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Decision Making Criteria in Oncology

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Abstract
Decision making is one of the most complex skills required of an oncologist and is affected by a broad range of parameters. For example, the wide variety of treatment options, with various outcomes, side-effects and costs present challenges in selecting the most appropriate treatment. Many treatment choices are affected by limited scientific evidence, availability of therapies or patient-specific factors. In the decision making process, standardized approaches can be useful, but a multitude of criteria are relevant to this process. Thus, the aim of this review is to summarize common types of decision criteria used in oncology by focusing on 3 main categories: criteria associated with the decision maker (both patient and doctor), decision specific criteria, and the often-overlooked contextual factors. Our review aims to highlight the broad range of decision criteria in use, as well as variations in their interpretation.

Introduction

The process of clinical decision-making is the essence of everyday clinical practice. Various factors influence our judgments and decisions. For various reasons, multiple options are often available for oncological problems [1]. Decision makers' individual characteristics (decision maker as a person), decision-specific characteristics (the nature of the decision itself), and contextual factors (environment in which the decision is being made) shape our decisions [2, 3]. Medical decision making can be particularly complex and multi-layered, involving diagnostic and therapeutic uncertainties, patient preferences and values, and includes the complexities of the healthcare environment. Many decisions made in oncology are not based solely on evidence-based medicine, that is, clinical experience and the best available research. Consequently, eminence-based decision making, representing the opinion of an experienced colleague for example, comes into play [4]. In addition, decision making in medicine ideally involves the patient and thus can be characterized as shared decision making [5]; however, this process is

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often far from perfect [6]. Decision making in oncology involves the consideration of a complex set of diagnostic, therapeutic and prognostic uncertainties, potentially leading to considerable disagreement about the best course of action. This narrative review aims to reflect on various aspects of decision criteria in clinical oncology. Due to the lack of conceptual models for decision making criteria in this context, we built on the model developed in the managerial decision making context by Papadakis et al. [2] and later revised by Elbanna [3]. Our review highlights the broad range of decision criteria, the variation in the interpretation of these criteria, as well as practical approaches dealing with the complexity of everyday decision making.

Existence of Multiple Decision Criteria

Due to a variety of cancers, healthcare systems, treatment options, and individual factors, a plethora of different criteria are being implemented in routine clinical decision making in oncology. This has been demonstrated in decision making analyses of clinical experts. For example, treatment algorithms for the first-line systemic therapy for metastatic clear cell renal cell carcinoma from 11 international experts were analyzed and up to 6 different treatment options were identified for the same specific presentation of the disease. These treatment options were selected based on 7 differentiating treatment criteria [7], excluding universal factors such as, for example, informed consent.

In this review, decision making criteria used in oncology are categorized into 3 categories developed in the field of managerial decision making [2, 3]. We first concentrate on decision maker-related characteristics, including both the physician and the patient. Attributes, such as capabilities, confidence, self-efficacy, emotions, frames of reference, and degree of expertise, also influence decision making [8]; all of these factors affect the decision maker. Second, we consider decision-specific criteria. These involve classical clinical criteria, such as performance status, age, presence of comorbidities, cancer stage, biomarkers, or expected treatment toxicity. Third, we discuss contextual factors that are often overlooked in medical decision making. These factors include the patient's socioeconomic status, the health care system, treatment costs, or influence from the pharmaceutical industry. We use these 3 domains to categorize decision making criteria in oncology (Fig. 1).

Decision Maker-Related Criteria

Traditionally, decision making has been viewed as involving 2 forms of information processing – rational and non-rational modes of thinking [9]. Behavioral science approaches decision making from the perspective that humans do not make decisions as rational, profit-maximizing individuals. Aligned with this perspective, recent studies show that decision making is influenced by factors such as cognitive biases, or emotions [10–12]. Decision makers are often confronted with the trade-off between decision accuracy (how good decisions are) and decision speed (how quickly decisions are made) [13–15]. Especially when multiple options need to be considered, balancing between accuracy and speed in decision making is challenging. To cope with this challenge, decision makers use intuition [16–18], which draws on our ability to synthesize information quickly and effectively and is often based on expertise [19]. Potentially, this non-rational approach is reflected in eminence-based medicine (EBM) and other alternatives strategies to evidence-based medicine [20]. The importance of shared decision making has been increasingly recognized over the past decades and thus both the patient and the physician act as decision makers.

Patient-Related Criteria

Patient-related criteria are central to decision making. Decisions made in tumor boards might be overruled by patients or care-givers – for various reasons, for example, a patient's adherence to treatment or inappropriate behavior that may influence adherence (e.g., disorganized life style and frequent non-attendance at follow-up appointments) or a decision against active cancer treatment (e.g., for best supportive care and focusing on quality of life instead of survival). Non-adherence in cancer patients is a prevalent problem with varying adherence rates reported in literature (16–100%) [21–23]. There are many psychological factors involved when patients consider treatment options, including prior experience, quality of life during or after treatment, life expectancy, opinion of their care provider, and preference of the patient's family. Studies show that if patient preferences and individual goals are being heard, they are more likely to be satisfied and compliant with treatment regimens [24].

Physician-Related Criteria

The knowledge level of the physician affects the process of treatment decision-making. Ideally, decision making is based on high-level evidence, and making good de-

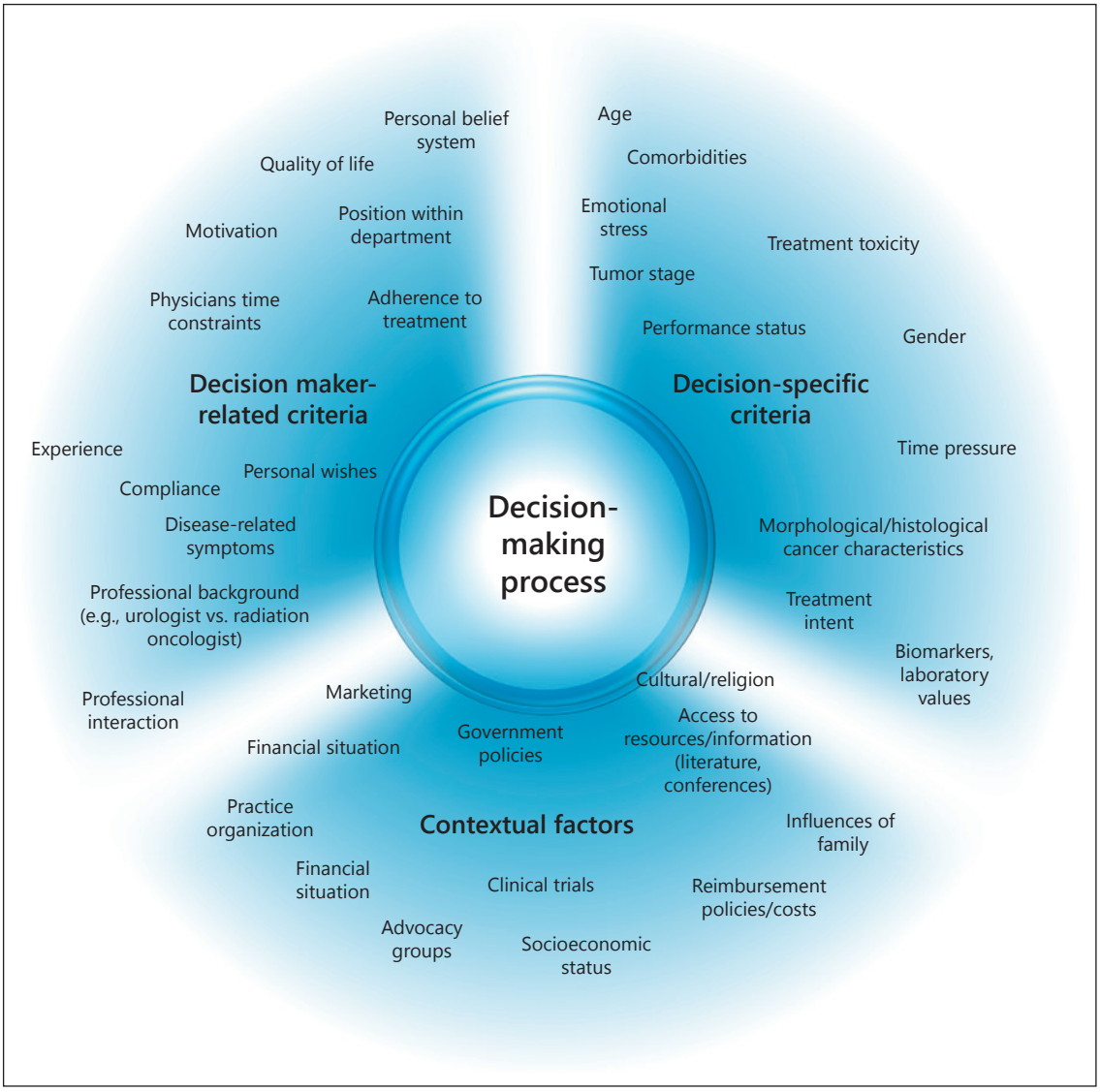

Fig. 1. Conceptual model of decision making criteria in oncology. The 3 main categories of decision criteria with examples are displayed.

cisions requires familiarity with current evidence and the ability to interpret and apply this in a clinical setting. The professional background of the physician is also a relevant factor. A national survey by Fowler et al. [25] reported that urologists tend to prefer surgery, while radiation oncologists tend to favor radiation therapy in managing patients with localized prostate cancer. Another survey [26] showed similar discipline-specific recommendations: gastroenterologists tend to favor surgery, while hematologists and medical oncologists preferred conservative therapy for treating gastric lymphoma. Based on the National Lung Cancer Audit in the United Kingdom, patients with lung cancer first seen in thoracic surgery centers were 51% more likely to have surgery compared to those seen in non-surgical centers (surgery being the strongest determinant of outcome) [27]. Physician-behavior may influence treatment decisions as well: physician's time constraints and work overload in clinical routine can impact recommendations.

Patient-Physician Interaction

The patient-physician interaction also influences decision making. It is important to recognize that both patient and physician may approach the clinical encounter with

different priorities. Physicians often seek to diagnose and treat an illness based on the patient's symptoms and objective information derived from physical examinations, laboratory tests, or the patient's medical history. Conversely, patients may only seek care when symptoms signal there is a problem because of disruptions in their work or social life. Including patient preferences in medical decision-making helps treatment selection, especially when no clear treatment preference exists based on objective outcomes. Even though shared decision making is a laudable goal and routine medical decision making is moving toward this model, there are several limitations to shared decision making, as it is exposed to a variety of biases [6]. Especially in the setting of poor evidence, many clinicians are still more familiar with the paternalistic model [28, 29]. Additionally, in this model, physicians exert control over information and decision making, and the patient may simply comply with what the physician recommends. This approach impacts the decision-making process and influences outcome [30], leading to the undertreatment of elderly women with breast or ovarian cancer [31].

A substantial proportion of individuals making preference-sensitive cancer-related decisions experience decisional conflict. For example, 43% of patients with advanced cancer were uncertain about whether to receive end-of-life care at home or in a health care institution [32]. In another study of cancer patients with advanced non-small-cell lung cancer, only 30% felt sure about choosing chemotherapy or best supportive therapy [33]. Key factors contributing to patients' decisional conflict across these studies included feeling uninformed, having uncertainty about their values, and being unsupported in decision making.

Optimal physician-patient communication has the potential to help regulate patients' emotions, facilitate comprehension of medical information, and allow for better identification of patients' needs, perceptions, and expectations. Trust is one of the central features of patient-physician relationship. A positive relationship and good communication between the patient and physician may lead to higher-quality outcomes and better satisfaction, lower costs of care, greater patient understanding of health issues, and better adherence to the treatment process [34].

Each physician or patient brings their own personal values and beliefs to the decision-making process. Physicians might rank comorbidity and trial results as important factors in treatment decision-making, while patients might rank family preference, family burden, and physician's opinion as important factors in making treatment decisions. To avoid this dissonance, well-organized interdisciplinary collaboration may be essential to facilitate adequate treatment considering all aspects of care, especially including patient preference.

Decision-Specific Characteristics

Decision-specific characteristics are related to the nature of the decision itself. These include all basic decision criteria used in clinical practice. Referring to Elbanna [3] these are criteria important for a decision motive, decision uncertainty and for the importance of a decision. Under acute stress (short-lived, high intensity) we focus on short-term rapid responses at the expense of complex thinking. This type of response can be life-saving when we need to react to immediate danger, but can also lead to "tunnel vision" and ill-thought-through decisions [35]. We need to keep this in mind when we jump to clear conclusions.

Age is a commonly used criterion in oncology. There are different treatment recommendations for children/adolescents (≤18 years of age) and for adults; for example, medulloblastoma patients are treated with different doses of radiation therapy depending on age [36]. Similar impacts of age are observed in the elderly [37]. Elderly patients may not tolerate treatments as well as their younger counterparts. There is emerging evidence that "elderly" people are offered less intensive treatment [38, 39]. However, the interpretation of what "elderly" means and how it is interpreted can be very heterogeneous [40]. Underrepresentation of elderly patients in clinical trials adds to our dilemma in dealing with this population [41, 42].

Comorbidities may result in more conservative treatment, despite evidence that more active treatments may be well tolerated [43]. The evidence concerning potential benefits and harms of cancer treatments among patients with comorbidities is scarce. Clinicians may overestimate potential toxicity or effectiveness of treatments among patients with comorbidities, or underestimate their life expectancies, both leading to potential undertreatment. This has been shown in referral and treatment recommendation patterns [44]. Decisions made for patients with comorbidities or elderly people are less likely to be concordant with clinical guidelines. Vinod et al. [45] reported that 29% of lung cancer patients reviewed in tumor boards were treated outside of guide-

lines, and comorbidity was the cause in 1 out of 4 cases [43].

For many treatment options, a good performance status is a prerequisite. The Karnofsky performance status and the Eastern Cooperative Oncology Group Performance Status scales [46] are commonly used to quantify performance status. When in experienced hands, their measurement can be consistent [47]; however, the cut-off values for decision making are widely variable in clinical routine [40].

The entity of a tumor and the tumor-stage play an important role in the decision making process. Treatment is based largely on the stage/extent of the cancer. Treatment recommendations for localized tumors are different to more advanced disease or metastasized tumors. The position of a single lymph node may determine operability.

Biological features can support decision making as well. An example for such parameters is the promoter methylation of the gene encoding for MGMT in glioblastoma patients. MGMT methylation is a predictive factor of favorable survival in glioblastoma patients undergoing chemotherapy with alkylating agents [48]. Especially for the elderly subpopulation, phase III trials showed that overall survival in methylated patients was better if temozolomide treatment was applied, whereas in unmethylated patients, radiotherapy alone was more effective [49, 50]. Another example for biological features influencing decision making in oncology is OncoType DX assay. Jaafar et al. [51] reported that the use of the assay was associated with a significant change in treatment decisions and an overall reduction of chemotherapy use. Also, the Ki-67 Index, although there is no objectively established cutoff point [52–54], has predictive and prognostic value and is a utilized marker in clinical practice, for example, it independently improves the prediction of treatment response and prognosis in a group of breast cancer patients receiving neoadjuvant treatment [55].

Deciding on the goal of a treatment is sometimes a problem. For oligo-metastatic prostate cancer [56], do we want to improve progression-free survival, androgen deprivation therapy free time or even overall survival? Deciding on one of these goals in order to improve quality or quantity of life will influence the recommendation to treat or not to treat, the level of data available to support the decision and potentially the level of side effects the patient is willing to risk. The chosen goal of a specific therapy influences the selection of decision criteria.

Contextual Factors

Papadakis et al. [2] described contextual factors referring to external corporate environment and internal firm characteristics. Translated to medicine, these are factors that include for example the structure of an institute, the environment including government policies, reimbursement, structure of the healthcare provider as well as the patient's socioeconomic status.

While the physician recommendation plays a major role in decision making, insurance coverage cannot be ignored. In some settings, clinical benefit may be considered relevant, but reimbursement is rejected on the grounds of insufficient cost-effectiveness [57]. Insurance coverage influences many medical decisions, including which tests and procedures are implemented, sometimes even determining which patients are cared for. The increasing costs of cancer care impacts all elements of the healthcare system. Decisions in healthcare policy and individual clinical problems require careful weighing of risks and benefits and are commonly a trade-off of competing objectives: maximizing quality of life versus maximizing life expectancy vs. minimizing the resources required. Hopefully costs are not the primary driver when choosing treatments, but they must be acknowledged. Nadler et al. [58] reported that for most oncologists, costs do not influence their clinical practice and should not limit access to what they consider effective care. Around 80% of physicians would prescribe effective therapy regardless of cost, but the majority did not believe that these therapies necessarily offered good value [58]. Associated factors such as insurance status, availability of technology/drugs, and even rural or urban location influence decision making [1, 59–61].

The type of practice (e.g., private vs. public), size, and organization might influence decision making [62–64]. Physicians practicing in client-dependent practices respond more readily to the wishes of patients. On the other hand, physicians practicing in a colleague-dependent practice respond more readily to influences from their professional community [63]. Physicians are more likely to be early adopters of new drugs if they are involved in the medical community, for example, having regular contact with colleagues and hospital consultants [65–67].

Medical representatives visiting physicians can affect prescribing practices [68]. One of the major generators of the scientific output is the industry, a known influencer of clinical decision making [69]. A study in Saudi Arabia [70] reported 41% of the physicians' decisions regarding

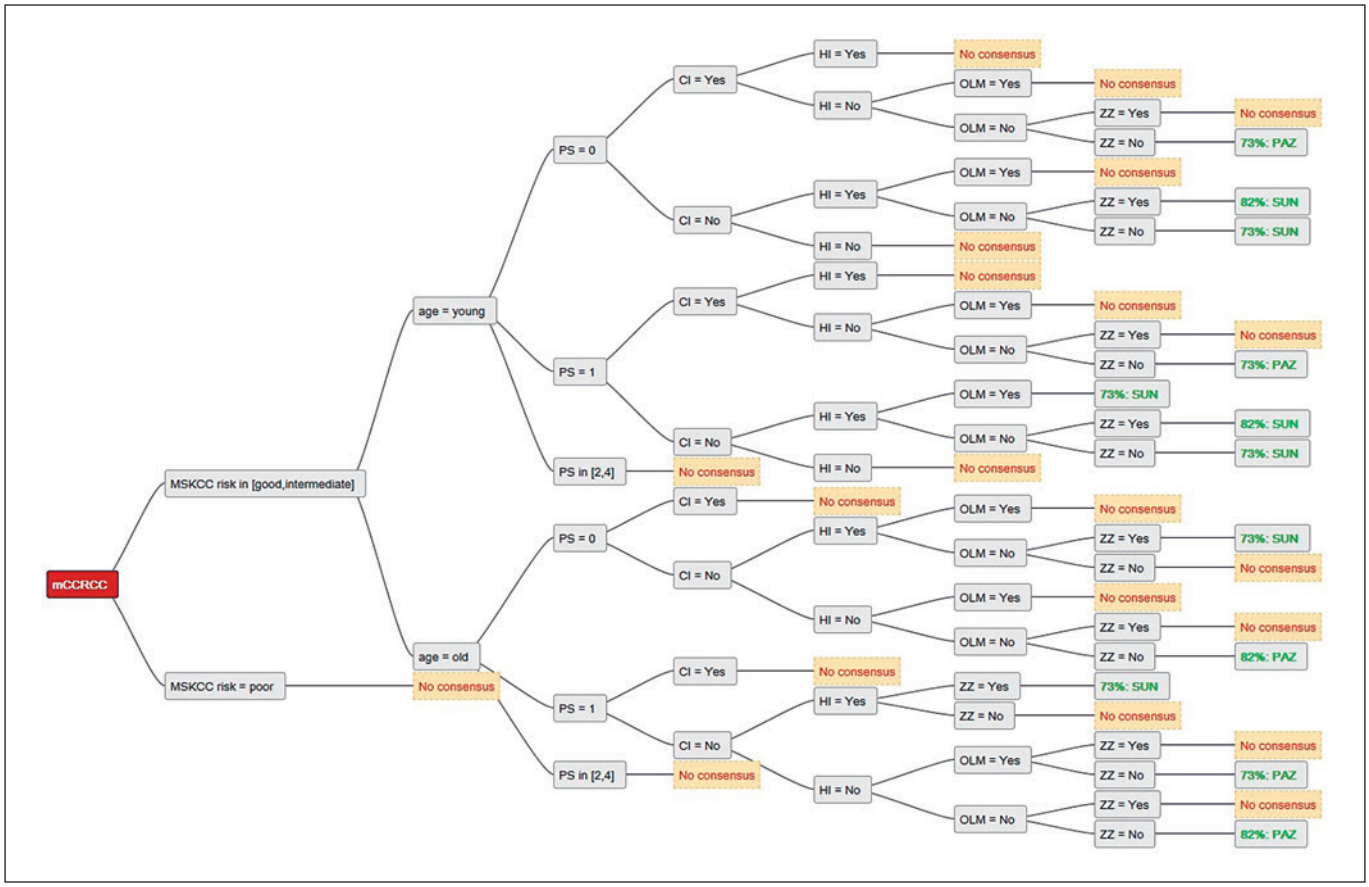

Fig. 2. The consensus for 11 decision trees for systemic therapy of metastatic clear-cell renal cell cancer. A decision tree showing combinations of decision criteria where at least 8 of 11 centers agreed on the same recommendation. All relevant criteria are displayed and combined to reach every possible combination. For example, for the top-most row, when these criteria are fulfilled there is no consensus. For the fourth row, the most common recommendation is pazopanib in 73% (8 out of 11 centers recommend PAZ). CI, cardiac insufficiency; mccRCC, metastatic clear cell renal cell carcinoma; MSKCC, Memorial Sloan Kettering Cancer Center; OLM, only or mainly lung metastases; PAZ, pazopanib; PS, performance status; SUN, sunitinib; ZZ, zugzwang (the compulsion to move).

drug prescriptions were influenced by medical representatives.

Clinicians who engage in EBM need to acknowledge the social and cultural factors that affect the health-care encounter, understand the important role of those factors in health-care decision making, and expand the paradigm of EBM to incorporate sociocultural influences more explicitly.

Process of Decision Making

Most recommendations in oncology are not based solely on high-level evidence [71, 72]. While guideline adherence can rightfully be viewed as positive, one should be aware that only 6% of the recommendations found in NCCN guidelines are based on high-level evidence [73]. Even in the clinical routine of academic oncology centers, most treatments are not based on high-level evidence [74]. In these settings, lower levels of evidence are used, for example, the results of phase II trials or observational studies. Where none of this evidence is available, recommendations are based on expert opinion.

Decision theory and related research concentrates on choice – the selection of the best option from a choice set containing 2 or more options, and the process of reasoning over multiple options [75]. Clinical recommendations in the form of decision trees, ideally based on high-level evidence, aim to identify the best option from a predefined set based on parameters (branches of the decision

tree). When multiple options are considered, pre-choice (or screening) is important, as it reduces the decision maker's workload and risk for wrong choices [75, 76]. An approach purely based on clinical algorithms (e.g., decision trees) and traditional EBM alone may be insufficient, especially when the limited availability of information and complexity of the patient and the environment are not sufficiently considered.

Using structured approaches to decision making involving multiple criteria can provide insight into objective parameters of decision making. An example for such an approach is the objective consensus methodology [77]. By analyzing and comparing decision trees based on the same rules and terminology, information on medical decision making among medical experts can be obtained. Based on information from multiple sources in the decision tree format, treatment recommendations can be assessed for every possible parameter combination (permutation; Fig. 2) [7]. For various cancer forms and settings, even among highly specialized medical centers or experts, the use of decision criteria varies considerably [7, 40, 78–80].

How criteria are weighed is influenced by the healthcare setting, the institution or the individual physician as well as the patient. The decision making process is very complex. Variable criteria weights and different aggregation rules lead to a multitude of possible interpretations and implications. Also, the impact of each of the abovementioned categories of decision criteria varies, the lines between these categories can blur at times and there is interaction between these categories. For example, the "contextual" factors may dominate in some settings when they influence the number of available options: selecting from treatment options is only possible when the infrastructure for these treatments is available. In highly symptomatic patients, for example, due to the tumor-related compression of the spinal canal, the need for quick intervention dominates and thus the "decision-specific" criteria define the decision making pattern. In such a scenario, zugzwang (the compulsion to move) is based in decision-specific factors (the disease requiring urgent treatment); however, the compulsion is perceived by the patient, or even the physician [7].

Conclusion

When oncologists and patients are confronted with multiple decision options, their choice is influenced by several factors extending beyond rational or analytical decision making models. For decision makers, whether they are individuals or committees, it is challenging to process and evaluate all relevant information. As demonstrated, a myriad of different decision criteria is used in oncology. While the list presented is by far not exhaustive, it demonstrates the complexities and variability of decision making criteria in oncology. For any improvements in our decision making to be possible, we first need to acknowledge the complexity of decision making criteria and the impact they have.

Disclosure Statement

The authors declare they have no competing interests.

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