Human costs are one of the cost elements included in economic evaluations and play an important role in disease costing and in the techniques that form part of the so-called cost benefit approach [1, 2], comprising cost benefits (CBA), cost effectiveness (CEA) and cost utility analyses (CUA).

At present the costs are classified into three aggregates: direct, indirect and intangible or human [3, 4]. Before examining the third type of cost, the subject matter of the present paper, we shall briefly consider the other two types.

Direct costs refer to the costs for diagnosis, therapy and rehabilitation – generally speaking healthcare. To such medical costs other direct, non-medical costs should be added, such as, for example, transport costs for reaching and returning from healthcare structures, plus the time needed for these journeys. These costs are the easiest to quantify even if it is necessary to distinguish the elements to be included in an economic analysis from those useful for financial evaluation, and which could differ from the former both as regards the type and method of evaluation.

Before beginning with some theoretical issues related to the human costs, we present some financial data about the Italian market for antimigraine drugs. The main reason of that is related to the idea of direct costs for the national healthcare service (NHS) and for citizens. The antimigraine market, even though is not so large as the antihypertensive one, has a quite important weight. Another reason is to take this market as an example of behaviours by pharmaceutical companies: introduction of a new type of drug (e.g. triptans in 1992) has lastly changed the structure of the market (for example today of the market of antimigraine is about triptans). So it means that when a new effective molecule is introduced into the market, it is able to “absorb” it.

Here, we found another point to think about CBA.

Some countries (Australia, the Netherlands, and others) started to require a type of CBA (usually CEA), mainly for financial reasons. The introduction of a new molecule implies to modify some cultural paradigms: a cost-effectiveness analysis needs to be developed using a “meta-analysis”
approach. In other words, we need some models that design some theoretical behaviours, and from such assumptions starting to focus on effects of a new drug. Quite often it is just a theoretical approach that after 2–4 years could be changed by some empirical data. As first conclusion we can state that many CBAs could be affected by many theoretical assumptions that have to be changed when the researchers have new data.

A financial point of view develops peculiar issues different from an economic point of view. From that, we can analyze healthcare actor’s behaviours (NHS, pharmaceutical industries, physicians, and citizens). Then the CBA implies a more macroeconomic methodology than traditional micro-analysis.

A last general point to be discussed about is connections between outcome research and industrial value of drugs. We have implied two different values that often are quite far between them. When we use the “outcome approach” we imply to use only healthcare meaning for medicine. In other words, we see the medicine as merely a “tool” to be better (or to suffer less); we focus only on the “good” use to go over sickness.

In practice, as we show later, many types of measurement studies focus on the “health” value of a drug, and they should be integrated with some other measurements that consider the “social” value of a medicine. Besides the “health” value of a medicine, a concept of a drug as an “industrial product” also exists. Industrial product means to consider a drug as a final step of research, marketing, commercial steps and so on.

These dimensions affect the market price that not necessarily means the opportunity cost, in other words the social value. Moreover when we compute direct costs we have to consider the market price.

*Indirect costs* refer to costs accruing from production losses caused by illness. As such they were the first to be taken account of in economic evaluation. Their inclusion is related to the human capital approach that initially had the objective of attributing an explicit monetary value to human life or disability. The founder of this method is reputed to be Sir William Petty, a seventeenth century statistician and physician, even if in the Babylonian Hammurabi law, the first written legal codes going back to 1792 B.C., contained an evaluation of such damage [5]. However, despite the fact that the human capital method is used in today’s courts of law and by insurance companies to assess damages due to injured persons, together with other components specific to this approach, all attempts to obtain an explicit monetary value of disability or loss of life on the basis of an individual’s present or future earned income have been abandoned for purposes of economic evaluation. Nevertheless, indirect costs, or in other words, production losses, remain one of the elements taken into calculation of the social cost of illnesses.

*Human costs* refer to the health of an individual and a population considered as such, regardless of the resources involved and production losses. They refer to the fact of falling ill or dying, along with the associated suffering and pain. Such costs are usually referred to as intangible on account of the presumed impossibility to quantify them. The lack of a definition of *health* that would allow objective measurements to be made of variations from “the state of being healthy” contributes to this state of affairs. If, for example, we took the definition of the World Health Organization, of a complete state of psychophysical and social well-being and not only the lack of sickness, the definition would not help us to establish a precise “quantity” of health, and far less reductions in it as a outcome. Researchers consequently decided to revert to proxies, in the form of health indicators, and to consider different aspects on a one by one basis. In this manner a vast literature has been built up ranging from indicators that only consider aspects of physical limitation to complex, multi-dimensional indices that combine physical with psychological or relational aspects. Before discussing these indices it should initially be noted that the first measurements of human cost were wholly objective and based on statistical-epidemiological methods. Thus human cost was expressed by means of mortality and morbidity rates, which are, in fact, methods that enable cost to be expressed as a quantity. In this type of indexing the only elements of uncertainty derive from the use of subjective probability calculations. In other words, without sufficient historical knowledge to allow for the construction of objective frequencies, subjective estimates must be used, often made by physicians, epidemiologists or other experts, which consequently makes the measurements “not objective”. In addition, according to a theory of thought that considers a patient’s judgement final, there is the widespread idea that the subjective probabilities that correspond to the estimates made by patients on the risk of dying or falling sick should, in all cases, be used insofar as they are more in line with the so-called principle of *consumer sovereignty*, rather than preferences expressed by physicians and those constructed on the objective probabilities.

Successively in 1947, Dempsey introduced the concept of potential years of life lost (PYLL). This indicator takes into account not only the fact of dying but also the age of death. PYLL is constructed in such a way as to comprehend the average statistical life of various individuals [6]. In most cases life-expectancy at birth or age at death is used, but they could also be calculated differently, for example, by taking into consideration the moment when a diagnosis was made and calculating the time intervening before death. As this is also based on “natural units” (number of deaths, age, life-expectancy) they must be regarded as objective indices of human cost. The only element of uncertainty is due to the estimate of probability, which is necessary when *ex ante*
evaluations are made. This is found, as stated, in the case of subjective probabilities or when estimates are based on populations other than those being examined. An example is the calculation of PYLL of headache in Italy using specific rates, by age, calculated in the USA or in another country.

Successively, from such objective indicators, there was a movement to subjective and, therefore, less objective measurements. This took place in 1968 after Klarman and some of his colleagues in Great Britain attributed a different weighting to the years of life lived after a transplant with respect to those lived under dialysis, for patients affected by kidney failure [7]. They argued that the quality of life achieved thanks to a kidney transplant was better than that for patients who had to undergo continuing dialysis sessions and added 25% to the number of years of life so that the two types of patient could be compared qualitatively and quantitatively. This means that one year of life after a transplant guarantees the same “utility” (situation of indifference) of 1 year and 3 months under dialysis.

Including quality of life (QoL) has led to the development of a variety of measurements among which the most well known are the quality adjusted life years (QALYs) and disability adjusted life years (DALYs) [8, 9]. Although the calculation of these healthcare indices does involve any significant practical difficulties, the indices themselves do present problems, commencing from the tools for weighing life quantity, the latter being calculated along lines similar to PYLL.

In this context we shall not discuss the difference between QALYs and DALYs preferring to treat them as similar types of measurement. We shall merely point out that the former weighs the quantity (years, months, days life) of a positive element, quality of life. Generally speaking these weights have 0 and 1 value limits, where the first value expresses a state of health so deteriorated as to be comparable to death and the second to express a state of good health, sometimes considered as a state of normal health. Without making any further comment, we shall limit ourselves to saying that as good health is a theoretical situation that cannot, in practice, be attained, it is necessary to commence from the conditions that, in the absence of pathologies, are normal for every single individual.

In the DALYs index, health is regarded in relation to negative situations that limit the activities or the functions of the individual: the value 1, therefore, refers to maximum disability while the value 0 indicates no disability. Therefore 0.9 is an acceptable health condition when referred to QALYs, although it is very negative in relation to DALYs. More simply it can be stated that the two values in the two indices can be regarded as reciprocal and thus mathematically translatable.

However, it remains to be seen if these two indices, as well as being conceptually similar, are an “objective” measure or not and, if not, what the level of uncertainty is.

The “utility”, understood as a year of life weighed for quality, expresses a “preference”. Therefore, the first question is “who” must evaluate quality of life: the physician or other specialists with a “more expert” knowledge of the problem or the patients as they are the best judges of their own state of health. Should this mean only the actual patients affected by the pathology in question, or all “citizens” insofar as potential patients? It is clear that the average value of the same state of health can vary as between these three groups of individuals (physicians or other experts, patients, citizens), as well as varying within each group. Some attempts have been made to overcome these limits using indices that take account of the various preferences.

As regards practical tools, it must be immediately stated that the literature on the quality of life is exceedingly vast even if few indicators have actually emerged, designed to obtain the weightings used for QALYs or other similar indicators. There have been frequent attempts to adapt measurements designed for other purposes, i.e. indices used to express in general terms the quality of life in relation to the seriousness of various pathologies. Among these measurements there are single-dimension indices that consider health solely in terms of physical restriction, as well as bi- or tri-dimensional (physical, psychological or social health) and even multidimensional, among which the so-called health profiles. The latter tend to break down the various components (for example motor functionality, physical suffering, psychological unease, domestic activities, social relations or relations with a partner, working activities) and attribute values to every single area, but these are only occasionally brought together in a synthetic measurement. However, for this purpose, the values involved must be cardinal - and thus summable - and not ordinal. For example the value 0.8 expresses a quality of life two times greater than 0.4 and not only that the former is higher than the second.

With respect to specific indicators for single pathologies, a series of experiments has been initiated to obtain evaluations on the quality of life of the entire population, among which we cite SF36 and EQ5 [10].

Hitherto, utility has been considered a synthetic measure of the quality of life, but in fact there are profound differences linked to the summability of various components of quality of life. The QALY index contains the term quality even if, more rigorously, it represents a measure of utility, a fact that emerges from the use of the term utility in a type of economic analysis where the QALYs index is widely used. The analysis in question is the constitution utility analysis, which distinguishes itself from CEA insofar as the latter uses indicators whose results are expressed in natural units (death or case of illness, or potential years of life gained).

The problem is complex and, in our view, takes us back
to the two major meanings of the term utility. The first is the most familiar to economists by being related to the general principles of the “welfare theory”, particularly for the part referring to the satisfaction of consumers, which was amply and lucidly discussed by Arrow (1951) with his celebrated “impossibility theorem”. The second, instead, derives from the “theory of utility”, which owes its origin to a contribution by von Neumann and Morgenstern (1944). Leaving aside the details of this problem, the discussion can be restated in terms of QALYs [11]. This index adapts itself to the theory of utility not only because decisions are normally taken in conditions of uncertainty, and not certainty as usually premised in the theories of consumer utility, but also because utilities are always considered in cardinal and not ordinal terms, where collective preferences can be obtained as the sum of individual preferences, thus overcoming the obstacles posed by the impossibility theorem.

This is the concept to which those attempts refer that try to aggregate the various aspects making up the quality of life understood as utility, or the preference associated with a specific state of health.

We conclude this brief theoretical discussion on human costs with some ethical considerations. For this purpose we distinguish “technological” type economic evaluations from “allocative” evaluations. In the first case the patients are all affected by a specific pathology and it must only be decided what the most efficient technology would be (in terms of cost effectiveness or cost utility). In the second case, the comparison is inter-sectorial, and concerns groups of patients affected by different pathologies. The evaluation is above all useful for regional planning. The groups of patients in this case could have different ages and, therefore, indicators such as QALYs and the DALYs could be open to the criticism of ageing: all things being equal, such as costs and quality of life, the younger patients are advantaged with respect to older patients because they have a longer life-expectancy due to their age and not to the specific characteristics of the pathology. This happens when human costs are calculated on the basis of the incidence and not according to the prevalence method. The DALYs index does not run this risk because it is designed to give a relative annual value to the social cost of various pathologies, or groups of them, thus avoiding the extension of the evaluation to the entire life span of the patients. Even when DALYs are calculated according to the method proposed by Murray, as used in the Global Burden of Disease Study, which uses a function to yield a value for the various ages, the trade off between patients of different ages does not exceed a ratio of 1 to 3, while this limit is easily exceeded with the QALYs.

In addition, by primarily addressing developing countries, the maximum value is obtained in intermediate ages, the productive ages, given the high rates of infant mortality and the short life-expectancy found in such countries. In the QALYs index, on the contrary, the lower an individual’s life-expectancy the lower his or her implicit value. Therefore, given the present tendency in industrialised countries where the weight of chronic-degenerative pathologies is ever greater, the difference expressed in QALYs among the various ages is increasingly evident.

The advantage of DALYs is that the function used to express the value of the various age is easily understood as a function of utility: it is derived from preferences expressed for age and not from a mechanical method as in the QALYs index [12]. It is sufficient to create a function based on a different system of preferences in order to modify the relative values, if necessary annulling all age differences. Thus by calculating the human cost for each single year, only the differences due to conditions of disability would emerge.

After this brief evaluation it can be concluded that the importance to attach to the quality of life can be easily included in the calculation of human costs with respect to merely quantitative indicators. This, of course, means that the estimates become less objective and leave more space for preferences, but this does not entail that the evaluations are less significant. If anything, the results are enriched by the inclusion of new information.

Unfortunately, much more needs to be done to find measurements that can obtain, if not unanimous approval, at least a vast consensus. However, if we review the progress made, we must also recognise the considerable efforts made in this direction, all addressed to providing precise indications on the human cost of various illnesses. As always, the greater the spaces opened up by discussion on these themes the further the progress that can be made, so long as there is the desire to find a common basis for development rather than accentuating, as in the past, differences in attempts to demonstrate the usefulness of one tool with respect to another.

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