



Meet Our Presenters:



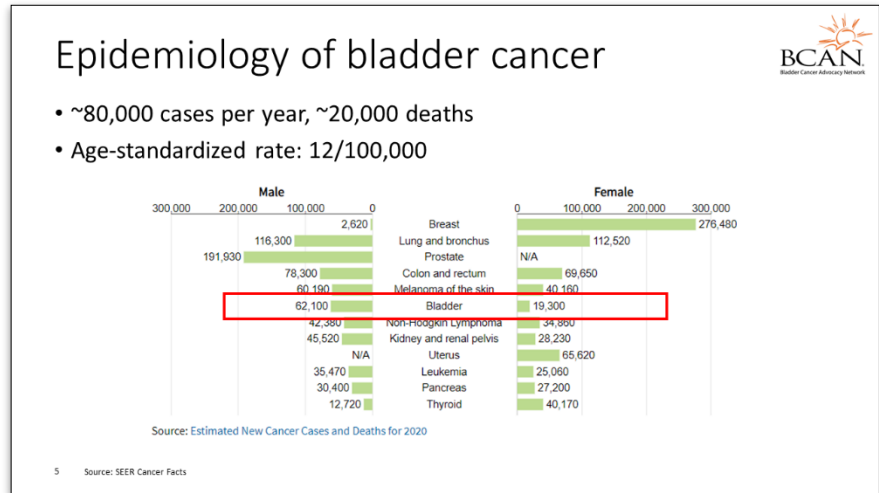
laparoscopic, and robotic approaches.

Richard S. Matulewicz: Dr. Matulewicz is an Assistant Professor of Urology and Population Health at NYU Grossman School of Medicine and a fellowship trained urologic oncologist. Dr. Matulewicz graduated from Tufts University School of Medicine in Boston and completed residency at Northwestern Memorial Hospital in Chicago. This was followed by a Society of Urologic Oncology (SUO) clinical fellowship in urologic oncology at Memorial Sloan Kettering Cancer Center in New York City. Dr. Matulewicz is trained in all aspects of urologic oncology disease management including endoscopic, open,



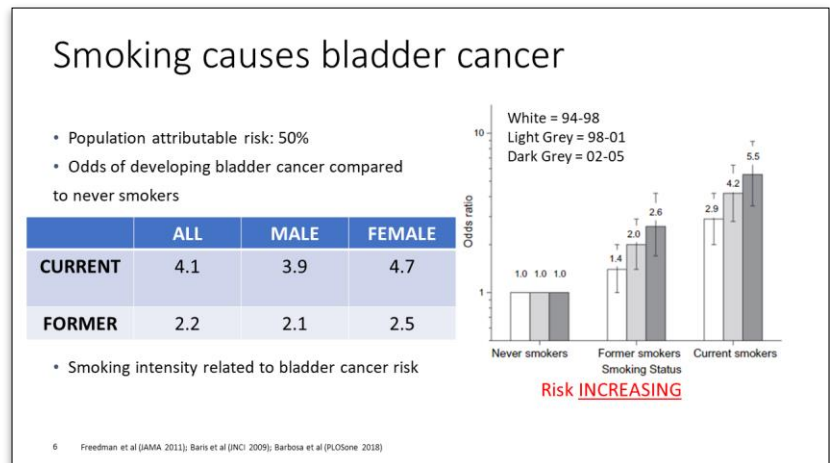
Marc Bjurlin: Dr. Bjurlin DO received his medical degree from Midwestern University and completed his residency at the Cook County Hospital in Chicago. After residency, Dr. Bjurlin completed a fellowship in urologic oncology at New York University along with a master of science degree in clinical investigation through the New York University School of Medicine. Prior to joining UNC, Dr. Bjurlin was Assistant Professor of Urology and Director of Urologic Oncology at NYU Langone Hospital in Brooklyn .

Dr. Matulewicz: All right. Thank you so much for the opportunity to be here today; to discuss this important topic. With that said, I think it's important to really understand the landscape, not only of bladder cancer, but also of how smoking relates to bladder cancer before we really start to do a deep dive into the rest. Bladder cancer in the United States is diagnosed in about 80,000 cases per year; 80,000 patients per year.



Unfortunately this results in about 20,000 deaths per year, specifically due to bladder cancer. As you can see here, there is a male to female predominance about a three to four times the increased risk of being diagnosed with bladder cancer, between males and females. Throughout the world, this incidence and this prevalence translates into about 1.5 to 2 million bladder cancer survivors after diagnosis which really gives us the understanding of just how important a topic this is for the 2 million people who have had bladder cancer. Some of which may be smokers previously.

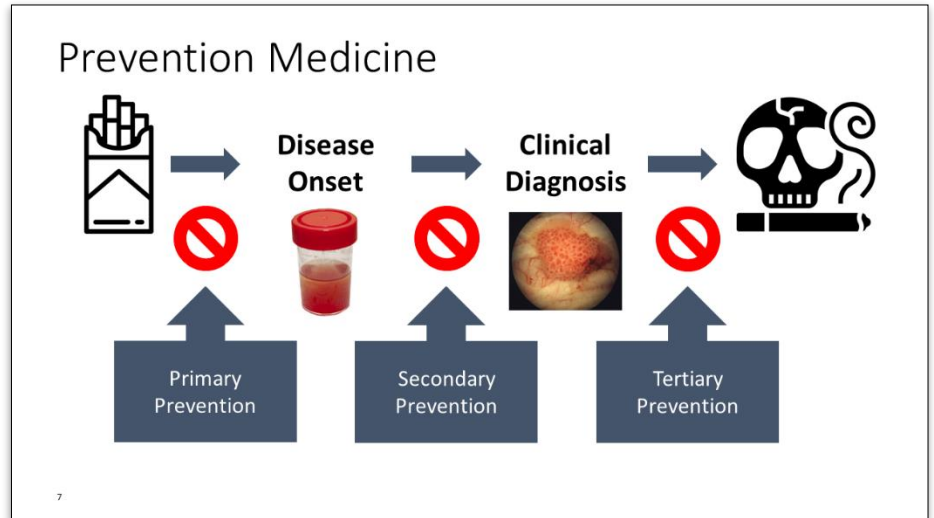
What we do know, also, is that smoking causes bladder cancer and about 50% of all cases of bladder cancer can actually be directly attributable to cigarette smoking. Looking here at the odds of patients who are former smokers compared to never smokers and current smokers compared to never smokers; What you can see is that a current smoker has a four times greater odds of being diagnosed with bladder cancer than a never smoker and even a former smoker, regardless of when quit, has about a two times greater odds of being diagnosed with bladder cancer, then a never smoker. These persist within male and female genders.



What we also know is that smoking intensity is related to bladder cancer risks. So the longer, and the more number of pack years that someone smokes the higher their cancer risk is.

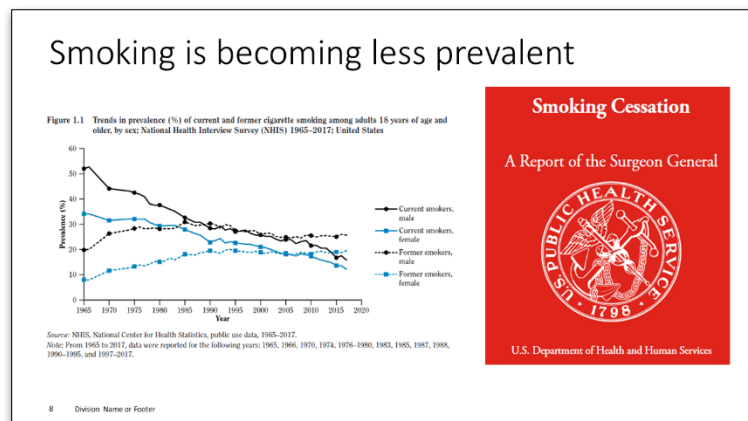
Dr. Matulewicz: Additionally, one of the things that we discovered in recent years, which has been nicely demonstrated in epidemiologic studies is that risk is actually increasing for current smokers. Although cigarettes have changed over the years, there is some thought that some of the way the tobacco is packaged and treated now actually portends a greater risk in the more modern era of cigarettes than past. So this is not only a problem that is quite prevalent, it actually may be getting worse.

Taking a step back and talking about prevention strategies in medicine, you have really three different means of prevention. The first being primary prevention, as you can see here, this is really trying to prevent the onset of disease. So this would be a lot of the things that have been done at the population level, which I'll talk about in a second, public policy changes that have reduced the number of smokers. This actually, is something that the goal is to prevent the onset; someone getting bladder cancer. This is something, again that's done by the government has done at the population level.



Whereas, these tertiary and secondary preventions, this is really more the space that urologists and patients need to partner together to, to address. And this is secondary prevention here is basically after the onset of disease or after diagnosis. This is stopping the agents in this case, cigarette smoking that can actually lead to worse outcomes before a disease develops and progresses similar with tertiary prevention. This is once a disease has started to show symptoms. These are really where the urologist and the patient can partner to prevent worse outcomes down the road.

The good news in all of this is that smoking actually is becoming less prevalent. We know from the time of the first report of the surgeon general for smoking cessation back in 1965, which is really the marker in the sand as to when the public really was told that smoking causes cancer. As you can see here in the subsequent almost 60 years, there have been some declines in the amount of patients who are currently smoking at any given time in the United States. This has definitely been very impactful in reducing the amount of tobacco related disease in the United States.

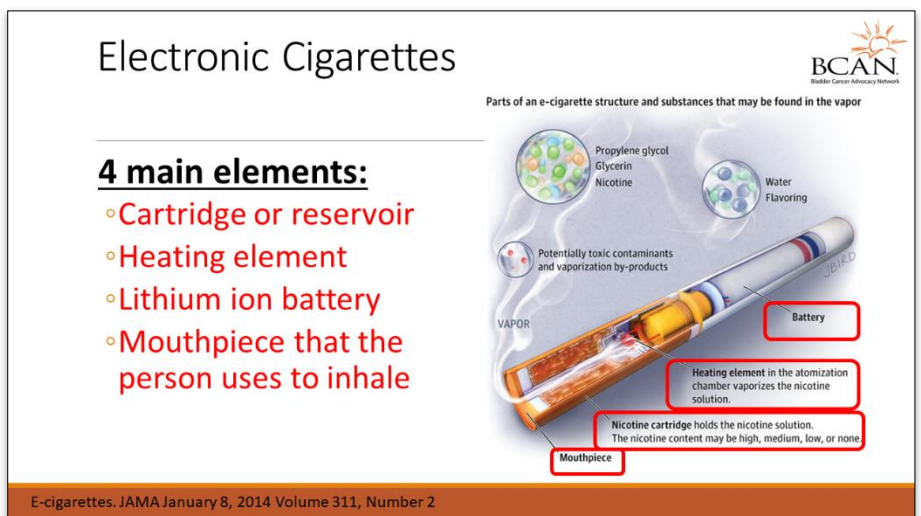
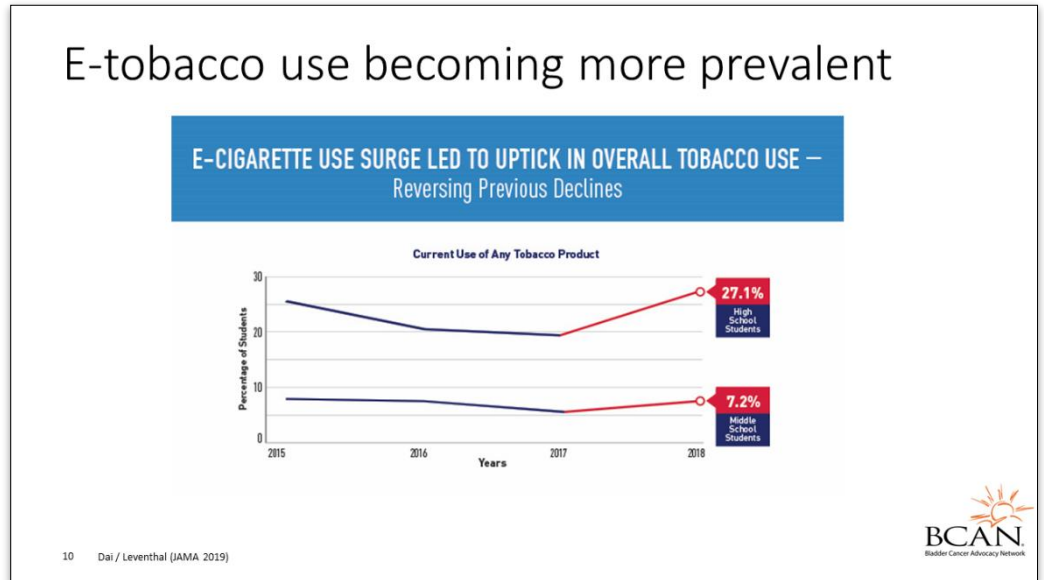


Dr. Matulewicz: Unfortunately, one of the trends we are seeing, although cigarette smoking is decreasing eat tobacco use and tobacco products like vapes and Juul pens have actually increased in prevalence. Most importantly and most concerning actually; these trends are increasing among youth which are at very high risk for subsequent tobacco related illness given the fact that they are starting tobacco use very early and have many years down the road of, of continuing if it persists. I'm going to turn it over to Dr. Bjurlin now to give a nice explanation as to what really relates to the bladder cancer risk in cigarette and e-cigarette users.

Dr. Marc Bjurlin: All right. All right, next we'll transition into discussing the topics of cigarettes and e-cigarettes and why they actually may place smokers at risk for developing bladder cancer. To get kind of a 30,000 foot overview of electronic cigarettes... E-cigarettes came on the US market somewhere around 2007 and really have exploded. They are now over a \$10 billion industry. And their use has really become a public health

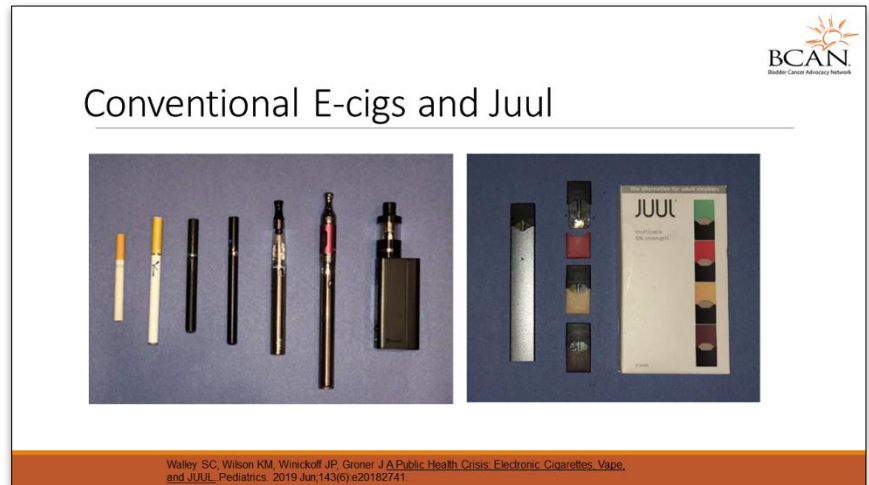
crisis, with an exponential rise over the last three to five years. E-cigarettes are considered an alternative to conventional cigarettes for a number of reasons. One being their appealing appearance, number two being their taste, and the third is perhaps their actual use characteristics, which make them popular among many age groups, particularly adolescents and young adults.

However, the definitive safety profile of e-cigarettes has really not been fully characterized. And given this large an increase in use in e-cigarettes, there's a pressing need to understand the health implications of vaping. So to have a general idea of how electronic cigarettes work, we can see here that they do have four main elements to them. One is the cartridge or reservoir, and this is part of the e-cigarette that holds the what's called e-liquid or e-juice that has the nicotine in it. There's the heating element that will heat this juice. And then also there's a lithium ion battery, similar to your



Tesla car or your electronic lawnmower that will again, heat this device. And then lastly, there's the mouthpiece that's used to actually inhale the aerosol from the electronic cigarette.

Dr. Marc Bjurlin: So this slide shows some pictures of e-cigarettes on the left and the specific brand of e-cigarette called JUUL on the right, which really highlights some of the design variability among these devices. So seen on the far left, here is a conventional cigarette and the earlier e-cigarettes, the first generations, had a very similar shape and size similar to a conventional e-cigarette. You can see them on the second, third and fourth from the left. The second generation e-cigarettes here are shown on the fifth and sixth from the left, had these clear reservoirs that were filled with the e-liquid. And these were conventionally known as vape pens. The third generation in cigarettes shown on this far right here, have the ability to modify the wattage and the voltage, and thus are known as mods. And then when someone uses an e-cigarette it's colloquially known as vaping.



On the right here is the actual brand of e-cigarette called JUUL, and these have recently received a number of significant media attention because of their rapid uptake in adolescents. Part of the appeal of these JUUL devices, is there a small, sleek shape that you can see here and their ability to use these devices surreptitiously, in that they can often hide them from the teachers when the adolescents use them. The JUUL device looks actually like a USB flash drive and actually can be plugged into a USB port in order to recharge it. The device does have some pre-filled cartridges shown here. These are referred to as pods and each one of these contains just less than one milliliter of unique solution that's referred to the e-juice or the e-liquid. And then each of these individual pods is marketed to be equivalent to one pack of cigarette in terms of puffs.

So an average pack of cigarettes, a user gets about 200 puffs. An average pod of a JUUL device has about 200 puffs. And then commonly, when someone uses a JUUL device, it's referred to as JUULing rather than vaping, which is commonly used for electronic cigarettes.

E-cigarette solutions, often referred to as either e-juice or e-liquid, are actually even more diverse than the devices themselves. The solutions commonly are advertised to contain three different types of chemicals. One being a humectant, the second being nicotine, and the third being a variety of flavors. The two humectants that are most

commonly used are either one, propylene glycol, or number two, vegetable glycerin. And these are additives that are used to reduce moisture loss.

Dr. Marc Bjurlin: And both of these solutions are generally recognized as safe for ingestion, but to date, there's really little evidence about their safety profile for long-term inhalation. The majority of e-cigarette solutions are advertised to contain nicotine. And this may actually range from no nicotine at all to up to more than 24 milligrams per milliliter of solution of nicotine. And the level of nicotine actually has been reported to vary quite substantially from what is actually advertised that's in the liquid to what is actually in the liquid when it's tested by an analytical chemistry assay.

Most brands of electronic cigarettes solutions are available in a variety of flavors. And these range from fruits, desserts, candies, sodas, to traditional tobacco flavor. Menthol is actually a common compound found in both mint and tobacco flavored e-cigarettes, and there's also some coffee and chocolate flavored e-cigarettes that actually have 42% or 52% levels of caffeine in some of these. You can see on the right side of the slide that these e-liquids are marketed quite similar to actual food sources that adolescents may use. You can see here that the food product shown on the right is an apple juice. And there's a juice box of apple flavored e-liquid. On the bottom, you can see the Sour Patch Kids as a sour flavor, and then e-liquid, also as a candy flavored sour flavor that you can add to the e-liquid or e-juice. So there are quite a variety of devices, and even more so e-liquid or e-juices.

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