

**Health Impact Review of HB 1932
Concerning vapor products (2019 Legislative Session)**

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Full review

The full Health Impact Review report is available at:

<https://sboh.wa.gov/Portals/7/Doc/HealthImpactReviews/HIR-2020-01-HB1932.pdf>

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Executive Summary
HB 1932, Concerning vapor products (2019 Legislative Session)

Evidence indicates that HB 1932 would likely decrease initiation and use of vapor products and other tobacco products among youth and young adults, thereby improving health outcomes. It is unclear how the bill would impact health inequities.

BILL INFORMATION

Sponsors: Pollet, Jinkins, Tarleton, Stanford, Appleton, and Valdez

Summary of Bill:

This summary highlights all provisions in the bill. However, this analysis was scoped to assess only the provisions prohibiting the sale of flavored vapor products.

- Prohibits the sale of flavored vapor products and flavored marijuana vapor products, beginning January 2020, and regulates vapor product advertising.
- Establishes a vapor products stewardship program to require producers of vapor products, including marijuana vapor products, to finance the collection, transportation, recycling, and disposal of vapor products sold for use in Washington State.
- Grants the Department of Health authority to develop vapor product labeling requirements including disclosures of ingredients and potential harmful effects.

HEALTH IMPACT REVIEW

Summary of Findings:

This Health Impact Review found the following evidence for relevant provisions in HB 1932:

- **Strong evidence** that prohibiting the sale of flavored vapor products will likely decrease initiation and use of vapor products among adolescents and young adults.
- **Strong evidence** that decreasing initiation and use of vapor products among adolescents and young adults will likely decrease initiation and use of tobacco products among these populations.
- **Very strong evidence** that decreasing use of vapor products among adolescents and young adults will likely improve health outcomes.
- **Very strong evidence** that decreasing use of tobacco products among adolescents and young adults will improve health outcomes.
- **Unclear evidence** of the bill's impacts on health inequities. Other factors may influence how this bill impacts inequities such as access to flavored vapor products on tribal lands and military bases and use of other flavored tobacco products. These factors are analyzed in more detail in the full Health Impact Review.

Introduction and Methods

A Health Impact Review is an analysis of how a proposed legislative or budgetary change will likely impact health and health disparities in Washington State ([RCW 43.20.285](#)). For the purpose of this review ‘health disparities’ have been defined as the differences in disease, death, and other adverse health conditions that exist between populations ([RCW 43.20.270](#)). This document provides summaries of the evidence analyzed by State Board of Health staff during the Health Impact Review of House Bill 1932 ([HB 1932](#)).

Staff analyzed the content of HB 1932 and created a logic model depicting possible pathways leading from the provisions of the bill to health outcomes. We consulted with experts and contacted key informants about the provisions and potential impacts of the bill. We conducted an objective review of published literature for each pathway using databases including PubMed, Google Scholar, and University of Washington Libraries. More information about key informants and detailed methods are available upon request.

The following pages provide a detailed analysis of the bill including the logic model, summaries of evidence, and annotated references. The logic model is presented both in text and through a flowchart (Figure 1). The logic model includes information on the strength-of-evidence for each relationship. The strength-of-evidence has been defined using the following criteria:

- **Not well researched:** the review of literature yielded few if any studies or only yielded studies that were poorly designed or executed or had high risk of bias.
- **A fair amount of evidence:** the review of literature yielded several studies supporting the association, but a large body of evidence was not established; or the review yielded a large body of evidence but findings were inconsistent with only a slightly larger percentage of the studies supporting the association; or the research did not incorporate the most robust study designs or execution or had a higher than average risk of bias.
- **Strong evidence:** the review of literature yielded a large body of evidence on the relationship (a vast majority of which supported the association) but the body of evidence did contain some contradictory findings or studies that did not incorporate the most robust study designs or execution or had a higher than average risk of bias; or there were too few studies to reach the rigor of “very strong evidence;” or some combination of these.
- **Very strong evidence:** the review of literature yielded a very large body of robust evidence supporting the association with few if any contradictory findings. The evidence indicates that the scientific community largely accepts the existence of the association.

This review was subject to time constraints, which influenced the scope of work for this review. The annotated references are only a representation of the evidence and provide examples of current research. In some cases only a few review articles or meta-analyses are referenced. One article may cite or provide analysis of dozens of other articles. Therefore the number of references included in the bibliography does not necessarily reflect the strength-of-evidence. In addition, some articles provide evidence for more than one research question, so are referenced multiple times.

Analysis of HB 1932 and the Scientific Evidence

Summary of relevant background information

- In June 2009, the Family Smoking Prevention and Tobacco Control Act (2009 Tobacco Control Act) was signed into law in part to reduce smoking rates among adolescents.¹ It gave the U.S. Food and Drug Administration (FDA) authority to regulate the manufacture, distribution, and marketing of tobacco products.¹ The Tobacco Control Act banned flavors, except menthol and tobacco, in cigarettes¹ specifically as one strategy to reduce the use of cigarettes among young people.
- In May 2016, the FDA finalized a rule to extend its authority over all tobacco products, known as the ‘Deeming Rule.’² Newly regulated products, including electronic cigarettes, are required to comply with all Federal Food, Drug, and Cosmetic Act and FDA regulations specific to tobacco products.²
- In 2018, the FDA took action to reduce youth access to e-cigarettes. The FDA:
 - Issued 1,300 warning letters and fines to “retailers who illegally sold JUUL and other e-cigarette products to minors,” marking the “largest coordinated enforcement effort in the FDA’s history.”³ As of September 11, 2019, FDA had issued more than 8,600 warning letters and more than 1,000 fines to retailers (both online and brick-and-mortar stores) for sales of ENDS and their components to minors.⁴
 - Issued letters to the top five-selling e-cigarette brands (which comprise 97% of the U.S. e-cigarette market) requiring each company to submit plans detailing how they will limit marketing and youth access to their product.³
 - Launched “The Real Cost” youth e-cigarette prevention campaign.⁵
 - Issued a directive that all “flavored [electronic nicotine delivery system] products (other than tobacco, mint, and menthol flavors or non-flavored products) must be sold in age-restricted, in-person locations and, if sold online, under heightened practices for age verification.”⁵
 - Issued a Notice of Proposed Rulemaking to ban menthol in combustible tobacco products, including cigarettes and cigars.⁵
- In November 2018, JUUL Labs, which has more than 70% of the U.S. e-cigarette market share, announced that it would suspend sales of most of its flavored e-cigarette pods in retail stores and would discontinue its media promotions.⁶ By early 2019, competitors quickly filled the market demand with similar flavored products or JUUL-compatible flavored nicotine cartridges.⁷
- In December 2018, the Office of the Surgeon General issued an advisory about e-cigarette use among youth.⁸ The statement noted that, “any e-cigarette use among young people is unsafe, even if they do not progress to future cigarette smoking.”⁸
- In 2019, the Washington State Legislature passed EHB 1074 (Chapter 15, Laws of 2019), Protecting youth from tobacco products and vapor products.⁹ The law increases the legal age of sale of tobacco and vapor products from 18 to 21 years of age and permits the Governor to seek government-to-government consultations with tribes about raising the

minimum legal age of sale in cigarette tax compacts. The law is effective January 1, 2020.

- In July 2019, FDA launched its first youth e-cigarette prevention TV ads educating youth about the dangers of e-cigarette use.¹⁰
- In July 2019, the Centers for Disease Control (CDC), FDA, state and local health departments, and other clinical and public health partners began investigating outbreaks of lung injury associated with e-cigarette use.¹¹ As of September 17, 2019, CDC had received reports of 530 cases of lung injury associated with use of e-cigarettes or vaping products from 38 states and 1 U.S. territory.¹¹ Seven deaths were confirmed in 6 states.¹¹ CDC received complete sex and age data on 373 of 530 cases: 67% of cases are 18-34 years old; 16% of cases are under 18 years of age; and the majority of cases are male.¹¹ While this investigation is ongoing, CDC stated, “All patients have a reported history of e-cigarette product use, and no consistent evidence of an infectious cause has been discovered. Therefore, the suspected cause is a chemical exposure.”¹¹
 - On September 11, 2019, Public Health – Seattle & King County (PHSKC) announced the first confirmed Washington State case of severe pulmonary disease associated with e-cigarette use in a King County teenager.¹²
 - On September 16, 2019, the Washington State Department of Health (DOH) confirmed two new cases (a patient in their teens and a patient in their twenties) identified by the Spokane Regional Health District.¹³
- In September 2019, Michigan became the first state to prohibit the sale of flavored vapor products.¹⁴ California, Massachusetts, and New York are considering similar proposals.¹⁴
- On September 9, 2019, FDA issued a warning letter to JUUL Labs Inc. for marketing unauthorized modified risk tobacco products to consumers, including statements made by a JUUL representative to youth in a school.¹⁵ The Acting FDA Commissioner stated, “before marketing tobacco products for reduced risk, companies must demonstrate with scientific evidence that their specific product does in fact pose less risk or is less harmful [than cigarettes].”¹⁵
- On September 11, 2019, the Federal administration announced that FDA would “outline a plan within the coming weeks for removing flavored e-cigarettes and nicotine pods from the market, excluding tobacco flavors.”¹⁴ Prohibited flavors would include mint and menthol.

Summary of HB 1932

- Prohibits the sale of flavored vapor products and flavored marijuana vapor products beginning January 2020, and regulates vapor product advertising.
- Establishes a vapor products stewardship program to require producers of vapor products, including marijuana vapor products, to finance the collection, transportation, recycling, and disposal of vapor products sold for use in Washington State.

- Requires vapor product retailers and certain marijuana retailers to accommodate stewardship organizations and make opportunities available for the collection of unwanted vapor products to the general public during all business hours.
- Grants the Department of Ecology rule-making and enforcement authority to administer the stewardship program, establishes civil penalties, and authorizes an administrative fee on vapor product retailers and certain marijuana retailers.
- Grants the Department of Health authority to develop vapor product labeling requirements, including disclosures of ingredients and potential harmful effects.

Health impact of HB 1932

Evidence indicates that HB 1932 would likely decrease initiation and use of vapor products and other tobacco products among youth and young adults, thereby improving health outcomes. It is unclear how the bill would impact health inequities.

Pathway to health impacts

The potential pathway leading from the provisions of HB 1932 to decreased health inequities are depicted in Figure 1. There is strong evidence that prohibiting the sale of flavored vapor products will likely decrease initiation and use of vapor products among adolescents and young adults.¹⁶⁻²⁷ There is also strong evidence that decreasing initiation and use of vapor products among adolescents and young adults will likely decrease initiation and use of tobacco products among these populations.^{17,28-33} There is very strong evidence that decreasing use of vapor products among adolescents and young adults will likely improve health outcomes for these individuals.^{28-30,32-45} There is also very strong evidence that decreasing use of tobacco products among adolescents and young adults will improve health outcomes for these individuals.⁴⁶⁻⁴⁸ Finally, it is unclear how the bill will impact health inequities.⁴⁹⁻⁵⁴ Other factors may influence how this bill impacts inequities such as access to flavored vapor products on tribal lands and military bases and use of other flavored tobacco products. These factors are analyzed in more detail beginning on page 15.

Scope

This analysis focuses on the provisions in the bill related to prohibiting the sale of flavored vapor products. Provisions regulating the advertising of vapor products and the establishment of a vapor products stewardship program are not included in this analysis.

Due to time limitations, we only researched the most direct connections between the provisions of the bill and decreased health inequities and did not explore the evidence for all possible pathways. Therefore, this Health Impact Review focused on the impact that prohibiting the sale of flavored vapor products would have on health outcomes and health equity for adolescents and young adults. Additional potential pathways are discussed in “Other Considerations” beginning on page 17. We did not evaluate potential impacts related to:

- The economic impacts of prohibiting the sale of flavored vapor products on industry or businesses.
- Enforcement and compliance efforts for retailers. HB 1932 authorizes the Washington State Liquor and Cannabis Board (Board), in conjunction with law enforcement agencies, to “conduct random and unannounced inspections of a retailer to investigate whether flavored vapor products are sold or offered for sale”

and allows the Board to “seize any flavored vapor products found during such inspections.” Compliance violations may result in the Board revoking the retailer’s license and/or a civil penalty (\$1,000 per day, up to \$10,000). Key informants in San Francisco shared that it is vital to conduct education and outreach (e.g., mailings and in person visits) with retailers following the passage of such legislation to answer their questions before enforcement begins (San Francisco Department of Public Health [SFDPH] and San Francisco Tobacco-Free Coalition, personal communication, September 2019). For example, outreach in San Francisco allowed the department to develop a list of ‘questionable’ flavored tobacco products from retailers’ perspectives and to provide clear guidance of what did or did not qualify as a flavored product.⁵⁵ Additionally, outreach efforts allowed retailers to indicate which languages they needed materials in to serve staff and customers.⁵⁵

Magnitude of impact

Estimates suggest there are over 460 brands and 8,000 flavors of e-cigarettes on the U.S. market.^{56,57} According to JUUL, 85% of its sales are from mint and other flavors.¹⁴

Adolescents and young adults

Overall, tobacco product use among middle and high school students decreased from 2011 to 2017 nationally.⁵⁸ Contrary to these declines, e-cigarette use has increased dramatically among middle and high school students, and e-cigarettes are now the most commonly used tobacco product among youth.^{5,8,28,58} E-cigarette use statistically significantly increased from 1.5% of high school students in 2011 to 20.8% of high school students in 2018.⁵⁹ For middle school students, 0.6% reported using e-cigarettes in 2011 compared to 4.9% in 2018.⁵⁹ The 2016-2017 Youth Risk Behavior Surveillance System also found that 42.4% of students had ever used an electronic vapor product and 13.2% currently used e-cigarettes.⁵⁰ In addition, CDC found that e-cigarette use increased 78% (from 11.7% to 20.8%) among high school students and 48% (from 3.3% to 4.9%) among middle school students from 2017 to 2018, reversing previous trends suggesting use may be declining.^{5,8,59} The next most popular tobacco products among high school students were cigars (7.7%) and cigarettes (7.6%).⁶⁰ In a Morbidity and Mortality Weekly Report, CDC attributed the increase in e-cigarette use from 2017 to 2018 to “recent popularity of e-cigarettes shaped like a USB flash drive, such as JUUL.”⁵⁹ The Office of the Surgeon General cited evidence that JUUL sales increased 600% from 2016 to 2017.⁸ Data from the 2019 Monitoring the Future Survey show the prevalence of past month nicotine vaping was more than 1 in 4 students in 12th grade; 1 in 5 in 10th grade; and 1 in 11 in 8th grade.⁶¹ Results show that “vaping prevalence more than doubled in each of the three grades from 2012 to 2019.”⁶¹

In Washington State, results of the 2018 Washington State Healthy Youth Survey (HYS) indicate the prevalence of current (i.e., past 30-day) vapor product use among 6th graders (3%), 8th graders (10%), 10th graders (21%), and 12th graders (30%) has significantly increased since 2016.⁵¹ However, these results may underestimate the true prevalence of e-cigarette/vapor product use. Evidence indicates that some adolescents and young adults do not consider using JUUL (i.e., JUULing) as using e-cigarette/vapor devices and may not report relevant behaviors when surveyed about vaping.⁶⁰ HYS data indicate that the most commonly reported substances “vaped” among current users across grade levels contain nicotine or flavor only (i.e., no nicotine

or tetrahydrocannabinol [THC]). However, it is likely that adolescents and young adults may not realize that products they are using contain nicotine (personal communication, August and September 2019). A 2019 analysis of convenience store and mass market sales data (2013-2018) found that zero-nicotine products accounted for less than 1% of the dollar market share across all years analyzed.⁶² Finally, HYS results also show greater statewide prevalence of past 30-day use of both e-cigarettes and cigarettes as grade level increases (6th grade: <1%, 12th grade: 6%).⁵¹

Effective January 1, 2020, the legal age of sale of tobacco and vapor products will increase from 18 to 21 years of age in Washington State (Chapter 15, Laws of 2019). The Health Impact Review of ESSB 1074 found that evidence indicates that this policy change would likely decrease use of tobacco and vapor products among youth and young adults, thereby improving health outcomes. However, while the policy change also permits the Governor to seek government-to-government consultations with tribes about raising the minimum legal age of sale in cigarette tax compacts, the legislation did not impact the purchase age on tribal lands or military bases, and young adults ages 18 to 20 could still purchase tobacco and vape products on tribal land or military bases.

Adults

Results of the 2017 National Health Interview Survey indicate an estimated 2.8% (6.9 million) of U.S. adults currently use e-cigarettes.⁶³ Moreover, 40.5% of current tobacco product users were daily users of e-cigarettes.⁶³ Among current tobacco product users who reported using 2 or more tobacco products the most prevalent tobacco product combination was cigarettes and e-cigarettes (30.1%).⁶³ Primary reasons for e-cigarette use among adults include “curiosity, flavoring, cost, consideration of others, convenience, and simulation of cigarettes, as well as to attempt to quit smoking.”⁶³

Logic Model

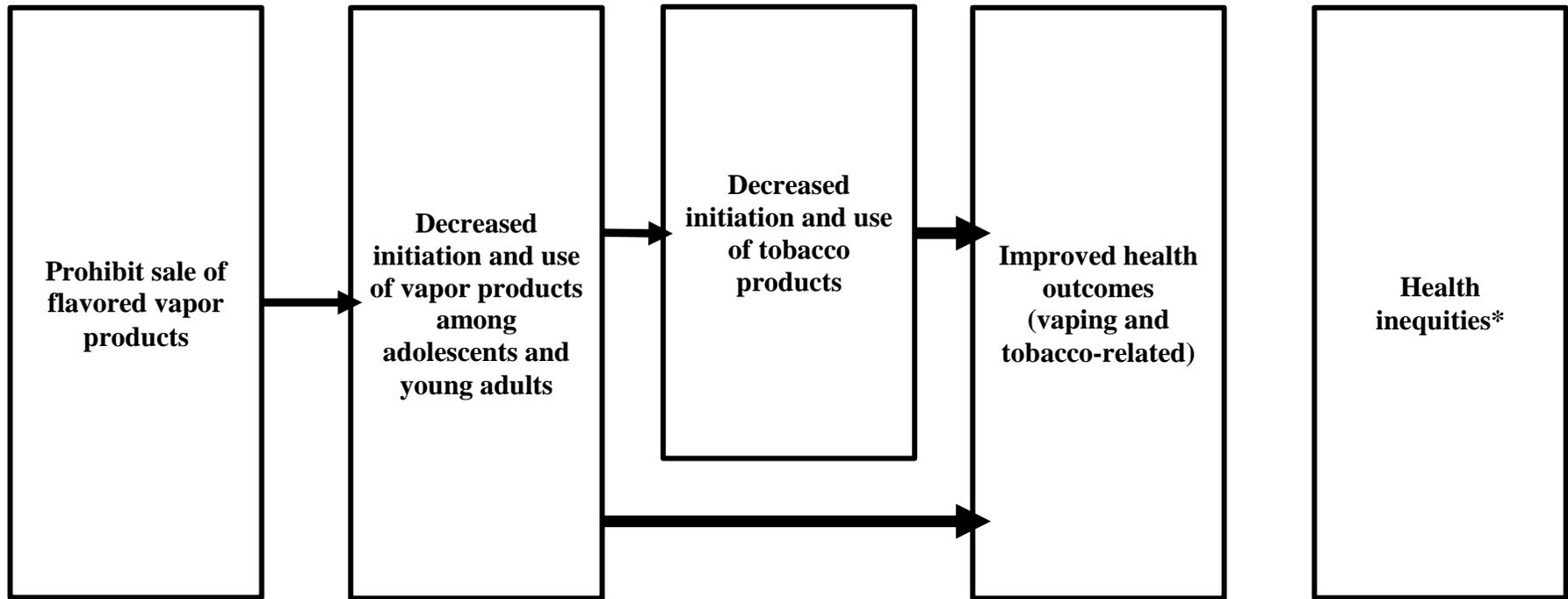
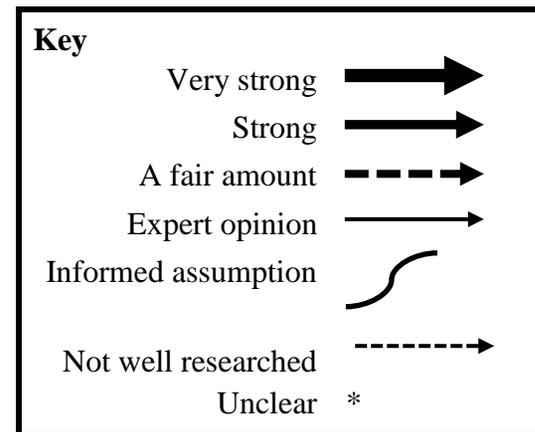


Figure 1:
Concerning vapor products
HB 1932



Summaries of Findings

Will prohibiting the sale of flavored vapor products decrease initiation and use of vapor products among adolescents and young adults?

There is strong evidence that prohibiting the sale of flavored vapor products (e.g., e-cigarettes, vapes, and JUUL) will likely result in decreased initiation and use of vapor products among adolescents and young adults.¹⁶⁻²⁷

In June 2018, voters in San Francisco, California passed Proposition E, which prohibited the sale or distribution of flavored tobacco products (including e-cigarettes).^{64,65} Analysts contacted staff at the San Francisco Department of Public Health (SFDPH) to determine if prohibiting the sale and distribution of flavored vapor products would result in compliance among retailers. Following its passage, the SFDPH and partners visited 801 retail sites to conduct education and outreach efforts with retailers to support compliance with the new ordinance.⁵⁵ Site visitors distributed posters, offered to supply written materials in additional languages, and collected questions regarding potentially flavored tobacco products. From December 2018 to March 2019, 13 SFDPH inspectors conducted 693 tobacco compliance inspections (out of 761 locations).⁵⁵ Of the inspections conducted in 2018 (n=360), flavored tobacco products were present at 284 locations (versus 58 with no flavored tobacco products present).⁵⁵ Of the inspections conducted from January through March of 2019 (n=362), flavored tobacco products were identified at just 50 locations (versus 279 with no flavored tobacco products present).⁵⁵ Researchers at Stanford University also conducted a compliance check of retailers in San Francisco, and unpublished results of their independent check indicate high compliance rates among retailers (SFDPH, personal communication, September 2019). Results suggest prohibiting the sale and distribution of flavored tobacco and nicotine products can result in compliance among retailers, thereby limiting access to flavored products.

Moreover, research consistently shows that flavors, and associated advertising, contribute to the appeal, initiation, and use of tobacco products, including vapor products, particularly among adolescents and young adults.¹⁶⁻²² For example, among adolescents (12-17 years old) in Texas who used e-cigarettes, 72.9% reported using e-cigarettes because they “come in flavors I like.”¹⁹ Flavors have been shown to increase positive (e.g., euphoria, relaxation) and decrease negative (e.g., nausea, coughing) subjective experiences among novice users.¹⁷ Such positive subjective experiences are associated with initiation and sustained cigarette smoking, whereas negative experiences may be associated with reduced odds of sustained cigarette use.¹⁷ Preferences for specific flavors (i.e., fruit, dessert, and alcohol) and the total number of flavors preferred have also been associated with more days of e-cigarette use among adolescents, “indicating that flavor preferences may play an important role in adolescent e-cigarette use.”²¹ A 2019 study found adolescents (12-17 years) and young adults (18-24 years) were more likely (4.58 times and 2.28 times, respectively) than adults 25 years of age and older to concurrently use multiple flavors.²² Results of a study of 3,878 U.S. adults showed 8% of participating e-cigarette users reported flavors as a reason for first trying e-cigarettes.⁶⁶ Meanwhile, 53% of respondents reported first using e-cigarettes out of curiosity and 30% reported first using them because they wanted to quit or reduce smoking.⁶⁶

Sweet and fruit flavors, in particular, strongly appeal to adolescents and young adults.^{18,20,21} Evidence from a small (n=20) double-blind laboratory study of young adults aged 19 to 34 who vape indicated that e-cigarette solutions that “stimulate orosensory perceptions of sweetness (in and of themselves) may be primary drivers of appeal.”²⁰ After controlling for flavor and nicotine, perceived sweetness was significantly positively associated with appeal ratings.²⁰ Specifically, “each one point increase in sweetness rating (0–100) was associated with an estimated 0.51 increase in ‘liking,’ a 0.51 increase in ‘willingness to use again,’ and a \$0.04 increase in ‘amount willing to pay for a day’s worth of the solution.’”²⁰ Meanwhile, “throat hit” (from nicotine) ratings were not positively associated with appeal and were inversely associated with liking.²⁰ Researchers re-analyzed data from those who reported non-sweet flavor preferences to determine if pre-existing flavor preferences influenced study outcomes. Findings from the overall sample held true for the sub-sample that preferred non-sweet flavors.²⁰

Evidence also suggests that advertisements for flavored vapor products, particularly for fruit and sweet flavors, are attractive to adolescents and young adults and are perceived as targeted toward them. For example, a majority of adolescents and young adults (14-21 years) surveyed believed advertisements for flavored e-liquids “target individuals about their age, not older adults.”²³ A 2018 study assessed whether nonsmoking young adults (ages 18-25 years) perceive sweet/fruit flavor e-cigarette advertisements more like sweets and fruits and less like tobacco, despite being equivalent to tobacco flavored e-cigarettes.¹⁸ Results showed “a significant impact of advertising for sweet/fruit flavors on increased neural cue-reactivity” compared to tobacco flavor e-cigarette advertisements.¹⁸ Sweet/fruit flavor advertising was also associated with “poorer memory for health warnings, increased visual attention to advertising content and decreased visual attention to warning labels, and relatively increased liking and intent to try these products.”¹⁸ This increased brain response to sweet/fruit versus tobacco flavored e-cigarette advertisements provides evidence of a relative product preference for sweet/fruit flavor e-cigarettes in nonsmoking young people.¹⁸

Additionally, study authors found that participating young adults who spent more time viewing the advertising content and less time viewing the warning label “reported greater liking and intentions to use e-cigarettes.”¹⁸ Authors concluded that advertising for sweet/fruit flavors “may increase positive associations with e-cigarettes and/or override negative associations with tobacco, and interfere with health warnings.”¹⁸ This evidence aligns with findings of a 2018 systematic review in which evidence from five studies show flavored tobacco products, including e-cigarettes, are perceived as less harmful than non-flavored products by younger participants.¹⁶

Evidence also indicates that restricting flavors in e-cigarettes and other tobacco products has the potential to substantially reduce use of these products by youth (12-17 years)²⁴ and young adults (18-29 years).^{24,25} While more than 90% of youth and young adult e-cigarette users surveyed in Texas reported using flavored products, approximately three-quarters of these “flavored e-cigarette users said that they would *not* use an e-cigarette if it was not available in a flavored form (e.g., candy, fruit, mint/menthol, etc.).”²⁴ While reported discontinued use was highest among e-cigarette users and hookah users, results suggest eliminating flavors in other tobacco products (i.e., cigar products, smokeless tobacco) would also decrease the use of these products among adolescents and young adults.²⁴ Another analysis of cross-sectional surveys of youth (12-

17 years old), young adults (18-29 years old), and older adults (30+ years old) found that fruit and candy flavors predominated for all age groups.¹⁹ Authors concluded, “restricting the range of e-cigarette flavors (e.g., eliminating sweet flavors, like fruit and candy) may benefit youth and young adult prevention efforts. However, it is unclear what impact this change would have on adult smoking cessation.”¹⁹

Removing availability of flavored products may also decrease initiation and use. The 2018 HYS found that, accessing products through non-social sources (e.g., buying from a store, the internet, or a vending machine) was most common among 12th graders (26%) compared to 10th (14%) and 8th graders (16%).⁵¹ A separate survey of over 1,700 youth aged 15 to 17 who reported vaping in the past 30 days found that 78.2% owned their own vaping device, with 32.2% purchasing their device online and 22.3% purchasing it in a vapor shop or lounge.⁶⁷ A survey with 9th and 12th grade students in California found that 9.3% reported buying tobacco products (including hookah, e-cigarettes, and cigarettes) from retailers directly.⁶⁸

Social availability was also a large access point, with 72.8% of youth reporting using someone else’s vaping device in the past 30 days, and 80.5% who borrowed stating that they borrowed from a friend.⁶⁷ In Washington State, results of the HYS found roughly 65% of students currently using tobacco and electronic vapor products reported accessing them through social sources (e.g., giving money to someone, “bumming”, from a person 18 or older, and taking from a store or family).⁵¹ A survey with 9th and 12th grade students in California found that 55% reported getting tobacco products (including hookah, e-cigarettes, and cigarettes) from peers.⁶⁸ One researcher suggested that, “social sources might be even more important for vaping than for smoking cigarettes; cigarette smokers likely get cigarettes from other people only when they do not possess their own, but vapers use others’ devices even when they have their own.”⁶⁷

Lastly, the 2009 Tobacco Control Act banned flavored cigarettes (except menthol and tobacco) as a result of evidence that flavored products attract youth.^{26,27} Research evaluating adolescent tobacco use before and after the ban found that banning flavored cigarettes was associated with a 17% decrease in cigarette smoking.²⁷ However, use of menthol cigarettes, cigars, and pipe tobacco increased significantly “implying substitution toward the remaining legal flavored tobacco products.”²⁷ Even with an overall 14% increase in the use of other flavored tobacco products, banning flavored cigarettes resulted in a net 6% decrease in the probability of adolescents using any tobacco product.²⁷ Study authors concluded that, “the results suggest the 2009 flavored cigarette ban did achieve its objective of reducing adolescent tobacco use, but effects were likely diminished by the continued availability of menthol cigarettes and other flavored tobacco products.”²⁷

Overall, there is strong evidence that prohibiting the sale and distribution of flavored vapor products will likely decrease initiation and use of products by adolescents and young adults.

Will decreasing initiation and use of vapor products among adolescents and young adults decrease initiation and use of other tobacco products among these populations?

There is strong evidence that decreasing initiation and use of vapor products among adolescents and young adults will likely result in decreased initiation and use of other tobacco products by these populations.^{17,28-32}

Evidence shows the use of e-cigarettes among youth is associated with future use of combustible cigarettes,²⁸⁻³³ potentially increasing risk of long-term negative health outcomes and resulting in an overall net negative impact on public health.^{5,28} Evidence suggests that adolescents and young adults who start using e-cigarettes may be more likely than their peers to begin using combustible cigarettes and other tobacco products.^{31-33,60} In a national survey of 12 to 17 year olds, researchers found that ever-using e-cigarettes was associated with 2.53 times greater odds of subsequently smoking cigarettes.²⁹ Another study found that using e-cigarettes was strongly and consistently associated with greater risk of cigarette smoking initiation among adolescents and young adults, and that e-cigarette use was an independent risk factor for cigarette smoking, even after controlling for multiple additional risk factors.³⁰ Moreover, results of a 2018 analysis of a pooled sample of U.S. adolescents found the risk of past-30-day smoking and of more frequent smoking after initiation was higher among those who at baseline had ever used e-cigarettes compared to those who had never used e-cigarettes.³¹

Additionally, the use of flavored e-cigarettes among adolescents and young adults increased significantly from 2013 to 2018, and use of flavored tobacco products by adolescents has been associated with increased risk of multiple tobacco product use (dual and poly tobacco use).¹⁷ An analysis of 2017 National Youth Tobacco Survey results found, after controlling for covariates, “[f]lavored tobacco use [among adolescent respondents] was significantly correlated with a greater risk of dual and poly tobacco use (2.09 times greater risk and 5.54 times greater risk, respectively), relative to single product use.”¹⁷ For dual and poly tobacco users, the most commonly used flavored tobacco products were e-cigarettes followed by cigars and conventional cigarettes.¹⁷ Research also indicated that 95% of adult smokers begin smoking before they turn 21⁶⁹ and early smoking onset is associated with greater likelihood of addiction and decreased likelihood of cessation.^{5,70}

Overall, there is strong evidence that reducing initiation and use of vapor products among adolescents and young adults will likely result in decreased initiation and use of other tobacco products among this population.

Will decreasing use of vapor products among adolescents and young adults improve health outcomes?

Evidence related to the impact of vapor product use on health is still emerging. Although some evidence has suggested that e-cigarettes may pose less risk to individuals than combustible cigarettes,^{28,34,35} the use of e-cigarettes has been shown to have negative impacts on health for adolescents and young adults,^{3,5,8,28,36} and there is very strong evidence that decreasing use of vapor products among adolescents and young adults will likely improve health outcomes for these individuals.^{28-30,32-45}

Generally, research has shown that e-cigarette use has numerous negative health impacts, including respiratory, cardiac, and digestive system effects; unintentional and intentional poisonings; and injuries due to explosion.⁷¹ In a 2018 report about the public health consequences of e-cigarettes, the National Academy of Sciences stated that, although e-cigarette use poses less risk to individuals than combustible cigarettes, there is conclusive evidence that use of e-cigarettes has multiple adverse impacts on health.²⁸ They found evidence that e-cigarettes can explode and cause burns and injuries; intentional or accidental exposure to e-

liquids can result in seizures, anoxic brain injury, vomiting, lactic acidosis, and other effects; and intentionally or unintentionally drinking or injecting e-liquids can be fatal.²⁸ From 2011 to 2017 the Washington Poison Center received 2,966 total cases related to nicotine exposure among children 0 to 12 years of age.³⁷ The majority of cases were in children under 5, and 22% (653) of cases were related to e-cigarettes.³⁷ In 2018, the Washington Poison Center received 136 cases specific to e-cigarettes, including 79 cases among children 0 to 12 years of age.⁷² Children were primarily exposed through ingestion, and experienced symptoms like vomiting, coughing/choking, drowsiness/lethargy, and pallor.³⁷

The National Academy of Sciences also found substantial evidence that e-cigarette use results in symptoms of dependence on e-cigarettes, formation of reactive oxygen species/oxidative stress, increased heart rate shortly after nicotine intake, and exposure to chemicals capable of causing DNA damage and mutagenesis, suggesting the possibility that long-term exposure could increase risk of cancer and adverse reproductive health outcomes.^{28,71} Overall, the report concluded that e-cigarettes contain and emit numerous potentially toxic substances (e.g., metals, mercury, formaldehyde, and other cancer-causing nitrosamines),^{28,73,74} and that nicotine intake among adult e-cigarette users is comparable to intake from combustible tobacco cigarettes.^{28,75} In addition, a study of JUUL products found levels of menthol at concentrations known to increase nicotine intake.⁷⁵ Lastly, a study of adolescents aged 13-18 years old who use e-cigarettes found that, compared to non-users, users had three times greater levels of five volatile organic compounds in their urine and saliva, most of which are known carcinogens.³⁸

A large body of recent research also found that solvents and flavor chemicals in e-cigarettes cause harm at the cellular level and are cytotoxic.^{50,57,71} Propylene glycol and glycerin are the most common solvents used in vapor products. While both are ‘generally recognized as safe’ for ingestion, propylene glycol and glycerin have been found to be cytotoxic when aerosolized through vaping.^{71,74} One study found that e-liquid refills containing glycerin were the most cytotoxic, and 91% of glycerin-based refill fluids were cytotoxic when aerosolized.⁷¹

There is also research showing that flavor chemicals are cytotoxic in both e-liquid and aerosol form. While many flavor chemicals used in vaping products have been approved for ingestion, they have not been tested for inhalation safety or toxicity.^{26,57,71,76} Flavor chemicals are not typically listed on e-cigarette packaging,²⁶ and most e-liquids contain multiple flavor chemicals. Many have been shown to contain harmful aerosol components and aldehydes, which impair lung function.^{26,57} One study found that nicotine and flavoring chemicals were equally responsible for compromising lung function.⁵⁷ A study evaluating 36 e-cigarette refill fluids representing a range of brands and flavors found that 54% were cytotoxic in both the fluid and aerosol form, and 23% were cytotoxic in the aerosol but not the fluid form.⁷¹ Another study looking specifically at flavor chemical concentrations in the eight pre-filled JUUL e-cigarette pods available on the market found that all e-liquids and corresponding aerosols were cytotoxic to human lung epithelial cells.⁷⁷ One study demonstrated that a single exposure to cinnamaldehyde flavoring in e-cigarettes impairs lung function, potentially resulting in the development or exacerbation of respiratory disease.^{40,78} Other studies have also shown that cherry-flavored products (benzaldehyde)⁷⁶ and chocolate-flavored products (2,5-dimethylpyrazine)⁷⁹ are potentially harmful.⁷¹ Flavor chemical concentrations have also been

found in some e-cigarette products at levels that exceed daily occupational exposure limits from inhalation.²⁶

Additional emerging research also supports the Institute of Medicine's finding that smoking e-cigarettes is associated with adverse effects such as airway and lung obstruction.³⁶ One study found that e-cigarette use is independently and significantly associated with increased odds of heart attack.³⁹ Data from 96,467 respondents to the 2014, 2016, and 2017 National Health Interview Survey found that adults that used e-cigarettes were 34% more likely to have a heart attack and 25% more likely to have coronary artery disease compared to adults that did not use e-cigarettes.⁵⁶ Users were at increased risk of heart attack and coronary artery disease regardless of whether they vaped occasionally or daily.⁵⁶ Other studies have found that e-cigarette devices emit particulate matter and that passive or secondhand exposure to vaping products could impact health.^{45,80} For example, a study among youth in Florida found that secondhand exposure to aerosol from electronic nicotine delivery systems was associated with higher odds of asthma attacks among youth with asthma.⁸⁰

In July 2019, CDC, FDA, state and local health departments, and other clinical and public health partners began investigating outbreaks of lung injury associated with e-cigarette use.¹¹ As of September 17, 2019, CDC had received reports of 530 cases, including 7 deaths, from 38 states and 1 U.S. territory.¹¹ The majority of patients have been between 18 and 34 years old.¹¹ Three cases have been confirmed in Washington State.¹³ While the disease investigation is ongoing, all reported cases have a history of using e-cigarette products containing nicotine, THC, or both.¹¹ A recent Morbidity and Mortality Weekly Report briefing from CDC explained that, "no consistent e-cigarette product, substance, or additive has been identified in all cases, nor has any one product or substance been conclusively linked to pulmonary disease in patients."⁸¹ However, "all patients have a reported history of e-cigarette product use, and no consistent evidence of an infectious cause has been discovered. Therefore, the suspected cause is a chemical exposure."¹¹ Among other recommendations, CDC recommended that youth and young adults never use e-cigarette products.⁸¹ CDC also noted that long-term treatment and impacts to lung function for these patients are unknown.⁸²

Lastly, evidence shows that most adolescents and young adults do not use e-cigarettes to quit smoking.^{31,60} For example, data from the National Youth Tobacco Survey (2016) showed only 7.8% of respondents cited cessation as a reason for e-cigarette use.³¹

Overall, there is very strong evidence that decreasing use of vapor products among adolescents and young adults will likely improve health outcomes for these individuals.

Will decreasing use of tobacco products among adolescents and young adults improve health outcomes?

There is very strong evidence that decreased use of tobacco products improves health outcomes.⁴⁶⁻⁴⁸ Because this connection is widely accepted, less time was dedicated to researching this relationship.

Tobacco use is the leading cause of preventable disease and death in the U.S.⁴⁶ A very strong body of evidence has shown a causal link between combustible cigarette smoking and diseases in nearly every organ, diminished health status, exacerbation of asthma, inflammation, impaired

immune function, age-related macular degeneration, harms to the fetus, diabetes, erectile dysfunction, arthritis, cancer, and premature death.⁴⁷ CDC has found that tobacco use is causally associated with at least 12 types of cancer, including cancer of the oral cavity and pharynx; esophagus; stomach; colon and rectum; liver; pancreas; larynx; lung, bronchus, and trachea; kidney and renal pelvis; urinary bladder; cervix; and acute myeloid leukemia.⁴⁶ Other research found that higher average cigarette use during adolescence was associated with poorer academic performance, mental health, physical health, and social functioning as well as with greater academic unpreparedness, physical ailments, and delinquency.⁴⁸

Will improving health outcomes for adolescents and young adults impact health inequities?

Overall, it is unclear from the available evidence how prohibiting the sale of flavored vapor products would impact health inequities in Washington State. We did not find any research looking at the impact of prohibiting the sale of flavored vapor products by subpopulations or communities.

While little research has looked specifically at the impact of prohibiting flavoring in vapor products across subpopulations, inequities in e-cigarette use are documented⁴⁹⁻⁵⁴ and presented below.

Inequities by race/ethnicity

Data from the 2018 HYS show e-cigarette use was significantly higher than cigarette use for all grade levels and all races/ethnicities.^{49,83} Survey results indicate that current use of e-cigarettes/vapor products among 10th and 12th graders is higher among American Indian/Alaska Native (AI/AN), multi-racial, and white students than their peers.⁴⁹ Among 8th graders, current use of e-cigarettes/vapor products was higher among Hispanic/Latino, AI/AN, multi-racial, and Black/African American students than other racial/ethnic groups.⁴⁹

Current law ([RCW 43.06.455](#)) allows the Governor to enter into cigarette tax compacts with tribes, and applies to the sale of all tobacco and vape products sold on tribal lands. While tribes could choose to prohibit the sale of flavored vapor products, HB 1932 does not apply to products sold on tribal lands. Therefore, if tribal retailers continue to sell flavored vape products, it is possible that use and initiation rates among AI/ANs and other Washingtonians living on or accessing goods on tribal land will not be as positively impacted by HB 1932. If this leads to a greater decline in vaping use among other subpopulations, this could exacerbate the vaping inequities that currently exist for AI/AN communities in Washington.

For example, following a menthol cigarette ban in Ontario, Canada, “22% of the daily menthol cigarette users reported purchasing menthol cigarettes after the ban” compared to 5% of the occasional menthol users and 0.3% of the non-menthol smokers.⁸⁴ The primary source for purchasing menthol cigarettes was on First Nation Reserves.⁸⁴ This purchasing pattern did not increase over time among prior daily menthol smokers (21% at both short-term and long-term follow-up).⁸⁴ Results were consistent with previous research findings that “25% of menthol smokers claim that they would find some way to purchase menthol cigarettes despite a ban.”⁸⁴

Overall, it is unclear how the bill would impact communities in Washington, especially for AI/AN youth and other youth living on or accessing flavored vape products on tribal land.

Further discussion specific to the initiation and use of other flavored tobacco products is on page 17.

Inequities by sexual orientation and gender identity

Nationally, students identifying as gay, lesbian, and bisexual were more likely to use e-cigarettes than students who identify as heterosexual (17.5% versus 13.2%, respectively).⁵⁰ Results of the 2018 HYS show that current use of e-cigarette/vapor products varied by sexual orientation.⁴⁹ Among 10th graders, 32.1% of gay, lesbian, or bisexual students; 23.6% of those who indicate they are “questioning, something else fits;” and 20.8% of students identifying as heterosexual reported current e-cigarette use.⁴⁹

Additionally, results of the 2018 HYS show that current e-cigarette use among 10th graders varied by gender identity. Transgender students reported the greatest current use (44.7%) followed by students who felt something else fits better (30.0%), students questioning/not sure of their gender identity (24.4%), cis-gender female students (22.4%), and cis-gender male students (20.8%).⁵¹

Overall, it is unclear how the bill would impact LGBTQIA adolescents and young adults. See discussion specific to the initiation and use of other flavored tobacco products on page 17.

Inequities by socioeconomic status

Generally, lower socioeconomic status (SES) is associated with greater exposure to tobacco cigarette advertising and cigarette use.^{52,85} However, evidence from Connecticut found “higher SES was associated with greater [e-cigarette specific] advertising exposure. Furthermore, exposure to more advertising was significantly associated with using e-cigarettes more frequently.”⁵² This aligns with information shared by a key informant in California who indicated the higher initial costs (compared to other flavored tobacco products) of vapor starter kits (typically \$30-\$50) make these products more accessible to higher SES adolescents and young adults (SFDPH, personal communication, September 2019). Results of the 2017-2018 California Student Tobacco Survey show the prevalence of current e-cigarette use among students (8th, 10th, and 12th grades) in San Francisco and San Mateo Counties (20.8%) is nearly double that of current use among their peers statewide (10.9%).⁵³ In 2017, the median household income in both San Mateo County (\$116,653) and San Francisco County (\$110,816) were well above the statewide median (\$71,805).⁸⁶ Additional research is necessary to examine the association between SES and e-cigarette use over time.

Available evidence and information shared by key informants indicate that prohibiting the sale of flavored vapor products may disproportionately benefit adolescents and young adults of higher SES. Meanwhile, the sale of other flavored tobacco products (e.g., blunt wrappers), which are sold at lower price points, would still be available. See discussion specific to the initiation and use of other flavored tobacco products on page 17.

Inequities by military status

National data indicate that active duty military members are more likely than the general population to report currently smoking or currently using e-cigarettes.⁵⁴ In 2015, 35.7% of military personnel reported ever trying e-cigarettes compared to 12.6% of the general population and 11.1% reported being daily e-cigarette users compared to 3.7% of the general population.⁵⁴

While purchase data for e-cigarettes specifically on military bases is not available, the Health Related Behavior Survey for Active Duty Service Members found that 80.7% of military personnel reported buying cigarettes on a military base, suggesting that purchase of tobacco products on base may be high generally.⁵⁴ Since HB 1932 would not affect vapor products sold on military bases in Washington, it is possible that this bill could have a smaller impact on decreasing use of vaping products among active duty military personnel, thereby potentially creating a disparity or exacerbating inequities that already exist at the national level.

Overall, there has not been a large enough body of evidence established to determine how laws prohibiting the sale of flavored vapor products may impact different subpopulations and communities in Washington State, and the impact on health inequities is unclear.

Other considerations

This Health Impact Review focused on the most direct pathway between provisions in the bill and health outcomes and health equity. Evidence for other potential pathways are discussed below.

Initiation and use of other flavored tobacco products

Other flavored tobacco products include cigars, cigarillos/little cigars, blunt wraps, smokeless tobacco, hookah, cigarettes (allowed flavors menthol/mint), and others. Like vapor products, these flavored options disproportionately appeal to young people and serve as an entry point to the tobacco market. For example, an analysis of national data from 2004 to 2014 found that adolescent smokers aged 12 to 17 years old were the most likely group to use menthol cigarettes compared to all other age groups.⁸⁷ Moreover, according to the FDA's scientific evaluation, "menthol has a physiological impact on smoking that increases initiation and progression to regular cigarette smoking, increases nicotine dependence and decreases smoking cessation success."⁸⁴ Findings are consistent with results of a 2017 systematic review in which "longitudinal studies demonstrate initiation with menthol cigarettes facilitates progression to established use in young smokers."⁸⁸

The tobacco industry also has a long, well-established history of marketing products (including flavors) to people in low-income communities, communities of color,⁸⁹⁻⁹¹ and LGBTQIA communities.⁹² For example, companies used targeted advertisements in community press, cigarette giveaways, philanthropy, and sponsorship of cultural activities (e.g., Black History Month events) to appeal to specific communities and develop a market for products.^{89,92} Targeted advertising for menthol cigarettes has contributed to their wide use among Black/African American (89%), Native Hawaiian (80%), Puerto Rican (62%), Filipino (58%), and Latino smokers (47%).⁹⁰ Smokers who identify as LGBT are also significantly more likely to smoke menthol cigarettes (more than 36%) than those who identify as heterosexual.⁹² Disproportionate use of menthol cigarettes contributes to inequities experienced by these populations as menthol makes cigarettes easier to smoke and harder to quit.^{89,90,92}

Because marketing for other tobacco products has targeted communities that have been marginalized, prohibiting the sale of flavors in vapor products alone may exacerbate existing inequities (personal communications, August to September 2019). Those who use flavored vapor products only are more likely to benefit, while those who are disproportionately exposed to and

use other flavored tobacco products (single, dual, or poly use) may be less impacted by the legislation.

Additionally, there is concern that prohibiting the sale of some flavored products may result in some consumers switching to other flavored tobacco products (product substitution) rather than simply discontinuing use of vapor products (personal communications, August to September 2019). As flavored vapor products and policies regulating them are relatively new, it is unclear to what extent different groups will either quit using vapor products or switch to/increase use of other tobacco products. Analysts reviewed evaluations of regulations restricting flavors in other tobacco products (i.e., cigarettes, menthol cigarettes, and cigars) in the U.S.; Providence, Rhode Island; and Canada to assess the potential for switching. While this literature is less generalizable, it provides insight into the potential impact of prohibiting the sale of flavored products.

In the U.S., research evaluating the 2009 Tobacco Control Act prohibiting the sale and distribution of flavored cigarettes found that, while use of cigarettes decreased following the law's implementation, use of menthol cigarettes, cigars, and pipe tobacco increased significantly "implying substitution toward the remaining legal flavored tobacco products."²⁷ Study authors concluded that, "the results suggest the 2009 flavored cigarette ban did achieve its objective of reducing adolescent tobacco use, but effects were likely diminished by the continued availability of menthol cigarettes and other flavored tobacco products."²⁷

Similarly, in January 2013, the city of Providence, Rhode Island, began enforcing a restriction on the retail sale of all non-cigarette tobacco products with a characterizing flavor other than tobacco, menthol, mint, or wintergreen. Researchers assessed the policy impact (January 2012-December 2016) on cigar sales, which represented 95% of flavored non-cigarette tobacco product sales in the city.⁹³ Results showed, "policy implementation was associated with a five-times greater decrease in average weekly sales of all cigars ([flavored] and otherwise) from prepolicy to postpolicy periods in Providence as compared with the more modest decrease observed in the [rest of the state]."⁹³ However, researchers found increases in sales of several brands of cigars labelled with concept-flavor names (e.g., Jazz) rather than explicit-flavor names (e.g., Watermelon Mist).⁹³ They also identified some evidence of product substitution and cross-border purchasing.⁹³ Despite these challenges, sales of all cigars decreased significantly (31%) in Providence following the flavor restriction policy compared to the rest of the state.⁹³

In 2009, the Canadian government passed federal regulations restricting flavors (excluding menthol) in small cigars. To assess the policy's effect, researchers analyzed wholesale data (2001 through 2016) to estimate changes in sales of cigars with and without flavor descriptors and analyzed changes for each flavor type over time.⁹⁴ Results show the Federal flavor regulations were "associated with a reduction in the sales of [flavored] cigars by 59 million units."⁹⁴ While increases in sales of cigars with descriptors other than flavors (e.g., color) were observed (9.6 million increase), the overall level (decline of 49.6 million units) and trend of sales of cigars (6.9 million units per quarter) declined following the ban.⁹⁴ Authors concluded flavor regulations "have the potential to substantially impact tobacco sales. However, exemptions for certain [flavors] and product types may have reduced the effectiveness of the ban, indicating the need for comprehensive, well-designed regulations."⁹⁴

Another Canadian study assessed the impact of Ontario’s menthol cigarette ban on smoking behavior of participants who reported current smoking (i.e., daily, occasional, and non-menthol cigarette smokers) at baseline prior to the ban.⁸⁴ At follow-up, “20% of occasional menthol smokers and 24% of daily menthol smokers reported quitting in the long terms, which exceeded what was predicted by smokers at baseline.”⁸⁴ Overall, daily menthol smokers had significantly higher rate of reporting having quit smoking and were more likely to have tried to quit after the ban compared with non-menthol smokers, controlling for smoking and demographic characteristics.⁸⁴ Findings suggested an increased rate of quitting 1 year following Ontario's ban on the sale of menthol tobacco products.⁸⁴ However, the impact was observed in older adults but not younger adults (16 to 29 years).⁸⁴ “The difference may be due to younger adults not having a brand preference and switching to other tobacco or nicotine products.”⁸⁴ Authors noted a combustible tobacco menthol ban would be more impactful for at-risk subpopulations of youth and young adults if there was less availability of other flavored tobacco or nicotine products.⁸⁴

Additionally, a key informant shared that, since Canada implemented restrictions on some flavored tobacco products (e.g., cigars, cigarettes, and hookah), the tobacco industry has adopted new tactics to appeal to former flavor buying customers. For example, companies have introduced ‘add on’ flavor products (dry or liquid options) which customers can now purchase and add to tobacco products (personal communication, 2019). Currently, these add on flavors have not gained the same traction that flavored products showed. This is likely due to inertia—it takes more effort for customers to purchase and use the flavor add on than it did to buy the ready-made flavored product (personal communication, August 2019). Companies have also found loopholes in the regulations that have allowed them to create product descriptors other than flavor. For example, companies have provided retailers with sales materials to guide customers to the new brand product (e.g., color) which most closely matches the previous product’s flavor descriptor (personal communication, August 2019).

While Canada and other jurisdictions have implemented multiple narrowly defined tobacco policies to restrict flavors, San Francisco policymakers adopted a more comprehensive approach. The San Francisco Health Code defines “tobacco product” broadly to include those “products containing, made, or derived from tobacco or nicotine that is intended for human consumption” and “any device or component, part, or accessory that delivers nicotine alone or combined with other substances [...] whether or not the device or component is sold separately.”⁶⁴ This language was crafted so that established tobacco regulations will apply to future products brought to market (SFDPH, personal communication, September 2019).

Overall, it is unclear how and to what extent HB 1932 will affect initiation and use of other flavored tobacco products by adolescents and young adults. Therefore, we did not include this pathway in the logic model on page 8.

Cessation

E-cigarettes are not approved by the FDA as an aid to quit smoking.⁹⁵ The U.S. Department of Health and Human Services stated that, “so far, the research shows there is limited evidence that e-cigarettes are effective for helping smokers quit.”⁹⁵ However, the FDA has approved several smoking cessation products designed to help users gradually withdraw from smoking (i.e.,

nicotine replacement therapy) in which flavors are approved—nicotine chewing gum and nicotine lozenges.⁹⁶ Vapor product manufacturers may apply to have their product reviewed by FDA for approval as a cessation option which could include flavors. Due to confidentiality laws, the Division of Drug Information in the FDA’s Center for Drug Evaluation and Research (CDER) cannot provide information related to drug applications that may have been submitted to the agency (CDER, personal communication, September 2019), and analysts were unable to determine whether any vapor product manufacturers have applied to have their product reviewed as a cessation device.

Overall, there is mixed evidence that e-cigarettes provide opportunity for cessation for adult combustible cigarette smokers.^{5,28} While some studies suggest that e-cigarettes may be useful cessation tools or may help smokers decrease their use of combustible cigarettes, other studies have found that e-cigarette use is associated with a decreased likelihood of quitting combustible cigarettes and increased consumption of combustible cigarettes.⁴¹⁻⁴⁴ A 2016 meta-analysis concluded that e-cigarettes, as they are currently being used, are actually associated with lower quit rates among adult combustible cigarette smokers.⁴⁴ National Health Interview Survey data (2014 to 2016) indicate the dominant pattern of e-cigarette use in adults is dual use of both combustible cigarettes and e-cigarettes.⁶⁰ As part of the interim guidance issued by CDC to address the outbreak of severe pulmonary illness associated with e-cigarette use, CDC recommended that, “adult smokers who are attempting to quit should use evidence-based smoking cessation treatments, including counseling and FDA-approved medications.”⁸¹ In sum, the National Academy of Sciences stated that, “the net public health effect, harm or benefit, of e-cigarettes depends on three factors: their effect on youth initiation of combustible tobacco products, their effect on adult cessation of combustible tobacco products, and their intrinsic toxicity.”²⁸ They concluded that “there would be net public health harm in the short and long terms if the products do not increase combustible tobacco cessation in adults.”²⁸

Since there is mixed evidence that e-cigarettes provide opportunity for combustible tobacco cessation in adults and since evidence suggests that most adolescents and young adults do not use e-cigarettes to quit smoking,^{31,60} we did not include this pathway in the logic model on page 8.

Flavored marijuana products

Analysts also explored the potential impacts of the bill on the initiation and use of flavored marijuana products meant for consumption through aerosolization or vaporization (marijuana vapor products). We ultimately did not include this pathway in the logic model on page 8 because the health impacts of marijuana vapor products and the impacts of the flavors in these products have not been well researched.

Key informants noted multiple research limitations including federal regulations, state funding, and technical challenges specific to marijuana. First, federal funding requirements limit research on marijuana to strains cultivated at one specific source farm in Mississippi. Key informants noted that the strains grown at the designated source farm more closely resemble strains available in the 1970s than strains developed since states began legalizing marijuana for various purposes (e.g., medicinal, recreational) (personal communication, August 2019). More recent advances in production are capable of yielding strains with significantly higher THC content,

making research available using product from the source farm less generalizable to today's market. Second, Washington State law ([RCW 69.50.540](#)) limits appropriations available for research on the short and long-term effects of marijuana use (and the dissemination of this research) to 1.0% of funds collected through Initiative 502.⁹⁷ With limited funding and multiple research priorities, the health impacts of flavors have not been well researched for marijuana vapor products. Finally, key informants shared that THC and cannabiniol (CBD) are extremely difficult to completely parse out. Therefore, both are nearly always present, which makes conducting health focused research specific to either chemical challenging and less generalizable.

The science of marijuana vapor product flavors is also more nuanced than that of flavored e-cigarettes. While flavored e-cigarettes contain almost exclusively flavor chemicals, marijuana vapor products generally get their flavor from naturally derived terpenes that contribute to the flavor profile and/or added fruit oils or extracts (personal communication, September 2019). However, cannabis oils can have manufactured (e.g., non-cannabis derived) terpenes and terpene additives (e.g., not derived from a regulated plant) added as flavorants (personal communication, September 2019). These additives are typically not well regulated, and may contain contaminants that could pose health risks and/or not be designed for aerosolization (personal communication, September 2019). Currently, there is no research on how these flavor components specifically affect the long-term health of users. However, some jurisdictions have adopted regulations to restrict their use. For example, New York State Department of Health regulations prohibit the use of “any additional active ingredients or materials to any approved medical [marijuana] product that alters the color, appearance, smell, taste, effect or weight of the product unless it has first obtained prior written approval of the department.”⁹⁸ Furthermore, “excipients [i.e., inactive ingredients] must be of pharmaceutical grade and approved by the department.”⁹⁸ As manufactured terpenes are not pharmaceutical grade, they are prohibited under New York's medical marijuana regulations (personal communications, September 2019).

While health literature specific to flavor chemicals used in nicotine and tobacco products may not be generalizable to flavored marijuana vapor products, the literature pertaining to the appeal of flavors is generalizable, and the presence and advertising of flavored marijuana vapor products increases their appeal to adolescents and young adults.

Annotated References

1. **Family Smoking Prevention and Tobacco Control Act, 123 (2009).**

The 111th U.S. Congress found that "virtually all new users of tobacco products are under the minimum legal age to purchase such products" and that "tobacco advertising and marketing contribute significantly to the use of nicotine-containing tobacco products by adolescents." For this and other reasons, "It is in the public interest for Congress to enact legislation that provides the Food and Drug Administration with the authority to regulate tobacco products and the advertising and promotion of such products." Section Chapter IX--Tobacco Products, Section 907. Tobacco Product Standards (a)(1)(A) specifically bans the use of artificial or natural flavor (other than tobacco or menthol) or an herb or spice that is a characterizing flavor of the tobacco product or tobacco smoke in cigarettes. The full text of the Tobacco Control Act is available at <https://www.govinfo.gov/content/pkg/PLAW-111publ31/pdf/PLAW-111publ31.pdf>.

2. **Administration U.S. Food and Drug. Summary of the Deeming Final Rule. Silver Spring, Maryland: U.S. Food and Drug Administration.**

In this document the U.S. Food and Drug Administration (FDA) summarizes the Deeming Tobacco Products to be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Restrictions on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products ('Deeming Rule'). The final rule was published on May 10, 2016. It extends the FDA's "tobacco product" authorities to "all other categories of tobacco products meeting the statutory definition of 'tobacco product' in the Federal Food, Drug, and Cosmetic Act (FD&C Act), except accessories of such products." The newly regulated products include currently marketed products (e.g., electronic cigarettes, cigars, waterpipe (hookah) tobacco) and future tobacco products. The Deeming Rule requires these tobacco products to comply with all provisions regarding "tobacco products" found in the FD&C Act and FDA regulations. The full text of the rule is available at <https://www.federalregister.gov/documents/2016/05/10/2016-10685/deeming-tobacco-products-to-be-subject-to-the-federal-food-drug-and-cosmetic-act-as-amended-by-the>.

3. **FDA News Release -- FDA takes new steps to address epidemic of youth e-cigarette use, including a historic action against more than 1,300 retailers and 5 major manufacturers for their roles perpetuating youth access [press release]. 2018.**

In September 2018, the U.S. Food and Drug Administration issued 1300 warning letters and fines to retailers who illegally sold JUUL and other e-cigarette products to minors. The FDA news release stated that this was the "largest coordinated enforcement effort in the FDA's history." FDA Commissioner Scott Gottlieb stated, "we see clear signs that youth use of electronic cigarettes has reached an epidemic proportion, and we must adjust certain aspects of our comprehensive strategy to stem this clear and present danger. This starts with the actions we're taking today to crack down on retail sales of e-cigarettes to minors." The FDA also issued letters to the top five-selling e-cigarette brands (which comprise 97% of the U.S. e-cigarette market) , including JUUL, Vuse, MarkTen XL, blu e-cigs, and Logic requiring each company "to submit to FDA within 60 days plans describing how they will address the widespread youth access and use of their product." The FDA also committed to increasing enforcement efforts for e-cigarette manufacturers and retailers.

4. FDA News Release -- Trump Administration Combating Epidemic of Youth E-Cigarette Use with Plan to Clear Market of Unauthorized, Non-Tobacco-Flavored E-Cigarette Products [press release]. Silver Spring, MD: U.S. Food and Drug Administration, 11 September 2019 2019.

This news release from the U.S. Food and Drug Administration (FDA) outlines the Trump Administration's announcement that as part of its ongoing work to address the epidemic of youth e-cigarette use, the agency will finalize a compliance policy that prioritizes enforcement of the premarket authorization requirements for non-tobacco-flavored e-cigarettes. Preliminary data from the National Youth Tobacco Survey show "that more than a quarter of high school students were current (past 30 day) e-cigarette users in 2019 and the overwhelming majority of youth e-cigarette users cited the use of popular fruit [65.9%] and menthol or mint [63.9%] flavors." Effective August 8, 2016, "all electronic nicotine delivery system (ENDS) products were expected to file premarket tobacco product applications with the FDA within two years. ENDS products currently on the market are not being legally marketed and are subject to government action. The compliance policy the FDA anticipates announcing in the coming weeks will outline enforcement policy addressing non-tobacco-flavored e-cigarette products that lack premarket authorization moving forward." FDA has issued more than 8,600 warning letters and more than 1,000 fines to retailers for sales of ENDS and their components to minors. Many e-liquid products resembling kid-friendly juice boxes, cereal, and candy have been removed from the market as the result of FDA warning letters--many written in collaboration with the Federal Trade Commission (FTC). On September 9, 2019, FDA issued a warning letter to JUUL Labs Inc. for "marketing unauthorized modified risk tobacco products by engaging in labeling, advertising, and/or other activities directed to consumers, including a presentation given to youth at a school."

5. FDA Statement--Statement from FDA Commissioner Scott Gottlieb, M.D., on proposed new steps to protect youth by preventing access to flavored tobacco products and banning menthol in cigarettes [press release]. 2018.

FDA Commissioner Scott Gottlieb outlines a "policy framework [that] reflects a re-doubling of the FDA's efforts to protect kids from all nicotine-containing products." He states that, "if we're to break the cycle of addiction to nicotine, preventing youth initiation on nicotine is a paramount imperative." He cites research showing that 90% of current adult smokers started smoking before 18 years of age, 95% started smoking before 21 years of age, and only 1% started smoking after 26 years of age. Research with the Centers for Disease Control and Prevention found that e-cigarette use among high school students increased 78% from 2017 to 2018, and 48% among middle school students- reversing prior trends from 2015 to 2017 suggesting that use was declining. To address these trends, FDA has taken a number of recent actions as part of their Youth Tobacco Prevention Plan, including increasing enforcement against retailers, targeting e-liquid manufacturers marketing to youth, working with eBay to remove products from their website, and launching "The Real Cost" Youth E-Cigarette Prevention Campaign. Dr. Gottlieb stated, "I repeatedly said that, although we continue to believe that non-combustible tobacco products may provide an important opportunity to migrate adult smokers away from more harmful forms of nicotine delivery, these opportunities couldn't come at the expense of addicting a generation of kids to nicotine." This statement includes two directives from the FDA. First, FDA requires that all "flavored [electronic nicotine delivery systems] products (other than tobacco, mint, and menthol flavors or non-flavored products) must be sold in age-restricted, in-

person locations and, if sold online, under heightened practices for age verification." Second, FDA issued a "Notice of Proposed Rulemaking that would seek to ban menthol in combustible tobacco products, including cigarettes and cigars." Data indicate that youth are more likely to use menthol cigarettes than any other group and that, "more than half (54 percent) of youth smokers ages 12-17 use menthol cigarettes, compared to less than one-third of smokers ages 35 and older." In addition, approximately 70% of African American youth use menthol cigarettes. In response, FDA is proposing a policy to ban flavors in cigars. Dr. Gottlieb emphasized that, "If youth trends don't move in the right direction, we will revisit all of these issues."

6. Kaplan Sheila, Hoffman Jan. Juul Suspends Selling Most E-Cigarette Flavors in Stores. *The New York Times*. 13 November 2018, 2018;Health.

This article from The New York Times reported on the decision by Juul Labs to suspend sales of most of its flavored e-cigarette pods in retail stores and to discontinue its social media promotions. Juul said it would "keep mint, tobacco and menthol flavors for its devices in retail stores" to prevent some users from reverting to menthol cigarettes. The announcement came before the FDA's unveiled a series of measures to curb teenage vaping. "More than three million middle and high school students reported using e-cigarettes, according to preliminary, unpublished government data, with about one-third of them saying the flavors were a big factor in their choice." Juul's announcement also stated it would renew sales of suspended flavored products "at retail outlets that invested in age-verification technology."

7. Kaplan Sheila. 'Juul-alikes' Are Filling Shelves With Sweet, Teen-friendly Nicotine Flavors. *The New York Times*. 13 August 2019, 2019;Health.

The New York Times reported that after Juul Labs, under pressure from the FDA, suspended sales of most of its popular flavored nicotine pods in stores in fall 2018, upstart competitors began producing their own fruity and candy-flavored versions. The proliferation of 'Juul-alikes' "shows just how entrenched the youth vaping problem became and that voluntary measures are unlikely to solve it." Juul "has filed patent infringement claims against 21 manufacturers and seller of copycat devices and pods." According to Juul, three companies have not agreed to stop selling their similar products. One of these competitors, Eonsmoke generated an estimated \$5.3 million in revenue in 2018. In 2019, the company's business has an estimated \$43.6 million in tracked sales as of mid-July. According to a 16-year-old quoted in the story, adolescents are attracted to the wide range of flavors. Additionally, he noted, "[s]ome of my friends use Eon pods because they have a higher nicotine percentage, because they want a bigger head rush." Eonsmoke is under investigation by both the F.D.A. and the attorney general of Massachusetts.

8. Surgeon General's Advisory on E-cigarette Use Among Youth [press release]. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2018.

In December 2018, the Office of the Surgeon General issued a statement "emphasizing the importance of protecting our children from a lifetime of nicotine addiction and associated health risks by immediately addressing the epidemic of youth e-cigarette use. The recent surge in e-cigarette use among youth, which has been fueled by new types of e-cigarettes that have recently entered the market, is a cause for great concern. We must take action now to protect the health of our nation's young people." The statement included background information that e-cigarette use increased dramatically from 2017 to 2018, and that e-cigarette aerosol can negatively impact

health. The Surgeon General noted that e-cigarette aerosol and flavorings can expose users and bystanders to metals, volatile organic compounds, and ultrafine particles that can be inhaled deeply into the lungs. The statement also includes information about JUUL. The sale of JUUL increased 600% from 2016 to 2017, and the Surgeon General stated that "all JUUL e-cigarettes have a high level of nicotine. A typical JUUL cartridge or 'pod' contains about as much nicotine as a pack of 20 regular cigarettes." In addition, JUUL uses nicotine salts which allow nicotine to be inhaled more easily and with less irritation than tobacco products and other e-cigarettes. The statement noted that, "any e-cigarette use among young people is unsafe, even if they do not progress to future cigarette smoking."

9. ACT Relating to protecting youth from tobacco products and vapor products by increasing the minimum legal age of sale of tobacco and vapor products, Revised Code of Washington(2019).

In 2019, Washington State legislators passed Engrossed House Bill 1074, An act relating to protecting youth from tobacco products and vapor products by increasing the minimum legal age of sale of tobacco and vapor products. The legislation prohibits selling or giving tobacco or vapor products to a person under the age of 21 and permits the Governor to seek government-to-government consultations with tribes about raising the minimum legal age of sale in cigarette tax compacts. The law is effective January 1, 2020.

10. FDA News Release -- FDA launches its first youth e-cigarette prevention TV ads, plans new educational resources as agency approaches one-year anniversary of public education campaign [press release]. Silver Spring, MD, 22 July 2019 2019.

On July 22, 2019, the U.S. Food and Drug Administration announced the launch of its first e-cigarette prevention TV ads educating kids about the dangers of e-cigarette use. Part of FDA's "The Real Cost" Youth E-Cigarette Prevention Campaign, a \$60 million effort, the new ads highlight emerging science which indicates that "teens who vape are more likely to start smoking cigarettes, putting them at risk of a lifetime of addiction to smoking and related disease." Specifically, "compared with non-users, youth who use e-cigarettes are more likely to try conventional cigarettes in the future. This was also a conclusion reached in a National Academies of Sciences, Engineering, and Medicine report in 2018 on the Public Health Consequences of E-Cigarettes." The ads will run on television networks aimed at youth (e.g., TeenNick, CW, MTV), as well as on music streaming sites, social media networks, and other teen-focused media channels. Highlighted messages include, that e-cigarettes, like cigarettes, put youth at risk for addiction and other health consequences; nicotine can rewire the brain to crave more nicotine; and that e-cigarettes can contain dangerous chemicals.

11. Outbreak of Lung Injury Associated with Using E-cigarette Use, or Vaping. 2019; Available at: https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html. Accessed 19 September 2019.

In 2019, CDC, U.S. Food and Drug Administration, state and local health departments, and other clinical and public health partners began investigating outbreaks of severe pulmonary disease associated with e-cigarette use. As of September 17, 2019 at 5pm, 530 cases of lung injury associated with use of e-cigarettes or vaping products had been reported to the CDC by 38 states and 1 U.S. territory. Seven deaths have been confirmed in 6 states. CDC received complete sex and age data on 373 of 530 cases: 72% of cases are male; 67% of cases are 18-34 years old; 16%

of cases are under 18 years of age; and 17% are 35 years or older. While the investigation is ongoing, CDC noted "All patients have a reported history of e-cigarette product use, and no consistent evidence of an infectious cause has been discovered. Therefore, the suspected cause is a chemical exposure." They noted that, "the investigation has not identified any specific substance or e-cigarette product that is linked to all cases. Many patients report using e-cigarette products with liquids that contain cannabinoid products, such as tetrahydrocannabinol (THC)." However, "No consistent e-cigarette or vaping product, substance, or additive has been identified in all cases, nor has any one product or substance been conclusively linked to lung disease in patients." Patients have reported symptoms like coughing, shortness of breath, and chest pain; nausea, vomiting, and diarrhea; and fatigue, fever, and weight loss. Symptoms have not been responsive to antibiotic treatment, and are not associated with an infection. Among other recommendations, CDC recommends that youth and young adults, women who are pregnant, and adults who do not currently use tobacco products not use e-cigarette products.

12. Bogan Sharon. First Case of Vaping-Related Lung Illness Confirmed in King County. Seattle, Washington: Public Health - Seattle & King County; 2019.

This article from Public Health - Seattle & King County (PHSKC) staff reported the first confirmed case of severe lung disease associated with e-cigarettes in Washington State. The patient (male, late teens) was hospitalized in August for fever, cough, and shortness of breath. He was treated in an intensive care unit for 5 days before being released to recover at home. The teenager reported vaping nicotine with propylene glycol as well as saffron, but PHSKC's investigation is ongoing and details about the type of vaping device, where the products were obtained or if other substances were also used were unknown at the point of publication. Dr. Jeff Duchin, Health Officer for PHSKC, noted that "e-cigarettes and vaping are not safe [...] Youth, young adults and pregnant women should never use e-cigarettes or vapes." Duchin also noted that "[a]lthough e-cigarettes are not approved as a cigarette smoking cessation method, we are aware that some people use them in this way. People who want to quit or reduce cigarette smoking should consult with their health care provider for effective treatment options."

13. Severe Lung Illness: Severe Lung Illness linked to use of vaping products in Washington State. 2019; Available at:

<https://www.doh.wa.gov/Emergencies/SevereLungIllness>. Accessed 9/17/2019.

Washington State Department of Health is monitoring cases in Washington State connected to the ongoing investigation of severe pulmonary disease conducted by Centers for Disease Control and Prevention. As of September 16, 2019, there were three confirmed cases in Washington State, including one in King County and two in Spokane County. All three cases were in patients aged 10-29 years old.

14. Kaplan Sheila. Trump Administration Plans to Ban Flavored E-Cigarettes. *The New York Times*. 11 September 2019, 2019.

This article reported the Trump administration's announcement on Wednesday, September 11, 2019, that it would ban the sale of most flavored e-cigarettes. The announcement is in response to the outbreak of severe pulmonary disease associated with vaping. Michigan became the first state to prohibit the sale of flavored e-cigarettes. New York, Massachusetts, and California are also considering similar measures. The Secretary of Health and Human Services (HHS), Alex

Azar II, stated that JUUL's removal of fruit flavor from stores simply prompted youths to shift to using menthol and mint flavors rather than to stop vaping altogether.

15. FDA News Release -- FDA warns JUUL Labs for marketing unauthorized modified risk tobacco products, including in outreach to youth [press release]. Silver Springs, MD: U.S. Food and Drug Administration, 9 September 2019 2019.

This U.S. Food and Drug Administration news release the agency details the warning letter issued to JUUL Labs Inc. requesting more information on concerning outreach and marketing practices (targeting students, tribes, health insurers, and employers) raised during a Congressional hearing in July 2019. The letter underscores that law requires "companies must demonstrate with scientific evidence that their specific product does in fact pose less risk or is less harmful [than cigarettes]. JUUL has ignored the law, and very concerningly, has made some of these statements in school to our nation's youth," stated Acting FDA Commissioner Ned Sharpless, M.D. According to testimony, "a JUUL representative speaking with students at his presentation in a school stated that: JUUL 'was much safer than cigarettes' and that 'FDA would approve it any day.'" FDA has requested JUUL provide a written response describing its corrective actions and its plan for maintaining compliance.

16. Huang L. L., Baker H. M., Meernik C., et al. Impact of non-menthol flavours in tobacco products on perceptions and use among youth, young adults and adults: a systematic review. *Tob Control*. 2017;26(6):709-719.

Huang et al. conducted a systematic review examining the impact of non-menthol flavors in tobacco products on tobacco use perceptions and behaviors among youth, young adults, and adults. Four databases were searched through April 2016. Of 1688 articles identified, authors excluded articles that were not English-language, were not peer-reviewed, were qualitative, assessed menthol-flavored tobacco products only and did not contain original data on outcomes that assessed the impact of flavors in tobacco products on perceptions and use behavior. "[Two] researchers extracted the data independently and used a validated quality assessment tool to assess study quality." Overall, 40 studies met the inclusion criteria (0% published between 2010 and 2016), and 17 of those studies examined e-cigarettes (10 U.S. based studies, 7 Non-U.S. based studies). Results showed that "tobacco product packaging with [flavor] descriptors tended to be rated as more appealing [6 studies] and as less harmful by tobacco users and non-users [5 studies]. Many tobacco product users, especially adolescents, reported experimenting, initiating [7 studies] and continuing to use [flavored] products [7 studies] because of the taste and variety of the [flavors]." For example, a U.S. study of 13,651 adolescents found "product flavoring was consistently reported as the most common reason for use across all product types, including e-cigarettes (81.5%), hookah (78%), cigars (73.8%), smokeless tobacco (69%) and snus pouches (67.2%)." The systematic review found, those who used many flavored tobacco products also showed "decreased likelihood of intentions to quit compared with non-[flavored] tobacco product users." Authors concluded, flavors in most tobacco products "appear to play a key role in how users and non-users, especially youth, perceive, initiate, progress and continue using tobacco products. Banning non-menthol [flavors] from tobacco products may ultimately protect public health by reducing tobacco use, particularly among youth."

17. **Mantey D. S., Omega-Njemnobi O., Montgomery L. Flavored tobacco use is associated with dual and poly tobacco use among adolescents. *Addict Behav.* 2019;93:269-273.**

Mantey et al. examined the relationships between flavored tobacco use and single, dual, and poly tobacco product use, among adolescents. Researchers obtained cross-sectional data from the 2017 National Youth Tobacco Survey (NYTS). Participating adolescents (N=2,042) were past 30-day tobacco users. Tobacco use was assessed for 9 products (cigarettes, e-cigarettes, hookah, cigar products (i.e., cigars, little cigars, cigarillos), smokeless tobacco, snus, pip tobacco, bidis, and dissolvable tobacco. "Multivariable multinomial logistic regression models were used to assess the relationship between flavored tobacco use and past 30-day single, dual, and poly (three or more) tobacco product use." Data were weighted to be representative of U.S. middle and high school students, adjusting for nonresponse and probability of selection. Researchers conducted two analyses using different categories as referent groups "to allow for a comprehensive examination of the relationship between all groups. Covariates included sex, grade level, race/ethnicity and exposure to tobacco marketing." Data showed flavored tobacco use prevalence differed significantly by race/ethnicity ($p < 0.001$); non-Hispanic whites had the greatest prevalence (74.7%) followed by Hispanic/Latinos (66.5%). Additionally, "[s]ingle, dual, and poly tobacco use prevalence differed significantly by race ($p = .035$). Single product use prevalence was greatest among non-Hispanic blacks (66.5%). Dual product use was greatest among non-Hispanic whites (21.3%). Poly tobacco use was greatest among Hispanic/ Latinians (28.9%)." Approximately half of all participating adolescent tobacco users (45.7%) reported use of more than one product, and most adolescent tobacco users reported using flavors (69.4%). Specifically, analysis of 2017 National Youth Tobacco Survey results found that among dual and poly tobacco users, the most commonly used flavored tobacco products were e-cigarettes (34.3% and 44.6%, respectively), cigars (23.8% and 41.5%, respectively), and convention cigarettes (21.9% and 33.9%, respectively). After controlling for covariates, "[f]lavored tobacco use was significantly correlated with a greater risk of dual (RRR: 2.09) and poly (RRR: 5.54) tobacco use, relative to single product use." Moreover, "flavored tobacco use was significantly correlated with a greater risk of poly (RRR: 2.66) tobacco use, relative to dual tobacco use, controlling for covariates." Overall, authors noted a positive relationship for flavored tobacco use and multiple tobacco product use. Authors conclude, "[f]indings suggest the need to consider stronger regulations of flavored tobacco products [...] [and] the need to emphasize flavored tobacco use in prevention and education programs."

18. **Garrison K. A., O'Malley S. S., Gueorguieva R., et al. A fMRI study on the impact of advertising for flavored e-cigarettes on susceptible young adults. *Drug Alcohol Depend.* 2018;186:233-241.**

Garrison et al. tested a brain biomarker of product preference for sweet/fruit versus tobacco flavor e-cigarettes, and whether advertising for flavors interfered with warning labels. The study included college-age young adult participants (N=26; aged 18-25 years) who had tried an e-cigarette and were susceptible to future e-cigarette use but were nonsmokers. The study sample was 54% male; 65% white, 15% black, 8% Asian, 8% white Hispanic, and 4% black Hispanic. Participants viewed advertisements in functional magnetic resonance imaging (fMRI), which has been used to objectively measure the effects of advertising (beyond self-report) by "testing whether the neural signal in response to advertisements can predict product preferences and purchasing." Participants viewed advertisements (taken from online media) for sweet (i.e.,

candy/desserts and fruit flavor and tobacco flavor e-cigarettes, menthol and regular cigarettes, and control images of sweets/fruits/mints with no tobacco product. "Cue-reactivity was measured in the nucleus accumbens, a brain biomarker of product preference. Advertisements randomly contained warning labels [formatted to meet current FDA requirements, FDA 2016b], and recognition of health warnings was tested post-scan. Visual attention was measured using eye-tracking." Immediately following scanning, participants performed an unannounced recognition memory test of health messages. Results showed "a significant effect of e-cigarette condition (sweet/tobacco/control) on nucleus accumbens activity, that was not found for cigarette condition (menthol/regular/control)." Specifically, "[n]ucleus accumbens activity was greater for sweet/fruit versus tobacco flavor e-cigarette advertisements and did not differ compared with control images of sweets and fruits." Additionally, "[g]reater nucleus accumbens activity was correlated with poorer memory for health warnings." Overall, authors concluded results of this study and other exploratory eye-tracking findings suggest that "advertising for sweet/fruit flavors may increase positive associations with e-cigarettes and/or override negative associations with tobacco, and interfere with health warnings, suggesting that one way to reduce the appeal of e-cigarettes to youth and educate youth about e-cigarette health risks is to regulate advertising for flavors."

19. Harrell M. B., Weaver S. R., Loukas A., et al. Flavored e-cigarette use: Characterizing youth, young adult, and adult users. *Prev Med Rep.* 2017;5:33-40.

Harrell et al. investigated how the use of flavored e-cigarettes varies between youth (12-17 years old), young adults (18-29 years old), and older adults (30 + years old). Cross-sectional surveys of school-going youth (n = 3907; Texas Adolescent Tobacco and Marketing Surveillance System [TATAMS]) and young adult college students (n = 5482; Marketing and Promotions Across Colleges in Texas Project [M-PACT]) in Texas, and young adults and older adults (n = 6051; Tobacco Products and Risk Perceptions Survey [TPRPS]) nationwide were administered in 2014-2015. "Most e-cigarette users said their first and 'usual' e-cigarettes were flavored." Results show that "at initiation, the majority of Texas school-going youth (98%), Texas young adult college students (95%), and young adults (71.2%) nationwide said their first e-cigarettes were flavored to taste like something other than tobacco, compared to 44.1% of older adults nationwide." Most youth, young adult, and adult e-cigarette users reported the "'usual' e-cigarette they used in the past 30 days were flavored, with the majority reporting that it was flavored to taste like something other than tobacco." Fruit and candy flavors predominated for all groups (Texas youth: 76% endorsed fruit and 57% endorsed candy; Texas young adult college students 83% and 52%, respectively; young adults nationwide: 74% and 50%, respectively; and older adults nationwide: 47% and 27%, respectively). Tobacco was the least commonly reported usual flavor among all age groups. Flavors were particularly important for Texas youth as a reason to use e-cigarettes; 72.9% reported using e-cigarettes because they "come in flavors I like" compared to 57.4% of young adult college students in Texas and 64.8% of young adults nationwide. "Among adults, the use of tobacco flavor at initiation was common among dual users (e-cigarettes + combustible tobacco), while other flavors were more common among former cigarette smokers (P = 0.03)." Authors conclude, "restricting the range of e-cigarette flavors (e.g., eliminating sweet flavors, like fruit and candy) may benefit youth and young adult prevention efforts. However, it is unclear what impact this change would have on adult smoking cessation."

20. **Goldenson N. I., Kirkpatrick M. G., Barrington-Trimis J. L., et al. Effects of sweet flavorings and nicotine on the appeal and sensory properties of e-cigarettes among young adult vapers: Application of a novel methodology. *Drug Alcohol Depend.* 2016;168:176-180.** Goldenson et al. used a double-blind, cross-over design laboratory protocol to assess whether: "(1) sweet flavorings and nicotine affect e-cigarette appeal; (2) sweet flavorings increase perceived sweetness; (3) nicotine increases throat hit; and (4) perceived sweetness and throat hit are associated with appeal." Double-blind laboratory conditions help control for exogenous factors (e.g., marketing strategies, cultural trends, pre-existing expectations about product effects, and social influences) that can influence the perceived appeal of certain e-cigarette products. Eligible participants were young adult vapers (N=20) ages 19-34 years who used e-cigarettes one or more times per day/week for one or more months; smoked 15 or fewer conventional cigarettes per day; were not using smoking cessation medication; and were not pregnant or breastfeeding. The study sample was 55% male; average age 26.3 years; 45% white, 35% African American, and 20% Other race/ethnicity. On average, participants reported low to medium e-cigarette dependence (based on PSECD) and vaping for 3 years. Eleven participants reported regularly vaping a sweet flavor, and 9 reported usually using a non-sweet flavor. Participants self-administered "20 different e-cigarette solutions (10 flavors × 2 nicotine concentrations) that were separated into two counterbalanced blocks (nicotine and placebo). Within each block, 10 different e-cigarette solutions (6 sweet, 3 non-sweet and 1 flavorless) were presented in random order—constituting a Flavor (sweet vs. non-sweet vs. flavorless) × Nicotine (nicotine vs. placebo) within-participant full factorial design." Evidence indicates that participants remained blind to the characterizing flavor they received (average accuracy rate in identifying administered flavor 9.7%; did not differ by Flavor condition). Participants followed a prescribed standardized puff sequence to test each solution. They then rated appeal (liking, willingness to use again and perceived monetary value), perceived sweetness and throat hit strength after each administration." Results showed sweet-flavored solutions produced greater appeal and perceived sweetness ratings compared to non-sweet and flavorless solutions ($p < 0.0001$). Secondly, nicotine produced greater throat hit ratings than the placebo. However, presence of nicotine did not significantly increase appeal ($p = 0.25-0.59$) nor interact with flavor effects on appeal ($p = 0.76-0.99$). "Controlling for flavor and nicotine, perceived sweetness was positively associated with appeal ratings ($p < 0.0001$)." Specifically, "each one point increase in sweetness rating (0–100) was associated with an estimated 0.51 increase in 'liking,' a 0.51 increase in 'willingness to use again,' and a \$0.04 increase in 'amount willing to pay for a day's worth of the solution.'" Meanwhile, throat hit ratings were not positively associated with appeal, and were inversely associated with liking ($p = 0.01$). To assess whether pre-existing flavor preferences influenced study outcomes, researchers re-analyzed data from those who reported non-sweet flavor preferences separately. "As in the overall sample, all appeal outcomes were positively associated with sweetness ratings ($p < 0.0001$); willingness to use again and subjective value were not associated with throat hit [...] and liking was *inversely* associated with throat hit ($p = 0.02$)." Findings suggest that "e-cigarette solutions that stimulate orosensory perceptions of sweetness (in and of themselves) may be primary drivers of appeal." Authors concluded, "[f]urther identification of compounds in e-cigarette solutions that enhance sensory perceptions of sweetness, appeal, and utilization of e-cigarettes are warranted to inform evidence-based regulatory policies."

21. **Morean M. E., Butler E. R., Bold K. W., et al. Preferring more e-cigarette flavors is associated with e-cigarette use frequency among adolescents but not adults. *PLoS One*. 2018;13(1):e0189015.**

Morean et al. examined whether: 1) "preferences for e-liquid flavors and the total number of flavors preferred differed between samples of adolescent and adult e-cigarette users" and 2) "preferences were associated with e-cigarette use frequency for adolescents or adults, respectively." The study's adolescent sample consisted of past-month e-cigarette users (n=396) from "5 Connecticut high schools who completed an anonymous, school-based survey in Fall 2014 (56.1% male; 16.18 [1.18] years; 42.2% past-month smokers)." The adult sample included past-month e-cigarette users (n=590) who "completed an anonymous, MTurk survey in Fall 2014 (53.7% male; 34.25 [9.89] years; 51.2% past-month smokers)." Researchers assessed preferences for "10 e-liquid flavors (i.e., tobacco, menthol, mint, fruit, coffee, vanilla, dessert/candy, spices, alcohol, and other) and the total number of flavors preferred by each group." The analysis found that compared to adults, "a larger proportion of adolescents preferred fruit, alcohol, and 'other'-flavored e-liquids, whereas adults disproportionately preferred tobacco, menthol, mint, coffee, and spice-flavored e-liquids (p-values < .05). Adults also preferred a greater total number of flavors compared to adolescents and used e-cigarettes more frequently (p-values < .001)." However, flavor preferences were associated with frequency of e-cigarette use within the adolescent sample. Specifically, "the total number of flavors preferred was associated with more days of e-cigarette use [p<0.001], as were preferences for fruit [p<0.01], dessert [p<0.01], and alcohol-flavored [p<0.01] e-liquids." Authors concluded, "[f]lavor preferences differed between adolescent and adult samples. While youth reported less frequent e-cigarette use overall, their preferences for specific flavors and the total number of flavors preferred were associated with more days of e-cigarette use, indicating that flavor preferences may play an important role in adolescent e-cigarette use."

22. **Soneji S. S., Knutzen K. E., Villanti A. C. Use of Flavored E-Cigarettes Among Adolescents, Young Adults, and Older Adults: Findings From the Population Assessment for Tobacco and Health Study. *Public Health Rep*. 2019;134(3):282-292.**

Soneji et al. examined the types of e-cigarette flavors used by adolescent (aged 12-17), young adult (aged 18-24), and older adult (aged ≥25) e-cigarette users. Researchers "assessed the prevalence of flavored e-cigarette use within the past month by flavor types and concurrent use of multiple flavor types among past-month e-cigarette users sampled during Wave 2 (2014-2015) of the Population Assessment for Tobacco and Health Study among 414 adolescents, 961 young adults, and 1711 older adults." Weighted logistic regression models were used for the use of fruit-, candy-, mint/menthol-, tobacco-, or other-flavored e-cigarettes and concurrent use of multiple flavor types. Authors considered covariates including "demographic characteristics, e-cigarette use frequency, cigarette smoking status, current use of other tobacco products, and reasons for e-cigarette use." For example, cigarette smoking status varied by age with 35.8% of adolescent e-cigarette users, 14.1% of young adults users, and 3.6% of older adult users reporting having never smoked cigarettes. Additionally, 14.7% of adolescent users, 37.4% of young adult users, and 48.5% of adult users were current cigarette smokers who had tried to quit smoking in the past year. The number one reason for e-cigarette use among both adolescent (77.9%) and young adult users (90.3%) was the availability of appealing flavors. Meanwhile, appealing flavors was the 7th most commonly reported reason among older adult users (first - beliefs may be less harmful than cigarettes to themselves and others; 2 - acceptability of e-cigarette use in

places where cigarettes are not allowed. Overall, "the leading e-cigarette flavor types among adolescents were fruit, candy, and other flavors; among young adults were fruit, candy, and mint/menthol; and among older adults were tobacco or other flavors, fruit, and mint/menthol." Compared with older adults, adolescents and young adults were more likely to use fruit-flavored e-cigarettes (adjusted odds ratio [aOR] = 3.35; 95% confidence interval [CI], 2.56-4.38; and aOR = 2.31; 95% CI, 1.77-3.01, respectively) and candy-flavored e-cigarettes (aOR = 3.81; 95% CI, 2.74-5.28; and aOR = 2.95; 95% CI, 2.29-3.80, respectively) and concurrently use multiple flavor types (aOR = 4.58; 95% CI, 3.39-6.17; and aOR = 2.28; 95% CI, 1.78-2.91, respectively)." Analysis by race/ethnicity found "the odds of mint/menthol-flavored e-cigarette use were higher among non-Hispanic black users (aOR = 3.81; 95% CI, 2.78-5.22) and Hispanic users (aOR = 1.60; 95% CI, 1.18-2.18) than among non-Hispanic white users." Authors concluded, "Regulation of sweet e-cigarette flavors (eg, fruit and candy) may help reduce the use of e-cigarettes among young persons without substantially burdening adult e-cigarette users."

23. McKelvey K., Baiocchi M., Ramamurthi D., et al. Youth say ads for flavored e-liquids are for them. *Addict Behav.* 2019;91:164-170.

McKelvey et al. showed adolescents and young adults (ages 14 to 21 years) advertisements for flavored e-liquids and asked which age group they thought advertisements targeted. Data were collected in 2016 (June through September) as part of a larger survey, a random sample of 255 youth from across California. The sample was 62.4% female; mean age=17.5, SD=1.7 [range 14-21]; 25.6% ever-used e-cigarettes; 24% white, 27% Asian/Pacific Islander, 36% Latino, and 12% Other. Participants viewed "eight ads, presented in randomized order, for fruit-, dessert-, alcohol-, and coffee-flavored e-liquids and indicated the age group they thought the ads targeted: younger, same age, a little older [18-24 years], or much older than them." Respondents could choose anywhere from 0 to 4 age groups as target age groups for each flavor ad. Researchers estimated population means and 95% confidence intervals using bootstrapping (100,000 replicate samples). Results show 93.7% of participants indicated "the cupcake man flavor ad targeted an audience of people younger than they." More than half of respondents believed ads for smoothie (68.2%), cherry (63.9%), vanilla cupcake (58%), and caramel cappuccino (50.4%) flavors targeted their age group. Overall, "for no flavor ad did most feel the primary target age group was much older." Results indicate "youth believe ads for flavored e-liquids target individuals about their age, not older adults." Authors conclude, "findings support the need to regulate flavored e-liquids and associated ads to reduce youth appeal, which ultimately could reduce youth use of e-cigarettes."

24. Harrell Melissa B., Loukas Alexandra, Jackson Christain D., et al. Flavored Tobacco Product Use among Youth and Young Adults: What if Flavors Didn't Exist? *Tobacco Regulation Science.* 2017;April(2):168-173.

Harrell et al. conducted a study to determine "the potential for reductions in the prevalence of young people's e-cigarette and tobacco use if characterizing flavors were not present." Authors used two parallel cross-sectional surveys of 2,483 youth aged 12-17 years (TATAMS: Texas Adolescent Tobacco and Marketing Surveillance System) and 4,326 young adults aged 18-29 years (M-PACT: Marketing and Promotions across Colleges in Texas) in Texas (Houston, Dallas/Ft. Worth, San Antonio, Austin), which included questions related to current use of e-cigarettes and other tobacco (cigarettes, cigar products, hookah, smokeless tobacco). Those who used e-cigarettes and other tobacco products were asked: "When you use [product], do you

usually use any of the following flavors?" Those who used flavored products were asked: "Would you continue using [product] if it were not flavored?" Results showed "[f]lavored tobacco use was high for both youth (89%) and young adults (83%)" and "use of flavored e-cigarettes and hookah was most common (>90% of past 30-day users)." However, if characterizing flavors were not present three-quarters of flavored tobacco users reported they would discontinue using the product. Furthermore, reported discontinued use was highest for e-cigarettes and hookah and lowest for cigarettes. Findings show, "[s]ignificantly more young adult females than males reported they would not use the product if it were not flavored [e-cigarettes: 77% vs. 69%, p=.03]." Results indicate that "these reductions would be expected to impact adolescent boys and girls across middle school and high school in Texas about equally. However, restricting or removing flavors may have a larger impact on young adult female than male e-cigarette and other tobacco product use." Authors noted, "[a]lthough youth often start their tobacco use with flavored products, this study reinforces that use of flavored tobacco products among current users after initiation and experimentation is also high." Authors concluded that "[r]estricting flavors in tobacco products would not eradicate e-cigarette or other tobacco use among young people, but the potential for substantial reductions in the prevalence of young people's e-cigarette and other tobacco use seems high if flavors were removed." Limitations of the study include: data are from school-going participants and may not be generalizable to out-of-school youth or young adults; cross-sectional data do not allow for direct estimation of flavors influence on initiation or cessation among young people. Authors cite menthol cigarette specific research which "suggests many menthol smokers, including young adults, support a ban on the use of this characterizing flavor in this product and would try to quit if such a ban were put into place."

25. **Pesko M. F., Kenkel D. S., Wang H., et al. The effect of potential electronic nicotine delivery system regulations on nicotine product selection. *Addiction*. 2016;111(4):734-744.** Pesko et al. estimated the "effect of potential regulations of electronic nicotine delivery systems (ENDS) among adult smokers, including increasing taxes, reducing flavor availability and adding warning labels communicating various levels of risk." Researchers performed a discrete choice experiment (DCE) among a national sample of 1200 adult smokers. A total of 1200 adult smokers from the United States were recruited to participate in the study. Participants were presented with hypothetical purchase choice of cigarettes, nicotine replacement therapy and a disposable ENDS. Results showed restricting flavor availability in ENDS to tobacco and menthol was associated with a 2.1 percentage point reduction in ENDS selection ($P < 0.001$) among participating adults. Young adult smokers were 3.7 percentage points more likely to choose ENDS when multiple flavors were available than older adults ($P < 0.001$). Findings suggest reducing flavor availability may reduce ENDS use by young adult smokers.

26. **Tierney P. A., Karpinski C. D., Brown J. E., et al. Flavour chemicals in electronic cigarette fluids. *Tobacco Control*. 2016;25(e1):e10-15.** Tierney et al. measured the flavor chemical components of 30 e-cigarette fluids from two brands: BLU and NJOY. The authors noted that, "adoption of e-cigarettes has far out-paced our understanding of their implications for health, including the initial composition of the e-cigarette fluids as well as presence of harmful by-products formed during 'vaping.'" Flavor compounds are not typically listed on e-cigarette packaging. However, flavoring has been a focus of e-cigarette marketing strategies despite the fact that flavored cigarettes were banned in 2009 based on

evidence that flavors attract youth. The authors also quote the Flavor Extracts Manufacturers Association that, "the Flavor Extracts Manufacturers Association Expert Panel does not evaluate flavor ingredients for use in tobacco products including e-cigarettes or other products that are not human food, or products that result in exposures other than ingestion...E-cigarette manufacturers should not represent or suggest that the flavor ingredients used in their products are safe because they have [Flavor Extracts Manufacturers Association 'generally recognized as safe' status for use in food because such statements are false and misleading." Tierney et al. found that flavor chemicals comprised 1-4% of the total fluid, and that six of the 24 isolated chemicals were aldehydes. Aldehydes are "a compound class recognized as 'primary irritants' of mucosal tissue of the respiratory tract." They also found that the majority of tobacco flavored e-cigarettes were found to contain confectionary flavor chemicals, rather than tobacco extracts. Overall, they concluded that, "the concentrations of some flavour chemicals in e-cigarette fluids are sufficiently high for inhalation exposure by vaping to be of toxicological concern." In 13 of the 30 e-liquids tested, flavor chemicals comprised more than 1% by weight. Based on these concentrations, the authors concluded that e-liquid consumption rates may be twice the recommended daily occupational exposure limits by inhalation for benzaldehyde and vanillin flavor chemicals.

27. Courtemanche C.J., Palmer M.K., Pesko M.F. Influence of the Flavored Cigarette Ban on Adolescent Tobacco Use. *American Journal of Preventive Medicine*. 2017;52(5):e139-e146.

Courtemanche et al. cite previous research findings that 17 year olds were three times as likely to use flavored cigarettes than smokers older than 25 years of age. In addition, the majority of tobacco users state that the first product they tried was a flavored product, "supporting the concern that these products may serve as a gateway to tobacco addiction." The 2009 Family Smoking Prevention and Tobacco Control Act banned all flavored cigarettes (except menthol) as a step to limit youth tobacco use and initiation. Courtemanche et al. evaluated the impact of the 2009 ban on flavored cigarette products on adolescent tobacco use. They used data from the National Youth Tobacco Survey (NYTS) from 1999 to 2013 to look at a number of variables before and after the ban, including: past 30-day cigarette use, number of cigarettes smoked in the past 30 days, use of menthol cigarettes among smokers, and past 30-day use of any other tobacco product besides cigarettes. Control variables included age, gender, race/ethnicity, price indices for cigarettes and other tobacco products, inflation, and youth unemployment rates. Their sample included 197,834 youth aged 11 to 19 years of age. Overall, the authors found that banning flavored cigarettes was associated with a 17% decrease in the likelihood of being a cigarette smoker ($p < 0.001$) and a 58% decrease in cigarettes smoked ($p = 0.005$). However, use of menthol cigarettes increased by 45% among smokers ($p < 0.001$), use of cigars increased by 34% ($p < 0.001$), and use of pipe tobacco increased by 55% ($p < 0.001$). The authors stated these findings imply "substitution toward the remaining legal flavored tobacco products." The likelihood of using at least one non-cigarette tobacco product increased 14%. However, after taking into account these increases in other forms of tobacco, the authors found an overall net 6% decrease in the probability of using any tobacco product (including cigarettes) (< 0.001). They concluded, "the results suggest the 2009 flavored cigarette ban did achieve its objective of reducing adolescent tobacco use, but effects were likely diminished by the continued availability of menthol cigarettes and other flavored tobacco products." This study did not account for hookah and e-cigarette use, as questions about these products were not included in the NYTS

until 2011. However, the authors noted that 89% of adolescents that use hookah and 85% of adolescents that use e-cigarettes use flavors.

28. Sciences National Academy of. *Public Health Consequences of E-Cigarettes.* Washington, D.C.: The National Academies Press; 2018.

The U.S. Food and Drug Administration requested the National Academy of Sciences complete a report about the health impacts of e-cigarettes. As part of this white paper, the National Academy of Sciences evaluated existing published literature to determine whether there was conclusive, substantial, moderate, limited, insufficient, or no available evidence to determine the link between e-cigarette use and health outcomes. They stated that, "the net public health effect, harm or benefit, or e-cigarettes depends on three factors: their effect on youth initiation of combustible tobacco products, their effect on adult cessation of combustible tobacco products, and their intrinsic toxicity." E-cigarette use among youth and young adults has increased, and in 2016, e-cigarette use was higher than cigarette smoking or use of any other tobacco product. Use was also higher among boys and Hispanic and non-Hispanic whites. They reached 9 conclusions about the make-up of e-cigarettes. They found conclusive evidence that: 1) E-cigarette use increases airborne concentrations of particulate matter and nicotine in indoor environments. 2) Exposure to nicotine from e-cigarette use is variable and depends on product characteristics and operation. 3) E-cigarettes contain and emit numerous potentially toxic substances in addition to nicotine. 4) The number, quantity, and characteristics of potentially toxic substances in e-cigarettes are highly variable and depend on product characteristics and operation. They found substantial evidence that: 5) Nicotine intake from e-cigarettes among experienced adult e-cigarette users is comparable to that from combustible tobacco cigarettes. 6) Under typical use, except for nicotine, there is lower exposure to potentially toxic substances from e-cigarettes compared to combustible tobacco cigarettes. 7) E-cigarettes contain metals. They found limited evidence that: 8) E-cigarette use increases levels of nicotine and other chemicals on indoor surfaces. 9) the number of metals in e-cigarettes could be greater than the number of metals in combustible cigarettes. The National Academy of Sciences also made 26 conclusions about the impact of e-cigarettes on health outcomes. They concluded that, "the implications for long-term effects on morbidity and mortality are not yet clear. Use of e-cigarettes instead of combustible tobacco cigarettes by those with existing respiratory disease might be less harmful." They found conclusive evidence that: 1) E-cigarette devices can explode and cause burns and injuries. 2) Intentional or accidental exposure to e-liquids can result in seizures, anoxic brain injury, vomiting, and lactic acidosis, among other effects. 3) Intentionally or unintentionally drinking or injecting e-liquids can be fatal. They found substantial evidence that: 4) Components of e-cigarettes can promote formation of reactive oxygen species/oxidative stress. 4) E-cigarette use results in symptoms of dependence on e-cigarettes. 5) E-cigarette use increases heart rate shortly after nicotine intake. 6) Chemicals in e-cigarettes are capable of causing DNA damage and mutagenesis, suggesting the possibility that long-term exposure could increase risk of cancer and adverse reproductive outcomes. Related to initiation and cessation, they found 7 conclusions. They found mixed evidence that, "while e-cigarettes might cause youth who use them to transition to use of combustible tobacco products, they might increase adult cessation of combustible tobacco products." They found substantial evidence that "e-cigarette use increases risk of ever using combustible tobacco cigarettes among youth and young adults." Overall, the National Academy of Sciences found that the evidence across a range of outcomes suggests that, "e-cigarettes pose less risk to an individual than combustible tobacco cigarettes." They also

concluded that "there would be net public health harm in the short and long terms if the products do not increase combustible tobacco cessation in adults."

29. **Watkins S. L., Glantz S. A., Chaffee B. W. Association of Noncigarette Tobacco Product Use With Future Cigarette Smoking Among Youth in the Population Assessment of Tobacco and Health (PATH) Study, 2013-2015. *JAMA Pediatrics*. 2018;172(2):181-187.** Watkins et al. used data from the national Population Assessment of Tobacco and Health (PATH) survey to determine whether adolescents use of electronic cigarettes, hookah, noncigarette combustible tobacco, or smokeless tobacco led to cigarette smoking initiation. The authors stated that, "in addition to their direct health effects, how these products affect youth cigarette smoking is a major consideration in determining their net influence on public health." PATH is a nationally representative survey of 12 to 17 year olds, and the authors completed a longitudinal evaluation of survey responses for 10,384 youth from 2013 and 2015. At baseline, approximately 9% of youth had never tried a cigarette and had tried at least one non-cigarette tobacco product. They found that cigarette imitation was higher among youth that had used e-cigarettes, hookah, noncigarette combustible tobacco, or smokeless tobacco. Overall, "the odds of past 30-day cigarette use at follow-up were approximately twice as high among baseline ever users of e-cigarettes (odds ratio [OR], 1.87; 95% CI, 1.15-3.05), hookah (OR, 1.92; 95% CI, 1.17-3.17), noncigarette combustible tobacco (OR, 1.78, 95% CI, 1.00-3.19), and smokeless tobacco (OR< 2.07; 95% CI, 1.10-3.87)." The authors found that "ever use of e-cigarettes was associated with 2.53 times greater odds of subsequent cigarette use." Using two or more types of non-cigarette tobacco products was associated with 4 times greater odds of past 30-day cigarette smoking at follow-up (OR, 3.95, 95% CI, 2.65-5.90, P<.001). The authors cite previous research showing that "approximately 90% of adult smokers first tried a cigarette by 18 years of age, and even infrequent smoking in adolescence is associated with established adult smoking."

30. **Soneji S., Barrington-Trimis J.L., Wills T.A., et al. Association Between Initial Use of e-Cigarettes and Subsequent Cigarette Smoking Among Adolescents and Young Adults-- A Systematic Review and Meta-analysis. *JAMA Pediatrics*. 2017;171(8):788-797.** Soneji et al. conducted a systematic review and meta-analysis of longitudinal studies to determine whether initial use of e-cigarettes leads to subsequent cigarette smoking among youth and young adults. They included 9 studies in their analysis. Overall, they found that e-cigarette use was strongly and consistently associated with greater risk for cigarette smoking initiation (OR 3.50, 95% CI 2.38-5.16) and past 30-day cigarette smoking (OR 4.28, 95% CI 2.52-7.27) among youth and young adults. In addition, their analysis found that e-cigarette use is an independent risk factor for cigarette smoking, after controlling for multiple additional risk factors.

31. **Barrington-Trimis Jessica L. , Kong Grace , Leventhal Adam M. , et al. E-cigarette Use and Subsequent Smoking Frequency Among Adolescents. *Pediatrics*. 2018;142(6).** E-cigarette use is associated with cigarette initiation. Barrington-Trimis et al. pooled data from 3 prospective cohort studies in California and Connecticut (baseline: 2013-2014; follow-up: 2014-2016; N = 6,258) to assess whether e-cigarette use is associated with more frequent cigarette use after initiation or whether adolescent cigarette or dual product users transition to e-cigarette use or nonuse. Authors found that fewer never e-cigarette users (at baseline) began smoking (7%) compared to those who had used e-cigarettes at baseline (21% reported smoking cigarettes at

follow-up). "Baseline exclusive e-cigarette users had higher odds of reporting exclusive e-cigarette use at follow-up (OR = 7.28; 95% CI: 4.86–10.9), exclusive cigarette use at follow-up (OR = 3.84; 95% CI: 1.80– 8.19), or dual product use at follow-up (OR = 8.86; 95% CI: 5.08–15.4)." Once youth began smoking cigarettes (either never e-cigarette users or e-cigarette users at baseline) the amount that they smoked was similar. Researchers found, "Among baseline never smokers, e-cigarette users had greater odds of subsequent experimental (odds ratio [OR] = 4.58; 95% confidence interval [CI]: 3.56–5.88), infrequent (OR = 4.27; 95% CI: 2.75–6.62) or frequent (OR = 3.51; 95% CI: 1.97–6.24) cigarette use; the 3 OR estimates were not significantly different." Whereas, "[b]aseline past-30-day exclusive cigarette use was associated with higher odds at follow-up of exclusive cigarette or dual product use than of exclusive e-cigarette use."

32. Leventhal Adam M., Strong David R., Kirkpatrick Matthew G., et al. Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence.(Report). 2015;314(7):700.

Leventhal et al. cite evidence that electronic cigarettes are being used among teens who have never used combustible cigarettes. They cite a 2014 estimate that in the United States 43% of 10th graders who reported using e-cigarettes in the previous 30 days reported never having tried combustible cigarettes. Leventhal et al. analyze data from a longitudinal survey of high school students from a convenience sample of 10 public high schools in the Los Angeles, California area. They collected data in three waves: baseline (fall 2013; 9th grade), 6-month follow-up (spring 2014), and 12-month follow-up (fall 2014; 10th grade). The final sample included students who completed all three waves of the survey (n=2,530). They found that students who reported e-cigarette use at baseline were also more likely to report use of combustible tobacco products in the previous 6 months. After adjusting for potential confounding factors, the authors found that baseline e-cigarette use was also associated with a higher likelihood of using combustible tobacco products (cigarettes, cigars, or hookah) at follow-up (averaged across the two follow-up periods OR 2.73 [95% CI 2.00-3.73]). This trend was also true for combustible cigarettes specifically (OR 3.25 [95% CI 2.29-4.62]).

33. Thomas A Wills, Rebecca Knight, James D Sargent, et al. Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. *Tobacco Control*. 2016.

Wills et al. analyzed 2013 and 2014 longitudinal school-based survey data from Hawaii. The baseline sample included 2,338 9th and 10th graders. Students who were not smokers at baseline but who had used e-cigarettes were significantly more likely to have smoked combustible cigarettes at the one-year follow-up than their non-smoking peers who had never tried e-cigarettes (OR 2.87 [95% CI 2.03-4.05]). Among students who had tried combustible cigarettes at baseline, using e-cigarettes was not significantly related to changes in their frequency of smoking traditional cigarettes at follow-up.

34. Pisinger Charlotta, Dossing Martin. A systematic review of health effects of electronic cigarettes. *Preventive Medicine*. 2014;69:248.

Pisinger and Døssing conducted a systematic review of the literature on the health consequences of vaping products published before August 14, 2014. The authors identified 76 studies which met their inclusion criteria. They found that 34% of the studies' authors had a conflict of interest (e.g. the study was funded or somehow influenced by electronic cigarette manufacturers or

consultants for manufacturers of medicinal smoking cessation therapy). Many studies found that product labels did not show the concentrations of solvents and flavoring and that products labeled nicotine free were sometimes found to actually contain nicotine in high concentrations. There was also variability in product concentrations from cartridge-to-cartridge. The authors conclude that the studies had many methodological problems and that the body of evidence is inconsistent, lack long-term follow up, and don't allow any firm conclusion on the safety of vaping products. They conclude that these 76 studies indicate that electronic cigarettes cannot be regarded as safe. The available evidence does indicate that at least some vaping products are toxic to human cells and contain toxic compounds such as metals, traces of carcinogenic nitrosamines, formaldehyde, mercury, and other potentially harmful components. Vaping was associated with significant airway and lung obstruction in the short term and other adverse effects in the mouth/throat. Some studies indicate that vaping may have less adverse effects or result in less exposure to harmful substances than combustible cigarettes. Some studies suggest that electronic cigarettes may be useful as a smoking reduction/cessation aid, but the evidence on their efficacy is conflicting.

35. Hocharoen Chanalee. An evaluation of potential harm of electronic cigarette aerosol exposures and directions for research and regulation. In: Taft D, ed: ProQuest Dissertations Publishing; 2015.

Hocharoen conducted a systematic review of the literature on electronic cigarettes published between January 1, 2009 and January 31, 2015. Thirty-nine articles met the inclusion criteria. Three of these studies examined inflammatory markers, cytokines, and chemokines, all of which found that interleukins (cellular messengers for immune response) increased with electronic cigarette exposure. One study found that interleukin 6 decreased with e-cigarette exposure. Seven studies examined cytotoxicity (cell toxicity) or mutagenicity (ability to cause genetic mutations). These studies looked at the impacts of e-vapors of liquids on lung, throat, and mouth specific embryonic stem cells, and various fibroblasts. Six of these seven studies found cytotoxic effects, decreased cell viability, changes in cell morphology, reduced ATP detection, and cell mutagenicity for at least one of the measured flavors or e-liquid components. The seventh study found no cytotoxicity from e-liquids for epithelial carcinoma cells or Chinese Hamster ovary cells. The author concludes that cell viability is affected by e-cigarettes and that vapor products sometimes contain "carcinogens, metals, and other potentially harmful constituents." The author notes that while physiological effects of e-cigarettes have been found in the literature, potential adverse long-term effects have not been studied.

36. General Office of the Surgeon. E-Cigarette 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 of Smoking and Health; 2016.

This report was prepared by the Centers for Disease Control and Prevention's National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. It focused on examining the research around the epidemiology and health effects of e-cigarette use among youth and young adults in the United States. They note that, "the initial drafts of the chapters were written by 27 experts who were selected for their knowledge of the topics addressed. These contributions are summarized in five chapters that were evaluated by approximately 30 peer reviewers. After peer review, the entire manuscript was sent to more than 20 scientists and other

experts, who examined it for its scientific integrity." The chapters outline the following topic areas: (1) historical background, (2) patterns of e-cigarette use among U.S. youth and young adults, (3) health effects of e-cigarette use among U.S. youth and young adults, (4) activities of e-cigarette companies, and (5) e-cigarette policy and practice implications.

37. Center Washington Poison. 2017 Annual Toxic Trend Report: Nicotine and E-Cigarette. 2017.

This brief report from the Washington Poison Center provides summary data from calls about nicotine exposure among children 0 to 12 years of age. From 2011 to 2017, the Washington Poison Center received 2,966 total cases related to nicotine exposure. The most cases occurred in 2015, with 521 total cases of nicotine exposure. In 2017, the Center had 440 cases of nicotine exposure and 373 (84.8%) cases were among children 0-5 years of age. About half of nicotine exposures come from cigarette/cigar exposure, 22% are related to e-cigarettes, and 22% are related to chewing tobacco. Children are primarily exposed through ingestion (94.5% of cases are due to ingestion), and common symptoms of nicotine exposure include vomiting, coughing/choking, drowsiness/lethargy, and pallor. Washington Poison Center noted that exposure reporting is voluntary, and that these numbers likely underrepresent nicotine exposure.

38. Rubinstein M.L., Delucchi K., Benowitz N.L., et al. Adolescent Exposure to Toxic Volatile Organic Chemicals from E-Cigarettes. *Pediatrics*. 2018;141(4).

Rubinstein et al. analyzed urine and saliva samples from adolescents aged 13-18 years old who use electronic cigarettes to evaluate the presence of volatile organic compounds. More adolescents use e-cigarettes than cigarettes, and chemicals found in e-cigarettes are known to be harmful to human health. However, the authors noted that, "there are no data on toxicant exposure in adolescent e-cigarette users. However, there is great concern because exposure to toxicants during adolescence may result in greater harm than exposure in adulthood, given vulnerability to the acute and chronic effects of toxicants in general and from their cumulative exposure if started early." This study included adolescents participating in a larger longitudinal study of the effects of e-cigarettes on adolescents in the San Francisco Bay Area. Adolescents who used e-cigarettes were scheduled for a baseline appointment within 24 hours of use and provided saliva and urine samples for analysis. Saliva samples were analyzed for cotinine, a metabolite of nicotine. Urine samples were analyzed for NNAL (a potent carcinogen) and eight volatile organic compounds that are toxic environmental or tobacco smoke constituents. They used use categories based on self-report as well as chemical levels so that, "conservative criteria for group definitions meant that the e-cigarette-only group was clearly differentiated from the dual user group, and any [volatile organic compounds] found in the e-cigarette-only group could be clearly attributed to e-cigarette use." Based on their criteria, samples were analyzed for 67 e-cigarette-only users, 16 dual users, and 20 controls. They found that the presence of 5 volatile organic compounds was significantly higher in e-cigarette-only users compared with controls ($p < .05$ for all compounds), but lower than in dual-users. For e-cigarette-only users, levels were statistically significantly higher for users that used e-cigarettes with nicotine all or some of the time and for users that reported more sessions of e-cigarette use per day. They also found that "levels of 3 other significant and likely toxic [volatile organic compounds] were just as high in users of nonnicotine products as in those using nicotine." The authors concluded, "Adolescent e-cigarette-only users had levels of 5 [volatile organic compound] toxicants detected in their urine in quantities up to 3 times greater than in matched controls...levels of toxicant exposure in dual

users were up to 3 times higher than in those who used only e-cigarettes." Many of these compounds are known carcinogens.

39. Alzahrani T., Pena I., Temesgen N., et al. Association Between Electronic Cigarette Use and Myocardial Infarction. *American Journal of Preventive Medicine*. 2018;55(4):455-461.

Alzahrani et al. evaluated 2014 and 2016 National Health Interview Survey data to determine whether electronic cigarette use could increase the risk of myocardial infarction. This was the first study to examine the relationship between e-cigarette use and heart attack. E-cigarette use has been shown to stimulate similar reactions as traditional cigarette use in otherwise healthy individuals, including endothelial dysfunction, oxidative stress, inflammation, platelet activation, and activation of the sympathetic nervous system. Interviewees were classified as never, former, and current e-cigarette and cigarette users. However, the definition of former use was not consistent between e-cigarette users and cigarette users. Based on NHIS responses, 25.8% of current e-cigarette users were former smokers and 66.2% of current e-cigarette users were also current cigarette smokers. Overall, the authors found that daily e-cigarette use was independently associated with increased odds of myocardial infarction (OR= 1.79, 95% CI= 1.20, 2.66, p-value= 0.004). Former and some day e-cigarette use were not associated with increased risk of heart attack. Former, some day, and current cigarette use were all associated with increased risk of heart attack. The authors also found that, "dual use of e-cigarettes and conventional cigarettes appears to be more dangerous than using either product alone." The authors state that their study likely underestimates the increased risk of heart attack from using e-cigarettes, and that more research is needed to fully understand the health impacts of former or some day e-cigarette use. They state that, "it is not known when the [myocardial infarctions] occurred relative to e-cigarette use, and it is likely that some of the heart attacks subjects reported occurred before e-cigarettes became available in the U.S. (around 2009). This situation will bias the [odds ratio] estimates toward the null, meaning that the study results likely underestimate the true risks associated with e-cigarette use."

40. Clapp P., Lavrich K., Reidel B., et al. The E-Cigarette Flavoring Cinnamaldehyde Suppresses Mitochondrial Function and Transiently Impairs Cilia Beat Frequency in Human Bronchial Epithelial Cells. Paper presented at: Epithelial Function in Health and Disease- Poster Discussion Session; May 23, 2018, 2018; San Diego, California.

In this abstract, Clapp et al. explain that compounds in cigarettes impair mitochondrial function and reduce cilia beat frequency, impairing lung function. They note that cinnamaldehyde, which is commonly used to flavor e-cigarette products, has similar structural properties to compounds in cigarettes. They determined the content of cinnamaldehyde in e-cigarette products and exposed human bronchial epithelial cells to various levels to evaluate a dose-response relationship. Overall, the authors concluded, "data suggest that cinnamaldehyde, a ubiquitous flavoring agent commonly used in e-cigarettes, adducts to mitochondrial proteins, disrupts mitochondrial function, and significantly reduces intracellular ATP levels, which correlates with impaired [cilia beat frequency] in airway epithelial cells...inhalational exposures of cinnamaldehyde may increase the risk of respiratory infections in e-cigarette users."

41. **Gmel Gerhard, Baggio Stéphanie, Mohler-Kuo Meichun, et al. E- cigarette use in young Swiss men: is vaping an effective way of reducing or quitting smoking? *Swiss medical weekly*. 2016;146:w14271.**

Gmel et al. summarize the current evidence on the impact of e-cigarettes on combustible cigarette usage, noting that the literature is conflicting—with some studies finding that vaping is associated with using fewer cigarettes but with being less likely to completely quit smoking combustible cigarettes, and other studies finding an increase in combustible cigarette usage and decreased likelihood of quitting, and still other studies finding that e-cigarettes were associated with more quit attempts and continued abstinence than NRT or using no aid. The authors used data from the Cohort Study on Substance Use Risk Factors in Switzerland. While 7,556 participants (all young men) provided consent to participate, 79.2% (n=5,987) completed the baseline questionnaire and 79.7% (n=6,020) completed the follow-up questionnaire. A total of 91.5% of the baseline respondents (n=5,476) also completed the follow-up questionnaire. Among those who did not smoke at baseline, those who were vaping at follow-up were more likely to start smoking and to become occasional or daily smokers at follow-up than were non-vapers. Among those who were occasional smokers at baseline, non-vapers were more likely to become non-smokers and less likely to become daily smokers than vapers. Among those who did not smoke at baseline, vapers were 6 times more likely to be occasional smokers and 12 times more likely to be daily smokers at follow-up than non-vapers. Among non-smokers at baseline, vapers smoked significantly more (10 times more) cigarettes weekly at follow-up than did non-vapers. Weekly cigarette use increased between baseline and follow-up for occasional smokers and decreased for daily smokers but these changes were not significantly between vapers and non-vapers.

42. **Grace Randolph C., Kivell Bronwyn M., Laugesen Murray. Estimating cross- price elasticity of e- cigarettes using a simulated demand procedure. *Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco*. 2015;17(5):592.**

Grace et al. collected data from a convenience sample of 210 daily smokers in New Zealand who were 18 years of age or older and who had no intention to quit smoking before January 1, 2013. They excluded any smokers who had ever used e-cigarettes. They interviewed participants between February and March of 2013 (response rate not noted). The researchers had participants complete a written survey and three additional validated surveys, complete the Cigarette Purchase Task (CPT), sample an e-cigarette, and then answer questions about their intentions to purchase e-cigarettes and their regular tobacco product. The CPT is used to measure demand for tobacco products across a range of prices. The authors used the CPT completed before sampling the e-cigarette as a baseline to determine the demand for combustible cigarettes in the absence of e-cigarettes. The participants also indicated their intentions to purchase e-cigarettes and combustible cigarettes after trying the e-cigarette. The authors found that the simulated demand for e-cigarettes increased as the price of regular cigarettes increased, with an average cross-price elasticity of 0.16 (indicating that a 10% increase in the cost of combustible cigarettes was associated with a 1.6% increase in the demand for e-cigarettes). However, the simulation also found that the low-cost availability of e-cigarettes did not decrease the demand for regular cigarettes at a higher price and that a significantly lower proportion of participants said that they would quit smoking tobacco completely if e-cigarettes were available than if they were not. This finding suggests that the availability of low-priced e-cigarettes could actually encourage people who would otherwise have quit smoking completely as a result of raising tobacco prices to

instead continue to use combustible cigarettes perhaps in tandem with lower-cost e-cigarettes. So, while the study found that smokers may substitute e-cigarettes for combustible cigarettes as the cost of the later increases (with the cost of the former staying low), low-cost e-cigarette availability may actually discourage combustible cigarette smokers from quitting entirely as combustible cigarette prices increase.

43. **Rahman M. A., Hann N., Wilson A., et al. E- Cigarettes and Smoking Cessation: Evidence from a Systematic Review and Meta- Analysis. *PLoS One*. Vol 102015.**

Rahman et al. conducted a systematic review of the literature on combustible cigarette consumption or cessation after the use of e-cigarettes. Six studies met their inclusion criteria. They found that e-cigarettes with nicotine were more effective as a cessation tool than those without nicotine. The authors pooled data from two randomized control trials and found a risk ratio of 2.29 (95% CI 1.05-4.97). They also found that use of e-cigarettes was associated with smoking cessation and reduction in the number of cigarettes used—though three of the six studies did not include a control group. The authors note that they were only able to consider the efficacy of nicotine vs. non-nicotine e-cigarettes and were not able to compare the efficacy of e-cigarettes to other cessation interventions.

44. **Kalkhoran Sara, Glantz Stanton A. E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis. *The Lancet Respiratory Medicine*. 2016;4(2):116-128.**

Kalkhoran et al. conducted a systematic review and meta-analysis to evaluate the association between e-cigarette use and combustible cigarette cessation among adults. Thirty-eight studies met their inclusion criteria for the systematic review, 20 of which had control groups and were included in the meta-analysis. They found that the odds of combustible cigarette cessation among those who used e-cigarettes was 28% lower than for those who did not use e-cigarettes (OR 0.72 [95% CI 0.57-0.91]). When the authors only included studies of smokers with an interest in quitting, they did not find a significant difference from the overall findings. The authors conclude that e-cigarettes, as they are currently being used, are associated with lower quit rates among combustible cigarette smokers.

45. **Protano C., Avino P., Manigrasso M., et al. Environmental Electronic Vape Exposure from Four Different Generations of Electronic Cigarettes: Airborne Particulate Matter Levels. *International Journal of Environmental Research and Public Health*. 2018;15(2172).**

Protano et al. evaluated the levels of airborne particulate matter emitted by four generations of e-cigarette models in use in Italy. They found that all e-cigarette devices emitted particulate matter of a size that can be inhaled into the lungs (including PM10, PM4, PM2.5, and PM1). Newer models emitted greater levels of small particulate matter as a result of increased operating power. Overall, their findings suggest that passive vaping does occur, supporting "the need for legislative interventions to regulate e-cigs use in public places and other enclosed environments, in order to protect the health of any subject who is potentially exposed."

46. **Gallaway M.S., Henley S.J., Steele C.B., et al. Surveillance for Cancers Associated with Tobacco Use--United States, 2010-2014. *Morbidity and Mortality Weekly Report, Centers for Disease Control and Prevention*. 2018;67(12):1-42.**

In this Surveillance Summary, the Centers for Disease Control and Prevention evaluates tobacco-associated cancer incidence for 12 types of cancer associated with tobacco use from 2010 to 2014. They find that tobacco use contributes "to at least 12 types of cancer, including acute myeloid leukemia (AML) and cancers of the oral cavity and pharynx; esophagus; stomach; colon and rectum; liver; pancreas; larynx; lung, bronchus, and trachea; kidney and renal pelvis; urinary bladder; and cervix." They used cancer incidence data covering approximately 99% of the U.S. population from CDC's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results program. Approximately 3.3 million new tobacco-associated cancer cases were reported from 2010 to 2014, or approximately 667,000 cases per year. They found that incidence remains high among whites, blacks, non-Hispanics, and individuals living in rural areas.

47. **Centers for Disease Control and Prevention National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. *The Health Consequences of Smoking: 50 Years of Progress. A Report of the Surgeon General. U.S. Department of Health and Human Services; 2014.***

The analysts writing the Surgeon General's reports on the health effects of smoking use a set of criteria to rank the strength of evidence that a causal relationship exists. For each health indicator, the analysts synthesize the evidence and then apply the criteria to the body of evidence. The report is then vetted by a series of external editors who are tasked with ensuring the accuracy of the report. This comprehensive analysis includes hundreds of references. The 2014 report concludes that since the 1964 Surgeon General's report, a very strong body of evidence has shown a causal link between cigarette smoking and diseases in nearly every organ, cancer (e.g. lung, liver and colorectal cancer), diminished health status, exacerbation of asthma, inflammation, impaired immune function, age-related macular degeneration, harms to the fetus, diabetes, erectile dysfunction, arthritis, and premature death. Research also shows that secondhand smoke causes cancers, reparatory disease, cardiovascular disease, stroke, and harms to infant and child health. This report also summarizes the evidence indicating that tobacco use may have a different impact on adolescents than adults. The authors indicate that adolescence is a vulnerable stage of brain development, and that nicotine exposure during this age may have lasting adverse effects on brain development.

48. **Dunbar M.S., Tucker J.S., Ewing B.A., et al. *Ethnic Differences in Cigarette Use Trajectories and Health, Psychosocial, and Academic Outcomes. Journal of Adolescent Health. 2018;62:327-333.***

Dunbar et al. presented previous research that, "youth who initiate smoking and continue to smoke demonstrate poorer academic and occupational outcomes, social difficulties, behavioral problems, and more physical and mental health problems in young adulthood relative to individuals who abstain entirely or desist after a period of experimentation." They also summarized previous research suggesting that youth alcohol and marijuana use may impact academic performance and physical health disproportionately for some racial/ethnic groups. In this study, they examined adolescent smoking trajectories and academic, health, and social outcomes by race/ethnicity for students at the end of high school. The authors followed students who were in sixth or seventh grade in 2008 through their completion of high school in 2016. Approximately 6500 students from 16 middle schools in Los Angeles, California completed annual surveys during physical education classes. Surveys asked about current cigarette

smoking, sociodemographics and race/ethnicity, academic orientation, academic unpreparedness, physical ailments/symptoms, physical health, mental health, social functioning, and delinquency. Overall, they found that higher average cigarette use was associated with poorer academic performance, mental health, physical health, and social functioning as well as with greater academic unpreparedness, physical ailments, and delinquency. Controlling for cigarette use trajectories, "racial/ethnic minority youth showed poorer outcomes in multiple domains--notably physical health and physical impairments." The authors concluded, "after adjusting for similar use patterns over time, as well as an index of socioeconomic status (mother's education), cigarette smoking during adolescence is associated with poorer outcomes for racial/ethnic minority youth compared with white peers, and these disparities in health, academic, and other functional domains are evident as early as high school."

49. QxQ Analysis: E-Cigarette/Vapor Product Use by Race/Ethnicity, Sexual Orientation, and Gender Identity. Looking Glass Analytics; 2018.

<http://www.askhys.net/Analyzer>. Accessed September 2019.

Washington State Healthy Youth Survey data from 2018 indicate that among 8th grade respondents the highest rate of vaping was reported among Hispanic students (15.4% [95% CI 12.0-18.8%]), followed by American Indian or Alaska Native (AI/AN) students (14.6% [95% CI 9.4-19.8%]) and black students (13.6% [95% CI 8.5-18.7%]). Among 10th grade respondents, AI/AN students (28.0% [95% CI 18.7-37.3%]) and multi-racial students (24.4% [95% CI 20.7-28.1%]) reported higher smoking rates than their peers. The percent of students who had reported using e-cigarette/vapor products at all in the past 30 days was highest among 12 grade respondents. AI/AN students (38.3% [95% CI 24.6-52.0%]) and multi-racial students (35.2% [95% CI 30.8-39.7%]) reported higher rates of using e-cigarettes/vapor products than their peers. Among 12th graders, the lowest rates of e-cigarette/vapor product use were reported by Asian and Black/African American students. These data suggest that in Washington State, AI/AN, and multi-racial, and Hispanic youth have disparately high rates of current e-cigarette/vapor product use. It is important to note that the current race/ethnicity categories aggregate diverse subpopulations into one category—so disparities within these categories may be masked. For example, API subpopulations likely have very different smoking rates but they are aggregated into one category so these differences may be missed. White respondents in 10th and 12th grade also report high e-cigarette/vapor product current use compared to cigarette use. Students from the subsample of schools who participate in the extended form version of the Healthy Youth Survey also answered questions about their sexual orientation. Eighth grade respondents who identified as lesbian, gay, or bisexual were more likely to report using e-cigarettes/vapor products at all in the last 30 days (16.5% [95% CI 10.8-22.2%]) than their peers who identified as straight (10.1% [95% CI 7.9-12.3%]). This disparity also existed among 10th graders (32.1% [95% CI 27.4-36.8%] vs. 20.8% [95% CI 17.7-23.9%]) and 12 graders (35.4% [95% CI 29.9-40.9%] vs. 28.1% [95% CI 24.3-31.9%]). Finally, the Healthy Youth Survey also asks students about their gender identity. Eighth grade and 12th grade data were suppressed due to fewer than 5 responses in at least one category. Among 10th grade respondents who identified as transgender were more likely to report using e-cigarettes/vapor products at all in the last 30 days (44.7% [95% CI 26.6-62.8%]) than their peers who identified as cisgender female (22.4% [95% CI 19.3-25.5%]) or cisgender male (20.8% [95% CI 17.5-24.1%]). Disparities also exist for students who report something else fits better (30.0% [95% CI 14.8-45.2%]), questioning/not

sure of my gender identity (24.4% [95% CI 12.4-36.4%]), and who selected more than one response (28.0 [95% CI 14.0-42.0%]).

50. **Kann L., McManus T., Harris W.A., et al. Youth Risk Behavior Surveillance--United States, 2017. *Morbidity and Mortality Weekly Report, Centers for Disease Control and Prevention*. 2018;67(8).**

This MMWR Surveillance Report provides updated findings from the 2016-2017 Youth Risk Behavior Surveillance System (YRBSS) on the leading causes of morbidity and mortality among youth, including unintentional injuries and violence; tobacco use; alcohol and drug use; sexual behaviors; dietary behaviors; and physical inactivity. It presents data on health behaviors and health disparities by sex, race/ethnicity, grade in school, and sexual orientation. This is the first YRBSS survey that reports on questions added in 2015 related to sexual orientation. Washington State did not participate in the 2016-2017 YRBSS. Specific to tobacco use, this version of YRBSS either changed the wording of the question or response or asked a question for the first time related to the following measures: "having first tried cigarette smoking before age 13 years; having usually gotten their own electronic vapor products by buying them in a store; current, current frequent, and current daily smokeless tobacco uses; current cigarette, cigar, or smokeless tobacco use; current cigarette, cigar, smokeless tobacco, or electronic vapor produce use; having tried to quit using all tobacco products." From 1991 to 2017, the prevalence of ever trying cigarette smoking significantly decreased from 70.1% to 28.9% nationally. Male, white, and gay, lesbian, and bisexual students were more likely to have ever tried cigarette smoking compared to other students. In addition, this YRBSS asked for the first time about cigarette smoking before 13 years of age, and results indicated that 9.5% of students had tried cigarette smoking before 13 years of age. From 1991 to 2017, the prevalence of current cigarette use (smoked a cigarette at least once in the past 30 days) also significantly decreased from 27.5% to 8.8% nationally. Among students that currently used cigarettes, the prevalence was higher for males (9.8%) than females (7.8%), and whites (11.1%) compared to Hispanic (7.0%) or black (4.4%) students. Current cigarette use was almost twice as high among gay, lesbian, and bisexual students (16.2%) compared to heterosexual students (8.1%). Nationally, 2.6% of students had smoked cigarettes on 20 or more days in the past 30 days, and 2.0% of students had smoked cigarettes on all 30 days. Frequent cigarette use was higher among whites and gay, lesbian, and bisexual students. Nationally, 42.4% of students had every used an electronic vapor product (e.g. e-cigarettes, e-cigars, e-pipes, vape pipes, vaping pens, e-hookahs, hookah pens), and 13.2% of students currently used e-cigarettes (used an electronic vapor product at least once in the past 30 days). Among students that currently used e-cigarettes, the prevalence was higher for males (15.9%) than females (11.8%); whites (15.6%) compared to Hispanic (11.4%) or black (8.5%) students; and gay, lesbian, and bisexual students (17.5% compared to 13.2% of heterosexual students). Nationally, 3.3% of students had used an electronic vapor product on 20 or more days in the past 30 days, and 2.4% of students had used an electronic vapor product on all 30 days. Frequent vapor product use was higher among male, white, and gay, lesbian, and bisexual students. Among students that currently used electronic vapor products, 13.6% had gotten their own electronic vapor products by buying them in a store. Nationally, 5.5% of students currently used a smokeless tobacco product (e.g. chewing tobacco, snuff, dip, snus, or a dissolvable tobacco product). Approximately 24% of students had used any tobacco product during the past 12 months. Of these students, 41.4% had tried to quit and females, whites and Hispanics, and gay, lesbian, and bisexual students were more likely to have tried to quit. Overall, males were

more likely to have engaged in tobacco use risk behaviors than females. White students were more likely to have engaged in tobacco use risk behaviors than Hispanic or black students. Gay, lesbian, and bisexual students were more likely to have engaged in tobacco use risk behaviors than heterosexual students, and the prevalence for current, current frequent, and current daily cigarette use was twofold or greater for gay, lesbian, and bisexual students compared to heterosexual students. The prevalence for current frequent and current daily cigarette use, and current frequent and current daily cigar use was twofold or greater for students who had sexual contact with only the same sex or with both sexes compared to students who had sexual contact with only the opposite sex.

51. Healthy Youth Survey Fact Sheets: Tobacco Use and Tobacco & Vapor Product Use. Healthy Youth Survey Fact Sheets. Looking Glass Analytics; 2018.

Analysts reviewed Washington State Healthy Youth Survey Fact Sheets for Tobacco and Tobacco & Vapor Product Use for grade levels 8, 10, and 12. These fact sheets provide current use trends for tobacco products (vapor products, cigarettes, and smokeless tobacco), statewide current use by race/ethnicity, single and dual use (cigarettes and vapor products), reported substance "vaped", and source. The most commonly reported substances "vaped" among current users across grade levels contain nicotine or flavor only (no nicotine or THC). The most commonly reported substance vaped among 8th graders is flavor only (44%), followed by nicotine in it (39%), THC (marijuana) in it (17%), and substance unknown (14%). Among 10th and 12th graders, the most commonly reported substance vaped contains nicotine (56% and 62%, respectively), followed by flavor only (33% and 26%), THC in it (21% and 24%), and substance unknown (10% and 8%).

52. Simon Patricia , Camenga Deepa R. , Morean Meghan E. , et al. Socioeconomic status and adolescent e-cigarette use: The mediating role of e-cigarette advertisement exposure. *Preventive Medicine*. 2018;112(2018):193-198.

Simon et al. examined "exposure to e-cigarette advertisements as a mediator of the relationship between [socioeconomic status (SES)] and adolescent e-cigarette use." While low SES is associated with "greater exposure to tobacco cigarette advertising and cigarette use," associations among SES, e-cigarette advertising, and e-cigarette use are not yet well understood. Authors used anonymous survey data collected from adolescents (N = 3,473; 51% Female) attending 8 high schools in Connecticut in Spring 2015. "Mediation analysis was used to examine whether the total number of sources of recent e-cigarette advertising exposure (e.g., TV, radio, billboards, magazines, local stores [gas stations, convenience stores], vape shops, mall kiosks, tobacco shops, social media) mediated the association between SES (measured by the Family Affluence Scale) and past-month frequency of e-cigarette use." Researchers "clustered for school and controlled for other tobacco product use, age, sex, race/ethnicity and perceived social norms for e-cigarette use in the model." The sample had recently seen e-cigarette advertisements via 2.1 (SD = 2.8) advertising channels. "Mediation was supported (indirect effect: $\beta = 0.01$, SE = 0.00, 95% CI [0.001, 0.010], $p = 0.02$), such that higher SES was associated with greater recent advertising exposure, which, in turn, was associated with greater frequency of e-cigarette use." Results suggest that "regulations to reduce youth exposure to e-cigarette advertisement may be especially relevant to higher SES youth." Authors recommend future research "examine these associations longitudinally and evaluate which types of advertisements target different SES groups."

53. Zhu Shu-Hong, Zhuang Yue-Lin, Braden Katherine, et al. Results of the Statewide 2017-18 California Student Tobacco Survey. San Diego, California: Center for Research and Intervention in Tobacco Control (CRITC); 2019.

This report summarized the main results from the 2017-18 California Student Tobacco Survey (CSTS), which was administered to 8th, 10th, and 12th grade students from September 2017 to June 2018. Random selection of California middle and high schools resulted in 333 schools and 151,404 students participating in the survey. Results show that students in San Mateo and San Francisco Counties reported current e-cigarette use at nearly double (20.8%) the use statewide (10.9%).

54. Defense Department of. 2015 Health Related Behavior Survey for Active Duty Service Members. 2015.

The Health Related Behavior Survey for Active Duty Service Members is a Department of Defense survey used to track health indicators for all branches of active-duty military personnel. Survey data from 2015 indicated that e-cigarette use has been increasing among military personnel. In 2015, 35.7% of military personnel reported ever trying e-cigarettes compared to 12.6% of the general population and 11.1% reported being daily e-cigarette users compared to 3.7% of the general population. The survey also found that 80.7% of military personnel reported buying cigarettes on a military base. Use also varied by branch and rank. All forms of tobacco use, including e-cigarette use, were highest among the Marine Corps (16.1%). E-cigarette use was also higher among lower ranking personnel. For example, 20% of junior enlisted personnel currently used e-cigarettes compared to 10.8% of mid-level enlisted personnel, 6.1% of senior enlisted personnel, 3.4% of warrant officers, 2.2% of junior officers, and 0.9% of mid-grade or senior officers. Active-duty military members "aged 17-24 were almost ten times more likely to be a current e-cigarette smoker than service members aged 45 or older." By age, 22.8% of personnel aged 17-24 currently used e-cigarettes, 10.8% of personnel aged 25-34, 5.4% of personnel aged 35-44, and 2.5% of personnel older than age 45. Military personnel identifying as Hispanic and personnel having high school education or less also used e-cigarettes at a higher rate.

55. Smith Derek. San Francisco vs. Goliath: how communities of color fought to protect our youth against Big Tobacco *Step 2 - Implementing Innovation. San Francisco, California: San Francisco Department of Public Health; 2019.

This presentation from the San Francisco Department of Public Health provides an overview of how it implemented the city ordinance prohibiting the sale and distribution of flavored tobacco products and cigarettes. It discusses outreach and education efforts as well as results of initial compliance inspections. Overall, inspections indicate that the majority of retailers are in compliance with the law. Based on prior non-compliance, 150 locations were prioritized for inspections. Those found to be selling received a Notice of Correction. In 2019, SFDPH's annual mailing shared details on how to comply with state and local laws. It has also expanded its quitting offerings to support the flavor restrictions. For example, it has funded and supported community contracts to meet African American youth needs as well as trans folks and Spanish-speaking smokers. The next round of priority populations include Chinese speaking men, African American adults, youth who use Juul, and Pacific Islander folks. In fall 2019, it will launch its Connect to Quit media campaign.

56. E-cigarettes linked to heart attacks, coronary artery disease and depression [press release]. 2019.

This American College of Cardiology press release summarizes results from a study by Vindhyal et al. presented at the ACC's 68th Annual Scientific Session (2019). Vindhyal et al. reported that there are over 460 brands and 7,700 flavors of e-cigarettes. Vindhyal et al. analyzed data from 96,467 respondents to the National Health Interview Survey from 2014, 2016, and 2017. They found that adults who use vapor products are significantly more likely to have a heart attack, coronary artery disease, and depression compared to those that do not use vape products. For example, after controlling for age, sex, body mass index, high cholesterol, high blood pressure, and smoking combustible cigarettes, adults that used e-cigarettes were 34% more likely to have a heart attack and 25% more likely to have coronary artery disease compared to adults that do not use e-cigarettes. Users were at increased risk of heart attack and coronary artery disease regardless of whether they vaped daily or occasionally. The authors noted that further longitudinal data is needed to establish causation. However, the authors stated that the results "show a clear association between any kind of smoking and negative health outcomes."

57. Gerloff J., Sundar I. K., Freter R., et al. Inflammatory Response and Barrier Dysfunction by Different e-Cigarette Flavoring Chemicals Identified by Gas Chromatography-Mass Spectrometry in e-Liquids and e-Vapors on Human Lung Epithelial Cells and Fibroblasts. *Appl In Vitro Toxicol.* 2017;3(1):28-40.

There are over 8,000 flavors of e-cigarettes on the market. Gerloff et al. looked at the impact of e-cigarette flavoring chemicals on lung function. Specifically, they looked at impact of various chemicals on the release of proinflammatory cytokine (interleukin-8) in human lung epithelial cells and human lung fibroblasts in vitro, and on barrier dysfunction in human bronchial epithelial cells. They looked at the impact of various e-liquids at three different concentrations to evaluate dose-response impacts after 24 hours of exposure. The authors stated that, "flavored e-cigs are a public health concern not just because they attract youth for experimentation (gateway for initiating tobacco products) but also due to the presence of chemicals that serve as flavorings that may lead to their own health hazards. Flavoring chemicals contain harmful aerosol constituents, such as maltol, vanillin, acetoin, and diacetyl apart from nicotine, vegetable glycerin, and propylene glycol/glycerol." In addition, "recent studies have shown that cytotoxic effects posed by e-liquids are mainly due to increasing concentrations of the flavoring agents." The authors noted that there is a lack of data about potential short and long-term health impacts and toxicity from inhaling flavored chemicals. This study found that acetoin, diacetyl, maltol, and ortho-vanillin significantly induced the release of interleukin-8 in human bronchial epithelial cells. Acetoin, pentanedione, maltol, and ortho-vanillin also induced release of interleukin-8 among human primary lung fibroblast cells. None of the flavorings produced a significant proinflammatory response in lung epithelial cells. E-cigarette flavoring chemicals had a dose-dependent impact on lung epithelial cells and fibroblasts. The authors also found that flavoring chemicals impact barrier dysfunction in human bronchial epithelial cells, which can increase access of pollutants, bacteria, and viruses into the lungs. They authors stated, "previously, it has been shown that soluble components of e-cig, including nicotine exposure, caused a dose-dependent loss of lung endothelial barrier function associated with oxidative stress and inflammatory response. Our data show that nicotine and e-cig flavoring agents...differentially affect epithelial barrier function time dependently. This suggests that both nicotine and flavoring

chemicals in e-cigs are equally responsible for compromising epithelial integrity/[tight junctions], which allows particles to cross the epithelial barrier.” The authors noted that “food flavoring chemicals approved and evaluated as safe by FEMA for ingestion are now widely being used in [electronic nicotine delivery systems] without knowing their safety and inhalation toxicity.” This study confirmed that inhaling diacetyl can cause damage to lung cells. They also cited a previous study that found that cytotoxicity was correlated with the total number and concentration of chemicals present in flavored e-cigarettes. Another study found that 30 puffs from cherry-flavored e-cigarettes contained higher levels of benzaldehyde than combustible cigarettes. The authors concluded that, “our finds suggest that flavoring chemicals are present in e-liquid/e-cigar aerosols, which are proinflammatory and long-term exposure to flavoring chemicals may lead to lung injurious responses.”

58. Wang T.W., Gentzke A., Sharapova S., et al. Tobacco Product Use Among Middle and High School Students--United States, 2011-2017. *Morbidity and Mortality Weekly Report, Centers for Disease Control and Prevention. 2018;67(22):629-633.*

Centers for Disease Control and Prevention and the Food and Drug Administration evaluated data from the National Youth Tobacco Surveys from 2011 to 2017. They estimated nationwide current use of tobacco products for students in middle and high school. Overall, they found that tobacco use decreased from 24.2% of high school students (grades 9-12) in 2011 to 19.6% of high school students in 2017, and from 7.5% of middle school students (grades 6-8) in 2011 to 5.6% of middle school students in 2017. E-cigarettes were the most commonly used tobacco product across all grades. Although use of tobacco products decreased overall, e-cigarette use increased from 1.5% of high school students in 2011 to 11.7% of high school students in 2017. E-cigarette and hookah use also increased from 2011 to 2017 for middle school students. Currently, "in 2017, approximately one in five high school students (2.95 million) and one in 18 middle school students (0.67 million) currently used a tobacco product." The authors note that, "several factors continue to promote and influence tobacco product use among youths, including exposure to tobacco product advertising and imagery through various media, as well as the availability of flavored tobacco products."

59. Cullen K.A., Ambrose B.K., Gentzke A.S., et al. Notes From The Field: Use of Electronic Cigarettes and Any Tobacco Product among Middle and High School Students--United States, 2011-2018. *Morbidity and Mortality Weekly Report, Centers for Disease Control and Prevention. 2018;67(45).*

E-cigarettes entered the U.S. market in 2007, and were the most commonly used tobacco product among youth by 2014. This *Morbidity and Mortality Weekly Report* update provides a summary of adolescent e-cigarette use in the U.S. from 2011 to 2018. Using data from the National Youth Tobacco Survey, this update shows that e-cigarette use among high school and middle school students statistically significantly increased between 2011 and 2018. For high school students, 1.5% of students reported using e-cigarettes in 2011 and 20.8% reported using e-cigarettes in 2018 ($p < 0.001$). For middle school students, 0.6% reported using e-cigarettes in 2011 and 4.9% reported using e-cigarettes in 2018 ($p < 0.001$). Both groups experienced large increases between 2017 and 2018, with high school use increasing by 78% (11.7% to 20.8% of students, $p < 0.001$) and middle school use increasing by 48% (3.3% to 4.9% of students, $p = 0.001$). The authors attribute the increase in e-cigarette use between 2017 and 2018 to "recent popularity of e-cigarettes shaped like a USB flash drive, such as JUUL."

60. **Bhatnagar A., Whitsel L. P., Blaha M. J., et al. New and Emerging Tobacco Products and the Nicotine Endgame: The Role of Robust Regulation and Comprehensive Tobacco Control and Prevention: A Presidential Advisory From the American Heart Association. *Circulation*. 2019;139(19):e937-e958.**

In its Presidential Advisory on New and Emerging Tobacco Products, the American Heart Association (AHA) highlighted the dramatic increase in use of electronic cigarettes (e-cigarettes), particularly among adolescents and young adults, as a significant health concern. AHA stated, “[a]lthough these products may benefit by helping some smokers to quit or to move to a less harmful product, the long-term health effects of these products and the net public health effect associated with their use remain unclear and widely debated.” Evidence indicates that use of e-cigarettes by youth “seems to be nearly exclusively for recreational purposes because youth use does not seem to be associated with quit attempts or quit contemplation.” The National Academies of Sciences, Engineering, and Medical summary of the latest research on e-cigarettes indicates that these products “contain fewer numbers and lower levels of toxicants than combustible tobacco cigarettes and that exposure to nicotine and toxicants from aerosolization of e-cigarette constituents depended on the characteristics of the device and its use.” Upon review of the evidence, the committee found that “e-cigarettes likely pose less risk than continuing to smoke cigarettes”, but that e-cigarettes are “not without adverse biological effects in humans.” Population dynamic modeling conducted before the rise in JUUL use indicated that, “assuming that the use of e-cigarettes increases the net cessation rate of combustible cigarettes among adults, the use of these products could generate a net public health benefit, despite the increased use of combustible tobacco products by young adults.” However, the modeling also showed that “in some scenarios in which e-cigarette toxicity was much higher or the gateway effects from e-cigarette use to combustible cigarette use were much stronger, the public health benefit was substantially less or e-cigarette use was even associated with net harm. Moreover, if e-cigarettes do not promote cessation of combustible tobacco products in adults, the policy model projected that there would be net public harm in both the short and long terms.” The committee therefore “prioritized research to determine whether e-cigarettes promote smoking cessation.” AHA noted that data documenting the increasing use of e-cigarettes among adolescents and young adults may underestimate the true prevalence because evidence indicates that “some youth self-report that they are not using e-cigarettes when they are using electronic hookah, JUUL, and other similar products.” A growing body of evidence shows that young people who use e-cigarettes, particularly products with higher nicotine content, “are more likely than those not using these products to try and to continue cigarette smoking.” Evidence also indicates that e-cigarettes may contribute to former smokers reinitiating tobacco use and sustaining nicotine use. A population-based, prospective cohort study found “no evidence that e-cigarette use helps adult smokers quit at rates higher than when these products are not used.” Moreover, while dual users may smoke fewer cigarettes, they tend to compensate with more e-cigarette use, which increases their overall exposure to nicotine. “Therefore, even though e-cigarettes might help maintain smoking reduction and lower withdrawal symptoms, the long-term health impact of dual use remains largely unknown.” AHA noted that, to date, “there is no experimental evidence to support the view that flavors help adults switch from combustible tobacco products or to quit tobacco altogether.” However, evidence suggests restricting flavoring in all tobacco can reduce the appeal of these products to adolescents and young adults.

61. **Miech Richard , Johnston Lloyd , O'Malley Patrick M. , et al. Correspondence: Trends in Adolescent Vaping, 2017-2019. *The New England Journal of Medicine*. 2019.** Miech et al. used data from Monitoring the Future to assess "whether adolescents' vaping of nicotine continued to increase from 2018 to 2019, after the previous year's record increase, the largest for any substance tracked by Monitoring the Future over the past 44 years." The survey collects data from a nationally representative samples of 12th, 10th, and 8th-grade students. Data indicate that across the 2017, 2018, and 2019, response rates were equal to or greater than 80% for each grade level (12th grade 80%, 10th grade 86%, and 8th grade 88%), with most nonresponse due to students' absence. A randomly selected subset (1/3 of total year sample) received questions on nicotine vaping. The analysis found that from 2017 to 2019 vaping prevalence more than doubled in each of the three grades. "In 2019, the prevalence of use during the previous 30 days was more than 1 in 4 students in 12th grade, more than 1 in 5 in the 10th grade, and more than 1 in 11 in the 8th grade." Daily nicotine vaping (i.e., vaping on at least 20 of the past 30 days) was reported by 12% of 12th grade students, 7% of 10th grade students, and 2% of 8th grade students.

62. **Romberg A. R., Miller Lo E. J., Cuccia A. F., et al. Patterns of nicotine concentrations in electronic cigarettes sold in the United States, 2013-2018. *Drug Alcohol Depend.* 2019;203:1-7.** Romberg et al. examined changes in nicotine concentrations of e-cigarette products sold from 2013 to 2018. Authors used sales data aggregated in 4-week periods from March 2, 2013 to September 8, 2018 (66 months) for convenience stores and mass market channels. Internet and vape shop sales were not available. "Internet searches were used to supplement information for nicotine concentration and flavor. Products were categorized by nicotine concentration, flavor, type (disposable or rechargeable), and brand." Authors assessed dollar sales, unit sales, and average nicotine concentration. Results show that "during 2013-2018, the average nicotine concentration in e-cigarettes sold increased overall, for all flavor categories, and for rechargeable e-cigarettes." Furthermore, during that time period "the proportion of total dollar sales comprised of higher nicotine concentration e-cigarettes (>4% mg/mL) increased from 12.3% to 74.7%." Authors found, "Zero-nicotine products accounted for less than 1% of dollar market share across all years analyzed." Authors note that higher concentrations of nicotine may influence patterns of e-cigarette use.

63. **Wang Teresa W., Asman Kat, Gentzke Andrea S., et al. Tobacco Product Use Among Adults -- United States, 2017. *Morbidity and Mortality Weekly Report*. 2018;67(44):1225-1232.** The National Health Interview Survey (NHIS) is an annual, nationally representative, in-person survey of the noninstitutionalized U.S. civilian population. In 2017, the adult sample included 26,742 adults aged 18 years and older. The response rate was 53.0%. The survey assessed adult use of five tobacco products: cigarettes; cigars (cigars, cigarillos, or filtered little cigars); pipes (regular pipes, water pipes, or hookahs); e-cigarettes; and smokeless tobacco (chewing tobacco, snuff, dip, snus, or dissolvable tobacco). Data were weighted to adjust for differences in selection probability and nonresponse and to provide nationally representative estimates. Overall, an estimated 2.8% (6.9 million) of U.S. adults currently used e-cigarettes in 2017. Among current tobacco product users, 40.5% were daily users of e-cigarettes. "Overall, 3.7% of U.S. adults (9.0 million; 19% of current tobacco product users) used [2 or more] tobacco products." The most

prevalent tobacco product combination was cigarettes and e-cigarettes (30.1%). Young adults (i.e., aged 18-24 years) reported the highest use of e-cigarettes (5.2%) despite having lower use of any tobacco product than those 25-44 years of age and 45-64 years. Primary reasons for e-cigarette use among adults include curiosity, flavoring, cost, consideration of others, convenience, and simulation of cigarettes, as well as to attempt to quit smoking. Authors noted that "[d]ifferences in tobacco product use across population groups might be related to multiple factors, including targeted advertising, differing perceptions regarding the relative harm or social acceptability of tobacco use, and differences in tobacco product prices and levels of access to cessation resources."

64. **Article 19H: Permits for the Sale of Tobacco, San Francisco Health Code(2016).** Section 19H.2. of the San Francisco Health Code defines "Tobacco Product" as "(1) any product containing, made, or derived from tobacco or nicotine that is intended for human consumption, whether smoked, heated, chewed, absorbed, dissolved, inhaled, snorted, or sniffed, or ingested by any other means, including, but not limited to, cigarettes, cigars, little cigars, chewing tobacco, pipe tobacco, bidis or snuff; (2) any device or component, part, or accessory that delivers nicotine alone or combined with other substances to the person using the device including but not limited to electronic cigarettes, cigars, or pipes, whether or not the device or component is sold separately. "Tobacco Product" does not include any product that has been approved by the United States Food and Drug Administration for use as a tobacco cessation product where such product is marketed and sold solely for such an approved purpose."

65. **Article 19Q: Prohibiting the Sale of Flavored Tobacco Products, San Francisco Health Code(2018).** Article 19Q.1-19Q.8 of the San Francisco Health Code was added by Ordinance 140-17, approved July 7, 2017. However the ordinance was suspended by the filing of a referendum petition. The law was adopted by the voters as part of Proposition E at the June 5, 2018 election and became effective 30 days after the election results were declared. Under 19Q.3 "(a) The sale or distribution by an Establishment of any Flavored Tobacco Product is prohibited." and "(b) There shall be a rebuttable presumption that a Tobacco Product, other than a Cigarette, is a Flavored Tobacco Product if a Manufacturer or any of the Manufacturer's agents or employees, in the course of their agency or employment, has made a statement or claim directed to consumers or to the public that the Tobacco Product has or produces a Characterizing Flavor, including, but not limited to, text, color, and/or images on the product's Labeling or Packaging that are used to explicitly or implicitly communicate that the Tobacco Product has a Characterizing Flavor." Section 19Q.4 applies the same statutory language to flavored cigarettes.

66. **Pepper Jessica K. , Ribisl Kurt M. , Emery Sherry L. , et al. Reasons for Starting and Stopping Electronic Cigarette Use *Int J Environ Res Public Health*. 2014;11(2014):10345-10361.** Pepper et al. assessed reasons cited by adult e-cigarette users for starting and then stopping electronic cigarette (e-cigarette) use. "Among a national sample of 3878 U.S. adults who reported ever trying e-cigarettes, the most common reasons for trying were curiosity (53%); because a friend or family member used, gave, or offered e-cigarettes (34%); and quitting or reducing smoking (30%)." Researchers found nearly two-thirds (65%) of those who started using e-cigarettes later stopped using them. "Discontinuation was more common among those whose

main reason for trying was not goal-oriented (e.g., curiosity) than goal-oriented (e.g., quitting smoking) (81% vs. 45%, $p < 0.001$). The most common reasons for stopping e-cigarette use were that respondents were just experimenting (49%), using e-cigarettes did not feel like smoking cigarettes (15%), and users did not like the taste (14%).” Results suggest there are “two categories of e-cigarette users: those who try for goal-oriented reasons and typically continue using and those who try for non-goal-oriented reasons and then typically stop using.” Authors recommend additional research focus on distinguishing “e-cigarette experimenters from motivated users whose decisions to discontinue relate to the utility or experience of use. Depending on whether e-cigarettes prove to be effective smoking cessation tools or whether they deter cessation, public health programs may need distinct strategies to reach and influence different types of users.”

67. Pepper J. K., Coats E. M., Nonnemaker J. M., et al. How Do Adolescents Get Their E-Cigarettes and Other Electronic Vaping Devices? *American Journal of Health Promotion*. 2018;890117118790366.

Pepper et al. conducted an online survey of 1,729 adolescents aged 15-17 who reported vaping in the past 30 days (using an e-cigarette or similar device) to determine how youth obtain or access vaping devices. Adolescent use of e-cigarettes increased significantly between 2011 and 2015, and in 2016 11% of U.S. 10th graders and 12% of U.S. 12 graders reported vaping. Minimum purchase age for e-cigarettes was established nationally as 18 years in 2016. While prior studies have found that social sources are the main way adolescents access cigarettes, little is known about how adolescents access e-cigarettes and other devices. Approximately half of respondents reported smoking cigarettes in the past 30 days, and one-third of respondents reported using other tobacco products in the past 30 days. They found that 78.2% of adolescents surveyed owned their own vaping device, with 32.2% purchasing their device online and 22.3% purchasing it in a vapor shop or lounge. Sources varied significantly by sex, race/ethnicity, and poly tobacco use. In addition, 72.8% reporting using someone else's vaping device in the past 30 days, with 80.5% who borrowed stating that they borrowed from a friend. Adolescents were more likely to borrow a vaping device if they vaped more often, did not own their own, vaped in social situations, or had been refused purchase. The authors suggested that, “social sources might be even more important for vaping than for smoking cigarettes; cigarette smokers likely get cigarettes from other people only when they do not possess their own, but vapers use others' devices even when they have their own.”

68. Meyers M. J., Delucchi K., Halpern-Felsher B. Access to Tobacco Among California High School Students: The Role of Family Members, Peers, and Retail Venues. *Journal of Adolescent Health*. 2017;61(3):385-388.

Meyers et al. surveyed 772 adolescents in California to determine how they obtain cigarettes, e-cigarettes, and hookah. They recruited 9th and 12th grade students from 8 high schools in California to participate in a longitudinal study related to tobacco access, perceptions, social norms, marketing, and use. In general, 32.7% of students reported using hookah, 28.7% reported using e-cigarettes, and 19.2% reported using cigarettes. Approximately 55% of respondents reporting getting their tobacco products from peers, and “adolescents [were] significantly more likely to obtain hookah, e-cigarettes, and cigarettes from a friend than any of the other sources addressed.” Of students who purchased tobacco products, students were significantly more likely to purchase e-cigarettes or hookah from a smoke shop than any other retailer. The authors found

that, "9.3% of participants under the age of 18 reported purchasing tobacco products themselves...thus, despite legislation banning the sale to minors, [adolescents and young adults] continue to directly purchase tobacco products at alarming rates." However, this survey was completed before California enacted their Tobacco 21 law.

69. Knox B. Increasing the Minimum Legal Sale Age for Tobacco Products to 21.: Campaign for Tobacco-Free Kids; 2016.

In this report, the author presents an overview of the issues surrounding tobacco use among youth in the United States and outlines potential benefits to increasing the tobacco purchasing age to 21. Key points discussed include the modeling predictions from the 2015 Institute of Medicine report, tobacco company marketing towards youth, the success of raising the minimum drinking age to 21 and lessons learned, as well as the overall benefits to a Tobacco 21 approach.

70. Lydon David M., Wilson Stephen J., Child Amanda, et al. Adolescent brain maturation and smoking: What we know and where we're headed. *Neuroscience and Biobehavioral Reviews*. 2014;45:323-342.

Lydon et al. conducted a review of the literature on adolescent brain development and nicotine dependence. They cite evidence that smoking is most likely to be initiated during adolescence and that most adults who smoke daily initiate smoking by 18 years of age. The authors also note that once adolescents begin smoking, they are more likely than adults to continue smoking because they experience heightened positive effects from nicotine and are more susceptible to developing nicotine addiction than adults. Research also indicates that individuals who smoked their first cigarette at a younger age and who had a more pleasant experience are more likely to smoke additional cigarettes. Early-initiation smokers also tend to develop nicotine dependence faster and have higher daily cigarette consumption rates than later-initiation smokers. The authors cite a 1996 study by Breslau and Petterson which found that early smoking onset is associated with decreased likelihood of cessation. The likelihood of quitting was lowest for youth who initiated smoking at 13 or younger, with likelihood of quitting increasing with each year that initiation was delayed for adolescents.

71. Behar R. Z., Wang Y., Talbot P. Comparing the cytotoxicity of electronic cigarette fluids, aerosols and solvents. *Tob Control*. 2017;27(3):325-333.

Behar et al. evaluated the cytotoxicity of e-cigarette refill fluids and corresponding aerosol as well as propylene glycol and glycerin (common solvents) using three different types of human cells. Overall, they found that various brands and flavors of e-cigarette fluids are cytotoxic. The authors conducted a previous study evaluating the cytotoxicity of chemicals used to flavor e-cigarette refill fluids. That study found that, "cinnamon-flavoured products were particularly cytotoxic, and cinnamaldehyde was identified as the most potent additive in these fluids. We also reported that cinnamaldehyde is widely used in refill fluids, including popular fruity and sweet flavours, and that it produces adverse effects on cells at doses that do not cause cell death." Other studies have also shown that cherry-flavored products (benzaldehyde) and chocolate-flavored products (2,5-dimethylpyrazine) are potentially harmful. They also cite other research showing that e-cigarette use has numerous health effects, including respiratory, cardiac, and digestive system effects, unintentional and intentional poisonings, and injuries due to explosion. They also stated that in vitro studies have found that e-cigarettes can cause cell inflammation, apoptosis, and DNA damage. In this study, the authors evaluated 36 e-cigarette refill fluids representing a range

of brands and flavors. Fluids testing included tobacco-flavored, propylene glycol, vegetable glycerin, and pure nicotine liquid. In addition, the authors produced corresponding aerosols using a smoking machine. The fluids and aerosols were tested using three types of cells. Human pulmonary fibroblasts are a cell type that is first exposed to inhaled aerosol and are involved in the development of lung diseases. Lung epithelial cells are cells commonly used in toxicological inhalation testing. Pluripotent human embryonic stem cells were also used to approximate potential impacts to human embryos. All of the tests included dose-response experiments. The authors found that 34 of the 35 products were significantly more toxic at high concentrations than at low concentrations. Creamy/buttery, mint/menthol, tobacco, and fruit flavoring categories were the most potent. The six most potent flavorings were in the creamy/buttery category and included flavorings like Swiss Dark, Butterfinger, Caramel, and Butterscotch. In general, the embryonic stem cells were more sensitive to e-cigarette fluids and aerosols than adult lung cells. Overall, 54% (19 products) were cytotoxic in both the fluid and aerosol form; 23% (8 products) were cytotoxic in the aerosol form but not the fluid form; and 3% (1 product) were cytotoxic in the fluid form but not the aerosol form. Twenty percent (7 products) were found to be non-cytotoxic in both the fluid and aerosol form. In addition, refills containing glycerin were the most cytotoxic, and 91% of glycerin-based refill fluids were cytotoxic when aerosolized. Vegetable glycerin alone was also cytotoxic when aerosolized, and was found to be more cytotoxic than propylene glycol alone. The authors noted that many flavoring liquids may be approved for ingestion, but have not been tested for safety of inhalation.

72. Center Washington Poison. Washington Poison Center 2018 Annual Data Report: Nicotine. 2018.

In 2018, the Washington Poison Center addressed 483 cases of nicotine exposure, including 353 cases of nicotine exposure among 0-5 year olds. 87% of exposures were due to ingestion, and included gastrointestinal, neurological, respiratory, ocular, cardiovascular, and dermal symptoms. Washington Poison Center also addressed 136 cases specific to e-cigarettes, including 77 cases among 0-5 year olds, 2 cases among 6-12 year olds, 23 cases among 13-20 year olds, 26 cases among 21-59 year olds, and 1 case among 60 years and older.

73. IOM. Public health implications of raising the minimum age of legal access to tobacco products. Washington D.C.: The National Academies Press; 2015.

The Tobacco Control Act of 2009 directed the Food and Drug Administration (FDA) to convene a panel of experts to conduct a study on the health impacts of raising the minimum purchase age for tobacco products and submit a report to Congress. The FDA contracted with the Institute of Medicine (IOM) to convene a committee to examine the existing literature and use modeling to predict the likely impacts of increasing the minimum purchase age to 21 or 25 years of age. The committee concluded in their report that increasing the minimum purchase and possession age for tobacco products would likely prevent or delay initiation of tobacco use by adolescents and young adults and therefore also lead to a “substantial reduction in smoking-related mortality.” The authors also concluded that while (for a purchase age of 21) 18 to 20 year olds would be affected, the largest reduction in tobacco initiation would likely be among 15 to 17 year olds. They note that increasing the purchase age to 19 would likely have a modest impact on decreasing tobacco access to minors compared to increasing the age to 21. The authors cite evidence that younger age of smoking initiation is associated with heavier smoking later in life, a higher likelihood of continuing to smoke through the lifespan, and increased risk of adverse

health outcomes. The report also summarizes the literature on the effect of tobacco purchase, use, and possession (PUP) laws. A 2008 study conducted in California by Rogers et al. found that in the previous 12 months, across all 249 enforcement agencies statewide, an average of 24.1 citations were issued per agency. A study by Gottlieb et al. also found that African-American and Hispanic students were significantly more likely than their White counterparts to receive a PUP citation. Jason et al. (2007b) found that youth who were fined for PUP violations were more likely than youth in a tobacco prevention education program to reduce or quit tobacco use. However Gottlieb et al. (2004) found that receiving a PUP citation was only associated with reduced smoking intention in some of the sample schools. The committee conducted modeling (informed by the existing scientific literature) and estimated that raising the tobacco purchase age to 21 would lead to the following reductions in tobacco initiation: 15% (range: 12.5-18%) reduction for those under 15 years of age, 25% (range: 20.8-30%) reduction for those 15-17 years, 15% (range 12.5-18%) reduction for those 18-20 years. Their modeling predicts that with an age 21 minimum, by 2040-2059 there would be 0.2-0.8% reduction in deaths (8.2-9.9% by 2080-2099); 0.5% reduction in years of life lost (9.3% by 2080-2099); 0.3% reduction in lung cancer deaths (10.5% by 2080-2099); 12.2% reduction in low birth weight cases; 13% reduction in pre-term birth cases; and 18.5% reduction in sudden infant death syndrome (SIDS) cases.

74. Caporale A., Langham M.C., Guo W., et al. Acute Effects of Electronic Cigarette Aerosol Inhalation on Vascular Function Detected at Quantitative MRI. *Radiology*. 2019;00:1-10.

Caporale et al. provided background research about each component of e-cigarettes, including the solvents, metals generated by the heating elements, and flavorants. They noted that, “the basic constituents of e-liquids, primarily propylene glycol and glycerol, can form irritant acetals even at room temperature and carcinogens at typical working device temperatures.” The heating elements produce fine and ultrafine metal particles that have been shown to cause nose, throat, and respiratory irritation, lung inflammation, and nervous system damage. Caporale et al. conducted a prospective study with 31 healthy, adult non-smokers (aged 18 to 35) to determine the impact of smoking nicotine-free e-cigarettes. Participants had healthy BMI ranges, no history of smoking, and no obvious cardiovascular or neurovascular disease. Participants underwent an MRI before and after smoking 16 inhalations of nicotine-free e-cigarettes containing propylene glycol, glycerol, and flavor. They measured, “peripheral hyperemia in response to cuff-induced ischemia, cerebrovascular reactivity in response to breath hold, aortic pulse wave velocity, and an indicator of aortic stiffness.” Overall, after vaping, they found, “reductions after vaping in luminal flow-mediated dilation (-3.2 of 9.4; -34%; $P < .001$), reactive hyperemia peak velocity (-9.9 of 56.6 cm/sec; -18%; $P < .001$), and acceleration (-3.9 of 15.1 cm/sec²; -26%; $P < .001$) as representative of macrovascular alterations; a reduction in precuff occlusion S_{vo2} (-13 OF 65 %hBO₂; -20%, $P < 0.001$), which indicated transient microvascular impairment; a marginal increase in aortic pulse wave velocity (0.19 of 6.05 m/sec/ 3%; $P = .05$), which suggested aortic stiffening; and no statistically significant alterations in cerebrovascular reactivity measured by breath-hold index.” The authors noted that they did not determine whether the effects were due to the solvent, flavor, or thermal degradation.

75. Erythropel H.C., Davis L.M., de Winter T.M., et al. Flavorant-Solvent Reaction Products and Menthol in JUUL E-Cigarettes and Aerosol. *American Journal of Preventive Medicine*. 2019;57(3):425-427.

Erythropel et al. examined the composition of JUUL aerosol. They evaluated 8 flavors of JUUL brand e-cigarettes to evaluate the reaction between vanillin flavoring and propylene glycol, glycerol, menthol, and nicotine benzoate to understand how common JUUL components may interact. JUUL products contain higher concentrations of nicotine than other e-cigarette brands (5% versus 0.3%-2.4%) because they use nicotine benzoate salt that “is perceived as more satisfactory and less harsh” than other products. The authors analyzed e-liquids and used a vaping machine to capture aerosol for analysis. They found that JUUL aerosols include quantities of nicotine similar to cigarettes and levels of acetals known to cause irritation and contribute to inflammation. They explained that, “the average vanillin puff concentration was 101 mg/m³. In comparison, chronic inhalational exposure to vanillin in occupational environments is limited to 10 mg/m³, raising the question of what long-term effects regular inhalation of vanillin at such doses and frequency (200 puffs/pod) might have.” They also found levels of menthol in JUUL products (some of which are not labeled as containing menthol) at levels known to increase nicotine intake.

76. Kosmider L., Sobczak A., Prokopowicz A., et al. Cherry-flavoured electronic cigarettes expose users to the inhalation irritant, benzaldehyde. *Thorax*. 2016;71(4):376-377.

Kosmider et al. tested 145 e-cigarette products for the presence of benzaldehyde, a common ingredient in fruit flavored e-cigarettes and a chemical known to cause respiratory irritation in animal and occupational studies. They tested e-liquid aerosols for the presence of benzaldehyde and compared levels from 30 puffs with levels from one combustible cigarette as well as with levels predicted to be inhaled occupationally during an 8 hour work shift. The authors detected benzaldehyde in 108 out of 145 e-cigarette products, most commonly in cherry-flavored products. At levels found, 30 puffs of e-cigarettes flavored with benzaldehyde were higher than doses inhaled from conventional cigarettes and more than 1000 times lower than occupational exposures. The authors noted, “although many flavourings used in e-cigarettes are generally recognized as safe when used in food products, concerns have been raised about the potential inhalation toxicity of these chemicals.” There is a lack of data about the long-term health impacts of inhaling chemicals used in e-cigarette flavorings.

77. Omaiye E. E., McWhirter K. J., Luo W., et al. High-Nicotine Electronic Cigarette Products: Toxicity of JUUL Fluids and Aerosols Correlates Strongly with Nicotine and Some Flavor Chemical Concentrations. *Chem Res Toxicol*. 2019;32(6):1058-1069.

Omaiye et al. evaluated the flavor chemical concentrations and nicotine concentrations of the eight pre-filled JUUL e-cigarette pods available on the market (i.e., Cool Mint, Classic Menthol, Mango, Fruit Medley, Cool Cucumber, Crème Brulee, Classic Tobacco, and Virginia Tobacco). The authors tested concentrations in the vape fluid before puffing, after puffing, and in the corresponding aerosol. Overall, JUUL pods contain solvents, flavor chemicals, and varying concentrations of nicotine. Among the eight flavored pods, the authors identified 59 different flavor chemicals. The concentration of flavor chemicals in JUUL pods ranged from 0.2-15.6 mg/mL, with the highest concentrations of menthol, vanillin, and ethyl maltol. The nicotine concentration of JUUL pods was significantly higher than other e-cigarette products. Most products had nicotine concentrations between 1.6-34.3 mg/mL; JUUL pods had nicotine concentrations between 59.2-66.7 mg/mL. This concentration is also higher than in a pack of cigarettes (40 mg/pack). The transfer of flavor chemicals from the e-liquid to the corresponding

aerosol was over 50%, and the transfer of nicotine was between 56%-75%. The authors also found that JUUL fluids were cytotoxic for all pod flavors. All of the pod fluids were found to be cytotoxic to lung epithelial cells. Most were cytotoxic at 0.2% to 1.8% concentration, with a maximum effect at 10% concentration. Corresponding aerosols were also cytotoxic, and were cytotoxic at levels lower than observed with fluids with maximum effect at 0.2%- 1.8%. Omaiye et al. also tried to determine the relative contribution of nicotine, total flavor chemicals, and individual flavor chemicals to cytotoxicity. They found that nicotine concentration most closely aligned with cytotoxicity. However, the correlation between cytotoxicity and all components was statistically significant. The authors concluded that, “our data clearly identify a [sic] concern related to the high nicotine concentration in JUUL products, i.e., the potential for high levels of nicotine, as well as flavor chemicals such as ethyl maltol, to damage or even kill cells at the concentrations used in JUUL pods.”

78. Widely used e-cigarette flavoring impairs lung function [press release]. 2018.

In this press release, the American Thoracic Society summarizes recent research by Clapp et al. entitled, "The E-cigarette Flavoring Cinnamaldehyde Suppresses Mitochondrial Function and Transiently Impairs Cilia Beat Frequency in Human Bronchial Epithelial Cells." The study found that a single exposure to cinnamaldehyde in e-cigarettes impairs lung function. In the press release, the authors state that, "our data suggest that when used in e-cigarettes cinnamaldehyde, like toxic aldehydes in cigarette smoke, significantly disrupts normal cell physiology in ways that may have implications for the development and exacerbation of respiratory disease...our finding that cinnamaldehyde impairs normal airway cilia motility is significant because it demonstrates that a common, food-safe flavoring agent, in the context of e-cigarette use, is capable of dysregulating a critical anti-bacterial defense system in the lungs." The authors note that flavoring agents, while safe for ingestion, may not be safe for inhalation. In addition, since flavoring agents are used in high concentrations in e-cigarettes, individuals may be exposed to higher doses of the agent. Authors state, "The two principles of toxicology- 'The Dose Makes the Poison' and 'The Route of Exposure Affects Toxicity'- clearly apply here."

79. Sherwood C. L., Boitano S. Airway epithelial cell exposure to distinct e-cigarette liquid flavorings reveals toxicity thresholds and activation of CFTR by the chocolate flavoring 2,5-dimethylpyrazine. *Respir Res.* 2016;17(1):57.

Sherwood and Boitano evaluated the impact of e-liquid flavoring chemicals on bronchial epithelial cells, which “provide the first line of defense against inhaled particulates, pathogens, and toxicants.” They found that 5 out of 7 flavoring chemicals were cytotoxic and produced effects consistent with cell death. Vanillin and 2,5-dimethylpyrazine, used to provide chocolate flavoring, also compromised cell function at subcytotoxic levels. Very low concentrations (0.02%) of 2,5-dimethylpyrazine “induced distinct cellular impedance changes indicative of a cellular signaling event.” This type of reaction, “alters the capability of airway epithelial cells to respond to signaling molecules key in the proper functioning of airway cell physiology.”

80. Bayly J.E., Bernat D., Porter L., et al. Secondhand Exposure to Aerosols from Electronic Nicotine Delivery Systems and Asthma Exacerbations Among Youth With Asthma. *CHEST.* 2018; Ahead of print.

Bayly et al. analyzed data from the 2016 Florida Youth Tobacco Survey to determine whether there was a relationship between secondhand exposure to aerosol from electronic nicotine

delivery systems (ENDS) and asthma exacerbation among youth with asthma. They examined survey responses for youth aged 11 to 17 years old from middle and high schools in Florida. Overall, approximately one-third of youth reported secondhand exposure to ENDS aerosols. The authors found that secondhand exposure to aerosol from ENDS was significantly associated with higher odds of asthma attacks among youth with asthma ($p < 0.01$; OR 1.27, 95% CI 1.11-1.47). The authors concluded that, "secondhand exposure to ENDS aerosols may be related to asthma symptoms in youth...future research is necessary to evaluate the longitudinal relationship between secondhand ENDS aerosol exposure and asthma control."

81. Schier J.G. et al. Severe Pulmonary Disease Associated with Electronic-Cigarette-Product Use-- Interim Guidance. *Morbidity and Mortality Weekly Report*. 2019;68:2-4.

On September 6, 2019, Centers for Disease Control and Prevention issued interim guidance related to the outbreak of severe pulmonary disease associated with e-cigarette use. This *Morbidity and Mortality Weekly Report* states that, "based on available information, the disease is likely caused by an unknown chemical exposure; no single product or substance is conclusively linked to the disease...until a definitive cause is known, persons should consider not using e-cigarettes." In addition, "e-cigarette products should never be used by youths, young adults, pregnant women, or by adults who do not currently use tobacco products. Adult smokers who are attempting to quit should use evidence-based smoking cessation treatments, including counseling and FDA-approved medications." They note that most patients have presented with hypoxemia, which has progressed to acute or subacute respiratory failure, requiring some patients to receive oxygen, intubation, or mechanical ventilation. Case studies with 53 patients in Illinois and Wisconsin, 6 patients in Utah, and 5 patients in North Carolina, have found that all patients, "have had abnormal radiographic findings, including infiltrates on chest radiograph and ground glass opacities on chest computed tomography scan." Ground glass opacities refers to findings showing a filling of air spaces or a thickening or collapse of lung alveoli. The authors explained that, "no consistent e-cigarette product, substance, or additive has been identified in all cases, nor has any one product or substance been conclusively linked to pulmonary disease in patients." All patients have used vapor products containing THC, nicotine, or both.

82. Davidson K. et al. Outbreak of Electronic-Cigarette-Associate Acute Lipoid Pneumonia-- North Carolina, July-August 2019. *Morbidity and Mortality Weekly Report, Centers for Disease Control and Prevention*. 2019;68:1-3.

In this *Morbidity and Mortality Weekly Report* case study, Davidson et al. describe cases associated with the acute lipoid pneumonia outbreak in North Carolina. Five patients presented at two hospitals between July and August 2019. All five patients were 18-35 years old and had used e-cigarettes products containing THC purchased on the street. They experienced symptoms, including dyspnea, nausea, vomiting, abdominal discomfort, fever, tachypnea, hypoxemia, and bilateral lung infiltrates. All five patients were hospitalized for respiratory failure, and all patients survived. All five patients tested negative for bacterial pathogens, influenza, mycoplasma, and legionella and were not responsive to antibiotics. The authors explained that, "one potential explanation for acute lipoid pneumonia among these patients is that aerosolized oils inhaled from e-cigarettes deposited within their distal airways and alveoli, inciting a local inflammatory response that impaired vital gas exchange. Lipoid pneumonia has long been described from aspiration of oil into the lungs and has been associated with e-cigarette use in

some case reports.” The authors also noted that the optimal treatment course and the long-term impacts of lipoid pneumonia are unknown.

83. QxQ Analysis: Cigarette Use by Race/Ethnicity, Sexual Orientation, and Gender Identity. Looking Glass Analytics; 2018. <http://www.askhys.net/Analyzer>. Accessed September 2019.

Washington State Healthy Youth Survey data from 2018 indicate that among 8th grade respondents American Indian/Alaskan Native (AI/AN) students (5.8% [95% CI 2.9-8.5%]) and black students (5.0% [95% CI 2.4-7.6%]) reported higher smoking rates than their Asian or Asian American, Native Hawaiian or other Pacific Islander (Asian/NHOPI) (1.8% [95% CI 0.9-2.7%]), white (2.2% [95% CI 1.5-2.9%]), and Hispanic peers (3.4% [95% CI 2.4-4.4%]). Among 10th grade respondents, black students (6.0% [95% CI 4.0-8.0%]), Hispanic/Latino students (6.0% [95% CI 4.7-7.3%]), and students of more than one or other race/ethnicity (6.4% [95% CI 4.9-7.9%]) reported higher smoking rates than their peers. Generally, the percent of students who had reported smoking at all in the past 30 days was highest among 12 grade respondents. AI/AN (10.5% [95% CI 4.2-16.8%]) respondents and those who selected more than one or other race/ethnicity (10.2% [95% CI 7.4-13%]) reported higher cigarette smoking rates than their peers with 9.5% (95% CI 7.7-11.3%) of white youth smoking. These data suggest that in Washington State, AI/AN, black, and multi or other racial/ethnic youth have disparately high rates of current cigarette use. It is important to note that the current race/ethnicity categories aggregate diverse subpopulations into one category—so disparities within these categories may be masked. For example, API subpopulations likely have very different smoking rates but they are aggregated into one category so these differences may be missed. Students from the subsample of schools who participate in the extended form version of the Healthy Youth Survey also answered questions about their sexual orientation. Eighth grade respondents who identified as lesbian, gay, or bisexual were more likely to report smoking cigarettes at all in the last 30 days (5.3% [95% CI 3.2-7.4%]) than their peers who identified as straight (1.9% [95% CI 1.3-2.5%]). This disparity also existed among 10th graders (10.8% [95% CI 8.4-13.2%] vs. 3.7% [95% CI 3.1-4.3%]) and 12 graders (16.0% [95% CI 11.9-20.1%] vs. 5.9% [95% CI 4.8-7.0%]). A similar disparity exists across grade levels for students who report either questioning their sexual orientation or who feel something else (besides gay, lesbian, bisexual, or straight) fits better. Finally, the Healthy Youth Survey also asks students about their gender identity. Eighth grade data were suppressed due to fewer than 5 responses in at least one category. Among 10th grade respondents who identified as transgender were more likely to report smoking cigarettes at all in the last 30 days (22.4% [95% CI 12.6-32.2%]) than their peers who identified as cisgender female (4.3% [95% CI 3.2-5.4%]) or cisgender male (4.4% [95% CI 3.6-5.2%]). This disparity also existed among 12th graders (transgender students: 37.3% [95% CI 20.9-53.7%] vs. cisgender female 5.5% [95% CI 3.9-7.1%] or cisgender male (7.9% [95% CI 6.0-9.8%])). Similar disparities exists across grade levels for students who report questioning/not sure of my gender identity, something else fits better, and who selected more than one response.

84. Chaiton M. O., Nicolau I., Schwartz R., et al. Ban on menthol-flavoured tobacco products predicts cigarette cessation at 1 year: a population cohort study. *Tob Control*. 2019.

Chaiton et al. conducted a population cohort study to analyze the long-term impact of a menthol ban in Ontario, Canada, on smoking behavior. Authors cited evidence from the FDA's scientific

evaluation that "menthol has a physiological impact on smoking that increases initiation and progression to regular cigarette smoking, increases nicotine dependence and decreases smoking cessation success." Menthol sales account for 5% of the cigarette sale market in Canada, while in the U.S. menthol cigarettes account for 35% of the market. The FDA also noted younger populations, women, and black Americans were more likely to smoke menthol cigarettes--which "perfectly matched the targeted marketing strategies employed by the tobacco industry." Similar to the U.S., a considerable number of Canadian youth report smoking menthol cigarettes. "According to the 2010–2011 Canadian Youth Smoking Survey, as many as 32% of current cigarette smokers used menthol cigarettes, and in the 2012–2013 iteration, almost 15% of students from grades 10–12 reported using [flavored] tobacco (including menthol products)." Baseline survey results were collected before the menthol ban (September-December 2016) and follow-up surveys were conducted 1 year after the implementation of the ban (January-August 2018). Participants included residents of Ontario, Canada, ages 16 years and older who reported current smoking (past 30 days) at baseline and completed a follow-up survey. Of participants, 58% were female; 84% were over age 30 years; 83% were white; 71% had more than a high school degree; 39% smoked from 11-20 cigarettes a day; and 10% were non-daily smokers. Researchers assessed past year use of menthol cigarettes prior to the ban and current use of menthol and non-menthol cigarettes following the ban. Researchers evaluated "quitting" as the primary outcome and "quit attempts" as a secondary outcome. Quit attempts were defined as "self-reporting making a serious quit attempt since the beginning of the menthol cigarette ban in January 2017." Additionally, all those who reported not smoking at follow-up were considered to have made a quit attempt. The use of e-cigarettes or cigars since the ban was also assessed. Of participants with complete data (n=913), 21% (187) reported smoking menthol cigarettes daily, 46% (420) reported smoking menthol cigarettes occasionally, and 34% (306) were non-menthol cigarette smokers. "Daily and occasional menthol smokers were more likely to be female, non-white and have more than a high school education than non-menthol smokers." The highest percentage of young adult (i.e., 16 to 29 years of age) smokers was seen among those who smoked menthol cigarettes occasionally. "At follow-up, 0.3% of the non-menthol smokers at baseline, 5% of the occasional menthol users and 22% of the daily menthol users reported purchasing menthol cigarettes after the ban ($p < 0.001$). The primary source for purchasing menthol cigarettes was on First Nation Reserves, but this purchasing pattern did not increase over time among prior daily menthol smokers (short-term follow-up: 21%; long-term follow-up: 21%)." This is consistent with previous research findings that "25% of menthol smokers claim that they would find some way to purchase menthol cigarettes despite a ban." Among the overall study sample, 19% of baseline smokers reported successfully quitting smoking, and 56% reported making a quit attempt after the ban. Quit rates reported by non-menthol smokers were "consistent with a previous population-representative longitudinal studies of quit rates in Ontario (8.9% sustained self-reported quit rate)." Meanwhile, "[d]aily menthol smokers had significantly higher rate of reporting having quit smoking after the ban (adjusted rate ratio [AAR] 1.62; 95% CI 1.08 to 2.42) compared with non-menthol smokers, controlling for smoking and demographic characteristics." Daily menthol smokers were also more likely to have tried to quit than non-menthol smokers (AAR 1.25; 95% CI 1.03-1.50), after adjustment. Both findings were statistically significant ($p < 0.05$). Sensitivity analyses, which included those who did not complete the follow-up survey (N=1,738) as having continued smoking did not change the significance of results "nor did it greatly alter the magnitude of estimates." Study results found that "menthol smokers who intended to substitute with other means had substantial levels of

quitting behavior." Specifically, "20% of occasional menthol smokers and 24% of daily menthol smokers reported quitting in the long terms, which exceeded what was predicted by smokers at baseline." Moreover, findings suggested an increased rate of quitting 1 year following Ontario's ban on the sale of menthol tobacco products. However, the impact was observed in older but not younger adults. Authors postulated that "the difference may be due to younger adults not having a brand preference and switching to other tobacco or nicotine products." Authors noted a combustible tobacco menthol ban would be more impactful for at-risk subpopulations of youth and young adults if there was less availability of other flavored tobacco or nicotine products. Finally, there was no public education campaigns informing the public of the menthol ban, and the ban was implemented without noticeable controversy. Authors conclude that "[C]onsidering that menthol smokers may be more nicotine dependent and have reduced cessation success, our findings that daily menthol smokers were significantly more likely to reporting smoking cessation relative to non-menthol smokers after the ban suggest that the menthol ban could have tremendous public health impact at the population level in Canada and in other jurisdictions as well from an overall reduced level of cigarette smoking."

85. Christenson T., Weisser, J. Health of Washington State Report: Tobacco Use. Washington State Department of Health; 2015.

Combined 2012-2014 Behavioral Risk Factor Surveillance System (BRFSS) data indicate that AI/AN adults in Washington have significantly higher rates of current cigarette use than their white, black, Hispanic/Latino, and Asian counterparts. Cigarette use also decreased significantly as educational attainment or income increased. This report also indicates that smoking rates among gay, lesbian, and bisexual respondents were significantly higher than for their straight counterparts. These BRFSS data and 2014 Healthy youth survey data also show that smoking prevalence is highest in late adolescence and early adulthood, peaking among 25-34 years old for men and women. Pregnancy Risk Assessment Monitoring System (PRAMS) data from 2010-2012 indicate that the smoking rates among pregnant women before and during pregnancy are highest among mothers younger than 20 (36% [95% CI 28-45%]). Thirty-two percent of mothers age 20-24 also reported smoking before and during pregnancy (95% CI 27-37%) compared to 9% (95% CI 6-12%) of mothers 35 years or older. These data also indicate that smoking before pregnancy is highest among AI/AN (50% [95% CI 45-55%]) and low-income mothers. Because women often are not aware that they are pregnant until several weeks into their pregnancy, the smoking rates in the months leading up to pregnancy can have an important impact on fetal development and growth.

86. San Mateo County, CA. Data USA 2018; Available at: <https://datausa.io/profile/geo/san-mateo-county-ca/>. Accessed September, 2019.

Data USA is a collaboration by Deloitte, Datawheel, and Professor Cesar Hidalgo at the MIT Media Lab and Director of Collective Learning. It presents public US Government data from multiple data sources. Analysts accessed 2017 median household income data for San Mateo County, San Francisco County, and California.

87. Villanti Andrea C , Mowery Paul D , Delnevo Cristine D , et al. Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004–2014. *Tobacco Control*. 2016;25:ii14-ii20.

Villanti et al. analyzed National Survey on Drug Use and Health data from 2004 to 2014 to estimate the prevalence of menthol cigarette use among persons aged ≥ 12 years. Researchers used self-reported menthol status for selected brands that were either exclusively menthol or non-menthol were adjusted based on retail sales data. Data were then weighted to provide national estimates. The analysis found that "although overall smoking prevalence has decreased, the proportion of past 30-day cigarette smokers using menthol cigarettes was higher (39%) in 2012–2014 compared to 2008–2010 (35%). Youth smokers remain the most likely group to use menthol cigarettes compared to all other age groups." Moreover, "Menthol cigarette prevalence exceeded non-menthol cigarette prevalence in youth and young adult smokers in 2014." Estimates showed menthol cigarette prevalence increased in white, Asian, and Hispanic smokers since 2010. Authors concluded, "The youngest smokers are most likely to use menthol cigarettes."

88. Villanti A. C., Collins L. K., Niaura R. S., et al. Menthol cigarettes and the public health standard: a systematic review. *BMC Public Health*. 2017;17(1):983.

Villanti et al. conducted this systematic review to update the evidence synthesis regarding the role of menthol in initiation, dependence, and cessation. Researchers ran a search for peer-reviewed literature on menthol cigarettes (through May 9, 2017) using PubMed and reviewed the National Cancer Institute's Bibliography of Literature on Menthol and Tobacco and the FDA's 2011 report and 2013 addendum for additional publications. "Included articles addressing initiation, dependence, and cessation were synthesized based on study design and quality, consistency of evidence across populations and over time, coherence of findings across studies, and plausibility of the findings [...] Eighty-two studies on menthol cigarette initiation (n = 46), dependence (n = 14), and cessation (n = 34) were included." Authors found, "Large, representative studies show an association between menthol and youth smoking that is consistent in magnitude and direction." Additionally, "One longitudinal and eight cross-sectional studies demonstrate that menthol smokers report increased nicotine dependence compared to non-menthol smokers." Finally, "Ten studies support the temporal relationship between menthol and reduced smoking cessation, as they measure cessation success at follow-up." Overall, authors concluded "The strength and consistency of the associations in these studies support that the removal of menthol from cigarettes is likely to reduce youth smoking initiation, improve smoking cessation outcomes in adult smokers, and in turn, benefit public health."

89. Tobacco is a social justice issue: Racial and ethnic minorities. Washington, DC: Truth Initiative; 2017.

This article from the Truth Initiative provides an overview of how tobacco use disproportionately affects marginalized populations. In particular, the article focuses on how the tobacco industry has targeted communities of color by capitalizing on culture (e.g., community press and traditions) and establishing a clear presence in communities of color. For example, "a 2011 review concluded that *Ebony* magazine was almost 10 times more likely than *People* magazine to contain advertisements for menthol cigarettes." Moreover, a 2013 study found "black children were three times more likely to recognize advertisements for Newport, the most popular menthol brand among that group, than other children." Tobacco companies have also sponsored cultural activities (e.g., events related to Black History Month, Asian/Pacific American Heritage Month, and Hispanic Heritage Month). Point-of-sale promotions, density of tobacco display ads inside

and outside of stores, and cheaper prices for menthol cigarettes in predominantly black communities, have all contributed to disparities.

90. Gardiner Philip, McGruder Carol. Adopt Citywide Restriction on the Sale of Menthol and all Other Flavored Tobacco Products, Including Flavored E-Juices in the City of New York. In: Health NYCCCo, ed: The African American Tobacco Control Leadership Council; 2019.

This letter from the African American Tobacco Control Leadership Council (AATCLC) to the New York City Council Committee on Health highlights the rising use of menthol cigarettes in the face of decreasing non-flavored tobacco cigarettes. Co-chairs Gardiner and McGruder cite evidence which shows that menthol cigarettes are increasingly being used among Latino, Black, and White youth and adults. They present menthol smoking data by race/ethnicity to indicate the disproportionate use among communities of color. For example, 85% of African American adult smokers and 94% of Black youth who smoke use menthol products. Additionally, female smokers and smokers within the LGBTQ community are also more likely to use menthol cigarettes. Authors cite evidence that the presence of menthol makes cigarettes harder to quit compared to other cigarettes.

91. Achieving Health Equity in Tobacco Control 8 December 2015 2015.

This report was a joint publication of a consortium of organizations coordinating efforts around the 50th anniversary of the U.S. Surgeon General's report on smoking and health. Organizations endorsing this report are the African American Tobacco Control Leadership Council; the American Cancer Society; American Heart Association; American Lung Association; Asian Pacific Partners for Empowerment, Advocacy and Leadership (APPEAL); Campaign for TobaccoFree Kids; the Intercultural Cancer Council; LGBT Healthlink at CenterLink: The Community of LGBT Centers; NAATPN, Inc.; National Latino Alliance for Health Equity; the Smoking Cessation Leadership Center; Truth Initiative; and the University of Southern California Keck School of Medicine. While authors acknowledge and celebrate the advancements made since the Surgeon General's initial report, they highlight the persistent gaps in health equity. Authors note that smoking disproportionately affects those most in need including those living in financial poverty, people experiencing homelessness, racial/ethnic minorities, LBGT persons, and those suffering from mental illness and substance use disorders. Authors state, "We need to continue the population based policies and programs that have produced such dramatic results, including results that have benefited many racial and ethnic populations, but also expand efforts that incorporate and embrace fundamental principles of health equity that afford equal treatment of all individuals/groups (horizontal) and provide supplementary support for individuals/groups that are marginalized (vertical)." The report summarized key facts on prevalence, cessation, health effects, and marketing among demographic groups more severely impacted by the tobacco epidemic. Disparities are discussed by socioeconomic status; education level; race/ethnicity; LGBT; mental illness and substance use disorders; and homelessness status.

92. Tobacco in LGBT Communities. Washington, DC: Truth Initiative; 2018.

This Truth Initiative fact sheet provides an overview of the disproportionate impact tobacco has on the LGBT community. Tobacco companies began advertising in gay press publications in the 1990s. For example, A 1997 industry document stated: "A large percent of Gays and Lesbians

are smokers. In order to increase brand share and brand awareness [...] it is imperative to identify new markets with growth potential. Many Gay and Lesbian adult smokers also have a preference for menthol brands." Corporate philanthropy (e.g., donations from Philip Morris to AIDS research and programs) also facilitated access to the LGBT market. "R.J. Reynolds created a marketing strategy called 'Project SCUM' (Sub-Culture Urban Marketing) to boost cigarette sales by targeting gay men and homeless individuals with advertisements and displays placed in communities and stores." The industry also provided free giveaways and hosted "LGBT bar nights" featuring specific brands. These tactics contributed to the disproportionately high smoking rates seen today. For example, lesbian, gay, and bisexual adults smoke at rates up to 2.5 times higher than straight adults. Bisexual women are up to 3.5 times more likely to smoke. "LGBT smokers are significantly more likely to smoke menthol cigarettes: more than 36 percent of LGBT smokers report that they usually smoke menthols."

93. Rogers Todd , Feld Ashley , Gammon Doris G , et al. Changes in cigar sales following implementation of a local policy restricting sales of flavoured noncigarette tobacco products. *Tobacco Control*. 2019:1-8.

Rogers et al. used non-cigarette tobacco sales data obtained from the Nielsen Company to assess the impact of Providence, Rhode Island's restriction on the retail sale of all non-cigarette tobacco products with a characterizing flavor other than tobacco, menthol, mint or wintergreen. Researchers focused on cigar sales, which comprised 95% of flavored non-cigarette tobacco products sold through conventional tobacco retail outlets (e.g., convenience stores, supermarkets) in Providence. Authors used weekly retail scanner sales data (January 2012 to December 2016). They categorized cigar sales into "products labelled with explicit-flavour (eg, Cherry) or concept-flavour (eg, Jazz) names." Researchers ran regression models to assess changes in sales in Providence and the rest of the state (ROS) before and after policy implementation. Overall, "Average weekly unit sales of flavoured cigars decreased prepolicy to postpolicy by 51% in Providence, while sales increased by 10% in ROS (both $p < 0.01$). The Providence results are due to a 93% reduction in sales of cigars labelled with explicit-flavour names ($p < 0.01$), which did not change significantly in ROS." Meanwhile, "sales of cigars labelled with concept-flavour names increased by 74% in Providence and 119% in ROS (both $p < 0.01$)." In sum, sales of all cigars (flavored and otherwise) decreased by 31% in Providence ($p < 0.01$). Authors detected "some evidence of product substitution and cross-border purchasing." Despite limitations, "the Providence policy had a city-specific impact on retail sales of flavoured cigars, which was attenuated by an increase in sales of concept-flavour named cigars." Authors concluded, "Products with concept-flavour names may avoid enforcement agency detection, and their continued sale undermines the intent of the policy."

94. Chaiton M. O., Schwartz R., Tremblay G., et al. Association of flavoured cigar regulations with wholesale tobacco volumes in Canada: an interrupted time series analysis. *Tob Control*. 2019;28(4):457-461.

Chaiton et al. examined the association of Federal Canadian regulations passed in 2009 addressing flavors (excluding menthol) in small cigars with changes in cigar sales. Researchers analyzed quarterly wholesale unit data as reported to Health Canada (2001 through 2016) using an interrupted time series analysis. They estimated changes in sales of cigars with and without flavor descriptors, adjusted data by seasonal, and assessed changes for each flavor type over time. Results show the Federal flavor regulations were "associated with a reduction in the sales

of flavoured cigars by 59 million units (95% CI -86.0 to -32.4)." While increases in sales of cigars with descriptors other than flavors (e.g., color or other ambiguous terms) were observed (9.6 million increase (95% CI -1.3 to 20.5), "the overall level (decline of 49.6 million units (95% CI -73.5 to -25.8) and trend of sales of cigars (6.9 million units per quarter (95% CI -8.1 to -5.7)) declined following the ban." Moreover, sensitivity analysis showed that "there was no substantial difference in effect over time comparing Ontario and British Columbia, suggesting that other provincial tobacco control legislation [enacted in Ontario] was not associated with the changes in levels." Finally, "analyses suggested that the level change was sensitive to the specification of the date." Authors conclude, results demonstrate that flavor regulations "have the potential to substantially impact tobacco sales. However, exemptions for certain [flavors] and product types may have reduced the effectiveness of the ban, indicating the need for comprehensive, well-designed regulations."

95. **What we know about electronic cigarettes. 2019; Available at. Accessed 9/9/2019.**

The smokefree.gov website outlines information about e-cigarettes and health risks. The site also explains that, "e-cigarettes are not approved by the FDA as a quit smoking aid. So far, the research shows there is limited evidence that e-cigarettes are effective for helping smokers quit." The site states that e-cigarettes still contain nicotine and other harmful substances.

96. **Want to Quit Smoking? FDA-approved products can help. 2019; Available at: <https://www.fda.gov/consumers/consumer-updates/want-quit-smoking-fda-approved-products-can-help>. Accessed 9/13/2019.**

The U.S. Food and Drug Administration provides information about cessation devices.

97. **Dedicated marijuana account--Appropriations, RCW 69.50.540 Revised Code of Washington(2019).**

According to this statute, funds available for research on the short and long-term effects of marijuana use are limited to 1.0% of those collected through Initiative 502. Up to 0.6% can be allocated to the University of Washington and 0.4% to Washington State University for these purposes.

98. **Title 10 | Chapter XIII - Medical Use of Marihuana | Part 1004 - Medical Use of Marihuana | Title: Section 1004.11 - Manufacturing requirements for approved medical marihuana products, New York State(2017).**

Section 3369-a of the Public Health Law gives the Commissioner of Health for the State of New York statutory authority to regulate the use of medical marihuana. Note: Although 'marijuana' is the standard spelling, the public health law and the penal law have spelled it with an 'h' and that is the official New York State statutory spelling. According to the Official Compilation of Codes, Rules and Regulations of the State of New York (Volume E, Title 10 [Health], Chapter XIII, Section 1004.11[7][d]), "The registered organization shall not add any additional active ingredients or materials to any approved medical marihuana product that alters the color, appearance, smell, taste, effect or weight of the product unless it has first obtained prior written approval of the department. Excipients must be pharmaceutical grade and approved by the department."