

## PERSPECTIVE

## LESS IS MORE

## The Gold Standard for Current Cancer Treatment

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Invited Commentary

**A couple of months** before Elaine died from peritoneal cancer, we hired Anila, a cheerful, hearty Albanian housecleaner. On her first visit, Anila saw that Elaine was bedridden. “Kerosene can save her,” she said. “There is science. Look it up on the Internet.” Later, Elaine and I had a good laugh over it. She said, “Maybe that’s all they have available in Albania.” But in retrospect I’ve thought, “Could it be any worse than the treatment she got here?”

Elaine was a bright light to those who knew her, one of those rare people whose inherent grace put others at ease and made them feel special. A trained pianist, she was also a gifted and productive artist who in her last year painted and gave away more than a dozen original pieces to friends and family (Figure).

When she drew the cancer card, Elaine began studying everything she could about her illness and the agents that were being deployed against it. Pragmatic and disciplined, she was the model of an engaged patient, hungry to know as much as possible. When we received a detailed report on her tumors, Elaine became fluent in genetic mutations and protein overexpressions. She wanted to knowledgeably participate in the decisions that would have an effect on her health, and she was open and honest with her physicians about her conclusions.

Even so, on major treatment decisions we tended to unquestioningly follow the advice of our oncologist, acknowledging his expertise and good intentions. On several occasions we discussed the next treatment regimen after the last one had failed. Our physician referred to each new round of therapy as the “gold standard,” meaning the approach that scientific evidence shows works the best. What patient in a difficult situation could resist faith in the gold standard?

What we did not appreciate then was how little evidence there is that Elaine’s gold standard treatments produce outcomes that actually matter to patients and families. Two oncologists recently published a study<sup>1</sup> that reinforced this. Between 2008 and 2012, two-thirds of cancer drugs approved by the US Food and Drug Administration were found to “have unknown effects on overall survival or fail to show gains in survival.” The drugs were approved on the basis of surrogate endpoints, like progression-free survival, a clinical metric that describes how long the tumor remains dormant before beginning to grow again. Drug company representatives have told me that surrogate endpoints help get important drugs to market more quickly, making them available to more patients who need them. This study<sup>1</sup> demonstrated that those surrogate end points had only spotty correlation with either length of life or quality of life.

Of course, extending life is different from the patient’s experience of that life. Discussions of cancer treatment can focus on the trivial, like hair loss, but anyone who has lived day-to-day with chemotherapy knows the wretchedness of life that becomes worn to the nub by adverse effects: loss of feeling in the hands and feet, deep bone aches, severe headaches brought on by blood pressure spikes, nausea, digestion that moves back and forth from diarrhea to concrete, and on and on. The symptoms can be so debilitating that they steal from life all of the pleasures of seeing family and friends, of being engaged, of looking forward to the remaining moments.

Our failure to be more diligent about demanding the evidence cost Elaine dearly. While her disease presented tremendous challenges, the interventions made in the name of prolonging her life were by far the greater source of her miseries. Several of her hospitalizations and her most challenging symptoms were the direct result of conventional treatments—for example, third line chemotherapy regimens that have nominal efficacies at best.

Advanced cancer lies at the convergence of disease, high technology, immense dollars, and death, and so engenders inordinate fear and blind compliance. With prognoses that are generally grim and toxic effects that take terrible tolls, even the most modest improvements, like a few extra weeks of life, are cheered, distorting our perceptions of success. For those of us who have gone through it, though, it feels wrong to label a treatment a gold standard when it often causes the patient more suffering while offering so little positive in return.

Oncologists have told me that patients in this situation are desperate for solutions and want every possible chance. I don’t doubt this. But I also suspect that most cancer patients’ outlooks are based on incomplete information about the ordeal ahead and their odds of success.

As we struggled with our circumstances, there were questions that mattered to us, and that I suspect should be part of any informed discussion about advanced stage cancer. How much time—worst, medium, and best cases—is each treatment likely to buy? Given the treatment agents involved, what are the likely adverse effects and their characteristics, and what will they realistically mean to the patient’s capacity to enjoy remaining life? Will the struggle be worth the benefit? How would you advise your loved ones in this situation?

It also would have been valuable for our oncologists to show us research that asks patients who have been through aggressive therapy and are nearing death whether it was worth it and whether they would do it again. Elaine and I talked about this. Given the chance

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Figure. Keys Heron



Reproduced with permission. Keys Heron by Elaine Waples. Painted in Islamorada, Florida in January, 2013.

to do it over, would she have gone through 3 lines of “gold standard” chemotherapy again, with their profound impacts and the remote chances of success? The tradeoffs between hope and quality of life were simply too great. Her answer was an unequivocal no.

Elaine and I had a wonderful gynecologic oncologist—deeply caring, smart, well-trained and open minded—and it has occurred to me that for him, and for many other oncologists, it must be extremely demoralizing, and take extraordinary commitment, to sit every day with people you know will die despite your best efforts. Still, I wonder why well-intentioned, well-trained clinicians urge patients to have intense, high-cost interventions—surgery, radiation, chemotherapy—that often induce tremendous additional suffering without a real

world likelihood of providing significant benefit. An easy answer is the money oncologists make on interventions. But that can't be all of it. Perhaps, in futile circumstances, they hope to convey that they are responding meaningfully. Maybe they are trying to instill hope as an antidote to hopelessness.

Elaine once wrote that “the truths we come to know lie in the depth and clarity of our bonds.”<sup>2</sup> Cancer care must find its way back to clarifying the delicate bonds between patients and clinicians by reasserting what is best, first, for patients. Getting there will advance the cause of cancer care and, most importantly, reinfuse oncology with the deep humanity and purposefulness that moved so many oncologists to focus on these patients in the first place.

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