Multi-Criteria Decision Analysis in Healthcare

Its usefulness and limitations for decision making
Multi-Criteria Decision Analysis in Healthcare

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ABREVIATIONS

6MWT 6 Minutes Walk Test
AHRQ Agency for Healthcare Research and Quality
ASCO American Society of Clinical Oncology
AVF Advanced Value Framework
BRAT Benefit-Risk Action Team
CADTH Canadian Agency for Drugs and Technologies for Health
CDC Center for Disease Control and prevention
CHAQ Child Health Assessment Questionnaire
COMP Committee for Orphan Medicinal Products
COPD Chronic Obstructive Pulmonary Disease
DALY Disability-Adjusted Life Year
EE Economic Evaluation
EMA European Medicines Agency
EU European Union
EUnetHTA European network for HTA
EVIDEM Evidence and Value: Impact on Decision-Making
FEV Forced Expiratory Volume
FVC Forced Vital Capacity
G-BA Gemeinsame Bundesausschuss
HIV Human Immunodeficiency Virus
HTA Health Technology Assessment
IC Inhaled Corticosteroids
ICC Intraclass Correlation Index
ICER Incremental Cost-Effectiveness Ratio
ICVR Incremental Cost-Value Ratio
iFOBT Immunochemical Fecal Occult Blood Test
IHME Institute for Health Metrics and Evaluation
IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
ISPOR International Society for Pharmacoeconomics and Outcomes Research
KCE Belgian health care knowledge centre
LABA Long-Acting β2 Agonist
LAMA Long-Acting Muscarinic Antagonist
MAUT Multi-Attribute Utility Theory
MAVT Multi-Attribute Value Theory
MCDA Multi-Criteria Decision Analysis
MEA Managed Entry Agreements
MPS Mucopolysaccharidosis
MRP Medication-Related Problems
mu Monetary units
NICE National Institute for Health and Clinical Excellence
OD Orphan Drugs
OECD Organisation for Economic Co-operation and Development
PASFTAC Programa d’Avaluació, Seguiment i Finançament dels Tractaments d’Alta Complexitat
PBAC Pharmaceutical Benefits Advisory Committee
PBMA Programme Budgeting and Marginal Analysis
PDA Personal Development Analysis
PRO Patient-Reported Outcomes
QALY Quality-Adjusted Life-Years
RD Rare Diseases
RSA Risk-Sharing Agreement
SD Standart Deviation
SET Substitute Enzyme Treatment
TPR Therapeutic Positioning Reports
USA United States of America
WHO World Health Organization
I am very pleased to preface this book about multi-criteria decision analysis in healthcare, and I feel sure that it will become a basic reference in our field. Top-level experts in health economics in Spain have contributed their academic, clinical or management vision, giving shape to this work. The document is conceived as an interesting combination between a manual and a reference book. This is what enriches its content, which I foresee will prove to be a great contribution, not only to scientific dissemination but also to practical learning about the use of supporting tools when making health decisions.

The demographic changes that we have been experiencing during the last few decades generate changes in people's needs, due not only to ageing but also to a real change from the epidemiological pattern of non-communicable diseases, which generate chronic conditions of great impact on the quality of life of those who suffer from them and their families. Moreover, the great advances in diagnosis and treatment, and the associated cost of health care, push our healthcare system towards uncertainty about its sustainability if we do not adopt compromises and correct decisions.

In this context, in the current debate about how to combine innovation and sustainability with the needs of people, a tool such as multi-criteria decision analysis now appears.

It is not surprising that these methods are being increasingly used to inform decision-making about financing and prioritisation of techniques, technologies and procedures in the healthcare sector. Although their use began with orphan drugs, their application is essential for all types of pathologies, because it allows us to consider the holistic value of health technologies for society, and explains the importance of each element considered.

This work offers us a broad panorama of the usefulness of multi-criteria decision analysis, which positions it as a method that enriches the decision-making process by providing it with greater transparency, consistency and legitimacy.

Nevertheless, as with any other emerging tool, its use will improve over time, but first we must understand it well and understand its advantages and limitations, through practical examples. In this sense, this book is an undoubted help, by exposing the ideas on which the tool is based and by developing a very coherent perception of the applicability of multi-criteria analysis in the healthcare field. Something that infuses the text with practicality is the inclusion in some chapters of practical examples, applicable to different decision cases which we face in our daily healthcare management at different levels -macro, meso or micro- and which are cases through which the reader's understanding of the model is facilitated.
I convey my congratulations to the authors for the excellent work done, because they have managed to combine the theoretical aspects of the method with practical experiences of its use, both nationally and internationally.

The text facilitates the understanding of key issues that arise when performing or interpreting an analysis of this type, in which different analytical techniques are used to inform decision-making in contexts such as ours, in which there are multiple criteria which may be in conflict. This type of analysis is an opportunity to integrate, among other criteria, for example, the perspective of the patient, into a system that we want and believe to be centred on the person, and on their needs and expectations. Incorporating new information for the analysis that comes from people’s experience, values and preferences helps to legitimise the decision-making.

The work ultimately leads the authors to reflect critically about multi-criteria decision analysis, and to develop a compendium of recommendations to enhance its usefulness.

At the Spanish Ministry of Health, Consumption and Social Welfare we are committed to the quality and equity of our healthcare system, to whose sustainability we are all committed. In this sense, multi-criteria decision analysis, complementing other techniques, can help us to make decisions about the prioritisation and use of resources based on evidence, and to improve commitment, transparency and accountability to citizens.

I encourage readers who would like to become more familiar with this topic, or to study it more deeply, to read this book carefully; it explains in a clear and readable way how a multi-criteria decision analysis should be carried out and what practical usefulness it can bring to the decision-making process which we face in healthcare management, with the ultimate aims of ensuring that these decisions serve to improve people’s quality of life and contribute to the sustainability of the system.

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CHAPTER 3

MULTI-CRITERIA DECISION ANALYSIS: WHAT IS IT AND WHAT IS IT FOR?

Jaume Puig-Junoy
3.1 INTRODUCTION

The purpose of this introductory chapter about Multi-Criteria Decision Analysis (MCDA) is to present the basic concepts of its application in decisions about the evaluation and prioritisation of drugs, medical technologies and healthcare programmes. First, the need for a ‘multi-criteria’ rationale, as opposed to the rationale of cost-effectiveness analysis and of opportunity cost, is analysed. Secondly, it describes what an MCDA consists of, as well as the main methods and stages for carrying out an analysis of this type. Thirdly, a hypothetical illustration of the use of MCDA is presented in order to show the conditions for its appropriate use in each of the three main methods. It concludes by reviewing the conceptual and empirical debate, in the field of health technology evaluation, about the complementarity or substitutability between the cost-effectiveness analysis and the MCDA.

3.2 MULTIPLE CRITERIA IN HEALTHCARE DECISION-MAKING

In recent years, several OECD countries have adopted measures to incorporate economic evaluation (EE) into the set of health technology assessment (HTA) tools that guide the strategies for coverage and reimbursement of drugs and medical technologies (Auraaen et al., 2016; Angelis et al., 2017). Many of them, in addition to comparative or incremental efficacy and the incremental cost-effectiveness ratio (ICER), also require and use budget impact studies which, from the outset, should not be interpreted so much as a conflict between the rules of efficiency and budgetary rules, but, instead, as the way in which insurers take into account the opportunity cost. Cost-effectiveness thresholds cannot be established independently of budget availability in a context of maximising health outcomes (Culyer, 2017). However, the magnitude of the budgetary impact in itself does not provide a good representation of the opportunity cost in relation to lost profits (McCabe et al., 2007). Thus, for example, the case of the new oral agents in the treatment of chronic hepatitis has highlighted the fact that the cost-effectiveness analysis does not adequately take into account the budgetary impact, since it focuses its attention on individual treatments without assessing the impact on the healthcare system as a whole (Neumann and Cohen, 2015). The OECD countries have been adopting different decision-making processes in their respective attempts to include information coming from the economic evaluation of health technologies (Angelis et al., 2017).

From the social perspective, the concepts of therapeutic usefulness and degree of innovation of the new medicines must be related to the social value which they add compared with the available treatment alternatives, and to the added costs that they entail, that is, their ICER. The rationale of incremental cost-effectiveness may be appropriate for the decisions of public insurers about coverage for a particular treatment, the price that one is willing to pay for it, and the clinical situations and groups of patients for which it is recommended. The incremental cost-effectiveness analysis and the establishment of a threshold indicative of the maximum cost that one is willing to pay for ‘quality-adjusted life-years’ (QALYs) gained — as a reference to the opportunity cost — are the essential elements of this rationale, which does not require setting the price of new drugs at the threshold of willingness to pay.

In practice, HTA procedures to assess and evaluate clinical evidence differ in each country in terms of, for example, the levels of evidence required, the variables of clinical outcome
adopted (mortality, morbidity, survival or quality of life), the criteria for the choice of compara-
tor to evaluate comparative efficacy or the use of measurements of clinical benefit such as QALYs or discrete scales of classification of the added value of innovations. In the same vein, the stakeholders involved (citizens/patients, clinical and economic experts, public payers/public regulators, healthcare professionals/provider institutions/industry) and their role and influence in the evaluation process are variable from one HTA to another. It is not surprising that on many occasions HTA agencies reach different conclusions about the value of the clinical benefit of the same technology.

These decisions of the HTA agencies face some common problems, added to the more specific controversies about the function and the details of the application of economic evaluation techniques, among which two stand out: the limited availability of evidence at the time of carrying out the evaluation, and the difficulties in establishing and justifying a cost-effectiveness threshold above which it is considered that innovations are not cost-effective (Auraaen et al., 2016).

Although cost-effectiveness is widely recognised as a necessary element to guide decision-making with limited resources, none of the HTA agencies that take EE into account use the ICER as the only measurement. This practice recognises that the criterion of efficiency/opportunity cost is a necessary but insufficient condition to guide the allocation of health resources and the need to consider distributive effects on costs and results. From a conceptual point of view, the vast majority of economic evaluations carried out neither incorporate criteria of equity (one year of life or a QALY are valued independently of the disease, the age and the group of patients), nor claim to be, at least from an extra-welfarist approach, the only decision criterion with a metric based solely on the ICER. The very logic of using cost per QALY relies on extra-welfarist theories, and this approach is the one that provides theoretical bases for the inclusion of other criteria in the MCDA (Culyer, 1991; Garau and Devlin, 2017). The main justification, beyond the specific limitations of the QALY — which do not need to be reviewed in detail here — (Angelis and Kanavos, 2016; Nord, 2017), is that the ICER corresponds only to the criterion of efficiency (Devlin and Sussex, 2011; Drummond et al., 2015).

The cost-effectiveness approach implies prioritising not only according to effectiveness but also according to the balance between the comparative costs and health outcomes of one intervention and those of its best alternative, but it does not imply a single threshold (see, for example, the case of the criteria for treatments at the end of life or for rare diseases), nor does it imply that the cost-effectiveness threshold is the only criterion for prioritisation (Culyer, 2017; Neumann and Cohen, 2015). Thus the decision to cover or finance a treatment with an ICER above the threshold could be interpreted in this context as a measure of the opportunity cost of taking into account the 'other' factors in the decision-making in addition to the cost-effectiveness.

In practice, decisions about the allocation of health resources of HTAs take into account, in addition to comparative efficacy and safety, the ICER and the budgetary impact, five groups of 'other' factors: a) the incidence, prevalence and severity of the illness; b) the affected population group; c) the availability of therapeutic alternatives; d) the quality of the available evidence; and e) the degree of technological innovation (Devlin and Sussex, 2011; Regier and Peacock, 2017; Garau and Devlin, 2017). This list of factors could be somewhat more
extensive in certain therapeutic areas, for example, in the case of orphan drugs (Paulden et al., 2014) and is also quite variable between countries, and even between decision-makers.

An international review of the literature of 11 countries about criteria for prioritising technologies groups them into three major groups of principles: a) need, adequacy and clinical benefits; b) efficiency (including cost-effectiveness); and, c) equality, solidarity and other ethical or social values (Golan et al., 2011). Table 3.1 presents the enumeration of allocation principles and the criteria that are associated with them according to this review of the literature.

Decision-making, whatever the level of resource allocation, requires the prioritising and weighting of these criteria in such a way that implicit interchange relationships are established between them. For example, the Dutch healthcare system uses four prioritisation criteria in a rather complex decision process: care must be necessary, effective and efficient, and cannot be left to individual responsibility (Stolk and Poley, 2005). France classifies pharmacological innovations into three levels: essential, important and ease of administration, associating with these categories public financing of 100%, 65% and 35% respectively (Sandier et al., 2004).

**TABLE 3.1. MAIN CRITERIA AND ‘OTHER’ CONSIDERATIONS USED INTERNATIONALLY TO PRIORITISE NEW HEALTH TECHNOLOGIES**

<table>
<thead>
<tr>
<th>PRINCIPLES OF ALLOCATIVE JUSTICE</th>
<th>CRITERIA</th>
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<tr>
<td>Need</td>
<td>General</td>
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<tr>
<td></td>
<td>Severity of the condition</td>
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<td>Availability of alternatives</td>
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<td>Appropriateness</td>
<td>Efficacy and safety</td>
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<td></td>
<td>Effectiveness</td>
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<tr>
<td>Clinical benefits</td>
<td>General</td>
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<td></td>
<td>Effect on mortality (life saving)</td>
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<td></td>
<td>Effect on longevity</td>
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<td>Effect on health-related quality -of-life</td>
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<tr>
<td>Efficiency</td>
<td>Cost -effectiveness /benefit</td>
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<tr>
<td></td>
<td>Budgetary impact</td>
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<td></td>
<td>Cost</td>
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<tr>
<td>Equality</td>
<td>General</td>
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<td></td>
<td>Accessibility to the service</td>
</tr>
<tr>
<td></td>
<td>Affordability to the individual</td>
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<tr>
<td>Solidarity</td>
<td>Autonomy</td>
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<tr>
<td>Other ethical or social values</td>
<td>Public health value</td>
</tr>
<tr>
<td></td>
<td>Impact on future generations</td>
</tr>
<tr>
<td>OTHER CONSIDERATIONS</td>
<td>Strategic issues consistency with previous decisions and precedents</td>
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</table>

Source: Golan et al., 2011.

A pragmatic and widely-shared conclusion from the practice observed in the HTA agencies, without going into considerations of its theoretical foundations, is not whether multiple criteria should be taken into account, but, rather, how they should be taken into account with
transparency and consistency and without omission of relevant information. In this sense, for example, when an agency of HTA affirms that in its decisions ‘other’ factors are considered in addition to cost-effectiveness, the decisional problem is far from being solved, and there are immediate doubts about the manner of applying this multi-criteria approach.

Moving away from the approach of cost-effectiveness or opportunity cost towards the multi-criteria approach, far from solving the problem, makes it essential to give an adequate response to the need to be explicit about the ‘other’ factors that influence decisions: it requires improving the transparency and accountability of the decision-making process; improving the consistency of the process; taking account of the preferences of the different social agents involved in decision-making and giving precise signals to the industry about the aspects of innovation that are valued (Devlin and Sussex, 2011; Angelis and Kanavos, 2016). By way of example, in many multi-criteria decision-making processes, the way to incorporate the ‘other’ factors in the decision-making process is not clear in respect of: a) the weight assigned to each of these factors and how they are balanced among themselves and with respect to the ICER; b) whether the effect on the decision is of an additive or multiplicative nature; and c) whether the list of explicit criteria, when there is an explicit list, is or is not exhaustive (Devlin and Sussex, 2011). For example, in the case of England and Wales, when the decisions taken by the National Institute for Health and Clinical Excellence (NICE) in the period 2004-2009 are analysed retrospectively, a significant association is observed between the recommendations of that agency and four variables: a) evidence of clinical superiority of the primary outcome variable in clinical trials; b) the ICER; c) the number of drugs included in the same assessment; and d) the year of the evaluation (Cerri et al., 2013). In Australia, the retrospective review of the decisions taken between 1993 and 2009 (n=425) by the Pharmaceutical Benefits Advisory Committee highlights the fact that an increase of A$10,000 in cost per QALY reduces the average probability of public funding from 37% to 33%, but if it is a treatment for a life-threatening disease that has no effective alternatives, then these two conditions together are considered as being equivalent to an increase of A$46,000 in the cost per QALY (Harris et al., 2015). Contrary to what some authors have affirmed (Drummond et al., 2007) for the case of chronic diseases, it does not seem true that the real experiences of HTA are based on the application of a pure criterion of efficiency in a unique way (Laupacis, 2009).

The recent profusion of scales for measuring the innovation value of new drugs (‘innovometers’), quite possibly in response to proposals for pricing based on value and the high prices of technological innovations (Neumann and Cohen, 2015; Walton et al., 2016; Zaragozá and Cuéllar, 2017; Angelis and Kanavos, 2017), especially in the field of oncology, is a good example of the risks of inappropriate use of multi-criteria decision-making processes. The non-systematic and ad hoc use of value dimensions and the lack of transparency in judgments and preferences about value can often lead to inconsistencies and arbitrariness in the process of evaluating these scales (Angelis and Kanavos, 2016). Simple comparisons of some of these scales of innovation value highlight the fact that there is no consensus about the criteria that must be taken into account, and the fact that they use different strategies to weight the criteria and calculate an overall score. The simple sum of the value scores of each criterion does not necessarily result in an overall score that is consistent with the preferences of the parties (Neumann and Cohen, 2015). Also, in most cases these scales lack any theoretical basis for the measurement of value, which would require, among other things, “an estimate of the rate at which stakeholders are willing to forgo one attribute of health for another” (Walton et al., 2016). All these limitations and criticisms directly affect, for example, the quantitative
scale of innovation value of new drugs recently proposed for Spain by a working group led by the Ministry of Health, Social Services and Equality (Zaragozá and Cuéllar, 2017).

The difficulty of decision-making lies in the multiplicity of criteria to evaluate the alternatives, with objectives that may enter into contradiction and with different groups of stakeholders involved in the decision-making, with different preferences. The traditional methods of MCDA constitute a tool at the service of this type of decisions by providing a formalised method of assisting multi-criteria decision-making that comes from operational research models (Belton and Stewart, 2002). In this sense, the need for MCDA in the HTA, despite what some authors claim (Angelis and Kanavos, 2016), cannot be sustained as an alternative to the sole rationale of cost-effectiveness or opportunity cost — which has hardly ever been a unique logical proposal by the economic literature or used in a unique way by the agencies — but can be upheld as an instrument to bring order (transparency, consistency and being comprehensive) in an explicit manner into multi-criteria decisions (Belton and Stewart, 2002; Thokala and Duenas, 2012; Drummond et al., 2015; Regier and Peacock, 2017). MCDA is a set of techniques to help the deliberative processes of multi-criteria decision-making, that is, a support instrument without prescriptive value, and which does not replace decision-making.

Although the application of MCDA to healthcare decisions is relatively recent (Devlin and Sussex, 2011; Marsh et al., 2014; Adunlin et al., 2014; Wahlster et al, 2015; Thokala et al., 2016), these methods have been widely used during recent decades, both in the public sector and in the private sector, as an aid to decisions about transport, immigration, investments, the environment, energy, defence, etc. (Thokala et al., 2016; Communities and Local Government, 2009). It is necessary to recognise that part of the recent interest in MCDA falls within the political debate in order to get away from some HTA processes which, according to some stakeholders, are too concerned with the threshold of the maximum cost per QALY. One has to recognise that there are results or benefits beyond those related to health, and to explore methods of measuring everything that may be relevant for patients. The theoretical and political debate about value-based assessment in the United Kingdom could be interpreted as an attempt to complement the maximisation of QALYs with the explicit consideration of other factors or attributes of value such as the severity of the disease.

In spite of the above, it would be a mistake to regard MCDA merely as a simple alternative to a cost-effectiveness analysis: the correct performance of an MCDA is much more complex than most simple exercises that have so far been disseminated in the literature. Most issues to be resolved and most cost-effectiveness problems affect MCDA with the aggravating circumstance that they extend to other attributes or dimensions: “Without a proper assessment of the other attributes of benefit forgone, decisions may reduce both health and the other attributes of benefit that originally motivated the use of MCDA” (Garau and Devlin, 2017).

### 3.3 WHAT IS MCDA?

The starting point that justifies the use of MCDA by decision-makers who have to choose between two or more alternatives is that they take into account more than one objective when judging the desirability of a given alternative. Rarely, one alternative is superior to the other or others in respect of all the objectives, that is, it is dominant with respect to the others. The most common situation is that each alternative satisfies the objectives at different levels, and the decisions involve conflicts and relationships of exchange between the degrees of fulfil-
ment of the objectives. In any environment, multi-criteria or not, the choice of one alternative over the others implies an opportunity cost. Thus, the logic of applying MCDA to evaluate alternatives has as its starting point some simple basic assumptions (Regier and Peacock, 2017). First, decisions are made in a context of limited resources, and any decision involves forgoing the benefits of the others (opportunity cost). Secondly, the objectives or criteria that the decision-makers take into account correspond to their discretionary scope and cannot be determined in a normative way by means of ethical or economic theories such as utilitarianism or social justice. Thirdly, an alternative or programme is not a homogeneous benefit, but is described by its multiple characteristics as the combination of several levels for each criterion or dimension. And fourthly, it is possible to establish the relative importance of each criterion and the relationships of exchange between them that allow scores to be obtained and alternatives to be ordered in consequence.

The common purpose of MCDA methods is to take into account explicitly the multiple criteria involved in individual or group decision-making (Belton and Stewart, 2002; Thokala et al., 2016). In a somewhat broader way, Devlin and Sussex, 2011, define MCDA as a set of methods and techniques to help decision-making, applicable when they are based on more than one criterion, which explicitly deal with the impact on the decision of each of the criteria applied, as well as the relative importance of each of them. Two MCDA conditions are particularly relevant for HTA: the replicability and the transparency of the decisions. In fact, the same measurements of quality of life related to state of health that are used to calculate QALYs in a cost-utility analysis are still a form of MCDA — for example, the scale of quality of life EQ-5D-5L takes into account six criteria (survival and five quality-of-life criteria), with five scores for each of them (Drummond et al., 2015).

In a multi-criteria decision context, there are three main issues to be resolved (Drummond et al., 2015), which will be decisive in reaching the recommendation or decision. First, the criteria that will be used in the MCDA, that is, the criteria of the benefit or result that will be evaluated together with the improvement in health. Secondly, how to assign weights to the value of the attributes of each criterion. And thirdly, the characteristics or dimensions of benefit that are lost or forgone if additional costs are incurred (opportunity cost).

Any application of MCDA in the healthcare sector or in other sectors includes the following phases (Figure 3.1): identification of alternatives and decision criteria (structuring the problem), construction and use of the model, and development and action plans. The criteria included in the structuring of the problem must fulfil some essential conditions: they must be non-redundant, independent, complete, operational and measurable (Belton and Stewart, 2002; Regier and Peacock, 2017). Each criterion must contribute to the result or benefit independently of the others and avoiding duplication. In the phase of modelling or constructing the model, the information or evidence collected is the subject of quantification and will be used as input in mathematical models to identify the best alternative by incorporating explicit weights and scores of the criteria and attributes. The way in which these models are constructed is what differentiates the different MCDA methods. Their construction involves the production of behavioural models that quantitatively represent the preferences or value judgments of the decision-makers, which, ideally, should reflect the preferences of society. These models have in common that preferences are expressed for each criterion of each alternative and that the aggregation model allows the criteria to be compared with each other in order to combine the estimates of preferences.
The main MCDA methods can be classified into the following three groups (Devlin and Sussex, 2011; Thokala and Duenas, 2012; Mühlbacher and Kaczynski, 2015; Thokala et al., 2016; Garau and Devlin, 2017): models for measuring value, outranking models and models by objectives or reference levels (Figure 3.2).

The **value measurement models** calculate and compare numerical scores which synthesise the overall value of each alternative as an expression of the degree to which one is preferred to another. The scores of each of the individual criteria are aggregated into a figure that represents the overall value of the alternative. This is the most widely preferred method, almost the only one, in HTA, with the additive aggregation method (the weighted sum method) being the most used. The additive method of aggregation requires that the condition of additive independence be satisfied, that is, that the conflicts between two criteria do not depend on the level of the other criteria (Diaby and Dias, 2017). In a systematic review of the applications of MCDA in the healthcare sector, for the period 1980-2013, it is observed that 60 of the 66 studies selected only used value functions (Diaby and Dias, 2017). Budget programming and
marginal analysis and the analytical hierarchical process are similar techniques that can be included within this group of methods.

Two alternative methods of measuring value functions are identified: the multi-attribute utility theory (MAUT) and the multi-attribute value theory (MAVT). The main difference between the two is that the MAUT uses utility functions which take into account the decision-makers' attitudes to risk, using the concept of lotteries, as opposed to the MAVT, which builds an overall value function for each alternative to obtain the overall score of each alternative based on the decision criteria, using the concept of intensity of preferences. The MAVT’s models for measuring value require strict compliance with certain conditions related to criteria and weights: independence and transitivity of criteria preferences and weights that fulfil the requirements of the exchange relationship between criteria. The independence of preferences requires that the decision be based on criteria in which the alternatives appear as different. The relative weights of criteria $i$ and $k$ ($w_i$, $w_k$) must be such that the ratio of relative weights ($w_i/w_k$) represents the change in the value of the score of criterion $k$ for alternative $A$, $v_k(A)$, which is necessary to compensate for a loss of one unit in the value of the score of criterion $i$, $v_i(A)$. The techniques for obtaining these weights are analysed in detail in Chapter 4 of this book. Likewise, the methods of scoring and weighting the criteria are described in detail in Chapter 5 of this book and in Marsh et al., 2017. The theoretical bases of the various methods can be found in Regier and Peacock, 2017.

The use of value measurements or functions implies accepting that a low result in one criterion can be compensated with a better result in one of the other criteria. These methods may not be appropriate when these compensatory effects are not considered adequate for the decision process: for example, when the criteria relate to different stakeholders (patients vs. professionals or hospitals) or when the criteria relate to very different dimensions of the value (economic versus social) (Diaby and Dias, 2017).

In outranking models, the alternatives are initially compared by pairs in terms of each criterion, in order to confirm the degree of preference (dominance) of one relationship over the other for each specific criterion. If the two alternatives are very similar, they cannot be compared. Next, one adds the degree of preference of the different criteria between the alternatives, in order to establish the overall level of preference of one over the other. This method is based on a direct comparison of the characteristics of the alternatives, and it is appropriate for the HTA despite having been little used so far.

Modelling by objectives or reference levels is based on determining which alternative is closest to predetermined levels of results for each criterion. The use of a cost/utility threshold in pricing based on value would be similar to the way of proceeding in this group of methods based on mathematical programming techniques. Programming by objectives implies minimising deviations from the objectives, taking into account the relative importance of each objective or criterion. The two main techniques used in this group of methods are programming by objectives and lexicographic programming by objectives, which differ in the way of prioritising and reaching the optimal solution (Thokala and Duenas, 2012).

Table 3.2 presents the comparison of these three groups of MCDA, in relation to the weights used, the measurement of the performance of the criteria, the complexity of the MCDA model, the presentation of results and the treatment of uncertainty.
## TABLE 3.2. COMPARISON OF MCDA METHODS

<table>
<thead>
<tr>
<th></th>
<th>VALUE MEASUREMENT MODELS</th>
<th>OUTRANKING MODELS</th>
<th>GOAL PROGRAMMING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weights</strong></td>
<td>Swing weights are used to capture both the effect of measurement scales and the importance of the criteria. Weights need to satisfy the preferential independence of criteria and the trade-off requirements.</td>
<td>Weights are un influenced by the scale of the value functions. They convey the relative importance of criteria in the assertion that one alternative is better than the other. Weights do not have to satisfy any conditions.</td>
<td>Weights are attached to the deviations and represent the relative importance of criteria by specifying an overall measure of deviations from the goals. Weights do not have to satisfy any conditions.</td>
</tr>
<tr>
<td><strong>Measuring the performance of the criteria</strong></td>
<td>Performance scores $v_i(a)$, monotonic functions of the attribute values $z_i(a)$, need to be developed for all criterion $i$. Significant effort is needed to develop these performance scores.</td>
<td>Outranking approach can use either performance value scores $v_i(a)$ or the attribute values $z_i(a)$, saving on the effort needed to develop performance scores.</td>
<td>Goal programming method operates directly on the attribute values, $z_i(a)$. No need to develop performance scores.</td>
</tr>
<tr>
<td><strong>Complexity of the MCDA model</strong></td>
<td>Weighted sum approach is easy to understand and use by the decision makers. The parameters can be changed in real time to observe their effect.</td>
<td>Intuitive and easy to follow. With right software, assumptions can be changed and results can be observed almost instantaneously.</td>
<td>Easy to understand but requires significant computational time to provide results. Real-time updating is not possible.</td>
</tr>
<tr>
<td><strong>Presentation of the results</strong></td>
<td>Easy to follow and enables further deliberation, well suited for good visual presentation of the results.</td>
<td>Moderately easy to follow. Can be presented visually but difficult with multiple alternatives.</td>
<td>Results easy to follow, but they cannot be represented visually.</td>
</tr>
<tr>
<td><strong>Incorporating uncertainty</strong></td>
<td>Probabilistic sensitivity analysis can be used to propagate parameter uncertainty quite easily.</td>
<td>Moderately difficult to include uncertainty, needs specialist software.</td>
<td>Quite difficult to include uncertainty, complex stochastic programming techniques are needed.</td>
</tr>
</tbody>
</table>

*Source: Thokala and Duenas, 2012.*

From a practical point of view, the phases for the performance of an MCDA can be summarised as the following five (Angelis and Kanavos, 2016), although there are authors and guides that present more detailed schemes or stages (Devlin and Sussex, 2011; Thokala et al., 2016): problem structuring, model building, model assessment, model appraisal and action plans.

In the first stage, structuring the problem, in which researchers and decision-makers intervene to establish the context of the decision: the problem about which a decision has to be made and the objectives to be pursued, as well as the decision-makers and parties involved. For example, the decision problem could be to assess the benefits and costs of a new technology from the social perspective and compared with usual clinical practice, in order to identify the intervention that contributes more value to the healthcare system. The decision-makers, in this context, could be the payers or the insurers; and the parties involved would be health professionals, patients and their caregivers, the supplier industry and experts in methods.
In the second stage, model building, researchers and decision-makers also intervene. This phase consists basically of the selection of criteria and attributes that reflect the decision-makers’ objectives and concerns, the selection of alternatives and the obtention of evidence for the results of the alternatives for the selected criteria. For example, in the evaluation of a new drug compared with a previous, more effective one, the selected criteria could be the therapeutic benefit, the safety profile, the burden of the disease, the level of innovation, the socio-economic impact and the quality of the evidence.

The third stage of the MCDA consists of the assessment of the performance of options against the identified criteria: the score for each criterion that provides information for the intra-criterion comparison, and weighting of the criteria according to their relative importance that contributes information for combining criteria. This phase generally requires the construction of value functions by means of various techniques (see Chapter 5 of this book), transforming the values of the results into scores on the value scale. The appraisal requires the obtention of an indicator of added value from the combination of scores and weights, the technical details of which are different depending on the MCDA method adopted (Diaby and Dias, 2017). The result of this phase, subject to the performance of a sensitivity analysis, consists of an arrangement of the alternatives based on the value score obtained with the MCDA.

3.4. WHAT CAN MCDA BE USED FOR? A SIMPLE ILLUSTRATION

MCDA can be useful as an aid to decision-making in the healthcare sector, which, in addition to the HTA, can include authorisation decisions, about prioritisation of coverage or financing of benefits, prioritisation of access to treatment for patients, classification of diseases, allocation of resources for R&D, etc. (Thokala et al., 2016; Marsh et al., 2016; Mülhbacher and Kaczynski, 2016). Castro et al., 2017, present an interesting description of three case studies of the application of MCDA in the HTA for various countries and regions (Colombia, Lombardy and Belgium), which are explained in detail in sections 4.3 and 7.3.7. Also, a review of the experiences in the application of MCDA in the prioritisation of benefits and treatments in low- and middle-income countries can be found in Tromp et al., 2017.

Included in this section is a simple illustration of a hypothetical case of using the various MCDA methods to evaluate two pharmacological treatments A and B, being A the current treatment and B the new treatment. This illustration is based on a summary presentation of the case study published by Thokala and Duenas in 2012. Table 3.3 presents the main characteristics of the two drugs under evaluation based on five criteria: cost/effectiveness (in terms of net benefit), equity, innovation, adherence to treatment and quality of evidence. The cost-effectiveness ratio is presented as a net benefit calculated from a willingness to pay per QALY or 20,000 monetary units (mu). The net monetary benefit is the difference between the monetary value of the QALYs and the cost of treatment (Hounton and Newlands, 2012). Let us assume that the net benefit of drug A depends on the price (x) according to the following function: \[ f(p) = 25,000 - 1,000x \]. If the logic of cost-effectiveness is used alone, treatment B would be recommended. Nevertheless, let’s see what might happen if the three MCDA methods mentioned above were used. In this hypothetical example, the opportunity cost is not included as a criterion, but only the net benefit of both alternatives.
As a step prior to the application of the three MCDA methods, table 3.4 presents the performance scores for each of the five criteria according to an objective measure or scale. For each criterion, desirable performance levels have been identified. When there is a linear relationship between the value of the attribute and the value of the result of the criterion, as in the case of adherence, the same value of the attribute can be taken as a measure of result. In most cases, for which this linear relationship cannot be assumed, it is necessary to construct a scale to represent the performance of each alternative in which the highest values are preferred. For criterion i, the performance score $v_i(A)$ is a non-decreasing function of the attribute value $z_i(A)$. More generally, for any criterion i the score of any alternative is defined as $v_i = f(z_i)$, the function f being the same for the alternatives (pharmacological treatments) compared. These scores are generally presented standardised on a scale ranging from the least desirable to the most desirable value (1, 10 or 100). Here we shall assume that we have defined these functions and that the scores are those presented in table 3.4. Once these scores have been obtained, we are ready to start applying each of the three MCDA methods.

**TABLE 3.3. CHARACTERISTICS OF THE DRUGS IN THE APPRAISAL PROCESS**

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>DRUG A $z(a)_i$</th>
<th>DRUG B $z(b)_i$</th>
</tr>
</thead>
<tbody>
<tr>
<td>C/E (in terms of NB)</td>
<td>£15,850</td>
<td>£25,600</td>
</tr>
<tr>
<td>Equidad (%) Equity (%)</td>
<td>0.14</td>
<td>0.08</td>
</tr>
<tr>
<td>Innovation</td>
<td>Innovative</td>
<td>Less Innovative</td>
</tr>
<tr>
<td>Patient compliance (%)</td>
<td>0.93</td>
<td>0.85</td>
</tr>
<tr>
<td>Quality of evidence</td>
<td>Good</td>
<td>Good</td>
</tr>
</tbody>
</table>

C/E: cost-effectiveness.

* $z(a)_i$ and $z(b)_i$ are values of attribute i for drug A and drug B respectively.

**Source:** Thokala and Duenas, 2012.

**TABLE 3.4. PERFORMANCE SCORES OF DRUGS**

<table>
<thead>
<tr>
<th>CRITERION (i)</th>
<th>DRUG A $v(a)_i$</th>
<th>DRUG B $v(b)_i$</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIE</td>
<td>0.72</td>
<td>0.84</td>
</tr>
<tr>
<td>Equity(%)</td>
<td>0.14</td>
<td>0.08</td>
</tr>
<tr>
<td>Innovation</td>
<td>0.91</td>
<td>0.62</td>
</tr>
<tr>
<td>Patient compliance</td>
<td>0.93</td>
<td>0.85</td>
</tr>
<tr>
<td>Quality of evidence</td>
<td>0.82</td>
<td>0.79</td>
</tr>
</tbody>
</table>

C/E: cost-effectiveness.

* $v(a)_i$ and $v(b)_i$ are values of the result of attribute i for drug A and drug B respectively.

**Source:** Thokala and Duenas, 2012.
Value measurement models. In order to achieve a single overall score for each alternative, the performance levels of both drugs are constructed for each criterion (preference modeling) as we did in table 3.4 (partial value function), in this case, on a scale between 0 and 1. A partial value function reflects how the value of an attribute varies for the decision-maker along the scale of measurement. It can be a function for an attribute such as quality of life, or decreasing, as for cost. Next, to each criterion a weighting or relative weight $w_i$ is assigned that depends on the scale of the value function of each criterion and indicates its relative importance. Next, the partial value functions are aggregated, taking into account the weightings. If an additive aggregation function (weighted sum approach) is adopted, then:

$$V(a) = \sum_{i=1}^{n} w_i \cdot v_i(a).$$

Assuming that we have identified the following relative weights ($w_i$) using the most appropriate technique: cost-effectiveness (8), equity (1), innovation (3), adherence to treatment (2) and quality of evidence (3), then one obtains $V(a)= 12.95$ and $V(b)= 12.73$. With this method, alternative A is preferred to alternative B, contrary to the recommendation with the sole use of cost-effectiveness, since the best results of A in the other 4 criteria more than compensate for the disadvantage in the cost-effectiveness criterion.

Outranking approach. The first step in estimating the agreement or disagreement is to construct the matrix of outranking relations from the individual scores of the alternatives in each criterion (Table 3.4), as shown in table 3.5. With this method, alternative A is preferred to B only if $v_i(A) - v_i(B)$ is greater than a certain ‘indifference threshold’ ($t_i$). In our case, for example, if the threshold for the quality of the evidence is 0.05, then the difference observed is less than this threshold, and the alternatives for this criterion cannot be compared. This method also requires the estimation of relative weights for each criterion, which may be different from those of the value measurement model since they only represent the relative importance of the different criteria that allows us to affirm that one alternative is better than the other (they do not need to be exchange relations between criteria). In this example, the concordance index $C(A,B)$ is calculated by the ELECTRE I method, which consists of the ratio between the sum of the weights of the criteria in which A is at least as good an alternative as B ($Q$ weights) and the sum of weights of all criteria ($m$ weights):

$$C(A,B) = \frac{\sum_{i \in Q(A,B)} w_i}{\sum_{i=1}^{m} w_i}.$$  

Alternatively, we could also have calculated a discordance index $D(A,B)$ which can be defined as:

$$D(A,B) = \begin{cases} 1 & \text{if } v_i(B) - v_i(A) > t_i \frac{V_i}{\sum w_i} \\ 0 & \text{otherwise} \end{cases}$$

For our hypothetical example, the concordance index of A against B is $C(A,B)= 8/18= 0.44$ and the concordance index of B against A is $C(B,A)= 10/18= 0.56$. Supposing now that we define a veto threshold for the cost-effectiveness criterion $t_1 = 0.1$ table 3.4 shows that B is better than A in cost-effectiveness by 0.12, which is higher than the veto threshold $t_1$. If, for example, the threshold of agreement $C'$ were less than 0.56: then, with this method it could be concluded that alternative B is better than A provided that the thresholds of the other criteria are respected and in accordance with the threshold of agreement adopted.
TABLE 3.5. OUTRANKING RELATIONS AND WEIGHTS

<table>
<thead>
<tr>
<th>CRITERION (i)</th>
<th>WEIGHTS ( w_i^* )</th>
<th>DRUG A</th>
<th>DRUG B</th>
</tr>
</thead>
<tbody>
<tr>
<td>C/E (in terms of NB)</td>
<td>10</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>Equity(%)</td>
<td>2</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Innovation</td>
<td>1</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Patient compliance (%)</td>
<td>3</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Quality of evidence</td>
<td>2</td>
<td>✔</td>
<td></td>
</tr>
</tbody>
</table>

C/E: Cost-Effectiveness. NB: Net Benefit.
* \( w_i^* \) is the weighting of criterion i.


Goal programming. With this method, first, objective values are defined for each criterion of the alternatives, understood as the desired levels of results for each criterion. In table 3.6 these values of the \( g_i \) objective are defined. Thus, in our example we define objectives for the criteria cost-effectiveness, equity and adherence. We shall assume that whereas cost-effectiveness can be modified through changes in price, equity and adherence cannot be modified.

TABLE 3.6. ATTRIBUTES OF DRUGS, THE GOALS AND WEIGHTS AGAINST DIFFERENT CRITERIA

<table>
<thead>
<tr>
<th>CRITERION (i)</th>
<th>DRUG A ( z(a)_i )</th>
<th>DRUG B ( z(b)_i )</th>
<th>GOALS ( g_i )</th>
<th>WEIGHTS ( w_i^{**} )</th>
<th>WEIGHTS ( w_i^{***} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>C/E (in terms of NB)</td>
<td>£15.850</td>
<td>£25.600</td>
<td>£20.000</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Equity(%)</td>
<td>0.14</td>
<td>0.08</td>
<td>0.20</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Innovation</td>
<td>Innovative</td>
<td>Less Innovative</td>
<td>-</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patient compliance (%)</td>
<td>0.93</td>
<td>0.85</td>
<td>0.95</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Quality of evidence</td>
<td>Good</td>
<td>Good</td>
<td>-</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

C/E: Cost-Effectiveness. NB: Net Benefit.
* \( z(a)_i \) and \( z(b)_i \) are values of attribute i for drug A and drug B respectively.
** Weights of the first level of priority.
*** Weights of the second level of priority.
\( \Omega^+_i \) and \( \Omega^-_i \) are the weights related to the deviations of criterion i from the objective \( g_i \).


We shall use the lexicographical method of goal programming, with cost-effectiveness being the criterion with the highest priority and the others with the next priority. We know that the net benefit of A (C/E) varies with the price according to the following function: \( f(x) = 25,000 - 1,000x \) (where x is the unit price of A). If we use the net benefit function of A, this alternative would only reach the level of the net profit objective if the price were equal to 5 mu, that is, 45% less than the initial price (9.5 mu). Only if both treatments attain the objective of net benefit can we proceed to the next step. Now that, with the price reduction, the objective of top priority has been attained, we can move on to the next level of priority, which includes the other criteria. Calculat-
ing the weighted sum of the deviations from the objective value, for the other two criteria with a non-zero relative weight, for each alternative we obtain: $D(A) = (5 \times 0.06) + (5 \times 0.02) = 0.4$ and $D(B) = (5 \times 0.12) + (5 \times 0.1) = 1.1$. So with this method we can conclude that drug A is superior to drug B, being closer to the objectives of equity and adherence, provided that the price of A is reduced by 45% to reach the cost-effectiveness objective.

**3.5 GOOD PRACTICES IN MCDA: ADVANTAGES AND RISKS**

MCDA applied to healthcare decisions has some advantages which are widely mentioned in the literature, but it also has its disadvantages or limitations, which can be amplified if this method moves away from the conditions of good practice on which the validity and advantages attributed to it are based. One useful function of MCDA is its consideration of complex information when making decisions such as those in which multiple criteria intervene and which may be in conflict; complexity is ‘cognitively demanding’ and can lead to incongruent decisions. Some of the most important advantages come from the greater transparency of the process through which a decision or recommendation is reached, as well as its congruence or coherence and the fact that it can be easily replicated (Devlin and Sussex, 2011; Garau and Devlin, 2017). Additionally, from the point of view of the political decision-makers, it is important to bear in mind that an explicit focus on criteria and weights or weightings, such as that of MCDA, may also have its disadvantages when compared with less formal and explicit processes of decision-making, since decision-makers can perceive that it contributes to reducing the discretion and degrees of freedom of their decisions (the cost of being "too explicit"; Garau and Devlin, 2017).

In the actual application of MCDA in the wide range of healthcare decisions in which it may be applicable, it is essential to observe the desirable properties of the criteria, attributes, weights and aggregation method, as well as compliance with good practice guidelines such as those of the ISPOR’s Task Force (Thokala et al., 2016) or those identified by other authors (Marsh et al., 2016; Thokala and Duenas, 2016) (see Chapter 6 of this book). There are still few MCDA studies in the health field which prove that the criteria have been defined in such a way that they fulfil the requirements of this analysis, such as the avoidance of double counting. Table 3.7 summarises a detailed set of 16 principles of good practice in MCDA in the healthcare sector covering all stages of conducting such an analysis.

Even when the application of MCDA in healthcare decisions respects the conditions of good practice, there are some important costs and risks which may affect the use of this method. In this section, starting from the literature reviewed, three groups of practical risks are identified, leaving the subject of opportunity cost for more detailed comment in the next section.

First, MCDA can be used generically for all decisions with the same purpose (for example, decisions about reimbursement and price), or it can be applied in a specific way, *ad hoc* for each specific case. In this second case, the criteria, weights, value functions and aggregation functions may be different for each drug or technology evaluated, whereas in the first case, they are the same for all evaluations. With a generic MCDA approach, the preferences represented must be those of society, with the added difficulty of appropriately capturing these preferences. A case-by-case approach in which criteria, weights and functions of *ad hoc* value are chosen for each decision can be a serious limitation to the consistency of, and coherence between, the decisions adopted (Garau and Devlin, 2017), with negative implications for the allocative efficiency of the decisions, in addition to reproducing the discretion and inconsist-
ency which MCDA precisely tries to mitigate. The limited practical experience indicates that, the greater the uncertainty about the criteria and the weights, the greater the likelihood that the HTA committees and agencies will be tempted to convert the MCDA into a case-by-case analysis in which each of them is concerned in a different way (Thokala and Duenas, 2012).

**TABLE 3.7. PRINCIPLES OF GOOD PRACTICE IN MCDA IN THE HEALTHCARE SECTOR**

<table>
<thead>
<tr>
<th>STAGE</th>
<th>PRINCIPLE OF GOOD PRACTICE</th>
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<tbody>
<tr>
<td>Establishment of the context</td>
<td>1. Define the limits of the problem.</td>
</tr>
<tr>
<td>of the decision</td>
<td>2. Identify the objectives and key actors.</td>
</tr>
<tr>
<td></td>
<td>3. Explore the context and issues with the group.</td>
</tr>
<tr>
<td>Identification of alternatives</td>
<td>4. Establish a clearly defined set of requirements for the options.</td>
</tr>
<tr>
<td>and criteria</td>
<td>5. Establish a defined set of operational criteria.</td>
</tr>
<tr>
<td></td>
<td>6. Make sure that the criteria are not redundant.</td>
</tr>
<tr>
<td></td>
<td>7. Make sure that there is no double counting in and between criteria.</td>
</tr>
<tr>
<td></td>
<td>8. Make sure that the criteria are mutually independent of preferences.</td>
</tr>
<tr>
<td></td>
<td>9. Iterate between options and objectives to create a set of requirements for each one.</td>
</tr>
<tr>
<td>Scoring of the alternatives</td>
<td>10. Make sure that the evaluators understand the type and meaning of the scale of preferences.</td>
</tr>
<tr>
<td></td>
<td>11. Conduct consistency tests during and after scoring the options.</td>
</tr>
<tr>
<td>Weighting of criteria</td>
<td>12. Make sure that the comparison ranges are taken into account when the trade-offs are valued.</td>
</tr>
<tr>
<td></td>
<td>13. Keep it simple.</td>
</tr>
<tr>
<td>Calculation of weighted scores</td>
<td>14. Use an algorithm to add evidence and criteria.</td>
</tr>
<tr>
<td>Analysis of results</td>
<td>15. Use software to present the results in the form of graphs and tables.</td>
</tr>
<tr>
<td>Sensitivity and scenario analysis</td>
<td>16. Explore the robustness of the conclusions by means of sensitivity and scenario analysis.</td>
</tr>
</tbody>
</table>

*Source: author’s preparation from Phillips, 2017.*

Secondly, there is a risk that the choice of preferences could be influenced by pressure groups, as predicted by the theory of public choice. If the preferences to be taken into account in the MCDA are those of the members of the decision committees, as representatives of social preferences in a generic approach, or those of the parties involved in a case-by-case approach, there is a risk that parties with a more self-serving interest in the decision will be selected instead of those who are really involved. The transaction cost of the participation in a deliberative process of the groups most directly affected, and who have the most to gain or lose as a result of the decision (for example, groups of patients with a certain disease) is much lower than the cost for the rest of society or for the insured parties who bear the opportunity cost of that decision, but with a smaller and more dispersed individual impact (Devlin and Sussex, 2011).

And thirdly, the limitations deriving from uncertainty about the evidence relating to the characteristics of the criteria chosen for each of the alternatives are, at least, the same in a traditional HTA and in an MCDA. In an MCDA, the areas of uncertainty include the structuring...
of the problem (choice of the most appropriate MCDA model, criteria, level of detail, etc.), the evidence for each alternative and the variation in preferences (uncertainty about scores, weights of criteria, thresholds, etc.) (Thokala and Duenas, 2012). In an MCDA, the degree of uncertainty is still potentially greater than when the incremental cost-effectiveness ratio is used as the sole decision criterion because of the multiple attributes of the asset or benefit (Garau and Devlin, 2017). For example, is a measurement of uncertainty necessary for each criterion? The influence of uncertainty on healthcare decisions has still been studied very little, and depends, for example, on the parties’ attitude to the risk and on the adequate understanding of the uncertainty. In practice, the MCDA must ensure that the parties whose preferences are to be used have an adequate understanding of the uncertainty which exists in the information available for each decision, in addition to using appropriate methods to capture this uncertainty (scenario analysis, multi-attribute utility theory, diffused logic, stochastic analysis of multi-criteria acceptability).

By way of summary, it is of interest for any application of MCDA in HTA, in addition to reviewing the criteria of good practice, to make explicit, to both the decision-makers and the users of the results, the list of key issues to be resolved in order to incorporate MCDA in HTA with guarantees that this will not make things worse (Table 3.8).

### 3.6. The ‘Multi-Criteria’ Rationale versus the Rationale of Opportunity Cost: Are They Alternatives or Complementary?

The growing literature about MCDA in healthcare decisions points out three reasons why this group of methods may represent an alternative to economic appraisal in HTA procedures (Angelis and Kanavos, 2016): 1) the inclusion of a comprehensive list of value dimensions in an explicit manner, beyond what traditional economic evaluation methods capture; 2) the assignment of quantitative weights across the different evaluation criteria, so that their relative importance is incorporated explicitly, thereby improving the transparency of the preference-elicitation process; 3) the stakeholder participation and the possibility of including them all in the value assessment process, which helps to increase the legitimacy of the process.

The previous potential advantages may be contrasted with the difficulty of the MCDA, if not the failure to consider the opportunity cost. The inclusion of the opportunity cost in an MCDA requires, in theory, all the benefits lost and potentially produced as a result of implementing an intervention to be compared, and this requires having a threshold or maximum limit to understand the opportunity cost. The efficient allocation of limited resources between alternative interventions cannot, under any pretext about the dimensions of value, set aside or neglect consideration of the opportunity cost (taking into account the budgetary constraint), that is, the benefits that are not going to be obtained because of the displacement of resources towards the selected or recommended intervention. Beyond the correct application of the MCDA method (Table 3.7) and the appropriate resolution about the key aspects of an MCDA (Table 3.8), the main problem, and the source of the most important criticisms presented by the use of MCDA in HTA, derives from the difficulty to adequately consider the logic of opportunity cost (the value of the lost benefit when considering the ICER as a decision criterion).

Table 3.8 shows the two conventional options for taking into account the opportunity cost (Garau and Devlin, 2017). The first option is to consider it as one more criterion, together with the other factors. In this case it is necessary, at least, to avoid the risk of overlapping
with other criteria (for example, between cost and cost-effectiveness). As an example, the EVIDEM framework (Goetghbeur et al., 2008) incorporates the compared cost (‘economic consequences of the intervention’) as one of the five criteria considered as representative of value, together with need, compared results, type of benefit and knowledge about the intervention. For example, Angelis and Kanavos, 2017, propose an Advanced Value Framework (AVF) which includes a criterion of socio-economic impact together with the burden of the disease, the therapeutic impact, the safety profile and the level of innovation. The value of the socio-economic impact criterion is based on three intermediate criteria: public health (risk reduction and prevention), direct incremental costs (medical and non-medical) and incremental indirect costs (absenteeism, presentism, premature abandonment, premature mortality and caregivers). The inclusion of cost, be it the total cost or the incremental cost, as a criterion or dimension of the value of the intervention has been the subject of criticism, since if what is pursued is to obtain a value index, then the criteria should represent attributes of benefit. The AVF tries to evade this criticism by considering not the cost of the intervention, but the incremental cost, as a measurement of the impact on costs instead of the total cost or the cost of acquisition. The treatment of opportunity cost in the majority of currently available MCDA schemes and software only partially deals with the subject of opportunity cost (Garau and Devlin, 2017). When cost is treated as an individualised value criterion, a careful definition of this criterion is necessary to avoid overlapping with other criteria (for example, when both cost and cost-effectiveness are included), and additional information is needed to identify whether it represents good value for money (whether it is efficient). In most applications there is a need to know where the adoption boundary is located (the maximum cost per incremental point) to the extent that the decisions affect a limited budget.

The second option for taking into account the opportunity cost in the framework of an MCDA would be to construct a composite measure of the benefit (net), compared with the cost (net), an incremental cost-value ratio (ICVR) (Angelis and Kanavos, 2016). This option, the incremental approach of MCDA, requires the establishment of an acceptable level or threshold of incremental cost per benefit point which reflects the opportunity cost and, for consistency, that the cost itself has not been included as one of the criteria in the construction of the value index. The ICVR aims to be used as a guide for the allocation of resources in a similar way to the ICER. It is obvious to point out that, among other conditions, value scores must guarantee conditions of comparability so that interventions can be prioritised according to the incremental cost per point of value. This option would be no more than an ICER with an extended measurement of value.

The MCDA can be used in complementary way to the ICER to adjust it, taking into account additional dimensions of value, the ‘other’ factors that are not measured with the QALYs (complementary approach). In this case, the criticism of the inclusion of cost as a criterion within the MCDA and the explicit absence of the lost benefit as an opportunity cost gains weight. A particular case of the application of this rationale could be, for example, a decision process in two stages. In the first one, the ICER is considered in comparison with the maximum cost threshold per QALY. When the ICER is higher than this threshold, in a second stage the appraisal is complemented by obtaining a value index through the MCDA. Possibly the outranking approach is better suited to a two-stage process of this type than the value-measurement approach.

With a different perspective, although very rare, MCDA can be used as a single method (the pure approach) to estimate the value of an intervention without using the ICER (or, only includ-
TABLE 3.8. KEY ISSUES FOR THE USE OF MCDA IN HTA

<table>
<thead>
<tr>
<th>OPTIONS</th>
<th>ISSUES TO CONSIDER</th>
</tr>
</thead>
</table>
| **Which criteria and weights?** | 1. Set in advance; similarly in all decisions.  
2. Selected case-by-case and varying throughout technologies or disease areas. | 1. It allows the use of the same metric to measure losses and added benefits; it considers consistently all the criteria.  
2. Flexible method. Even so, a systematic consideration of all the criteria and the predictability of decision-making can be difficult. |
| **Which criteria?** | 1. The current criteria of the HTA agencies.  
2. Those of the members of the HTA committee, representing those of the healthcare system.  
3. Reflection of the opinions of the general public. | 1. It is assumed that there is an obligation to consider these criteria.  
2. The involvement of holders of the budget for healthcare can promote an alignment of objectives through various decision-makers in the healthcare system.  
3. They reflect the opinions of the users of the healthcare system/taxpayers. |
| **Which are the preferences for weighting the criteria?** | 1. Any of those involved, defined by the decision-maker.  
2. Members of an HTA committee.  
3. Members of the general public. | 1. In congruence with the current extra-welfarist principles of the HTA. Also, the variations of those involved throughout the diseases require flexible weights.  
2. A paradigmatic method that can avoid carrying out large studies based on preferences.  
3. Consistent with the method used to assess the quality of life in QALYs. |
| **How are opportunity costs incorporated?** | 1. Different criteria for costs.  
2. An aggregate measure of benefits (net) to be set against costs (net). | 1. Risk of overlapping with other criteria (for example, cost and cost-effectiveness).  
2. Requires the fixing of an ‘acceptable cost per increase in the benefit/score scale’. |
| **How can uncertainty be dealt with?** | 1. A separate, different criterion for uncertainty.  
2. Sensitivity analysis techniques. | 1. Measuring and assessing this criterion presents difficulties. Different criteria can be associated with different types and degrees of uncertainty.  
2. One ensures that the fragility of the premises about key evidential issues is taken into account. Similarly, the question of how the results of the sensitivity analysis should affect decision-making is left unanswered. |

QALY: Quality-Adjusted Life-Years.

Source: Garau and Devlin, 2017.

The pure approach could better reflect the opportunity cost of the resources used, provided a threshold is established, although it is very likely that the limitations derived from the specific context and the preferences of the stakeholders included, represent still more serious limitations for the points of value than for the QALYs and the ICER (see Tables 3.7 and 3.8).

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