

## Are We Finally Winning the War on Cancer?

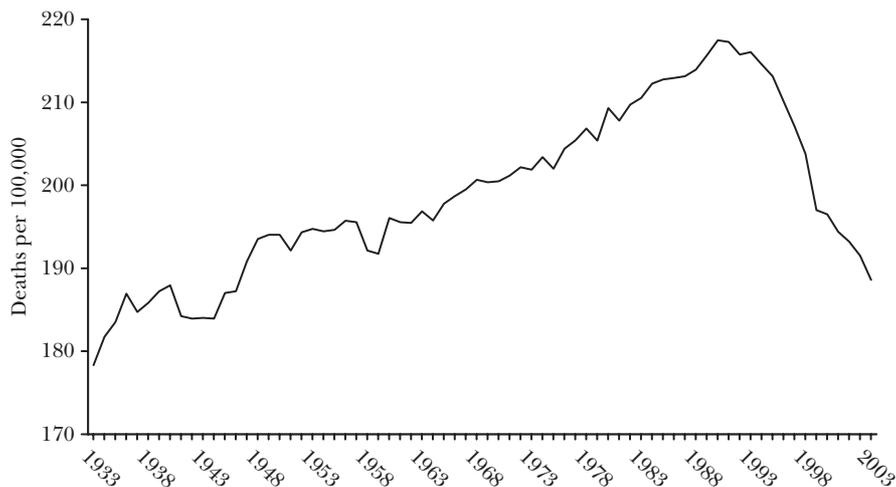
David M. Cutler

**P**resident Nixon declared what came to be known as the “war on cancer” in 1971, when he said in his State of the Union address (reproduced at <http://www.gutenberg.org/dirs/etext04/sunix11.txt>): “I will also ask for an appropriation of an extra \$100 million to launch an intensive campaign to find a cure for cancer, and I will ask later for whatever additional funds can effectively be used. The time has come in America when the same kind of concentrated effort that split the atom and took man to the moon should be turned toward conquering this dread disease. Let us make a total national commitment to achieve this goal.” At the time, cancer was the nation’s second leading cause of death, trailing only heart disease. After Nixon’s declaration, research budgets rose five-fold in real terms from 1971 to 2005 (National Institutes of Health, 2008). Spending on cancer treatment rose from \$15 billion in 1972 to \$74 billion in 2005 (both in 2005 dollars), a 4 percent real per capita increase (National Cancer Institute, 2007).

Despite this increase in resources, however, the war on cancer went poorly. Age-adjusted cancer mortality increased by 8 percent between 1971 and 1990, twice the increase from 1950 through 1971, as shown in Figure 1. An article in the *New England Journal of Medicine* in 1986 argued that “some 35 years of intense effort focused largely on improving treatment must be judged a qualified failure” (Bailar and Smith, 1986, p. 1231). A 1997 article by the same authors in the same journal was titled “Cancer Undefeated” and declared that “with 12 more years of data and experience, we see little reason to change [the earlier article’s] conclusion” (Bailar and Gornick, 1997, p. 1573).

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Figure 1  
**Age-Adjusted Cancer Mortality, 1933–2004**



Note: Data are adjusted to the 2000 population distribution and corrected for changes in the classification of deaths over time.

Since 1990, however, the situation has changed. Between 1990 and 2004, age-adjusted cancer mortality fell by 13 percent. This drop translates into an increase in life expectancy at birth of half a year—roughly a quarter of the two-year increase in life expectancy over this time period and a third of the increase in life expectancy at age 45. The decline brings cancer mortality to its lowest level in 60 years. In the war on cancer, optimism has replaced pessimism. The American Cancer Society (1996) has set a goal to halve cancer deaths by 2015. The National Cancer Institute issued a “challenge goal” of eliminating suffering and death due to cancer by 2015 (von Eschenbach, 2005), which is not meant to imply a cure for cancer, but rather preventing many cancers and treating the others so that cancer becomes primarily a chronic long-term condition, rather than an often-fatal acute condition.

In this paper, I evaluate the reasons for the reduction in cancer mortality and the implications of that decline. I highlight three factors as leading to improved survival. Most important is cancer screening: mammography for breast cancer and colonoscopy for colorectal cancer. These technologies have had the largest impact on survival, at relatively moderate cost. Second in importance are personal behaviors, especially the reduction in smoking. Tobacco-related mortality reduction is among the major factors associated with better health, likely at a cost worth paying. Third in importance, and more controversial, are treatment changes. Improvements in surgery, radiation, and chemotherapy have contributed to improved survival for a number of cancers, but at high cost. The major challenge for cancer care in the future is likely to be the balancing act between what we are able to do and what it makes sense to pay for.

## The Major Faces of Cancer

Cancer is a disease characterized by abnormal growth and spread of cells. Almost all cells in the body divide to promote growth when young and repair injury when older. Appropriate cell division occurs when necessary and ends when no longer needed. Cancer cells divide without reason or limit. Ultimately, cancer cells pile up into a nonstructured mass, called a tumor. Benign tumors grow but do not spread. Malignant cancers spread, destroying the organs they invade. Left uncontrolled, malignant cancer will result in death.

While all cancers share certain characteristics, they differ in important ways. Generally, the difference is associated with the part of the body where the cancer originated. Breast cancer cells will always resemble breast cancer cells, even if the cancer spreads to another organ. Thus, treatment is customized to the origin of the cancer. Over 100 types of cancer have been identified. In practice, though, most cancer mortality is associated with a few principle sites. I consider the major solid tumors: lung and other tobacco-related cancers; colorectal cancer; female breast cancer; and prostate cancer.

Solid tumors come in two basic flavors: localized (located only in the originating tissue) and metastatic (having spread to other parts of the body). Localized cancer isn't fatal; metastatic cancer is both lethal and incurable—even with recent treatment advances. It follows that there are three ways to reduce cancer deaths. First, the cancer can be prevented from occurring at all. Second, the cancer can be caught when it is still local, reducing the chance of a metastatic progression. Many local cancers are detected through screening. Third, treatment of the localized disease can be improved. Surgery is often the first option, with radiation and chemotherapy as supplements. Prevention, screening, and treatment are thus the keys to cancer control.

Table 1 displays the primary cancers that I analyze, their risk factors, screening technologies, and primary treatments. Not all risk factors are known for certain—the risk factors noted in Table 1 are those classified as “definite” by Colditz et al. (2000). In some cases, studies since 2000 have expanded on our knowledge of risk factors. Still, most of the important developments in the war on cancer relate to these definite risk factors.

### Tobacco-Related Cancers

Lung cancer (including cancer of the trachea and bronchus) is the leading cancer-related cause of death, accounting for 28 percent of cancer deaths. Lung cancer is almost entirely a result of behavioral and environmental insult, especially tobacco smoke and airborne particulates such as asbestos. The risk of developing lung cancer is 10 times higher among heavy smokers (people smoking 25 or more cigarettes per day) than among nonsmokers (this ratio is termed the relative risk). Lung cancer is not the only tobacco-related cancer. Cancers of the lip, larynx, bladder, pancreas, and esophagus are also strongly related to tobacco smoke. The relative risk associated with heavy smoking compared with nonsmokers is 3.0 for bladder cancer and 2.5 for pancreatic cancer.

*Table 1*  
**Characteristics of Major Solid Tumors**

<i>Cancer site</i>	<i>Behavioral/environmental risk factors</i>		<i>Screening</i>	<i>Treatment</i>	<i>Five-year survival rate</i>
	<i>Factor</i>	<i>Relative risk</i>	<i>Major options</i>	<i>Major options</i>	
<b>Tobacco-related</b> (40% of cancer deaths; 22% of mortality decline)	Tobacco <sup>a</sup>	10.0	Chest CT (rare)	Surgery <sup>g</sup> Chemotherapy Radiation	15%
	Occupational exposure	—			
	Vegetables <sup>b</sup>	0.7			
<b>Colorectal</b> (10% of cancer deaths; 22% of mortality decline)	Obesity	1.5	Colonoscopy, sigmoidoscopy, fecal occult blood test	Surgery <sup>g</sup> Chemotherapy Radiation	64%
	Inflammatory bowel disease	1.5			
	Regular aspirin	0.7			
	Screening	0.5			
	Folate	0.5			
<b>Female Breast</b> (7% of cancer deaths; 18% of mortality decline)	Ionizing radiation	2.0	Mammography	Surgery <sup>g</sup> Chemotherapy Radiation Hormonal therapy	89%
	Estrogen replacement	1.7			
	Age at first birth <sup>c</sup>	1.5			
	Height <sup>d</sup>	1.3			
	Age at menopause <sup>e</sup>	1.2			
	Number of births	1.1			
	Age at first period <sup>f</sup>	0.8			
<b>Prostate</b> (5% of cancer deaths; 15% of mortality decline)			prostate-specific antigen (PSA) test	Surgery <sup>g</sup> Radiation Hormonal therapy Chemotherapy	99%

*Note:* Relative risk is the risk of developing cancer for a person with the risk factor divided by the risk for a person without the risk factor. Tobacco-related cancers include cancer of the lung/trachea/bronchus, lip, larynx, bladder, pancreas, and esophagus. Risk factors are definite risk factors, as defined by Colditz et al. (2000). The relative risk is the ratio of mortality for people with the risk factor compared to people without the risk factor. A value greater than 1.0 indicates a higher risk among people with the characteristic; a value less than 1.0 indicates that the characteristic is protective for cancer. Five-year survival is survival for cancer patients relative to the demographically adjusted population as a whole.

<sup>a</sup> Impact of heavy tobacco use on lung cancer. Moderate use has a relative risk of 5.0. Light use has a relative risk of 2.0.

<sup>b</sup> Impact on lung cancer.

<sup>c</sup>  $\geq 35$  versus  $\leq 20$ .

<sup>d</sup>  $>5$  foot 7 inches.

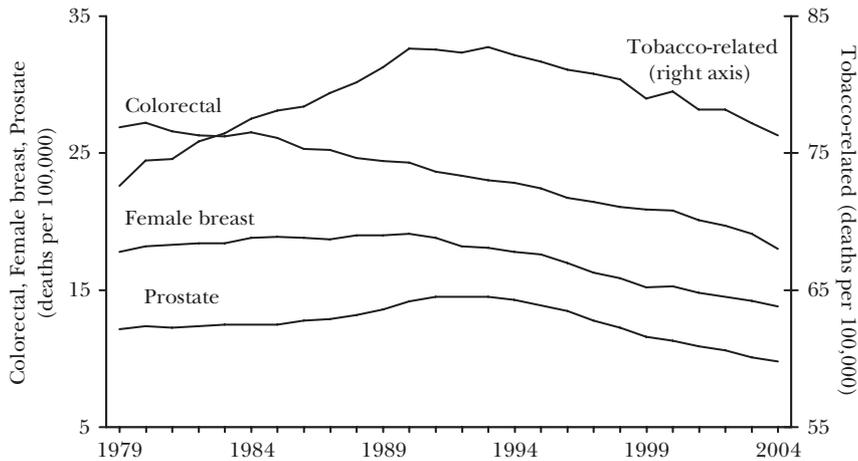
<sup>e</sup> five-year increment.

<sup>f</sup>  $\geq 15$  vs.  $\leq 11$ .

<sup>g</sup> Local or regional stage

I group these cancers along with lung cancer into a tobacco-related cancer group, which accounts for 40 percent of cancer. Seventy percent of tobacco-related cancers are due to lung cancer, so the specific discussion refers to that site.

Figure 2  
**Age-adjusted Mortality for Major Solid Tumors, 1979–2004**



Note: Tobacco-related mortality rate is measured along the right axis; colorectal, female breast, and prostate mortality rates are measured along the left axis.

Tobacco-related cancer incidence and mortality rose markedly prior to 1990 and has declined since then (as shown in Figure 2), mirroring—with a lag—the trend in smoking. Between 1990 and 2004, tobacco-related cancer mortality fell by 8 percent, accounting for 22 percent of the total reduction in cancer-related deaths over this time period.

There is relatively little screening for tobacco-related cancers. Traditional lung cancer screening involved chest x-rays or sputum analysis, but the use of these tests was never shown to be associated with improved survival. More recently, helical CT (in which the X-rays move as a spiral or helix—thus the name) has offered the possibility of better images. Still, consensus guidelines do not recommend their use. The U.S. Preventive Services Task Force (2004) found that while lung cancer screening led to detection of lung cancer at earlier stages, it did not improve survival. Further, the false positive rate is high, leading to some harm from testing. Most lung cancers are detected during a clinical examination.

Surgery is an option for cancers confined to the lung, but two-thirds of lung cancers are not detected until the cancer has spread beyond its initiation point, with half of those cases displaying significant involvement of other organs.<sup>1</sup> Che-

<sup>1</sup> Cancer is typically divided into stages: in situ (the original tissue only); stage I (relatively small, with no lymph node involvement or spread to other organs); stage II (slightly larger tumors, or tumors spread to a small number of nearby lymph nodes); stage III (greater lymph node involvement); and stage IV (spread to other organs or lymph nodes farther away). Tumors with lymph node involvement are referred to as regional cancer, and stage IV cancer is metastatic cancer. In some cases, cancer stages will be subdivided to reflect the extent of cancer spread.

motherapy and radiation are more common treatments in such situations. Chemotherapy for lung cancer has advanced over time, with an increase from one primary chemotherapy agent in the 1980s to many more in the 1990s. Still, therapy for lung cancer remains not very effective, and medical care is often only palliative. Relative five-year survival rates for lung cancer—survival compared to the demographically matched population as a whole—are only 15 percent.

### **Colorectal Cancer**

Colon and rectal cancers are the second leading cancer-related cause of death, accounting for 10 percent of cancer mortality. Colorectal cancer mortality declined by 26 percent between 1990 and 2004, accounting for 22 percent of the overall reduction in cancer deaths, the same share of the reduction as tobacco-related cancers.

Many factors lead to colorectal cancer. The largest modifiable factor is obesity, which raises the risk of colorectal cancer by 50 percent. Since obesity has increased over time, this factor implies an increased cancer risk. A history of inflammatory bowel disease also increases colorectal cancer risk, although this condition is rare. Colorectal cancer incidence declines with regular aspirin use and folate consumption (generally in the form of multivitamins). Use of these preventive measures has increased over time (Knudsen, 2005; Vogelaar et al., 2006).

There are a number of screening technologies for colorectal cancer: fecal occult blood testing (looking for blood in the stool), sigmoidoscopy, and colonoscopy (the latter two involve looking at the inside the colon with a flexible camera). The screening tests differ in their effectiveness, price, and discomfort. The most important screening development was colonoscopy, which has a preventive as well as a screening purpose. During a colonoscopy, cancerous or pre-cancerous polyps are often found and removed, reducing subsequent cancer occurrence. Colonoscopy was approved for use in 1978. Thirty percent of age-recommended people had received a colonoscopy by 1990, and 39 percent had by 2000.

For people diagnosed with colorectal cancer, treatment options include surgery, chemotherapy, and radiation, with the three often used in concert. Surgery has been standard in colorectal cancer for many years, but process innovations have improved its effectiveness over time. Chemotherapy has also advanced. Clinical trials supporting the use of chemotherapy in adjuvant settings (as a companion to other therapies) were published in the late 1980s, and quickly became the treatment standard. In the late 1990s and early 2000s, several new chemotherapy agents were developed, including some of the most expensive drugs on the market today. Typically, the new drugs are used in combination with each other or older drugs.

Partly as a result of better treatment and partly as a result of earlier detection, the five-year relative survival rate for colorectal cancer is nearly two-thirds. Figure 2 shows that colorectal cancer mortality has been declining since 1980, with a particularly rapid decline since 1999.

### **Breast Cancer**

Breast cancer is the third leading cause of cancer mortality (second among women), accounting for 7 percent of all cancer deaths. Breast cancer mortality declined after 1990, as shown in Figure 2. The cumulative decline is 28 percent, or 18 percent of the total reduction in cancer deaths.

A substantial amount is known about risk factors for breast cancer. Older age, family history, use of estrogen replacement therapy, fewer children, and later start to childbearing are all associated with increased breast cancer risk. The impact of these factors is modest, however, and most studies suggest they do not play a major role in breast cancer mortality trends, and if anything would increase the underlying rate (Berry et al., 2005).

Mammography is a common and relatively inexpensive screening test for breast cancer. Mammography dates back to the 1960s but widespread use to screen for cancer became common in the early 1980s. By 1987, nearly one-third of women were being screened; the share was 70 percent in the early 2000s (Breen et al., 2007).

Breast cancer treatment has seen advances as well. Prior to the 1980s, mastectomy was virtually the only treatment choice, either with or without radiation. Mammography continues to be used, with breast-conserving surgery, developed in the mid-1980s, as an alternative surgical option. Adjuvant chemotherapy agents began to be widely used in the mid-1970s, first independently and later in concert with other treatments. Hormonal therapy was approved for metastatic cancers in 1977 and for adjuvant therapy in the early 1980s. Newer developments since 1990 include more aggressive chemotherapy agents, and aromatase inhibitors as hormonal substitutes or additional therapy.

### **Prostate Cancer**

Prostate cancer is the fourth leading cancer-related cause of death, accounting for 5 percent of total deaths (13 percent among men). As Figure 2 shows, mortality for prostate cancer has a hump shape; it increased in the late 1980s and fell subsequently. The reason for the hump is discussed below. The overall decline from 1990 to 2004 is 31 percent, or 15 percent of the total reduction in cancer deaths.

Very little is known about the behavioral and environmental causes of prostate cancer. Age, race, and family history are the only definite risk factors for the disease: for example, African-Americans have a higher risk, and Asians have a lower risk. Diet is probably associated with prostate cancer, but the studies are not entirely consistent.

Prostate cancer screening involves a prostate-specific antigen (PSA) test, a blood test for levels of prostate-specific antigens in the blood. Higher values indicate probable prostate cancer. The PSA test was approved by the FDA in 1986, and its use spread rapidly.

Since many prostate cancers are slow-growing, watchful waiting is a frequent treatment option for men with the disease, particularly those who have a life

expectancy of less than 10 years. In cases where treatment is undertaken, surgery and radiation are usually the first options, especially with early-stage cancer. Surgery is typically removal of the prostate, although other possibilities also exist. Both surgery and radiation techniques have improved over time. Hormonal therapy is an option for men with more advanced prostate cancer. Reducing testosterone production can slow the growth of prostate tumors; for example, surgical removal of the testes is one way to prevent testosterone production. More common, however, is medication to reduce testosterone production, a number of which were developed in the 1980s and 1990s. Chemotherapy has traditionally been used only in men with metastatic prostate cancer that is unresponsive to hormone therapy, although clinical trials increasingly suggest use in patients with earlier stage disease.

Because watchful waiting is a common strategy for the (many) slow-growing prostate cancers, and because treatment has significant side effects, routine use of PSA screening is not generally recommended (Harris and Lohr, 2002). Rather, physicians are encouraged to talk about the PSA test with their patients, who should then make an individual decision.

Lung, colorectal, breast, and prostate cancers form the bulk of cancer-related mortality. Sixty-two percent of all cancers deaths are attributable to these causes. More importantly, they explain 78 percent of the reduction in cancer mortality between 1990 and 2004. Thus, they are the cancers I analyze in most depth. The residual contributors to improved cancer survival are spread across a variety of sites. Some blood-related cancers have also experienced major mortality reductions, including leukemia and non-Hodgkin's lymphoma. Stomach cancer has also declined significantly, as has testicular cancer. If one went back in time, childhood cancers used to be more important, but many are now curable (for example, acute lymphoblastic leukemia, osteosarcoma, and Ewing's sarcoma). I focus on the more recent period, however. I turn now to why mortality has declined.

## **Cancer and Other Conditions**

Cancer is but one cause of death, and trends in cancer mortality will be affected by changes in death from other causes. Death from cardiovascular disease (the heart and blood vessels) has fallen rapidly since 1970, so it is natural that more people will die of cancer. Some of these changes will be picked up with age adjustment. If cancer rates rise simply because more people reach ages where cancer is common, age-adjusted cancer rates will not change, and the data would accurately show no progress or retreat on cancer.

The issue of correlated risks is more complex, however. Smokers and obese people are at increased risk of both heart disease and cancer. If fewer smokers and obese people are dying of heart disease, age-specific rates of cancer would rise, as a greater share of those alive are at high risk for cancer. This is the standard "competing risk" problem.

The true contribution of cancer changes to survival improvement cannot be

estimated without making assumptions on the nature of the competing risks. Honoré and Lleras-Muney (2006) place bounds on the contribution of cancer to overall survival, taking account of changes in cardiovascular disease mortality. Their bounds are large in many cases, but suggest that reductions in cancer mortality from 1970 to 2000 were about twice as large as the estimates assuming independence of competing risks suggest. Most of the additional reductions were in the 1990s, the period I consider in detail, though some occurred earlier. Thus, the effect of the changes I find here are perhaps understated.

## **Explaining the Mortality Reduction**

The previous discussion suggested three reasons why cancer mortality might have declined: changes in environmental and behavioral risk factors led to reduced incidence of disease; improved screening led to earlier detection and thus more successful treatment; and treatment for cancer improved. With good data on disease incidence and stage-specific survival, we could differentiate among these three explanations.

Data on diagnosis of cancer and survival after diagnosis are very good. The National Cancer Institute has sponsored the Surveillance, Epidemiology, and End Results (SEER) program since 1973 (created in one of the early acts of the War on Cancer) to learn about cancer incidence and treatment. Currently, SEER covers 17 regions of the country, accounting for one-quarter percent of the U.S. population. SEER coverage has increased over time; for most of the time period I consider, SEER had 13 sites. SEER contains very detailed information on the nature of the tumor, the date of death, and cause of death.

## **Difficult Inferences after Earlier Detection**

The difficulty is not the availability of data, but the fact that many cancers are asymptomatic until they grow sufficiently invasive to present clinical symptoms. Because many cancers grow slowly, however, they would never be detected clinically were screening not undertaken; the person would die of another disease before the cancer became manifest.

As cancer screening became more common, many of these nonclinical cases of cancer were detected. Reported incidence of cancer thus rose greatly. In addition, because these nonclinical cases never metastasized, survival after cancer treatment appears extremely high; any treatment looks good when the underlying disease will not result in death! As a result, reported data suggest large increases in cancer incidence, alongside significant increases in case-specific survival.

Prostate cancer is a prime example of this phenomenon. Prostate cancer is extremely common, but often slow-growing. Autopsy studies on deaths not resulting from prostate cancer suggest that 30 percent of men who die in their 50s have prostate cancer, as do 80 percent of men who die in their 70s (Breslow et al., 1977). Because of the cancer's slow growth, it was not the cause of death: patients died *with*

the cancer, not *because of* the cancer. But with the advent of PSA testing, prostate cancer was detected in many more men. Further, when death occurs, prostate cancer that has been detected becomes a possible attribution. The increase in prostate cancer mortality in the early 1990s is frequently attributable to greater detection rather than a true change in prevalence (Feuer, Merrill, and Hankey, 1999).

Breast cancer follows a similar trend, although to a somewhat smaller extent (Kessler, Feuer, and Brown, 1991). In the 1980s, the growth of screening mammography led to a 29 percent increase in breast cancer incidence. Autopsy studies suggest that about 9 percent of women who die from causes other than breast cancer have some form of breast cancer (Welch and Black, 1999).<sup>2</sup> Thus, greater screening leads to increased incidence of breast cancer and seemingly higher short-run mortality from that cause.

The diagnosis issue is less serious in colorectal cancer, although not totally eliminated. It is estimated that 2–3 percent of men who die of noncancerous causes have colorectal cancer at autopsy, and 10–33 percent have colonic polyps (Correa, Strong, Reif, and Johnson, 1977). The reported incidence of colorectal cancer rose modestly from 1978 through the mid-1980s, the period when colonoscopy was developed and thus more polyps and cancers were identified. Mortality fell rapidly thereafter. Lung cancer is the only cancer I analyze where this type of bias is believed to be very small. As noted, screening is rare and most detected cases are far advanced and ultimately fatal.

### **Microsimulation Models**

For most cancers, there is no definitive way to separate the importance of prevention, detection, and treatment based on aggregate data alone. To surmount this difficulty, cancer researchers have built microsimulation models for a variety of cancer sites. These models start with a natural history of the cancer: the appearance of cancerous cells, and their growth and spread through the body. The models superimpose on this disease progression a pattern of screening and treatment. Using Monte Carlo analysis, they then simulate incident cases of cancer, screened and clinical detection of disease, and survival with the disease.

Several microsimulation models are available for three out of the four cancers I consider. These models have been developed as part of the Cancer Intervention and Surveillance Modeling Network (CISNET), a research consortium sponsored by the National Cancer Institute (<http://cisnet.cancer.gov/about/>). Like all simulations, cancer simulations are not perfect. They are only as accurate as the data and models that underlie them. The best models have been validated against trends in time periods without successful treatment, however, and perform reasonably

<sup>2</sup> This is mostly ductal carcinoma in situ (DCIS), a non-invasive form of breast cancer. Although it is typically treated the same way as early-stage breast cancer, there remains some controversy about the benefits of identifying these cancers, nearly all of which are identified by screening mammography.

Table 2

**Explanations for the Reduction in Cancer Mortality, 1990–2004**

<i>Factor</i>	<i>Consideration</i>	<i>Contribution to total</i>
<b>Behavioral</b>		<b>23%</b>
Reduced smoking	Reduction in tobacco-related cancer incidence	22%
	Reduction in colorectal cancer incidence	1%
Vitamin use	Increase in folate for colorectal cancer prevention	1%
Increased obesity	Increase in colorectal cancer incidence	–1%
<b>Screening</b>		<b>35%</b>
Mammography	Earlier detection of breast cancer	8%
Colonoscopy, sigmoidoscopy, fecal occult blood testing	Earlier detection of colorectal cancer; Removal of polyps	18%
PSA testing	Earlier detection of prostate cancer	9%
<b>Treatment</b>		<b>20%</b>
Breast cancer	Adjuvant use of chemotherapy; new chemotherapy agents	4%
	Hormonal therapy	5%
Colorectal cancer	Adjuvant use of chemotherapy; new chemotherapy agents	4%
Prostate cancer	Hormonal therapy and surgery	6%
<b>Other Cancers</b>		<b>22%</b>
<b>Total</b>		<b>100%</b>

*Note:* Lung cancer estimates are based on the assumption that smoking trends explain the entire reduction in incidence. Breast cancer estimates are based on Berry et al. (2005). Colorectal cancer estimates are based on Knudson (2005) and Vogelaar et al. (2006). Prostate cancer estimates are based on Etzioni et al. (2008). “PSA testing” is prostate-specific antigen testing.

well. I use the results of these models to decompose observed changes in cancer mortality into prevention, screening, and treatment.

Table 2 shows the results of this analysis. Tobacco-related cancers are the least well-analyzed. While there are lung cancer microsimulation models, these models have not been used to understand trends in outcomes over time. Fortunately for my purposes here, lung cancer analysis is relatively straightforward. Since most lung cancer cases are detected clinically, changes in incidence are a good guide to true cases of lung cancer. Lung cancer incidence fell by 10 percent between 1990 and 2004, roughly the same as the 8 percent reduction in lung cancer mortality over this time period. At the same time, stage-specific five-year survival rose by only 0.1 percentage point. The vast bulk of improved mortality from lung cancer is thus a result of fewer cases.

Almost certainly, the reduction in lung cancer incidence is a result of reduced rates of smoking. Lung cancer incidence follows smoking trends (with a lag), and studies suggest that reductions in smoking can explain the bulk of trends in lung cancer incidence (Holford, Zhang, Zheng, and McKay, 1998). Environmental factors may be important as well (the reduction in asbestos in particular), but no studies have compared this to the effect of reduced smoking. For simplicity, I attribute all of the reduction in smoking-related-cancer deaths to reduced smoking.

I show this in the first row of Table 2 as a 22 percent reduction in cancer mortality due to reduced deaths from smoking-related cancers.

Two simulation models have examined trends in colorectal cancer incidence and mortality over time (Knudsen, 2005; Vogelaar et al., 2006). While the studies differ somewhat, the broad conclusions are similar. In each case, the most important factor in reduced mortality is increased colonoscopy screening. As noted above, screening works partly by catching cancers earlier, and partly by removing polyps that may become cancerous. Knudsen estimates that 80 percent of reduced colorectal cancer is a result of increased screening; Vogelaar et al. do not give specific estimates, but note that this screening has a major impact on survival. Risk factors play a relatively small role in reduced mortality, accounting for 4 and 7 percent of reduced mortality in the two models. In part, the impact of risk factor changes is relatively small because different risk factors move in different directions (obesity has increased as smoking has declined). Also, risk factors play a smaller role than screening because colorectal cancer grows only slowly. As a result, past risk factor changes have yet to play out fully.

Increased use of chemotherapy in adjuvant settings (meaning “in addition to other therapies”) plays a small but important role in reduced mortality, explaining about 10 percent of the total. This partly reflects the fact that traditional therapy was relatively effective; chemotherapy regimens that were common in the 1980s reduced mortality in the groups using them by 30 percent compared to no treatment; regimens in 2000 are estimated to have a 40 percent mortality reduction. Since 2000, the development of even newer medications might lead to a reduction in mortality, but these have not yet been modeled.

Looking again at Table 2, we can see how changes in prevention, screening, and treatment for colorectal cancer contributed to the overall cancer mortality reduction. The biggest single impact is increased screening, which rivals tobacco cessation in its impact on overall cancer mortality (18 percent of the total). Behavioral changes on net led to essentially no change in mortality, and improved treatment accounted for 4 percent.

Of the four cancers I consider, breast cancer is the one with the most modeling work. Seven microsimulation models have been developed for breast cancer, and the seven models have been compared to understand changes in breast cancer mortality between 1975 and 2000 (Berry et al., 2005). As noted above, changes associated with the various risk factors for breast cancer were small; all of the studies estimated that behavioral and environmental trends were modestly increasing the risk of breast cancer over time. Screening and treatment are both significant. Averaged across the seven models, an average of 46 percent of the improved survival is attributable to increased screening. The remainder is attributable to improved treatment. Six of the models divide treatment into the impact of chemotherapy (both new agents and expanded use of existing agents) and increased use of hormonal agents. On average, 56 percent of the improvement in treatment comes from greater use of the hormonal agents. The rest is a result of greater use of existing chemotherapies and the development of newer agents.

Two models have analyzed the contribution of PSA screening to reductions in prostate cancer mortality since 1990 (Etzioni et al., 2008). Prostate cancer analysis is particularly difficult to model because data on natural progression of the disease are scarcer than for the other cancers. Still, both studies suggest that prostate cancer incidence would have increased mildly in the absence of PSA testing and advances in treatment; this continues a trend seen before the PSA era. Both studies estimated that PSA screening contributed to the reduction in deaths relative to trend; the share of the decline explained by PSA testing was 45 percent in one model and 70 percent in the other model. The difference between the models is not entirely clear; I use an average of 57 percent. The remainder of the mortality decline is almost certainly a result of better treatment—increasing use of radical prostatectomy over time, and use of adjuvant hormone therapy for men with locally advanced cancers. The division between the impacts of these two treatments are not addressed in either model; I record the joint impact of hormonal therapy and surgery in Table 2.

### **Summary**

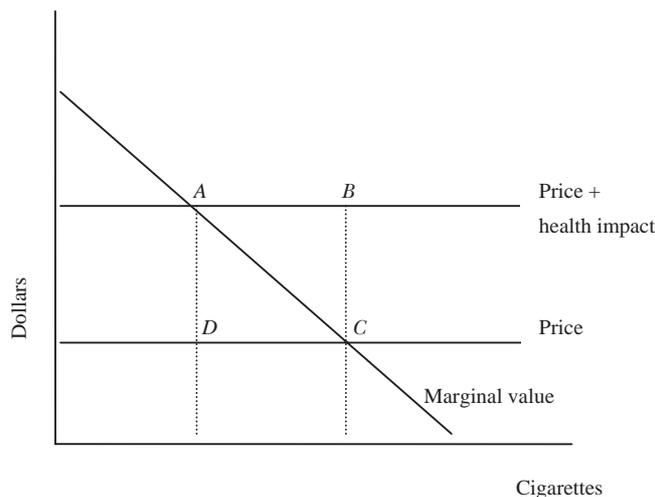
Overall, Table 2 shows that behaviors, screening, and treatment advances for the four cancers I consider were each important in improved cancer survival. Together, they explain 78 percent of the reduction in cancer mortality between 1990 and 2004. Thirty-five percent of reduced cancer mortality is attributable to greater screening—partly through earlier detection of disease, and partly through removal of precancerous adenomas in the colon and rectum. Behavioral factors are next in importance, at 23 percent; the impact of smoking reductions on lung cancer is the single most important factor in this category. Finally, treatment innovation is third in importance, accounting for 20 percent of reduced mortality.

The relative importance of these different strategies seems surprising, but it is easily understandable. Despite the vast array of medical technologies, metastatic cancer remains incurable and fatal. The armamentarium of medicine can delay death, but cannot prevent it. Thus, technologies in metastatic settings have only limited effectiveness. Far more important is making sure that people do not get cancer in the first place (prevention) and that cancer is caught early (screening), when it can be successfully treated.

### **Was the Increase in Cancer Survival Rates Worth It?**

The increase in cancer survival came at great expense. Medical spending on cancer rose from \$15 billion in 1972 to \$74 billion in 2005 (both in 2005 dollars). Behavioral change is costly as well. The important question is whether the improved survival was worth it. The answer to this question is not completely clear, but some informed guesses are possible.

Figure 3

**The Cost of Reduced Smoking**

*Note:* The figure shows an individual rationally deciding to smoke, given the value of cigarettes to the smoker and the perceived cost. See text for details.

**Behavioral Change**

The most important behavioral change in reduced cancer mortality was the decline in smoking. The percent of adults who smoke regularly fell from 42 percent in 1965 to 26 percent in 1990 to 21 percent in 2004. Over the same time period, the number of cigarettes smoked fell in half.

Most of the reduction in smoking is a result of people voluntarily quitting cigarettes, without aids or other expense. The cost of this change is not monetary (although public health messages have a moderate expense), but psychic. Because the costs are not monetary, comparing these costs to the health benefits of reduced smoking is not straightforward; it depends on why people smoked to begin with. A benchmark model of smoking is the rational model; people smoke because they enjoy it and quit when the costs of smoking are greater than the benefits. In this model, the costs of behavioral change will be approximately equal to half of the health benefits.<sup>3</sup>

Figure 3 shows the reasoning behind this conclusion. The figure shows an individual rationally deciding to smoke, given the value of cigarettes to the smoker and the perceived cost. Suppose that initially there is no adverse health information, so the cost of cigarettes is just the monetary cost. Information concerning the health costs of smoking adds to the perceived cost of smoking. As a result of the

<sup>3</sup> I am grateful to Kevin Murphy, who brought this result to my attention.

effective price increase, some people will decide to cut back on smoking. The gain to the individual from cutting back the number of cigarettes they consume is area ABCD: the health cost per cigarette times the number of cigarettes given up. The cost to the individual of giving up smoking is the foregone consumer surplus of not consuming the cigarettes. This is the triangle ACD—the benefits above what the individual would pay for the cigarettes. If the costs and health benefits of reduced smoking are linear in the number of cigarettes given up, the foregone pleasure of smoking will be equal to half of the health benefits.

To put this in context, conventional estimates suggest that the value of a year of life in good health is about \$100,000 (Cutler, 2004). Using the \$100,000 estimate and the pattern of smoking-related mortality by age, the present value of the benefits of a one-year increase in life expectancy resulting from reduced smoking would be about \$35,000 as of age 35. The implied cost of reduced smoking is therefore half this amount, about \$17,500 per year of additional life. Of course, using a higher value of a life—Murphy and Topel (2006) use a value of \$200,000—will increase these values.

In nonrational models, the cost of reduced smoking may be higher or lower than this amount. Models of hyperbolic discounting (Laibson, 1997) suggest that the costs could be lower. In these models, smokers are overly sensitive to short-run costs. Because the costs of quitting smoking are largely front-loaded (the loss of pleasure from an addicted person going without) while the benefits are longer term (the person gets to enjoy more years of life), even small costs of quitting can discourage hyperbolic smokers from quitting cigarettes. In other models, the cost of reduced smoking may be greater than the health benefits. Viscusi (1992) argues that smokers overestimate the risks of smoking-related death (though this argument is controversial; see Schoenbaum, 1997). If the argument holds true, some people who give up smoking may value cigarettes more than the true health cost, and for them, quitting smoking can thus reduce welfare.

The right model of behavioral change is not completely clear, and thus the costs of behavioral change are not completely known. A benchmark estimate of a \$17,500 cost per year of additional life is perhaps reasonable.

## Screening

Screening involves both monetary and nonmonetary costs like travel time and psychic costs. I focus on the monetary cost, where more analysis has been performed. Typically, costs for these analyses are taken from Medicare reimbursement or claims from private insurers. The same simulation models that allow researchers to determine why health outcomes have changed can also be used to evaluate the costs and benefits of changes in screening and treatment. The analysis of screening is complicated, because the cost-effectiveness of screening depends on how frequently it is performed: if screening is either too frequent or too infrequent, it will have high costs relative to benefits. Most of the models take a lifetime perspective. They start with individuals of a given age—perhaps 40—and simulate their life

*Table 3*  
**Cost-Effectiveness of Screening for Cancer**

<i>Cancer Site</i>	<i>Technology</i>	<i>Cost</i>	<i>Cost-effectiveness</i>
Lung	Helical CT	\$300	\$2,500–\$116,000 / QALY
	Follow-up if positive	\$600	
Colorectal	Fecal occult blood test	\$15	\$10,000–\$25,000 / LY
	Sigmoidoscopy	\$200	
	Colonoscopy	\$500	
	Colonoscopy with polypectomy	\$800	
Female breast	Mammography	\$70	\$37,000 / QALY
	Follow-up if positive	\$500	
Prostate	PSA test	\$50	\$14,000–\$500,000 / LY
	Follow-up if positive	\$700	

*Sources:* See Mahadevia et al. (2003) for lung cancer; Pignone, Saha, Hoerger, and Madelblatt (2002) for colorectal cancer; Stout et al. (2006) for breast cancer; and Coley, Barry, Fleming, Fahs, and Mulley (1997) for prostate cancer.

*Note:* Costs apply to about the year 2000. A “PSA test” is a prostate-specific antigen test.

expectancy and medical costs over their remaining lifetimes. Typically, one simulation will include screening—often at the level recommended by official guidelines, sometimes as actually performed—and a second simulation will omit screening. The comparison indicates the change in cost and life expectancy from screening.<sup>4</sup>

All studies measure the impact of screening on length of life. A number of studies also include quality of life, which is a significant issue for many cancers. Treatment of prostate cancer, for example, may lead to greater survival, but it frequently leads to reduced quality of life—impotence and incontinence are common side effects. For cancers where treatment is not very effective or where cancer would often not be a cause of death, treatment may even reduce quality-adjusted life expectancy.

Table 3 presents data on the costs and cost-effectiveness of cancer screening. The direct cost of screening is generally modest. Stool tests for colorectal cancer and PSA tests for prostate cancer typically cost \$50 or less; imaging of one sort or another (mammography or helical CT) costs up to a few hundred dollars; and more invasive testing (colonoscopy) costs \$500 to \$800. False positive tests add to the cost of screening. A positive finding on a screening mammogram leads to diagnostic mammogram and a biopsy, for example, which cost about \$500. To put the numbers in perspective, total spending on mammography is about \$2 billion annually and spending on colonoscopies is about \$3 billion. Studies suggest that follow-up care for false positive findings adds about one-third to the cost of screening mammography (Elmore et al., 1998). By comparison, about \$7.5 billion

<sup>4</sup> Recommendations about how to handle discounting and other issues are presented in Gold, Siegel, Russell, and Weinstein (1996). A 3 percent discount rate is common.

is spent treating breast cancer, and the cost of treating colorectal cancer is just below that. Screening is not that expensive relative to treatment; the important question is whether it is effective in improving survival.

The cost-effectiveness of cancer screening varies greatly with the specific cancer and screening technology. Estimates of the cost-effectiveness of lung cancer screening are extremely variable. As noted above, the impact of CT scanning on lung cancer mortality is uncertain, depending on how effective early detection and treatment are assessed to be. Studies suggesting that many cases caught by screening will have good prognoses find a low cost per additional life-year gained—as low as \$2,500 per quality-adjusted life year. However, the favorable cost-effectiveness studies are not widely believed; rather, most researchers believe that lung cancer screening has a cost-effectiveness ratio well above \$100,000 per quality-adjusted life year, if it has any benefits at all.

Screening for colorectal cancer is far more cost-effective. A consensus from a number of studies is that colorectal cancer screening costs \$10,000 to \$25,000 per life year added (in this case, the studies generally do not consider quality of life). By virtually any criterion, this investment is worthwhile.

Breast cancer screening is similarly cost effective, since catching breast cancer earlier leads to significant improvements in survival. Stout et al. (2006) suggest that mammography screening as currently practiced has a cost of about \$37,000 per quality-adjusted life year. This is somewhat above the cost-effectiveness of the most cost-effective screening strategy for breast cancer, but not enormously so. Other studies give relatively similar estimates, though based on older data and more selected samples (for example, Lindfors and Rosenquist, 1995).

As with lung cancer screening, uncertainty about the benefits of PSA testing leads to substantial uncertainty about the cost-effectiveness of PSA testing. Favorable sets of assumptions suggest that prostate cancer screening has a cost-effectiveness of just over \$10,000 per life year. Less favorable estimates suggest a cost-effectiveness of about \$500,000 per life year (even that ignores possible reductions in quality of life). Most researchers suspect that the higher cost-effectiveness estimates are more accurate.

The overall assessment of screening is thus mixed. In two of the four cases (colorectal cancer and breast cancer), screening is highly cost-effective. Indeed, the major question is how to get even more people screened. In two other cases (lung cancer and prostate cancer), the return is very uncertain, and screening is not universally recommended. In one of these cases, lung cancer, screening is still infrequent. Screening is still common for prostate cancer, however. About 15 million men in the United States have a PSA test for prostate cancer annually, which is probably above the optimal number.

## **Treatment**

Evaluating the cost-effectiveness of treatment changes is more difficult than evaluating the cost-effectiveness of screening. Screening is a fairly homogenous activity; treatment is not. One component of treatment may be cost-effective, while

*Table 4*  
**Cost-Effectiveness of Therapies for Cancer**

<i>Cancer site</i>	<i>Life expectancy (years)</i>			<i>Lifetime cost 1984–90</i>	<i>Approximate cost change</i>	<i>Approximate cost/LY</i>
	<i>1990</i>	<i>2004</i>	<i>Change</i>			
Lung	1.8	1.8	0.0	\$40,325	\$23,205	—
Colorectal	5.7	6.0	0.3	\$71,664	\$41,239	\$137,464
Female breast	11.0	11.3	0.3	\$69,707	\$40,113	\$133,709
Prostate	5.5	5.6	0.1	\$67,269	\$38,710	\$387,100

*Note:* Lifetime costs are from Riley, Potosky, Luitz, and Kessler (1995) and are based on Medicare claims for Medicare patients only. I adjust costs to 1995 dollars. To calculate life expectancy in 1990, I use data on relative survival from the SEER investigators (Ries et al., 2007) combined with 1990 U.S. life tables. I weight the age and sex life expectancy by the distribution of cancer cases in 1990. To calculate how treatment changes affect life expectancy, I proportionately adjust cancer-specific mortality in each year after the cancer so that the total mortality rate from that cancer, averaged over people having had it for all previous years, changes by the percent indicated by the simulation models. Using the new relative survival rates, I recalculate life expectancy for each age and sex and weight to the same national totals. Costs and benefits are discounted using a 3 percent discount rate.

another is not. In addition, the same service—surgery, for example—may change in effectiveness and cost over time, as physicians get more experience with it. To be sure, screening evolves over time as well (for example, reading of images is not always straightforward), but the changes are likely greater in treatment than in screening. Finally, because of the multiplicity of inputs to treatment, the marginal product of care may differ from the average product. For example, perhaps chemotherapy as a whole is worth it, but the marginal chemotherapy agent may not be. That much said, I present some guesses about average productivity.

Table 4 shows data on the life expectancy and treatment cost for people with cancer. The first column shows life expectancy for people with cancer around 1990. Life expectancy for people with cancer differs greatly by the site of the cancer. Life expectancy for people diagnosed with lung cancer is low—under two years. Life expectancy is moderately higher for men diagnosed with prostate cancer and men and women diagnosed with colorectal cancer—nearly six years in each case. Life expectancy is highest for female breast cancer, about eleven years, reflecting a large number of cancers caught at an early stage and a high likelihood of survival in those cases.

The next column estimates life expectancy in 2004, translating the mortality decline from the microsimulation models to additional years of life. Based on the calculations above, there is no increase in life expectancy resulting from improved lung cancer therapy. Increases in life expectancy for those diagnosed with colorectal and breast cancer are somewhat larger, although still not overwhelming: 0.3 years each, or about 4 months. The increase in life expectancy for those diagnosed with prostate cancer is modest: 0.1 years, or roughly 1.2 months. Even

though mortality from prostate cancer declined rapidly, the cancer is concentrated at advanced ages, when mortality from other causes is high.

To determine cost-effectiveness, we need to compare these increases in life expectancy to the additional spending required to produce them. Spending on cancer is generally U-shaped with time from diagnosis. Costs are high immediately after diagnosis, decline as the cancer goes into remission (if it does), and then increase substantially at the end of life. To estimate the cost per cancer patient, one needs to add these costs over a person's entire life.

Riley, Potosky, Luitz, and Kessler (1995) estimate costs for cancers diagnosed in the 1984–90 period. The next column presents their results, adjusted to 2005 dollars. Lung cancer is the cheapest of the cancers. Since so many people with lung cancer die rapidly, lifetime spending from the disease is only about \$40,000. Lifetime spending on colorectal, breast, and prostate cancer, in contrast, is about \$70,000.

We do not have estimates of lifetime spending on cancer for recent years. Thus, I cannot examine the change in cancer costs directly. An approximation can be made by assuming that cancer costs for all stages and all sites grew by the increase in real, per person spending on medical care over the time period, adjusted for the change in cancer prevalence (National Cancer Institute, 2007).<sup>5</sup> The next column of the table shows the implication of this assumption. The implied increase in cancer costs is about \$20,000 for lung cancer, and about \$40,000 for the other three cancers.

The last column shows the implied cost per additional year of life. Overall, the cost of treatment per year of life gained is large. For lung cancer, the situation is clear: costs increased but survival did not. In Woodward, Brown, Stewart, Cronin, and Cutler (2007), my coauthors and I estimate that very modest improvements in survival—about half a month between the early 1980s and the late 1990s—led to a cost-effectiveness ratio of \$400,000 per year of life saved. For prostate cancer, the cost of the additional years of life gained is nearly \$400,000 per year of life, well above typical estimates of the value of a year of life. The costs per year of life extension for people with colorectal and breast cancer are over \$130,000, which is modestly above the benchmark \$100,000 noted above.

Several factors explain the poor cost-effectiveness of much of cancer treatment. One important factor is the significant amount of treatment provided to metastatic cancer patients, which so far has yielded little average benefit. Earle, Neville, Landrum, Ayanian, Block, and Weeks (2004) show high and increasing numbers of admissions to intensive care units, emergency room visits, and new chemotherapy regimens in the few months before death from cancer during the

<sup>5</sup> Considering the total cost of care is consistent with a social cost-effectiveness calculation. There are some complications with pharmaceuticals, though. Part of the cost of pharmaceuticals is a transfer (to the pharmaceutical companies), not a resource cost. The appropriate calculation would net out the transfers, less that part used to fund the R&D. In the absence of better data, I assume that transfers net of R&D spending are small.

mid-1990s. The reimbursement system facilitates the provision of this care, as does the hope of a miracle cure in patients with nothing else to lose (Becker, Murphy, and Philipson, 2007).

These estimates of cost-effectiveness do not incorporate changes in quality of life. Clearly, quality of life for cancer survivors is far from perfect; thus, one should look for a cost per life-year below \$100,000 to be welfare improving. On the other hand, quality of life for cancer survivors has been improving over time, as new (and expensive) supportive care drugs have been introduced. Because quality of life is poorly measured, the impact of these changes is not known. It is unlikely that changes in quality of life would affect the very poor cost-effectiveness of lung and prostate cancer, but could make the analysis of colorectal and breast cancer more favorable.

## **Gazing Into the Future**

After several decades of setbacks, we finally seem to be winning the War on Cancer. Thanks to improved behaviors and better screening, the number of cancer deaths is declining, and is doing so at an increased rate.

The cloud on the horizon is the cost of treatment: high, growing, and increasingly directed in situations where it brings little value. In the early 1990s, the most expensive cancer therapy was Taxol (used for treating breast cancer), which sold for about \$4,000 per year. In 1998, Herceptin was introduced, and cost about \$20,000 per year (also for breast cancer). Gleevec, approved in 2001 for the treatment of chronic myeloid leukemia, costs over \$30,000 per year. Since then, drugs such as Avastin and Erbitux (both approved in 2004 for advanced colon cancer and other cancers) sell for \$50,000 to \$100,000 per year. While touted as wonder drugs, these new medications have so far had only modest survival impact. Avastin, for example, extends life in patients with metastatic colorectal cancer by about five months.

Of course, pharmaceutical companies can charge so much because cancer patients are near death, and most have good insurance. Thus, any therapy seems worth trying in such a situation. Other countries are not so sanguine. The National Institute of Clinical Excellence (NICE) in the United Kingdom has judged both Avastin and Erbitux to be not cost-effective, and thus they are not covered. The United States does not approve medications by cost-effectiveness criteria. As a result, Avastin and Erbitux are both covered by most insurance companies. Still, the strain of high costs is increasingly apparent (Kolata and Pollack, 2008).

This dynamic will surely repeat itself. Cancer is one of the most active areas of biomedical research, accounting for 40 percent of pharmaceutical company R&D; there are over 500 drugs in oncology clinical trials. Thus, there will be new advances, and accompanying high costs. The funding issue will become increasingly severe.

But the cancer dynamic will involve more than this. Many of the new, expensive drugs are tested first in metastatic settings because that is where clinical trials are easiest to conduct. Only later are tests done in non-metastatic cases. It is possible—even likely—that the effectiveness of new medications will be greater in non-metastatic settings. Since prices rarely rise after subsequent approvals (one reason why the drugs are priced so high in the metastatic setting), the cost-effectiveness profile of cancer care could improve over time.

In addition, research is likely to help tailor medications to particular patients. Cancer therapy traditionally involved a one-size-fits-all approach: all patients with a given tumor type and stage were recommended to receive the same treatment. Scientific advances have increasingly refined the effective population for some therapies, however. For example, the drug Herceptin has been shown to be effective in women with some, but not all breast cancers, and is now recommended for only those women. The impact of subgroup, or even individualized, therapy is complex. The number of patients taking each medication will fall, limiting spending, although prices might increase given the tailored effectiveness. Because prices are already high, however, the price increase may be limited, and the cost-effectiveness of care could thus improve.

Screening and prevention are sure to change as well. Advances over time have improved imaging quality (see Haus, 2002, for mammography quality), and these will surely continue. An equally big issue in screening is getting people to be screened regularly. Only two-thirds of women in 2005 had had a mammogram in the previous two years, a slight reduction from the value in 2000 (Breen et al., 2007). Colonoscopy screening is even lower. Price, inconvenience, and other factors limit the frequency of screening. If the amount that consumers have to pay for care increases or if inconvenience rises, screening rates could decline. Conversely, a reorientation of the medical system to focus on prevention and care management could lead to more regular screening.

Some of the biggest possibilities in cancer control are with prevention. Smoking rates have declined over time, although that trend may be leveling off. Obesity rates have increased markedly. Public or private interventions that continue the reduction in tobacco use and reduce the increase in obesity would have enormous impact on tobacco-related cancers, colorectal cancer, and cancers of other sites.

New medical techniques are also being developed for prevention. The recently introduced vaccine for cervical cancer is one example of medically-oriented prevention. More expensive, and intensive, prevention efforts include prophylactic chemotherapy or mastectomy for women at high risk of breast cancer. Because of the high cost of cancer treatment, cervical cancer vaccination is very cost-effective (Elbasha, Dasbach, and Insinga, 2007), as is prophylactic treatment for breast cancer in high-risk women (Anderson et al., 2006).

Whether the United States will reach the goal of halving cancer deaths, or reducing cancer to just another chronic condition, cannot be foretold. The tools are in place for significant advances in fighting cancer. Whether they will be used effectively is the major question in cancer care, as it is in all of medicine.

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