

## SHORT REPORT

# MULTI-CRITERIA DECISION ANALYSIS FOR THE APPRAISAL OF MEDICAL NEEDS: A PILOT STUDY





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## ■ FOREWORD

There are some mantras – politically correct truisms – that are right by definition. In this project we are fortunate, because we combine two of these: need-driven healthcare policy and patient involvement. But to get from the slogan to workable implementation in the field, quite a bit more thought and study is needed. And some time and space for those involved to adopt the new approach.

The *unmet needs* programme of the RIZIV/INAMI [*National Institute for Health and Disability Insurance*] is a first step in that direction. Admittedly, the programme as it exists today is still limited entirely to the area of medicinal products, and the proposals for the list of unmet needs are therefore still largely driven by what the companies have in the pipeline. But you must begin somewhere. And at least these needs are explicitly included in consideration of the priorities.

And the patient's voice must also have a place in this. That seems obvious, but here we must take care not to upset the equilibrium. This involves after all weighing unmet needs against each other. It cannot be the intention to put the decision in the hands of the patients themselves, as that would amount to pitting people with different disorders and needs against each other. Moreover, when priorities in health insurance are involved, the public also has something to say about this.

So a good policy must deal with this carefully. For a number of years the KCE has been making progress in this in close consultation with the RIZIV/INAMI, but also in coordination with the relevant activities of the King Baudouin Foundation. Gradually we have built up insights and a methodology in which the patient *and* the public have a place. Today you have the results of a first pilot test of this methodology before you, and they are encouraging; because beyond the objective of a needs-driven and patient-informed policy, this method also allows complex decisions to be made more transparently and more consistently. This is a small step in the direction of *accountability for reasonableness* that we put forward as a framework a number of years ago. Our country is among the pioneers in this; that should also be said.

Christian LÉONARD  
Deputy general director

Raf MERTENS  
General director



## ■ SYNTHESIS

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## 1. BACKGROUND

### 1.1. Early access to promising medicines for unmet medical needs

Access to innovative medicines for high unmet medical needs has been a concern for policy makers since many decades. On the one hand, health authorities want to give access to promising treatments for patients suffering from severely debilitating or life-threatening health conditions for which no treatment currently exists as soon as possible. These patients are often willing to take a risk by following a treatment that has not received market authorization yet, i.e. before the benefit-risk of the treatment has been assessed based on good clinical research. On the other hand, the authorities want to protect patients by not allowing unreasonably risky or potentially unsafe treatments to the market.

In 2006, two programmes for early access to promising medicines for unmet medical needs were established in Belgium, following the European regulation (EC) 726/2004, Article 83: the medical needs programme and the compassionate use programme. Both had the same objective: to grant quicker access to promising drugs for “a chronic, seriously debilitating or life-threatening condition for which no satisfactory alternative authorized treatment is available”. The difference between the programmes is related to whether the product is already on the market for another indication or not. In both cases, the product has not received marketing authorization (yet) for the indication under consideration.

It is a difficult and delicate balance between ensuring safety and providing early access to treatments for high unmet needs. Health authorities cannot be too lenient because patients trust that what is on the market has been extensively tested and judged safe and beneficial. If this judgment is ongoing or the evidence on the benefit-risk of a product has not been established yet because trials are ongoing, the level of need should be sufficiently high to justify a procedure that deviates from the standard marketing authorization procedure.

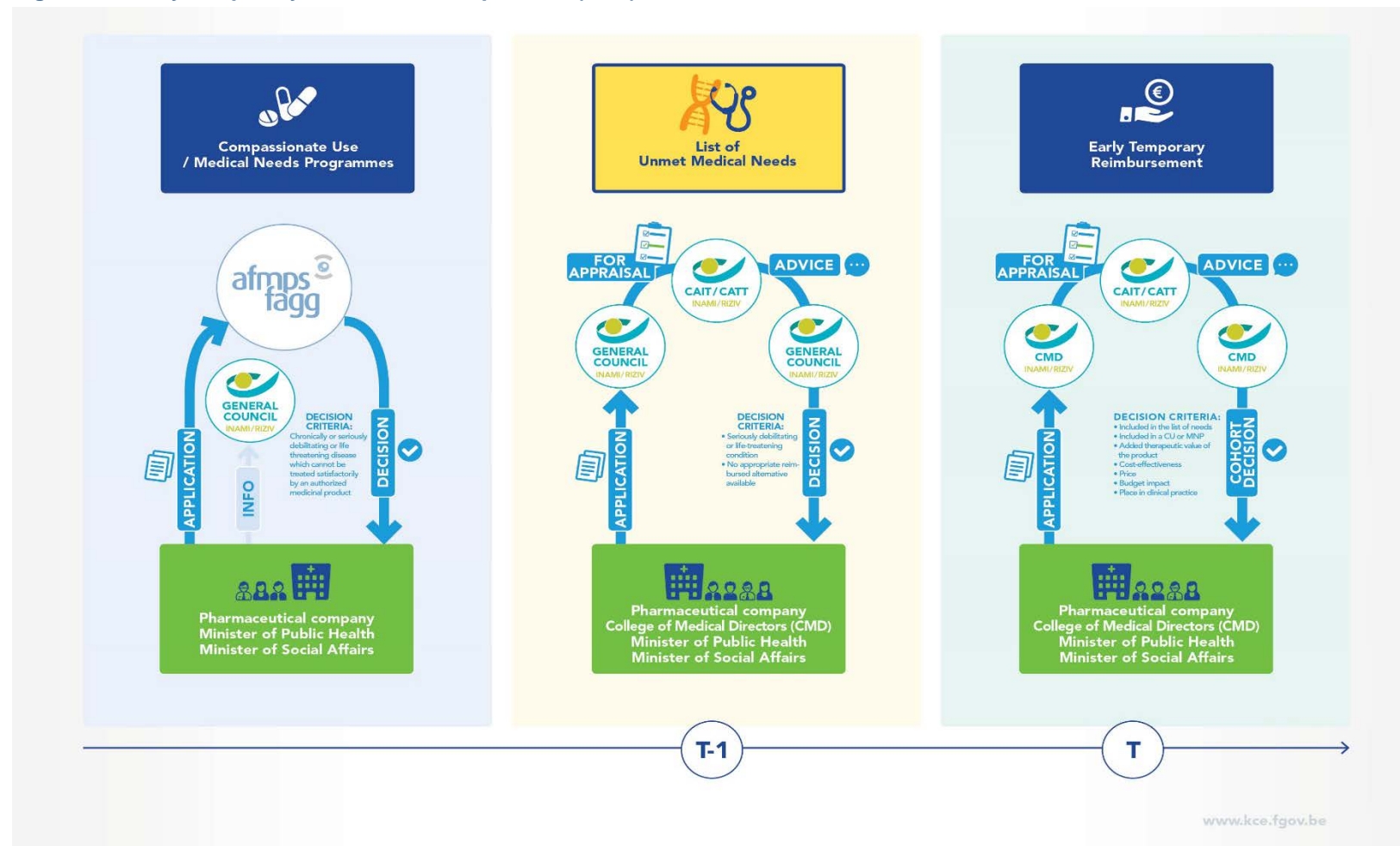
The compassionate use and medical needs programmes regulate *the use* of medicinal products that have not yet received marketing authorization for a particular unmet medical need. They do **not** automatically imply *reimbursement* by the National Institute for Health and Disability Insurance (RIZIV/INAMI). National governments have to ensure the sustainability of the health system and therefore have to consider carefully what can and what cannot be reimbursed. It is clear, though, that access is not only determined by availability on the market but also by reimbursement. Therefore, a law was established in 2014, organising the possibility to grant a temporary compensation to companies providing their promising products that have not received marketing authorization (yet) to patients with unmet medical needs. The decision is taken by the College of Medical Directors (CMD) within the NIHDI for a cohort of patients.

The initiative to submit a request for early temporary reimbursement (ETR) to the CMD can come from a company, the CMD itself or the minister of public health and social affairs. Compared to other countries, the ETR in Belgium is different, as it does not concern a real ‘reimbursement’ but rather a compensation of medication costs. The principle is that the product will not be reimbursed at some established price, but that because of its “early” and “temporary” nature, only a cost compensation will be provided. The actual price setting should happen afterwards, when a reimbursement request is submitted to the Drug Reimbursement Committee.

The process of the cohort decisions is presented in Figure 1



Figure 1 – Early temporary reimbursement process (ETR)



AFMPS / FAGG = Federal Agency for Medicines and Health Products

CMD = College of Medical Directors

MNP = medical needs programme

CAIT / CATT = Commission d'avis en cas d'intervention temporaire pour l'utilisation d'un médicament /

Commissie voor advies in geval van tijdelijke tegemoetkoming voor het gebruik van een geneesmiddel  
CU = compassionate use programme





To be able to judge whether a product is eligible for ETR, a list of unmet medical needs is created by the “Commission for advice on temporary reimbursement of a pharmaceutical product” (CAIT / CATT). This commission was established to advise the CMD about the appropriateness of a cohort decision.

Proposals to put a particular disease or condition on the list of unmet medical needs have to be appraised by the committee members.

Accountability for reasonableness presumes that this is done in a transparent and consistent manner. The appraisal of the medical need in a particular disease involves the consideration of multiple criteria. It is not easy to balance these different criteria in a consistent manner across diseases.

KCE has developed a possible multi-criteria appraisal methodology to create a rank ordered list of needs that satisfies the requirements of transparency and consistency. The development, pre-testing and pilot-testing of this methodology is described in the current report.

## 1.2. The philosophy behind the list of unmet medical needs

The list of unmet medical needs is used in the context of the unmet medical needs programme, which is targeted at promising new drugs for treating patients with severe diseases for which no effective treatment is currently available. Its relevance and importance is, however, larger. The philosophy behind the unmet medical needs list and the unmet medical needs programme is that a needs-driven health system is to be preferred over a supply-driven health system. This is related to the objectives of the health system, which are generally defined as system sustainability, equity and quality of care. A supply-driven system is subject to the interests and objectives of developers, which are not always concurrent with those of the health system. For example, a reason for bringing a new drug on the market may be its high profit potential. It should not necessarily respond to a high need to be highly profitable. In other words, the rationale behind the unmet medical needs programme is that the health system should strive towards meeting the health needs of patients, and give priority to those patients with the highest needs.

Through the list, the domains in healthcare that deserve priority in terms of research and development of (new) treatments are highlighted. Research investments, both public and private, can be more targeted towards those areas with many unmet needs. The solutions for these needs are not necessarily medicinal. Although the unmet medical needs programme now still focusses on medicinal products, we considered this to be a pragmatic decision, in order to field test the programme in one domain with the objective to extend it in the future to other domains.

In this study, we did not bind ourselves to the current application of the unmet medical needs list, but followed the underlying philosophy of the programme and its expected future application. Therefore, the definition of unmet medical need used in this study is larger than the definition used in the unmet medical needs programme (see next paragraph).

## 1.3. Medical versus therapeutic and societal needs

Medical needs are rarely, in developed health care systems, entirely unmet. Even if no curative treatment is available for a given health condition, patients receive symptomatic treatment or supportive care. What happens more often is that specific aspects of a disease are not effectively treated and are considered to be needs by patients. Moreover, need has gradations. The extent to which needs are met may vary, even with an existing treatment.

Therefore, we prefer using the term “therapeutic need” instead of unmet medical need. “Therapeutic need” refers to the need for a better treatment than the treatment currently reimbursed, from the perspective of the patient. By defining need in this way, also conditions which are partially met, either because some issues remain unresolved or the current treatment is only moderately effective, can get into the list of needs, and not only those conditions for which no appropriate treatment is currently available or reimbursed. The current legislation is subject to interpretation. It states that conditions can come on the list if it is a seriously debilitating or life-threatening condition for which no appropriate reimbursed therapy is available. The “appropriateness” of a therapy could be interpreted as its effectiveness, and a condition could be interpreted as any symptom of a disease that is not under control. We apply this broad interpretation, as it is in line with the previously described rationale behind the unmet medical needs programme.



Besides therapeutic need, we also include the concept of societal need. Societal need refers to the need for a better treatment than the currently available treatment for societal reasons. Societal reasons can be, for instance, disease-related public expenditures or contagiousness. It should be noted that within the current legal framework, the CMD will not be able to take a cohort decision based on a high societal need because societal need is not part of the definition of “unmet medical need” in this framework.

## 2. OBJECTIVES OF THE STUDY

The general objective of this study is to develop and assess the applicability of a multi-criteria decision analysis (MCDA) approach for the appraisal and ranking therapeutic and societal needs in healthcare. MCDA is “*a set of methods and approaches to aid decision-making, where decisions are based on more than one criterion, which make explicit the impact on the decision of all the criteria applied and the relative importance attached to them.*”<sup>1</sup>. MCDA can help decision-makers to structure complex decisions that involve multiple criteria. “Decision” can be replaced by appraisal, which is the weighing and balancing of different elements that are relevant for the decision.

An MCDA can take several forms. This study does not assess or analyse the pros and cons of different forms of MCDA. Rather, it develops and assesses the applicability and acceptance of *one* MCDA approach for Belgium. Also, the study does not produce a list of therapeutic and societal needs that can be used in real life. The lists resulting from the pilot study are produced for research purposes only.



### 3. METHODS

#### 3.1. Previous research

The proposed MCDA approach builds upon results of previous KCE research (KCE report 147 on drug reimbursement decision processes<sup>2</sup>, KCE report 195 about the feasibility and acceptability of citizen- and patient participation in health policy<sup>3</sup>, and KCE report 234 on the relative importance of decision criteria according to the general public in Belgium<sup>4</sup>) and research of the King Baudouin Foundation<sup>5</sup>. Each of these studies provided a justification or an input for the current study.

In report 147, we developed a framework to improve the accountability for reasonableness of drug reimbursement decision processes. We explained that multiple criteria should be considered in the appraisal of therapeutic and societal need and that this should happen prior to the assessment and appraisal of a new product.

In report 195, we examined through a qualitative study which models for citizen- and patient involvement in health policy were considered acceptable and feasible for different stakeholders in health policy. The study showed that stakeholders considered involving citizens and patients to be important. They would see them in a consultative role. Citizens would be consulted for more strategic decisions, e.g. about healthcare priorities, whereas patients would be consulted more in the context of operational decisions, e.g. drug reimbursement decisions. Patients would have a role as experts by experience, whereas citizens would play a role as “payers for healthcare and potential patients”. Because it would be impossible to consult citizens about important decisions in health policy, we searched for alternative ways to set up a one-time consultation that could deliver results that would be useful for many decisions, at least for a certain period of time. This was the topic of a next report.

In report 234, we defined, based on a scientific process with expert consultation, the relevant criteria for the appraisal of therapeutic and societal need. We also measured the relative importance according to the Belgian general public of these criteria for the appraisal of therapeutic and societal need as well as for the appraisal of added therapeutic value. We performed a large population survey using discrete choice experiments, with the same criteria for therapeutic and societal need as the ones used in the current

study. The discrete choice experiments resulted in a weight for each criterion.

The general public was hence consulted about the relative importance of decision criteria, as recommended in report 195, and thereby increases the accountability for reasonableness of decision makers who decide on behalf of the public.

The identified criteria and their weights are two essential components of the MCDA that was applied in the current pilot study. They hence provided important inputs for the current study. The next step in the MCDA process is to judge the ‘performance’ of diseases on the relevant criteria and bringing the scores and the weights together to obtain an overall score reflecting the therapeutic or societal need. These judgments are expressed as scores on a pre-determined scale.

#### 3.2. Criteria in the current MCDA approach

The criteria that are considered relevant for the appraisal of needs and their relative weight (on a 0-1 scale) are presented in Table 1. The relative weights express the relative importance of the criterion for judging the therapeutic or societal need. The higher the weight, the more important is the criterion.

**Table 1 – Criteria for defining therapeutic need and societal need and their weights**

Therapeutic need	Weight
• Impact of the condition on <b>quality of life</b> , given current treatments available	0.43
• Impact of the condition on <b>life expectancy</b> , given current treatments available	0.14
• <b>Inconvenience</b> of current treatment	0.43
Societal need	Weight
• Condition-related <b>public expenditures per patient</b>	0.65
• <b>Frequency</b> of the condition (prevalence or incidence)	0.35

Source: Cleemput et al. 2014<sup>4</sup>



The criteria were defined as follows:

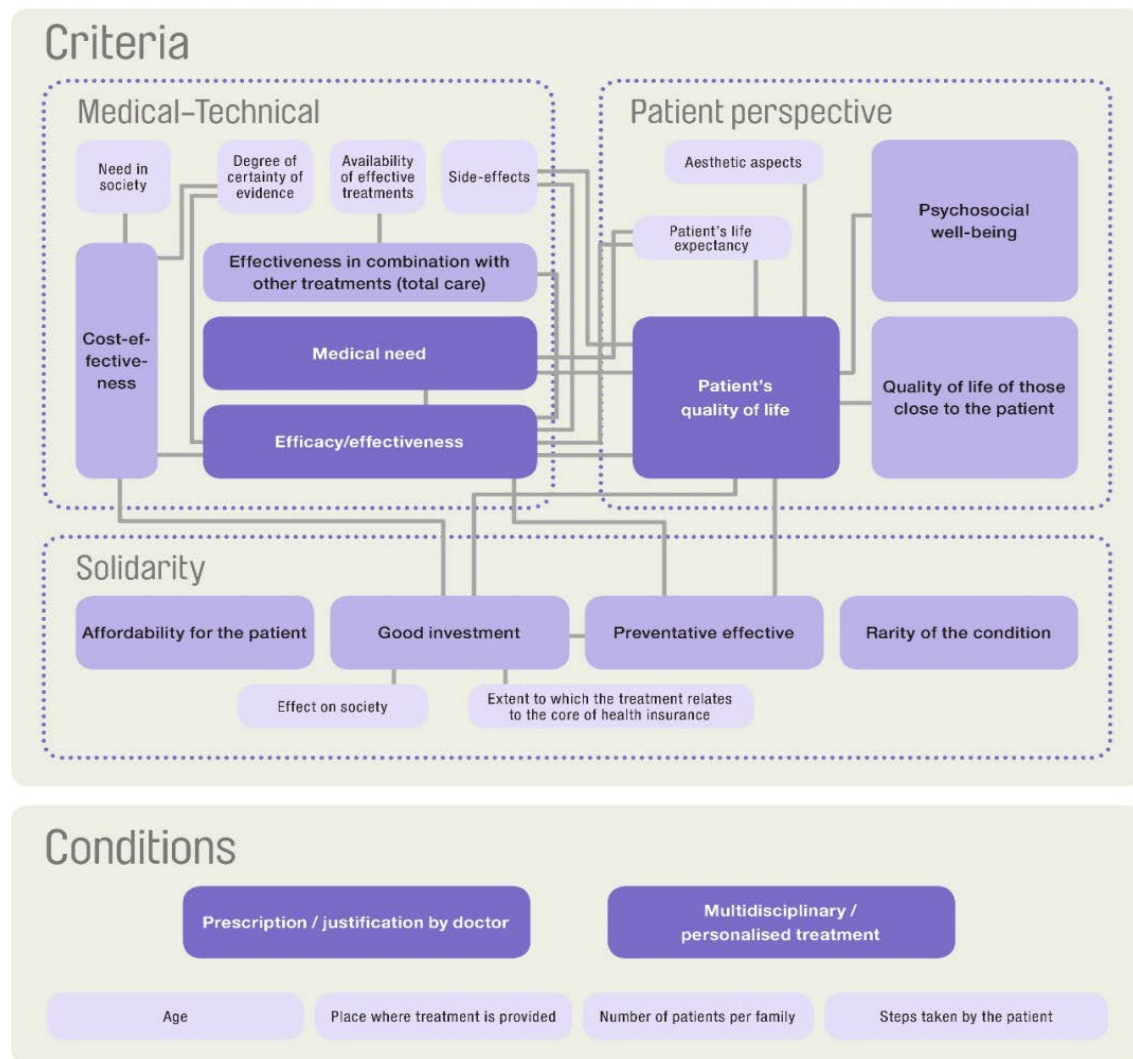
- Impact of the condition on quality of life, given current treatments available refers to the extent to which the disease has an impact on the five dimensions of the EQ-5D, which is a frequently used quality of life instrument in research: mobility, self-care, usual activities, pain/discomfort, anxiety/depression. Mobility refers to the ability to walk about, self-care to the extent to which patients are able to wash and dress self, usual activities to the extent to which they are able to participate in social activities and go to work or school.
- Impact of the condition on life expectancy refers to the extent to the number of years people lose due to their disease, as compared with patients of the same age without the disease.
- Inconvenience of current treatment refers to the inconvenience caused by for instance the frequency of use (e.g. taking a drug once or more times a day), the administration route (e.g. syringes, oral drugs, via perfusion, by the patient him- or herself or by someone else), the place of administration (in hospital, at home, in a doctor's cabinet), the side-effects. It should be noted that inconvenience has a broad meaning. It does not relate only to medication. For example, dialysis treatment is usually considered very inconvenient, be it at home or at the hospital. This type of inconvenience is clearly of a different order than the inconvenience of having to take a pill twice a day instead of once a day. This may explain the high weight of 'inconvenience' in our population survey.
- The frequency of disease refers to the prevalence or, for acute diseases, the incidence of the disease.
- The disease-related public expenditures refer to the total public expenditures per patient with the disease, including health care expenditures and invalidity benefits.

The King Baudouin Foundation (KBF) performed in 2015 citizen consultations about values and criteria that should guide decisions about the reimbursement of health interventions. Additional criteria that are relevant for the appraisal of need, as compared to the ones identified by KCE, emerged from this qualitative research (see Figure 2 for an overview). Quality of life was defined as being the main priority. Psychosocial well-being of patients and the quality of life of those close to the patients (informal caregivers, family and friends) were, however, also considered of very high importance. Respect for the sick person's autonomy and attention for the interests of his or her environment were also considered very important. Personal responsibility for own health should not, according to the participants, be an argument to give lower priority to patients. Nevertheless individual responsibility could be used as a trigger for prevention. Convenience of treatment was not identified as an important criterion by the citizen panel. However, it is a criterion for reimbursement according to the Belgian law.<sup>6</sup>

The criteria identified by the KBF are used as another input in the MCDA approach tested in the current study.



Figure 2 – Criteria and conditions for reimbursement identified by the citizen panel



Source: Raeymaekers, 2015<sup>7</sup>



### 3.3. Phases in a multi-criteria decision analysis

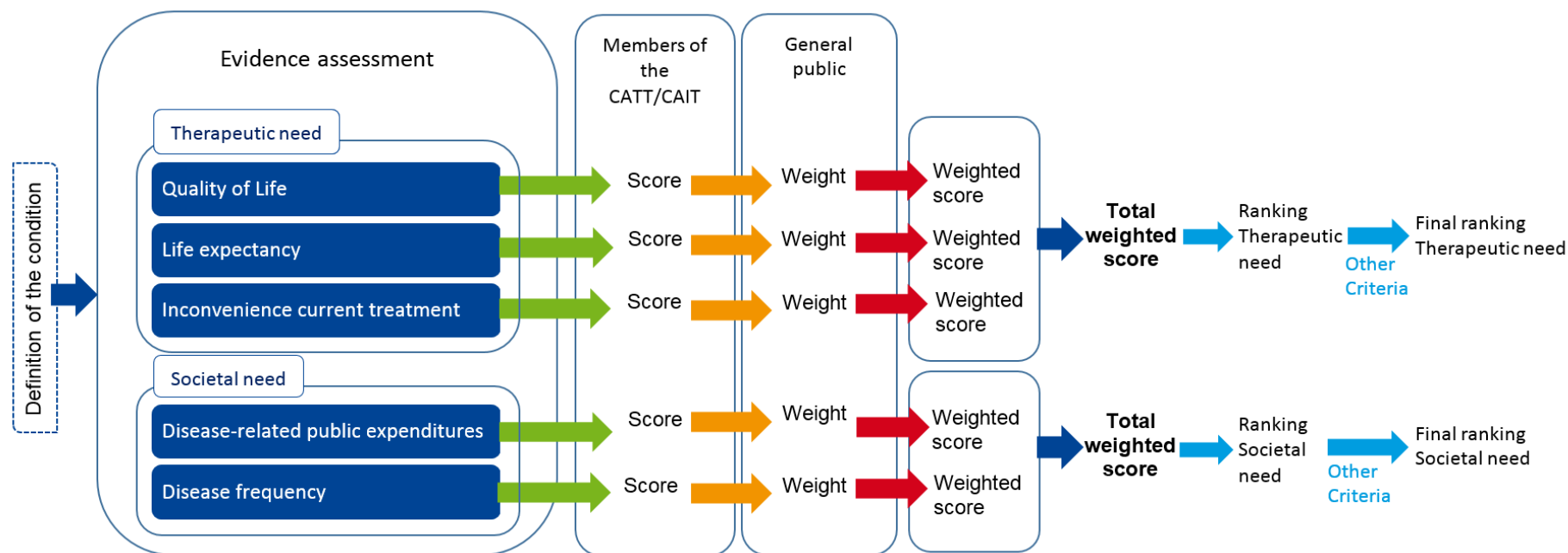
Once the relevant decision criteria and their weights are determined, the following steps need to be taken for a MCDA for ranking needs (Figure 3):

- The diseases or conditions as well as the patient population under consideration needs to be well-defined.
  - For each disease or condition, an evidence report needs to be prepared, assessing the quality and summarizing the evidence with respect to the various relevant appraisal criteria. If evidence is missing, primary data collection should be considered. Especially for the criteria “impact of disease on quality of life” and “inconvenience of current treatment” evidence collected from patients may have an added value.
  - Based on this evidence, the members of the CATT / CAIT assign scores to the criteria on a predefined scale (e.g. from 0 to 3), representing the “performance” of the disease on each of the criteria. For example, a score of 0 for impact of the disease on life expectancy means that the CAIT / CATT member judges that the evidence did not demonstrate an impact of the disease on mortality. Criteria for which there is significant disagreement amongst members, for which there is major uncertainty or for which the evidence is of low quality need to be discussed during a meeting.
- The scores are then weighted, using the criteria weights obtained from the general public (cfr supra).
  - The weighted scores of the criteria relevant for assessing therapeutic need are summed to obtain a total weighted score for the therapeutic in the disease under consideration; similarly, the weighted scores of the criteria relevant for assessing societal need are summed to obtain a total weighted score for the societal need related to that same disease. This appraisal process had to be repeated for every disease under consideration.

The individual total weighted scores for therapeutic, respectively societal need, are then aggregated to obtain an “average” weighted score for therapeutic, respectively societal, need for each disease. Diseases can then be ranked according to their average total weighted score, giving a first idea of the relative level of need in each these diseases.
  - After this process, the commission needs to consider the relevant criteria that have not yet been assessed in the quantitative part of the MCDA: psychosocial well-being, impact of the disease on the quality of life of people close to the patients. The commission should judge in a plenary session the relevance of these additional criteria and justify how they should alter the ranking resulting from the quantitative part of the MCDA, if necessary.



Figure 3 – MCDA process in decision making



It should be clear that the proposed MCDA is not purely quantitative in nature. The discussions about the criteria scores and the deliberation about the rankings are an inherent part of the proposed approach. The crucial feature of MCDA is that it makes qualitative assessments explicit and transparent. Deliberation can be used to define the inputs for MCDA and is not in contradiction with MCDA principles.





### 3.4. Methodological choices

For the development of a practical MCDA tool, a number of methodological choices had to be made. First, a scale for scoring diseases on the different criteria had to be chosen. There is no strong evidence base for choosing such a scale. Based on experiences described in literature and one review, a four-point ordinal scale was chosen (paragraph 3.4.4. in the [scientific report](#)).

Second, a procedure for weighting the scores and aggregating the weighted scores had to be chosen. Several options exist: first aggregating and then weighting, first weighting and then aggregating, taking the mean of the weighted scores or the median, etc. The approach chosen was to weight the individual scores first, sum the individual weighted score for the criteria determining therapeutic need and then calculate the mean total weighted score to obtain an aggregate weighted score for therapeutic need. The same is done for societal need (see paragraph 3.4.5. in the [scientific report](#)).

Third, it had to be decided whether we would merge the aggregated weighted scores of therapeutic need and societal need to obtain one score for need. We decided not to do so, to maintain the clear distinction between needs from the patients' point of view and needs from the societal point of view. A procedure for dealing with the two separate ranking of need was worked out (see paragraph 3.4.8. in the [scientific report](#)).

Fourth, a decision had to be made on how to deal with criteria or values that are not covered by the criteria of the MCDA yet, such as the criteria resulting from the KBF research. Should these also be scores on the same scale as the other criteria and weighted against these other criteria or treated separately in a deliberative process? For reasons explained in paragraph 3.4.7 of the [scientific report](#), it was decided to choose the latter approach.

### 3.5. Summary of the features of the tested MCDA

A summary of the features of the MCDA approach tested in this study is presented in the following table.



**Table 2 – Features of the proposed MCDA approach**

<b>Decision problem / objective of the MCDA</b>	Ranking diseases according to their therapeutic and societal need.
<b>Criteria</b>	<p>Criteria included in the tested MCDA are:</p> <p>For therapeutic need:</p> <ul style="list-style-type: none"><li>• Impact of disease on quality of life, given current treatment</li><li>• Impact of disease on life expectancy, given current treatment</li><li>• Inconvenience of current treatment</li></ul> <p>For societal need:</p> <ul style="list-style-type: none"><li>• Disease-related public expenditures</li><li>• Frequency of the disease (prevalence or incidence)</li></ul> <p>Additional criteria, to be considered qualitatively, after the MCDA results have been produced, are:</p> <ul style="list-style-type: none"><li>• psychosocial well-being / patient frailty</li><li>• impact of the patients' disease on carers' quality of life</li><li>• autonomy</li></ul>
<b>Collecting and presenting evidence</b>	Evidence with respect to each MCDA criterion is collected, critically appraised and summarized for each disease and summarized in "summary of evidence tables". The evidence-base comes from literature and direct patients' or caregivers' input.
<b>Scoring criteria</b>	<p>A labelled 4-point ordinal scale is used for individual scoring the performance of a disease on each of the criteria.</p> <p>Criteria with a large variation in scores between individuals are discussed. During the discussion, participants can justify their score. After the discussion, a second round of scoring is performed. The adjusted scores are used in further analyses.</p>
<b>Weighting of scores</b>	The individual scores are weighted by the weights assigned to the criteria by general public. Still on the individual respondent's level the weighted scores of the criteria defining therapeutic need, respectively societal need, are summed. This gives an individual total weighted score per disease for therapeutic, respectively societal, need.
<b>Aggregation and preliminary ranking</b>	The mean of the individual total weighted scores for therapeutic and societal need are calculated for each disease. These aggregated scores allow the creation of a preliminary ranking for therapeutic and societal need.
<b>Deliberation on final ranking</b>	The CAIT / CATT will have to agree on the final ranking. At this stage, additional criteria, not yet included in the MCDA, might need to be discussed. If rankings have to change based on these discussions, they need to be justified, using the arguments related to the additional criteria emerging from the research of the KBF.



A flowchart presentation is provided in Figure 4

Figure 4 – Flowchart of MCDA process





### 3.6. Test of the chosen MCDA approach

The MCDA approach described above was first pre-tested in 11 experts from KCE with a medical background. Eight diseases were described by means of 5 summary-of-evidence tables per disease (one summary-of-evidence table per criterion). The selected diseases were: invasive meningococcal disease, major depression, severe heart failure, refractive errors, Amyotrophic Lateral Sclerosis (ALS), mesothelioma, Alzheimer's disease, deep mixed partial thickness burns of the skin in children, representing a good balance between mental and physical diseases, rare and frequent diseases, diseases causing sudden death and diseases not causing sudden death. Evidence tables were based on previous KCE reports or submissions made by the pharmaceutical industry to the CAIT / CATT.

For each criterion a 4-point scale was presented underneath the evidence tables, with criterion-specific labels. The panel of pre-testers was asked to assign scores to all criteria for every disease. The scoring exercise was followed by two meetings: one to discuss the methodological aspects, one to discuss the criteria with large variation across individuals and the ranking. Based on the feedback of the pre-testers, adjustments were made to the content of the evidence tables and labels of the scoring scales. Also a vade mecum was added to the pilot test package following the feedback of the pre-testers to clarify difficult concepts used in the evidence tables.

The pilot test was run in 13 members of the CAIT / CATT. A first meeting was organized to explain the MCDA approach and the assignment.

For the pilot test, the feasibility of an approach to collect data directly from patients, their representatives or caregivers to complete the evidence tables for aspects related to the impact of the disease on patients' and caregivers' quality of life and the inconvenience of current treatment, was tested for Alzheimer's disease and for burns.

The scoring was done in LimeSurvey. Room for making written comments was provided. Participants were invited to a second meeting to discuss the criteria with large variation in scores, the final ranking and the overall process and methodology. Criterion scores were discussed as soon as at least three different scores were given by the group of participants.

For example, if for a particular criterion 8 respondents give a score of 3 (high impact), 4 respondents give a score of 2 (moderate impact) and one respondent gives a score of 1 (some impact). The participants got the opportunity to change their score after the discussion during the meeting. For practical reasons, the impact of changes in scores on the variation in scores and the ranking of the diseases could only be examined after the meeting.

Of the 13 members who participated in the pilot test, only 6 could be present on the second meeting, which was postponed due to unforeseen circumstances (terrorist attacks in Brussels). This reduced our ability to measure the impact of the discussion on the variation in scores and the ranking.



## 4. RESULTS

### 4.1. Methodological issues raised by the members of the CAIT / CATT

The following methodological issues were raised during the second meeting:

- It is difficult to give one overall score for each criterion for the diseases with both a life-threatening acute phase and a chronic phase with possible sequelae such as invasive meningococcal disease. The evidence provided encompasses both phases and some trade-off must be made between the seriousness of a bad outcome in the acute phase and the severity of possible sequelae, both occurring only in a subgroup of patients.
- It is difficult to appraise the quality of the evidence provided. Mostly, study results are presented as ranges rather than as exact figures. This is not surprising, but renders the scoring more difficult. The suggestion of KCE to involve an independent expert to make a critical assessment of the submitted evidence was considered useful.
- The role of patients and patient organisations should be worked out because it is felt that the appraisal by the committee members may be biased by personal experiences (or absence thereof) with the conditions under consideration. Involvement of patients in the process may improve all committee members' understanding of the impact of a disease. This should happen in a scientifically valid way, e.g. through robust qualitative research.
- The 4 level scale was considered insufficient for some disease-criteria combinations.
- The definition of "inconvenience of current treatment" needs to be made very clear, as it is expected that the evaluation of "impact of the disease on quality of life" will influence the score for inconvenience. Although definitions were provided at the front page of the pilot package, we can conclude from this feedback that it is important to repeat the definitions on the pages relating to the criteria to allow the committee members to get used to the definitions.

- The evidence tables should avoid suggestive language at all times. For example, statements like "patients support the treatment generally well" should be avoided.

### 4.2. Discussion about the criteria scores

In total, 19 criteria out of 40 scored over all diseases, showed a 'large' variation, as defined above (see full report paragraph 4.2.4. for a graphical presentation of the response frequencies per criterion per disease).

On eleven occasions, only one respondent was 'responsible' for there being three different scores within the group. For example, for the frequency of major depression, 12 respondents gave a score of 3 and one respondent gave a score of 1. The committee members did not consider this to be problematic and were not in favour of trying to achieve a consensus score or more aligned scores. They concluded that these differences are legitimate and should not be discussed.

However, for some criteria there was clear disagreement between the respondents. For example, in ALS, the entire scoring scale was used: not inconvenient (2), somewhat inconvenient (5), highly inconvenient (4) and extremely inconvenient (2).

Three criteria were discussed in more detail. Eventually, only two respondents changed one of their scores. The ranking of the diseases for both therapeutic need and societal need were not impacted by these changes.

The discussions revealed two causes of large variation in scoring:

- Respondents give different implicit weights to different aspects of treatment when appraising the inconvenience of treatment or of quality of life when appraising the impact of a disease on quality of life. For example, ventilation of ALS patients at an advanced stage of their disease may get a high weight for some respondents when assessing the inconvenience of ALS treatment, even if the other aspects of treatment (medication with no adverse effects) may not be considered very inconvenient. Also when respondents score the impact of the disease on quality of life, where the evidence is highly variable, different implicit weights are given by the respondents to different aspects of quality of life. For example, if amputation of a limb is a possible outcome of meningococcal infection, a respondent can give a high weight to this



outcome, even if it only occurs in a small proportion of the patients initially infected, and hence assign a high score to impact on quality of life.

- Respondents interpret the criteria differently, despite the definitions provided in the handouts and vademecum. This demonstrates the importance of the repetition of these definitions during the discussion after the individual scoring. Also repeating the definitions on the scoring sheets might prove to be useful. Efforts should be made to establish unambiguous definitions and to give examples. Some aspects of interpretation will never be resolved by a written definition, however, as also this definition needs to be interpreted by the respondents.

From the discussion we conclude that it is important to have a discussion on the criteria for which there is large variation in scores; not to reach a consensus score or change the implicit weights given to sub-criteria of specific criteria but to ensure that all respondents have interpreted the meaning of the criteria correctly. Variation due to different implicit weighing can be considered as legitimate variation, while variation due to differences in interpretation of the criteria cannot.

### 4.3. Discussion about the rankings

Both the ranking of therapeutic needs and the ranking of societal needs made sense according to the committee members present at the second meeting. The distinction made between therapeutic and societal need was perceived as particularly useful. Examples were mentioned where societal need was low and the therapeutic need high, as well as examples where societal need was high and therapeutic need was low.

The ranking of therapeutic needs is presented in Table 3. The use of the median weighted scores versus the mean weighted scores for setting up the ranking did not change the ranking of diseases much. Only heart failure and depression were switched, but their scores were rather close.

**Table 3 – Ranking of therapeutic needs in pilot study before discussion**

Rank	Disease	Median weighted score	Disease	Mean weighted score
1	Mesothelioma	2,57	Mesothelioma	2,46
2	Burns in children	2,29	Burns in children	2,42
3	ALS	2,14	ALS	2,26
4	Meningococcal infection	2,00	Meningococcal infection	1,90
5	Alzheimer's disease	1,86	Alzheimer's disease	1,69
6	Heart Failure	1,57	Depression	1,57
7	Depression	1,43	Heart Failure	1,52
8	Refractive errors	0,86	Refractive errors	0,75

Referring to the results of the citizens labs of the KBF, one participant noted that for the chronic conditions the impact of the disease on the quality of life of patients' environment (family, caregivers, friends) can be higher because of the longer duration of the disease. This would be an argument to put Alzheimer's disease higher on the list. Ironically, this impact cannot be an argument for severe life-threatening diseases (e.g. mesothelioma), because the impact on the patient's environment is high for a relatively short period of time while it remains high for several years in chronic deteriorating conditions.

The ranking of societal need is presented in Table 4.

**Table 4 – Ranking of societal needs in pilot study before discussion**

Rank	Disease	Median weighted score	Disease	Mean weighted score
1	Alzheimer's disease	2,35	Alzheimer's disease	2,16
2	Major Depression (shared 1 <sup>st</sup> rank)	2,35	Major Depression	2,10
3	Heart failure	1,35	Burns in children	1,56
4	Burns in children	1,30	Heart failure	1,43
5	ALS (shared 4 <sup>th</sup> rank)	1,30	Refractive errors	1,30
6	Mesothelioma (shared 4 <sup>th</sup> rank)	1,30	ALS	1,25
7	Refractive errors	1,05	Mesothelioma	1,23
8	Meningococcal infection	0,65	Meningococcal infection	0,80

Because of the small number of criteria used to create the list of societal needs, more ties are observed when the median weighted score is used to establish the ranking than when the mean is used.

## 5. DISCUSSION

### 5.1. Reflections on the legal framework for unmet medical needs

There is an anomaly in the law in that the budget estimate is based on a list of unmet medical needs, while the treatments for those needs have, in theory, not been defined yet. Moreover, the treatments seem to be limited to pharmaceutical treatments. It is therefore assumed that the law intends to define the list of pharmaceutical treatments meeting an unmet need, rather than a list of needs as such. This is in contrast with the spirit of a demand-driven, in contrast to a supply-driven system. If the healthcare system is to become more demand driven, i.e. driven by the real needs rather than by the new interventions launched on the market, it is necessary to define a list of unmet medical needs independent of the interventions that are in the pipeline. Besides the stakeholders currently allowed to submit proposals, also patients, healthcare providers and other professionals should be allowed to propose the inclusion of conditions in the list of unmet medical needs.

The focus on conditions rather than on interventions under development implies, however, the impossibility to estimate beforehand the required budget for next year's cohort decisions. This does not mean that it is not possible to define a budget for innovations coming to the market, independent of what is already in the pipeline. This could be pharmaceutical innovations but equally so surgical innovations, organisational innovations, (supportive) care innovations, etc. There is no reason to limit this budget to pharmaceutical interventions only.

It should be noted that the needs of patients often cannot be met by new pharmaceutical treatments. The needs are often on a different level. For instance, the conclusion of the citizen labs organised by the King Baudouin Foundation was that citizens value psychosocial well-being and quality of life of the patient's environment more highly than life expectancy.





## 5.2. Medical needs programmes versus unmet medical needs program

The law of 7 February 2014 and the Royal Decree of 12 May 2014 consistently use the term “unmet medical needs”, which is defined as a pharmaceutical product for the treatment of a severe or life threatening condition for which **no reimbursed alternative** treatment is available. In the regulation of the European Commission (EC 726/2004), used by the FAMHP for judging the eligibility of a product for the compassionate use or medical needs programme, the definition of an unmet need is, however, more restrictive: it only refers to chronically or seriously debilitating diseases or diseases considered to be life threatening and that cannot be treated satisfactorily **by an authorised medicinal product**.

This implies that the indication for which a product that has received approval from the FAMHP for a medical needs programme does not necessarily have to figure high on the list of unmet medical needs. If the indication under consideration can be managed satisfactory by a non-medical treatment, that indication can be judged as a low medical need. This is legitimate and should not be regarded as problematic.

## 5.3. Validity of the current study

This study tested one specific MCDA approach. Other MCDA approaches are possible (e.g. discrete choice experiments), and other choices could have been made within the approach applied in this study (e.g. other techniques or populations for determining criteria weights, other scoring scales etc.). The conclusions of this report are only applicable for the MCDA approach presented. However, the conclusion that a MCDA approach is acceptable to decision making bodies is valuable in general. Moreover, it is important to emphasise the **merit of any MCDA system is that it provides an approach that encourages transparency and an explicit accounting of the judgments involved**. It is important to present the evidence with a sufficient level of detail, to allow for a fully evidence-based appraisal. This means also that the knowledge about a disease and its current treatment amongst the decision makers needs to be brought to the same level and hence also attention should be given to a good description of the disease and its current management options. The appraisal of evidence on the impact of a disease of several criteria is a subjective process. Variations in

scores may be legitimate. MCDA is not going to resolve disagreements between decision makers in their appraisals of a problem. MCDA is not purely a quantitative exercise.

The discussions about criteria with a large variation in scores between respondents and the deliberation about the intermediate ranking (based on the quantitative part of the MCDA) are inherent to the proposed approach.

Several countries are using MCDA in decision making processes (Colombia, Italy (Lombardy region), Spain), but none of them have used this approach to rank needs. MCDA is most often suggested in the context of coverage decisions. Severity of disease or medical need is, in these MCDAs, considered to be a criterion within the analysis. We argue that needs and disease severity are also multidimensional and are independent of the new treatment being considered for reimbursement. Therefore, they should therefore be considered separately from the treatment-related criteria.

## 5.4. Dealing with two lists of needs

The MCDA approach tested in this study gives rise to two rankings: one for therapeutic need, one for societal need. The proposed MCDA model does not aggregate the median total weighted scores of therapeutic and societal need to obtain one overall score or ranking for need. One reason was lack of evidence or data regarding the relative importance of therapeutic (individual) needs and societal needs. There was thus no scientifically valid way to combine the two types of needs.

The advantage of keeping the distinction between the societal and patient perspective, however, is that it remains clearer for future cohort decisions on which aspects any new intervention should show an improvement to meet the actual need: if a new intervention is developed for a need that is high on the societal needs list, it should either reduce the frequency of the disease (i.e. be curative) or reduce the public expenditures per patient. If both perspectives are merged by aggregating the weighted scores, for instance, the risk that new interventions are accepted for cohort compensation for the wrong reasons, increases (e.g. the target indication is high on the list because the prevalence is high, but the intervention only offers added benefit in terms of quality of life). By keeping them separate, it will be easier for the commission to keep focus on the criteria that ought to



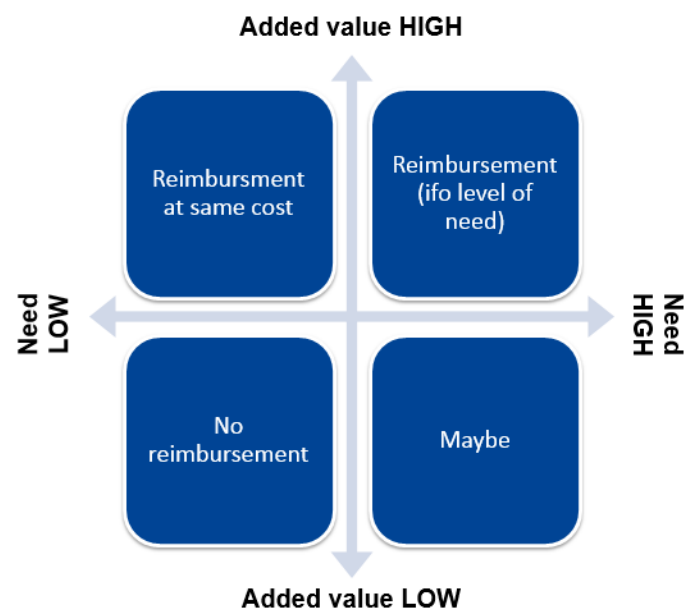
be improved by the new intervention asking for compensation in the context of the unmet medical needs procedure.

It is clear, for instance, that the overall need will be judged higher if both therapeutic and societal need have a high total weighted score, and the overall need will be judged lower if the total weighted score for one of the types of need is low.

Future research could help in finding ways to combine the two concepts and perspectives of needs.

In Figure 5, representing the decision framework, this will translate into a higher or lower value on the X-axis, but if either therapeutic or societal need is high, always at the right side of the origin.

**Figure 5 – Decision framework for cohort decisions**



### 5.5. Practical tools to support the implementation of the MCDA approach

To facilitate the future application of the MCDA presented in this study by the CAIT / CATT for the appraisal of needs, we developed a number of new tools and recommend the use of a number of existing tools. These can be found on the web-site of KCE.

- A tool for assessing and reporting the quality of evidence regarding a criterion
- A template for summarizing by-criterion-evidence for each disease (which can serve as a submission template for the unmet medical needs list)
- A template for collecting additional written information from external experts, including patients or patient groups, developed by the HTAi Interest Group on Patient and Citizen Involvement in HTA.
- A demo version of a practical spreadsheet for calculating the weighted scores and aggregating the individual weighted scores, presenting also the rank order of diseases in terms of therapeutic need and societal need.





## ■ RECOMMENDATIONS<sup>a</sup>

### TO THE BELGIAN LEGISLATOR

- To move from a supply-driven health care system to a real needs-driven health care system, by creating a list of unmet medical needs that is independent of what is in the pharmaceutical industry's pipeline and by
  - expanding the list of stakeholders who can submit proposals for inclusion on the unmet medical needs list to patients, informal caregivers, healthcare providers and other professionals. Exploration of how to organise this is needed,
  - not earmarking budgets for innovative medicinal treatments but allow other types of innovations in the healthcare sector, in order to really respond to the needs of patients. This requires a modification of the regulation for the unmet medical needs programme, which now only allows cohort decisions for pharmaceuticals.

### TO THE BELGIAN REPRESENTATIVES IN THE EUROPEAN LEGISLATIVE INSTANCES

- To define “medical needs” in the context of compassionate use as needs of patients with seriously debilitating or life-threatening conditions for which no effective alternatives exist, including non-medicinal alternatives

### TO THE NATIONAL INSTITUTE OF HEALTH AND DISABILITY INSURANCE (RIZIV / INAMI)

- To add, besides therapeutic need, the concept of societal needs in the definition of “unmet medical needs” but assess them separately.
- Create the limitative list of unmet needs that is needed for the allocation of the budget of the unmet medical needs programme in two phases: first create a ranking of unmet needs, and then determine to which of the highest ranked diseases public resources could be spent in the context of the unmet medical needs programme.
- To implement an independent assessment of the quality of the evidence submitted by stakeholders. A quality assessment tool is provided on the web-site of KCE
- To complete the evidence tables with information collected directly from patients or patient organisations regarding the impact of the disease on quality of life and the inconvenience of current treatment. Patient umbrella organisations can help to facilitate the contacts with individual patient organisations.

### TO THE CAIT / CATT

<sup>a</sup> The KCE has sole responsibility for the recommendations.



- To request the use of the templates for by-criterion summary of evidence tables for the submission of proposals for the unmet medical needs list.
- To use a multi-criteria decision analysis approach to rank therapeutic and societal needs, taking preferences of the general public into account.
- To use the tools made available by KCE on its web-site to implement the multi-criteria decision approach.
- To repeat on a regular basis (i.e. during each appraisal round) the definitions of the criteria to ensure they are interpreted in the same way by all voting commission members.
- To discuss criteria with large variability in scoring to make sure all committee members have interpreted the criteria in the same way.



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