CHAPTER X

ECONOMIC STUDIES

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Currently, clinicians have the feeling of being confronted with a double pressure: one emanating from the public authorities who would like to see them become actors in a policy of controlling health expenditure, the other coming from patients who would ask benefit without limit from medical technological innovations, which are often costly.

Faced with these constraints, it becomes more and more difficult to preserve this fundamental ethical fact that the medical decision must remain an individual contract between the clinician and the patient. Because health expenditure is increasing nearly twice as fast as national wealth, it is clear that policies to control health expenditure will continue to weigh on the medical profession for a long time to come.

Assuming that the problem of the long-term balance of Social Security accounts no longer arises, the question of the efficient use of resources in the health system would still remain, since the available financial resources are never infinite. Any inefficient use in the health sector sacrifices the possibility of producing greater welfare for the community, either in the sector itself or in the rest of the economy. The measures taken to control the health expenditure undertaken only accelerate awareness that any medical decision has concrete consequences in terms of the allocation of resources and implies an (implicit) choice to no longer be able to use the resources thus consumed at other purposes.

The empowerment of clinicians, who commit the use of collective resources, in a policy of controlling health expenditure, requires knowledge of the economic evaluation tools applicable to medical practice.

In this chapter, we will endeavor to put into perspective the economic analyzes applied to health strategies in relation to these debates on the functioning of the health system as a whole.

In a number of situations, the concern to optimize the allocation of resources, which is the primary purpose of the economic analysis, is in no way in contradiction with the interests of the patients: eliminating an obsolete or useless examination means avoiding a economic waste, but it is above all acting in the interest of the patient; similarly, favoring a medical strategy that provides the most efficiency at constant expenditure is to contribute both to improving the economic performance of the system, to reducing the costs of health insurance and to ensuring that the use of resources brings maximum benefit to patients.

Two confusions are too frequent. The first is that which reduces the economic evaluation to the sole concern of "saving money": developing a new health strategy source of increased expenditure can prove to be economically profitable when this additional cost leads to an

additional benefit for the community (for example, a gain in life expectancy or quality of life). The second confusion that often arises from the first is that which identifies the collective economic interest with the point of view of a particular agent, such as the health insurance fund or the hospital: the management of patients with a chronic illness in an outpatient way or by a home care organization can be a source of budgetary savings for the hospital, but it does not automatically guarantee the interest of the community, because home care can increase costs for patients or their families.

A methodological clarification of the main elements of economic evaluation may prove useful to clinicians in order to optimize their decisions. A number of health strategies inevitably obey a law of diminishing returns, i.e. the increase in the means of production leading to a lower additional return.

The progress of neonatal resuscitation illustrates this evolution: what it costs today to resuscitate a premature infant weighing less than 1 kg is out of all proportion to what was spent a decade ago for a newborn; it has been estimated that resuscitating a premature infant weighing less than 1 kg costs twice as much as for a premature infant weighing between 1 kg and 1.5 kg, and seven times more if it is estimated in years of life without disability.

Because it is not conceivable to "do everything for everyone", the question of the legitimate thresholds to be set for the health strategy frequently arises. A tension may result between the medical requirement that "the physician may not in the context of an individual case place the interests of society above those of the individual" and the management of medical resources. Contrary to the received idea which opposes medical ethics and economics, this notion is written into the code of medical ethics by its article 2, which specifies that the doctor is at the service of the individual and of public health. Clinicians are closely involved in finding ways to reconcile their decision-making autonomy and the collective interest of the healthcare system.

Here again, a better knowledge of the tools of economic evaluation constitutes an essential prerequisite for transparent debates on the limits of the health strategy and on the regulatory systems.

I - THE DIFFERENT TYPES OF ECONOMIC ANALYSIS

The basic principle of economic analysis within the framework of economic theory applied to public investments is the determination of a choice between different alternatives for the use of resources. It helps identify the most effective strategy. The economic evaluation cannot therefore be limited to a descriptive analysis of costs; it involves analyzing the different options while simultaneously considering the costs and the consequences, which distinguishes it from other forms of medical evaluation *(Table 1)*. In some cases the alternative may be the simple absence of a program.

Table 1 - Specificity of economic evaluation in medicine

		Are the costs and consequences of the alternatives measured?	
		yes	no
Is there a comparison alternatives?	yes	economic evaluation	therapeutic trial
	no	cost accounting clinical study	consumption statistics

Three types of analysis can be defined depending on the nature of the problem and the choice to be made *(Table 2).*

Table 2 *- Typology of economic evaluation studies of health strategies*

Type	cost measurement	identification of consequences	measure of consequences
cost minimization	euros	identical consequences for all alternatives compared	none
cost-effectiveness	euros	one-dimensional effectiveness indicator	physical unit
cost-utility	euros	multidimensional efficiency indicator	QALY Quality-adjusted life expectancy
cost-benefit	euros	efficiency indicator with one or more dimensions	euros

A - Cost minimization analysis

Cost minimization analysis aims to identify the least costly health strategy to provide a certain service. It is expressed in monetary units per patient treated.

This analysis is only justified if it has been demonstrated that the various health strategies studied have the same consequences in terms of therapeutic efficacy, which is rarely the case.

In addition, it is often important to verify that, with equal effectiveness, the social consequences are also similar.

This type of study can be adapted to the hospital situation. Indeed, we thus place ourselves from the point of view of the institution providing care and we compare the direct medical costs of two procedures, for example of two antibiotic treatments, one being administered orally, the other by intravenous.

B - Cost-effectiveness and cost-utility analyzes

Cost-effectiveness analysis makes it possible to compare strategies that differ in their costs and effects. It is expressed in monetary units per medical efficiency indicator (for example, in euros per year of life saved).

For example, a French study carried out by the PREMISS group (Protocol in Resuscitation for the Medico-Economic Evaluation of an Innovation in Severe Sepsis) [1] assessed the cost-effectiveness ratio of drotrecogin alfa (DA) compared to conventional management in the treatment of severe sepsis in real practice. Thanks to a "before" / "after" type model, a cost-effectiveness ratio of 20,300 euros per year of life gained was highlighted. The threshold used was that of acceptability proposed by the World Health Organization (3 times GDP per capita). For this willingness-to-pay value, the probability that AD would be cost-effective was 79%.

Similarly, if kidney transplantation, hospital dialysis or home dialysis differ in terms of the number of years of life saved, it is possible to compare them thanks to their ratio of years of life saved per euro spent.

In some cases, the single-dimension effectiveness indicators appear unsuitable, in particular the programs evaluated act both on the duration and the quality of life of the people who benefit from them.

To deal with these situations, "cost-utility" type studies have been developed, where the result indicator becomes the number of years of life gained adjusted for the quality of life related to health (QALY: Quality Adjusted Life Years).

To be usable in cost-utility type studies, health-related quality of life measures must be determined on an interval scale including perfect health and death: we then speak of cardinal preferences, as opposed to ordinals resulting from the use of a ranking method (psychometric quality of life questionnaire). For this, innovative experimental tools are used to determine preferences leading to an indirect estimation of the quality of life of patients. The use of a visual analogue scale, the standard bet or time arbitration, are the three most commonly used tools which meet the methodological requirements underpinning tending to carry out cost-utility type analyses.

An alternative option to these methods consists in using multi-attribute health state classification systems which are pre-scored, and which therefore avoid the long and delicate work of evaluating individual patient preferences: the three main systems are the Quality of Well Being (QWB), the Health Utilities Index (HUI) and the Euroquol (EQ-5D), whose "scoring" functions are based respectively on categorical scale measurements for the QWB, standard wager for the HUI and a visual analog scale for Euroquol.

For example, a cost-utility study evaluating different therapeutic strategies in the case of fistulized perianal forms of Crohn's disease was carried out [2].

In this work, a Markov model was used to simulate a one-year treatment period. The reference strategy, consisting of the 6-mercaptopurine and metronidazole combination, was compared with 3 interventions: the first involved 3 infliximab infusions (at 0, 2 and 6 weeks) with the 6- mercaptopurine and metronidazole in second line in case of failure; 3 infliximib infusions (also at 0, 2 and 6 weeks) with episodic reinfusion in case of failure, for the second; and finally for the third, the combination of 6-mercaptopurine and metronidazole with infusions of Infliximab (at 0, 2 and 6 weeks) more or less associated with episodic reperfusions in the event of failure.

The chosen efficacy endpoint was survival adjusted for quality of life, the unit of which is the QALY. For an almost similar effectiveness, the 3 interventions evaluated were much more expensive. The cost-utility ratios were $355,450/QALY (Intervention I), $360,900/QALY (Intervention II), and $377,000/QALY (Intervention III), respectively. The real question emerging from this analysis was: is society willing to pay more than $350,000 for each quality-adjusted life year?

Cost-effectiveness or cost-utility analyzes can lead to 4 types of situation:

- The strategy studied is less costly and at least as effective as the reference strategy, therefore efficient (and called "dominant"): it can be recommended from a medico-economic point of view.
- The strategy studied is more costly and less effective than the reference strategy, so it is not efficient (known as "dominated") and cannot be recommended.
- The strategy studied is less costly and less effective than the reference. This situation raises the question of whether the resulting savings are sufficient to compensate for a drop in efficiency.
- The strategy studied is more expensive and more effective than the reference. This is the most common situation. It is then necessary to arbitrate in order to know if the increase in cost is acceptable from the point of view adopted by the study with regard to the gain in efficiency obtained.

This trade-off is carried out by calculating a differential cost-effectiveness ratio (Incremental Cost Effectiveness Ratio – ICER) which calculates the ratio of the difference in the cost of 2 strategies to the difference in their effectiveness. It is interpreted as the additional cost generated by the strategy to gain an additional unit of efficiency compared to the reference strategy. Although it is possible to compare simple cost-to-outcome ratios for each of the health strategies, the correct comparison is that of incremental costs with incremental outcomes in order to establish an appropriate measure of final results and constitute a decision support criteria.

Once the incremental cost-effectiveness ratio has been calculated, it is a matter of deciding whether or not the amount that should be allocated to obtain this additional efficiency gain is acceptable. This raises the question of determining the threshold ratio, i.e. the ratio up to which the community is ready to go to obtain this additional gain. Depending on the country, this threshold varies. In England, the National Institute for Clinical Excellence (NICE) uses a threshold range of £20,000 to £30,000 per QALY gained, but debate is still ongoing over the use and level of threshold values for the ICER.

Some countries have tried to derive a threshold value for the implicit ICER based on past resource allocation decisions. Australia has estimated a threshold value of AU$69,900/QALY, New Zealand of NZ$20,000/QALY and Canada has defined an acceptance range from the cost of a dominant intervention up to 80,000 CAN$/QALY with a rejection range of 31,000 to 137,000 CAN$/QALY (Threshold values for cost-effectiveness in health care, KCE reports 100B, 2008).

In France, the use of "twice the gross national product (GNP)" per inhabitant is mentioned by certain authors who suggest that below 50,000 euros per year of life gained, certain strategies could be accepted without discussion [3]. . It would be necessary to discuss their validity for those between 2 and 6 to 8 times the GNP per capita. Finally, those exceeding the figure of 150,000 to 200,000 euros per year of life gained would be rejected.

C - Cost-benefit analysis

Cost-benefit analysis aims to compare the cost of a strategy and its benefit. In a study of this type, the real costs and consequences are expressed in monetary units. This analysis aims to calculate the net benefit for the community of the health strategy studied and to determine which of the various possible strategies "maximizes the net social surplus". It helps to determine if a certain goal is worth achieving.

Several profit measurement techniques are available. In the first, which emerged in the 1960s and is referred to as the “human capital” method, benefit is measured as the result of improved (or impaired) production by the health program. This method has been heavily criticized, particularly because of its assertion that the main goal of society is the increase of the national product per capita, which implies that non-productive people cannot have an improvement in their state of health. Another technique called “revealed preference” is based on estimating monetary trade-offs made by the individual in terms of risk taking. This method aims, for example, to estimate the willingness to pay for a reduction in morbid or fatal risk, by observing wage differentials associated with a risk differential on the labor market. We can thus deduce a statistical estimate of the price of human life. The last technique called “stated preference” is based on the expression of preferences declared by individuals in a fictitious market. Among the techniques for estimating stated preferences, contingent valuation consists in proposing to an individual a hypothetical market situation on which the respondent must indicate the maximum monetary amount that he is ready to consent to access the proposed good [4][5]. This amount is an indicator of the usefulness or satisfaction that this good brings to him.

For example, a French study evaluated, by simulation, the opportunity in terms of costs and clinical benefits of a vaccination campaign against tick-borne encephalitis among French soldiers on mission in Kosovo, versus the absence of vaccination [6]. The authors valued the cost of not vaccinating (from a “human capital” perspective), and compared it to the cost of the vaccination program. The judgment criterion for the economic evaluation corresponded to the benefits of vaccination in monetary terms (valued by the human capital method) measured by the number of cases of tick-borne encephalitis avoided, i.e. ultimately in avoided costs. These avoided costs are those related to mortality and morbidity of the disease. For this, the authors used the value of human life expressed in Francs (French money preceding Euros) according to the pension paid by the Ministry of Defense to the beneficiaries in the event of death in service. The cost of the sequelae, meanwhile, was obtained by the guide-scale of invalidities paid under military pensions (Guide-scale of invalidities applicable under the code of military pensions for invalidity and victims of war, provided by the Department of Veterans Affairs). The results were as follows: 143 cases of tick-borne encephalitis could be prevented by vaccination/4 years, including 3 deaths and 17 patients with disabling sequelae; the total costs of vaccination were 25.0 MF and the total costs “avoided by the vaccination program” amounted to 27.1 MF.

Whatever the type of study, uncertainties on the estimation of costs or consequences may exist; therefore, it is recommended to carry out a sensitivity analysis in each case. This verifies whether or not the modification of the values taken by the main variables leads to a modification of the results of the analysis.

II - THE DIFFERENT PERSPECTIVES OF ECONOMIC ANALYSIS

Several points of view are possible for an economic analysis. The costs, the results, the benefits can be envisaged in four ways: according to the payer, the service provider (the hospital), the patient and society.

A - The cost for the payer and for the hospital

The cost for the payer (health insurance) is equal to the pricing allowed by the latter, while this same cost is for the hospital the real cost of providing the service whatever the pricing. To determine the real cost for the hospital, it is often necessary to have cost accounting in the establishment, that is to say an accounting system allowing the calculation of the cost per patient stay.

For example, a study established by determining the cost of the work of nursing staff and the necessary supplies, that delivering an antibiotic in one daily dose instead of several doses allowed savings of 6 euros per patient and per day for the same therapeutic efficacy. This interesting saving for the hospital is nevertheless without repercussion for the payer.

B - The cost for the patient

The cost for the patient is the amount to be paid not covered by health insurance for the provision of a service, that caused indirectly by the treatment or the illness (workday not performed, travel not covered, etc.) and that of the subjective costs (anxiety, pain, etc.). If day surgery, which allows the reduction of hospitalization, is a source of savings for the payer, it can be for the patient a source of additional expenses varying according to different reimbursement methods. The interests are then contradictory according to the analytical perspective.

C - The cost to society

The cost to society is the total net cost for the various economic agents of this society, including the loss of productivity of the patient and the total expenses caused by the disease and its management. It thus represents the opportunity cost measuring the sacrifice of resources made for a given program and which cannot be used for another effect.

Thus, the diffusion of innovations in the field of prenatal diagnosis of genetic anomalies by molecular biology techniques is currently slowed down; the application of these methods results, for the hospitals which practice them, in additional costs without sufficient compensation, whereas the overall profitability for society would undoubtedly be high.

III - THE DIFFERENT TYPES OF COSTS

Different types of costs make up the total cost: direct cost (medical and non-medical) and indirect costs (indirectly linked to treatment).

A - Direct costs

The direct cost is the value of the resources directly consumed for the analyzed program.

The direct medical cost usually includes hospitalization costs, drugs, biological and radiological examinations, medical fees, rehabilitation care and necessary long-term care.

Its estimation poses methodological problems, in particular because the absence of a real market price system in the health sector means that health expenditure is not always representative of the real value of medical costs. Indeed, cost must be distinguished from pricing. Pricing is imposed by a regulatory system, which often does not reflect the real cost of producing a good or service.

In addition, many other direct non-medical costs must be considered: food, non-medical transport to establishments health care, equipment or adaptation of the home… They are caused by the illness or the treatment but have not led to the consumption of a medical service. Some of these sums may be paid directly by the patient or the patient's relatives: a study has shown that the family of a child with cancer uses a quarter of its income for non-medical expenses due to treatment and usually not reimbursed.

B - Indirect costs

The indirect costs represent the productivity losses linked to the disease, that is to say the hours of work lost following a morbid episode.

The determination of the loss of productivity is done by measuring the number of hours or days of work lost due to the illness and its management. This number is measured by ad-hoc surveys. Three methods exist for the monetary quantification of these losses (Methodological guide for the economic evaluation of health strategies, College of Health Economists, 2003):

- The theory of human capital

This theory leads to quantifying the impact of the disease by the production losses it induces, by multiplying the number of working days lost by the value of this production, expressed by the GDP per active person, related to the working day. Simple to implement, this approach is unrealistic insofar as it is based on the assumption of a full employment economy in which the loss of a working day has a proportional and mechanical impact on production.

- The friction cost approach

This approach, more realistic than the previous one, considers that the loss of production is not exactly proportional to the number of working days and proposes a macroeconomic modeling of the impact of work stoppages on the labor market. It therefore requires specific, important, permanently updated empirical work in order to be applied.

These first two approaches do not take into account unpaid work, in particular domestic work, or the time of inactive people such as retired people or people outside the labor market due to a disability.

- The theory of well-being

The third approach is derived from welfare theory and is applied in cost-per-QALY or cost-benefit studies with willingness to pay. This approach consists in evaluating the inconveniences related to work stoppages by integrating them into the evaluation made by patients of their state of health following a given treatment. The so-called indirect costs are included in the denominator of the cost-results ratio.

The extent of the costs taken into account must be judged according to the context and the objective of each study: limiting oneself to direct medical costs alone can be entirely appropriate when comparing two neighboring therapeutic protocols in the same hospital context; on the other hand, neglecting the indirect costs biases the evaluation when a hospital management strategy for psychiatric disorders is compared with a community intervention strategy.

IV – DISCOUNTING AND INFLATION

A- Update:

According to economic theory, a sum paid today does not have the same value if it is paid later: there is a preference for the present, because the immediate availability of resources allows them to be invested with interest, ensuring later a higher sum. The reasoning applies to the costs and to the results, when these are valued in monetary terms (cost-benefit analysis).

Discounting is an economic calculation that standardizes costs over time. It is based on a discount rate r which links C_n costs borne in year n, to their present value C_0; you can use tables [7] or a formula. Assuming that the costs incurred at the beginning of the year, therefore not discounted in the 1st year, the present value PV of a cost is:

$$PV = \Sigma C_n(1+r)^{-n} = C_0+C_1/(1+r)+C_2/(1+r)^2+\ldots+C_n/(1+r)^n$$

The rate r is often chosen at 5%; a sensitivity study is recommended (see below) to assess the impact of different possible rates on the results of the study.

B- Inflation :

When the annual price increase is significant (example of the 1970s in France), or applies differently to the actions or programs being compared, it must be included in the analysis.

V - CONCLUSION

With regard to the definition of public health policies, national prevention programs, allocations of investments in equipment or heavy means, recourse to economic analysis is "natural" to help define, as we have seen, the optimal modalities of an intervention.

With regard to the direct integration of economic evaluation in the optimization of clinical strategies, we must, on the other hand, avoid any normative logic and accept, as we have pointed out above, the tensions between collective ethics and individual ethics. It is in order to promote the transparency of such debates that we have proposed, throughout this chapter, a rapprochement between economic thinking and clinical practice.

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