

Virtual Mentor
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Virtual Mentor

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FROM THE EDITOR

Clinical Cures, Ethical Questions

Cancer. The disease that has touched so many of us, in one way or another, immediately commands attention and engenders questions of life, death, values, and meaning.

Each passing year brings a vast array of new drugs, technologies, and guidelines that introduce new dimensions to age-old questions of ethics and caregiving that medicine—and society at large—are still grappling with. As is increasingly being recognized, cancer is not a single disease, but rather a diverse collection of diseases differing in pace, expression, and challenges. The way in which it is experienced, then, varies dramatically from patient to patient and caregiver to caregiver, setting the stage for a clinical environment rife with particularly complex ethical situations.

Navigating these dilemmas to ensure the best possible outcomes for patients requires direct, empathic communication on the part of caregivers. But initiating such difficult conversations has not always been the norm—and is something that the medical community continues to struggle with today. Thomas P. Duffy, MD, describes how the culture of American medicine—devoted to conquering disease at all costs and still uncomfortable with death and dying—often prevents physicians from having vitally important end-of-life discussions with their patients.

These emotionally trying discussions are layered with additional complexity when there is a disconnect between doctor and patient about realistic goals of treatment and appropriate courses of action. If initial treatment regimens fail and disease progresses, patients and families may request increasingly risky and unproven treatments. When physicians believe a drug is likely to do more harm than good, are they obligated to refuse treatment or should they strive to maintain patient autonomy? In their case commentary, Laura L. Tenner, MD, and Paul R. Helft, MD, explore strategies for preserving the therapeutic relationship and promoting the patient's best interests near the end of life. At times, these issues expand beyond the clinic and into the courtroom. Valarie Blake, JD, MA, discusses landmark judicial cases questioning patients' constitutional right to experimental therapies and current FDA regulations.

Doctors confront different aspects of autonomy, beneficence, and shared decision making when caring for children. In their case commentary, Cristie M. Cole, JD, and Eric Kodish, MD, explore the ethics of withholding terminal diagnoses from pediatric patients, weighing a minor's right to know against the possible psychological and physiological harms of disclosure.

Patient and physician experiences are also inextricably linked to the larger health care delivery system. This connection becomes acutely apparent when doctors confront difficult treatment decisions precipitated by scarce resources. Over the past decade, cancer drug shortages have become an increasingly problematic and unpredictable component of providing oncologic care. Liza-Marie Johnson, MD, MPH, MSB, and Deena Levine, MD, discuss a challenging clinical case created by drug shortfalls and the criteria for ethical allocation of scarce resources.

At the same time that shortages of proven generic drugs threaten to compromise effective cancer care, the medical system has been flooded with expensive—and often only marginally effective—new cancer treatments. This situation is heightened during an era in which the exorbitant cost of health care is seen as unsustainable. In her discussion of Tito Fojo's and Christine Grady's thought-provoking article, "How much is life worth: Cetuximab, non-small cell lung cancer, and the \$440 billion question," Nancy Berlinger, PhD, explores the high and growing cost of cancer care and the physician's role in helping patients recognize and understand value.

The unsustainable cost of medical care, and wide disparities in quantity and quality of care delivered, were in part the impetus for the health care reform measures introduced by the Affordable Care Act (ACA). In their op-ed, Thomas W. LeBlanc, MD, MA, and Amy P. Abernethy, MD, PhD, explore the factors contributing to substantial variations in cancer treatment across the United States, and offer a promising path forward. Michael K. Gusmano, PhD, examines the ACA's potential to reduce disparities in cancer screening and treatment through comparative effectiveness research. And James F. Thrasher, PhD, Amira Osman, MPH, and Dien Anshari, MS, describe a recent public health effort to reduce the burden of cancer: the FDA mandate that cigarette packaging carry graphic images of the negative health consequences of smoking. The authors summarize existing evidence regarding the effectiveness of pictorial warnings, as well as the tobacco industry's arguments and legal challenges against the mandate.

As we enter the age of personalized medicine, advances in genomic sequencing hold great promise for tailored, sophisticated diagnosis and anti-cancer therapy. Erin Hofstatter, MD, and Allen Bale, MD, explore the science of whole-genome sequencing for real-time oncologic diagnosis, challenges of implementation, and ethical issues going forward. The past several decades have seen great advancements in cancer care, and many patients today enjoy longer, richer lives than they did in the past. In her essay, Gayle Sulik, PhD, discusses what it really means to be a cancer survivor and the positive and problematic aspects of the survivorship culture.

The issue closes with a podcast interview with Ronald DePinho, MD, president of MD Anderson Cancer Center, who discusses the future of cancer research and treatment, as well as the powerful, symbolic message of striking a red line through the word "cancer" on the center's logo (click on the podcast tab).

From prevention to treatment, patient to doctor, the lab bench to Capitol Hill, every component of cancer care brings its own set of promises and dilemmas. The widespread and deadly nature of the disease makes finding and adopting ethically responsible solutions of the utmost importance. In a field in which the rate of new technologies often exceeds society's capacity to fully comprehend their consequences, frequent and robust discussions of ethics, empathy, and equity will be required. This issue of *Virtual Mentor* seeks to extend and strengthen that conversation.

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ETHICS CASE

Minors' Right to Know and Therapeutic Privilege

Commentary by Cristie M. Cole, JD, and Eric Kodish, MD

“Why do I feel so bad, doctor?”

Dr. Marion's heart broke as she looked at the adorable 9-year-old girl who asked the question. Jill had been diagnosed with acute lymphocytic leukemia almost 5 months earlier, and Dr. Marion had quickly grown attached to the young girl. When Dr. Marion first started caring for Jill, it appeared that she was responding to treatment quite well. But over the past several weeks, Jill was in the hospital more often—the combined result of frequent infection and the toxic agents needed to treat her leukemia.

Throughout Jill's treatment course, her parents had insisted she not be told about her diagnosis. A friend at school had died from cancer, and the loss had affected Jill profoundly. For months afterward, Jill had not wanted to go back to school and refused to sleep in her own room, preferring to be close to her parents. Not long after Jill seemed to be recovering from the most intense effects of her schoolmate's death, she was diagnosed with leukemia. Her parents feared that telling her she had leukemia would compromise her emotional health and well-being. They asked Dr. Marion and others involved in Jill's care to refrain from disclosing her diagnosis to her.

Dr. Marion—and the rest of the medical staff—had thus far respected their wish, but felt strongly that Jill was mature enough to understand her condition and that she deserved to know what was going on, given that her leukemia might be life-limiting. Once, when her parents were not around, Jill asked what was wrong with her, and Dr. Marion offered an explanation that did not mention cancer but focused on side effects of medications. Now, Jill was asking again.

Commentary

Jill's parents are not alone. Families are generally concerned that knowledge of a life-threatening diagnosis will harm the patient's psychological and physiological well-being [1-5]. In the past, physicians routinely withheld medical information from a patient if they believed the information would harm the patient's overall health, justified by what is known as “therapeutic privilege” [1-3, 6, 7]. While not exclusive to pediatrics, the ethical dilemmas raised by nondisclosure requests are complicated further when made by a parent of a minor patient [8-11]. Dr. Marion and her team must grapple with reconciling their obligations to Jill with Jill's parents' authority to make decisions on behalf of their 9-year-old child [10].

Pediatric Decision Making: Reconciling Parental Authority, Physician Obligations, and a Child's Developing Autonomy

Informed consent is a cornerstone of patient-centered medical decision making. Rooted in respect for patient autonomy, it focuses on the process as much as on consent itself [8, 9, 12-15]. The goal is to elucidate the patient's values and preferences, given the decision and surrounding circumstances [8-11, 13]. Even for most adults lacking capacity, a surrogate strives to make decisions based on the adult patient's previously expressed preferences in accordance with the standard of substituted judgment [16].

In pediatrics, informed consent is at best an imperfect fit [8-10, 15]. Generally, a pediatric patient is not and never has been legally competent to make medical decisions. Until the child reaches 18, legal authority is vested in the patient's parents to determine what is in their child's best interest. Unlike decisions made by an adult's surrogate decision maker, such decisions cannot be based on the child's previously expressed values and beliefs, and so are based on the parents' values and beliefs [8, 9, 15, 16]. Instead of seeking informed consent, then, the American Academy of Pediatrics advises physicians to obtain "parental permission" and, when developmentally appropriate, *assent* (willingness to undergo the proposed treatment) from the young patient. Reframing informed consent as parental permission plus assent respects parental authority and recognizes its limitations. While substantial discretion is afforded to parents in child rearing, the interests of the child and the interests and obligations of the physician, state, and society at large act as limitations. Conflicts are rare, but, when they do arise, the interests and obligations of the stakeholders should be carefully weighed in light of the moral considerations and contextual factors [8-10].

In cases of nondisclosure requests from parents, the child's emerging autonomy and the physicians' obligation to provide appropriate treatment to the young patient must be balanced against parental authority [5, 10]. Of primary importance when thinking about medical decision making is the obligation to foster the child's capacity to make medical decisions [8, 9, 17]. This does not require treating the child as a fully autonomous decision maker [8, 9]. Rather, as a young patient matures, his or her role in medical decision making should also evolve. The physician and parents have an obligation to enable the young patient's participation in accordance with the patient's cognitive and emotional capacity [8, 9, 17]. The process of assent embodies this obligation because it allows the child to take a more active role in decision making once he or she has sufficiently matured. Like informed consent, assent seeks to elucidate the child's willingness to undergo the proposed medical intervention in a developmentally appropriate manner [8, 9]. Out of respect for the person, a broader concept than respect for autonomy, assent (or dissent) should only be sought if the child's expressed preference will be seriously considered [1, 8, 9]. If it will not, then this should be clearly communicated to the child [8, 9].

While each child should be assessed based on his or her own capabilities, a 9-year-old such as Jill generally has sufficient capacity to assent to at least some medical

interventions [8]. Regardless, some information about the medical condition and treatment should be provided in a developmentally appropriate manner for even the youngest patients [8, 9]. Disclosure fosters not only the patient's decision-making capacity but also trust in the clinician from an early age [5, 8-10, 18].

Therapeutic Privilege and a Minor's Right to Know (or Not Know)

Patient autonomy was not always a defining value in medical ethics [2-4, 7]. As late as the 1970s, paternalism was the cornerstone of the physician-patient relationship and reflected a general belief that the physician's fiduciary obligation to act in the patient's best interest was of paramount importance [2-4, 7, 19]. The physician was the primary decision maker and not required to solicit or consider the patient's preferences [2-4, 7]. Therapeutic privilege embodies this fiduciary duty by protecting the patient from information the physician deems to be potentially harmful and that the patient does not have an overriding interest in [2-4, 7]. The American Medical Association itself endorsed the practice in its 1847 *Code of Medical Ethics*, stating that a physician has "a sacred duty...to avoid all things which have a tendency to discourage the patient and depress his spirits" [20].

In contemporary medical practice, paternalism has given way to patient autonomy and the corresponding values of bodily dignity and self-determination [3, 19]. Medical decision making is a partnership between the physician and the patient. The physician is obligated to disclose information that the patient needs to meaningfully participate in and make decisions regarding medical care [3, 7, 12]. While pediatric patients are not generally treated as fully autonomous decision makers, the young patient's developing autonomy warrants respect [1]. The same values upon which informed consent is founded also support a physician's obligation to engage children in medical decision making proportionate to their cognitive and emotional development [5, 8, 9, 17]. Consistent with this shift in philosophical priorities, the American Medical Association's *Code of Medical Ethics* now states that "it is a fundamental ethical requirement that a physician should at all times deal honestly and openly with patients. Patients have a right to know their past and present status and to be free of any mistaken beliefs concerning their *conditions*" [13].

Under some circumstances, respect for patient autonomy can paradoxically support withholding medical information. If a patient expresses a desire not to know all or some medical information, then the physician should respect that decision and withhold that information [21, 22]. This is distinguished from therapeutic privilege because the physician is acting in accordance with the patient's preferences rather than on his or her own judgment [21]. The patient's religious or cultural beliefs may indicate preferences, but they should not be attributed to the patient without corroborating them with him or her [22-25]. The physician should offer the truth, speaking in general terms about categories of information to avoid mistakenly revealing information while also soliciting the patient's preferences [21].

Exercising therapeutic privilege also risks undermining trust in the physician-patient relationship. One risk of nondisclosure is the patient's discovering the withheld

information from another source [2, 5, 10]. A family member or another clinical team member could mistakenly reveal the withheld information. The patient could also find the information on his or her own, whether through medical records, the Internet, or accidentally hearing a voicemail. If a patient discovers that the physician intentionally withheld information, trust is compromised, which could prove detrimental to the patient's care [2, 3, 10, 26].

Clinical Realities of Nondisclosure: Problems and Unintended Harms

Yet, some parents and even physicians are tempted to withhold a life-threatening diagnosis from pediatric patients [26-28]. Not disclosing a diagnosis, though, is fraught with its own obstacles and harms [1, 5, 10]. More often than not, the child is aware of the hushed whispers and discussions among grown-ups and can ascertain that a secret exists that is not to be discussed [29-31]. The child may know to some degree what that secret is, whether he or she knows the specific disease, the severity of the illness, or that he or she is dying from the disease [5, 29-32]. In the context of the terminally ill child, this is often called "mutual pretense"—all parties including the child know the child is dying but act as if he or she were not [31, 32].

Research shows that withholding information may result in the child's imagining a worse scenario or at least a much different scenario [5, 27]. Without understanding why he or she feels bad, the child may begin to ascertain his or her own explanation for secrecy, including that the illness or treatment is a form of punishment [5]. Research shows that children not aware of their diagnosis do not experience any less distress and anxiety than those who are told about their life-threatening illness [6, 29], and in some cases may actually experience *more* [6, 33]. Openness, by contrast, appears to contribute to good long-term adjustment [27, 33]. Practically speaking, not understanding a diagnosis may also prevent compliance with treatment recommendations, particularly in older children [26, 33].

Nondisclosure also raises the question of how to respond to inquiries from patients about their condition, just as Jill asked Dr. Marion. Several strategies may be used to evade questions, including providing contingent answers, narrow answers, non-answers, or questions [28]. These strategies, however, do not directly resolve the underlying moral dilemma, i.e., reconciling parental authority in pediatric decision making with the physician's obligation to be honest with the young patient.

Conclusion

The desire to protect Jill from knowledge of her own mortality is understandable, particularly given her experience with the death of her friend. This experience, her age, her developmental status, and the impact this information may have on her health should all be factors influencing how and even when the diagnosis is disclosed. These factors do not however justify withholding the diagnosis from Jill indefinitely. Ultimately, Jill's developing autonomy and Dr. Marion's obligations to Jill outweigh Jill's parents' desire to protect her from the knowledge of her life-threatening illness. In discussions with Jill's parents, Dr. Marion should be careful not to appear to be seeking parental permission for diagnostic disclosure. Rather, she

should clearly communicate that the diagnosis will be disclosed within a finite period of time [11]. Allowing Jill's parents some control in choreographing how the disclosure takes place may help facilitate acceptance of disclosure and demonstrates respect for Jill's relationship with her parents. Dr. Marion could offer three options: (1) Jill's parents tell Jill alone; (2) Dr. Marion tells Jill alone; or (3) Dr. Marion and Jill's parents tell Jill together. Explaining that diagnostic disclosure is a process and that prognosis may be treated separately may also help Jill's parents accept diagnostic disclosure.

Lying to Jill is not an option. If Jill asks a direct question, then Dr. Marion has an obligation to answer it honestly and in a developmentally appropriate manner. She should clearly convey this obligation to Jill's parents. Even absent Jill's questions, Dr. Marion at the very least has an obligation to offer 9-year-old Jill the truth and assess whether Jill wants to know about her diagnosis and if so, how much she wants to know.

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ETHICS CASE

Allocation of Drugs in Short Supply

Commentary by Liza-Marie Johnson, MD, MPH, MSB, and Deena Levine, MD

Dr. Simpson, a busy oncologist, had been hearing about impending drug shortages for some time but had never given the issue much thought until the day he called the pharmacy and received the unpleasant news that there was a “severe shortage” of the drug he had started several patients on the previous month.

“Are you sure?” he asked incredulously. The drug in question wasn’t some expensive, novel chemotherapeutic agent. It was a reasonably priced generic that had been available for years to treat a variety of cancers.

Dr. Simpson thought about how best to use the limited supply of the drug his practice would receive. He had started both David and Justin on the drug the month before and wanted to switch one of them to another drug now, rather than making a change later in the treatment course. After looking into other chemotherapeutic agents, Dr. Simpson believed the effectiveness of this particular drug combined with its limited side effects made it the preferred agent for both patients.

He recalled the conversation he had with David, his 71-year-old patient whom he had treated for cancer several years earlier, and who had since been in remission. David had recently come into the hospital after experiencing progressive and severe back pain for several weeks. His cancer had metastasized to his spine. Solemnly, Dr. Simpson told David and his family that now the aim of treatment was not to cure, but to lengthen and improve the quality of his life. David had tolerated the drug well in the past, and, because of its favorable side-effect profile and David’s relative ill health, Dr. Simpson said it was the best choice going forward. If David reacted to the drug as he had in the past, the treatment could again extend his life by months or even years.

Dr. Simpson also thought of the last time Justin came into his clinic. A jovial man in his early 60s, Justin had recently been diagnosed with a primary cancer and was otherwise in good health. Despite his diagnosis, Justin remained quite positive—and with good reason: Dr. Simpson believed Justin had a very good chance of cure with this drug. There were other drugs Dr. Simpson thought could be substituted, but those had less robust evidence supporting their use, were more expensive, and often had more side effects.

Commentary

Medications shortages have become an increasingly frequent problem in the United States health care system and threaten quality patient care. The number of drug shortages tripled from 2005 to 2010, affecting major classes of therapeutics including oncology agents (28 percent), antibiotics (13 percent), and electrolytes/nutritional agents (11 percent) [1]. The majority of shortages involve sterile injectable medications (80 percent), primarily due to problems at manufacturing facilities (43 percent), delays in manufacturing or shipping (15 percent), or shortage of the active ingredient (10 percent) [1]. These drug shortages are often unpredictable and may persist over the short or long term. It is important for clinicians such as Dr. Simpson to apply ethical reasoning to allocating scarce resources when drug rationing becomes necessary in clinical practice.

Physicians have a fiduciary responsibility to promote the welfare and best interests of their patients, so it can be uncomfortable to ration a drug or other limited resource (e.g., ICU bed) and thus promote the best interest of one patient over that of another. In some cases it may be possible to substitute for the drug in short supply with an equivalent alternative agent, but often no acceptable substitute exists. This is frequently the case in oncology therapeutics. When there is no equivalent alternative to a scarce resource, physicians are in the “unconscionable position” of being forced to choose who receives the scarce resource and who does not [1]. It is critical that physicians use evidence-based medicine and ethical analysis of treatment goals, rather than relying on emotional biases or social-worth criteria, in prescribing a medication of limited availability.

Allocation of a scarce medication or medical resource should be made with evidence-based criteria, transparency, and consistency, with mechanisms for appeal in place should patients or their family members feel that a decision was unfair [2]. Unless a demonstrable public health benefit exists (e.g., vaccination of health care workers during a pandemic) all those in similar clinical situations should be treated fairly, with no patient having increased access to the limited resource due to perceived importance or social worth [2]. Clinicians should promptly and thoroughly evaluate the available medical literature for evidence of clinical benefit. The primary criterion for allocating a scarce drug to one patient over another should be evidence of a superior therapeutic effect in that particular patient [2].

While drug shortages clearly have a significant impact on all fields of medicine, in oncology the repercussions of drug shortages have been keenly felt. Chemotherapy shortages lead to adverse patient outcomes with increased toxicities, inferior efficacies, and elimination of curative options associated with alternative regimens [3]. In a study of pediatric patients with Hodgkin lymphoma, Metzger et al. demonstrated that substituting a promising alternative for a proven effective chemotherapy agent that had become unavailable due to a shortage led to inferior event-free survival at 2 years (75 percent with the alternative agent, rather than 88 percent with the standard agent) and resulted in exposure to increased toxicity [4]. Oncology drug shortages force physicians to make difficult choices about resource

allocation with unfortunate clinical consequences; however, the decisions can and should be facilitated by using an ethical framework that prioritizes beneficence and justice and applies evidence.

In the present case, Dr. Simpson has reviewed the evidence and believes that Justin has a very good chance of cure with this drug and that no therapeutically equivalent substitute exists. Based on the ethical framework presented, the limited supply of the drug should be allocated to Justin due to “demonstrable evidence of superior clinical therapeutic effect” [2] when compared to expected results for David. No evidence base supports use of the drug for David, and its intent is not curative but rather life prolonging. During a drug shortage, use of the drug should be restricted to those patients for whom it is likely to be most effective, and new courses of treatment with the scarce drug should not be initiated in other patients unless there is a reasonable expectation that sufficient quantities of the drug will be available to complete their treatment plan.

This does not mean that Dr. Simpson is without options to offer David for lengthening and improving the quality of his life. Now is the time to support those goals by offering David palliative care—reducing his disease-related symptoms to improve his quality of life. Dr. Simpson should have an honest, compassionate discussion with David in which he discloses that the drug previously used is currently in short supply and only available to those patients in whom there is evidence to support a superior therapeutic effect, as in the case of a patient with an primary cancer diagnosis where the expectation of cure from the drug is quite high. Dr. Simpson can present David and his family with the alternative chemotherapy agents, as well as symptom-based therapies, and give them time to weigh the possibility of life prolongation from the alternative agents against their possible adverse effects.

Medication shortages are becoming increasingly common in the United States. Individual physicians like Dr. Simpson should educate themselves on drugs that are in short supply, the degree of shortage, and the estimated duration of the shortage. This information is readily available through the United States Food and Drug Administration website [5]. Clinicians may wish to partner with other health care professionals and institutions that may still have sufficient supply of the medication and are willing to provide it for a patient who is expected to benefit greatly from receiving it.

We can also educate the public about the silent crisis of medication shortages and work with national physician organizations (such as American Society of Clinical Oncology) to advocate for change. Root cause analyses are needed to uncover the reasons for the shortages and suggest mechanisms to eliminate the bottleneck in drug manufacturing and distribution of critical therapeutic agents. In the interim, there is an immediate need for researchers to add to the evidence-based literature and conduct studies that compare outcomes from medications in short supply and their

potential alternatives to help clinicians make informed decisions about scarce resource allocation in what has become reality.

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ETHICS CASE

End-of-Life Decisions and Off-Label Drug Use

Commentary by Laura L. Tenner, MD, and Paul R. Helft, MD

With a mix of sympathy and admiration, Dr. Smith looked down at Mr. Johnson, sleeping uncomfortably on his hospital bed. Mr. Johnson had been diagnosed with lung cancer nearly 2 years before, at 70, and had remained remarkably upbeat and optimistic despite a very difficult treatment course.

“I still have a lot to live for, doc,” he routinely told Dr. Smith. “I’m gonna fight this thing. I want to be there for my family.”

Mr. Johnson had been through three rounds of chemotherapy and was now on his fourth regimen. Initially, he responded quite well, but over the past several months, his tumors continued to grow, and the side effects of treatment were becoming increasingly difficult to tolerate. He was constantly nauseated and severely fatigued. Yet he remained devoted to continuing treatment and exploring new options.

Dr. Smith had spoken with Mr. Johnson and his family several times about the possibility of moving from disease-directed therapy to palliative and end-of-life care. He felt that more chemotherapy would be likely to cause a further decline in Mr. Johnson’s quality of life without having any effect on his cancer and worried that it might even shorten Mr. Johnson’s life. Mr. Johnson’s family said they understood that prospects for recovery were bleak, but wanted to exhaust “all available options before giving up.” They approached Dr. Smith about a new drug that a family friend—also a physician—had mentioned. Dr. Smith had previously considered the drug but decided against using it for several reasons: it carried a very significant side effect profile, it had not been approved for use in Mr. Johnson’s cancer, there was only limited evidence that it had the potential to improve survival by 1 or 2 months, and it was extremely expensive.

Given this profile and Mr. Johnson’s poor condition, Dr. Smith believed starting this treatment would be an inappropriate course of action. However, both Mr. Johnson and his family seemed determined to pursue further treatment with this drug. As he contemplated how to proceed with the family meeting, Dr. Smith wondered whether he should respect Mr. Johnson’s desire to continue further cancer therapy even at the end of his life.

Commentary

This case scenario involves some of the most difficult issues practicing oncologists face in treating patients with advanced cancer nearing the end of their lives. Trying to provide compassionate, respectful, and appropriate care while navigating patient and family expectations is a challenge for any physician. Especially in the setting of

a longstanding relationship with a patient, the oncologist may find it difficult to say no to further disease-directed therapy near the end of life. Though oncologists have patients' best interest at heart, refusing to provide further therapy that has limited efficacy can often cause a rift in the patient-physician relationship.

In situations where the patient and the physician remain in disagreement over the correct therapeutic course, the patient may choose to search out other institutions or other physicians to provide the desired treatments. This is a less-than-ideal outcome insofar as the patient-physician relationship has been severed and the patient may still be exposed to further harm. Skillful and empathic communication can often aid physicians in avoiding such outcomes. While these patient and family discussions are fraught with complexity, some tools can help direct the shared decision-making process and preserve the patient-physician relationship. We address several of the concerns in this case vignette, including the ethical and communicative dimensions, and suggest ways of reframing aspects of the interaction that are among the most challenging.

An important component of any communication strategy is to validate the complex emotions the patient is experiencing. As in the above vignette, the patient told Dr. Smith that he was going to “fight this thing” because he wants to be there for his family. Timothy Quill, Robert Arnold, and others have pointed out that such statements are better understood not as literal directives about patients' preferences for therapy but rather as reflective of emotional distress [1]. In response to such statements, one adaptive strategy can be to address them as a plea for emotional support: “I hear you saying that the most important thing in your life is your family, and, more than anything else, you don't want them to have to live without you.” By reiterating the sentiments, you are hearing the patient's concerns, validating his or her emotions, and allowing further exploration of fears, hopes, and wishes, but without fostering unrealistic or harmful conceptions of goals. Eliciting concerns and expressing empathy can help patients cope with negative emotions [2].

Another important part of such patient and family discussions is defining the patient's preferences and goals. In the above vignette, the patient and family are equating stopping chemo with giving up. This is a common belief among patients and families. Reframing the idea of “giving up” can be helpful. Discontinuing ineffective treatments that are more likely to cause harm than good does not mean that one is giving up. Indeed, sometimes withdrawal of chemotherapy leads to an improved quality of life that allows patients to eat more, sleep better, and become more active. In addition, therapeutic interventions often come with the risk of significant adverse events. Explaining to patients that, though some interventions may control disease by months or slow progression, this may not extend overall survival or improve quality of life [3]. Reframing the cessation of aggressive disease-directed therapy as an opportunity to refocus efforts on maximizing the quality of the patient's life can allow the patient to turn away from equating cessation of disease-directed therapy with giving up or “doing nothing.”

Other points to consider are the physician's responsibility to uphold the ethical principles of beneficence (the promotion of well-being) and nonmaleficence (the avoidance of harm) [4, 5]. Though patient preferences should guide physician care, the physician should not feel ethically bound to provide aggressive disease-directed therapy that he or she deems to offer a poor risk-benefit ratio. If the physician truly feels that the therapy is more likely to harm than benefit the patient, then the value of the principles of nonmaleficence and beneficence should outweigh the value of preserving the patient's autonomy. In other words, a patient's request or demand for treatment does not obligate a physician to provide it, if the physician thinks it will cause more harm than good. *Primum non nocere*.

Mr. Johnson has already experienced significant side effects from the four regimens, and the off-label treatment he is requesting carries a significant side-effect profile with limited data to support its benefits. For off-label treatments, especially, substantial evidence of safety and efficacy must be present before they are considered for use outside a clinical trial [6]. In the setting of a decrease in overall functioning and significant accumulated side effects from prior treatments, further off-label experimental drugs will most likely cause more harm than benefit.

The number one recommendation on the American Society of Clinical Oncology's "top five list" of tests and treatments that are commonly performed in oncology despite a lack of evidence that they provide meaningful benefit states that "for patients with advanced solid-tumor cancers who are unlikely to benefit, do not provide unnecessary anticancer therapy, such as chemotherapy, but instead focus on symptom relief and palliative care" [7]. The physician is ethically obligated to refuse to offer a therapy with an unacceptably poor risk-benefit ratio. It is essential, however, to stress that this "compassionate refusal," must emphasize that the reasons for refusal arise from of the physician's resolute commitment to the patient's best interest.

Cost considerations, mentioned in the vignette may play a role in physician decision making or shared decision making, but it is unknown whether physicians feel comfortable exploring this avenue of discussion with patients. In a 2010 *New England Journal of Medicine* article, Cooke claims that "being a physician is not just about finding benefit for patients; it is also about helping them to understand value" [8]. As in our case above, the great expense coupled with limited data on efficacy suggest that using an unproven therapy such as the drug the patient requests represents poor value. Further challenges are that cost consideration must be, as Cooke states, explicit, transparent, and consistent, and, furthermore, "physicians must be provided with the skills to discuss value with patients honestly, effectively and compassionately" [9]. Further study in cost communication with patient and family members is needed, so that physicians can feel better prepared to engage in conversations about costs with patients.

In conclusion, physicians should not feel bound to provide care that they think will harm the patient. However, physicians should, without compromising their values, maintain the physician-patient relationship to the best of their ability through open

communication and empathic listening, incorporating the techniques of emotional validation and goal-directed therapy.

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CONLEY ESSAY

2012 Winning Essay

Joey Knows Best? Balancing Conflicts and Defending a Child's Best Interest in Difficult Clinical Decisions

Mariam O. Fofana

After experiencing morning headaches, vomiting, and increasing lethargy for about 3 months, Joey, 12 years of age, was found to have a medulloblastoma. He had surgery to remove as much of the tumor as possible. Joey had a postoperative MRI that showed no focal metastatic sites. His treatment plan called for radiation immediately following the surgery and then chemotherapy.

Joey's oncologist, Dr. Burnet, told his mother that an ongoing study was investigating the use of lower-than-standard doses of craniospinal radiation in a subset of children like Joey. The study was testing the hypothesis that the lower radiation dose followed by high-dose chemotherapy would produce the same survival rates as the standard high radiation dosage while reducing the neurocognitive side effects of the radiation.

When Joey and his mom met with Dr. Burnet, his mom told Dr. Burnet that she did not want Joey to participate in the experimental treatment regimen. Joey didn't say anything during the meeting, but on the way home he told his mother that he wanted to be a part of the experimental treatment study. She asked him why. Joey, who had always been a curious kid, loved school, and was proud of his ability to excel at his studies, said, "Mom, they think this is going to be better than what they're doing now. I don't want to be a cancer-free dummy..."

Joey's mother and father were separated, and, although Joey lived with his mom, his father remained close to both of them and involved in his son's life. When Joey's mother told him about the treatment decision they were being asked to make, Joey's dad said, "I think we should let Joey decide. He's old enough to understand what the risks and possible benefits are. It's his life." The mother and father were alone, and Joey's mom was fighting back tears. "I can't say yes to this experiment; I just want our son to live," she said.

The three of them went to Dr. Burnet together so that they all could hear what Dr. Burnet had to say. In the meantime, they learned as much as they could from the Internet, and what they were able to find just confirmed what Dr. Burnet had said. This time Joey spoke up in the office, telling Dr. Burnet that he wanted to participate in the lower-dose radiation study.

“Because this regimen is experimental,” Dr. Burnet told Joey’s folks, “Joey’s assent is really important, but it’s best for everyone if all of you to agree to the treatment. I’m sure you can see why it’s critical that everyone be on board when you’re facing a possibly life-changing decision. We have a physician-ethicist on staff,” Dr. Burnet continued, “who might be able to help you sort out some of the questions you have. The key one, as I see it, is who gets to decide what is in Joey’s best interest. Would you like to meet with our physician-ethicist, Dr. Klein?”

Response

Joey’s story presents the difficult situation of a child facing a life-threatening illness and potentially harmful treatment. Decision making for children is significantly more complex than in adult cases as minors are not deemed capable of deciding for themselves, raising the question of how to weigh children’s and parents’ preferences. Joey’s situation is all the more complicated because his parents disagree with each other. Dr. Burnet did well to recognize the complicated nature of this case and the necessity to parse out the ethical questions involved. In his discussion with the family, Dr. Klein will need to combine the Belmont report’s primary bioethics principles (nonmaleficence/beneficence, respect for persons, justice) with an analytic framework that reflects the particularities of pediatric clinical decision making [1, 2].

Research Participation as a Treatment Option

Because the experimental offered to Joey is part of a research study, concerns specific to research (as opposed to routine clinical care) must be addressed. We may conclude from the vignette that the family is adequately informed of the potential benefits and harms of the study and alternative options and that Dr. Burnet has no conflict of interest. This does not mean that Dr. Burnet is an impartial actor in the discussion regarding Joey’s treatment: his duty is to advocate for Joey’s best interests. Secondly, we must make sure that Joey and his family understand the distinction between treatment and research. The therapeutic misconception, the mistaken perception that treatments being researched are intended for therapeutic benefit, is common among participants in clinical research, and patients faced with life-threatening illnesses are particularly vulnerable due to their desperation for any chance to prolong life and well-being; this is especially true in pediatric oncology, where the lines between clinical care and research are often blurred [3].³ Dr. Klein must ensure that the family understands that the purpose of the study is to compare the experimental treatment to traditional treatment, and that it is unclear whether the experimental treatment is superior—in fact, it may lead to a much worse outcome if the reduced radiation dose causes higher mortality and does not prevent side effects as hypothesized. Finally, it must be made clear to Joey’s family that they can discontinue their participation in the study whenever they wish.

Does Joey’s Opinion Count?

The first question that Dr. Klein must address is whether and how much Joey’s opinion matters—that is, the question of Joey’s autonomy. In assessing the value of a minor’s treatment preferences, one must take into account maturity and decisional capacity [4]. Clearly, a 3-year-old would not be fit to choose her radiation treatment

but we might afford a 17-year-old nearly as much decisional authority as an adult. What of children who, like Joey, are “in the middle”? Based on studies of cognitive development, some authors and institutions have advocated thresholds of 7 or 14 years of age to involve children in clinical decisions by obtaining their assent [5, 6]. However, the use of a threshold seems exceedingly arbitrary. A gradualist and individualist approach, which recognizes that the development of decisional capacity is a gradual rather than discrete process and that individual children progress differently toward maturity is more likely to result in a fair assessment of each case.

Joey seems an intelligent and mature 12-year-old; and indeed, the experience of serious illness can make children “grow up” faster than their age peers [7]. Joey has demonstrated his understanding of his treatment options and potential consequences, and an ability to manipulate these facts and his own values to arrive at a decision, thus meeting commonly used criteria for decisional capacity [8]. Moreover, because children generally have a tendency to go along with their parents’ decision (less so as they mature), Joey’s openly voiced disagreement indicates a capacity for independent judgment and the fervor of his desire to participate in the study [9, 10].

The nature of Joey’s illness also affects the value of his preference. Children in end-of-life situations may be given more say in deciding between life-extending measures and comfort care that optimizes quality of life, reflecting an understanding that, the more life-altering the situation, the more difficult it is for a surrogate decision maker to comprehend the patient’s experience and the tradeoff involved in the decision [11, 12]. Although Joey is not necessarily in an end-of-life situation, he has a life-threatening illness and faces the risk of significant decrease in quality of life. Given his demonstrated level of maturity and his illness, Joey’s preferences must be taken in serious consideration. However, this does not imply that Joey’s position should be adopted unequivocally. Certainly, legal statutes require that Joey’s parent(s) approve and, ethically speaking, the gradualist approach mentioned above allows us to recognize that, although Joey’s opinion matters, we cannot consider him to have full decisional autonomy as we would an adult or older adolescent.

Can Parents Decide for Their Children?

Parents, as the primary caretakers, are generally assumed to be best suited to decide in children’s stead. For adults, surrogate decision-making relies on the notion of substituted judgment; that is, a surrogate decision-maker is expected to make the choice that best represents the patient’s own judgment [13].¹³ Thus, for adults, it is crucially important *who* decides, as this person must be familiar with, and able to honor the patient’s preferences. However, in pediatrics, substituted judgment is not truly applicable, as parents’ decisions cannot be deemed to reflect the judgment that their children would make if they had full decisional capacity [13]. Although children often eventually adopt values similar to their parents’, it is impossible to know what Joey would have decided as a fully autonomous adult. Parents’ choices reflect their values and, often, their own interests [14]. This may lead to a conflict when, for example, a parent opts to forego extreme life-saving measures for a child

who could have survived, but with significant neurologic deficits, because the burden of caring for the child would be too onerous. Although it is clear from her emotional distress that Joey's mother wants the best for him, she also has an interest in protecting herself from the immense grief of losing one's child. Thus, because parental decision making is not equivalent to true *consent*, it may be more accurate to refer to parental *permission* [12]. In our case, both parental permission and Joey's assent are necessary.

One consequence of the ethical inferiority of parental permission to true consent is that the question of *who* decides is less relevant than the question of which decision upholds the child's *best interests* [13]. In Joey's case, an attempt to choose an appropriate decision maker would lead to a dead end. Joey's mother may be considered better suited than his father to decide as she is the custodial parent and may know him better, but Joey's father is very involved in his life and thus his preferences cannot *a priori* be discounted. Because the permission of only one parent is typically required for studies in which the participants may benefit, Dr. Burnet could conceivably enroll Joey with just the father's consent.¹² However, Dr. Burnet rightfully recognized that this would have been an unwise and unethical decision in its disregard for the mother's concerns and the risk of discord within the family. It is clearly in Joey's best interest that consensus be achieved and the integrity of the family relationships be maintained.

In sum, Dr. Klein's task rests in determining whether Joey's interests are best served by "vetoing" his treatment preference or abiding by it. Dr. Klein will have to have the family identify and weigh the potential benefits and harms of each option to determine which best upholds the principles of beneficence and nonmaleficence.

Determining Joey's Best Interests: Harms vs. Benefits

A comprehensive and systematic analysis of harms and benefits must encompass the magnitude and likelihood of both direct and indirect consequences, including physical, psychological, social, and economic outcomes. Here, knowledge about the clinical (physical) outcomes of the two treatment options is insufficient to make a definite determination; while some clinical decisions have a clear answer regarding the child's best interest (e.g., protection of a vaccine vs. transient pain of the injection), there is no such easy answer to the tradeoff between potentially decreased chance of survival and potential (but not guaranteed!) protection from neurocognitive side effects.

However, the psychological and social impacts of each option do offer valuable insight. First, regardless of the final decision, there is a risk of discord between Joey's parents and consequent psychosocial stress for Joey. If Joey is allowed to participate in the study, the mother may feel slighted that her opinion was not respected. On the other hand, the father might feel slighted if Joey is not allowed to participate. Because the risk of parental discord exists with both decisions and can reasonably be assumed to be equally likely, it does not enlighten our decision

process. (Nevertheless, mitigation through counseling support throughout the treatment process is essential.)

If Joey were not allowed to participate in the study, he is likely to develop resentment towards his parents (especially his mother) and the treatment team, with potential consequences including decreased engagement in the treatment plan (and poorer compliance) and a long-term rift in his relationship with his parents. If Joey does develop cognitive impairment, he will also bear the pain of living with a disability that he had explicitly sought to avoid, an added psychological cost on top of the burden of the cognitive impairment itself. On the other hand, allowing Joey to enter the study presents the potential benefit of validating his developing sense of autonomy. Of course, if the experimental treatment were unsuccessful, this could result in tremendous guilt on the parents' part for opting for the less certain treatment, but in weighing Joey's best interests the parents' guilt matters primarily insofar as it affects Joey, which would not be the case here.

With no further factual details, this analysis indicates that, taking into account potential psychosocial outcomes, and given the lack of a clearly clinically superior option, the best decision is to respect Joey's preference and allow him to enter the study. One test of the robustness of this decision framework is to apply it to the converse situation, that is, if Joey did not want to participate in the study but his mother wanted him to. Here again, assuming similar potential clinical outcomes, the psychosocial consequences of deciding against Joey's desires would weigh most heavily and guide us towards respecting Joey's decision. Of course, parental permission remains paramount—our conclusion serves only in making recommendations to the family as to the *decision process* rather than the actual *treatment*.

Conclusions

Dr. Klein faces the delicate task of guiding a family facing a very difficult clinical decision for a pre-adolescent child with a life-threatening illness. In discussing the family's options, Dr. Klein must be empathetic to the deeply emotional nature of the situation and to each family member's viewpoint, acknowledging the valid reasons for each preference. Joey and his parents should be given sufficient time to reflect upon their decision (albeit with consideration for the need for prompt treatment to optimize outcomes). In seeking consensus, Dr. Klein must emphasize the importance of Joey's level of decisional capacity and his understanding of the choice he faces. He should then walk the family through the potential benefits and harms outlined above and elicit any additional concerns and the family's own assessment of the magnitude and likelihood of these potential outcomes. It is crucial that the ethical analysis take into account the family's unique circumstances in order to properly weigh the potential benefits and harms and arrive to the right conclusion for this specific family. Nevertheless, the steps above offer a systematic, comprehensive, and robust approach to achieving a decision process that puts the entire family at ease and allows them to face Joey's illness as a united front.

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CONLEY ESSAY

2012 Runner-Up Essay

Pediatric Assent in Clinical Research: A Patient-Centered Perspective Using Motivational Interviewing

William Sveen

After experiencing morning headaches, vomiting, and increasing lethargy for about 3 months, Joey, 12 years of age, was found to have a medulloblastoma. He had surgery to remove as much of the tumor as possible. Joey had a postoperative MRI that showed no focal metastatic sites. His treatment plan called for radiation immediately following the surgery and then chemotherapy.

Joey's oncologist, Dr. Burnet, told his mother that an ongoing study was investigating the use of lower-than-standard doses of craniospinal radiation in a subset of children like Joey. The study was testing the hypothesis that the lower radiation dose followed by high-dose chemotherapy would produce the same survival rates as the standard high radiation dosage while reducing the neurocognitive side effects of the radiation.

When Joey and his mom met with Dr. Burnet, his mom told Dr. Burnet that she did not want Joey to participate in the experimental treatment regimen. Joey didn't say anything during the meeting, but on the way home he told his mother that he wanted to be a part of the experimental treatment study. She asked him why. Joey, who had always been a curious kid, loved school, and was proud of his ability to excel at his studies, said, "Mom, they think this is going to be better than what they're doing now. I don't want to be a cancer-free dummy..."

Joey's mother and father were separated, and, although Joey lived with his mom, his father remained close to both of them and involved in his son's life. When Joey's mother told him about the treatment decision they were being asked to make, Joey's dad said, "I think we should let Joey decide. He's old enough to understand what the risks and possible benefits are. It's his life." The mother and father were alone, and Joey's mom was fighting back tears. "I can't say yes to this experiment; I just want our son to live," she said.

The three of them went to Dr. Burnet together so that they all could hear what Dr. Burnet had to say. In the meantime, they learned as much as they could from the Internet, and what they were able to find just confirmed what Dr. Burnet had said. This time Joey spoke up in the office, telling Dr. Burnet that he wanted to participate in the lower-dose radiation study.

"Because this regimen is experimental," Dr. Burnet told Joey's folks, "Joey's assent is really important, but it's best for everyone if all of you to agree to the treatment.

I'm sure you can see why it's critical that everyone be on board when you're facing a possibly life-changing decision. We have a physician-ethicist on staff," Dr. Burnet continued, "who might be able to help you sort out some of the questions you have. The key one, as I see it, is who gets to decide what is in Joey's best interest. Would you like to meet with our physician-ethicist, Dr. Klein?"

Response

Joey's dilemma disrupts the typical framework of ethical research practices because the concepts of autonomy and informed consent do not apply in pediatrics. Instead, they are replaced by parental authority and patient assent. However, strong parental authority without the child's assent undermines the developing capacity of the child to engage in decision making. As a result, clinical ethicists must strive to reach consensus within the family. Motivational interviewing provides techniques that the ethicist can use to facilitate a patient-centered, semi-directive discussion in attempt to break down the communication barriers among the patient, parents, and healthcare team.

The Problem of Autonomy

Clinical bioethics in the United States revolves around the concepts of autonomy and, by extension, informed consent. Medical autonomy is the ability of an individual to direct his or her own decision making. Due to the complexities of many medical therapies, autonomy is manifested in informed consent, the process of providing the patient with adequate information to make medical decisions free from coercion.

Capacity, the ability to understand the risks and benefits of a proposed treatment and choose a treatment plan that corresponds to his or her values, is a prerequisite for autonomy. Determining medical capacity is a key aspect of many ethical consultations in adults due to the wide range of decision-making ability. Following this model, an adult with decision-making capacity has the autonomy to direct his or her own care and involvement in research.

However, this model does not hold in pediatrics, namely because children lack full decisional capacity. It is generally understood that children slowly gain capacity as they develop and mature from an infant with no capacity to a young adult with nearly full capacity, but it is difficult to determine where on the spectrum of capacity an individual child exists. Therefore, children are not fully autonomous, but they become more autonomous as they develop [1].

Furthermore, using the informed consent model in pediatrics is problematic because informed consent implies a sense of self. Informed consent by proxy is technically misleading since the patient remains uninformed. Because of these ethical distinctions, pediatricians do not utilize the language of autonomy and informed consent but instead refer to parental authority and patient assent [2].

Parental Authority

Parental authority stems from the traditional role of parenting. Our culture grants parents the responsibility of decision making for their children and does not morally

oppose a parent's decision to direct most aspects of their children's lives. This is comparable to the principle of respecting patient autonomy in adults. From an ethical standpoint, parental authority is based on the principle of beneficence, acting in the best interested of their child [1].

At times the parental authority conflicts with the child's wishes. For example, very few children want routine vaccinations. They cry. They yell. They scream. They may become aggressive, verbally denounce their parents and physician, and attempt to flee. If any healthy adult behaved like this, the clinician would immediately stop treatment. However, since the child lacks the capacity to understand the future benefit of vaccinations, he or she is exposed to temporary pain against his or her wishes.

This does not mean that parental authority is absolute. In 1944, the United States Supreme Court ruled that parental authority could be limited for the protection of children [3]. In regards to medical treatment, the American Academy of Pediatrics states that "all children are entitled to medical treatment that is likely to prevent serious harm, or suffering, or death" regardless of parental desire to do otherwise [1]. Children are also protected from being enrolled in clinical research that has no direct benefit to them or puts them at high risk. Finally, the emerging autonomy of adolescents is often respected in the sensitive discussions of sex, smoking, drugs, and alcohol, since parental involvement may decrease trust in the physician.

Patient Assent

Although children lack full capacity for informed consent, they should still be involved in their medical decision making whenever possible using the model of patient assent, the process of agreeing to a treatment plan chosen by an outside authority. This respects the relative capacity of the child and centers care on the patient. Even at a young age, allowing a child to make simple decisions such as deciding in which arm to get a vaccination helps them understand and participate, even if they are not responsible for the actual decisions.

Pediatric patients should not be excluded from decision making without specific reasons. Explanation of medical care to the child should be developmentally appropriate for the child's understanding, include the risk and benefits of treatment and entail an assessment of the comprehension and response of the child. For the best outcomes, parents and physicians should seek the assent of the patient for all medical decisions [1, 2].

Patient-Centered Approach to Decision Making

Tension occurs in pediatric decision making when the child disagrees with the parents' plan. The American Academy of Pediatricians proposes three models for decision making in pediatric research that balance paternal authority and patient assent based on the patient's age [2, 4]. Decisions with infants and young children center on parental authority accompanied, if possible based on the age of the patient, by assent. For school-aged children such as Joey, parental permission with assent is used to account for the increasing capacity of the child. As patients become

adolescents, parental permission continues, but informed consent can be used in specific situations as the patient nears adulthood.

Irresolvable disagreement between parents and the child inevitably occurs. Ultimately, parents have the power to select care for their child provided that care is in the best interest of the child. However, physicians should withhold treatment, even if only temporarily, in order to assess the values of a noncompliant patient. Coercion should only be used as a last resort. Continued treatment without assent can undermine the child's trust in both the physician and the parents, causing problems in the therapeutic and family relationships. Finally, legal action including court-appointed guardianship or emancipation should be reserved for only the most severe cases when all other means of reaching consensus have failed [2].

Motivational Interviewing in Ethical Consultations

From a patient-centered perspective, the role of the ethicist, Dr. Klein, is to facilitate conversation between the individuals involved with the final goal of reaching rational consensus for the patient and parents. Dr. Klein cannot make the decisions for Joey's family. Instead, he must expertly mediate a discussion that helps the family solve the dilemma for themselves. This can be a difficult task since individuals are often resistant or ambivalent to decision making, but the principles of motivational interviewing may help resolve these barriers.

Motivational interviewing is a semi-directed and patient-centered approach to physician-patient communication that began in the 1980s as a technique to help alcoholics quit drinking. It has been successfully applied in numerous health care settings to help patients adjust behavior, especially addiction. More recent studies have shown that motivational interviewing techniques help in difficult conversations with patients, such as palliative care consultation, even though not all of the concepts of motivational interviewing apply because no behavioral changes are involved [5].

Motivational interviewing has three main principles: collaboration, autonomy, and evocation. Collaboration occurs when the ethicist and patient work together to make decisions. Dr. Klein is the expert on the application of ethical principles, but Joey's parents, and ultimately Joey himself, are experts on the patient. The ethicist must also respect autonomous decision making, or, in Joey's case, parental permission with patient assent. Dr. Klein cannot have preconceived notions about Joey's decision. In directing the conversation toward consensus, he must be careful not to direct it toward a specific decision. Finally, evocation involves eliciting information from the patient and family about their internal motivations. Evocation benefits everyone involved because people often have not processed their own values on complex dilemmas. The family is encouraged to reflect on the spoken values of the patient and each other.

Dr. Klein has a number of motivational interviewing techniques at his disposal. He can ask open-ended questions to explore each individual's values. He can summarize and restate each individual's values for the benefit of Joey and his parents. He can encourage Joey to reflect on his values and ask his parents to do the same. Instead of working to overcome resistance from the family, he can acknowledge the difficulty

of decision making and reframe the discussion. This avoids an unproductive series of arguments and counterarguments while encouraging further discussion. Throughout this process, he should keep the conversation civil and query any extreme remarks that may lead to unnecessary confrontation.

Application to Joey's Case

Based on Joey's age, the decision-making model in this case should be parental permission with patient assent. It is clear that Joey wants to participate in the trial. The research trial is deemed ethical even though it is high-risk because of the possibility of direct benefit to Joey. However, it is certainly not clear if participating in the trial is in Joey's best interest because the efficacy of low-dose radiation is not known. His parents would not be abusing their parental authority by either allowing or refusing his participation. Still, Joey's parents disagree. His mother wants to refuse Joey's participation while his father supports his decision. Not just the parents but the entire family needs to reach consensus because this will help Joey engage in his care, whether he participates in the trial or not.

Joey did not voice his opinions during the initial appointment with Dr. Burnet. While there could be many reasons for this, Dr. Klein needs to overcome that by first focusing on Joey and evoking his values and emotions. Joey excels in school and told his mother that he doesn't "want to be a cancer-free dummy." Dr. Klein should discuss Joey's desire to retain full neurological function, validate his values, and restate them aloud. Dr. Klein should also ask about Joey's fears of participating in the trial to assess if Joey comprehends the risks involved.

After focusing on Joey, Dr. Klein should direct his attention to the parents, using motivational interviewing to prompt them to name any resistance or ambivalence they have toward the decision-making process. Both parents are likely motivated by fear and the desire to protect their child, and rightly so. A majority of parents claim they would rather participate in a similar trial themselves than allow their children to participate [6]. The discussion should focus on common themes parents encounter with enrolling their children in clinical trials such as the stress of living in a tragic event, desiring the best for their child, wanting to help future children with cancer, accepting the potential consequences of their decisions without regrets, feeling overwhelmed by the sheer number of serious decisions in a short period of time, and navigating relationships with the health care team [7].

Joey's mother wants her son to live but does not describe the values that motivate her to refuse the trial. Dr. Klein should validate her concern but explore her emotions and reasoning. She displays resistance toward accepting Joey's opinion, admitting "I can't say yes to giving him less treatment." Motivational interviewing techniques can help her name her resistance and reframe the issue.

Dr. Klein should explore why the father claims Joey is "old enough to understand what the risks and possible benefits are." What informs that judgment? Does the mother agree? Or is he being ambivalent by allowing Joey to decide?

No method guarantees that a consensus will be reached, but motivational interviewing techniques emphasize the importance of finding agreement. Caring for a child with cancer is stressful, and Joey's parents need to be able to support each other and their child. Joey needs to feel his opinions are valued throughout this process. Failure to do so may result in regret, resentment, and distrust among the members of the family and the health care team. This patient-centered approach seeks to avoid those consequences while respecting the concepts of parental authority and patient assent in pediatrics.

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CONLEY ESSAY

2012 Runner-Up Essay

Keeping Joey at the Center of the Conversation: Ethical Considerations in a Challenging Pediatric Case

B. Corbett Walsh

After experiencing morning headaches, vomiting, and increasing lethargy for about 3 months, Joey, 12 years of age, was found to have a medulloblastoma. He had surgery to remove as much of the tumor as possible. Joey had a postoperative MRI that showed no focal metastatic sites. His treatment plan called for radiation immediately following the surgery and then chemotherapy.

Joey's oncologist, Dr. Burnet, told his mother that an ongoing study was investigating the use of lower-than-standard doses of craniospinal radiation in a subset of children like Joey. The study was testing the hypothesis that the lower radiation dose followed by high-dose chemotherapy would produce the same survival rates as the standard high radiation dosage while reducing the neurocognitive side effects of the radiation.

When Joey and his mom met with Dr. Burnet, his mom told Dr. Burnet that she did not want Joey to participate in the experimental treatment regimen. Joey didn't say anything during the meeting, but on the way home he told his mother that he wanted to be a part of the experimental treatment study. She asked him why. Joey, who had always been a curious kid, loved school, and was proud of his ability to excel at his studies, said, "Mom, they think this is going to be better than what they're doing now. I don't want to be a cancer-free dummy..."

Joey's mother and father were separated, and, although Joey lived with his mom, his father remained close to both of them and involved in his son's life. When Joey's mother told him about the treatment decision they were being asked to make, Joey's dad said, "I think we should let Joey decide. He's old enough to understand what the risks and possible benefits are. It's his life." The mother and father were alone, and Joey's mom was fighting back tears. "I can't say yes to this experiment; I just want our son to live," she said.

The three of them went to Dr. Burnet together so that they all could hear what Dr. Burnet had to say. In the meantime, they learned as much as they could from the Internet, and what they were able to find just confirmed what Dr. Burnet had said. This time Joey spoke up in the office, telling Dr. Burnet that he wanted to participate in the lower-dose radiation study.

“Because this regimen is experimental,” Dr. Burnet told Joey’s folks, “Joey’s assent is really important, but it’s best for everyone if all of you to agree to the treatment. I’m sure you can see why it’s critical that everyone be on board when you’re facing a possibly life-changing decision. We have a physician-ethicist on staff,” Dr. Burnet continued, “who might be able to help you sort out some of the questions you have. The key one, as I see it, is who gets to decide what is in Joey’s best interest. Would you like to meet with our physician-ethicist, Dr. Klein?”

Response

On the surface, one might think that pediatrics is simply adult medicine in younger people. A trained clinician however, knows that there are differences so distinct that many physicians devote their entire lives to just treating this select population. In addition to obvious anatomical, pharmacokinetic, and developmental differences, the *practice* of medicine is also slightly different. Physicians not only treat their patient but must also interact with the patient’s parents. Indeed pediatric cases can be more complex and emotionally demanding, and decisions are often made by individuals other than the patient. These difficult cases often intersect the field of bioethics in the important areas of research ethics and consent. Physicians may feel overwhelmed by the ethical complexities of a particular case, and just as a pediatrician may refer their patient to an oncologist, an oncologist may likewise ask for a clinical ethicist to lend expertise as they navigate the various moral quandaries.

One such example could be the following case. Joey is a 12-year-old boy found to have a medulloblastoma. Following a successful surgery that removed all visible tumor and a post-surgical workup showing no metastasis, his treatment plan called for immediate radiation and then chemotherapy. Dr. Burnet, Joey’s oncologist, informed Joey and his family that Joey could participate in an experimental treatment regime that was determining if a lower radiation dose would produce the same survival rates as the higher standard radiation dosage while reducing the neurocognitive side effects. Because several moral issues are at play in this case, Dr. Burnet requested Dr. Klein—a physician-ethicist—be included in the subsequent discussions. This paper provides a structure that Dr. Klein could follow as he explores the various ethical aspects of this case. First a basic framework for the consultation will be mentioned, followed by a brief examination of the study. Prior to a comprehensive discussion of pediatric consent, the family will be reminded of their decision-making roles and how they can enhance the discussion. This will lead to an exploration of Joey’s values and interests, ending with a similar examination of his parents’ values and interests.

While Dr. Burnet may be familiar with an ethics consultation, it is likely that Joey and his family are not. It is therefore critical that Dr. Klein establish realistic expectations about the ethics consultation and flesh out the various issues that need to be addressed. Joey and his family should understand that the role of Dr. Klein is similar to Dr. Burnet’s in that each offers expertise, clinical ethics and oncology respectively, with the goal of improving Joey’s care. In leading the discussion, and because there initially appears to be a conflict between Joey and his mother, Dr.

Klein should employ a style consistent with mediation. In doing so, Dr. Klein should create a space where all parties are encouraged to tell their story and express their interests in an environment free of judgment. Along those lines, Dr. Klein should not take Joey and his parents' initial statements as clear unambiguous expression of their positions. Instead, Dr. Klein should be encouraged to solicit and explore each individual's underlying values and interests that support those initial positions. This will provide Dr. Klein some room to maneuver as he attempts to build a consensus that, given any initial conflicts, advances everyone's understanding of what is best for Joey. Joey and his family should also understand the limit of Dr. Klein's and Dr. Burnet's roles. While Dr. Klein is interested in Joey's health and recovery, he is only contributing to this very narrow aspect of Joey's care.

Critical to the limit of Dr. Burnet's role is his relationship to the study that Joey may participate in. For Joey to participate, it is absolutely essential that Dr. Burnet not be involved in any aspect of the study. If this were violated, Dr. Burnet would have to simultaneously balance the interests of Joey against the interests of the study—an inherent conflict of interest best avoided by a morally sound physician-scientist. Equally critical is that the study be approved by an Institutional Review Board—an institutional body responsible for ensuring the scientific merit and balancing the risks and benefit of the research protocol.

While Drs. Klein and Burnet bring additional expertise to the discussion, Joey and his family should be reminded of the various competencies they contribute. The thought that Joey has a brain tumor can be incredibly frightening and difficult to process, much less manage. Joey should be reminded that his surgery was successful and without complications and that his family has remained a strong cohesive unit despite his parents being separated. This is no small task and deserves explicit recognition. Also commendable is their initiative to educate themselves about Joey's disease and the treatments available. Perhaps most praiseworthy is Joey's participation in this process. His parents should be extolled for encouraging their son to take additional ownership of his life by contemplating the consequences of his decisions. Joey should equally be praised for participating and should continue to take advantage of his parents' guidance.

Of particular importance to this case is the role of pediatric assent—or Joey's decision to participate in a specific treatment plan. Part D of the Common Rule details the relevant federal regulations. For the study in question, Joey's treatment would be greater than minimal risk—defined as “the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests” [1]—but also present the prospect of direct benefit to Joey. Participation of this type of study requires (1) Joey's assent and (2) informed permission from his parents [2].

In contrast to adult informed consent where the goal is self-determination, pediatric assent prioritizes the best interests of the child over principles of autonomy. Indeed

parental permission originates from beneficence and the nonmaleficence of unjustified risks, whereas pediatric assent reflects the respect of the child's *developing* autonomy. More practically, this position maintains that minors lack the life experience necessary to prevent actions that they may regret later. Providers may therefore be justified to intervene when necessary and proportionally restricting their liberty for the purposes of promoting their health and minimizing harms [3]. Critical to note is that the absence of dissent does not qualify as assent.

Turning our attention to Joey, it's critical to ascertain his values, preferences, and goals of treatment. Joey is presented as a curious kid who excels at his studies, and Dr. Klein should be encouraged to engage Joey's character to best determine Joey's values. Dr. Klein could continue the discussion by exploring why Joey remained silent during his initial meeting with Dr. Burnet. There are limitless reasons of varying significance for why he was initially quiet, but to ignore it would be a disservice. Joey states that he doesn't "want to be a cancer-free *dummy*..." (emphasis added), indicating he places significant importance on and is very averse towards any reduction in his cognition. Dr. Klein should be especially sensitive to Joey's '...' when describing why he wants to participate in the experimental treatment regimen. The pause could be insignificant, but it might indicate there is more to be solicited and requires further investigation. Equally important is Dr. Klein's verification that Joey understands his medical condition and the study to the best developing cognitive abilities.

Integrating all this information, Dr. William Bartholome defined the four elements of pediatric assent as (1) a developmentally appropriate understanding of the disease; (2) disclosure of the proposed intervention and what it involves; (3) an assessment of the child's comprehension of the information provided and the influences that may sway the child's evaluation of the situation; and (4) a solicitation of the child's expression to willfully accept the intervention [4]. A discussion between Drs. Klein and Burnet should occur beforehand to determine what extent of understanding, of which specific elements in the experimental protocol, would be required for Joey to assent. Dr. Klein should be particularly aware of two beliefs that adolescents may occasionally exhibit; (1) a bias toward the nearer future—Joey may choose immediate benefits (cognitive ability) over his interest of remaining cancer free in the distant future—and (2) the invulnerability hypothesis wherein Joey may underappreciate his own vulnerability to certain types of harm [3]. There is no indication that Joey displays either behaviors, however it would be advisable that Dr. Klein be alert of these possibilities as he continues his consultation.

Similar to Joey, his parents' values, preferences, and goals of treatment should be solicited and explored. Parental involvement is critical, not only because society entrusts them to protect their children, but because Joey is literally dependent on his parents. Joey's father believes that he is "old enough to understand what the risks and possible benefits are". As previously recommended, Dr. Klein should resist temptation to accept this at face value and solicit specific examples that define Joey's father's position. Turning our attention to Joey's mother, she states that she "can't

say yes to giving *less* treatment” (emphasis added). Parental permission follows criteria similar to pediatric assent, namely it is critical that Joey’s parents understand the study to the best of their ability. To recommend the experimental treatment regimen Dr. Burnet, as an advocate for Joey’s health and recovery, would have to believe that both treatments are in clinical equipoise; a genuine uncertainty about which treatment is more efficacious. It therefore follows that the in this clinical scenario, and what should be clearly communicated to Joey’s mother, both treatments are believed to be *equal* when looking at survival rates.

The experimental treatment regimen *may* produce similar survival rates, or it may be more or less efficacious—this is what the study is trying to determine. What is believed is that the experimental treatment regimen would reduce the neurocognitive side effects. This tradeoff is the crux of the decision on whether to participate. Joey’s mother continues by saying “I just want our son to live.” This initial statement, at face value, appears to be in conflict with Joey’s goals of care. Whereas Joey places his cognition at a premium and appears to be concerned with recurrence secondarily, his mother seems to be less averse to the neurocognitive side effects of the treatment—valuing the prevention of recurrence more. To overcome this impasse Dr. Klein must be able to ascertain their fundamental values and goals of care, find common ground, and craft a solution that advances each stakeholder’s interest. Dr. Klein should be keenly aware that statements similar to Joey’s mother’s can be infused with guilt, and that possibility should be evaluated and addressed if appropriate.

In closing the discussion Dr. Klein should, irrespective of whether a decision was made regarding Joey’s participation in the experimental treatment regimen, describe a plan that includes an additional consultation, if necessary, as well as any subsequent tasks that need to be completed. All parties should be thanked for their participation and contributions, and a note summary should be made in the Joey’s health record. Dr. Burnet should be recognized because, while many physicians have knowledge and experience in several areas touched by this case, patient care really benefits when one acknowledges one’s own limits and utilizes local resources available. This is undoubtedly a difficult case that involves the management of multiple parties, exploring their interests, and an effective command of several highly complicated and still developing ethical topics.

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MEDICAL EDUCATION

The Medical Student and Care at the End of Life

Thomas P. Duffy, MD

Almost 20 years ago, care of the dying was described by Daniel Callahan as an “open moral wound” in the American health care system [1]. He attributed the continued festering of this lesion to the American veneration of self-mastery and self-realization that cannot submit to the inevitable reality of death. He also cited the secularization of death, with a religious/spiritual response replaced by a medico-technical assault, as a contributor. Physicians exaggerated and prolonged this injury by the avoidance behavior generated in them by encounters with death and dying. There was a reticence to initiate discussions about advance health care planning, a failure to elicit patients’ values in these matters, and a propensity to ignore directives even when they were in place.

The Patient Self-Determination Act, passed more than 2 decades ago to correct this situation by encouraging discussion of end-of-life (EOL) issues, saw only a modicum of success in reversing physicians’ disinclination to make such discussions a priority. Even a multimillion-dollar interventional study (SUPPORT) to improve patient-physician communication with critically ill patients succeeded only in documenting the extent and frequency of this communication gap in modern medicine [2].

Physicians’ reluctance to initiate and flesh-out patient preferences regarding EOL care has been defended (and excused) on the grounds that such discussions threaten the patient’s ability to maintain hope. This long-adhered-to but now outmoded belief and practice resulted in “benevolent” deception being the primary communication style in EOL care of the past. Physicians’ problems with a personal sense of failure in the face of death, a disproportionate belief in the mastery of science over disease, and unacknowledged anxiety over their own deaths all contributed to this physician-centered rather than patient-centered approach to end-of-life care. The shift from curing to the caring stance required during the dying process is not an easy transition for physicians trained in the ethos of delaying death at all costs. The financial and time constraints of modern-day practice have only accentuated the omission of end-of-life conversation from encounters with patients.

This serious oversight persisted even in the face of the expressed desires of their patients to be engaged in EOL conversation [2]. A major reason for this was the way in which physicians were educated throughout the last century. The Flexnerian biomedical model of medical education was strongly anchored in scientific ideas with less emphasis on or inclusion of professional ideals. Generations of physicians

were not schooled in the artful care of the dying; death and dying were absent from the medical curriculum as topics and almost nonexistent in medical texts. Communication skills were taken for granted. Death, which inhabits the halls of every hospital, was excluded from the discourse of physicians' daily lives. Physician interest and attention to patients appeared to dwindle as the battle against dying was lost. This twentieth-century professionalization of physicians determined a way of life that paradoxically failed our patients' expressed concerns and needs.

Healing of this wound has become the major moral responsibility of the medical profession in the twenty-first century, and major alterations and emphases in how students are trained are being implemented. Bioethics has played a huge role in the healing and has been a gadfly, energizing the profession to address and correct the omission. Palliative care teams, nonexistent until only a few years ago, now work alongside the health care team in a therapeutic and educational role. The dialogue on this subject has, to some degree, become mainstream. Popular TV programs such as Bill Moyer's PBS series in 2000 on dying "On One's Own Terms" and films specifically created to address this topic have helped put "power-of-attorney" and "advance directives" into most patients' vocabularies. The modern plague of AIDS made it impossible for anyone to escape confronting dying and death. The debate over the legality of physician assistance in dying and its approval in Oregon, Washington, Vermont, and Montana have catapulted "how we die" into the forefront of concerns for the medical profession and its patients.

A rapid correction to the problem, analogous to a surgical closure of a wound, is, however, not possible. The solution requires a departure from the type of professionalization in which many of the current ranks of physicians were schooled. It rests in training medical students to be more comfortable in the territory of death and dying and to be more skilled in discussing these topics with their patients. This is essential for cultivating the habit and skillful practice of "benevolent" disclosure. Such physicians will be better prepared to support their patients in living while dying and in helping to orchestrate a "good death." The movement is already well under way in most medical institutions in America, with attention and emphasis on this aspect of care across the curriculum. Initiatives such as the EPEC (Education in Palliative and End-of-life Care) project are serving to heighten physician awareness and engagement in EOL care [3].

The new importance EOL care is being accorded is emphasized by its introduction early on alongside the previously sacred terrain of basic science. The cadaver introduces students not only to anatomical detail but to the more complicated and awesome territory of dealing with death and dying. Studies have documented that student attitudes and adjustments to dealing with death begin early in medical school with students' encounters with the cadaver [4]. And integration of this material continues across the curriculum throughout the 4 years of training. Special emphasis is being placed on nurturing the development of effective communication skills; professional actors are portraying patients in clinical scenarios in which students acting as physicians deliver bad news or discuss EOL issues [5].

Medical school ethics courses contain a heavy concentration of EOL issues. Hospice visits are part of most medical clerkships. Clinical ethical reasoning proceeds hand-in-hand with classical clinical reasoning. Incorporating questions about patients' preferences concerning death and dying into student learning of routine history taking strongly dispels the tendency to avoid these subjects. Giving this information equal importance with other parts of the history makes both patients and physicians more at ease with such discussions. No longer should there be a need to introduce this essential dialogue at the bedside of a dying patient; knowledge of the patient's wishes should have evolved from conversation that has become a natural part of the patient-physician encounter.

The issues that must be considered in end-of-life care are multidimensional, and the skills physicians must possess are many. Ethical grounding for discussing end of life with patients is rooted in the principles of respect for patient autonomy, beneficence, nonmaleficence, and justice. Truth telling and informed consent are central to the task. The legal implications of living wills, advance directives, durable power of attorney, competency, and surrogacy must be understood. The use of agents to relieve pain must be mastered and skillfully employed to the patient's advantage.

Patient Narratives and the Student's Role in End-of-Life Care

None of the many goals of end-of-life care can be met without what is often the medical students' most valuable contribution—elicitation of the story of the patient's life and the conversations that identify the values, wishes, needs, fears, and, most importantly, the goals of the patient. The importance of eliciting the patient's narrative in EOL care is a surprisingly recent realization. An ongoing conversation to understand where patients are coming from, where they now are in their illness, and to where they will return, depending on the outcome of the illness, was not recognized for its defining role in care decisions until, perhaps, 15 years ago. History taking had been taught as a distiller's art—the distillate of the disease was removed from the rich and oftentimes messy details of human life and illness.

This oversight is now being corrected. Courses in narrative medicine even have their own place in some medical schools [6]. The narrative not only promotes a more empathic understanding of patients, it is an essential resource for addressing and helping resolve moral issues in patient care [7]. This perspective has its origin in the belief that moral judgments cannot be properly made unless the circumstances of an individual's life are identified and considered.

It becomes easy to see that the student's role in EOL care is critical when one recognizes the value of eliciting the patient's story in its fullest detail. It is often the student's sympathetic and earnest listening that evokes the narrative that lays the groundwork for a team's understanding of the patient. The elicitation of the story identifies each patient's uniqueness and determines how each patient's management will be tailored to his or her needs. Engagement with the patient in the act of attentively listening incorporates the listener into the developing narrative and helps

cultivate trust in the relationship. Equipped with this knowledge, the student is better prepared to learn from and even question decisions about a patient's care. The opportunities to witness the delivery of bad news by members of the team become richer occasions for learning. The artful engagement of an attending physician in EOL discussions becomes embedded in the student's repertoire of clinical knowledge.

The term "personalized" medicine—referring to treatments that genomic analyses make possible—is evoking tremendous excitement. But the term is misapplied to genomic medicine. Treatments that arise from genomics will be "individualized" to the patient's cancer cells, but they will treat the cancer, the disease, the way medicine has long treated the disease. "Personalized" medicine treats the person with the disease—the illness experience. And true "personalized" medicine is the domain of narrative medicine and is the proper possession and pursuit of all physicians [8]. It is through the understanding of stories—not genomes—that personalized medicine is realized.

Medical students are equal players in that process and have the same access to the stories of patients' lives that William Carlos Williams claimed afforded him entrance to the "secret gardens of the self" [9]. This generation of medical students is fortunate in being able and encouraged to enter these gardens and use this training in all of their patient interactions, especially in the circumstances of EOL care.

When former trainees of the physician Paul Beeson were questioned about the source of his persisting influence on current generations, they opined that it was the fashion in which he encountered each patient that was the basis for their ongoing admiration [10]. His habit was always to draw a chair to the patient's bedside and listen attentively to the patient's story. It is that simple act that is the key to the gardens of our patient's lives, the entrance to the discovery of our patients' fears and apprehensions.

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JOURNAL DISCUSSION

Why Clinical Oncologists Should Talk about the Price of Cancer Drugs

Nancy Berlinger, PhD

Fojo T, Grady C. How much is life worth: cetuximab, non-small cell lung cancer, and the \$440 billion question. *J Natl Cancer Inst.* 2009;101(15):1044–1048.

Cost is an ethical issue in three ways: price, value, and burden. In the United States, the high prices of potentially life-sustaining treatments and technologies that are set by manufacturers are frequently characterized as unsustainable for public and private insurance programs and for patients [1]. This problem, well documented in cancer care [2], is due not only to the large number of cancer cases (cancer is the second leading cause of death in the U.S., after heart disease) and the ever-growing number of drugs to treat different types of cancer, but also to highly problematic ways of describing—and marketing—drugs as “breakthroughs,” in part to justify extremely high prices. In their important article, Tito Fojo and Christine Grady make a compelling ethical case to their fellow oncology professionals: “We must stop deluding ourselves” that high-priced cancer drugs “are an aberration,” and we must change our prescribing practices so that we do not “signal” to manufacturers our tacit acceptance of ever-higher prices as the status quo [3].

They describe a kind of game—or gaming—in which the annual meeting of their field’s major professional society was used as a platform to present a marginally beneficial cancer drug as a “breakthrough,” a “new standard,” and “first-line treatment” [3]. These practices, and automatic Medicare coverage of FDA-approved drugs, including those with scant evidence of being any more effective than existing drugs, serve the marketing interests of manufacturers, who charge extremely high prices for these drugs. They justify doing so on the grounds that they need to recoup their research costs, although Fojo and Grady question whether drugs that can offer marginal benefits at best should be in development in the first place.

Other commentators note that some so-called breakthrough drugs are, in fact, variations on existing drugs, and that, for a few highly effective cancer drugs, profit margins are enormous [4]. They also challenge manufacturers’ implicit or explicit assertion that high prices are justified because a drug is potentially lifesaving, noting that this is far from true for the majority of cancer drugs, some of which may, at best, extend life for only a few weeks or months, accompanied by toxicity and other side effects. As Bruce E. Hillner and Thomas J. Smith concluded in a 2009 editorial in the *Journal of Clinical Oncology*, “We think advocacy groups should be rallying for reductions in price when drugs do not work that well” [5]. And, they added, “even if

we cannot influence the price, as oncologists we have to discuss these issues with our patients” [5].

Hillner and Smith identified the deliberate conflation of a drug’s price with a drug’s value as “profiteering,” an activity unethical on its face and akin to intentionally driving up the price of life-saving medication during an epidemic [5]. The marketing of marginally beneficial drugs as lifesaving “breakthroughs” or “advances” is, in a way, even worse. During a public health emergency, medicine or vaccines may indeed save lives. This does not justify profiteering but could justify costs, such as increased production costs that may reasonably be reflected in a drug’s price. But a “marginally” beneficial drug *cannot* save a person’s life. Suggesting that it can is wrong no matter what the price of the drug is. Playing on this suggestion to justify a high price is doubly wrong.

In 2012 and 2013, prominent oncologists began to do what Fojo and Grady and Hillner and Smith had called for, to take a moral and professional stand against ever-increasing prices for cancer drugs. Memorial Sloan-Kettering Cancer Center announced that its doctors would refuse to prescribe a drug for the treatment of colorectal cancer priced at more than \$11,000 per month that, according to evidence, offered no advantage over an existing drug [4]. In an editorial describing this decision, MSKCC oncologists noted that the typical patient with colorectal cancer is on Medicare, which would not cover the full cost of this drug, and that a Medicare patient’s monthly out-of-pocket costs for this drug alone would be “more than \$2,200,” an amount “greater than the monthly income for half of Medicare participants” [1]. In other words, half of Medicare patients would have *no money to live on* as soon as they started this drug. This is not, remotely, a tenable situation for cancer patients and their families, and it is an unnecessary situation, given that a cheaper (though still expensive) drug with the same potential benefits was already on the market. This public stance on the part of the MSKCC oncologists led the manufacturer to “cut the price in half” [4].

This brings us to cost as value. People who have been diagnosed with cancer usually value their own lives, and research by Thomas Smith and colleagues suggests that when presented with treatment options, people with cancer will continue to opt for chemotherapy even when they are near the end of life, in part because treatment—the next drug, and the next, and the next—is being offered to them by their oncologists [5]. When oncologists fail to explain what a treatment can and cannot do for a patient, in the context of the patient’s diagnosis, prognosis, and current condition, or offer treatments that are unlikely to provide any physiological benefit to a patient, this is a failure of informed choice. The act of offering the drug implies that the drug has value. High price may further imply that the drug is newer, better, more “worth it.” Clinical oncologists should challenge and seek to change how manufacturers characterize a drug’s value to patients in a way that translates into a high price. Oncologists should, at the same time, make every effort to learn *what* a patient values in life—longer life? longer life together with quality life? relationships? being able to do certain things? staying out of the hospital?—and to

translate these values and preferences into goals of care as a framework for considering the benefits and burdens of different treatment options [6].

Finally, cost can be experienced as a burden by patients and their families. This is true when a drug offers only marginal benefit. It is true even when a cancer drug offers tremendous benefit. This is true of imatinib (trade name, Gleevec), which was introduced in 2001 for the treatment of chronic myeloid leukemia (CML) and has succeeded in transforming a life-threatening form of cancer into a chronic disease that can be managed long-term through daily medication. The annual cost of Gleevec is \$92,000, and newer drugs for CML are entering the market priced at well over \$100,000 for a year of therapy. Is it appropriate to charge such a high price for one of the rare cancer drugs that is, in fact, lifesaving? No, in the opinion of more than 100 experts in the treatment of CML, who state that “the current prices” of imatinib and similarly effective CML drugs “are too high, unsustainable, may compromise access of needy patients to highly effective therapy, and are harmful to the sustainability of our national healthcare systems” [7]. Patients who are able to benefit from a cancer drug will be greatly burdened by high price, as they “have to pay the high price annually to stay alive” [7]. These experts in the management of cancer as a chronic disease build on the ethical framework of Fojo and Grady in describing the issue of drug pricing as an urgent moral concern for oncologists, in that high price, questionable value, or both can “harm our patients and societies” [7]. All oncology professionals should be familiar with these issues, as practitioners who must confront the reality of “financial toxicity” as an immense problem for cancer patients, and as effective advocates for these patients [8, 9].

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STATE OF THE ART AND SCIENCE

The Promise and Pitfalls of Genomics-Driven Cancer Medicine

Erin W. Hofstatter, MD, and Allen E. Bale, MD

Mrs. J is a 45-year-old woman with metastatic breast cancer. Her cancer has proved resistant to several standard chemotherapy treatments. Her doctor has become aware of a new clinical trial, which offers whole genome sequencing of the patient's tumor to select treatment based on specific mutations found in the cancer. To properly interpret somatic mutations found in the tumor, the study also requires a sample of germline DNA. Mrs. J agrees to participate in the trial. Several weeks later, testing reveals a PTEN mutation in her breast cancer that qualifies her for targeted chemotherapy based on this finding. However, germline DNA sequencing incidentally reveals a PSEN1 mutation, which is known to cause a heritable form of early-onset Alzheimer dementia. Mrs. J presents to clinic to find out the results of her testing. With her 21-year-old daughter by her side, she asks, "Doctor, what did my tests show?"

Over the last decade, the field of cancer medicine has witnessed an explosion in technological advances, now allowing rapid and inexpensive sequencing of the entire human genome. These advances hold great promise in our ability to understand and treat cancer and to develop true "genomics-driven cancer medicine" based on a patient's individual tumor profile. However, with these advances come significant challenges, both technical and ethical. As the case illustrates, while so-called "next-generation sequencing" (NGS) can successfully guide therapy, it can also reveal significant incidental findings that patients, families, and physicians may not be prepared to handle and may not want to know. In this article, we aim to provide an overview of NGS and its role in cancer medicine. We then highlight some of the technical issues and ethical challenges we must face as we use this technology in real-time oncologic care.

Genomics-Driven Cancer Medicine

Defined as the study of genes and their functions, the field of genomics addresses the interrelationships of all genes and their combined influence on the development and growth of an organism [1]. This discipline applies sophisticated laboratory technology and bioinformatics to analyze the sequence, broader structure, and function of genomes. Whereas the field of genetics focuses on single genes, genomics seeks to understand an organism's entire complement of DNA [1, 2].

Cancer is inherently a genomic disease. In other words, most cancers accumulate an array of mutated genes that interact over time to initiate neoplasia and fuel its progression [3]. The introduction of high-throughput, massively parallel ("next-

generation”) sequencing to evaluate all of the bases in the human genome has revolutionized our ability to study and understand the cancer genome. Although methodology varies among NGS platforms, all are designed in such a way that an extremely large number of DNA molecules are spatially arranged onto a solid matrix. The many thousands to millions of DNA strands are then sequenced simultaneously. All NGS sequencing results in a huge volume of raw data, generating hundreds of millions to even trillions of data points, in a single instrument run [4]. These data must then be processed and interpreted by comparison with a reference genome (e.g., the human genome in the case of medical genomics) requiring complex biostatistical and bioinformatics analysis [5].

To put the impact of NGS in context, sequencing of the first human genome was completed in 2001 after more than two decades of work and at the cost of \$2.7 billion [4, 6]. With the introduction of NGS in 2005 and continued improvement in NGS instrumentation, we can now sequence a human genome within days at a cost of approximately \$5,000 [7]. This dramatic drop in cost and turnaround time has allowed for broad use of NGS for cancer research and advanced clinical diagnostics. With the potential to quickly detect all mutations in a tumor and an expanding library of targeted anticancer agents, oncology is serving as a proving ground, unique among medical specialties, for genomics-driven therapy [3].

The application of NGS to oncology, or “genomics-driven cancer medicine,” is conceptually logical and simple: First, the genome of a patient’s tumor is sequenced, and all genetic differences from the standard human reference genome are identified. Because all human beings have many normal genetic variants that differ from the reference genome, the tumor sequence is compared with the patient’s constitutional (“germline”) genome to determine which alterations in the tumor are somatic (and therefore potentially pathogenic) and which are germline (and probably not cancer-related). Next, the somatic mutation list is filtered through a database of mutations that may render tumors sensitive to established and emerging anticancer drugs. Finally, an annotated list is provided to the treating physician to be used in clinical decision making and clinical research design [3, 8]. However, several technical and ethical challenges must be addressed before real-time application of NGS can become a reality in cancer medicine.

Technical Challenges

Though the advantages of NGS for cancer medicine seem obvious, clinicians and researchers alike must be wary of several potential pitfalls when applying this technology to patient care. First, the quality of the data generated depends heavily on the quality of the sample provided. The percentage of tumor cells within a given sample can vary widely, and furthermore one tumor may harbor different genetic changes in different geographic regions (“tumor heterogeneity”) [4, 5]. Availability of ample, representative, high-quality biospecimens may prove scarce in real-time oncology NGS diagnostics.

A second major technical pitfall relates to the ability to accurately interpret genomic data. Bioinformatics and computational biology are rapidly evolving, but considerable risk remains of false positive results, false negative results, and misinterpretation of gene mutations [4, 9]. Because almost all malignancies are genetically unstable, tumors accumulate a large number of random genetic alterations not related to their pathogenesis. The causative or so-called “driver” mutations seen in tumor DNA can be difficult to distinguish from the more common random, “passenger” mutations that do not contribute to disease [5]. Even among somatic alterations in genes known to cause cancer, many are variants of uncertain significance (VUS), in which the effect of the DNA change on protein function cannot be predicted using current informatics tools [9]. To select a cancer therapy based on a mutation that does not truly “drive” the given cancer would likely lead to ineffective treatment for the patient.

A third possible pitfall of using NGS in real-time oncology is that, even when we can correctly identify a driver, treatments that target it may not exist. Indeed, the pace of sequencing technology has far exceeded our ability to develop and use targeted drugs in the research and clinical settings. In fact, fewer than 30 percent of all cancer patients screened with NGS receive a genomically directed therapy [5]. This phenomenon calls into question the cost-benefit ratio of NGS in the cancer setting, where most patients are not seeing “clinically actionable” results from their testing [3].

Ethical Challenges

The ethical challenges raised by the use of genome-scale sequencing in guiding cancer therapy relate to germline variants detected in the process of comparing tumor DNA to constitutional DNA. The great majority of patients undergoing genome sequencing will be found to carry a handful of deleterious autosomal recessive alleles [10]. These recessive genes result in a phenotype only when present in the homozygous state and do not cause symptoms in heterozygous carriers. While potentially relevant to offspring and other relatives, autosomal recessive genes generally don’t have much impact on the cancer patient. Of greater concern are X-linked recessive diseases in males and autosomal-dominant diseases in males or females, as in the hypothetical case described above. These mutations are much rarer than autosomal recessive mutations but still are present in a substantial fraction of patients [11]. So-called “incidental findings” that are unintentionally discovered when NGS is used for cancer genome testing can pose a significant ethical problem for patients, their families, and their physicians.

It has been recognized for some time that even targeted genetic testing for somatic mutations in cancer can identify germline mutations that indicate the presence of hereditary cancer predisposition. Identifying a BRCA mutation in a breast tumor, when testing the tumor for sensitivity to PARP inhibitors, simultaneously predicts that the patient has a hereditary cancer syndrome since virtually all tumor BRCA mutations are also present in the germline [12-14]. The possibility of finding a mutation that predicts hereditary cancer predisposition can be discussed ahead of

time with patients undergoing tumor testing because results of this nature are not unanticipated. In the context of colorectal cancer, some groups advocate specifically including hereditary cancer genes when testing tumors for mutations in order to identify patients with genetic cancer predisposition [15].

However, genetic diagnoses not closely related to the disease for which testing was originally ordered are more problematic. Which incidental findings to report and whether to report incidental findings at all have been fiercely debated among genetic researchers, clinical laboratories, and direct patient care providers. The American College of Medical Genetics recently published guidelines recommending mandatory reporting of incidental findings in 57 genes that lead to “actionable” genetic disease [11], but quickly revised its guidelines after an outcry from the genetics community over what was felt to represent major violations of informed consent [16].

Though a consensus has yet to be found, most agree that there is, at a minimum and in certain contexts, a “duty to warn” a patient when results that indicate predisposition to a life-threatening disease are found [17]. Incidental findings from genomic testing have been compared to incidental findings in medical imaging, where case law suggests that clinicians may face liability for failing to disclose information that would have offered an opportunity to improve health outcomes [18]. On the other hand, results that predict the presence of or predilection to an untreatable disease, as in the present case, would seem to have limited personal utility or clinical value. Nevertheless, the lay public expresses concern about health care professionals filtering data and failing to provide complete information [19].

To prevent the ethical dilemmas associated with “incidentalomes,” clinical laboratories and those in direct patient care relationships should make explicit decisions, in advance of testing, about what in the genome will be queried and reported [20]. Choosing a selected set of genes to analyze would reduce the risk of false positives and incidental findings. It would also theoretically allow for the patient to better understand what results may stem from a given test and to provide informed consent for testing. However, obtaining true informed consent for testing for a single gene mutation is already complicated and lengthy; NGS has exponentially multiplied the difficulty in ensuring that a patient truly understands the implications of testing. A patient’s “right not to know” is a widely held value in medicine and has been a thorny issue in NGS testing [21]. Some have suggested a tiered approach to result reporting as a solution to this issue, in which patients can choose which results will be disclosed based on clinical utility, disease implications, and potential for heredity [17, 20, 22]. It remains to be seen whether this ostensible patient consent would protect a health care provider who fails to reveal actionable information.

Conclusions

Modern sequencing technologies have dramatically changed the face of cancer medicine in recent years, and the future holds great promise. NGS has made

genomic-driven cancer medicine a reality, with hopes of tailoring cancer therapy to individual patients. To be sure, NGS is not without its challenges. But with foresight, careful planning, collaboration among researchers, clinicians and patients, and adequate funding, NGS may very well lead us to the end of cancer as we know it.

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HEALTH LAW

The Terminally Ill, Access to Investigational Drugs, and FDA Rules

Valarie Blake, JD, MA

Abigail Burroughs was in her late teens when she was diagnosed with head and neck cancer. A year into her treatment, her doctors had exhausted all standard therapies but Abigail's condition had not improved [1]. Abigail's oncologist believed she might benefit from an experimental cancer drug that targeted the same receptors as her cancer but that was only being studied in patients with colon cancer. Another cancer trial would not enroll her and, when she was finally accepted to a clinical trial several months later, she was by then too ill to travel. She died a month later at the age of 21 [1].

To honor his daughter, Abigail's father formed the Abigail Alliance, a patient rights group that advocates for expanded access to experimental drugs for terminally ill cancer patients [2]. The group sued the Food and Drug Administration for broadened access, critiquing FDA's existing compassionate use regulations (discussed in greater detail later). The suit launched a legal battle over two questions: is there a fundamental constitutional right to experimental therapies, and should the terminally ill be permitted to expose themselves to unusually great research risks for a small chance of benefit? This paper explores relevant legal cases and the FDA's response to this evolving area of law.

U.S. v Rutherford (1979)

Before the Abigail Alliance suits (and before the FDA had introduced specific rules allowing compassionate use of experimental therapies), terminally ill cancer patients and their spouses brought suit against the FDA to enjoin it from interfering in the marketing and distribution of Laetrile [3]. Laetrile was an extract of apricot pits and almonds, available outside the U.S. and widely believed to be an effective cancer treatment. Parties to the suit believed Laetrile was their last and only option [3, 4]. The FDA had blocked approval for marketing of the drug and was waiting for greater clinical research data on efficacy and safety [3, 4].

Recognizing the limited options that terminal cancer patients faced, the U.S. Supreme Court in *Rutherford* stood by the FDA actions and concluded that the right to access unproven therapies did not exist in this case [3]. Acknowledging that there is a clear protected right to refuse life-saving treatment, the Court distinguished this from a positive right to access a particular treatment or medication. It argued that a drug is as unsafe for the terminally ill as for anyone else if its prospects of death and physical injury are not outweighed by its potential for benefit, and the FDA had not yet found evidence that Laetrile was safe and effective [3]. Furthermore, the Court

asserted, the government (specifically the FDA) has an interest in regulating unsafe drugs and protecting the public's health [3]. The Court believed that if patients were to have expanded access to Laetrile, the question would more appropriately be handled by the FDA or the legislature than by the judiciary [3].

Abigail I (2006)

Almost three decades later, the U.S. Court of Appeals for the District of Columbia heard *Abigail Alliance for Better Access to Developmental Drugs v. Von Eschenbach* and was asked to address the same fundamental question raised in *Rutherford* [5]. While the FDA by then had special procedures in place that gave some individuals access to developing drugs, the alliance rejected these procedures as “effectively inoperative” and called for greater rights for the terminally ill [6].

A three-judge panel held in favor of the alliance and a right to access experimental therapies [5]. They framed the question as one of whether terminally ill patients have a fundamental right to make informed decisions that may prolong their lives, specifically access to experimental therapies that have completed phase I testing [5]. They saw this right as arising from due process clause, the part of the Fifth Amendment to the Constitution that guarantees that no person shall be deprived of life, liberty, or property without due process [5]. The due process clause protects rights and traditions that are deeply rooted in our nation's history and are implicit in the concept of liberty [5]. The three-judge panel pointed to a longstanding tradition in America of protecting a right to control one's body, demonstrated in the right to self-defense and self-preservation (including an exception to violate some laws in order to preserve one's life, for example to damage another's property). And while there is no long-standing general duty to rescue or save another's life, there is long-standing liability for interfering with an individual's ability to save him- or herself [5].

In contrast with these age-old traditions in the law, the regulation of drugs by the government is fairly new, not undertaken until 1906 [5]. Drug safety did not become a significant regulatory issue until 1938, and drug efficacy only became a requirement for FDA approval in 1962 [5]. Thus, for half of American history, patients could obtain drugs without any government interference, and important aspects of patient access still remain unregulated, for example the provision of off-label prescriptions [5]. Relating this to *Cruzan* (the renowned 1990 Supreme Court case affirming a fundamental due process-derived right to *withdraw* life-saving medical care) [7], the finding in favor of the alliance was based not on a positive right to access something, but on a negative right to be free from governmental intrusion [5].

Abigail II (2007)

The FDA appealed the three-judge panel's determination and sought an *en banc* review (meaning a larger pool of Appellate Court judges to hear the case). In a landmark decision, the *en banc* review overturned the appeals court's decision in *Abigail I* and agreed with the FDA that there is no fundamental right to access

experimental therapies for anyone, including the terminally ill. [8]. This time, the court “reframed the issue not as a personal autonomy right to control one’s body but as a right to access something that is presently inaccessible: drugs that FDA has not yet approved for marketing and use by the public” [9]. Moreover, the court in *Abigail I* had not recognized a strong argument about the government’s interest in regulating drug *safety* [8]. Here, the *Abigail II* court found a long-standing regulatory history. At the state level, regulation of dangerous drugs had begun as early as 1736, with a Virginia law limiting the dispensing of drugs to amounts that were necessary but not harmful [8]. By the 1850s at least 25 states had some regulation related to adulterated and unsafe drugs [8]. Therefore, FDA prohibitions on the sale of drugs were seen by the court as “entirely consistent with our historical tradition” [8].

And while expanded access to experimental therapies might be akin to self-defense, such a right can always be limited by the legislature [8]. For example, a group arguing for access to medical marijuana was denied it because the drug had already been forbidden under the Controlled Substances Act [8, 10]. Similarly, the FDA (through the legislature) has already acted to limit access to unsafe drugs [8, 11]. While the *Abigail I* court agreed with a long-standing history of forbidding interference with a person’s ability to save or rescue him- or herself, the *Abigail II* court disagreed that the FDA was preventing the terminally ill from rescuing themselves [8]. Instead, clear science and medical communities were protecting the terminally ill from unsafe drugs that had not been approved for marketing [8]. The court suggested that the law could someday strike a balance between access to experimental drugs and appropriate risk taking, but the specific question before this court was whether the Constitution itself demands that terminally ill people have access to nonapproved drugs [8]. Like the *Rutherford* court, the *Abigail II* decision insinuated that this was an issue perhaps better handled by the legislature, nodding to recent efforts by the FDA to expand access [8].

FDA Regulations

In bringing *Abigail I* and *II* to court, the Abigail Alliance for Better Access to Developmental Drugs did not pay much attention to the existing FDA regulations that allow some expanded access for terminally ill patients to experimental drugs. Perhaps this is because it was trying to win the much larger battle of establishing a recognized Constitutional right and, additionally, found the FDA expanded-access rules too limiting and ineffective to warrant greater attention.

To date, there are several channels that patients like Abigail Burroughs might consider. The FDA updated the policies in 2009 (and as recently as May 2013 provided draft guidance on their implementation [12]). There are currently three possible channels for expanded access for patients. (1) The FDA allows expanded access on a case-by-case basis for individual patients if the probable risk of ill effects from the drug is not greater than the probable risk posed by the disease and if the patient cannot gain access to the drug in other ways. A drug sponsor or physician must file the paperwork to open this channel [13]. (2) Small groups of patients can gain access to experimental therapies if they do not qualify for an experimental trial

and there is sufficient evidence of experimental therapy's safety and efficacy [14]. (3) Lastly, larger groups may gain access to the drug once it has passed phase III (or rarely, with strong evidence of safety and effectiveness, phase II) and the sponsor is seeking marketing approval [15]. These channels have been critiqued as slow and burdensome for patients. The FDA sometimes defers decisions on these requests until there is greater knowledge of the safety and effectiveness of drugs, which can be too slow a process for some patients [4, 9]. In 2011, approximately 1,200 patients received some form of early access under FDA's compassionate use channels [16].

This issue, despite prior legislation and the ongoing development of FDA rules, continues to be presented before the courts. There was, for example, a 2008 case in the Third Circuit Court of Appeals in which a pharmaceutical company was held not to have an obligation to provide a promising treatment in phase II studies to a patient with Duchenne muscular dystrophy [17]. Ongoing innovation and development in medicine is bound to increase the tension over how early to provide access to non-FDA-approved drugs to patients who have no other treatment options available.

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POLICY FORUM

Overcoming Inequalities: The Affordable Care Act and Cancer Treatment

Michael K. Gusmano, PhD

A regrettable feature of the debate leading up to the adoption of the Patient Protection and Affordable Care Act (ACA) in 2010 was the controversy over whether the new law would lead to inappropriate “rationing” of cancer screening and treatment. In particular, opponents of the law pointed to a recommendation from the U.S. Preventive Services Task Force (USPSTF) [1]—that had nothing to do with the ACA or the comparative effectiveness research it now funds—as an example of how the new law would limit access to care and undermine the quality of the health care system by placing cost control ahead of quality. Not only did these attacks have little merit, they distracted attention from the more likely effect of the ACA on cancer screening and treatment. By extending public and private health insurance to approximately 30 million Americans and prohibiting a number of health insurance practices that limit coverage, the ACA has the potential to reduce ethically troubling disparities in access.

Is “Comparative Effectiveness Research” Really a Threat to Cancer Care?

The controversy over the USPSTF’s recommendation against routine mammography screening among women ages 40 to 49 without other risk factors for breast cancer was caught up in a large debate about the role of comparative effectiveness research (CER). This debate reached a fever pitch during the health reform deliberations of 2009-2010. CER is the effort to compare the effectiveness of competing health care technologies and advocates hope it will generate evidence that can be used to improve the quality and efficiency of the health care system [2]. The Obama administration signalled its enthusiasm for this research when it invested \$1.1 billion in CER as part of the American Recovery and Reinvestment Act (ARRA) in 2008. The ACA expanded this investment and created the Patient-Centered Outcomes Research Institute (PCORI) to direct federal CER efforts.

Despite its laudable goals, CER often generates fear because opponents are concerned that it may be used to deny coverage for effective treatments on the basis of inadequate data [3]. Furthermore, CER is often confused with economic evaluation of health technology (cost-benefit analyses) in which the health benefits of a technology are compared with its costs. To guard against this criticism, the ACA prohibits the government from conducting economic evaluation and prohibits the Center for Medicare and Medicaid Services (CMS) from using CER to make coverage and reimbursement decisions. And even if the ACA *did* call for economic evaluation of health care technologies, it is not clear that the results would significantly reduce spending on cancer screening and treatment.

Spending on cancer screening and treatment continues to climb, but many studies claim that these investments have been “worth it” when the economic value of the health gains is compared with the cost. Studies from the U.S. and other Organization for Economic Co-operation and Development (OECD) countries have found that aggressive use of breast cancer screening, coupled with advances in treatment, have reduced breast cancer deaths significantly in recent decades. For instance, a host of studies have found that radiotherapy, hormone treatment, and chemotherapy are all cost effective [4-7].

There is considerable disagreement among policymakers, health care professionals, policy analysts, and the general public about how to value gains in longevity, but few doubt that such gains have great economic value. As new, and more expensive, treatment options are developed, it is important for researchers and government agencies to review the clinical evidence continually and identify the health gains associated with these treatments. In doing so, they should make every effort to capture gains in functional status and quality of life, not merely gains in longevity. Regardless, without substantial changes, the ACA will not allow the federal government to incorporate the results of such research into policy.

The ACA and Inequality in Cancer Treatment

There is little evidence that the ACA will restrict access to cancer screening and treatment, and there are good reasons to believe it will *expand* access to such treatment. By doing so, it may help to reduce indefensible inequalities in cancer treatment and outcomes. Based on national health interview survey data, Ward and colleagues found that, compared with people with private insurance, women ages 40 to 64 who were uninsured at the time of interview were significantly less likely to report having a mammogram during the preceding 2 years (38 percent vs. 75 percent). Uninsured women ages 18 to 64 were significantly less likely than women with private health insurance to have had a Pap test within the preceding 3 years (68 percent vs. 88 percent). Similarly, uninsured adults ages 50 to 64 were significantly less likely to have been screened for colorectal cancer (19 percent vs. 48 percent) than their counterparts with private health insurance [8]. Halpern and colleagues found that people without insurance were more likely to be diagnosed with late stage (III or IV) vs. early state (I or II) than cancer patients with private insurance [9].

What are the consequences of these inequalities in access to care? The contribution of health care to health outcomes can be measured, in part, by focusing on “unnecessary untimely deaths” or “avoidable’ mortality” [10, 11]. These are deaths caused by conditions for which there are effective public health and health care interventions. Among the causes of premature death that experts believe to be amenable to medical care are cancers of the breast, cervix, colon, uterus, skin, and testis [10]. The concept of amenable mortality assumes that all premature deaths due to causes for which there are effective interventions, including breast cancer, are all *potentially* avoidable, but it recognizes that it may be impossible for health care interventions to eliminate all of these deaths [12]. Unfortunately, not all Americans benefit from interventions that could reduce their odds of dying prematurely from

cancer. In a previous analysis of geographic inequalities in avoidable mortality in Manhattan, we found that residents of the lowest-income neighborhood of Manhattan, in which rates of insurance coverage were much lower than the rest of the borough, were significantly more likely to die prematurely from diseases that are amenable to medical care, including the forms of cancer listed above [13].

By extending health insurance coverage to millions of Americans, the ACA should help reduce inequalities in cancer screening and treatment. First, the law's minimum essential coverage provision, known as the "individual mandate," requires most people to purchase a minimum level of health insurance for themselves and their dependents starting in 2014. Second, the law calls for a major expansion of the Medicaid program that will expand the availability of public insurance coverage for many adults in states that had low eligibility levels. Although the U.S. Supreme Court ruled in *National Federation of Independent Business v. Sebelius* that the federal government may not force states to participate in the Medicaid expansion by withdrawing federal matching for the existing Medicaid program, most, if not all states are likely to expand their Medicaid programs rather than walk away from enormous federal funding [14]. Together, the individual mandate and Medicaid expansion will extend health insurance protection with more than 20 million people.

Equally important, the "essential health benefit" provision of the law means that this insurance will include substantial coverage for cancer screening and treatment [15]. Beyond this, the ACA also includes several provisions designed to improve access to preventive services, including cancer screening. Under the law, for example, Medicare beneficiaries do not have to pay for preventive services that have received a grade of A or B (i.e., "strongly recommended" or "recommended") by the U.S. Preventive Services Task Force, and the deductible for colorectal cancer screening is waived. Finally, the ACA regulates private health insurance and prohibits a number of practices that limited access to health insurance for people diagnosed with cancer. Health insurance companies are no longer allowed to rescind policies when people make mistakes on their applications and they are no longer allowed to place lifetime caps on the dollar amount of coverage. Health insurance companies are prohibited from denying coverage for children with a pre-existing condition and, starting in 2014, they will be prohibited from doing so for anyone.

Conclusion

Years of investment in medical technology have improved our capacity to detect and treat many forms of cancer. Although some types of screening may be problematic because they generate too many false positives, most are effective at detecting cancer at an early stage and improving the prognosis of patients. Similarly, advances in treatment have helped cure many patients and extended the lives of many others. Unfortunately, the benefits of these interventions are not shared by all. In the U.S., members of marginalized racial and ethnic groups and patients without health insurance often do not receive timely and appropriate care. The ACA will not solve this problem, but, by extending access to health insurance to millions of Americans, it should significantly reduce inequalities in access to care.

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MEDICINE AND SOCIETY

What Cancer Survivorship Means

Gayle Sulik, PhD

“What patients see through the glass is not a world outside cancer, but a world taken over by it—cancer reflected endlessly around them like a hall of mirrors.”

--Siddhartha Mukherjee, *The Emperor of All Maladies* [1]

According to the National Cancer Institute Office of Cancer Survivorship, a person is considered a cancer survivor at the time of cancer diagnosis and remains so for the remainder of his or her life [2]. By this definition there were about 13.7 million cancer survivors in the United States as of January 2012, a number projected to reach 18 million in the next decade. Sixty-four percent of the 2012 survivor population had survived 5 or more years; 40 percent had survived 10 or more years; and 15 percent had survived 20 or more years [3]. But, contrary to the common definition of survival (i.e., to live), many cancer survivors do not actually survive cancer—according to an 18-year study by the American Association for Cancer Research, just over half of people labeled cancer “survivors” ultimately died of cancer [4]. This contradiction creates confusion about the meaning of survivorship for patients, caregivers, and health practitioners. What’s more, it influences social support, policy guidelines, health care delivery and research, and survivors’ lives.

There is a blog on health care by a trained oncologist turned breast cancer patient, now “survivor,” that paints a picture. In one of her blog posts [5] she writes about a chance meeting with a colleague several years after being treated for cancer. In response to the usual “How have you been?” question, the oncologist-blogger mentioned that she’d been out of touch for a while “because of some health problems...[including] breast cancer.” The colleague said, “Who doesn’t have breast cancer?” Without a nod of acknowledgement toward what the oncologist-blogger had experienced, the conversation quickly shifted to a discussion of medical offices. The oncologist-blogger was taken aback by her colleague’s glib remark and apparent lack of concern. To her readers, she wrote:

My hair was curly for most of a year. My breasts are gone. My bones are thinner and I’m estrogen-deprived. Sound depressing? It is, for as many as 30 to 40 percent of women at some point after their diagnosis. It’s not a minor experience in the physical, emotional or life-changing sense.

The conversation between the two oncologists, one diagnosed with cancer and the other not, brings to light a common misunderstanding about survivorship. There is an

odd impression in American society that cancer is a passing inconvenience for most, an opportunity for personal growth for all, and a badge of honor for those who “survive.” In reality, survivorship operates in multiple spheres with conflicting meanings, creating ambivalence about what survivorship means for people dealing with cancer and for those offering support, guidance, and treatment.

While individuals and survivorship groups have made inroads in communicating their experiences with cancer and its latent effects to the medical system, cultural and other systemic factors impede understanding of survivorship experiences and needs. Stories about courageous survivors abound, but the realities of many people’s lives look nothing like the celebratory events, sound bites, or marketing materials that pervade the cultural landscape. The remainder of this essay describes three overlapping social spheres in which the “survivor” label operates, with varying degrees of utility.

First is the patient advocacy sphere, which was a collective response to the failure of the health care system to provide coordinated and comprehensive follow-up care to cancer patients when treatment stops. A seminal report by the Institute of Medicine (IOM), *From Cancer Patient to Cancer Survivor: Lost in Transition* [6], described a state of limbo wherein survivors were caught between an orderly system of medical care and a non-system. There were few evidence-based guidelines on how to deal with lingering health problems, latent effects, psychosocial difficulties, and other hardships. The term “survivor” was crucial for making a case for ongoing, coordinated, and comprehensive support for the duration of a person’s life. The report recommended survivorship care plans and the need for clear standards of care. It was a step forward, and there were isolated attempts to deal with survivorship, but it took years before additional guidelines were developed [7-12].

On March 14, 2013 an alliance of 23 leading cancer centers (as the National Comprehensive Care Network) announced new survivorship guidelines to help practitioners assess the needs of cancer survivors on a routine basis [13]. They provide a general framework for screening, evaluating, and treating common consequences of cancer and treatment. For instance, at least half of those treated for cancer suffer latent treatment effects such as pain and fatigue; 19 percent meet the diagnostic criteria for post-traumatic stress syndrome; 29 percent face anxiety and depression; and cancer treatments themselves too often lead to the development of other conditions, including heart disease and other cancers [13]. Sleep disorders, cognitive impairment, suppressed immune systems, and sexual problems are also common. How these descriptions translate to clinical practice is unclear. However, they are a move toward focusing on some key aspects of post-treatment patients’ real lives—something survivorship groups have demanded as they pressed for a cooperative and comprehensive model of care.

The second sphere of survivorship is the self-help arena [14]. Over the course of many years, the term “survivor” replaced “victim” as a way to encourage personal empowerment. As the survivor identity gained social status, public discourse started

to focus almost exclusively on inspiration, pride, and transformation. “Share your stories of hope,” say the countless calls for survivors’ voices from popular magazines, news outlets, and nonprofit organizations. With the goal of providing comfort and hope to those facing cancer, for example, the American Cancer Society encourages people to share their stories on its website [15]. With courage, strength, and optimism inextricably tied to “winning the war” on cancer, however, what started as social support later morphed into a profitable entertainment venue. Fundraisers and public spaces brought cancer survivors to the forefront as audiences sang songs and purchased survivor gear. Heightened attention to celebration and triumph made survivorship a multibillion-dollar industry. While the celebration resonated with some, it left the difficult realities of cancer on the sidelines, isolating those with terminal conditions and creating a backlash against survivorship culture itself.

Those who protested the “survivor” label typically recognized that, while optimistic attitudes may help people to feel better emotionally, they do not positively impact cancer progression or survival. Evidence supports this belief. People who think positively get cancer and die from cancer at the same rates as people who do not [16]. Yet the cultural mandate to demonstrate a can-do attitude in the face of cancer thrives within many survivor communities and in the broader culture. The optimism and triumph of the iconic cancer survivor sometimes has the unintended effect of encouraging people to suppress emotions that are not socially accepted, especially anger, disappointment, and fear. Doing so contributes to stress (well known for its deleterious health effects) as well as denial and depression. It also increases the likelihood that the needs of survivors will not be met. After all, if “survivors” are to be strong, courageous, and self-motivated, they surely do not need help. Tragically, the image of the triumphant survivor who cheerfully lives on suggests implicitly that those who do not survive were simply not optimistic enough.

When combined with the third sphere, medical consumerism, the term “survivor” is more loaded. In this realm the ideal survivor is armed with medical knowledge to confidently and aggressively seek medical intervention. The consumer movements of the 1960s and 1970s challenged the dominance of the medical system, arguing that those who purchase health care services have a right to play an active role in making informed choices [17]. By the 1990s, more patients sought information, questioned doctors, and asked for second opinions. At the same time, corporate medicine infiltrated survivor communities, medical communities, and the public sphere [18]. Most clinical research privatized, and huge pharmaceutical companies started to spend more on direct-to-consumer-advertising than on research and development [19-23]. The pharmaceutical industry sought to shape consumer choice and develop new markets, including the survivor population and healthy people at risk.

An example in the cancer world is the “previvor”—a term coined in 2000 for the survivor of a *predisposition* to cancer who has not had the disease. Commonly used in the breast and ovarian cancer survivor communities, the term made *Time* magazine’s top ten buzzwords list in 2007 [24]. The term typically refers to people

who have a cancer-predisposing genetic mutation on the so-called breast cancer genes, BRCA1 and BRCA2. Although not everyone who inherits mutations in these genes develops cancer, the genetic mutations have been found to increase the overall risk of breast, ovarian, prostate, pancreatic, testicular, and male breast cancers.

Angelina Jolie's shocking reveal in a *New York Times* editorial of [25] her family history of cancer, her inherited genetic mutation, and her decision to have prophylactic surgeries to reduce her risk of developing breast and ovarian cancer set off a public discussion about pre-survivorship, medical intervention, genetic testing, gene patenting, access and choice in health care, and personal responsibility. Though only 5 to 10 percent of all breast cancer cases and 10 to 15 percent of ovarian cancers among white women in the United States are associated with BRCA gene mutations, the Mayo Clinic reports that removing the breasts reduces the chances of developing breast cancer by 90 percent and removing the ovaries reduces the risk of ovarian cancer by 80 to 90 percent [26]. As an astute medical consumer at high risk, Jolie's decision to remove her healthy body parts as a way to reduce her probability of possibly developing a future cancer seemed to make sense. While some called her decision brave [27-30], others pointed to the fact that such medical intervention in a culture of fear around cancer is extreme and that too many women struggle with what they feel are "all around bad choices" [31-33]. This case demonstrates how the spheres of patient advocacy, self-help, and medical consumerism both antagonize and unite survivors.

On the one hand, survivors of all types want to be heard, want control, and want choice. More than anything else, they want health, longevity, and quality of life. On the other hand, the road to these outcomes is riddled with obstacles involving profit motives, medical uncertainty, treatment modalities, access to quality care, social expectations, and other factors affecting health. The medical system is not yet prepared to deliver survivorship care, let alone presurvivorship care. There is already too little survivorship research, inadequate reimbursement for services, variation in care models, and a lack of health care providers [34]. Without an infrastructure to handle the needs of the survivor population, the social and economic burden of cancer will continue to grow along with the sheer numbers of people dealing with cancer risks, diagnoses, and the aftereffects of treatment. Until health practitioners become actively involved in survivorship at all levels of care and keep detailed histories on patients as new evidence emerges, survivors will continue to "see cancer reflected endlessly around them like a hall of mirrors."

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IMAGES OF HEALING AND LEARNING

Images in Cigarette Warning Labels: How Should They Warn?

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Tobacco use remains the leading cause of preventable death in the United States [1]. To reduce tobacco's impact on public health, the U.S. Food and Drug Administration (FDA) was given regulatory authority over tobacco products in the Family Smoking Prevention and Tobacco Control Act of 2009 [2]. The act's mandate to the FDA included selection of "color graphics depicting the negative health consequences of smoking" to accompany nine different text messages for health warning labels (HWLs) that will cover 50 percent of the front and back of cigarette packages. The messages consist of the word "WARNING" paired with one of the following: "Cigarettes are addictive," "Tobacco smoke can harm your children," "Cigarettes cause fatal lung disease," "Cigarettes cause cancer," "Cigarettes cause strokes and heart disease," "Smoking during pregnancy can harm your baby," "Smoking can kill you," and "Tobacco smoke causes fatal lung disease in nonsmokers." This policy is consistent with recommendations by the World Health Organization Framework Convention on Tobacco Control (WHO-FCTC) [3, 4], the world's first global health treaty. As of 2012, 56 countries had implemented prominent pictorial HWLs on cigarette packs, and seven more countries are scheduled to do so in 2013 [5]. The U.S. was to join these countries in 2012, but tobacco industry litigation has delayed implementation of this key tobacco control policy.

The tobacco industry has argued that the images the FDA selected for HWLs violate their First Amendment rights by compelling them to engage in speech that is against their interests [6]. The industry claimed that many of the selected images were designed to provoke emotional responses that go beyond the goal of informing consumers about the consequences of tobacco use [6]. The Washington, D.C. District Court effectively halted implementation of pictorial HWLs in February 2012 [6], judging the industry's argument to have merit, a judgment that was upheld by the U.S. Court of Appeals in August 2012 [7]. In March 2013, the FDA decided not to appeal the case to the U.S. Supreme Court [8]. Nevertheless, in April 2013, the U.S. Supreme Court let stand a prior appellate court ruling that clears the way for the FDA to propose a new set of images to accompany the already-legislated textual content of the HWLs [9]. These new pictorial HWLs will most likely need to overcome additional legal challenges from the tobacco industry. This essay reviews the primary tobacco industry arguments and the public health arguments against the industry, including those from the ruling and dissenting opinions in the appeals court case, while reflecting on existing scientific evidence and ethical considerations raised by this issue.

Pictorial Health Warning Labels

The inclusion of textual HWLs on the side of cigarette packs to warn consumers of the health risks associated with smoking began in the U.S. in 1965 [10]. The content and format of these warning labels was last revised in 1984 [11]. Evidence shows that these warnings are unnoticed by consumers and they have failed to convey relevant information in an effective way. According to the Institute of Medicine, “the current warnings are inadequate even when measured against an informed choice standard, but they are woefully deficient when evaluated in terms of proper public health criteria” [12]. The tobacco companies do not challenge the factual accuracy of the text statements proposed for the new HWLs [7], nor could they reasonably do so, given the scientific consensus that tobacco products are dangerous and a leading cause of many diseases. The main legal challenges in this case revolve around the graphic images selected by the FDA to accompany the factually accurate text statements.

In determining the legal framework against which to judge the tobacco industry’s case, the U.S. Court of Appeals had to assess whether the pictorial HWLs that the FDA selected were “reasonably related to the State’s interest in preventing deception of consumers” [13]. Because the FDA did not design the pictorial HWLs to correct specific deceptive claims by the industry about their products, the appeals court viewed the FDA’s recommended HWLs as going beyond this goal and agreed with the tobacco industry contention that the HWLs aimed to discourage consumers from buying the company’s products. This narrow interpretation of the FDA’s role in correcting deceptive claims did not consider the long history of systematic tobacco industry campaigns to deceive consumers and regulators about the harms of tobacco and to enhance the addictiveness of their products [14, 15]. In 2012, the U.S. District Court for the District of Columbia upheld charges against the industry using the Racketeer Influenced and Corrupt Organizations (RICO) Act for proven “misstatements and acts of concealment and deception...made intentionally and deliberately...as part of a multi-faceted, sophisticated scheme to defraud” [16]. The government’s interest in implementing pictorial HWLs should be examined against this broad backdrop and long history of industry deceit.

Indeed, the dissenting opinion of the appeals court highlights the implications of this deceit by citing studies done between 2000 and 2007, which found that many current and potential smokers were not adequately informed about the range and magnitude of tobacco-related risks or about the addictive nature of tobacco use. In one survey, for example, 28 percent of smokers and 18 percent of non-smokers were not aware that smoking shortens one’s life [17], and a high proportion of consumers had inaccurate assessments of the fatality of smoking compared with other risks to which they were exposed, such as car accidents [17, 18]. Moreover, smokers generally did not fully understand the implications of tobacco addiction for quitting and underestimated their risk relative to other smokers and to nonsmokers [19].

This tendency to underestimate risks appears particularly pronounced in adolescents, who have been shown to express unrealistic optimism about their ability to quit

smoking after they start smoking [18-20]. For example, only 3 percent of twelfth-grade daily smokers reported that they would still be smoking in 5 years, but 63 percent were daily smokers 7 to 9 years later [21]. The addictiveness of tobacco is clear when one considers that 40 percent of smokers try to quit in any particular year, and only 5 percent succeed [18]. Misperceptions of the addictiveness of smoking and its harms are particularly tragic given that smoking remains the leading cause of preventable death in the US, causing smokers to die 10 years earlier than nonsmokers [22]. HWLs are a cheap means of delivering important health information on the addictiveness and dangers of smoking to consumers and potential consumers.

The appeals court ruling did not view HWLs as a corrective to tobacco industry fraud, and therefore concluded that the FDA's intent was to "encourage current smokers to quit and dissuade other consumers from ever buying cigarettes" [23]. They highlighted the lack of scientific evidence for a substantial impact of pictorial HWLs on smoking prevalence. Indeed, scientific study of pictorial HWL policy effects is complicated by the simultaneous implementation of pictorial HWLs with other tobacco control measures, all of which could help explain subsequent declines in consumption. Existing evidence for the population impact of pictorial HWLs on consumption suggests a relatively small effect size, but it is in the direction that favors public health [24]. Relatively small behavioral effects are not unexpected from interventions like this, but their impact can be significant because of their broad reach, regularly exposing all smokers.

The appeals court indicated that the broader goal of reducing smoking supersedes the FDA's stated "primary goal, which is to *effectively* convey the negative health consequences of smoking on cigarette packages and in advertisements" [25]. Hence, the appeals court did not seriously consider consumer misperceptions of smoking-related risks, the tobacco industry's role in perpetuating these misperceptions, or the evidence showing how pictorial HWLs can increase consumer knowledge of smoking risks. Indeed, HWLs are a prominent source of health information for smokers and nonsmokers; they can increase health knowledge and perceptions of risk and can promote smoking cessation [26, 27]. Larger, more prominent warnings are more effective than smaller warnings, and warnings that contain pictures that illustrate the consequences of smoking are more likely than warnings with only text to capture the attention of consumers, to produce greater processing of the information, and to be remembered [27]. Moreover, graphic HWLs that elicit strong emotional reactions have been found to be more effective than more symbolic or abstract representations of risk [28-30]. It is the FDA's goal to adopt HWLs that are most likely to promote changes in knowledge, attitudes, and behaviors, and the evidence suggests that large graphic HWLs work best.

Tobacco industry arguments against pictorial HWL content also hinged on whether the images were considered "purely factual and uncontroversial" [6, 7]. The industry argument about the need for more factual HWLs is grounded in their concern that the FDA analyzed consumers' emotional responses to HWLs in order to select the most

effective pictorial content [6, 7]. This allegation that the emotive quality of the images conflicts with the purpose of communicating facts is particularly hypocritical coming from an industry that has been at the forefront of using emotive, image-based advertising to persuade people to consume its products. Persuasive messages that effectively change beliefs, attitudes, and behaviors often involve arousing negative emotions [31, 32], and the most effective tobacco control campaigns employ this strategy [33, 34]. Although some of the graphic images the FDA selected may evoke emotional reactions, it is undisputed that smoking can cause the health consequences these images depict (see figure 1). The emotive quality of the selected images does not necessarily undermine the HWLs' factual accuracy, but in selecting the next round of HWL imagery, the FDA will most likely need to strengthen arguments about the linkage between images and the text messages that they illustrate.



Figure 1. Example of FDA-proposed pictorial health warning label [35]

Information that Facilitates Smoking Cessation Efforts

One area of concern for the selection pictorial HWL content in the U.S. involves the inclusion of a toll-free phone number where smokers who want to quit can find help (i.e., “quitline”). Both the majority and dissenting opinions in the U.S. Court of Appeals highlighted how the inclusion of this “1-800-QUIT-NOW” quitline on pictorial HWLs went beyond the FDA’s mandate to disclose factual information about the health consequences of smoking. In other countries, pictorial HWLs that include such content have raised awareness about quitlines [36, 37] and increased the volume of calls they receive [38-41]. Indeed, pictorial HWLs that increase awareness of smoking-related dangers without providing behavioral recommendations or information to help with quitting violate basic principles of public health communication [42] while raising ethical concerns.

As public health communications, HWLs should provide members of the population with reasonable opportunities to pursue the behavior change needed to avoid the negative outcome [32]. Providing information on the addictiveness of tobacco and the harmfulness of smoking unaccompanied by cessation assistance information assumes that consumers have a free choice and personal responsibility to stop or avoid smoking or to pursue information on smoking cessation programs. However, nicotine addiction makes cessation extremely difficult, and when combined with the lack of knowledge about or access to cessation programs, smokers may blame themselves or their “weak” character for not quitting.

A further ethical concern associated with justice could be raised [32], inasmuch as socioeconomically disadvantaged populations, which have the highest rates of smoking, may have the least access to cessation programs [43]. Providing disadvantaged populations with information on free quitline services is crucial to advance the FDA's interest in reducing smoking rates. If the inclusion of quitline information on cigarette package HWLs is considered beyond the FDA mandate, then alternative means of providing smokers with this information should be considered. In Canada, for example, all packs contain either "onserts" or leaflets that include quitline information and smoking cessation advice (see figure 2).



Figure 2. One of eight “onserts” included in all cigarette packs sold in Canada [44]

Conclusion

In its April 2013 decision, the U.S. Supreme Court cleared the way for the FDA to propose a new set of pictorial HWLs for inclusion on cigarette packages [9]. In so doing, it has implicitly signaled its recognition of the FDA's mandate to inform consumers about the risks of tobacco products, and there is ample evidence to favor the efficacy of pictorial HWLs for achieving this goal. This policy measure is necessary to combat a long history of tobacco industry deceit about the magnitude and range of tobacco-related harms. Existing scientific evidence suggests that HWLs that graphically illustrate the harms of smoking should be considered for implementation in order to effectively inform consumers and would-be consumers about these risks.

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OP-ED

Defining Quality, Disseminating Evidence, and Enforcing Guidelines for Cancer Treatment

Thomas W. LeBlanc, MD, MA, and Amy P. Abernethy, MD, PhD

Dr. Robert Bristow and colleagues recently reported on the quality of cancer care provided to a large group of patients in California. In reviewing more than 13,000 cases from 1999 through 2006, they found that only about 37 percent of women with ovarian cancer had received the recommended standard treatment for their disease, as laid out in the National Comprehensive Cancer Network (NCCN) guidelines at the time [1]. This staggering finding is unfortunately just the latest piece of evidence in the evolving story about tensions between quality and cost in U.S. health care. Though we spend more of our gross domestic product on health care than any other country in the world, many of our outcomes are no better than those of other industrialized nations [2]. Our health care system has the uncanny ability to simultaneously provide the most expensive, unproven care to many and fail to consistently provide proven, guideline-recommended interventions. Or so it seems.

These recent findings are of course gut-wrenching and seemingly unfathomable. Who would deny appropriate treatment to so many women with a life-threatening disease? The underlying roots of the problem, however, are far from clear; its causes are complex and insidious, stemming from a tangled web of issues implicating physicians, payers, systems, and patients—all well-intentioned, yet sometimes contributing to the provision of inadequate care. Key contributors that we will highlight here include: (1) difficulty getting new evidence incorporated into clinical consciousness, (2) disagreements about definitions and measures of quality and problems with guidelines (conflict with other guidelines, failure to reflect the latest evidence and innovations, and so on), and (3) the challenges of enforcing adherence to guidelines.

Defining Quality and Disseminating Information

While reasonable people can agree that no patient should receive substandard care, we face enormous struggles in changing physician behavior and incorporating new knowledge into clinical practice [3]. Consider the following example. A general gynecologist finds an unexpected pelvic mass while doing a routine hysterectomy. She sees just a handful of ovarian cancer cases each year and is not trained in the intricacies and latest evidence on its surgical management. The patient is already in the operating room at a small community surgery center with no local gynecologic oncologist, so she proceeds to remove the mass, unfortunately resulting in its rupture and spillage of contents into the pelvis. No lymph nodes are sampled, the omentum is not removed, and no other biopsies are obtained. Thus, the patient leaves the

operating room without complete cancer staging and with a suboptimal resection that is likely to worsen her prognosis and necessitate another surgery.

The caring decision to quickly remove a newly found pelvic mass thus becomes an instance of suboptimal (if not negligent) care, despite good intentions. Should the gynecologist have stopped the operation, closed the incisions, and referred the patient to a specialist as an outpatient, resulting in a delay prior to another surgery and perhaps much distress? Reasonable people might disagree on the definition of quality care in a case like this, and agreed-upon definitions might conflict with reasonable views on how to help this particular patient when an expert is not available.

Such is the challenge of actually defining “quality.” Experts often disagree on the standard by which to measure quality care. As we increasingly focus on value-based care and more consciously consider costs, however, we *must* have some sort of yardstick by which to measure the care we provide. Unfortunately, these measures can be quite imperfect; sometimes we choose the wrong measure or fail to recognize downstream consequences of our choices. For example, current pneumonia treatment guidelines require the provision of antibiotics within 4 hours of presentation to the emergency department. The goal, of course, is timely provision of appropriate care. One of many unintended consequences, however, may be the overtreatment of less serious conditions (viral bronchitis, for example, which generally should not be treated with antibiotics) in an attempt to avoid a possible penalty for missing the 4-hour window for a patient who is later found to actually have pneumonia. Downstream, this could lead to antibiotic resistance, along with unnecessary drug costs. Outcomes like this reflect Goodhart’s famous axiom from the financial world: “When a measure becomes a target, it ceases to be a good measure” [4].

As this example demonstrates, appropriate referral to experts is certainly an important part of the solution to closing the quality chasm. Indeed, the “clinician comfort level” problem described here is precisely why gynecologic-oncology fellowships exist, why subspecialty board exams are important, and why specialists have their own conferences. Would those things really have helped in this case, though, since a gynecologic oncologist was not available to join in on the surgery? Even when experts abound, the challenge of getting evidence incorporated into practice remains; this process tends to be slow, inefficient, and inconsistent, even among experts themselves.

Continuing education activities are helpful but insufficient to keep physicians up to date with fast-paced changes [5, 6]. This is especially true in oncology, given how complex and diverse our options have become and the pace with which new therapies are being released to the market. Furthermore, many academic centers that pride themselves on staying “ahead of the curve,” provide promising therapies before there is truly mature data about their efficacy or appropriateness as standards of care or in conjunction with proven therapies. (This does not mean it is wrong to provide new treatments, which may in some cases be better for a particular patient.) Where

guidelines do exist, the recommendations of one frequently conflict with those of another, and many oncologists disagree with the specifics. Furthermore, available guidelines may change annually due to the speed of evidence development. All this conspires to make quality monitoring in oncology a rather precarious endeavor. Our evidence base is quite imperfect; we often really do not know which treatment is best.

Guideline Enforcement

If measuring quality is a tricky business, so too is enforcing adherence to guidelines and recommendations. Pay-for-performance initiatives and penalties for complications and errors are emerging strategies to enforce quality guidelines. Such initiatives have yet to emerge meaningfully in oncology, however. One promising development is the “5 things campaign,” meant to encourage reflection about high-value, cost-conscious care by highlighting five specific costly, unproven treatments to avoid; unfortunately the campaign lacks any enforcing “teeth” [7].

To promote adherence to proven, standard therapies, on the other hand, rather than discourage ineffective ones, is a much different and more challenging task. One potentially promising strategy to promote adherence is the use of so-called “care pathways.” These pathways are effectively “roadmaps” that seek to standardize cancer treatment on the basis of some reasonably agreed-upon set of evidence or guidelines, within the confines of a particular center or group of patients. Whether this strategy will catch on, eventually to the point that payers provide actionable incentives for sluggish systems to adopt it, remains unclear. From a behavioral economics standpoint, however, it is plausible and intuitively desirable. Evidence suggests that “defaults” are quite powerful in their impact on people’s eventual choices—several countries have capitalized on this phenomenon to increase the rate of organ donation, enacting policies of presumed consent by default [8]—and care pathways would effectively standardize some definition of “quality cancer care” as the default for all patients from which clinicians would opt out if they did not apply in a particular case. Making guideline-based care the “default” option would very likely increase quality, at least by this measure.

Care pathways only scratch the surface of what needs to be done, however. “Learning health care systems,” such as the American Society of Clinical Oncology’s CancerLinQ, have the potential to operationalize quality measures more effectively, bringing on-the-fly quality monitoring and feedback to individual clinicians and practices [9, 10]. Learning systems and electronically available data can also facilitate clinical decision support, tying specific details about the patient (e.g., age, disease, preferences) with clinical options to present the best possible approach in real-time at the point of care. This recursive provision of feedback will not only enhance adherence to agreed-upon guidelines, imperfect as they may be, but also simultaneously help us study and develop the quality measures of the future by making data collection and analysis more of an active part of routine clinical care. Even the clinical practice guidelines or care pathways can “learn” in such a system—being iteratively updated as outcomes data highlight optimal choices at the decision

nodes in the pathway. Such is the future. CancerLinQ brings us a step closer to the reality.

Conclusion

In the end, clinicians are generally good people, trying to do a good job, working to help patients who face devastating diagnoses. Despite this, we still sometimes fail to provide optimal care. How can we improve the status quo? We must be thoughtful about how we proceed. This is a time of major growing pains, as medical practice is changing from a more individual, experience-based phenomenon to a more systematized, guideline-based, value-driven, regulated provision of care by teams. As we focus increasingly on quality and value, there will be more attention on guideline-based care, and this is probably good for patients.

“Care pathways” appear to be a promising way to make care that is consistent with the latest high-quality evidence a “default” option. However, we must be careful not to treat pathways as the be-all and end-all of medical practice; medicine is complex, and not every patient should get the same treatment. Clinicians must retain the autonomy to deviate from these pathways when appropriate. We must demand that pathways be personalized, combined with a patient’s unique information; we must tailor the recommendations to personal circumstances and ensure that pathways be continuously evaluated and updated by aggregating information. Such is the difficulty of standardizing cancer care, but we owe it to our patients to do better than 37 percent.

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Suggested Readings and Resources

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Virtual Mentor

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Theme Issue Editor

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