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Using threshold values for cost per quality-adjusted life-year gained in healthcare decisions

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Background: In many countries, the incremental cost-effectiveness ratio (ICER) is used to assess whether an intervention is worth its costs. At the same time, policy makers often feel uncomfortable with refusing reimbursement of any intervention purely on the basis of the fact that the ICER exceeds a specific threshold value. Reluctance to define a single threshold value for the ICER seems to have been stronger in social security systems than in national healthcare services systems. This study explores how basic differences between healthcare systems impact upon the potential usefulness of an ICER threshold value.
Methods: This study is a narrative review of literature about the theoretical foundations of the ICER threshold value approach and its practical relevance in different types of healthcare systems.
Results: A single ICER threshold value cannot be maintained, defined, or measured and should not be used as a policy-making tool. None of the solutions presented up until now to make the ICER threshold approach a valuable policy-making tool overcome the important weaknesses of the approach.
Conclusions: ICERs and ICER threshold values are insufficient for assessing interventions' value for money. Rather, they should be considered as one element in the decision-making process. Complete rationalization of the decision-making process by means of quantitative decision criteria is undesirable and not feasible. Increasing transparency in the criteria used for a decision and explicitness about the relative importance of each criterion should, therefore, be the major goal.

Keywords: Cost-effectiveness Analysis, Decision making, Healthcare rationing/economics, Quality-adjusted life years, Healthcare costs

The purpose of cost-effectiveness analyses (CEA) is to inform policy makers about the extent to which an intervention represents efficient use of scarce healthcare resources (30). The basic goal of CEA is to inform healthcare policy makers about which combination of health programs would maximize health gains, given the limited resources available for funding these programs. However, several issues—apart from the methodological ones—reduce the practical value of CEA for policy making.

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A CEA estimates an intervention's incremental cost-effectiveness ratio (ICER)—i.e., the additional cost per extra unit of "effect" in terms of, for example, quality-adjusted life-year (QALY) gained—of an intervention compared with an appropriate comparator. It is not always straightforward to give a meaning to ICERs or to use them in a real decision-making context. There is a basic difference between "representing efficient use of resources" and "being worthwhile." ICERs only help in answering the efficiency question, but decision makers have to decide on whether an intervention is worthwhile, taking into account broader societal considerations. For example, Belgian policy makers will have to judge whether €33,000 per QALY gained is reasonable for vaccinating all 12-year-old girls against the human papilloma virus (24); South African policy makers will have to judge whether society is willing to pay €986 per QALY gained for an anti-retroviral (HIV) therapy (3). They have to make a judgment about the maximally acceptable cost-per-QALY or, in short, the "threshold value" above which an intervention can no longer be considered worthwhile.

An overview of the use of ICER threshold values in eleven countries showed that very few countries define an explicit threshold value (4). England and Wales use an ICER threshold range of £20,000 to £30,000 per QALY gained, but the discussion about the use of ICER threshold values, and their level, is still ongoing at the National Institute for Health and Clinical Excellence (NICE). NICE's struggle with its threshold value for the cost-per-QALY is demonstrated by its recent decision to allow an exception to the threshold rule for specific end of life drugs (21;25). This decision was not consistent with the health maximization objective.

Most countries do not define an ICER threshold value. Some have tried to derive implicit threshold values from past resource allocation decisions: Australia (AU$69,900/QALY), New Zealand (NZ$20,000/QALY), and Canada (acceptance up to CAN$80,000/QALY, rejection from CAN$31,000 to CAN$137,000/QALY) (4).

ICER threshold values or ranges proposed by individuals or institutions were found in the USA ($50,000/QALY), the Netherlands (€80,000/QALY), and Canada (CAN$20,000–$100,000/QALY). The basis for these thresholds is unclear.

Finland, Sweden, Norway, Denmark, and Belgium do not identify or suggest an ICER threshold value (4).

All countries have in common that other assessment elements become more important if the ICER is high and that interventions with a low ICER are more likely to be accepted than interventions with a high ICER.

This article reflects upon possible reasons why most countries have not defined and used ICER threshold values as explicitly as NICE. It focuses on the impact of differences in characteristics between healthcare systems for the relevance and applicability of ICER threshold values, starting from the theoretical assumptions underlying the ICER threshold value approach.

Our reflections are based on a narrative review of the literature on ICERs and ICER threshold values. Literature was mainly retrieved through identification of relevant papers from reference lists of papers that were identified through a key-word search in Medline (PubMed).

THEORETICAL FOUNDATIONS FOR THE ICER THRESHOLD VALUE

Neo-classical welfarist economic theory shows that, under a fixed budget constraint, an ICER threshold value can be defined above which interventions do not improve efficiency and below which they do improve efficiency (13). Efficiency is defined as maximizing total health from the available resources. The ICER threshold value is the ICER of the last intervention in a league table of ICERs that would still (fully or even partially) be financed from a given fixed budget.

The ICER threshold value thus obtained is based on several assumptions (29): (i) The healthcare budget is fixed, that is, it cannot be exceeded in a given year. (ii) The one and only aim of healthcare decisions is to maximize health benefits in terms of QALYs within the population. (iii) Complete information on the ICERs of all interventions is available. (iv) Programs are perfectly divisible, that is, they can be reduced to each desirable level. (v) Programs offer constant returns to scale, meaning that an extension of a program causes the same proportional increase in the costs as in the effects, thereby not influencing its ICER. (iv) Health programs are independent from each other, meaning that changes in one program have no impact on other programs.

This ICER threshold value is the result of a health maximization model that applies to a specific context (budget, model of healthcare organization, and health insurance), at a specific moment in time and under specific conditions. Therefore, the ICER threshold value is not a static value but changes over time, subject to changes in the budget, the interventions funded and the productivity of health care (14). A fixed budget context, therefore, requires a variable ICER threshold value. A fixed ICER threshold value would require a flexible healthcare budget to be able to respond to changing conditions in the healthcare system (i.e., development of new interventions with an ICER below the fixed threshold value).

THEORY VERSUS PRACTICE IN DIFFERENT HEALTHCARE SYSTEMS

The neo-classical welfarist assumptions for the ICER threshold value approach are clearly unrealistic. First, the theoretical ICER threshold value cannot be *identified* in practice due to a lack of information. Second, even if the ICER threshold value could be identified, it could not be *applied* because certain theoretical conditions are not fulfilled: budgets are not necessarily strictly fixed and in case of variable budgets

the opportunity costs of additional investments in health programs is not constant, health maximization is not the only concern of health policy makers as equity concerns always arise when resources have to be allocated, health programs may not show constant returns to scale and programs may not be perfectly divisible. Some of these conditions may be considered more important than others, depending on the healthcare system.

We consider three types of healthcare systems: Bismarck (or social security)-type, Beveridge (or national health service)-type, and private insurance systems (28). The Bismarck-type healthcare systems, such as in Belgium, Germany, and France, are generally characterized by a strong influence of stakeholders (healthcare providers, insurers, and government) in the decision-making process. In Beveridge-type systems, such as in the UK, Italy, and Spain, the influence of stakeholders on the decision-making process is less pronounced. This has implications for the possibility to introduce "rationalized" decision rules, such as cost-per-QALY threshold values.

A second basic difference between the Bismarck- and the Beveridge-type healthcare systems is the way healthcare services are financed. Patient copayments are much more common in social security systems than in National Health Service (NHS) systems. In a NHS, the budget is set by the parliament and, therefore, considered to be more or less fixed within a given year (6). Patients' out-of-pocket expenditures are relatively small compared with public expenditures. The budget to be allocated efficiently is, therefore, clearly defined. In a system with patient copayments (fixed amount) or coinsurance (percentage), it is unclear which amount of money needs to be allocated efficiently. As the policy makers do not define limits for the total out-of-pocket payments made by the population as a whole, the total "budget" for health care (public + private payers) remains undefined (4). This also applies to other societal costs, such as productivity losses or informal care.

To overcome this issue, NICE requires CEA to be performed from the perspective of the NHS, including only costs borne *by* the NHS. This approach, that ignores patient copayments or other societal costs in CEA, is consistent with NICE's remit of allocating the fixed NHS budget efficiently (19).

In social security systems, the proportion of healthcare expenditures borne by patients is relatively large and cannot be ignored. Social security systems have more opportunities to respond to equity considerations in reimbursement decisions by changing the public reimbursement rate. Such decisions are taken on a intervention-by-intervention basis. Equity considerations include, for instance, the potential financial implications for patients of a less than full reimbursement. As such, treatments for chronic or life-threatening conditions are more likely to be fully reimbursed than treatments for trivial diseases such as antibiotics for the treatment of an infection (4).

What does all of the above mean for the applicability of a threshold value for the cost-per-QALY in social security systems?

First, defining the perspective of the CEA and the budget to be spent efficiently is problematic. Limiting the perspective to that of the public payer is not an option, because in that case interventions with higher copayments would be more likely to be cost-effective than interventions with lower copayments. Consider two interventions with identical total incremental costs and incremental effects but one with higher patient copayments than the other (e.g., because the first intervention is a treatment for the flu whereas the second is a treatment for cancer). The treatment for flu would be more efficient from the public payers' point of view, but from a societal point of view reimbursement of the cancer treatment might be more desirable. Taking the perspective of all healthcare payers, that is, patients and public payer, struggles with the problem of an undefined total healthcare budget and, as a consequence, the threshold value.

Second, the ICER threshold value suggests which interventions present efficient use of resources but does not help to determine the optimal reimbursement rate. If an intervention's cost per QALY is lower than the threshold value, but the disease for which the intervention is meant is considered to be of low societal priority, the policy maker may decide to reimburse only a small part of the intervention or not reimburse the intervention at all. Inconsiderate use of a single ICER threshold value, for example, reimbursing all interventions with a low ICER at 100 percent, may lead to undesirable societal outcomes.

An additional consideration with respect to the explicit definition of a single ICER threshold value is that it risks becoming a legitimization in itself, while decision makers may sometimes wish to give more weight to other criteria in their decision than to health maximization.

ALTERNATIVES TO ICERS AND ICER THRESHOLD VALUES

Alternatives to the neo-classical welfarist ICER threshold value have been suggested in literature, differing in the extent to which they support the notion of an ICER threshold value as a guiding principle for resource allocation.

Most economists recognize there might be legitimate reasons for wanting to sacrifice efficiency for more equity (1;9;26). However, many do not support the adaptation of the threshold value for the cost-per-QALY on a case by case basis because this makes the rational decision-making process unmanageable. Some researchers suggest to weigh QALYs accruing to different patient groups to incorporate equity considerations in the objective function of healthcare policy making (8;27). In the UK, relative societal values for health gains according to the populations receiving these gains have been collected from the general public to be able to assign "equity weights" to QALY gains (10). The premise of this

approach is that moral judgments can and should be quantified to make the right decisions from the societal point of view. The weighting will, however, always be disputable. Especially in healthcare systems where reimbursement decisions are the result of a deliberative process between stakeholders, stakeholders will not fail to identify exceptional factors that have not been taken into consideration in the QALY weights.

Instead of defining the ICER threshold value as the ICER of the least cost-effective intervention still financed, the ICER threshold value could be defined in terms of the societal willingness to pay (WTP) for a QALY (11;17). The societal WTP approach is appealing because it is explicitly based on the societal value of health but there are two major problems with the approach. First, it is impossible to measure the maximum societal WTP for *a* generic QALY because a "QALY gained" cannot be separated from any concrete context. Societal WTP for a QALY depends, for instance, on the characteristics of the patient population gaining the QALYs, or the total number of QALYs gained. Second, a fixed value for the societal WTP for a QALY suggests the assumption of constant opportunity costs of additional investments in health care. From a societal point of view this does not make sense, as the opportunity costs of additional investments in health care are likely to increase: the more resources are drawn away from other sectors, the higher the value of the benefits lost in these other sectors will be. The alternative of re-defining the societal WTP for a QALY on a case-by-case or group of cases basis avoids the measurement problem of societal WTP for a generic context-independent QALY but risks to result in untenable budget requirements. Looking at decisions in the past is another suggested way to identify the societal WTP for a QALY. However, empirical ICER threshold values or a range of ICER threshold values observed in past decisions should always be interpreted within their budgetary, societal, and political context. As decisions are never inspired by economic considerations only, past decisions will never give a pure estimate of the societal willingness to pay for *a* QALY but could merely give an indication of a range of potentially acceptable values.

Another option is to weigh the ICER implicitly or explicitly against other elements in the decision-making process (2;7;18;22;31). This approach requires measuring and/or objectifying all the elements believed to be relevant for the decision-making process. The ICER can be used as the element reflecting on the economic value interventions. The actual weight of each decision element can be made explicit or remain implicit. Remaining implicit about the relative weights, however, reduces the transparency of the decision-making process. Defining explicit weights reduces the need for repeated discussions about the relative importance of each decision criterion. It will prove difficult though to determine the actual weights. Discussions will remain necessary because every decision is affected by particular circumstances and local conditions.

Another approach is defining a threshold value for the *average* cost-effectiveness ratio, for example, the average gross domestic product (GDP) per capita. This should reflect the citizens' "fair share" of a nation's wealth (32). The problem with this approach is that it could *in extremis* lead to a situation where the entire GDP (or even more) would have to be devoted to health care.

The opportunity cost approach abandons the idea of an ICER to guide decisions. It argues that the health benefits lost from other interventions that have to be abandoned to finance the new intervention should be made explicit and directly compared with the new intervention's health benefits. Implementation of this approach on the national level may be difficult, especially if budgets are not strictly fixed, because it is not always clear whether and which other services will have to be cut down.

Finally, the cost-consequences approach pleads for a disaggregated presentation of all economically relevant elements. ICERs and CEA might only have a limited meaning to healthcare policy makers (5;12;16). Modeling inputs as well as outputs that are "hidden" in the ICER estimate should be presented in a disaggregated form to allow the decision maker to weigh explicitly the economic elements against other elements (5).

The different approaches described can be considered as complementary methods to achieve more transparency in the role of economic considerations in decision making.

THE ROLE OF CEA IN HEALTHCARE DECISION MAKING

Decision making is a complex process moving beyond rational assessment of problems, weighing of alternatives and formulation of best solutions (33). Effectiveness and cost-effectiveness are only two of the many elements taken into consideration in policy making. Only when health maximization is the only concern of the policy maker, cost-effectiveness would be the sole decision criterion. Neither theory nor empirical evidence supports this assumption (4;6;15;23).

"Rationalization" of the healthcare decision-making process can never be complete, but from a social justice and democratic perspective it would at least be expected that the decision-making process is transparent and that decision makers are accountable for their decisions.

CONCLUSIONS AND POLICY IMPLICATIONS

The ICER is insufficient as a measure for evaluating an interventions' value for money. The ICER threshold value against which interventions' ICERs should be compared is unknown and variable over time. There are fundamental differences in the potential value of threshold values for the cost per QALY between different healthcare systems. The ICER threshold

value approach might make more sense in a national health service system where healthcare budgets are well-defined and more fixed than in a social security system where the maximum level of the total copayments of the entire population is undefined. In no system healthcare decision making can be reduced to a simple rational process of using a single ICER threshold value that fits all decisions because the ICER is in practice unable to take societal values such as equity, preference for life-saving treatments, etc., adequately into account.

Nevertheless, all policy makers would recognize that neglecting economic considerations is unethical, as spending resources on one health program reduces the resources available for other health programs, especially in a fixed budget situation (20). Because the ICER cannot provide the magic solution to decision making, the focus should primarily be on transparency in the decision criteria and their relative importance of each of the criteria in each decision. To allow policy makers to be transparent, economic modelers should present the results of their CEA in disaggregated form, including "unpacking" the ICER but also presenting all other relevant outcome parameters that can be derived from the CEA but that are potentially concealed in the ICER estimate because the ICER is a ratio between two values.

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CONFLICT OF INTEREST

All authors report having no potential conflicts of interest.

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