Zorginstituut Nederland

Package advice in practice

Deliberations for arriving at a fair package

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| **Van goede zorg verzekerd** |

Content

A priori

The Health Insurance Act and the Long-Term Care Act determine which care is included in the basic insurance. Together, these two acts form the basic package. Whether care belongs in the basic package is assessed based on four criteria:

Necessity
- is the disease serious enough?
- is the treatment so expensive that patients cannot pay for it themselves?

Effectiveness: is there evidence that the treatment works?
Cost-effectiveness: is the ration between the costs and the benefits of the treatment acceptable:
Feasibility: is including the treatment in the package feasible in practice?

Zorginstituut Nederland advises the Minister of VWS about this.

Though criteria are fixed, the outcome of the process is far from fixed. The process leaves a lot of leeway for consulting medical experts, patients associations and professional associations and parties in health care. This report describes the process of gathering arguments, of assessing and deliberating in order to arrive at a justifiable division of the available funds.

Preface

It is with great pleasure that I present the report “Package advice in practice: deliberations for arriving at a fair package”. This report is the latest in a series of publications in which we explain how we use the package criteria necessity, effectiveness, cost-effectiveness and feasibility in practice. This information is brought together in “Package advice in practice” and we demonstrate how relevant arguments are assessed and considered. We reveal which societal perceptions form the basis of the package criteria.
Package advice cannot be seen separate from its context, and this is what makes advising on the package much more than a mere box-ticking exercise relating to technical information on the most objective criteria possible. We are faced with the task of finding the right balance between what society wants and what society can realise in respect of package compilation, a task that we fulfil by adhering to a meticulous process.
We realise that our advice will not always meet everyone’s approval, but our aim is to ensure that our advice can always be explained and that it was arrived at meticulously.

Arnold Moerkamp,
Chairman of the Executive Board of Zorginstituut Nederland

Summary

The public debate pays a lot of attention to how we can continue to pay for health care in the future. A question that the *Zorginstituut* feels is equally important is whether health care, and the available funding, is shared fairly. After all, all citizens aged eighteen years and older contribute to the basic insurance and it is important that they remain willing to make this contribution. Insight into the evaluation process and the criteria for reimbursing care helps to guarantee this solidarity. *Zorginstituut Nederland* has written this report to provide insight into how this works in practice.

Relevant and fair

This report is a follow-up to the report on Cost-Effectiveness in Practice that the *Zorginstituut* issued in June 2015. In that report we explained why we regard cost-effectiveness as a relevant and fair criterion, though opinions in society differ on this matter. In addition, we explained how the *Zorginstituut* evaluates the cost-effectiveness of care. Unfavourable cost-effectiveness does not automatically result in negative advice, and favourable cost-effectiveness does not always result in positive advice. Whether we accept an unfavourable cost-effectiveness depends on other compelling arguments.

Conflicting values

In this report, the *Zorginstituut* shows which arguments can lead to us advising the Minister to reimburse a therapy or provision that has an unfavourable cost-effectiveness. These arguments can generally be traced back to package criteria, though this is not always the case. Arguments are often specific for a given situation.
This report cites examples illustrating how values can conflict with one another. In such cases it is important to determine which argument carries most weight. The fact that interventions sometimes get included in the basic package and then removed again on numerous occasions shows that such an evaluation may change over time.

Not an automatic process

In other words, arriving at package advice is not an automatic process with a predictable outcome, even though the criteria are known in advance. This is why the process demands so much attention. The *Zorginstituut* follows the principles of the ethnical framework of Daniels and Sabin (Accountability for Reasonableness, often abbreviated to A4R). This means that we make use of a so-called deliberative process, whereby all parties make a contribution, e.g., parties in health care, the *Zorginstituut* and its advisory committees. This interactive process results in us giving the Minister well-balanced advice about whether or not to reimburse care from the basic insurance.

Room for new arguments

Examples are given to show the underlying values of package criteria and other arguments, and how social values can conflict with one another. It is important that the process always allows room for new arguments. It would be impossible to provide an exhaustive summary of all criteria and arguments that can play a role in package advice. This is because new arguments can always emerge. What's more, the importance that society attaches to certain arguments may change over time. The basis of this balancing process is, however, constant: the application of criteria in a process of deliberative and interactive policy.

Introduction

The question about how – together – we can maintain good, accessible and affordable health care in the Netherlands now, and in the future, is high on the political agenda. In political circles the discussion focusses mainly on affordability. This is an important topic, as money can only be spent once. Money spent on health care cannot be spent on other important matters, such as security, education and social security.

Solidarity

The *Zorginstituut* feels that the matter of sharing care and the available funds fairly is equally important. All adults in the Netherlands are obliged to pay towards the basic insurance via a flat-rate and an income-dependent premium, irrespective of whether they take advantage of the insurance. We look upon this solidarity between the old and the young, and between people who are ill and those who are healthy, as a major collective asset. If we want to retain that solidarity, then people must feel that funds are being spent fairly.

A link exists between this solidarity and the available budget. If health care costs are so high that the premiums consume too much of our available income, this puts pressure on solidarity. This is an important reason for keeping an eye on the total expenses.

Fairness

Two factors determine whether people feel that their premiums are being spent fairly.
First, whether they support the criteria for accepting care into the basic package. We call this distributive justice. These criteria are based on values within society. In society, however, we do not always agree on social values and they may even conflict with one another. This is why it is equally important that a basis of support exists for the process whereby package decisions are made. This is known as procedural justice.

Zorginstituut Nederland advises the Minister of Health on which care should be reimbursed collectively. This takes place based on our mission, that all citizens have access to good care. No more and no less than is necessary. In drawing up package advice we make use of so-called package criteria: necessity, effectiveness, cost-effectiveness and feasibility.

Various publications of the *Zorginstituut* explain these criteria and their operationalisation[1]. We explain the package criteria, discuss the requirements that information must fulfil and describe how this information is assessed (the assessment).

This report, however, is about the so-called *appraisal*, in which arguments for and against reimbursement are weighed up to arrive at advice for the Minister.

1 *CVZ (College van Zorgverzekeringen, the predecessor of Zorginstituut Nederland). Package management in practice, part 3. Diemen, 2013. Zorginstituut. Cost-effectiveness in practice. Diemen, 2015. Zorginstituut. Burden of disease in practice. Diemen, 2017 (draft under consultation). Zorginstituut. Assessment of established medical science and medical practice. Diemen, 2015. All available on www.Zorginstituutnederland.nl*

2. Points of departure of the advisory process

The *Zorginstituut* fulfils its package management task within a social climate. Support exists for the evaluation system that has been developed, but not always for the outcome of the process. The fact is that a package evaluation is not a rigid process, with predictable advice as the outcome, even though the criteria are known in advance. This is because package criteria are not value-free. Differences of opinion may even exist about the evaluation of a criterion like effectiveness. For instance, on the matter of which research is needed to demonstrate effectiveness, or the matter of whether the evidence is sufficient to justify reimbursement from collective resources.

Context-sensitive

A role is sometimes played by arguments that are not directly related to a package criterion. Not only criteria but also arguments may conflict with one another. They too are often context-sensitive; in one situation they will be accorded a different weight than in another situation. This is why the process that leads to package advice must be transparent.

Procedural justice demands that all values that could be relevant in arriving at package advice are involved in the process. Choices must be explicitly named and substantiated.
The ethical framework of Daniels and Sabin (Accountability for Reasonableness; often abbreviated to A4R) is a method frequently used for making these choices based on a deliberative process[2]. We define a deliberative process as: arriving at substantiated advice on the desirability of reimbursement by means of logical deliberation and questioning, and confrontation with other opinions and arguments. The advisory process of the *Zorginstituut* is based on this ethical framework.

Deliberative process

A number of points of departure and conditions apply to a deliberative process:

- Relevance: all relevant values are taken into consideration in a decision.
- Publicity: the advice and its substantiation are public.
- Subject to challenge and revision: an appeal can be lodged against advice that is perceived as unreasonable, to solve differences of opinion and to revise advice if more information and evidence becomes available.
- Legislation: the decision-making process is described in regulations in order to be certain that it fulfils the above-described requirements.

The *Zorginstituut* has interpreted these conditions as follows:

- Relevance: the arguments were taken from an evaluation framework with a political basis of support. With some degree of regularity, the *Zorginstituut* presents the evaluation framework and developments therein to the Lower House (the VWS Permanent Parliamentary committee). Various perceptions exist within society, for instance, on the matter of whether costs and cost-effectiveness should be allowed to play a role. Thus, in some cases, this relevance is disputed. These opinions are also included in our final evaluation.
- Publicity: the advice of the *Zorginstituut* and its substantiation are public. This also applies to the deliberations of the Insured Package Advisory Committee (ACP), an important advisor of the *Zorginstituut*. This committee assesses the societal consequences of package advice. Draft advice is also made publicly accessible to parties for the purpose of consultation.

2 *Daniels N, Sabin JE. Setting limits fairly: Can we learn to share medical resources? Oxford: Oxford University Press, 2002*

- The possibility of challenge and revision: various possibilities exist for entering into discussion with the *Zorginstituut* and its committees about the arguments, or to introduce supplementary arguments. The same applies to the Scientific Advisory Board (WAR) which monitors the underlying evidence and advises the *Zorginstituut*. The *Zorginstituut* will revise its opinion when it receives new information or well-substantiated opinions.
- The *Zorginstituut* listens to all parties involved (patients' associations, manufacturers, care-providers, care professionals and health care insurers) and eventually forms an independent decision on the draft advice. This advice is then offered to the Minister of VWS. An appeal against a decision of the Minister can be lodged with the court of appeal.
- Legislation: the task of the *Zorginstituut* as package manager is defined in the Zorgverzekeringswet (Health Insurance Act). The same law and the Explanatory Memorandum state the criteria for admission to the basic insurance. The *Zorginstituut* has described how this is interpreted in various documents.

The *Zorginstituut* is of the opinion that the advisory process fulfils the criteria for procedural justice. Because the basis of support is important, every now and again we assess our advice, both from a substantive perspective and as a process.

3. Design of the advisory process

The advisory process is comprised of steps in which information and arguments are collected and assessed. Many parties play a role here.

3.1. The parties involved

Package advice is drawn up in close collaboration with people inside and outside the *Zorginstituut*. These parties are:

The *Zorginstituut* and its employees: *Zorginstituut* employees draw up advice and coordinate the logistics surrounding advice and its communication. They maintain contact with stakeholders (patients' organisations, care professionals, care-providers, manufacturers and health insurers), prepare reports and meetings, and collect the necessary information. The Executive Board approves the advice.

Package advice committees: The Scientific Advisory Board (WAR) advises the *Zorginstituut* about the scientific evaluation. The Insured Package Advisory Committee (ACP) advises on societal aspects of arguments. These independent committees are comprised of external experts who are authoritative in their field. The statutory basis of the WAR can be found in the regulations of the *Zorginstituut*, that of the ACP in the Health Insurance Act.

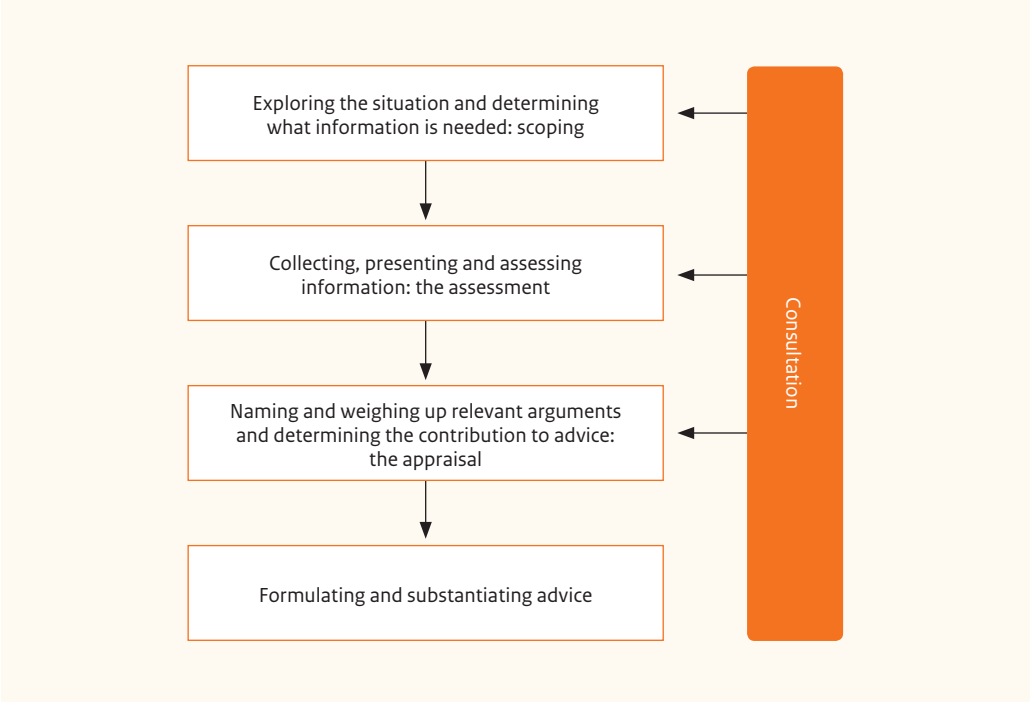
Parties in health care: patients' organisations, care professionals, care-providers, manufacturers and health insurers provide their expertise and experience in various phases of the process. They can ask questions, respond to draft documents and consultation documents and have discussions with the ACP.

3.2. The advisory process

There are four phases to the advisory process.

- Exploring: establishing relevant arguments and the need of information (scoping).
- Collecting, presenting and assessing relevant information in relation to the criteria and other arguments (assessment).
- Naming arguments, determining their role and whether they contribute to positive or negative advice (appraisal).
- Formulating (positive or negative) advice with the support of the arguments.

It can be depicted in the following diagram:



The advice is offered to the Minister of VWS

Explanation of the various steps

Exploring the situation and determining what information is needed: scoping

The advice trajectory starts with scoping, an exploration of the relevant question. This may include a question about domain, e.g. whether care is involved as defined in the Zorgverzekeringswet (Health Insurance Act). Also clarified is which arguments will play a role in the advice. In this way, we quickly establish what information is needed in order to formulate advice. A so-called PICO(T) is drawn up for the scientific assessment. This involves determining the relevant group of patients (P for Patient), the intervention (I for Intervention), comparative treatment (C for Comparator), outcome parameter (O for Outcome) and duration of follow-up (T for Time). *Zorginstituut* employees put the topics to the Insured Package Advisory Committee (ACP) and the Scientific Advisory Board (WAR)[3]. The WAR and the ACP collaborate where common ground exists. For instance, regarding the question as to whether certain effect parameters are sufficiently relevant within society to warrant reimbursement. Sometimes a meeting is organised with stakeholders, so we can ask them what they feel is relevant and what they regard as important considerations within the trajectory. This may take place in writing or in other ways.

Collecting, presenting and assessing information: the assessment

A well-balanced assessment demands sufficient – and reliable – information about the intervention being assessed[4]. It is important that all relevant questions are asked and answered. This is what makes the explorative or scoping phase so important.

3 *For more information on this, see the publication: Zorginstituut. Assessment of Established Medical Science and Medical Practice. Diemen, 2015. Available via www. Zorginstituutnederland.nl.*

4 *To find out which information is collected and which requirement it has to fulfil, see the report "Package Management in Practice 3" and the further elaboration of the package criteria necessity, effectiveness, cost-effectiveness and burden of disease in, respectively "Assessment of Established Medical Science and Medical Practice"; "Cost-effectiveness in Practice" and "burden of disease in practice".*

Together with our European partners in EUnetHTA[5], the *Zorginstituut* has developed the HTA core-model (see framework). This model helps us to be as complete as possible, to present information in a structured manner and to carry out more evaluations in collaboration with other countries. We want to use this model more frequently, e.g., when an evaluation is carried out for several member states or when it involves an intervention involving all nine of the domains mentioned.

EUnetHTA core-model

This basic model describes nine domains.
The model facilitates the exchange of information within Europe. Each country can subsequently use this generic information within its own evaluation framework.
The nine domains are:

1 Health problem and current use of technology
2 Description of the intervention and its characteristics
3 Safety
4 Clinical effectiveness
5 Costs and economic evaluation
6 Ethical analysis
7 Organisational aspects
8 Social aspects
9 Legal aspects

These nine domains display a lot of overlap with our four package criteria.

If necessary, we also collect information about additional arguments that were identified in the scoping phase. We record this information in documents.

Scientific reports are presented to the Scientific Advisory Board, which assesses the scientific substantiation of the criteria effectiveness, cost-effectiveness and burden of disease. In relation to the evidence for clinical effectiveness, the WAR issues a summarising conclusion on:

- The value of the effect
- The size of the effect
- The probability of the effect[6]

Furthermore, the WAR issues a statement on the correctness of the (assumptions for the) calculation of the burden of disease and about uncertainty margins.
After the WAR has assessed the reports, draft versions are sent to the parties involved for comments. In certain cases, the WAR discusses the report anew, before it is approved by the *Zorginstituut*. This completes the assessment phase and the appraisal phase starts. For the sake of clarity, we discuss these phases sequentially, though in reality the dividing line is less strict.

Naming and weighing up relevant arguments: the appraisal

In this phase, the information from the last two steps is translated into arguments. The arguments are weighed up and the contribution of each argument to our advice is determined (positive or negative; strong or not so strong).
These matters are publicly debated within the ACP. A baseline situation is first established (favourable or unfavourable), based on the criteria effectiveness, burden of disease and cost-effectiveness. All other arguments can subsequently influence this baseline situation. This results in positive or negative advice. This is described in more detail in the next section.

5 *This is a European collaboration of HTA organisations*
6 *This is in keeping with the scores used within the GRADE system. For more information, see the report: "Assessment of established medical science and medical practice."*

Criteria and arguments that play a role in the advice may conflict with one another. It is therefore important that the societal debate is structured properly. A useful technique for this is Multi-Criteria Decision Analysis (MCDA). Many versions of MCDA exist, varying from a more mathematical form that allocates fixed weights to criteria, to a more deliberative form.

The *Zorginstituut* uses a deliberative form of MDCA[7]. This not only gives the process a clear structure but also provides room for involving unique circumstances. The criteria, the corresponding evidence and the additional arguments are presented systematically. This allows us to demonstrate on which arguments the parties agree. The discussion can subsequently focus on arguments over which the parties' opinions are divided.

Formulating and substantiating advice
During the public debate, the ACP presents the outline of its advice to the *Zorginstituut*. After the meeting, the ACP elaborates on the formulation and issues its advice to the Executive Board of the *Zorginstituut*. Subsequently, the Executive Board approves the advice for sending to the Minister, having heard the (previous) advice of the WAR and the ACP and the opinions of all parties. The *Zorginstituut* informs the parties what has been done with points they had introduced.

The Minister finally makes a decision and incorporates it, if necessary, in laws and legislation.

Consultation of the parties
Consulting the parties is not included as a separate phase in the process because it is interwoven in the various steps of the process. This enables the parties to contribute during scoping and the evaluation of the information. They can debate with the ACP and, after the discussion within the ACP, there is generally an administrative consultation. Consultations take place according to the procedure that has been agreed between the *Zorginstituut* and the parties.

7 *Bærøe K., *Baltussen R. Legitimate Healthcare Limit Setting in a Real-World Setting: Integrating Accountability for Reasonableness and Multi-Criteria Decision Analysis. Public Health Ethics 2014, 1-14*

4. Criteria, social values and arguments

4.1 An on-going domain-related discussion

The *Zorginstituut*'s Package Management task is specified by law in the Zorgverzekeringswet (Zvw, Health Insurance Act) and the Wet langdurige zorg (Wlz, Long-Term Care Act). The Zvw focuses mainly on curing diseases and on preventing the exacerbation of diseases. The Wlz is to provide vulnerable citizens with long-term care.

Before the *Zorginstituut* assesses a form of care substantively, we need to know whether the insurance is actually intended for that care. This is not always clear; societal discussions are possible. Examples are the treatment of dyslexia and the reimbursement of maternity care, contraceptives and dietary products. In the past, discussions also arose about addiction care and about the treatment of infertility. Another recurring debate is about whether preventive care belongs in the insured package, e.g. vaccinations and prenatal screening.

A question that is increasingly being asked, due to the increasing medicalisation of society, is what actually constitutes insured care and what is simply a part of life, e.g., inconveniences, coping with misfortune and ailments due to old age. And, thus, what should not be covered by health insurance. We will not discuss this further at this point. The dividing line between what should and what should not be covered by health insurance is determined not so much by laws as by what society thinks about the matter.

4.2 Package criteria and conflicting values

The *Zorginstituut* advises whether care belongs in the basic package based on four criteria: necessity, effectiveness, cost-effectiveness and feasibility. These criteria ('Dunning's Funnel') were drawn up in 1991, at the Minister's request, by the Choices in Care Committee8.[8] In general, these criteria do not give rise to much discussion. They do sometimes cause reactions when they are applied to individual interventions. This is why it is important that we keep abreast of perceptions in society about these evaluation criteria, about situations in which they are applied and about the process within which this takes place.

The *Zorginstituut* feels it is important that the available resources are divided as fairly as possible. But what is fair? Economists might reply: the maximum possible health gains for the euros invested. But does this apply to everyone and always? Aiming to realise health gains for the entire population may be at the expense of the health of a few. People may perceive this as unfair. For this reason, other possible goals are:

- reducing inequality of health between people;
- giving precedence to the treatment of certain severe disorders;
- increasing or improving the health of people who need it most.

These goals may conflict with one another and which goal is favoured will often depend on the situation. This requires a societal debate in which all relevant arguments are specified and weighted. The ACP was appointed by law to assess proposed package advice. Societal debate within the ACP concentrates around the four basic questions that correspond with the package criteria necessity, effectiveness, cost-effectiveness and feasibility:

- Is there an important health problem?
- Is there a treatment that can solve this problem?
- Are the effects of the treatment reasonably well-balanced with the costs?
- Are the costs of the treatment beyond the reach of an individual and within the reach of society?

The following is an elaboration of these four questions, whereby we demonstrate that it is not always easy to answer these seemingly simple questions. We sketch the conflicting values that can arise. There is no cut-and-dried answer as to how we deal with conflicting values and other possible additional arguments. A characteristic of a deliberative process as described above is that the arguments are specified and weighted.

8 *Take it or leave it; report of the committee, Choices in health care (Dunning Committee). Rijswijk: Ministry of Welfare, Public Health and Culture, 1991.*

Is there an important health problem?

This question relates to the medical necessity of treating a disorder. In our opinion, entitlement to insured care must be linked to a given severity of the disorder. We can map out this severity of a disorder, e.g. by getting patients to complete questionnaires about the quality of their life. But also by paying attention to how long people live with a given disorder. This means we know how many life-years and how much quality of life people lose as a consequence of a disorder.

Sometimes people's lives are not shortened by a disorder, but they do suffer pain or inconvenience due to their illness. In that case they do not lose life-years, but they do lose quality of life. Life-years and quality of life can be expressed jointly as QALYs (Quality-Adjusted Life-Years), life-years that have been adjusted according to quality of life. One QALY is a life-year in full health. We can determine how many QALYs a patient loses due to a disorder. This is referred to as burden of disease. This burden of disease can be compared with the burden of disease of other disorders. Society feels it is fair that people with a higher burden of disease take precedence over people with a lower burden of disease.

In the autumn of 2017 the *Zorginstituut* will publish the Burden of Disease in Practice report. That report explains which approach to the concept of burden of disease is most fair. Since 2001[9] the *Zorginstituut* has used the so-called proportional shortfall-approach. This method makes no distinction between younger and older people[10]. The ACP wondered whether this approach was still sufficiently in line with current concepts of fairness in society, and decided that it should be reviewed. In the report, we propose a broad presentation of burden of disease data: both qualitative and with numerous calculations that do justice to the different concepts of fairness. We are keeping an eye on the development of new methods, such as the capability-approach. This method is based on the degree to which the functioning of people is limited by a disorder. This type of approach is more suited, for example, to long-term care and mental health care.

Conflicting values

Once we have mapped out burden of disease, the next question is to which consequences it must be linked. Should one give precedence to an intervention that reduces severe burden of disease to moderate burden of disease? Or an intervention that reduces average burden of disease to low burden of disease or even no burden of disease? In the first instance, you are helping people with the highest burden of disease, but in the second case, the health gains are larger.
Another question is whether we should in fact reimburse an intervention for a disorder with a very low burden of disease. It is sometimes argued that people have their own responsibility here. On the other hand, people may decide against treatment if it is not reimbursed. This could cause a disorder to worsen, which may result in higher costs. These higher costs would be at the expense of health insurance.

Is there a treatment that can solve the problem?

This question is about the effectiveness of a treatment, defined by law as 'established medical science and medical practice'. The law states that all care that is reimbursed by health insurance must fulfil this criterion. The *Zorginstituut* feels it is appropriate that only if treatment is really likely to help does society allow people to contribute towards the costs of other people's treatment. How we determine this is elaborated upon in the report *Assessment of Established Medical Science and Medical Practice*[11].

Conflicting values

Clearly, agreement is needed on whether treatment is or is not effective. This is not always easy, because the minimum level of evidence this requires is often lacking. For instance, because a given treatment does work for a number of people, but not for others, without a clear indication in advance of which patients will benefit from the treatment. In that case, the average effect may be deemed too low.

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9 *In that year the Zorginstituut (then still the Sickness Funds Board) published the report "Breadth of the medicines package", in which the criterion burden of disease was used for the first time*

10 *Zorginstituut. Burden of Disease in Practice. Diemen, 2017 (draft in consultation). Available via www.Zorginstituutnederland.nl*

11 *Zorginstituut. Assessment of Established Medical Science and Medical Practice. Diemen, 2015. Available via www.Zorginstituutnederland.nl*

This argument applies in particular when assessing drugs for rare diseases (orphan drugs) and for disorders for which no other treatment exists. In these case, the parties often demand positive advice, even with a low average effect. However, this is not a valid argument if the proposed treatment seems to have little to offer.

The *Zorginstituut* has adopted the position that orphan drugs should be assessed just as non-orphan drugs are, but taking into account that it will be impossible to fulfil some requirements[12]. For instance, because there is only a small group of patients on whom research into the drug can be carried out.

A criticism frequently heard is that the evaluation framework relies too heavily on principles of evidence-based medicine and not enough on patient experience and the experience of professionals in clinical practice. Evidence-based medicine means there must be scientific evidence that care is effective. The *Zorginstituut* feels it is important to involve as many data as possible in the evaluation. However, good research is often lacking. For this reason we have drawn up guidelines on how to cope with lack of evidence or a lower level of evidence (Appropriate Research) when carrying out an evaluation. This shows that positive advice is still possible even when there is less evidence. This is in keeping with the GRADE[13] system that we use when assessing evidence.

The *Zorginstituut* feels that it is fair to stipulate requirements regarding the substantiation of effectiveness, specifically because people who pay health care premiums are contributing towards the costs of treatment. Money that has been spent on treatment that is insufficiently effective can no longer be spent on more effective treatment. Furthermore, patients may experience negative effects which are not offset – or insufficiently – by favourable effects. For the rest, the *Zorginstituut* does include patient experience and experience in clinical practice in its evaluations, as long as these are obtained in a reliable way. A favourable development is the growing amount of research determining which groups of patients (sub-populations) experience most effect, e.g., using predictions based on genotyping for the treatment of tumours.

Are the effects of treatment reasonably well-balanced with the costs?

The idea behind cost-effectiveness is that we want to achieve the greatest possible health gains at the lowest possible costs. If treatment is very expensive and less effective, its cost-effectiveness is un-favourable. A possible consequence of reimbursing care that is not cost-effective – while the budget remains stable – is that other forms of treatment cannot be reimbursed. This so-called crowding out is at the expense of total health gains. Research in England has shown, for example, that mental health care became a victim of reimbursing interventions that were not cost-effective, such as certain expensive drugs[14]. The *Zorginstituut* has commissioned research into which care may have been crowded out as a consequence of reimbursing care that is not cost-effective. The results of this research are expected in December 2017[15].

The matter of cost-effectiveness follows close on the heels of the matter of effectiveness. We examine at what costs health gains are realised. There is also a relationship with the question regarding burden of disease. Where burden of disease is expressed in QALYs lost, the effectiveness of health gains can be expressed in QALYs gained.

Costs per QALY are determined by dividing the costs of an intervention by the effect (expressed in QALYs). We refer to this as the cost-effectiveness or costs per life-year gained. If we divide the difference in the costs of a new treatment compared with the "old" treatment by the difference in the effect of the new treatment compared with the "old" treatment, this gives us a so-called incremental cost-effectiveness ratio or ICER.

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12 Zorginstituut Nederland. Package Management Orphan Drugs. Diemen, 2015. Available via www.Zorginstituutnederland.nl

13 See the report "Assessment of Established Medical Science and Medical Practice".

14 Karl Claxton et al. Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold, February 2015

15 For this research the Zorginstituut commissioned a consortium of Radboud University/Ecorys/Universities of Utrecht and Maastricht

How do we determine whether therapy is cost-effective? To do this we need a framework of reference. In the *Cost-Effectiveness in Practice report*, the *Zorginstituut* defined three classes of reference values (with a range of 10,000 to 80,000 euro/QALY) which vary according to the burden of disease[16]. When the cost-effectiveness for a given burden of disease falls within these classes, one can speak of favourable cost-effectiveness. If it falls outside these ranges, one can speak of unfavourable cost-effectiveness. For the rest, these reference values are not synonymous with the maximum amount a treatment is allowed to cost. If 10 QALYs are gained using a certain treatment on a patient with the highest category burden of disease, then this treatment is allowed to cost, in total (i.e., life-long), 800,000 euro (10 times 80,000) more than the current treatment. If the sum is far higher, then the cost-effectiveness is very unfavourable. This could be because the effect is small (it does not benefit a patient much), or because the price is very high, or both.
According to the evaluation framework, there must be other compelling arguments if this unfavourable cost-effectiveness is to be accepted.
The two examples in section 5 show the type of arguments that can be involved.

Conflicting values
By and large, the dilemmas when assessing effectiveness also apply when assessing cost-effectiveness. Especially when the intervention is expensive and it has a large effect on some patients while on others it has no effect or a negative effect, the ICER is likely to be unfavourable. This can be an incentive to improve the cost-effectiveness, e.g., by applying stricter start–stop criteria for treatment and by negotiating with the manufacturer on the price of an intervention.
If improving the cost-effectiveness proves impossible, then society has a difficult balancing task. Are there compelling arguments for accepting the unfavourable cost-effectiveness and advising that the intervention should nevertheless be reimbursed?

Are the costs of the intervention beyond the reach of the individual but within the reach of society?
This question is about where solidarity begins and where it ends. In principle, citizens are responsible for their own health and for the costs this involves.
People who lack the financial resources can appeal to solidarity. People with lower incomes receive a care allowance to compensate the health care premium.
Statutory entitlements to care apply to everyone irrespective of their income position. Whether a treatment should be reimbursed collectively should therefore depend only on the costs of the intervention, and not on whether everyone could afford these costs. Financial compensation is available, for instance, via municipal or fiscal arrangements, for people who cannot even afford relatively small sums.

When the costs are too high for individuals, the question is whether society should pay them. An important barometer in this respect are the total costs of including an intervention in the insured package. This is referred to as budget impact. Costs of health care can be too high for individuals, but also for society as a whole. In that case, the budget impact (total costs of the treatment times the number of patients who are eligible for it) is too large. The budget impact can rise spectacularly if treatment is too expensive and it is being given to many patients. The impact is smaller if the number of patients is small, even though the treatment does cost a lot of money. For example, in the case of rare diseases.

Conflicting values
Parties often tell us that people in vulnerable positions cannot afford even low costs. They are often confronted with other care costs (accumulation of costs). Sometimes their income is lower due to their poor health. However, costs are often increased if we include relatively cheap forms of treatment in the basic package. This is because a 'guaranteed turnover' is created and there is little competitive incentive. This results in care costs – and thus also the premiums – being increased unnecessarily. However, if we do not reimburse these costs, people may decide against treatment and their symptoms will worsen.

16 *See report "Cost-Effectiveness in Practice"*

This can cause more damage for patients and extra costs for society. This argument also applies to many preventive interventions.

Another claim is that budget impact is limited in relation to an expensive treatment for a small number of patients. This is said to favour reimbursement. But one could also claim that it is unjustifiable to reimburse an expensive treatment for a small group of patients, but not to reimburse it when large numbers are involved. Patients with an orphan disease should not be given precedence above patients with a disorder that is more prevalent, such as cancer or diabetes. This is why, during an evaluation, a role is played not only by budget impact but also by the cost-effectiveness of treatment.

4.3 Other societal arguments

In a deliberative process, all relevant arguments have to be considered. These arguments usually emerge from the evaluation of the package criteria. However, arguments also exist that are not directly related to a package criterion. Such arguments are often specific to a given situation. For instance, they emerge when draft advice does not seem to stroke with current societal perceptions. We illustrate this with two examples.

Example 1: Giving up smoking

In April 2009[17], the *Zorginstituut* published package advice on whether or not to include the Give up smoking (SMR) intervention (a combination of nicotine-replacement drugs and GP guidance). The evaluation of the package criteria revealed, as decisive argument, that the costs of the treatment were so low that these could be borne by the patient. This argument was also reinforced as people save a lot of money if they no longer have to purchase tobacco products.
However, research showed that more people would stop smoking if treatment were to be included in the basic insurance. In the end, the *Zorginstituut* attached greater value to the argument favouring the societal goal of getting as many people as possible to give up smoking than to the 'at one's own expense' argument. For this reason, the *Zorginstituut* advised the Minister of VWS to include SMR in the basic insurance. The Minister adopted this advice.

Example 2: Contraceptive pill for women under 21 years of age

In April 2010[18] the *Zorginstituut* issued advice on whether or not to remove the pill from the basic package. Until then, the pill had been in the package for all women. The deciding argument that emerged from the evaluation of the package criteria was that the costs of the pill were so low that people could pay for it themselves. Even young people with a limited budget. It seemed only natural, therefore, to scrap it entirely.
However, research showed that the number of teenage pregnancies and abortions might rise if the pill were removed from the package. More value was attached to this negative effect than to the 'at one's own expense' argument. The *Zorginstituut* advised that it was best to retain the pill in the package for women up to and including the age of 21 years. The Minister adopted this advice and only scrapped the pill from the basic insurance for women older than 21 years.

These examples show that societal considerations exist that have a correcting effect on other arguments. In the last section we mentioned that society may have other social values alongside – or instead of – maximising health gains.
Examples are:

- combatting inequality of health between people (often the consequence of the unequal distribution of welfare);
- giving precedence to severe diseases that receive a lot of attention in society (e.g., dementia and cancer);
- giving precedence to patients whose need is greatest (e.g. people with rare diseases and/or life-threatening diseases).

17 *CVZ. Package Advice 2010. Publication number 276. Diemen, 2009*
18 *VZ. Package Advice 2010, sub-report, medical devices. Preventing pregnancy and contraception in the Health Insurance Act. Publication number 286. Diemen, 2010.*

The deliberative process must allow room for this type of corrective arguments. However, it is important that this takes place in a consistent manner. Otherwise there is the danger that, following a meticulous consideration, an opportunist argument suddenly causes advice to take an entirely different course. Advice must at all times be meticulously motivated.

It is impossible to provide a list, in advance, of 'other societal arguments'. The examples show that they depend on the situation. They are often related to a package criterion, but naming all arguments properly is more important than being able to categorise them.

Many arguments are introduced by the parties concerned during the scoping phase because they are well-informed about the topic and know current opinions of the parties they represent. For package advice to be accepted, it is important that;
- all relevant arguments are in the picture;
- it is clear how they are weighted in respect of one another;
- it is clear which argument or arguments is/are decisive in arriving at advice and why.

Arguments also exist that may not play a role in our considerations because they contradict laws and legislation, e.g. article 1 of the Constitution (non-discrimination principle). This could apply to[19]:
- Age
- Gender
- Ethnicity
- Sexual preference
- Social-economic status
- Geography
- Lifestyle and high-risk behaviour

For the rest, these criteria can be included when they influence the effectiveness of an intervention. An intervention that turns out to be more effective on women than on men can (and may) lead to a different decision for men than for women.

The following explains the lifestyle and behaviour argument. In the public debate of package advice surrounding, e.g., giving up smoking and the treatment of alcohol addiction, it was argued that treatment should not be reimbursed if it is necessary as a consequence of a person's own unhealthy behaviour. Not only is proving a causal relationship difficult, the question is to what extent the behaviour really is culpable. Does smoking and obesity actually involve a conscious choice, with consequences of which people are aware? And if so, should we also stop reimbursing the treatment of sport injuries, while this is actually desired behaviour?

It is to avoid this type of discussion that the Health Insurance Act (art. 15(2)) stipulates that "the health insurer is not competent to refuse an insured provision in part or in full if the insured person is to blame for the occurrence of the insured risk". This is in fact an exception to article 952 of Book 7 of the Dutch Civil Code, which states that an insurer does not have to pay out if damage is a consequence of the insured client's high-risk behaviour. In this way, legislation has established solidarity between people with a healthy lifestyle and those with an unhealthy lifestyle. This is why the 'own fault argument' has never yet played a role in the *Zorginstituut*'s package advice.

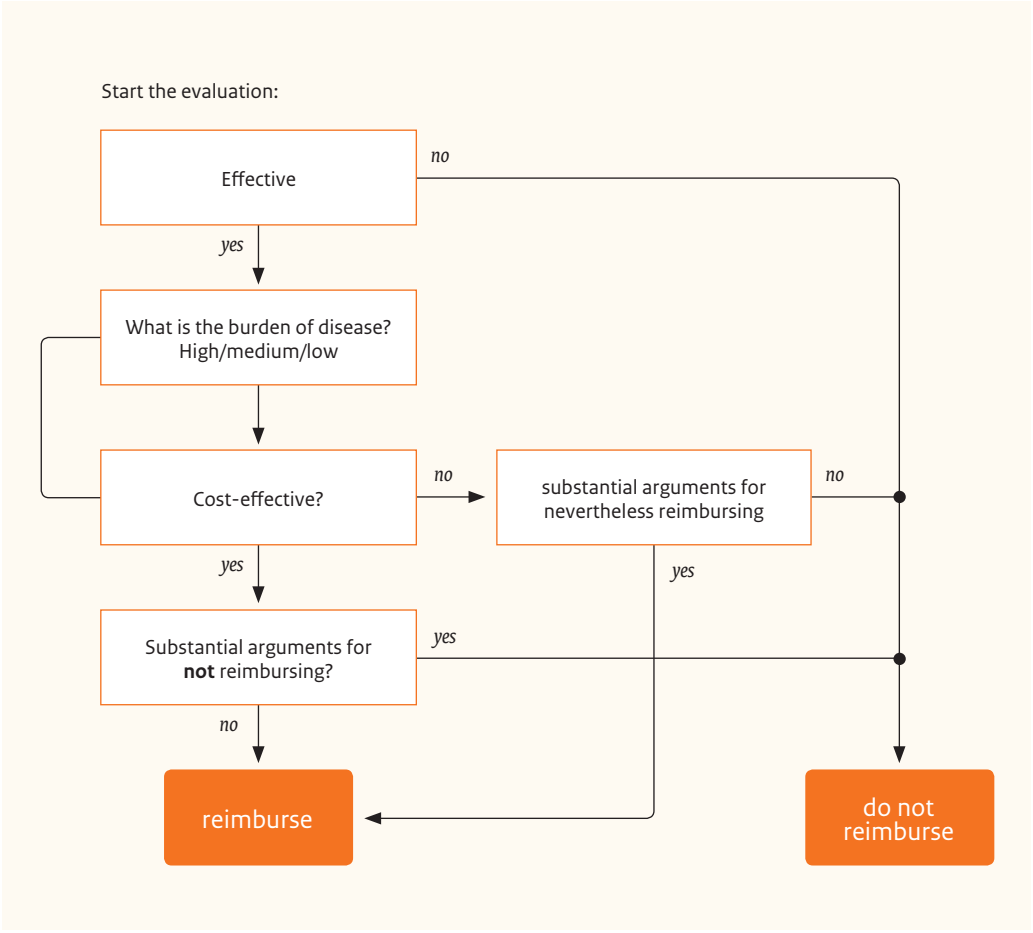
19 Text taken from the report of the Council for Public Health. Equitable and sustainable health care. Publication number 07/04, The Hague. 2007

5. Combination of process and content: weighing up all the arguments

Ever since 'Dunning's Funnel' came into existence, there has been a debate on whether package criteria should be assessed sequentially or simultaneously. In the first case, an evaluation will never reach the next phase if it has a negative score on an earlier question or criterion.
This is referred to as a threshold criterion or 'knock-out criterion'. The criterion 'effectiveness' was given this status by law. The *Zorginstituut* assesses the four package criteria integrally, but a positive outcome on the criterion effectiveness is a condition for progressing further in the evaluation process. Once this threshold has been reached, all information from the evaluation is involved in the further trajectory, i.e., also information about effectiveness. In order to structure an evaluation, we keep to a specific sequence, though no conclusions are as yet formulated in the sense of a decision.

After establishing that an intervention is effective, it is time to assess its cost-effectiveness. If the cost-effectiveness is favourable, then attention is given to whether serious arguments exist for nevertheless issuing negative advice. If the cost-effectiveness is unfavourable, next comes the question of whether serious arguments exist for nevertheless issuing positive advice.

This is illustrated in the following flow diagram.



In the diagram, the blocks ‘compelling arguments for reimbursing’ and ‘compelling arguments for not reimbursing’ form the core of the deliberative process. What type of compelling arguments might these be? Arguments for not reimbursing a cost-effective treatment generally issue from a low burden of disease, low costs or possible undesired consequences of reimbursement (increased demand, increased consumption, substitution), often in combination with one another. The outcome could be that the intervention will have to be funded privately, even though it is an effective and cost-effective intervention.
Arguments for reimbursing treatment that is not cost-effective generally issue from arguments relating to justice, fairness and equality. We discussed this in the previous paragraph.

Effectiveness and cost-effectiveness can themselves be deciding arguments for positive or negative advice. Particularly for expensive drugs we often see that unfavourable cost-effectiveness is often caused by a (very) high price. It may be possible to negotiate a lower price with the manufacturer, and thus improve the cost-effectiveness. In that case the *Zorginstituut* can advise the Minister only to reimburse the drug (or intervention) if the price is reduced to the extent that the cost-effectiveness becomes acceptable.

Below, using two examples, we illustrate that a favourable cost-effectiveness can nevertheless result in negative advice and that an unfavourable cost-effectiveness can result in positive advice.

Example 1: effective and cost-effective, but compelling reasons for non-reimbursement

Vitamins, minerals and paracetamol 1000 mg[20]
In December 2016, the *Zorginstituut* issued package advice after the Minister had asked whether these products still belonged in the insured package based on the criterion necessity.

Information gathered
- The burden of disease varies for a number of disorders for which these products are prescribed. For instance the burden of disease is not very high for osteoporosis (indication vitamin D with calcium), but it is very high when a bone is fractured. This can be avoided by taking vitamin D with calcium.
- All products are effective and cost-effective (because the costs are often low and the effect is good).

This is, thus, a case of favourable cost-effectiveness.
Relevant question: are there compelling reasons for not reimbursing?

Arguments for reimbursing
- Costs are accumulated (excess deductible, multiple disorders)
- The products are often prescribed to vulnerable groups of people (often the elderly).
- The products are medically necessary: non-reimbursement leads to loss of health because people may not take them.
- Proper guidance is lacking when people starting purchasing and using products themselves.

Arguments against reimbursement
- The costs are often low (less than 50 euro per year).
- Many of these products are sold OTC (drug-store), often at even lower costs.
- Reimbursement via insurance makes reimbursement per prescription product unnecessarily expensive.
- Products may be regarded as self-care products and are mainly put to preventative use (personal responsibility).

Weighing up arguments and *Zorginstituut*'s advice
The arguments against reimbursing outweigh the arguments in favour of reimbursement. The most important argument is that some of these products can be freely purchased in a drug-store. Our advice was to remove this group of products from the package.
Although the *Zorginstituut* is of the opinion that other (cheap) products that can only be purchased in a pharmacy could also be removed from the package, little support existed among the stakeholders for this advice. We proposed holding a societal debate on the question of what should be at patients' own expense. Where does solidarity start in relation to health insurance?
Due to the lack of a basis of support, the *Zorginstituut* did not advise removing from the package the group of cheap products that are not sold OTC.

The Minister has not yet decided on this advice; it will be left to the next cabinet.

20 Advice "Do vitamins, minerals and paracetamol 1000 mg (still) belong in the insured package? Diemen, 2016. Available via www.Zorginstituutnederland.nl

Example 2: effective, but not cost-effective, but compelling arguments for reimbursing

Eculizumab for aHUS[21]

The main question with this advice was whether eculizumab should continue to be reimbursed for patients with aHUS. aHUS is a rare disease involving damage to the blood cells and blood vessels. This causes severe damage, particularly to the kidneys.

Information gathered

- The burden of disease is high; people have severe symptoms (highest class).
- The product is effective; people can lead a normal life (almost) with this product. Without treatment this is not possible because they were dependent on blood transfusions and suffered from tiredness.
- The cost-effectiveness was insufficiently substantiated, but in view of the price, very unfavourable.

Relevant question: are there compelling reasons for reimbursing the product?

Arguments for reimbursing

- The product is very effective
- Patients have a poor state of health but with this product they can lead a reasonably normal life.
- The patients and doctors have drawn up their own guidelines, according to which the product is used not on a life-long basis but temporarily. This could result in the costs being much lower. Such an initiative should be honoured.

Arguments against reimbursement

- A very unfavourable cost-effectiveness results in replacement. Reimbursing this treatment is at the expense of reimbursing the treatment of other patients.
- The minister will probably be unable to negotiate a price that will lead to a favourable ICER.

Weighing up arguments and *Zorginstituut*'s advice

The health of patients improves considerably with this product. For this reason, the cost-effectiveness argument has a different weight to that of nivolumab, a product for metastatic lung cancer. This not only improves the health of patients considerably, but extends their lives by 'only' a few more months. Furthermore, the joint initiative of the patients and their doctors, which is not free of risk, has paid off. The advice is therefore: reimburse, but only according to the new protocol. And enter into price negotiations.

The Minister has followed this advice.

21 *Package advice eculizumab (Soliris) for the treatment of aHUS patients. Diemen, 2016. Available via www.Zorginstituutnederland.nl*

6. Conclusion

In this report we have demonstrated the role criteria and arguments play in package advice, which views of fairness play a role and what course the advisory process takes. The core of this process is that all relevant arguments are defined and weighed up in a deliberative process. Many actors are involved in this. The process focuses on allowing them all to contribute their knowledge and opinions. An independent opinion is subsequently given based on societal criteria that have been agreed in advance and on current views of fairness.

A summary of all criteria and arguments that play a role in package advice will never be exhaustive, because new arguments can always arise. The weight given to certain arguments can change over time if society's perceptions of these arguments change. The basis of the evaluation process will remain the same: making use of criteria in a deliberative and interactive process.

Colophon

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