

REVIEW

A taxonomy of the factors contributing to the overtreatment of cancer patients at the end of life. What is the problem? Why does it happen? How can it be addressed?

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Many patients with cancer approaching the end of life (EOL) continue to receive treatments that are unlikely to provide meaningful clinical benefit, potentially causing more harm than good. This is called overtreatment at the EOL. Overtreatment harms patients by causing side-effects, increasing health care costs, delaying important discussions about and preparation for EOL care, and occasionally accelerating death. Overtreatment can also strain health care resources, reducing those available for palliative care services, and cause moral distress for clinicians and treatment teams. This article reviews the factors contributing to the overtreatment of patients with cancer at the EOL. It addresses the complex range of social, psychological, and cognitive factors affecting oncologists, patients, and patients' family members that contribute to this phenomenon. This intricate and complex dynamic complicates the task of reducing overtreatment. Addressing these driving factors requires a cooperative approach involving oncologists, oncology nurses, professional societies, public policy, and public education. We therefore discuss approaches and strategies to mitigate cultural and professional influences driving overtreatment, reduce the seduction of new technologies, improve clinician–patient communication regarding therapeutic options for patients approaching the EOL, and address cognitive biases that can contribute to overtreatment at the EOL.

Key words: advanced cancer, overtreatment, end-of-life care, palliative care, communication, informed consent

INTRODUCTION

In the management of patients with far-advanced cancer, oncologists are motivated by the desire to maintain hope and to promote the interests of their patients. In doing so, they walk a fine line between delivering effective treatments that make a meaningful difference in how well and how long patients live, and overtreatment. Overtreatment refers to the use of medical interventions that are unlikely to provide meaningful clinical benefit to a patient, with a high probability of causing more harm than good.¹ Harms

may involve direct patient harms or societal harms from the nonbeneficial use of limited health care resources.

Despite advancements in palliative care and a growing emphasis on patient-centered approaches, 10%-40% of patients with cancer are overtreated with various anti-cancer treatments in their final weeks of life.²⁻¹² The proportion of patients who are overtreated is higher in males, younger adults, children, and patients with hematological malignancies.^{11,13} In recent years there has been a rising incidence of overtreatment with immunotherapy and molecularly targeted therapy.^{3,12,14}

There are three major classes of overtreatment, which in clinical practice frequently co-occur: overtreatment related to diagnostic modalities, to treatment modalities, and to patient factors (Table 1). Overtreatment related to treatment modalities may involve excessive use of systemic anticancer therapies (including chemotherapy, targeted therapies, and immunotherapy), radiation therapy, or

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Table 1. Types of overtreatment		
Category	Type of overtreatment	Description
Overtreatment caused by diagnostic modalities		
Overdiagnosis	Identification of cancer unlikely to cause harm	Early detection of slow-growing or indolent cancers
Overtreatment related to treatment modalities		
Unnecessary surgery	Inappropriate extensive surgery when less-invasive methods are suitable	Surgical plan not appropriate to tumor characteristics, age, overall health, or goals of care
	Inappropriate use of expensive technologies (such as robotic- or laser-assisted surgery)	Use of expensive therapies when equivalent outcomes could be achieved with lesser expense
Excessive systemic cancer therapies	Inappropriate treatment selection	Availability of less-intensive options with better risk-to-benefit ratio
	Inappropriate dosing and duration	Dose intensification or extended duration of therapy not supported by adequate evidence
Excessive radiation therapy	Inappropriate, nonevidence-based treatment	Off-label use unsupported by clinical research data
	Not cost-effective	Use of expensive therapies when equivalent outcomes could be achieved with lesser expense
	Inappropriate treatment selection	Availability of less-intensive options with better risk-to-benefit ratio
	Inappropriate dosing	Dose intensification or fractionation
	Inappropriate fractionation	Use of many fractions when single-fraction treatment is adequate
	Inappropriate use of advanced technology	Use of stereotactic body radiation therapy or proton beam therapy when standard treatment approaches provide similar outcomes
Overtreatment due to patient factors		
Age-inappropriate treatment	Aggressive treatment for older patients with comorbidities	Lack of consideration of comorbidity burden and ability to tolerate side-effects
Inappropriate treatment for patients with poor performance status	Aggressive treatment for patients with low functional capacity	Disregard for overall health and ability to function
Inappropriate treatment for patients near the end of life	Aggressive treatment for patients with very poor prognosis near the end of life	
Ignoring patient preferences	Treatment not aligned with patient goals	Lack of shared decision making and prioritizing survival over quality of life

surgery.^{11,15,16} This paper focuses on the nonbeneficial use of anticancer therapies at the end of life (EOL).

While patients with treatment-resistant advanced cancer who have good performance status and physiological reserve may benefit from further trials of treatment or participation in clinical research, patients with poor performance status, with or without advanced vital organ involvement, are more likely to be harmed than helped by further therapies. Overtreatment in this latter setting is often characterized as ‘medically futile’. However, because ‘futility’ is subjective, the use of this term is discouraged, and the term ‘medically nonbeneficial’ is generally preferred.¹⁷ Consequently, overtreatment should be distinguished from other scenarios of advanced cancer management such as participation in early-phase research studies, or when well-informed, fit patients request a trial of treatments with low but evidence-based prospects of meaningful benefit.

The American Society of Clinical Oncology’s (ASCO) Choosing Wisely recommendations admonish against overtreatment: “Don’t use cancer-directed therapy for solid tumor patients with the following characteristics: low performance status (3 or 4), no benefit from prior evidence-based interventions, and no strong evidence supporting the clinical value of further anticancer treatment.¹⁸ Cancer-directed treatments are likely to be ineffective and more toxic for solid tumor patients who meet the above-stated criteria.” This admonition is followed by two qualifications: (i) ‘Exceptions may include when disease

characteristics (e.g. an extremely chemo-sensitive tumor, or a sensitive and targetable alteration in the tumor) suggest a high likelihood of a response to therapy that may reverse functional limitations related to the cancer,’ and (ii) ‘While this Choosing Wisely statement originally referred to cytotoxic chemotherapy, it also applies to novel, purportedly less-toxic treatments such as immunotherapy and off-label targeted therapy in patients who meet the above-stated criteria.’ The strength of this admonition reflects the level of concern regarding the adverse consequences and harms of overtreatment. This approach is also incorporated in the European Society of Medical Oncology (ESMO) guidelines regarding the care of patients at the EOL.¹⁹

While there is some evidence that patients with advanced cancer and short life expectancy may be willing to accept considerable toxicity for a small chance of benefit,²⁰ other studies indicate that patients and their families often expect much greater benefits than are likely.^{16,21,22} Indeed, treatments often offer much less survival benefit than patients report would justify additional treatment.^{21,23,24}

Survival gain thresholds for which patients would consider having further anticancer treatments have been evaluated in several studies. A German study by Mende et al.²¹ assessed the attitudes of 134 patients previously treated with chemotherapy for advanced cancer. The median additional survival gain threshold for which patients would consider having further chemotherapy was 33 months for patients with colorectal cancer and 18 months for patients with other cancers. In a study involving 71

patients with unresectable and metastatic pancreatic cancer by Pihlak et al.,²² the minimal survival gain threshold for [‘additional’?] treatments was 1-5 years for 32% of respondents and >5 years for 11%. In a study by Patil et al.,²⁴ of 200 patients with advanced head and neck cancer and anticipated survival of <1 year, the minimum expected increment in life expectancy for taking palliative chemotherapy was >1 year in 190 patients.

Adverse consequences and harms of overtreatment in the setting of advanced cancer

The reflexive prescribing of further anticancer treatment to patients with advanced and refractory cancers promotes a collusive illusion of limitless therapeutic solutions,²⁵ with many resultant risks and harms.

The nonbeneficial nature of overtreatment for patients with advanced cancer was demonstrated in a recent study. Canavan et al.²⁶ evaluated the impact of aggressive systemic anticancer therapies on overall survival. They evaluated 78 446 patients with six common solid tumors in 144 practices from the time of diagnosis of metastatic disease to death. The study found no significant difference in survival outcomes between patients treated in practices with the highest rates of treatment for highly advanced cancer and practices with the lowest rates.

Specific patient harms may include a high risk of adverse effects,^{27,28} increased likelihood of hospital or even intensive care unit admission,^{27,28} and diminished quality of life.^{16,29-31} Furthermore, the emotional strain of enduring nonbeneficial treatments can contribute to the patients’ anxiety and depression.¹⁶ Overtreatment close to the EOL is associated with substantial opportunity costs for both patients and their families, particularly when life expectancy is short; time devoted to treatments is often at the expense of time with family or time devoted to other meaningful life goals and/or pleasures.^{32,33} This has been called ‘time toxicity’. The presentation of inflated expectations from treatments with a low likelihood of benefit to patients and their families in this setting also undermines true informed consent and delays important discussions about EOL priorities and care planning.³⁴⁻³⁶

There are also economic harms and harms at the level of the treating clinicians. Economic harms include the strain on public health care resources^{37,38} and, if patients are paying out of pocket, the personal resources of patients and their families.^{38,39} From a public health perspective, the very high cost of providing these treatments diverts resources that could be better applied elsewhere, including the development of more robust palliative care services than the limited services currently available.^{38,40,41}

For treating clinicians, especially for the oncologists and the nursing staff involved in the delivery of treatment, overtreatment can cause moral distress, guilt, and remorse.⁴²⁻⁴⁵ All of these responses can contribute to clinician burnout.⁴⁶

DECISION MAKING ABOUT TREATMENT IN THE SETTING OF FAR-ADVANCED CANCER

Oncologists and their patients with advanced cancer who are approaching the EOL confront difficult decisions in fateful and emotionally charged circumstances. The evolving understanding of the intricacy of the decision-making process now increasingly recognizes the complex interaction between objective considerations (such as prognosis and likelihood of benefits and harms), culture, emotion, and cognitive factors.⁴⁷ This complex interplay of factors affects decision making by oncologists, patients, and family members (Figure 1 and Table 2).

PSYCHOLOGICAL FACTORS

Fear and ‘the counterphobic determination to treat’

The fear of death can be a potent motivator for patients, their families, and physicians. For patients and their families, the fear of death can lead to a desperate clinging to anticancer treatments, even when potential benefits are marginal or possibly even nonexistent.^{34,48,49} Aggressive treatment may be seen as a way of fighting back against an otherwise inevitable outcome, offering a sense of control over the situation. Indeed, oncologists often perceive that anticancer treatment toward the EOL is patient-driven, rationalizing its prescription as an effort to palliate emotional distress.³⁴

Oncologists may unintentionally reinforce the determination to treat by presenting an overly optimistic prognosis or an exaggerated likelihood of benefit from treatments, by not being explicit about the limitations of treatments, and by not addressing important issues surrounding EOL care, such as opportunity costs, time toxicity, and financial toxicity.⁵⁰

Justifiably, oncologists commonly fear causing emotional distress, shattering the hopes of patients and their loved ones, and then needing to deal with this distress. These fears sometimes lead to an avoidance of crucial conversations regarding care at the EOL.³⁵ It is much easier for oncologists to suggest another line of treatment or consideration of a phase I study with emphasis on the potential benefits of a new treatment than to discuss EOL issues.³⁴⁻³⁶ This is especially true among physicians who have difficulty initiating and guiding conversations about transitioning to a palliative and supportive care approach and those who have limited access to dedicated and effective palliative care teams and resources.^{34,35} Professor Margaret Lederberg, a psycho-oncologist at Memorial Sloan Kettering Cancer Center, described this as a ‘counterphobic determination to treat’ (personal communication).

Hope preservation

Hope can be a powerful motivator for patients to continue anticancer treatments, even when the likelihood of benefit is limited.⁵¹⁻⁵³ For patients and their families, the uncertain

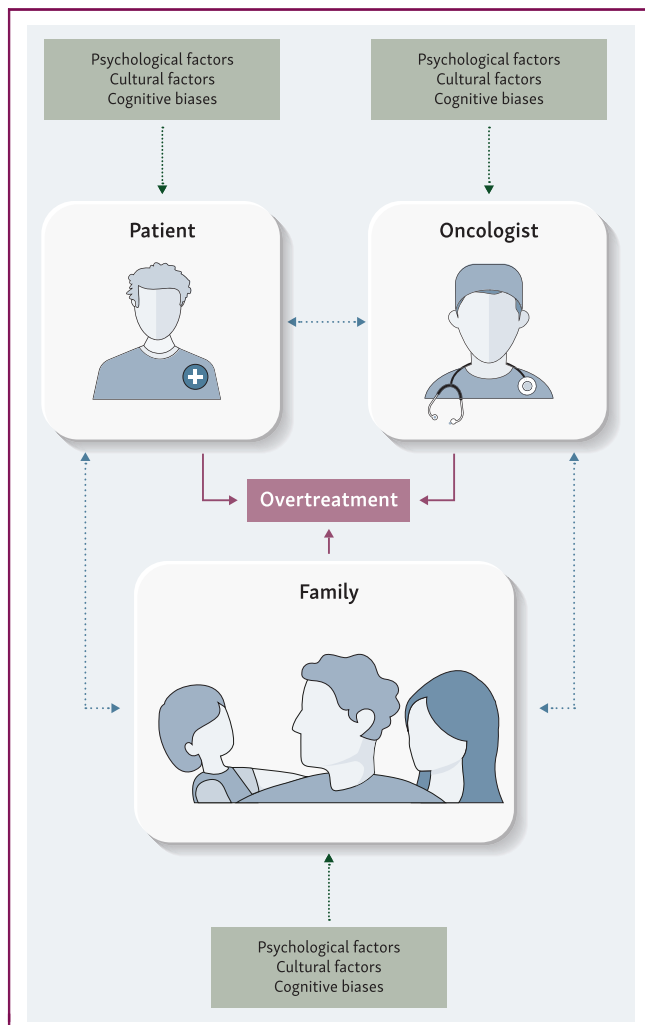


Figure 1. Factors contributing to overtreatment at the end of life.

possibility that a new treatment may generate some added benefit is often preferred to the perceived certainties associated with a palliative care option with no anticancer treatments.^{34,35} Some oncologists perceive that their professional role is to sustain hope and, consequently, not to guide patients to EOL care options, which patients perceive as a loss of hope.^{34,35}

Denial and anger

Denial can prevent patients from fully understanding the implications of far-advanced and refractory cancer⁵⁴ and lead them to prioritize aggressive intervention over informed decision making, even when the treatment may carry a greater likelihood of harm than benefit. Anger can also play a role, pushing patients toward a ‘fight back’ mentality that may prioritize anticancer treatment regardless of its side-effects.⁴⁹

Desire for control

Some oncologists and their patients view continuing treatment as a way of asserting control over the cancer⁵⁵; the

Psychological factors	Fear and ‘the counterphobic determination to treat’ Hope preservation Denial and anger Desire for control Decision fatigue Oncologist–patient relationship
Social and cultural factors	Societal norms and expectations Cultural and religious beliefs Emotional pressure from family Medical culture Professional norms within oncology Institutional and departmental culture Financial and legal considerations Oncologist workload and time constraints
Cognitive biases and heuristics	Optimism bias Confirmation bias Novelty bias (the seductiveness of new technologies) Availability (recall) bias Overconfidence bias Loss-aversion bias Bandwagon heuristic Anchoring bias Affect heuristic Framing bias

idea of transitioning to palliative care or hospice is equated with relinquishing control and becoming dependent on others. By contrast, the act of ‘doing something’ can promote a sense of control, even when control may not objectively exist. This can lead oncologists to recommend further treatments, and patients to persist in treatments, even when the likelihood of benefit is minimal.

Decision fatigue

The complex decision-making process associated with cancer treatment, often coupled with the emotional stress of the illness, can, over time, cause mental exhaustion resulting from the repeated need to make choices. The sheer volume of information presented during consultations, along with emotional distress, can contribute to decision fatigue, in which patients feel overwhelmed by choices and rely on treatment continuation as a default.³³ Medical jargon such as ‘palliative care’, ‘quality of life’, and ‘end-of-life care’ can be confusing, especially if patients are not familiar with these terms. As a result, patients may not fully comprehend the gravity of their situation or the rationale behind their oncologist’s recommendation to limit treatment.³³

The oncologist–patient relationship

The dynamics of the oncologist–patient relationship impact treatment decisions. Unless the patient has a high level of medical literacy, the relationship has a clear power imbalance wherein physicians have the power because of their knowledge of what they choose to discuss or disclose, and how they present issues such as prognosis and the likelihood of benefit from further treatments.

Inadequate communication lacking open and candid discussions regarding goals of care,³³ prognosis, and relative risks and benefits of treatment options^{36,56} often results in unrealistically optimistic expectations about the effectiveness of further treatments. Consequently, many patients only get filtered information that reflects the biases and values of their treating oncologist. Empiric data indicate that oncologists frequently choose not to disclose the limited likelihood or scope of benefits of proposed anti-tumor therapies in the setting of advanced cancer⁵⁷⁻⁶⁴ and that many patients often receive less information than they want.⁶⁵⁻⁶⁷

Furthermore, even when there is a candid discussion of treatment options, there is often a major gap between the information provided by health care professionals and the patient's or family's understanding of that information. Even when oncologists present treatment options with a clear explanation of risks, benefits, and likely outcomes, many patients do not fully grasp the limitations of treatment. For instance, they may interpret 'chance of remission' as a 'guarantee of cure', rather than an improvement in symptoms or temporary disease control. These misunderstandings can drive the continued pursuit of aggressive therapies.

Sometimes, patients pressure their oncologists to pursue overtreatment even when further treatment is no longer medically advisable. Despite oncologists' efforts to explain that continuing treatment would be ineffective, some patients persist in their demands. In some cases, patients may even threaten legal action if treatment is not provided, or resort to emotional pleas such as crying to compel oncologists to proceed.⁴⁹ Complying with such requests may be a 'path of least resistance' that is much easier than dealing with emotionally charged discussions about impending death,⁴⁹ or an expression of what has been called 'necessary collusion', whereby patients and physicians avoid discussing prognosis openly, leading to continued treatments that may not be beneficial.⁶⁸

Despite the former considerations, patients who perceive their oncologists as trustworthy, caring, and empathetic are more likely to accept the option of palliative care as the preferred strategy for EOL care.^{69,70} However, these qualities are difficult to achieve in settings where there is poor continuity of care.⁷¹

SOCIAL AND CULTURAL FACTORS CONTRIBUTING TO OVERTREATMENT

Cultural norms and expectations

Cultural norms and beliefs about death and dying significantly influence treatment decisions. In many cultures, death is viewed as a defeat or a failure, leading to a preference for antitumor treatments to defer death rather than a focus on palliative care to address the process of dying.^{72,73}

Societal expectations to fight cancer aggressively can pressure patients and clinicians toward overtreatment.⁷⁴ There is a cultural glorification of 'fighting' disease, often

reflected in a language such as 'battling cancer'. This 'warrior' mentality can create pressure to pursue all possible treatments, however remote the benefits, overlooking the potential downsides of specific treatments.^{49,74} The narrative framing cancer treatment as a 'battle' can further contribute to the social stigma associated with palliative care and hospice, which are often viewed as 'giving up' rather than as stage-appropriate treatments focusing on comfort and quality of life. This stigma can lead to resistance from patients and families to opting for palliative care.

The hype regarding medical progress by lay press,⁷⁵ cancer centers,^{76,77} patient social media influencers,⁷⁸ and treating physicians⁷⁹ fosters inappropriately high expectations that new treatments and interventions will substantially prolong life even for patients with far-advanced and refractory cancers. In countries where direct-to-consumer pharmaceutical advertising is allowed, a barrage of TV commercials touting new cancer treatments gives false hope that there is always one more treatment to try.⁸⁰ This can result in a preference for new treatments and technologies even when the current prognosis is poor and the likelihood of actual benefit is very low.

Cultural and religious beliefs

In some cultural and religious frameworks, enduring pain or 'fighting' the disease may be viewed as morally or spiritually commendable.^{81,82} The idea of ceasing aggressive treatment can be seen as dishonorable, a moral failure, or a reflection of a lack of faith in a higher power.

In certain religious contexts, some patients and families believe that miracles can occur, even in the most advanced stages of illness.^{83,84} This belief may lead to the continued pursuit of treatment even when there is little to no clinical benefit expected. Refusing further interventions may be seen as expressing a lack of faith, which reinforces the drive for overtreatment.

Emotional pressure from family

Patients are commonly influenced by the emotions and desires of family members. Particularly in cultures with strong familial bonds, family members sometimes want to 'do everything possible' to extend the life of their loved ones, even if the treatments cause harm or prolong suffering.^{85,86} Family members, especially those who may feel guilty for not having been able to support the patient earlier, may push for continued treatments as a way of showing love and commitment.^{87,88} Patients may agree to aggressive treatments not because they believe the treatments will help, but because they do not want to let their family down.⁸⁵

Medical culture

Physicians' attitudes and beliefs about death, dying, and the effectiveness of treatments play a substantial role in overtreatment.⁴⁹ Many physicians feel that it is their duty to exhaust all options.⁸⁹ This is called the 'therapeutic

imperative'.⁹⁰ Combined with optimism about and confidence in the efficacy of new medical technologies and treatments,⁴⁹ this therapeutic imperative can overshadow critical evaluation of the effectiveness and suitability of treatments for patients approaching the EOL.

Professional norms within oncology

Professional norms within oncology can contribute to overtreatment. The training and professional identity of oncologists often emphasize life-prolonging approaches.^{48,49,91} Some oncologists perceive that their expert subspecialty knowledge provides added value in care planning. However, this knowledge often pertains to very late-line niche therapies in fit patients that often translate poorly to the standard low-performance-status patient with far-advanced cancer.

Many oncologists receive limited training in EOL care, including communication about prognosis and palliative care options.⁹¹⁻⁹⁴ Palliative care generally receives low priority in oncology training.^{94,95} This is reflected in the content of oncology professional congresses and journals. Indeed, some oncologists do not consider EOL care to be part of their professional role.^{30,91} This gap in education can contribute to a default approach of continuing the search for another treatment.

Some oncology professionals view a reluctance to intervene aggressively with further lines of therapy as a form of therapeutic nihilism.³⁶ Indeed, the ongoing use of anti-cancer therapies avoids peer criticism for 'giving up' on patients prematurely.⁴⁸ This orientation can make it difficult for oncologists to shift to a focus on palliative care even at the EOL.

In addition, some studies have shown that oncologists worry that honest prognostic communication may take away patients' hope, consequently undermining patients' quality of life and possibly even causing them to die sooner.^{34,91}

Another driver of EOL overtreatment may be that oncology training and faculty academic promotion heavily incentivize clinical trial enrollment and drug discovery. Oncologists often feel pressure to enroll patients in early-stage clinical trials,⁹⁶ often phase I dose-finding trials, which rarely offer a survival benefit and can bring an additional treatment burden (such as frequent visits, infusions, and blood draws).^{96,97} Discussion about the competing pressures of clinical trial enrollment and stopping therapy to pursue holistic EOL care is often taboo at specialized cancer centers, which are evaluated and funded largely on the basis of their research success.

Institutional and departmental cultures

There are substantial differences in the cultures of care between different hospitals and different oncology departments,^{98,99} particularly regarding the aggressiveness of anticancer care at the EOL, the degree of integration of palliative care, and the availability of palliative care services.¹⁰⁰

Financial and legal considerations impacting oncologists

Financial incentives, such as fee-for-service payments to oncologists (e.g. commissions on medicines used or on total billing, or per-fraction billing for radiotherapy) can incentivize overtreatment.^{49,101,102} In addition, the threat of litigation can lead to a practice of 'defensive medicine', in which physicians recommend more aggressive treatment plans to minimize the risk of malpractice claims, even if the risk of litigation is small and the potential treatment benefit is minimal.⁴⁹

Oncologist workload and time constraints

Oncologists often face demanding schedules with high patient loads, administrative tasks, and urgent cases. This time pressure can limit their ability to have thorough, empathetic discussions about EOL care options, patient values, and goals.¹⁰³ Consequently, patients may not fully understand their prognosis or the limited benefits of aggressive treatment in advanced disease stages and there may be less opportunity to explore alternatives such as palliative care, leading to default decisions for continued treatments.

COGNITIVE BIASES AND HEURISTICS

Clinical decision making is a complex endeavor involving both intuitive and analytic processes. It has been estimated that people spend ~95% of their time in the intuitive mode, with a much smaller proportion of time dedicated to deliberate, focused, analytical thinking.¹⁰⁴ The intuitive mode of decision making is characterized by shortcuts called heuristics¹⁰⁴ which are vulnerable to systematic errors, or cognitive biases.¹⁰⁴ These cognitive shortcuts become anchoring defaults that allow us to apply our mental and emotional energy elsewhere. Cognitive biases commonly impact clinical decision making^{105,106} and contribute to overtreatment in oncology.^{107,108}

These intuitive heuristics and biases are derived from four processes.¹⁰⁹ Some were naturally selected in our evolutionary past for their adaptive value. Some are regulated by our emotions of happiness, sadness, fear, surprise, anger, and disgust. A third group is developed through overlearning and repeated exposures. A final group is acquired through an unintentional and unconscious osmosis process called 'implicit learning'. In an example of implicit learning, oncology trainees might subtly acquire biases by simply spending time with more senior clinicians who express these biases in their practice, even though the bias is never deliberately articulated or overtly expressed. This has been called the 'hidden curriculum'.¹⁰⁹

Optimism bias

Optimism bias refers to the tendency to overestimate the likelihood of positive outcomes and underestimate the likelihood of negative outcomes. In oncology care, optimism bias contributes to overestimating patient prognosis¹¹⁰ or the likelihood of benefit from a particular treatment and underestimating the risks of harm and the burden of

treatment.¹¹¹ The optimism bias of oncologists can lead them to communicate unrealistically optimistic expectations to patients and their families, which undermines authentic informed consent. Contributing factors include wishing to maintain hope and a lack of feedback to oncologists regarding the accuracy of their prognosis, the effectiveness of their treatments, adverse effects, and other patient and family harms such as financial toxicity and time toxicity. Optimism bias among patients can be reflected in a sense of hope that they will be an exception to the typical outcomes, sometimes due to hearing about anecdotes of recovery in others with advanced-stage cancer.

Confirmation bias

Confirmation bias, which commonly coexists with optimism bias, refers to the tendency to seek out information that confirms one's existing beliefs and to disregard information that contradicts them.^{105,108,112} This can lead oncologists to focus on evidence that supports their initial diagnosis or proposed treatment plan while neglecting alternative possibilities. Confirmation bias can influence how oncologists interpret the findings of new clinical research, causing them to focus on the benefits (even when they are small), and to minimize or ignore the consequences of adverse effects or bias in the study's implementation or interpretation.

Novelty bias (the seductiveness of new technologies)

Novelty bias, sometimes called 'the seductiveness of new technologies', refers to the allure and excitement surrounding new 'breakthroughs'. It is driven by the initial excitement and hype for better outcomes and/or enhanced precision and by the desire to want to practice cutting-edge oncology.⁷⁴

The novelty bias that new treatments are better can synergize with confirmation bias, and both can lead to a suspension of critical evaluation, an overlooking of bias in the design and/or implementation of supporting studies, an overestimation of potential benefits, an overlooking of patient harms, and prioritizing adoption of new technologies over established treatments even when their efficacy and safety profiles are not well characterized.

There are substantial downsides to the rapid adoption of new therapies that are supported by limited and often low-level evidence for efficacy.¹¹³ Many new agents have unique adverse effects, some with long-term consequences, and they can involve substantial financial toxicity to the health care system or to patients and their families. Often there is a large gap between anticipated outcomes and actual outcomes, and some approvals are subsequently withdrawn due to lack of confirmatory data.¹¹³

Factors contributing to the seductiveness of new treatments and technologies include corporate promotion and hype. Pharmaceutical companies and device manufacturers heavily promote their latest products, and this pressures clinicians to incorporate these treatments and technologies into their practice.^{114,115} Often, this is exacerbated by financial incentives such as industry-sponsored research

grants, consulting fees, and speakers' fees, all of which can lead to a subconscious bias toward using the promoted medicines or technology.^{102,115} Patients and their families may also be incentivized to request or even expect new treatments or diagnostic tests based on the hype generated by media coverage,⁷⁵ peer recommendations, and the perception of innovation.¹¹⁶ Clinicians may feel pressured to meet patient expectations for the latest treatments in response to patient demand, overriding considerations of clinical necessity, cost-effectiveness, or evidence-based practice.

Availability (recall) bias

Availability bias, also called recall bias, refers to the tendency to overestimate the likelihood of events based on recall.¹⁰⁴ Oncologists are more likely to remember exceptional responders who are still in follow-up than patients who die despite having received nonbeneficial, last-ditch treatments at the EOL.¹¹⁷ Several quality measures endorsed by the ASCO and the National Quality Forum aim to provide data that can counter the 'positive response' recall bias, including rates of systemic therapy given within 14 days of death, or rates of hospital, emergency department, and intensive care unit admission in the 30 days preceding death.^{118,119}

Overconfidence bias

Overconfidence bias refers to the tendency to overestimate the accuracy of one's judgments, leading one to disregard potentially important information or alternative perspectives.¹²⁰ Among oncologists, this bias may lead to overlooking relevant data or expertise from other sources, reluctance to seek second opinions or consider alternative approaches, and to not taking advantage of peer input through multidisciplinary tumor boards.

Loss-aversion bias

Losses loom larger than gains in our decision making.¹⁰⁴ Oncologists, patients, and families may worry that they will regret not trying 'everything possible', leading them to choose treatments even when the potential benefit is marginal. Coupled with misleading expectations, this loss-framing messaging may promote behaviors that can lead to harm in the form of the toxicities and/or quality-of-life costs associated with nonbeneficial therapies.¹¹⁷

The bandwagon heuristic bias

The bandwagon heuristic is a cognitive bias that leads individuals to adopt an opinion or behavior because of the popularity of that choice. People are wired to conform to social norms and majority views, seeking safety and validation in numbers. The bandwagon heuristic can contribute to overtreatment in oncology through several mechanisms. When a particular treatment approach is widely adopted (such as immunotherapy or biologically personalized therapeutics for patients with far-advanced cancer), there is a

tendency to favor evidence supporting its use while downplaying potential drawbacks.¹¹² Oncologists may feel pressure to adhere to prevailing treatment practices or departmental norms.¹²¹ This can affect the decision making of individual oncologists and even tumor boards.

Anchoring bias

Anchoring bias refers to the tendency to rely too heavily on the first piece of information encountered when making a decision.¹⁰⁴ It can lead clinicians to overlook other patient-related considerations once an initial treatment plan has been made. Anchoring bias is closely related to the cognitive bias of premature closure, whereby one prematurely stops searching for information or alternative solutions.

Affect heuristic

Oncologists' decisions are influenced by emotions and feelings when working with patients with advanced cancer. The affect heuristic is a cognitive shortcut used to make judgments and decisions based on emotional responses. Oncologists commonly report more emotional relief when presenting either a positive prognosis or another treatment option than when discussing EOL care.^{34,48}

Framing bias

Framing bias refers to how the presentation of information influences decision making—how oncologists perceive the magnitude of benefit and how they communicate it. How clinicians present treatment options has a critical impact on the patient's perception of the likely benefit of the treatment. Oncologists often frame potential outcomes from new treatments in probabilistic terms which are easily misunderstood (e.g. 'There's a 20% chance this treatment may help', which patients may misinterpret as a 20% likelihood of cure). In this example, an oncologist may frame, and a patient may understand, a small chance of improvement as a reason to continue aggressive treatment, even when the likelihood of improving the patient's well-being or substantially prolonging survival is very low.

RECOMMENDATIONS FOR ADDRESSING OVERTREATMENT AT THE EOL

Reducing overtreatment at the EOL in oncology is challenging. Indeed, despite multiple trials of various interventions, well-established approaches are lacking.¹²² This is not surprising given the complexity of the patient, clinician, and family dynamics in play, each with social, psychological, and cognitive factors driving overtreatment.

The first step in addressing overtreatment is the acknowledgment that overtreatment is a problem that causes harm and needs remediation. This is a nontrivial task, especially in treatment settings where aggressive treatment toward the EOL is common practice. Clinical audits to identify the prevalence of ongoing anticancer treatments in the last 2-4 weeks of life can help to identify

the scale of overtreatment in a practice setting.¹² Addressing the factors that drive overtreatment requires the cooperative effort of oncologists, professional societies, public policy, and public education.

Use of established guidelines

Guidelines can guide and support oncologist recommendations to de-escalate treatment as patients approach the EOL. ASCO¹⁸ and ESMO¹⁹ guidelines emphasize shared decision making and regular discussions about prognosis, treatment goals, and patient preferences; integrating palliative care early in the disease trajectory for patients with advanced cancer; and discourage using further trials of systemic therapies in patients with poor performance status, progressive disease despite multiple lines of therapy and limited life expectancy.

Workload and time management

Discussions with patients approaching the EOL require more time than routine clinical encounters. These consultations should be treated as complex consultations and should be scheduled for longer appointments (e.g. 60-90 minutes) specifically for EOL discussions.

Palliative care teams can take on some of the responsibilities related to EOL conversations and decision making, especially when they have been introduced early. Furthermore, multidisciplinary team care with social work, psychologists, and chaplaincy services can assist in addressing nonmedical aspects of care, such as emotional support, advance directives, and family dynamics.

Appreciating and acknowledging the limitations of anticancer therapies

The law of diminishing marginal returns (or diminishing benefit) is an economic rule that is salient to the oncologic care of patients with advanced cancer. In this context, the law of diminishing returns refers to the idea that as more aggressive interventions or treatments are administered to a patient with terminal or incurable cancer, the additional benefits (in terms of symptom control, quality of life, or survival) may decrease relative to the increasing effort, cost, or side-effects involved.

In the management of patients with far-advanced cancer, there is a tipping point at which the benefits of further treatment are outweighed by the risk of harms or reduced quality of life. Appreciating and acting upon this critical consideration is part of the medical commitment to avoid harm. These are the core skills and tasks in the oncologic care of patients with far-advanced cancer that require emphasis in routine practice and in oncologist training.^{18,19,50}

Upstreaming palliative care for patients with advanced cancer

The timely introduction of palliative care that is initiated when patients are diagnosed with incurable metastatic

cancer—not just at the EOL—allows patients more time to better understand their prognosis and treatment options. Palliative care highlights the importance of managing symptoms, reducing suffering, and maintaining dignity as important issues in their own right, independent of issues related to disease modification. Despite this change in focus, several studies have demonstrated improved survival among patients receiving early palliative care, and none have demonstrated reduced survival.^{123,124}

Palliative care should be initiated early as part of the comprehensive care strategy for patients with advanced cancer.¹²⁵⁻¹²⁷ This approach is strongly supported by randomized controlled trials showing that patients who receive early palliative care report higher quality of life, experience less depression, and are less likely to receive aggressive EOL care that does not improve survival outcomes.¹²⁸⁻¹³¹ Expert opinion^{100,132} and data from patients and their family members support these findings.^{133,134} Early integration of palliative care is also endorsed by oncology professional societies including the ASCO¹³⁵ and ESMO.¹²⁶

Introducing palliative care as a legitimate and important focus of care at an earlier stage of the disease trajectory, alongside efforts to modify the natural history of the disease, diminishes the trauma of the transition to a more palliation-focused approach and reduces the likelihood of aggressive care at the EOL.^{12,126,127,130,136-139} The development of a preexisting trusting and empathetic relationship between oncologists and patients can make discussions of the relative merits and potential harms of disease-modifying treatment more effective in situations where such treatment is unlikely to be beneficial.^{126,127,140,141}

Integrating palliative care specialists into multidisciplinary care teams can ensure a comprehensive evaluation of patient needs and preferences. These teams can provide balanced perspectives and reduce the burden on oncologists to make unilateral decisions, promoting more holistic and appropriate care.^{38,142} If honest prognostic disclosure occurs early and is revisited as the disease progresses, patients and families will be more ready to make the transition away from nonbeneficial disease-focused treatments.¹⁰⁰ In addition, patients often fear abandonment by their treating oncologist when they are no longer receiving anticancer treatments.¹⁴³ A better transition occurs when the oncologist and palliative care physician are part of the same team in the ambulatory setting.¹⁰⁰

Enhanced communication skills training

Effective communication between oncologists, patients, and families is critical to making informed and balanced treatment decisions. Oncologists and health care teams should prioritize clear, compassionate communication to help patients understand their prognosis and the realistic likely outcomes of treatments. Visual aids, simplified explanations, and multiple conversations about prognosis and treatment options may help patients better understand their choices. This is especially true in the care of patients

with far-advanced cancer. Training programs such as Vital-Talk^{144,145} and the ‘Serious Illness Conversation Guide’¹⁴⁶ teach oncologists how to have empathetic, clear, and honest conversations with patients about their prognosis and the risks/benefits of continuing aggressive treatments, and can significantly improve the quality of discussions about prognosis, treatment options, and EOL care.¹⁴⁷ In addition, training can help mitigate oncologists’ fears that may lead them to avoid these discussions by shifting focus to adding further lines of treatment.¹⁴⁷

Empathetic communication. Oncologists should be trained in empathetic communication techniques to better understand and address the emotional and informational needs of patients and their families.¹⁴⁸ This includes active listening, validating patient emotions, and providing clear and compassionate explanations about the prognosis and treatment options.¹⁴⁸ Observing experienced physicians performing these discussions is an important part of role modeling and medical socialization, reinforcing the importance of this part of oncologic care.¹⁴⁹

Values clarification. Without an understanding of the patient’s values and preferences, it is not possible to make a shared treatment decision that focuses on achieving the patient’s goals. Explicit values clarification methods have demonstrated benefits in reducing values-incongruent choices and decisional conflict, and even in reducing the subjective impact of harms that do occur from treatment.¹⁵⁰ This process can be undertaken informally, formally, as part of an advanced care plan, or integrated into a decision aid.

Delivering bad news. Specialized training on how to deliver bad news can help oncologists, nurses, general practitioners, and other health care professionals convey difficult information in a way that is both sensitive and clear.¹⁵¹⁻¹⁵⁴ This can reduce misunderstandings and help patients and families make more informed decisions. Honest, sensitive, and empathetic discussions regarding prognosis convey care and respect and may dissuade patients from choosing low-value anticancer treatments over comfort-oriented care.¹⁵⁵

Discussing EOL care. Structured training modules that focus on discussing EOL care can help oncologists initiate conversations about palliative care and patient priorities for themselves and their families as they approach the EOL. In addition, using the resources of a multidisciplinary team, discussion can be assisted by oncology nurses, palliative medicine clinicians, social workers, and/or chaplains. These conversations are crucial for aligning treatment goals with patient preferences and reducing unnecessary aggressive interventions.

Negotiating the hope/honesty ‘tightrope’. Oncologists navigate a delicate balance (tightrope) between providing patients with hope and their ethical responsibility to advise patients when further anticancer treatment may not be the best course of action. Honesty regarding prognosis, the

likelihood of benefits and harms from the different relevant treatment options, and a focus on patient autonomy and well-being are crucial to ensuring that patients feel supported and empowered throughout their cancer journey.²⁵

When a patient asks, ‘Why not try? I have nothing to lose’,¹⁵⁶ it is important to address potential harms including time toxicity, risk of adverse effects, financial toxicity, and the opportunity cost of time at home with loved ones. A structured approach to difficult conversations can help facilitate these discussions (Table 3).

Support for the emotional and psychological needs of patients and their caregivers

Providing patients with emotional support, including counseling and mental health services, can help address their anxiety and fear of death.^{157,158} Cognitive-behavioral interventions may assist in processing difficult emotions and coping with a terminal diagnosis.¹⁵⁹ Several standardized therapies directed toward the individual patient or toward patient–caregiver dyads have been shown to improve psychological outcomes, including depression, anxiety, hopelessness, and spiritual well-being, in patients with advanced cancer.^{160–163} Distress screening should be conducted routinely to identify patients who are in the most urgent need of specialized psychosocial services.¹⁶⁴

Family caregivers of patients with advanced cancer may have psychological distress exceeding that of the patients they care for and may themselves benefit from

psychoeducational or supportive interventions.^{165,166} Involving family members in discussions about EOL care can help reduce pressure on patients to continue aggressive treatment.¹⁶⁷ Family counseling and education about advanced cancer care options can help align expectations and decisions around the patient’s best interests.

Mitigating the seduction of new technologies

The key tools to the mitigation of the seduction of new technologies are evidence-based medicine and critical appraisal. Evidence-based medicine starts with the critical evaluation of the evidence supporting new technologies that prioritize well-researched treatments with substantial patient benefits. Clinical trial data supporting efficacy and the magnitude of likely benefit need critical evaluation of the study design, implementation, and analysis.¹⁶⁸ Many clinical studies include weak surrogate endpoints, weak control arms, substandard postprogression treatment, lack of quality of life data, informative censoring, substandard reporting of adverse effects, and *post hoc* subgroup analysis without adjustment for multiplicity.¹⁶⁸ Medical journals should enforce publication standards for clinical trials. The absolute benefit of a treatment over months or years should be emphasized over the relative benefit (percentage improvement). By maintaining a balanced approach to innovation and evidence-based practice, oncologists can ensure that the integration of new treatments enhances rather than compromises the quality of cancer care.

Table 3. A structured approach to difficult conversations with patients with advanced and treatment-refractory cancer

1. First, acknowledge that this is going to be a difficult conversation.
2. Prioritize honesty and transparency when discussing diagnosis, prognosis, treatment options, and expected outcomes.
3. Explore what matters most to the patient: quantity of life versus quality of life, symptom management, and spending time with loved ones.
4. Set realistic expectations regarding the likely outcomes of the different treatment options including the option of palliative and supportive care without further disease-modifying treatment.
5. Recognize that this is a deeply personal patient decision and that authentic decision making requires accurate information.
6. Be empathetic and provide effective and responsive support frameworks. These may be required during sensitive conversations and certainly in providing care in the last phases of life.
7. Do not hasten the discussion and decision making. Suggest not making an immediate decision and discussing the relevant issues with important personal contacts.
8. Acknowledge that just as there is courage in pursuing treatment, there is no less courage in stopping anticancer treatments when they are not likely to help.
9. Offer psychological and/or spiritual counseling to help patients cope with the emotional challenges of their illness and end-of-life decisions.
10. Help patients to find hope beyond disease-modifying treatments: hope that they can enjoy their important relationships, hope that they can fill the remaining time with activities and relationships that are meaningful and important to them, and hope that this time will be rich as possible and that they will be comfortable.
11. Finally, even if there are no further disease-modifying treatments, commit to nonabandonment and that you will always be available if needed.
12. If, despite all these considerations, patients still request treatment: If the treatment does not place an unreasonable burden on limited health care resources, agree to a ‘limited time trial of therapy’ with an agreement to discontinue the therapy in the event of harm or lack of benefit.

Improved prognostic understanding

Better prognostic understanding allows oncologists to tailor treatment strategies that are appropriate for the patient’s condition. This is facilitated through honest and transparent conversations with patients and their families about realistic outcomes and expectations. It can reduce the pressure for aggressive treatments and give patients more control over their EOL decisions, potentially leading to a preference for comfort care.

Oncologists need ongoing training in the science of prognostication, particularly around the factors that influence survival in advanced cancer. These include understanding disease trajectories for various cancer types and recognizing clinical and laboratory indicators of proximity to death. The use of a validated prognostic tool, such as the Palliative Prognostic Score¹⁶⁹ or the Glasgow Prognostic Score,¹⁷⁰ may reduce subjective bias in prognostication. Machine learning algorithms can integrate patient data, tumor characteristics, and treatment responses to predict outcomes more accurately. In a recent randomized clinical trial, a machine learning-based intervention to identify patients at enhanced risk of death in the coming month increased the initiation of serious illness conversations focusing on setting goals and advanced care planning and decreased the use of EOL systemic therapy among patients with cancer.¹⁷¹ Integrating these tools into routine clinical practice can improve the precision of survival predictions

and help oncologists identify patients who are unlikely to benefit from further antitumor therapies.

Cognitive debiasing

As heuristics and bias influence so many decision-making processes, oncologists need to exercise vigilance regarding the risks that their intuitive thinking may interfere with effective diagnostic and therapeutic decision making.^{109,172}

The process of cognitive debiasing is a multistep one. First, one must become aware that biases can influence one's decision making and develop the ability to identify when it is happening. Second, one must consider trying to make a change. Third, one must decide to change. Fourth, one must initiate strategies to accomplish change. Finally, one must maintain the change.^{172,173}

Successful debiasing only happens when there is self-awareness of the direction in which the bias is leading and its severity and when there is motivation for change.¹⁷³ Debiasing is variably successful; clinicians who are successful become sensitive to the potential consequences of their bias and develop diligence to avoid the same thinking traps. This may involve having the ability to detect the need for bias override and to actively disengage from the bias.¹⁷⁴

Nonetheless, cognitive biases are difficult to change. The major barriers to bias correction are a lack of awareness of the impact of bias in clinical reasoning and clinicians' overconfidence in their own judgment. Even oncologists who are aware of the potential impact of biases may not believe that they themselves are vulnerable to them.¹²⁰ This underscores the value of decision reviews in oncology mortality meetings, in which peer discussion and review may highlight biases that may have influenced the care decisions for patients with far-advanced cancer.

Mindful reflective practice

Reflective practice aims to challenge biases that place practitioners at risk of incorrect decision making. Beyond building the capacity to critically reflect upon decisions,¹⁷⁵ it promotes a version of shared decision making that is founded in empathetic honesty and transparent discussions regarding treatment goals and potential harms and risks, as well as an accurate appraisal of the likely outcomes (not only the best possible outcomes).

Mitigating cultural influences driving overtreatment

Altering cultural perceptions of death. Many Western societies view death not as the closing of the circle of life but as an anathema.⁷³ The recent Lancet Commission on Death And Dying aimed to present death as a relational and spiritual process rather than simply a physiological event.⁷³ This radical reframing requires networks of care to support people who are dying, caring, and grieving. It can be promoted by media presenting conversations and stories about everyday death, dying, and grief and highlighting that even in death, there can be medical success: success in ensuring

that life was lived as well as possible, comfort was optimized, relationships nurtured, and loved ones supported.¹⁷⁶

Public health campaigns and societal education should focus on normalizing discussions about death and dying, promoting the idea that a good death, centered on comfort and dignity, is a positive outcome. This cultural shift can help alleviate the fear of transitioning to palliative care.

Professional societies, institutions, and departments.

Oncology professional societies and educators have the potential to impact the professional culture of oncology by giving enhanced emphasis to holistic care that is focused on individualized goals, and by promoting a more patient- and family-centered approach.¹⁷⁷ For patients with advanced cancer and those approaching the EOL, oncologists can emphasize their role as stewards in the cancer journey to ensure that patients receive the best care appropriate to their condition.¹⁷⁷⁻¹⁷⁹

Professional societies, cancer centers, and individual departments should emphasize the importance of symptom management, pain control, and psychological support throughout the care journey.^{177,178} They should focus on outcomes that matter most to patients, such as physical comfort, emotional well-being, and maintaining functional independence for as long as possible.

Improving the education and training of oncologists in EOL care can help them make better treatment decisions and communicate more effectively with patients and their families.^{94,177,178} This should include an emphasis on the importance of early palliative care with a timely cessation of anticancer therapy.¹⁸⁰ The presence of role models and mentors who practice patient-centered and palliative care can influence trainees to adopt similar approaches.^{94,181}

Policy and system-level changes. Systemic changes in health care policy and institutional practices are necessary to create an environment that supports appropriate EOL care and reduces overtreatment. Health policy reforms that incentivize quality of life over quantity of care can shift the focus from aggressive treatments to palliative care.¹⁸² Payment models that reward patient-centered outcomes rather than volume of services can also discourage overtreatment.^{183,184} In addition, legal protections for physicians prioritizing palliative care can mitigate the fear of litigation.

Clinical guidelines. Up-to-date clinical guidelines developed by professional organizations can help standardize care and reduce variability in treatment decisions for patients approaching the EOL.^{18,135,185} Disease-specific oncology guidelines need to emphasize the importance of palliative care and provide clear recommendations for when to prioritize the quality of life over further antitumor treatment. Regular updates and dissemination of these guidelines are essential to ensure their effectiveness.

Patient decision aids. These tools provide patients and caregivers/families with clear, concise, and balanced information about the potential benefits and risks of different treatment options.^{186,187} Decision aids can include

brochures, videos, or interactive online tools that help patients understand their choices and the likely outcomes. They facilitate informed discussions between patients and oncologists, promoting decisions that reflect the patient's values and preferences.¹⁸⁷

CONCLUSIONS

By fostering open communication with antibiasing strategies, integrating palliative care early, emphasizing outcomes that matter most to patients, and implementing health care system reforms, we can ensure that patients with advanced cancer receive care that aligns with their values and maximizes their remaining time. Ultimately, the goal is to shift the paradigm toward a patient-centered approach that prioritizes quality of life, respects patients' autonomy during this critical phase of their lives, and achieves the outcomes that matter most to them.

In some cases, despite all of the above, patients will choose to undergo treatments that are likely to be medically nonbeneficial and possibly even harmful. In such circumstances, treatment can be administered as a 'trial of therapy' with a limited time agreement to discontinue the therapy in the event of harm or lack of benefit after an agreed period. This should be conducted within the framework of informed consent. This approach respects patient autonomy and provides the understanding for families that they 'have done everything' in difficult circumstances while preserving also the fiduciary responsibilities to avoid harm and the societal responsibility of prudent use of limited health care resources. Physicians are not obliged to and should not continue treatments that are causing actual harm.¹⁸⁸

Further research is crucial in:

1. Refining prognostic tools to improve accuracy in predicting life expectancy at the EOL.
2. Evaluating the impact of physician education on decision making, particularly regarding communication skills training and antibiasing interventions.
3. Developing optimal communication strategies that empower patients and families to make informed decisions about EOL care, considering cultural and religious beliefs.
4. Policy and payment reform to incentivize improved EOL outcomes such as quality of life, days spent at home, and caregiver support.

This can be achieved through a collaborative effort involving oncologists, palliative care specialists, health care systems, and researchers. By working together, we can ensure that patients with advanced cancer receive care that is both compassionate and evidence-based, allowing them to face the EOL with dignity and peace.

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