Big Questions

CanCer’s

This year nearly 550,000 Americans will die of cancer, the second most common cause of death in the United States after heart disease. How can we best prevent, screen for and treat this formidable opponent? We asked medicine’s brightest minds to weigh in on the most debated questions about cancer. Here’s what they had to say.

What role do lifestyle choices play in cancer risk?
Only 5 to 10 percent of all cancers are strongly hereditary. Most have been linked to exposure to chemicals, radiation and cigarettes and to obesity and other lifestyle factors. Tobacco will kill about 174,100 Americans this year—that’s nearly a third of all cancer deaths. Poor nutrition, excess weight and physical inactivity will contribute to about a quarter to a third of new cancer cases. “The new frontier in cancer prevention is nutrition and physical activity,” declares Dr. Otis Brawley, the chief medical officer for the American Cancer Society.

How do we improve cancer research?
Randomized clinical trials, which can take years (even decades) to complete, don’t always reflect what happens in any given physician’s office. “It’s a very different ball game to evaluate treatments in actual clinical practice where patients and also pro-
viders may be quite different from those in the trial," says Dr. Cary Gross, director of the Yale School of Medicine’s Cancer Outcomes, Public Policy and Effectiveness Research Center. “We need to do a better job of testing whether treatments are effective in actual clinical practice.”

**What’s the best way to screen for breast cancer?**

“Mammography is the only screening test shown to reduce a woman’s incidence of dying from breast cancer,” says Dr. Therese Bevers, medical director of the Cancer Prevention Center at MD Anderson Cancer Center in Texas.

Traditional 2-D mammography isn’t perfect (about 80 percent of abnormal mammogram readings turn out to be benign) and new 3-D mammography is promising but not ready for widespread use. “At this time, we don’t know if 3-D can take the place of 2-D,” Bevers says. “If you get it, it’s an add-on. It’s not a replacement.” As radiologist Dr. Jafi Lipson of the Stanford Cancer Center points out, “that’s twice the dose of radiation.”

Bevers’ recommendation: “Screen according to your level of risk.” A woman who has a strong family history of cancer may be a good candidate for an MRI in addition to a mammogram. Ultrasound is an option for women with dense breast tissue who have an intermediate lifetime risk of breast cancer but who aren’t able to undergo a breast MRI. Neither, though, is without risk—ultrasound gives too many false positives to be a universal screening tool and MRI is expensive ($3,000 versus $100 for a mammogram) and yields more false positives than a mammogram.

**Are there too many preventive mastectomies?**

Prophylactic double mastectomies are “tremendously overdone,” says American Cancer Society medical director Otis Brawley, who notes that women who have them are often not at high risk. And the surgery itself doesn’t entirely eliminate cancer risk since it removes only 90 percent of breast tissue. “Women should be aware that bilateral mastectomies may lower risk, but they clearly do not lower risk to zero,” he says. Except for women with the BRCA gene mutation, women with cancer in one breast are at very low risk of developing breast cancer in their other breast, no greater risk than women in the general population, says Sarah Hawley, an associate professor of general medicine at the University of Michigan. Yet about 8 percent of breast cancer patients have a double mastectomy.

“I’ve had many women who want to do bilateral mastectomies when it’s the cancer that’s in the breast at the time that’s likely to hurt them in the future,” says surgical oncologist Dr. Ingrid Meszoely, clinical director of the breast center at Vanderbilt Medical Center. “In most women, their risk of having a second cancer in the other breast is somewhere between .5 and 1 percent per year.”

**Why is the PSA test controversial?**

About 1 out of every 6 men will develop prostate

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**WE ASKED**

How can we better control the cost of cancer?

By using the most effective and efficient means of treatment, it’s an unfortunate fact that if you’re a patient with a particular cancer and you go to six different cancer doctors, you’ll likely get six different opinions about how to care for your cancer. That’s really not acceptable in today’s environment.

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Dr. Scott Ramsey, Fred Hutchinson Cancer Research Center in Seattle
Big data
Bringing to Cancer

Eric Schadt, Icahn Institute for Genomics & Multiscale Biology at Mount Sinai School of Medicine

Big data is comfortable with chaos. In his work life, he collaborates with 10 or more scientists at a time, produces two dozen or more scientific papers a year and harnesses massive amounts of data. His mission: push the brightest minds in science to embrace complexity.

Rather than honing in on single genes or linear pathways of disease, Schadt says, we need to understand the vast network of genes, metabolites, proteins and environmental factors that drive the function of the human body. "If we want to figure out how complex biological systems work, we need to understand how the different components talk to each other," he says. "The goal is to use the digital universe of information analyzed with powerful supercomputers to create models of the living world that are nearly as complex as we are."

Schadt’s approach is hypothesis-free, big data-driven and based on the premise that we don’t understand the root causes of disease. "In the same way sophisticated predictive mathematical models drive decision making in the financial markets—what stocks to buy, how much to buy, when to sell—we want to give doctors tools to use in their decision making."

He projects that in five to ten years, medicine will be so personalized that physicians will be able to pinpoint what disrupted the network that caused a person’s cancer, predict the disease course and determine how best to treat or even prevent it. — A. P.

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With a nonprofit called F*** Cancer and the official title of "chief cancer f*****," 26-year-old Yael Cohen doesn’t mince words. And she’s determined to change the way that we talk about cancer. Her target: generation Y. Her vehicle: letsfcancer.com, a resource that empowers its audience with real-world tools to communicate about the disease rather than cower in fear.

"Kids can teach their parents something more important than how to use their smartphones," Cohen says. "Most kids don’t know how to start the conversation, so we built a campaign to teach them what they should discuss with their parents."

It all started in 2009, on the heels of her own mother’s breast cancer diagnosis. Cohen had a shirt made for her mom that said F*** Cancer. "It was such a summation of everything I was feeling," she says. "I never thought Mom would wear it in public. She’s a classy lady who doesn’t say the word f***, never mind wear it."

But when her mom did wear the shirt, the response was remarkable. "I knew we had something powerful when strangers would hug Mom," Cohen says. "The foundation of what we do and why we have this following is because of our name. The whole point is to meet people where they are, to let them be brave, vulnerable and uncensored in what is often a really censored experience."

Cohen’s strategy of channeling the power of humor into a serious movement has worked. People all over the globe have contacted her with stories of finding cancer and convincing their reluctant parents to get screened. She recalls one young man whose father had an unrelenting cough. "He kept asking his dad to go to the doctor and his dad ignored him," she says. "Then he used the lines from our site and told his dad, ‘This isn’t about you; this is about me. I’m worried.’ His dad went to the doctor and was rushed into emergency surgery for lung cancer. That’s when I realized, ‘Holy s***, we did that.’" — A. P.
cancer, called the prostate health index, which is based on a new form of PSA called the pro-PSA. “It’s significantly more accurate than the PSA test and has a tendency to identify the more life-threatening prostate cancers,” Catalona says.

**Is there a better way to screen for colon cancer?**
Colon cancer screening saves lives. Yet half of the people over the age of 50 do not get screened. Is there a better option than a colonoscopy every 10 years? Otis Brawley, the American Cancer Society’s chief medical officer, says patients could have a stool sample tested for blood (a sign of polyps) every year at a cost of $10 or so per test (versus $3,000 for a colonoscopy). There are many reasons why this isn’t common, says Brawley—the reluctance of patients to collect stool samples, our tendency to embrace high-tech solutions and the financial incentive of promoting higher-cost procedures.

**Is proton beam therapy the best way to treat prostate cancer?**
There’s been a building boom in centers that treat prostate cancer with proton beam therapy. Only three such facilities existed before 2006. Ten are in operation today, with another 20 or 30 in the works, at a cost of about $100 million to $200 million for the equipment alone.

While proton beam therapy theoretically reduces radiation exposure to normal tissue and causes fewer side effects than standard radiation therapy, so far studies have failed to prove that it’s any better than other treatments. And there’s a significant cost difference—$80,000 for proton beam therapy versus $15,000 to $20,000 for traditional radiation. Medicare reimburses for both procedures.

“It’s less about cost and more about value—value being what can you do to increase patient outcomes and not have excessive cost,” says Dr. Dale Shepard, a physician in the department of solid tumor oncology at the Cleveland Clinic Taussig Cancer Institute. “Right now we don’t have the data on proton therapy, but the government is covering proton therapy to the tune of twice what they’d pay for traditional radiation therapy.” And whereas standard radiation is available just about everywhere, proton therapy isn’t and can require seven weeks of five-day-a-week treatment. “People are traveling very long distances for proton radiation. It’s not 100 percent clear whether it’s worth that,” says Dr. James Yu, director of the department of therapeutic radiology’s prostate and genitourinary cancer program at the Yale School of Medicine. “The current evidence is supporting at most a modest benefit.”

Radiation oncologist Dr. Ronald Chen of the University of North Carolina is conducting a study of 1,500 men receiving various treatments for prostate cancer (about 40 percent of men in the United States choose surgery and about a third choose radiation). Chen isn’t convinced yet that proton therapy is more accurate than traditional radiation. “We’ve seen very clearly a trend in our country of patients and physicians wanting to use new and more expensive treatments even though they put them back in the lab and change therapy where we have a new experimental therapy where we take a patient’s T cells and change them in the lab so that they actually target their leukemia cells when we put them back in the child.” —Dr. Anne Reilly, Cancer Center medical director, Children’s Hospital of Philadelphia

From Doctor to Patient

**Dr. Susan Love, Dr. Susan Love Research Foundation, Santa Monica**

She’s long been one of the most respected women’s health specialists in the country and is the author of what’s been called the bible of breast cancer books. Yet, Dr. Susan Love’s most life-changing role has been as a cancer patient. Diagnosed in June 2012 with acute myelogenous leukemia, Love is newly emboldened in her quest to focus on the causes of cancer.

Love had no symptoms, no family history and no warning of her cancer and ran five miles the day before a routine checkup revealed abnormal blood cells. “There’s a sense of shock when it happens to you,” Love says. “Even as an expert, you sort of forget everything you know and you’re scared just like anybody else.”

That paralyzing fear is not just about the cancer, it’s also about toxic treatments. “The medical profession underestimates the collateral damage from surgery, radiation and chemotherapy,” Love says. “There’s this sense that you’re lucky to be alive. They don’t care that you have nerve pain, numb toes or that your brain doesn’t work right.”

Love is committed to transforming medicine so that women don’t develop the disease in the first place. There’s no reason we can’t do this, she says, citing cervical cancer as an example. A few decades ago, it was routine for women with abnormal pap smears to have total hysterectomies. Now there’s a vaccine that protects women from the infections that cause almost all cervical cancers.

“Cancer of the cervix went from being a disease that robbed women of their fertility, if not their lives, to having a vaccine to prevent it,” she says. Love’s nonprofit research foundation is committed to better connecting scientists and the public, with the goal of making sure that researchers ask the questions that address the cause of breast cancer. —A. P.
haven’t been proven to be better than the current standard treat-
ments,” he says. “For something to be twice as expensive, it has to be
proven to be better. If it’s twice as expensive and no better, we don’t
think that’s good. If it’s twice as expensive and worse, that’s no good
either. We have proven that proton therapy is more expensive, but
we haven’t proven at all that it is more beneficial.”

What role can corporate America play in cancer prevention?
We asked Ronald Nelson, chairman and CEO of Avis Budget Group and a member
of CEOs Against Cancer.

How can America’s CEOs help the fight against cancer?
We can use the bully pulpit to set expectations for employees and
to challenge them to strive for improvement in a lot of different
areas, most importantly their health.

What are some of the anticancer initiatives you have implemented at Avis Budget?
All of our facilities in the U.S. are now tobacco free. If you are a
smoker in our health care plan, you pay a premium. If you don’t want
to pay that premium, you have to agree to sign up for a smoking
cessation program. We are very proud of our success rate; about
60 percent of people who sign up for the program quit smoking. We
also have Biggest Loser contests to encourage people to lose weight.
We provide employees with mammograms, Pap smears and
physical exams free of charge. We offer discounts at health clubs and
healthy menus in our cafeteria.

What’s the most impactful way a CEO can make a difference in
the fight against cancer?
It’s one thing to preach a good and healthy lifestyle. It is quite another
thing to demonstrate that you practice what you preach. I lost
70 pounds over the course of the last three or four years. I am a real
evangelist about how losing weight impacts your health and impacts
it pretty quickly. I was a late 50s guy who took Lipitor because my
cholesterol was too high and took blood pressure medicine because
my blood pressure was too high. I was a great candidate for a stroke
or heart attack. Within six months of losing most of my weight, my
cholesterol was back down to normal, my blood pressure was
back down to normal and I slept better at night. —Stephanie Taylor
hen Steve Jobs paid $100,000 to have his genes sequenced—a process known as whole genome sequencing—it demonstrated the allure of this proliferating new science. It also demonstrated that these are very early days for genome sequencing, especially as it relates to cancer treatment. After all, whole genome sequencing didn’t save Jobs’ life. The Apple founder died of pancreatic cancer in 2011.

The outcome might have been different had Jobs been diagnosed with an inherited genetic disease such as cystic fibrosis or neurofibromatosis. Genetic sequencing has generally been more successful at identifying the basis of heredity conditions than it has for even the most common forms of cancer.

Whereas heredity genetic diseases are typically caused by mutations in a single gene, most forms of cancer are caused by many mutations in many genes, says Heidi Rehm, director of the Laboratory for Molecular Medicine at Partners Healthcare Center for Personalized Genetic Medicine in Boston.

It is also easier to genetically sequence blood samples used to get a read on hereditary genetic diseases than it is to pull apart and analyze the labyrinth of genetic insertions, deletions and other mutations in pathways exploited by cancer tumors. And cancer changes, moves and adapts.

“You get a first mutation that allows it to grow into a small set of cells,” Rehm says. “Then you get another mutation that allows it to grow further. Then another that allows the blood supply to grow into the tumor so that it can feed itself. Then another mutation that allows it to invade neighboring tissues so that it can metastasize. You treat it with an effective drug, but then it develops another mutation that makes it resistant to that drug.”

Getting ahead of that evolution will be costly and complex. When the first genome was sequenced, it cost about a penny a base pair, or $3 billion. Sequencing is less expensive today (though still out of range for most consumers). Last year, Complete Genomics reported that it had produced more than 3,000 whole genome sequences at roughly $5,000 each.

Many clinical researchers now steer away from sequencing whole genomes, even as they retain the methodology of the process. They focus instead on the smaller, more well-understood portion of the genome, sometimes referred to as the “exome.”

Foundation Medicine of Cambridge, Massachusetts, boasts the first “next-generation sequencing-based diagnostic product” to be made broadly commercially available to oncologists, especially those not practicing inside academic medical centers. To the extent that cancer genes get sequenced at all—still a relative rarity—oncologists customarily have ordered test after test searching for the most commonly known cancer mutations in one specific tumor type that are linked to treatments.

Insurers have balked at continuing to finance that approach, says Dr. Michael Pellini, president and CEO of Foundation Medicine, whose FoundationOne™ test looks at only the known alterations from within the exome. That generates more comprehensive, less costly genomic profiles, Pellini says, allowing doctors to more efficiently assign targeted therapies or divert patients to clinical trials.

John D. Carpten, division director of cancer genomics and deputy director of basic research at Translational Genomics Research Institute in Phoenix, acknowledges that genomic sequencing as a treatment tool is in its earliest clinical trial phases,
but he says it holds tremendous potential. While clinical trials tend to sequence only patients with advanced cancer, Carpten would like there to be more longitudinal studies that begin sequencing tumors at first diagnosis—even before therapies are applied. Tumors could then be tracked through their evolution, with their genetic mutations mapped in almost real time.

For new treatments, data is needed—lots of data, compiled through genetic testing and clinical research. “My genome in isolation isn’t really very valuable, but my genome compared to millions of other genomes starts to be enormously valuable,” says Randy Scott, chairman and CEO of InVitae, a commercial clinical lab that plans to release an assay that tests for 500 conditions (not all cancer) by the end of the year. For Scott, the current state of genomic sequencing is akin to when the Internet was first catching on.

“Once you could connect to millions of other users on the Internet, everything changed,” he says. “Likewise in cancer, what we need is not just cheap sequencing. We need really large data sets from millions of individuals.” That will take informatics advancements to process and analyze masses of collected data. But as data accumulates, more pieces of the massive human genome puzzle will fall into place. “The more pieces we put into place,” Scott says, “the better our understanding is and the closer we are to the cure.”

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IN-DEPTH

Dr. Shahla Masood,
medical director of
the Shands
Jacksonville Breast Health Center in Florida

What’s the most pressing issue today in breast cancer?
Making sure people understand what kind of breast cancer they have. Hopefully, by becoming knowledgeable about their disease, they will be able to ask their physicians the right questions so they can choose a therapy that speaks to the extent and biology of their disease. There are tumors that have a limited ability to progress and compromise a patient’s life, and they should be treated conservatively versus breast cancers that are more aggressive.

You have pushed for more integrated, multidisciplinary care. Have we achieved this?
There have been tremendous strides in promoting integrated and multidisciplinary breast care. This has been my professional focus. The establishment of breast centers across the country has provided a unique opportunity for women to be treated in places where all of the disciplines communicate and consult with each other to provide a personalized type of therapy.

Breast cancer arguably gets more attention and advocacy than any other cancer. What is your response to people who say we should be further along in finding a cure?
Breast cancer is one of the most polarizing diseases in the world. It has received so much attention because of the power of advocacy. Advocating patients have been very effective in providing more research funding and more attention to breast cancer. But despite all of the efforts, a large number of patients still die from this disease. We still do not know what causes breast cancer, and we really still don’t have a simple cure for it. What we have is the ability to detect it earlier, and when it is detected early, long-term outcomes are much better.

—Sydney Berry

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Does Your Hand Shake When You...

Drink a glass of water? Write a note? Dial a phone number?
If so, you may be suffering from Essential Tremor. Dr. Ronald Young from the Swedish Radiosurgery Center has successfully treated over 1,000 patients — more than any other physician worldwide — using Gamma Knife, a non-surgical approach to treat Essential Tremor.

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