THE HEALTH AND SAFETY IMPLICATIONS OF E-CIGARETTE USE BY YOUTH

REPORT BY THE COLUMBIA/BOONE COUNTY BOARD OF HEALTH

July 26, 2021

THE HEALTH AND SAFETY IMPLICATIONS OF E-CIGARETTE USE BY YOUTH REPORT BY THE COLUMBIA/BOONE COUNTY BOARD OF HEALTH

July 26, 2021

TABLE OF CONTENTS

Key Findings and Recommendations Pages 2-7			
Report on the Health and Safety Implications of E-Cigarette Use by Youth Pages 8-3			
Appendices			
Appendix A	Tobacco 21 Compliance Program 2020 Outcomes	Pages 34-35	
Appendix B	Tobacco Retail Store Assessments, Boone County, Missouri, January-February 2020	Pages 36-47	
Appendix C	How Schools Can Help Students Stay Tobacco-Free https://www.tobaccofreekids.org/assets/factsheets/0153.pdf	Pages 48-51	

KEY FINDINGS AND RECOMMENDATIONS

Health and Safety Implications of E-Cigarette Use by Youth

Report by the Columbia/Boone County Board of Health

July 15, 2021

The Columbia/Boone County Board of Health began studying the health effects of adolescent vaping in October 2019 due to community concerns about the steadily increasing proportion of teens affected. The Board reviewed the scientific literature and data from local, state and national youth surveys. We heard from university researchers, anti-tobacco advocates, Columbia/Boone County Public Health and Human Services (DPHHS) staff, school administrators, and members of the Columbia Youth Advisory Council. See list of those who testified on page 7.

The Board sent a letter of concern to the City Council in October, 2019 and the Council requested a report on the subject. After a long hiatus due to the COVID-19 pandemic, the Board finalized the attached, which was drafted by Board member Dr. Leona Rubin.

The key findings of the Board's inquiries are summarized below. We encourage local policymakers including the Columbia City Council, Boone County Commission, and school boards and administrators to consider the information and implement needed policy and program changes. The harmful health and mental health effects of youth e-cigarette use (vaping) are far-reaching, and additional interventions are needed to bring down the number of young people whose lives are marred by nicotine addiction.

1. Vaping harms youth physical and mental health

Nicotine is a significant ingredient in e-cigarettes. Nicotine derived from smoking has well-documented negative health effects on youth, and although the research is still evolving, those effects can also be attributed to nicotine delivered via e-cigarettes.

Nicotine exposure during adolescence can cause addiction and increases the likelihood of smoking traditional cigarettes. Physiological dependence occurs at a much lower level of use than previously thought. Adolescents are more susceptible to the addicting/reward effects of nicotine than adults and are more likely to exhibit an increase in drug-seeking behaviors.

The nicotine in e-cigarettes elicits the same cardiovascular responses as smoking and thus is likely to provoke the same deleterious cardiovascular diseases into adulthood.

Nicotine can harm the developing adolescent brain. Nicotine exposure (in animal models of adolescence) results in deficits in attention and cognition, mood disorders, and increased anxiety and fear disorders, all of which can extend into adulthood.

E-cigarettes and vaping exposes users to many other chemicals known to have adverse health effects. Many are known lung irritants, immunological activators or carcinogens. In 2018-19 a cluster of severe lung damage and multiple deaths was traced to cannabinoid vaping solutions containing Vitamin E oil. Most youth users choose liquids with flavoring ingredients, which when heated and inhaled form dangerous compounds that evoke immune responses, damage lung tissue, and can have estrogenic effects that alter developmental changes during puberty. Vaping increases the likelihood of viral transmission and COVID-19 infection in youth and increases severity of disease.

The manufacture of e-cigarettes and other electronic nicotine delivery systems is mostly unregulated, and these devices can cause harm through fires, leakage and heavy metal toxicity. Most (90%) are manufactured in China, and many are poor quality counterfeits, difficult to identify and usually cheaper, thus more likely to be used by youth.

2. Youth vaping is a significant problem in Missouri and Boone County

Prior to the pandemic, youth e-cigarette use across the nation more than doubled from 2017-2019. Data collection was difficult during 2020, but CDC recently released the results of the 2020 National Youth Tobacco Survey showing that the national rate of current use among high school students dropped from 27.5% in 2019 to 19.6% in 2020. Among middle schoolers the rate dropped from 10.5% to 4.7%. The reasons for the apparent decline in usage are not clear but probably reflect pandemic disruptions of retail businesses and schools (e.g., masking, social distancing and parental supervision during online schooling). As schools, household routines and the economy return to more normal conditions the rates are likely to increase again.

The 2020 Missouri Student Survey data for Boone County showed that 11.7% of students in grades 6-12 reported using e-cigarettes in their lifetime, and 3.6% reported using them in the past 30 days. However, nearly 90% of Boone County survey respondents were in middle school. Statewide and national data show that e-cigarette usage rates are higher among high school students than middle schoolers, so the lack of data from high school students probably resulted in an underestimate of actual usage rates.

Flavors are a key factor in enticing youth to start vaping. E-cigarettes are sold in over 15,000 flavors, from mint and menthol to gummy bear and cotton candy. According to the 2020 National Youth Tobacco Survey, flavored e-cigarettes were preferred by 85% of high school users and 74% of middle school users in 2020, with fruit and mint flavors the most popular. The 2020 survey also showed a dramatic shift among youth to disposable and menthol e-cigarettes.

Multiple cities around the nation are working toward prohibiting the sale of flavored tobacco products, including vaping fluids. The US Food and Drug Administration (FDA) has been very slow to assess and regulate vaping products. Although prefilled flavored cartridges (except for menthol) were banned by the FDA in 2019, the ban does not apply to refillable vape tanks and delivery devices, or to disposable e-cigarettes, which are increasingly popular among youth.

School policies can reduce student vaping behavior. The Board received information about Columbia Public Schools (CPS) policies that prohibit all nicotine products on campus. We heard from CPS representatives that awareness and enforcement of the policies varied markedly between two of the local high schools, one of which confiscated large numbers of vaping devices while the other seemed generally unaware of vaping violations. Unfortunately, CPS data regarding disciplinary actions did not distinguish vaping from other offenses. We were also given anecdotal reports of high rates of vaping and other tobacco use in rural Boone County schools.

Columbia and Boone County have adopted ordinances prohibiting the sale of tobacco products, including vaping products, to anyone under 21 years of age. The DPHHS hired a Tobacco Education and Enforcement Officer in 2020 to carry out retail compliance audits. The violation rate declined significantly over the

course of 2020, from almost 30% to around 5%, indicating that the compliance program is having a positive effect. See Appendix A.

E-cigarettes are also readily available via the internet, with lax procedures for age verification. We were not able to find data regarding online purchasing, but since other online shopping has increased during the pandemic the same may hold for e-cigarettes. This points to the need additional interventions targeting youth and their parents to increase awareness of the hazards of vaping and especially of counterfeit devices sold online.

3. Additional interventions are needed to reduce teen vaping rates in Boone County

Improve awareness of the hazards of youth vaping through effective parental and youth education. Advertising campaigns and packaging portray vaping as safe and many seem to believe that. Columbia/Boone County DPHHS conducted a grant-funded social media campaign for youth in 2019-20, "Stand Up for Your Health," consisting of posters and ads on SnapChat, Instagram, iheartradio, and Spotify. The theme, researched and tested on youth, was "Don't let the tobacco industry choose for you." The social media advertisements were targeted at people age 13-24 and reached a total of 80,729 individual social media users in 2019 and 104,985 in 2020. Fewer Boone County middle and high school students reported recent use of e-cigarettes after the campaign (3.6% in 2020) than before (9.6% in 2018). The proportion of students who viewed e-cigarettes as harmful rose from 60% in 2018 to 73.5% in 2020. The Board recommends that this type of social media campaign be funded and resumed with the addition of messaging targeted to parents.

Continue to actively enforce the Tobacco 21 ordinances and extend them to more Boone County municipalities.

Enforce existing school vaping policies more consistently. Data regarding disciplinary actions should identify vaping violations for comparison across schools, in order to identify problem spots as well as schools that may not be enforcing the policies. Although prevention of use is preferable to discipline for use, vaping should be recognized by all concerned as a "big deal."

Develop model policies and educational interventions for Boone County school districts. The recommended components can be found in the Tobacco Free Kids publication, "How Schools Can Help Students Stay Tobacco-Free," found in Appendix C.

Expand cessation services for youth. Better pathways for addicted youth to receive cessation support are needed. There are high barriers to treatment for youth who are already vaping and little in the published literature about effective vaping cessation programs. There are age barriers to FDA-approved cessation products such as nicotine gum and patches, and online apps and counseling for youth have not been well studied. The Board recommends that the various interested parties in Boone County (MU, CPS and other school districts, health care providers, etc.) continue to monitor treatment developments and collaborate to implement better cessation support as alternatives develop.

Implement stronger policies and ordinances to prevent youth vaping. While Columbia and Boone County have implemented effective policies to reduce youth access to tobacco/vaping products, including Tobacco 21 sales restrictions and tobacco-free campus and workplace policies, youth are still vaping using products purchased by adults. Three additional effective policy interventions have not yet been adopted here.

- Zoning restrictions on vape shops. Vape shops are permitted to operate in close proximity to schools (e.g., directly across the street from Hickman High School), thus normalizing and signaling availability of e-cigarette products to teens. A 2020 assessment of 111 tobacco retail stores in Boone County, performed by the North Carolina-based nonprofit organization Counter Tools, found that two-thirds had exterior advertising and 74.7% of those advertised e-cigarette products (see Appendix B). Retail tobacco sales outlets should be required to be distant from schools (similar to the limitations for pornography shops and marijuana dispensaries).
- 2. **Prohibit the sale of flavored vaping products.** This has been shown to be an effective intervention. Most youth enter the world of nicotine addiction through flavored products and are less likely to vape if flavors aren't available. Several US cities and states are moving toward such policies in collaboration with the Tobacco Free Kids "Flavors Hook Kids" initiative.
- 3. Explore the feasibility of an excise tax on e-cigarettes and other electronic nicotine delivery systems and products. Many states and local jurisdictions have imposed higher taxes on vaping products to increase the cost and thus reduce use by youth. We recommend the city and county explore this option.

Board of Health Speakers on Youth E-Cigarette Use

10/10/19

Ginny Chadwick, Preventing Tobacco Addiction Foundation Michelle Shikles, DPHHS Staff

1/9/20

Danielle Mondloch, Substance Abuse Advisory Council Cassandra Walker-Suggs, Dean of Students, Hickman High School Brandon Kim, Youth Advisory Council representative Rockbridge High School Blaine Ravert, Youth Advisory Council representative Hickman High School Robin Dianics, Ellis Fischel Cancer Center

2/13/20

Dr. Lisa Nieuwenhuizen, Assistant Principal, Rockbridge High School

Dr. Kevin Everett, MU Family and Community Medicine

Health and Safety Implications of E-Cigarette Use by Youth

Introduction and Background

Lighting a cigarette mixes tobacco with oxygen, creating an inhalable smoke containing nicotine, as well as about 7,000 by-products of which ~70 are known to cause cancer. In addition to cancer, it is well established that smoking tobacco increases cardiovascular and respiratory diseases, each of which increase morbidity and mortality for those who partake. Smoking also has detrimental effects on non-smokers through exposure to second-hand or possibly even third-hand smoke. Smoking also negatively impacts fetal development in pregnant women who smoke. Thus, there is considerable effort by medical, public health, and government agencies to stop individuals from smoking tobacco including: prohibiting smoking in indoor public spaces such as restaurants, hotels and public buildings; monetary rewards offered by employers for smoking cessation; and health insurance company motivations through reduced premiums or free coverage for smoking cessation programs. A major challenge to smoking cessation efforts is, and has been, the strong addictive properties of nicotine, a primary component of tobacco and a major driving force for continued tobacco use. Thus, national and regional regulations on the sale and availability of tobacco products have targeted prevention of first-time tobacco use, particularly by youth.

The highly addictive properties of nicotine have led to development of alternative methods to deliver nicotine to the body without the detrimental health outcomes of burning and smoking tobacco, primarily for smoking cessation efforts. Nicotine patches or nicotine gum are available to adults attempting to stop smoking, usually assisted by medical personnel. Consumers, on the other hand, have supplemented or replaced their use of traditional smoking products with electronic nicotine delivery systems (ENDS), which provide the nicotine but without most of the combustible tobacco smoke components. One of the earliest ENDS was an "e-cigarette", invented by the Chinese pharmacist, Hon Lik, in 2003, presumably to assist him with smoking cessation (reportedly unsuccessful). These first-generation e-cigarettes used a piezoelectric heating element to vaporize a propylene glycol solution containing nicotine which the user then inhales. Manufacturers and marketing agencies promote the idea that it is the combustion of tobacco, not the nicotine, that is responsible for most of the health problems associated with smoking, including cancer, heart problems and lung disease, medical authorities disagree. E-cigarettes were first marketed and sold in Asia but soon became available worldwide through internet sales. They were introduced to the American market in 2007 by major tobacco companies seeking an alternative commercial outlet for tobacco products. While the tobacco companies focused on the



Figure 1. Examples of a few of the electronic nicotine delivery devices on the market. These devices continue to evolve in their sophistication and socially acceptable appearance.

extracted nicotine solution, most of the ENDS for delivering the nicotine were, and still are, manufactured in China.

ENDS are quite variable in appearance and size but consist of three main components: 1) a battery, 2) a vaporizing chamber with a heating coil and 3) a cartridge (tank) that contains the volatile liquid. Initially ENDS were designed to look like traditional cigarettes to replicate the visual, sensory, behavioral and social aspects of smoking. These devices were mostly disposable and classified as first-generation ecigarettes. The second-generation ENDS were larger, the battery became rechargeable (via USB port) and they contained a separate tank that could be replaced or refilled. Third generation ENDS are essential a larger version of the second generation and are called "mods" because they come in a variety of shapes and sizes and the user can customize how much e-liquid is in the tank and how much voltage or power the device can output. The fourth and most recent generation are the most powerful and advanced devices on the market consisting of a stainless-steel cylindrical tank with a temperature regulating system and lower resistance coils that can produce bigger more flavorful vapors. The production of the inhaled vapor by all devices is



Figure 2. Different types and generations of E cigarettes. Image from the Center for Disease Control and Prevention: E cigarettes, or Vaping, Products Visual Dictionary page 15.

why the process of using any of these electronic devices is termed "vaping". Examples of some of the mods on the market are shown in Figures 1 and 2.

ENDS Marketing

Clearly, ENDS represent a significant and growing consumer market that is expected to gain traction owing to increasing product demand from millennials and an increase in variety of options. ENDS generated \$4.2 billion in US sales in 2018, \$15.1 billion in 2020, and is expected to generate \$18.47 billion in 2021 at a growth rate of 28.1%. By 2028, the industry will generate \$104.51 billion in revenue (E-Cigarette And Vape Market Size & Share Report, 2021-2028 (E-cigarette And Vape Market Size & Share Report, 2021-2028 (grandviewresearch.com)). Contributing to this market growth, especially among youth and young adults is 1) the cost-effectiveness of these devices compared to the rising price of traditional cigarettes, 2) addition of flavors 3) youthtargeted marketing, mostly online, with reward programs, subscriptions, and pyramid schemes (called Partner Programs) for online sales, and 4) marketing claims and assumptions that "ecigarettes" are a safer and healthier alternative to traditional cigarettes. E-cigarettes do contain fewer toxic chemicals, including carcinogens, than cigarettes, so switching could translate to lower rates of smoking-related disease[1]. But it is too simple to look only at "known" carcinogens. It is not yet clear what impact some of the ingredients unique to e-cigarettes could have on health, and the products have not been around long enough for scientists to know how they affect the body over decades.

Nonetheless, surveys of youth and young adults indicate they believe vaping is less harmful than smoking and many do not realize the major ingredient in both is the addictive drug, nicotine [2-4]. Youth and young adults who have never experienced a "smoking world" are particularly susceptible to big tobacco and online retainer marketing methods that appeal to the "being cool", "insider crowd" and "young rebel" mentality of teens [5-7]. Online retailers use names for devices that appeal to youth such as "WTF Target Mini Vaporizer" or a friendly web site name "Vapingpapa.com" that proports to provide user information as well as sales. Online Partner Programs encourage young people to sell ENDS for commissions, usually to other people they know. They simply set up a website or send an email with images and links to a supplier and any visitor to their site, who then purchases from the supplier, earns the original lister a commission. Thus, it is financially beneficial to encourage your friends to shop from your site. While most web sites indicate you must be of a certain age to purchase, it is unclear how that restriction is managed, and there is little doubt that the marketing of ENDS, from flavors to web-site gimmicks, is directed at a young, new consumer for these products.

The most comprehensive research and analysis of youth-targeted marketing can be found in a series of articles in Time Magazine by Jamie Ducharme: <u>How Juul Hooked Teens on Vaping and Ignited a Health Crisis | Time</u>, September 19, 2019; and <u>Juul: Inside the Rise and Fall of the Vaping Company | Time</u>, May 17, 2021. Although his work focuses on Juul, all makers of ENDS have adopted the Juul marketing model of making "Vaping" and vaping devices "cool" to the youth market, Juul just had a decade head start on other companies (see Text Box Quote from May 17,

Pax—the parent company that made and marketed Juul products—had spent much of its marketing budget on advertisements that appeared in convenience stores and other retail spaces, as well as on the Times Square billboard and in a print ad that appeared in Vice, which called itself part of the "#1 youth media company in the world." But social media marketing was valuable to the scrappy startup too, in no small part because it was cheap. If influencers were seen using the Juul, their followers would want to try it. And once their followers tried it, they would post about it and tell their friends. But this social media marketing strategy, unlike most utilized by startups, hinged on promoting an age-restricted and highly addictive nicotine product on platforms beloved by teenagers.

2021 Times article).

Juul is now being sued by the attorney general of North Caroline for intentionally targeting teens for sale of its nicotine products and underlying a generation of nicotine addiction by youth. This will be a challenging case in tobacco rich North Carolina. ENDS manufacturers, like Juul, have targeted youth through deployment of flavored nicotine solutions, in addition to MOD design. It is now not surprising that the current Juul website features a headline banner indicating nicotine is addictive and a large photo of a middle-aged couple. Juul now touts itself as a smoking alternative for adults only and effective July 2021 agreed to settle the lawsuit for \$40 million. Unfortunately, Juul is only one of many companies and retailers targeting youth and legal age limitations do not appear to prevent youth from obtaining products either in person, from their parents, or online [8, 9].

Federal Regulation of ENDS

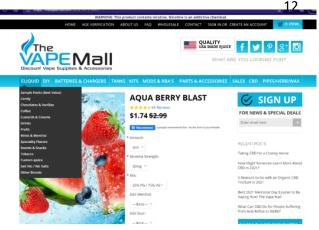
The 2009 Tobacco Control Act gave FDA the necessary tools to reduce society's toll from tobacco, including e-cigarettes. However, the agency has only recently exerted its powers to slow the youth e-cigarette epidemic. Indeed, until very recently, e-cigarette manufacturers enjoyed a market with few barriers. Repeated regulatory delays gave e-cigarette manufacturers more than a decade to

operate with minimal federal oversight. Not until 2016 did the FDA begin to address the ecigarettes market and request premarket applications (known as PMTAs) to determine whether these new tobacco products are "appropriate for the protection of public health" before they are allowed on the market. Of course, they are already "on the market". After years of delays, in 2017 FDA extended the deadline for completed applications to August 2022. When several public health groups, sued FDA, a federal court ordered the agency to require applications be submitted by September 9, 2020, and FDA has begun reviewing thousands of applications to determine if those products meet the public health standard set by the Tobacco Control Act. While the agency is supposed to conduct its review of those products in one year, FDA's Center for Tobacco Products director has admitted "the likelihood of FDA reviewing all of these applications during the oneyear review period is low," foreshadowing yet more delays in necessary and urgent regulatory action. Thus, the products being ingested, inhaled and vaporized into the environment remain unregulated and the impact on youth unknown. Much of this information comes from the 2020 Truth Initiative newsletter focused on youth and e-cigarette regulations (<u>E-cigarettes: Facts, stats</u> and regulations (truthinitiative.org).

Opposing any US government regulation is the lobby group, Sevia USA comprised of Chinese electronic cigarette manufacturers (<u>SeviaUSA</u>). Sevia stands for Shenzhen E-Vapor Industry Association. The companies involved are the leading companies making mostly high quality, innovative vaping devices and products (Aspire, Joyetech, Innokin, Smok, iJoy, Sense, Wotofo, Tesla, and Kangertech). Sevia is lobbying to prevent what they consider to be stifling FDA regulations if it specifies that electronic cigarettes are classified as a tobacco product. Sevia is the largest funder of the Right 2B Smoke Free lawsuit that promotes use of ENDS. Sevia's stated mission is:

- 1. The FDA should create a streamlined process that allows companies to submit more reasonable applications for the vapor market.
- 2. Congress SHOULD NOT regulate vapor products as tobacco products, considering these products **DO NOT actually contain tobacco leaf**.
- 3. The FDA should modify the grandfather date to allow products currently on the market in order to avoid the Pre-Market Tobacco Application (PMTA) process.

Sevia's membership represents reputable Chinese makers of ENDS, most of which have partnerships with global tobacco companies such as Altria Group, Inc., British American Tobacco, Imperial Brands, Japan Tobacco, Philip Morris International Inc., and R.J. Reynolds Vapor Company which produce the nicotine solution. Partnerships and rebranding between ENDS makers and tobacco companies make it extremely difficult to track ownership and provides even greater opportunities for counterfeiting and cloning of these products. As described below, tobacco leaf should not be the determining factor in whether vaping is classified as a tobacco product, but rather the addictive product of tobacco leaf, nicotine. The FDA ban on flavored prefilled cartridges (except menthol) during the Trump administration in 2019 will certainly hurt the profit margin of some ENDS companies such as Juul Inc, valued at \$38 billion before this ban with \$2 billion in 2018 revenue. Unfortunately, many teens and young adults are likely already addicted and willing to jump to non-flavored options or purchase refillable vape tanks, MODS or PODS as **flavored e-liquids were not banned**. For example, the online retailer, The Vape Mall (The Vape Mall: Discount Vaping Supplies, E-Juice &



Accessories) allows the buyer to select the e-liquid volume, milligrams of nicotine in that volume, and the flavor (even extra flavor if desired). Thus, it is possible to put 30mg of nicotine into 5ml of solution for nicotine delivery near or exceeding that of traditional cigarettes, and with flavor. Vapor4Life (Best Vape Juice & Cartomizer Flavors | Vapor4life) offers flavors by category, Fruit Flavors, Dessert Flavors, Coffee Flavors, and Beverages (lemonade, orange juice etc). While 5ml of vape juice with 30mg nicotine only cost \$1.74, vape tanks (\$30-\$60), and MODS (\$40-\$80) are expensive for youth users. Oh, and by the way, the Vape Mall is in Wentzville, Missouri.

Witnessing vaping on TV (for example, Mare of Easttown) and in online advertisements by famous personalities is reminiscent of big Tobacco advertising and adds to the challenges of preventing youth vaping. An FDA warning letter (September 9, 2020) was sent to three ENDS manufacturers to remove their products from the market; *XL Vape LLC* for lack of premarket authorization (deadline for the application was September 9, 2020), and *Flavour Warehouse LTD* (Vampire Vape) and *Pretty Women UK LTD* (Coil2oil Mad Kingdom Liquids) for illegally marketing and advertising e-cigarettes through use of cartoon images (vampires and kings) that appeal to youth. These actions were taken in response to the 2020 National Youth Tobacco Survey demonstrating increased use of disposable e-cigarette Use, Concerning Uptick in Use of Disposable Products [FDA]. Sadly, as detailed above, the FDA is considerably late in its recognition of the health impact of vaping on our youth and no effort has been made to ban or curtail sale of flavored e-liquids that appeal to youth.

Data on Youth E-Cigarette Use

Each year, the CDC and FDA collaborate, along with local and state health agencies, to implement the National Youth Tobacco Survey (NYTS) (Tobacco Product Use Among Middle and High School Students — United States, 2020 | MMWR (cdc.gov) for high school (grades 9-12) and middle school (grades 6-8) students to gather data on youth tobacco use. The NYTS is a cross sectional, voluntary, school-based, self-administered electronic survey and represents students in public and private schools. The surveys are traditionally conducted in the classroom and starting in 2019 was administered electronically on a tablet preloaded with the questionnaire. A web-based version also exists for students who may have been absent during the survey. According to NYTS data, in 2019, 6.2 million youth used some form of tobacco product. The overwhelming choice for tobacco use was electronic delivery with over 5 million students indicating e-cigarettes use within the last 30 days. One million students said they used e-cigarettes daily and the preferred brand was Juul. The use of e-cigarettes among youth has steadily increased since 2011 while traditional cigarette use

has declined from 16% of high school youth tobacco users in 2011 to 5.8% of users. Middle school students also reported a decline in traditional cigarette use (2011, 4.5% to 2019, 2.3%).

The NYTS for 2020 demonstrated an overall decline in youth tobacco use with 4.47 million students reporting tobacco use within the last 30 days (compared to 6.2 million in 2019). Student use of e-cigarette also declined (3.58 million users) but continued to be the prevalent product choice (See Info graphic). Conducting the in-person survey in 2020 was challenging due to the COVID pandemic. Only 50% of the schools selected were available for the survey and the time frame for data collection was reduced from 4 months (Jan 16 thru May 15) to 2 months (ended March 16) due to widespread school closures. However, data was collected from 14,533 students (~50% high school and 50% middle school), only ~3000 fewer than in 2019 and CDC researchers demonstrated with confidence that the change in sampling was not responsible for the overall decline in tobacco use. It would be encouraging if the decline in vaping by youth resulted from public health and school official efforts to educated youth on the dangers of vaping. However, it is also possible this decline is a result of factors associated with the Covid-19 pandemic, such as, reduced retail access, mask wearing in schools and reduced access (6 ft social distance) to the places students tend to congregate and vape, bathrooms and lockers. Interviews with high school students suggest they are knowledgeable of vaping behaviors in their schools [10]. Youth behavior changes due to Covid-19 may underlie some of the reported decline in youth vaping such as avoiding small spaces where aerosol vapers could spread Covid-19 and reduced sharing of ENDS devices among friends which might underlie the increase in disposable e-cigarettes reported in the 2020 NYTS.

ENDS and Youth Health Issues

While the ENDS devices themselves may pose physical harm to youth users, as discussed later in this report, the products they deliver, primarily nicotine, have detrimental effects on health and development of youth users. While considerable data exists on the adverse effects of the drug, nicotine, less information is available regarding other components present in vaping solutions or about the vaping process itself. As was true for research with conventional cigarettes and cigarette smoke, the real impact of vaping will require long-term population studies, as well as research with animal models. In addition, our understanding of health effects is somewhat hindered by the variability in vaping components. The concentration of nicotine, presence, or absence of flavorings, and/or the use of other e-liquid constituents contribute to the challenges of assessing the human health risk of vaping. Further, the concentration of aerosolized constituents delivered to the user varies by the type of device and the voltage of the device [11]. For example, commercial vaping products (e-liquids) can contain as little as 0 milligrams/milliliter (mg/mL) to as much as 36.6 mg/mL of nicotine; can be mislabeled [12, 13]; can vary by propylene glycol (PG)/vegetable glycerin (VG) ratio; and, can contain one or more of several thousand available flavorants [14]. Some liquids intended for use in ERMS contain adulterants not even named on ingredient lists [15], and under at least some user conditions, the aerosolization process, which involves heating, produces additional toxicants that may present health risks [16-19]. These issues will be discussed later in more detail. To add to these real and potential health harms is the fact that users of MODS, PODS and tanks can create their own solutions or purchase off-market, black-market solutions, which can have devastating life and death consequences as demonstrated by the multiple deaths associated with vaping tetrahydrocannabinol (THC) dissolved in an oil-base vitamin E solution

13

[20]. It is striking that a substance with so many variables, apparent unregulated content, and such high probability of harm, can reach youth users at all.

Vaping Solutions with Nicotine

Nicotine is the primary ingredient in most e-cigarettes and ENDS possibly reaching 4% of the volume in e-cigarettes and as high as 6mg/ml in tank refills. Depending on the battery voltage and experience of the person vaping, at least 50% of the solution can be aerosolized. Puff durations of e-cigarette among experienced e-cigarette users may be twice as long (~4 sec) [21-23] as puff duration of conventional cigarettes. Puff duration is causally related to the nicotine content of the e-cigarette aerosol (i.e., the yield or dose) [16]. Thus, a JUUL pod, which contains more than 41mg of nicotine can deliver at least 20mg to the user. While the average pack of conventional cigarettes contains 204mg of nicotine, only about 10% gets inhaled (~20mg total). Thus, some e-cigarettes and ENDS deliver as much nicotine as cigarettes. Given that the primary ingredient in ENDS (so far) is nicotine, and that considerable data already exist demonstrating negative health effects of nicotine, we can assume that regardless of mode of delivery, nicotine will have negative health consequences for youth especially as some e-cigarettes can deliver sufficient nicotine to reach plasma levels comparable to or higher that conventional cigarettes [23, 24]. In fact, the physiological effects of nicotine, whether delivered by conventional cigarettes or vaping, is similar [25]. Thus, at present, a primary concern of health officials regarding e-cigarettes use in adolescence and young is the presence of nicotine.

Nicotine and Youth Addiction Behaviors

Nicotine is the key chemical ingredient that causes and sustains the addicting effects of tobacco products and is the primary ingredient in most e-cigarette solutions. Young people are more sensitive to nicotine than adults and can become dependent on nicotine much faster than adults [26] Preventing Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General (nih.gov) 2016, Surgeon General's Report: E-Cigarette Use Among Youth and Young Adults | CDC. In three independent populations of European origins, early nicotine exposure (younger than 16 years of age), is mechanistically linked to genes associated with the severity of nicotine addiction, and subsequent adult nicotine addiction [27]. The ability of e-cigarettes raises concerns about e-cigarette use generating nicotine dependence among young people [28] [29, 30]. The reported blood levels achieved with e-cigarettes likely cause physiological changes to nicotinic acetylcholine receptors in the brain that sustain nicotine addiction in youth [31, 32]. This is particularly concerning for youth and young adults, as early exposure to nicotine increases the severity of future nicotine dependence [30] The Health Consequences of Smoking - 50 Years of Progress: A Report of the Surgeon General (nih.gov).

Animal studies using rodent models demonstrate that the nicotinic acetylcholine receptor pathway is still actively changing during adolescence, with higher expression and functional activity in the forebrain of adolescent rodents compared to adult rodents [33-37]. Rats and mice are among the most commonly used animal models in behavioral neuroscience research. They are well-suited model organisms, as they display a variety of behaviors that are relevant to human behavior and disease. Both perform well in many of the standard neuropharmacalogical tasks, and their size makes it easier to perform more invasive procedures. Mice, and more recently rats, also are amiable to genetic manipulation, an essential tool in neuroscience research, allowing scientists to

investigate the impact of individual genes on development and behavior. Relative to this report, reward-seeking is an easy behavioral measure in rats and this behavior is enhanced by nicotine. Importantly, nicotine enhances the neuronal activity in reward-seeking regions of the rat brain and does so more robustly in adolescent rats than in adults [38-45]. An increased sensitivity to nicotine in the reward-seeking pathways of adolescent rat brains is associated with enhanced behavioral responses for continued administration of nicotine, rats seek out solutions with nicotine. Enhanced nicotine addiction in adolescent rodents compared to adults is supported by considerable behavioral research and highlights the likelihood that human adolescents are particularly vulnerable to developing dependency to and continuing to use nicotine containing e-cigarettes or advance to more conventional cigarettes [46].

Nicotine enhancement of neuronal activity in reward-related regions of the adolescent rat brain also is associated with increased drug-seeking behaviors in general [31, 47] and has been termed "The Gateway Effect" or "Gateway Hypothesis". Multiple studies of adolescent rodents demonstrate that nicotine exposure in adolescence increases the reinforcing effects of other drugs of abuse, including cocaine, methamphetamine, and alcohol, without having a major impact on responding to other rewards (food, play) [44, 48-50]. These studies showed that exposure to even low doses of nicotine for a few days during early adolescence, but not late adolescence or adulthood, increased self-administration of other abused drugs [44, 48, 51-54]. These behavioral changes were associated with alterations in dopamine receptors in regions of the brain known to control impulse behaviors suggesting nicotine exposure during adolescence induces persistent neuronal remodeling of reward-processing centers and potentially enhances the addictive effects of drugs of abuse.

Epidemiological studies of human adolescents suggest use of nicotine in general during high school is a good predictor of current or future drug abuse [54-56]. A recent survey of high school students demonstrated that of the 1 out of 10 (10%) that had vaped cannabis in the last 30 days, a significant majority also used e-cigarettes [57]. The association between drug use and e-cigarettes was stronger than that with other forms of nicotine exposure (chewing, pipe, smoking). This association may be related to the similarity and ease of the delivery mode for both cannabis and nicotine solutions via vaping.

Aerosolized Nicotine and Cardiovascular/Pulmonary Function

Acute administration of nicotine elicits a variety of well-characterized, dose- and route-dependent physiological effects in adults, including alterations in cardiovascular functions, such as increasing heart rate and blood pressure (BP) causing greater cardiac output which leads to an increase in myocardial oxygen demand [58, 59]. Decades of research with cellular models or animal studies has established the biologic underpinnings of nicotine induced physiological changes in both cardiac and vascular tissues and cells [60-63]. Vaping and e-cigarette use elicit similar cardiovascular changes (for review, [64] [65-68] suggesting vaping will elicit similar long-term nicotine mediated morbidity and mortality as other forms of nicotine delivery. A cross sectional study of smokers, non-smokers and sole e-cigarette users demonstrated that vascular stiffness, due to reduced nitric oxide (vasodilator) production was similar for smokers and e-cigarette users [69, 70]. Vascular stiffness is a hallmark of hypertension. Nicotine also induced the production of various inflammatory mediators implicated in the atherosclerotic pathway [66, 71], and at the cellular level, nicotine induces C-reactive protein ((CRP) a marker for inflammation) expression in macrophages that contribute to pro-inflammatory and pro-atherosclerotic effects [72]. Thus,

nicotine, regardless of the mode of delivery is likely to lead to increased blood pressure and future atherosclerotic manifestations in adult and future adults of youth users.

Aerosolized nicotine also elicits detrimental respiratory changes and potential lung damage. Although e-cigarettes do not require inhalation of the combustible product of traditional cigarettes, the aerosolized vapor of e-cigarettes containing nicotine elicited similar respiratory mechanical changes (increased resistance) and increased inflammatory markers in both human and animal studies [73-77]. While findings of increased lung mechanical resistance [78] in e-cigarette users is equivocal, due possibly to different study populations (health vs asthmatic), a common and verified finding is cytokine-dependent lung inflammation due either to the nicotine directly or the solvents present in all nicotine solutions used in e-cigarettes and vaping devices [73, 74]. Nicotine solvents are discussed later.

Long-term population studies, beginning in adolescence, of the detrimental effects of inhalation of nicotine (and solvents) without the combustion products of conventional cigarettes have not been conducted. E-cigarette use is a more recent phenomenon without the decades of research that accompanied conventional cigarette use. However, to date, when e-cigarettes induce a measurable increase in plasma nicotine concentration, they also induce physiological effects similar to conventional cigarettes [79-85] suggesting some of the long-term outcomes of nicotine exposure may well be similar and detrimental.

Nicotine and Brain Development and Cognition in Youth

Brain Development:

There exists considerable scientific evidence to suggest nicotine negatively influences both adolescent and prenatal brain development (for review, USDHHS 2014 <u>The Health Consequences of Smoking - 50 Years of Progress: A Report of the Surgeon General (nih.gov)</u>. While there exists limited direct human experimental data regarding the effects of nicotine exposure on the developing adolescent brain, there exists considerable data using animal models that are relevant to human impact and responses [86]. Animal studies offer significant advantages compared to human studies due to better control for confounding factors, and the ability to limit nicotine exposure to differing levels of physical and neural development. Such studies are pivotal for understanding the neural substrates associated with adolescence and nicotine. Using a variety of study designs and research paradigms, research in this area provides convincing evidence for a neuroteratogenic and neurotoxic role of nicotine in the developing adolescent brain [87-89].

The brain is not fully developed at birth and undergoes significant neurobiological development during adolescence and young adulthood, which are critical periods of sensitivity to neurobiological insults [90-95]. Although maturation occurs in different regions of the brain at different rates, a similar process occurs in all areas characterized by the rapid formation of synaptic connections in early childhood, followed by a loss of redundant or unnecessary synapses (called pruning) and the formation of myelin, the fatty sheath that covers and insulates neurons. Myelin allows nerve cells to transmit information faster thus providing for more complex brain processes. Pruning allows for more focused concentration. Both pruning and myelination are important for efficient cognitive processing. The human brain continues to change (plasticity) and adapt throughout life, not only because of normal neural growth and development but also because of changes in environmental neurobiological exposures such as injuries, behaviors, thinking, emotions, and mind-altering drugs such as nicotine [96].

Across species, including humans, adolescence is a key period of increased plasticity and rapid growth of brain circuits that regulate social, emotional, and motivational processes and decision making. During adolescence and into young adulthood, myelination occurs rapidly in the frontal lobe. The prefrontal cortex, which is involved in higher level regulatory control of complex behaviors (executive functioning, planning, reasoning, decision-making skills, self-discipline, and impulse control) continues normal structural and functional development well into young adulthood, to about 25 years of age [97-101]. Because of the immaturity and rapid growth of the prefrontal cortex, adolescents and young adults normally exhibit moody, risk-taking, and unpredictable impulsive behaviors [102-106]. Brain development in juvenile rodents displays patterns that resemble those of human beings, making the rodent model relevant to studying the neurobiological underpinnings of brain maturation in teenagers[107].

Attention and Cognition:

Both cognitive improvements and cognitive deficits have been reported after nicotine exposure in healthy human adults, while smoking during adolescence impairs cognition and attention processes [108-111]. Results of a twin study from the Netherlands Twin Registry indicated a larger increase in attention problems from adolescence to adulthood in twins who smoked compared to their never-smoking co-twins [112]. In another study, adolescent smokers were found to have chronic impairments in the accuracy of their working memory (e.g., in processing information from two sensory modalities simultaneously), which were more severe with an earlier age of onset of smoking [113]. Thus, longitudinal studies in humans provide support for the hypothesis that adolescent use of conventional cigarettes has both acute and long-term effects on attention and memory and appears to be worse when smoking is initiated at a younger age. Although in these studies of nicotine exposure in humans, nicotine cannot be cited as the sole cause of cognitive defects, animal studies have shown that nicotine exposure in adolescent rats induces lasting synaptic changes in the prefrontal cortical regions critical for normal attention, memory, and cognition that likely underlie observed impairments in attentional and cognitive function [114]. In addition, adolescent, but not post-adolescent, rats treated with nicotine demonstrated diminished attention span and enhanced impulsivity in adulthood [115, 116]. The biological causes of these cognitive disturbances (reduced attention span and impulse control) were associated with reduced regulation of synaptic metabotropic glutamate receptor 2 (mGluR2) in the prefrontal cortex [115, 117, 118]. These rodent studies have implications for human adolescents and suggest that exposure to nicotine during youth may lead to long-lasting changes in behavioral and neuronal plasticity into adulthood.

Anxiety and mood disorders:

A meta-analysis showed consistent evidence that both tobacco use and dependence on tobacco products among adolescents increased their risk for anxiety disorders [119]. Other studies demonstrate that early onset of smoking is associated with a shorter time to first onset of an anxiety disorder [120], and there is a positive association between adolescent smoking, particularly through a nicotine pathway, and anxiety in early adulthood [121]. Relationships between adolescent smoking and disruptive disorders (e.g., ADHD; oppositional defiant disorder [ODD] [122] as well as depression [123] also have been reported, while a longitudinal birth cohort found evidence to support a causal relationship between teen smoking and onset of depression [124]. Although these findings are complex and warrant further study using comparisons of genetic polymorphisms associated with smoking or twin and sibling studies [125, 126], they do suggest that nicotine exposure during adolescence could contribute to long-term mental health disorders.

Findings from animal studies support the theory that adolescent nicotine exposure results in long-term alterations in emotional response, specifically enhanced anxiety and fear [127, 128], and in persistent alterations in serotonin systems involved in mediating mood disorders by reprogramming the systems response to nicotine [129]. Even a single day of nicotine treatment in adolescent rats can enhance sensitivity to aversive stimuli later in life and result in a depression-like state in adulthood that is normalized by treatment with nicotine or antidepressants [130]. In summary, given the existing evidence from human and animal studies of the detrimental impact of nicotine exposure on adolescent brain development, the use of nicotine-containing e-cigarettes by youth should be of concern. Both preadolescence and adolescence are developmental periods associated with increased vulnerability to nicotine addiction, and exposure to nicotine during these periods may lead to long-lasting changes in behavioral responses and neuronal plasticity.

Negative Health Effects of Other Ingredients Present in e-Cigarette Solutions

The nicotine used in e-liquids is extracted from tobacco leaf. The extraction process may produce some potentially harmful **tobacco-specific impurities**, including minor alkaloids like nornicotine, anatabine, anabasine, myosmine, cotinine, nicotine-N-oxides (cis and trans isomers), β -nicotyrine, and β -nornicotyrine [131-136]. The correlation between nicotine and the concentrations of minor alkaloids is much stronger in conventional tobacco products [137] than in e-cigarettes [135]. Nonetheless, these alkaloids are present in ENDS solutions and occur at differing concentrations most likely due to poor quality control of e-liquid products during manufacturing and purification [135]. The long-term impact of these alkaloids is unclear.

Propylene glycol (PG) and/or glycerin (VG) are the primary nicotine solvents used in ENDS. Upon heating, PG and VG vaporize to create the nicotine aerosol. PG and CG also decompose under heat to form carbonyl compounds such as the carcinogens formaldehyde and acetaldehyde and the toxic compound, acrolein. The amount of carbonyl carcinogens increases with increasing heat, due to increased device voltage [138-141]. In some devices the temperature near the central coil can reach or exceed 350°C essentially ensuring chemical conversion of PG and VG to harmful levels of carcinogens [142]. Acrolein is a known respiratory and ocular irritant and in animal models plays a role in cancer formation [143-145], production of proinflammatory cytokines [146], development of COPD [147], and progression of atherosclerosis and cardiovascular disease [148-153]. It is unclear if this extreme heat results in production of other harmful compounds since it is not always clear what other components exist in e-cigarette solvents which is for the most part, unregulated.

Negative health effects of **other ingredients** present in vaping solutions are highly probable as many are known lung irritants, immunological activators or carcinogens. Most of these studies have been conducted in animal models or in vitro conditions. In addition, many ENDS, specifically tank models, contain flavorings, which although safe to ingest, have not been studied as aerosols and upon heating have been shown to form significantly dangerous compounds that evoke immune responses and damage lung tissue[154]. Some flavorings also decompose to bioactive drugs [155] and others are estrogenic, potentially altering developmental changes during puberty [156]. Further, package labeling of "other" compounds or ingredients is not required or complete and some flavoring chemicals can reach or exceed 1% by weight in e-cigarettes [157]. Extracts of flavored

vapor solvents lacking nicotine were shown to be cytotoxic on mouse neuronal stem cells and human embryonic stem cells [158]. A partial list of identified, non-nicotine, components found in ENDS solutions is provided below.

Compounds Found in Vapor Solutions	Potential or Known Impact on Health	
Cinnamon-related chemicals (CAD, 2-	Cytotoxic [154], CAD has been used as chemotherapeutic	
methoxycinnalamdehyde) (flavorings)	[159], and insecticide [160, 161]	
Diacetyl (buttery flavoring)	Decline in respiratory function or obstructive lung disease when inhaled [162, 163]	
Acetyl propionyl (flavoring)	Structurally related to diacetyl and inhalation causes airway epithelial damage similar to diacetyl [164]	
Tobacco specific nitrosamines (tobacco nicotine extraction process)	Potent human carcinogens [132, 165, 166]	
Amino-tadalafil (contaminant?)	Tadalafil is active ingredient in Cialis [155]	
Rimonabant (contaminant?)	Weight loss drug removed from the market [155]	
Diethyl phthalate (contaminant?) Solvent used	Estrogenic and antiandrogenic ([136]	
in cosmetics, plastics production and aerosol		
sprays		
Diethylhexyl phthalate (contaminant?) Plasticizer for PVC manufacturing	Estrogenic and antiandrogenic, carcinogenic (IARC) [136]	
Heavy metals (tin, lead, nickel, cadmium)	Heavy metals are known to cause respiratory distress and	
(contaminants from the device due to the	disease [167-170]	
heating mechanism or poor-quality control)		
Vitamin E acetate	Lung damage, death [20, 171]	
Gamma-butyrolactone (Juul liquid pods)	Industrial solvent used recreationally as a CNS depressant.	
	DEA regulated drug [172]	

Effects of ENDS/E-cigarette Use on Oral Health

There is growing evidence from dental research to suggest ENDS vapors cause gum and tissue damages (for review, [173-178]. The formaldehyde that forms in e-cigarette aerosols following the heating of the solvent propylene glycol, is both a gum irritant and carcinogen [179] as are many of the nicotine extraction byproducts [180]. E-cigarette flavorings used in the cartridges induce production of proinflammatory markers and pro-senescence markers in human gingival epithelium and periodontal fibroblasts [181]. The vapors have also been shown to alter the microbiome of the oral cavity [182], change the antibacterial properties of saliva [183] and increase expression of the cisplatin transporter thereby making oral cancer cells more resistant to drug treatment [184]. These changes are highly likely to increase the incidence of gum disease [185] and lead to increases in oral as well as head and neck cancers [186, 187]. Importantly, the impact of e-cigarettes vapors on oral health are worsened by the amount of constituents present, which is directly related to the voltage applied [188] making 3rd and 4th generation e-cigarettes more harmful. Dentists and oral health professionals are in a unique position to try and stem the rise of e-cigarette use among their clients due to its direct effect on the oral cavity [189, 190].

Second-Hand Exposure To Vaping Aerosol

Covid and Other Airborne Illnesses

In response to COVID-19 and the possible association between smoking and illness severity in adults [191, 192] as well as the spread of COVID due to tobacco user behaviors (spitting, exhaling vapors and smoke near others) some countries have banned tobacco sales (notably India and South Africa) [193]or attempted to reduce tobacco and specifically smokeless tobacco use. It is estimated that only 20% of the e-cigarette vapor is actually inhaled with the remaining 80% carried out into the immediate environment. Smoking, spitting of tobacco, vaping, and waterpipe use are likely to increase virus transmission through direct transmission or by generating respiratory or aerosolized droplets (WHO/Europe | Coronavirus disease (COVID-19) outbreak - Resources for tobacco use control as part of COVID-19 response). Thus, youth use of ENDS in bathrooms, classrooms in social situations poses increased risk to other students and staff for viral exposure. A recent study from Stanford University Medical School suggests teens who vape were 5-7 times more likely to get infected with the coronavirus that causes Covid-19 [194]. There could be several reasons for vapers' heightened transmission risk. E-cigarettes can damage lungs and alter the immune system, making each coronavirus exposure more likely to trigger an infection, or the aerosol emitted from e-cigarettes have droplets containing coronavirus. Teens who smoke or use e-cigarettes also are more likely to get seriously ill with COVID-19 although the exact medical/physiological link is unclear [195, 196]. Students are also known to share ENDS and vaping always requires removing the mask. Thus, both smoking and ENDS increases risk of infection and illness in youth users.

ENDS and Youth Safety Issues

The components of ENDS, batteries and heating elements, have potential safety issues that may be more prevalent in young users who are 1) likely to seek less expensive and potentially counterfeit products and 2) less willing or able to recognize certified safety labeling of products. There are conditions under which batteries can short circuit or the battery chemistry can change, causing the ENDS batteries to overheat and vent or explode, potentially causing scalds, flame or contact burns, chemical burns, or blast injuries to the user [197, 198] (US Fire Administration New Report on E-Cig Vape Battery Safety - Levin Simes Abrams). Although sever injury to the face or hands has been reported [199, 200], a recent FDA funded study using data from the National Electronic Injury Surveillance System indicates that of the estimated 1007 injuries in a single year (2016), 80% were thermal injuries, and 77% of these injuries occurred to the upper leg or lower trunk, presumably when the device was located in a pocket. Thus the majority of injuries could potentially be prevented through improved battery design requirements, and/or better battery testing standards. From 2015-2019 there were 3369 e-cigarette related I juries reported to US emergency hospitals suggesting the number of injuries is not declining with improved device manufacturing [201, 202]

When considering the safety and testing standards of electronic products such as ENDS, it is relevant to discuss the manufacturing source for ENDS. Until recently (last 4-5 years), all ENDS were manufactured in the same industrial park in Shenzhen, China. There are reportedly over 600 factories producing ENDS, but only a dozen or so advertise UL Certification of their product (all US products are UL Certified). UL LLC, or Underwriters Laboratories, is a global safety certification company with offices in 46 countries that participates in the safety analysis of new technologies.

A search of the UL website indeed demonstrates that components of vaping devices can and have been UL Certified (<u>E-Cig and Vape Battery and Electrical Certification | UL</u>), specifically the batteries and charging devices. The following statement appears on the UL website regarding vaping devices.

"Both electronic cigarettes (e-cigs) and similar vaping devices, often called vap mods, use a rechargeable battery system to power the rapid heating of manufactured consumables. Customized heating elements instantly convert the compatible consumable into a vapor or atomized mist state for inhalation via the user's mouth. Unfortunately, a number of potential failure scenarios including poor mechanical ecig/vape device design, incompatible battery management system design, operator misuse, or environmental exposures can trigger catastrophic battery failure resulting in fire or explosion. Serious injuries and death have been reported."

Of the dozen or so Chinese manufacturers that have sought UL Certification, the certification is for a specific product and not every device manufactured by the company may be certified. The first company to seek UL certification was Joyetech, a global ENDS producer, as recently as October of 2018. Thus, most studies and reports of thermal injuries represent non-certified devices and prompted some ENDS manufacturers in China to seek UL certification. ENDS manufactures publicize their UL certification on their website and actively warn consumers against use of counterfeit devices. Counterfeit devices are made to look like the product of a major company and may even exhibit a fake UL certification. However, counterfeit devises are produced more cheaply with inferior batteries and are known to use lower grade metals for their heating coils. Thus, users are potentially exposed to toxic metals in the vapor as well as possible thermal injuries from unstable batteries if they use counterfeit ENDS.

Counterfeiting in the ENDS market potentially represents a billion dollars a year and includes both ENDS devices and cartridges containing liquid product. The most notable occurrence of unregulated and counterfeit vaping solutions occurred in 2018-2020 involving cannabinoid solutions containing Vitamin E acetate [20]. These solutions resulted in severe lung damage (EVALI, e-cigarette or vaping use-associated lung injury) requiring hospitalization of more than 2800 users, mostly youth or young adults, and the death of 68 (2% mortality) as of February 2020. Like many other additives in e-cigarettes, vitamin E acetate may be fine to use externally on your skin and appropriate for oral ingestion but can cause massive destruction of lung tissue when inhaled [171]. Given how easy it is to add ingredients to the tank solution, this will likely not be the last incident of EVALI.

A quick internet search of "counterfeit e-cigarettes" yielded pages of law enforcement reports or lawsuits concerning counterfeit ENDS. Recommendations for identifying counterfeit ENDS include: 1) Price. If it is cheap, it is likely counterfeit. 2) Poor packaging. Most major produces are using high quality, exquisite packaging that corresponds to the product price. 3) Product quality. If parts are loose, scratched or dented, you have a fake. 4) Serial number or Authenticity Code verification. Manufactures have begun etching serial numbers on devices or under package scratchoff sites that can be verified on their website.

Unfortunately, youth are likely active users of and a target for counterfeit ENDS. Youth are more likely to seek less expensive products. They are more likely to buy from online sellers or from friends of friends through pyramid schemes. They are less likely to look for UL codes or authentication codes and even if they find the device to be counterfeit, there is little recourse as devices cannot be returned. Thus, coupled with increased risk seeking or less risk-avoidance behavior, youth are more likely to keep and use a counterfeit device putting themselves in harm's way for possible thermal burns, oral injuries, and health effects associated with inhalation of potentially toxic metals from inferior heating coils.

References

- 1. George J, Hussain M, Vadiveloo T, Ireland S, Hopkinson P, Struthers AD, Donnan PT, Khan F, Lang CC: Cardiovascular Effects of
- Switching From Tobacco Cigarettes to Electronic Cigarettes. Journal of the American College of Cardiology 2019, **74**(25):3112-3120.
- East KA, Hitchman SC, McNeill A, Thrasher JF, Hammond D: Social norms towards smoking and vaping and associations with product use among youth in England, Canada, and the US. Drug & Alcohol Dependence 2019, 205:107635.
- 3. Keamy-Minor E, McQuoid J, Ling PM: Young adult perceptions of JUUL and other pod electronic cigarette devices in California: a qualitative study. 2019.
- 4. Tsai J, Walton K, Coleman BN, Sharapova SR, Johnson SE, Kennedy SM, Caraballo RS: **Reasons for Electronic Cigarette Use Among Middle and High School Students -National Youth Tobacco Survey, United States, 2016**. *Mmwr-Morbidity and Mortality Weekly Report* 2018, **67**(6):196-200.
- Struik LL, Dow-Fleisner S, Belliveau
 M, Thompson D, Janke R: Tactics for
 Drawing Youth to Vaping: Content

CBP, FDA Seize Counterfeit, Unauthorized E-Cigarettes

www.fda.gov > news-events > press-announcements > c...

Jan 13, 2021 — CBP's trade **enforcement** mission places a significant emphasis on intercepting illicit products that could harm American consumers. In fiscal year 2020, CBP seized 93,590 units of **ecigarettes** that did not meet U.S. federal **regulations**. In July 2020, the FDA issued a warning letter to Cool Clouds Distribution Inc.

Police Seize More Than 33K Counterfeit E-Cigarettes

www.cspdailynews.com > tobacco > police-seize-more-...

Jan 15, 2021 — U.S. Customs and Border **Police** (CBP) officers seized 33681 **counterfeit e-cigarette** units resembling the Puff Bar brand.

<u>CBP Officers in Chicago Capture \$1.5 Million in</u> <u>Counterfeit Vaping Pens | U.S. Customs and Border</u> <u>Protection</u>

March 11, 2021. **CHICAGO–**U.S. Customs and Border Protections officers at Chicago O'Hare's International Mail Branch seized more than 77,000 Rick and Morty Vape Pens on March 9. The shipment, originating from Shenzhen, China, was heading to a distribution company in Georgia.

FDA Seizes \$720,000 of Counterfeit and Unauthorised Vapes • VAPE HK

US Customs and Border Protection (CBP), in conjunction with the FDA, have recently seized a shipment of over 33,000 counterfeit and unauthorized e-cigarettes while in transit from China to Texas.

Analysis of Electronic Cigarette Advertisements. *Journal of Medical Internet Research* 2020, **22**(8):e18943.

- 6. Hammond D, Reid JL, Burkhalter R, Rynard VL: E-cigarette Marketing Regulations and Youth Vaping: Cross-Sectional Surveys, 2017-2019. *Pediatrics* 2020, 146(1):07.
- Gilley M, Beno S: Vaping implications for children and youth. Current Opinion in Pediatrics 2020, 32(3):343-348.
- 8. Cwalina SN, Braymiller JL, Leventhal AM, Unger JB, McConnell R, Barrington-Trimis JL: **Prevalence** of Young Adult Vaping, Substance Vaped, and Purchase Location Across 5 Categories of Vaping Devices. *Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco* 2020.
- 9. Green MJ, Gray L, Sweeting H: Youth vaping and smoking and parental vaping: a panel survey. BMC Public Health 2020, **20**(1):1111.
- 10. Greenhill R, Dawkins L, Notley C, Finn MD, Turner JJD: Adolescent Awareness and Use of Electronic Cigarettes: A Review of Emerging Trends and Findings. *Journal of Adolescent Health* 2016, **59**(6):612-619.
- 11. Cobb NK, Brookover J, Cobb CO: Forensic analysis of online marketing for electronic nicotine delivery systems. *Tobacco Control* 2015, **24**(2):128-131.
- 12. Peace MR, Baird TR, Smith N, Wolf CE, Poklis JL, Poklis A: **Concentration of Nicotine and Glycols in 27 Electronic Cigarette Formulations**. *Journal of Analytical Toxicology* 2016, **40**(6):403-407.
- 13. Peace MR, Mulder HA, Baird TR, Butler KE, Friedrich AK, Stone JW, Turner JBM, Poklis A, Poklis JL: **Evaluation of Nicotine and the Components of e-Liquids Generated from e-Cigarette Aerosols**. *Journal of Analytical Toxicology* 2018, **42**(8):537-543.
- 14. Zhu S-H, Sun JY, Bonnevie E, Cummins SE, Gamst A, Yin L, Lee M: Four hundred and sixty brands of e-cigarettes and counting: implications for product regulation. *Tobacco Control* 2014, 23:3-9.
- 15. Varlet V, Farsalinos K, Augsburger M, Thomas A, Etter J-F: **Toxicity Assessment of Refill Liquids for Electronic Cigarettes**. *International Journal of Environmental Research and Public Health* 2015, **12**(5):4796-4815.
- 16. Talih S, Balhas Z, Eissenberg T, Salman R, Karaoghlanian N, El Hellani A, Baalbaki R, Saliba N, Shihadeh A: Effects of User Puff Topography, Device Voltage, and Liquid Nicotine Concentration on Electronic Cigarette Nicotine Yield: Measurements and Model Predictions. Nicotine & Tobacco Research 2015, 17(2):150-157.
- Talih S, Salman R, El-Hage R, Karam E, Karaoghlanian N, El-Hellani A, Saliba N, Shihadeh A: Characteristics and toxicant emissions of JUUL electronic cigarettes. *Tobacco Control* 2019, 28(6):678-680.
- Talih S, Salman R, El-Hage R, Karam E, Salam S, Karaoghlanian N, El-Hellani A, Saliba N, Shihadeh A: A comparison of the electrical characteristics, liquid composition, and toxicant emissions of JUUL USA and JUUL UK e-cigarettes. *Scientific Reports* 2020, 10(1).
- 19. Talih S, Salman R, Soule E, El-Hage R, Karam E, Karaoghlanian N, El-Hellani A, Saliba N, Shihadeh A: Electrical features, liquid composition and toxicant emissions from 'pod-mod'-like disposable electronic cigarettes. *Tobacco control* 2021.
- 20. Blount BC, Karwowski MP, Shields PG, Morel-Espinosa M, Valentin-Blasini L, Gardner M, Braselton M, Brosius CR, Caron KT, Chambers D *et al*: **Vitamin E Acetate in Bronchoalveolar-Lavage Fluid** Associated with EVALI. *The New England journal of medicine* 2020, **382**(8):697-705.
- 21. Farsalinos KE, Romagna G, Tsiapras D, Kyrzopoulos S, Voudris V: **Evaluating nicotine levels** selection and patterns of electronic cigarette use in a group of "vapers" who had achieved complete substitution of smoking. *Substance abuse : research and treatment* 2013, **7**:139-146.
- Farsalinos KE, Spyrou A, Stefopoulos C, Tsimopoulou K, Kourkoveli P, Tsiapras D, Kyrzopoulos S, Poulas K, Voudris V: Nicotine absorption from electronic cigarette use: comparison between experienced consumers (vapers) and naive users (smokers) (vol 5, 11269, 2015). Scientific Reports 2015, 5.

- 23. Spindle TR, Breland AB, Karaoghlanian NV, Shihadeh AL, Eissenberg T: **Preliminary Results of an Examination of Electronic Cigarette User Puff Topography: The Effect of a Mouthpiece-Based Topography Measurement Device on Plasma Nicotine and Subjective Effects**. *Nicotine & Tobacco Research* 2015, **17**(2):142-149.
- 24. Lopez AA, Hiler MM, Soule EK, Ramoa CP, Karaoghlanian NV, Lipato T, Breland AB, Shihadeh AL, Eissenberg T: Effects of Electronic Cigarette Liquid Nicotine Concentration on Plasma Nicotine and Puff Topography in Tobacco Cigarette Smokers: A Preliminary Report. *Nicotine & Tobacco Research* 2016, **18**(5):720-723.
- 25. Tsai M, Byun MK, Shin J, Crotty Alexander LE: **Effects of e-cigarettes and vaping devices on cardiac and pulmonary physiology**. *Journal of Physiology* 2020, **598**(22):5039-5062.
- 26. Colby SM, Tiffany ST, Shiffman S, Niaura RS: **Are adolescent smokers dependent on nicotine? A review of the evidence**. *Drug and alcohol dependence* 2000, **59 Suppl 1**:S83-95.
- 27. Weiss RB, Baker TB, Cannon DS, von Niederhausern A, Dunn DM, Matsunami N, Singh NA, Baird L, Coon H, McMahon WM *et al*: A Candidate Gene Approach Identifies the CHRNA5-A3-B4 Region as a Risk Factor for Age-Dependent Nicotine Addiction. *Plos Genetics* 2008, **4**(7).
- 28. Dawkins L, Munafo M, Christoforou G, Olumegbon N, Soar K: **The Effects of E-Cigarette Visual Appearance on Craving and Withdrawal Symptoms in Abstinent Smokers**. *Psychology of Addictive Behaviors* 2016, **30**(1):101-105.
- 29. Etter J-F: Characteristics of users and usage of different types of electronic cigarettes: findings from an online survey. *Addiction* 2016, **111**(4):724-733.
- St Helen G, Ross KC, Dempsey DA, Havel CM, Jacob P, 3rd, Benowitz NL: Nicotine Delivery and Vaping Behavior During ad Libitum E-cigarette Access. *Tobacco regulatory science* 2016, 2(4):363-376.
- 31. Kandel DB, Kandel ER: A Molecular Basis for Nicotine as a Gateway Drug REPLY. New England Journal of Medicine 2014, **371**(21):2038-2039.
- 32. Yuan M, Cross SJ, Loughlin SE, Leslie FM: Nicotine and the adolescent brain. *Journal of Physiology* 2015, **593**(16):3397-3412.
- 33. Britton AF, Vann RE, Robinson SE: **Perinatal nicotine exposure eliminates peak in nicotinic acetylcholine receptor response in adolescent rats**. *Journal of Pharmacology and Experimental Therapeutics* 2007, **320**(2):871-876.
- 34. Kota D, Martin BR, Robinson SE, Damaj MI: **Nicotine dependence and reward differ between** adolescent and adult male mice. *Journal of Pharmacology and Experimental Therapeutics* 2007, 322(1):399-407.
- 35. Doura MB, Gold AB, Keller AB, Perry DC: Adult and periadolescent rats differ in expression of nicotinic cholinergic receptor subtypes and in the response of these subtypes to chronic nicotine exposure. *Brain Research* 2008, **1215**:40-52.
- 36. Doura MB, Lee NH, Perry DC: Chronic nicotine exposure differentially alters gene expression in VTA from adolescent and adult rats. *Biochemical Pharmacology* 2009, **78**(7):914-915.
- 37. Doura MB, Luu TV, Lee NH, Perry DC: **PERSISTENT GENE EXPRESSION CHANGES IN VENTRAL TEGMENTAL AREA OF ADOLESCENT BUT NOT ADULT RATS IN RESPONSE TO CHRONIC NICOTINE**. *Neuroscience* 2010, **170**(2):503-513.
- 38. Schochet TL, Kelley AE, Landry CF: **Differential behavioral effects of nicotine exposure in** adolescent and adult rats. *Psychopharmacology* 2004, **175**(3):265-273.
- 39. Schochet TL, Kelley AE, Landry CF: **Differential expression of arc mRNA and other plasticity**related genes induced by nicotine in adolescent rat forebrain. *Neuroscience* 2005, **135**(1):285-297.
- 40. Schochet TL, Landry C, Kelley AE: **Differential contextual conditioning to nicotine in adolescent versus adult rats**. *Society for Neuroscience Abstracts* 2001, **27**(1):595-595.
- 41. Shram MJ, Funk D, Li Z, Le AD: **Periadolescent and adult rats respond differently in tests measuring the rewarding and aversive effects of nicotine**. *Psychopharmacology* 2006, **186**(2):201-208.

- 42. Shram MJ, Le AD: Adolescent male Wistar rats are more responsive than adult rats to the conditioned rewarding effects of intravenously administered nicotine in the place conditioning procedure. *Behavioural Brain Research* 2010, **206**(2):240-244.
- 43. Shram MJ, Li Z, Le AD: Age differences in the spontaneous acquisition of nicotine selfadministration in male wistar and long-evans rats. *Psychopharmacology* 2008, **197**(1):45-58.
- 44. Dao JM, McQuown SC, Loughlin SE, Belluzzi JD, Leslie FM: Nicotine Alters Limbic Function in Adolescent Rat by a 5-HT1A Receptor Mechanism. *Neuropsychopharmacology* 2011, 36(7):1319-1331.
- 45. Dao JM, Soria AM, Tran A-HT, Leslie FM: Age-Related Neural Changes After Brief Exposure to Nicotine. *Faseb Journal* 2009, 23.
- 46. Owotomo O, Stritzel H, McCabe SE, Boyd CJ, Maslowsky J: **Smoking Intention and Progression From E-Cigarette Use to Cigarette Smoking**. *Pediatrics* 2020, **146**(6).
- 47. Owotomo O, Maslowsky J: Association between e-cigarette and marijuana use in a national sample of 8th and 10th grade never-smokers of conventional cigarettes, 2014-2015. *Pediatrics* 2018, 142.
- 48. McQuown SC, Belluzzi JD, Leslie FM: Low-dose nicotine treatment during adolescence increases subsequent cocaine reward. *Faseb Journal* 2007, **21**(6):A781-A781.
- 49. Dickson PE, Miller MM, Rogers TD, Blaha CD, Mittleman G: Effects of adolescent nicotine exposure and withdrawal on intravenous cocaine self-administration during adulthood in male C57BL/6J mice. Addiction Biology 2014, **19**(1):37-48.
- 50. Pipkin JA, Kaplan GJ, Plant CP, Eaton SE, Gil SM, Zayala AR, Crawford CA: **Nicotine exposure beginning in adolescence enhances the acquisition of methamphetamine self-administration, but not methamphetamine-primed reinstatement in male rats**. *Drug and Alcohol Dependence* 2014, **142**:341-344.
- 51. McQuown SC, Dao JM, Belluzzi JD, Leslie FM: Age-dependent effects of low-dose nicotine treatment on cocaine-induced behavioral plasticity in rats. *Psychopharmacology* 2009, 207(1):143-152.
- 52. Mojica CY, Belluzzi JD, Leslie FM: **Age-dependent alterations in reward-seeking behavior after brief nicotine exposure**. *Psychopharmacology* 2014, **231**(8):1763-1773.
- 53. Mojica CY, Dao JM, Yuan M, Loughlin SE, Leslie FM: **Nicotine modulation of adolescent dopamine** receptor signaling and hypothalamic peptide response. *Neuropharmacology* 2014, **77**:285-293.
- 54. Boccio CM, Jackson DB: Adolescent nicotine and marijuana vaping activity and the use of other illicit substances. *Drug and Alcohol Dependence* 2021, **219**.
- 55. Lewinsohn PM, Rohde P, Brown RA: Level of current and past adolescent cigarette smoking as predictors of future substance use disorders in young adulthood. *Addiction* 1999, **94**(6):913-921.
- 56. Kirst M, Mecredy G, Borland T, Chaiton M: Predictors of Substance Use Among Young Adults Transitioning Away from High School: A Narrative Review. Substance Use & Misuse 2014, 49(13):1795-1807.
- 57. Kowitt SD, Osman A, Meernik C, Zarkin GA, Ranney LM, Martin J, Heck C, Goldstein AO: **Vaping** cannabis among adolescents: prevalence and associations with tobacco use from a crosssectional study in the USA. *BMJ open* 2019, **9**(6):e028535.
- 58. Price LR, Martinez J: Cardiovascular, carcinogenic and reproductive effects of nicotine exposure: A narrative review of the scientific literature. *F1000Research* 2019, **8**:1586.
- 59. Benowitz NL, Gourlay SG: **Cardiovascular toxicity of nicotine: implications for nicotine replacement therapy**. *Journal of the American College of Cardiology* 1997, **29**(7):1422-1431.
- 60. Espinoza-Derout J, Hasan KM, Shao XM, Jordan MC, Sims C, Lee DL, Sinha S, Simmons Z, Mtume N, Liu Y *et al*: **Chronic intermittent electronic cigarette exposure induces cardiac dysfunction and atherosclerosis in apolipoprotein-E knockout mice**. *American Journal of Physiology-Heart and Circulatory Physiology* 2019, **317**(2):H445-H459.

- 61. Sinha-Hikim I, Friedman TC, Falz M, Chalfant V, Hasan MK, Espinoza-Derout J, Lee DL, Sims C, Tran P, Mahata SK *et al*: **Nicotine plus a high-fat diet triggers cardiomyocyte apoptosis**. *Cell and Tissue Research* 2017, **368**(1):159-170.
- 62. Hanna ST: **Nicotine effect on cardiovascular system and ion channels**. *Journal of Cardiovascular Pharmacology* 2006, **47**(3):348-358.
- 63. Shao XM, Lopez B, Nathan D, Wilson J, Bankole E, Tumoyan H, Munoz A, Espinoza-Derout J, Hasan KM, Chang S *et al*: **A mouse model for chronic intermittent electronic cigarette exposure exhibits nicotine pharmacokinetics resembling human vapers**. *Journal of Neuroscience Methods* 2019, **326**.
- 64. Tsai M, Byun MK, Shin J, Alexander LEC: **Effects of e-cigarettes and vaping devices on cardiac and pulmonary physiology**. *Journal of Physiology-London* 2020, **598**(22):5039-5062.
- 65. Mayyas F, Aldawod H, Alzoubi KH, Khabour O, Shihadeh A, Eissenberg T: **Comparison of the** cardiac effects of electronic cigarette aerosol exposure with waterpipe and combustible cigarette smoke exposure in rats. *Life Sciences* 2020, **251**.
- 66. Chaumont M, de Becker B, Zaher W, Culie A, Deprez G, Melot C, Reye F, Van Antwerpen P, Delporte C, Debbas N *et al*: Differential Effects of E-Cigarette on Microvascular Endothelial Function, Arterial Stiffness and Oxidative Stress: A Randomized Crossover Trial. *Scientific Reports* 2018, 8.
- 67. Kerr DMI, Brooksbank KJM, Taylor RG, Pinel K, Rios FJ, Touyz RM, Delles C: Acute effects of electronic and tobacco cigarettes on vascular and respiratory function in healthy volunteers: a cross-over study. *Journal of Hypertension* 2019, **37**(1):154-166.
- Bessri M, Sultan AS, Magdy E, Hynes N, Sultan S: Nicotine e-vaping and cardiovascular consequences: a case series and literature review. European heart journal Case reports 2020, 4(6):1-7.
- 69. Fetterman JL, Keith RJ, Palmisano JN, McGlasson KL, Weisbrod RM, Majid S, Bastin R, Stathos MM, Stokes AC, Robertson RM *et al*: **Alterations in Vascular Function Associated With the Use of Combustible and Electronic Cigarettes**. *Journal of the American Heart Association* 2020, **9**(9).
- Antoniewicz L, Brynedal A, Hedman L, Lundback M, Bosson JA: Acute Effects of Electronic Cigarette Inhalation on the Vasculature and the Conducting Airways. Cardiovascular Toxicology 2019, 19(5):441-450.
- 71. Lau D, Baldus S: **Myeloperoxidase and its contributory role in inflammatory vascular disease**. *Pharmacology & Therapeutics* 2006, **111**(1):16-26.
- 72. Mao C, Li D, Zhou E, Zhang J, Wang C, Xue C: Nicotine exacerbates atherosclerosis through a macrophage-mediated endothelial injury pathway. *Aging-Us* 2021, **13**(5):7627-7643.
- 73. Khan N, Gong M, Sundar I, Rehan VK, Rahman I: E-Cigarette Vapor Containing Nicotine Induces Inflammatory Response and Dysregulated Repair Via Alpha 7 Nicotinic Acetylcholine Receptor in Mice Lung. American Journal of Respiratory and Critical Care Medicine 2019, 199.
- 74. Glynos C, Bibli S-I, Katsaounou P, Pavlidou A, Magkou C, Karavana V, Topouzis S, Kalomenidis I, Zakynthinos S, Papapetropoulos A: **Comparison of the effects of e-cigarette vapor with cigarette smoke on lung function and inflammation in mice**. *American Journal of Physiology-Lung Cellular and Molecular Physiology* 2018, **315**(5):L662-L672.
- 75. Garcia-Arcos I, Geraghty P, Baumlin N, Campos M, Dabo AJ, Jundi B, Cummins N, Eden E, Grosche A, Salathe M *et al*: **Chronic electronic cigarette exposure in mice induces features of COPD in a nicotine-dependent manner**. *Thorax* 2016, **71**(12):1119-1129.
- 76. Lappas AS, Tzortzi AS, Konstantinidi EM, Teloniatis SI, Tzavara CK, Gennimata SA, Koulouris NG, Behrakis PK: **Short-term respiratory effects of e-cigarettes in healthy individuals and smokers with asthma**. *Respirology* 2018, **23**(3):291-297.
- 77. Staudt MR, Salit J, Kaner RJ, Hollmann C, Crystal RG: Altered lung biology of healthy never smokers following acute inhalation of E-cigarettes. *Respiratory Research* 2018, **19**.
- 78. Chaumont M, van de Borne P, Bernard A, Van Muylem A, Deprez G, Ullmo J, Starczewska E, Briki R, de Hemptinne Q, Zaher W *et al*: **Fourth generation e-cigarette vaping induces transient lung**

inflammation and gas exchange disturbances: results from two randomized clinical trials. American Journal of Physiology - Lung Cellular & Molecular Physiology 2019, **316**(5):L705-L719.

- 79. Vansickel AR, Shihadeh A, Eissenberg T: Waterpipe tobacco products: nicotine labelling versus nicotine delivery. *Tobacco Control* 2012, **21**(3):377-379.
- 80. Vansickel AR, Eissenberg T: Electronic Cigarettes: Effective Nicotine Delivery After Acute Administration. *Nicotine & Tobacco Research* 2013, **15**(1):267-270.
- Nides MA, Leischow SJ, Bhatter M, Simmons M: Nicotine Blood Levels and Short-term Smoking Reduction with an Electronic Nicotine Delivery System. American Journal of Health Behavior 2014, 38(2):265-274.
- Yan XS, D'Ruiz C: Effects of using electronic cigarettes on nicotine delivery and cardiovascular function in comparison with regular cigarettes. *Regulatory Toxicology and Pharmacology* 2015, 71(1):24-34.
- 83. Benowitz NL, Burbank AD: Cardiovascular toxicity of nicotine: Implications for electronic cigarette use. *Trends in Cardiovascular Medicine* 2016, **26**(6):515-523.
- 84. Bhatnagar A: Cardiovascular Perspective of the Promises and Perils of E-Cigarettes. *Circulation Research* 2016, **118**(12):1872-1875.
- 85. Bhatnagar A: Are Electronic Cigarette Users at Increased Risk for Cardiovascular Disease? Jama Cardiology 2017, 2(3):237-238.
- 86. Stevens HE, Vaccarino FM: **How Animal Models Inform Child and Adolescent Psychiatry**. *Journal of the American Academy of Child and Adolescent Psychiatry* 2015, **54**(5):352-359.
- 87. Lydon DM, Wilson SJ, Child A, Geier CF: Adolescent brain maturation and smoking: What we know and where we're headed. *Neuroscience and Biobehavioral Reviews* 2014, **45**:323-342.
- England LJ, Bunnell RE, Pechacek TF, Tong VT, McAfee TA: Nicotine and the Developing Human A Neglected Element in the Electronic Cigarette Debate. American Journal of Preventive Medicine 2015, 49(2):286-293.
- 89. England LJ, Aagaard K, Bloch M, Conway K, Cosgrove K, Grana R, Gould TJ, Hatsukami D, Jensen F, Kandel D *et al*: **Developmental toxicity of nicotine: A transdisciplinary synthesis and implications for emerging tobacco products**. *Neuroscience and Biobehavioral Reviews* 2017, **72**:176-189.
- 90. Spear LP: Neurobehavioral changes in adolescence. *Current Directions in Psychological Science* 2000, **9**(4):111-114.
- 91. Dahl RE: Adolescent brain development: A period of vulnerabilities and opportunities Keynote address. In: Adolescent Brain Development: Vulnerabilities and Opportunities. Volume 1021, edn. Edited by Dahl RE, Spear LP; 2004: 1-22.
- 92. Dahl RE: Adolescent development and the regulation of behavior and emotion Introduction to part VIII. In: Adolescent Brain Development: Vulnerabilities and Opportunities. Volume 1021, edn. Edited by Dahl RE, Spear LP; 2004: 294-295.
- 93. Dahl RE, Lerner J, Hariri AR, Ladouceur C, Carter C, Ryan ND: Affective influences on decision making in adolescents. *Neuropsychopharmacology* 2004, **29**:S4-S5.
- 94. Walker DM, Bell MR, Flores C, Gulley JM, Willing J, Paul MJ: Adolescence and Reward: Making Sense of Neural and Behavioral Changes Amid the Chaos. *Journal of Neuroscience* 2017, 37(45):10855-10866.
- 95. Spear LP: Adolescent neurodevelopment. *The Journal of adolescent health : official publication of the Society for Adolescent Medicine* 2013, **52**(2 Suppl 2):S7-13.
- 96. Dow-Edwards D, MacMaster FP, Peterson BS, Niesink R, Andersen S, Braams BR: **Experience during** adolescence shapes brain development: From synapses and networks to normal and pathological behavior. *Neurotoxicology and teratology* 2019, **76**:106834.
- 97. Selemon LD: A role for synaptic plasticity in the adolescent development of executive function. *Translational psychiatry* 2013, **3**:e238.
- 98. Giedd JN, Rapoport JL: Structural MRI of Pediatric Brain Development: What Have We Learned and Where Are We Going? *Neuron* 2010, 67(5):728-734.

- 99. Somerville LH, Casey BJ: **Developmental neurobiology of cognitive control and motivational systems**. *Current Opinion in Neurobiology* 2010, **20**(2):236-241.
- 100. Casey BJ, Jones RM, Levita L, Libby V, Pattwell SS, Ruberry EJ, Soliman F, Somerville LH: **The Storm and Stress of Adolescence: Insights From Human Imaging and Mouse Genetics**. *Developmental Psychobiology* 2010, **52**(3):225-235.
- Somerville LH, Jones RM, Ruberry EJ, Dyke JP, Glover G, Casey BJ: The Medial Prefrontal Cortex and the Emergence of Self-Conscious Emotion in Adolescence. *Psychological Science* 2013, 24(8):1554-1562.
- 102. Maslowsky J, Owotomo O, Huntley ED, Keating D: Adolescent Risk Behavior: Differentiating Reasoned And Reactive Risk-taking. *Journal of Youth and Adolescence* 2019, 48(2):243-255.
- 103. Romer D: Adolescent risk taking, impulsivity, and brain development: implications for prevention. *Developmental psychobiology* 2010, **52**(3):263-276.
- 104. Romer D, Reyna VF, Satterthwaite TD: Beyond stereotypes of adolescent risk taking: Placing the adolescent brain in developmental context. *Developmental cognitive neuroscience* 2017, 27:19-34.
- 105. Willoughby T, Good M, Adachi PJC, Hamza C, Tavernier R: **Examining the link between adolescent** brain development and risk taking from a social-developmental perspective. *Brain and cognition* 2013, **83**(3):315-323.
- 106. Konrad K, Firk C, Uhlhaas PJ: **Brain development during adolescence: neuroscientific insights into this developmental period**. *Deutsches Arzteblatt international* 2013, **110**(25):425-431.
- 107. Spear LP: Adolescent brain development and animal models. Annals of the New York Academy of Sciences 2004, **1021**:23-26.
- 108. Jasinska AJ, Zorick T, Brody AL, Stein EA: **Dual role of nicotine in addiction and cognition: A review of neuroimaging studies in humans**. *Neuropharmacology* 2014, **84**:111-122.
- 109. Hall BJ, Cauley M, Burke DA, Kiany A, Slotkin TA, Levin ED: Cognitive and Behavioral Impairments Evoked by Low-Level Exposure to Tobacco Smoke Components: Comparison with Nicotine Alone. *Toxicological Sciences* 2016, **151**(2):236-244.
- 110. Leslie FM: Unique, long-term effects of nicotine on adolescent brain. *Pharmacology, Biochemistry* & *Behavior* 2020, **197**:173010.
- 111. Poorthuis RB, Goriounova NA, Couey JJ, Mansvelder HD: **Nicotinic actions on neuronal networks for cognition: General principles and long-term consequences**. *Biochemical Pharmacology* 2009, **78**(7):668-676.
- 112. Treur JL, Willemsen G, Bartels M, Geels LM, van Beek JHDA, Huppertz C, van Beijsterveldt CEM, Boomsma DI, Vink JM: **Smoking During Adolescence as a Risk Factor for Attention Problems**. *Biological Psychiatry* 2015, **78**(9):656-663.
- 113. Jacobsen LK, Krystal JH, Mencl WE, Westerveld M, Frost SJ, Pugh KR: **Effects of smoking and smoking abstinence on cognition in adolescent tobacco smokers**. *Biological Psychiatry* 2005, **57**(1):56-66.
- 114. Bergstrom HC, McDonald CG, French HT, Smith RF: **Continuous nicotine administration produces** selective, age-dependent structural alteration of pyramidal neurons from prelimbic cortex. *Synapse* 2008, **62**(1):31-39.
- 115. Counotte DS, Goriounova NA, Li KW, Loos M, van der Schors RC, Schetters D, Schoffelmeer ANM, Smit AB, Mansvelder HD, Pattij T *et al*: Lasting synaptic changes underlie attention deficits caused by nicotine exposure during adolescence. *Nature Neuroscience* 2011, **14**(4):417-419.
- 116. Counotte DS, Spijker S, Van de Burgwal LH, Hogenboom F, Schoffelmeer ANM, De Vries TJ, Smit AB, Pattij T: Long-Lasting Cognitive Deficits Resulting from Adolescent Nicotine Exposure in Rats. *Neuropsychopharmacology* 2009, **34**(2):299-306.
- 117. Goriounova NA, Mansvelder HD: Short- and Long-Term Consequences of Nicotine Exposure during Adolescence for Prefrontal Cortex Neuronal Network Function. *Cold Spring Harbor Perspectives in Medicine* 2012, **2**(12).

- 118. Goriounova NA, Mansvelder HD: Nicotine Exposure during Adolescence Leads to Short- and Long-Term Changes in Spike Timing-Dependent Plasticity in Rat Prefrontal Cortex. *Journal of Neuroscience* 2012, **32**(31):10484-10493.
- 119. Moylan S, Jacka FN, Pasco JA, Berk M: Cigarette smoking, nicotine dependence and anxiety disorders: a systematic review of population-based, epidemiological studies. *Bmc Medicine* 2012, 10.
- 120. Jamal M, Van der Does AJW, Penninx BWJH, Cuijpers P: Age at Smoking Onset and the Onset of Depression and Anxiety Disorders. *Nicotine & Tobacco Research* 2011, **13**(9):809-819.
- 121. Moylan S, Gustavson K, Karevold E, Overland S, Jacka FN, Pasco JA, Berk M: The Impact of Smoking in Adolescence on Early Adult Anxiety Symptoms and the Relationship between Infant Vulnerability Factors for Anxiety and Early Adult Anxiety Symptoms: The TOPP Study. Plos One 2013, 8(5).
- 122. Griesler PC, Hu M-C, Schaffran C, Kandel DB: **Comorbid psychiatric disorders and nicotine dependence in adolescence**. *Addiction* 2011, **106**(5):1010-1020.
- 123. Tjora T, Hetland J, Aaro LE, Wold B, Wiium N, Overland S: **The association between smoking and** depression from adolescence to adulthood. *Addiction* 2014, **109**(6):1022-1030.
- 124. Boden JM, Fergusson DM, Norwood LJ: Cigarette smoking and depression: tests of causal linkages using a longitudinal birth cohort. *British Journal of Psychiatry* 2010, **196**(6):440-446.
- 125. Munafo MR, Araya R: Cigarette smoking and depression: a question of causation. *British Journal* of *Psychiatry* 2010, **196**(6):425-426.
- 126. Leventhal AM, Zvolensky MJ: Anxiety, Depression, and Cigarette Smoking: A Transdiagnostic Vulnerability Framework to Understanding Emotion-Smoking Comorbidity. *Psychological Bulletin* 2015, **141**(1):176-212.
- 127. Slawecki CJ, Gilder A, Roth J, Ehlers CL: **Increased anxiety-like behavior in adult rats exposed to nicotine as adolescents**. *Pharmacology Biochemistry and Behavior* 2003, **75**(2):355-361.
- 128. Smith LN, McDonald CG, Bergstrom HC, Brielmaler JM, Eppolito AK, Wheeler TL, Falco AM, Smith RF: Long-term changes in fear conditioning and anxiety-like behavior following nicotine exposure in adult versus adolescent rats. *Pharmacology Biochemistry and Behavior* 2006, **85**(1):91-97.
- 129. Slotkin TA, Seidler FJ: **Nicotine Exposure in Adolescence Alters the Response of Serotonin Systems to Nicotine Administered Subsequently in Adulthood**. *Developmental Neuroscience* 2009, **31**(1-2):58-70.
- 130. Iniguez SD, Warren BL, Parise EM, Alcantara LF, Schuh B, Maffeo ML, Manojlovic Z, Bolanos-Guzman CA: Nicotine Exposure during Adolescence Induces a Depression-Like State in Adulthood. Neuropsychopharmacology 2009, **34**(6):1609-1624.
- 131. Etter J-F, Zather E, Svensson S: Analysis of refill liquids for electronic cigarettes. *Addiction* 2013, **108**(9):1671-1679.
- 132. Farsalinos KE, Gillman G, Poulas K, Voudris V: **Tobacco-Specific Nitrosamines in Electronic Cigarettes: Comparison between Liquid and Aerosol Levels**. *International Journal of Environmental Research and Public Health* 2015, **12**(8):9046-9053.
- 133. Farsalinos KE, Gillman IG, Melvin MS, Paolantonio AR, Gardow WJ, Humphries KE, Brown SE, Poulas K, Voudris V: Nicotine Levels and Presence of Selected Tobacco-Derived Toxins in Tobacco Flavoured Electronic Cigarette Refill Liquids. International Journal of Environmental Research and Public Health 2015, 12(4):3439-3452.
- Farsalinos KE, Kistler KA, Gillman G, Voudris V: Evaluation of Electronic Cigarette Liquids and Aerosol for the Presence of Selected Inhalation Toxins. Nicotine & Tobacco Research 2015, 17(2):168-174.
- 135. Lisko JG, Tran H, Stanfill SB, Blount BC, Watson CH: Chemical Composition and Evaluation of Nicotine, Tobacco Alkaloids, pH, and Selected Flavors in E-Cigarette Cartridges and Refill Solutions. Nicotine & Tobacco Research 2015, **17**(10):1270-1278.

- 136. Oh J-A, Shin H-S: **Identification and Quantification of Several Contaminated Compounds in Replacement Liquids of Electronic Cigarettes by Gas Chromatography-Mass Spectrometry.** *Journal of Chromatographic Science* 2015, **53**(6):841-848.
- 137. Jacob P, 3rd, Yu L, Shulgin AT, Benowitz NL: Minor tobacco alkaloids as biomarkers for tobacco use: comparison of users of cigarettes, smokeless tobacco, cigars, and pipes. *American journal of public health* 1999, **89**(5):731-736.
- 138. Kosmider L, Sobczak A, Fik M, Knysak J, Zaciera M, Kurek J, Goniewicz ML: **Carbonyl Compounds in Electronic Cigarette Vapors: Effects of Nicotine Solvent and Battery Output Voltage**. *Nicotine & Tobacco Research* 2014, **16**(10):1319-1326.
- 139. Jensen RP, Luo W, Pankow JF, Strongin RM, Peyton DH: **Hidden Formaldehyde in E-Cigarette Aerosols**. *New England Journal of Medicine* 2015, **372**(4):392-394.
- 140. Jensen RP, Strongin RM, Peyton DH: **Solvent Chemistry in the Electronic Cigarette Reaction Vessel**. *Scientific Reports* 2017, **7**.
- 141. Korzun T, Lazurko M, Munhenzva I, Barsanti KC, Huang Y, Jensen RP, Escobedo JO, Luo W, Peyton DH, Strongin RM: E-Cigarette Airflow Rate Modulates Toxicant Profiles and Can Lead to Concerning Levels of Solvent Consumption. *Acs Omega* 2018, **3**(1):30-36.
- 142. Kosmider L, Cox S, Zaciera M, Kurek J, Goniewicz ML, McRobbie H, Kimber C, Dawkins L: **Daily** exposure to formaldehyde and acetaldehyde and potential health risk associated with use of high and low nicotine e-liquid concentrations. *Scientific Reports* 2020, **10**(1).
- 143. Cohen SM, Garland EM, St John M, Okamura T, Smith RA: Acrolein initiates rat urinary bladder carcinogenesis. *Cancer research* 1992, **52**(13):3577-3581.
- 144. Kuntic M, Daiber A, Munzel T: **Acrolein, e-cigarettes, and pulmonary and vascular damage**. *European heart journal* 2020, **41**(15):1524.
- 145. Rubinstein ML, Delucchi K, Benowitz NL, Ramo DE: Adolescent Exposure to Toxic Volatile Organic Chemicals From E-Cigarettes. *Pediatrics* 2018, **141**(4).
- 146. Moretto N, Bertolini S, ladicicco C, Marchini G, Kaur M, Volpi G, Patacchini R, Singh D, Facchinetti F: Cigarette smoke and its component acrolein augment IL-8/CXCL8 mRNA stability via p38 MAPK/MK2 signaling in human pulmonary cells. American journal of physiology Lung cellular and molecular physiology 2012, 303(10):L929-938.
- 147. Moretto N, Volpi G, Pastore F, Facchinetti F: **Acrolein effects in pulmonary cells: relevance to chronic obstructive pulmonary disease**. *Annals of the New York Academy of Sciences* 2012, **1259**:39-46.
- 148. DeJarnett N, Conklin DJ, Riggs DW, Myers JA, O'Toole TE, Hamzeh I, Wagner S, Chugh A, Ramos KS, Srivastava S *et al*: **Acrolein exposure is associated with increased cardiovascular disease risk**. *Journal of the American Heart Association* 2014, **3**(4).
- 149. Hazari MS, Griggs J, Winsett DW, Haykal-Coates N, Ledbetter A, Costa DL, Farraj AK: A single exposure to acrolein desensitizes baroreflex responsiveness and increases cardiac arrhythmias in normotensive and hypertensive rats. *Cardiovascular toxicology* 2014, **14**(1):52-63.
- 150. Perez CM, Hazari MS, Ledbetter AD, Haykal-Coates N, Carll AP, Cascio WE, Winsett DW, Costa DL, Farraj AK: Acrolein inhalation alters arterial blood gases and triggers carotid body-mediated cardiovascular responses in hypertensive rats. *Inhalation toxicology* 2015, **27**(1):54-63.
- 151. Zirak MR, Mehri S, Karimani A, Zeinali M, Hayes AW, Karimi G: **Mechanisms behind the atherothrombotic effects of acrolein, a review**. *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association* 2019, **129**:38-53.
- 152. Henning RJ, Johnson GT, Coyle JP, Harbison RD: Acrolein Can Cause Cardiovascular Disease: A Review. *Cardiovascular toxicology* 2017, **17**(3):227-236.
- 153. Luo J, Hill BG, Gu Y, Cai J, Srivastava S, Bhatnagar A, Prabhu SD: **Mechanisms of acrolein-induced myocardial dysfunction: implications for environmental and endogenous aldehyde exposure**. *American journal of physiology Heart and circulatory physiology* 2007, **293**(6):H3673-3684.
- 154. Behar RZ, Davis B, Wang Y, Bahl V, Lin S, Talbot P: **Identification of toxicants in cinnamon-flavored** electronic cigarette refill fluids. *Toxicology in Vitro* 2014, **28**(2):198-208.

- 155. Hadwiger ME, Trehy ML, Ye W, Moore T, Allgire J, Westenberger B: **Identification of aminotadalafil and rimonabant in electronic cigarette products using high pressure liquid chromatography with diode array and tandem mass spectrometric detection**. *Journal of chromatography A* 2010, **1217**(48):7547-7555.
- 156. Oh J-A, Shin H-S: **Identification and Quantification of Several Contaminated Compounds in Replacement Liquids of Electronic Cigarettes by Gas Chromatography-Mass Spectrometry.** *Journal of chromatographic science* 2015, **53**(6):841-848.
- 157. Tierney PA, Karpinski CD, Brown JE, Luo W, Pankow JF: Flavour chemicals in electronic cigarette fluids. *Tobacco Control* 2016, **25**(E1):E10-E15.
- 158. Bahl V, Lin S, Xu N, Davis B, Wang Y-h, Talbot P: **Comparison of electronic cigarette refill fluid** cytotoxicity using embryonic and adult models. *Reproductive Toxicology* 2012, **34**(4):529-537.
- 159. Nagle AA, Gan F-F, Jones G, So C-L, Wells G, Chew E-H: Induction of Tumor Cell Death through Targeting Tubulin and Evoking Dysregulation of Cell Cycle Regulatory Proteins by Multifunctional Cinnamaldehydes. *Plos One* 2012, **7**(11).
- 160. Cheng S-S, Liu J-Y, Huang C-G, Hsui Y-R, Chen W-J, Chang S-T: Insecticidal activities of leaf essential oils from Cinnamomum osmophloeum against three mosquito species. *Bioresource technology* 2009, **100**(1):457-464.
- 161. Cheng S-S, Liu J-Y, Lin C-Y, Hsui Y-R, Lu M-C, Wu W-J, Chang S-T: **Terminating red imported fire ants using Cinnamomum osmophloeum leaf essential oil**. *Bioresource technology* 2008, **99**(4):889-893.
- 162. Egilman DS, Schilling JH, Menendez L: **A proposal for a safe exposure level for diacetyl**. International journal of occupational and environmental health 2011, **17**(2):122-134.
- 163. Clark S, Winter CK: **Diacetyl in Foods: A Review of Safety and Sensory Characteristics**. *Comprehensive Reviews in Food Science and Food Safety* 2015, **14**(5):634-643.
- 164. Hubbs AF, Cumpston AM, Goldsmith WT, Battelli LA, Kashon ML, Jackson MC, Frazer DG, Fedan JS, Goravanahally MP, Castranova V *et al*: **Respiratory and olfactory cytotoxicity of inhaled 2,3**-**pentanedione in Sprague-Dawley rats**. *The American journal of pathology* 2012, **181**(3):829-844.
- 165. Hecht SS: **DNA adduct formation from tobacco-specific N-nitrosamines**. *Mutation research* 1999, **424**(1-2):127-142.
- 166. Cheng T: Chemical evaluation of electronic cigarettes. *Tobacco Control* 2014, 23:11-17.
- 167. Zalups RK, Ahmad S: **Molecular handling of cadmium in transporting epithelia**. *Toxicology and Applied Pharmacology* 2003, **186**(3):163-188.
- Williams M, Villarreal A, Bozhilov K, Lin S, Talbot P: Metal and Silicate Particles Including Nanoparticles Are Present in Electronic Cigarette Cartomizer Fluid and Aerosol. *Plos One* 2013, 8(3).
- 169. Farsalinos KE, Voudris V, Poulas K: **Are Metals Emitted from Electronic Cigarettes a Reason for Health Concern? A Risk-Assessment Analysis of Currently Available Literature**. *International Journal of Environmental Research and Public Health* 2015, **12**(5):5215-5232.
- 170. Mikheev VB, Brinkman MC, Granville CA, Gordon SM, Clark PI: **Real-Time Measurement of Electronic Cigarette Aerosol Size Distribution and Metals Content Analysis**. *Nicotine & Tobacco Research* 2016, **18**(9):1895-1902.
- 171. Ind PW: E-cigarette or vaping product use-associated lung injury. *British Journal of Hospital Medicine* 2020, **81**(4):1-9.
- 172. Holt AK, Poklis JL, Cobb CO, Peace MR: **The Identification of Gamma-Butyrolactone in JUUL** Liquids. *Journal of analytical toxicology* 2021.
- Javed F, Kellesarian SV, Sundar IK, Romanos GE, Rahman I: Recent updates on electronic cigarette aerosol and inhaled nicotine effects on periodontal and pulmonary tissues. Oral diseases 2017, 23(8):1052-1057.
- 174. Kumar PS, Clark P, Brinkman MC, Saxena D: **Novel Nicotine Delivery Systems**. *Advances in dental research* 2019, **30**(1):11-15.

- 175. Andrikopoulos GI, Farsalinos K, Poulas K: Electronic Nicotine Delivery Systems (ENDS) and Their Relevance in Oral Health. *Toxics* 2019, **7**(4).
- 176. Ebersole J, Samburova V, Son Y, Cappelli D, Demopoulos C, Capurro A, Pinto A, Chrzan B, Kingsley K, Howard K *et al*: Harmful chemicals emitted from electronic cigarettes and potential deleterious effects in the oral cavity. *Tobacco induced diseases* 2020, **18**:41.
- 177. Yang I, Sandeep S, Rodriguez J: **The oral health impact of electronic cigarette use: a systematic review**. *Critical reviews in toxicology* 2020, **50**(2):97-127.
- 178. Rouabhia M: Impact of Electronic Cigarettes on Oral Health: a Review. Journal (Canadian Dental Association) 2020, 86:k7.
- 179. Klawinski D, Hanna I, Breslin NK, Katzenstein HM, Indelicato DJ: Vaping the Venom: Oral Cavity Cancer in a Young Adult With Extensive Electronic Cigarette Use. *Pediatrics* 2021, **147**(5).
- 180. Bustamante G, Ma B, Yakovlev G, Yershova K, Le C, Jensen J, Hatsukami DK, Stepanov I: **Presence** of the Carcinogen N'-Nitrosonornicotine in Saliva of E-cigarette Users. *Chemical research in toxicology* 2018, **31**(8):731-738.
- 181. Sundar IK, Javed F, Romanos GE, Rahman I: E-cigarettes and flavorings induce inflammatory and pro-senescence responses in oral epithelial cells and periodontal fibroblasts. Oncotarget 2016, 7(47):77196-77204.
- 182. Chopyk J, Bojanowski CM, Shin J, Moshensky A, Fuentes AL, Bonde SS, Chuki D, Pride DT, Crotty Alexander LE: **Compositional Differences in the Oral Microbiome of E-cigarette Users**. *Frontiers in microbiology* 2021, **12**:599664.
- 183. Cichonska D, Kusiak A, Kochanska B, Ochocinska J, Swietlik D: Influence of Electronic Cigarettes on Selected Antibacterial Properties of Saliva. International journal of environmental research and public health 2019, 16(22).
- 184. Manyanga J, Ganapathy V, Bouharati C, Mehta T, Sadhasivam B, Acharya P, Zhao D, Queimado L: Electronic cigarette aerosols alter the expression of cisplatin transporters and increase drug resistance in oral cancer cells. *Scientific reports* 2021, **11**(1):1821.
- 185. Atuegwu NC, Perez MF, Oncken C, Thacker S, Mead EL, Mortensen EM: Association between Regular Electronic Nicotine Product Use and Self-reported Periodontal Disease Status: Population Assessment of Tobacco and Health Survey. International journal of environmental research and public health 2019, 16(7).
- 186. Ji EH, Elzakra N, Chen W, Cui L, Lee ES, Sun B, Messadi D, Xia T, Zhu Y, Hu S: **E-cigarette aerosols** induce unfolded protein response in normal human oral keratinocytes. *Journal of Cancer* 2019, 10(27):6915-6924.
- 187. Flach S, Maniam P, Manickavasagam J: **E-cigarettes and head and neck cancers: A systematic review of the current literature**. *Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery* 2019, **44**(5):749-756.
- 188. Zhou Y, Irshad H, Dye WW, Wu G, Tellez CS, Belinsky SA: Voltage and e-liquid composition affect nicotine deposition within the oral cavity and carbonyl formation. *Tobacco control* 2020.
- Holliday R, Hong B, McColl E, Livingstone-Banks J, Preshaw PM: Interventions for tobacco cessation delivered by dental professionals. *The Cochrane database of systematic reviews* 2021, 2:CD005084.
- 190. Holliday R, Chaffee BW, Jakubovics NS, Kist R, Preshaw PM: Electronic Cigarettes and Oral Health. *Journal of dental research* 2021:220345211002116.
- 191. Patanavanich R, Glantz SA: **Smoking is associated with worse outcomes of COVID-19 particularly among younger adults: A systematic review and meta-analysis**. *medRxiv : the preprint server for health sciences* 2020.
- 192. Patanavanich R, Glantz SA: **Smoking Is Associated With COVID-19 Progression: A Meta-analysis**. *Nicotine & Tobacco Research* 2020, **22**(9):1653-1656.
- 193. Chakma JK, Kumar H, Bhargava S, Khanna T: **The e-cigarettes ban in India: an important public health decision**. *The Lancet Public health* 2020, **5**(8):e426.

- 194. Gaiha SM, Cheng J, Halpern-Felsher B: Association Between Youth Smoking, Electronic Cigarette Use, and COVID-19. *Journal of Adolescent Health* 2020, 67(4):519-523.
- 195. Adams SH, Park MJ, Schaub JP, Brindis CD, Irwin CE, Jr.: Medical Vulnerability of Young Adults to Severe COVID-19 Illness-Data From the National Health Interview Survey. Journal of Adolescent Health 2020, 67(3):362-368.
- 196. Kumar G, Adams A, Hererra M, Rojas ER, Singh V, Sakhuja A, Meersman M, Dalton D, Kethireddy S, Nanchal R *et al*: **Predictors and outcomes of healthcare-associated infections in COVID-19** patients. International Journal of Infectious Diseases 2021, **104**:287-292.
- 197. Walsh K, Sheikh Z, Johal K, Khwaja N: Rare case of accidental fire and burns caused by e-cigarette batteries. *BMJ case reports* 2016, **2016**.
- 198. Brownson EG, Thompson CM, Goldsberry S, Chong HJ, Friedrich JB, Pham TN, Arbabi S, Carrougher GJ, Gibran NS: **Explosion Injuries from E-Cigarettes**. *New England Journal of Medicine* 2016, **375**(14):1400-1402.
- 199. Harrison R, Hicklin D, Jr.: Electronic cigarette explosions involving the oral cavity. *Journal of the American Dental Association (1939)* 2016, **147**(11):891-896.
- 200. Roger JM, Abayon M, Elad S, Kolokythas A: **Oral Trauma and Tooth Avulsion Following Explosion** of E-Cigarette. Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons 2016, **74**(6):1181-1185.
- 201. Rossheim ME, Livingston MD, Soule EK, Zeraye HA, Thombs DL: Electronic cigarette explosion and burn injuries, US Emergency Departments 2015-2017. *Tobacco control* 2019, 28(4):472-474.
- 202. Rossheim ME, McDonald KK, Soule EK, Gimm GW, Livingston MD, Barnett TE, Jernigan DH, Thombs DL: Electronic cigarette explosion/burn and poisoning related emergency department visits,
 2018-2019. The American journal of emergency medicine 2020, 38(12):2637-2640.

Appendix A

TOBACCO 21 COMPLIANCE PROGRAM 2020 OUTCOMES (6/9/21)



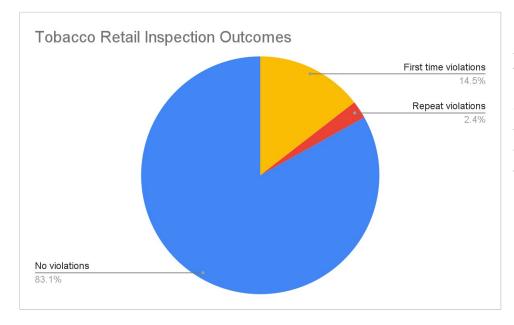


The Tobacco 21 Compliance Program began in January 2020 with an educational brochure and introductory letter which was delivered in standard mail and email to all tobacco retailers in the City of Columbia on file with the Business License Manager in the Finance Department.

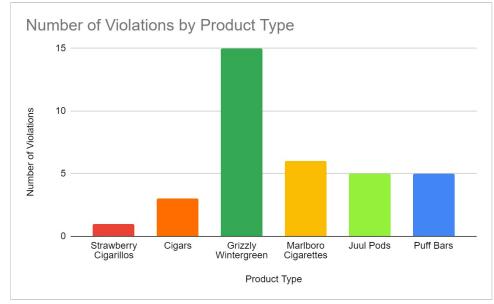
After retailers received education and notice that compliance audits would be occurring, PHHS began audits. Compliance audits are conducted with an official youth buyer attempting to purchase any tobacco product. If a purchase is completed, the Tobacco Enforcement and Education Officer issues a violation to the retailer. Violations are sent to the City of Columbia Prosecuting Attorney.



There was a decrease in the violation rate from February to December 2020. No inspections were completed in April and May due to Covid-19 Stay-At-Home Order. The downward trend provides good evidence that the compliance program is effective.



As of December 22, 2020, a total of 207 inspections were completed and 35 violations were issued. Five (5) of the 35 violations were repeat violations. This demonstrates that the vast majority of retailers are compliant and repeat violators are rare.



Youth buyers attempted to make purchases on a variety of products. More violations were made with Grizzly Wintergreen than any other product. Puff Bars are a disposable e-cigarette product.



Youth buyers were aged 18-20. We trained 2-3 new youth buyers every few months. We hired both male and female buyers. Nationally, female buyers tend to have higher violation rates. Locally, 57% of the violations occurred with the purchase by a male youth buyer. We do not have the rate of violations for males and females at this time.

APPENDIX B



Tobacco Retail Store Assessments Boone County, Missouri

January – February 2020

Background

In 2018, Counter Tools and Truth Initiative developed a set of retail tobacco store assessment questions specifically focused on menthol and other flavored tobacco products, building on the Standardized Tobacco Assessment for Retail Settings (STARS) form. This set of questions, called fSTARS, was piloted initially in two cities (Dayton and Cleveland, OH) that are located within Tobacco Nation, a geographic area identified by Truth Initiative as a cluster of states where the smoking prevalence exceeds the national average as well as the prevalence in many of the most tobacco-dependent countries in the world.¹ One factor that contributes to the disparate smoking rates in this region is the lack of tobacco control policies in comparison to the rest of the United States.

The Standardized Tobacco Assessment for Retail Settings (STARS) form was designed for practitioners to inform state and local tobacco control policies pertaining to the point of sale. The STARS form and training materials resulted from a collaboration of SCTC researchers with stakeholders from five state health departments, the CDC, and the Tobacco Control Legal Consortium. The assessment items, which include tobacco product availability, price, promotion, and placement were selected exclusively for their policy relevance. Similarly, Counter Tools and Truth Initiative sought to design and test a set of questions specifically focused on menthol and other flavored tobacco products that had direct policy relevance and that could facilitate localities' consideration of flavor-based policies and other point-of-sale tobacco control policies.

Following the initial pilot in 2018-2019, the form was revised to reflect the evolving market for flavored ecigarette products, to be able to better compare flavored and non-flavored products, and to compare local data with national trends in disparities in the availability and marketing of flavored products. The revised form was piloted in Columbia and Boone County in 2020, along with two other cities: one within and one outside of Tobacco Nation (Lee's Summit, MO and Evanston, IL, respectively).

Boone County, Missouri has a population of 180,463.^{II} Missouri, part of Tobacco Nation, has the nation's lowest cigarette excise tax at \$0.17 and does not yet have a comprehensive smokefree air law statewide.^{III} Missouri's adult smoking rate in 2018 was 19.6%, higher than the national average of 13.7%.^{IV} Boone County's adult smoking rate in 2017 was 19%.^V Boone County's residents are 81.4% non-Hispanic white, 9.8% Black or African American, 5.0% Asian, 3.5% Hispanic or Latino, 0.5% American Indian or Alaska Native, 0.1% Native Hawaiian or Other Pacific Islander, and 3.2% two or more races.^{VI} In Boone County, 20.4% of residents are under the age of 18.^{VII}

Methodology

Using a list of all tobacco retailers in Boone County, Missouri, provided by Columbia/Boone County Public Health and Human Services, data collectors visited 134 retailers within city limits and were able to complete store assessments at 124 retailers, 111 of which sold tobacco.

Data analysis was completed by Counter Tools. Available store data rather than only complete store data was utilized in analysis; therefore, the total number of assessments summarized for each assessment item may vary depending on the amount of data that was available (or missing) for the particular assessment item.

Tobacco Retailer Types Surveyed (n=111)		
Convenience store with gas	55.9%	
Convenience store without gas	4.5%	
Grocery store	13.5%	
Beer, wine, or liquor store	8.1%	
Mass merchandiser	2.7%	
Drug store or pharmacy	1.8%	
Vape shop	8.1%	
Tobacco shop	5.4%	

Retailer Characteristics

- 18 of 110 (16.4%) accepted SNAP
- 19 of 110 (17.3%) accepted WIC
- 97 of 110 (88.2%) also sold alcohol
- 10 of 111 (9.0%) had a pharmacy counter

Convenience stores, which are frequented by youth,^{viii} were the most common type of tobacco retailer.

Flavored tobacco products were available for sale at all 110 of 110 (100%) retailers surveyed. Youth are more likely to initiate tobacco use with a flavored product. In fact, over 80% of youth who have ever used tobacco started with a flavored product.^{ix}

Exterior Advertisements

Exposure to tobacco marketing and advertising contributes to youth tobacco use initiation.^x Children and adolescents more frequently exposed to point-of-sale tobacco promotion have 1.6 times higher odds of having tried smoking and 1.3 times higher odds of being susceptible to future smoking compared to those less frequently exposed.^{xi}

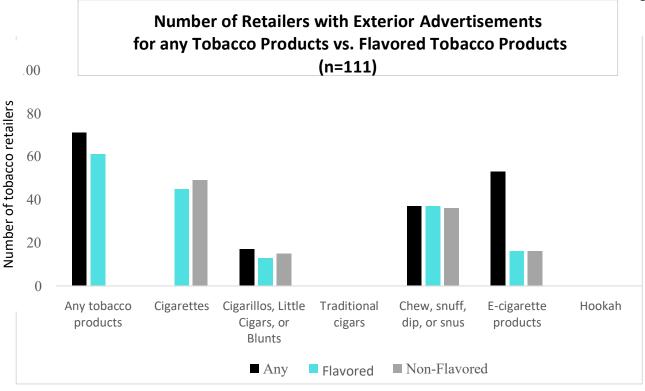
71 of 111 (64.0%) retailers in Boone County had exterior ads for tobacco products.

- 61 of 71 (85.9%) had exterior ads for any flavored tobacco products
- 49 of 70 (70.0%) had exterior ads for non-menthol cigarettes
- 45 of 70 (64.3%) had exterior ads for menthol cigarettes

Exterior Advertisements: Other Tobacco Products

Table interpretation: Of the 71 of 111 (64.0%) of retailers that had exterior ads for any tobacco product, 17 of 71 (23.9%) had exterior ads for cigarillos, little cigars, or blunts. Of those retailers, 13 of 17 (76.5%) had ads for flavored cigarillos, little cigars, or blunts and 15 of 17 (88.2%) had exterior ads for non-flavored cigarillos, little cigars, or blunts. The percentages reported for each assessment item only include stores for which data was available (excludes missing data).

	% of retailers with any exterior tobacco ads n of N (%)	% of retailers with exterior ads for flavored products n of N (%)	% of retailers with exterior ads for non-flavored products n of N (%)
Cigarillos, little cigars, or blunts	17 of 71 (23.9%)	13 of 17 (76.5%)	15 of 17 (88.2%)
Traditional cigars	0 of 70 (0%)		
Chew, snuff, dip or snus	37 of 71 (52.1%)	37 of 37 (100%)	36 of 37 (97.3%)
E-cigarette products	53 of 71 (74.7%)	16 of 53 (30.2%)	16 of 52 (30.8%)
Hookah	0 of 71 (0%)		



Exterior Advertisements at Retailers Near Schools

When there are more tobacco retailers near schools, youth are more likely to experiment with smoking,^{xii} and schools with more retailers within walking distance have higher smoking prevalences than schools with fewer retailers nearby.^{xiii}

- 18 of 111 (16.2%) of tobacco retailers surveyed were located within 1000ft of a school.
- 6 of the 18 (33.3%) surveyed retailers located within 1000ft of schools had exterior advertisements for flavored tobacco products, as did 55 of 93 (59.1%) of surveyed retailers located greater than 1000ft away from a school

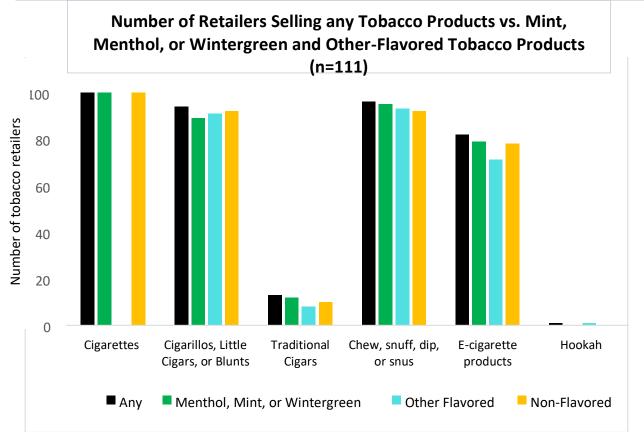
Exterior Advertisements by Neighborhood Demographics

Menthol cigarettes have been disproportionately targeted to African Americans for decades. Marketing for menthol tobacco products is more prevalent in urban neighborhoods and neighborhoods with black residents.^{xiv} Neighborhoods with a greater proportion of Black or lower-income residents also have more marketing for little cigars and cigarillos.^{xv} While we compared the proportion of retailers with exterior advertisements for menthol cigarettes and the proportion of retailers with exterior advertisements for flavored little cigars, cigarillos, or blunts in census tracts with the least proportion of African American residents to the census tracts with the most African American residents, as well as in census tracts with the most households living below the poverty level to census tracts with the lowest proportion of households living below the poverty level, we are not reporting these percentages. Given the small number of retailers in each tract, we are not able to draw any conclusions about this data.

Product Availability

Table interpretation: 82 of 110 (74.6%) of retailers sold e-cigarettes, of which 80 (97.6%) sold any flavored ecigarettes, 79 (96.3%) sold mint, menthol, or wintergreen flavored e-cigarettes, 71 (86.6%) sold otherflavored e-cigarettes, and 78 (95.1%) sold non-flavored e-cigarettes. The percentages reported for each assessment item only include stores for which data was available (excludes missing data).

Product Sold	Any n of N (%)	Any Flavor n of N (%)	Menthol- Flavored n of N (%)	Other- Flavored n of N (%)	Non- Flavored n of N (%)
Cigarettes	100 of 110 (90.9%)	N/A	100 of 100 (100%)	N/A	100 of 100 (100%)
Cigarillos, little cigars, or blunts	94 of 110	92 of 94	89 of 92	91 of 92	92 of 94
	(85.5%)	(97.9%)	(96.7%)	(98.9%)	(97.9%)
Traditional cigars	13 of 110	12 of 13	12 of 13	8 of 13	10 of 13
	(11.8%)	(92.3%)	(92.3%)	(61.5%)	(76.9%)
Chew, snuff, dip, or snus	96 of 110	96 of 96	95 of 96	93 of 96	92 of 96
	(87.3%)	(100%)	(99.0%)	(96.9%)	(95.8%)
E-cigarette products	82 of 110	80 of 82	79 of 82	71 of 82	78 of 82
	(74.6%)	(97.6%)	(96.3%)	(86.6%)	(95.1%)
Hookah	1 of 110 (0.9%)	1 of 1 (100%)	0 of 1 (0%)	1 of 1 (100%)	0 of 1 (0%)



40

- Nationally, e-cigarettes are the most common product used by youth, though cigarillos, little cigars, and blunts youth is also growing, particularly among males. Both of these products are often sold in flavors that are appealing to youth, such as candy or fruit flavors.
- Cigarillos, little cigars, and blunts are very widely available in Boone County. While they are just as dangerous as cigarettes, they are sold in a wide variety of flavors that appeal to youth and are often available for less than \$1.

Availability of Specific Flavored Tobacco Products

- Ambiguous flavor names: 49 of 94 (52.1%) retailers that sold cigarillos, little cigars, or blunts sold them with ambiguously named flavors such as "Tropical Fusion" and "Wild Rush." These flavors can present challenges for enforcement of flavored tobacco restrictions, and may be a tactic the tobacco industry is using to circumvent some definitions of characterizing flavors.
- **Menthol cigarettes:** Menthol cigarettes were widely available in Boone County and sold in all surveyed stores that sold cigarettes.
- **Cigarettes with menthol capsules:** 93 of 100 (93.0%) retailers that sold cigarettes also sold cigarettes with menthol capsules in the filter (e.g. Camel Crush, Marlboro NXT)

A wide range of e-cigarette products are available on the market today. While the first generation of ecigarettes were disposable and largely looked similar to conventional cigarettes, now newer generations of e-cigarette products come in both disposable and rechargeable varieties. Many are designed with refillable tanks or cartridges designed to be used with flavored nicotine solution or "e-liquid." New 4th generation "pod mod" styles of ecigarettes allow the user to replace cartridges or "pods" that can be refillable or pre-filled with flavored nicotine e-liquid. The pod mod device may be sold separately from the pre-filled pods or together in a "starter kit." These pods also typically use nicotine salts rather than the freebase nicotine used in previous generations of e-cigarettes, which allows the user to easily inhale and absorb high levels of nicotine.^{xvi}

This data was collected in between January 24, 2020 – February 21, 2020, during a time when the U.S. ecigarette market was shifting, and so were youth e-cigarette consumption patterns. E-cigarette use rates among youth have risen to epidemic proportions in recent years, driven largely by the youth-friendly pod mod e-cigarette brand Juul. Juul had captured about 75% of the e-cigarette market in the United States by the end of 2018.^{xvii} While the 2020 National Youth Tobacco Survey (NYTS) shows that current e-cigarette use among high school students decreased from 27.5% to 19.6% and current use among middle school students decreased from 10.5% to 4.7%,^{xviii} e-cigarettes remain the most common product used by youth. In addition, many youth are vaping frequently, with 22.5% of high school students reporting daily use as well as 9.4% of middle school students.^{xix}

In response to the youth e-cigarette epidemic, on January 2, 2020, the FDA announced a federal ban on the sale of flavored pre-filled cartridge-based e-cigarette products (like Juul) other than menthol or tobacco flavor. However, this restriction did not apply to e-liquids used in refillable e-cigarette devices or to disposable e-cigarettes. Retailers were given 30-days to sell off their remaining stock of these newly prohibited products, during which time this data collection began.

Use of menthol-flavored e-cigarette products also grew during this time. Prior to the federal restriction, ecigarette company Juul voluntarily stopped selling flavors other than menthol and tobacco in retail locations, starting with their fruit- and dessert-flavored pods in October 2018,^{xx} and then mint-flavored pods in November 2019.^{xxi} Between August 2019 and May 2020, menthol sales grew from 11% to 52% of total e-cigarette sales.^{xxii} While in previous years, menthol was not assessed independently, 2020 NYTS data shows that nearly half of youth and young adults who use e-cigarettes have used a menthol flavored pre-filled pod or cartridge and one quarter have used a menthol flavored disposable vaping product. Sales data also show a shift from mint to menthol.^{xxiii}

With the federal restrictions on the sale of flavored e-cigarette products in place, youth consumption shifted to new products like Puff Bar, a disposable e-cigarette that mimicked Juul's design but was still available in sweet and fruity flavors. The 2020 NYTS data show that while pod mods remained the most commonly used type of e-cigarette for 48.5% of high school students, rates of disposable e-cigarette use grew by roughly 1000% among high school students, jumping from 2.4% in 2019 to 26.5% in 2020.^{xxiv} In addition, 72.6% of disposable sales were for flavors banned from pod mods, indicating that youth were shifting to these products for the flavors.^{xxv} In July 2020, Puff Bar received a warning letter from the FDA instructing the company to remove its products from the marketplace since the product had not received the required premarket authorization,^{xxvi} and while the company first declared that they would cease all operations in the United States, they later declared they would only cease online sales in the United States. Puff Bar remains on the market and continues to grow its market share.^{xxvii} Other copycat products have also emerged.^{xxviii}

Product	Availability n of N (%)	
E-cigarette products (any)	82 of 110 (74.6%)	
E-liquid in droppers	7 of 82 (8.5%)	
Single disposable e-cigarettes	24 of 82 (29.3%	
Pod mods	82 of 82 (100%)	
Pod mod devices	76 of 82 (92.7%)	
Pod mod cartridges	78 of 81 (96.3%)	
• Pod mod starter kits	22 of 81 (27.2%)	
"Zero nicotine" e-cigarettes	6 of 82 (7.3%)	

Availability of E-Cigarette Products

Tobacco Product Prices

• Of the 94 of 110 (85.5%) of retailers that sold cigarillos, little cigars, or blunts, 79 of 94 (84.0%) sold singles, and 92 of 94 (97.9%) advertised them for less than \$1.

\$5.79

Avg. Newport Menthol cigarette pack

\$3.85

Avg. cheapest non-menthol cigarette pack Most common brand: Pall Mall

\$3.84

Avg. cheapest menthol cigarette pack Most common brand: Pall Mall

E-Cigarette Product Prices

- Avg. cheapest advertised price of e-liquid (n=7): \$7.99
 Avg. size of the cheapest dropper of e-liquid: 3.2oz
- Avg. cheapest advertised price for a single disposable e-cigarette (n= 24): \$7.99
- Avg. cheapest advertised price for a "pod mod" device (n=76): \$3.93
- Avg. cheapest advertised price for a pack of "pod mod" cartridges (n=78): \$11.35
 Avg. # of cartridges in a pack: 1.7
 - Packs with 1 cartridge: 37 of 69 (53.6%)
 - Packs with 2 cartridges: 24 of 69 (34.8%)
 - Packs with 4 cartridges: 8 of 69 (11.6%) \circ Avg. price per cartridge in the cheapest pack: \$6.68
- Avg. cheapest advertised price for a "pod mod" starter kit (n=22): \$15.37

Price variation by neighborhood youth population:

• Prices were cheaper on average in neighborhoods with the most youth, who are a more price-sensitive group. The average price of the cheapest pack of cigarettes was \$3.94 in census tracts with the lowest proportion (7.44% or less) of households with youth ages 5-17 vs. \$3.38 in census tracts with the highest proportion of youth ages 5-17 (18.98% or more)

Price variation by neighborhood income levels:

Lower-income smokers are more likely to purchase discount brand cigarettes.^{xxix} However, the average cheapest prices overall were not found in the areas of greatest poverty in Boone County. The average cheapest pack of cigarettes (for both menthol and non-menthol cigarettes) was \$4.31 in census tracts with the greatest proportion of households living below the poverty line (38.39% or more), whereas the average cheapest pack of cigarettes was \$3.91 and the average price of the cheapest pack of menthol cigarettes was \$3.92 in census tracts with the lowest proportion of households living below the poverty in the poverty of the poverty below the poverty

line (6.21% or less). However, the price for a pack of Newport menthol cigarettes was lowest (\$5.54) in census tracts with the greatest proportion of households living below poverty, compared to \$5.67 in census tracts with the lowest proportion of households living below poverty. Overall, 16.8% of Boone County's residents have household incomes below the poverty line.^{xxx}

Price variation by neighborhood racial demographics:

Nationally, research has shown Newport menthol cigarettes to be cheaper in geographic areas with a higher proportion of African American residents.^{xxxi} The store assessment results in Boone County, which is 9.8% Black or African American^{xxxii}, showed this pattern for Newport menthol cigarettes but not for the cheapest pack of menthol cigarettes. The average price of Newport menthol cigarettes was cheaper, at \$5.54 in census tracts with the greatest proportion of Non-Hispanic Black residents (14.45% or more), compared to \$5.67 in census tracts with both the lowest proportion of non-Hispanic Black residents (2.23% or less). However, the average cheapest advertised price for any pack of menthol cigarettes did not follow this same pattern, with an average price of \$4.31 in census tracts with greatest proportion Non-Hispanic Black residents but an average price of \$3.92 in census tracts with the lowest proportion of Non-Hispanic Black residents.

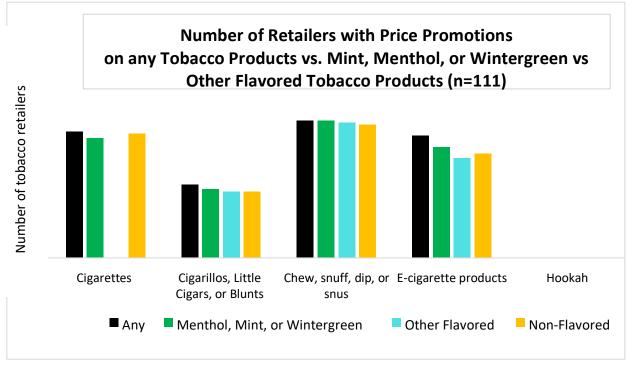
Tobacco Product Price Promotions

Tobacco companies spent over 85% of their total marketing expenditures for cigarettes and smokeless tobacco in 2018 on price discounts.^{xxxiii} Raising the price of tobacco products is one of the most effective strategies for reducing initiation, decreasing consumption, and increasing cessation.^{xxxiv} Price promotions and cheap prices can make flavored tobacco products even more appealing to youth and other price-sensitive groups.

Price Promotions

Table interpretation: 55 of 81 (67.9%) retailers that sold e-cigarettes had price promotions on any ecigarettes. 50 of 54 (92.6%) of those retailers had price promotions on mint-, menthol-, or wintergreen-flavored e-cigarettes, 45 of 49 (91.8%) had price promotions on other-flavored e-cigarette, and 50 of 55 (90.9%) had price promotions on any-flavored e-cigarettes, while 47 of 54 (87.0%) had price promotions on non-flavored e-cigarettes. The percentages reported for each assessment item only include stores for which data was available (excludes missing data).

Product	Any n of N (%)	Menthol- Flavored n of N (%)	Other- Flavored n of N (%)	Any- Flavored n of N (%)	Non- Flavored n of N (%)
Cigarettes	57 of 100 (57.0%)	54 of 56 (96.4%)	N/A	N/A	56 of 57 (98.3%)
Cigarillos, little cigars, or blunts	33 of 94	31 of 32	30 of 32	32 of 32	30 of 32
	(35.1%)	(96.9%)	(93.8%)	(100%)	(93.8%)
Chew, snuff, dip, or	62 of 96	62 of 62	61 of 62	62 of 62	60 of 61
snus	(64.6%)	(100%)	(98.4%)	(100%)	(98.4%)
E-cigarette products	55 of 81	50 of 54	45 of 49	50 of 55	47 of 54
	(67.9%)	(92.6%)	(91.8%)	(90.9%)	(87.0%)
Hookah	0 of 1 (0%)				



• 17 of 107 (15.9%) retailers surveyed indicated that they accepted mobile tobacco coupons

Product Placement

While cigarettes and smokeless tobacco products are required by federal law to be kept behind the counter, other tobacco products, including flavored products, are often displayed within easy reach of youth without clerk assistance.

Retailers with Tobacco Products in Self-Service Displays

Table interpretation: Of the retailers that sold cigarillos, little cigars, or blunts, 7 of 94 (7.5%) had them in self-service displays. The percentages reported for each assessment item only include stores for which data was available (excludes missing data).

Cigarillos, little cigars, or blunts	7 of 94 (7.5%)
Traditional cigars	4 of 13 (30.8%)
E-cigarette products	3 of 82 (3.7%)
Hookah	1 of 1 (100%)

- 1 of 111 (0.9%) retailers had any tobacco products places within 12 inches of youth products, such as candy, ice cream, soda, or toys.
- 5 of 109 (4.6%) retailers had any tobacco advertisements placed within 3 ft of the floor, right at kids' eye level.

Percent Inventory

Data collectors were asked to estimate the percent of each store's inventory that menthol flavored tobacco products, other-flavored tobacco products, and non-flavored tobacco products each comprised. Across stores in Boone County, data collectors most commonly estimated that:

- Menthol tobacco products comprised 26-50% of the total tobacco inventory Other-flavored tobacco products comprised 11-25[%] of the total tobacco inventory
- Non-flavored tobacco products comprised 11-25% of the total tobacco inventory.

References

```
<sup>ix</sup> Ambrose BK, Day HR, Rostron B. Flavored Tobacco Product Use Among US Youth Aged 12-17 Years, 2013-2014.
JAMA. 2015; 314(17): 1871-1873. doi:10.1001/jama.2015.13802
```

[×] National Cancer Institute. The Role of the Media in Promoting and Reducing Tobacco Use. Tobacco Control Monograph No. 19. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute. NIH Pub. No. 07-6242, June 2008.

^{xi} Robertson L, Cameron C, McGee R, Marsh L, Hoek J. Point-of-sale tobacco promotion and youth smoking: a metaanalysis. Tobacco Control. 2016;25:e83-e89. doi:10.1136/tobaccocontrol-2015-05286

^{xii} McCarthy WJ, Mistry R, Lu Y, Patel M, Zheng H, Dietsch B. Density of tobacco retailers near schools: effects on tobacco use among students. American Journal of Public Health. 2009;99(11)2006-13 doi: 10.2105/AJPH.2008.145128.

^{xiii} Henriksen L, Feighery EC, Schleicher NC, Cowling DW, Kline RS, Fortmann SP. Is adolescent smoking related to the density and proximity of tobacco outlets and retail cigarette advertising near schools? Preventive Medicine. 2008;47(2):210-4. doi:10.1016/j.ypmed.2008.04.008.

^{xiv} Lee JGL, Henriksen L, Rose SW, Moreland-Russell S, Ribisl KM. A systematic review of neighborhood disparities in point-of-sale tobacco marketing. American Journal of Public Health. 2015;105(9):E8-E18. doi:

^{xv}Kong AY, Queen TL, Golden SD, Ribisl KM. Neighborhood Disparities in the Availability, Advertising, Promotion, and Youth Appeal of Little Cigars and Cigarillos, United States, 2015. Nicotine & Tobacco Research. 2020. ntaa005, https://doi.org/10.1093/ntr/ntaa005

^{xvi}CDC. E-Cigarette, or Vaping, Products Visual Dictionary. Accessed November 8, 2020.

https://www.cdc.gov/tobacco/basic_information/e-cigarettes/pdfs/ecigarette-or-vaping-products-visualdictionary-508.pdf

^{xvii} Public Health Law Center. Juul & The Guinea Pig Generation Revisited: Juul's Spawning of the Youth Vaping Epidemic. July 2020. Accessed November 8, 2020.

ⁱ Truth Initiative. Tobacco Nation: An ongoing crisis. https://truthinitiative.org/tobacconation. Accessed November 13, 2020.

ⁱⁱ US Census Bureau. QuickFacts: Boone County, Missouri. Accessed November 13, 2020. https://www.census.gov/quickfacts/fact/table/boonecountymissouri/

ⁱⁱⁱ American Lung Association. State of Tobacco Control Report: Missouri. Accessed November 13, 2020. <u>https://www.lung.org/research/sotc/state-grades/missouri</u>

^{iv} Campaign for Tobacco Free Kids. The Toll of Tobacco in Missouri.

https://www.tobaccofreekids.org/problem/tollus/missouri. Accessed October 26, 2020.

^v 2017 BRFSS data via County Health Rankings & Roadmaps.

https://www.countyhealthrankings.org/app/missouri/2020/measure/factors/9/map. Accessed November 13, 2020. ^{vi} US Census Bureau. QuickFacts: Boone County, Missouri. Accessed November 13, 2020.

https://www.census.gov/quickfacts/fact/table/boonecountymissouri/

^{vii} US Census Bureau. QuickFacts: Boone County, Missouri. Accessed November 13, 2020.

https://www.census.gov/quickfacts/fact/table/boonecountymissouri/

^{viii} Sanders-Jackson A, Parikh NM, Schleicher, NC, Fortmann SP, Henriksen L. Convenience store visits by US adolescents: Rationale for healthier retail environments. Health & Place.2015;34: 3-66. *doi:10.1016/j.healthplace.2015.03.011*

https://www.publichealthlawcenter.org/sites/default/files/resources/JUUL-and-the-Guinea-Pig-GenerationRevisited.pdf

^{xviii}Wang TW, Neff LJ, Park-Lee E, Ren C, Cullen KA, King BA. E-cigarette Use Among Middle and High School Students
 United States, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1310–1312. DOI:

http://dx.doi.org/10.15585/mmwr.mm6937e1external icon.

^{xix}Wang TW, Neff LJ, Park-Lee E, Ren C, Cullen KA, King BA. E-cigarette Use Among Middle and High School Students
 — United States, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1310–1312. DOI:

http://dx.doi.org/10.15585/mmwr.mm6937e1external icon.

^{xx}CBS News. Juul halts sales of fruit and dessert flavors for e-cigarettes. October 17, 2019. Accessed November 8, 2020. https://www.cbsnews.com/news/juul-halts-sales-of-fruit-and-dessert-flavors-for-e-cigarettes-vaping-today-2019-10-17/

^{xxi} Campaign for Tobacco Free Kids. Juul's Decision to End Sales of Mint Pods Is Not a Substitute for FDA Action to Remove All Flavored E-Cigarettes. November 7, 2019. Accessed November 8, 2020.

https://www.tobaccofreekids.org/press-releases/2019_11_07_juul_mint

^{xxii} Diaz MC, Donovan EM, Schillo BA, *et al*. Menthol e-cigarette sales rise following 2020 FDA guidance. *Tobacco Control Published* Online First: 23 September 2020. doi: 10.1136/tobaccocontrol-2020-05605

^{xxiii} Ali FRM, Diaz MC, Vallone D, et al. E-cigarette Unit Sales, by Product and Flavor Type — United States, 2014– 2020. MMWR Morb Mortal Wkly Rep 2020; 69:1313–1318. DOI:

http://dx.doi.org/10.15585/mmwr.mm6937e2external icon

^{xxiv}Wang TW, Neff LJ, Park-Lee E, Ren C, Cullen KA, King BA. E-cigarette Use Among Middle and High School Students
 — United States, 2020. MMWR Morb Mortal Wkly Rep 2020; 69:1310–1312.

DOI: http://dx.doi.org/10.15585/mmwr.mm6937e1external icon.

^{xxv}Truth Initiative. New federal data: Flavored e-cigarettes continue to drive youth vaping epidemic, with disposable use up 1,000\$ among high schoolers. https://truthinitiative.org/research-resources/emerging-

tobaccoproducts/new-federal-data-flavored-e-cigarettes-continue-drive. Accessed November 2, 2020.

^{xxvi} U.S. Food and Drug Administration. FDA Notifies Companies, Including Puff Bar, to Remove Flavored Disposable E-Cigarettes and Youth-Appealing E-Liquids from Market for Not Having Required Authorization. July 20, 2020. Accessed November 8, 2020. <u>https://www.fda.gov/news-events/press-announcements/fda-notifies-</u> companiesincluding-puff-bar-remove-flavored-disposable-e-cigarettes-and-youth

^{xxvii} Campaign for Tobacco Free Kids. FDA Action Against Puff Bar and Other Disposable E-Cigarettes Is a Positive Step to Protect Kids, but Not a Substitute for a Ban on All Flavored Products. July 20, 2020. Accessed November 8, 2020. <u>https://www.tobaccofreekids.org/press-releases/2020_07_20_fda-puff-bars</u>

^{xxviii} Truth Initiative. What we know and don't know about Puff Bar right now. August 19, 2020. Accessed November 8, 2020. <u>https://truthinitiative.org/research-resources/emerging-tobacco-products/what-we-know-and-dontknow-about-puff-bar-right-now</u>

^{xxix}Cornelius ME, Driezen P, Fong GT, et al. Trends in the use of premium and discount cigarette brands: findings from the ITC US Surveys (2002-2011). Tobacco Control. 2013; 23: i48-i53. doi:10.1136/tobaccocontrol-2013-051045 ^{xxx} U.S. Census Bureau. QuickFacts: Boone County, Missouri.

https://www.census.gov/quickfacts/boonecountymissouri. Accessed October 20, 2020.

 ^{xxxi} Henriksen L, Schleicher NC, Barker DC, Liu Y, Chaloupka FJ. Prices for Tobacco and Nontobacco Products in Pharmacies Versus Other Stores: Results from Retail Marketing Surveillance in California and in the United States.
 American Journal of Public Health. 2016;106 (10): 1858-1864. doi:10.2105/AJPH.2016.303306
 ^{xxxii} U.S. Census Bureau. QuickFacts: Boone County, Missouri.

https://www.census.gov/quickfacts/boonecountymissouri. Accessed October 20, 2020.

^{xxxiii} Federal Trade Commission. FTC Releases Reports on Cigarettes and Smokeless Tobacco Sales and Marketing Expenditures for 2018. December 30, 2019. Accessed October 16, 2020. https://www.ftc.gov/news-

events/pressreleases/2019/12/ftc-releases-reports-cigarette-smokeless-tobacco-sales-marketing

^{xxxiv} U.S. Department of Health and Human Services. Preventing Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2012.

APPENDIX C



HOW SCHOOLS CAN HELP STUDENTS STAY TOBACCO-FREE

Schools are in a uniquely powerful position to play a major role in reducing the serious problem of smoking and other tobacco use by kids. Children spend almost a third of their waking time in school, or about 135 hours per month; and much of the peer pressure kids feel regarding whether or not to use tobacco occurs in school.¹ Nearly 90 percent of adult smokers begin smoking at or before age 18.²

A national survey in 2020 found that 2.2 percent of eighth graders, 3.2 percent of tenth graders, and 7.5 percent of twelfth graders had smoked in the past month.³ Unfortunately, this problem can begin long before high school or even junior high. Though very little data about smoking is regularly collected for kids under 12, the peak years for first trying to smoke appear to be in the sixth and seventh grades (or between the ages of 11 and 13), with a considerable number starting even earlier.⁴ In 2015, 3.8 percent of eighth grade students reported having had their first cigarette by the end of fifth grade (ages 10 to 11).⁵ If current trends continue, 5.6 million kids under the age of 18 who are alive today will ultimately die from smoking-related disease.⁶

Nicotine is a highly addictive drug; and adolescents, who are still going through critical periods of growth and development, are particularly vulnerable to its effects.⁷ Symptoms of serious addiction, which can lead to years of tobacco use and dependence, can appear within weeks or even days after occasional smoking begins.⁸ Smoking and other tobacco use causes numerous immediate, sometimes irreversible, health effects and risks that can seriously damage kids' health well before they leave school or reach adulthood.⁹

Because of the addictive power of nicotine, about three out of four teen smokers ends up smoking into adulthood, even if they intend to quit after a few years.¹⁰ Smoking may also be a "gateway" to illegal drug use. Studies show that nicotine addiction often precedes the use of other drugs and is a risk factor for future use of drugs and alcohol.¹¹

The Role of Schools in Reducing Youth Smoking and Other Tobacco Use

For schools to effectively prevent and reduce youth tobacco use among their students, they must create an environment that encourages anti-tobacco beliefs and behaviors. This fact sheet offers a brief summary of suggested anti-tobacco policies and programs for schools recommended by the U.S. Centers for Disease Control and Prevention and other youth tobacco prevention experts.¹² For more detailed information, please refer to the cited references.

Forbid tobacco use by students, staff and visitors on all school grounds and at all school- sponsored events. School tobacco-free policies that are clearly and consistently communicated, applied and enforced reduce tobacco use among students.¹³ While just making sure that no kids use tobacco at school is helpful, also prohibiting tobacco use by teachers, other school staff, and visitors sends a much more powerful and constructive tobacco-free message. And while adopting firm tobacco-free policies for all school properties and events will have a strong positive impact in and of themselves, these policies are even more effective when accompanied by prevention and cessation education.¹⁴ Many schools are already required to prohibit smoking because the Federal Pro Children's Act of 1994 prohibits

smoking in facilities that regularly provide certain Federally-funded children's services.¹⁵

- Provide comprehensive tobacco prevention education. School-based education programs to prevent and reduce youth tobacco use work, but they have to be done right.¹⁶ To work best, such programs should comprehensively address all aspects of tobacco use, including the short- and long- term negative health effects, social acceptability, social influences, negative social consequences, peer norms and peer pressure, resistance and refusal skills, and media literacy as it relates to tobacco marketing and advertising.¹⁷ In addition, it is not enough to offer anti-tobacco education only in middle school or early high school. Students should receive this instruction and guidance, in one form or another, throughout their educational experience.¹⁸ Effective youth tobacco prevention programs are grade and age sensitive, with the most intense instruction in middle school and reinforcement throughout high school.¹⁹
- Provide program-specific training for teachers. When teachers are trained to properly deliver tobacco prevention curriculum, the success of the overall program is greatly improved.²⁰ Effective training should include a review of curriculum content, modeling of program activities by skilled trainers and the opportunity for teachers to practice implementing program activities.²¹
- Involve parents and families in school efforts to prevent tobacco use. Families have an enormous influence on students' tobacco perceptions and attitudes, and family members should be involved in school tobacco-free efforts as much as possible. Programs that include interactive homework assignments that educate and involve parents and other family members not only increase family discussions on this important topic but can lead to better home policies about tobacco use and even encourage adult tobacco users to try to quit.²²
- Provide program-specific training for teachers. When teachers are trained to properly deliver tobacco prevention curriculum, the success of the overall program is greatly improved.²⁰ Effective training should include a review of curriculum content, modeling of program activities by skilled trainers and the opportunity for teachers to practice implementing program activities.²¹
- Involve parents and families in school efforts to prevent tobacco use. Families have an enormous influence on students' tobacco perceptions and attitudes, and family members should be involved in school tobacco-free efforts as much as possible. Programs that include interactive homework assignments that educate and involve parents and other family members not only increase family discussions on this important topic but can lead to better home policies about tobacco use and even encourage adult tobacco users to try to quit.²²
- Offer interactive tobacco-free projects for students. To reinforce the school's tobacco-free policies and strengthen its related programs, schools should offer students opportunities to work on projects to reduce the pro-tobacco influences in their communities. For example, students could do a survey of stores near their school that advertise and sell tobacco products, and then write letters to the store owners urging them to reduce or eliminate their externally visible tobacco-product ads. Similarly, students could start a letter-writing campaign to encourage magazines available in the school library to stop running any tobacco-product advertisements. The Campaign for Tobacco-Free Kids' Kick Butts Day activity guide describes additional antismoking projects for students that can be done independently or as part of Kick Butts Day each year: http://www.kickbuttsday.org/.²³
- Help tobacco-using students and staff quit. Efforts to reduce tobacco use among school kids must focus on more than just preventing kids from starting. Too many kids already use tobacco products, and these kids need help quitting. Most smokers want to quit smoking. In 2019, nearly half (47.6%) of high school tobacco users tried to quit using tobacco.²⁴ In 2015, 55.4 percent of adults tried to quit smoking, but only 7.4 percent were successful in staying quit for six months or more.²⁵ Schools can improve these quitting percentages by providing effective cessation assistance to their students and staff who use tobacco. If school-run cessation programs are not possible, schools can still provide students and staff with information on how to quit and on how to link up with community-based cessation programs—or even bring program representatives to the schools. If there is a shortage of available cessation programs, schools can play an important

role in developing new ones by partnering with community health, youth, and other volunteer organizations. In any such efforts, schools should be mindful of the fact that successful cessation approaches differ for kids and adults. Cessation programs for adolescents, for example, should focus more on immediate consequences, offer specific attainable goals, and use contracts that include rewards.²⁶

- Adopt a firm school policy of not accepting any funding, curricula or other materials from any tobacco company. Tobacco companies produce and market incredibly harmful and addictive products, and they rely on kids to replace their adult customers who die or quit. For that reason, schools should be completely off limits to tobacco companies. But the major cigarette companies still try to get schools to accept all sorts of assistance—like book covers, industry sponsored tobacco prevention curricula and "anti-youth-smoking" funding books—as part of their much broader public relations and political strategies. Some schools say that the only way they can offer tobacco prevention programs and materials to their students is by taking these tobacco-company "gifts." Yet, in many cases, the schools have not even tried to find or develop alternative sources of income or assistance. Regardless, accepting tobacco company funding and materials always benefits the tobacco companies a lot more than the school, and it's always a bad deal for our kids.²⁷
- Evaluate the school's tobacco-free programs at regular intervals. Schools should regularly evaluate their success at implementing smoke-free policies, programs and curriculum components, as well as their success at decreasing students' tobacco use. Such evaluations are necessary for schools to determine which areas of their program need improvement, as well as to demonstrate the positive effects of the program to students, parents and the community, as well as to other schools who have not adopted tobacco prevention programs.

By taking some or all of these steps, schools can have an enormous impact on the current and future health and well-being of their students.

Campaign for Tobacco-Free Kids, December 16, 2020

¹ See e.g., Jackson C, "Initial and experimental stages of tobacco and alcohol use during late childhood: relation to peer, parent, and personal risk factors," *Addictive Behaviors* 22(5):685-98, Sept-Oct 1997. See, also, Banks, M, et al., "Adolescent attitudes to smoking: their influence on behavior," *Int'l Jnl of Health Education* 24(1):39-44, 1981.

² United States Department of Health and Human Services. Substance Abuse and Mental Health Services Administration. Center for Behavioral Health Statistics and Quality. National Survey on Drug Use and Health, 2014. ICPSR36361-v1. Ann Arbor, MI: Inter-university Consortium for Political and Social Research [distributor], 2016-03-22. <u>http://doi.org/10.3886/ICPSR36361.v1</u>.

³ University of Michigan, Monitoring the Future Study, 2020, <u>http://monitoringthefuture.org/data/20data.html#2020data-drugs</u>. [This school-based study does not survey kids who have dropped out of school, who tend to have higher smoking rates].

⁴ Miech, RA, et al., *Monitoring the Future National Survey Results on Drug Use*, 1975-2015: Volume 1, Secondary School Students, Ann Arbor, Institute for Social Research, The University of Michigan, 2016. <u>http://www.monitoringthefuture.org/pubs/monographs/mtf-vol1_2015.pdf</u>.

⁵ Miech, RA, et al., *Monitoring the Future National Survey Results on Drug Use, 1975-2015: Volume 1, Secondary School Students*, Ann Arbor, Institute for Social Research, The University of Michigan, 2016. <u>http://www.monitoringthefuture.org/pubs/monographs/mtf-vol1_2015.pdf</u>.

⁶ HHS, "The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General," 2014, <u>http://www.surgeongeneral.gov/library/reports/50-years-of-progress/index.html</u>.

⁷ HHS, "The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General," 2014, <u>http://www.surgeongeneral.gov/library/reports/50-years-of-progress/index.html</u>.

⁸ DiFranza ,JR, et al., "Initial symptoms of nicotine dependence in adolescents," *Tobacco Control* 9:313-19, September 2000.

⁹ HHS, "Preventing Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General," 2012, <u>http://www.surgeongeneral.gov/library/reports/preventing-youth-tobacco-use/full-report.pdf</u>. See also, Campaign for Tobacco-Free Kids (TFK) factsheet, *Smoking's Immediate Effects on the Body*, <u>http://tobaccofreekids.org/research/factsheets/pdf/0264.pdf</u>.

¹⁰ HHS, "Preventing Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General," 2012, http://www.surgeongeneral.gov/library/reports/preventing-youth-tobacco-use/full-report.pdf.

¹¹ HHS, *Preventing Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General,* HHS, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2012. See also, TFK factsheet, *Smoking and Other Drug Use*, <u>http://tobaccofreekids.org/research/factsheets/pdf/0106.pdf</u>.

¹² Information and recommendations for school policies have been derived from CDC, *Guidelines for School Health Programs to Prevent Tobacco Use and Addiction, MMWR*, 43(RR-2), February 25, 1994, www.cdc.gov/mmwr/preview/mmwrhtml/00026213.htm.

¹³ Grimes, J, et al., "Educational factors influencing adolescent decision-making regarding use of alcohol and drugs," *Jnl of Alcohol and Drug Education* 35:1-15, Fall 1989.

¹⁴ Pentz, M, et al., "The power of policy: the relationship of smoking policy to adolescent smoking," *American Jnl of Public Health (AJPH)*, 79:857-62, July 1989.

15 Title 20 USC 6081.

¹⁶ See TFK fact sheet, School-Based Programs Reduce Tobacco Use, <u>http://www.tobaccofreekids.org/research/factsheets/pdf/0050.pdf</u>.

¹⁷ Flay, B, "Psychosocial approaches to smoking prevention: a review of findings," *Health Psychology* 4(5):449-88, Sept 1985. See, also, Best, J, et al., "Preventing cigarette smoking among school children," *Annual Reviews of Public Health* 9:161-201, 1988.

¹⁸ National Cancer Institute, "School programs to prevent smoking: the National cancer Institute's guide to strategies that succeed", 1990, HHS publication no. (NIH) 90-500.

¹⁹ Glynn, T, "Essential elements of school-based smoking prevention programs," *Jnl of School Health* 59(5):181-8, May 1989. Murray, D, et al., "Five- and six-year follow-up results from four seventh-grade smoking prevention strategies," *Jnl of Behavioral Medicine* 12(2):207-18, 1989. See, also, Flay, B, et al., "Six-year follow-up of the first Waterloo School Smoking Prevention Trial," *AJPH* 79(10):1371-6, October 1989.

²⁰ Connell, D, et al., "Summary of findings of the school health education evaluation: health promotion effectiveness, implementation, and costs," *Jnl of School Health* 55(8):316-21, October 1985. See, also, Gold, RS, et al., "Summary and conclusions of the THTM evaluation: the expert work group perspective," *Jnl of School Health* 61(1):39-42, January 1991.

²¹ Tortu, S, et al., "School-based smoking prevention: the teacher training process," *Preventive Medicine* 18(2):280-90, March 1989. See, also, Perry, C, et al., "Evaluating the statewide dissemination of smoking prevention curricula: factors in teacher compliance," *Jnl of School Health* 60(10):501-4, December 1990.

²² Perry, C, et al., "Parental involvement in cigarette smoking prevention: two pilot evaluations of the 'Unpuffables Program," *Jnl of School Health* 60(9): 443-7, November 1990.

²³ For more information on Kick Butts Day, visit <u>www.kickbuttsday.org</u>.

²⁴ CDC, 2019 High School Youth Risk Behavior Survey Data. Available <u>https://yrbs-</u>explorer.services.cdc.gov/#/tables?guestionCode=H39&topicCode=C02&year=2019. Accessed on August 21, 2020.

²⁵ <u>CDC</u>, Quitting Smoking Among Adults—United States, 2000-2015," *MMWR* 65(52): 1457-1464, January 6, 2017, <u>https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6552a1.pdf</u>.

²⁶ Weissman W et al., "Development and preliminary evaluation of a cessation program for adolescent smokers," *Psychology of Addictive Behaviors* 1(1):84-91, March 1987. See, also, HHS, *The health consequences of smoking: nicotine addiction – a report of the Surgeon General*, 1988.

²⁷ See, e.g., American Heart Association, American Cancer Society, et al., Letter to state boards of education, August 16, 2001; TFK factsheets on industry youth prevention programs, <u>http://www.tobaccofreekids.org/facts_issues/fact_sheets/industry/prevention/</u>.