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# Spanish recommendations on economic evaluation of health technologies

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**Abstract** The economic evaluation of health technologies has become a major tool in health policy in Europe for prioritizing the allocation of health resources and the approval of new technologies. The objective of this proposal was to develop guidelines for the economic evaluation of health technologies in Spain. A group of researchers specialized in economic evaluation of health technologies developed the document reported here, following the initiative of other countries in this framework, to provide recommendations for the standardization of methodology applicable to economic evaluation of health technologies in Spain. Recommendations appear under 17 headings or sections. In each case, the recommended requirements to be satisfied by economic evaluation of health technologies are provided. Each recommendation is followed by a commentary providing justification and compares and contrasts the proposals with other available alternatives. The economic evaluation of health technologies should have a role in assessing health technologies, providing useful information for decision making regarding their adoption, and they should be transparent and based on scientific evidence.

**Keywords** Economic evaluation · Health economics · Health policy · Decision making · Spain

**JEL Classification** H0 · I0 · J0

## Preface

Over the last few years, the economic evaluation of health technologies (EEHT) has become an important tool for European health policy decision makers when formulating strategies to prioritize the allocation of health resources and

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when evaluating new technologies for approval. European health policy makers must ensure that advances in medical technology that improve quality of life and life expectancy are made available to patients, and they are responsible for investing in measures aimed at disease prevention. However, there is little doubt that such improvements usually require an increase in spending and that indiscriminately adopting these measures would pose a serious risk to the health system. There has been significant debate around the creation of the National Institute for Health and Clinical Excellence (NICE), which has produced certain cultural changes. Indeed, the work it has carried out since its inception has undoubtedly altered the perceived responsibilities of the Health Technology Assessment Agencies (HTAA), emphasizing the potential consequences of their recommendations.

Spain has pioneered the standardization of methodology applicable to economic evaluation studies. In the 1990s, the Spanish Ministry of Health and Consumer Affairs commissioned a working group to produce a proposal to establish a standard methodology for the economic evaluation of health technologies and programs, including drugs. However, due to various political and administrative circumstances, the methodology devised was never put into practice. In a global context, initial efforts by Australia and Canada found support in a number of European countries, where it was acknowledged that the information obtained from economic evaluations is useful to coherently allocate the available health resources. In this context, curiously, Spain is now one of the few European countries that have yet to adopt a clear position on this question.

The authors assume that in the near future, the common practice in Spain will be to present evidence of the economic value of new health technologies financed by the National Health System based on common practices. Such values will be based on comparisons with the costs associated to alternative technologies, although at this point in time, stakeholders have yet to agree upon a clear and concise set of rules regarding the technical and methodological issues that EEHT should take into account. Hence, the aim of this proposal was to develop guidelines for the EEHT in Spain. This work was financed by the Spanish Ministry of Health and Social Policy.

The coordinators, Julio López-Bastida (JL-B) and Juan Oliva (JO), selected a group of experts with a wide perspective and proven experience in the fields of health economics, health policy, and EEHT (FA, AG-A, RG, JM, JP-J). After reviewing the EEHT guidelines in a number of countries[1] and following two discussion sessions, a first draft of the proposal was presented to experts from the Spanish HTAA. A second revised draft was then discussed with other experts (see "Acknowledgments"), and their responses were collected by the coordinators. The inclusion of these suggestions in the final paper was debated by the entire working group (JL-B, JO, FA, AG-A, RG, JM, JP-J). The recommendations laid out here appear under 17 headings or sections. In each case, the recommended requirements that should be satisfied by the EEHT are indicated in bold, and in the full version, each recommendation is followed by a justifying comment that may also contrast the proposal with other available alternatives.

[1] Germany, Australia, Canada, Spain (previous proposal), the United States of America, France, Netherlands, Hungary, England and Wales, Ireland, Italy, Norway, Sweden, and Switzerland.

## Objectives and scope of the economic analysis

Recommendations

1. Establish clear objectives and formulate well-defined questions in terms of the objectives of the study.
2. Carry out a general economic evaluation on a clearly and precisely defined study group, and use data that will determine whether differences in age, gender, disease severity, and risk factors have a significant impact on either effectiveness or costs.

The first step in any economic evaluation is to clearly define the clinical problem (situation under evaluation) or the issues raised. Bearing this in mind, the decision to perform an economic evaluation might be coupled with the need to evaluate the efficiency or effectiveness of an action in relation to an alternative measure, or to performing the same action at a later date. In the latter case, performing an economic evaluation would only make sense where sufficient information was available on the relative benefits and risks of a certain technology or intervention in comparison with alternative technologies. The economic evaluation should be relevant for the decision makers it intends to inform, and thus, one must bear in mind that EEHT primarily intends to facilitate the decisions made by the authorities. When planning an EEHT, it may be useful to identify the main audience for whom the study is intended, as the formal aspects, methodology, and outcome presentation can be adapted depending on the intended audience. The target group must be clearly specified, and the study must be based on a significant sample of the specific group. The research question should clearly define the study group (its clinical and demographic characteristics, morbidity or risk factors, healthcare setting, geographical location, usual rates of adherence or typical patterns of treatment, as well as levels of risk for a single clinical condition), the intervention to be evaluated, and the comparison of interventions (as the case may be), as well as the relevant outcomes.

## Perspective

Recommendations

1. Adopt a societal perspective.
2. Include the perspective of the third-party National Health System (NHS) in the analysis.
3. Differentiate and present the societal and NHS perspectives separately.

The societal perspective considers all the outcomes that are significant from a societal perspective, and this is preferred as it represents the most general perspective. The societal perspective provides most information on the relative and actual importance of an illness; that is, all the benefits derived from the application of an intervention (compared with alternatives) and the related costs. On the other hand, the perspective of the payer refers to all therapeutic benefits derived from the application of an intervention (compared with other alternatives) and the related costs incurred by the NHS when implementing or making new technology available. Where certain debilitating illnesses of a chronic nature are concerned, it may be reasonable to consider the combined perspective of the NHS and of the Healthcare System implicated in the Autonomy and Care of Dependent Persons. Although the societal perspective is recommended, the perspective of the payer (mainly the NHS) should also be considered, as it represents the main audience for an EEHT.

## Options for comparison

Recommendations

1. Compare the technology under study with the standard technology used in current health care practices.
2. Justify the choice of alternative technologies for comparison.

The choice of technologies for comparison is crucial to the analysis and one of the key determinants of increased cost-effectiveness ratios. Although evident, it should be emphasized that economic evaluations involve a comparative analysis. Current practice calls for drawing comparisons with the technology normally applied to the largest group of patients. There may be specific instances in which a new technology has recently become available but has not yet become standard practice, although it may do so in the near future. In this situation, it may be best to choose a new technology that is on the market for comparison. Any technology that is held up as a "gold standard" should be included in the comparison. Likewise, the decision "to do nothing" or "to take no action" may be considered as a possible alternative where clear justification exists.

## Type of economic evaluations

Recommendations

1. In theory, any of the four analysis methods (cost minimization, cost effectiveness, cost utility, and cost benefit) may be used for EEHT. Nevertheless, the choice of the method should clearly be based on its suitability to address the question raised in the study.
2. Develop a cost-minimization analysis when there is evidence that the technologies under examination have equivalent outcomes in terms of health and well-being.
3. Develop a cost-effectiveness analysis when there is a clinically significant effect (improvement in health) and sufficient information is not available to perform a cost-utility analysis.
4. Develop a cost-utility analysis when there is a gain or improvement in quality-adjusted life years (QALY) as a result of the health care intervention (due to an improvement in life expectancy, in health-related quality of life, or in both), as this provides the most relevant outcomes for decision makers to allocate resources.
5. Despite its limited use in the field of health care, a cost-benefit analysis is similarly valid. This model provides a comparison of alternative interventions in which costs and outcomes are quantified in common monetary units.
6. The various ways of measuring effects on health and, therefore, the different types of analyses, should not be considered as mutually exclusive. Rather, they should be seen as complementary ways of presenting the results of a single study.

## Data on efficacy and effectiveness

Recommendations

1. Outcomes may be obtained under conditions that are ideal (efficacy) or reflect real practice (effectiveness). Both types of sources should be used whenever possible, as the information they provide is often complementary.
2. When the outcomes are based on a single study of efficacy, both the methodology and results should be discussed in full: sample group, selection criteria, criteria for assignment to the study, and control groups, whether analyzed by treatment intention or under a cohort study, the size of the effect with confidence intervals, etc.
3. When the outcomes are based on more than one study of efficacy, describe the methods by which outcomes from different studies are combined to obtain a

quantitative estimate of the overall effect of a particular intervention or variable on a defined outcome (search strategies, selection criteria, etc.).
4. When effectiveness data are not available, use appropriate statistical techniques. Variables, values, assumptions, and structures should be described in detail. Every hypotheses used in these extrapolations should be explicitly formulated and checked closely using a sensitivity analysis.
5. In retrospective studies that involve the outcomes of standard treatment for existing patients (effectiveness), the differences in data on efficacy and effectiveness should be compared and contrasted.
6. If there is evidence revealing a large gap between the outcomes obtained using efficacy and effectiveness data, the analysis should be repeated using the most recent data available.

Although policy makers might prefer information on the real impact that an intervention might have for real-life patients (effectiveness), two issues should be considered. The first is that an EEHT is usually performed when data on effectiveness may not be available, either because the decision to include a technology has yet to be approved or because the technology has been implemented so recently that it has not yet been the subject of a formal analysis. The second issue refers to the fact that randomized clinical trials provide information on efficacy under controlled conditions. Well-performed trials may offer an internal validity far superior to that offered by a study on treatments received under routine conditions. Furthermore, one should bear in mind that studies on efficacy and effectiveness are not interchangeable but, rather, provide different types of information. The introduction of a new technology would logically lead one to study its efficacy and follow-up with information based on outcomes (effectiveness) in order to re-evaluate it.

## Valuing outcomes

Recommendations

1. In a cost-effectiveness analysis, outcomes are related to the primary endpoint of the underlying clinical trial. The outcomes should be expressed in clinically relevant terms, and where intermediate outcomes are used, the connection to final outcomes must be clear and scientifically proven.
2. In a cost-utility analysis, health benefits or outcomes are measured in QALY gained. The scale to assign values must be validated on the basis of sample groups representative of the general population.
3. A willingness-to-pay (WTP) methodology should be included in a cost-benefit analysis.
4. Analysts should provide details on the valuation scales employed to measure patient preferences (utilities).

In a cost-effectiveness analysis, a connection should be drawn between the outcomes and the primary endpoint of the clinical trial an observational study or review of where the data to be analyzed was obtained. Outcomes should be measured in a manner that has clinical significance and that is generally accepted by the scientific community for the type of health problem examined. It is usual to apply a cost-effectiveness analysis in EEHT, because the outcomes are measured in terms that are most similar to those used in clinical practice. Nevertheless, policy makers at macro- and middle-management levels are increasingly demanding analyses using data that link quantity and quality of life. Health-related quality of life (HRQOL) refers to the impact of health on a person's general well-being. Several methods to measure HRQOL have been developed, and some are designed to be applied to specific populations or groups with specific health problems, whereas others are generic methods designed to study the general population. In a cost-utility analysis, the recommended unit of measurement is QALY, due to its clarity, simplicity, ease of application and validity. Preferences scores can be measured direct or indirectly. Direct measurements are obtained by surveying people who suffer from the health problem under study to ascertain their preferences or utilities for different states or changes in health. Indirect measures are obtained through previously validated HRQOL patient surveys. Although patients are scored or grouped according to their answers, the numerical values given to individual answers are not obtained directly from the patients but depend rather on the social values previously estimated for the questionnaire. Indirect methods to measure utilities are preferable, as they are easier to obtain, compare, and interpret. However, these considerations do not rule out direct measurements when their use and scientific validity is justified for the study in question. Irrespective of the approach used, the study must provide separate data on changes in both quantity and quality of life, and it must combine the data in a transparent manner. Current assumptions with regards quality of life must also be discussed, as well as the methods used to estimate QALY.

## Allocation of resources and costs

Recommendations

1. A full description of the chosen perspective should be provided, as this may affect the decision to include or exclude certain costs.

2. The physical units of resources used (amounts) should be treated separately from their unit cost or price. The best available source should be used to show the opportunity cost of the resources. Unit costs should preferably be taken from official publications, the accounts of centers, market prices, and lastly the rates applied to NHS service provision contracts. The data source should be fully justified.
3. If the costs of labor production losses or lost time are included, the method chosen must be justified.
4. The cost of informal care (caregivers) should be included in the evaluation when the perspective used so requires. The method used to calculate caregiver costs should be described and justified.
5. Health care costs, labor losses, time loss, and informal care should be readily distinguished to ensure that such costs are not counted twice.

The perspective of the study will determine which resources are included or excluded from the analysis. Thus, from the perspective of the health care payer, production losses caused by illness, the costs associated with nonremunerated care provided by family members and friends (informal care), as well as the costs of private home assistance and the support given by social services, would not be included in the analysis. The inclusion of data on the social services provided by the public sector will depend on whether the payer is considered to be the authorities in general or one of the various funding bodies. In any case, all of these are relevant from the societal perspective. Costs should be evaluated based on opportunity cost (i.e., the best available alternative). The aim is to measure the long-term marginal cost (additional unit cost of the resources needed to give a long-term additional unit). Non-health-care costs should be identified individually and in detail using surveys designed for this purpose. In free or loosely regulated markets, market prices should be used to evaluate the use of resources. However, under the Spanish Health System, many prices are strongly regulated and resources are largely provided by public suppliers. Accordingly, it is probably more useful to rely on official publications, accounts of health care centers, and the fees applied to NHS service provision contracts. The time lost by patients and caregivers due to a health problem should be quantified separately, as it will probably have an important impact on the outcome of the analysis. Analysts and decision makers from several countries have yet to come to an agreement on the conditions and methods that should be used to quantify the loss of time. It is useful to distinguish between paid employment–labor production losses (measured using the Human Capital or the Friction Costs method), unpaid work–housework and informal care time (measured based on opportunity costs, replacement cost, or declared preference method), and leisure time (based on shadow costs as a proxy to opportunity costs).

## Time horizon

Recommendations

1. The time horizon should capture all relevant differences in costs and in the effects of health treatments and resources. In some cases, the time horizon will have to be extended to the individual's entire life.
2. When the analysis is based on a short clinical trial, the use of models to extrapolate data to estimate outcomes over a long time horizon should be used.

The time horizon should be sufficiently long to capture all significant differences in costs and outcomes affected by the intervention and its alternatives. In this regard, the natural history of the disease and how it can be modified using the treatments under evaluation should be taken into account. In the case of chronic diseases, the entire anticipated length of the patient's life must be taken into consideration. Any analytical decision to shorten the time horizon for practical reasons (lack of relevant information, minimal long-term effects) should be justified and include an estimate of the possible bias that this might introduce.

## Modelling

Recommendations

1. Modelling techniques should be developed in different situations to: (a) extrapolate progression of the clinical outcome (i.e., survival) beyond that observed in a trial (e.g., model the progression of AIDS in asymptomatic patients); (b) translate intermediate outcomes into final outcomes (e.g., modelling survival and chronic heart disease (CHD) events based on cholesterol levels); (c) model the relationship between production input and output based on models to estimate or distribute the use of resources; (d) model data from several sources to establish parameters necessary to analyze decisions; (e) model evidence obtained from trials or systematic reviews of trials to reflect possible circumstances in different clinical situations or populations.
2. The chosen model and its key parameters should be justified.

The model must be designed in accordance with the aim of the study. It must represent the natural progression of the disease or problem under study and must contain relevant information for the decision makers for whom it is

intended, presented in a clear and comprehensible manner. No one model is *ex ante* better than any other, and the most suitable model in each case will depend on the problem under study as well as the availability of sound data on efficacy/effectiveness and the use of resources. In any event, comprehensive details should be given on the strengths and limitations of the model used, justifying its choice over other alternatives and presenting its key parameters in a transparent manner. It is necessary to identify and evaluate data, report sources from which they were obtained, and describe their strengths and limitations. Evidence should also be gathered regarding the key parameters of the model, and suitable techniques should be used.

## Discounting

Recommendations

1. An annual discount rate of 3% should be used for the reference case, and 0% and 5% can be applied to the sensitivity analysis for comparison with other studies.
2. Whenever possible, cost flows and health effects should be presented separately and in detail, both discounted and nondiscounted.

In EEHT, costs and outcomes should be evaluated on the basis of a reference year, updating cost flows and results to the reference year chosen by applying a discount rate. At present, neither the scientific community nor international regulatory agencies have reached a consensus on the discount rate applicable to costs and outcomes or whether or not to apply discounts at all. Accordingly, any proposal along these lines will be controversial. However, there is a consensus that using a homogenous set of criteria in all economic evaluations improves comparisons and is critical for the transferability of results. It is recommended to use discount costs and outcomes at the same rate to avoid logical inconsistency in the analysis. For the same reason, it is recommended that both costs and results be discounted when the time horizon is longer than 1 year. With regards the value of the discount rate, it should reflect the social opportunity cost of foregoing the present consumption in exchange for investing resources in order to obtain a future benefit. An annual discount rate of 3% is recommended as the preferred rate for the reference case, both for costs and outcomes in the main analysis. The rate chosen should remain constant over several periods and be revised in the future. We also recommend that analysts apply a zero discount rate for health benefits in a sensitivity analysis, experimenting with greater flexibility in the rate for costs and health benefits within a range of 3–5%.

## Variability and uncertainty

Recommendations

1. Carry out a sensitivity analysis to account for uncertainty and justify modifications made to the sensitivity analysis with respect to the reference case.
2. Provide details on the method used (e.g., one-way or multiway sensitivity analysis, threshold analysis), and justify the choice of variables for the sensitivity analysis and the interval over which they vary.
3. Whenever possible, carry out a probabilistic sensitivity analysis.
4. Statistical distribution of the variables analyzed should be as transparent as possible.
5. Any statistical tests performed should be presented and the confidence intervals analyzed for the main variables.

The presence of uncertainty is inherent to several aspects of the EEHT. This is caused by uncertainty regarding the natural course of the illness itself and how it is affected by the therapeutic alternatives analyzed, as well as by uncertainty regarding the consumption of the resources used. All scenarios used in an analysis must be set out and justified, including their limitations. A sensitivity analysis should be performed to discern the degree to which outcomes depend on each scenario. Finally, one-way sensitivity analyses should be applied. If they turn out to be insufficient, multiway analyses should be applied. Whenever feasible, probabilistic analyses should be added, since they ensure the broadest evaluation of the uncertainty associated with the model input and of the relationship between the variables analyzed. Other models, such as Bayesian analysis, discrete choice models, etc., may be recommended depending on the type of illness and the technologies evaluated.

## Equity

Recommendations

1. The criterion underlying equity in economic evaluation is equality of the valuation of outcomes; apart from this, it is not obligatory to include any other criterion a priori in the economic evaluation.
2. If other social justice arguments are to be taken into consideration, they should be reported in a descriptive manner, or a parallel analysis may be carried out separately and independently from the reference case.

The term "equity" is understood as equality guided by principles of social justice. As it refers to social justice, its definition and scope mainly lie in the hands of the

health-care decision makers who represent the interests of society. EEHTs mainly concentrate on analyzing efficiency. The standard of equity implicit in the analysis resides in the fact that an additional QALY should receive the same weight as any other QALY, without taking into account the characteristics of the individuals who receive the health benefit ("a QALY is a QALY"). This leads to the principle of maximizing health outcomes using the available resources. If necessary for the decision maker, other analyses may be presented that express other criteria of equity or distributive justice. To avoid confusion, the distributive analysis should be presented transparently, separately, and independently from the reference case.

## Transferability of results

Recommendations

1. Transparency in methods, data, and results is essential to assess the validity of the analysis. It can also help health-care agents generalize or transfer the elements of an economic evaluation to new contexts.

Data, methods, and outcomes of a given study are transferable when: (a) potential users can assess their applicability in the context of their particular interest; and (b) when they are applicable to that context. To date, proposals for measuring transferability refer to check lists that can be summarized and drawn up in the form of indices. The lists contain concepts relating to the quality of the studies, even if they are not of high quality, and whether they are transferable or not is of no interest. Accordingly, these lists contain elements common to those included in good evaluation practice guides, such as some of those included in this guide, some from other countries, and some from renowned journals. Some elements, such as sensitivity analyses on certain parameters, can help explain the economic evaluations in other contexts (i.e., to make them more transferable). Accordingly, when studies are drawn up, it should be taken into account that other people may be able to use the same study to make decisions in a different context.

## Presentation of results

Recommendations

1. Results should be presented as an incremental analysis (incremental cost per incremental health outcome unit obtained), comparing relevant alternatives, and separating the perspectives (if analyzed from the perspective of society and that of a third-party payer) and subgroups.
2. Present the main outcomes (cost and health outcomes) both separately and together.
3. When a probabilistic analysis is carried out, include a cost-effectiveness/cost-utility plane and the acceptability curve in the findings.
4. Present data and assumptions considered in the analysis as transparently as possible so that any analyst can reproduce the study.

In describing the findings of the study, the main emphasis must be on transparency, in accordance with many of our previous recommendations. The relevant quotient is that which relates the additional costs with the additional health benefits (incremental cost-effectiveness ratio or incremental cost-utility ratio). Describing data separately also makes the information provided more transparent. If the study deals with primary data representing the direct short-term effects obtained from clinical trials and data modelled for long-term outcomes, the short- and long-term outcomes should be presented separately. A probability tree of the clinical efficacy/effectiveness and for the costs data for the relevant options may greatly clarify analysis. Authors should establish all cases, conducts, and actions carried out in their studies in great detail, including how consistency and quality of the process were verified and documented. The sensitivity analysis should play an important role in enabling the reader to evaluate the strength of the study's conclusions.

## Study limitations

Recommendations

1. The main limitations or weaknesses of the study should be presented in a critical manner

Any EEHT will contain limitations with regards sources of information used, and the models employed may be subject to criticism, or there may be doubts regarding the scope of the transferability or external validity of outcomes. Accordingly, the authors should clearly and critically address any aspects of the study that could be improved in the future if the analysis were to be repeated. The main strengths may be cited in a transparent manner if desired, but special attention should be given to any weak points. Any possible discrepancies between outcomes of the economic evaluation and those of previous analyses should also be discussed, and the authors should indicate new studies to be performed in accordance with outcomes obtained to explore any areas not fully resolved in the evaluation.

## Conclusions

Recommendations

1. Conclusions should answer the research questions posed in a clear and concise manner and must be supported by the results obtained.

## Conflict of interest

Recommendations

1. Who commissioned the study and who provided the financial support should be clearly stated.
2. The authors must declare any potential conflict of interest.

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