Danish Regions' methodological framework for the Danish Health Technology Council

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Methodological framework for the Danish Health Technology Council

1. Introduction

This chapter describes how the methodological framework should be understood and how it can be supplemented by additional products. The chapter also describes the objectives of the Danish Health Technology Council and defines several key concepts relating to the Council's activities and the basis for its methods.

Below is a description of the methodological framework for the Danish Health Technology Council's work. The methodological framework is the foundation for the more in-depth methodological guidelines to be prepared by the Danish Health Technology Council secretariat. These guidelines will provide a more detailed version of the framework described below.

In addition to the methodological guidelines, the Danish Health Technology Council secretariat will prepare a number of other tools and products to guide stakeholders proposing topics to be addressed by the Council, including an application template based on elements and requirements described in the methodological guidelines, a catalogue of unit costs for cost analyses (see chapter 3) and a tool for assessing cost neutrality or cost savings. Furthermore, internal tools and templates will be developed for evaluation reports, synthesis reports and decision bases.

The methodological guidelines, the application template and other documents and tools will assist the secretariat, as well as Council and expert committee members in their work. Furthermore, they are intended as a set of standards to guide stakeholders eligible to propose topics for evaluation by the Danish Health Technology Council, including companies, hospitals, and regional governments. Proposal submitters are responsible for providing evidence for the health technology they wish to have evaluated, and they should do so within the framework of the methodological guidelines. The expert committee will assess and supplement this evidence, assisted by the secretariat.

The methodological framework should be understood in the context of the process guide.

The Danish Health Technology Council conducts evaluations and analyses. The difference between the two depends on the topic addressed. Danish Health Technology Council *evaluations* focus on a single or a few technologies or interventions, including marketed medical devices. Danish Health Technology Council *analyses* have a broader scope and evaluate several (sometimes several *different*) technologies or complete treatment approaches or treatment areas.

The methodological framework described below covers both evaluations and analyses. In the following, both analyses and evaluations will be referred to as evaluations.

This methodological framework document presents the Danish Health Technology Council's approach to evaluations and possible sources of evidence, including requirements for these sources. Furthermore, the document presents the methodological core elements and the types of conclusions and recommendations that can be given on the basis of an evaluation.

The objective of the Danish Health Technology Council

The primary objective of the Danish Health Technology Council is to target Danish health care resources at the technologies and interventions that provide best value for money; in other words, the objective is to identify the most cost-effective health technologies, raising the quality of health services and reducing cost pressure in the health care system. The Danish Health Technology Council works within and on the basis of the following guiding principles: providing optimal value for money (the most cost-effective health technologies), maintaining professionalism and independence from the political system, and ensuring transparency and equality. Furthermore, the Council operates in accordance with the seven principles for prioritisation of hospital drugs set out by the Danish Parliament.

The Danish Health Technology Council can make recommendations for the use of new or existing medical devices and health technologies. The term 'health technologies' denotes any use of procedures, treatments and systems, including associated knowledge and skills, to solve a health problem or to improve quality of life. The term 'cost-effective' means that a health technology offers a reasonable relationship between outcomes/effectiveness and costs for the health care system. With regard to medical devices, the Council can only evaluate products with CE marking.

The aim is to always evaluate health technologies and treatments on the basis of their assessed (added) value, and technologies will be compared with the best existing, already implemented technologies or treatments. The assessment of the value of a technology includes an assessment of its effectiveness and any implementation needs (typically organisational), as well as the financial considerations required to enable and support the Council's guidance.

Broad remit

When carrying out evaluations, the Danish Health Technology Council must take account of the specific conditions pertaining to the topic under review.

Medical devices are often continuously adjusted and fine-tuned so that their effectiveness and cost-effectiveness are improved along a learning curve. Effectiveness is often also affected by the training, skills and experience of users. On the cost side, it is essential to separate acquisition costs and start-up costs from operating costs, including maintenance costs and the like.

For technologies used for diagnostics, it is especially important to consider outcomes and costs over the full treatment pathway, because the outcomes often rely on the subsequent intervention and treatment.

The Danish Health Technology Council can also evaluate products for use across hospitals, municipalities and general practice. Such evaluations are conducted in close coordination with the Danish Medicines Council. Medicines accompanied by a diagnostic test, such as a biomarker, are assessed by the Danish Medicines Council.

The secretariat will elaborate on the factors touched upon above and will describe how to deal with them in evaluations and analyses.

2 Content of evaluations and the sources and assessment of evidence

This chapter describes how the contents of an evaluation are determined. The process starts by clearly defining a set of review questions relevant to the individual case. In addition, the possible sources of evidence are presented, as is the approach to assessing the quality of the evidence.

The Danish Health Technology Council must make cross-cutting decisions concerning different technologies and disease areas. It is therefore important to analyse the benefits for users, such as clinicians or patients, and the financial significance for the overall health care system, using a consistent and transparent approach that is framed in the same way each time.

Framing and PICO

The evaluation should define and identify what are to be included as central elements in the assessment of a specific technology. This is achieved by determining PICO questions.

PICO stands for:

- P - Patient, problem, population
- I – Intervention, exposure
- C – Comparison (comparator(s))
- O – Outcome (for example death, disease, pain, quality of life)

The evaluation addresses a number of questions based on these four elements.

The full treatment pathway (across sectors) covered by the technology must be considered when answering the questions. For diagnostic technology in particular, pathways can be long and relatively complex because diagnostics are embedded in a larger technology and

treatment regime.

Outcomes and costs associated with the use of the new technology must be assessed in comparison with the relevant alternative(s). The alternatives should be a real alternative, relevant in a Danish context. The most relevant alternative is the alternative that will be replaced if the technology under evaluation is taken into use.

The secretariat will specify the use of the PICO model as the framework for evaluation and analysis, and how the PICO model is to be used to frame review questions.

Sources of cost and outcome evidence

The quantity and quality of evidence relating to medical devices and diagnostics are generally lower than for medicines. Clinical outcomes associated with medical devices, particularly new technologies, are often limited. For example, in certain situations, there is a lack of studies comparing the technology in question with suitable alternatives. For diagnostic devices, in certain situations, there will be a lack of end-to-end studies, i.e. studies that follow the patient from testing, over treatment, to the final outcome(s). The Danish Health Technology Council therefore does not limit itself to including only certain types of evidence. Evidence may range from quantitative studies and literature on clinical outcomes and costs to qualitative evidence from patients, expert statements, and information from ongoing research or other.

Sources of information may include:

- Literature
  The PICO questions determine the literature to search for and select. The objective of searching and using literature is to identify, for example, outcomes, user-friendliness and safety, and possibly health economic studies, and studies concerning the patients' perspective. The literature search is carried out in relevant databases, including databases with primary literature, registers or databases for systematic reviews, meta-analyses, HTAs, etc. Grey literature may also be included, as well as unpublished data/studies.
- Documentation from manufacturer(s)
  Knowledge from relevant manufacturer(s) should always be included. For example, product specifications, the company's own data or estimates with regard to costs or management of the technology, including knowledge about any organisational or structural requirements for the technology, etc.
- Expert statements
  Experts can be clinicians, technicians or others with relevant knowledge

about the technology or treatment under evaluation. In many cases, experts will be a part of the expert committees, but expert statements may also be obtained from outside the expert committees. Expert statements can be included as part of the organisational or implementation analysis, or they can be used to assure the quality of information provided by others.

- Patients/relatives as sources

  There will always be patients involved in an evaluation. The patient perspective and patients' experiences are included on par with all other evidence provided. To the extent possible, patients with first-hand experience of the health technology or topic in question will be included in the work of expert committees. For example, through facilitated inputs, e.g. via focus-group interviews with patients in connection with expert committee meetings.

  As far as possible, patients will be selected on the basis of whether they are representative of the user group. Relevant patient associations will appoint patients with relevant experience to the expert committees. Patients will be involved and heard on their own terms. One of the patients participating in the expert committee will also participate in the presentation of the evaluation to the Council. In the analysis of the patient perspective, focus is on experience, recommendations, preferences, values and expectations with regard to health, disease, services and treatment. The overarching themes could be to identify how patients experience the burden of life with the relevant disease, experience with use of the existing technology or treatment, and experience with and expectations of a (new or) another technology or treatment.

In the methodological guidelines, the secretariat will specify relevant sources and methods for validating and assessing the quality of data, including how to involve experts and patients and how to include their statements in the overall analysis.

The expert committee assesses the quality of the evidence

The expert committee assesses the quality of the evidence. The expert committee uses the GRADE method as a tool to assess the quality of evidence, where relevant. Furthermore, the expert committee uses its expert and clinical knowledge about the technology and the therapeutic area to assess the degree to which the findings generated by the qualitative and quantitative evidence are credible.

The significance attached to the various types of evidence depends on the quality of the

evidence and on whether a given type of evidence is suited to address a specific problem. Furthermore, the expert committee has to consider that the requirements for evidence are higher for high-risk technologies, while greater uncertainty may be accepted in other situations. In general, evidence based on quality studies, e.g. randomised trials with low risk of bias, will be afforded the highest significance and weight.

The secretariat will elaborate on the use of GRADE and the hierarchy of evidence in the methodological guidelines.

3 Method for evaluation

This chapter presents the evaluation method and the methodological core elements: outcomes, costs, organisation/implementation aspects, and ways to compare costs and outcomes. For each core element there are guidelines and possible sources, as well as requirements for quality assessment.

The Danish Health Technology Council can evaluate a number of different health technologies and treatments, and how a method is applied may vary accordingly. The more complex an evaluation, the more complex the methods and the longer the evaluation process.

An evaluation starts with factual descriptions of the technology and the indication/disease area, the target group, etc.

This could be by describing:

- The objective of the technology or treatment under evaluation; whether the technology or treatment supplements or is already part of existing Danish practice, including whether it should be considered as a replacement for an existing technology or is expected to constitute a new treatment or an add-on to existing treatment; the indications towards which the technology is targeted (the intended use/purpose); and for which the technology has obtained CE marking (if relevant).
- The disease area with which the technology or treatment under evaluation is associated, including characteristics of the area such as organisation, technological advancements, etc. The disease for which the technology or treatment is used, including prevalence and incidence in Denmark. The existing standard treatment in Denmark and the prognosis with current treatment options. Also if there are no existing treatment options.
- The patient group for which the technology or treatment under evaluation is effective, including number of patients. What consequences/disease groups do use of the technology focus on? How is the disease/condition diagnosed/treated, how often is the technology used, and are there any observed variations in use across regions or in other contexts?

The secretariat can specify further how the description of the technology or treatment, disease area, and target group can be summed up and included in the overall assessment.

Methodological core elements

An evaluation covers at least three elements: outcomes, costs and implementation/organisation. The content and breadth of the three fixed elements will vary. Further aspects should be included where relevant.

Outcomes

An evaluation examines the outcomes that are initially defined in the PICO. Generally, the aim is to examine how the technology works in practice and under normal, everyday circumstances. The effects of the technology should be considered over the full treatment pathway, which may extend beyond the hospital to include the patient's own home, the general practice, and the municipal health service.

The aim is therefore to determine the extent of clinical and/or health benefits and drawbacks brought by the technology for the patient or users, compared to current practice.

An outcome must be relevant for clinicians, patients or users, and it must be valid, reliable and, preferably, sufficiently sensitive to register changes over time.

An outcome can be *direct,* i.e. situations in which the technology only has a direct impact for the patient or user. Or the outcome target can be *indirect*, i.e. situations in which the technology has an indirect impact on the patient as part of an overall treatment pathway and the technology is considered to be a mediating or intermediate outcome in the treatment of the patient (for example a diagnostic test that indicates whether a given treatment is right for a given patient or estimates how much treatment should be given to a specific patient group), and, finally, in which it is the treatment itself that has a direct impact on the patient.

In general, outcome can be divided into the following categories:

- *Health-related quality of life*
  Quality of life should always be included in assessments where relevant and should as far as possible be measured directly by patients, e.g. by use of generic (such as EQ-5D) or disease-specific, validated questionnaires.
- *Morbidity, symptoms, adverse effects and safety*
  The choice of outcome representing adverse effects depends on the technology in question and the specific disease for which the technology is assessed. Adverse effects can be assessed through their prevalence, manageability, reversibility, and severity. Relevant adverse effects could be the change in the percentage of or number of patients experiencing specific adverse effects or experiencing adverse effects in general, or in the

number of patients leaving a study due to adverse effects. Aspects pertaining to safety, including direct harm (mortality; morbidity, e.g. associated with exposure to radiotherapy; toxicity; hypersensitivity, etc.) or indirect harm (e.g. due to inadequate training or experience); as well as lack of device maintenance or wrong choice of patient group should be described to the extent possible.

- *Mortality/survival rate*
  Outcomes related to mortality or survival must be included where relevant and should be expressed as the reduction/difference in risk or similar.
- *Use*
  Outcomes related to the use of a technology, e.g. user-friendliness, availability, compliance or similar which relate to the use a technology or treatment.

When relevant, the time period should be defined, for which the outcome is estimated. This is important because the occurrence of outcomes and adverse effects may vary over time, so whether you measure the outcome over weeks or months, for example, may make a difference.

Once outcomes have been determined, they are presented in a manageable way along with their sources. Studies behind outcome assessments are presented on the basis of characteristics such as:

- Study design
- Intervention and comparator
- Follow-up period
- Outcomes in the study
- Characteristics of patients included (broken down by treatment arms)

This is supplemented by a discussion of knowledge from expert sources, including from patients, unpublished data, etc. The quality and validity of the sources are also discussed.

The actual analysis of the improvement in outcomes can have various scopes and degrees of complexity depending on the subject, risk class, disease area, etc. The requirements for the outcome analysis and the quality of evidence increase relative to aspects such as:

- The severity of the problem the technology is intended to solve
- The scope of the problem the technology is intended to solve
- The scope of the negative financial impacts of implementing the technology

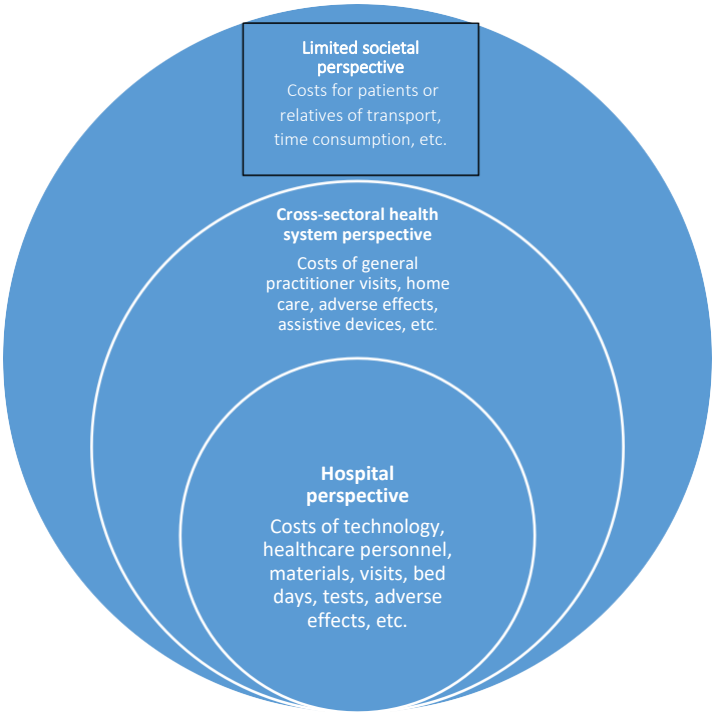
The outcomes analysis will be presented as a summary of the outcomes found from the selected studies and other qualitative evidence compared to the standard treatment. Where relevant, complex analyses will be used, such as comparative studies including multiple comparators.

The secretariat will specify how the outcomes analysis can be performed (including the use of more complex analyses, such as network meta-analyses), and how it can be presented.

Costs

Evaluations always include analyses of costs. A broad understanding of costs is applied. The costs that change as a consequence of the change in use of a technology or treatment include both direct costs from resource use and costs derived from resource use following from the effects and adverse effects of the technology in all sectors. To identify and compare the changes, the resource use for each technology included in the evaluation must be identified, quantified and valued.

The figure below shows some of the costs that can be included:



The assessment of changes in resource use should be based on the evaluation's PICO questions.

In this way, the content of the analysis will be defined on the basis of the relevant population and comparator(s).

It is important that the cost analysis clearly outlines the most influential cost drivers in the analysis because these elements will be most relevant for the Danish Health Technology Council in its assessment of a technology or treatment.

As a general rule, the cost analysis should be based on average cost estimates. Sources of cost data can be studies, expert statements or a combination.

For the most typical types of resources to be used in the economic analyses, the Danish Health Technology Council will produce and maintain a catalogue of unit costs or source references indicating how to best estimate the unit costs.

Direct costs should be divided into two, separately reported elements: Consumed quantities, for example hospital admissions or home care hours, and the associated unit costs.

DRG/DAGS rates can be used as average estimates for costs.

The price of the health technology under investigation should be included as a cost in submitted applications. An evaluation process can include a price negotiation to determine a (new) procurement price. For example, this can be in situations with a new product that has yet to be priced, or in situations where a number of products are compared which have not previously been subject to competition. See also the process guide.

The secretariat is expected to further clarify how resource use can be estimated and valued, and the secretariat will moreover prepare a catalogue of unit costs.

The following describes a number of elements to be included in a cost analysis, including when to document whether a technology is cost-neutral or cost-saving:

- Perspective and highlighting consequences for various actors

  A limited societal perspective must be applied. This means that all relevant treatment-related costs should be included, regardless of who pays them. This also applies to derived costs resulting from the treatment of adverse effects, etc. If the technology under evaluation affects costs in general practice or municipalities, these costs must be included in the analysis. The same requirements apply with respect to the validity and argumentation as for the other costs. In evaluations that include health-related costs in other sectors, all results must be presented both including and excluding these costs, because these costs are often more uncertain than treatment-related costs. The analysis is to provide an overview of how the financial impacts distribute across actors (hospitals, actors in the primary sector, etc.). Productivity losses/gains (labour market benefits, etc.) should not be included in the analysis so as not to bias the analysis with regard to age/labour market attachment.

  The costs incurred by patients and their relatives due to use of the technology (such as transport costs and time consumption) should be included, if relevant and sufficiently documentable. The results of the analysis should be presented both including and excluding these costs.

- Population

  The cost analysis should include a description of the patient population that the costs relate to. The patient population should reflect the population defined in the PICO process. Separate cost estimates can be performed for various subgroups if the technology is expected to have substantially varying costs for the various subgroups (such as separate cost estimates for men and woman and different age groups).
- Time horizon, discounting and extrapolation

  The time horizon for the cost analysis should be long enough to capture all significant differences in resource use. Benefits and costs should be converted to present values. A discount rate corresponding to the current socio-economic discount rate from the Danish Ministry of Finance should be applied. It will often be necessary to extrapolate (effects and) costs to achieve the relevant time horizon. Assumptions in connection with extrapolation should be described and reasoned for.

The secretariat will prepare a catalogue of unit costs and will clarify and exemplify which types of costs can be included.

Implementational and organisational aspects

In addition to outcomes and costs, an evaluation should describe implementational and, often, organisational aspects. This is to identify and describe matters considered essential for successful implementation of the technology or treatment under evaluation.

The analysis of aspects pertaining to implementation and organisation identifies the organisational prerequisites for and consequences of implementation and/or use of the new technology (compared with the existing technology). Some of the organisational elements are included in the context of the cost analysis, where staff resources etc. are valued.
Elements in the analysis could include:

- Training and management:

  Identification of matters such as the need for education and training of relevant staff; the need for changes to the organisational framework for performance of the tasks linked to the technology; changes to work procedures, work tasks and workflows of the relevant staff; and changes pertaining to collaboration, interaction and communication. Furthermore, there should be a description of management and responsibility aspects in relation to the technology or treatment, for example with regard to setting goals for use and deployment, etc.

- Norms and routines:

  Could be about how a technology or treatment can be included in or change existing routines, traditions or norms, and whether it will be perceived as beneficial or disadvantageous by various staff groups. Furthermore, the more social aspects, such as accessibility of the technology for certain subgroups of patients, can also be examined, if relevant.

Sources in the analysis of implementational and organisational matters can be multifarious and will often depend on expert statements from relevant staff or from others, possibly supplemented by literature, document reviews or primary data in the form of interviews or observation, where relevant.
The implementation aspects should be summarised and synthesised with a description of special focus areas, and the validity of transferability of the sources should be discussed.

The secretariat will further outline the implementational/organisational analysis, including sources, summary and how the analysis should be included in the overall assessment.

Cost-effectiveness

An economic evaluation should be carried out as both outcomes and costs have been identified and these must be compared. There are various ways this can be done, depending on the data available.

An economic evaluation is defined as a comparative analysis of two or more alternative options for action, including both costs and effects/consequences. The objective of economic evaluations is to illustrate the relationship between costs and impacts of the (new) health technology compared with the relevant alternative(s). Searching for and finding solid economic evaluations can make other analyses superfluous.

Otherwise, the choice of the type of economic evaluation depends on the objective and on availability of suitable data.

The difference between possible types of economic evaluations is based on how health effects are measured and valued.

- For evaluations of technologies that are either cost-neutral or cost-saving, the objective of the health economic evaluation is to assure the quality and validity of the

analysis submitted. This includes determining whether relevant elements have been included and sufficiently examined, as well as whether assumptions in the analysis are relevant and fair.

- For technologies that are cost-driving, a cost-utility analysis (CUA) should be performed, if possible. This is a cost-effectiveness analysis that uses utility, such as quality-adjusted life years (QALYs) as effect measure.
- Alternatively, a cost-consequence analysis can be carried out, presenting and describing the disaggregated costs and effects.

All economic analyses are subject to uncertainty. The uncertainties in the analysis should therefore always be identified, described, analysed and discussed. It is important that uncertainties are presented systematically to make transparent how the uncertainties affect the cost-effectiveness. This should be investigated through sensitivity analyses.

The economic evaluation should be supplemented with a budget impact analysis estimating the budgetary impact on regional governments.

Economic evaluations of diagnostic tests/technologies differ from evaluations of other health technologies in certain respects. When identifying costs in connection with diagnostics, all costs associated with the technology should be included. This means that, in addition to the costs of the test itself, the analysis should include costs of organisational aspects pertaining to the procedure, additional examinations and follow-ups, as well as any treatment costs.

Economic evaluations of diagnostic tests should also consider the sensitivity and specificity of the technology; the number of positive and negative results (true and false, i.e. positive predictive value (PVV) and negative predictive value (NPV)); as well as the consequences of false positive and false negative results. The potential benefits of better diagnostics include a more timely diagnosis which allows for more timely treatment and, thus, reduced morbidity or mortality. The potential drawbacks are the false positives that could mean a risk of overdiagnosis and, thus, a risk of overtreatment. The evaluation should include such possible effects and assess their impact on other outcomes.

The secretariat will specify the process for validation of submitted analyses of cost-neutral or cost-saving technologies and how to manage uncertainties and budget impact analyses.

4. Overall assessment

This chapter presents the final assessment and synthesis of the results of an evaluation by the expert committee and the relationship between the committee's conclusions and the possible recommendations from the Danish Health Technology Council.

An evaluation ends with an overall assessment by the expert committee, while the Council makes the final decision on a recommendation.

The overall assessment of the expert committee includes the risk class of the technology, the size of the (patient) population, and the rarity of the disease, etc.

Results are summarised and discussed based on the expert committee's expert, clinical, economic, analytical and patient-reported experience and are assessed against a Danish setting. Results are presented in a form that is manageable, precise and easy to understand, and sub-results are weighted and assessed to provide one or more summary conclusions and recommendations. Emphasis should therefore be on achieving the greatest possible transparency about documentation, methodology and the assessment process, so that it is possible to form the best possible basis for any subsequent decision-making process. This will include explicitly highlighting any limitations linked to the results.

The expert committee provides an overall assessment and conclusion about the evaluation to support and inform one of the Council's categories of recommendation:

a) The technology is recommended for use or implementation. In this situation the expert committee assesses:

- That there is sufficient evidence and knowledge to conclude that the technology has at least the same benefits for all or parts of the target group, or for the health care system as a whole, compared with standard practice, and that the costs are lower; or
- That there is sufficient evidence and knowledge to conclude that the technology has benefits for all or parts of the target group, and/or for the health care system as a whole, compared with standard practice, and that the costs are the same; or
- That there is sufficient evidence and knowledge to conclude that the technology has better benefits for all or parts of the target group, and/or for the health care system as a whole, compared with standard practice, and the costs are higher, but the technology is considered cost-effective.

b) The technology is recommended for knowledge building. In this situation the expert committee assesses:

- That there is not sufficient evidence and input from experts and patients to recommend implementing the technology, but that the technology is showing promising results; and/or
- That the treatment regime of which the technology forms part needs a health technology solution, and that more evidence and knowledge should be gathered about such solution.

c) The technology is not recommended. In this situation the expert committee assesses:

- That there is not sufficient evidence and input from experts and patients to justify a recommendation of the technology.
- That the available evidence indicates that the technology examined is inferior to one or more alternative technologies.

For analyses of technology areas, the specific wording of the recommendations will consider that the analysis may have involved assessments and/or comparisons of several competing technologies. However, for the individual technology, the possible recommendations are the same as in connection with evaluations, i.e. the individual technology can either be recommended, recommended for knowledge building, or not recommended.

The secretariat will prepare a template for the expert committee's recommendation to the Council concerning a possible recommendation.