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Pharmacoeconomic studies: pitfalls and problems[1]

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ABSTRACT

The literature on economic evaluation of pharmaceuticals is growing rapidly. Although there are substantial methodological advances, there remain serious problems and pitfalls. The presentation focuses on three aspects i.e. use (and abuse) of evaluation studies, methodological problems and the quality of published studies.

The use of evaluation studies for decision-making at the micro or macro level is not clear. There are ethical concerns toward priority setting dictated by economic evaluation studies. Especially in drug evaluation, the objectives of evaluation studies are not always clear.

Some aspects of the methodology are settled, leading to generally accepted guidelines for evaluation. However, serious principal problems of methodology remain, especially in how to value health status effects. Apart from differences of opinion on the proper methodology, compiling and generating the required data for practical analysis is marred with difficulties.

Recent surveys evaluate the quality of published evaluation studies, using generally accepted guidelines for evaluation. It shows that a large percentage of published evaluation studies is of substandard quality.

The literature on economic evaluation, and especially on evaluation of pharmaceuticals, is growing rapidly. Project and program evaluation started in the late fifties. Health evaluation is even more recent than that. The number of publications within the domain of health evaluation is increasing fast. In an article on the growth and composition of the literature, ELIXHAUSER et. al. (1993) found that the annual number of CBA and CEA studies increased from about 20 in 1970 to more than 250 in 1990.

Although there are clear methodological advances, there still remain serious problems and pitfalls. This presentation focuses on three aspects i.e. 1. the use (and possible abuse) of evaluation studies, 2. problems of methodology and measurement and 3. the quality of published studies.

1. THE USE OF EVALUATION STUDIES

Most economists (and especially health economists) strongly advocate the use of evaluations studies - cost analysis (CA), cost minimization analysis (CMA), cost effectiveness analysis (CEA), cost utility analysis (CUA) or cost benefit analysis (CBE) - to guide resource allocation in health care. In some countries or states (Australia, Ontario), economic evaluation according to specific guidelines, is already mandatory for listing of new drugs (HENRY 1992). In other countries, economic analysis is required to support drug price reviews or reimbursement status (DRUMMOND et. al. 1993)

Are these countries examples to be followed? Should economic evaluation studies of drugs become a standard instrument of regulatory authorities? At first glance, the answer to this question seems evidently positive. However, a closer look shows that such policies are not free of problems.

First, economic evaluation is an imperfect tool. As HUTTON (1993) recently argued, economic evaluation exhibits many features of a "half-way technology", i.e. it is rarely

used routinely, it requires specific expertise, it is expensive to carry out, riddled with uncertainty in its methods and more of an art than a science. Underlining this status is the fact that, within pharmaceutical companies, economic evaluation analysis is typically the concern of the marketing department rather than that of the science division. For some drugs - e.g. with well-defined and ineffective comparators, ample data on various health effects, clear-cut therapeutic effects, etc. - economic analysis is relatively ease to perform and perhaps not even necessary[3]. In other cases - many rival drugs or therapies, minimal data on selected health effects, guesstimate (rather than estimates) on outcomes, etc. - economic analysis is often merely a tool to organize data and thinking. It is not clear if it is wise to let a "half-way technology" govern policy making, let alone, clinical decision-making.

Second, there is the problem of sponsoring and selectivity bias. Most academic research on economic evaluation of pharmaceuticals is sponsored by the pharmaceutical industry. Economic evaluation is often a mutually beneficial undertaking to both academics and the industry. Academics are ever more pushed to find new sources of funds. At the same time, pharmaceutical marketing benefits if an "independent" academic research team reports on the cost-effectiveness of their products. Several authors (HILLMAN et. al. 1991, DRUMMOND 1992) have argued that this symbiosis between academia and industry is a possible source of bias.

Pharmaceutical companies evidently prefer favorable results on their products as they bring higher reimbursement status, better price and increased sales. This leads to a double selectivity bias. First, companies are more likely to sponsor studies expected to generate positive results than negative results. Second, only those studies with positive outcomes will be published. This bias is reinforced by the tendency of scientific journals to accept "positive" publications more willingly than "negative" publications. As academics want to get published, massaging data, selective reporting and downright fraud is not unknown.

[3] A manager, responsible for business development in a pharmaceutical firm, put it as follows: "if we need cost-benefit analysis, it means we are in trouble showing that we have a good product".

Due to the half-way technology status of economic evaluation, there is ample scope for favorable data assumptions, possibilities in selecting the most favorable health outcome measures or the worst of comparators. Researchers and companies are able to manipulate results in order to obtain favorable results. Furthermore, public decision makers often lack the appropriate expertise to assess the methodological standards of these studies and to interpret results adequately. Some have suggested government funding of evaluation research as a way out of these biases. However, government agencies are no angels either, especially if they are heavily pressured to stay within budgetary constraints. In that case, a bias toward negative results of evaluation studies might be expected.

HILLMAN et. al. (1991) formulated several recommendations to counter selectivity bias. They suggest that pharmaceutical companies should provide global research grants to universities, rather than contract with individuals or individual universities. They also make several practical recommendations in conducting unbiased evaluation research. Perhaps the most important recommendation is that any research contract should stipulate that, if the company does not publish results within a reasonable time after completion, the researcher has the right to publish findings regardless to their nature. It is our experience that this clause often seriously inhibits sponsoring from pharmaceutical companies as well as from government agencies.

Third, fundamental objections to the use of economic evaluation at a global level might be raised. Some countries have a decentralized and rather "liberal" system of health care. In these countries regulation is achieved through providing the proper incentives for health insurance and health care providers. Regulators in such countries prefer the use of "market-type-mechanisms" (OECD, 1993) to allocate resources rather than "command-and-control". Other countries have a more centralized and planned system of public health care where regulation is more by directive or "command-and-control" mechanisms of regulation.

In countries with a tradition of decentralized decision-making and "médicine libérale", rigorous use of economic analysis to decide on global drug formulary, drug

reimbursement status or drug prices, etc. will be far less acceptable by those regulated than in a public health service environment. Providers will object and, if possible, simply not abide to laid down rules, as it clearly impinges on "clinical autonomy" and "therapeutical freedom"[4]. They will prefer more decentralized decision-making processes to determine drug formularies so that far more specific treatment guidelines for drug use can be taken into account. For a description of such decision-making process see e.g. NASH et. al. (1993). It is all very well to decide not to list a particular drug on a national formulary because it does not withstand the (imperfect) test of an economic evaluation, but the wisdom of such decision is less clear if it provokes or calls into existence the creation of private (legal or illegal) markets for non-listed drugs where ability and willingness to pay then governs access.

Finally, mandatory use of economic evaluation of drugs would undoubtedly strengthen the regulatory grip of public authorities on pharmaceutical companies. It is likely that economic evaluation studies would be used by health care regulators to negotiate price concessions, to withhold approval of high-priced drugs, to tie reimbursement rates to price concessions, etc. Evidence shows (see SCHERER 1993) that in countries with an already strong regulatory tradition (e.g. the European nations) have on average lower drug prices compared with countries where free pricing is the rule (e.g. U.S.)[5]. American drug manufacturers and government officials have complained that through regulatory interventions outside the U.S., these nations are free-riding or cheap-riding on drug development efforts of U.S. firms, paid for by the American public.

Government bodies regulating prices and reimbursment are often myopic and might be tempted to use this new tool to strengthen drug price regulation or limit the use of high-priced drugs, without taking into account the long-run detrimental effects on R&D and technological progress. As the amount of resources going into R&D

[4] In some case, they are even followed by the Courts if they can show it is in their patients' interest not to abide to regulation.

[5] SHERER makes an exception for Japan.

depends in part on the expected mechanisms to finance the provision of health care determining the expected rewards, a change toward more restrictive regulatory attitudes is likely to slow down technological progress. In a review on the relationship between prices, profits an technological progress in the pharmaceutical industry, SCHERER concludes that regulating drug prices in the U.S. could seriously impair the industry's incentives for investment in new products. A similar but more global argument was made by WEISBROD (1991). He argues that the gradual shift from retrospective financing toward more prospective methods of financing health care in a dominant health care market such as the U.S., leads to slower technological growth in health care.

It is not clear if the effect of introducing mandatory evaluation on technological development leads to desirable or non-desirable side-effects.

There might be a detrimental trade-off between static and dynamic efficiency as cost effectiveness and cost utility analysis offers no guidance about the global willingness to pay for health care. Although static allocative efficiency within a given budget might be improved upon by rigorous application of economic drug evaluation, it is perhaps at a cost in dynamic efficiency. This trade-off is not yet fully understood.

On the other hand, equalization of cost effectiveness or cost utility ratios at the margin might lead to gains in dynamic as well as static efficiency as it may lead to a redirection of research and development expenditures from less cost effective drugs to more cost effective uses of resources.

In sum, it would be unwise to adopt economic analysis blindly in guiding resource allocation and use it without qualification. However, it is even more risky to allocate scarce resources without any reference to cost effectiveness or cost utility. Despite caveats and pitfalls, economic analysis certainly has its merits, if used properly.

2. METHODOLOGICAL ISSUES

Economic evaluation of health care technology certainly has progressed substantially, especially during the last decade or so. The result is that there is consensus on what constitutes a proper economic evaluation of health care technologies. Perhaps the most widely used list is GUYATT et. al. (1986) or DRUMMOND et. al. (1987). These principles are covered in depth in other presentations. The main items on such a list are in table 1. Despite agreement on many methodological issues several aspects of evaluation are still hotly debated in the literature. In this paper, but a few issues are singled out for discussion.

Table 1: Some basic standards for economic evaluation

1. Identify the viewpoint(s) for the analysis (society, government, industry,...)
2. Consider all relevant alternatives (choice of comparator)
3. Use the appropriate form of economic evaluation (CA, CMA, CEA, CUA, CBE)
4. Measure all relevant (opportunity) costs and benefits
5. Use incremental (or marginal) cost and benefits
6. Allow for differential timing of costs and benefits (discounting)
7. Allow for uncertainty in costs and benefits (sensitivity analysis)
8. Present and discuss results appropriately (omitted costs and benefits, equity aspects, ...)

2.a. OUTCOME MEASUREMENT AND VALUATION

In the recent years, there has been a shift from intermediate outcome measures (e.g. the number of cases treated) or partial outcome measures (e.g. the number life years saved) to more global and comprehensive measures such as Quality Adjusted Life Years gained (QALYs), Healthy Years Equivalent gained (HYEs) or Disability

Adjusted Life Years gained (DALYs). Partial or intermediate outcome measures limit analysis to cost-effectiveness analysis (CEA), whereas more global and comprehensive measures allow for cost-utility analysis (CUA).

These global measures (QALYs, HYEs and DALYs) estimate the number of life years gained from a therapy, but each life year gained is adjusted for quality of life. The adjustment factor for quality of life corresponds to a value on a scale from unity (perfect health) to zero (death) or even a negative number (states worse than death) assigned to various health states. QALYs[6] are the most widely used measure. Several standardized non-disease specific and multidimensional scaling instruments are available nowadays to adjust life years for quality of life. Some of the most famous scales are the Quality of Well-being scale (QWB), the MacMaster Health Classification System, the Rosser/Kind index and the EuroQol Instrument.

QALYs are used at micro levels of decision-making e.g. by clinicians facing a choice between alternative treatments and at the macro level, whereby marginal cost per QALY gained for different treatments (so called "QALY League Tables") are used to select priorities where to spend additional resources.

Although the concept of QALYs and related concepts such as HYEs[7] and DALYs are a great step forward in the methodology of cost utility analysis, their use is not straightforward.

1. Some discussions in the literature are related to fundamental issues such as to what extent QALYs measure the social value of a health program rather than the increase in the production of healthy years from that program. Most authors recognize that QALYs measure production of health (MOONEY & OLSON 1991, BROOME 1992,

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[6] QALYs are a University of York invention (WILLIAMS)

[7] There has been an exchange of views in recent literature whether or not QALYs and HYEs are conceptually equivalent. GAFNI et. al. (1993) argue that HYEs - on the basis of a two-stage lottery procedure - are superior to QALYs for economic evaluation of health care. CULYER & WAGSTAFF (1993) argue that QALYs obtained from time trade offs are the same as HYEs.

NORD et. al. 1993) rather than social welfare. The fundamental problem of interpersonal comparisons of utility is not solved by the use of QALYs and the use of QALYs does not imply that fairness and equity in health care is taken into account automatically. However, in most of the applied cost-utility literature, QALY gains have been implicitly interpreted as a measure of social value. The practice to determine spending priorities using "QALY League Tables" (or a list of marginal cost/QALY gained of different health care interventions) is in line with this view. The ethical view underlying the latter practice is called "quasi-utilitarianism" (MOONEY & OLSON 1991) in which social welfare equals a weighted average of individually determined utilities in which weights ensure that each person's life-year is equally important. Most of these discussions have been in theoretical terms. However, a recent study by Nord and collegues (NORD et. al. 1993) indicates that some scaling techniques (such as the Rosser/Kind index) are more reflective of social values than others (QWB, EuroQol, McMaster). Also the person trade off technique[8] recently proposed by OLSON (1994) - i.e. a technique to elicit health status valuations - seems promising to obtain health status valuations more closely reflecting social values.

2. There are very serious measurement problems in determining QALYs or equivalent concepts. To elicit a value for a particular health state several techniques are available viz. the standard gamble, the time trade-off, the person trade-off technique, category scaling and magnitude estimation[9]. The problem is that these techniques give widely different results. This inconsistency and lack of robustness is

[8] Subjects are asked to state the number of persons p each of whom gains a long duration T of a health quality improvement which is considered equally as good as a given number of persons P each gaining a shorter duration t of the same health quality improvement. From this an implicit annual social weight rate is derived.

[9] In the standard gamble, a subject has the choice between 1. state A for the rest of his life and 2. a gamble, with a probability p to be healthy for the rest of his life and a probability 1-p of immediate death. The value of state A corresponds to the probability p so that he is indifferent between both alternatives. In the time trade-off approach, the subject has to decide the number of years in perfect health (t) equivalent to T years in health state A. The value of state A corresponds to the ration t/T. Health status values based on rating scales (EuroQol, QWB) are a weighted average of a subject's or a community's rating of different functions of symptom/problem coplexes. Some rating scale instruments are based on magnitude estimations (e.g. Rosser/Kind). They are similar to rating scales except that they use a reference state. Subjects are asked "how many times more ill" a patient is in another state compared to the reference state.

often used as justification to use arbitrary health-state values in applied cost-utility analysis. In a review of 15 studies, NORD (1993) found that 2/3 of valuations used were based on the author's own personal judgment.

Output valuation is serious problem in applied cost-effectiveness and cost-utility analysis. Outcome valuation usually consists of three steps. First, descriptions of scenarios of the relevant health status have to be constructed. Next, different health states relatively to each other should be value on a scale from one (perfect health) to zero (death) or less than zero (states worse than death). Finally, obtained values are subject to further corrections to take into account equity considerations. In each step, the analyst is faced with serious difficulties of measurement.

In practical applications the choice of technique to elicit health status values is crucial, but little practical guidance is offered to the analyst on what technique is most suitable for specific health states. Each different technique handles risk aversion differently. E.g. standard gambles inevitably reveal subjective attitudes toward risk; category scaling or magnitude estimation are less prone to bias due to specific risk attitudes.

There is no agreed standard method for constructing scenarios on health status. The analyst is left to his own devices to develop scenarios. E.g. there is no best practice about the the duration of health status considered or the level of detail in describing and assessing various health states. Scenario description may range from very detailed descriptions, amply supported with audiovisual material, to very brief and concise descriptions covering only the most vital characteristics. Discussing some practical methodological issues on measuring utility values, SMITH and DOBSON (1993) refer to several studies showing that framing and labelling systematically affect utility values. One technique advocated by SMITH and DOBSON (1993) is the use of representative focus groups, a technique similar to consumer clinics used in marketing research, whereby a small group (say about 10 people) is loosely guided to discuss a particular health state in an open way. These sessions are recorded and information is used to develop scenarios.

Another unresolved issue is whose values to take? Should the valuations of health care providers and professionals be used, or should preference be given to the values of healthy people or the values of patients? Or is a random sample drawn from the population the appropriate group? How should the aggregation problem be solved i.e. how does one combine different individual values to construct one aggregate value reflecting a societal valuation of a particular health state?
There is no agreement in the literature on this point, although elicited values seem to vary widely among different groups.

2.b. COST MEASUREMENT AND VALUATION

Estimation of relevant costs is quite often not an easy task in a specific economic evaluation. Again, problems and pitfalls arise due to methodological intricacies and measurement problems.

1. Evaluation used for policy purposes usually takes the societal point of view[10]. Such an evaluation should cover all costs, direct as well as indirect. However, to what extend indirect cost should be included is not always clear. E.g. should medical costs in extended years of life be included? Concerning medical costs due to the health care intervention under study, there is widespread agreement. They should be included. However, whether or not to include additional costs merely due to a longer life is less clear. RUSSELL (1986) argues not to include such costs, whereas DRUMMOND et. al. (1987) advocates their inclusion. A similar argument concerns the handling of indirect benefits such as production gains in cost effectiveness and cost utility studies. Most authors (e.g. DRUMMOND 1992, JONSSON 1987, WEINSTEIN 1990) recommend to keep production gains separate from other costs in

[10] This is usually the point of view that is recommended by economists. However, policy-makers are usually more interested in who gains and who loses by a decision. Therefore, it is perhaps more useful to report from different viewpoints (e.g. society, public expenditure, insurers, providers, drug companies, households, etc.), preferably using a common set of data and facts, acceptable to the different players involved.

calculating the C/E ratio, whereas some others include such gains by subtracting them from costs.

2. Furthermore, all cost should reflect opportunity costs i.e. the value of the next best alternative forgone in developing an activity. For certain cost elements, market prices are available, such as charges (e.g. hospital charges), market prices (e.g. drugs) or fees (e.g. physician fees). However, these valuations can only be used for inputs if they represent the value of the input in its best alternative use. Economic theory teaches us that a market price only equals opportunity cost in a perfectly competitive clearing market. This condition does certainly not hold in the health care industry as many prices are negotiated and do not take into account the real value of foregone options. E.g. the opportunity cost of physician time in Belgium (with a physician surplus) is substantially smaller than fees suggest. The same argument applies in valuing cost (or benefits) of patient time lost or gained. Market wage rates are most frequently used as the value of time per unit forgone or gained, whereas the shadow price of time (or the opportunity cost of time) is far less under present conditions of massive unemployment. The use of shadow prices - which is a fairly standard practice in non-health related cost-benefit studies - is not yet standard practice in economic evaluation in health care.

3. Problems of measurement are abound. Most often, cost data for an economic evaluation are gathered retrospectively from different sources: billings, cost statements, expert opinion, accounting data. Such data are marred with uncertainty. They often rest on subjective estimates.

More economic evaluation studies are being made within the context of randomized clinical trials (RCTs). RCTs are considered to the best source of information about the clinical effectiveness of a drug. At first, it was thought to be very useful to combine economic evaluation with the clinical study. It was hoped this would lead to more reliable cost information and would be less expensive than retrospective collection of information. Recently, several disadvantages became obvious and there is much less optimism (DRUMMOND & DAVIES 1991).

First, it is not clear whether cost data from clinical trials are relevant for the economic evaluation. Medical services delivered in the controlled environment during clinical trials are very often very different from daily medical practice. Patients are followed far more closely so that clinical problems are more rapidly recognized or even avoided. This clearly has an impact on costs. Also the rate of non-response is normally smaller in RCTs than in the non-controlled real world.

Another disadvantage is the heavy burden it puts on clinical RCT-studies as it requires the collection of a lot of additional data, not routinely collected in RCTs (e.g. time input of medical staff, relatives and friends, costs of special diet...). Furthermore, time horizons and sample sizes for economic studies may differ from that of the clinical evaluation.

2.c. DISCOUNTING

Most interventions lead to costs and benefits that accrue in different periods of time. Comparisons between interventions are complicated due to differences in timing of costs and benefits. Discounting - i.e. weighting costs and benefits less the more they accrue in the future - is the standard procedure recommended to make flows comparable over time. One rationale for discounting is that people prefer current consumption over future consumption, even in a world with zero inflation and no uncertainty about the future (time preference rationale). Another argument for discounting is that the real cost of a program does not only include the resources invested in a program, but also the future real return of a forgone alternative investment (opportunity cost of capital argument). Still another reason for discounting (economic growth effect) stems from positive economic growth combined with diminishing marginal utility of wealth implies that an additional unit of wealth today adds more to utility than an additional unit of wealth tomorrow, when people are more wealthy.

There is widespread agreement among economists on the principle of discounting if applied to costs. On discounting health benefits measured in terms of QALYs or some equivalent notion, there is some dissidence. Seminal authors (e.g. DRUMMOND et.al. 1987, FINEBERG & WEINSTEIN 1980) recommend discounting benefits. MOONEY & OLSON (1991) argue that QALYs should be left undiscounted when ranking alternative programs, as empirical estimates on the time preference rate for health are very poor. They note that when positive individual time preference for health is observed using gambling approaches, a competing explanation can be found such as risk aversion. Some authors (SHELDON 1992) critisize discounting benefits on the grounds that this discriminates against preventive and other public health programs as discounting favors interventions resulting in short-term benefits and against longer-term benefits. Others (KATZ & WELCH 1993) suggest the use of differential discounting, i.e. discounting monetary costs/benefits at a higher rate than QALY-type health benefits, to reflect longitudinal equity among cohorts and altruistic preferences of the present generation with regard to the next one.

2. Apart from this principal issue on discounting benefits, there is the empirical problem of the appropriate discount rate. In a perfectly competitive market economy in long-term equilibrium, the market rate of interest equals the social rate of time preference and the marginal rate of return on investment. The appropriate discount rate is simply the market interest rate. But, the real world differs from the model world and there is no simple rule to determine the appropriate discount rate. Various rules to estimate the appropriate social discount rate were discussed at length in the non-health related cost-benefit analysis offering some guidance but no consensus (GRAMLICH, 1990: 92-114).

Again, this uncertainty leads to a wide variation in discount rates used in actual practice. PETROU et. al. (1993) report on discount rates used in 35 economic evaluations and find ranges from zero to 20 percent. Program rankings are highly sensitive to discount rates used, especially those with costs and benefits extending over long periods of time. Sensitivity analysis is absolutely necessary to inform

decision-makers on the effect of the discount rate on final cost-efficiency or cost-utility ratios.

3. THE QUALITY OF THE PRACTICE OF CEA AND CUA

Two recent reviews (UDVARHELYI et. al. 1992, ADAMS et. al. 1992) check whether published CEA and CBA studies in the medical literature, have adhered to basic analytical principles. The results of these surveys give reason for concern.
UDVARHELYI et. al. (1992) analyzed whether published CEA and CBA have adhered to basic analytical standards. They reviewed systematically 77 articles published in general medical, general surgical and medical subspecialty journals either in the period from 1978 to 1980 or from 1985 to 1987. These articles were reviewed to assess if they adhered to six basic principles of analysis, derived from widely cited textbooks or articles on methodology. Performance was rather poor. Only three articles adhered to all six principle, the median number of correctly applied principles per article was three. Table 2 reproduces some results of this analysis. Also, no improvement in performance was observed over this almost ten year period. Articles in general medical journals performed better than articles in general surgical or medical subspecialty literature [11].

[11] It would have been interesting to see if economists outperformed non-economists.

Table 2. Adherence to analytic principles (UDVARHELYI et. al. 1992)

Principle	Adherence in %
perspective explicitly stated	18
benefits explicitly stated	83
side effects or morbidity costs included	30
averted costs included	25
induced cost included	4
discounting used if needed	48
sensitivity analysis used	30
average C/B or C/E ratio only	29
incremental and average C/B (C/E) ratio	13
no C/E or C/B ratio	47

ADAMS et. al. (1992) found similar results. They assess the prevalence and completeness of economic analysis in RCTs published for January 1966 until June 1988. Only 121 of the more than 50,000 published RCTs included economic analysis. For a random sample of 51 articles out of these 121 a detailed assessment of quality was made. They used a detailed set of quality questions, predominantly based on the comprehensive list in DRUMMOND, STODDART and TORRANCE (1987). Two reviewers independently scored all 51 studies and reached consensus by discussion in case of difference. Each article obtained a completeness score, simply adding item scores.

The mean completeness score of articles in the survey is 0.52 on a scale from 0 to 1 with a range extending from 0.32 to 0.94. ADAMS et. al. could not find a correlation between the quality of the RCT and that of the economic evaluation. They did find a

modest positive correlation of 0.28 ($p=0.046$) between the date of publication and completeness score, indicating some progress on adhering to standards.

4. CONCLUSION

Economic evaluation should not be presented as a simple and straightforward routine exercise. As is clear from the above, there are many problems and pitfalls. Despite problems on methodology debated in the scientific literature, from what is known, guidelines of good practice can be established. With proper training, it is feasible to judge the quality of an economic evaluation and to perform an acceptable evaluation analysis on the basis of these guidelines. Bias and manipulation of results - either by pharmaceutical companies wanting to promote their products by presenting favorable results or by regulatory authorities wanting to limit expenditures by presenting unfavorable results - by selective choice of methodology is relatively easy to check upon.

More important than methodological problems are the empirical and measurement problems encountered in practical CEA or CUA. In this area, the scope for bias and manipulation is very wide and very difficult to check. Also, research efforts in this field seem to concentrate more on the more glamorous fundamental aspects of evaluation rather than on the nitty-gritty practical problems of measurement.
In view of the many problems and pitfalls, economic evaluation should not be offered to policy-makers and decision-makers as some kind of a philosopher's stone and policy-makers should not be blinded by the elegance and sophistication of this new set of tools. However, this does not imply that this method is to be discarded. Despite its limitations, economic analysis offers a rational approach to discriminate between many options in health competing for scarce resources. Therefore, economic evaluation is undoubtedly a valid tool to guide resource allocation and decision-making in the health care industry, that should be perfected though by practice and application.

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