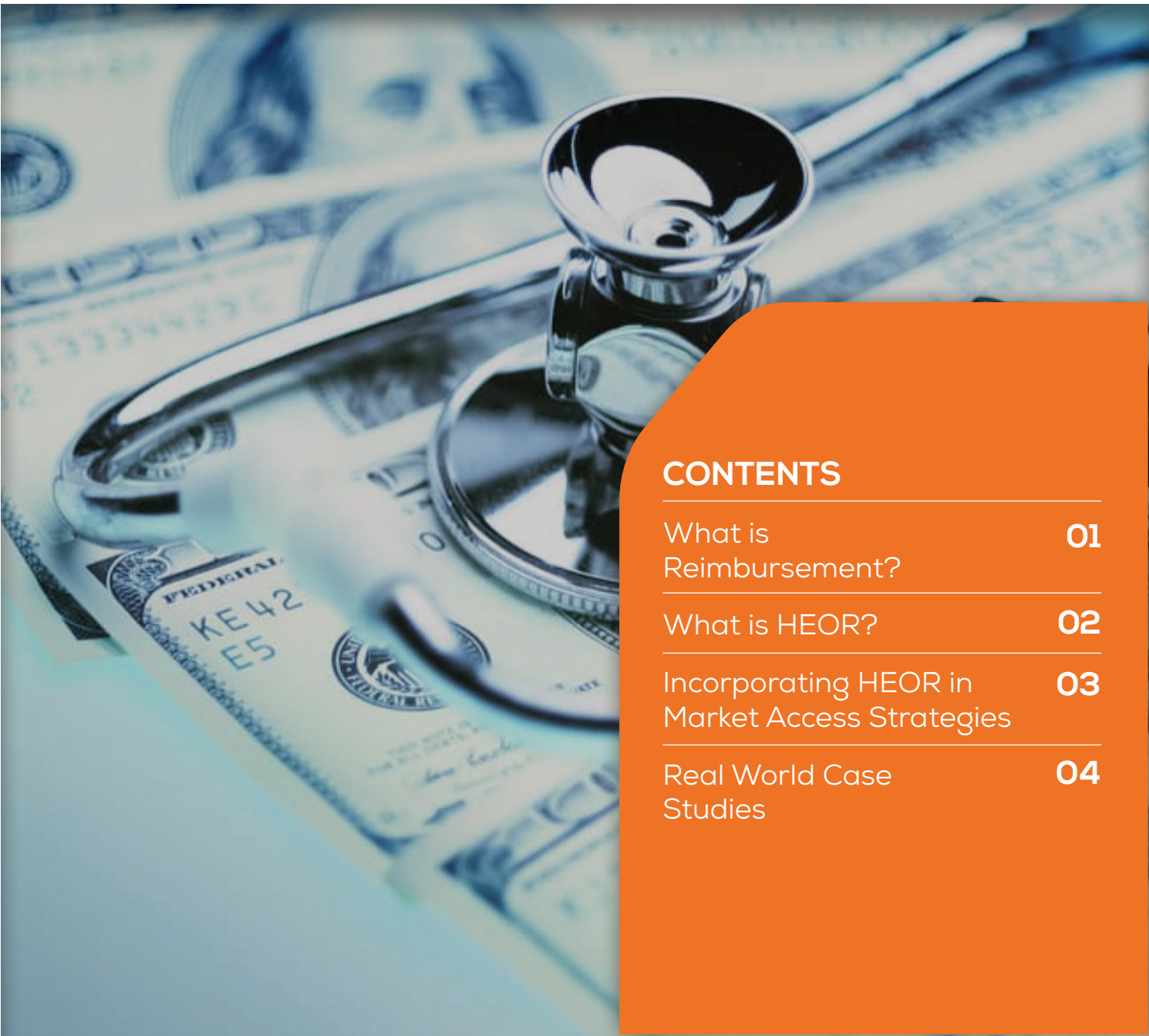

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WHAT IS REIMBURSEMENT?

Reimbursement is the **payment** of a public or private insurer **to a health care provider**.

This payment should cover the costs that the provider has sustained while using a medical device, a treatment, or performing a procedure.

Whether a device or procedure is reimbursed, and at what amount, can have a significant impact on:

provider's ability to access a technology

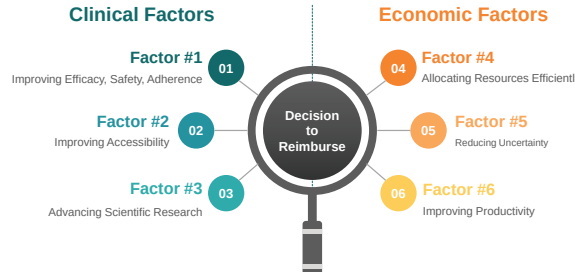
manufacturer's ability (or willingness) to provide a technology

REIMBURSEMENT DECISION MAKERS IN THE USA

The U.S. market is comprised of nearly 1,000 payers. **Medicare Administrative Contractors (MACs)** *are influential local payers* who handle Medicare. Nearly all **private payers look to MACs** in their own coverage decisions.

Another option is to apply for national coverage decision, where Centers for Medicare & Medicaid Services, or CMS, make a single decision of reimbursement that will be applied by private local insurers. Clearly, this process is more risky and less preferred with respect to making numerous local negotiations. However, if there is certainty on the clinical and economic benefits of a technology, it may be a more efficient way to negotiate.

The National Coverage Decision is a high stakes process, overseen by CMS.



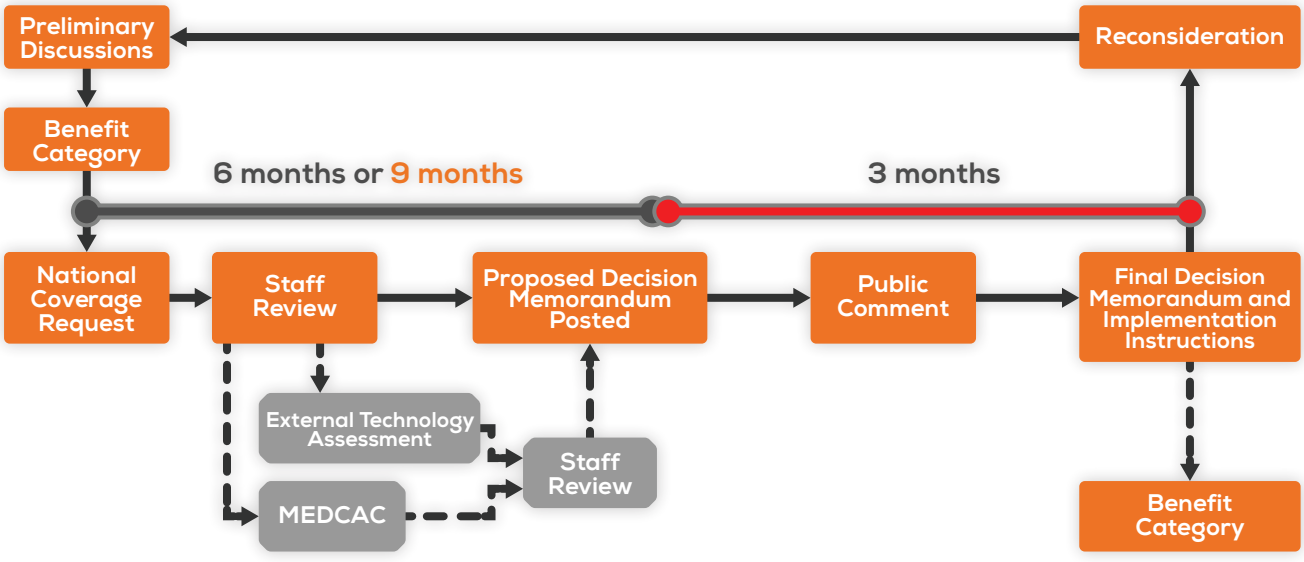
DETERMINANTS OF REIMBURSEMENT

Whether a therapy or device is reimbursed by insurers depends on a number of factors:

First and foremost, there are clinical factors that determine the reimbursement level of drugs and medical devices. These can be the extent to which technologies improve efficacy, safety, adherence, accessibility, or even the development of scientific knowledge in general.

Even in health, however, resources are scarse and have to be allocated wisely, given the cost of health technologies. Therefore, a number of economic factors have been increasingly considered by decision makers, as for example the ability of technologies to improve allocation of resources or the productivity of citizens, or to reduce uncertainty on future spending.

MEDICARE NATIONAL COVERAGE PROCESS



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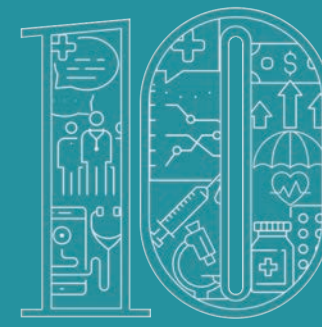
WHAT IS HEOR?

HEALTH ECONOMICS AND OUTCOMES RESEARCH (HEOR) IS A FIELD IN WHICH **ECONOMIC AND STATISTICAL EVIDENCE ON PHARMACEUTICALS AND DEVICES** IS PRODUCED TO *SUPPORT HEALTHCARE AND ACCESS DECISIONS.*

2020 Top 10 HEOR Trends[1]

1. Real world evidence
2. Drug Pricing
3. Novel Curative Therapies
4. Overall Healthcare Spending
5. Universal Health Coverage
6. Value-Based Alternative Payment Models
7. Price Transparency
8. Digital Technologies
9. Aging population
10. Precision Medicine



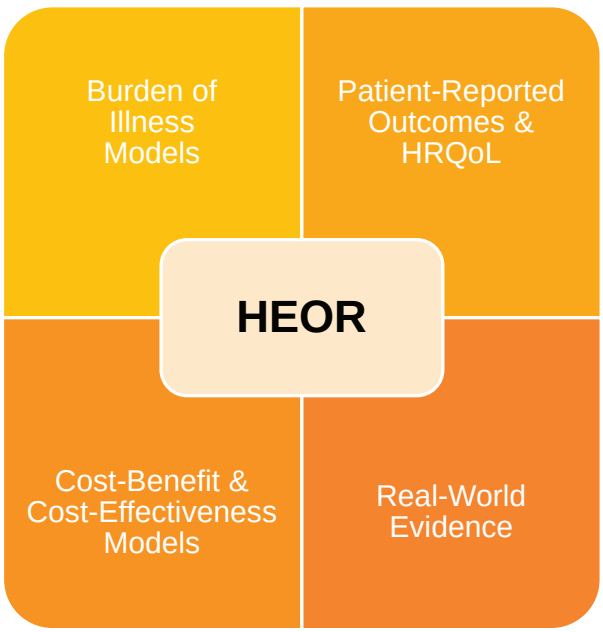
HEALTH ECONOMICS AND OUTCOME RESEARCH

In this field health economists, statisticians, data experts, and so on, produce economic evidence that can support market access and reimbursement decisions.

The main tools or analyses used are:

Burden of illness models, analyses on patient-reported outcomes and health-related quality of life, cost-benefit and cost-effectiveness models, and analyses on real-world evidence. These types of evaluations have been consolidated in the past decades and they can affect the decision of reimbursement.

Keep in mind that health economics is part of a system that is much larger than prices and reimbursement. According to a survey carried out on health economists, there are a variety of health topics, like digital technologies, precision medicine, ageing population, and universal coverage, that are increasingly falling within their scope. This is to understand the transversality of this field of research. In the case where one can incorporate economic evidence, it can truly complement clinical data and is highly valued by the majority of decision makers.



An example of this is how the health insurer may need to choose between two technologies with similar clinical outcomes. This is the classic situation in which the decision maker would benefit from having extra information. So in addition to what is being considered, one would also need to factor in drug prices and application limitations. Which would show that the first drug has a medium price, but needs to be administered every day in the hospital. While the second drug has a higher price, but can be taken orally. At this point, economic data could show that the second drug, while having a higher price is actually less costly.

Further insights:

HEOR is used to **complement traditional clinical development information** in guiding healthcare coverage and access decision for specific therapies.

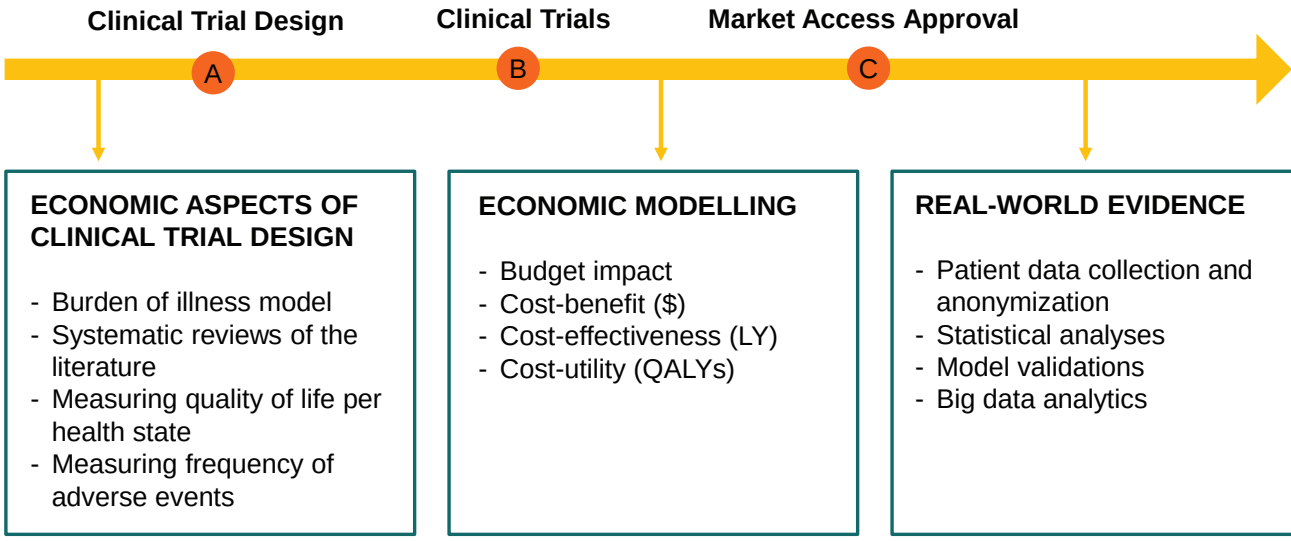
The majority of decision makers in the USA use HEOR evidence when making formulary and coverage decisions.

Unmet needs:

In the USA economic evidence is not required for obtaining market access, and therefore there a clear framework is missing.

Companies must design their own winning strategies for the production of economic evidence than can support access decisions.

PLANNING HEOR INTO MARKET ACCESS STRATEGY



HEOR IN MARKET ACCESS STRATEGY

This timeline shows a clinical trial design to market access approval to better illustrate how health economics aspects can be incorporated at different points in time.

We start from the point in which a new drug is developed, and a clinical trial is designed. Given the cost of clinical trials, it may be a good idea to explore the opportunities in the market before designing endpoints. In this case the economic discussion would revolve around two main topics:

- *The first is the current cost of the illness. Usually assessed with burden of illness models,*
- *The second is the current use of resources for the illness. Usually, systematic reviews of the literature can provide for insights on similar patient populations.*

Awareness on resource use and cost of illness may help clinical research organizations to identify which aspects should be measured in the trial. Apart from survival, it may be adherence, or safety, or quality of life. Speaking of, safety and quality of life actually have to be measured if economic modelling is going to be performed. After the actual execution of the trial comes economic modelling. Different models can be developed.

The first is the budget impact model, which estimates the additional expenditure, or the savings, that payers can expect when a new technology is introduced in the market. We will discuss this later.

Then, we have three models that are quite similar: cost-benefit, cost-effectiveness, and cost-utility. All of these models show how much the payer would pay for an additional unit of health.

- *If health is associated to a monetary value, then the it is a cost-benefit model.*
- *If health is measured in additional years of life, then it's a cost-effectiveness model.*
- *If health is measured in additional quality-adjusted years of life, or QALYs, then it is a cost-utility model. QALYs, are life years multiplied utility, which is a measure of quality. Utility ranges from 0 to 1, where 0 is death and 1 is perfect health. So if a patient lives for an entire year with poor quality of life, the QALY will be equal to a couple of months.*

Finally, there is real-world evidence, which is data collected on real-life patients after market access approvals. With respect to clinical trial data, real-world evidence is on a much larger scale of patients and obviously more realistic. After all, clinical trials are conducted in highly controlled settings. For this reason, many regulatory bodies ask for the submission of real world evidence after market access approval.

In this case, health economists can contribute with the design of tools for the collection and anonymization of patient data, with statistical analyses on significant and representative samples, but most importantly they can validate models by considering real life data inputs, which can decrease the uncertainty associated to model outcomes. Big data is an emerging topic in most industries, and in health its applications fall within real-world evidence.

REAL LIFE CASE STUDY: HEOR IN ITALY

ECONOMIC MODELING FOR AIFA

The Italian Medicines Agency (AIFA) requires companies to provide for the results of economic modelling as part of the technical report for national reimbursement approval. Detailed guidelines and templates have been provided.

In order to file for reimbursement, in Italy a technical report is submitted to the Italian medicines agency or AIFA, in which the technology is presented, clinical data is provided, and pricing and revenue aspects are described.

Since 2020, the AIFA specifically requests that the methodology and results of economic modelling are also attached to the technical report. Detailed guidelines and templates have been designed in order to ensure that the data provided for different technologies is somewhat standardized. In this way decision-makes can incorporate a pre-defined set of key indicators in the approval process.

In the guidelines, AIFA specifically asks for two types of models: budget impact model and the cost-utility model.

BUDGET IMPACT MODEL

The Budget Impact model, which is used to measure the change in the expenditure of the payer if it were to approve a new technology.

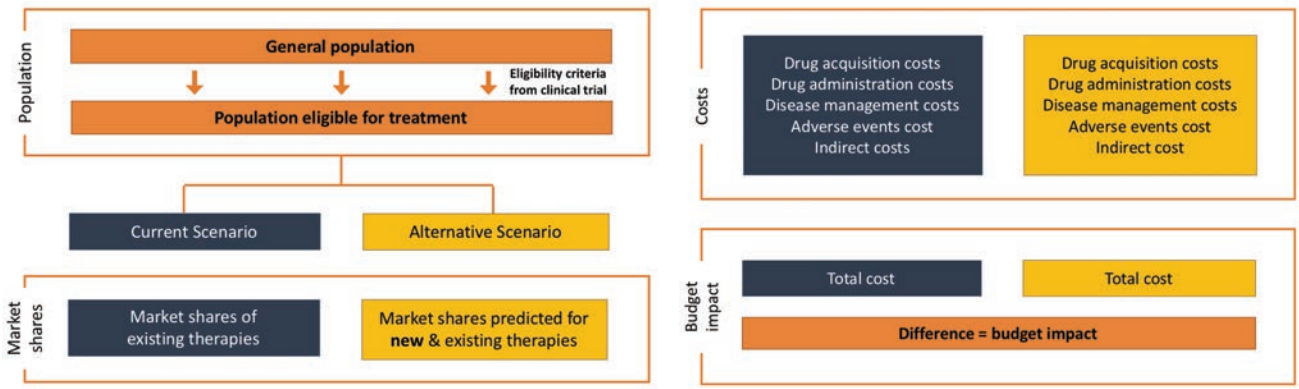
Basically, we consider two scenarios, one in which patients are treated with existing therapies, and one in which the new therapy is also available.

The patient population is assigned to different treatments according to the market shares. Each treatment as a different cost, which includes drug acquisition, administration, disease management, adverse events, and indirect costs. The total cost to treat the entire patient population with the different therapies is calculated.

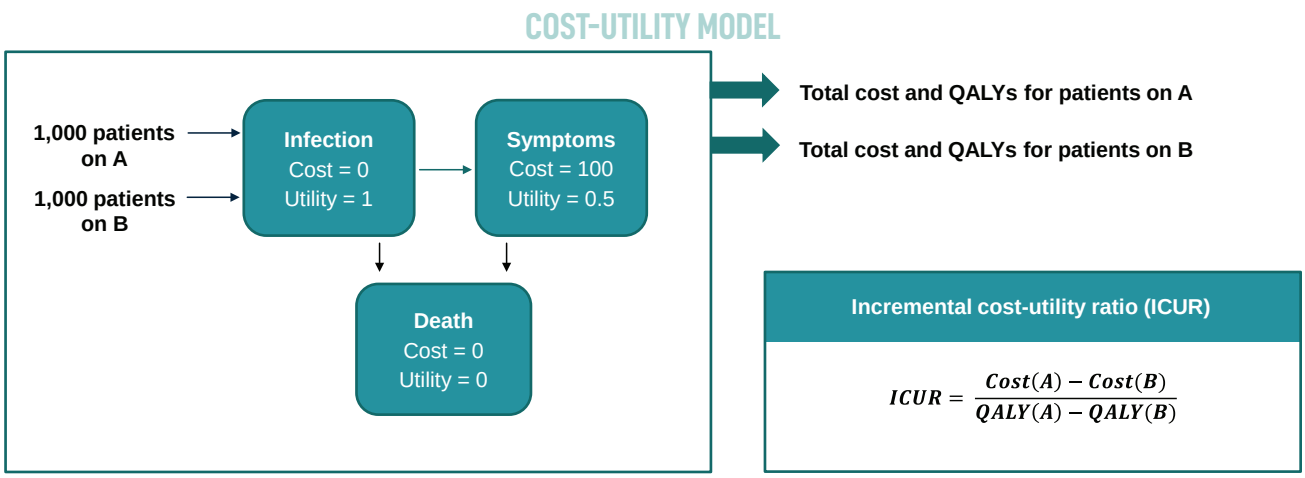
The cost difference between the two scenarios is the budget impact, or the difference in spending of the payer if it were to introduce the new treatment within the mix of therapies available.

The most common situation is that spending increases when the new technology is introduced, as a consequence of higher drug acquisition costs. This is okay, as long as the payer knows that there is some health benefit and how much it is spending for that additional health benefit, and this is where the cost-utility analysis jumps in.

BUDGET IMPACT MODEL



REAL LIFE CASE STUDY: HEOR IN ITALY



COST UTILITY MODEL

The Cost-Utility model is used to measure how much the payer will pay for an additional unit of health benefit. In this case, as we said earlier, health is measured as **QALYs, or quality-adjusted life years**.

Initially, a model structure is devised. For example, as written here, infected, symptomatic, dead. Each health state is associated to a **cost** and a **utility**. Utility as we said before is a measure of quality that is used to adjust life years for quality of life.

The way in which patients transition from one state to the other is simulated by the model usually over 20-to-40 years, once assuming that all patients take treatment A and a second time only taking treatment B. The treatment affects how patients transition from one state to the other. For example with treatment A patients that are infected remain asymptomatic for longer, and therefore there are more patients with zero costs and full utility. The model measures all the cumulative costs and the quality-adjusted years lived by the patient cohort for each treatment.

The main result is the **Incremental Cost-Utility Ratio or ICUR**, which is a ratio of incremental costs to incremental benefit of the option A with respect to the option B. Basically, it should be interpreted as the additional cost for option A for the every additional **QALY** that it generates. A technology is said to be cost-effective if the **ICUR** falls below certain benchmark, called the willingness to pay threshold.

If the **ICUR** is higher that this benchmark, it means that each additional **QALY** generated by the new technology is too costly. In Italy, the threshold is around € 30,000 per **QALY.**

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What is your opinion on the analysis of HEOR? Stay intouch!
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