Guidelines on Health Economic Evaluation

Consensus paper

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Introduction

In view of the scarcity of resources, diagnostic, therapeutic and preventive procedures in medicine must no longer be analysed purely in terms of their effectiveness, but also in terms of their cost-effectiveness - the ratio between the resources used and the related effects. This is done by means of health economic evaluation studies. If health economic evaluations are to serve as a direct aid in decision-making, a minimum of methodology and transparency is necessary. It is for this reason that the following guidelines have been developed.

As regards the content and structure of the recommendations, it should be pointed out that these guidelines have been formulated as "broadly" as possible to allow room for individual solutions and the progress in methodology. However, they must be sufficiently precise to avoid vagaries in study design. In this respect, they must also comply with international state-of-the-art.

The initiative

The Institute of Pharmaeconomic Research (IPF) and the Association of Pharmaceutical Companies (PHARMIG) decided jointly to establish the "Pharmacoeconomic Guidelines: International Status and Consequences for Austria" project. The following procedure was agreed: to begin with, the contents of national and international guidelines were analysed. The resultant status quo then served as a basis for further discussions. This initiative was supported by a group of experts. The kick-off meeting took place in November 2004. The experts had already been involved in the basic question about the scope of the guidelines and in defining the initial direction of the methodology. This was done by means of a written questionnaire. In total, questionnaires were sent out to 17 experts (2 people received a questionnaire on request) and 14 questionnaires were returned. The difference between the number of questionnaires sent out and those returned was due to the fact that experts from one and the same institution completed a questionnaire jointly. The questionnaires were analysed in March 2005 and presented to the whole team of experts at a workshop. In addition, the survey results were published in a special issue of the Journal PHARMIG info in September 2005.

On the basis of the survey results, the Euromet Guidelines and the German recommendations for health economic evaluation (Hannover consensus), a proposed set of guidelines was drawn up by the IPF, which was discussed in February 2006 with the team of experts. The aim of the expert panel meeting was to achieve consensus on the individual points of content. <u>A consensus was reached on all points.</u>

The initiators and members of the team of experts were:

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Guidelines

The guidelines presented below relate solely to comparative analyses of health economic evaluations in general, i.e. the present guidelines do not apply solely to the evaluation of pharmacological alternatives. They are therefore not purely pharmacoeconomic guidelines.

1 Study design

The health economic evaluation should be designed in accordance with scientific state-of-the-art knowledge. This means that the research question must be clearly defined, the hypotheses must be derived precisely, the methodology must be presented and justified, the perspective must be defined, the choice of therapeutic alternatives must be justified and the target population must be stated. The study design should be chosen to reflect reality as closely as possible.

For health economic analyses, both a prospective and a retrospective study approach can be adopted.

The health economic evaluation can be undertaken as part of a clinical study and reflect "efficacy" or it can portray "effectiveness" statistically by means of modelling. The methodological procedures of modelling (e.g. decision analyses, stochastic simulations, etc) are not standardised as this is difficult to do in comparison with clinical trials. For this reason, a high degree of transparency is required in the relevant model calculations.

2 Methods of analysis

Comparative health economic analyses can be classified according to the type of comparison of the costs and consequences. Depending on the type of analysis, the assessment of the outcome ranges from non-assessment through assessment in non-monetary, naturalistic units to monetary assessment. **The choice of method of analysis depends on the research question and must be justified.**

Method of analysis	Measurement / assessment of costs	Measurement / assessment of outcome	Cost-outcome comparison
Cost-minimisation analysis (CMA)	Monetary	None	None
Cost-effectiveness analysis (CEA)	Monetary	Natural units	Costs per outcome unit
Cost-utility analysis (CUA)	Monetary	Utility values	Costs per QALY
Cost-benefit analysis (CBA)	Monetary	Monetary	Net costs

Cost-minimisation analysis

The cost-minimisation analysis is an economic study in which two or more therapeutic alternatives with the same effectiveness or efficacy are compared in terms of net costs in order to establish the cheapest alternative. The equivalence of the comparators in terms of efficacy must be presented transparently and comprehensibly.

Cost-effectiveness analysis

The cost-effectiveness analysis is an economic study in which the costs are expressed in monetary units and the results in non-monetary units. Non-monetary units may for example be: (1) years of life gained, (2) hospital days prevented, (3) clinical parameters (e.g. response or remission rates, reduction in cholesterol, etc).

Cost-utility analysis

The cost-utility analysis follows the same principle as the cost-effectiveness analysis. Costs are assessed in monetary units and the benefit is measured as a non-monetary but utility-adjusted outcome, the quality adjusted life year (QALY). The concept combines life expectancy and quality of life. If quality of life is an important aspect of therapy, this form of analysis should be chosen.

Cost-benefit analysis

The cost-benefit analysis assesses all effects, including health effects, in monetary units. The disadvantage of the cost-benefit analysis is that a monetary assessment of clinical results must be made even though methodologically this is difficult to perform. Because of these methodological difficulties, this method of analysis is not used.

On the basis of these methods of analysis, supplementary questions can then be considered, such as the cost impact.

3   *Perspective*

The perspective is the point of view from which the costs and benefits are recorded and assessed. The choice of perspective must be derived logically from the research question. Apart from the societal/economic perspective, which

represents the most comprehensive approach, other perspectives are possible, e.g. the health system, social insurance, other service providers (hospitals), etc. The choice of perspective must be justified. If several perspectives are included in the analysis, the results must be presented separately for each study perspective.

4   Comparators

The aim of comparative economic analyses consists in assessing competing measures. The choice of alternatives must be appropriate to the research question and the state of science. The chosen alternatives should be described as fully as possible and comply with Austrian clinical practice. In other words, in the analysis a comparison should be made first of all with **standard therapy** in the case of alternative forms of treatment. If the standard therapy cannot be clearly established, the **most frequent therapy** or the **most effective therapy** can likewise be chosen. The choice of alternative(s) must be justified.

5   Cost determination

Fundamentally, all costs relevant to the chosen perspective must be determined and included in the analysis. In health economics, costs are defined in the economic meaning of the term and understood as the financially quantified consumption of resources.

Direct costs comprise all consumption of resources resulting from a treatment or therapy and directly attributable to this. Direct costs include direct medical and direct non-medical costs. Direct medical costs arise directly from the treatment (e.g. diagnosis, drug therapy, medical care, in-patient treatment, etc). Direct non-medical costs arise from the consequences of the disease or treatment (e.g. transport costs, care services, etc.).

Changes in resources that occur not directly in relation to the treatment of the disease are recorded and quantified as **indirect costs**. This includes losses of productivity resulting from illness and premature death. If impairment of capacity to work is to be considered together with absence from the workplace, this procedure must be presented separately.

A marginal consideration should be attempted in order to quantify the costs of an additionally consumed unit. Mean values should only be used if marginal values are not available.

In order to make the whole consumption of resources transparent, unit quantities and prices should be defined. Ideally, resource consumption should be quantified by means of opportunity costs. Opportunity costs describe the value of the next best use of resources. In a competitive market, this value is represented by market prices (e.g. drugs, medical devices, etc.). If there is no competitive market but scales of charges or fees or other forms of administrative reimbursement, then these should be used. In other cases, substitute quantities or "shadow prices"

should be used. If there are no published data for the cost survey, calculations and individual assessments (estimates, mean values, exploration of published data for the whole of Austria) should be performed.

Losses of productivity should be quantified by the **human capital approach**, i.e. the period-related income of the patient group concerned. If no specific data are available for the patient group considered, average values can be used from official statistics.

$$Loss\ of\ productivity = Incapacity\ for\ work\ x\ \frac{Wage\ costs}{Dependent\ employees\ x\ 365\ days}$$

In determining the loss of productivity, gender, age and social components must be considered, depending on the question.

It is also possible in the case of long-term absence from work or death to consider the current labour market situation, i.e. workplaces can be filled again within a relatively short space of time. Only the period until the workplace is filled again (friction period) is assessed as loss of production. Likewise, it is conceivable in the event of a very short period of absence from work for the absence to be covered by colleagues.   The use of the **friction cost approach**, however, must be justified.

6   *Outcome parameters*

The choice of outcome parameters depends both on the indication as well as on the research question. The effects of a medical intervention can be defined in various ways. At the same time the choice determines the method of analysis. The outcome parameters must be selected in advance and justified. The following outcome parameters can be chosen:

Economically oriented outcome measures such as hospital days, days of incapacity for work, etc.

Clinical outcome parameters include physiological or biochemical, morbidity- or mortality-related parameters. Final endpoints, intermediate endpoints and surrogate endpoints can be used as a measure of outcome. Hard clinical endpoints should be preferred. Because of the short analysis periods of randomised clinical studies, intermediate and surrogates endpoints can be selected optionally if these have a high degree of predictability of a hard clinical endpoint. If multiple outcomes are selected, they must all be presented separately.

As the relationship between clinical outcome parameters and subjective patient well-being is only very indirect, in specific indications - particularly where the medical treatment does not hold out the prospect of either a cure or a significant

prolongation of life - the **health-related quality of life** is the appropriate outcome indicator.

If the quality of life is to serve as an outcome variable, it must be ensured that the variable measured is also an appropriate measure for comparing the chosen treatment alternatives. Outcomes of this kind, in other words utilities, can be determined in the following way:
- specific scales (rank scales),
- game theory procedures (e.g. standard gamble, time-trade off, etc),
- psychometric scale procedures which include generic and disease-specific procedures as well as one-dimensional and multidimensional instruments.

These individual measures are suitable for combining with quantitative objective measurements such as survival time in the form of quality adjusted life years (**QALYs**).

In all study contexts, the methodological feasibility and the current state of science of quality of life measurement must be re-assessed. Comparison of different evaluation studies is facilitated by the choice of outcome parameters that are validated and current in the literature.

Whatever the outcome parameter chosen, it must be sensitive, valid and consistent.

7   *Incremental cost-effectiveness*

The incremental cost-effectiveness shows the difference in the cost-effectiveness of two alternatives or the additional costs of the net effect. Health economic analyses should include the description of the incremental cost-effectiveness.

8   *Data sources*

Health economic evaluation studies contain clinical, economic and epidemiological data. All the data sources used must be described exactly, their choice justified and their suitability and validity assessed. This involves scrutinising both internal and external validity.
The evidence level of the data is given below:

Clinical data

The underlying clinical data in health economic evaluations are assessed according to the following evidence levels and should be assessed in this order of priority according to availability:

1) Meta-analyses of randomised, controlled studies with masked assessment of the results
2) Representative, randomised, controlled studies with masked assessment of the results
3) Systematic reviews with an assessment of the results
4) Smaller randomised, controlled studies
5) Observational studies
6) Treatment guidelines
7) Expert opinions

Economic data

In Austria, economic data is not systematically recorded or published. For this reason, health economic evaluations should refer primarily to data from the following sources:

1) Austrian data from cost calculations published in cost studies
2) Global schedule of fees of the Central Association or a mixed tariff from several schedules of fees (e.g. Vienna, Upper Austria, Styria and Tyrol) or a tariff list from a regional health insurance fund,
3) All tariff and price lists of social insurance institutions, hospitals, care homes, rehabilitation centres, geriatric centres, health spa clinics and chambers of physicians and pharmacists (e.g. list of products).
4) LKF [Austrian DRG System] list of public fund hospitals
5) Data from cost calculation by hospitals
6) Cost estimates from Delphi surveys
7) Empirical surveys
8) Expert opinions

Epidemiological data

Epidemiological surveys performed directly in Austria or relating to Austria are extremely rare.

1) Published Austrian data or data surveys from Austria (plausibility check with other countries)
2) Published data from comparable neighbouring countries (e.g. Germany, countries of the European Union or Switzerland, etc)
3) Other available data (e.g. expert statements, published data from non-European countries)
4) Expert opinions

9   Time horizon

The choice of time horizon depends on the research question and can range from a few weeks to several years (e.g. remaining life expectancy). In choosing the time horizon, it should at all events be ensured that the chosen outcome and the resource consumption of the treatment alternatives are observable in this period.

10   Discounting

Often, in health economic analyses, costs and/or outcomes are considered over a period of more than a year. If this is the case, the calculation of current values is necessary, i.e. long-term considerations require discounting of the costs and benefits at a particular reference point - usually the time at which the study is set up. Discounting allows two different treatment alternatives in which costs and benefits of a particular reference point generally occur at different times to be compared.

As an annual discount, a rate of 5% is adopted, while a sensitivity analysis with higher and lower rates (e.g. 3% and 10%) should verify the robustness of the results. Non-monetary outcomes should be discounted in a separate calculation.

11   Uncertainty

Data for a health economic analysis are derived from various sources (e.g. pooled data sets, meta-analyses, unverifiable assumptions). As this is to some extent incomplete and affected by uncertainties, assumptions are frequently made about certain parameter values. Stochastic approaches such as deterministic sensitivity analyses should examine the effect of uncertain and/or estimated parameters on the outcome of the evaluation.

Ranges of variation are defined for the variation in exogenous parameters. The definition of the plausible range of variation is based on the following options, depending on the study design for sensitivity analyses: (1) confidence intervals from clinical studies, statistical studies, (2) assumptions from the scientific literature, (3) expert opinions, etc.

A sensitivity analysis is unnecessary if the parameters have already been presented with their dispersion.

The results of the sensitivity analysis must be discussed critically.

12   Presentation of the results

The results and procedure of the health economic evaluation must be reproduced transparently. The results should be presented in the same way as for a publication in journals (peer review) (details of the author, sponsoring, etc). Negative results also should be published.

Descriptions relevant to the research question and significant results should be presented in an aggregated and disaggregated way (e.g. according to cost components, perspectives, etc). The different viewpoints should be presented comparatively. An additional clear and brief description of the results should present the cost-effective (i.e. dominant) strategy.