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BRIGHT FUTURE
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THE TRUCK STOPPED
AT 2 A.M. SOMEWHERE
IN THE SUDANESE DESERT.
MERHAWIT’S JOURNEY
WAS JUST BEGINNING.
IN THE SINAI,
THINGS WOULD GET MUCH WORSE.
Electronic cigarettes are everywhere: on commercials, in magazine ads and in the hands of their users—who are not called smokers, but “vapers.” That’s because while cigarettes burn tobacco, creating smoke, e-cigarettes heat liquid nicotine, creating vapor.

Some say the gadgets are a gateway to the greater danger of smoking, while others hope they might help eradicate that cancer-causing habit. Bloomberg School researchers interested in this issue—and a host of others posed by e-cigarettes—led a symposium on the topic May 2.

Patented in the U.S. in 1962, the nicotine-vaporizing device was commercialized by a Chinese pharmacist and for a decade has been marketed aggressively. Today, e-cigarettes come in some 250 varieties that resemble everything from cigarettes and cigars to pipes, hookahs, flutes and flasks. Their prices vary, as do the flavors—from mint to mango.

They differ from standard cigarettes, which burn tobacco, paper and additives to create smoke that delivers nicotine to the lungs—and ultimately the brain—in seconds. Traditional “combustibles” throw off about 7,000 toxins, more than 60 of which are known carcinogens. E-cigarettes, on the other hand, heat liquid nicotine, water and other chemicals, creating vapor.

“E-cigarettes expose the user and those around them to nicotine and a few other chemicals,” says K. Michael Cummings, PhD, MPH, a professor in Psychiatry and Behavioral Sciences at the Medical University of South Carolina. “But the aerosol generated is clearly less toxic than cigarette smoke.”

E-cigs are “much, much safer than cigarettes,” says symposium keynote speaker David B. Abrams, PhD, a professor in Health, Behavior and Society at the Bloomberg School and executive director of the Schroeder Institute for Tobacco Research and Policy Studies. “They are much less likely to cause the big diseases: heart disease, cancer, and chronic pulmonary disease.”

**All Steamed Up  ARE E-CIGS THE ANTI-TOBACCO OR GATEWAY GADGETS?**
Joanna Cohen, director of the Bloomberg School’s Institute for Tobacco Control and an organizer of the event, agrees. “The expert opinion at this point is that they are much less harmful to the individual,” she says. “The question you have to ask from a public health perspective is, What are the implications at the population level?”

A primary public health concern is that e-cigs will renormalize smoking. “Young people say it’s not cool to smoke cigarettes right now. With this new device, we worry they will say it is cool,” says Maciej L. Goniewicz, PhD, PharmD, assistant professor of Oncology in the Department of Health Behavior at the Roswell Park Cancer Institute.

Cool, and wildly accessible. E-cigarettes, largely unregulated, are used where cigarettes now are forbidden; they are advertised in media where cigarettes have long been taboo. Some call it “the Wild West”—lawless and possibly full of potential. “This is a disruptive technology,” says Abrams. “For the first time in a century we have a product that could make cigarettes obsolete. It’s the beginning of a revolution.”

Those who stand to benefit are smokers who make the switch from cigarettes, Cohen says, citing small studies that suggest that they might help some to quit smoking. While FDA-approved smoking-cessation products like gum, patches and lozenges are slow to deliver nicotine to the bloodstream, some e-cigs have the potential to mimic the quick-hit of standard cigarettes. That, plus the fact that e-cigs can look and feel like the “real thing,” might make them helpful to the can’t-quit contingent.

“A nicotine patch is not a very good reward for a smoker craving nicotine,” explains Cummings. “It’s like telling my dog to wait two hours to get her treat. She learns much better if I give her the reward right away.”

However, if smokers keep on smoking and take up e-cigarettes, there’s no health gain. In fact, this kind of “dual use”—smoking when permitted and vaping when not—might extend rather than curtail a smoking habit.

“If you smoke an e-cig rather than a Marlboro, that’s a good thing,” says Cummings. “The problem is people who add an e-cigarette to their Marlboro smoking might not get any benefit.”

Researchers concur that regulating the sale and content of e-cigs is a good idea, as they can be packed with contaminants. While foes want to see them taxed and restricted like standard cigarettes, proponents of the product say careful regulation can help shape a healthier future. “I call it the Goldilocks formula,” says Abrams. “Not too hot and not too cold.” If e-cigs can be positioned at a lower price point with a higher nicotine punch, consumers may abandon cigarettes altogether, he says.

That sounds just right to some, but others are proceeding with caution. “There aren’t a lot of data yet,” Cohen says. “People can give a lot of opinions; they aren’t right or wrong. We don’t know yet.”

—Leah Eskin

Sales of e-cigs more than doubled from 2012 to 2013 to $1.7 billion.

In 2011, 5% of high school students said they’d tried e-cigs. In 2012, 10% had.

Second-hand exposure from e-cigs is about 1/10th that of cigarettes.

About 40% of American smokers have tried e-cigs.
When a school kid in just about any developing country has an epileptic seizure, chances are that fellow students and even teachers will shy away instead of trying to help. Tenacious superstitions that epilepsy sufferers are either possessed or contagious surround this disease, which afflicts 65 million worldwide.

Of that number, almost 90 percent live in developing countries where causal factors are not addressed and cases remain severely under- and misdiagnosed despite effective and available and relatively affordable treatment.

“This is a disorder of children, youth and working-age adults mostly, and when there is inadequate diagnosis and limited treatment, the cost to society is potentially very high,” says Farrah Mateen, MD, PhD ’14, who started working in the Kingdom of Bhutan in 2009. She has been back several times and plans to go again this summer.

Mateen is focused on interventions and low-cost diagnostics for brain disorders with the goal of facilitating a “technological leap” in resource-limited settings. Along with doctoral studies at the Bloomberg School, Mateen simultaneously completed a fellowship in the Division of Neuroimmunology and Neurological Infections at the Johns Hopkins School of Medicine. “This training allowed me to develop clinical expertise with vulnerable populations in Baltimore and abroad,” she says.

Now a neurologist and faculty member at Massachusetts General Hospital of Harvard Medical School, and the University of Ottawa, Mateen is conducting a clinical trial in Bhutan to test a low-cost mobile electroencephalography (EEG) device that could become a routine tool in developing countries for the diagnosis of people with seizure disorders. There are an estimated 10,000 cases of epilepsy in Bhutan.

The device takes the form of a “shower cap,” with roughly a dozen leads that are attached to a patient’s scalp for 20–30 minutes to monitor the brain’s electrical signals. The signals are fed into a smartphone app that records the EEG.

Health care workers who give the test don’t require formal medical training, and the data are easily transmitted for expert interpretation. That’s helpful in a country like Bhutan, which has not a single neurologist and just one non-functioning, stationary EEG machine at the main hospital in the capital Thimphu, days of walking away for many of the country’s 900,000 citizens.

The device, operating on open software developed at the Technical University of Denmark, costs $275, compared to approximately $15,000 for current stationary EEGs. The work is funded by Grand Challenges Canada, which rewards technological innovations in projects with other social and economic benefits, as well as the Thrasher Foundation.

Mobile technologies particularly benefit young children who can suffer small, non-violent seizures that might be mistaken for staring spells, according to Mateen.

Once a diagnosis of epilepsy is made, doctors can then prescribe a medication. The government of Bhutan provides anti-epileptic drugs free of charge.

This technology has the potential to improve the diagnosis of epilepsy in other developing countries, including in Africa where a dozen countries with a combined population of 26 million lack a neurologist, and 23 other countries have four or fewer neurologists.

“Populating the world with neurologists, which involves training of a decade or more, is impossible, but we can roll out technology that is cheap and simple to use,” says Mateen. —Ken Stier

**A Shower Cap EEG in Bhutan**

PROBLEM: In the Kingdom of Bhutan, there are 10,000 people with epilepsy, one stationary EEG and not a single neurologist.

SOLUTION: See Farrah Mateen.
It’s not easy to study and prevent malaria transmission because people are always on the move.

From home to work, or village to country, they can pick up and carry the *Plasmodium* parasite. Traditional surveys often fail because they capture only what people remember and care to share. And public health programs often end abruptly at national borders not recognized by *Anopheles* mosquitoes. All this leads to glaring information gaps and sets the stage for malaria’s resurgence. Cross-border foot traffic, in particular, can reignite epidemics.

How big is this threat? And how can it be prevented? These are issues epidemiologist William Moss, MD, MPH, wants to investigate at three NIH-funded sites in sub-Saharan Africa that belong to the International Centers of Excellence for Malaria Research. Each site has a distinctive history that’s influenced by the presence—or absence—of cross-border foot traffic.

Recently, a tiny pocket of rural Zambia lit up with GPS signals. Each belonged to a community member going about everyday activities with a wristwatch-like GPS device in tow. Moss remembers how cautiously his colleagues approached study participants about the project. “It turns out that they thought it was really cool to wear [the devices],” Moss says. Before long, other people were asking to wear a bracelet. It was an auspicious start to a series of studies Moss plans to conduct, exploring how both small- and large-scale human movements impact malaria prevention efforts.

The GPS study is being run out of Choma District, a region in southern Zambia where recent antimalaria efforts have been successful. Yet even here, transmission hotspots remain, threatening to reverse the region’s gains. By tracking participants’ daily routines, and then overlaying them on a malaria risk map, Moss and his colleagues hope to discover how local travel can promote hotspots.

The program’s second site, Mutasa District, lies on Zimbabwe’s eastern border with Mozambique.

Family ties transcend these political boundaries, and cross-border trips are second nature to residents. For 40 years, public health programs in Zimbabwe loosened malaria’s grip. But since the programs ended in 1990, malaria’s made a comeback. Although cross-border transmission is frequently blamed, no one really knows if it’s playing a major role in the area. Using samples from 2012 and onward, Moss and colleagues plan to genotype the parasites found in patients, distinguishing “local” parasites from “imported” ones. Their results could benefit other border regions attempting to sustain public health gains in the face of dwindling budgets.

The third NIH-funded research site, in northern Zambia, also lies on an international border—this time with the Democratic Republic of Congo (DRC). For years, political instability has led the international community to steer clear of the DRC, leaving Africa’s fourth most populous country to fight malaria largely on its own. Despite the country’s violent reputation, Moss envisions creating a sister research program in the DRC to share ideas and information. Moss traveled with Peter Agre, MD, director of the Johns Hopkins Malaria Research Institute, to the DRC in February 2014. They found the country’s health minister and counterparts at Kinshasa’s Congo Protestant University eager to collaborate. Now the issue is finding funding for a DRC site. Moss is hopeful. “I think everyone recognizes that malaria can’t be controlled in sub-Saharan Africa without addressing malaria in the DRC. It’s a place where there are huge needs but also huge opportunities.”

—Rebecca Widiss

**Danger: Plasmodium Crossing**

Among the challenges in preventing malaria transmission: People move, and mosquitoes don’t recognize borders.
After the rash of mass shootings in recent years, some politicians and pundits have lobbied for sweeping policies barring people with mental illness from owning guns. But that may not be the most effective strategy. A history of violent acts or serious substance abuse, not mental illness alone, should determine who is allowed to own a gun and who isn’t, according to new recommendations by the Consortium for Risk-Based Firearm Policy. The report recognizes that the vast majority of people with mental health conditions are not violent and calls for developing evidence-based criteria for determining who is more likely to commit acts of violence and prohibiting them from owning guns.

“Past behavior is the best indication of future behavior, and that’s where we’re going to be effective in concentrating our efforts on gun violence prevention policy,” says Shannon Frattaroli, PhD ’99, MPH ’94, an associate professor in the Center for Gun Policy and Research, who served on the consortium.

The consortium—composed of approximately 30 of the country’s leading researchers, practitioners and advocates in gun violence prevention and mental health—convened last spring at the Bloomberg School and in December 2013 issued two reports with recommendations for both state and federal policymakers.

Looking at current epidemiology, the group concluded that strategies focused solely on restricting access to guns by those diagnosed with a mental illness are too broad and therefore unlikely to significantly reduce overall rates of gun violence.

“When we think about the risk factors for gun violence, and where we can intervene, what we really need to be doing is focusing on behaviors and not diagnoses,” says Frattaroli. Center for Gun Policy and Research colleagues—Daniel Webster, ScD ’91, MPH; Jon Vernick, JD, MPH ’94; Beth McGinty, PhD ’13; and graduate assistant Anna Grilley who will earn her MSPH this May—also participated in the consortium.

The report calls for temporary restrictions on the purchase and possession of firearms by people subject to temporary domestic violence restraining orders, and restrictions of up to five years by individuals convicted of violent misdemeanors, or more than one drug or DUI/DWI within a certain period. These behaviors are all associated with an elevated risk of violence, even when not accompanied by a record of mental illness. Researchers recommended maintaining current provisions that permanently disqualify individuals from possessing firearms following involuntary commitment to a mental health facility.

Josh Horwitz, executive director of the Education Fund to Stop Gun Violence and a visiting scholar at the Bloomberg School, says that in the wake of the Sandy Hook shooting, the time was right.

“We were having these shootings by people who were clearly affected by mental illness, but at the same time, I was cognizant that most shootings aren’t committed by the mentally ill,” says Horwitz, who organized the consortium. “I thought it was really important to get everybody in the same room and ask, ‘What is the state of knowledge, and what can we confidently say about the intersection of guns and mental health that would potentially reduce gun violence?’”

—Joe Sugarman

Gauging Gun Risks

Guns, Mental Illness and Violence

- On the day of the Sandy Hook Elementary School massacre, an estimated 85 others died from gun-related injuries in the U.S.
- Only 4% of violence in the U.S. is attributable to mental illness.
- Mental illness is much more strongly linked with suicide. 60% of gun deaths in the U.S. are suicides.
- In the U.S., an estimated 31,000 people die and 74,000 suffer non-fatal gunshot injuries annually.
- Unless they have other risk factors, individuals with common mental health conditions are not much more likely than others to be violent.
- Most people with serious mental illnesses are more likely to be victims than perpetrators of violence.
- Congress enacted the Gun Control Act of 1968, following the assassinations of Dr. Martin Luther King, Jr. and Robert F. Kennedy.
Sound Medicine

Three years ago, at a conference involving traumatic brain injury, Linda Maguire’s two worlds—music and neuroscience—merged in a particularly dramatic fashion.

There was a flurry of urgent text messages: Was she available in a few hours to fill in for a soloist who was ill?

“I had to leave the conference and sing Verdi’s ‘Requiem’ that night at the Strathmore concert hall in North Bethesda, Maryland, and darn if I didn’t pull it off,” recalls Maguire, MA, a Master of Health Science student in Mental Health.

A classically trained vocalist with numerous performances of leading opera roles and classical music recordings to her credit, Maguire is equally devoted to science. Her research into music and the brain, mainly in Alzheimer’s patients, continues to blend her two passions.

What was for years an amateur interest became a serious academic pursuit not long after she visited a friend with Alzheimer’s in a facility for dementia patients. She witnessed behaviors characteristic of the condition—lonthargy, aggression, confusion.

Then she began to play the piano.

“Music not only calmed and redirected them, it clearly provided access to brain networks while nothing else could,” recalls Maguire, who cut back her performing schedule to study cognitive and behavioral neuroscience, earning a master’s in psychology last year.

Now she’s working to harness the power of music—using a science-based approach—to improve the lives of Alzheimer’s patients.

Maguire’s focus is on the use of “prescriptive” music to elicit specific physiological changes that, in turn, bring about positive and measurable responses such as decreases in blood pressure, heart rate and stress hormones.

It’s well established that music can powerfully benefit dementia patients. What’s missing from the equation is an understanding of how musical characteristics—including rhythm, structure, tone, instrumentations, melody and vibration intensity—drive behavioral and cognitive changes.

She likens her “prescriptive music model” to a physician’s use of prescription drugs. “There’s a difference between entertainment and prescriptive value,” says Maguire. “I’m working on developing a foundation to use music as a true and legitimate clinical intervention.”

Nancy Hodgson, PhD, RN, an assistant professor at the Johns Hopkins School of Nursing and Maguire’s thesis advisor, says that her research into music as a precisely targeted clinical intervention holds promise as an effective non-pharmacological approach to enhance Alzheimer’s care.

“I think she’s onto something very innovative,” Hodgson says. “Her proposed design is attentive to detail, and she brings the perspective of a well-established, highly regarded musician.”

Maguire is currently conducting a review of the literature on the physiological response to develop a computerized prototype targeted to dementia patients. Her model relies on a comprehensive physiological and psychological assessment to design personalized music prescriptions that “escort” patients to desired outcomes in mood, cognition and activity levels.

One component of her thesis focuses on “sundowning syndrome” in Alzheimer’s patients to mitigate problematic behaviors that typically occur with more frequency in the late afternoon hours.

The music selection might start with a favorite hymn, a selection that often connects with dementia patients in an agitated state.

“You can build from that point to take them to other arenas,” Maguire says.

Continuing to alleviate the anxiety, Bach’s “Air on G” or Josef Rheinberger’s “Cantilena”—pieces that can trigger relaxation responses—might figure in the repertoire.

“It gradually establishes a physiological domain where anxiety can’t happen because it doesn’t have the physiological ingredients to happen,” Maguire explains.

Although her primary focus is on Alzheimer’s disease, Maguire says that the medical music model is applicable to patients with PTSD, depression, schizophrenia, autism and other conditions.

“A lot of vets with PTSD love heavy metal because that’s what they’re living,” she says. “If you play something sweet and classical, they’re going to reject it.”

Looking ahead, Maguire hopes to develop a website of archived clinical music programming that can be accessed by health care providers and delivered on a professional level.

“I’m just putting together a very logical model, based on empirical research,” she says. “It might serve as a turning point in music medicine.”

—Jackie Powder

When musician and brain researcher Linda Maguire began playing the piano at the care facility, she noticed a dramatic change: “Music not only calmed and redirected [Alzheimer’s patients], it clearly provided access to brain networks while nothing else could.”
Finally, the “How” of ALS

If gene mutations were people, the mutation commonly found on a gene called C9ORF72 would be a notorious criminal. About two years ago, researchers first linked this mutation to the fatal, muscle-wasting disease amyotrophic lateral sclerosis (ALS)—Lou Gehrig’s disease. Since then, the mutation has been implicated in an ever-expanding list of ailments including Alzheimer’s disease, frontotemporal dementia and Huntington’s disease. But, like detectives without a murder weapon, researchers haven’t understood how the C9ORF72 mutation derails normal cell functions. Now, Jiou Wang, PhD, an assistant professor in Biochemistry and Molecular Biology, and colleagues may have an answer. In a study focused on ALS and recently published in Nature, the team reports discovering a cascade of molecular events from mutation to pathology, potentially opening avenues to treat the disease’s root cause, not merely its symptoms. In recognition of this finding, Wang was awarded the 2014 Shikani/El Hibri Prize for Discovery & Innovation.

Like all genes, C9ORF72 consists of a sequence of bases (represented by letters) within a larger strand of DNA. A normal C9ORF72 gene contains a string of six letters, GGGGCC, which may be repeated a few times. In its mutated counterpart, this sequence repeats dozens to tens of thousands of times. Yet the familiar mutation story—alter a gene, alter the protein it codes for—doesn’t necessarily apply, as this region doesn’t code for a protein. Still, Wang’s team thought the repeats must be up to something. It took two years to confirm this hunch.

Step one in the team’s process was to create artificial DNA sequences with GGGGCC repeats. In these regions, the two strands of DNA pulled apart. One side folded over itself to form G-quadruplexes, stacks of square-shaped molecules that resemble a miniature, low-rise building. Meanwhile, the other side formed rare, long-lasting bonds with RNA, called R-loops.

In cells taken from patients, this bulbous, hybrid RNA-DNA crippled the machinery used to make standard RNA, which acts as a template for protein production. It’s as if the machinery hit “a series of speed bumps or the occasional roadblock,” says Wang (above left, with ScM student Tushar Chakravarty). Rather than creating one long RNA strand, the machinery produced many stunted ones. Worse still, these mini-strands attracted and diverted proteins that would otherwise be performing important cellular functions. When the team compiled a list of 280 proteins waylaid by this “toxic RNA,” a protein called nucleolin stood out as highly susceptible.

The team was onto something big. In healthy cells, nucleolin is concentrated in the nucleolus, a chamber within the nucleus where protein assembly begins. But in the cells of ALS patients, nucleolin is widely dispersed throughout the entire nucleus. Though the details aren’t clear yet, this dispersion puts stress on cells, sometimes causing their death. And it’s cell death that manifests in ALS patients as progressive movement problems. In short, by focusing on the structure of the C9ORF72 mutation, the team had found a probable root cause for ALS.

There’s much more to study. But Wang and his colleagues are eager to put their insights to use developing therapies. And they’re hopeful that, as researchers study over 30 other diseases linked to similar repeat regions, the basic process they’ve discovered will prove to be a “smoking gun” many times over.

—Rebecca Widiss
An Alarming Trend in Maternal Health

Maternal death is dropping in many countries—globally the number of women dying from pregnancy-related causes has fallen from 376,000 in 1990 to 293,000 last year. However, the rate in the U.S. doubled during the last decade, and the incidence of near-death has also spiked.

Maternal mortality has not declined in the U.S. for a quarter century, according to Andreea Creanga, MD, PhD ’09, who leads the CDC’s Pregnancy Mortality Surveillance System.

“It’s an alarming statistic,” she says.

Creanga’s job involves collecting vital statistics data from all 50 states and then painstakingly analyzing each individual case of maternal death. About 650 women die annually nationwide; about a third of these deaths are preventable.

Generating a clear and up-to-date picture of the problem at a population level is no easy feat. The death rate rise in the U.S. can, at least in part, be attributed to improvement in how maternal deaths are identified, Creanga notes.

But that’s hardly the whole story.

Among the significant risk factors for maternal death is a mother’s age; the number of U.S. women delaying childbearing has increased in recent years. Obesity is another risk factor. So is having hypertension and diabetes, both of which contribute to high-risk pregnancies. Being foreign-born as opposed to U.S.-born is a risk factor. So is race. Black women have a three- to four-times higher risk of maternal mortality, but no clear evidence exists to explain the disparity.

Ascertaining the true nature of the problem can be tricky given the relatively small number of cases of maternal death, Creanga explains. “We need larger numbers to be able to draw reliable conclusions.”

“No woman should be dying from pregnancy-related complications in the U.S. in 2014. Yet, many are dying every year. We need to know why.”

—Andreea Creanga, CDC

The complexity of maternal death at the population level is heightened by the fact that it's a moving target, Creanga explains. “Things are changing every year, and we want to know about these changes.”

To help provide an all-important context for understanding what’s behind the trend, Creanga has co-authored research that measures the incidence of maternal near-death cases to combine with mortality data.

One notable new finding: Traditionally, hypertension, hemorrhage and embolism were the leading causes of maternal mortality. Lately, there’s been a shift to cardiovascular conditions as the main contributor to maternal death, Creanga notes.

“The more we know about risk factors and causes of deaths, the more we can do something to prevent maternal deaths,” she says.

Her office is now collaborating with a wide assortment of clinical and professional partners on an initiative that focuses on “patient safety bundles”—standardized sets of evidence-based guidelines, practices and tools that health care practitioners and hospitals can employ to improve outcomes. The first bundle involves a hemorrhage management protocol to prevent death. “We are now putting together bundles for hypertension and embolism,” Creanga says. “Going forward, we’ll be creating bundles that address obesity and cardiovascular disease.”

Her work can be very sad, Creanga says, especially recreating scenarios involving the death of young mothers. “But it’s what we have to do. No woman should be dying from pregnancy-related complications in the U.S. in 2014. And yet, many are dying every year. We need to know why.”

—Maryalice Yakutchik

In Memoriam

 Timothy D. Baker, MD, MPH ’54, who in the 1960s was instrumental in founding the world’s first Department of International Health, died December 17, 2013, at age 88. A professor in International Health, he also founded the General Preventive Medicine Residency Program and helped to establish the School’s first endowed professorship. Baker's work as a health systems consultant and his pioneering health workforce studies took him to dozens of countries on five continents.

Baker came to the School in 1959 as the assistant dean and an associate professor of public health administration.

Alan Ross, PhD, MS, professor emeritus in the Department of Biostatistics, which he joined in 1964, died September 7, 2013, at age 87. Chair of Biostatistics from 1967 to 1981, Ross also served as chief biostatistical consultant to the Federal Aviation Administration and advised WHO on medical care utilization and designing and analyzing population surveys.

Raymond Seltser, MD, MPH ’57, a professor in Epidemiology and associate dean at the School from 1967 to 1976, died February 16, 2014. The author of seminal studies on the risk factors involved in smoking, radiation exposure and stroke, Seltser was deputy director of the Johns Hopkins Oncology Center from 1977 to 1981, and later served as dean of the University of Pittsburgh Graduate School of Public Health.