

FEATURE STORY

# When Illnesses Compete

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*In an aging population, cancer is rarely a solo act.*

"If I was a horse, I would have been shot a long time ago," jokes breast cancer survivor Robin McIlvain. Diagnosed with breast cancer in 1999, McIlvain was already grappling with a long list of medical conditions, including high cholesterol, Graves' disease, arthritis, osteoporosis and biliary duct disease.

McIlvain, then 50, received a lumpectomy, radiation therapy and a five-year prescription for tamoxifen—a preventive breast cancer drug that blocks the estrogen that breast cancer cells require to survive and grow. Though side effects forced her to stop taking the drug, McIlvain has now been in remission for seven years.

McIlvain's experience illustrates an increasingly recognized fact that cancer doesn't exist in a vacuum. Recent studies suggest that at least half of people diagnosed with cancer already suffer from at least one other illness, or comorbidity, such as heart disease, diabetes, hypertension or arthritis—some of which can be life-threatening in their own right.



Robin McIlvain had already been diagnosed with numerous other illnesses when she was diagnosed with breast cancer. Photo by

Cancer therapy is habitually approached with a single-minded zeal, says Jane Geraci, MD, an internist at M.D. Anderson Cancer Center in Houston. “There is often an attitude that if we can’t beat the cancer, nothing else matters,” she says. But this approach is misguided, as a comorbid illness affects all aspects of cancer care, from early diagnosis to treatment options and prognosis. In fact, with cancer patients living longer than ever, comorbid illnesses have an even greater impact on long-term health.

A recent study of more than 17,000 cancer patients showed that those with preexisting illnesses were less likely to survive their cancer and were also at greater risk for recurrence. This was true for all types of cancer, but particularly for breast and prostate cancer for whom an overall survival rate of 50 percent in otherwise healthy individuals dwindles to 3 to 5 percent in those with severe comorbid illnesses.

A similar trend was recently reported by Jeffrey Meyerhardt, MD, a gastrointestinal oncologist at Dana-Farber Cancer Institute in Boston. In his study, the average post-surgery survival time for patients with stage 2 and 3 colon cancer was about 11 years. Add diabetes and these patients survived only half as long. In other words, says Dr. Geraci, “it really does matter how you deal with your diabetes or other illness while you treat cancer.”

### An Onus of the Elderly

The burden of cancer and comorbid illness falls most heavily on the elderly—a rising population in the United States. Currently 63 percent of all cancer patients in the United States are at least 65 years old, and that percentage is expected to rise as baby boomers turn 65 beginning in 2011. To put the numbers in perspective, while the 65-and-up group currently numbers 36 million, that figure will jump to 72 million by 2030 and 86.7 million by 2050.

“Comorbidity issues in elderly patients may not be reflected in younger patients with cancer,” says Lodovico Balducci, MD, chief of the Senior Adult Oncology Program at H. Lee Moffitt Cancer Center in Tampa, who is spearheading multiple clinical trials focused on optimizing the treatment of elderly patients with cancer. Dr. Balducci says comparing cancer treatment in young and old patients is like comparing apples and oranges, but that is exactly what is happening since many decisions about cancer treatment in the elderly are based on clinical trial data from younger populations.

To help fill this information void, Dr. Balducci is conducting trials aimed at establishing prognostic measures that can help oncologists determine the best treatment for elderly patients. “We’re trying to identify a way to predict which patients will do better by receiving aggressive care and which will not.” Dr. Balducci’s studies focus not only on clinical measures of health, but also on quality of life and functional capacity. “In some cases we can shoot for a cure,” says Dr. Balducci, citing non-metastatic leukemia and breast cancer as examples. “In others, we can only try to improve the patient’s quality of life.”

## The Patient as a Whole

Multiple illnesses affect not only the prognosis of the cancer patient but also the treatment. Thus, for patients to get the most appropriate and effective treatment, they must be evaluated as a whole—each with their entire laundry list of health problems. This can be a daunting prospect both for patients, who may not be aware of all their health problems, and for physicians, who are usually trained in a single medical specialty.

The whole-patient approach is important in part because cancer drugs often have side effects that exacerbate preexisting medical conditions.

Considering the Tumor

Velcade® (bortezomib), for example, is a highly effective drug used to treat multiple myeloma, but it can also cause pain and numbness in the hands and feet—a condition known as neuropathy that is made worse in patients with diabetes, who are already prone to nerve damage.

Diabetes can also flare up when patients are treated with steroids as part of their standard chemotherapy regimen. Just ask 52-year-old chemistry teacher Wilbern Laughlin, whose blood sugar spiked while on the steroid prednisone after being diagnosed with non-Hodgkin's lymphoma in 2005. "It blew my diabetes out of the water," Laughlin recalls. Dr. Geraci notes that corticosteroids also tend to increase blood sugar because of their interference with insulin production.

Another class of breast cancer drugs called aromatase inhibitors may cause problems in patients with osteoporosis. These drugs blunt the production of estrogen, but since estrogen helps maintain healthy bones, blocking it can aggravate osteoporosis. Other cancer drugs are bad news for patients with heart disease or hypertension, conditions prevalent among the elderly. Anthracyclines, such as Adriamycin® (doxorubicin) and Ellence® (epirubicin), help shrink solid tumors but also trigger the production of free radicals that damage heart cells. Another commonly used drug with heart-damaging effects is the breast cancer drug Herceptin® (trastuzumab).

## Evaluating Risk

Side effects do not mean that certain anticancer drugs cannot be given to patients with comorbid illnesses since doctors may adjust the dosage of medication—both for the cancer and comorbidity—to allow patients the option of receiving the most effective cancer therapy. In addition, elderly patients shouldn't automatically receive less aggressive cancer therapy than younger patients, says Dr. Meyerhardt, noting that older people with stage 3 colon cancer tend to receive less chemotherapy after surgery, despite studies demonstrating its benefit. "Age alone or comorbidity alone doesn't mean you won't benefit from aggressive therapies," he says.

The reason elderly cancer patients are often treated with kid gloves is the prevalence of comorbid illness as well as the perception that older people are less likely to benefit from and cope with the stress of potent treatment. But reality doesn't always support this perception. Recent studies have shown that elderly patients with non-small cell lung cancer respond to chemotherapy as well as younger patients. Despite suffering from more comorbid illnesses, the older patients in the studies fared equally well in terms of overall survival and quality of life.

Richard Donnelly has first-hand experience with the tendency to treat older patients more conservatively. When Donnelly, a 76-year-old retired lawyer, was diagnosed with prostate cancer last May, his primary care physician and urologist recommended two options: radiation therapy or “watchful waiting”—doing nothing and waiting to see if the cancer progresses.

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—Jeffrey Meyerhardt, MD

“But I wanted to get rid of this thing,” says Donnelly, who began his own research that prompted him to inquire about robotic-assisted laparoscopic prostatectomy, or RLP, a less invasive, state-of-the-art alternative to open prostate-removal surgery that is associated with a more rapid recovery and fewer post-operative complications. Neither his urologist nor his HMO, however, was supportive, insisting that his age, diabetes and weight excluded him from having the procedure. It took months of appeals to his HMO for Donnelly to get coverage for the RLP in early October.

Donnelly's story illustrates the obstacles faced by patients as well as physicians, who must make treatment recommendations without information on how comorbid illnesses affect the course of a particular type of cancer and how the cancer treatment in turn affects the comorbid illnesses. This paucity of information is due in part to a lack of clinical trials designed to address these issues. In fact, elderly individuals and those with multiple illnesses are typically excluded from cancer trials, as they introduce unwanted variation into trial data. But this variation is precisely what must be measured in order to provide these individuals with the best possible care, especially considering that issues arising from comorbid conditions that influence physical functioning and quality of life are different from those that affect mortality.

## The Road Forward

Understanding the impact of comorbid disease on cancer, notes Dr. Geraci, will first require more accurate assessment techniques. Most current indices used to gauge the impact of comorbid illness on cancer, the most common of which is the Charlson Comorbidity Index, fail to consider the severity of the comorbid illness.

Although a number of studies aimed to increase understanding of the relationship between cancer and comorbidity, many of the clinical trials that have been conducted so far have tended to overlook complexities such as functional status of the patient and available social support.

Sanjay Asthana, MD, a gerontologist at the University of Wisconsin Comprehensive Cancer Center, hopes to improve this situation with a unique clinical trial to assess how cancer treatment affects both physical function and memory in elderly patients. The study will follow patients for two years and evaluate drug interactions, or “polypharmacy,” an important issue for elderly patients, who take an average of six to eight prescription medications. Dr. Asthana anticipates preliminary data from his trial by mid-2007.

Research at the University of Wisconsin is the result of a grant from the National Cancer Institute and National Institute on Aging that is funding eight centers around the country to study a variety of issues related to aging and cancer. But improving care for cancer patients with comorbid illnesses will also require better communication between primary care doctors and oncologists—no small feat considering the increasingly fragmented nature of medical care and the shortage of primary care physicians and gerontologists.

In the meantime, patients like McIlvain have taken the reins in managing their care. She totes around a list of her 11 daily prescription drugs and has become accustomed to detailing her medical problems to different doctors. Laughlin simply looks at the practical side of things. About managing his medications, he says, “You don’t gripe about it. You just do it.”