Only a broad expanse of expertise—including that of scientists and sociologists, patients and physicians, researchers and regulators—can battle and subdue this disparate family of diseases. Here, we listen in as experts converse about the latest medical advances poised to someday render cancer a manageable and predictable condition. Equally important are the lessons that this new “war” can teach us about innovation in general, and its value to society.
TACKLING A COMPLEX DISEASE

INNOVATIVE THERAPIES AND A HOST OF OTHER ADVANCES ARE HELPING MANY OF TODAY’S CANCER PATIENTS NOT ONLY TO SURVIVE, BUT TO THRIVE

Five thousand years ago, an Egyptian medical expert wrote about cancer in the Edwin Smith Papyrus and concluded that there was no effective treatment. But thousands of years of medicine—particularly the last four decades—have changed that prognosis. Today, cancer patients often move ahead to fulfilling healthy lives, all because of ongoing advances in medical technology and other areas of the healthcare industry.

Perhaps most important of all, more people than ever survive cancer. In just the past two decades, deaths from cancer dropped in the United States by about 20%, and that rate continues to fall. The five-year survival numbers paint an even clearer picture: in the 1970s, less than half of the cancer patients in the United States survived more than five years after being diagnosed, according to the US National Cancer Institute; in recent years that figure climbed to nearly 70%. That’s about a 40% improvement in a little more than three decades. In combination, these statistics show that the cancer patients of today are undoubtedly living longer.

A wide range of scientific and medical advances account for the increasing survival of people diagnosed with cancer. For one thing, pharmaceutical companies have developed better means of screening for safe and effective cancer drugs. Simultaneously, advances in pathology have allowed oncologists to analyze cancer in deeper ways. Rather than just diagnosing a patient with, say, lung cancer, an oncologist can determine the specific type, such as non-small cell lung cancer. Furthermore, our growing knowledge of basic biology—especially molecular components and pathways—provides even more information about a patient’s cancer. For instance, sequencing the genes in a tumor reveals its specific molecular profile, providing a fingerprint of sorts for a person’s disease. Those differences expose the potential sites where the cancer can be defeated. Indeed, the more that science and medicine learn about cancer, the more it emerges as a collection of individual diseases (see “One by One”). Understanding that individuality allows for the personalization of treatment.

In addition to improving diagnostics and therapies, basic science uncovers new ways to combat cancer. For example, increasing our familiarity with the underlying processes that drive the disease can help us discover its vulnerable pathways and targets. In some cases, these pathways could comprise the very mechanisms that set cancer off in the first place (see “Synthetic Sabotage”).

Many cancer-fighting strategies combine modern drug-screening capabilities with advanced diagnostics. One of the best-known examples of this is the drug Herceptin, which the US Food and Drug Administration approved in 1998 for treating HER2-positive breast cancer. The result of a gene mutation, this cancer type is characterized by overproduction of the human epidermal growth factor receptor 2 (HER2) protein, which promotes cancer growth. Only about 20% of breast cancer is HER2-positive, and Herceptin proves effective in battling solely those cases of the disease. Thus, Herceptin is a pioneer in the field of targeted therapy. Others have followed, and many more are sure to lie ahead.

The continued development of advanced oncology treatments, however, is not simply dependent upon further innovation in basic and medical science. Our entire health system must evolve to treat and manage today’s and tomorrow’s cancer patients. For example, the growing population of cancer survivors will create a burden—albeit a happy one—on healthcare spending. Many people attribute rising healthcare costs to the price of new drugs. In fact, new medicines have the opposite effect. Other aspects of the system often contribute more to the expense of treating cancer. To control the spending, even regulatory agencies should consider new approaches (see “Seeds of Change”).

In the end, countries and communities evaluate cancer care on its results, and those are measured by the number of lives saved. In the past 25 years, advances in cancer treatments saved more than 42 million life years. Not only do today’s cancer patients live longer, but they also live better. Many cancer patients graduate to cancer survivors, who then set and achieve new goals in life (see “Miles Beyond Myeloma”). Increasingly, medicine is finding innovative ways to treat cancer effectively. It is not unrealistic to predict that medicine will one day make all cancers survivable.
ONE BY ONE
The ultimate in customized care treats each cancer differently

JUST AS AN EARLY DIAGNOSIS MAKES ALL OF THE difference in treating cancer, obtaining a molecular profile of the disease can aim an oncologist at a precise, effective treatment. In the past, says Christine Cournoyer, CEO of N-of-One in Waltham, MA, “One of the biggest challenges in treating cancer was the ability to profile a tumor.” Such a profile identifies the genes in cancer cells that have mutated and how they have done so. But the declining price of gene sequencing, she explains, has made this increasingly possible. At N-of-One, the results from sequencing a patient’s tumor—along with a database of clinical and therapeutic knowledge—can provide the oncologist with an arsenal of targeted therapeutic options.

After analyzing more than 4,000 tumors at N-of-One, Jennifer Levin Carter, founder and chief medical officer at the company, says, “Every cancer differs at the molecular level, and understanding those differences is critical for developing the right treatment strategy.” In fact, nearly three-quarters of the cases evaluated at N-of-One resulted in treatments that went above and beyond the standard of care. This shows that combining the data from the molecular profile of a tumor with information from a huge range of clinical data often leads to unexpected treatment options.

But while the N-of-One approach sounds straightforward enough, many challenges remain. “When it comes to individualized cancer care, the system overall struggles with education and reimbursement,” Cournoyer says. For example, the sheer volume of information it encompasses—thousands of molecular tests, platforms analyzing thousands of genes, over 10,000 ongoing clinical trials, etc.—is too much for most physicians to keep track of. Finding ways to ensure that individualized cancer treatment gets paid for is also a frequent hurdle in the current healthcare system.

Most important of all, moving toward personalized cancer care demands broader outcome studies, says Cournoyer. The healthcare community has plenty of anecdotal evidence that targeted therapies can make a positive impact, but it needs more outcomes data to support greater adoption and reimbursement for the cost of diagnostic testing and associated treatment, including clinical trials.

SYNTHETIC SABOTAGE
Harnessing the mechanisms of cancer could lead to its undoing

OUR GENETIC MATERIAL IS CONSTANTLY UNDER attack. The sun, cigarette smoke, the foods we eat and cosmic radiation can injure our genes. As Nicola Curtin, professor of experimental cancer therapy at Newcastle University, in Newcastle upon Tyne, UK, says, “These things are forever damaging your DNA.” Although the estimates vary wildly, the number of environmental insults our cells endure on a typical day ranges in the tens of thousands. Luckily, they are equipped with several primary and backup defenses—a “belt and braces” approach—to repair most of that damage. If the repair process fails, a tumor may develop. Conversely, this failure to repair DNA efficiently also occurs in tumor cells, and, if we can learn to exploit it therapeutically, that could prove to be cancer’s Achilles’ heel.

The trick involves taking advantage of the loss of one repair pathway, the belt, in the cancer cells by targeting their backup repair pathway, the braces. This approach is called synthetic lethality. Even better, this kind of therapy, Curtin says, “will be toxic to cancer cells but not the rest of the body, which still has ‘the belt.’”

Making synthetic lethality work, however, depends on inhibiting the right target with the right agent. For example, Curtin works on one target, poly(ADP-ribose) polymerase (PARP), which plays a role in DNA repair. Initial research on this target began in the 1980s with the idea that using PARP inhibitors might make antitumor drugs more effective. “But that approach was not cancer-cell specific,” Curtin explains. “As we get more sophisticated in identifying synthetic lethal interactions, our use of PARP inhibitors becomes more targeted.”

Current research indicates that PARP inhibitors could be effective in treating a range of cancers, including breast and ovarian. A search of ClinicalTrials.gov on October 14, 2013, turned up more than 100 clinical trials underway or enrolling patients for studies related to PARP. “Agents might need to inhibit PARP almost completely for synthetic lethality to work clinically,” says Curtin. Nonetheless, exploiting DNA repair defects in tumors could be among tomorrow’s fundamental cancer treatments.
SEEDS OF CHANGE
Finding the savings in tomorrow’s cancer care

THE HEALTHCARE INDUSTRY STARTED PROMISING changes in cancer care decades ago, but the biggest changes could lie just over the horizon. “We are at the cusp of something that will change how we treat cancer,” says Scott Gottlieb, a resident fellow at the American Enterprise Institute in Washington, DC, and a venture partner at NEA, a venture capital firm. “We can look inside tumors and see discrete differences that let us target treatments.” That change is already driving clinical advances and much more.

Providing context to an overall discussion of cancer care, Gottlieb says, “The total amount spent on cancer has been flat for decades, at about 5% of all healthcare spending.” He adds, “The survival rates are going up, so we’re getting more for what we’re spending.”

To improve care for cancer patients, people must see beyond medications. For example, Gottlieb says, “The cancer drugs are expensive, but that cost is not going to affect the overall budget one way or the other.” He points out that worldwide spending on cancer drugs rose only 6% from 2007 to 2011. That accounted for only 0.8% of total healthcare spending, and only 0.4% came from higher-priced, newer medications.

Instead of focusing on cancer drug costs, Gottlieb notes, “a lot of inefficiency and waste is in hospitals, but it’s hard to make policy to deal with complex instruments like that.” He should know, since he has served as the deputy commissioner for medical and scientific affairs at the US Food and Drug Administration (FDA) and as a senior official at the Centers for Medicare and Medicaid Services.

Some policy changes, such as regulatory improvements, will circle back to drugs. “Clearly,” says Gottlieb, “the FDA has increased the regulatory hurdles for getting new drugs to the market.” To reduce some of the cost associated with new drugs, he says, “we should not tolerate uncertainty around safety, but we should tolerate uncertainty around benefit.” This strategy will reduce the cost of development and drive more innovation, all while reducing costs to consumers.

MILES BEYOND MYELOMA
With a single pill, a patient with terminal cancer maintains his status as a marathon machine

WEARING A YELLOW VISOR, DON WRIGHT SLIPPED past other runners on his way to the finish line. On that sunny December day in 2012 in Honolulu, he completed his goal of running a marathon in each of the 50 states, having participated in 70 marathons overall. Few 71-year-olds could accomplish that, especially nearly a decade after being diagnosed with multiple myeloma, a cancer of the blood cells. Even when caught at the earliest stages, the average patient with this cancer survives only five years beyond the diagnosis.

Wright beat that five-year death sentence, surpassing it by two times so far. But he got off to a rough start. Right after his first marathon—the “Grandma’s Marathon” in Duluth, MN, in June 2003—he received the diagnosis. Although his first two forms of treatment failed, he kept running.

After Wright’s first marathon, he wondered if he could qualify for Boston. He did, and he ran it. And he kept running.

He is able to do all that running because of a once-a-day pill keeps his myeloma at bay. “It’s so easy to take,” he says, “and I don’t have any side effects.”

In fact, Wright feels so good that even a marathon in every state was not enough for him. “We’re going to go to 100 marathons,” he says. “When we get there, we’ll go for 101.” As of early October 2013, Wright had carved the 74th notch into his marathon belt.

He is the first to say that his running, and his health, are the result of a team effort. His wife, who is 74, and his 43-year-old daughter run too. “They’ve also done 50 states,” Wright says. His wife and daughter run together, often doing a half-marathon while Wright runs all 26.2 miles. In addition, Wright supports Team Continuum. “It’s a very interesting organization that provides funds for people with cancer,” he explains. “It helps them pay their regular bills they couldn’t pay otherwise.”

Other than some runner’s knee, Wright has no physical complaints. As he says, “I know people [my age] who don’t have cancer who have lots worse problems than me.”
Those of you who listened to radio in the B.P.—before podcasts or Pandora—era might know that Lake Wobegon was the fictional home of Garrison Keillor, the host of “A Prairie Home Companion.” Keillor started each broadcast with: “Welcome to Lake Wobegon, where all the women are strong, all the men are good-looking and all the children are above average.” The Lake Wobegon Syndrome is the tendency to overestimate one’s capabilities in relation to others. Its principal manifestation is the belief that you are something special just because you view yourself as such.

Increasingly, it seems, many aspects of biomedical research are hailed as innovations. Instead of relying on so much hype, innovation should be clearly defined. It is not, for example, just doing research—running experiments and generating information. Likewise, the products in development seeking support on Kickstarter or Indiegogo do not always consist of innovations. Furthermore, being part of a LinkedIn community, a Twitter follower or an attendee at a gathering marketed as a “biomarker innovation summit” does not make a person an innovator any more than showing up at a Star Trek convention makes someone a crewmember of the Enterprise. Rather, as British journalist Sir Harold Evans stated in 2010 in a lecture to the Royal Society for the Encouragement of Arts, Manufactures and Commerce: “Innovation is not simply invention; it is inventiveness put to use. Invention without innovation is a pastime.”

The emphasis here is on “use”—as in “useful relative to other products or services.” Before there were iPads and iPhones, there were Palm Pilots and MP3 players. Before Google, there was AltaVista. What was the difference? MIT Sloan School of Management’s Michael Schrage wrote in a 2004 issue of the MIT Technology Review: “Innovation isn’t what innovators do; it’s what customers, clients and people adopt. Innovation isn’t about crafting brilliant ideas that change minds; it’s about the distribution of usable artifacts that change behavior.”

Most of what the medical research community does is basic research or clinical development. The same is true of the multiplicity of digital-health businesses. Companies should be encouraged to invest in new technologies. But we shouldn’t confuse that important activity with innovation, and neither should wannabe innovators, especially in the world of cancer care.

Understanding Innovation Inflation
The failure to make that distinction means that much time and money are invested in activities that reinforce a mistaken approach to innovation. That mindset underlines innovation in two ways. First, as Joshua Lederberg, the late Nobel Prize Laureate in Physiology or Medicine, regularly stated, “The belief that clinicians and patients should bow down in great gratitude to the illuminations provided by the basic scientists is...
out of observations that did not fit prevailing scientific doctrine, wrong.” Rather, “The most revolutionary discoveries have arisen of availability of [grant] funding.” In other words, the valley of companies [who are seeking venture funding, and the contraction portfolios and spinning out record numbers of [new com-
university-based tech-transfer offices focused on buildingpat-
site, that this so-called valley of death “is the acceleration of
Adam Rubinstein told Pharmalot, a pharmaceutical news web-
the hour of their greatest need. Nonetheless, venture capitalist
for investor’s risk-averse behavior.
In reality, a product, such as a new cancer therapy in develop-
ment, whose time has come will get financing. Private capital—
most of which comes from existing biopharmaceutical compa-
ies—funds innovations that bring about a change in practice
or thinking that leads to even more innovation. On the other
hand, public funding agencies have ignored more than a few
important innovations. For example, the discovery that DNA,
rather than proteins, controls genetic function emerged from
Rockefeller University researcher Oswald Avery's development
of a more accurate diagnostic and a better treatment for pneu-
monia, but his re
volutionary insight was ridiculed until the
diagnostic went commercial.
Similarly, the NIH rejected Craig Venter’s grants for work
on his rapid sequencing system—used to create a commercially
viable genomic database for clinical research—until his compa-
ny began to commercialize the technology. Before Venter’s suc-
cess, only one slow and ponderous method allowed scientists to
understand a single gene, let alone characterize how genes in-
fluence the interaction of regulatory and developmental path-
ways. His faster, cheaper approach spawned a cadre of users
seemingly overnight.
Generally speaking, innovations become indispensable be-
fore we even know it. They seem to come out of nowhere to
change our behavior and thinking. Innovations are the em-
bodyment of technological progress that allows us to be and do
things that we always imagined but never thought possible.

Innovation from Inhibition
As Robert Hariri, founder of Celgene Cellular Therapeutics,
points out: “Real innovation surprises even the most well-

informed,” because it succeeds in replacing “the existing equations
that a scientific culture is based on.” Celgene’s
first drug is a case in
point. Its precursor, thalidomide, was as-
associated in the 1950s and 60s with birth
defects when pre-
scribed to pregnant women. Decades later, Celgene adopted
the drug, an angiogenesis inhibitor, to develop treatments for
HIV-related conditions and multiple myeloma, while enacting
a program to guard against the danger of birth defects.
Once approved for use by the US Food and Drug Adminis-
tration, that new drug created a whole new set of consumers.
Beyond blocking angiogenesis, this drug resets the imbalance

NEW TRENDS IN TEAMWORK
Today’s technology offers a broader network of data and expertise to fight disease

PEOPLE FROM AROUND THE WORLD TRAVEL TO renowned cancer clinics in hopes of
getting the best treatments, but the same options could soon be available
at any medical facility. “Increasingly, we are providing the decision-support
tools that enable country oncologists to have the same information and
knowledge available at one of the comprehensive cancer clinics,” says G. Steven
Burrill, CEO at Burrill & Company in San Francisco, CA.
This sort of information will grow ever more important in cancer care. “The
world of oncology is moving from acute intervention to chronic care,” Burrill
explains. “We will be spending less time
in a cell’s immune system that is essential to the progression of many diseases. Furthermore, because it works on a web of inflammatory factors at the cellular level, it can be used as an oral therapy, making treatment more convenient, safer and more powerful. Consequently, immunomodulation has become a template for exploring other ways to improve health. Hariri saw that even before he worked for the company.

As a neurosurgeon, Hariri was doing an obstetrics rotation at Cornell University when his wife was pregnant with their first child. He recalls “looking at the ultrasound and being struck by the fact that the placenta had already developed into a full organ, even though it was very early in the development of our baby. It occurred to me that the placenta might be an excellent source for large quantities of immature stem cells.”

Angiogenesis supports fetal development because stem cells recruit other cells to produce the placental vasculature. In turn, the placental cells also create the right balance of immune factors essential to sustaining infants from conception. Birth defects due to thalidomide were a result of the drug’s angiogenesis inhibition choking off the source of immune factors necessary to protect the fetus and repair any damage it was exposed to in the uterus. Hariri believed, based on the use of Celgene’s immunomodulators, that these stem cells could be programmed to stop disease progression and grow healthy cells.

**Overcoming the Crowdsourcing Complex**

Finally, there is another trap that self-defined innovators—especially patient advocacy groups—fall into: confusing open-source collaboration and the rapid decline in the cost of analyzing and sharing data with the development of truly usable technologies. It could be called “the crowdsourcing complex.” The cost of sequencing genomic information, collecting gene-expression data and analyzing clinical information is dropping. The speed of connecting with others who are interested in these activities is increasing. Therefore, some people believe that any project using these new tools qualifies as “innovative.” Crowdsourcing—in which users change or add to existing products—is already taking the place of traditional innovation in many areas, and it’s only a matter of time before it does so in medicine and biotechnology. However, open sourcing is not de facto innovation. Rather, open sourcing speeds up the diffusion of innovation to a greater number of users. And as Schrage points out in the article mentioned above: “The accelerating spread of innovation ultimately amounts to the greatest revolution in choice the world has ever known. The diffusion of innovation is about the diffusion of choice—both good and bad. The more choices you have, the more your values matter.” Many patient groups, including the Sarcoma Alliance and the National Psoriasis Foundation, are using crowdsourcing to influence product design and user experience.

Indeed, the digitization of health information and biology is already creating a whole new generation of users who can experience and organize life in different ways. Eric Topol, the author of *The Creative Destruction of Medicine*, recently stated on the Medscape website that the ability to control our own DNA and data means that we will “learn from it, read it, and get facile with it. That will extend to genomics and understanding the drug interactions with one’s own genome. It’s going to extend in every which way where there’s a data information domain in the hands of consumers.”

That shifts the source of innovation. As Topol also told Medscape: “There was always an information asymmetry whereby the high priests or the doctors [held the information]; now we’re moving from information asymmetry to information parity.” Topol believes this change is “leading to the most exciting time in the history of medicine.” Not because the scientific establishment will be cut down to size, but because these technologies will reduce the cultural, political and regulatory obstacles that stand in the way of spreading innovation. This will, he says, “lead to better health at lower costs for many generations to come.”

Innovations ultimately are tools and templates for making the unexpected an indispensable source of human sustainability. In the future, something real could replace the Lake Wobegon Syndrome. Hopefully, the replacement will stir real innovation that makes cancer easier to manage.

Robert Goldberg is vice president of the Center for Medicine in the Public Interest (CMPI.org) and founder of its Value of Medical Innovation project (valueofinnovation.org).
A CALCULATED WIN USING THE POWER OF NUMBERS TO OUTSMART CANCER

Obtaining a wealth of data to draw upon is fundamental to the fight against cancer. And as health science experts around the world gather more and more data—from numbers that describe the production of specific proteins to information about insurance premiums—more patients will prosper.

In some instances, a simple statistic can unveil a critical relationship in science. For example, statistics show that increased spending on healthcare R&D drives the decline of patient death rates from all causes. Indeed, in response to higher levels of R&D investment, the mortality rate in the United States has plummeted by about 40% since 1960.

Data on cancer also reveal many improvements in care. The statistics on non-Hodgkin lymphoma, for example, bring good and bad news. Since 1975, the incidence of this cancer has kept climbing—nearly tripling, in fact. Nonetheless, the deaths caused by this form of cancer started dropping about a decade ago. The incidence and mortality data for breast cancer over the past 30 years show similar trends: increasing incidence but decreasing, or at least stable, deaths per year.

The improvements in treating non-Hodgkin lymphoma, breast cancer and many other forms of cancer depend heavily on R&D investment. In the United States alone, the pharmaceutical industry invests more in R&D, based on per employee spending, than any other industry—nine times more, to be specific. And the benefits of such investment are clear: Cancer research continues to yield new strategies for battling this deadly disease (see “Stamping Out Resistance”).

However, bringing these advances in cancer treatment to the patients who need them requires considerable funding. Although some people think of cancer drugs as extremely expensive, one expert considers them from an economic perspective to counter that perception (see “The Price of Progress”). In some cases, adjustments in insurance premiums—smaller than people might think—could provide better coverage for cancer treatments. On the other hand, employers might be able to offer better cancer care to their workers. That’s just what Life Technologies in Carlsbad, CA, had in mind when it recently teamed up with N-of-One in Waltham, MA. If one of Life Technologies’s roughly 10,000 employees or their dependents faces a cancer diagnosis, N-of-One will provide a personalized assessment and treatment plan. This includes genomic profiling of the cancer and a molecular diagnostic strategy, with no cost to the employee.

Examples like these show the value of teamwork in fighting cancer. The breadth of teamwork needed, though, stretches from researchers and patients to companies and government organizations (see “Managing Multiple Fronts”). By making better use of the existing data on cancer, collecting further information about the disease might exploit. Then, converging chemo-forces could wipe out the enemy.

STAMPING OUT RESISTANCE
Identifying the mechanisms of cancer-drug interactions will lead to more remissions

WHEN A CHEMOTHERAPEUTIC ATTACKS CANCER, IT MAY ONLY KILL some of the tumor cells—the drug-sensitive ones. Tumors, however, frequently consist of various subtypes of cells, and some of them—the drug-resistant ones—might be unaffected by the drug. Often the treatment works at the beginning, fighting back the cancer, but the resistant cells survive and multiply. “You get Darwinian selection for the resistant population,” says Daniel Longley of the drug resistance group at the Centre for Cancer Research and Cell Biology at Queen’s University in Belfast, UK. As a result, the tumor rebounds, and the drug fails to stop it. Understanding this process could lead to treatments that prevent such resistance.

Analyzing a tumor for all of its subtypes is a good start. Armed with this knowledge, an oncologist can prescribe drugs that battle the specific tumor’s various factions, beating them all back to prevent Darwinian selection from even beginning.

Resistance can also arise from adaptation. An anti-cancer therapeutic may turn off a molecular pathway that is critical for the tumor’s survival and succeed in killing the cancer. Nonetheless, human biology generally provides overlapping pathways, or more than one way to do any job. Thus, shutting down one pathway can turn on another compensatory one. “By understanding those mechanisms,” says Longley, “we can give a drug combination that simultaneously hits the primary pathway and the adaptive compensatory pathways.”

Some researchers are adopting a new mindset for exploring potential treatments. “People are starting to think of ‘orthogonal’ therapies that act in completely different ways,” says Longley. “If all of the therapies act on the same pathway, the resistance mechanism could be fairly simple for the cancer.” By attacking a cancer from different directions, so to speak, therapies stand a better chance of cutting off escape routes that the disease might exploit. Then, converging chemo-forces could wipe out the enemy.
THE PRICE OF PROGRESS
Do the benefits justify the costs?

WHILE THE COST OF BRINGING CUTTING-EDGE cancer treatments to the public is a subject of endless debate, few will argue with the results of effective cancer care. To the patient facing a devastating illness, these results are priceless. “There’s a lot of pushback against current prices, especially in the United States,” says Tomas J. Philipson, the Daniel Levin Professor of Public Policy Studies in the Irving B. Harris Graduate School of Public Policy at The University of Chicago. “But that’s somewhat misguided, in the sense that people are extraordinarily willing to pay for cancer care. That means that people value these treatments very highly.”

Research by Philipson and his colleagues (Health Affairs 31, 667–675, 2012) demonstrates that higher spending on cancer care in the United States, versus ten European countries, benefits patients with longer rates of survival. In large part, the financial burden those undergoing treatment must absorb comes in the form of copayments. “This is an issue of insurance failure,” says Philipson. “You want insurance to cover expensive treatment when you really need it.” By raising insurance premiums just a few percent, however, companies could cover these cancer expenses.

When it comes to the cost of cancer drugs, Philipson is mindful of the alternative: “No available treatment is like an infinitely priced product.” As an example, he points out that, before highly active antiretroviral therapy (HAART) for HIV, “you couldn’t buy longer life for any price. So the price for longer life was infinite.” When HAART became available, HIV patients could undergo treatment and extend their lives. The cost was high, but not immeasurable. In this way, Philipson says, “Innovation lowers the price of a healthy life.”

To keep filling the innovation pipeline, the pharmaceutical industry needs markets to purchase its products. In the coming decade, Philipson predicts, “Two big forces will drive the incentive to innovate.” First, financial uncertainty in the United States and Europe—where governments pay for about 50% and 90% of the healthcare, respectively—“will lead to lower reimbursement for healthcare, including cancer,” he says. Conversely, he believes that healthcare markets will expand in Brazil, Russia, India, China and South Africa over the same period. “It is not clear which one will win out on the world return for innovation,” he says. But it is clear that the affordability of healthcare around the globe will depend on continuing market growth.

about treatments and the range of cancers, and developing even more advanced ways of analyzing and using those data, healthcare hopes to soon turn this deadly suite of illnesses into manageable conditions, in which patients get treated—perhaps continue treatment, akin to a diabetic taking insulin—and then go on with their lives, developing new goals and pursuing them.

To turn this hope into reality, the entire cancer community must not underestimate the power of optimism. “We are just unraveling how a person’s mental state impacts the physical state,” says Robert Hariri, chairman, founder and chief science officer for the cellular therapeutics division at Celgene, as well as a neurosurgeon. “Anyone who thinks your mental state doesn’t impact your immune system has not been keeping up with the literature.” More than one cancer survivor has used brainpower in combination with treatment to fight the disease (see “Up the Odds with Attitude”).

Despite the advances in diagnostics and treatments, the battle against cancer is far from won. During the past 30 years, the rates of cancer for people 55 years of age or older increased around the world, especially in developed countries. In the next 20 years, the compound annual growth rate, according to the World Health Organization, will be 1.5% for the developed world and 3.3%—more than double—for the developing world. Consequently, teamwork will be more important than ever in the near future. This is the time to make the most of the data that we have on cancer to take away its killing power.
MANAGING MULTIPLE FRONTS
Winning the war on cancer demands vigilance on numerous battle lines

THE LEADING ADVANCES IN CANCER HEALTHCARE TODAY—FROM DRUG development to patient care—provide us with just a glimpse of what innovations lie ahead. “The biggest shift is the way we think about treating cancer,” says Louis J. DeGennaro, chief mission officer and executive vice president of the Leukemia & Lymphoma Society (LLS) in White Plains, NY. Turning that shift into reality, however, depends on considerable teamwork.

For one thing, says DeGennaro, “From a public-policy perspective, there is not enough focus on cancer prevention.” He adds, “Currently, healthcare is in the mode of thinking about treating cancer after it happens, but we should be challenging ourselves in the near term to put more resources into ways to prevent cancer.” Nonetheless, he admits that there is not an obvious prevention strategy for most cancers, except maybe stopping smoking to reduce lung cancer. With no existing methods of prevention or early screening for most blood cancers, DeGennaro explains that the focus now is on finding cures.

Consequently, new treatments propel innovation in cancer healthcare. As one great advance, DeGennaro points to “using the patient’s own immune system to attack the cancer.” For instance, he explains that Carl June of the University of Pennsylvania and his colleagues are able to take a leukemia patient’s own immune system cells—specifically, T cells—and modify them genetically to train them to kill cancer cells before injecting them back in the patient. The results look very promising so far, with 80% of patients achieving a complete remission.

Despite being more advanced, tomorrow’s drugs might be developed more economically. “You could put human tissue on a chip and test drugs in the lab in a predictive system that reflects how human cells react,” says DeGennaro. “That could help both the pharmaceutical industry and the US Food and Drug Administration judge new therapies, and could greatly reduce drug development costs.” Such advances make him optimistic about the price of cancer care in the future. “The smart application of good science will help us find ways to lower the cost of the development of drugs and lower their ultimate prices,” he says.

To reach that affordable future, teams of experts and patients must collaborate. “What’s going to make this work,” DeGennaro says, “is a closer working relationship between and among the cancer stakeholders: the academic side, biotechs and pharmas, regulatory agencies and payers, and—very importantly—patients and patient advocates.”

UP THE ODDS WITH ATTITUDE
Defeating lymphoma with treatment and optimism

IN JANUARY 2009, ACHEs AND PAINs crept into the hips and legs of then 49-YEAR-OLD Chad Flaig. Despite being an athlete all of his life, this felt unfamiliar. Flaig’s first visit to an orthopedist turned up nothing, but a second opinion was ominous—possible bone cancer. After several consultations with leading experts around the United States, Flaig’s oncologist diagnosed his condition as indolent non-Hodgkin’s lymphoma.

The ride ahead turned rough. He underwent months of chemotherapy that ran into the fall of 2009. In the following months, his strength improved, with the cancer going into remission. By January 2010, however, the lymphoma returned. Flaig then endured radiation, a staph infection, a stem-cell transplant (with cells donated by his younger brother) at the Nebraska Medical Center in Omaha, and after that, more radiation.

In Omaha, though, he got back in touch with some friends through a CaringBridge website, which he and his wife, Jenny, used to keep people updated on his treatments and condition. “With a lot of the people, I started having private conversations, and it was a good remedy for me,” he says. “Since then, we’ve been contacting people who need support and encouragement. We know how good it made us feel to get love and support during our struggles.”

All of the support and encouragement—plus the optimism that he and his wife shared—worked for Flaig. In the fall of 2011, he returned to his teaching job at Shroder High School in Cincinnati, OH. And, just months later in July 2012, he celebrated the end of his treatment when a surgeon removed his chemotherapy port.

Now, Flaig wants to help others survive cancer. He recently trained to be a volunteer in the Leukemia & Lymphoma Society’s First Connection program, which provides support for people recently diagnosed with cancer. When asked what advice he might give other cancer patients, he says, “There are only so many things that you can control, and one is your attitude. I know a good attitude will make life during treatment better.”
Robert Hariri is chairman, founder and chief science officer of the cellular therapeutics division at Celgene in Summit, New Jersey. As a serial entrepreneur in both biomedicine and aerospace, he has a broad view of innovation’s far-reaching potential. Recently, he discussed this topic with Scientific American’s Custom Media group.
other technologies, including the family of related compounds as well as our investment in drugs for solid tumors.

Celgene also invested in cell therapy early. We saw the biology of stem cells as fundamentally interesting, relevant to cancer and inflammation, and thought that perhaps this technology could be developed into a practical tool that could be delivered to patients for a variety of indications. We are now using that technology to treat a range of diseases. It also served as a basis for Celgene's expertise to be deployed in the emerging field of cellular immunotherapy for cancer.

Celgene leveraged its investments and innovations in cell therapy and expertise in hematological oncology to become a leader in the engineering of T cells that can target and destroy cancer. We can take a patient’s own immune cells, T lymphocytes, and engineer them to specifically target his or her cancer. In the clinic, this so-called chimeric antigen receptor therapy, or CART, is creating complete and total remission in diseases that are resistant to pharmaceuticals. Here, we’ve supercharged nature’s way of attacking cancer. We’re turbocharging the process on the outside by taking your cells and engineering them to go after your cancer. We will apply this technology for treating hematological cancers to solid tumors and beyond.

People die from cancer for many reasons, such as the fundamental decline of the body during the course of this disease. So every complementary approach that gives patients a physical benefit adds an opportunity to enhance their overall survival. As an example, oral therapies that can be taken without the need for doctor visits result in a preservation of quality of life that translates into an improved overall response to therapy and extends survival. Every incremental contribution that we make in a disease is a building block.

**Q:** How important are combination therapies?

**RH:** Today’s scientific tools let us figure out why combination therapies work and how to customize them for different patients. Genomic and proteomic tools are in our hands now. In large part, employing these tools and fully exploiting their value was a bioinformatics hurdle. So much data being generated, and the complexity of this information, makes it difficult to connect the dots and understand the causal relationships between observations and the treatments. Why does a patient respond so well to one combination of drugs and not to others?

We are investing heavily in answering this question. We will customize treatments so that patients get the maximum benefit from our products. For instance, we have a very big effort led by Tom Daniel, president of research for Celgene, in the epigenetics of cancer. As we generate knowledge about how the genome is changing in people with cancer, we will be able to control these changes and customize therapy. We already have products that are epigenetic-modifying drugs.

We can explore such advances because of Celgene’s culture, which is innovative, aggressive, enthusiastic and passionate about the patients we serve. The optimism at Celgene energizes our employees and boosts the confidence of our patients. Our value-in-innovation theme is central because we see tangible returns for the company’s hard work. By funneling back those returns, we continue this great journey, and we will keep on doing just that.

For example, Celgene was convinced that placental stem cells—cells recovered from the leftovers of a healthy birth—held the same therapeutic potential as embryonic stem cells, but could be developed outside of the controversy over the source of these powerful biological tools. We invested to create the manufacturing technology to take a piece of tissue from what is basically a waste product of birth and make thousands of therapeutic doses from a single placenta. That required considerable innovation in engineering and manufacturing science, but helped create one of the best cell-therapy platforms in clinical development today. It also served as a basis for Celgene’s investment in drugs for solid tumors.

**Q:** How would you describe the cost–benefit ratio to patients of today’s cancer therapies?

**RH:** In my own family, two very close relatives are battling cancer, and I can tell you there’s no doubt in my mind that every week and month that we can provide quality survival is meaningful and valuable to the family as a whole. We provide the opportunity for other approaches to extend the person’s life. The longer a patient survives has calculable benefits to those affected and provides an opportunity to access new treatments that are in the pipeline.

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