

PCANCER Prevention

NEW RESEARCH

HIGH LEVELS OF EXERCISE TIED TO REDUCED RISK FOR 13 CANCERS

IN LARGEST SUCH STUDY EVER CONDUCTED, EFFECT HELD EVEN WHEN RESEARCHERS ACCOUNTED FOR WEIGHT, SMOKING STATUS

The largest study of its kind finds that people who exercise regularly may reap a dividend, cutting their odds for 13 types of cancer.

The research involved a pooled analysis of data from 12 prospective U.S. and European studies that together followed more than 1.4 million people for a median of 11 years.

Compared to participants in the bottom 10 percent in terms of physical activity, those in the top 10 percent had markedly lower risks for cancers of the liver, lung, kidney, gastric cardia (upper stomach), endometrium (uterine lining), colon, head-and-neck, rectum, bladder and breast, as well as lower risks of myeloma, esophageal adenocarcinoma and myeloid leukemia.

The reductions in risk weren't simply because the "high-exercisers" were thinner than their more sedentary peers, or less likely to smoke, the researchers said.

"Most of these associations were evident regardless of body size or smoking history," wrote a team led by Stephen Moore, PhD, of the U.S. National Cancer Institute. They published their findings earlier this year in *JAMA Internal Medicine*.

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GENETIC SCREENING FOR CANCER PREVENTION: MANY CHOICES

Sequencing the human genome for the first time cost about the same as building an aircraft carrier. But now, large genetic tests are available for about the same price as bicycles. Whole genome and exome (the part of the genome that is most important for human disease) sequencing has now become mainstream for diagnosing rare disorders and cancer therapy targets.



Steven Monroe Lipkin MD, PhD

As costs have declined, the trend is moving towards using it in broader groups of people for more precise estimation of disease risk, including for cancer prevention.

For children who develop cancer, genetic testing can identify mutations to explain the cause in about one in 10, and an additional one in six had a mutation in their tumor that could guide therapy in the event of cancer recurrence. For adults with more than one close relative with breast, colorectal or certain rare tumors, about one in 10 to one in 15 will have a mutation identified by genetic testing that alters cancer screening. For men with prostate cancer that has spread beyond the local stage, almost one in five will carry a mutation in a gene linked to DNA repair and cancer risk, and their families can potentially benefit from more intensive screening.

Even for people without a strong personal or family history of any disease, screening 76 genes that by expert medical consensus influence clinical management (including cancer screening) will identify about one in 20 who carry a mutation in an "actionable" disease – that is, one that will influence their medical care.

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Cancer Prevention also has a Web site. Please visit us at www.nypcancerprevention.org

LETTER FROM THE EDITORS

In this issue of *Cancer Prevention*, we report on a recent study that demonstrates a significant protective effect of physical activity on risk for many types of cancer.

This may not seem so eye-opening when one looks around us at all the individuals who are jogging, bike riding, going to the gym to use the treadmill or the pool, or the people who are doing Zumba. All of them would tell you that, at least in part, they are undertaking this regular exercise in order to improve their health and prevent disease.

And they would be right in their reasoning – but, for the most part, the benefits of physical activity have generally been associated with cardiovascular disease rather than cancer.

Indeed, the highly influential paper by Sir Richard Doll and Richard Peto in 1981, that was a milestone in listing and ranking the key causes of cancer that are still considered crucial today, failed even to include physical activity as a preventive strategy. It was not until the early 1980s that occupational physical activity began to be recognized and later sports and recreation were also explored.

We live in a world where a focus has been placed on tobacco control, obesity management, hypertension control, dietary fat reduction, and the use of aspirin for health, largely because of their impact on cardiovascular disease. The result has been a dramatic decline in cardiovascular mortality since 1980.

Since cancer and cardiovascular disease share many of the same risk factors, the control of these risk factors promises to lead to a significant reduction in the cancer burden. Based on a growing body of evidence – including the study that is featured in this issue – one hopes that increased physical activity will contribute to a reduction in both cancer incidence and mortality. ■

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SUSAN G. KOMEN: PIECING TOGETHER THE PUZZLE OF BREAST CANCER PREVENTION

With 1 in 8 women in the U.S. likely to be diagnosed with breast cancer within her lifetime and more than 240,000 new cases of breast cancers diagnosed in the U.S. this year alone, many argue that preventing this disease is the only way we will ever conquer it, while others wonder whether breast cancer can be prevented.

Unfortunately, right now there isn't one surefire way to prevent breast cancer, but that hasn't stopped us from trying. As a leading breast cancer organization, Susan G. Komen has invested more than \$52 million in over 85 research grants, including more than 20 clinical trials focused on discovering ways to keep breast cancer from ever happening.

Vaccines are usually thought of as the first line of defense in preventing a disease, especially those caused by infections. But, since breast cancer isn't caused by an infection, some researchers – like Komen Scholar, Dr. Keith Knutson of the Mayo Clinic – are using the vaccine concept to try to target other potential drivers of breast cancer, like proteins that appear only on cancer cells.

The hope is that women at high risk can receive a vaccine that will stimulate their own immune system to find these proteins and destroy cancer cells before they become invasive.

Another Scholar, Dr. Nora Disis of the University of Washington, is investigating whether vaccines can block obesity-related inflammation, with the ultimate goal of reducing the incidence of breast cancer in obese women.

Other exciting possibilities focus on dietary approaches – including the Komen-funded Zumba Global Research Grant for Breast Cancer Prevention at the University of Kansas



Victoria Wolodzko
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Susan G. Komen

Medical Research Institute. Hoping to find a new method for breast cancer prevention in high-risk women, Dr. Carol Fabian and her team are studying a cheap and readily accessible plant-based product, lignin, found in flaxseed, called SDG (secoisolariciniresinol diglycoside).

So far, the team has shown that an amount of SDG equivalent to one flaxseed muffin per day inhibits the abnormal growth of breast cells that precedes the development of breast cancer in mice. In other words, SDG helped prevent the development of breast cancer in mice.¹ This team is currently completing a clinical trial in high-risk women that holds great promise, especially for those who cannot afford expensive medications or who are limited by inadequate healthcare infrastructures, such is often the case in rural areas in the United States and around the world in developing countries.

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For more information on cancer prevention, please visit our website
www.nyp.org/cancerprevention

ISSUES & INSIGHTS

STOPPING CANCER BEFORE IT STARTS: THE PROMISE OF THE PRE-CANCER GENOME ATLAS

Imagine, in the not-too-distant future, a routine visit to your doctor's office. As usual, samples of blood or urine are taken for testing. Then, a bit later, you get the news: Special "biomarkers" in those samples suggest you are at especially high risk of developing a specific type of cancer.

Appropriate preventive methods are then ordered – lifestyle change, chemopreventive drugs, other interventions.

"data points" focused on processes that push healthy cells to become cancerous ones.

"The idea behind the Pre-cancer Genome Atlas is to identify those genomic, cellular and molecular changes that characterize pre-cancer as an evolving cancer," he explained. "Because if we intercept the disease earlier in the process – in the pre-disease state – we'll have much more

expensive process. However, in the past decade, there's been an explosion in less costly and rapid sequencing technologies that are now in common use at most major research centers.



Avrum Spira, MD, MSc

"...if we intercept the disease earlier in the process – in the pre-disease state – we'll have much more success in preventing disease from happening, maybe even reverse the disease process once it's begun."

And the cancer – which could have threatened your life – has been stopped before it began.

Sound like science fiction? It could soon be science fact, once a bold, collaborative project dubbed the Pre-cancer Genome Atlas gets underway.

Dr. Avi Spira directs the BU-BMC Cancer Center at Boston University and is a leading light behind the project. He envisages a global collaboration of scientists combing through millions of

success in preventing disease from happening, maybe even reverse the disease process once it's begun."

This would represent a paradigm shift in cancer care, Spira believes.

"We want to eradicate cancer, that's the goal here: Eradicate it, because it never happened."

Key advances

According to Spira, recent innovations in medical research technology have paved the way for a project such as the Atlas.

"First are the advances in next-generation gene-sequencing technology," he said.

In years past, cataloging the intricacies of DNA and RNA molecules – the cell's "blueprint" components – was an arduous,

Alongside that has come a revolution in computational science, "that's allowed us to make sense of the data and identify genomic changes that characterize pre-malignant states," Spira said.

There have also been new insights at the molecular level into how the body's immune system either fights off cancer – or is compromised and weakened.

That's important, Spira explained, because every human being's immune system is naturally fighting off "pre-cancers" all the time.

"The real challenge is that we don't know which of these pre-cancers is going to go on to become a full-blown lethal cancer," he said. "If we could find those that are and intercept them early, we'd be much more effective in preventing the disease."

Early examples

The first of these "pre-malignancy" tests are, in fact, already here. For example, Cologuard, which looks for genomic "biomarkers" of either pre-cancerous or cancerous colon lesions in stool, was approved by the U.S. Food and Drug Administration in 2014.

Cologuard's effectiveness relies on spotting "some of the mutations in genes that characterize an early colorectal cancer," Spira explained.

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SPOTLIGHT ON.....

SIR RICHARD PETO, FRS

*Professor, Medical Statistics and Epidemiology
Co-director, Clinical Trial Service Unit and Epidemiological
Studies Unit
University of Oxford, U.K.*

The battle against tobacco has been a long one, but finally – in Western nations at least – smoking rates have begun to fall.

And most experts in cancer prevention would credit at least some of that achievement to the work of Sir Richard Peto.

Knighted in 1999 by Queen Elizabeth for his service to the field of epidemiology, Peto helped revolutionize that discipline by introducing ‘meta-analyses’ – studies that pool information from related trials to come up with powerful datasets that guide research.

From their base at Oxford’s Clinical Trial Service Unit, Peto and Sir Richard Doll collaborated for more than 30 years to highlight links between smoking and many health issues, especially cancer.

Using data sources from around the globe, their groundbreaking work helped confirm the importance of tobacco as a key carcinogen.

Most importantly, Peto and Doll were able to communicate their findings to the public in a lucid, persuasive way – helping to turn the tide against the most important cancer risk factor.

For example, their research helped delineate the benefits of quitting smoking at particular ages – hard facts that smokers could use to make the tough decision to quit.

Governments around the world, and the World Health Organization, also used data from the Oxford team to help inform their anti-smoking policies and targets.

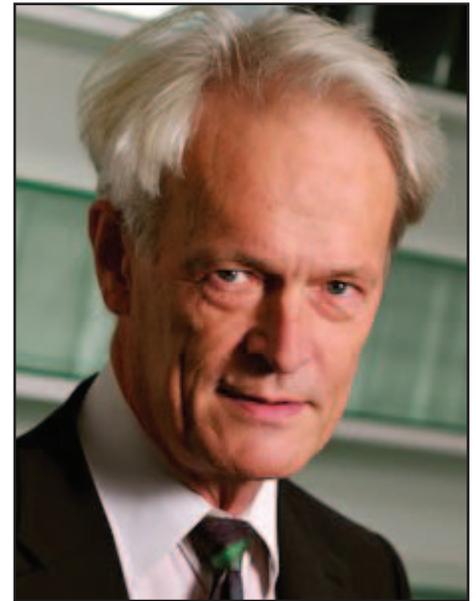
In one landmark study, Peto worked with Alan Lopez of the World Health Organization to calculate deaths from smoking in the 20th Century – and beyond. In a 2014 interview with Cancer Control, Peto summarized the grim statistics.

“In the last century, there were about 100 million deaths from smoking,” he said. “If current smoking patterns persist – with 30 percent of young adults becoming smokers and most not stopping – in the second half of the [21st] century we are going to end up finishing up with more than 100 million tobacco deaths per decade. That’s something like a billion deaths this century if we keep on as we are.”

However, sounding the alarm in this way – always based on rigorous science – Peto has helped reduce the likelihood that smokers will “keep on” as they are.

Smoking rates are already falling dramatically in the West, and Peto continues to advocate for legislative interventions such as higher taxes on tobacco products or plain cigarette packaging.

Peto was born in 1943 and studied natural sciences at Cambridge. In 1989 he was made a Fellow of the Royal Society of London for his pioneering work in epidemiology. Peto’s work extends beyond cancer prevention, and he has collaborated recently on studies on



Sir Richard Peto, FRS

alcohol use in Russia and malaria in Africa and India.

However, Peto’s efforts in the cancer prevention arena are far from over. He points to countries such as China and India, where the death toll from smoking remains enormous.

Speaking to the BBC in 2011, Peto said “there are a million deaths from smoking in China [annually] and things are getting worse rather than better. There are another million in India.”

Still, a world without smoking remains a real possibility, Peto believes.

“If they stop we’ll all be out of work,” he said, “It’ll be lovely.” ■



January is designated as Cervical Health Awareness Month. Cervical cancer was once one of the most common causes of cancer death for American women. But over the last 30 years, the cervical cancer death rate has gone down by more than 50%. The main reason for this change was the increased use of screening tests.

PREVENTING LUNG CANCER IN PEOPLE WHO HAVE NEVER SMOKED

While there is general knowledge that tobacco smoking is a powerful cause of lung cancer, indeed the cause of most cases in the United States and worldwide, lung cancer does occur in never smokers. Cases of lung cancer were documented before the cigarette smoking epidemic took hold in the early 20th century; lung cancer occurs in populations where there is no or very little smoking; and workers who do not smoke develop lung cancer because of cancer-causing workplace contaminants.

There are also other ubiquitous causes of lung cancer aside from smoking, including radon indoors and air pollution outdoors and indoors, particularly from burning of biomass fuels in low-income countries. However, our understanding of lung cancer in never smokers is incomplete, reflecting the relatively small numbers of such cases and the resulting limitation to research.

How important is lung cancer in never smokers? The death rate for lung cancer in never smokers is around 10 per 100,000 per year, about 5 % of the rate in smokers of a pack of cigarettes per day. This year there will be about 20,000 cases in the United States, producing around 15,000 lung cancer deaths out of a total of more than 158,000 lung cancer deaths per year.

For comparison, mortality from breast cancer will be about 41,000 and from prostate cancer about 26,000. In fact, lung cancer in never smokers ranks as the seventh leading cause of cancer death in the United States.

Global estimates are highly uncertain; there are an estimated 1.8 million lung cancer cases worldwide and if 10-15% are in never smokers the count ranges from about 180,000 to 270,000 in people who never smoked.

There is also uncertainty about whether the rate at which lung cancer occurs in never smokers has increased in recent decades, potentially reflecting changes

in the environmental factors that cause lung cancer.

To answer that question, researchers put together data from 13 large studies from around the world and also examined the records of cancer registries. Over a timespan that reached back to the 1930s, they did not find any indication that lung cancer in never smokers was becoming more common.

They did find that the rates of new cases were similar in men and women and that rates were highest in Asian men and women. One hypothesis is that never-smoking Asian women have a high lung cancer frequency because of exposure to cooking fumes, particularly from high-temperature cooking in woks.

What are the causes of lung cancer in never smokers? The list includes three environmental agents: radon indoors, outdoor and indoor air pollution, and secondhand smoke or SHS—the mixture of sidestream smoke from the smoldering cigarette and the exhaled mainstream smoke.

There are also agents that workers are exposed to, including radon in underground mines, asbestos, silica dust, beryllium, arsenic, formaldehyde, and benzo-a-pyrene. Most of the occupational causes were identified through epidemiological studies of workers who had exposures far higher than those that would generally be found today in regulated workplaces. Nonetheless, occupational lung cancer remains a problem worldwide, particularly in some countries where workplace exposures are not yet sufficiently controlled.

A past history of tuberculosis is also associated with increased risk, perhaps because of the scarring of the lung. Genes that might increase risk have been sought for both smokers and never smokers. The search has proved challenging, particularly in never smokers, but there are promising leads under investigation.

From a clinical perspective, lung cancer in never smokers varies in important ways in comparison to cancers in smokers. The spectrum of mutations in the

DNA differs between the two groups. There are potential therapeutic implications, particularly in regard to the high incidence of mutations of the gene encoding the epidermal growth factor receptor in never smokers.

Also, overall survival tends to be better in never smokers than in smokers with lung cancer.

While the understanding of lung cancer in never smokers is incomplete, there are effective ways to reduce its occurrence. First, exposure to secondhand smoke has dropped greatly over the last three decades and can be pushed lower; second, exposure to radon can be reduced by following the recommendation of the US Environmental Protection Agency to measure indoor radon concentration and to take steps to control radon if the concentration exceeds guidelines; third, improvements in outdoor air quality in the United States should reduce lung cancer burden; and fourth, the burden of occupational cancer should continue to fall in the United States, reflecting the impact of regulations implemented decades ago and subsequently tightened for some agents. ■



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As the researchers noted, prior studies have found strong links between higher rates of leisure-time physical activity and decreased risks for colon, endometrial and breast cancers.

However, the new study assessed the benefits of exercise against a broad range of tumor types, gathering data on a huge number of people tracked prospectively.

The report found especially high rates of risk reduction – 20% or more – for the “top exercisers” for seven different tumor types: esophageal adenocarcinoma (42% reduction), liver (27%), lung (25%), kidney (23%), gastric cardia (22%) endometrial cancers (21%) and myeloid leukemia (20%).

There were less dramatic, but still significant, reductions in risk for six other tumor types – myeloma, colon, head and neck, rectal, bladder and breast.

Overall, a person’s odds of developing any cancer fell by 7% if they exercised at a high level, the researchers reported.

The risks for melanoma actually rose for the high-exercisers, Moore’s team noted. However, the 27% higher risk for the skin cancer observed in this group

may be, “because physical activity is frequently done outdoors in light clothing,” the researchers reasoned.

Factoring in a person’s body mass index (BMI) didn’t seem to affect the results for most tumor types. And that’s important, the researchers said, “because not all persons who engage in high levels of physical activity have low body weights.”

Lauren McCullough, PhD, Kathleen McClain, MS, and Marilie Gammon, PhD wrote an accompanying journal commentary. They said the findings are “exciting,” but raise as many questions as they answer.

For example, “issues that remain unclear are the exact timing, intensity, and dose of physical activity required for cancer risk reduction,” they said. As well, the “underlying mechanism” driving the link between physical activity and cancer prevention remains largely unknown.

Finally, they said, what types of exercise – walking, biking or other activities – work best, and for how long?

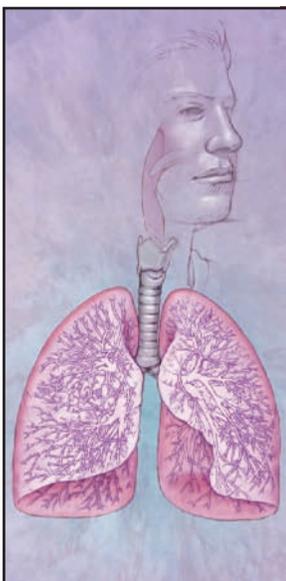


“It is currently unknown whether physical activity should be initiated during adolescence, can be intervened on during mid-life, or must be sustained across the entire life course to reduce the risk of cancer development,” the experts wrote.

One thing is clear, however: far too few people get enough exercise.

According to one 2012 study, 51 percent of Americans and 31 percent of people worldwide fail to meet recommended physical activity levels.

According to Moore’s team, that means that, “promotion of physical activity may be important for population-wide cancer prevention.” ■



November is National Lung Cancer Awareness month.

Lung cancer (both small cell and non-small cell) is the second most common cancer in both men (after prostate cancer) and women (after breast cancer). It accounts for about 14% of all new cancers.

The American Cancer Society’s most recent estimates for lung cancer in the United States for 2016 are:

- 224,390 new cases of lung cancer will be diagnosed (117,920 in men and 106,470 in women).
- There will be an estimated 158,080 deaths from lung cancer (85,920 in men and 72,160 among women). About 1 in 4 cancer deaths are from lung cancer.

Lung cancer is by far the leading cause of cancer death among both men and women. More people die of lung cancer than of colon, breast, and prostate cancers combined.

One of the keys to success in reducing the number of these deaths is prevention. Overall, the chance that a man will develop lung cancer in his lifetime is about 1 in 14; for a woman, the risk is about 1 in 17. These numbers include both smokers and non-smokers. For smokers the risk is much higher.

Despite the very serious prognosis of lung cancer, some people with earlier stage cancers are cured. More than 430,000 people alive today have been diagnosed with lung cancer at some point.

ARE SODAS, OTHER SUGARY DRINKS FALLING OUT OF FAVOR WITH AMERICANS?

City taxes on sweetened beverages, falling sales might help curb obesity – a known cancer risk factor

This June, Philadelphia became the first major U.S. city to pass a tax on sugary beverages such as sodas – one more sign that Americans' love affair with the fattening drinks might be on the wane.

The trend could have real implications in the fight against cancer: The American Cancer Society says obesity is "clearly linked" with cancers of the breast (in postmenopausal women), colon, uterine lining (endometrium), esophagus, kidney and pancreas, and may be linked to other tumor types as well.

As reported by *The New York Times*, on June 16 Philadelphia mayor Jim Kenney spearheaded a successful effort to slap a tax of 1.5 cents per ounce on the sale of sugary or artificially sweetened drinks sold in the city.

Similar efforts at a "soda tax" have failed with voters in New York City and other major U.S. urban centers, with the soft drinks industry casting such efforts as an intrusive "nanny tax." However, Kenney portrayed his city's soda tax as a healthy and effective means of raising much-needed funds to help boost popular city programs, such as universal prekindergarten classes.

"If we go five years ahead and look back, I think this is going to be a watershed moment," said Jim Kreiger, executive director of Healthy Food America, an advocacy group that helps push for soda taxes across the country. "This is really going to provide momentum," he told the *Times*.

Success in passing the tax in Philadelphia may be another nail in the coffin for sodas, which have seen

their reign as one of Americans' favored drinks teeter in recent years.

In early June, a report from drinks-industry tracker Beverage Marketing predicted that bottled water will soon replace soda as the most consumed beverage in the United States.

The report found that Americans' consumption of bottled water jumped 120 percent between 2000 and 2015 – while carbonated beverage sales slipped by 16 percent over the same period.

Beverage Marketing now predicts that bottled water will become Americans' drink of choice by 2017.

People are increasingly reaching for water to replace a wide variety of drinks, including sodas, juices and alcoholic beverages, Beverage Marketing CEO

Michael Bellas told *USA Today*. "It was really one of the very first beverages to start to be consumed for health reasons," he said.

A younger generation is also switching away from high-calorie sodas, according to the U.S. Centers for Disease Control and Prevention.



In June, the CDC released the latest data from the annual National Youth Risk Behavior Survey, which surveys the habits of more than 15,000 high school students nationwide.

Among the findings: "There was a significant decrease in drinking soda one or more times a day from 27 percent [of high school students] in 2013 to 20 percent in 2015," the CDC said. ■

GENETIC SCREENING FOR CANCER PREVENTION: MANY CHOICES

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Thus, currently about 6% of the American population belong to families with a known genetic disease mutation, a little less than one percent of which relates to cancer risk.

“There are now a wide range of genetic tests available to healthy individuals concerned about their longevity...”

There are now a wide range of genetic tests available to healthy individuals concerned about their longevity that can be ordered by a physician to assess cancer risk, ranging from the very expensive to the very affordable. Direct-to-consumer genetic tests (ordered without a physician or genetic health professional) for cancer risk individualization have come under increased scrutiny by the US Food and Drug Administration, which regulates medical testing.

On the high end in terms of cost, Human Longevity Sciences offers the HealthHub. Geared towards concierge medicine, patients visit their offices in La Jolla, California, London, Singapore or other locations. Patients have their whole genomes sequenced in addition to an analysis of their gastrointestinal microbiome; screening with new preventative medicine technologies such as brain-fast MRI; atherosclerosis scanning and wearable technology monitoring of blood pressure, heart rate and other real-time datastreams.

The cost is many thousands of dollars for an initial visit, with annual follow-up visits at an additional cost. Patients

receive recommendations for individualized cancer screening for breast cancer (e.g., MRI, mammography), colorectal, lung, prostate and other cancers that they follow up with their regular physicians.

Whole exome sequencing, which screens all 20,000 human genes, is also available – with a price tag of many thousands of dollars. This screens for

“spelling mistakes” that cause mutations for both common and rare genetic causes of cancer, along with all other diseases. However, depending on the testing laboratory, some miss mutations that rearrange large parts of genes (called structural variants), and so people interested in whole exome sequencing should be sure to go to a physician or genetic health professional who is well-versed in the technical details of laboratory testing.

There are about 150 genes whose mutation has been associated with increased cancer risk, although some of these are extremely rare. There are a variety of more focused gene panel tests, ranging from one gene to dozens that are usually oriented around increased risk of specific malignancies, such as breast and ovarian cancer. Most (but not all) laboratories performing gene panel tests detect both spelling mis-

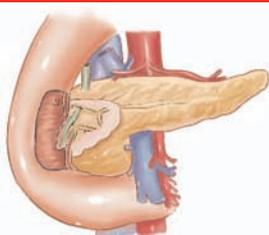
takes and structural variants, and so can actually be superior to whole exome sequencing.

For individuals who have strong personal or family histories of specific constellations of malignancies – for example, colorectal and endometrial cancer – many insurers will cover testing ordered by a physician or genetic health professional.

However, for individuals whose medical insurance will not cover genetic testing, the price of high quality gene panels has recently become much more affordable. Invitae, a San Francisco based genetic testing company, has high-quality gene panel tests that cost a few hundred dollars when billed directly to patients and which covers up to 79 cancer risk genes. Invitae is also coming out with another panel-based test for the same price that covers 76 genes (including both cancer and non-cancer genes) that genetic professional experts agree should directly influence medical care. Color is another company offering a 24-gene panel for breast/ovarian cancer, again priced at a few hundred dollars.

Another option is to participate at no cost in the Precision Medicine Initiative Cohort Program. The Precision

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November is National Pancreatic Cancer Awareness Month. Rates of pancreatic cancer have been fairly stable over the past several years. The American Cancer Society estimates that there will be about 27,670 men and 25,400 women diagnosed with pancreatic cancer in 2016. Pancreatic cancer will cause about 41,780 deaths (about 7% of cancer deaths).

GENETIC SCREENING FOR CANCER PREVENTION: MANY CHOICES

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Medicine Initiative Cohort will build a large research cohort of 1,000,000 or more Americans. Stated official goals include developing quantitative estimates of risk for a range of diseases by integrating environmental exposures, genetic mutations, and gene-environment interactions; identification of determinants of individual variation in the efficacy and safety of commonly used therapeutics, and the discovery of biomarkers that identify people with increased or decreased risk of developing common diseases.

“...for individuals whose medical insurance will not cover genetic testing, the price of high quality gene panels has recently become much more affordable.”

The Precision Medicine Initiative Cohort will commence recruiting patients in November 2016 from all geographic regions of the United States. However, it is likely that not all PMI-enrolled individuals will have their genomes sequenced, as there are currently no funds dedicated for this purpose, and there is no timeline for when participants will have genome sequencing performed, and genetic information returned to them, if at all.

A question frequently raised by patients is whether having genetic tests will change the premiums that they pay for insurance. In May 2008, President George W. Bush signed into law the Genetic Information Non-Discrimination Act, or GINA. This legislation prohibits genetic discrimination in both employment and health coverage.

Specifically, insurers and employers who have more than 15 employees are not allowed to request genetic informa-

tion to be used in any of their decisions. However, small businesses are exempt because of concerns over the cost of administration. Also importantly, GINA

“There are about 150 genes whose mutation has been associated with increased cancer risk, although some of these are extremely rare.”

does not protect against discrimination involving life, disability, and long-term care insurance.

This is not theoretical, but a real-life situation, and I have patients who have been denied life insurance because of a genetic diagnosis. As an example, I will discuss one patient in my practice

because of your positive finding of a mutation in the MSH2 gene, which causes the Lynch syndrome, as noted in your medical records.

because of your positive finding of a mutation in the MSH2 gene, which causes the Lynch syndrome, as noted in your medical records.

If you received any correspondence prior to this letter that you interpret as coverage, please disregard it. You do not have coverage. Also, if you have an existing policy that you were replacing, please continue paying the premiums on that policy.”

Consequently, many people who are interested in having genetic testing may want to obtain life, disability and/or long-term care insurance prior to tests.

In summary, there are currently many different options for genetic testing for cancer prevention. Genetic testing has many complicated technical, legal and

who has Lynch syndrome. This is a genetic cancer susceptibility disease that increases the risk for colorectal, uterine, ovarian and other cancers and is caused by mutations in MSH2, MLH1

“Genetic testing has many complicated technical, legal and social details that can influence whether testing is appropriate for each person.”

and other genes. My patient is in her 50s and had surgery to remove her colon, uterus and ovaries. She has never developed any cancer and is diligent in keeping up with cancer screening in order to work and take care of her family. Despite her meticulous care to stay healthy, my patient was denied life insurance, largely because of her genetic diagnosis. The denial letter from her insurer read:

“Like all insurance companies, we have guidelines that determine when cover-

social details that can influence whether testing is appropriate for each person. The best course of action is for a person who is considering having testing to meet in person with a physician or genetic counselor regarding whether genetic testing is right for them. ■

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For information on ongoing cancer prevention clinical trials, please visit our Web site,
www.nypcancerprevention.org

URUGUAY'S LEGAL VICTORY MAY RE-IGNITE GLOBAL FIGHT AGAINST BIG TOBACCO

International court upholds tiny South American country's efforts to curb smoking

It's a true David-and-Goliath story: Uruguay, a South American nation with a population of less than 4 million, has been successful in beating back a legal challenge to its anti-smoking laws launched by one of the world's biggest tobacco companies.

In July, the independent World Bank court known as the International Center for Settlement of Investment Disputes, settled in favor of Uruguay continuing its aggressive anti-smoking efforts.

The plaintiff in the case, tobacco behemoth Philip Morris International, not only lost the case but has been ordered by the court to pay Uruguay about \$7 million in legal fees, *Bloomberg* reported.

The victory is seen as a watershed moment in the growing fight between nations bent on lowering smoking rates and the companies that market tobacco to their citizens.

After the unanimous decision from the court in favor of Uruguay, "I got phone calls from everywhere," said Eduardo Bianco, a cardiologist in Uruguay who is also president of the Tobacco Epidemic Research Center, an anti-smoking organization.

He told *Bloomberg* that, as a result of the July decision, "We are almost certainly going to be seeing other countries taking more aggressive measures to protect public health."

The story began in the mid-2000s, when Uruguay's then-president Dr. Tabare Vazquez – an oncologist – banned smoking in public and also ordered that half of the area of cigarette packs be covered with health warnings. Those warnings included gruesome images of victims of cancer and other smoking-linked illnesses.

Vazquez left office in 2010, but not before extending those warnings to cover 80 percent of the front and back of each cigarette pack, and mandating that tobacco companies only use one packaging design for all their brands.

Tobacco taxes are also high, comprising two-thirds of the average cost of a pack of cigarettes.

All of these anti-smoking efforts seem to have paid off: Adult smoking rates in Uruguay dropped from 32 percent in 2006 to 22 percent in 2013, Bianco told *Bloomberg*, and smoking rates for teens plunged even more dramatically.

None of this happened without a fight from Big Tobacco, however.

Phillip Morris brought its claim to the World Bank court, saying that Uruguay's new rules infringed on the company's intellectual property rights and curtailed competition. The company also made the claim that anti-smoking efforts like those made by Vazquez' government don't work, and only encourage a black market in cigarettes. Phillip Morris asked for \$25 million in damages.

As the court battle dragged on, Uruguay elected a new president in 2010 – a heavy smoker and ex-guerrilla fighter, Jose Mujica. According to *Bloomberg*, Mujica upheld his predecessor's anti-smoking initiatives, saying tobacco products required regulation.

Mujica's term ended in 2015 and Vazquez was returned to office as president.

Experts believe that Uruguay's legal win has implications that extend far beyond the small country's borders.

Paul Reichler was lead counsel for Uruguay in the World Bank arbitration. He believes that Philip Morris launched the suit to send a message to other countries that efforts to curb smoking could be very costly.

"If a state knows it could cost tens of millions of dollars to pursue a case, and then possibly pay hundreds of millions of dollars [in] damages, clearly it's going to think twice about taking legal action," he told *Bloomberg*. "This was typical intimidation."

Instead, experts say, Uruguay's victory may now boost efforts in countries worldwide that are mulling actions similar to those carried out in Uruguay.

However, even Uruguay has a long way to go to cut smoking rates.

As reported by *Bloomberg*, Euromonitor – a group that tracks global tobacco markets – reported that cigarette sales actually rose by 8 percent in Uruguay between 2010 and 2014. Anti-smoking advocates believe that even though more Uruguayans are quitting the habit, smokers who remain may be smoking more intensely. ■



March is National Colorectal Cancer Awareness Month. Excluding skin cancers, colorectal cancer is the third leading cause of cancer-related deaths in the U.S. when men and women are considered separately, and the second leading cause when both sexes are combined. It is expected to cause about 49,190 deaths during 2016. The American Cancer Society estimates that there will be 95,270 new cases of colon cancer and 39,220 new cases of rectal cancer in 2016 in the United States.

STOPPING CANCER BEFORE IT STARTS: THE PROMISE OF THE PRE-CANCER GENOME ATLAS

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People who test positive from the screen are recommended to undergo colonoscopy.

Spira, a lung cancer specialist, also pointed to a test he helped develop called Percepta. The test analyzes key genomic alterations in bronchial airway cells to gauge a patient's risk for the number one cancer killer.

Tests focused on mutations in BRCA genes – long tied to breast and ovarian cancers – are also examples of “pre-malignancy” screens that help guide decisions on cancer prevention.

“Now we have modalities available for screening colorectal, lung, breast and several other malignancies, and that’s allowed us to potentially identify the

pre-malignant lesions before they become cancer,” Spira said. “But we still struggle to identify which of these precancerous lesions is destined to become an invasive and lethal cancer”

The Road Ahead

A handful of tests is a good beginning of course. But high-powered data mining – conducted in a collaborative, multi-disciplinary way – could usher in many new insights into premalignancy.

The Pre-cancer Genome Atlas represents just that sort of concerted approach to this new field, Spira said.

“The idea is to create a sort of ‘Manhattan Project,’ if you will – a biomedical research community consortium where we collect these premalignant samples when we can and study them thoroughly, comprehensively, with the latest and greatest molecular tools,” he explained.

“Through our computational biology, we may then understand the sequence of events that lead to cancer and –

potentially – have a better way of identifying who is truly incubating a cancer that’s likely to kill them,” Spira said.

How long would it take to complete the Pre-cancer Genome Atlas? Once it got up and running, perhaps 5 to 10 years, but it is difficult to predict, Spira said.

An article outlining the promise of the approach, published early in 2016 in the journal *Cancer Prevention Research*, has already generated great interest.

“That paper was a call to arms,” Spira said.

“Will it ever get to that ‘Manhattan Project’ that I am envisaging?” Spira said. “I hope so – we’re not there yet, but that would be the goal.”

The final goal is routinely stopping cancer before it starts.

“An ounce of prevention is worth a pound of cure,” he said. “If you can get in early, you can have a much bigger impact on the disease process.” ■

SUSAN G. KOMEN: PIECING TOGETHER THE PUZZLE OF BREAST CANCER PREVENTION

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In an effort to better understand the scientific “landscape” of research into breast cancer prevention, Komen commissioned the Institute of

Medicine’s foundational report, *Breast Cancer and the Environment – A Life Course Approach*, to move us toward greater opportunities for breast cancer prevention. That report revealed that there were insufficient data in a number of areas and that more research was needed.

In response, Komen offered Environmental Challenge Grants in

FY13. These grants focused on: the impact of radiation exposure on breast cancer development and in treatment; the impact of pollutants in areas where cancer rates are disproportionately high; the impact of air pollution on breast cancer development; and the role of synthetic chemicals called phthalates. Through these grants, we hope to move beyond theories to

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Interested in learning about cancer prevention meetings and events? Please visit our Web site, www.nypcancerprevention.org, to view the Calendar of Events.

SUSAN G. KOMEN: PIECING TOGETHER THE PUZZLE OF BREAST CANCER PREVENTION

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a solid base of scientific evidence to understand the specific role of environmental exposures and breast cancer development.

All of these projects are helping to lay the groundwork for someday being able to truly prevent breast cancer, but it will require a deeper understanding of all aspects of prevention – everything from environmental causes to diet, exercise, alcohol, chemicals and more – to get us to that point.

Fortunately, our organization is well versed in both patience and persever-

ance. We have made significant advances in our understanding of risk, lifestyle factors and genetics, but breakthroughs happen over time, not overnight. We intend to follow through on the promise that founded our organization – to end breast cancer forever – and will continue to invest in innovative prevention research that will someday help make this goal a reality. ■

For reference information please go to our Web site,
www.nypcancerprevention.org.



Visit our website, www.nypcancerprevention.org, and click 'Resources' for Congressional, White House, and federal agency contact information, should you like to learn more about government efforts to prevent cancer.

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