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Behind the Vapor

Chasing the facts about e-cigarette health risks



By Sara Rimer • Photos by Cydney Scott • Video by Devin Hahn

Less than a decade ago, the e-cigarette was an obscure product marketed as a safe, tobacco-free alternative to conventional cigarettes by a single company in China. Seven years ago, the electronic nicotine delivery device entered the US market. Today, health officials, policy makers, and researchers are all scrambling to keep up with a rapidly expanding, wildly controversial, and largely unregulated [\\$3 billion global industry](#) that has, at last count, 466 brands, 7,764 flavors (bubblegum, cherry crush, bacon, java jolt, menthol), and slick, youth-oriented Big Tobacco marketing designed to create the perception that e-cigarettes are not only safe, but cool.

\$3B

Global Industry

466+

Brands

7,764+

Flavors



Video: Josh Jason on the pleasures of vaping.

Pulmonologist Avrum Spira on how what we don't know could hurt us.

Public Health Professor Michael Siegel on the lesser of two evils.

With the public health community sharply divided over the potential benefit and harm of the popular device—and with conclusive scientific evidence in short supply—the World Health Organization (WHO) [released a report](#) in August 2014 that raised serious questions about the health impact of e-cigarettes and called for a ban on indoor use and sales to minors. The report expressed “grave concern” over the growing role of multinational tobacco companies, warning that they could turn e-cigarettes into a gateway for a new generation of smokers at a time when a decades-long public health campaign has successfully reduced smoking rates in the US and other developed countries.

“In theory—and how they’re marketed—e-cigarettes are a safer product because they don’t have tobacco, which has known carcinogens,” Spira says. “The question is: does safer mean safe?”

Also in August 2014, the Centers for Disease Control (CDC) reported that more than a quarter million youth who had never smoked a cigarette used e-cigarettes in 2013, three times the number of users since 2011. The Food and Drug Administration (FDA) proposed bringing e-cigarettes under its control alongside tobacco in the spring of 2014, but that proposal is enmeshed in debate and lawsuits. Dozens of states and cities across the country, including Boston, have already banned the use of e-cigarettes indoors.

At Boston University, Avrum Spira (ENG’02), a pulmonary care physician and School of Medicine professor of medicine and pathology and bioinformatics who studies genomics and [lung cancer](#), was one of the first scientists to receive funding from the FDA to investigate the health effects of e-cigarettes. “In theory—and how they’re marketed—e-cigarettes are a safer product because they don’t have tobacco, which has known carcinogens,” Spira says. “The question is: does safer mean safe?”

Across BU’s Medical Campus from Spira, [Michael Siegel](#), a physician and professor of community health sciences at the School of Public Health, has emerged as perhaps the country’s most high-profile public health advocate for e-cigarettes. Siegel, who is not currently researching e-cigarettes, says he believes that the device could potentially help large numbers of smokers quit, or drastically decrease, a habit that is the leading cause of preventable deaths in the US. He points out that despite all the existing smoking cessation products on the market,

only a small fraction of cigarette smokers manage to quit. Only 4 to 7 percent break the habit without some nicotine replacement or medication, according to the American Cancer Society. At the same time, Siegel says, more research is needed on the health effects of e-cigarettes as well as their effectiveness in helping people quit smoking.

Josh Jason:

“There’s no way e-cigarettes are totally safe. The only things our lungs were meant to take in is oxygen.”

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Josh Jason, a 21-year-old junior at BU’s College of Communication, is just the sort of consumer (young and hooked on smoking) who the e-cigarette industry is targeting and researchers want to better understand. Thinking it might be time to try to quit smoking, he bought his first e-cigarette a year ago. Jason says “vaping,” as the e-cigarette habit is known, helped him cut way back—until the battery on his device died and, in need of a quick nicotine fix, he bummed a cigarette from a friend. Now, he is a dual user, trading off between vaping and smoking, depending on which form of nicotine delivery he has on hand. He buys his vaping supplies online (online sales are brisk) or at stores specializing in the product, and prefers e-cigarettes made by independent companies rather than Big Tobacco.

“I hate Big Tobacco,” Jason says. “They know about the risks of cigarettes. They’re pussyfooting around the fact that these things will probably kill you.”

As much as he enjoys e-cigarettes, Jason is not unmindful of the risks. “There’s no way e-cigarettes are totally safe,” he says. “The only things our lungs were meant to take in is oxygen.” On the other hand, he notes, vaping doesn’t make him a social outcast the way smoking does. It doesn’t smell bad or make his breath reek. “Hopefully, I’ll move toward vaping rather than smoking,” he says.

Siegel is among those experts critical of the WHO report who worry that overregulation could spell the end of what he and others believe could be the most disruptive public health tool to have come along in some time in the war on smoking. “Electronic cigarettes represent one of the greatest threats to cigarette smoking in many years,” says Siegel, who has been battling Big Tobacco, cigarette smoking, and the harmful effects of secondhand smoke for well over two decades. “The WHO is trying to protect cigarettes from the threat posed by these fake cigarettes.”

With research still in the early stages, here are things consumers currently don’t know about e-cigarettes, according to the FDA:

- The potential risks when used as intended. How much nicotine or other potentially harmful chemicals are being inhaled during use.
- Whether there are any benefits of using them.

HOW DO E-CIGARETTES WORK?

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RECHARGEABLE BATTERY
ATOMIZER
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E-cigarettes are battery-powered—many can be recharged through USB ports—and while there are a dizzying array of varieties, they come in three main categories: cigalikes, which look like conventional cigarettes; eGos, which are larger than cigalikes and usually come with a removable tank that can be refilled with a liquid containing varying amounts of nicotine and a syrupy synthetic liquid called propylene glycol, a chemical that has been shown to be generally safe to consumers except at very high levels; and modular e-cigarettes (mods), which are usually larger than eGos and can be endlessly customized.

7,764+ flavors and dozens of devices

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E-cigarette users inhale a vapor made by heating the nicotine-containing liquid and flavoring. Nicotine is a highly addictive substance, but e-cigarette users get their fix without the deadly carcinogenic tar that comes with combustible cigarettes. And yet, Spira says, there are crucial unanswered questions about just what e-cigarette users are inhaling into their lungs along with nicotine. “This is not a tobacco product,” he says, “but when you burn a liquid, it changes the composition, and when you inhale that liquid, you get nicotine plus other chemicals. The question is, are those other chemicals harmful or not?”

Spira’s preliminary research, using genomics to test the effects of the nicotine vapor on human bronchial cells, suggests that e-cigarettes may not be benign.

“It’s cause for concern,” Spira says. “We need to learn a lot more.”

Avrum Spira says e-cigarettes may be safer than regular cigarettes, but that doesn’t mean they’re safe.

Avrum Spira is a Boston University School of Medicine professor of medicine and pathology and bioinformatics, the Alexander Graham Bell Professor of Healthcare Entrepreneurship, and chief of the Division of Computational Biomedicine. He is a pulmonologist at Boston Medical Center. With funding from the National Institutes of Health and, more recently, the Department of Defense, he has been working to develop molecular tests for [early detection of lung cancer](#). Spira talked with *BU Research* about his research into the health effects of [e-cigarettes](#), which is being funded by the FDA.

BU Research: You're a pulmonary researcher who has done groundbreaking work on early-stage lung cancer detection. You're also a pulmonary care physician and you've spent years treating patients with advanced lung cancer who had been heavy smokers. What are your concerns about e-cigarettes?

Spira: It took decades after cigarettes were introduced to sort out the health effects, which were devastating. Many people got addicted and they couldn't quit once the health effects became clear. The devastation is truly hard to imagine; according to the 2014 [Surgeon General's report](#), more than 20 million deaths have been attributed to smoking in the US since the 1960s. The tobacco companies have recognized for many years that their product is hurting their customers, which also impacts their sales. So they have recently started to develop "safer" products. There is a lot of controversy around this. How do we know a "safer" product is really safer?

But before the big tobacco companies got involved, weren't e-cigarettes introduced and produced by independent companies as a way to get a nicotine hit without the tobacco and carcinogenic tar—as a safe alternative to cigarettes?

Yes, we could say that e-cigarette products have exploded in the marketplace, specifically in terms of brands, delivery devices, flavors, nicotine concentrations, as well as the delivery liquids. It's a complicated, fascinating, and rapidly moving space. There are currently a myriad of ingredients that can be combined in different ways to produce the vapor. This does present a challenge for researchers looking to identify the agents that are harmful, as each e-cigarette product is potentially different than the next. The FDA is trying to get a handle on standardization and potential risks of e-cigarette products by funding groups like ours to develop systems to rapidly assess these factors. But the research community is still scrambling to keep up with the rapid and unanticipated changes in this field.

Can you explain how e-cigarettes work?

E-cigarettes are a device that delivers nicotine—which is one of the addictive substances in cigarettes—without any actual tobacco, or tar. Tar has hundreds of known carcinogens. E-cigarettes have a battery-powered cartridge that heats a liquid containing nicotine and potentially a flavoring, which creates an aerosol that is inhaled. The e-cigarette community refers to this as "vaping," where traditionally we'd call it "smoking." Now, when you heat a liquid, it changes the chemical composition of that liquid and additional chemicals can form (e.g., formaldehyde, acetaldehyde, and acrolein), which are then inhaled by the user. The question is: are those other chemicals harmful or not?

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Avrum Spira (MED) on the dangers of regulation without research

What do you think about the public health argument Professor Michael Siegel (of the School of Public Health) and others make, that e-cigarettes are an important tool for helping cigarette smokers quit who might not otherwise be able to?

I understand his perspective and don't entirely disagree. If there's a smoker who can't quit but who can use this product instead, that has a health benefit. This is almost certainly better than smoking traditional tobacco cigarettes. If this is a vehicle for quitting or a better alternative to traditional cigarettes, it could have a huge public health benefit. There are 45 million current smokers, adults in the US, who are unable or unwilling to quit. It's still a major public health problem. The other side of the debate is that this normalizes smoking behavior, that it's an entry point for younger people. A 15-year-old, an 18-year-old, says, "Okay, this is safe product," and gets addicted and it becomes a gateway to other products, including traditional cigarettes.

What does your research tell us about the health effects of e-cigarettes?

Our group was one of the first, in collaboration with [Dr. Steve Dubinett](#) (a pulmonologist at UCLA) to get funding from the FDA to study the health consequences of vaping. Our approach to evaluating e-cigarettes is based on what we've done with tobacco cigarettes, where we've developed genomic signals of exposure and, to take that a step further, signals of disease risk (e.g., lung cancer and chronic obstructive pulmonary disease, or COPD).

The question is: Does exposure to e-cigarettes create the same genomic changes in the airway as tobacco cigarettes do? Our prior work, over the past decade, has characterized a large number of genomic changes that traditional cigarette smoke causes in epithelial cells that line the upper airway (e.g., the windpipe) and has identified a smaller subset of changes that are associated with development of lung cancer and/or COPD among smokers. We are currently evaluating whether e-cigarettes produce similar gene expression changes as traditional cigarettes. In addition, we can correlate these genomic signatures to signatures of disease risk and begin to assess the chronic potential harmful impact of these products.

We decided to do our research in two phases. We started off with cells in culture. We took human bronchial epithelial cells that contained some mutations found in smokers at risk of lung cancer and cultured them with media that contains everything that comes out of an e-cigarette. The idea is that you're "smoking" the cells.

We found that the electronic cigarette was able to cause cells to become more cancer-like—they grew more quickly than a cell should be able to. That is one of the things that cancer cells do. That is the only thing we found—that it did change their growth rate significantly, more than smoking nothing and similar to smoking regular tobacco. That raised concerns on our end. Then we looked at the cells' genome and found that many

of the same genes turned off and on by tobacco cigarette smoke are being turned on and off by e-cigarettes.

And you're now in Phase Two of your study? Can you tell us about that?

Our ultimate objective in Phase Two is to take people who smoke tobacco cigarettes, have them switch to e-cigarettes for at least two months, and sample the cells in their windpipe and their nose both before and after they switch. We would then perform genomic profiling on these samples. This entails measuring the activity of all 20,000 genes in your cells, which we can do in 24 to 48 hours. This produces a large amount of data, so this is where computation comes in.

We are able to compile all of the data for all of the people we profiled and ask general questions, such as: when individuals switch to e-cigarettes, do their gene expression patterns or profiles resemble that of a former smoker? This would suggest that the product is potentially safer. Alternatively, does your genetic profile continue to look abnormal? And in that case, we would argue that e-cigarettes aren't necessarily safer.

With regard to disease, some smokers' genes turn on differently and that puts them at risk for cancer. So we can also look and see whether electronic cigarette exposure produces similar genomic changes that are associated with lung cancer.

Should e-cigarette users be concerned? Should they stop vaping?

We're not saying that e-cigarettes cause cancer. We can't say that based on this data. What we're saying is that we have evidence from cells in culture that e-cigarettes could have effects that are similar to tobacco smoking and that many more studies are needed before we can say this is a much safer product. That's where this fits into the whole public health debate. The FDA wants the academic community to come to the table with new approaches. That is what we responded to. The FDA has made a significant investment in our group and many other groups across the country to help study this in far greater depth. While it will likely take years via longitudinal studies to be absolutely certain of the safety of this new product, we're in the process of getting more data in the short term that will give us some more insight into the potential risks of e-cigarettes, so that potential users have that information.

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John Carroll (COM) on the genius of Big Tobacco's ad machine

What about the public health history in terms of cigarette smoking and the lessons learned there?

We don't want to go down the road we did with cigarette smoking. It took 20, 30 years until the epidemiologic data came out convincingly that cigarettes cause cancer and other diseases. For many people, it was too late, as they were unable to quit and/or had already developed disease.

The genomic technology we have today—these approaches weren't available back then. It took long-term epidemiologic data before risks of exposure became clear.

We are in a new era of science and technology and medicine where we can do new types of translational studies. This type of science can potentially be done very quickly. We're not there yet and we won't be in a few months. Maybe in a couple years...but it need not be decades. We don't have to repeat the past. More science needs to be done as quickly as possible. We need to take a very careful look at this product and come to some preliminary conclusions. It's going to be very difficult to put the genie back in the bottle—the longer people use it, the more difficult it becomes to stop.

Why do you care so much about this research?

My passion is to care for patients with diseases. An ounce of prevention is worth a pound of cure. Most people start smoking when they're young. I take care of them many years later when they become a patient. I wish I could go back and stop them from starting smoking. I feel like this is my opportunity with a different product to perhaps prevent young folks from engaging in a behavior that could be harmful—so at least they're armed with information. E-cigarettes are, in theory, a safer product. They don't have a lot of the components found in tobacco. It's just—they may be safer, but they may not be safe. We need to clarify and I think it's important the public have that information. Even if e-cigarettes are not as bad as tobacco, it's important that we know what their health impacts are.

When I became a lung doctor, I was seeing a huge population of smokers who were getting diagnosed with lung cancer at this institution at an advanced stage where I couldn't offer them any effective treatment. We need to detect this disease earlier and prevent it. Once you're diagnosed with lung cancer, your survival rate is very poor.

What do you think about people who smoke cigarettes?

I'm okay with someone eating wrong, not exercising, smoking—as long as they know about the consequences of that behavior. I take care of a lot of people who smoke. A lot of them started when they didn't know it was bad to smoke. Smoking was a cultural phenomenon. People didn't know the health effects—and it's addictive. Later you can say, "Now we know," but if you're doing an addictive behavior for 20, 30 years, it's really hard to stop.

I don't judge smoking at all. I take care of patients unable to quit. That's why I see Siegel's argument. I know how hard it is to quit. Even some patients with lung cancer still can't quit.

Public Health professor Michael Siegel says concerns are premature and overblown

BY Lisa Chedekel and Sara Rimer

Michael Siegel, a Boston University School of Public Health professor of [community health sciences](#), is a nationally known expert on the health risks, marketing, and regulatory policies [concerning cigarettes](#). He argues that the controversy over e-cigarettes is misguided, and that it clouds the important benefits of the devices to help people quit smoking. Because only about 6 percent of cigarette smokers who try to quit are successful, and because the tobacco industry will continue to sell cigarettes despite tobacco's known health risks, Siegel is concerned that the government's focus on the potential harms of e-cigarettes will detract from their potential benefits to those who want to stop smoking.

BU Research discussed the controversy with Siegel.

***BU Research:* CDC director Tom Frieden has said the findings of increased teen use are “deeply troubling,” deeming e-cigarettes a gateway drug to a lifelong addiction to nicotine and regular cigarettes. Do you disagree?**

Siegel: Well, first, it's important to point out that this alarming conclusion is premature. There is no evidence that electronic cigarettes are serving as a gateway to a lifelong addiction to nicotine and conventional cigarettes.

There is something that Dr. Frieden didn't mention. The overwhelming majority of the youths who reported experimenting with e-cigarettes were already smokers. So the fact that these smokers are experimenting with e-cigarettes is not really a problem. The concern would be if nonsmokers were using electronic cigarettes, and then moving on to regular cigarettes. But the prevalence of nonsmokers experimenting with e-cigarettes in the CDC study was only 0.5 percent. Moreover, the study did not document any examples of youth starting to smoke as a result of first trying electronic cigarettes.

While there is every reason to be concerned about the potential for electronic cigarettes to become popular among youth, there is no reason to be alarmed at this point. It is essential that we continue to carefully monitor this. It is also important that the FDA promulgate regulations that will help prevent the use of electronic cigarettes by youth.

What do we know about the rising number of people who are using e-cigarettes as devices to quit smoking?

We do know that the predominant reason so many people are using e-cigarettes is that they want to quit smoking in order to improve their health. While we don't have a lot of quantitative studies about the effectiveness of e-cigarettes in smoking cessation, a clinical trial published recently found that e-cigarettes are just as effective as the nicotine patch for smoking cessation. Unfortunately, the e-cigarettes tested were a first-generation product that did not deliver nicotine very well. It is possible that more advanced products could actually surpass the nicotine patch in their effectiveness.

Josh Jason, the BU junior you talked with on [our video](#), said he started vaping with the idea that it might help him quit smoking and is now vaping and smoking. Is he the “dual user” people are talking about?

Yes, he is an example of the classic “dual user.” I can't predict what will happen for an individual, but we do know on a population basis that many dual users do go on to quit smoking completely. So it is simply not the case that someone who becomes a dual user will always be a dual user. For many smokers, dual use is a step along the progression to quitting smoking completely.

Do you think the intense government focus on e-cigarettes' potential negative effects is misplaced?

It is certainly reasonable to carefully scrutinize any consumer product like this. However, what I have a problem with is the fact that the FDA has given its seal of approval to the irredeemably toxic regular tobacco cigarettes—while they are doing everything they can to discourage people from switching to the much safer fake ones. That makes no sense from a public health perspective.

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Leonard Glantz (CAS'70, LAW'73) on the wisdom of risk reduction

What about the WHO report that came out in August calling for some of the toughest regulations yet proposed on e-cigs, raising serious concerns about their health effects and expressing “grave concern” about the growing market encroachment of Big Tobacco? What do you think about the WHO's tough stance on e-cigarettes and do you share its concern about the tobacco companies' growing industry role?

There is no question that the WHO is overreacting to the supposed “threat” posed by electronic cigarettes. In fact, not only is the WHO overreacting, but it is taking exactly the wrong approach with respect to these products. Electronic cigarettes represent one of the greatest threats to cigarette smoking in many years. These products have already helped hundreds of thousands of people to quit smoking or to substantially cut down on the amount that they smoke. The WHO is actually taking the side of trying to protect cigarettes from the threat posed by these fake cigarettes. The WHO has consistently

discouraged smokers from quitting by using e-cigarettes. This invariably has discouraged many smokers who might have quit successfully from trying to quit at all. In addition, the WHO has drawn shoddy scientific conclusions that are not backed up by the actual science. I'm afraid that the WHO has done a lot of public health harm on this issue.

But is there conclusive scientific evidence that e-cigarettes help smokers quit?

No, there isn't. We need more research. There needs to be a randomized trial. I want to do that study. The way to do it is to take a group of smokers and get them to switch to e-cigarettes and follow them over time. A randomized trial is the gold standard, but it would cost about \$4 million. It's very difficult to get funding for that kind of study.

Are you concerned that big US tobacco companies, such as Altria and Reynolds, have entered the e-cigarette business, given the type of marketing they might do?

There are actually some benefits to having the major tobacco companies become players in the e-cigarette field. For one thing, they have better access to large retail outlets, and it is possible that their entrance into the market may greatly expand the access smokers have to these products.

In terms of marketing practices, it is essential that the FDA allow companies to tell the truth about the intended use of these products—that they are intended to be used for smoking cessation. That would avoid the need for companies to resort to some sort of glamorized marketing campaign that glorifies smoking behavior.

You've long opposed Big Tobacco and cigarettes, but now, ironically, are you on the same side as Big Tobacco when it comes to e-cigarettes?

I don't think it's fair to say that I'm on the same side as Big Tobacco regarding electronic cigarettes. It's a very complex issue. I think that the tobacco companies see a prospective niche market—there are many smokers who want to quit and e-cigarettes are a potentially lucrative business. So it makes economic sense for tobacco companies to try to derive some of their income from noncombustible nicotine products. In fact, I think the industry can see long term that the field is changing and that the combustible market will eventually shrink. They want to expand their offerings so that they can derive income from noncombustible sources.

Are you worried that e-cigarette advertising and photos of celebrities vaping will make cigarette smoking—a behavior you've spent your career trying to decrease drastically—glamorous again?

I don't think that e-cigarette advertising glamorizes smoking. I think it glamorizes vaping. However, I do think that the more advertising is focused on marketing these products as ways to quit smoking, the more public health benefit will come from these products.

Right now, if an e-cigarette company marketed its product for smoking cessation, it would run the risk of being deemed as having made a therapeutic claim and having the FDA pull it off the market. My opinion is that the FDA should explicitly allow companies to tell the truth about the intent of the product without having it considered a therapeutic claim.

Most scientists believe nicotine, while highly addictive, is not what causes cancer in smokers or people exposed to secondhand smoke. Has there been any scientific research into the negative health effects of e-cigarettes?

It is very true that nicotine is not the main component of the tobacco smoke that is responsible for most of the adverse health effects. Because electronic cigarettes deliver nicotine without most of the tens of thousands of other chemicals—and without the more than 60 known carcinogens—it is clear that electronic cigarettes are much safer than tobacco cigarettes.

The scientific research conducted so far suggests that electronic cigarettes are much safer than regular cigarettes, and that in particular, they carry a greatly reduced risk of lung cancer, other cancers, and chronic obstructive lung disease. Evidence presented just recently suggests that they also likely present a lower risk of heart disease. We need more research to understand whether there may be long-term adverse effects. But what we can say for sure is that they are much safer than the real cigarettes.

Do you think science will settle the debate over e-cigarettes that has divided the public health community?

I don't think science will settle this because many opponents of e-cigarettes are so biased in their views that I don't think they will objectively look at the science. In fact, this is already happening. A large group of researchers has already concluded that e-cigs are a gateway to smoking, but the science doesn't support such a conclusion.

How did you get interested in e-cigarettes?

I have been following the issue of electronic cigarettes since they entered the US market several years ago. My interest was piqued by the response that these products received from public health and antismoking groups.

Rather than embracing these products as a potential way to get thousands of smokers to quit smoking, antismoking groups have attacked these products and discouraged smokers from quitting by using them. This is so contrary to the principles of public health that it caught my attention—and I continue to be puzzled by this inane public health response.

The only hypothesis I have come up with is that the ideology in the antismoking movement is so strong that the very thought of condoning a behavior that looks like cigarette smoking is just something that these groups are not capable of doing—even though it is likely saving the lives of thousands of ex-smokers.

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Mike Seigel (SPH) on the balancing act of public health

What is the most effective smoking cessation tool we have?

Unfortunately, we don't have an effective cessation tool. The best available treatments, such as Chantix and nicotine replacement therapy, only work long-term for about 8 percent or so of the population. We need to do better than that.

Why do you feel so passionately about e-cigarettes?

Because I've seen them save the lives of thousands of individual smokers who would not have quit smoking without them.

Listen to Michael Siegel discussing e-cigarettes during an interview with [WBUR's On Point here](#).

Discuss this story on [BU Today](#).