1. Purpose

1.2 Background

One of the duties of the Norwegian Medicines Agency, represented by its Department of pharmacoeconomics, is to prepare recommendations and, where relevant, pass resolutions concerning acceptance of drugs to the reimbursement scheme (in Norway known as "blue prescription reimbursement" blåreseptrefusjonen). As of 01.01.2002 all applications to the Norwegian Medicines Agency regarding acceptance to the drug reimbursement scheme (blårecept ordningen) must include an analysis of the pharmacoeconomic repercussions of use of the drug.

The Norwegian guidelines shall serve as a standard for preparation of pharmacoeconomic analyses to be included in applications for reimbursement. The development of guidelines
is a result of a position on the part of the public authorities that pharmacoeconomic information shall constitute a portion of the basis for decisions pertaining to reimbursement applications.

- The Norwegian guidelines for pharmacoeconomic analyses were developed by the Norwegian Medicines Control Authority (now the Norwegian Medicines Agency), at the Department for pharmacoconomics, as commissioned by the Ministry of Health and Social Affairs. A number of key persons from different fields with expertise and background from the profession contributed to development of the guidelines which were presented for the first time in the autumn of 2000.

It was recognised that users of the guidelines would need some time to acquire the necessary expertise in this area. A transitional period was therefore introduced, with voluntary submission of analyses in connection with reimbursement applications up until 1 January 2002. The preparation of pharmacoeconomic analyses in connection with applications for reimbursement would be obligatory subsequent to 1 January 2002.

The requirement for pharmacoeconomic analyses is implemented through the existing legislation. In connection with this, an evaluation and revision of the guidelines has been carried out, to be subsequently revised according to need and experience gained. This calls for an open dialogue between users - on the part of the pharmaceutical industry and other relevant parties, the public authorities, the Department of pharmacoconomics, and the Norwegian Medicines Agency. The latter is open to discussions of methods, conditions and parameters in connection with preparation of pharmacoeconomic analyses. Such discussions can be held both during the start-up phase and during the process of preparing the application.

The guidelines are relatively open, without many restrictions with respect to method. Pharmacoconomics is a relatively new professional field and it is necessary to take into account the ongoing developments in the field, in the sense of not imposing requirements so strict that their practical implementation becomes impossible, or that they inhibit the desired development of the field and prevent the public authorities from carrying out their administrative obligations. The guidelines are not intended as a textbook on pharmacoeconomic analysis, but rather as guidelines determining which elements that are to be included in an analysis in connection with reimbursement applications.

On the basis of reimbursement applications submitted, including pharmacoeconomic analyses, as well as the Norwegian Medicines Agency’s own reports, cost effectiveness data and overall cost and health outcomes given reimbursement of the individual drug will be evaluated. The Norwegian Medicines Agency will come to a decision on its own or make a recommendation to the Ministry of Health concerning reimbursement applications based on an overall assessment of medical, social and health economic information related to the drugs.

1.2. Pharmacoeconomic analyses
The purpose of the pharmacoeconomic analyses in this context is primarily to identify the relation between changes in cost and health outcomes associated with treatment with the drug in question, compared with already existing treatment programmes. The result shall demonstrate the cost effectiveness of the new treatment compared with already established treatment. Analyses should be carried out in accordance with the Norwegian guidelines and reasons given for any deviation from these.

2. Specification of requirements

Pharmacoeconomic analyses shall be performed for all drugs for which an application for reimbursement is submitted, with the exception of:

- Drugs with the same active agent as drugs for which reimbursement has already been granted, hereunder: generic drugs, parallel-imported preparations and preparations in new packaging. This holds under the condition that the drug for which the application is being made has the same approved indication as the reimbursement-approved drug and that the costs are not higher, or the health outcomes different than that of a drug with which comparison is natural.
- Drugs where a new formulation clearly does not change the costs and health outcomes of treatment.

3. Introduction to the analysis

3.1. Assumptions and liabilities

The problem presented in the analysis is to be worded in such a way as to clearly illustrate the questions it aims to answer. The assumptions upon which the analysis is based, both the qualitative and quantitative basis for the parameters used in the analysis, and the limitations to the analysis must be defined and described so as to be as credible and transparent as possible for the users.

3.2. Responsibility

The reimbursement applicant is responsible for preparation of the pharmacoeconomic analyses to be enclosed in the application for reimbursement. The person(s) who has/have been responsible for preparation of the analysis, collaborating partners who have participated and how the analysis has been financed shall be stated.

3.3. Language

Pharmacoeconomic analyses and appendices are to be written either in Norwegian or English.

4. Description of the drug and its use

4.1. Description of the new drug.
The analysis shall contain the name of the preparation, the ATC-code and approval date for preparations registered in Norway.

Information about the drug and its mode of action should be primarily based on the Summary of Product Characteristics (SPC) or corresponding documentation from the marketing license application.

The approved indication shall serve as the basis for performance of the health economic analysis. Reimbursement of a drug, pursuant to Article 9, is granted only for use with medically approved indications. The description shall make clear whether the pharmacoeconomic analysis covers the indication in its entirety, or if there are limitations to the use of the drug implicit to the premises of the analysis.

4.2. Description of illness and patient group

The analysis must contain a description of the illness(es) and/or disease(s) for which the drug shall be used, and a profile of the patient group(s) making up the target group(s) for the drug with the given indication. The anticipated number of patients in Norway (prevalence and incidence figures) for each of the coming five years subsequent to introduction of the drug shall be given. Beyond this, the projected market share, or the number of patients who will use the new drug under the condition that reimbursement is granted, shall be submitted for the same years.

If the drug is regarded as being the most cost effective for a narrower patient group than the one covered by the indication, this must be specified.

4.3. Description of treatment

Daily dosage and expected treatment period with use of the drug must be specified along with expected frequency of repetition treatments. Experiences pertaining to compliance shall be accounted for. It should be stipulated whether any other drugs or forms of medical treatment can be expected to be used concomitantly. If the treatment is expected to lead to a reduction in the use of other drugs/additional therapy, this should be specified and reasons given.

4.4 Health outcome

The drug's documented primary effects with direct clinical relevance for the indication shall be given. Testing methods and parameters used must be described. If intermediary/surrogate endpoints are used to describe the effects of the drug, the relation of these to the final end points relevant to the medically approved indication must be clarified. Should the documented outcome include only parts of the patient group, outcome must be presented through sub-group analyses.

4.5 Adverse reactions
Adverse reactions of drugs may be decisive with respect to choice of treatment and can also affect the cost of treatment. The adverse reaction profile of the drug which is analysed must therefore always be described. It can be both relevant and expedient to treat the documented differences in adverse reaction profiles between alternative treatment programmes as differences in health outcomes.

5. Choice of basis for comparison

5.1. Choice of reference alternatives

A pharmacoeconomic analysis consists of a comparison of one medical treatment programme with one or more other medical treatment programme(s).

The drug for which an application for reimbursement is submitted is called the treatment alternative. This is compared with other relevant medical treatment programmes, known as comparators or reference alternatives.

The analysis shall account for the most significant medical treatment possibilities for the disease in question and the established treatment programme for the given indication. Treatment programmes which are chosen as reference alternatives should either be the most prevalent treatment, or the most inexpensive treatment, while other alternatives can also be used. Comparison with "no treatment" is acceptable where this is the relevant treatment alternative (the only offer to the patient). Resources and costs in connection with this alternative shall also be calculated. Where there are other relevant treatments than "no treatment" these shall always be analysed.

It is a condition that the chosen reference alternatives and the calculation alternative are relevant for the same patient group and indication. Several reference alternatives can be used in an analysis. The choice of alternatives perceived as relevant is a matter of assessment and whether medication-related or not, such a choice is of great significance to the results of the analysis. The grounds for the choice shall therefore be given in detail.

The most prevalent medical treatment programme or first choice of therapy is recommended as the reference alternative.

5.2 Description of reference alternative

Clinical experience regarding the of the reference alternative shall be presented. Any difference with regard to other countries’ treatment traditions should be discussed. All important costs and consequences for each alternative shall be given, in the same manner as for the drug for which the application is being made. Dosage of the drugs used as reference alternatives in the analysis should be within the approved dosage scale and reflect common clinical practice. This also pertains to duration of treatment. Reasons must be given for any deviation. The drug’s documented primary effects shall be presented in the same manner as for the treatment alternative. The adverse reaction profile of reference alternatives shall be described. Should there be differences in
precautionary measures and/or contraindications for the different treatment programmes, these shall also be described.

6. Time perspective of the analysis

Calculations in the analysis should have a time perspective which either

- corresponds with the documented effect in clinical studies

or

- corresponds with the period in which all the significant economic and health consequences of the treatment are clarified. The clinical data may be extrapolated by way of calculation models should this prove expedient. The time period should be adapted to the anticipated duration of treatment. Method and basis of extrapolation shall be described and reasons given.

7. Data collection methods

The pharmacoeconomic analysis shall be based on a complete presentation of all available documentation of the effects and adverse reactions of the treatment alternatives for the given indication. This implies a comprehensive, systematic literature search in relevant databases. A presentation of the criteria used for the literature search including the databases used and criteria for inclusion and exclusion of identified studies shall be given. Additionally, all non-published reports addressing the treatment alternative for the indication are to be presented. A summary of all presented abstracts is also recommended.

7.1. Use of data from different types of studies

Currently the most common method for gathering clinical data as a basis for pharmacoeconomic studies is randomised controlled studies (RCT), and to a certain extent epidemiological observation studies (e.g. cohort-studies and case control-studies). Data from randomised controlled studies where the treatment alternative is compared directly with relevant reference alternative(s) is recommended. The results from randomised clinical studies will be characterised by the study design, inclusion/exclusion criteria, choice of treatment programmes, number of patients and duration of the study. This will feasibly reduce the transfer value of the outcome results from clinical studies to outcome in common clinical practice.

Epidemiological studies (e.g. cohort-studies and case control-studies) can be useful because data from such studies can thoroughly explicate the effects of drugs in common clinical practice to a greater extent than RCT studies. The results from such studies can however, be influenced by so-called confounding factors (factors which have a connection both to the use of the drug and the health outcome one wishes to measure) and systematic errors (bias) to a greater extent than with randomised studies.
7.2. Systematic summaries

Outcome data on drugs from individual studies can be presented as systematic summaries or meta-analyses, wherein data from two or more studies is aggregate analysis as a unit. It is often advantageous if the pharmacoeconomic analysis is based on a systematic summary or meta-analysis because this can lead to more representative and easily generalised data than results obtained in a single study. Systematic summaries and meta-analysis should be based on methods in accordance with accepted guidelines (such as the Cochrane Library). The chosen method for acquiring an overview of published randomised studies must be described in detail and with clearly illustrated criteria for inclusion and exclusion of studies. Additionally, the country of origin for the clinical studies shall be clearly stated.

When carrying out a pharmacoeconomic analysis, there will often be a need to combine data acquired through different methods in order to ensure the best possible basis for assessment of the drug’s outcome/adverse reactions in clinical practice.

7.3. "Efficacy" and "effectiveness"

In randomised controlled clinical studies, the drug’s outcome is usually gauged as "efficacy". One seeks to test the effect of the drug under standardised conditions by reducing systematic effects of other factors which can influence the outcome of the drug.

In clinical practice however, there will often be a number of factors which contribute to an outcome which differs from that from testing done in random clinical studies. The resulting outcome of the drug in common clinical practice is called "effectiveness".

Ideally, health economic studies should be made up of the evaluation of the outcome of treatment programmes as these are found in a clinical every-day setting ("effectiveness") for the relevant patient groups. It is recommended that studies of drugs’ "effectiveness" be carried out to an increasing extent, also as a basis for pharmacoeconomic analyses. This will provide a better and balanced view of the drugs’ "efficacy" and "effectiveness".

7.4. Pharmacoeconomic models

Models of drugs’ cost effectiveness are intended to provide a theoretical structure and illustrate the drugs’ consequences and costs as these appear in clinical practice. Pharmacoeconomic models can serve as an alternative when relevant health outcomes or costs for different reasons are not measurable or have not been measured directly. There are a number of different approaches to creating such health economic models (e.g. decision trees, Markov models). Reasons for choice of approach must be presented.

The conditions, assumptions and data creating the basis for the pharmacoeconomic models must be clearly presented in such a manner as to make them relevant, understandable and re-examinable. The data basis used must be as relevant as possible with regard to the indication and treatment context of the drug in clinical practice.
Economic analyses based on "number needed to treat" (NNT) can be acceptable, but can be misleading and should be supplemented by other analyses indicating the validity of the NNT-analysis.

Foreign model analyses can be used, but must be adapted to Norwegian standards both with regard to clinical practice, costs and any health outcomes. Adjustments made for Norway must be clearly stated. If no adjustments have been made, the reasons for this must be given, along with the consequences this lack of adjustment can have for the final results.

An explanation must be given for any deviance between the data used in the theoretical model and the presented data basis. The consequences of such deviance is to be analysed in a sensitivity analysis (see Chap. 14).

8. Analysis methods

There are a number of different basic methods which can be applied in pharmacoeconomic analyses. The names of the methods are international and can be difficult to translate into Norwegian. The international expressions are therefore often used, so as to remove any doubt concerning the method being addressed.

8.1. Cost-of-illness analyses

Cost-of-illness analyses show what the illness costs society over the course of a given time period, e.g. one year. Cost-of-illness analysis is purely a cost analysis. Health-related consequences of treatment alternatives are not considered. In such cases the total costs and not the marginal costs are calculated and totalled.

The method will not gave a satisfactory analysis in a reimbursement context, because the result only describes the illness-related costs and does not show the cost-effectiveness in treating the patient. Such analyses can however be used as a basis for calculation of costs in cost-effectiveness analyses, which in turn can be applied to a reimbursement context.

8.2. Cost-effectiveness analyses

Cost-effectiveness analyses shall show the relation between costs and health outcome when comparing two or more treatment programmes. The treatment programme which has the lowest additional cost per gained health outcome unit has the highest cost effectiveness.

Cost-minimisation: Through comparison of measures which give the same result (different procedures for the same patient group) it is possible to explore which measure will cost the least. This is called cost-minimisation. Note that the "same result" includes the adverse reaction profile, a relatively rare occurrence.
For comparison of measures which give different results a number of different analysis types are available (see details in the Appendix):

**Cost-effectiveness:** Patient utility indicated in natural units such as gained life years or mortality avoidance. Health outcomes are related to cost of measures in utility-cost ratios.

**Cost-utility:** Patient utility in terms of gained life years and improved function/quality of life is measured with a common measurement index – quality adjusted life years (QALY). The number of gained QALYs is related to cost of measures in utility-cost ratios.

**Cost-value:** Patient utility in terms of gained life years and improved function/quality of life is emphasised due to societal priority setting based on degree of severity. This societal assessment of health outcomes is related to cost of measures in utility-cost ratios.

**Cost-benefit:** Results are measured in Norwegian kroner (NOK). Usually one then looks at the results in the form of production gains and avoided subsequent treatment costs. One can in addition to this estimate patient utility of health improvements by measuring people’s willingness to pay for such improvements. If the sum of the results, measured monetarily, is greater than the cost of the programme, implementation of the programme will result in welfare gains for society.

**Recommendation:** An analysis should be done which includes the patient utility (outcome). It can be expedient to use a number of different methods to illuminate the problem. Reasons for choice of method(s) shall be given. If improved functionality and/or quality of life – hereunder alleviation of adverse reactions – is a significant part of the patient utility, a method should thus be chosen which includes this dimension. If a cost-utility analysis is done, it is a good idea to supplement this with a cost-value analysis, as stipulated in the Appendix and subsection 9.1.

The methods are described in greater detail in Appendix, Part A.

9. Use of clinical and economic data from abroad

9.1. Clinical data

Clinical data of satisfactory quality based on foreign conditions will often be suitable for use as a starting point for further calculations in pharmacoeconomic analyses. Whether or not the Norwegian treatment context corresponds with the context described in the foreign studies with regard to therapeutic tradition, patient characteristics, reference alternative, etc. should be addressed. If deviance is likely, this must be taken into consideration and given particular attention. In such cases the deviance should be confirmed by relevant Norwegian expertise on the widest possible basis (e.g. clinical, socio-medical and epidemiological expertise). It is a condition that the drug is used in accordance with the approved indication in Norway.
In some cases it may be relevant to submit cost-utility analyses performed by parent companies abroad. In such analyses, the values for health status (‘utilities’) are often stipulated using an index for measuring health status of the type EuroQol, Health Utilities Index, 15 D or something similar. The transfer value of the utility-index from one country to another is to a very great extent variable and must be addressed separately. Uncertainty about the utility-index must also be reflected in sensitivity analyses.

There is also a significant variation between the values which such indices give for the same conditions. The results of cost-utility analyses can therefore be sensitive to the choice of health-status index. Analyses of different drugs, based on different utility-indices, are for this reason often not directly comparable.

Some functions are proposed for the transformation of values from different health-status indexes to values which also reflect the societal emphasis on the degree of severity in priority setting (cost-value analysis). Each index has a specific transformation function. With such transformation the analyses are thereby more consistent with societal values. Analyses based on different indices are also more comparable to one another. It is therefore recommended that cost-utility analyses be supplemented with cost-value analyses based on transformed values, see Appendix.

9.2. Economic data

Resource-use and costs of treatment with the same type of patient group can vary significantly from country to country. A health economic analysis which is carried out abroad can have little relevance to a Norwegian context because of differences in clinical practice, in the national health service’s capacity and organisation and different reimbursement systems. Information on cost-related consequences of treatment from abroad must therefore often be replaced by or supplemented with Norwegian data in order to adapt the analysis to a Norwegian context.

10. Cost perspective of the analysis

Pharmacoeconomic analyses performed in the given context shall be evaluated on behalf of society and should therefore be performed both from a societal perspective or where relevant a health service perspective, and the perspective of the payer, i.e. the National Insurance Administration. This means accordingly that the economic consequences which the illness and any interventions will have for society as a whole and the National Insurance scheme should at all times be clear. All relevant costs must be included in the analysis, regardless of who is to bear them. Costs borne by society in general and the National Insurance in particular are to be presented separately.

A presentation of the patient’s costs in the event of reimbursement not being granted shall be given. Costs falling to different parties and budgets can be illustrated using a table or other type of clear presentation.

11. Costs
Distinctions are made between different types of costs:

1. Direct costs are resources which are *used* as a result of illness and treatment and consist of:
   - Direct costs within the health care sector (cost of diagnostics, prevention, treatment costs, stay in hospital or institution).
   - Direct costs outside of the health care sector (medical equipment, patient costs, costs to relatives)
2. Indirect costs are resources which are *lost* as a result of illness and death and consist of:
   - Loss in production
3. Intangible costs:

   Non-measurable costs such as grief, pain and suffering. This cost can alternatively be evaluated as a change in terms of quality of life and measured as a health outcome.

The different types of costs are described in Appendix, part B.

All direct costs must be included in the analysis, regardless of who shall bear the costs (societal perspective). The analysis must make a clear distinction between identification of cost components, consumption of such components and valuation (in NOK) of the individual components. If possible, costs should be given on the individual/patient level or as precisely as possible.

It is the incremental cost of the treatment alternative compared to the reference that is to be calculated. Where it is deemed relevant to include indirect costs in incremental costs, reasons for this shall be given. In such cases the incremental costs must always also be presented excluding indirect costs.

It is important to make a distinction between expenses and costs. Ideally, a pharmacoeconomic analysis must calculate cost. It is however often the case that it is difficult to identify real costs, and in such cases calculation of expenses can be acceptable. It must be clearly defined which measure is used. For example, the medical fees submitted need not be the actual cost of a given service. Expenses for medical fees do not therefore necessarily reflect costs, but can be used if no better estimate of actual costs is available.

Estimated use of resources and expense basis for estimation of costs shall reflect the relevant Norwegian conditions based on common medical practice. Costs which are related to other illnesses, which have no connection with the analysed illnesses/diseases, shall neither be calculated. Transfer payments, such as sickness benefits and VAT are not included in health economic calculations, due to the risk of double-entries or other errors.

**12. Discounting**
A cost Y or health outcome X currently in effect, is commonly assessed as higher than that which is realised for the same cost/health outcome in the future. For analyses of treatment where the health outcomes and/or costs are distributed over more than one year, discounting should be carried out, in other words a depreciation of the value of costs and any health outcomes. Costs shall be discounted, while health outcomes should be illustrated both with and without discounting.

Given a lack of international consensus with regard to a discounting rate, it is recommended that a rate fixed between 2.5 and 5% be used. A sensitivity analysis will be performed to illuminate the significance the discounting rate would have for the end result of the analysis. The recommendation is that the discounting rate vary from 0 % to 8 % in the sensitivity analysis.

For further discussion on discounting, see Appendix, part C.

13. Results

The results of the cost-effectiveness analysis shall be presented in a separate section and be based on the main parameters and conditions of the analysis. The results are reported as difference in costs (marginal costs) in relation to difference in health outcomes (marginal health outcomes) i.e. cost effectiveness.

How the results are reported will be contingent upon the choice of analysis method. Examples of results are: costs per avoided heart attack (CEA), costs per gained life-year (CEA), costs per quality adjusted life-year (CUA), etc.

In addition, the total costs and health outcomes are to be reported separately. This provides a clear overview of the total economic and health-related consequences for the treatment.

14. Sensitivity analysis

A sensitivity analysis must be done for all key parameters in the analysis, in order to test the validity of the conclusion. The most prevalent method involves changing the value of these parameters within a defined area to control whether it will change the conclusions of the analysis. Varying the parameters one by one (one-way sensitivity analysis) is accepted, but two-way and three-way analyses are deemed more expedient.

Examples of methods are found in the Appendix, part D.

15. Discussion and conclusion

The analysis shall contain a discussion of submitted data, methods and results. The transferability of results based on studies and any foreign data to common Norwegian clinical practice shall be accounted for (e.g. efficacy vs. effectiveness).
The discussion must present any existing published and, where relevant, unpublished pharmacoeconomic analyses on the analysed illness. This overview shall be based on a systematic literature search indicating where the search has been done. If the analysis deviates from any earlier publications, the reasons for such deviance must be discussed.

The discussion shall also state whether or not another analysis method or model would change the result, and whether other conditions and parameters should be tested in the sensitivity analysis.

The discussion should also address the social consequences of introduction of the new therapy in Norway.

16. List of references

Finally, the report shall include a reference list of all reference sources comprising the data basis of the analysis and its conditions. References are set up in accordance with the Vancouver-convention.

17. Summary of analysis structure

- Introduction
- Description of the drug and its use
- Comparison therapy
- Time perspective of the analysis
- Choice of analysis method
- Use of data from abroad
- Cost perspective of the analysis
- Costs
- Discounting
- Results
- Sensitivity analysis
- Discussion and conclusion
- List of references

APPENDIX

A. Analysis methods:

1. Cost-minimisation analysis

The cost-minimisation method presupposes that the health outcomes (including adverse reactions) of the treatment methods to be compared are identical. The analysis therefore consists of a comparison of costs of the therapies only. The condition of identical health
outcomes for different treatment programmes is seldom fulfilled, but the method is recommended in cases where this occurs.

2. **Cost-effectiveness analysis**

Cost-effectiveness analyses calculate the health outcomes in intermediary (surrogate) or final (hard) end points. As an example we have, respectively, a reduction in cholesterol level, in percent, and number of avoided heart attacks. These are measurable end-points.

The result of such an analysis is easy to understand as it will be represented as e.g. NOK 100 000 per avoided heart attack per annum, or NOK 1 500 000 per gained life-year after cancer treatment (random figures). The method for measuring health gains is equivalent to that we often see in the clinic.

With calculation of intermediary outcome measure, it is important to describe/document the connection between the intermediary and final health outcome, such as cholesterol level and development of heart/vascular disease or death.

Cost-effectiveness analyses can be used when the treatment programmes to be compared give the same type of health outcome, e.g. two drugs which reduce the number of epileptic seizures. In such a case the health outcomes can be compared. The method cannot be used when one wants to compare the value of different treatment programmes which have different forms of health outcomes, such as treatment of gastric ulcers vs. treatment of migraines.

3. **Cost-utility analysis**

In a cost-utility analysis it is assumed that the value of a health improvement in connection with a treatment programme can be quantified as a product of the improvement in life quality the patient will achieve and the number of years he/she will benefit from the improvement. Cost-utility analyses show health outcomes in terms of morbidity and mortality in a health outcome measure which is common for all treatment alternatives. Life quality improvements are expressed on a scale from zero (equivalent to dead) to one (perfect health). A gained life-year in perfect health receives the value one. This gain is called a gained quality adjusted life-year (QALY). It is used as a measurement unit for all types of health gains, whether these consist of symptom alleviation, functional improvement or prolongation of life, and regardless of the type of symptom alleviation or functional improvement (Torrance, 1986).

A number of indices have been developed to assist in performing QALY-calculations, for scoring complex health profiles on a life quality scale from zero to one (e.g. ‘EuroQol’ (Brooks et al, 1996; Nord, 1996a).

The cost-utility method is well established. The advantage is that in principle the method makes it possible to compare the value of scanty resource funding for entirely different, competing applications.
On the other hand, research in recent years has shown that priority setting between programmes according to the cost--per-QALY-method in many cases does not correspond well with the societal perspective of what is fair and ethical. The QALY-approach is based on a wish to maximise health production. But a society such as the Norwegian society primarily seeks to prioritise according to degree of severity, where effective treatment does exist. This can mean for example that moderate improvements for the critically ill are sought prioritised above large improvements for the moderately ill.

Technically speaking there are two reasons why the QALY-calculations can be misleading as a basis for decisions involving societal priority setting. One is that the life quality scores (on a zero-one scale) attributed to different health problems are often too low. The consequence of this is that programmes for moderate health problems are given far too great an emphasis in the analysis compared to programmes for serious health problems, and symptom alleviation and functional improvement are generally given too great a value compared to live-saving measures. The second reason is that the QALY-approach places an excessive importance on the number of years for which patients will benefit from a treatment. This can lead to the value of treatment programmes for elderly patients being set too low compared to the value of treatment programmes for younger patients.

4. Cost-value-analysis

A set of alternative values for health conditions of various types has been proposed which is more in harmony with societal preferences for priority setting than the prevalent life quality scores in the QALY literature (Nord, 1996b). In the alternative set of values, the value of less serious conditions is set at just below one. Analyses which use such alternative values are called cost-value analyses. The alternative values can be used as weights for life-years, as is the case with conventional life-quality scores in the QALY-approach. If a cost-utility analysis is performed based on the values from a health index of the type EuroQol, Health Utilities Index or 15 D, one can estimate alternative values using simple transformation functions, and perform a cost-value analysis as a supplement to the cost-utility analysis (Nord 2001).

5. Cost-benefit analysis

The result of the cost-benefit analysis shows the costs in NOK in relation to health outcomes measured in NOK. If the analysis only includes gains in the form of increased production ability on the part of the patients, the analysis is called the human capital approach. An analysis as narrow as this has a limited value for priority setting. It can, however, be expedient if regarded as a method solely used to calculate society’s net costs for a given programme.

Patient benefit of a treatment programme (such as improved quality of life and/or prolonged lifetime) is quantified in cost-benefit analyses in NOK instead of in physical units or QALYs. Quantification is usually based on hypothetical questions to the population about what they would be willing to pay for different types of health
improvement, if they lived in a system where they had to pay for improvements directly from their own pocket (the payment willingness principle). Cost-benefit analyses are used relatively seldom as pharmacoeconomic analysis, because there is great uncertainty concerning the validity of measurements of hypothetical willingness to pay for health services (Abel Olsen, 1997). It is difficult and controversial to express health outcomes in monetary value. Pharmacoeconomic analyses which are performed using this method must therefore be assessed with great caution and will not provide as many possibilities for comparison with analyses of other programmes and technologies as does the QALY-approach, simply because fewer analyses have been done based on payment willingness studies.

References:


B. Costs

Costs in cost-effectiveness analyses must reflect the marginal costs (added costs) expressed in monetary terms. The marginal cost is in principle the cost accrued with treatment of one extra patient.

Costs in health economic analyses are divided into three groups:

- Direct costs
- Indirect costs
- Intangible costs

Direct costs are the resources which are used as a result of the treatment and illness, while the indirect costs are resources lost as a result of the treatment and illness.

Intangible costs are personal strain as a result of the treatment which can not be measured in monetary terms, such as anxiety, grief and suffering.

1. Direct costs
Direct costs are, within health economics, the resources *used* in connection with the illness. For the societal perspective, all direct costs are to be included in the analysis. Direct costs can include purely medical costs such as expenses for diagnostics, drugs and hospital stay, as well as non-medical costs such as remedial aids, transport aids, special clothing and special food. VAT shall be excluded from all costs calculated in pharmacoeconomic analyses with the societal cost perspective.

2. Indirect costs

Indirect costs, within health economics, include the resources *lost* as a consequence of the illness. This is loss in productivity as a result of illness or death. This includes both paid and unpaid productivity loss (temporary sickness absenteeism, permanent functional impairment, premature death). Indirect costs can be measured using two methods:

1. **Human capital method**: Production loss measured in payroll costs. Number of hours the patient is absent from work multiplied by hourly cost.
2. **Friction-cost method**: What it would cost society to replace the lost work input.

There is a lack of professional consensus regarding choice of method and internationally, recommendations vary from country to country. The Norwegian authorities are open to the choice of method, but reasons for the choice must be given.

3. Intangible costs

Intangible costs represent costs as a consequence of the treatment not measurable in monetary terms. These costs can be pain, grief, suffering and the like. To the extent that intangible costs must be quantified, this should be done using approved outcome-measurement techniques.

The Norwegian authorities are open to the submission of such documentation.

4. Cost data sources

The cost analysis is based on identification, quantification and valuation of cost components. Valuation is usually based on an average cost unit. It is important to remember that the ideal is always to calculate the *costs*. Where the costs cannot be calculated, expenses may be used as a substitute, but the reasons for this must be given. The following is a list of some examples of relevant unit costs:

- Market price can be used where possible (medication, technical equipment, rental of premises, etc.).
- Cost of hospital stay can be based on the Ministry of Health and Social Affair’s DRG-list, available by contacting the Ministry.
- Cost per outpatient clinic consultation or procedure at a public outpatient clinic can be based on the hospital’s reimbursement rates available by contacting the Ministry of Health and Social Affairs. These do not necessarily reflect the socio-
economic costs. Sintef NIS in Trondheim can in such a case give information about relevant studies.

- Cost per consultation or procedure in a private general or specialist practice can be based on the rates of the standard wage scale (Normaltariffen) available by contacting the Norwegian Medical Association. The consultation rates shall include patient’s own payment and the share of the consultation grant (e.g. 4 200 consultations per annum for a general practice and 3 500 consultations per annum for a specialist practice). The rates do not necessarily reflect the socio-economic costs. Sintef NIS is working on analyses of costs in private specialist practices and the report on this may become available from Sintef NIS.

- Cost for stays in nursing homes and the like should be based on accounts from large municipalities (such as Oslo) where there is a representative selection of nursing homes. If any costs are left out (such as overhead-costs and capital costs) this must be specified.

Capital costs for buildings can be based on the market price for rent of equivalent areas or buildings.

C. Discounting

Costs incurred at different points in time cannot be added directly to arrive at total cost, because cost X is valued higher by most people today than the same cost in the future. In order to make costs comparable over time, they must be discounted so that the sum of the discounted costs represents the current value of the total discounted costs.

Example:

In the next three years the costs of a project will amount to NOK 110, NOK 120 and NOK 130. The discount rate is 5% per annum. This means that for each year the value will decrease by 5%. The current value of the costs for the project become thus:

\[
\text{NOK } 110/(1+0.05)^1 + 120/(1+0.05)^2 + 130/(1+0.05)^3 = \text{NOK 326}
\]

In contrast to the calculation:

\[
\text{NOK 110 + 120 + 130 = NOK 360}
\]

Discounting formula:

The current value of NOK 100 in a period t by discounting rate i

\[
100/(1+i)^t
\]

The discounting factor is: \(1/(1+i)^t\)

If there are several costs K over time, we get the following formula for current value:
D. Sensitivity analysis

The result of a health economic analysis is generally based on many assumptions and variables. Some of these will be uncertain. It is therefore important to test how changed assumptions will affect the result.

A common method is to change one variable or assumption at a time and report the result on a continuous basis. This should be illustrated using tables. By changing one assumption at a time, one can clearly see each individual variable’s effect on the result. A multi-directional analysis is also recommended, where two or more variables at a time are changed. A probability sensitivity analysis with a presentation of cost-effectiveness acceptability curves is clearly advantageous.

The suppositions and variables can alternatively be changed along a scale regarded as probable. For example, one can argue that a specific cost can vary from -10 % to +30 % in relation to the base case. Another method is to vary one component from one extreme end of a scale to another. One thereby shows results with extreme base cases, allowing the decision maker to easily imagine the cases in between. A base case is often reported supplemented by one optimistic and one pessimistic estimate for each variable (best case/worst case scenario).