BEYOND CIGARETTES

The Risks of Non-Cigarette Nicotine Products and Implications for Tobacco Control

The National Center on
Addiction and Substance Abuse

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Accompanying Statement by Samuel A. Ball, PhD, President and Chief Executive Officer

Since the early 1960's, tobacco use has been recognized as one of the most costly and deadly threats to the public's health. To minimize this threat, policymakers at all levels of government have enacted laws and regulations to try to reduce the accessibility of tobacco products--especially to youth--and to rein in the tobacco industry's efforts to perpetuate tobacco use by recruiting new customers and ensuring that existing customers keep using their products. The public health community has supported these government efforts by developing and implementing public awareness campaigns, school- and community-based prevention programs, and interventions to help people who use tobacco products cut back or quit.

It is widely recognized that cigarettes are the most harmful of all the available tobacco and tobacco-derived products, and that nicotine is the main ingredient that reinforces and maintains their use. Non-combustible tobacco products, such as chewing tobacco, are also harmful because their ingredients have carcinogenic effects along with other negative health consequences, but pose less of a risk to the non-smoking bystander. Further down on the continuum of harm (and potentially conferring some benefit if used in place of cigarettes) are products that contain nicotine but no tobacco, namely electronic nicotine delivery systems (ENDS) such as e-cigarettes and other "vaping" devices.

Whereas much is known about the effects of tobacco use, the current state of knowledge regarding non-cigarette nicotine products that do not contain tobacco is not robust enough to yield a definitive consensus regarding their relative risks and benefits. Although non-cigarette nicotine products, especially those that do not contain tobacco, have been heralded as safe alternatives to cigarettes, emerging research has called that assumption into question, highlighting the need for more research and a more cautious, well-informed approach to regulation, marketing, and use of these products. Historically lax regulation and oversight of the manufacture, marketing, and sales of these products already have resulted in sharp increases in their use, especially among youth, and in sharp reductions in perceptions of their harm or risk. These trends are becoming difficult to reverse despite accumulating evidence that non-cigarette nicotine products are more harmful than originally suspected.

In fact, research has already shown that non-cigarette nicotine products like e-cigarettes typically are not used exclusively or even primarily in place of smoked tobacco products, but rather in conjunction with them, and often by young people who do not smoke cigarettes and who were not planning to do so. The use of multiple nicotine products is common and--relative to the use of a single nicotine product--has been shown to elevate the risks of nicotine addiction, alcohol and other drug use, and other harmful consequences. There also is no clear proof of the efficacy of these products for tobacco cessation. To the extent that they encourage the initiation of smoking or delay or prevent smoking cessation rather than facilitate it, their proliferation carries the risk of preserving the role of tobacco use as the leading cause of preventable disease and death in the United States.

A recent report by the World Health Organization concluded that, "in order for there to be a potential population-wide net health benefit from ENDS at present usage rates, these products would need to be at least three times safer than cigarettes." The Surgeon General's recent report on e-cigarettes documents specific concerns about the use of these products among youth. Generally, the consensus among those steeped in the research is that the most reasonable and responsible strategy is to develop and enforce regulations that keep e-cigarettes and other nicotine products out of the hands of young people and to implement policies and programs that discourage those who do not smoke cigarettes from starting to use any type of nicotine product.

As of August 2016, the U.S. Food and Drug Administration (FDA) finally began to exercise its authority to regulate all tobacco and nicotine products, including e-cigarettes, aiming to implement a research-based approach to their regulation. However, this development has not fully eased concerns about the "wild west" of non-cigarette nicotine products. Instead, the growing influence of "big tobacco" companies in the market and their incessantly blatant role in lobbying Congress to restrict the power of FDA regulations are raising alarm that the remarkable progress made in reducing tobacco use in our nation will be stymied or even reversed.

Regardless of whether its delivery is through a smoked cigarette, an e-cigarette, a hookah pipe, or a cigar, nicotine remains one of the most addictive and potent "gateway drugs," associated with the later use of other addictive and dangerous substances. It is essential that the public, policymakers, and health professionals be better informed about the full range of non-cigarette nicotine products and their effects, especially on youth. It is critical that the actions taken by policymakers and health professionals are based on the research evidence, rather than on misinformation driven largely by the industry's financial interests.

Public health and policy efforts have been remarkably successful in reducing rates of cigarette smoking in the United States over the past few decades. However, both the commercial interests of the tobacco industry and the natural human proclivity toward risk-taking, pleasure seeking, and addictive behaviors require that we do not become complacent in allowing non-cigarette nicotine products to undo decades of hard-won progress in reducing the enormous health and financial costs of tobacco and nicotine use.

This report, *Beyond Cigarettes: The Risks of Non-Cigarette Nicotine Products and Implications for Tobacco Control,* addresses and updates the issues documented in the recent Surgeon General's report on e-cigarettes, but also covers a broader terrain in its examination of the use of all non-cigarette nicotine products among both youth and adults. It summarizes the evidence regarding the different types of non-cigarette nicotine products, presents analysis of data regarding the prevalence and patterns of use, describes the risk factors and consequences of use and the current regulatory landscape, discusses barriers to reducing their use, and offers concrete recommendations for overcoming these barriers. The ultimate goals of this report are to help the public, policymakers, and health professional make sense of the often-confusing and contradictory information that is available on the risks and benefits of these products and recommend reasonable strategies for limiting their recreational use. As ongoing research continues to shed light on the short- and long-term effects of non-cigarette nicotine products, we believe that regulatory efforts and clinical practice should err on the side of caution, especially with regard to preventing youth from using and becoming addicted to nicotine products and preventing the glamorization and renormalization of smoking behaviors.

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This report was prepared under the direction of Linda Richter, PhD, Director of Policy Research and Analysis. Key staff members who contributed to this report include Azure Thompson, DrPH, MPH; Adetutu Adekoya, MA; Nina Robertson; Nicole Piazza; Lindsey Vuolo, JD, MPH; and Aida Edwards. We thank Philip H. Smith, PhD, for his valuable advice regarding the analysis of data presented in Chapter III. David Man, PhD, MLS, assisted with the references for the paper. Andrea Roley, BA, Michelle Conley, MIPH, and Elizabeth Mustacchio, MBA, managed the communications, marketing, and distribution activities. Jennie Hauser managed the bibliographic database and provided administrative support.

While many contributed to this effort, the opinions expressed herein are the sole responsibility of The National Center on Addiction and Substance Abuse.

Chapter I
Introduction

The United States is at a critical juncture in recalibrating its tobacco control policies. Historically, such policies have focused on combustible tobacco products, specifically cigarettes. Decades of restrictions on the sale and marketing of tobacco products, prohibiting smoking in public places and workplaces, and educating the public about the hazards of smoking have all contributed to significant and life-saving declines in cigarette use on the population level.[1] The overall reduction in cigarette smoking, however, has slowed in recent years,[2] especially among youth,[3] while the use of non-cigarette nicotine products[*]--including cigars, smokeless tobacco, and water pipe/hookah--and non-tobacco products like electronic cigarettes (e-cigarettes) generally has been on the rise.[† 4]

> *Important strides have been made over the past several decades in reducing conventional cigarette smoking among youth and young adults. We must make sure this progress is not compromised by the initiation and use of new tobacco products, such as e-cigarettes.*
>
> --Sylvia Burwell
> Former Secretary
> U.S. Department of Health and Human Services
> *E-Cigarette Use Among Youth and Young Adults: A Report of the Surgeon General, 2016.*

The growing popularity of non-cigarette nicotine products has been met with mixed reactions. On the one hand, e-cigarettes and related electronic nicotine delivery systems (ENDS),[‡] as well as other products that contain nicotine but not tobacco, appear to be less harmful than tobacco-containing products (especially combustible tobacco products). They may serve as a safer replacement for people who are addicted to smoking and cannot or will not quit by using currently approved cessation aids.[5] On the other hand, the potential toxicity of these products (due to their flavorings, aerosols, and other harmful components) and the possibility that their use may encourage or perpetuate cigarette smoking and other substance use and addiction (due to the nicotine they contain) are troubling. These opposing perspectives underscore the needs for additional research to better understand the potential risks of non-cigarette nicotine products and for research-informed regulation of their manufacturing, marketing, and distribution.

Striking the right balance between regulating and controlling non-cigarette nicotine products to discourage non-smokers (especially youth) from using them while helping to foster reductions in cigarette smoking has been a difficult challenge. Opponents of strict regulation of these products--including their manufacturers and retailers, the tobacco industry, and some health professionals who are concerned primarily with reducing the deadly toll of cigarette smoking--tend to take a "harm reduction" approach,

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[*] Many terms have been used to refer to products other than combustible cigarettes that contain tobacco or nicotine, including "alternative tobacco products" and "emerging tobacco products." In this paper, we refer to any non-cigarette product that contains nicotine simply as "non-cigarette nicotine products" for several reasons. First, we would like to avoid the implication that these products necessarily are appropriate "alternatives" to cigarettes. Second, some of these products are new or emerging, but others are in mainstream use. Third, it is important to maintain the focus on nicotine--an addictive drug whether in the presence or absence of tobacco--and to examine the nature, risks, and benefits of these products through the lens of addiction science, prevention, and treatment.

[†] Recently published national data from the Monitoring the Future study, a school-based survey of 8th, 10th, and 12th graders, found small but mostly statistically significant declines in the use of most nicotine products between 2015-2016. If this pattern is sustained over the next few years, it is an encouraging sign that the rising trend of non-cigarette nicotine product use among youth may have peaked.

[‡] These include devices referred to as electronic cigarettes, e-cigarettes, e-cigs, cigalikes, vapes, electronic cigars, e-cigars, electronic hookah, e-hookah, hookah sticks, vaping devices, personal vaporizers, vape pens, mods, and tank systems.

acknowledging that these products are not risk-free, but clearly a much better alternative to cigarettes. They argue that over-regulation can impede their use among cigarette smokers looking to cut down or quit and that enacting stringent regulations to control their use is an unnecessary and potentially counter-productive overreach by public health professionals and policymakers. In contrast, proponents of strict regulation of all nicotine-containing products argue that a growing body of research calls into question their safety and that their use is skyrocketing among youth, even those who never smoked or intended to smoke a cigarette. They also argue that their efficacy in reducing cigarette smoking or aiding in cessation is questionable and that their unrestricted marketing and advertising is renormalizing smoking behavior and reversing years of progress in improving the public health.

What we do know with some degree of certainty is that, regardless of the device through which it is delivered, nicotine is not a harmless drug.[6] Once nicotine is ingested and absorbed into the body, it quickly travels to the brain where it triggers the release of chemicals that ultimately produce rewarding sensations.[7] The acute physiological effects of nicotine include an increase in blood pressure, respiration, and heart rate.[8] There is some evidence that nicotine adversely affects the nervous, cardiovascular, respiratory, and reproductive systems;[9] may contribute to cancerous tumor development;[10] and can be lethal if orally ingested.[11] Nicotine also is associated with poor reproductive health outcomes like preterm delivery and stillbirths, and exposure during fetal development and adolescence can have lasting effects on brain and lung development and is associated with cognitive, emotional, and behavioral deficits.[12]

Nicotine use is common among those with certain mental health conditions such as attention-deficit/ hyperactivity disorder, anxiety, and depression, who may use nicotine products in an attempt to self-medicate the symptoms associated with their disorders. It is especially difficult for people with a mental illness to quit once they have started using a nicotine product.[13] Nicotine use also is common among less educated, rural, and lower-income populations--with more negligible declines in use in these groups relative to those seen on the population level, highlighting the need to maintain and even bolster effective tobacco control policies.[14] Finally, nicotine has been shown to perpetuate the use of harmful tobacco products and increase the risk of nicotine addiction as well as alcohol and other drug use and addiction.[15]

The extent of nicotine's particular effects, including its addictive potential, depends in large part on the dose ingested and on the speed of absorption in the body. These factors vary by the device itself (e.g., cigarette, pipe, e-cigarette, hookah, nicotine replacement therapies), the mode of delivery (e.g., smoked, chewed, direct inhalation, skin patch, secondhand exposure), the rate and pattern of use, and an individual's genetic and other biopsychosocial characteristics. Although nicotine replacement therapies (medically-approved smoking cessation aids such as the nicotine patch, gum, or lozenge that are intended for short-term use) do deliver nicotine, their nicotine dose and mode of delivery limit their addictive potential relative to nicotine delivered through cigarettes, ENDS products, and most other nicotine products.

Most studies of the long-term health risks of nicotine have not explored its effects independent of tobacco or the many other toxic and unhealthy ingredients that most nicotine products contain. Much of the physiological harm associated with nicotine product use, apart from the risk of addiction and the risk to fetal development, can be attributed to these other toxicants rather than to nicotine itself.[16]

Given our current understanding of the risks and harms of tobacco and nicotine, most experts would agree with the following basic conclusions:

- The use of tobacco and nicotine products does not promote health and, depending on the nature and extent of their use, can pose significant health risks.
- Relative to combustible cigarettes, most other tobacco and nicotine products appear to be less harmful, unless they are used frequently and heavily.

- A key concern with regard to non-cigarette nicotine products is their propensity to lead to or perpetuate cigarette smoking and its associated risks, especially among youth.

There is little dispute that more quality research is needed to better understand the specific risks, harms and potential benefits of non-cigarette nicotine products, and the nature and consequences of their use, especially among youth, current cigarette smokers, and adult nonsmokers. This need is particularly acute with regard to ENDS use,[*] which is becoming increasingly popular despite accumulating evidence of its risk. For example, we now know with a high degree of confidence that the use of ENDS products among young people exposes them to nicotine at a time when their brains are still developing and particularly susceptible to its addicting effects. We know that their use among young people increases the risk of cigarette smoking and all its associated harms, even among those who were not inclined to smoke. We know that ENDS products contain toxic ingredients in addition to nicotine, such as those contained in its flavoring and the ultrafine particles that can cause adverse respiratory symptoms and other health effects. And we know that nicotine and the other toxic components in ENDS products are harmful to a developing fetus.[17] We also can safely assume that the use of ENDS alone (without the use of other tobacco products) confers less risk of morbidity and mortality than smoking cigarettes. What we are less sure about at this point is the extent to which ENDS products might possibly facilitate cigarette smoking reduction or cessation and whether their use can represent a net benefit to specific groups who are most vulnerable to the extensive harms associated with tobacco smoking.[18] However, attaining a more thorough account of the relative risks, harms, and benefits of non-cigarette nicotine products, including ENDS, is challenging and requires further research.

Research Challenges

Despite the near-daily dissemination of new research findings published in the academic literature and promulgated in the popular media, the current state of the science on non-cigarette nicotine products, especially ENDS, remains incomplete and inconclusive on several fronts. Due to practical and ethical constraints on how such studies can be conducted, it is difficult in most cases to tease out the effects of nicotine itself independent of the device that delivers it and the device's other ingredients. It also is difficult to discern the effects of a particular non-cigarette nicotine product independent of the effects of cigarettes, which commonly are used concurrently among those who use non-cigarette products. Finally, it is difficult to determine the extent to which the adverse health effects of nicotine product use and exposure that have been documented in animal-based studies are generalizable to humans. These difficulties are compounded by:

- The rapidly changing landscape of non-cigarette products, their technical terminologies and their many nicknames, and the lack of consistency across studies in the use of common terms and definitions related to them;
- The lack of consistent, valid, and reliable measures related to non-cigarette nicotine products and measures for determining the chemical components of individual products and their emissions;[19]
- The inevitable lag in surveillance studies in capturing current patterns and trends in use and perceptions of each product, due in large part to limited resources targeted to collecting and disseminating such data;
- The need to limit the number of questions asked in a given survey, which restricts the ability to conduct many meaningful analyses and tease apart complex associations;
- The high cost of conducting longitudinal studies that would allow for the assessment of longer-term patterns in use and consequences; and

[*] See Chapter II for a closer look at the current state of knowledge regarding ENDS products.

- The difficulty of capturing data from harder-to-reach populations that might be at increased risk of nicotine product use and its consequences.

Additional limitations in existing studies that the present report attempts to address or acknowledge to the extent possible are:

- The lack of distinction or control in many studies regarding specific categories of nicotine products, including those in which nicotine and tobacco are inhaled (i.e., smoked or combustible tobacco products like cigarettes, cigars, pipes, water pipe/hookah), products in which nicotine and tobacco are orally or nasally absorbed (i.e., smokeless tobacco products like chewing tobacco, snuff, snus, and dissolvables), and products in which only nicotine but no tobacco is inhaled (i.e., ENDS products).[*] There are critical differences in the patterns of use of products from each of these categories and in the consequent risk of addiction and other health effects.
- The lack of distinction or control in many studies between the exclusive use of non-cigarette nicotine products and the use of these products along with cigarettes. Research suggests that much of the harmful effects, including the risk of addiction, that appear to derive from non-cigarette nicotine product use might result from concomitant cigarette use. However, because most individuals who use nicotine products use more than one type, it is difficult to:
    - Isolate the unique adverse effects of nicotine relative to the tobacco and other toxic additives in smoked and smokeless tobacco products and in the flavors and other additives in non-tobacco nicotine products (ENDS); or
    - Calibrate the adverse effects of nicotine based on differences in dose, absorption, mode of delivery (e.g., inhalation), and exposure.
- The lack of distinction or control in many studies between nicotine product categories (i.e., smoked/combustible vs. smokeless vs. ENDS), types (e.g., cigarette only vs. cigar only vs. ENDS only), or nicotine content (ENDS or water pipe/hookah with vs. without nicotine), which precludes the ability to tease out the unique health effects of each category and type of product and the presence versus absence of nicotine.
- The lack of distinction or control in many studies between types of users of the various nicotine products in terms of their level of experience with using a specific nicotine product, the extent to which they are dependent on or addicted to nicotine, and the extent to which they may have other comorbid health behaviors or conditions that might account for the observed risks or harms associated with nicotine product use.
- The lack of a clear and consistent definition of nicotine addiction that can be applied validly and reliably across nicotine products. Current studies utilize a range of measures, nomenclature, and standards to categorize a tobacco use disorder or nicotine dependence or addiction. Some use the more comprehensive criteria outlined for tobacco use disorder in the Diagnostic and Statistical Manual of Mental Disorders (DSM), whereas others use a subset of symptoms designed primarily to assess addiction to cigarettes. Many studies do not adequately take into account the fact that the assessments they use may meaningfully be applied only to cigarette use and not to the use of the full range of non-cigarette nicotine products (e.g., daily use, use within 30 minutes of waking).

[*] Due to these important distinctions, the descriptions of nicotine products in Chapter II and the presentation of prevalence data in Chapter III are organized in line with these three categories.

Next Steps

Despite these extensive research challenges, the scientific community largely agrees that until additional quality research is completed, the most expedient and appropriate stance to take with regard to prevention and regulation, given the tragic lessons learned from our nation's history with cigarettes, is a conservative and precautionary one. The known health consequences associated with nicotine and the risk of addiction raise concerns about the proliferation of non-cigarette nicotine products, including those that do not contain tobacco, and underscore the importance of ensuring that these products are regulated in a way that best protects the public health and puts safety rather than the interests of the tobacco industry first. The onus must be on the tobacco industry and product manufacturers to prove that their products are safe or not harmful, rather than on research and health professionals to prove that they are not safe or harmful.

> *The burden of proof regarding product safety should be placed on those who wish to market and sell such tobacco products, rather than the public health community charged with protecting the public's health.*
>
> --U.S. Department of Health and Human Services
> *E-Cigarette Use Among Youth and Young Adults: A Report of the Surgeon General, 2016*

As non-cigarette nicotine products become more popular, a singular focus on reducing the burden of tobacco-related harms no longer suffices. Instead, the need to address carefully the potential risks of nicotine itself and the other potentially toxic components of non-cigarette nicotine products is becoming more prominent.

In May 2016, the U.S. Food and Drug Administration (FDA) finalized a rule that extends its oversight of tobacco products from cigarettes, cigarette tobacco, smokeless tobacco, and roll-your-own tobacco to electronic cigarettes, water pipe/hookah, cigars, dissolvables, and other previously unregulated tobacco/nicotine products.[20] These regulations went into effect on August 8, 2016, but much of it is under litigation. Nevertheless, this rule is a critical and promising first step in protecting the public from the many risks of tobacco and nicotine. Still, key knowledge and policy gaps remain to be filled, and a forceful push by the tobacco industry to curtail these regulations[21] must be met with solid, evidence-based policymaking. Importantly, given that the FDA is now authorized to regulate all current and future tobacco and nicotine products, additional regulations can be implemented to close these gaps in the future.

Taking into consideration the current state of knowledge on non-cigarette nicotine products and the limitations in the currently available data, this report, *Beyond Cigarettes: The Risks of Non-Cigarette Nicotine Products and Implications for Tobacco Control*, seeks to summarize research findings regarding the types of non-cigarette nicotine products that are available, their relative risks and benefits, the prevalence of their use, and the groups most at risk of using them. It highlights areas of inquiry where more research is needed to form solid conclusions and determine effective responses. It describes the current regulatory landscape regarding the control of these products and barriers to better protecting the public from their harms. Finally, it offers research-based recommendations for ensuring that the proliferation of these products is met with appropriate circumspection and an effective response that will simultaneously protect the public health and inform best practices in addressing all forms of nicotine product use.

Chapter II
Types of Non-Cigarette Nicotine Products and Their Effects

Nicotine products can be classified into three broad categories: smoked tobacco in which nicotine is delivered through combustion; smokeless tobacco in which nicotine is delivered through oral or nasal absorption; and electronic nicotine delivery systems (ENDS) such as e-cigarettes, in which nicotine is vaporized and inhaled through an aerosol.[1]

Types of Nicotine Products		
Smoked Tobacco	**Smokeless Tobacco**	**Electronic Nicotine Delivery Systems (ENDS)**
Cigarettes	Chewing tobacco	Electronic cigarettes (e-cigarettes, 'cigalikes')
Cigars (including large cigars, little cigars, and cigarillos)	Dry snuff/pouch	Vape pens
Pipes	Moist snuff	Modified electronic cigarettes Advanced personal vaporizers ('MODS')
Water pipe/hookah	Snus	Electronic water pipe/hookah
	Dissolvables	

The risk of addiction and other negative health effects from nicotine use varies by the type of nicotine product used, the means by which nicotine is ingested, and the nicotine concentration of the product; the risk for negative health effects also is influenced by the type and amount of other toxic components the product contains.[2]

The types of nicotine present in tobacco and nicotine products fall into two categories: unprotonated and protonated. Unprotonated nicotine is more readily absorbable than protonated nicotine, resulting in greater nicotine exposure. At higher pH levels,[*] the proportion of unprotonated nicotine increases, facilitating nicotine absorption.[3] Inhaled nicotine is quickly absorbed into the bloodstream and to the nicotine receptors in the brain. Nicotine reaches the brain approximately 20 seconds after being inhaled, quickly producing its reinforcing and addicting effects on the brain's reward system.[4]

Average Usage Patterns and Nicotine Levels in Nicotine Products				
	Unit		**Nicotine Levels**	
Nicotine Product	**Avg. duration of ingesting one unit**	**Avg. # of units consumed by typical user per day**	**Range of nicotine content per product unit (mg/g)**	**Average nicotine content per product unit (mg/g)**
Smoked Tobacco				
Cigarettes[† 5]	10 minutes[6]	13.04[7]	16.2-19.9	17.9
Cigars[8]	60 minutes[9]		6.3-15.6	10.0
Little cigars/cigarillos[10]			7.1-16.1	11.5

[*] An indicator of the acidity vs. alkalinity of a substance.
[†] Unfiltered and filtered U.S. brands (American Spirit, Camel, Kool Menthol, Marlboro, Newport Menthol).

Average Usage Patterns and Nicotine Levels in Nicotine Products (continued)				
	Unit		Nicotine Levels	
Nicotine Product	**Avg. duration of ingesting one unit**	**Avg. # of units consumed by typical user per day**	**Range of nicotine content per product unit (mg/g)**	**Average nicotine content per product unit (mg/g)**
Smoked Tobacco				
Pipes[11]		1[12]	30.1-50.9	38.2
Water pipe/hookah[* 13]	45-60 minutes[14]			
Smokeless Tobacco	69 minutes[† 15]	7[‡ 16]		
Dry snuff[17]			14.9-20.2	17.6
Dry snuff pouch[18]			10.5-14.0	11.7
Moist snuff[19]			4.4-25.0	11.9
Snus[20]			9.0-11.3	10.1
Dissolvables[21]			3.9-8.7	6.5
Electronic Nicotine Delivery Systems (ENDS)[§ 22]	10 minutes[23]	0-10[24]	0-29[25]	17.0

Non-Cigarette Smoked Tobacco Products

Whether ingested via smoked, smokeless, or vaped nicotine products, tobacco use carries risks. Although specific usage patterns--such as the extent of inhalation of smoke or the frequency of use--play a role in the likelihood of adverse health consequences, the composition of modern tobacco products contain ingredients such as tar, charcoal, and carcinogenic compounds that can be quite harmful to those who use these products.

Cigars

Cigars are rolled bundles of dried and cured tobacco consisting of three main parts: the tobacco filler, binder, and wrapper.[26] The wrapper typically is comprised of leaf tobacco or a substance that contains tobacco.[27] Cigars are differentiated by size, design, and flavoring[28] and they are classified into three types: large cigars, little cigars, and cigarillos:[29]

Large Cigars. Although their size may vary, large cigars typically weigh 5-17 grams and are 110-150 mm long.[30] They can accommodate a half ounce of tobacco or more.[31] The premium cigar is the largest type of cigar; it usually is hand-rolled, weighs up to 22 grams, and is 127-214 mm long.[32]

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[*] Water pipe/hookah nicotine content is measured by plasma nicotine concentration--the amount of nicotine in the blood--in nanograms per milliliter. Unlike the other products, it cannot be measured per unit. Average plasma nicotine concentration in water pipe/hookah is 9.8 ng/mL, which compares to an average of 9.4 ng/mL in one cigarette.

[†] Average of dry snuff, dry snuff pouches, moist snuff, and snus products. Does not include dissolvables.

[‡] Average of dry snuff, dry snuff pouches, moist snuff, and snus products. Does not include dissolvables.

[§] The majority of research on usage patterns and nicotine content for ENDS products are on e-cigarettes specifically.


Ivan Kurmyshov
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Little Cigars. Little cigars resemble cigarettes in shape, size, the use of filters,[33] and in their packaging (some brands are available in packs of 20).[34] They typically weigh about one gram and are 70-100 mm long.[35] Little cigars are available in various flavors.[36]


Zmurciuk Kirill
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Cigarillos. Slightly heavier and longer than little cigars (1.3-2.5 grams and 70-120 mm long), cigarillos hold more tobacco than little cigars. Like little cigars, they are available in multiple flavors and can be sold individually or in packages with as few as two units.[37]

Mode of Administration. Cigars are slowly burned to deliver tobacco and nicotine. As the cigar burns, cigar users typically puff but do not inhale the emerging smoke. When cigar smoke is drawn but not inhaled, nicotine is absorbed through the membranes of the mouth, the oral mucosa.[38] When cigar smoke is inhaled, as it is by many former smokers or those who use little cigars and cigarillos, it is inhaled in the same manner as cigarette smoke.[39] Inhaled cigar smoke is absorbed through the lungs, which is a faster route of administration than absorption through the mouth, making it more harmful.[40]

Nicotine Exposure. Nicotine content and concentrations vary depending on the size and type of cigar.[41] Exposure to nicotine also depends on smoke pH levels, inhalation behavior (whether one inhales or not), number of puffs, whether the cigar is kept in the mouth between puffs, and the amount of the cigar that is consumed.[42]

Factors Influencing Nicotine Exposure	
	Influence on Nicotine Exposure
Smoke pH level	The more basic (alkaline) the smoke/tobacco pH, the more readily it is absorbed through the oral mucosa--regardless of inhalation--and the greater the nicotine exposure.[43]
Inhalation behavior	More inhalation relates to greater absorption of nicotine through both the oral mucosa and the lungs, increasing nicotine exposure.[44]
Number of puffs	The greater the number of puffs, the greater the nicotine exposure.[45]
Length of time to finish the cigar	The longer the time spent using a cigar, the greater the nicotine exposure.[46]

Health Effects. Like cigarettes, cigars contain nicotine, tar, and other toxic ingredients[47] and increase the risk of decreased lung function; airflow obstruction;[48] coronary heart disease; cerebrovascular disease; aortic aneurysm; chronic obstructive pulmonary disease;[49] and oral, esophageal, pancreatic, and laryngeal cancer.[50] However, the health effects of cigar use vary depending on inhalation of the cigar smoke, the frequency of use, and whether cigars are used exclusively or in addition to cigarettes or other tobacco products.[51]

The nicotine in cigar smoke is more readily absorbed through the mouth than is the nicotine in cigarettes,[*] which means that to get the desired quantity of nicotine, cigarette smokers tend to inhale more than cigar smokers do. This tendency for cigar users to inhale less is one of the reasons for the generally lower risk of disease among those who use cigars exclusively versus those who use cigarettes exclusively or in addition to cigars.[52] Cigar users who do regularly inhale have a greater risk of health problems than those who do not or who only occasionally inhale. However, several studies have found that individuals who

[*] Cigar smoke is less acidic than cigarette smoke, with a higher proportion of unprotonated nicotine, making it more readily absorbed across the oral mucosa.

use cigars do typically inhale some of the smoke into their lungs during a smoking session, regardless of their reported inhalation behavior or cigarette smoking history.[53] Still, cigarette users, or those who have used both cigars and cigarettes, are more likely to deliberately inhale cigar smoke, exposing them to greater health risks.[54] Another contributor to the relatively lower risk of disease among exclusive cigar versus cigarette users is that they tend to smoke less frequently.[55]

CIGARS
Health Effects

Addiction

- Greater nicotine exposure is associated with a higher risk of addiction. Nicotine exposure depends on:[56]
  - Nicotine content in a cigar (varies significantly: large cigars typically have higher nicotine content than little cigars).
  - Tobacco and tobacco smoke pH levels (varies significantly: cigars with a higher smoke pH[*] level tend to deliver more nicotine).
  - Amount of cigar consumed (for larger cigars, more consumption leads to higher smoke pH levels and more nicotine exposure).
  - Whether or not smoke is inhaled (inhalation allows more nicotine to be absorbed).
  - Number of puffs taken (greater number of puffs taken is associated with more nicotine exposure).

Cardiovascular Disease

- Cigar users who inhale smoke are at increased risk of coronary heart disease, cerebrovascular disease, and aortic aneurysm.[57]

Cancer

- Cigar smoke particles, containing toxic and cancer-causing chemicals,[58] enter the lungs and increase the risk of lung cancer.[59] People who use both cigarettes and cigars are more likely to inhale cigar smoke and are at a higher risk of lung cancer than those who use cigars exclusively.[60]
- The risk of oral and pharyngeal cancers in cigar smokers is similar to that of cigarette smokers: both cigar and cigarette smokers are 7-10 times more likely to develop these cancers than nonsmokers.[61]
- Cigar smokers have a higher risk of laryngeal cancer than nonsmokers.[62] Research suggests that individuals who smoke five or more cigars per day or who inhale moderately or deeply are at the highest risk.[63]
- Cigar smokers have a higher risk of pancreatic cancer than nonsmokers.[64]

Respiratory Problems

- Cigar smokers who inhale smoke are at an increased risk of chronic obstructive pulmonary disease.[65]
- Cigar use is associated with decreased lung function and increased airflow obstruction.[66]

Oral Problems

- Cigar smokers have an elevated risk of gum disease and tooth loss, similar to cigarette smokers.[67]

Secondhand/Environmental Exposure

- Secondhand smoke from little cigars results in impairment of arterial flow-mediated dilation.[†] [68]
- Cigars can emit 9-30 times greater amounts of carbon monoxide than cigarettes.[69]

[*] A tobacco smoke pH value above 7.
[†] Arterial flow-meditated dilation measures vascular endothelial function, and is an indicator of cardiovascular risk.

Pipes

Tobacco pipes are comprised of the following main elements:

- the bowl or chamber, where the tobacco is held and burned;
- the shank and stem, where the tobacco smoke passes through;
- (usually) a filter cartridge between the stem and the mouthpiece; and
- the mouthpiece or bit, from which a pipe user draws in tobacco smoke.

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Mode of Administration. Tobacco is placed into the pipe bowl where it is burned and emits smoke. Pipe users typically do not inhale the tobacco smoke; rather they hold the smoke in their mouths and then exhale. However, inhalation behavior varies by user.[70]

Nicotine Exposure. There is very little research regarding the nicotine content in pipes. Given that tobacco from pipes is not commercially packaged and it is up to the user's discretion to determine how much tobacco goes in the pipe, nicotine content varies. Nicotine exposure depends on whether and to what extent the user inhales the tobacco smoke.[71]

Like cigars, pipe smoke is alkaline or less acidic than cigarette smoke, facilitating nicotine absorption through the mucous tissues of the mouth. Former and current cigarette smokers may be more likely than those who have never smoked cigarettes to inhale when using pipes.[72] Exclusive pipe users tend to have lower levels of plasma nicotine after pipe use compared to pipe users who also used cigarettes. This suggests that exclusive pipe users are not as likely as those who use both cigarettes and pipes to inhale tobacco smoke, and tend to have lower nicotine exposure.[73]

Health Effects. Pipe use is associated with lung, oropharyngeal, esophageal, colorectal, and laryngeal cancers as well as coronary heart disease, cerebrovascular disease, and chronic obstructive pulmonary disease.[74] However, because pipe smoking involves less inhalation than cigarette smoking and occurs less frequently, exclusive pipe users have a lower risk of disease relative to those who smoke cigarettes, except among heavy users who do inhale.[75] For example, the likelihood of cancer among pipe users is dose-dependent, increasing with the number of pipes smoked per day and years of pipe smoking.[76]

PIPES **Health Effects**
Addiction
• Greater nicotine exposure is associated with a higher risk of addiction. Nicotine exposure depends on: ➢ Nicotine content (typically higher than in cigarettes).[77] ➢ Whether or not smoke is inhaled[78] (inhalation allows more nicotine to be absorbed; exclusive pipe users are less likely to inhale tobacco smoke than those who use both pipes and cigarettes[79]).
Cardiovascular Disease
• Pipe users are more likely to develop coronary heart disease and cerebrovascular disease than individuals who have never used any tobacco product.[80]
Cancer
• Individuals with a history of pipe tobacco use have a higher risk of lung, oropharyngeal, esophageal, colorectal, and laryngeal cancers than non-users.[81] • Some studies have found that the likelihood of certain cancers among pipe users increases with the number of pipes smoked per day and years of smoking.[82]

PIPES Health Effects (continued)
Cancer (continued)
• The rate of lung cancer is significantly lower among exclusive pipe users than cigarette users, but there is less difference in the rates of other cancers.[83]
Respiratory Problems
• Current tobacco pipe users are more likely to have chronic obstructive pulmonary disease than non-users.[84] • Pipe smoking is linked to decreased lung function and increased airflow obstruction.[85]
Oral Problems
• The increased risk of gum disease, tooth loss,[86] and cancer of the oral cavity[87] among pipe smokers is similar to that among cigarette smokers.[88]

Water Pipe/Hookah

Water pipes, also referred to as hookah (as well as nargile, shisha, and hubble bubble), is a device typically used to smoke tobacco.[89] These devices may also be used to smoke nicotine- and tobacco-free products, such as dried herbs and herbal molasses. A water pipe/hookah is comprised of five main parts:

- the bowl where the tobacco and other ingredients are placed;
- the head where the charcoal is used to heat the tobacco;
- the base, usually filled with water or other liquid, which filters the smoke;
- the pipe that links the bowl and the base; and
- the hose and mouthpiece used to inhale the smoke.[90]

nata789
iStock/Getty Images

Water pipe/hookah products come in different shapes, and there are variations in the types of tobacco and other ingredients that can be smoked using the device.[91]

Mode of Administration. Water pipe/hookah use begins with placing charcoal in the head of the water pipe and water in the vase or bowl. The vapor from the burning tobacco is filtered through the bowl of water and then inhaled through the mouthpiece. While the device can be used individually, it is generally shared among a group of people until the tobacco has completely burned.[92] A session, which typically lasts 45 to 60 minutes, can involve refilling the tobacco bowl multiple times.[93]

Nicotine Exposure. Most water pipe/hookah use involves exposure to nicotine, but the extent of nicotine exposure varies by the device's design, the type of tobacco used, the temperature of the burning tobacco, the means of inhalation, the amount of puffs taken, and the duration of the session.[94] Almost all studies examining nicotine exposure from water pipe/hookah use have looked at individual use in laboratory settings even though these products often are used in social settings.[95]

The few studies that have quantified nicotine exposure from water pipe/hookah use display a wide range of findings. One study comparing toxicant exposure from water pipe/hookah and cigarettes found that blood plasma nicotine increased from 2 ng/ml to 8.5 ng/ml after 45 minutes of water pipe/hookah use (in comparison to 2.1 ng/ml to 4.1 ng/ml after 45 minutes of cigarette use).[96] Another found that blood plasma nicotine levels increased from 1.1 ng/ml to 60.3 ng/ml after 45 minutes of use among daily users.[97] The inconsistency in these findings could be attributed to different smoking behaviors and different amounts of nicotine in the tobacco.[98]

Health Effects. The exposure to toxins during water pipe/hookah use varies by the tobacco or charcoal used, the design of the device, and the nicotine content.[99] The immediate effects of water pipe/hookah use mostly resemble the acute effects of nicotine exposure, which include an increase in plasma nicotine concentration, heart rate, blood pressure, carboxyhemoglobin, and expired carbon monoxide.[100] The long-term health risks have not been as widely studied as the health risks associated with cigarette use. However, because water pipe/hookah use is associated with exposure not only to nicotine, but also to carbon monoxide and tobacco-specific nitrosamines,[*] there appears to be a link between its use and many of the same diseases as have been associated with cigarette use. These include lung and gastric cancer, chronic bronchitis, emphysema, respiratory and coronary artery disease, pregnancy-related complications such as low birthweight, osteoporosis, and mental health problems.[101] Carcinogenic components, volatile aldehydes, tar, phenolic compounds, and metals have been found in the charcoal and smoke of water pipe/hookah, increasing the risk of lung disease and other health conditions.[102] Water pipe/hookah use also involves exposure to high amounts of carbon monoxide, increasing the risk of poisoning and cardiovascular disease.[103] Because those who engage in water pipe/hookah use generally share mouthpieces, there is an increased risk of hepatitis, herpes, and tuberculosis.[104] Secondhand (passive) exposure to water pipe/hookah smoke exposes non-users to toxic particulate matter.[105]

Smoke exposure from a single session of use is greater than from a single cigarette smoking session.[106] Generally, a one-hour long session of using water pipe/hookah can result in the same amount of tobacco inhalation as smoking as many as 100 cigarettes.[107] The difference in smoke exposure could partly be attributed to the fact that water pipe/hookah users generally puff more often than cigarette users, which increases the likelihood of toxicant exposure and the risk of tobacco-related illness.[108]

WATER PIPE/HOOKAH
Health Effects

Cigarette Smoking

- Use of water pipe/hookah is associated with more susceptibility to cigarette smoking among young adults who are not established cigarette smokers.[109]

Addiction

- Greater nicotine exposure is associated with a higher risk of addiction. Nicotine exposure depends on:
  - Design of the device (varies based on size, water bowl capacity, and length of flexible hose).[110]
  - Type of tobacco used (flavored or unflavored; unflavored tobacco contains significantly higher nicotine content than flavored tobacco).[111]
  - Whether or not smoke is inhaled (inhalation of smoke allows for more nicotine exposure).
  - Number of puffs taken (greater amount of puffs increases nicotine exposure).
  - Duration of smoking session.[112]
  - Nicotine absorbed (daily water pipe nicotine absorption can be equivalent to that of smoking 10 cigarettes a day).[113]
  - Nicotine filtered (only small amounts of nicotine are filtered through the water pipe/hookah device, allowing for high levels of nicotine exposure).[114]

[*] A group of carcinogens present in tobacco and tobacco smoke that are formed from nicotine and related tobacco alkaloids.

WATER PIPE/HOOKAH Health Effects (continued)
Cardiovascular Disease
• Lifetime water pipe/hookah users (40 years or more) relative to non-users are at three times greater risk of severe stenosis, which increases the risk of coronary artery disease.[115] • Water pipe/hookah use may elevate heart rate and is associated with dysfunction in autonomic regulation of the cardiac cycles.[116]
Cancer
• Water pipe/hookah use is closely linked to lung and esophageal cancers.[117]
Respiratory Problems
• Both tobacco-free and tobacco-based water pipe/hookah products contain toxicants, which impair pulmonary function and increase the risk of lung disease.[118] • Long-term use of water pipe/hookah is associated with chronic bronchitis and emphysema.[119]
Pregnancy Outcomes
• Exposure to water pipe/hookah smoking appears to be associated with low infant birth weight.[120]
Secondhand/Environmental Exposure
• The charcoal used in water pipe/hookah smoking can lead to carbon monoxide poisoning.[121] • Venues that allow water pipe/hookah use have high concentrations of air pollutants and toxicants that lead to hazardous air quality, affecting visitors and employees.[122]

Smokeless Tobacco Products

Kris Hanke
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The term smokeless tobacco refers to any tobacco product that is administered without combustion or heat. Although there are wide global variations in the types of smokeless tobacco products available, those found in the United States typically consist of cut, ground, powdered, or leaf tobacco that is placed in the oral or nasal cavity. The ingredients and the process by which they are made vary by region, as do their nicotine concentration, pH levels, and the consequent health effects. The three main smokeless tobacco products typically found in the United States are chewing tobacco, snuff, and dissolvables.

Chewing tobacco is made of cured tobacco leaves that typically come in three forms: loose leaf, mounded together in "plug" form, or a twist form where the tobacco is twisted in the shape of a rope. Snuff includes dry snuff, moist snuff, and snus.[123] Dry snuff uses fire-cured tobacco leaves, which are turned into a powdered form of tobacco.[124] Moist snuff uses either air-cured or fire-cured tobacco leaves, which are cut into fine particles.[125] Snus essentially consist of moist snuff packaged in pouches the size of tea bags.[126] Dissolvable tobacco products are finely processed tobacco leaves turned into lozenges, orbs, or strips (similar in appearance to mints), sticks (similar in appearance to toothpicks), and breath strips.[127]

Mode of Administration. Smokeless tobacco is administered either orally or nasally. Chewing tobacco can be chewed or placed and held in the mouth between the cheek and the gum typically for up to one hour.[128] The juice emitted from chewing tobacco usually is spit out, but some people choose to swallow it.[129] Snuff is administered in the same manner as chewing tobacco, but also can be administered nasally.[130] Snus, unlike other types of snuff, is not typically spit out.[131] Dissolvable tobacco is administered orally and dissolves in the mouth over time.[132]

Nicotine Exposure. There is no standard amount of nicotine in smokeless tobacco products. Nicotine exposure depends on nicotine concentration, packaging, pouch size, moisture content, pH levels, and the amount of unprotonated (more readily absorbable) nicotine.[133]

In an evaluation of 53 smokeless tobacco products from five global regions,[*] nicotine concentration ranged from 0.16 to 34.1 mg/g and pH levels ranged from 5.2 to 10.1.[134] With such a wide range of pH levels, the proportion of readily absorbable nicotine ranged from 0.16 percent to 99.1 percent.[135] A study of domestic smokeless tobacco products[†] found that nicotine concentration ranged from 3.9mg/g to 40.1 mg/g, pH levels ranged from 4.7 to 7.9 and the unprotonated nicotine ranged from 0.01mg/g to 3.7 mg/g. Snus and dissolvable tobacco products had the highest levels of readily absorbable nicotine, and twist tobacco products had the highest levels of nicotine concentration.[136]

Health Effects. Smokeless tobacco has been associated with pancreatic and oral cancer as well as cancer of the esophagus, the pharynx, head, and neck. However, the research supporting these associations is limited and some studies did not take into account cigarette smoking.[137] Generally, the risk of cancer depends on the type of smokeless tobacco product used and the levels of carcinogens in the product.[138] Several studies have found high levels of toxicants and carcinogens in smokeless tobacco products as well as unprotonated nicotine, which may increase the risk of nicotine exposure and addiction.[139]

SMOKELESS TOBACCO
Health Effects

Addiction

- Greater nicotine exposure is associated with a higher risk of addiction. Nicotine exposure depends on:
  - Nicotine concentration (varies significantly between different products; twist smokeless tobacco products have the highest levels of nicotine concentration).[140]
  - Amount of unprotonated/absorbable nicotine (a greater amount of unprotonated nicotine is associated with greater nicotine exposure).[141]
  - pH levels of the tobacco (higher pH levels are associated with more unprotonated/ absorbable nicotine, making it more addictive. Snus and dissolvable smokeless tobacco products have the highest level of absorbable nicotine).[142]
  - Pouch size (increased pouch size is associated with a greater amount of nicotine).[143]
  - Moisture content[144] (moist snuff delivers more absorbable nicotine than dry snuff[145]).
- The risk of addiction to smokeless tobacco is similar to that of cigarettes.[146]

Cardiovascular Disease

- Smokeless tobacco users have a lower risk of cardiovascular disease than cigarette smokers.[147]
- The findings regarding the association between smokeless tobacco use and the risk of cardiovascular disease and stroke are inconsistent.[148]
- Smokeless tobacco users may have an increased risk of hypertension and metabolic syndrome relative to non-users.[149]

Cancer

- Those who use smokeless tobacco exclusively may have at least as high or even higher exposure to nicotine, cotinine, and carcinogens relative to those who use cigarettes exclusively.[150]
- Long-terms smokeless tobacco product use may be associated with oral cancer and cancer of the esophagus, pharynx, head, and neck, but the evidence regarding the risk of cancer is inconclusive.[151]

[*] Southeast Asia, Eastern Mediterranean, Africa, Europe, and the Americas.
[†] Including dry snuff pouch, dry snuff without pouch, twist, loose leaf, plug, snus, and dissolvable tobacco.

SMOKELESS TOBACCO Health Effects (continued)
Cancer (continued)
• Users of chewing and moist tobacco products appear to have a lower risk of oral cancer compared to users of dry snuff.[152] • A few studies report an association between smokeless tobacco product use and pancreatic cancer; people who use more than 2.5 ounces per week were found to be at an increased risk.[153] However, others have found no association.[154]
Pregnancy Outcomes
• Nicotine has been found to affect fetal development and, therefore, smokeless tobacco is not deemed safe for use during pregnancy.[155]

Electronic Nicotine Delivery Systems (ENDS)


NengLoveyou
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Electronic nicotine delivery systems (ENDS) are battery powered devices that heat a nicotine solution, called an e-liquid (made out of solvent carriers such as propylene glycol or glycerol/glycerin, nicotine, and flavoring), and deliver nicotine through aerosol instead of smoke.[156] The term 'vaping,' which is commonly used in reference to the use of ENDS, incorrectly implies that the gaseous substance produced by ENDS primarily contains water droplets. In fact, the substance emitted during ENDS use is an aerosol, which is a gaseous or airborne cloud of ultrafine particles that may contain toxic chemicals.[*] [157] ENDS include several types of devices with a range of distinguishing characteristics. Whereas researchers and public health advocates frequently use the term ENDS, that term is not as familiar to the public who more commonly refer to the whole class of ENDS products as e-cigarettes.[†] [158]

The first generation of ENDS most notably includes electronic cigarettes, also known as e-cigarettes, e-cigs, or cigalikes. These products are very similar to cigarettes in appearance; they are usually the same shape and size as a traditional cigarette and often mimic the experience of smoking a cigarette.[159] Depending on the device, they sometimes have a light-emitting diode (LED) that lights up when the user puffs.[160] They either can be disposable (single use) or rechargeable.[161]

Since the introduction of the e-cigarette to the U.S. market in 2007, the ENDS category has grown considerably. In addition to e-cigarettes, available ENDS products now include products referred to as vape pens, personal vaporizers, advanced personal vaporizers, modified vaporizers (MODs), electronic hookah, and electronic cigars. First generation ENDS most closely mimic the experience of smoking a cigarette,[162] whereas second and third generation ENDS are not modelled after cigarettes and generally are larger.[163] Unlike first generation devices, advanced generation devices allow users to modify parts of their device to enhance nicotine delivery.[164] Advanced generation devices typically have larger batteries than first generation devices and come in a greater variety of e-liquid flavors.[165] Electronic water pipe/hookah devices are similar mechanically to electronic cigarettes; however, they tend to deliver relatively less nicotine.[166]

[*] These potentially toxic particles can be inhaled deep into the lungs, causing damage.
[†] If that term used in research studies to refer to these products is not familiar to participants and not clearly defined, it may limit the accuracy of the research findings.

Distinguishing Factors of ENDS Products	
Type of ENDS	**Distinguishing Factors**
Electronic cigarettes (e-cigarettes) Cigalikes	• Physically similar to cigarettes • Come in disposable or refillable/rechargeable forms • Some emit a light when the user puffs • Relatively short battery life • Relatively less efficient nicotine delivery
Vaporizer (or vape) pen	• Comes in various sizes, does not resemble a cigarette • Comes in disposable or rechargeable forms • Slim like a pen • Can be modified
Modified nicotine delivery systems Advanced personal vaporizers ('MODs')	• Larger device • Most are rechargeable • Can be modified • Larger batteries and relatively long battery life • Relatively more efficient nicotine delivery
Electronic water pipe/hookah	• Electronic versions of traditional water pipe/hookah devices Relatively less efficient nicotine delivery

Mode of Administration. ENDS come in different shapes and sizes, but the mechanics of how they deliver nicotine are similar across products. ENDS function either via an airflow sensor in which the battery is activated through puffing or via manual activation in which the battery is activated by pressing a button.[167] Earlier generation devices mostly use an airflow sensor while later generation devices use manual activation.[168]

Once the battery is activated, it enables the atomizer in the device to heat the e-liquid solution and emit it in the form of an aerosol. E-liquid solutions generally consist of nicotine, propylene glycol, glycerol/glycerin, and artificial flavoring.[169] Earlier forms of ENDS had separate atomizers to heat the e-liquid solution and cartridges to hold the e-liquid solution.[170] In newer devices, the atomizer and cartridge frequently are combined.[171]

Components of an ENDS Device[172]	
Terms	**Description**
Battery	Power source
Heating element (atomizer, cartomizer)	Heats e-liquid solution/juice to a temperature of vaporization
Cartridge or tank	Holds e-liquid/juice
E-liquid solution/juice	Liquid solution of nicotine, propylene glycol, glycerol/glycerin solution, and sometimes flavoring contained in the cartridge or tank
Aerosol	The suspension of fine particles of liquid, solid, or both in a gas that is inhaled and exhaled

Nicotine Exposure. Levels of nicotine exposure are influenced by whether the ENDS product is a first or later generation device, the nicotine concentration within the e-liquid, the amount of unprotonated/ absorbable nicotine in the product and its nicotine pH levels, the puffing behavior of the individual using the product, and the individual's prior experience using an ENDS product.[173]

Type of Device. Later generation ENDs can deliver nicotine more efficiently than first generation products and thus expose users to more nicotine.[174] Some research indicates that later generation ENDS can deliver as much as or more nicotine than cigarettes.[175]

Nicotine Concentration. Nicotine concentration levels of e-liquids vary among and within brands, ranging from 0 mg/ml to 29mg/ml.[176] One study found that bottles of e-liquids can contain up to 720 mg of nicotine, several times the fatal dose of nicotine for an adult.[177]

Some devices only indicate the nicotine concentration in terms of high, medium, or low, without a precise measurement.[178] In a few cases, the nicotine level in a product is mislabeled, with actual nicotine levels being lower or higher than the label indicates, or with nicotine found in products that are labeled as nicotine free.[179]

Factors Associated with Use Patterns. Nicotine exposure varies by puffing behavior, the duration of use, the specific product being used, and the individual user's prior experience with ENDS products.[180] ENDS products tend to deliver less nicotine to inexperienced users than to experienced users.[181]

Health Effects. The chemical components within e-liquids, cartridges, and aerosols have a range of adverse health effects.[182] Although it is difficult to generalize the findings from studies of ENDS because there is wide variability in the ingredients and chemicals found in these products,[183] the documented acute effects include increased plasma nicotine, heart rate, and carbon monoxide concentration.[184] Short-term adverse effects include respiratory distress, impaired vascular function, and cell damage that can lead to oral disease.[185]

There is a wide variety of ingredients in e-liquid flavoring, refill solutions, cartridges, and aerosols--including solvent carriers (propylene glycol and glycerol/glycerin), tobacco-specific nitrosamines, carbonyl compounds, polycyclic aromatic hydrocarbons (PAHs), metals, and tobacco alkaloids[186]--some of which are carcinogens or contribute to respiratory and cardiac distress.[187] One recent study found detectable levels of more than 115 volatile organic compounds and semi-volatile organic compounds from a single puff[*] of an e-cigarette, and many of the potentially toxic chemicals found in the aerosol were not present in the e-liquid solution itself. This suggests that the aerosolization process itself might increase the risks associated with ENDS use.[188]

Of particular interest with regard to ENDS is the potential health risk to adolescents who are using these products in increasing numbers. While the research on the health consequences is relatively limited, the evidence generally suggests that adolescents who engage in exclusive ENDS use (in the absence of cigarette use) are less likely than those who exclusively use cigarettes or who use ENDS and cigarettes to experience mental health symptoms or to engage in alcohol and other drug use.[189] However, one recent longitudinal study of adolescents did find significantly higher increases in depressive symptoms among adolescents who reported sustained and frequent use of e-cigarettes over a 12-month period relative to those who did not use e-cigarettes.[190] With regard to physical health, research suggests an increased risk of chronic respiratory symptoms in adolescents who report using e-cigarettes.[191]

Recent studies also point to a practice among adolescents who use ENDS, which involves vaporizing the e-liquid at high temperatures by dripping some of the e-liquid directly onto the heating element of the device and quickly inhaling the aerosol (a practice known as "dripping") in order to produce thicker aerosol clouds and to intensify the flavor and 'throat hit' of the e-liquid. A recent survey in Connecticut found that more than one in four high school students who reported ever having used e-cigarettes said that they have engaged in dripping,[192] a practice that may lead to greater exposure to the toxins in e-liquids.[193]

[*] 40 mL

Ingredients in ENDS That May Pose a Health Risk. Propylene glycol, glycerol/glycerin, and in some cases ethylene glycol are solvent carriers that make up the majority of e-liquid refill solutions.[194] In nicotine-free electronic devices, there is an increased risk of exposure to high concentrations of these solvents since, in the absence of nicotine, they make up the majority of the e-liquid. These solvent carriers may result in irritation of air pathways.[195]

Carbonyls are organic compounds that may be present in either e-liquids or aerosol. Carbonyls found in ENDS products include formaldehyde, acetaldehyde, acrolein, acetone, propionaldehyde, propanal, glyoxal, methylglyoxal, butyraldehyde, o-tolualdehyde, propionic aldehyde, and crotonaldehyde.[196] Formaldehyde, acetaldehyde, and acrolein are the most commonly-detected carbonyls in ENDS products.[197] The ranges at which these carbonyl compounds are present in ENDS products vary by brand, with some well below exposure or hazardous limits and others well above the limit.[198] Levels of carbonyls in ENDS also vary based on the presence of propylene glycol as the main liquid solvent and on the level of the battery voltage, with a higher presence of carbonyls with increased output battery voltage.[199] Some carbonyls such as aldehydes are potentially carcinogenic.[200] Acrolein may be associated with multiple illnesses and diseases, including multiple sclerosis, Alzheimer's disease, cardiovascular disease, and diabetes.[201] On a molecular level, acrolein may play a role in a cellular damage, such as membrane damage and immune dysfunction.[202] Some researchers have noted that the presence of acrolein is at such a low level that it poses minimal risk to human health, and that formaldehyde does not form under conditions of normal use of ENDS products; others have called for extensive clinical research to determine if these compounds increase the risk of disease in ENDS users.[203]

Tobacco-specific nitrosamines are known carcinogens that are found in tobacco and tobacco smoke and, to a lesser degree, in e-liquids.[204] Certain metals--such as tin, copper, nickel, aluminum, chromium, zinc, cadmium, lead, and silver--also are found to varying degrees in ENDS e-liquids and aerosol.[205] The metals may derive from the actual ENDS device, specifically from the cartomizer, and carry over into the e-liquids and aerosol.[206] Some of these metals have been associated with respiratory irritation and illnesses, primarily in animal studies.[207]

The chemicals that comprise e-liquid flavorings can increase the risk of respiratory disease when inhaled, even though these chemicals may be 'generally recognized as safe' by the U.S. Food and Drug Administration when consumed in food.[208] Several studies have found that cinnamon flavor in e-liquids is the most toxic of all flavors, inhibiting cell survival among both embryonic and adult stem cells.[209]

Accidental/Unintentional Poisoning. The adverse effects of accidental or unintentional exposure to e-liquids include nausea, vomiting, coughing, chest pain and palpitations, dizziness, and oral irritation.[210] National data indicate that monthly calls to U.S. poison control centers about exposures to ENDS products or to e-liquids increased from 0.3 percent to 41.7 percent between September 2010 and February 2014. About half (51.1 percent) of these calls involved children ages 0 to 5 and the modes of exposure included ingestion, inhalation, eye exposure, and skin exposure.[211] Other national data indicate that whereas a higher percentage of calls to poison control centers between January 2012 and April 2015 were related to accidental exposure to cigarettes rather than to ENDS, children accidentally exposed to ENDS were five times more likely than those exposed to cigarettes to end up being hospitalized.[212]

Design Flaws and Risks. The rechargeable lithium batteries used in ENDS products carry a risk of explosion because their components are flammable or combustible.[213] Low-quality batteries and poorly designed or improperly used ENDS products increase the risk of battery explosions and serious injuries.[214]

ELECTRONIC NICOTINE DELIVERY SYSTEMS (ENDS)
Health Effects

Addiction

- Greater nicotine exposure is associated with a higher risk of addiction. ENDS products may contain the same amount or more nicotine than cigarettes.[215] Nicotine exposure depends on:
  - The generation of the device, with later generation ENDS delivering more nicotine than first generation devices.[216]
  - Nicotine concentration in the e-liquid (varies by product).[217]
  - User puffing behavior (a greater number of puffs increases nicotine exposure).[218]
  - Prior experience using ENDS products (ENDS typically deliver less nicotine to inexperienced users than to experienced users).[219]
  - Type of nicotine (unprotonated nicotine is more readily absorbable and results in higher nicotine exposure than protonated nicotine).[220]
  - The pH level of the e-liquid (higher levels are associated with more nicotine exposure). Menthol flavored products tend to have higher pH levels than those with other flavors.[221]

Cardiovascular Disease

- ENDS affect the cardiovascular system by increasing plasma nicotine, heart rate, and carbon monoxide concentration.[222]
- The combination of chemicals and fine particles contained in ENDS aerosols and liquids may increase the risk of heart distress.[223]

Cancer

- ENDS may contain solvent carriers, tobacco-specific nitrosamines, and metals that are carcinogenic.[224]

Respiratory Problems

- Some components in ENDS may contribute to respiratory distress.[225]
- Nicotine-free ENDS products can expose the user to high concentrations of solvent carriers like propylene glycol/glycerin, which increase the risk of air pathway irritation.[226]
- Inhalation of the chemicals in e-liquid flavorings may increase the risk of respiratory disease.[227]

Pregnancy Outcomes

- Nicotine can alter blood pressure and perivascular adipose tissue in developing organisms.[228]
- Research suggests that any amount of nicotine use is unsafe during pregnancy.[229]

Secondhand/Environmental Exposure

- ENDS aerosols generate potentially harmful fine particulate matter that may appear in high concentrations in areas where ENDS are used.[230]
- The aerosol remains in the air for shorter periods than cigarette smoke, resulting in relatively lower passive exposure in non-users.[231]
- Secondhand exposure to ENDS use is associated with an increased urge and desire to smoke and with actual smoking behavior (to a similar extent as produced by exposure to combustible cigarette use) among young adult cigarette smokers.[232]
- Reports of accidental/unintentional exposures to ENDS products increased between 2010 and 2014, with half of the cases involving young children, aged 0-5.[233] Accidental exposure to the nicotine in e-liquids may lead to nausea, vomiting, coughing, chest pain and palpitations, dizziness, and oral irritation.[234]
- There is a risk of explosions and fires as a result of malfunctioning in the rechargeable lithium batteries contained in ENDS devices.[235]

A Closer Look at Electronic Nicotine Delivery Systems:
The Current State of Science on the Risks and Potential Benefits

Many non-cigarette nicotine products are available on the market, but none has received as much attention or controversy in recent years as e-cigarettes and related electronic nicotine delivery systems (ENDS). Regulatory approaches to these products vary dramatically across the world, as do the attitudes of health professionals tasked with reducing the use of combustible tobacco products and their daunting toll on morbidity, mortality, and associated costs.

At its core, the debate surrounding ENDS products revolves around a key question:

Is the Net Effect of ENDS Use Beneficial or Harmful to the Public Health?

That is, are the known risks associated with ENDS products outweighed by their benefits, specifically with regard to their ability to serve as a replacement for combustible tobacco products among current smokers? To answer this question, researchers and public health experts are attempting to gather reliable information on the following issues that are essential for determining the risk/benefit ratio of ENDS products to the population at large and to specific sub-groups--particularly current cigarette smokers and youth. It is important to note that research surrounding these issues is limited and ongoing and it may take several more years to attain definitive answers, particularly with regard to questions about the long-term effects of using ENDS on other tobacco product use, health, and addiction.

In summing up the current state of the evidence, we present the following key conclusions, which coincide with those of the U.S. Surgeon General:[1]

- Use of any product that contains nicotine, including ENDS, is dangerous to youth, pregnant women, and fetuses. Any form of use of or exposure to these products in these groups is unsafe.
- The use of ENDS products is strongly associated with the use of other nicotine products, which increases overall nicotine exposure and the consequent risks of addiction and other negative health outcomes.
- Even ENDS products that do not contain nicotine are not safe. These products contain many potentially harmful ingredients in their flavorings, additives, and aerosols.
- ENDS products may benefit the health of current smokers who are unable or unwilling to quit through the use of medically-approved cessation methods, but only if they substantially or completely replace the use of cigarettes.

The current body of research is able to provide preliminary answers to the following two key questions:[2]

- Is the use of ENDS products among nonsmokers reliably associated with later cigarette smoking?

YES

- Is the use of ENDS products among smokers reliably associated with smoking reduction or cessation?

NO

Summary of Risks vs. Benefits of ENDS Products[3]	
Risks	**Benefits**
For Nonsmoking Youth	
Increased exposure to nicotine	
Nicotine addiction	
Increased risk of initiation of smoked cigarettes	
Adverse effects on brain development	
Future disease	
For Current Smokers	
Slower or delayed tobacco cessation	Reduced tobacco-related disease morbidity and mortality for those who switch to ENDS and significantly reduce or quit smoking cigarettes
Increased risk of nicotine exposure and addiction with continued dual use of ENDS and smoked cigarettes	
For Former Smokers	
Re-initiation of cigarette smoking	
Nicotine addiction	
For Nonsmokers and Society	
Secondhand aerosol exposure and associated health risks and costs	Reduced costs associated with tobacco-related disease morbidity and mortality
Re-normalization of smoking	
Accidental/unintentional poisoning	

A Closer Look at the Research Evidence

In December 2016, the U.S. Surgeon General published a report describing the growing public health concern of ENDS (e-cigarette) use among youth in the U.S. It described a 900 percent increase in use among high school students between 2011 and 2015. It documented what is known about the risks to youth of using these products and emphasized the point that there still are many unknowns and significant gaps in the scientific evidence. Yet, the report concluded that there is sufficient evidence to call for the prevention of any tobacco or nicotine product use, including ENDS, among youth and young adults.[4]

Below we present key questions relevant to the debate surrounding the risks and benefits of ENDS products and offer brief descriptions of up-to-date research findings that address these questions.

Who Are the Main Users of ENDS Products?

Youth or Adults?

Youth, including young adults, generally report higher rates of ENDS use than adults:

- National data indicate that 16.0 percent of high school students and 5.3 percent of middle school students reported current (past 30 day) use of ENDS products in 2015.[5]
- More recent national data from a school-based government survey indicate that the rate of use might be declining among teens: 9.9 percent of 8th, 10th, and 12th graders combined reported current use of ENDS in 2016, a significant decrease from 12.8 percent in 2015. More specifically, 12.5 percent of 12th graders, 11.0 percent of 10th graders, and 6.2 percent of 8th graders reported current use of ENDS

in 2016, all statistically significantly lower than the rates reported 1 year earlier (16.3 percent of 12th graders, 14.2 percent of 10th graders, and 8.0 percent of 8th graders).[6]

- Our analysis of national data on adults indicate that approximately 6.6 percent of adults, aged 18 and older, reported current use of ENDS in 2013-2014.[*] Rates of use among adults were highest among younger adults, aged 18 to 24.
- Other national data indicate that 22 percent of 18-24 year olds reported having tried an e-cigarette in their lifetime, and 13.6 percent said that they currently use e-cigarettes.[† 7]
- Newly-published results from a 2013-2014 survey of youth and adults found that young adults comprised the group with the highest rate of reported current e-cigarette use: 1.0 percent of 12-14 year olds, 5.3 percent of 15-17 year olds, 12.5 percent of 18-24 year olds, and 5.8 percent of adults aged 25 and older.[8]

Cigarette Smokers or Nonsmokers?

Most people who use ENDS also smoke cigarettes:

- Approximately three-quarters of youth[9] and adults[10] who report the current use of e-cigarettes also say they use combustible cigarettes.

However, there are many people who use ENDS, especially among youth, who never smoked a cigarette:

- A significant proportion of youth who do not use combustible cigarettes report using ENDS products.[11]
  - National data indicate that the use of e-cigarettes among middle and high school students who never smoked cigarettes increased more than three-fold between 2011 and 2013.[12]
  - Among middle school students in Connecticut who had used e-cigarettes, half (51.2 percent) reported that they were the first type of tobacco product they ever used (i.e., they had never used combustible cigarettes).[‡ 13]
  - Nearly 1 in 10 (9.7 percent) young adults, aged 18 to 24, in the U.S. who had never smoked a cigarette say they tried an e-cigarette.[§ 14]
  - A recent study found that less than a quarter of middle and high school students who reported e-cigarette use (and not cigarette use) fit the risk profile of a cigarette smoker, suggesting that the use of ENDS products is appealing to young people who are at low risk of smoking cigarettes, expanding rather than reducing the consumer base for nicotine products.[15]
- Among adults who reported using ENDS products, about one-third said they never smoked a cigarette or that they formerly but not currently smoke cigarettes (i.e., they already quit).[16]

Do Nonsmokers Who Use ENDS Products End Up Smoking Cigarettes?

Non-cigarette smoking youth who use ENDS products are significantly more likely than those who do not use ENDS to report intentions to smoke and to end up smoking combustible cigarettes in the near future:[17]

- National data indicate that middle and high school nonsmoking students who had ever used e-cigarettes were twice as likely to report intentions to smoke cigarettes[**] relative to those who never tried e-cigarettes (43.9 percent vs. 21.5 percent).[* 18]

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[*] These findings are presented in Chapter III.

[†] Persons who reported using electronic cigarettes at least once during their lifetime and now using electronic cigarettes every day, some days, or rarely.

[‡] Data collected in 2013.

[§] National data from 2014.

[**] Based on a composite measure of the two questions: "Do you think you will smoke a cigarette in the next year?" and "If one of your best friends were to offer you a cigarette, would you smoke it?" Response options were: definitely yes, probably yes, probably not, and definitely not.

- A recent longitudinal national survey of 12th graders found that students who never smoked cigarettes but recently started using e-cigarettes had more than four times the odds of smoking cigarettes a year later. This was true even among students who reported perceiving great risk from cigarette smoking at the time of the initial interview. The findings also indicated that those who never smoked but recently started using e-cigarettes were more than four times more likely to move away from their earlier perception of cigarettes as posing a 'great risk' of harm. This suggests that e-cigarette use reduces the perception of harm of cigarette smoking and desensitizes young people to cigarette smoking.[19]
- Nonsmoking high school students in Hawaii[†] who had ever used e-cigarettes had twice the odds of showing willingness to smoke cigarettes[‡] relative to those who had never used e-cigarettes (26 percent vs. 11 percent)[20] and nearly three times the odds of starting to smoke cigarettes 1 year later.[21]
- Nonsmoking high school students in California who used e-cigarettes were more susceptible than those who never used e-cigarettes to future cigarette use[§] (35 percent vs. 21 percent)[** 22] and had approximately six times the odds of starting to smoke cigarettes 16 months later.[†† 23]
- Nonsmoking high school students in California who reported more frequent e-cigarette use at baseline reported more frequent and heavier cigarette smoking 6 months later.[‡‡ 24]
- National data indicated that nonsmoking young adults, aged 18 to 29, who had used e-cigarettes were more likely to report being open to smoking cigarettes[§§] in the near future relative to those who had never tried an e-cigarette (46.1 percent vs. 14.2 percent).[*** 25]
- College students who reported in 2014 never having smoked cigarettes but that they had tried or currently use e-cigarettes were significantly more likely to report smoking cigarettes in 2015 than students who had not used e-cigarettes.[26]

What if They Had Initially Reported No Intention of Ever Smoking?

<u>Even non-cigarette smoking youth who specifically expressed no intention to smoke cigarettes in the future but used ENDS products are significantly more likely to end up smoking in the future than those who have not used ENDS products</u>:

- Adolescents and young adults who have used e-cigarettes are more likely than those who have not used e-cigarettes to smoke cigarettes in the future, even if they initially had no intention of or susceptibility toward doing so.[27]
  - National data indicate that nonsmoking youth, aged 16-26, who were deemed not susceptible to smoking cigarettes[*] but who had used e-cigarettes had eight times the odds of becoming

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[*] National data from 2011-2013.
[†] Data collected in 2013-2014.
[‡] Respondents were asked, "Suppose you were with a group of friends and there were some cigarettes you could have if you wanted. How willing would you be to ___: take one puff, smoke a whole cigarette, and take some cigarettes to try later?" Responses options were: not at all willing, a little willing, somewhat willing, and very willing.
[§] Based on the following three questions: "At any time in the next year do you think you will use these products?"; "Do you think in the future you will experiment with these products?"; and "If one of your best friends were to offer you these products, would you use them?" Response options were: definitely not, probably not, probably yes, and definitely yes. Those who responded "definitely not" to all three measures were considered to be not susceptible.
[**] Data collected in 2014 from a sample of 11th and 12th grade students.
[††] Data collected in 2014-2016 from a sample of high school students.
[‡‡] Data collected in 2014-2015 from students in public high schools in Los Angeles, California.
[§§] Based on the following two questions: "Do you think you will smoke a cigarette soon?" and "Do you think you will smoke a cigarette in the next year?" Response options were: definitely yes, probably yes, probably not, and definitely not.
[***] National data from 2012-2013.

susceptible to smoking and of starting to smoke cigarettes 1 year later relative to those who had never used e-cigarettes.[28]

- Nonsmoking 9th grade students in Los Angeles, California who had ever used e-cigarettes had two to four times the odds of reporting cigarette, cigar, and water pipe/hookah use 6-12 months later relative to those who had never used e-cigarettes.† [29]

- In an attempt to explain the pathway from e-cigarette to combustible cigarette use among youth, one recent study found that adolescents who use e-cigarettes may learn to find the physical process of using such a device (e.g., inhaling, exhaling, the motions involved) appealing, which can stimulate and promote positive expectations about cigarette use. Those who use e-cigarettes also may begin to affiliate more with peers who smoke cigarettes who can model that behavior.[30] Other research findings suggest that e-cigarette use desensitizes young people to the perceived risks of cigarette smoking.[31] Finally, a recent study found that middle and high school students who never smoked cigarettes but either used ENDS or were exposed to ENDS in their home or in advertisements were more likely to perceive peer and community acceptance of adult cigarette smoking and more susceptible to smoking themselves than those who were less exposed to ENDS. This finding suggests that exposure to ENDS and ENDS use may lead to the normalization of cigarette smoking.[32]

Do Cigarette Smokers Who Start Using ENDS Products End Up Quitting or Reducing Smoking or do They Continue to Use Both Types of Nicotine Products (i.e., "Dual Use")?

The findings related to this question are not conclusive.[33] Several studies suggest that ENDS that contain nicotine may help smokers cut back or stop smoking cigarettes[34] (one study found that the presence of nicotine is not so essential[35]). Other studies show that smokers who use ENDS generally are not more likely to reduce or quit smoking cigarettes and that many become 'dual users' of cigarettes and ENDS:

- A large-scale systematic review and meta-analysis found that the odds of quitting cigarette smoking are an estimated 28 percent lower among those who use e-cigarettes relative to those who do not.[36]
- National data indicate that middle and high school students who ever used e-cigarettes had six to eight times the odds of smoking relative to those who never used e-cigarettes. Among current smokers, current e-cigarette use was associated with higher levels of cigarette smoking. E-cigarette use was not associated with reports of attempting to quit smoking in the past year.‡ [37]
- National data indicate that middle and high school students who used both cigarettes and e-cigarettes were not more likely to quit smoking than those who did not use e-cigarettes, suggesting that e-cigarette users are engaging in dual use rather than smoking cessation.§ [38]
- A recent longitudinal national survey of 12th graders found that students who had smoked in the past and began using e-cigarettes had an increased likelihood of relapse to cigarette smoking and it was not related to smoking cessation among recent cigarette smokers.[39]
- College students who hadn't used e-cigarettes at the start of one study had more than twice the odds of reporting current cigarette use at the end of the study period (about 2-½ years later) if they had used e-cigarettes in the interim.** [40]
- A randomized controlled trial of young adult smokers who were not ready to quit and who were given either nicotine e-cigarettes or non-nicotine e-cigarettes (placebo) found that both groups reduced the number of cigarettes smoked over the course of the study period. However, although those who

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* Based on the following two questions: "If one of your friends offered you a cigarette, would you try it?" and "Do you think you will smoke a cigarette sometime in the next year?" Response options were: definitely yes, probably yes, probably no, and definitely no. Those who responded "definitely no" to both measures were considered non-susceptible nonsmokers whereas others were defined as susceptible.

† Data collected in 2014 from a sample of high school students.

‡ National data from 2011-2012.

§ National data from 2011-2013.

** Data collected from 2010-2013 from a sample of college students in North Carolina and Virginia.

received the nicotine e-cigarettes were more likely to have reduced the number of cigarettes they smoked, there were no differences between the groups in smoking cessation.[41]

- Adult cigarette smokers in California who smoked cigarettes and who had used e-cigarettes were less likely to reduce or quit smoking 1 year later relative to those who never used e-cigarettes.[*] [42]
- Adult cigarette smokers in Great Britain who reported daily use of e-cigarettes while smoking cigarettes reported more attempts to quit or reduce cigarette smoking, but not more success with smoking cessation. Non-daily use of e-cigarettes was not associated with cessation attempts, reduced smoking, or cessation.[43]
- Adult cigarette smokers who reported e-cigarette use at the start of one study were not more likely than those who did not use e-cigarettes to report intending to quit smoking or to actually have quit smoking 1 year later.[44]
- National data indicate that adult smokers who used e-cigarettes to facilitate quitting were less likely to have stopped smoking 1 year later compared to those who had never used e-cigarettes but tried to quit.[45]
- An international study of adult cigarette smokers found that those who reported at the start of the study that they were using e-cigarettes to quit smoking (85 percent) were not more likely to have quit 1 year later relative to those who did not use e-cigarettes.[46]

The adverse health effects of ENDS use associated with nicotine and other toxic ingredients,[47] along with the growing body evidence indicating that ENDS may increase the risk of cigarette smoking and not reliably facilitate smoking reduction or cessation lead to the following conclusion:

Even if they are less harmful than cigarettes and helpful to some individuals who smoke, the net effect of ENDS products is not beneficial and may be risky to the public health.

ENDS products are never safe for youth. Still, ENDS do appear to be less harmful than combustible cigarettes. Therefore, smokers who are unable to quit using medically-approved interventions may benefit from completely switching to ENDS. But only in cases in which the use of ENDS completely replaces or significantly reduces the use of cigarettes in existing smokers might there be a net benefit of ENDS products. Unfortunately, in the majority of cases, these products are used in addition to smoked cigarettes without lasting and significant declines in cigarette use, and often delay or prevent smoking cessation. Research indicates that merely cutting back on smoking or smoking intermittently does not eliminate the considerable health risks of cigarette use, and that prolonged smoking, even if only a reduced number of cigarettes due to ENDS use, can have profound negative health effects relative to completely quitting.[48] Without rigorous evaluation and subsequent approval by the U.S. Food and Drug Administration (FDA) as a cessation aid, ENDS products should not be promoted as cessation devices for smokers or touted as harmless for casual use.

[*] Data collected in 2011-2013 from a sample of adults, aged 18-59.

Chapter III
The Nature and Extent of Nicotine Product Use

The landscape of nicotine product use is changing. Fewer people in the United States are using cigarettes while more people, particularly youth, are using non-cigarette nicotine products.[1] Between 2011 and 2015, reported use of cigarettes in the past 30 days among high school students decreased from 15.8 percent to 9.3 percent, while current use of e-cigarettes increased tenfold, from 1.5 percent to 16.0 percent.[2] Other national data show that the rate of decline in cigarette smoking among middle and high school students over the past decade has not accelerated with the emergence of electronic nicotine delivery systems (ENDS), countering claims that ENDS product use among youth replaces cigarette smoking.[3] Still, data from a different national survey suggest small but significant declines in the use of e-cigarettes, water pipe/hookah, and some other non-cigarette nicotine products among 8th, 10th, and 12th grade students--a preliminary but promising sign that the recent steady rise in their use among young people may be stabilizing or reversing.[4] Most nationally representative surveys find that a significant proportion of people, adults and adolescents alike, who use nicotine products use more than one type.[5] While any nicotine product use is associated with an increased risk of nicotine addiction and alcohol and other drug use and addiction (especially when such use begins in early adolescence), use of multiple nicotine products increases those risks, especially for youth.[6]

To explore more thoroughly the prevalence and patterns of different types of nicotine product use among youth and adults, we conducted analyses of recent, publicly available, nationally representative data from the U.S. Centers for Disease Control and Prevention (CDC) on nicotine product use among middle and high school students and among adults, aged 18 and older, in the United States.* (See the Appendix for more details about the data sources used and the data analysis methodology.)

Key Findings

- **Prevalence.** One in four adults† (26.0 percent, 59.7 million) and one in seven middle and high school students,‡ (15.7 percent, 4 million) reported current§ use of at least one nicotine product.
  - Approximately 16.3 percent of adults and 14.7 percent of middle and high school students reported current use of a non-cigarette nicotine product.
  - Young adults, aged 18 to 24, were the age group most likely to report current use of a non-cigarette nicotine product (36.6 percent).
- **Most Commonly Used Nicotine Products.** The most commonly used nicotine products among adults, after cigarettes (17.6 percent), were cigars (7.0 percent) and e-cigarettes (6.6 percent).

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* Unless otherwise indicated, reported findings are from The National Center on Addiction and Substance Abuse's analysis of data from the CDC's 2013-2014 National Adult Tobacco Survey (NATS) and the 2014 National Youth Tobacco Survey (NYTS). Just prior to publication of this report, data from 2015 on middle and high school students became publicly available. However, as noted in the Appendix, we decided to present the data from 2014 so that it would be more comparable to the most recently available data collection period for the adult survey (2013-2014).

† Non-institutionalized U.S. adults, aged 18 years and older.

‡ In grades 6-12.

§ *Current nicotine product use* among adults was defined in the NATS survey as using one or more of the following eight nicotine products "now": cigarettes, cigars/cigarillos/little cigars, pipes, e-cigarettes, water pipe/hookah, chewing tobacco/snuff/dip, snus, and dissolvable nicotine products. *Current nicotine product use* among middle and high school students was defined in the NYTS survey as reported use in the past 30 days of one or more of the eight nicotine products listed above, with the addition of bidis.

Among middle and high school students, they were e-cigarettes (9.3 percent) followed by water pipe/hookah (6.4 percent) and cigarettes (6.3 percent).

- **Multiple Product Use.** Consistent with other recent studies,[7] the use of multiple nicotine products was common among those who reported current use of nicotine. More than one-third (37.5 percent) of adults and half (49.9 percent) of middle and high school students who engaged in current use of nicotine products indicated that they used more than one product. Among current users of nicotine products, 7.6 percent of adults and 19.6 percent of middle and high school students reported using more than one non-cigarette nicotine product. The use of multiple nicotine products elevates the risks of nicotine addiction, alcohol and other drug use, and other harmful consequences.
    - Cigarettes were the product most commonly used in combination with other nicotine products; nearly one-third of adults and middle and high school students who reported current use of nicotine products said they used cigarettes and a non-cigarette nicotine product.
- **Nicotine Addiction.** Few middle and high school students met the designated criteria for nicotine addiction; however, the majority of adults and young people who engaged in current use of a nicotine product did report at least one symptom consistent with addiction.
    - An estimated 15.0 percent of adults and 3.8 percent of middle and high school students who reported current use of a cigarette or non-cigarette nicotine product met the designated criteria for nicotine addiction; 77.9 percent of adults and 49.0 percent of middle and high school students reported at least one symptom of nicotine addiction.
    - An estimated 4.5 percent of adults and less than 1 percent of middle and high school students who reported using only non-cigarette nicotine products (and not cigarettes) in the past 30 days met the designated criteria for nicotine addiction. More than half of adults and half of middle and high school students who only used non-cigarette nicotine products (and not cigarettes) reported at least one symptom of nicotine addiction.
    - For both adults and students, the likelihood of reporting at least one symptom of nicotine addiction was greater among those who used cigarettes along with other nicotine products than among those who used multiple non-cigarette nicotine products.
- **Quit Attempts.** Nearly half of adults and nearly one-third of middle and high school students who engaged in the current use of nicotine products also reported attempting to quit using them in the past year.
- **Former Use.** Approximately one-half of adults and middle and high school students who reported ever having used a nicotine product indicated that they were no longer using them.

Current Nicotine Product Use and Addiction

Despite declines in cigarette use, the overall prevalence of nicotine product use has been stable over the past few years (25.2 percent in 2009-2010[8] and 25.5 percent in 2013-2014[9]), reflecting the rise in the use of non-cigarette nicotine products like ENDS and water pipe/hookah.[10] Still, adults continued to report the use of cigarettes at a higher rate than non-cigarette nicotine products (17.6 percent vs.16.3 percent). In contrast, middle and high school students reported the use of cigarettes at a much lower rate than non-cigarette nicotine products (6.3 percent vs. 14.7 percent).

Current Nicotine Product Use Among Adults

In 2013-2014, 26.0 percent of adults in the United States, aged 18 and older, reported current use of any nicotine product; 16.3 percent reported use of a non-cigarette nicotine product.

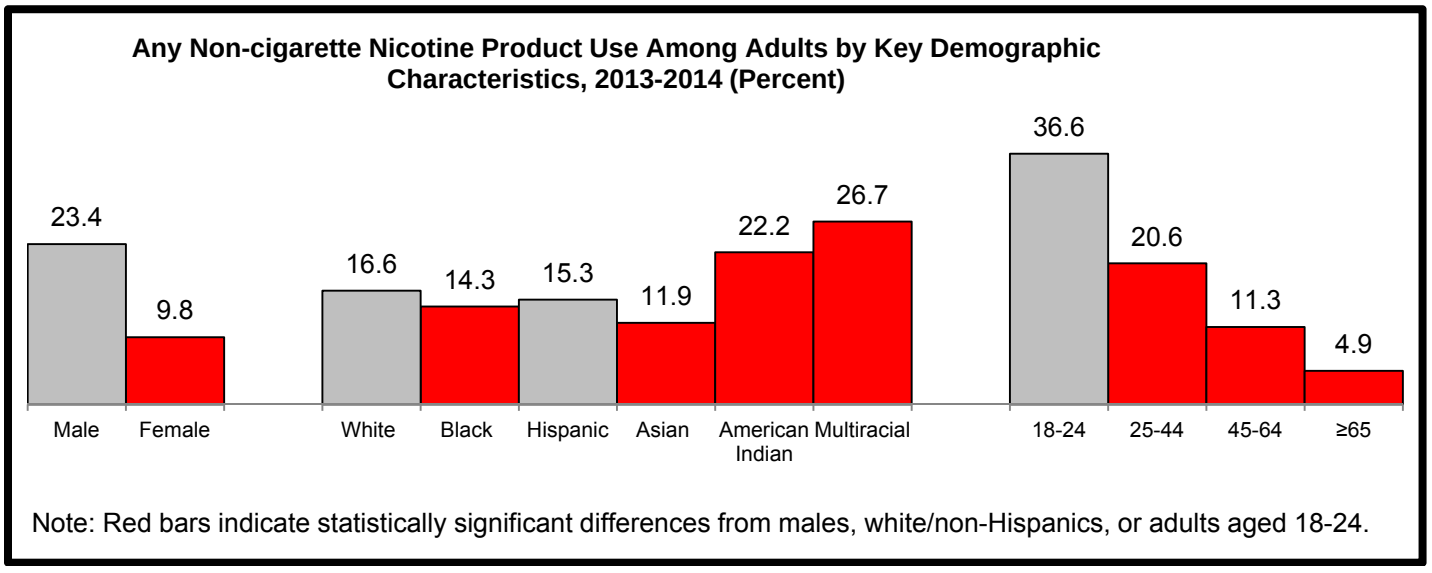
Demographic Differences. The prevalence of non-cigarette nicotine product use was higher among:

- Male than female adults (23.4 percent vs. 9.8 percent);
- Multiracial (26.7 percent) and American Indian (22.2 percent) adults than among white adults (16.6 percent); and
- Young adults aged 18 to 24 (36.6 percent) than among adults from all other age groups.

Current Nicotine Product Use Among Adults by Patterns of Use and Demographics, 2013-2014 (Percent)

	No Current Nicotine Product Use	Current Nicotine Product Use		
		Any Nicotine Product Use	Cigarette Use Only	Non-Cigarette Nicotine Product Use (with or without Cigarettes)
Total	**74.0**	**26.0**	**9.7**	**16.3**
Sex				
Male	67.1	32.9	9.5	23.4
Female	80.3	19.7	9.8	9.8
Race/Ethnicity				
White	74.4	25.6	9.0	16.6
Black	71.0	29.0	14.7	14.3
Hispanic	76.0	24.0	8.7	15.3
Asian	83.5	16.5	4.6	11.9
American Indian	61.0	39.0	16.8	22.2
Multiracial	58.9	41.1	14.5	26.7
Age				
18-24	58.4	41.6	5.1	36.6
25-44	68.3	31.7	11.1	20.6
45-64	76.8	23.2	11.9	11.3
≥65	88.8	11.2	6.3	4.9

Analysis of data from the 2013-2014 National Adult Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nats/).



Type of Product Used. Of the non-cigarette nicotine products assessed in the 2013-2014 NATS, adults most commonly reported using smoked products (10.1 percent), followed by ENDS (6.6 percent) and smokeless tobacco products (3.6 percent).*

Current Nicotine Product Use Among Adults by Type of Product Used,† 2013-2014 (Percent)	
Smoked (including cigarettes)	**23.0**
Cigarettes	17.6
Smoked (not including cigarettes)	**10.1**
Cigars/cigarillos/little cigars	7.0
Pipes	1.3
Water pipe/hookah	4.3
ENDS/E-cigarettes	**6.6**
Smokeless	**3.6**
Chewing tobacco/snuff/dip	3.4
Snus	0.8
Dissolvable products	0.0
Analysis of data from the 2013-2014 National Adult Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nats/).	

Frequency of Use. Among those who reported current use of nicotine products, daily use of non-cigarette nicotine products was not as common as daily use of cigarettes. Even among those who reported current use of cigars--the most commonly used non-cigarette nicotine product among adults--only 8.3 percent said they used them on a daily basis. Among adults who engaged in current use of nicotine products, chewing tobacco was the non-cigarette nicotine product most commonly used on a daily basis (46.1 percent) followed by ENDS (20.2 percent).

Frequency of Current Nicotine Product Use Among Adults by Type of Product Used 2013-2014 (Percent)			
	Daily	**Some Days**	**Rarely**
Smoked (including cigarettes)	**58.3**	**41.7**	
Cigarettes	74.5	25.5	
Smoked (not including cigarettes)	**7.2**	**18.2**	**74.6**
Cigars/cigarillos/little cigars	8.3	18.5	73.2
Pipes	8.5	19.2	72.3
Water pipe/hookah	1.8	12.2	86.1
ENDS/e-cigarettes	**20.2**	**30.2**	**49.6**
Smokeless	**44.3**	**24.1**	**31.6**
Chewing tobacco/snuff/dip	46.1	21.0	32.9
Snus	14.4	20.8	64.9
Dissolvable products	–‡	–	–
Analysis of data from the 2013-2014 National Adult Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nats/).			

* Smoked products include cigars/cigarillos/little cigars, pipes, and water pipe/hookah. Smokeless products include chewing tobacco/snuff/dip, snus, and dissolvable products.

† Categories are not mutually exclusive.

‡ A dash (–) indicates that the estimate is statistically unreliable because the sample size was less than 50.

Nicotine Addiction Among Adults

An estimated 15.0 percent of adults who reported current use of any nicotine product met the designated criteria for nicotine addiction, defined in accordance with a three-symptom index: reported daily use of any nicotine product, usually using a nicotine product within 30 minutes of waking, and having an unsuccessful quit attempt of all nicotine products in the past 12 months.[11] Other symptoms consistent with addiction that were not included in this index were strong craving or need to use, difficult to think of anything else except use, and feeling irritable when not using. The most commonly reported symptoms of nicotine addiction were daily use (60.8 percent) and a strong craving to use the product (55.9 percent). See the Appendix for more detail regarding the way nicotine addiction was assessed in the present analyses.

Demographic Differences. Among adults who engaged in current use of nicotine products, the prevalence of nicotine addiction was higher among:

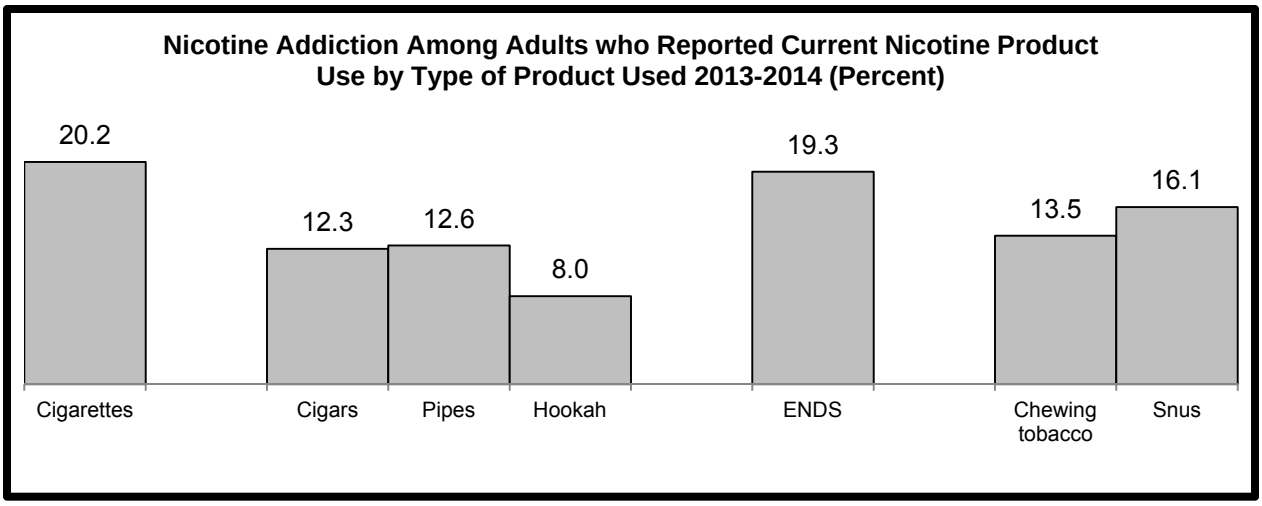
- Females than males (16.7 percent vs. 13.9 percent);
- White adults (15.7 percent) than among Hispanic (9.3 percent) and Asian (8.8 percent) adults; and
- Adults aged 25-44 (16.3 percent), 45-64 (18.2 percent), and 65 and older (11.7 percent) than among young adults aged 18-24 (8.8 percent).

Nicotine Addiction Among Adults Who Reported Current Nicotine Product Use by Patterns of Use and Demographics, 2013-2014 (Percent)

	Any Nicotine Product Use	Cigarette Use Only	Non-Cigarette Nicotine Product Use (with or without Cigarettes)
Total	**15.0**	**18.2**	**13.1**
Sex			
Male	13.9	17.3	12.5
Female	16.7	18.9	14.4
Race/Ethnicity			
White	15.7	19.6	13.6
Black	18.2	19.6	16.8
Hispanic	9.3	10.4	8.7
Asian	8.8	14.0	6.8
American Indian	18.1	21.2	15.8
Multiracial	14.0	12.5	14.8
Age			
18-24	8.8	11.8	8.4
25-44	16.3	19.1	14.7
45-64	18.2	19.6	16.7
≥65	11.7	14.0	8.8

Analysis of data from the 2013-2014 National Adult Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nats/).

Type of Product Used. The prevalence of nicotine addiction among adults who reported current use of non-cigarette nicotine products was highest for those who used cigarettes (20.2 percent), closely followed by those who used ENDS (19.3 percent).



Reports of at Least One Symptom of Nicotine Addiction. Although most adults who engaged in current use of non-cigarette nicotine products did not meet the designated criteria for nicotine addiction, more than three quarters (82.5 percent) did report at least one symptom of nicotine addiction.

The prevalence of reporting at least one symptom of nicotine addiction among adults who engaged in current use of nicotine products was higher among:

- Females than males (86.7 percent vs. 79.9 percent);
- American Indian adults (88.2 percent) than among white adults (83.4 percent); and
- Adults aged 25-44 (83.5 percent), 45-64 (88.9 percent), and 65 and older (87.4 percent) than among young adults aged 18-24 (68.6 percent).

Any Symptom of Nicotine Addiction Among Adults Who Reported Current Nicotine Product Use by Patterns of Use and Demographics, 2013-2014 (Percent)

	Any Nicotine Product Use	Cigarette Use Only	Non-cigarette Nicotine Product Use (with or without Cigarettes)
Total	**82.5**	**95.1**	**75.1**
Sex			
Male	79.9	94.2	74.1
Female	86.7	95.9	77.4
Race/Ethnicity			
White	83.4	96.1	76.5
Black	85.7	95.1	76.0
Hispanic	76.4	91.0	68.1
Asian	73.8	89.3	67.8
American Indian	88.2	94.7	83.2
Multiracial	85.2	96.9	78.9
Age			
18-24	68.6	89.7	65.6
25-44	83.5	95.0	77.2

Any Symptom of Nicotine Addiction Among Adults Who Reported Current Nicotine Product Use by Patterns of Use and Demographics, 2013-2014 (Percent) (continued)			
	Any Nicotine Product Use	**Cigarette Use Only**	**Non-cigarette Nicotine Product Use (with or without Cigarettes)**
Age (continued)			
45-64	88.9	96.1	81.4
≥65	87.4	95.1	77.5
Analysis of data from the 2013-2014 National Adult Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nats/).			

Current Nicotine Product Use Among Middle and High School Students

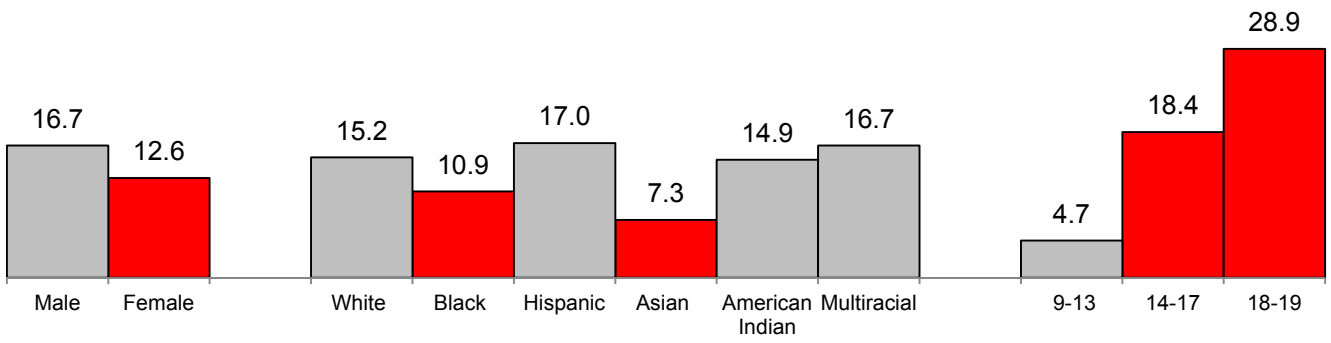
In 2014, 15.7 percent of middle and high school students in the United States reported current use of a nicotine product (used the products in the past 30 days); 14.7 percent used a non-cigarette nicotine product.

Demographic Differences. The prevalence of non-cigarette nicotine product use was higher among:

- Male than female students (16.7 percent vs. 12.6 percent);
- White (15.2 percent) than black (10.9 percent) and Asian (7.3 percent) students; and
- Students aged 14-17 (18.4 percent) and 18-19 (28.9 percent) than students aged 9-13 (4.7 percent).

Current Nicotine Product Use Among Middle and High School Students by Patterns of Use and Demographics, 2014 (Percent)				
	No Current Nicotine Product Use	**Current Nicotine Product Use**		
		Any Nicotine Product Use	**Cigarette Use Only**	**Non-Cigarette Nicotine Product Use (with or without Cigarettes)**
Total	**84.3**	**15.7**	**1.0**	**14.7**
Sex				
Male	82.3	17.7	1.0	16.7
Female	86.3	13.7	1.0	12.6
Race/Ethnicity				
White	83.7	16.3	1.1	15.2
Black	88.1	11.9	0.9	10.9
Hispanic	82.0	18.0	1.0	17.0
Asian	92.3	7.7	0.5	7.3
American Indian	83.8	16.2	1.3	14.9
Multiracial	82.2	17.8	1.1	16.7
Age				
9-13	94.9	5.1	0.3	4.7
14-17	80.2	19.8	1.3	18.4
18-19	69.4	30.6	1.7	28.9
Analysis of data from the 2014 National Youth Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nyts/).				

Any Non-cigarette Nicotine Product Use among Middle and High School Students by Key Demographic Characteristics, 2014 (Percent)



Note: Red bars indicate statistically significant differences from females, white/non-Hispanics, or students aged 9-13.

Type of Product Used. Of the non-cigarette nicotine products assessed in the 2014 NYTS, middle and high school students most commonly reported using ENDS (9.3 percent) and non-cigarette smoked products (9.3 percent), followed by smokeless products (3.7 percent).*

Current Nicotine Product Use Among Middle and High School Students by Type of Product Used,† 2014 (Percent)	
Smoked (including cigarettes)	**11.4**
Cigarettes	6.3
Smoked (not including cigarettes)	**9.3**
Cigars/cigarillos/little cigars	5.4
Pipes	1.1
Water pipe/hookah	6.4
Bidis	0.8
ENDS/E-cigarettes	**9.3**
Smokeless	**3.7**
Chewing tobacco/snuff/dip	3.8
Snus	1.3
Dissolvable products	0.5
Analysis of data from the 2014 National Youth Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nyts/).	

Frequency of Use. Similar to adults, daily use of non-cigarette nicotine products was uncommon among youth. For example, only 8.7 percent of middle and high school students who reported using cigar products said they did so every day. Chewing tobacco/snuff/dip was the non-cigarette nicotine product most likely to be used on a daily basis (28.3 percent).

* Smoked products include cigars/cigarillos/little cigars, pipes, water pipe/hookah, and bidis. Smokeless products include chewing tobacco/snuff/dip, snus, and dissolvable products.

† Categories are not mutually exclusive; values represent the percentage of the population that used the listed nicotine product.

Frequency of Current Nicotine Product Use* Among Middle and High School Students by Type of Product Used, 2014 (Percent)						
	Daily (30 Days)	**20-29 Days**	**10-19 Days**	**6-9 Days**	**3-5 Days**	**1-2 Days**
Smoked (including cigarettes)	**17.4**	**8.0**	**10.8**	**9.4**	**13.9**	**40.4**
Cigarettes	21.4	8.3	9.3	9.9	13.2	37.8
Smoked (not including cigarettes)	**8.7**	**4.5**	**9.4**	**8.7**	**18.1**	**50.6**
Cigars/cigarillos/little cigars	8.7	4.5	9.4	8.7	18.1	50.6
ENDS/E-cigarettes	**9.4**	**5.4**	**10.3**	**11.4**	**16.4**	**47.1**
Smokeless	**28.3**	**11.1**	**11.0**	**9.4**	**11.4**	**28.8**
Chewing tobacco/snuff/dip	28.3	11.1	11.0	9.4	11.4	28.8
Analysis of data from the 2014 National Youth Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nyts/).						

Nicotine Addiction† Among Middle and High School Students

The risk of becoming addicted to nicotine increases with earlier age of first use.[12] The increased vulnerability to addiction among youth who engage in any substance use appears to be due both to biological and psychological risk factors to which this age group is especially sensitive.[13] In adolescence, the brain is undergoing essential developmental changes that allow young people to learn quickly and adapt rapidly. However, this also means that their brains are more responsive to and affected by addictive substances, including nicotine, and that these effects--particularly those related to neural connectivity and behavioral regulation--can persist into adulthood.[14]

Only 3.8 percent of middle and high school students who engaged in current use of cigarettes, ENDS/e-cigarettes, cigars, or chewing tobacco met the designated criteria for nicotine addiction. This may be because addiction can take years to develop.[15] Similar to adults, the most commonly reported symptoms of nicotine addiction were a strong craving or need to use the product (31.5 percent) and an unsuccessful quit attempt (29.5percent).

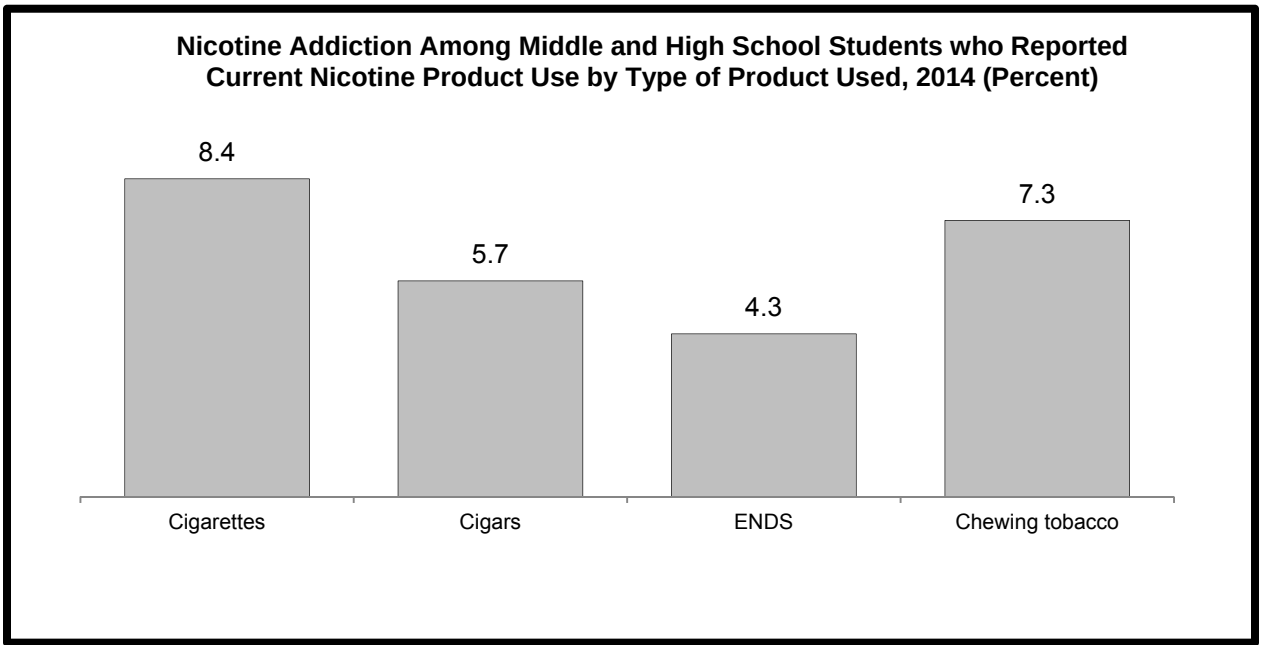
Demographic Differences. The prevalence of nicotine addiction did not differ significantly by sex, but was higher among:

- White students (4.9 percent) than among black (0.2 percent) and Hispanic (0.9 percent) students; and
- Students aged 14-17 (3.9 percent) and 18-19 (5.3 percent) than students aged 9-13 (0.9 percent).

* Frequency of use in the NYTS is assessed only for cigarettes, cigars, ENDS/e-cigarettes, and chewing tobacco.
† In the NYTS, addiction criteria data are available only for cigarettes, cigars, ENDS/e-cigarettes, and chewing tobacco.

Nicotine Addiction Among Middle and High School Students Who Reported Current Cigarette, Cigar, ENDS/E-cigarette, or Chewing Tobacco Use by Patterns of Use and Demographics, 2014 (Percent)			
	Cigarette, Cigar, ENDS/E-cigarette, or Chewing Tobacco Use	**Cigarette Use Only**	**Cigar, ENDS/E-cigarette, or Chewing Tobacco Use (with or without Cigarettes)**
Total	**3.8**	**4.6**	**3.7**
Sex			
Male	3.7	3.9	3.7
Female	4.0	5.4	3.8
Race/Ethnicity			
White	4.9	6.4	4.8
Black	0.2	–	0.3
Hispanic	0.9	–	0.8
Asian	1.6	–	1.8
American Indian	–	–	–
Multiracial	9.1	–	9.1
Age			
9-13	0.9	–	0.9
14-17	3.9	6.3	3.7
18-19	5.3	–	5.6
Analysis of data from the 2014 National Youth Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nyts/).			

Type of Product Used. The prevalence of nicotine addiction among middle and high school students who reported current use of cigarettes, ENDS/e-cigarettes, cigars, or chewing tobacco was highest for those who used cigarettes (8.4 percent) and chewing tobacco (7.3 percent), and lowest for those who used ENDS/e-cigarettes (4.3 percent).



Reports of at Least One Symptom of Nicotine Addiction. Although very few students met the designated criteria for nicotine addiction, nearly half (51.4 percent) of those who reported current use of nicotine products had at least one symptom of addiction.

The prevalence of reporting at least one symptom of nicotine addiction among students who engaged in current use of nicotine products did not differ significantly by age, but was higher among:

- Male than female students (53.9 percent vs. 47.9 percent); and
- White students (54.8 percent) than among black (39.1 percent) or Asian (36.2 percent) students.

Any Symptom of Nicotine Addiction Among Middle and High School Students Who Reported Current Nicotine Product Use by Patterns of Use and Demographics, 2014 (Percent)

	Any Nicotine Product Use	Cigarette Use Only	Non-cigarette Nicotine Product Use (with or without Cigarettes)
Total	**51.4**	**64.8**	**50.5**
Sex			
Male	53.9	59.6	53.5
Female	47.9	69.5	46.2
Race/Ethnicity			
White	54.8	76.4	53.2
Black	39.1	–	40.4
Hispanic	48.5	–	48.1
Asian	36.2	–	33.7
American Indian	–	–	–
Multiracial	50.4	–	49.3
Age			
9-13	52.0	–	53.0
14-17	51.2	68.4	50.0
18-19	51.6	–	50.7

Analysis of data from the 2014 National Youth Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nyts/).

Single vs. Multiple Nicotine Product Use and Addiction

A considerable proportion of adults and youth who use nicotine products say they use more than one type of product.[16] Although any nicotine product use can lead to addiction, the use of multiple nicotine products is associated with an increased risk of addiction, especially if cigarettes are one of the products used.[17]

Current Single vs. Multiple Nicotine Product Use Among Adults

In 2013-2014, more than a third (37.5 percent) of adults who reported current use of a nicotine product said they used more than one type. Consistent with other research,[18] our analysis indicates that 24.4 percent used two nicotine products (dual use) and 13.1 percent used more than two products (poly use). The most prevalent dual use combination was cigarettes with ENDS (10.2 percent) and the most prevalent poly use combination was cigarettes with ENDS and cigars (2.3 percent).

(See Appendix, Table 1 for more detail about the most prevalent combinations of nicotine product use among adults who reported current use.)

The prevalence of multiple (dual or poly) nicotine product use among adults who reported current use was higher among:

- Males than females (41.1 percent vs. 32.1 percent);
- White (38.7 percent) than black (28.1 percent) adults ; and
- Young adults aged 18-24 (55.2 percent) than adults from all other age groups.

(See Appendix, Table 2 for more detail about patterns of use and demographics.)

Nicotine Addiction Among Adults Who Reported Single vs. Multiple Nicotine Product Use. Adults who reported current use of multiple nicotine products were more likely than adults who reported use of a single nicotine product to have met the designated criteria for nicotine addiction (19.0 percent vs. 12.6 percent).

Consistent with other research,[19] the type of product used is important in determining the risk of addiction, with the highest prevalence of nicotine addiction found among those who reported using multiple nicotine products that included cigarettes.[20] One in 5 (22.6 percent) adults who reported using multiple nicotine products including cigarettes had symptoms consistent with nicotine addiction compared to 4.5 percent of adults who reported using multiple non-cigarette nicotine products.

(See Appendix, Table 3 for more detail about patterns of use and demographics related to nicotine addiction and Appendix, Table 4 for more detail about the symptoms of nicotine addiction reported among adults who engaged in single vs. multiple nicotine product use, by patterns of use and the types of products used.)

Current Single vs. Multiple Nicotine Product Use Among Middle and High School Students

In 2014, half (49.9 percent) of middle and high school students who reported current use of a nicotine product said they used more than one type. Our analysis indicates that 24.0 percent reported using two nicotine products (dual use) and 26.0 percent reported using more than two products (poly use). The most prevalent dual use combination was ENDS with water pipe/hookah (6.6 percent) followed by cigarettes and ENDS (4.3 percent), and the most prevalent poly use combination was cigarettes with ENDS and cigars (2.6 percent).

(See Appendix, Table 5 for more detail about the most prevalent combinations of nicotine product use among students who reported current use.)

The prevalence of multiple (dual or poly) nicotine product use among middle and high school students who reported current use was higher among:

- Male than female students (52.2 percent vs. 46.7 percent);
- White (34.9 percent) than black (18.0 percent), Hispanic (25.4 percent), and Asian (22.4 percent) students; and
- Students aged 14-17 (48.6 percent) and 18-19 (62.2 percent) than younger students aged 9-13 (39.4 percent).

(See Appendix, Table 6 for more detail about patterns of use and demographics.)

Nicotine Addiction Among Middle and High School Students Who Reported Single vs. Multiple Nicotine Product Use. Students who reported current use of multiple nicotine products were more likely than those who reported use of a single nicotine product to have met the designated criteria for nicotine addiction (5.9 percent vs. 1.0 percent).[*]

As was true of adults, middle and high school students who reported using multiple nicotine products including cigarettes had a substantially higher prevalence of nicotine addiction than those who reported using multiple non-cigarette nicotine products (9.2 percent vs. 0.7 percent).

(See Appendix, Table 7 for more detail about patterns of use and demographics related to nicotine addiction and Appendix, Table 8 for more detail about the symptoms of nicotine addiction reported among middle and high school students who engaged in single vs. multiple nicotine product use, by patterns of use and the types of products used.)

Quit Attempts of All Nicotine Products[†]

Nearly half of adults and nearly one-third of middle and high school students who reported current use of nicotine products also reported attempting to quit using them in the past year.

Quit Attempts Among Adults

Nearly half (47.8 percent) of adults who reported current use of any nicotine product said they attempted to quit in the past year. Non-cigarette nicotine products generally are perceived as a less harmful alternative to cigarettes,[21] a perception that likely contributes to their use as a smoking cessation aid. Research suggests that non-cigarette nicotine product use is indeed associated with an increased likelihood of attempting to quit cigarette smoking.[22] However, less is known about whether use of these products is associated with attempting to quit or discontinuing the use of all nicotine products, including non-cigarette products. Our analysis indicates that use of non-cigarette nicotine products relative to exclusive use of cigarettes was associated with a lower likelihood of attempting to quit using all nicotine products (46.4 percent vs. 50.1 percent).

Demographic Differences. Among adults who reported current use of non-cigarette nicotine products, the prevalence of reported quit attempts was higher among:

- Females than males (50.0 percent vs. 44.6 percent);
- Asian (57.2 percent), black (56.1 percent), and Hispanic (49.2 percent) adults than among white adults (42.5 percent); and
- Young adults aged 18-24 (47.4 percent) than among adults aged 65 and older (39.6 percent).

This latter finding is noteworthy since the age period between 18 and 24 is generally considered the period of transition from adolescence to adulthood and a time during which young adults experience new freedoms like being able to purchase nicotine products outside the scope of parental monitoring.[23] These years also have been considered the "missing link" between tobacco control efforts focused on youth smoking prevention and adult cessation. Still, nearly half (48.7 percent) of young adults, aged 18-24,

[*] Nicotine addiction in middle and high school student was assessed only among those who reported use of cigarettes, cigars, ENDS/e-cigarettes, or chewing tobacco.

[†] A quit attempt is defined as having reported "yes" to the following question: "During the past 12 months, did you stop using all kinds of tobacco products for more than one day because you were trying to quit using tobacco?"

who reported current use of any nicotine product said they attempted to quit in the past year. The prevalence of reported quit attempts was much higher among young adults who used cigarettes exclusively than among those who used non-cigarette nicotine products (with or without also using cigarettes) (57.9 percent vs. 47.4 percent).

(See Appendix, Table 9 for more detail about quit attempts by patterns of use and demographics.)

Quit Attempts Among Middle and High School Students

An estimated 29.5 percent of middle and high school students who reported current use of any nicotine product said they attempted to quit in the past year. Like adults, young people consider non-cigarette nicotine products to be less harmful than cigarettes.[24] And, as we found for adults, middle and high school students' reported use of non-cigarette nicotine products relative to exclusive use of cigarettes was associated with a lower likelihood of attempting to quit using all nicotine products in the past year (28.8 percent vs. 41.1 percent).

Demographic Differences. Among middle and high school students who reported current use of non-cigarette nicotine products, quit attempts did not differ significantly by sex or age, but were higher among:

- White students (28.9 percent) than among black students (23.3 percent).

(See Appendix, Table 10 for more detail about quit attempts by patterns of use and demographics.)

Former Use of Nicotine Products

About one half of adults and middle and high school students who reported ever using a nicotine product indicated that they were no longer using them.

Former Use Among Adults

More than half (53.0 percent) of adults in the United States who reported ever having used a nicotine product said they are not currently using them. Former use of nicotine products was less common among adults who reported every having used non-cigarette nicotine products (with or without cigarettes) than among adults who had used cigarettes exclusively (41.4 percent vs. 77.1 percent).

Demographic Differences. Former use of all nicotine products among adults who had ever used non-cigarette nicotine products was higher among:

- Males than females (42.5 percent vs. 39.1 percent);
- White adults (42.4 percent) than black (35.1 percent) or multiracial (32.4 percent) adults; and
- Adults aged 25-44 (37.9 percent), 45-64 (42.3 percent), and 65 and older (67.7 percent) than among young adults aged 18-24 (29.8 percent).

(See Appendix, Table 11 for more detail about former use by patterns of use and demographics.)

Former Use Among Middle and High School Students

Half (51.1 percent) of middle and high school students in the United States who reported ever having used a nicotine product said they no longer use them. Similar to adults, former use of nicotine products was less common among students who reported ever having used non-cigarette nicotine products (with or

without cigarettes) than among those who said they used cigarettes exclusively (46.6 percent vs. 91.1 percent).

Demographic Differences. Former use of all nicotine products among students who had ever used non-cigarette nicotine products was higher among:

- Female than male students (49.8 percent vs. 43.9 percent);
- Black (60.3 percent) and Asian (51.1 percent) students than among white students (46.1 percent); and
- Younger students aged 9-13 (61.1 percent) than among older students aged 14-17 (45.3 percent) and 18-19 (39.4 percent).

(See Appendix, Table 12 for more detail about former use by patterns of use and demographics.)

Special Populations

Relative to the general population, certain groups are at an increased risk of nicotine product use and the adverse consequences associated with nicotine use. For example, individuals with psychiatric disorders use cigarettes and other nicotine products at a relatively higher rate than other groups[25] and use among pregnant women is associated with preterm delivery, stillbirth, and other pregnancy complications.[26] Unfortunately, almost all of the research on the deleterious effects of nicotine on people with psychiatric disorders or on pregnant women involves use of cigarettes exclusively or in combination with other nicotine products. Few studies have evaluated the specific risks or harms associated with the use of non-cigarette nicotine products among these and other vulnerable population groups.

Individuals with Psychiatric Disorders[*]

The prevalence of cigarette, ENDS/e-cigarette, cigar, and pipe use generally has been found to be about twice as high among individuals with a psychiatric disorder than among those without a psychiatric disorder.[27] With regard to ENDS specifically, a national study found that individuals who had ever been diagnosed with a psychiatric disorder were more than twice as likely as those without such a diagnosis to report having tried (14.8 percent vs. 6.6 percent) and currently using (3.1 percent vs. 1.1 percent) ENDS products.[28] Other national studies generally find no significant difference by mental health status in smokeless nicotine product use.[29]

Women of Reproductive Age

Any use of nicotine products during pregnancy is associated with adverse reproductive health outcomes like preterm delivery and stillbirth;[30] even nicotine replacement therapy (NRT) is not recommended for use during pregnancy.[31] Because the NATS does not assess pregnancy status, our analysis examined nicotine use in women of reproductive age (ages 18-40) and found that 27.1 percent reported that they engaged in current use of a nicotine product. An estimated 17.4 percent reported using non-cigarette nicotine products; more women reported using smoked non-cigarette nicotine products (12.0 percent) than ENDS (8.1 percent) or smokeless products (0.8 percent). An estimated 10.5 percent reported using more than one nicotine product.

[*] Original analysis of data are not presented on nicotine product use among individuals with psychiatric disorders because mental health status was not assessed in the 2013-2014 NATS or the 2014 NYTS.

Current Nicotine Product Use Among Women of Reproductive Age by Type of Product Used, 2013-2014 (Percent)	
Any nicotine product	**27.1**
Smoked (including cigarettes)	**25.4**
Cigarettes	18.5
Any non-cigarette nicotine product	**17.4**
Smoked (not including cigarettes)	**12.0**
Cigars/cigarillos/little cigars	5.3
Pipes	8.5
Water pipe/hookah	1.1
ENDS/E-cigarettes	**8.1**
Smokeless	**0.8**
Chewing tobacco/snuff/dip	0.7
Snus	–
Dissolvable products	–
Analysis of data from the 2013-2014 National Adult Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nats/).	

One in seven (14.1 percent) women of reproductive age who reported current use of nicotine products met the designated criteria for nicotine addiction (20.1 percent of those who reported current use of multiple nicotine products, including cigarettes).

Chapter IV
The Regulatory Landscape

Laws and regulations,[*] coupled with funding and implementation of effective prevention, early intervention, and treatment initiatives, are critical means by which federal, state, and local governments can help to prevent and reduce tobacco and nicotine use and protect the public health. The primary aims of such laws and regulations are to:

- Prevent the initiation of tobacco or nicotine product use, particularly among youth;
- Help people who already use tobacco or nicotine products to quit or cut down; and
- Reduce the harmful effects caused by tobacco or nicotine product use.

Federal Laws and Regulations

Nearly all laws and regulations aimed at reducing tobacco use in the United States emerged after the publication in 1964 of the U.S. Surgeon General's report, *Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service*.[1] The report provided a comprehensive synthesis of the growing evidence on the health risks of cigarette smoking.[2] Informed by the science detailed in the report, the U.S. Government became one of the first authoritative bodies to declare cigarette smoking a public health threat and to act to implement laws and regulations to reduce that threat.[3]

While regulatory efforts to address the health risks of cigarette smoking intensified, efforts to address the effects of nicotine itself received little attention. Even the 1964 Surgeon General's report described "the tobacco habit" as "an habituation rather than an addiction…since once established there is little tendency to increase the dose; psychic but not physical dependence is developed; and the detrimental effects are primarily on the individual rather than society."[4] It was not until 1988 that a U.S. Surgeon General declared nicotine to be an addictive substance.[5] As a result, the regulation of non-cigarette nicotine products lags far behind that of combustible or smoked cigarettes.

The Promotion (and Restriction) of Public Information and Awareness

Upon publication of the 1964 U.S. Surgeon General's report, the first priority of the federal government was to educate the public about the health risks of smoking and to restrict tobacco product advertising.[6] For example, in 1965, the *Federal Cigarette Labeling and Advertising Act* was enacted, requiring warning labels on cigarette packages.[7] In 1969, the *Public Health Cigarette Smoking Act* strengthened this ruling by requiring a stronger health warning on cigarette packages and in cigarette print advertising (i.e., *"Warning: The Surgeon General Has Determined that Cigarette Smoking Is Dangerous to Your Health")* and prohibiting cigarette advertisements on television and radio.[8] As of January 1, 1971, advertising cigarettes or little cigars[†] on any medium of electronic communication subject to the jurisdiction of the Federal Communications Commission (FCC) became unlawful.[9] The *Comprehensive Smokeless Tobacco*

[*] Laws are passed by legislatures (U.S. Congress for federal laws, state legislatures for state laws) and typically are enforced through the executive branch. Regulations are standards and rules adopted by administrative agencies that govern how laws are enforced.

[†] The *Little Cigar Act* of 1973 defined little cigars as a roll of tobacco wrapped in leaf tobacco or any substance containing tobacco of which one thousand units weigh not more than three pounds.

Health Education Act of 1986 required the inclusion of three rotating health-warning labels on smokeless tobacco packages and advertisements and prohibited smokeless tobacco advertising on television and radio.[10]

These Acts marked the first time that science had been translated into tobacco policy[11] and, as the science base grew, so did the regulation of tobacco products. Unfortunately, the late 1960s and the 1970s also saw a spate of federal laws that reflected the tobacco industry's tremendous influence over government regulation and policy, even within those acts aimed at controlling tobacco and other substance use. Specifically, several acts were passed that included explicit restrictions on public information and awareness with regard to the risks of tobacco use. For example, the *Public Health Cigarette Smoking Act* of 1969 prevented states and localities from regulating or prohibiting cigarette advertising or promotion for health-related reasons; the *Controlled Substances Act* of 1970 excluded tobacco from the definition of a controlled substance; the 1976 amendment to the *Federal Hazardous Substances Labeling Act of 1960* indicated that the term "hazardous substance" shall not apply to tobacco and tobacco products; and the *Toxic Substances Control Act* of 1976 explicitly excluded tobacco products from the term "chemical substance."[12]

Minimum Legal Age of Access to Tobacco Products

With growing evidence that nearly all tobacco use begins in adolescence[13] and that adolescent tobacco use increases the risks of addiction and a host of health consequences, restricting youth access to tobacco became a high priority in the 1990s.[14]

In 1992, Congress enacted the *Alcohol, Drug Abuse, and Mental Health Administration Reorganization Act*, which included an amendment, known as the *Synar Amendment.*[*] The amendment indicated that in order for states[†] to receive their full Substance Abuse Prevention and Treatment Block Grant (SABG) awards, they would have to enact and enforce laws prohibiting the sale or distribution of tobacco products to individuals under the age of 18. The *Synar Amendment* also required states to conduct random inspections of tobacco retail outlets for adherence to this minimum legal age (MLA) requirement.[15]

By 1993, all 50 states enacted MLA restrictions, prohibiting the sale and distribution of tobacco products to individuals younger than age 18.[16] However, definitions of tobacco products vary by state, leaving gaps in tobacco products covered by MLA restrictions.[17] Even when the *Family Smoking Prevention and Tobacco Control Act* (TCA) was enacted in 2009 (see below), setting a national MLA of 18, the restriction was limited to combustible cigarettes, loose tobacco, roll-your-own tobacco, and smokeless tobacco products.[18] It was not until 2016 that the U.S. Food and Drug Administration's (FDA) 'final rule,' which expanded its authority to all tobacco products (see below), allowed for setting a MLA of 18 for sale of all tobacco and tobacco-derived products.[19]

Eighteen is not the only developmentally plausible age to set as a MLA to access tobacco. For example, the most recent national data indicate that while mostly all cigarette smokers have their first cigarette by the age of 18, nearly half progress to daily use after that age (one-third do so between the ages of 18 and 21).[20] Setting a higher MLA creates more distance between a young individual and social sources of tobacco (e.g., friends who are of the legal age)--a primary means by which youth under the age of 18 access tobacco products.[21] However, the TCA explicitly prohibited the FDA from setting a higher MLA than 18, while also directing the FDA to further study the issue.[22] The study concluded that increasing the

[*] Named for its sponsor, Congressman Mike Synar of Oklahoma.
[†] Including all states, the District of Columbia, Puerto Rico, the U.S. Virgin Islands, and six Pacific jurisdictions.

MLA will likely prevent or delay initiation of tobacco use by adolescents and young adults, and the age group most strongly affected would likely be youth between the ages of 15 to 17. The study also concluded that the impact of raising the MLA to 21 would be substantially greater than only raising it to 19 (e.g., 30 percent vs. 25 percent decrease in initiation for youth between the ages of 15 to 17 years).[23] Despite this, the 2016 FDA new ruling on tobacco products maintains the MLA as age 18.[24]

Although there is great public support for increasing the MLA to access tobacco,[25] and several states and localities have already increased it to age 21,[26] there is some concern that enacting age restrictions on non-cigarette nicotine products may inadvertently result in an increase in the use of smoked cigarettes.[27] For example, one national study found an increase in cigarette use among adolescents after states imposed minimum age purchasing restrictions for e-cigarettes. For some young people, the use of non-cigarette nicotine products might serve as a substitute for cigarettes or an aid to cigarette smoking cessation.[*] [28]

Limiting Youth Exposure to Tobacco Product Advertising and Marketing

Several federal laws from the late 1960s through the mid-1980s prohibited the advertising of tobacco products on television and radio. The Master Settlement Agreement (MSA) of 1998 was a settlement reached between the state Attorneys General of 46 states, 5 U.S. territories, the District of Columbia, and the 5 largest tobacco companies in America concerning the advertising, marketing, and promotion of tobacco products. The MSA specifically forbade participating cigarette manufacturers from directly or indirectly targeting youth in the advertising, promotion, or marketing of tobacco products.[29] As a blanket ban against targeting youth, this provision applied to all types of advertising, including transit, billboard, and magazine ads.[†] [30] However, the MSA is an agreement rather than a law, and is limited to those tobacco companies that were a part of the MSA.[31]

The MSA also does not apply to all non-cigarette nicotine products.[32] As a result, there is a considerable amount of tobacco and nicotine product advertising and marketing that still targets youth and that appears to be effective in making youth interested in trying these products. In particular, ENDS products currently are promoted heavily by industry-sponsored advertisements in the popular media, including on television, radio, and the Internet, and these messages are reaching young people. In 2014, nearly 7 in 10 middle and high school students were exposed to e-cigarette advertisements.[‡] [33] In 2015, 82 percent of 13-17 year olds and 88 percent of 18-21 year olds reported having seen an advertisement for e-cigarettes on at least one television channel that year.[34]

Comprehensive Federal Regulation: The 2009 Family Smoking Prevention and Tobacco Control Act (TCA)

In the 1990s, pressure began to mount for the federal government to regulate tobacco products. Cigarettes and other smoked products were increasingly recognized as addictive and deadly and, unlike other consumer products, subject to virtually no federal regulation.[35] Earlier attempts were made to regulate tobacco products at the federal level but it was not until 2009 that the *Family Smoking Prevention and Tobacco Control Act* (TCA) was signed into law, granting the FDA the authority to regulate the manufacture, distribution, and marketing of certain tobacco products.[36] Among its provisions, the TCA:

[*] See Chapter V for more discussion of this issue.
[†] With respect to magazines, "youth magazine" has been defined by the FDA as having either more than two million youth readers (younger than age 18) or more than 15 percent youth readership.
[‡] Sources of advertisement exposure were, in descending order of influence, retail stores, the Internet, television and the movies, newspapers and magazines.

- Restricts tobacco product marketing and sales to youth by banning: sales to minors, vending machine sales,[*] sale of packages of fewer than 20 cigarettes, tobacco brand sponsorships of sports and entertainment events or other social or cultural events, free giveaways of samples, and brand-name non-tobacco promotional items.
- Gives authority to the FDA to conduct inspections of tobacco product retailers to determine a retailer's compliance with federal laws and regulations and, when violations occur, to take corrective action by issuing:
    - Warning letters, the first time a tobacco compliance check inspection reveals a violation of the federal tobacco laws and regulations that the FDA enforces.
    - Civil Money Penalty Complaints, which impose a fine against a retailer with more than one tobacco compliance-check violation; fines can range from $250 to $11,000.
    - No-Tobacco-Sale Order Complaints, in which retailers with five or more violations within 36 months are prohibited from selling regulated tobacco products.
    - Seizures, injunctions, and criminal prosecution.
- Requires prominent graphic warning labels for cigarettes and larger, more visible text warnings for smokeless tobacco products.[†] [37]
- Prohibits the advertising or labeling of tobacco products with modified risk claims or reduced harm descriptors, such as "light," "low," or "mild," without support of scientific evidence.
- Requires the disclosure of ingredients in tobacco products.
- Requires tobacco companies to submit research on the health, toxicological, behavioral, and physiological effects of use of their tobacco products.
- Allows the FDA to implement standards for tobacco products to protect the public health, such as by regulating nicotine and ingredient levels (but it does not authorize the FDA to require that nicotine yields be reduced to zero).
- Prohibits the sale of cigarettes containing characterizing flavors (with the notable exceptions of menthol and tobacco).

Despite its broad reach with regard to effective tobacco control, the TCA only applies to the following specific tobacco products: cigarettes, loose tobacco, roll-your-own tobacco, and smokeless tobacco. It does not apply to other tobacco- and nicotine-containing products, leaving e-cigarettes, other ENDS products, cigars, pipe tobacco, nicotine gels, water pipe/hookah tobacco, and dissolvables completely outside the scope of federal regulation.

In April 2014, the FDA announced a proposal to extend its regulatory authority to these other tobacco and tobacco-derived products.[38] Finally, in May 2016, the FDA was authorized to extend its oversight to all tobacco and tobacco-derived products that previously were unregulated.[39]

[*] Except in 'adults only' facilities.

[†] This provision has not been implemented due to legal resistance by the tobacco industry, which claimed that the graphic warning label requirements violate their First Amendment rights. The FDA has indefinitely postponed implementation of the graphic warning label requirement. In October 2016, several anti-tobacco groups filed a complaint against the FDA to compel it to abide by the TCA and require it to undertake research to support a new rule mandating graphic warning labels.

The 2016 FDA Final Rule for all Tobacco Products

The new rule extends key provisions of the 2009 TCA to newly regulated tobacco products, and includes the following additional provisions:[40]

- Prohibits sales to children under age 18, requires retailers to verify age for over-the-counter sales for anyone under the age of 27, and provides for federal enforcement and penalties against retailers who sell to minors.
- Prohibits free samples.
- Restricts vending machine sales to 'adults only' facilities.
- Requires all tobacco products containing nicotine and advertisements for these products to carry an addiction warning label, and for cigars to carry one of four additional warnings; the ruling also allows states to add their own health warnings.
- Requires manufacturers to register with the FDA and to disclose product ingredients, potentially harmful additives, and other health-related effects.
- Authorizes the FDA to request additional documents related to research and marketing.
- Prohibits the introduction of new or changed products without prior FDA review and scientific evidence through a premarket review, demonstrating that allowing a product is "appropriate for the protection of public health."
- Prohibits manufacturers from claiming a tobacco product is less harmful without first providing the FDA with scientific evidence supporting the claim and demonstrating that it will benefit public health as a whole, and not just individual tobacco users.
- Authorizes the FDA to set standards governing the content of all tobacco products.

While broadening its regulatory coverage of tobacco products, the new FDA rule does not apply all of the restrictions that it currently places on cigarettes to all non-cigarette nicotine products.[41] For example:

- Unlike smoked cigarettes, for which characterizing flavors other than tobacco and menthol are prohibited, there are no restrictions on the flavorings that may be included in non-cigarette nicotine products.
- Unlike cigarettes, for which there are packaging requirements related to size,[*] warning labels, and ingredient disclosures,[42] no such requirements exist for non-cigarette nicotine products. Unlike cigarettes and smokeless tobacco products, which are prohibited from including brand names on non-tobacco products and brand name sponsorship of sporting and cultural events, no such prohibitions exist for other nicotine products.

The 2009 TCA gave the FDA the authority to determine whether new tobacco products covered under the TCA may enter the market, and the 2016 rule extended that authority to all tobacco products. Entry of new products onto the market can be accomplished via three pathways: the Premarket Tobacco Product Application; Substantial Equivalence Applications; and Exemptions from Substantial Equivalence Applications.[43]

[*] "No manufacturer, distributor, or retailer may sell or cause to be sold, or distribute or cause to be distributed, any cigarette package that contains fewer than 20 cigarettes."

- **Premarket Tobacco Product Application (PMTA).** The 2009 TCA requires tobacco manufacturers to get an order of exemption from the FDA before introducing new tobacco products[*] to the market via a PMTA. To obtain approval, the products must be assessed with regard to their risks and benefits to users and nonusers. The FDA's assessment includes reviewing the products' components, ingredients, additives, and health risks, as well as how the product is manufactured, packaged, and labeled. It also takes into account "the increased or decreased likelihood that existing users of tobacco products will stop using such products and the increased or decreased likelihood that those who do not use tobacco products will start using such products."[44] The FDA can deny an application for any product that does not protect the public health (primarily with regard to its effects on smoking initiation and cessation), that does not meet established manufacturing standards, that includes misleading or false labeling, or that does not meet a product standard set by the FDA.[45]

  The FDA has determined that any ENDS product that was not available commercially before February 15, 2007 and is not substantially equivalent to products that were on the market at that time is required to go through the premarket review process.[46] This essentially includes all existing ENDS products. However, enforcement of this requirement will be delayed for 1-2 years from the time the rule went into effect on August 8, 2016.[47] During this time, manufacturers may market the products as long as a PMTA has been submitted to the FDA. Any products that do not have a marketing authorization by the end of the compliance period may be removed from the market by the FDA.

  Critics of the decision to include all ENDS products in this PMTA requirement argue that the tobacco industry will be at an advantage relative to small business manufacturers since the PMTA is considered too expensive and burdensome of a process for small manufacturers of ENDS products to navigate successfully.[48] Proponents of more stringent PMTA enforcement argue that products currently on the market, many of which are completely unstandardized and may pose a threat to the public health, are permitted to continue to be sold for up to 2 years in their current form. They also argue that the FDA should shift its priorities regarding the products it reviews, from one in which products not yet on the market are reviewed prior to those already on the market to one in which potentially noncompliant products already on the market are reviewed first. Such a shift would facilitate the removal of products that do not comply with the FDA regulations over the introduction of new tobacco products.[49]

- **Substantial Equivalence Applications (SE).** Manufacturers wishing to introduce a new tobacco product that is similar to one that already had been marketed commercially as of February 15, 2007 (a "predicate" product) or that differs but does not raise public health concerns may use the SE pathway to FDA approval.[50]

- **Exemptions from Substantial Equivalence Applications (SE Exemption).** A third pathway for attaining FDA approval to market a new tobacco product is to request an SE exemption stating that the new product is so similar to a predicate product (e.g., an additive was removed) that a complete demonstration of its substantial equivalence is not necessary to protect the public health.[51]

The FDA's 2016 deeming rule requires that all tobacco product advertising and packaging, other than for cigars, include the following warning label: "*WARNING: This product contains nicotine. Nicotine is an addictive chemical*." Packaging and advertising for cigars must display either this warning or one of five

[*] New products are those commercially marketed in the United States for the first time after February 15, 2007.

other warnings specified in the rule.[52] The FDA is also authorized to take action against manufacturers who sell or distribute products with unsubstantiated, false, or misleading labeling or advertising claims.[53]

The new rule does not, however, fully address the issue of warning consumers about the risks of nicotine exposure (e.g., from e-liquid solutions), particularly to young children who may touch or ingest the potentially poisonous nicotine contained in many ENDS products. The FDA indicated that it does recognize "the importance of alerting consumers to, and protecting children from, the hazards from ingestion of, and eye and skin exposure to, e-liquids containing nicotine" and may in the future introduce regulatory actions with regard to requiring nicotine exposure warnings and child-resistant packaging.[54]

More Recent Actions by the FDA

In January 2017, the FDA proposed a tobacco product standard for smokeless tobacco products sold in the U.S. that would limit the amount of tobacco-specific nitrosamine (N-nitrosonornicotine, or NNN)--a potent carcinogen--to 1 microgram per gram of smokeless tobacco. The FDA estimates that implementation of this rule could prevent approximately 12,700 new cases of oral cancer and 2,200 oral cancer deaths over the course of 20 years, as well as reduce the risk of esophageal cancer and possibly pancreatic, laryngeal, prostate, and lung cancer. The proposed rule, which will be subject to a period of public comment prior to finalization, would also require an expiration date on smokeless tobacco products because this carcinogen builds up over time and that the product labels contain a manufacturing code, expiration date, and, if applicable, storage conditions for the product (e.g., refrigeration).[55]

State and Local Laws and Regulations

Aside from federal regulations that have begun to address non-cigarette nicotine products, there are other tobacco-control measures enacted at other levels of government that seek to address the availability and use of these products. However, the preemption doctrine, which applies when the laws of a higher level of government override or limit the laws of a lower level of government on a certain regulatory issue,[56] can interfere with these efforts. Specifically, federal preemption laws indicate that when there is a conflict between state and federal law, federal law overrides state law. Preemption also may apply to state laws displacing regulations enacted by local governments, especially when they are stricter than the law of the state. Preemption often applies to laws or regulations related to tobacco, alcohol, guns, and pharmaceuticals.[57]

While the TCA expressly preempts state and local governments with regard to certain tobacco regulations (e.g., premarket review, manufacturing practices, labeling), it does not preempt lower levels of government from enacting more stringent tobacco regulations with regard to sales and distribution restrictions, youth possession restrictions, taxes, and smoke-free laws.[58]

As more local governments--the level of government at which strong tobacco control policies traditionally have emerged due to grassroots community efforts[59]--passed tobacco-free and youth access restrictions laws, state preemption became a tactic promoted by the tobacco industry to fight local tobacco control initiatives.[60] Specifically, the tobacco industry used its political influence to promote the passage of state laws preempting local regulations of tobacco products.[61] Since 2008, there has been a surge in such state preemption bills, with most affecting local smoke-free laws.[62] As of July 2016, 13 states[*] had preemption of these local laws.[63]

[*] CT, FL, MI, NC, NE, NH, OK, PA, SD, TN, UT, VA, WI.

Smoke-Free (Clean Air) Laws and Regulations

In the 1960s, research regarding the hazards of environmental tobacco smoke exposure began to emerge,[64] but it was not until the 1986 publications of the U.S. Surgeon General's report, *The Health Consequences of Involuntary Smoking*,[65] and the National Research Council's report, *Environmental Tobacco Smoke: Measuring Exposures and Assessing Health Effects*,[66] that the science base was deemed conclusive enough to enact smoke-free legislation.[67] These reports detailed the hazardous effects of secondhand or environmental tobacco smoke on fetal development and on the health of adults and children.[68] Still, the authority of the federal government was limited in that it could only enact smoke-free policies in places in which it had jurisdiction, such as airplanes and federal office buildings.[69] The Federal Aviation Administration currently does not permit the use of ENDS products on any domestic or foreign airline flying to, from, or within the United States.[70]

States and localities do have the jurisdiction to enact smoke-free policies (or clean indoor/outdoor air policies) in public places such as bars, restaurants, and parks. While some localities enacted smoke-free regulations in public buildings during the 1970s and 1980s, it was not until the early 2000s that states began to implement comprehensive smoke-free laws.[71]

Smoke-free laws do not always apply to the use of non-cigarette nicotine products; however, some states have expanded their policies to include ENDS. As of October 2016, 36 states, the District of Columbia, American Samoa, the Northern Mariana Islands, Puerto Rico, and the U.S. Virgin Islands have laws that require non-hospitality workplaces and/or restaurants and/or bars and/or state-run gambling establishments to be 100 percent smoke-free.[72] Twenty-five states, Puerto Rico, and the U.S. Virgin Islands have such laws in all non-hospitality workplaces, restaurants, and bars.[73] Also as of that date, 12 states have laws restricting ENDS use in 100 percent smoke-free venues (i.e., workplaces, restaurants, bars, and sometimes gambling facilities), and 15 states have such laws in other venues (e.g., school property, prisons, trains, government buildings).[74]

Taxation

The oldest and most commonly implemented tobacco control regulation is taxation.[75] The earliest attempt to tax tobacco products in the U.S. was by Alexander Hamilton in 1794 when he introduced to Congress an excise tax on snuff.[76] Although this tax soon was repealed, federal tobacco excise taxes again were implemented during the Civil War. It was not until 1921 that a state, Iowa, successfully imposed an excise tax on cigarettes.[77] States throughout the U.S. soon followed Iowa's example and imposed taxes on cigarettes primarily as a means to produce state revenue.[78] Today, federal, state, and local governments tax cigarettes at widely varying levels,[79] primarily to produce revenue but also to help discourage the purchasing and use of tobacco products.[80]

Taxation of tobacco products extends to non-cigarette nicotine products. For example, as of July 2016, all states except Florida imposed a tax on at least one cigar product (cigars, cigarillos, or little cigars)[81] and all states tax chewing tobacco.[82] A growing number of state and local governments are enacting or proposing legislation to tax ENDS products as well. As of March 2016, four states[*] and the District of Columbia enacted, and 23 additional states considered, excise taxes on ENDS products.[83]

Because youth are especially price sensitive when it comes to tobacco product purchases, higher taxes consistently have proven to be an effective strategy for preventing or reducing youth tobacco use.[84] One recent study found that for every $1.00 increase in cigarette tax, there was an associated reduction of approximately two percentage points in smoking among 14- and 15-year olds.[85]

[*] KS, LA, MN, NC

Depending on assumptions of risk, differential tax policies can be applied to tobacco products: higher taxes to discourage the use of higher-risk products and lower taxes to encourage the use of lower-risk products, especially for smokers trying to cut down or quit.[86] For example, if the assumption is that ENDS products are lower risk than smoked tobacco products, the latter should be taxed higher than the former to discourage the use of smoked tobacco products and encourage switching to ENDS products.[87] However, because the evidence base regarding the risks of ENDS products and their effectiveness in aiding smoking cessation is inconsistent, some public health professional argue that, for now, all nicotine products should be taxed at an equivalent rate.[88]

Minimum Age Laws

Although the TCA prohibits the FDA from setting a MLA of sale higher than 18,[89] states and localities are allowed to do so. As of September 2016, six states[*] have MLA restrictions higher than 18 and have extended these age restrictions to non-cigarette nicotine products such as e-cigarettes.[90] Two states (CA and HI) have set the MLA of sale for tobacco products to age 21 and more than 200 localities have done so.[91]

Retail and Packaging Requirements

Some states have enacted retail-related regulations that go beyond federal regulations, such as requirements related to child-resistant packaging, sale of the product in the same minimum quantity as the manufacturer's container, sale of the product in its original factory wrapped packaging, and retailer licenses or permits for selling ENDS products.[92]

States with Regulations Related to the Retail and Packaging of ENDS Products (as of September 2016)[93]

State	Packaging Regulations	License/Permit Requirements
Arkansas	Yes: child-resistant packaging	Yes
California	Yes: child-resistant packaging	Yes
Connecticut	No	Yes
District of Columbia	No	Yes
Illinois	Yes: child-resistant packaging	No
Indiana	Yes: child-resistant packaging; "label must identify nicotine content, active ingredients," etc.	Yes
Iowa	No	Yes
Kansas	No	Yes
Kentucky	No	Yes
Louisiana	No	Yes
Maine	Yes: child-resistant packaging	Yes
Massachusetts	Yes: child-resistant packaging; "may not be opened, repackaged or sold in smaller quantities than the smallest package distributed by the manufacturer for individual consumer use"	No

[*] AL (age 19 legal age of purchase/possession); AK (age 19 legal age of sale/distribution); CA (age 21 legal age of sale); HI (age 21 legal age of sale/distribution and legal age of purchase/possession); NJ (age 19 legal age of sale/distribution); UT (age 19 legal age of sale/distribution).

States with Regulations Related to the Retail and Packaging of ENDS Products (as of September 2016)[94] (continued)		
State	**Packaging Regulations**	**License/Permit Requirements**
Minnesota	Yes: child-resistant packaging	Yes
Missouri	Yes: child-resistant packaging	Yes
Montana	No	Yes
New Jersey	Yes: child-resistant packaging	No
New Mexico	Yes: child-resistant packaging; "must be sold in original factory-sealed package"	No
New York	Yes: child-resistant packaging	No
North Carolina	Yes: child-resistant packaging; "must state the product contains nicotine"	Yes
North Dakota	Yes: child-resistant packaging	No
Ohio	Yes: "must be sold in the same minimum quantities as manufacturer's container"	No
Oregon	Yes: child-resistant packaging	No
Rhode Island	Yes: "must be sold in original factory-sealed package"	Yes
South Dakota	Yes: "must be sold in original manufacturer's packaging"	No
Tennessee	Yes: child-resistant packaging	No
Texas	Yes: child-resistant packaging	No
Utah	Yes: child-resistant packaging; "nicotine content displayed on label, and safety warning required"	Yes
Vermont	Yes: child-resistant packaging	Yes
Virginia	Yes: child-resistant packaging	No
Washington	Yes: child-resistant packaging; "liquid nicotine containers must be labeled with warnings concerning nicotine, keeping away from children, age restrictions, and must include nicotine content"	Yes
Wyoming	Yes: child-resistant packaging	No

Insurance Coverage for Tobacco Control

Expanding insurance coverage through laws and regulations to increase accessibility to tobacco prevention and cessation services is a core component of the effort to help people refrain from or quit nicotine product use and reduce its harmful consequences.[95] Federal initiatives have emerged over the past decade to expand tobacco prevention programs and coverage of cessation services, most notably the Patient Protection and Affordable Care Act (ACA).[*] [96] States have the opportunity to leverage the ACA to ensure coverage for tobacco prevention and cessation services.[97]

Federal Level

As of January 1, 2014, the ACA requires that all small and individual health plans cover 10 Essential Health Benefits (EHBs). One of these EHBs has direct implications for increasing accessibility to

[*] The Patient Protection and Affordable Care Act (2010) was amended by the Health Care and Education Reconciliation Act. Together, the two laws are known as the Affordable Care Act (ACA).

recommends that clinicians ask all adults about tobacco use, advise them to stop using tobacco, and provide behavioral interventions and FDA-approved pharmacotherapy for cessation to all those who use tobacco.[98]

The ACA also includes a number of other provisions related to chronic diseases, some of which specifically address tobacco control:[99]

- *The Prevention and Public Health Fund*: Established by the ACA, it invests billions of dollars in prevention, wellness, and public health activities, some of which are focused on tobacco prevention, including an investment in the Centers for Disease Control and Prevention's *Tips from Former Smokers* campaign.[100]
- *The National Prevention Strategy*: Released in 2011 by the National Prevention Council, which was created through the ACA, it is comprised of 20 federal departments, agencies, and offices and is chaired by the Surgeon General. The Strategy includes tobacco-free living as one of its seven main priorities and offers recommendations to government, businesses, health care professionals, educators, communities, and families to achieve that goal (e.g., support tobacco control policies, expand use of tobacco cessation services, use media to educate and encourage people to live tobacco free).[101]
- *The Medicaid Incentives for the Prevention of Chronic Diseases Model*: The ACA authorizes grants to states to provide incentives to Medicaid beneficiaries to participate in evidence-based prevention programs and to adopt healthy behaviors, including tobacco cessation.[102]

More generally, the ACA encourages community-based prevention through a variety of programs, such as:

- *Community Health Needs Assessment*: The ACA requires tax-exempt (nonprofit) hospitals to conduct a community health needs assessment every three years that incorporates input from the community.
- *Expansion of the health care workforce*: The ACA supports fellowship training in public health, provides grants to promote the community health care workforce, and provides billions of dollars for community health centers nationwide.[103]

State Level

Increasing the availability and utilization of tobacco prevention and cessation services also involves regulating health systems and insurance coverage at the state level. While the ACA establishes a federal standard for market reforms, states have the primary authority for enforcing these protections.[*] [104] According to our Center's recent report, *Uncovering Coverage Gaps: A Review of Addiction Benefits in ACA Plans*, the 2017 EHB benchmark plans for 26 states[†] were not in compliance with the ACA's requirement to cover tobacco cessation services.[105]

[*] If a state declines or substantially fails to enforce these protections, the federal government may step in.
[†] AL, AK, CA, CO, CT, FL, GA, HI, ID, IN, LA, ME, MA, NE, NV, NH, NM, OH, OR, RI, SC, SD, TN, UT, VT, WI.

Tobacco Cessation Minimum Service Coverage As Required By The ACA[106]
A group health plan or health insurance issuer will be considered to be in compliance with the ACA's requirement to cover tobacco interventions if it covers the following, without cost sharing or prior authorization: • screening of all patients for tobacco use; and • for enrollees who use tobacco products, at least two tobacco cessation attempts per year, with coverage of each quit attempt including: ➢ four tobacco cessation counseling sessions, each at least 10 minutes long (including telephone, group, and individual counseling), and ➢ any FDA-approved tobacco cessation medication (whether prescription or over-the-counter)* for a 90-day treatment regimen when prescribed by a health care provider.

While the ACA increases tobacco prevention and cessation coverage, it allows health insurers to charge subscribers who use tobacco up to 50 percent more for health insurance premiums than those who do not use tobacco.[107] As a result of the 2106 FDA rule,[108] non-cigarette nicotine products (including ENDS) can now be subject to that tobacco surcharge.[109] While imposing higher premiums might help motivate those who use nicotine products to quit, it might also lead to concealing use, avoiding cessation services, and even forgoing health insurance.[110]

States have the authority to prohibit insurers from charging tobacco users higher premiums or to reduce the maximum allowable surcharge increase.[111] As of February 2016, six states† and the District of Columbia have barred insurers from imposing higher premiums on smokers and several other states use surcharges that are lower than those allowed by the ACA.[112]

* FDA-approved tobacco cessation medications: Zyban® (bupropion), Chantix® (varenicline), and five forms of nicotine replacement therapy (NRT), including patch, gum, lozenge, nasal spray, and inhaler.
† CA, MA, NY, NJ, RI, VT.

Chapter V
Barriers to Reducing Nicotine Product Use

Despite significant declines in combustible or smoked cigarette use over the past few decades and increasing public awareness of the harms of tobacco,[1] our analysis of national data indicates that 26.0 percent of adults and 15.7 percent of middle and high school students reported having used at least one nicotine product in the past 30 days; 16.3 percent of adults used a non-cigarette nicotine product, as did 14.7 percent of youth.*

The growing popularity of non-cigarette nicotine products, such as e-cigarettes and other vaping devices known as electronic nicotine delivery systems (ENDS), coincides with a general public perception of these products as relatively harmless, as helpful for cigarette smoking cessation, and as adequate substitutes for smoked cigarettes that can be used at times and in places where tobacco products are prohibited.[2]

Historically, the focus of public policy and public health campaigns has been on the prevention and reduction of smoking rather than on the use of other nicotine products.[3] It has become clear in recent years, however, that the marketing of other nicotine delivery products, including ENDS and snus, as safer alternatives to or substitutes for cigarettes has shaped the public's perceptions of and decisions to use these products.[4]

The key barriers to reducing the use of nicotine products, in addition to their highly addictive nature, relate to factors that promote the initiation of nicotine use as well as those that interfere with successful cessation. Specifically, nicotine use is strongly influenced by tobacco industry practices, which include how these products are designed and marketed, as well as the exercise of undue influence on government policies and regulations. These factors, along with peer and family influences and inconsistency in scientific findings and clinical practice, shape public perceptions regarding the relative risks and benefits of nicotine products and individual decisions to use or cease using them.

Public Perceptions of Non-Cigarette Nicotine Products

The public generally recognizes that there is a continuum of harm associated with various nicotine products, with the greatest perceptions of harm typically reserved for cigarettes, followed by cigars and smokeless tobacco, and the least harm ascribed to water pipe/hookah and ENDS.[5] Yet, despite understanding that cigarettes pose the greatest harm, the inherent risks of non-cigarette nicotine products tend to be minimized or dismissed, especially if they are promoted in a way that emphasizes their reduced risk relative to cigarettes.[6]

The extent to which a product is seen as harmful is strongly related to the likelihood that an individual will use that product, and once an individual uses a nicotine product, he or she is less likely to perceive it as risky or harmful.[7] For example, a study of young adults who smoked water pipe/hookah found that 57 percent believed that it was not harmful to their health.[8] There is some evidence that water pipe/hookah is perceived by young adults to be the least harmful and addictive and the most socially acceptable nicotine product to use,[9] when the reality is that such use can be very harmful.[10] Misperceptions with regard to

* See Chapter III.

ENDS products abound as well, especially among adolescents. In a California study, 19.1 percent of high school student participants indicated a belief that the aerosol from e-cigarettes is water, 23.0 percent believed that e-cigarettes are not tobacco products, and 40.4 percent believed that the purpose of e-cigarettes is to aid smoking cessation.[11]

Recent national data, however, indicate that perceptions of harm and disapproval related to nicotine products among adolescents are slowly increasing. In 2016, relative to 2015, 8th and 10th grade students were more likely to perceive the regular use of e-cigarettes as harmful and to disapprove of their use.[12]

Many of the reasons reported for using non-cigarette nicotine products reflect the successful marketing and promotion activities of their manufacturers and distributors. Individuals report using certain non-cigarette nicotine products to cut down on or stop smoking cigarettes,[13] because they find that the taste or smell t more appealing than cigarettes,[14] because they enjoy the flavoring that many of these products have,[15] because they are able to use them in places where smoking is prohibited,[*] [16] and for relaxation or socializing purposes.[17] With regard to ENDS products specifically, additional reasons provided for using them are curiosity[18] and the perception that they are a healthier alternative to smoked cigarettes.[19] Adolescents report enjoying the flavor variety, the ability to control the nicotine content, and the ability to perform smoke tricks.[20] Adults are more likely than younger people to report using ENDS as a smoking cessation aid.[21]

Addiction as a Barrier to Reducing Nicotine Product Use

Probably the most prominent barrier to reducing nicotine use is that nicotine is one of the most highly addictive drugs.[22] People who meet the diagnostic criteria for a tobacco use disorder (which we refer to as nicotine addiction or dependence)[†] typically report symptoms consistent with other forms of addiction, such as craving, impaired functioning without the substance, and continued use despite adverse consequences.[23] Once someone is dependent on or addicted to nicotine, it is extremely difficult to quit or to sustain long-term abstinence.[24] Most smokers who try to quit on their own quickly relapse.[25] For those who start using nicotine products at a young age, symptoms of addiction can develop rapidly, even within weeks or days after nicotine use begins and even with infrequent use.[26] The addictive nature of nicotine products and the difficulty of cessation help ensure a loyal customer base for nicotine product manufacturers and retailers.

Nicotine's effects on the brain are similar in many ways to other addictive substances. It activates the reward pathways, or the areas of the brain that regulate pleasure, and long-term use of nicotine can create lasting changes in the brain circuitry as it becomes dependent on the continued presence of the drug. The extent to which a nicotine product is addictive, however, depends in large measure on its mode of delivery, which determines both the dose of the absorbed nicotine and the speed at which it is absorbed into the blood and enters the brain.[27] The risk of addiction varies between individuals based on their genetic profile which determines, in part, how quickly nicotine is metabolized,[‡] as well as by other biopsychosocial individual differences.[28] Unlike some other addictive substances, the effects of nicotine

[*] Specifically, smokeless tobacco products and ENDS.

[†] Defined in accordance with the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria for a "tobacco use disorder." Although the accepted term is "tobacco use disorder," it is nicotine specifically that leads to addiction, and addiction can occur in relation to non-tobacco products that contain nicotine.

[‡] Individuals who metabolize nicotine more slowly are at lower risk of nicotine addiction (e.g., men metabolize nicotine more slowly than women, and blacks and Asians metabolize nicotine more slowly than whites and Hispanics). However, there is some evidence that this pattern may not apply to adolescents or those in the early stages of nicotine use, when slower metabolism of nicotine may pose a higher risk of addiction.

dissipate relatively quickly, driving those who use it to seek more nicotine in order to perpetuate its pleasurable effects and stave off withdrawal symptoms.[29]

To a large extent, the risk of nicotine addiction falls along a continuum from minimal to high based on the nicotine delivery device,[*] with combustible tobacco products like cigarettes highest on the continuum, smokeless tobacco and ENDS products in the middle, and nicotine replacement therapies (NRT), like the nicotine patch, lowest on the continuum.[30] The amount of nicotine contained in NRT is less than in cigarettes and other nicotine products and is delivered and absorbed into the blood stream more slowly, limiting its misuse and addictive potential.[31] As a result, NRT products--such as nicotine patches, gum, nasal spray, inhalers, lozenges, and sub-lingual tablets--are approved by the U.S. Food and Drug Administration (FDA) as smoking cessation tools.

NRT, when used as directed, provides lower doses of nicotine at a slower rate than cigarette smoking, thereby easing nicotine withdrawal symptoms and reducing cravings.[32] Use of NRT increases the chances of successful quitting by an estimated 50 to 70 percent,[33] and approximately doubles abstinence rates over at least a 6-month period, relative to a placebo.[34] Still, the effectiveness of NRT is somewhat limited since it does not produce the subjective effects of nicotine that are experienced when using more efficient nicotine delivery devices such as cigarettes. Because of this limitation and the urgent need to reduce smoking and its numerous health consequences, some tobacco control professionals have become proponents of ENDS products, arguing that because nicotine delivery via ENDS is more efficient and the behavioral experience of vaping is more similar to smoking cigarettes, ENDS might provide a more effective transition to cessation than NRT. However, few studies have compared the use of ENDS to NRT for smoking cessation. Those that have examined the use of ENDS for smoking cessation have not found convincing evidence of its effectiveness[35] and some studies, to the contrary, have found that it delays cessation or encourages dual use of ENDS and cigarettes.[36]

Influence of the Tobacco/Nicotine Product Industry

The 2009 *Family Smoking Prevention and Tobacco Control Act* (TCA),[†] which gave the FDA the authority to regulate the manufacture, distribution, and marketing of certain tobacco products, greatly restricted the active marketing of these products.[‡ 37] In response, tobacco product manufacturers have shifted from actively marketing these products on media such as television and radio to more passive marketing through retail outlet advertisements and the Internet.[38] Products not covered under the TCA, such as ENDS, may be advertised and marketed actively on mainstream media and through these secondary channels and their appearance is pervasive throughout these outlets.[39]

The ability of the tobacco industry to saturate the physical and digital environment with tobacco product advertisements and promotions, often in a way that targets the most susceptible populations, is profound. Even marketers of ENDS that are not affiliated with established tobacco companies are promoting their products in ways that reflect old cigarette marketing tactics, pushing themes of independence, glamour, sexuality, sophistication, and rebelliousness, and making largely unsupported health benefit claims.[40] Beyond advertising, ENDS product manufacturers also utilize sophisticated marketing and product design techniques, including appealing packaging and flavorings, to boost sales. Finally, the influence of the industry on policymakers' decisions with regard to more restrictive regulations is significant and far-reaching.

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[*] See Chapter II.

[†] See Chapter IV.

[‡] Applied to cigarettes, loose tobacco, roll-your-own tobacco, and smokeless tobacco, but not to e-cigarettes, other ENDS products, cigars, pipe tobacco, nicotine gels, water pipe/hookah, or dissolvables.

Marketing and Exposure

The tobacco industry utilizes strategic advertising and promotional techniques to help make their products appear glamorous and fun to use while dispelling concerns about health risks. For example, both ENDS and--to a lesser extent in recent years--certain smokeless tobacco products such as snus have been marketed as healthier alternatives to smoked cigarettes, as useful for smoking cessation or reduction, and as a way to circumvent smoke-free laws.[41] Research consistently has found that tobacco product marketing influences tobacco initiation and use among youth,[42] rather than merely influencing brand choices among existing tobacco users, as the industry tends to assert.

Marketing. The tobacco industry is very adept at marketing their products in appealing ways, tailoring their advertisements to specific target groups, and masking the inherent risks of their products. The best example of this is cigarettes, but similar tactics have been used to market non-cigarette nicotine products as well. For example, in the 1980s, smokeless tobacco was promoted at fishing tournaments and tractor pull contests specifically to appeal to young men of lower socioeconomic status living in rural areas.[43] With the introduction of snus, a spit-less form of smokeless tobacco, consumer marketing shifted to appeal to professional, urban young men and to smokers wishing to use tobacco products in designated smoke-free-zones.[44] In recent years, tobacco companies have begun to acquire e-cigarette and other ENDS brands, and they are applying their vast experience in marketing cigarettes to the advertising and promotion of these increasingly popular nicotine products.

ENDS Product Brands Owned by Big Tobacco Companies	
E-cigarette Brand	**Tobacco Company**
blu	Imperial Tobacco[45]
Vuse	Reynolds America Inc.[46]
MarkTen	Altria Group, Inc.[47]
Green Smoke	Altria Group, Inc.[48]

As major tobacco companies enter the ENDS market, advertising expenditures are increasing dramatically.[49] Expenditures nearly tripled from $6.4 million in 2011 to $18.3 million in 2012, with the majority of expenditures (76.7 percent) going toward advertisements for blu e-Cigs, a company that was owned by Lorillard Tobacco Company in 2012.[50] ENDS advertising spending increased by 52 percent from 2013 to 2014, and now exceeds $100 million per year.[51]

These advertisements are making their way directly to youth. In 2014, 68.9 percent of middle and high school students reported exposure to e-cigarette advertisements from at least one source: retail stores, the Internet, television and movies, or print media.[52] Between 2014 and 2015, 82 percent of 13-17 year olds and 88 percent of 18-21 year olds reported having seen an e-cigarette advertisement. The highest awareness of e-cigarette advertisements was in relation to retail establishment marketing, followed by television and online marketing.[53]

The way these products are marketed can have a considerable impact on consumers' interest in them and decisions to use them.[54] Exposure to ENDS through advertising has been associated with positive perceptions, lower perceived harm, and greater interest in buying and trying them.[55] The odds of reported current use of these products were significantly greater among those who had been exposed to their advertisements compared to those with little to no exposure.[56]

Since there have been only limited point-of-sale or packaging restrictions on ENDS products, large store-front advertisements depicting their benefits with phrases such as "no tobacco smoke, only vapor" and equating them with independence and freedom have become quite common.[57] At the point-of-sale,

ENDS products are visible to young children and their packaging often resembles candy packaging that easily appeals to children of all ages.[58]

Retail Outlet Density and Proximity. In addition to exposure to advertising, ease of access to nicotine products is also associated with their use.[59] With regard to cigarettes, tobacco retail density is associated with greater intention to smoke cigarettes and the likelihood of smoking initiation.[60] Of note, there is a higher density of tobacco retail outlets (as well as tobacco product advertisements) in economically disadvantaged neighborhoods.[61] People living in high poverty census tracts and closer to tobacco retail outlets are less likely to refrain from smoking than those living farther away.[62] With regard to non-cigarette nicotine products, university students who indicated that the closest water pipe/hookah lounge was less than five miles away from their campus were more likely to report ever visiting one than those who stated that a lounge was farther away.[63] Greater density of ENDS retail outlets around schools has been associated with a greater probability of use among youth.[64]

The Internet and Social Media. In the last decade, the Internet has become an influential platform for the promotion of non-cigarette nicotine products.[65] Social media messages can influence public perceptions of these products and interest in using them.[66] Between 2012 and 2013, nearly $2 million were spent to promote nicotine products on the Internet, with the most money allocated to promote ENDS and snus and the least to smoked cigarettes.[67] Independent and smaller vape shops that sell ENDS products also use the Internet and social media to market their products.[68]

Online advertisements are proving to be a hurdle for tobacco control advocates given the Internet's wide reach and the limited federal regulations related to advertising non-cigarette nicotine products. Compared to traditional modes of marketing, social media marketing and exposure through the Internet have the potential to reach a larger audience because of the ability to "retweet" and repost.[69] Between May and June of 2012, the vast majority (90 percent) of tweets on Twitter that were related to e-cigarettes were commercial tweets and the majority of these (94 percent) had links to a website, many of which promoted or sold ENDS products.[70] Twitter messages related to ENDS, most of which are overwhelmingly positive, frequently link to scientific studies with favorable results about ENDS products or retweet users' personal messages about the benefits of their use.[71]

Age restrictions on who can watch videos on popular websites like YouTube are not effective and most videos in which people are using nicotine products or demonstrating how to use them typically are not age restricted.[72] Although ENDS products may not be marketed commercially as a smoking cessation aid in an explicit manner, they often are promoted this way through more implicit commercial-oriented messages on social media, along with reports of first person experiences. The majority (85.9 percent) of ENDS-related video content on YouTube is oriented toward marketing them, while about half addresses their safety. ENDS product companies and consumers tend to post videos that promote ENDS without noting the risks associated with use, while news videos are more likely to focus on their risks and safety.[73] One analysis of commercially-generated content in sponsored social media outlets and blogs found that the vast majority of leading ENDS brands used cessation-themed advertising; 82 percent of these implicitly promoted the products for cessation and 18 percent did so explicitly.[*] [74]

In addition to promotion, websites can act as communication boards for those who use non-cigarette nicotine products to share knowledge and information. Unlike traditional tobacco products like cigarettes, cigars, and smokeless tobacco, many ENDS users customize their devices and liquids to suit their personal preferences, in terms of flavors[75] and nicotine levels. An analysis of e-liquid flavors based

[*] An implicit claim used words such as "switch" or "alternative" without explicitly telling the viewer to quit, whereas explicit claims were those that had slogans that unambiguously indicated that ENDS are helpful for quitting smoking.

on information gathered from Reddit, a social media message board, found that while users expressed their preferred flavoring, some also shared their "DIY" (do-it-yourself) experience with regard to mixing flavors.[76] Sharing information on such websites can lead to misinformation and potentially dangerous outcomes, such as a user who follows bad advice and puts too much nicotine or flavorings in the e-liquid of a personalized device.

Product Design

The design and packaging of nicotine products can influence both consumers' perceptions and decisions regarding whether to buy and use them.[77] The changing design of ENDS is a good example. ENDS products have evolved from early models that closely resemble cigarettes to later generation devices that resemble pens or more elaborate mechanical objects. More than half of ENDS users began with first generation devices (commonly known as 'cigalikes' because of their physical resemblance to cigarettes), but most eventually transitioned to later generation devices, which allow the user to experience a more satisfying "hit."[78] Later generation devices deliver more nicotine than earlier ones and are more likely to be used by individuals with nicotine addiction.[79] People who use first generation device have an increased likelihood of dual use of ENDS and cigarettes because first generation devices may not adequately satisfy nicotine cravings.[80]

With regard to little cigars, an examination of tobacco industry consumer research and past marketing strategies illustrates how the tobacco industry historically used product design and other marketing techniques to increase sales and influence public perceptions of its products.[81] A planning proposal from 1968 highlights an attempt to market little cigars by advertising them as cigars with cigarette taste and mildness.[82] The reduced cigar size and the smoothness of filtered tips have also been promoted as distinct advantages of little cigars over cigarettes.[83] The overt design changes to create a market niche and distinguish little cigars from regular cigars and cigarettes underscore some of the methods used to attract more tobacco users.

Tobacco product design also plays a role in circumventing tobacco regulation. Recently, the FDA issued warning letters to four tobacco manufacturers for selling flavored cigarettes that were misleadingly labeled as little cigars or cigars to sidestep the prohibition on flavored cigarettes outlined in the 2009 *Family Smoking Prevention and Tobacco Control Act* (TCA).[84] The 2016 rule that provides the FDA the authority to monitor and regulate any product that is made or derived from tobacco now includes ENDS, cigars, and water pipe/hookah.[85] Still, the rule does not give the FDA the power to regulate all devices, particularly vaping devices, in which tobacco-derived products are used. So while the regulations do cover vaping devices that are sold with liquid nicotine, they do not regulate devices that are sold without nicotine or that are sold with nicotine-free e-liquid.[86] The absence of nicotine does not make these products safe. For instance, carbonyls and chemicals used in flavorings pose risks to users even in the absence of nicotine.[*] [87]

Flavors. The availability of a wide variety of flavorings for non-cigarette nicotine products increases their appeal relative to cigarettes,[88] which, according to the 2009 TCA, are prohibited from including flavors other than menthol or tobacco.[89] The ban on flavored cigarettes was associated with adolescent smokers switching to menthol cigarettes and to flavored non-cigarette nicotine products.[90] Menthol acts as a cooling agent to minimize the harsh taste of tobacco smoke, reinforces smoking behavior, and perpetuates nicotine addiction.[91] Menthol is particularly appealing to youth, blacks, and women who smoke.[92]

[*] See Chapter II.

Due to the TCA ban on other flavoring in cigarettes, tobacco companies have come out with many flavors for their non-cigarette products.[93] In the case of cigars, flavorings are added to mask the heavy cigar taste, reduce throat irritation, and ease the inhalation of smoke.[94] The sale of flavored little cigars over the Internet increased after the TCA ban on cigarette flavoring was introduced.[95] Most non-cigarette nicotine products contain high levels of synthetic sweeteners, sometimes exceeding by as much as 25-fold the levels or intensities of artificial sweeteners found in candy.[96] Adolescents and young adults are attracted to these flavors, which can incite curiosity and increase their willingness to try the products.[97] In fact, the majority of adolescents report flavoring as a reason for using all types of non-cigarette nicotine products.[98]

Approximately 8 in 10 adolescents who currently use nicotine products report that they first used a flavored product.[99] Approximately 7 in 10 middle and high school students who currently use nicotine products report that they have used at least one flavored product in 2014.[100] Most adults who use non-cigarette nicotine products likewise report using flavored products, especially with regard to ENDS and water pipe/hookah.[101]

ENDS products currently are sold in more than 7,000 unique flavors.[102] Most users say that the first ENDS products they used and the types they regularly use are flavored--usually fruit or candy. Among adults, the use of tobacco flavored ENDS at initiation is more common among those who use them along with cigarettes, while other ENDS flavors are more commonly used among former cigarette smokers.[103]

Flavored products tend to be perceived (inaccurately) by young people as less harmful than non-flavored products.[104] Children aged 11-16 who were exposed to advertisements for flavored e-cigarettes expressed greater interest in buying and experimenting with them than those who were exposed to advertisements for non-flavored e-cigarettes.[105] Adolescents are more likely to express an interest in trying ENDS that have menthol, candy, or fruit flavoring than in trying those that have tobacco flavoring.[106] Young adults who use ENDS find the sweet flavors most appealing, relative to tobacco- or non-flavored e-cigarettes.[107] Young adult cigarette smokers believe that fruit- and dessert-flavored products are more rewarding than non-flavored ENDS and tend to take more puffs, on average, of flavored e-cigarettes, increasing nicotine exposure and the risk of nicotine addiction.[108]

Despite evidence that flavored nicotine products are attractive to youth and young adults, the Obama administration recently overrode the FDA's call to ban all flavored nicotine products.[109] This decision came at a time when the availability of these products is increasing, along with their use, especially among youth. The rationale for the ruling was that flavored non-cigarette nicotine products appeal to current cigarette smokers and might help facilitate smoking cessation,[110] a rationale with some support in the research literature.[111] The heated debate surrounding the banning of flavored non-cigarette nicotine products underscores their critical role both in encouraging the initiation of nicotine product use and potentially helping those who smoke cigarettes to cut back or quit.

Industry Influence on Science, Policy, and Government Oversight

For decades, the tobacco industry has managed to capitalize on its influence over large segments of the scientific community as well as political officials to boost sales and limit regulation of its products. In the 1950s, when scientific evidence was mounting regarding the health risks of cigarettes, the tobacco industry responded by rallying scientists to discredit or distract from these findings. It contributed millions of dollars to the American Medical Association, which subsequently refused to endorse the 1964 Surgeon General's report that declared that cigarette smoking causes cancer, recommendations for placing warning labels on cigarette packages, or the 1971 ban on cigarette advertising in broadcast media. Dozens of Nobel Laureates have taken money from the tobacco industry for research, honoraria, or consulting.[112]

Since cigarettes and other nicotine products are legal, the tobacco industry has the right to lobby and attempt to influence legislation around its products. In 2015, tobacco companies spent over $20 million on political lobbying.[113] Tobacco firms have extensive state lobbying networks, organize advocacy campaigns and work with other allies to draft model legislation and resist proposed tobacco control regulations, including those that would restrict the availability or accessibility of ENDS--most notably higher tobacco taxes. They have given millions of dollars to state candidates, committees, and ballot initiatives nationwide, while key public health organizations that also engage in lobbying make minimal contributions to state politicians. The industry's efforts to protect their business interests, such as by limiting proposed tobacco tax increases, have shown success on the state level.[114] They run counter to tobacco control efforts and continue to be a barrier to smoking cessation and the prevention of nicotine product initiation and use.[115]

A 2011 report on menthol cigarettes by the Tobacco Products Scientific Advisory Committee (TPSAC)[*] indicated that menthol appeals to new smokers.[116] Just prior to its release, tobacco companies sought to nullify the findings by suing the FDA, the U.S. Department of Health and Human Services, and those agencies' leaders, arguing that three members of the committee had financial conflicts of interest.[† 117] In 2014, a judge ordered the removal of these members from the TPSAC and barred the FDA from using the menthol report.[118] More recently, some public health professionals have argued that the federal government's decision not to ban characterizing flavors in tobacco products may have reflected a tendency to put the interests of the tobacco industry before those of the public.[119]

Once large cigarette companies began entering the ENDS market several years ago, they started using the same tactics successfully used in the past to influence policymakers in their favor. Starting in 2010, tobacco companies began lobbying state policymakers to limit their restrictions on ENDS products; in 2013 and 2014 they spent more than $6 million on lobbying efforts in New York and California, far exceeding the amount spent by smaller, independent ENDS companies. In addition to lobbying, other strategies for influencing policies related to the regulation of ENDS included working through third parties (e.g., industry-funded think tanks, business organizations, hospitality associations, and front groups), mobilizing grassroots efforts (often through social media), making campaign contributions, and claiming that state regulations were unnecessary in the face of impending federal legislation. Local governments appear to have been more resistant to tobacco industry influence than state governments.[120]

More recently, members of Congress, along with a larger team of tobacco industry lobbyists, have sought to undermine the new 2016 FDA deeming rule which subjects ENDS and other previously unregulated tobacco-derived products to FDA regulation. They argue that the rule will harm public health by forcing out of business many ENDS companies that do not have the resources to comply with the new regulations, thereby limiting the availability of a product that many use to quit smoking. These members of Congress and the lobbyists introduced a bill to change the date on which new nicotine products are subjected to FDA premarket review from February 15, 2007 to 21 months after the date of enactment of the TCA. This change effectively would exempt many ENDS products from extensive FDA review since they were released to the market prior to that time. There is evidence that one member of Congress even introduced legislation that was copied verbatim from tobacco industry language included in draft legislation. The two most prominent supporters of curbing the FDA's control over ENDS products are among the top recipients in Congress of tobacco industry campaign contributions.[121]

[*] The TPSAC is charged with advising the Commissioner of Food and Drugs or a designee of the FDA on matters related to the regulation of tobacco products.

[†] The challenged TPSAC members acted as consultants to companies selling smoking cessation products.

Labeling and Packaging. The 2016 FDA ruling requires all tobacco or tobacco-derived product advertisements to include warning labels regarding the risks of using the products.[122] Graphic warning labels have been shown to help increase harm perceptions of tobacco products for those who have not used them.[123] This type of warning label is not required for non-cigarette nicotine products in the United States, and the attempt to include them on cigarettes, as mandated in the 2009 TCA, has been thwarted by lawsuits from tobacco companies.[124]

In addition to warning labels, other labeling issues can influence the marketability and public perceptions of a nicotine product, and tobacco companies have an interest in labeling their products in ways that will attract the most consumers. One way of doing this is to label a product as 'reduced risk.' The Modified Risk Tobacco Product application, which is overseen by the FDA, allows tobacco companies to alter warning labels and market tobacco products as 'reduced risk' only if the product has undergone extensive scientific review by the FDA attesting to the reduced risk of tobacco-related diseases (relative to other commercially marketed tobacco products).[125] Yet the FDA is reluctant to approve such labeling because it may encourage use of the product among non-users, particularly youth.[126] Lower harm perceptions have been associated with greater curiosity regarding a product--a key motivator of future use.[127] Even for those trying to reduce or quit smoking cigarettes, there is no evidence of population-level health benefits in the United States of reduced-risk labels.[128] The tobacco industry also incorporates harm-reduction and reduced-risk messages into their products' designs and promotions to present an image of corporate social responsibility.[*] However, some public health researchers argue that the focus on harm reduction is not genuine and is simply a tactic to influence policymakers.[129] Internal documents from British American Tobacco, one of the world's largest tobacco companies, indicate that the initial push for smokeless tobacco may have been influenced heavily by a desire to profit from declining cigarette sales rather than to promote a lower-risk alternative to cigarettes.[130]

As is true of cigarettes,[131] packaging for non-cigarette nicotine products can influence the product's appeal and the extent to which consumers consider the health risks associated with using it.[132] Individuals are more likely to perceive product packages that just have a text warning (compared to a graphic warning) and packages with corporate branding (compared to plain packaging) as more appealing and as the product that they would want to be seen using. Adolescents and young adults are more likely than adults to view packaging with flavor descriptors (compared to no descriptors) as appealing.[133] A 'low risk' label on snus and moist snuff packaging has been associated with reduced perceptions of harm of those products.[134]

In 2014, Swedish Match, a company that manufactures snus, tried to alter its warning label to convey a message of reduced risk to consumers.[135] Relying on international evidence of the reduced health risks of snus relative to cigarettes, Swedish Match applied for permission to include reduced-risk warning labels on their snus products.[136] The experts brought together by the FDA argued that a modified warning label did not accurately reflect snus' health risks.[137] Labels that reflect low or reduced risk can serve as an implicit marketing strategy or a promotional tool rather than a health communication tool.[138] Although the manufacturer failed to influence U.S. policy in this instance, Swedish Match North America had donated hundreds of thousands of dollars in the past to fund a university's endowed chair in tobacco harm reduction research, which was held by a researcher who supported lifting the European ban on snus and who promoted snus as an effective smoking cessation tool.[139]

[*] Corporate social responsibility is the idea that large companies can have a positive impact on the public through philanthropic or economic means.

Another fight taken on by the industry involves plain packaging rules for nicotine products.[140] Tobacco control advocates favor standardizing tobacco packaging by removing any distinctive and appealing colors, brands, designs, or logos, and making all tobacco product packages homogenous.[141] In December 2012, Australia became the first country to successfully implement a combination of plain tobacco packaging and graphic warning labels.[142] Opponents of plain packaging have argued against its effectiveness stating that the uniformity of packaging may incentivize tobacco companies to reduce sale prices, which may then increase use. They have also argued that plain packaging may act as a catalyst for illegal cigarette sales.[143] Yet research does not support these claims; in contrast, plain packaging can be an effective deterrent to tobacco product purchasing and use.[144] Despite tobacco industry resistance and threats of legal action,[145] other countries--including France, the United Kingdom, and Ireland--have signed legislation requiring plain packaging, and several more are considering this transition.[146] However, given the legal backlash from the tobacco industry against the TCA's required graphic tobacco warning labels, it is unlikely than plain tobacco packaging will be implemented in the United States in the near future.[147]

Social Influences

Social factors, such as peers' and family members' attitudes, perceptions, and behaviors with regard to nicotine product use are influential in determining one's interest in and use of these products, especially among youth.[148] However, the attitudes and perceptions of one's peers and family members are proximal social forces influenced, in turn, by larger and more distal factors, such as tobacco industry interests, the media's portrayal of nicotine product use, and public policy surrounding their regulation and use.

Over the past few decades, social influences around cigarette smoking have changed dramatically. Along with steep declines in cigarette smoking among youth, the negative social norms around smoking have increased dramatically. For example, in 2015, 85 percent of 12th grade students reported that their peers would disapprove of them smoking a pack or more of cigarettes per day, up from 69.2 percent in 1995.[149] Perceived peer disapproval of daily smoking is even higher among young adults.[150]

Changes in social norms surrounding cigarette smoking can be attributed to many factors, including accumulating and widely-promulgated research findings regarding its harmful effects, exposure of tobacco industry tactics to manipulate public perceptions of smoking, consequent tobacco control policies and regulations that restrict the accessibility of cigarettes, and regulatory restrictions on tobacco industry practices, including the marketing and distribution of cigarettes. Prevention and intervention programs--including school- and community-based initiatives, public awareness media campaigns, and improvements in smoking cessation interventions and insurance coverage--have all contributed to declines in smoking and to reversing the public's perceptions of smoking as cool, glamorous, or sexy.

Despite this hard-won public health success story, the tremendous gains achieved with regard to changes in social perceptions and acceptance of cigarette smoking over the past few decades are at risk of being undercut by the growing popularity of non-cigarette nicotine products. The advertising and promotion of ENDS products in ways that reflect old industry tactics for promoting cigarettes, the push by the tobacco industry to market little cigars with enticing flavors, and the proliferation of vape shops and hookah lounges in neighborhoods populated by young people have all begun to renormalize smoking behavior and build new barriers to eradicating nicotine use. It remains to be seen whether or to what extent these trends will undo years of progress in reducing tobacco use.

Peer Influences

Among high school students, use of cigarettes and cigars is perceived as incurring the most social risk (i.e., friends will be upset with you if you use them, you can get in trouble, they give you bad breath) and use of water pipe/hookah and ENDS is perceived as the least socially risky.[151] Students see water pipe/hookah followed by cigarettes and ENDS as the products most likely to confer social benefits--such as by making them look cool or more mature or helping them fit in--while cigars and smokeless tobacco are seen as the least likely to be socially beneficial.[152] Among college students, positive social norms are lowest for cigarettes and highest for water pipe/hookah; the perception of positive social norms is associated with use of a product.[153]

Social influences are especially important with regard to water pipe/hookah use.[154] One of the main reasons young people report for using water pipe/hookah is peer influence, including using it for social approval or 'to look cool.'[155] These products, typically used in communal settings, are associated with having friends who have used them and with socializing and partying.[156] Peer influence and the desire to please friends also are strong predictors of smokeless tobacco initiation[157] and of ENDS use.[158] Nearly half of students who use ENDS report having at least three friends who also used them.[159]

Family Influences

Family members' attitudes and behaviors with regard to nicotine product use are strong predictors of use by other family members, especially children.[160] Having parents who smoke cigarettes or living in a household with someone who smokes or uses ENDS is associated with youth initiation of both cigarette and ENDS use.[161] Living with someone who uses water pipe/hookah also is associated with an increased risk of using water pipe/hookah.[162]

The association between having a parent or living with someone who uses nicotine products and subsequent youth initiation may be influenced by the social norms that are created in a family environment or by the desire for youth to mimic their parents' or caretakers' behavior.[163] For example, adolescent males who use smokeless tobacco report that they either were emulating family members or were actively encouraged by male family members to use the product.[164] Lower levels of parental engagement or parental monitoring (e.g., parents' awareness of their children's whereabouts after school or who their friends are, openness and frequency of parent-child communication) also are associated with increased risk of using non-cigarette nicotine products.[165]

Limitations in Research and Clinical Practice

Developing a solid scientific evidence base regarding non-cigarette nicotine products is essential for counteracting the tobacco industry's push to dominate the messages the public receives about these products, specifically portraying them as relatively risk-free alternatives to cigarettes.

As outlined in Chapter I, barriers to establishing a strong evidence base include limited longitudinal and population-level studies,[*] conflicting research finding, methodological flaws,[†] and bias or conflicts of interest due to studies funded by the manufacturers of the products.[166] For example, with regard to ENDS--the non-cigarette nicotine product attracting the most attention in recent years--the current state of the scientific research makes it difficult to definitively answer critical questions related to the:

[*] Mostly in relation to water pipe/hookah and ENDS products.
[†] Such as the presence of confounding variables or inaccurate or limited naming of products in survey instruments.

- patterns of initiation and progression to regular use, use of smoked cigarettes, and addiction;
- the association between use of these products and successful smoking cessation, particularly in comparison to NRT and other cessation tools;
- long-term health effects; and
- the association between use of these products and other substance use and addiction.

Although research related to these questions is emerging at a fast pace, and is beginning to paint a clearer picture of the risk-benefit ratio with regard to these products, definitive conclusions cannot yet be drawn. Some public health professionals argue that a definitive evidence base is not necessary to enact policy when there is a potential harm to the public health.[167] However, there are drawbacks to precautionary policymaking. It may lead to inconsistent regulations across states and local regions. It also can potentially interfere with the use of these products among long-term cigarette smokers who certainly would benefit from completely switching over to tobacco-free products when accepted smoking cessation strategies have not been effective.[168]

There also is some concern that overly restricting the availability of ENDS products, specifically with regard to minimum purchase/sale age restrictions and higher taxes, can interfere with the trend toward reductions in youth cigarette smoking.[169] Research shows that changes in the relative cost of different tobacco products can encourage people to switch from more to less expensive products. As such, some public health researchers have proposed enacting differential taxes that would reflect the relative harm of different nicotine products and encourage switching from those that are most harmful (i.e., cigarettes) to those that appear to be relatively less harmful (i.e., ENDS). However, to continue to discourage initiation of ENDS or other non-cigarette nicotine product use among youth, taxes on these products should be set high, although not as high as taxes on combustible tobacco products.[170] Before implementing such proposals, however, research is needed to help policymakers enact regulations that do not inadvertently increase the risk of nicotine product initiation among youth while facilitating smoking cessation or reduction among cigarette smokers.

With regard to clinical practice, many physicians feel they are not well-informed about the risks versus benefits of non-cigarette nicotine products, especially ENDS, and their uncertainty and ambivalence about these products frequently are conveyed to patients.[171] A review of online patient-provider communications on a network that provides free medical advice found that about half of the providers' responses reflected a negative attitude toward ENDS (e.g., focusing on their risks and discouraging use), while 26 percent of the responses discussed them as smoking cessation aids. Another 20 percent presented overly positive views on ENDS (e.g., encouraging their use for smoking cessation). Among providers who recommended quitting smoking in response to patient inquiries, 31 percent suggested quitting 'cold turkey' or did not identify a formal cessation method and 15 percent recommended approved cessation techniques and did not include ENDS. Notably, more than half (54 percent) mentioned ENDS as cessation aids.[172] A national survey of pediatricians and family medicine physicians who provide primary care to adolescent patients found that an estimated 24 percent reported that they would recommend ENDS to adolescents for smoking cessation.[173] Another survey found that the majority (61 percent) of adult cigarette smokers who reported talking with their physicians about ENDS products said that their physician recommended using ENDS as a smoking cessation aid.[174] Such encouragement by physicians to use ENDS for smoking cessation is contrary to the conclusion of the United States Preventive Services Task Force (USPSTF)[*] that available evidence does not support the use of ENDS for tobacco cessation,[175] and the fact that ENDS are not approved by the FDA for this use.

[*] A panel of experts that reviews the scientific evidence related to clinical preventive health care services and develops recommendations regarding their use in primary care in the United States.

As more research evidence continues to accumulate, researchers will be able to better inform policymakers and health care professionals about the relative risks and harms of ENDS and other non-cigarette nicotine products, and recommend best practices to protect the public health. In the next chapter, we present recommendations for policy, practice, and research based on the current state of knowledge regarding non-cigarette nicotine products.

Chapter VI
Recommendations for Policy, Practice, and Research

Nicotine product use and addiction are not typically accorded adequate attention as health risks, particularly when tobacco and its considerable harms are not involved. However, non-cigarette nicotine product use itself is associated with adverse and costly health effects, including an increased risk of addiction and other substance use as well as relapse for those in treatment for alcohol and other drug addiction. Non-cigarette nicotine product use also may increase the risk of cigarette use and, in some cases, compromise smoking cessation efforts. Therefore, understanding and addressing non-cigarette nicotine product use should be a significant part of any comprehensive approach to addiction policy, prevention, and treatment and, more broadly, efforts to improve the public health.[1]

The growing popularity of non-cigarette nicotine products, coupled with a forceful push by the tobacco industry and other nicotine product manufacturers to encourage their use, underscore the need for an informed, measured, and evidence-based response. Such a response would encourage the reduction and cessation of cigarette smoking while simultaneously preventing the uptake of other, potentially risky nicotine products. A comprehensive approach is needed; one that results in well-conducted research that can inform health-promoting policies and regulations, and evidence-based prevention, early intervention, and treatment strategies.

Efforts to promote the use of non-cigarette nicotine products like ENDS in the absence of effective strategies that (1) reduce cigarette use, (2) prevent youth initiation of nicotine product use, and (3) prevent the dual use of cigarettes with non-cigarette nicotine products run the risk of increasing nicotine use and addiction on a population level, rather than decreasing it.

Based on the current state of knowledge and the regulatory landscape as of the publication date of this report, The National Center on Addiction and Substance Abuse presents the following recommendations for policy, practice, and research with regard to how best to understand and address all forms of non-cigarette nicotine product use and addiction.

Policy

Effective policies and regulations are critical for limiting youth access to nicotine-containing products, discouraging the initiation of nicotine product use, encouraging cessation, and protecting the health of nonusers exposed to environmental tobacco smoke and ENDS aerosols. Until recently, there was a significant lack of government regulation of most non-cigarette nicotine products, which allowed certain products that contained widely variable levels of nicotine, flavors, and other potentially toxic ingredients to be manufactured and sold to users of all ages without meeting basic standards of safety and labeling requirements.

Recently, this regulatory gap, which allowed nicotine products to flood the market unchecked at great cost to the public health, has begun to close. In May 2016, the U.S. Food and Drug Administration (FDA) announced a broad and significant extension of its oversight of tobacco products, granted under the 2009 *Family Smoking Prevention and Tobacco Control Act* (TCA), to include electronic cigarettes and other ENDS products, water pipe/hookah, cigars, dissolvables, and other previously unregulated tobacco and tobacco-derived (i.e., nicotine) products.[2]

This long-overdue regulatory authority, if effectively implemented and enforced, will go a long way toward bringing sensible guidelines, restrictions, and safety standards to a largely unrestricted market.

However, several critical components of a comprehensive approach to reducing the potential harms associated with nicotine-containing products remain unaddressed or insufficiently addressed within the new regulatory framework. Further, certain effective strategies, such as increasing the minimum legal sale/purchase age of all tobacco products to 21 and expanding clean indoor/outdoor air laws, lie outside of the FDA's authority, yet well within the lines of what state and local governments can do to fill in the gaps. Finally, many of the FDA provisions do not go into effect for several years, leaving ample opportunity for tobacco product manufacturers to continue to market products that may not comply with the new rules and that may threaten the public health, or to plan or initiate litigation to forestall the implementation of the new regulations.

In the face of these limitations, the FDA must do everything in its power to make all tobacco and nicotine products less toxic, less addictive, and less appealing, and to do so as quickly as possible. Congress must protect rather than undermine the FDA's regulatory authority. And state and local governments must try to fill existing gaps in federal regulation. With a few exceptions,[*] the 2009 TCA explicitly allows state and local officials to have authority over most aspects of tobacco control, permitting state and local governments to go beyond federal regulations.[† 3]

Consistent with the recommendations put forth by other leading public health organizations,[‡] we present the following recommendations for policymakers at all levels of government to help close the remaining gaps in regulatory control over the manufacture, sale, and marketing of all tobacco and nicotine-containing products.

The Federal Government

Despite not including these provisions in the May 2016 final rule, the FDA should exercise its new authority over all tobacco products and close the gaps in existing regulations by:

- Banning all characterizing flavors, including menthol, from all nicotine and tobacco products. Despite prohibiting "characterizing" flavors in cigarettes (with the exceptions of menthol and tobacco flavors), the FDA does not prohibit the use of flavors in any other nicotine product, including ENDS, little cigars, and water pipe/hookah, which typically include flavors that are highly appealing to youth.
- Restricting the advertising and marketing of all nicotine products, including ENDS, in the same way that cigarette and smokeless tobacco product advertising and marketing are restricted, and especially in ways that target or appeal to youth. This would include prohibiting product advertising on television and other media, brand name sponsorship of sporting and cultural events, and co-branding of non-tobacco products.
- Prohibiting "low-risk" or "reduced-harm" claims on all nicotine and tobacco products, as well as any implicit or explicit claims about their effectiveness as smoking cessation aids or relative

[*] The TCA prohibits state and local governments from adopting policies that are "different from, or in addition to" FDA standards related to "tobacco product standards, premarket review, adulteration, misbranding, labeling, registration, good manufacturing standards, or modified risk tobacco products."

[†] The TCA provides that state and local governments retain the authority to restrict or prohibit the "sale, distribution, possession, exposure to, access to, advertising, and promotion of, or use of tobacco products by individuals of any age." It also allows policies related to "fire safety standards for tobacco products," and permits states to require "information reporting to the State."

[‡] Including the American Academy of Pediatrics; the American College of Physicians; the Center for Tobacco Control Research and Education at the University of California, San Francisco; the Society of Behavioral Medicine; the Tobacco Control Legal Consortium at the Public Health Law Center; the Truth Initiative; and the World Health Organization.

addictiveness, unless adequate evidence is presented and the claims are approved by the FDA. If claims of reduced harm or utility as a smoking cessation aid are being made, the burden should not be on researchers to prove that the products are harmful, but rather on the industry to prove that they are safe before they can be marketed and sold.

- Implementing and enforcing product standards that minimize the health risks and addictive potential of all nicotine products (e.g., reducing the nicotine content).
- Resisting attempts by the tobacco industry to weaken or undermine the regulation of nicotine products and current efforts to protect the public health and safety.
- Prohibiting Internet sales of all nicotine products, including ENDS, their refill liquids, and water pipe/hookah products. Although the new regulations setting a minimum sale age of 18 for all tobacco products applies to online sales, this provision is very hard to enforce given the inadequate age verification procedures of most online vendors. Sites that sell nicotine products should require age verification and identification at the time of purchase and delivery.
- Setting minimum package size requirements and labeling requirements for all nicotine products.
- Requiring effective warning labels for all nicotine products regarding not only the addictive nature of nicotine, but also the health risks of the many ingredients and potentially toxic constituents that these products contain.
- Requiring manufacturers to monitor and report adverse effects of their products and removing any product from the market that does not comply with FDA regulations.
- Modifying the premarket review process for approving "new products" by prioritizing the review of products that are currently on the market and have not been reviewed (since these may be noncompliant with the new federal regulations yet are freely available) and then follow these with the review of new products that have not yet been introduced to the market.[4]
- Requiring child-resistant/tamper-evident containers and packaging on bottles and cartridges of concentrated liquid nicotine used in e-cigarettes and other ENDS products. The amount of liquid nicotine in any one package should be limited to a non-lethal dose in the event that the liquid is ingested by a child.[5]
- Encouraging and funding high impact, mass-reach health communication interventions that promote nicotine- and tobacco-free norms and inform the public of the risks of use, regardless of the delivery device. These interventions should address misconceptions in the public regarding the spectrum of risk of certain non-cigarette nicotine products. For example, they should convey that:
    - Despite being less harmful than cigarettes, ENDS products are not harmless. They contain nicotine, an addictive drug, and many contain varying amounts of other harmful ingredients and components.[6]
    - Water pipe/hookah use has similar health risks as cigarette smoking, including the ingestion of toxic chemicals, nicotine addiction, and the production of toxic environmental tobacco smoke.[7]
- Allocating funding to quality research on the prevalence, nature, correlates, and consequences of non-cigarette nicotine product use and on evidence-based prevention and early intervention initiatives that address all forms of nicotine use.
- Monitoring and evaluating the effectiveness of programs and policies targeted toward nicotine and tobacco control and prevention and making modifications based on the findings to improve outcomes.
- Encouraging Congress to reject amendments recently approved as part of the House appropriations bill, which funds the FDA. These provisions attempt to exempt certain cigars

from the new regulations[*] and restrict the FDA's requirements for new tobacco product approvals to those products that are released after the deeming regulations go into effect, rather than the February 15, 2007 grandfather date indicated in the current provisions ("the Cole-Bishop amendment").[8] These proposed provisions, if adopted by the House and Senate and signed into law, would significantly undermine the FDA's new regulatory authority over tobacco products.

State and Local Governments

State and local governments can contribute significantly to tobacco control efforts by implementing policies and regulations not covered by the FDA's rule, including:

- Increasing the minimum legal sale age for all nicotine products, including ENDS, to 21, a policy with broad public support.[9] This includes prohibiting youth under age 21 from entering hookah bars and other establishments that allow water pipe/hookah use.
- Broadening tobacco-free (smoke-free) clean indoor/outdoor air laws to include all nicotine products, including ENDS.
- Prohibiting the sale of all flavored nicotine products, including menthol.
- Prohibiting the sale of all non-cigarette nicotine products in any venues where the sale of cigarettes is prohibited.
- Instituting minimum pack size requirements on non-cigarette nicotine products, to reduce accessibility (via higher prices), and ensure that required package warnings can be displayed.
- Requiring warnings on packages that go beyond those required by the FDA regulations.
- Instituting or expanding the scope of tobacco retailer licensing laws to include non-cigarette nicotine products. This will help improve the surveillance of non-cigarette nicotine product sales and distribution and help to prevent sales to minors and evasion of tobacco excise taxes.
- Controlling retail outlet density and location by prohibiting sales and marketing of all nicotine-containing products near schools or youth-oriented facilities.
- Enhancing enforcement of laws restricting the sale of nicotine-containing products to minors by conducting routine retailer compliance checks and strengthening penalties for violators.
- Increasing pricing (through higher taxes) of nicotine products to help minimize youth initiation and use, discourage dual use, and encourage cessation.
    - Tobacco products should be taxed at a higher level than ENDS products both to discourage youth from initiating tobacco use or moving from ENDS to more harmful tobacco product use and to encourage smokers to cut back or quit.[10]
- Funding comprehensive and evidence-based programming related to prevention and cessation.
- Increasing tobacco cessation insurance coverage by:
    - Including tobacco cessation services in health care coverage provided by the state (e.g., through Medicaid, for state employees);[11]
    - Joining other states[†] in barring insurers from imposing higher premiums on cigarette smokers or using lower surcharges than those allowed by the Affordable Care Act;
    - Mandating private insurers to cover all FDA-approved treatments for nicotine addiction; and
    - Offering technical assistance to help health care organizations and providers implement and monitor policies and programs to prevent the initiation of tobacco/nicotine use and to encourage cessation.

[*] Cigars that would be exempted under the House bill would be premium and large cigars, including those that are hand rolled. Backers of the exemption argue that these cigars are generally bought and used by adults aged 45 and older.

[†] As of February 2016, CA, MA, NY, NJ, RI, VT.

Practice: Prevention, Screening, and Intervention

The best way to avoid the costly consequences of nicotine addiction is to invest in prevention and early intervention. Effective prevention is comprised of public education and awareness that helps to reduce the appeal of nicotine products, supported by laws, regulations, and policies that reduce their availability and accessibility, particularly to young people. Effective early intervention seeks to help those who already have started using nicotine products reduce or stop their use so that their health is improved, and prevent those who use nicotine from engaging in multiple nicotine product use and progressing to addiction.

Health Care Systems and Professionals

As part of routine patient care, health care professionals should do their part in preventing and treating nicotine use and addiction by:

- Being aware and knowledgeable about the risks of each type of nicotine product and about how to advise patients accordingly.
- Educating patients of all ages about the risks associated with nicotine use and identifying and correcting misconceptions about ENDS, water pipe/hookah, and other non-cigarette nicotine products. Important messages to deliver include the increased risk to youth relative to adults of developing nicotine addiction, the potential toxicants in ENDS aerosol, and the considerable health risks of non-cigarette nicotine products.[12]
- Screening all patients for all forms of nicotine product use and providing brief interventions and cessation services (counseling and pharmaceutical therapies) to those who screen positive, in accordance with the recommendations of the United States Preventive Services Task Force (USPSTF).[*] [13] Health professionals should be specific in their screening process since ENDS products come in many different forms and are referred to by different names (e.g., electronic cigarettes, e-cigarettes, e-cigs, electronic cigars, electronic hookah, e-hookah, hookah sticks, personal vaporizers, mechanical mods, vape pens, vaping devices). Health professionals should be aware that the USPSTF has concluded that the current available evidence does not support the use of ENDS for tobacco cessation.[14]
- Providing education and counseling interventions to children and adolescents to prevent the initiation of nicotine use and facilitate cessation, in accordance with the recommendations of the USPSTF.[15] Provide education and counseling to youth regarding the use of and exposure to ENDS products specifically, since their use is increasingly common among young people and there are many misperceptions among youth regarding their safety, addictive potential, and other risks.
- Screening all patients identified as engaging in nicotine product use or having nicotine addiction for alcohol and other drug use and providing them with appropriate intervention services. Nicotine use co-occurs at significantly high rates with the use of alcohol and other drugs.[16]

[*] A panel of experts that reviews the scientific evidence related to clinical preventive health care services and develops recommendations regarding their use in primary care in the United States.

Educators

The vast majority of people who use tobacco and other nicotine products initiate use during adolescence and young adulthood. Therefore, it is incumbent upon educators to play an important role in the prevention of nicotine use among youth by:

- Incorporating non-cigarette nicotine products into existing school-based tobacco prevention programs. The most effective prevention programs are age sensitive, delivered repeatedly throughout the academic career (with greatest intensity in middle school and reinforcement throughout high school and college), integrated into the curriculum, and bolstered by strong and consistent school policies that are health oriented rather than punitive in nature.[17]
- Implementing comprehensive prevention programming in a way that includes nicotine along with other addictive substances. Substance use prevention programming typically separates tobacco and nicotine use from alcohol and other drugs, perpetuating the perception of nicotine addiction as a relatively harmless form of addiction and glossing over the fact that tobacco/nicotine use and addiction overlap considerably with and increase the risk of alcohol and other drug use and addiction.[18]
- Incorporating non-cigarette nicotine products into existing surveys and assessments of student (and staff) tobacco use.
- Offering students who use nicotine products counseling, brief interventions, and cessation services or referring these students to qualified providers of these services. Educators should use a health-promoting rather than a punitive approach to encouraging students to quit.
- Offering smoking cessation services or facilitating access to such services for teachers and other school personnel. This will help promote a tobacco-free and healthy school environment and encourage and support educators to serve as positive role models for students.
- Including non-cigarette nicotine products in existing tobacco-free school and campus policies.
- Banning all types of nicotine product advertising and promotions on and near schools and campuses.
- Working with neighboring communities to promote policies that reduce nicotine product availability, accessibility, advertising, and promotion.
- Alerting parents, health care professionals, educators, clergy, and others responsible for the health and well-being of young people about the importance of preventing youth nicotine use and exposure to the second- and third-hand effects of nicotine product use; intervening early with those who show signs of risk; and addressing psychological, behavioral, and substance use problems that may co-occur with nicotine use and addiction.

Parents and Families

As is true of the prevention of all forms of substance use, parents and other adult guardians are the most important influence on whether or not a child will engage in nicotine product use. There are many things parents and other adult family members can do to help prevent youth from initiating nicotine use and to help those who already use cut back or quit, including:

- Establishing healthy patterns of communication with children, being involved in and monitoring their friendships and activities, and setting and enforcing rules regarding substance use and other risky behaviors.
- Setting a good example by not using nicotine products and, for those who do use, trying to quit.
- Conveying strong anti-use messages and educating children about the short- and long-term risks of nicotine use and the difficulty of quitting.
- Prohibiting cigarette smoking and other nicotine product use in the home and in family cars.

- Educating children about how tobacco and other nicotine product companies advertise and promote their products in ways that convey nicotine use as glamorous, mature, cool, and fun, rather than unhealthy and addictive.
- Encouraging schools and communities to be tobacco and nicotine free, to not accept funding or materials from the tobacco industry, and to implement effective and evidence-based prevention and intervention programs and policies.
- Encouraging and supporting federal, state, and local policies that reduce the availability and accessibility of all nicotine products to youth.[19]

Media

The tobacco industry has a long and sustained history of using a variety of media outlets to encourage nicotine product use. The promotion and advertising of cigarettes in the media are somewhat curtailed by federal regulations; however, limited regulations currently exist that restrict the advertising and promotion of most non-cigarette nicotine products. ENDS products currently are promoted heavily by industry-sponsored advertisements in the popular media, including on television, radio, and the Internet, and these messages are reaching young people. A recent survey found that 82 percent of 13-17 year olds and 88 percent of 18-21 year olds reported seeing an advertisement for e-cigarettes on at least one television channel in 2015.[20]

In the absence of adequate government regulation of the advertising and marketing of non-cigarette nicotine products, responsible media companies should help protect the public health and especially youth by:

- Restricting the advertising of non-cigarette nicotine products in the same way that they currently restrict cigarette advertising (especially to youth).
- Integrating anti-nicotine messages into media programming and avoid conveying the message that nicotine product use is mature, glamorous, cool, or fun.
- Encouraging studios and theaters to present evidence-based anti-nicotine use messages before any show or movie that includes nicotine product use.
- Banning brand identification of all nicotine products in television shows and movies.
- Including the presence of nicotine product use in determinations of ratings for movies, television shows, and video games.[21]

Research

In recent years, research examining the risks and benefits of non-cigarette nicotine products (on their own or in relation to cigarette use) has expanded dramatically, often yielding conflicting findings, particularly with regard to e-cigarettes and other ENDS products. One critical impediment to accurately assessing the prevalence, risks, and consequences (or benefits) of non-cigarette nicotine product use is the lack of available, up-to-date data that examine these products in depth.

Improve Surveillance

National data sets that track substance use typically do not include variables relevant to the full array of nicotine products or do not measure use of these products in any significant detail. Insufficient available data thwarts efforts to gauge:

- The prevalence of non-cigarette nicotine product use and rates of nicotine addiction;

- The populations most susceptible to using and becoming addicted to non-cigarette nicotine products (e.g., adolescents, people with psychiatric disorders) or experiencing their adverse health effects (e.g., adolescents, individuals with heart or lung disease);
- Perceptions of the harms and risks of these products;
- The short- and long-term risks and harms associated with their use or exposure to their smoke or aerosol, including the risk of:
    - initiating other tobacco/nicotine product use,
    - perpetuating cigarette smoking and addiction and impeding smoking cessation among smokers, or promoting smoking relapse among former smokers,
    - multiple tobacco/nicotine product use,
    - nicotine poisoning, respiratory complications, and other adverse health effects from intentional and unintentional exposure, and
    - alcohol and other drug use and addiction;
- The potential benefits of using these products on their own and relative to FDA-approved products in facilitating cigarette smoking cessation in a safe and effective way;
- The relationship between non-cigarette nicotine product use and alcohol and other drug addiction treatment success; and
- The association between exposure to advertising and marketing of these products and their use.

To begin to address these issues, national, state, and local surveys of tobacco and other substance use should expand the scope of their measures by including items related to a broader range of non-cigarette nicotine products, including ENDS, in their questionnaires. Critical research goals include:

- Assessing prevalence via detailed measures of recency, frequency, and intensity of use of the specific nicotine product and assessing nicotine use and addiction via measures that are applicable to non-cigarette nicotine product use.
- Administering questionnaires to youth and adults from a broad range of socio-demographic backgrounds.
- Including measures of alcohol and other drug use and addiction along with measures of nicotine product use to allow for the analysis of associations between nicotine and other substance use and addiction.
- Including measures related to the treatment of nicotine addiction in data sets that measure treatment seeking, processes, and outcomes.

Longer-term or longitudinal surveys that allow for determinations of the temporal relationships among relevant variables are the most informative way to assess the risk factors, correlates, and health consequences of non-cigarette nicotine product use; the effects of specific policies and regulations; and the benefits of prevention and intervention initiatives.[22] However, such surveys are costly to conduct. Therefore, funding should be made available to researchers to cover the costs of such longer-term investigations into the risks and benefits of non-cigarette nicotine products. Funding agencies, including the federal government, should prioritize funding for research grant applications that most effectively address key, outstanding questions in the literature. What is most needed now are well-conducted studies that directly address the current gaps in knowledge, use the most valid and reliable research techniques, allow for the generalizability of study findings to larger segments of the population, and restrict the number of caveats and limitations inherent in the study which tend to raise more questions than they answer and interfere with moving the field of knowledge forward.

An encouraging step in this direction has been the development of the *Population Assessment of Tobacco and Health (PATH) Study*, conducted jointly by the U.S. National Institutes of Health's National Institute on Drug Abuse and the FDA's Center for Tobacco Products. The *PATH Study* is a nationally

representative, longitudinal cohort study of 45,971 adults and youth in the United States, aged 12 years and older. Measures of tobacco-use patterns, risk perceptions, attitudes toward a broad range of tobacco products, initiation, cessation, relapse, and health outcomes are included in the study, as are bio-specimens collected from consenting adult participants, aged 18 years and older, to measure biomarkers of exposure and potential harm related to tobacco and nicotine product use.[23]

Improve Assessment Scales for Research and Clinical Purposes. Measures to assess or diagnose the presence of nicotine addiction both in clinical practice and for research purposes need to be adapted to non-cigarette nicotine products. The scales that are currently in common use include items specific to cigarette smoking, such as *"How soon after you wake up do you smoke your first cigarette?"*[24] However, several measures are being adapted, developed, and validated that can be applied to non-cigarette nicotine products.[25] Some researchers have called for product-specific measures of addiction since the risk of addiction varies by nicotine content and by the properties of the nicotine delivery device; however, this approach has certain disadvantages, especially in terms of being able to compare addiction across nicotine products.[26] More research is needed to develop scales that assess nicotine addiction independent of the product or delivery device and that can be validated by biomarkers of nicotine addiction.

Include Non-Cigarette Nicotine Product Use in Electronic Health Records. For both research and clinical purposes, data entered into electronic health records should include discrete and detailed information regarding the use of non-cigarette nicotine products, including ENDS, to allow for effective health surveillance, research, and clinical intervention.[27] From a population health perspective, this information can serve as a basis for epidemiological research on the prevalence and effects of ENDS and other non-cigarette nicotine products. Clinically, such information can help health care professionals initiate nicotine cessation interventions and identify adverse events or health risks that may be associated with the use of these products. Ideally, data entry should include as many of the following variables as possible: status of use; frequency and duration of use; type of nicotine products used; cessation attempts; side effects; and concurrent use of other nicotine products, alcohol, and other drugs.[28]

Improve Understanding and Documentation of the Contents (and Toxicity) of Non-Cigarette Nicotine Products

Until the new FDA regulations go into full effect, it will continue to be difficult to determine the exact contents of non-cigarette nicotine products, especially ENDS,[29] due to limited quality controls, standards, and requirements regarding their ingredients or design. Products vary dramatically (even within the same product type or brand) in nicotine content, flavoring, and other chemicals and toxicants. One result of this broad variability is that some products that are examined for adverse effects may reveal few, whereas others may reveal themselves to be even more toxic than cigarettes. Accurately assessing the components and ingredients of non-cigarette nicotine products is essential for determining their continuum of risk and the extent to which they might be less harmful alternatives to cigarettes, both for the user and for those environmentally exposed to them. Therefore, the FDA should require manufacturers of new or altered nicotine products to submit accurate information about all product devices, components, and ingredients--including additives, nicotine, flavorings--for review and to disclose such information and relevant warnings on their products' packaging.[30]

Conclusions

The physical health risks of non-cigarette nicotine products are well established: use can lead to addiction and other chronic diseases, including cancer. The federal government will now regulate these products in a manner similar to cigarettes.[31] But non-cigarette nicotine products do not contain all the same toxicants as cigarettes, potentially making them less harmful. There remains considerable debate regarding the

risks and potential benefits of non-cigarette nicotine product use, especially ENDS, both in absolute terms and relative to the use of cigarettes. If indeed they are proven to be less harmful, then over-regulating these products might interfere with their potential to help reduce the harm to the public health associated with tobacco product use. Determining the best approach to controlling the use of these products and protecting the public health depends in large part on accumulating more definitive evidence regarding their risks as well as their potential to facilitate smoking cessation. Still, emerging evidence appears to be pointing to the conclusion that the risks and harms of these products outweigh their benefits. And the evidence is clear that nicotine use, regardless of the delivery device, can lead to addiction and other adverse health effects.

The solution to the current lack of certainty regarding the risks and benefits of non-cigarette nicotine products is not inaction. Evidence-based government policies, health care practice, and prevention initiatives can help to protect people, especially youth, from the harms of nicotine and other addictive substances. The new FDA regulatory authority over all tobacco products is a critical first step in helping to ensure that the current proliferation of non-cigarette nicotine products do not become our nation's next public health crisis. But more needs to be done to implement a comprehensive, research-based approach to curbing all forms of tobacco and nicotine product use and their associated costly health effects.

Appendix

There are several national data sets that track and report information about nicotine product use among youth and adults. The surveys that focus specifically on tobacco/nicotine use are those conducted through a collaborative effort by the U.S. Centers for Disease Control and Prevention (CDC) and the U.S. Food and Drug Administration (FDA): the National Adult Tobacco Survey (NATS) and the National Youth Tobacco Survey (NYTS). Data from these surveys commonly are used to present prevalence estimates and patterns of different forms of nicotine product use in the United States.

Data Analysis Methodology in Chapter III

For the present report, The National Center on Addiction and Substance Abuse conducted analyses of the most recent publicly available data on adults (from 2013-2014) and on 2014 data on middle and high school students. Although 2015 data on students became available just prior to publication of this report, we decided to present the data from 2014 so that it would be more comparable to the data collection period for the adult survey. A comparison of the prevalence estimates from the 2014 and 2015 student surveys indicate that the only significant changes were in reported current use of e-cigarettes, which increased among middle school students (from 3.9 percent in 2014 to 5.3 percent in 2015), and in reported current use of water pipe/hookah, which decreased among high school students (from 9.4 percent in 2014 to 7.2 percent in 2015). No other statistically significant changes were found from 2014 to 2015, including in rates of reported use of e-cigarettes among high school students, use of water pipe/hookah among middle school students, or use of cigarettes, cigars, smokeless tobacco, pipe tobacco, or bidis among middle or high school students.[1]

National Adult Tobacco Survey (NATS): Data from 2013-2014

The National Adult Tobacco Survey (NATS) is a stratified, random digit dialed (RDD), telephone survey of non-institutionalized adults, aged 18 years and older. The purpose of the survey, conducted between October 2013 and October 2014, was to determine the prevalence and correlates of tobacco use behaviors among a nationally representative sample of adults in the United States.

A total of 75,233 qualified interviews were completed (70,487 full interviews and 4,746 eligible partial interviews). Eligible partial interviews consist of records where the respondent answered all the questions up to the first demographic question in the survey (marital status) and 59 percent of the total number of interview questions. The completion threshold of 59 percent was based on common industry practices for similar health-related surveys and ensured that eligible interviews included all questions needed to determine smoking status and use of all tobacco products included in the survey.

NATS data were weighted to provide national estimates of the non-institutionalized adult population, aged 18 years and older. Estimates were considered statistically unreliable for sample sizes of less than 50[2] and noted in the tables with a dash (–).

Statistical analyses were conducted for group comparisons that appear in the text of Chapter III. Chi-square tests were used to compare two groups (e.g., sex; single vs. multiple nicotine product users) and logistic regression analyses were used for comparisons between more than two groups (e.g., racial/ethnic categories). The comparison group for the analyses of differences by race/ethnicity was "white, non-Hispanic" and the comparison group for age-related analyses in the NATS was adults aged 18-24. Test results with a p-value of less than 0.05 were considered statistically significant and such differences are

described in the text of Chapter III with terms such as "higher" or "lower" (e.g., "nicotine addiction was higher among females than males").

Lifetime Use. Based on documented differences in the patterns of tobacco product use, NATS assessed varying thresholds of lifetime use to separate established users from experimenters and nonusers. Usage thresholds were as follows: cigarettes (≥100 times; n=32,359), cigars/cigarillos/filtered little cigars (≥50 times; n=8,459), regular pipes (≥50 times; n=4,611), water pipe/hookah (≥1 time; n=7,078), e-cigarettes (≥1 time; n=10,099), chewing tobacco/snuff/dip (≥20 times; n=6,105), snus (≥1 time; n=3,816), and dissolvable nicotine products (≥1 time; n=189).

Current Use. Respondents who met the lifetime thresholds were asked if they "now" used the product "every day," "some days," or "not at all." A response option of "rarely" was include for tobacco products other than cigarettes. The "rarely" option was added because cognitive testing suggested that some people who use non-cigarette nicotine products do not consider "some days" or "not at all" to accurately reflect their usage pattern. The number of respondents who indicated that they "now" use each tobacco product was as follows: cigarettes (n=10,195), cigars/cigarillos/filtered little cigars (n=3,867), water pipe/hookah (n=1,956), pipes (n=739), e-cigarettes (n=3,551), chewing tobacco/snuff/dip (n=2,015), snus (n=464), and dissolvable nicotine products (n=22).

Data Analysis for Measures of Current Nicotine Use, Addiction, Quit Attempts, and Former Use. Analysis of current use by type of product used, addiction, and quit attempts was conducted among respondents with no missing data on current nicotine product use. Of the 75,233 respondents, 73,507 had no missing data on current nicotine use (97.7 percent of the sample). Analysis of former nicotine use was conducted among respondents with no missing data on lifetime or current nicotine product use; those who indicated lifetime but no current use were defined as former users of nicotine products. Of the 75,233 adult respondents, 73,435 met these criteria (97.6 percent of the sample).

Sample Sizes Used for Analysis of NATS Data, 2013-2014		
	Sample Sizes for Analysis of Current Use by Type of Product Used, Addiction, and Quit Attempts (Among those with Complete Data on Current Use)	**Sample Sizes for Analysis of Former Use (Among those with Complete Data on Lifetime and Current Use)**
	N=73,507	**N=73,435**
Any nicotine product use	**14,986**	**38,610**
Any non-cigarette nicotine product use	**8,906**	**22,854**
Smoked (including cigarettes)	**13,118**	**36,564**
Cigarettes	10,195	31,570
Smoked (not including cigarettes)	**5,278**	**15,036**
Cigars/cigarillos/little cigars	3,876	8,244
Pipes	739	4,415
Water pipe/hookah	1,956	6,897
ENDS/E-cigarettes	**3,551**	**9,841**
Smokeless	**2,065**	**7,529**
Chewing tobacco/snuff/dip	2,015	5,889
Snus	464	3,721
Dissolvable products	22	182

Demographic Data

Sex. Respondents' sex was assessed by asking them to indicate if they considered themselves to be male (n=32,096) or female (n=42,234).

Race/ethnicity. Respondents' race/ethnicity was assessed by asking whether they were "Hispanic or Latino/a, or of Spanish origin." Respondents who reported "yes" were categorized as Hispanic (n=5,665) and respondents who reported "no" were asked which one or more of the following categories they considered themselves: white (n=56,972), black or African American (n=6,384), Asian (n=1,956), or American Indian or Alaska Native (n=1,043). Respondents who reported more than one racial/ethnic category were classified as multiracial (n=1,340). Due to small sample size, respondents who indicated they were Native Hawaiian/Pacific Islander (n=277) were not included in the comparisons by race/ethnicity.

Age. Respondents were asked "What is your age?" and grouped into four age categories based on the CDC's tobacco use reporting standards:[3] 18-24 (n=4,796), 25-44 (n=17,037), 45-64 (n=27,429), and 65 and older (n=24,806).

Missing Data. There were statistically significant sex and age differences in missing data. Males and older respondents were more likely than females and younger respondents, respectively, to have missing data on lifetime/current and current nicotine product use.

Complete (Non-missing) Nicotine Product Use Data by Sex and Age, NATS: 2013-2014

	Total	Complete Data for Lifetime/Current Use		Complete Data for Current Use	
	N	N	%	N	%
Total	**75,233**	**73,435**	**97.6**	**73,507**	**97.7**
Sex	**74,330**	**72,590**	**97.7**	**72,662**	**97.8**
Male	32,096	31,158	97.1	31,210	97.2
Female	42,234	41,432	98.1	41,452	98.2
Age	**74,068**	**72,408**	**97.8**	**72,408**	**97.8**
18-24	4,796	4,697	97.9	4,737	98.8
25-44	17,037	16,728	98.2	16,760	98.4
45-64	27,429	26,876	98.0	26,876	98.0
≥65	24,806	24,035	96.9	24,035	96.9

National Youth Tobacco Survey (NYTS): Data from 2014

The National Youth Tobacco Survey (NYTS) is a cross-sectional, school-based, self-administered, pencil-and-paper survey of U.S. middle and high school students. Information is collected to monitor the impact of comprehensive tobacco control policies and strategies and inform the FDA's regulatory actions. A three-stage cluster sampling procedure was used to generate a nationally representative sample of U.S. students who attend public and private schools in grades 6–12. Of 258 schools selected for the 2014 NYTS, 207 (80.2 percent) participated, with a sample of 22,007 (91.4 percent student participation rate) among 24,084 eligible students. The overall participation rate was 73.3 percent.

NYTS data were weighted to provide national estimates of middle and high school students. Estimates were considered statistically unreliable for sample sizes of less than 50[4] and noted in the tables with a dash (–).

Statistical analyses were conducted for group comparisons that appear in the text of Chapter III. Chi-square tests were used to compare two groups (e.g., sex; single vs. multiple nicotine product use). Logistic regression analyses were used for comparisons between more than two groups (e.g., race/ethnicity categories). The comparison group for the analyses of differences by race/ethnicity was "white, non-Hispanic" and the comparison group for age-related analyses was students aged 9-13. Test results with a p-value of less than 0.05 were considered statistically significant and such differences are described in the text of the chapter with terms such as "higher" or "lower" (e.g., "nicotine addiction is higher among females than males").

Lifetime use. Respondents were asked whether they ever used nicotine products. Usage thresholds were as follows: tried cigarettes, even 1 or 2 puffs (n=4,856); tried cigars/cigarillos/little cigars, even 1 or 2 puffs (n=3,796); and ever used bidis (n= 367), water pipe/hookah (n=2,980), pipe tobacco (n=716), e-cigarettes (n=4,214), chewing tobacco/snuff/dip (n=1,716), snus (n=672), or dissolvable tobacco products (n=275).

Current use. Respondents were asked on how many days during the past 30 days they used cigarettes (n=1,392), cigars/cigarillos/little cigars (n=1,194), pipe tobacco (n=244), water pipe/hookah (n=1,349), bidis (n=144), e-cigarettes (n=2,017), chewing tobacco/snuff/dip (n=795), snus (n=269), or dissolvable tobacco (n=111). Current use for each product was defined as use on one or more day during the past 30 days.

Data Analysis for Measures of Current Nicotine Use, Quit Attempts, and Former Use. Analysis of current use by type of product used and quit attempts was conducted among respondents with no missing data on current nicotine product use. Of the 22,007 respondents, 20,325 had no missing data on current nicotine use (92.4 percent of the sample). Analysis of former nicotine use was conducted among respondents with no missing data on lifetime or current nicotine product use; those who indicated lifetime but no current use were defined as former users of nicotine products. Of the 22,007 respondents, 19,476 met these criteria (88.5 percent of the sample).

Sample Sizes Used for Analysis of NYTS Data, 2014		
	Sample Sizes for Analysis of Current Use by Type of Product Used and Quit Attempts (Among those with Complete Data on Current Use)	**Sample Sizes for Analysis of Former Use (Among those with Complete Data on Lifetime and Current Use)**
	N=20,325	**N=19,476**
Any nicotine product use	**3,202**	**6,207**
Any non-cigarette nicotine product use	**2,985**	**5,572**
Smoked (including cigarettes)	**2,336**	**5,351**
Cigarettes	1,392	3,912
Smoked (not including cigarettes)	**1,892**	**4,148**
Cigars/cigarillos/little cigars	1,194	3,073
Pipes	244	569
Water pipe/hookah	1,349	2,504

Sample Sizes Used for Analysis of NYTS Data, 2014 (continued)		
Bidis	144	290
ENDS/E-cigarettes	**2,017**	**3,486**
Smokeless	**711**	**1,611**
Chewing tobacco/snuff/dip	795	1,388
Snus	269	538
Dissolvable products	111	209

Demographic Data

Sex. Respondents' sex was assessed by asking: "What is your sex?" (male n=11,150; female n=10,645).

Race/ethnicity. Respondents' race/ethnicity was assessed by asking whether they were "Hispanic, Latino/a, or of Spanish origin." Respondents who reported "yes" were categorized as Hispanic (n=6,081) and respondents who reported "no" were asked which one or more of the following categories they considered themselves: white (n=8,820), black or African American (n=3,226), Asian (n=932), Native Hawaiian/Pacific Islander (n=85), or American Indian or Alaska Native (n=333). Respondents who reported more than one racial/ethnic category were classified as multiracial (n=1,323).

Age. Respondents were asked "How old are you?" Options ranged from 9-19 years old and grouped into the following categories: 9-13 (n=8,078), 14-17 (n=11,910), and 18-19 (n=1,862).

Missing Data. There were statistically significant demographic differences in missing data on lifetime/current and current nicotine product use, with missing data more likely among males than females; among black, Hispanic, and American Indian students than among white and Asian students; and among students aged 9-13 and 18-19 than among those aged 14-17.

Complete (Non-missing) Nicotine Product Use Data by Sex, Race/Ethnicity, and Age, NYTS: 2014					
	Total	**Complete Data for Lifetime/Current Use**		**Complete Data for Current Use**	
	N	**N**	**%**	**N**	**%**
Total	**22,007**	**19,476**	**88.5**	**20,325**	**92.4**
Sex	21,795	19,365	88.9	20,197	92.7
Male	11,150	9,715	87.1	10,190	91.4
Female	10,645	9,650	90.7	10,007	94.0
Race/ethnicity	**20,715**	**18,554**	**89.6**	**19,312**	**93.2**
White	8,820	8,196	92.9	8,414	95.4
Black	3,226	2,777	86.1	2,935	91.0
Hispanic	6,081	5,219	85.8	5,518	90.7
Asian	932	870	93.4	896	96.1
American Indian	333	295	88.6	305	91.6
Multiracial	1,323	1,197	90.5	1,244	94.0
Age	**21,850**	**19,404**	**88.8**	**20,243**	**92.7**
9-13	8,078	7,156	88.6	7,478	92.6
14-17	11,910	10,640	89.3	11,082	93.1
18-19	1,862	1,608	86.4	1,683	90.4

Nicotine Addiction

The NATS and NYTS do not include a measure of nicotine addiction for non-cigarette nicotine products but instead assess a number of addiction-related symptoms. To estimate nicotine addiction, we relied on those symptoms measured in the NATS and NYTS questionnaires that were consistent with a three-symptom index developed by Strong and colleagues (2015):[5]

> "When selecting symptoms for an efficient index of ND [nicotine dependence] across tobacco-use groups, we established four primary criteria. We looked to (a) minimize redundancy of the content covered by symptom inquiries, (b) ensure coverage of a broad range of levels of ND, (c) select symptoms providing strong discrimination (information), and (d) select symptoms with least DIF [Differential Item Functioning] across use groups. Using these four guidelines, we selected a set of five symptoms: (1) want to/try to stop or cut down; (2) using just after getting up; (3) using tobacco more than intended; (4) using much more to get effect; and (5) nicotine withdrawal syndrome. We further selected a 3-symptom index using the same criteria and included symptoms 1, 2, and 4."

Symptoms we determined to be most consistent with Strong and colleagues' three-symptom index were: "reported daily use of any nicotine product,"* "usually using a nicotine product within 30 minutes of waking,"† and "a quit attempt of all nicotine products in the past 12 months" (unsuccessful because respondent still uses).‡ Respondents who reported these three symptoms were classified as having nicotine addiction in the present analyses. Other symptoms of addiction that were assessed in the surveys but not included in the addiction index were: a strong craving or need to use, difficulty thinking of anything else except use, and feeling irritable when not using.

The NYTS only included measures of daily use for cigarettes, cigars, ENDS/e-cigarettes, and chewing tobacco/snuff/dip. Therefore, nicotine addiction was assessed only among respondents who reported using those products and who had no missing data on current nicotine product use (n=2,800).

As discussed in Chapter I, the term "nicotine addiction" is defined inconsistently in the scientific literature; some researchers use the more comprehensive Diagnostic and Statistical Manual of Mental Disorders (DSM) diagnostic code for a tobacco use disorder, while others use a subset of symptoms considered to be indicative of physiological dependence. For example, in the case of cigarettes, smoking every day and within 30 minutes of waking and having unsuccessful attempts to quit have been considered key symptoms of addiction.[6] Unless otherwise indicated, the three-symptom definition of addiction outlined above was used to estimate the prevalence of nicotine addiction in the NATS and NYTS survey data.

Limitations

The findings presented in Chapter III and in the tables below are subject to several limitations. First, data were self-reported; therefore, the findings are subject to recall and response bias. Second, data related to nicotine product use were estimated only among respondents with no missing data on nicotine product

* For adults, reporting that they "now" use the nicotine product daily and, for students, reporting that they used the nicotine product on all 30 days during the past 30 days.
† For adults, reporting usually first using a nicotine product within 30 minutes after waking up and, for students, reporting wanting to use a nicotine product within 30 minutes after waking up.
‡ Reporting yes to the following question: "During the past 12 months, did you stop using all kinds of tobacco products for more than one day because you were trying to quit using tobacco?"

use, potentially skewing the generalizability of the results. Finally, NYTS only recruited middle and high school students from public and private schools in the United States; therefore, the findings might not be generalizable to young people who are home-schooled, have dropped out of school, or are in detention centers or otherwise institutionalized.

Detailed Data Tables for Analyses Presented in Chapter III

Current Single vs. Multiple Nicotine Product Use Among Adults by Nicotine Product

Table 1
Most Prevalent Combinations of Nicotine Product Use Among Adults Who Reported Current Nicotine Product Use, 2013-2014 (Percent)

Single product use	**62.5**
Cigarettes	37.3
Cigars	8.6
Chewing tobacco	5.5
Hookah	5.5
ENDS/e-cigarettes	4.8
Pipe	0.7
Snus	0.1
Dissolvable products	0.0
Dual product use combinations	**24.4**
Cigarettes and ENDS/e-cigarettes	10.2
Cigarettes and cigars	5.5
Cigars and water/pipe hookah	1.4
Cigarettes and chewing tobacco	1.3
Cigarettes and hookah	1.2
Poly-product use combinations	**13.1**
Cigarettes, ENDS/e-cigarettes, and cigars	2.3
Cigarettes, ENDS/e-cigarettes, and water pipe/hookah	1.6
Cigarettes, ENDS/e-cigarettes, cigars, and water pipe/hookah	1.2

Note: The table presents combinations of nicotine product use that were endorsed by more than 1 percent of respondents who reported current nicotine product use. There were 18 other combinations (4.8 percent total) of dual use patterns that did not exceed 1 percent and 86 combinations (8.1 percent total) of poly-product use patterns that did not exceed 1 percent.

Analysis of data from the 2013-2014 National Adult Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nats/).

Current Single vs. Multiple Nicotine Product Use Among Adults by Patterns of Use and Demographics

Table 2
Single vs. Multiple Nicotine Product Use Among Adults Who Reported Current Nicotine Product Use by Patterns of Use and Demographics, 2013-2014 (Percent)

	Single Nicotine Product Use			Multiple Nicotine Product Use		
	Any Single Nicotine Product Use	**Cigarettes Only**	**Non-Cigarette Nicotine Products Only**	**Any Multiple Nicotine Product Use**	**Non-Cigarette Nicotine Products (with Cigarettes)**	**Non-Cigarette Nicotine Products (without Cigarettes)**
Total	62.5	37.3	25.2	37.5	29.8	7.6
Sex						
Male	58.9	29.0	29.9	41.1	31.0	10.1
Female	67.9	50.0	17.9	32.1	28.4	3.7
Race/Ethnicity						
White	61.3	35.2	26.1	38.7	31.0	7.7
Black	71.9	50.7	21.2	28.1	24.0	4.0
Hispanic	61.2	36.3	24.9	38.8	28.7	10.1
Asian	64.0	28.0	36.0	36.0	25.5	10.5
American Indian	61.8	18.7	43.1	38.2	32.4	5.8
Multiracial	54.9	35.2	19.7	45.1	38.6	6.5
Age						
18-24	44.8	12.1	32.7	55.2	36.8	18.3
25-44	59.2	35.0	24.2	40.8	33.3	7.5
45-64	72.9	51.4	21.5	27.1	24.7	2.4
≥65	82.6	56.0	26.6	17.4	14.6	2.8

Analysis of data from the 2013-2014 National Adult Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nats/).

Nicotine Addiction Among Adults Who Reported Current Single vs. Multiple Nicotine Product Use by Patterns of Use and Demographics

Table 3
Nicotine Addiction Among Adults Who Reported Current Single vs. Multiple Nicotine Product Use by Patterns of Use and Demographics, 2013-2014 (percent)

	Single Nicotine Product Use			Multiple Nicotine Product Use		
	Any Single Nicotine Product Use	Cigarettes Only	Non-Cigarette Nicotine Products Only	Any Multiple Nicotine Product Use	Non-Cigarette Nicotine Products (with Cigarettes)	Non-Cigarette Nicotine Products (without Cigarettes)
Total	12.6	18.2	4.5	19.0	22.6	4.5
Sex						
Male	10.9	17.3	4.6	18.4	22.8	4.7
Female	15.0	18.9	3.9	20.2	22.3	3.9
Race/Ethnicity						
White	13.4	19.6	4.9	19.5	23.0	5.5
Black	15.3	19.6	5.2	25.6	29.0	5.4
Hispanic	6.6	10.4	1.0	13.6	17.6	2.2
Asian	8.6	14.0	4.3	9.2	12.9	0.0
American Indian	19.2	21.2	14.8	16.3	18.6	3.1
Multiracial	8.9	12.5	2.3	20.3	23.3	2.3
Age						
18-24	4.1	11.8	1.3	12.6	17.1	3.6
25-44	13.4	19.1	5.1	20.4	24.2	3.6
45-64	15.8	19.6	6.9	24.5	25.6	12.8
≥65	10.5	14.0	3.1	17.5	19.9	4.4

Analysis of data from the 2013-2014 National Adult Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nats/).

Symptoms of Nicotine Addiction Among Adults Who Reported Current Single vs. Multiple Nicotine Product Use

Table 4
Symptoms of Nicotine Addiction Among Adults who Reported Current Single vs. Multiple Nicotine Product Use by Patterns of use and Type of Product Used, 2013-2014 (Percent)

	Any Nicotine Product Use	Single Nicotine Product Use			Multiple Nicotine Product Use		
		Any Single Nicotine Product Use	Cigarettes Only	Non-Cigarette Nicotine Products Only	Any Multiple Nicotine Product Use	Non-Cigarette Nicotine Products (with Cigarettes)	Non-Cigarette Nicotine Products (without Cigarettes)
Any symptom of nicotine addiction	82.5	80.0	95.1	57.8	86.7	94.2	57.3
Daily use	60.8	56.5	46.5	11.6	68.0	38.1	3.7
Use within 30 minutes of waking	34.4	31.4	45.5	10.6	39.4	46.7	10.7
Unsuccessful quit attempt	47.8	46.2	50.1	40.2	50.4	54.0	35.9
Strong craving or need to use	55.9	50.0	67.5	24.1	65.7	75.1	29.4
Difficult to think of anything else except use	14.2	11.7	16.9	4.0	18.4	21.9	4.8
Irritable when not using	27.6	24.3	33.9	10.2	33.1	38.6	11.6

Analysis of data from the 2013-2014 National Adult Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nats/).

Current Single vs. Multiple Nicotine Product Use Among Middle and High School Students by Nicotine Product

Table 5
Most Prevalent Combinations of Nicotine Product Use Among Middle and High School Students Who Reported Current Nicotine Product Use, 2014 (Percent)

Single product use	**50.1**
ENDS/e-cigarettes	19.4
Hookah	11.8
Cigarettes	6.5
Cigars/cigarillos/little cigars	6.5
Chewing tobacco/snuff/dip	5.3
Pipes	0.2
Bidis	0.2
Dissolvable nicotine products	0.1
Snus	0.0
Dual product use combinations	**24.0**
ENDS/E-cigarettes and water pipe/hookah	6.6
Cigarettes and ENDS/e-cigarettes	4.3
Cigarettes and cigars	2.1
ENDS/e-cigarettes and cigars	2.0
Cigarettes and water pipe/hookah	1.9
Cigars and water pipe/hookah	1.5
Poly-product use combinations	**26.0**
Cigarettes, ENDS/e-cigarettes, and cigars	2.6
Cigarettes, ENDS/e-cigarettes, cigars, and water pipe/hookah	2.6
Cigarettes, ENDS/e-cigarettes, and water pipe/hookah	2.0

Note: The table presents combinations of nicotine product use that were endorsed by more than 1 percent of respondents who reported current nicotine product use. There were 17 other combinations (5.6 percent total) of dual use patterns that did not exceed 1 percent or that did not have a sample size greater than 50. There were 140 combinations (18.8 percent total) of poly-product use patterns that did not exceed 1 percent or that did not have a sample size greater than 50.

Analysis of data from the 2014 National Youth Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nyts/).

Current Single vs. Multiple Nicotine Product Use Among Middle and High School Students by Patterns of Use and Demographics

Table 6
Single vs. Multiple Nicotine Product Use Among Middle and High School Students Who Reported Current Nicotine Product Use by Patterns of Use and Demographics, 2014 (Percent)

	Single Nicotine Product Use			Multiple Nicotine Product Use		
	Any Single Nicotine Product Use	**Cigarettes Only**	**Non-Cigarette Nicotine Products Only**	**Any Multiple Nicotine Product Use**	**Non-Cigarette Nicotine Products (with Cigarettes)**	**Non-Cigarette Nicotine Products (without Cigarettes)**
Total	**50.1**	**6.5**	**43.6**	**49.9**	**30.3**	**19.6**
Sex						
Male	47.8	5.7	42.1	52.2	31.0	21.2
Female	53.3	7.6	45.7	46.7	29.5	17.2
Race/Ethnicity						
White	44.1	6.8	37.4	34.9	21.0	21.1
Black	70.2	7.9	62.3	18.0	11.8	12.1
Hispanic	55.2	5.4	49.8	25.4	19.4	19.4
Asian	57.1	5.9	51.2	22.4	20.4	20.1
American Indian	42.3	7.9	34.4	41.8	15.9	
Multiracial	50.2	6.3	43.9	28.7	21.1	21.1
Age						
9-13	60.6	6.8	53.8	39.4	28.2	11.2
14-17	51.4	6.7	44.7	48.6	29.3	19.3
18-19	37.8	5.6	32.3	62.2	36.3	25.8

Analysis of data from the 2014 National Youth Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nyts/).

Nicotine Addiction Among Middle and High School Students Who Reported Current Single vs. Multiple Nicotine Product Use by Patterns of Use and Demographics

Table 7
Nicotine Addiction Among Middle and High School Students Who Reported Current Single vs. Multiple Cigarette, ENDS/E-cigarette, Cigar, or Chewing Tobacco Use by Patterns of use and Demographics, 2014 (Percent)

	Single Nicotine Product Use			Multiple Nicotine Product Use		
	Any Single Nicotine Product Use	**Cigarettes Only**	**Non-Cigarette Nicotine Products Only**	**Any Multiple Nicotine Product Use**	**Non-Cigarette Nicotine Products (with Cigarettes)**	**Non-Cigarette Nicotine Products (without Cigarettes)**
Total	**1.0**	**4.6**	**0.3**	**5.9**	**9.2**	**0.7**
Sex						
Male	0.9	3.9	0.4	5.8	9.2	0.7
Female	1.2	5.4	0.0	6.1	9.3	0.6
Race/Ethnicity						
White	1.6	6.4	0.5	7.1	11.2	0.3
Black	0.0	–	0.0	0.6	1.0	–
Hispanic	0.5	–	0.0	1.2	1.4	1.0
Asian	–	–	–	–	–	–
American Indian	–	–	–	–	–	–
Multiracial	1.3	–	0.0	15.1	23.3	–
Age						
9-13	0.0	–	0.0	1.9	2.6	0.0
14-17	1.4	6.3	0.4	5.9	9.5	0.5
18-19	0.0	–	0.0	7.6	12.0	1.3

Analysis of data from the 2014 National Youth Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nyts/).

Symptoms of Nicotine Addiction
Among Middle and High School Students Who Reported Current Single vs. Multiple Nicotine Product Use

Table 8
Symptoms of Nicotine Addiction Among Middle and High School Who Reported Current Single vs. Multiple Nicotine Product Use by Patterns of use and Type of Product Used, 2014 (Percent)

	Any Nicotine Product Use	Single Nicotine Product Use			Multiple Nicotine Product Use		
		Any Single Nicotine Product Use	Cigarettes Only	Non-Cigarette Nicotine Products Only	Any Multiple Nicotine Product Use	Non-Cigarette Nicotine Products (with Cigarettes)	Non-Cigarette Nicotine Products (without Cigarettes)
Any symptom of nicotine addiction	51.4	34.9	64.8	30.4	68.0	79.6	50.0
Daily use	16.7	6.1	4.7	13.7	27.3	65.2	16.3
Use within 30 minutes of waking up	11.7	3.9	14.4	2.3	19.6	28.5	5.9
Unsuccessful quit attempt	29.5	20.9	41.1	17.9	38.2	46.2	25.9
Strong craving or need to use	31.5	17.7	42.7	14.0	45.2	59.1	23.8
Difficult to think of anything else except use	16.5	9.0	28.2	6.1	24.1	32.7	10.9
Irritable when not using	24.9	12.5	41.0	8.2	37.4	49.4	18.8

Analysis of data from the 2014 National Youth Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nyts/).

Quit Attempts
Among Adults by Patterns of Use and Demographics

Table 9
Quit Attempts in the Past Year Among Adults Who Reported Current Nicotine Product Use by Patterns of Use and Demographics, 2013-2014 (Percent)

	Any Nicotine Product Use	Cigarettes Only	Non-Cigarette Nicotine Products (with or without Cigarettes)
Total	**47.8**	**50.1**	**46.4**
Sex			
Male	46.3	50.3	44.6
Female	50.0	49.9	50.0
Race/Ethnicity			
White	44.0	44.7	42.5
Black	58.2	60.1	56.1
Hispanic	53.1	59.7	49.2
Asian	56.2	53.6	57.2
American Indian	48.3	46.9	49.4
Multiracial	48.9	46.3	50.3
Age			
18-24	48.7	57.9	47.4
25-44	49.8	53.7	47.7
45-64	46.4	47.9	44.8
≥65	41.2	42.5	39.6

Analysis of data from the 2013-2014 National Adult Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nats/).

Quit Attempts
Among Middle and High School Students by Patterns of Use and Demographics

Table 10
Quit Attempts Among Middle and High School Students Who Reported Current Nicotine Product Use by Patterns of Use and Demographics, 2014 (Percent)

	Current Nicotine Product Use		
	Any Nicotine Product Use	**Cigarettes Only**	**Non-Cigarette Nicotine Products (with or without Cigarettes)**
Total	**29.5**	**41.1**	**28.8**
Sex			
Male	30.1	45.3	29.2
Female	28.5	36.3	27.9
Race/Ethnicity			
White	30.1	47.6	28.9
Black	23.2	–	23.3
Hispanic	30.3	–	30.3
Asian	22.3	–	18.9
American Indian	–	–	–
Multiracial	31.0	–	29.7
Age			
9-13	34.2	–	34.7
14-17	29.2	42.8	28.2
18-19	27.6	–	26.7

Analysis of data from the 2014 National Youth Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nyts/).

Former Use of Nicotine Products
Among Adults by Patterns of Use and Demographics

Table 11
Former Nicotine Product Use Among Adults Who Have Ever Used a Nicotine Product by Patterns of Use and Demographics, 2013-2014 (Percent)

	Lifetime Nicotine Product Use		
	Any Nicotine Product Use	**Cigarettes Only**	**Non-Cigarette Nicotine Products (with or without Cigarettes)**
Total	**53.0**	**77.1**	**41.4**
Sex			
Male	49.8	75.5	42.5
Female	57.3	78.3	39.1
Race/Ethnicity			
White	55.8	82.2	42.4
Black	44.0	58.8	35.1
Hispanic	51.0	69.5	43.4
Asian	52.4	70.1	47.6
American Indian	43.2	62.6	36.4
Multiracial	39.5	67.3	32.4
Age			
18-24	30.0	37.3	29.8
25-44	42.6	62.6	37.9
45-64	56.4	74.7	42.3
≥65	80.3	89.5	67.7

Note: Former use was defined as having reported lifetime use but no use of the nicotine product "now."

Analysis of data from the 2013-2014 National Adult Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nats/).

Former Use of Nicotine Products
Among Middle and High School Students by Patterns of Use and Demographics

Table 12
Former Nicotine Product Use Among Middle and High School Students Who Have Ever Used a Nicotine Product by Patterns of Use and Demographics, 2014 (Percent)

	Lifetime Nicotine Product Use		
	Any Nicotine Product Use	**Cigarettes Only**	**Non-Cigarette Nicotine Products (with or without Cigarettes)**
Total	**51.1**	**91.1**	**46.6**
Sex			
Male	48.1	91.1	43.9
Female	54.6	91.3	49.8
Race/Ethnicity			
White	47.7	93.3	46.1
Black	63.6	86.3	60.3
Hispanic	49.9	87.7	46.1
Asian	58.0	–	51.1
American Indian	53.2	–	46.1
Multiracial	53.2	95.0	46.8
Age			
9-13	64.9	86.6	61.1
14-17	49.7	91.9	45.3
18-19	44.4	93.9	39.4

Note: Former use was defined as having reported "ever trying or using" the nicotine product but not using it in the past 30 days.

Analysis of data from the 2014 National Youth Tobacco Survey (http://www.cdc.gov/tobacco/data_statistics/surveys/nyts/).

Chapter I
Notes

[1] U.S. Department of Health and Human Services. (2014). *The health consequences of smoking-50 years of progress. A report of the Surgeon General* (January 2014. Printed with corrections). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

[2] Centers for Disease Control and Prevention. (2016). *Trends in current cigarette smoking by high school students and adults: United States, 1965-2014.* Retrieved from http://www.cdc.gov.

[3] Dutra, L. M., & Glantz, S. A. (2017). E-cigarettes and national adolescent cigarette use: 2004-2014. *Pediatrics, 139*(2), e20162450. doi:10.1542/peds.2016-2450.

[4] Agaku, I. T., King, B. A., Husten, C. G., Bunnell, R., Ambrose, B. K., Hu, S. S., et al. (2014). Tobacco product use among adults - United States, 2012-2013. *Morbidity and Mortality Weekly Report, 63*(25), 542-547.

Singh, T., Arrazola, R. A., Corey, C. G., Husten, C. G., Neff, L. J., Homa, D. M., et al. (2016). Tobacco use among middle and high school students - United States, 2011-2015. *Morbidity and Mortality Weekly Report, 65*(14), 361-367.

Johnston, L. D., Miech, R. A., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E. (2016). *Teen use of any illicit drug other than marijuana at new low, same true for alcohol: Data tables*. Retrieved from http://monitoringthefuture.org.

Loukas, A., Batanova, M., Fernandez, A., & Agarwal, D. (2015). Changes in use of cigarettes and non-cigarette alternative products among college students. *Addictive Behaviors, 49*, 46-51.

University of Michigan. (2017). *Press release: Vaping, hookah use by U.S. teens declines for first time*. Retrieved from http://ns.umich.edu.

[5] Niaura, R. (2016). *Re-thinking nicotine and its effects*. Washington, DC: Truth Initiative.

Truth Initiative. (2015). *The truth about: Electronic nicotine delivery systems.* Retrieved from http://truthinitiative.org.

Wagener, T. L., Floyd, E. L., Stpanov, I., Driskill, L. M., Frank, S. G., Meier, E., et al. (2016). Have combustible cigarettes met their match? The nicotine delivery profiles and harmful constituent exposures of second-generation and third-generation electronic cigarette users. *Tobacco Control*. doi:10.1136/tobaccocontrol-2016-053041.

[6] CASAColumbia. (2015). *Understanding and addressing nicotine addiction: A science-based approach to policy and practice*. New York: Author.

Klein, J. D. (2015). Electronic cigarettes are another route to nicotine addiction for youth. *JAMA Pediatrics, 169*(11), 993-994.

U.S. Department of Health and Human Services. (2016). *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, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

[7] CASAColumbia. (2015). *Understanding and addressing nicotine addiction: A science-based approach to policy and practice*. New York: Author.

DiFranza, J. R. (2015). A 2015 update on the natural history and diagnosis of nicotine addiction. *Current Pediatric Reviews, 11*(1), 43-55.

D'Souza, M. S., & Markou, A. (2013). The "stop" and "go" of nicotine dependence: Role of GABA and glutamate. *Cold Spring Harbor Perspectives in Medicine, 3(6). doi:10.1101/cshperspect.a012146.*

Mansvelder, H. D., Keath, J. R., & McGehee, D. S. (2002). Synaptic mechanisms underlie nicotine-induced excitability of brain reward areas. *Neuron, 33*(6), 905-919.

[8] Dani, J. A., Kosten, T. R., & Benowitz, N. L. (2014). The pharmacology of nicotine and tobacco. In C. A. Cavacuiti (Ed.), *Principles of addiction medicine: The essentials* (pp. 55-59). Philadelphia, PA: Lippincott Williams & Wilkins.

National Institute on Drug Abuse. (2012). *Research report series: Tobacco addiction* (NIH Pub No. 12-4342). Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Institute on Drug Abuse.

[9] Benowitz, N. L. (2009). Pharmacology of nicotine: Addiction, smoking-induced disease, and therapeutics. *Annual Review of Pharmacology and Toxicology, 49*, 57-71.

Benowitz, N. L., & Burbank, A. D. (2016). Cardiovascular toxicity of nicotine: Implications for electronic cigarette use. *Trends in Cardiovascular Medicine*. doi:10.1016/j.tcm.2016.03.001.

Middlekauff, H. R., Park, J., & Moheimani, R. S. (2014). Adverse effects of cigarette and noncigarette smoke exposure on the autonomic nervous system: Mechanisms and implications for cardiovascular risk. *Journal of the American College of Cardiology, 64*(16), 1740-1750.
Mishra, A., Chaturvedi, P., Datta, S., Sinukumar, S., Joshi, P., & Garg, A. (2015). Harmful effects of nicotine. *Indian Society of Medical and Paediatric Oncology, 36*(1), 24-31.
National Institute on Drug Abuse. (2012). *Research report series: Tobacco addiction* (NIH Pub No. 12-4342). Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Institute on Drug Abuse.
Schweitzer, K. S., Chen, S. X., Law, S., Van Demark, M. J., Poirier, C., Justice, M. J., et al. (2015). Endothelial disruptive pro-inflammatory effects of nicotine and e-cigarette vapor exposures. *American Journal of Physiology - Lung Cellular and Molecular Physiology, 309*(2), L175-L187.
Siqueira, L. M. (2016). Nicotine and tobacco as substances of abuse in children and adolescents. *American Academy of Pediatrics, 139*(1). doi:10.1542/peds.2016-3436.
[10] Benowitz, N. L. (2009). Pharmacology of nicotine: Addiction, smoking-induced disease, and therapeutics. *Annual Review of Pharmacology and Toxicology, 49*, 57-71.
Breuss, J. M., Froehlich, J. F., Steurer, S., Kaun, C., Binder, B. R., Huber, K., et al. (2004). Inhibition of smooth muscle cell migration by eptifibatide in vitro. Eptifibatide inhibits localization of integrin - Subunit to focal adhesions. *Poster Abstracts: Cardiovascular Pathology, 13*, s80-s138.
Chernyavsky, A. I., Shchepotin, I. B., Galitovkiy, V., & Grando, S. A. (2015). Mechanisms of tumor-promoting activities of nicotine in lung cancer: Synergistic effects of cell membrane and mitochondrial nicotinic acetylcholine receptors. *BMC Cancer, 15*, 152. doi:10.1186/s12885-015-1158-4.
Dasgupta, P., Rizwani, W., Pillai, S., Kinkade, R., Kovacs, M., Rastogi, S., et al. (2009). Nicotine induces cell proliferation, invasion and epithelial-mesenchymal transition in a variety of human cancer cell lines. *International Journal of Cancer, 124*(1), 36-45.
Grando, S. A. (2014). Connections of nicotine to cancer. *Nature Reviews Cancer, 14*(6), 419-429.
Zeidler, R., Albermann, K., & Lang, S. (2007). Nicotine and apoptosis. *Apoptosis, 12*(11), 1927-1943.
[11] Mayer, B. (2014). How much nicotine kills a human? Tracing back the generally accepted lethal dose to dubious self-experiments in the nineteenth century. *Archives of Toxicology, 88*(1), 5-7.
[12] Benowitz, N. L. (2009). Pharmacology of nicotine: Addiction, smoking-induced disease, and therapeutics. *Annual Review of Pharmacology and Toxicology, 49*, 57-71.
Dwyer, J. B., McQuown, S. C., & Leslie, F. M. (2009). The dynamic effects of nicotine on the developing brain. *Pharmacology and Therapeutics, 122*(2), 125-139.
England, L. J., Aagaard, K., Bloch, M., Conway, K., Cosgrove, K., Grana, R., et al. (2017). Developmental toxicity of nicotine: A transdisciplinary synthesis and implications for emerging tobacco products. *Neuroscience and Biobehavioral Reviews, 72*, 176-189.
England, L. J., Bunnell, R. E., Pechacek, T. F., Tong, V. T., & McAfee, T. A. (2015). Nicotine and the developing human: A neglected element in the electronic cigarette debate. *American Journal of Preventive Medicine, 49*(2), 286-293.
Kohlmeier, K. A. (2015). Nicotine during pregnancy: Changes induced in neurotransmission, which could heighten proclivity to addict and induce maladaptive control of attention. *Journal of Developmental Origins of Health and Disease, 6*(3), 169-181.
Smith, R. F., McDonald, C. G., Bergstrom, H. C., Ehlinger, D. G., & Brielmaier, J. M. (2015). Adolescent nicotine induces persisting changes in development of neural connectivity. *Neuroscience and Biobehavioral Reviews, 55*, 432-443.
U.S. Department of Health and Human Services. (1988). *The health consequences of smoking: Nicotine addiction: A report of the Surgeon General*. Rockville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
U.S. Department of Health and Human Services. (2016). *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, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
World Health Organization. (2007). *IARC monographs on the evaluation of carcinogenic risks to humans: Volume 89: Smokeless tobacco and some tobacco-specific N-nitrosamines*. France: International Agency for Research on Cancer.

Yuan, M., Cross, S. J., Loughlin, S. E., & Leslie, F. M. (2015). Nicotine and the adolescent brain. *The Journal of Physiology, 593*(16), 3397-3412.
[13] CASAColumbia. (2015). *Understanding and addressing nicotine addiction: A science-based approach to policy and practice*. New York: Author.
Kutlu, M. G., Parikh, V., & Gould, T. J. (2015). Nicotine addiction and psychiatric disorders. *International Review of Neurobiology, 124*, 171-208.
Schroeder, S. A., & Morris, C. D. (2010). Confronting a neglected epidemic: Tobacco cessation for persons with mental illnesses and substance abuse problems. *Annual Review of Public Health, 31*, 297-314.
[14] American Lung Association. (2012). *Cutting tobacco's rural roots: Tobacco use in rural communities*. Washington, DC: American Lung Association National Headquarters.
Jamal, A., Homa, D. M., O'Connor, E., Babb, S. D., Caraballo, R. S., Singh, T., et al. (2015). Current cigarette smoking among adults - United States, 2005-2014. *Morbidity and Mortality Weekly Report, 64*(44), 1233-1240.
Owusu, D., Aibangbee, J., Collins, C., Robertson, C., Wang, L., Littleton, M. A., et al. (2016). The use of e-cigarettes among school-going adolescents in a predominantly rural environment of Central Appalachia. *Journal of Community Health*. doi:10.1007/s10900-016-0297-0.
[15] Benowitz, N. L. (2009). Pharmacology of nicotine: Addiction, smoking-induced disease, and therapeutics. *Annual Review of Pharmacology and Toxicology, 49*, 57-71.
CASAColumbia. (2015). *Understanding and addressing nicotine addiction: A science-based approach to policy and practice*. New York: Author.
Fillon, M. (2015). Electronic cigarettes may lead to nicotine addiction. *Journal of the National Cancer Institute, 107*(3). doi:10.1093/jnci/djv070.
Jerry, J. M., Collins, G. B., & Streem, D. (2015). E-cigarettes: Safe to recommend to patients? *Cleaveland Clinic Journal of Medicine, 82*(8), 521-526.
Kandel, D. B., & Kandel, E. R. (2014). A molecular basis for nicotine as a gateway drug. *New England Journal of Medicine, 371*(21), 2038-2039.
Kutlu, M. G., Parikh, V., & Gould, T. J. (2015). Nicotine addiction and psychiatric disorders. *International Review of Neurobiology, 124*, 171-208.
National Institute on Drug Abuse. (2012). *Research report series: Tobacco addiction* (NIH Pub No. 12-4342). Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Institute on Drug Abuse.
Richter, L., Pugh, B. S., Smith, P. H., & Ball, S. A. (2016). The co-occurrence of nicotine and other substance use and addiction among youth and adults in the United States: Implications for research, practice, and policy. *American Journal of Drug and Alcohol Abuse, 43*(2), 132-145.
Schweitzer, K. S., Chen, S. X., Law, S., Van Demark, M. J., Poirier, C., Justice, M. J., et al. (2015). Endothelial disruptive pro-inflammatory effects of nicotine and e-cigarette vapor exposures. *American Journal of Physiology - Lung Cellular and Molecular Physiology, 309*(2), L175-L187..
Siqueira, L. M. (2016). Nicotine and tobacco as substances of abuse in children and adolsecents. *American Academy of Pediatrics, 139*(1). doi:10.1542/peds.2016-3436.
U.S. Department of Health and Human Services. (2012). *Preventing tobacco use among youth and young adults: A report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
World Health Organization. (2007). *IARC monographs on the evaluation of carcinogenic risks to humans: Volume 89: Smokeless tobacco and some tobacco-specific N-nitrosamines*. France: International Agency for Research on Cancer.
[16] Niaura, R. (2016). *Re-thinking nicotine and its effects*. Washington, DC: Truth Initiative.
[17] U.S. Department of Health and Human Services. (2016). *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, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[18] Niaura, R. (2016). *Re-thinking nicotine and its effects*. Washington, DC: Truth Initiative.
[19] Cheng, T. (2014). Chemical evaluation of electronic cigarettes. *Tobacco Control, 23 Suppl 2*, ii11-ii17.
Hutzler, C., Paschke, M., Kruschinski, S., Henkler, F., Hahn, J., & Luch, A. (2014). Chemical hazards present in liquids and vapors of electronic cigarettes. *Archives of Toxicology, 88*(7), 1295-1308.

[20] U.S. Food and Drug Administration. (2016). *Family Smoking Prevention and Tobacco Control Act: 21 CFR parts 1100, 1140, and 1143.* Retrieved from http://federalregister.gov.
[21] Cox, E., Barry, R. A., & Glantz, S. (2016). E-cigarette policymaking by local and state governments: 2009-2014. *Milbank Quarterly, 94*(3), 520-596.

Chapter II
Notes

[1] O'Connor, R. J. (2012). Non-cigarette tobacco products: What have we learnt and where are we headed? *Tobacco Control, 21*(2), 181-190.
Rom, O., Pecorelli, A., Valacchi, G., & Reznick, A. Z. (2015). Are e-cigarettes a safe and good alternative to cigarette smoking? *Annals of the New York Academy of Sciences*. 1340, 65-74.
[2] World Health Organization. (2007). *IARC monographs on the evaluation of carcinogenic risks to humans: Volume 89: Smokeless tobacco and some tobacco-specific N-nitrosamines.* France: International Agency for Research on Cancer.
[3] Brunnemann, K. D., Qi, J., & Hoffmann, D. (2002). Chemical profile of two types of oral snuff tobacco. *Food and Chemical Toxicology, 40*(11), 1699-1703.
Lawler, T. S., Stanfill, S. B., Zhang, L., Ashley, D. L., & Watson, C. H. (2013). Chemical characterization of domestic oral tobacco products: Total nicotine, pH, unprotonated nicotine and tobacco-specific N-nitrosamines. *Food and Chemical Toxicology, 57*, 380-386.
Richter, P., Hodge, K., Stanfill, S., Zhang, L., & Watson, C. (2008). Surveillance of moist snuff: Total nicotine, moisture, pH, un-ionized nicotine, and tobacco-specific nitrosamines. *Nicotine and Tobacco Research, 10*(11), 1645-1652.
[4] Dani, J. A., Kosten, T. R., & Benowitz, N. L. (2014). The pharmacology of nicotine and tobacco. In C. A. Cavacuiti (Ed.), *Principles of addiction medicine: The essentials* (pp. 55-59). Philadelphia, PA: Lippincott Williams & Wilkins.
El-Hellani, A., El-Hage, R., Baalbaki, R., Salman, R., Talih, S., Shihadeh, A., et al. (2015). Free-base and protonated nicotine in electronic cigarette liquids and aerosols. *Chemical Research in Toxicology, 28*(8), 1532-1537.
Lisko, J. G., Tran, H., Stanfill, S. B., Blount, B. C., & Watson, C. H. (2015). Chemical composition and evaluation of nicotine, tobacco alkaloids, pH, and selected flavors in e-cigarette cartridges and refill solutions. *Nicotine and Tobacco Research, 17*(10), 1270-1278.
[5] Malson, J. L., Sims, K., Murty, R., & Pickworth, W. B. (2001). Comparison of the nicotine content of tobacco used in bidis and conventional cigarettes. *Tobacco Control, 10*(2), 181-183.
[6] Klepeis, N. E., Ott, W. R., & Repace, J. L. (1999). The effect of cigar smoking on indoor levels of carbon monoxide and particles. *Journal of Exposure Analysis and Environmental Epidemiology, 9*(6), 622-635.
[7] Richardson, A., Xiao, H., & Vallone, D. M. (2012). Primary and dual users of cigars and cigarettes: Profiles, tobacco use patterns and relevance to policy. *Nicotine and Tobacco Research, 14*(8), 927-932.
[8] Henningfield, J. E., Fant, R. V., Radzius, A., & Frost, S. (1999). Nicotine concentration, smoke pH and whole tobacco aqueous pH of some cigar brands and types popular in the United States. *Nicotine and Tobacco Research, 1*(2), 163-168.
[9] Klepeis, N. E., Ott, W. R., & Repace, J. L. (1999). The effect of cigar smoking on indoor levels of carbon monoxide and particles. *Journal of Exposure Analysis and Environmental Epidemiology, 9*(6), 622-635.
[10] Henningfield, J. E., Fant, R. V., Radzius, A., & Frost, S. (1999). Nicotine concentration, smoke pH and whole tobacco aqueous pH of some cigar brands and types popular in the United States. *Nicotine and Tobacco Research, 1*(2), 163-168.
[11] Taghavi, S., Khashyarmanesh, Z., Moalemzadeh-Haghighi, H., Nassirli, H., Eshraghi, P., Jalali, N., et al. (2012). Nicotine content of domestic cigarettes, imported cigarettes and pipe tobacco in Iran. *Addiction & Health, 4*(1-2), 28-35.
[12] Rodriguez, J., Jiang, R., Johnson, W. C., MacKenzie, B. A., Smith, L. J., & Barr, R. G. (2010). The association of pipe and cigar use with cotinine levels, lung function, and airflow obstruction: a cross-sectional study. *Annals of Internal Medicine, 152*(4), 201-210.
[13] Cobb, C. O., Shihadeh, A., Weaver, M. F., & Eissenberg, T. (2011). Waterpipe tobacco smoking and cigarette smoking: A direct comparison of toxicant exposure and subjective effects. *Nicotine and Tobacco Research, 13*(2), 78-87.
[14] Jacob, P., Abu Raddaha, A. H., Dempsey, D., Havel, C., Peng, M., Yu, L., et al. (2011). Nicotine, carbon monoxide, and carcinogen exposure after a single use of a water pipe. *Cancer Epidemiology Biomarkers and Prevention, 20*(11), 2345-2353.
[15] Hatsukami, D. K., Stepanov, I., Severson, H., Jensen, J. A., Lindgren, B. R., Horn, K., et al. (2015). Evidence supporting product standards for carcinogens in smokeless tobacco products. *Cancer Prevention Research, 8*(1), 20-26.

[16] Hatsukami, D. K., Stepanov, I., Severson, H., Jensen, J. A., Lindgren, B. R., Horn, K., et al. (2015). Evidence supporting product standards for carcinogens in smokeless tobacco products. *Cancer Prevention Research, 8*(1), 20-26.
[17] Lawler, T. S., Stanfill, S. B., Zhang, L., Ashley, D. L., & Watson, C. H. (2013). Chemical characterization of domestic oral tobacco products: Total nicotine, pH, unprotonated nicotine and tobacco-specific N-nitrosamines. *Food and Chemical Toxicology, 57*, 380-386.
[18] Lawler, T. S., Stanfill, S. B., Zhang, L., Ashley, D. L., & Watson, C. H. (2013). Chemical characterization of domestic oral tobacco products: Total nicotine, pH, unprotonated nicotine and tobacco-specific N-nitrosamines. *Food and Chemical Toxicology, 57*, 380-386.
[19] Richter, P., Hodge, K., Stanfill, S., Zhang, L., & Watson, C. (2008). Surveillance of moist snuff: Total nicotine, moisture, pH, un-ionized nicotine, and tobacco-specific nitrosamines. *Nicotine and Tobacco Research, 10*(11), 1645-1652.
[20] Lawler, T. S., Stanfill, S. B., Zhang, L., Ashley, D. L., & Watson, C. H. (2013). Chemical characterization of domestic oral tobacco products: Total nicotine, pH, unprotonated nicotine and tobacco-specific N-nitrosamines. *Food and Chemical Toxicology, 57*, 380-386.
[21] Lawler, T. S., Stanfill, S. B., Zhang, L., Ashley, D. L., & Watson, C. H. (2013). Chemical characterization of domestic oral tobacco products: Total nicotine, pH, unprotonated nicotine and tobacco-specific N-nitrosamines. *Food and Chemical Toxicology, 57*, 380-386.
[22] Farsalinos, K. E., Gillman, I. G., Melvin, M. S., Paolantonio, A. R., Gardow, W. J., Humphries, K. E., et al. (2015). Nicotine levels and presence of selected tobacco-derived toxins in tobacco flavoured electronic cigarette refill liquids. *International Journal of Environmental Research and Public Health, 12*(4), 3439-3452.
[23] Behar, R. Z., Hua, M., & Talbot, P. (2015). Puffing topography and nicotine intake of electronic cigarette users. *PLoS One, 10*(2), e0117222. doi:10.1371/journal.pone.0117222.
[24] Behar, R. Z., Hua, M., & Talbot, P. (2015). Puffing topography and nicotine intake of electronic cigarette users. *PLoS One, 10*(2), e0117222. doi:10.1371/journal.pone.0117222.
[25] Bahl, V., Lin, S., Xu, N., Davis, B., Wang, Y. H., & Talbot, P. (2012). Comparison of electronic cigarette refill fluid cytotoxicity using embryonic and adult models. *Reproductive Toxicology, 34*(4), 529-537.
Etter, J. F., Zather, E., & Svensson, S. (2013). Analysis of refill liquids for electronic cigarettes. *Addiction, 108*(9), 1671-1679.
Farsalinos, K. E., Gillman, I. G., Melvin, M. S., Paolantonio, A. R., Gardow, W. J., Humphries, K. E., et al. (2015). Nicotine levels and presence of selected tobacco-derived toxins in tobacco flavoured electronic cigarette refill liquids. *International Journal of Environmental Research and Public Health, 12*(4), 3439-3452.
Kosmider, L., Sobczak, A., Fik, M., Knysak, J., Zaciera, M., Kurek, J., et al. (2014). Carbonyl compounds in electronic cigarette vapors: Effects of nicotine solvent and battery output voltage. *Nicotine and Tobacco Research, 16*(10), 1319-1326.
Lisko, J. G., Tran, H., Stanfill, S. B., Blount, B. C., & Watson, C. H. (2015). Chemical composition and evaluation of nicotine, tobacco alkaloids, pH, and selected flavors in e-cigarette cartridges and refill solutions. *Nicotine and Tobacco Research, 17*(10), 1270-1278.
[26] Shanks, T. G., & Burns, D. M. (1998). *Disease consequences of cigar smoking.* Retrieved from http://cancercontrol.cancer.gov.
[27] Centers for Disease Control and Prevention. (2016). *Cigars.* Retrieved from http://www.cdc.gov.
[28] American Cancer Society. (2015). *Is any type of smoking safe?* Retrieved from http://www.cancer.org.
[29] Shanks, T. G., & Burns, D. M. (1998). *Disease consequences of cigar smoking.* Retrieved from http://cancercontrol.cancer.gov.
[30] Shanks, T. G., & Burns, D. M. (1998). *Disease consequences of cigar smoking.* Retrieved from http://cancercontrol.cancer.gov.
[31] American Cancer Society. (2015). *Is any type of smoking safe?* Retrieved from http://www.cancer.org.
[32] Baker, F., Ainsworth, S. R., Dye, J. T., Crammer, C., Thun, M. J., Hoffmann, D., et al. (2000). Health risks associated with cigar smoking. *JAMA, 284*(6), 735-740.
[33] American Cancer Society. (2015). *Is any type of smoking safe?* Retrieved from http://www.cancer.org.
[34] Delnevo, C. D. (2006). Smokers' choice: What explains the steady growth of cigar use in the U.S.? *Public Health Reports, 121*(2), 116-119.
[35] Hoffmann, D., & Wynder, E. L. (1972). Smoke of cigarettes and little cigars: An analytical comparison. *Science, 178*(4066), 1197-1199.

Shanks, T. G., & Burns, D. M. (1998). *Disease consequences of cigar smoking.* Retrieved from http://cancercontrol.cancer.gov.
[36] King, B. A., Tynan, M. A., Dube, S. R., & Arrazola, R. (2014). Flavored-little-cigar and flavored-cigarette use among U.S. middle and high school students. *Journal of Adolescent Health, 54*(1), 40-46.
[37] Milam, A. J., Bone, L. R., Byron, M. J., Hoke, K., Williams, C. D., Furr-Holden, C. D., et al. (2013). Cigarillo use among high-risk urban young adults. *Journal of Health Care for the Poor and Underserved, 24*(4), 1657-1665.
[38] Armitage, A. K., Dollery, C. T., Houseman, T. H., Kohner, E. M., Lewis, P. J., & Turner, D. M. (1977). Absorption of nicotine by man during cigar smoking [proceedings]. *British Journal of Pharmacology, 59*(3), 493P.
[39] Chang, C. M., Corey, C. G., Rostron, B. L., & Apelberg, B. J. (2015). Systematic review of cigar smoking and all cause and smoking related mortality. *BMC Public Health, 15*, 390.
Jolly, D. H. (2008). Exploring the use of little cigars by students at a historically black university. *Preventing Chronic Disease, 5*(3), A82.
Koszowski, B., Rosenberry, Z. R., Kanu, A., Viray, L. C., Potts, J. L., & Pickworth, W. B. (2015). Nicotine and carbon monoxide exposure from inhalation of cigarillo smoke. *Pharmacology, Biochemistry and Behavior, 139*(Pt A), 7-14.
[40] Shanks, T. G., & Burns, D. M. (1998). *Disease consequences of cigar smoking.* Retrieved from http://cancercontrol.cancer.gov.
[41] Henningfield, J. E., Fant, R. V., Radzius, A., & Frost, S. (1999). Nicotine concentration, smoke pH and whole tobacco aqueous pH of some cigar brands and types popular in the United States. *Nicotine and Tobacco Research, 1*(2), 163-168.
[42] Henningfield, J. E., Fant, R. V., Radzius, A., & Frost, S. (1999). Nicotine concentration, smoke pH and whole tobacco aqueous pH of some cigar brands and types popular in the United States. *Nicotine and Tobacco Research, 1*(2), 163-168.
[43] Henningfield, J. E., Fant, R. V., Radzius, A., & Frost, S. (1999). Nicotine concentration, smoke pH and whole tobacco aqueous pH of some cigar brands and types popular in the United States. *Nicotine and Tobacco Research, 1*(2), 163-168.
[44] Funck-Brentano, C., Raphael, M., Lafontaine, M., Arnould, J. P., Verstuyft, C., Lebot, M., et al. (2006). Effects of type of smoking (pipe, cigars or cigarettes) on biological indices of tobacco exposure and toxicity. *Lung Cancer, 54*(1), 11-18.
McDonald, L. J., Bhatia, R. S., & Hollett, P. D. (2002). Deposition of cigar smoke particles in the lung: Evaluation with ventilation scan using (99m)Tc-labeled sulfur colloid particles. *Journal of Nuclear Medicine, 43*(12), 1591-1595.
Rodriguez, J., Jiang, R., Johnson, W. C., MacKenzie, B. A., Smith, L. J., & Barr, R. G. (2010). The association of pipe and cigar use with cotinine levels, lung function, and airflow obstruction: A cross-sectional study. *Annals of Internal Medicine, 152*(4), 201-210.
[45] Henningfield, J. E., Fant, R. V., Radzius, A., & Frost, S. (1999). Nicotine concentration, smoke pH and whole tobacco aqueous pH of some cigar brands and types popular in the United States. *Nicotine and Tobacco Research, 1*(2), 163-168.
[46] Henningfield, J. E., Fant, R. V., Radzius, A., & Frost, S. (1999). Nicotine concentration, smoke pH and whole tobacco aqueous pH of some cigar brands and types popular in the United States. *Nicotine and Tobacco Research, 1*(2), 163-168.
[47] Armitage, A. K., Dollery, C. T., Houseman, T. H., Kohner, E. M., Lewis, P. J., & Turner, D. M. (1977). Absorption of nicotine by man during cigar smoking [proceedings]. *British Journal of Pharmacology, 59*(3), 493P.
Baker, F., Ainsworth, S. R., Dye, J. T., Crammer, C., Thun, M. J., Hoffmann, D., et al. (2000). Health risks associated with cigar smoking. *JAMA, 284*(6), 735-740.
Rickert, W. S., Trivedi, A. H., Momin, R. A., Wagstaff, W. G., & Lauterbach, J. H. (2011). Mutagenic, cytotoxic, and genotoxic properties of tobacco smoke produced by cigarillos available on the Canadian market. *Regulatory Toxicology and Pharmacology, 61*(2), 199-209.
[48] Rodriguez, J., Jiang, R., Johnson, W. C., MacKenzie, B. A., Smith, L. J., & Barr, R. G. (2010). The association of pipe and cigar use with cotinine levels, lung function, and airflow obstruction: A cross-sectional study. *Annals of Internal Medicine, 152*(4), 201-210.
[49] Chang, C. M., Corey, C. G., Rostron, B. L., & Apelberg, B. J. (2015). Systematic review of cigar smoking and all cause and smoking related mortality. *BMC Public Health, 15*, 390.
Shanks, T. G., & Burns, D. M. (1998). *Disease consequences of cigar smoking.* Retrieved from http://cancercontrol.cancer.gov.

[50] Baker, F., Ainsworth, S. R., Dye, J. T., Crammer, C., Thun, M. J., Hoffmann, D., et al. (2000). Health risks associated with cigar smoking. *JAMA, 284*(6), 735-740.
Bertuccio, P., La, V. C., Silverman, D. T., Petersen, G. M., Bracci, P. M., Negri, E., et al. (2011). Cigar and pipe smoking, smokeless tobacco use and pancreatic cancer: An analysis from the International Pancreatic Cancer Case-Control Consortium (PanC4). *Annals of Oncology, 22*(6), 1420-1426.
[51] Armitage, A. K., & Turner, D. M. (1970). Absorption of nicotine in cigarette and cigar smoke through the oral mucosa. *Nature, 226*(5252), 1231-1232.
Armitage, A. K., Dollery, C. T., Houseman, T. H., Kohner, E. M., Lewis, P. J., & Turner, D. M. (1977). Absorption of nicotine by man during cigar smoking [proceedings]. *British Journal of Pharmacology, 59*(3), 493P.
Chang, C. M., Corey, C. G., Rostron, B. L., & Apelberg, B. J. (2015). Systematic review of cigar smoking and all cause and smoking related mortality. *BMC Public Health, 15*, 390.
National Cancer Institute. (1998). *Cigars: Health effects and trends.* Retrieved from http://cancercontrol.cancer.gov.
[52] Armitage, A. K., & Turner, D. M. (1970). Absorption of nicotine in cigarette and cigar smoke through the oral mucosa. *Nature, 226*(5252), 1231-1232.
Armitage, A. K., Dollery, C. T., Houseman, T. H., Kohner, E. M., Lewis, P. J., & Turner, D. M. (1977). Absorption of nicotine by man during cigar smoking [proceedings]. *British Journal of Pharmacology, 59*(3), 493P.
National Cancer Institute. (1998). *Cigars: Health effects and trends.* Retrieved from http://cancercontrol.cancer.gov.
[53] McDonald, L. J., Bhatia, R. S., & Hollett, P. D. (2002). Deposition of cigar smoke particles in the lung: Evaluation with ventilation scan using (99m)Tc-labeled sulfur colloid particles. *Journal of Nuclear Medicine, 43*(12), 1591-1595.
Rodriguez, J., Jiang, R., Johnson, W. C., MacKenzie, B. A., Smith, L. J., & Barr, R. G. (2010). The association of pipe and cigar use with cotinine levels, lung function, and airflow obstruction: A cross-sectional study. *Annals of Internal Medicine, 152*(4), 201-210.
[54] Armitage, A. K., Dollery, C. T., Houseman, T. H., Kohner, E. M., Lewis, P. J., & Turner, D. M. (1977). Absorption of nicotine by man during cigar smoking [proceedings]. *British Journal of Pharmacology, 59*(3), 493P.
National Cancer Institute. (1998). *Cigars: Health effects and trends.* Retrieved from http://cancercontrol.cancer.gov.
[55] Armitage, A. K., & Turner, D. M. (1970). Absorption of nicotine in cigarette and cigar smoke through the oral mucosa. *Nature, 226*(5252), 1231-1232.
Armitage, A. K., Dollery, C. T., Houseman, T. H., Kohner, E. M., Lewis, P. J., & Turner, D. M. (1977). Absorption of nicotine by man during cigar smoking [proceedings]. *British Journal of Pharmacology, 59*(3), 493P.
National Cancer Institute. (1998). *Cigars: Health effects and trends.* Retrieved from http://cancercontrol.cancer.gov.
[56] Henningfield, J. E., Fant, R. V., Radzius, A., & Frost, S. (1999). Nicotine concentration, smoke pH and whole tobacco aqueous pH of some cigar brands and types popular in the United States. *Nicotine and Tobacco Research, 1*(2), 163-168.
[57] Shanks, T. G., & Burns, D. M. (1998). *Disease consequences of cigar smoking.* Retrieved from http://cancercontrol.cancer.gov.
[58] Baker, F., Ainsworth, S. R., Dye, J. T., Crammer, C., Thun, M. J., Hoffmann, D., et al. (2000). Health risks associated with cigar smoking. *JAMA, 284*(6), 735-740.
[59] National Cancer Institute. (1998). *Cigars: Health effects and trends.* Retrieved from http://cancercontrol.cancer.gov.
Rodriguez, J., Jiang, R., Johnson, W. C., MacKenzie, B. A., Smith, L. J., & Barr, R. G. (2010). The association of pipe and cigar use with cotinine levels, lung function, and airflow obstruction: A cross-sectional study. *Annals of Internal Medicine, 152*(4), 201-210.
[60] Armitage, A. K., Dollery, C. T., Houseman, T. H., Kohner, E. M., Lewis, P. J., & Turner, D. M. (1977). Absorption of nicotine by man during cigar smoking [proceedings]. *British Journal of Pharmacology, 59*(3), 493P.
[61] Shanks, T. G., & Burns, D. M. (1998). *Disease consequences of cigar smoking.* Retrieved from http://cancercontrol.cancer.gov.
[62] Chang, C. M., Corey, C. G., Rostron, B. L., & Apelberg, B. J. (2015). Systematic review of cigar smoking and all cause and smoking related mortality. *BMC Public Health, 15*, 390.
Shanks, T. G., & Burns, D. M. (1998). *Disease consequences of cigar smoking.* Retrieved from http://cancercontrol.cancer.gov.
[63] Shanks, T. G., & Burns, D. M. (1998). *Disease consequences of cigar smoking.* Retrieved from http://cancercontrol.cancer.gov.

[64] Bertuccio, P., La, V. C., Silverman, D. T., Petersen, G. M., Bracci, P. M., Negri, E., et al. (2011). Cigar and pipe smoking, smokeless tobacco use and pancreatic cancer: an analysis from the International Pancreatic Cancer Case-Control Consortium (PanC4). *Annals of Oncology, 22*(6), 1420-1426.
[65] Shanks, T. G., & Burns, D. M. (1998). *Disease consequences of cigar smoking.* Retrieved from http://cancercontrol.cancer.gov.
[66] Rodriguez, J., Jiang, R., Johnson, W. C., MacKenzie, B. A., Smith, L. J., & Barr, R. G. (2010). The association of pipe and cigar use with cotinine levels, lung function, and airflow obstruction: A cross-sectional study. *Annals of Internal Medicine, 152*(4), 201-210.
[67] Albandar, J. M., Streckfus, C. F., Adesanya, M. R., & Winn, D. M. (2000). Cigar, pipe, and cigarette smoking as risk factors for periodontal disease and tooth loss. *Journal of Periodontology, 71*(12), 1874-1881.
[68] Liu, J., Wang, X., Narayan, S., Glantz, S. A., Schick, S. F., & Springer, M. L. (2016). Impairment of endothelial function by little cigar secondhand smoke. *Tobacco Regulatory Science, 2*(1), 56-63.
[69] Klepeis, N. E., Ott, W. R., & Repace, J. L. (1999). The effect of cigar smoking on indoor levels of carbon monoxide and particles. *Journal of Exposure Analysis and Environmental Epidemiology, 9*(6), 622-635.
[70] Chang, C. M., Corey, C. G., Rostron, B. L., & Apelberg, B. J. (2015). Systematic review of cigar smoking and all cause and smoking related mortality. *BMC Public Health, 15*, 390.
[71] Funck-Brentano, C., Raphael, M., Lafontaine, M., Arnould, J. P., Verstuyft, C., Lebot, M., et al. (2006). Effects of type of smoking (pipe, cigars or cigarettes) on biological indices of tobacco exposure and toxicity. *Lung Cancer, 54*(1), 11-18.
McDonald, L. J., Bhatia, R. S., & Hollett, P. D. (2002). Deposition of cigar smoke particles in the lung: evaluation with ventilation scan using (99m)Tc-labeled sulfur colloid particles. *Journal of Nuclear Medicine, 43*(12), 1591-1595.
Rodriguez, J., Jiang, R., Johnson, W. C., MacKenzie, B. A., Smith, L. J., & Barr, R. G. (2010). The association of pipe and cigar use with cotinine levels, lung function, and airflow obstruction: A cross-sectional study. *Annals of Internal Medicine, 152*(4), 201-210.
[72] Castleden, C. M., & Cole, P. V. (1973). Inhalation of tobacco smoke by pipe and cigar smokers. *Lancet, 2*(7819), 21-22.
Herling, S., & Kozlowski, L. T. (1988). The importance of direct questions about inhalation and daily intake in the evaluation of pipe and cigar smokers. *Preventive Medicine, 17*(1), 73-78.
Ockene, J. K., Pechacek, T. F., Vogt, T., & Svendsen, K. (1987). Does switching from cigarettes to pipes or cigars reduce tobacco smoke exposure? *American Journal of Public Health, 77*(11), 1412-1416.
[73] McCusker, K., McNabb, E., & Bone, R. (1982). Plasma nicotine levels in pipe smokers. *JAMA, 248*(5), 577-578.
[74] Carstensen, J. M., Pershagen, G., & Eklund, G. (1987). Mortality in relation to cigarette and pipe smoking: 16 years' observation of 25,000 Swedish men. *Journal of Epidemiology and Community Health, 41*(2), 166-172.
Henley, S. J., Thun, M. J., Chao, A., & Calle, E. E. (2004). Association between exclusive pipe smoking and mortality from cancer and other diseases. *Journal of the National Cancer Institute, 96*(11), 853-861.
Wyss, A., Hashibe, M., Chuang, S. C., Lee, Y. C., Zhang, Z. F., Yu, G. P., et al. (2013). Cigarette, cigar, and pipe smoking and the risk of head and neck cancers: Pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. *American Journal of Epidemiology, 178*(5), 679-690.
[75] Carstensen, J. M., Pershagen, G., & Eklund, G. (1987). Mortality in relation to cigarette and pipe smoking: 16 years' observation of 25,000 Swedish men. *Journal of Epidemiology and Community Health, 41*(2), 166-172.
Henley, S. J., Thun, M. J., Chao, A., & Calle, E. E. (2004). Association between exclusive pipe smoking and mortality from cancer and other diseases. *Journal of the National Cancer Institute, 96*(11), 853-861.
Higgins, I. T., Mahan, C. M., & Wynder, E. L. (1988). Lung cancer among cigar and pipe smokers. *Preventive Medicine, 17*(1), 116-128.
Lange, P., Groth, S., Nyboe, J., Mortensen, J., Appleyard, M., Jensen, G., et al. (1990). Decline of the lung function related to the type of tobacco smoked and inhalation. *Thorax, 45*(1), 22-26.
McCormack, V. A., Agudo, A., Dahm, C. C., Overvad, K., Olsen, A., Tjonneland, A., et al. (2010). Cigar and pipe smoking and cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC). *International Journal of Cancer, 127*(10), 2402-2411.
Tverdal, A., & Bjartveit, K. (2011). Health consequences of pipe versus cigarette smoking. *Tobacco Control, 20*(2), 123-130.
[76] Henley, S. J., Thun, M. J., Chao, A., & Calle, E. E. (2004). Association between exclusive pipe smoking and mortality from cancer and other diseases. *Journal of the National Cancer Institute, 96*(11), 853-861.

Wyss, A., Hashibe, M., Chuang, S. C., Lee, Y. C., Zhang, Z. F., Yu, G. P., et al. (2013). Cigarette, cigar, and pipe smoking and the risk of head and neck cancers: Pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. *American Journal of Epidemiology, 178*(5), 679-690.
[77] Taghavi, S., Khashyarmanesh, Z., Moalemzadeh-Haghighi, H., Nassirli, H., Eshraghi, P., Jalali, N., et al. (2012). Nicotine content of domestic cigarettes, imported cigarettes and pipe tobacco in Iran. *Addiction & Health, 4*(1-2), 28-35.
[78] Rodriguez, J., Jiang, R., Johnson, W. C., MacKenzie, B. A., Smith, L. J., & Barr, R. G. (2010). The association of pipe and cigar use with cotinine levels, lung function, and airflow obstruction: A cross-sectional study. *Annals of Internal Medicine, 152*(4), 201-210.
Wald, N. J., & Watt, H. C. (1997). Prospective study of effect of switching from cigarettes to pipes or cigars on mortality from three smoking related diseases. *BMJ, 314*(7098), 1860-1863.
[79] McCusker, K., McNabb, E., & Bone, R. (1982). Plasma nicotine levels in pipe smokers. *JAMA, 248*(5), 577-578.
[80] Henley, S. J., Thun, M. J., Chao, A., & Calle, E. E. (2004). Association between exclusive pipe smoking and mortality from cancer and other diseases. *Journal of the National Cancer Institute, 96*(11), 853-861.
[81] Henley, S. J., Thun, M. J., Chao, A., & Calle, E. E. (2004). Association between exclusive pipe smoking and mortality from cancer and other diseases. *Journal of the National Cancer Institute, 96*(11), 853-861.
[82] Henley, S. J., Thun, M. J., Chao, A., & Calle, E. E. (2004). Association between exclusive pipe smoking and mortality from cancer and other diseases. *Journal of the National Cancer Institute, 96*(11), 853-861.
[83] Tverdal, A., & Bjartveit, K. (2011). Health consequences of pipe versus cigarette smoking. *Tobacco Control, 20*(2), 123-130.
[84] Henley, S. J., Thun, M. J., Chao, A., & Calle, E. E. (2004). Association between exclusive pipe smoking and mortality from cancer and other diseases. *Journal of the National Cancer Institute, 96*(11), 853-861.
[85] Rodriguez, J., Jiang, R., Johnson, W. C., MacKenzie, B. A., Smith, L. J., & Barr, R. G. (2010). The association of pipe and cigar use with cotinine levels, lung function, and airflow obstruction: A cross-sectional study. *Annals of Internal Medicine, 152*(4), 201-210.
[86] Albandar, J. M., Streckfus, C. F., Adesanya, M. R., & Winn, D. M. (2000). Cigar, pipe, and cigarette smoking as risk factors for periodontal disease and tooth loss. *Journal of Periodontology, 71*(12), 1874-1881.
[87] Carstensen, J. M., Pershagen, G., & Eklund, G. (1987). Mortality in relation to cigarette and pipe smoking: 16 years' observation of 25,000 Swedish men. *Journal of Epidemiology and Community Health, 41*(2), 166-172.
[88] Albandar, J. M., Streckfus, C. F., Adesanya, M. R., & Winn, D. M. (2000). Cigar, pipe, and cigarette smoking as risk factors for periodontal disease and tooth loss. *Journal of Periodontology, 71*(12), 1874-1881.
[89] Centers for Disease Control and Prevention. (2015). *Hookahs.* Retrieved from http://www.cdc.gov.
[90] American lung Association. (2007). *An emerging deadly trend: Waterpipe tobacco use.* Retrieved from http://www.lungusa2.org.
[91] Aslam, H. M., Saleem, S., German, S., & Qureshi, W. A. (2014). Harmful effects of shisha: Literature review. *International Archives of Medicine, 7*, 16. doi:10.1186/1755-7682-7-16.
[92] Centers for Disease Control and Prevention. (2015). *Hookahs.* Retrieved from http://www.cdc.gov.
[93] American lung Association. (2007). *Hookah smoking: A growing threat to public health.* Retrieved from http://www.lung.org.
Jacob, P., Abu Raddaha, A. H., Dempsey, D., Havel, C., Peng, M., Yu, L., et al. (2011). Nicotine, carbon monoxide, and carcinogen exposure after a single use of a water pipe. *Cancer Epidemiology Biomarkers and Prevention, 20*(11), 2345-2353.
[94] Neergaard, J., Singh, P., Job, J., & Montgomery, S. (2007). Waterpipe smoking and nicotine exposure: A review of the current evidence. *Nicotine and Tobacco Research, 9*(10), 987-994.
[95] Eissenberg, T., & Shihadeh, A. (2009). Waterpipe tobacco and cigarette smoking: Direct comparison of toxicant exposure. *American Journal of Preventive Medicine, 37*(6), 518-523.
[96] Eissenberg, T., & Shihadeh, A. (2009). Waterpipe tobacco and cigarette smoking: Direct comparison of toxicant exposure. *American Journal of Preventive Medicine, 37*(6), 518-523.
[97] Shafagoj, Y. A., Mohammed, F. I., & Hadidi, K. A. (2002). Hubble-bubble (water pipe) smoking: Levels of nicotine and cotinine in plasma, saliva and urine. *International Journal of Clinical Pharmacology and Therapeutics, 40*(6), 249-255.
[98] Maziak, W., Rastam, S., Shihadeh, A. L., Bazzi, A., Ibrahim, I., Zaatari, G. S., et al. (2011). Nicotine exposure in daily waterpipe smokers and its relation to puff topography. *Addictive Behaviors, 36*(4), 397-399.

[99] Primack, B. A., Carroll, M. V., Weiss, P. M., Shihadeh, A. L., Shensa, A., Farley, S. T., et al. (2016). Systematic review and meta-analysis of inhaled toxicants from waterpipe and cigarette smoking. *Public Health Reports, 131*(1), 76-85.
[100] Blank, M. D., Cobb, C. O., Kilgalen, B., Austin, J., Weaver, M. F., Shihadeh, A., et al. (2011). Acute effects of waterpipe tobacco smoking: A double-blind, placebo-control study. *Drug and Alcohol Dependence, 116*(1-3), 102-109.
Cobb, C. O., Shihadeh, A., Weaver, M. F., & Eissenberg, T. (2011). Waterpipe tobacco smoking and cigarette smoking: A direct comparison of toxicant exposure and subjective effects. *Nicotine and Tobacco Research, 13*(2), 78-87.
Eissenberg, T., & Shihadeh, A. (2009). Waterpipe tobacco and cigarette smoking: Direct comparison of toxicant exposure. *American Journal of Preventive Medicine, 37*(6), 518-523.
El-Zaatari, Z. M., Chami, H. A., & Zaatari, G. S. (2015). Health effects associated with waterpipe smoking. *Tobacco Control, 24*(Suppl 1), i31-i43.
Jacob, P., Abu Raddaha, A. H., Dempsey, D., Havel, C., Peng, M., Yu, L., et al. (2013). Comparison of nicotine and carcinogen exposure with water pipe and cigarette smoking. *Cancer Epidemiology Biomarkers and Prevention, 22*(5), 765-772.
Maziak, W., Rastam, S., Shihadeh, A. L., Bazzi, A., Ibrahim, I., Zaatari, G. S., et al. (2011). Nicotine exposure in daily waterpipe smokers and its relation to puff topography. *Addictive Behaviors, 36*(4), 397-399.
[101] El-Zaatari, Z. M., Chami, H. A., & Zaatari, G. S. (2015). Health effects associated with waterpipe smoking. *Tobacco Control, 24*(Suppl 1), i31-i43.
Truth Initiative. (2015). *Hookah: Background.* Retrieved from http://truthinitiative.org.
Sibai, A. M., Tohme, R. A., Almedawar, M. M., Itani, T., Yassine, S. I., Nohra, E. A., et al. (2014). Lifetime cumulative exposure to waterpipe smoking is associated with coronary artery disease. *Atherosclerosis, 234*(2), 454-460.
[102] Al, A. R., Rastam, S., Ibrahim, I., Bazzi, A., Fayad, S., Shihadeh, A. L., et al. (2015). A comparative study of systemic carcinogen exposure in waterpipe smokers, cigarette smokers and non-smokers. *Tobacco Control, 24*(2), 125-127.
Al-Kazwini, A. T., Said, A. J., & Sdepanian, S. (2015). Compartmental analysis of metals in waterpipe smoking technique. *BMC Public Health, 15*, 153.
Al, R. M., Shihadeh, A., & Saliba, N. A. (2008). Volatile aldehydes in the mainstream smoke of the narghile waterpipe. *Food and Chemical Toxicology, 46*(11), 3546-3549.
Daher, N., Saleh, R., Jaroudi, E., Sheheitli, H., Badr, T., Sepetdjian, E., et al. (2010). Comparison of carcinogen, carbon monoxide, and ultrafine particle emissions from narghile waterpipe and cigarette smoking: Sidestream smoke measurements and assessment of second-hand smoke emission factors. *Atmospheric Environment (1994), 44*(1), 8-14.
Hammal, F., Chappell, A., Wild, T. C., Kindzierski, W., Shihadeh, A., Vanderhoek, A., et al. (2015). 'Herbal' but potentially hazardous: An analysis of the constituents and smoke emissions of tobacco-free waterpipe products and the air quality in the cafes where they are served. *Tobacco Control, 24*(3), 290-297.
Kadhum, M., Sweidan, A., Jaffery, A. E., Al-Saadi, A., & Madden, B. (2015). A review of the health effects of smoking shisha. *Clinical Medicine, 15*(3), 263-266.
Kumar, S. R., Davies, S., Weitzman, M., & Sherman, S. (2015). A review of air quality, biological indicators and health effects of second-hand waterpipe smoke exposure. *Tobacco Control, 24*(Suppl 1), i54-i59.
Monzer, B., Sepetdjian, E., Saliba, N., & Shihadeh, A. (2008). Charcoal emissions as a source of CO and carcinogenic PAH in mainstream narghile waterpipe smoke. *Food and Chemical Toxicology, 46*(9), 2991-2995.
Primack, B. A., Carroll, M. V., Weiss, P. M., Shihadeh, A. L., Shensa, A., Farley, S. T., et al. (2016). Systematic review and meta-analysis of inhaled toxicants from waterpipe and cigarette smoking. *Public Health Reports, 131*(1), 76-85.
Sepetdjian, E., Saliba, N., & Shihadeh, A. (2010). Carcinogenic PAH in waterpipe charcoal products. *Food and Chemical Toxicology, 48*(11), 3242-3245.
Sepetdjian, E., Abdul, H. R., Salman, R., Jaroudi, E., Shihadeh, A., & Saliba, N. A. (2013). Phenolic compounds in particles of mainstream waterpipe smoke. *Nicotine and Tobacco Research, 15*(6), 1107-1112.
Shihadeh, A. (2003). Investigation of mainstream smoke aerosol of the argileh water pipe. *Food and Chemical Toxicology, 41*(1), 143-152.

Shihadeh, A., Salman, R., Jaroudi, E., Saliba, N., Sepetdjian, E., Blank, M. D., et al. (2012). Does switching to a tobacco-free waterpipe product reduce toxicant intake? A crossover study comparing CO, NO, PAH, volatile aldehydes, "tar" and nicotine yields. *Food and Chemical Toxicology, 50*(5), 1494-1498.
Shihadeh, A., Eissenberg, T., Rammah, M., Salman, R., Jaroudi, E., & El-Sabban, M. (2014). Comparison of tobacco-containing and tobacco-free waterpipe products: Effects on human alveolar cells. *Nicotine and Tobacco Research, 16*(4), 496-499.
Shihadeh, A., Schubert, J., Klaiany, J., El, S. M., Luch, A., & Saliba, N. A. (2015). Toxicant content, physical properties and biological activity of waterpipe tobacco smoke and its tobacco-free alternatives. *Tobacco Control, 24*(Suppl 1), i22-i30.
St. Helen G., Benowitz, N. L., Dains, K. M., Havel, C., Peng, M., & Jacob, P. (2014). Nicotine and carcinogen exposure after water pipe smoking in hookah bars. *Cancer Epidemiology, Biomarkers and Prevention, 23*(6), 1055-1066.
Zhou, S., Weitzman, M., Vilcassim, R., Wilson, J., Legrand, N., Saunders, E., et al. (2014). Air quality in New York City hookah bars. *Tobacco Control, 24*(e3), e193-e198. doi:10.1136/tobaccocontrol-2014-051763.
[103] U.S. Department of Health and Human Services. (1983). *The health consequences of smoking: Cardiovascular disease: A report of the Surgeon General*. Rockville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
El-Zaatari, Z. M., Chami, H. A., & Zaatari, G. S. (2015). Health effects associated with waterpipe smoking. *Tobacco Control, 24*(Suppl 1), i31-i43.
La, F. G., Weiser, G., Steiner, I. P., & Shavit, I. (2012). Carbon monoxide poisoning in narghile (water pipe) tobacco smokers. *Canadian Journal of Emergency Medicine, 14*(1), 57-59.
Monzer, B., Sepetdjian, E., Saliba, N., & Shihadeh, A. (2008). Charcoal emissions as a source of CO and carcinogenic PAH in mainstream narghile waterpipe smoke. *Food and Chemical Toxicology, 46*(9), 2991-2995.
Shihadeh, A., & Saleh, R. (2005). Polycyclic aromatic hydrocarbons, carbon monoxide, "tar", and nicotine in the mainstream smoke aerosol of the narghile water pipe. *Food and Chemical Toxicology, 43*(5), 655-661.
von, R. J., Schonenberger, M., & Barlocher, L. (2014). Carbon monoxide poisoning following use of a water pipe/hookah. *Deutsches Ärzteblatt International, 111*(40), 674-679.
Zhang, B., Haji, F., Kaufman, P., Muir, S., & Ferrence, R. (2015). 'Enter at your own risk': A multimethod study of air quality and biological measures in Canadian waterpipe cafes. *Tobacco Control, 24*(2), 175-181.
Zhou, S., Weitzman, M., Vilcassim, R., Wilson, J., Legrand, N., Saunders, E., et al. (2014). Air quality in New York City hookah bars. *Tobacco Control, 24*(e3), e193-e198. doi:10.1136/tobaccocontrol-2014-051763.
[104] Kadhum, M., Sweidan, A., Jaffery, A. E., Al-Saadi, A., & Madden, B. (2015). A review of the health effects of smoking shisha. *Clinical Medicine, 15*(3), 263-266.
[105] Cobb, C. O., Vansickel, A. R., Blank, M. D., Jentink, K., Travers, M. J., & Eissenberg, T. (2013). Indoor air quality in Virginia waterpipe cafes. *Tobacco Control, 22*(5), 338-343.
Eissenberg, T., & Shihadeh, A. (2009). Waterpipe tobacco and cigarette smoking: Direct comparison of toxicant exposure. *American Journal of Preventive Medicine, 37*(6), 518-523.
Martinasek, M. P., Ward, K. D., & Calvanese, A. V. (2014). Change in carbon monoxide exposure among waterpipe bar patrons. *Nicotine and Tobacco Research, 16*(7), 1014-1019.
Truth Initiative. (2015). *Hookah: Background.* Retrieved from http://truthinitiative.org.
Zhang, B., Haji, F., Kaufman, P., Muir, S., & Ferrence, R. (2015). 'Enter at your own risk': a multimethod study of air quality and biological measures in Canadian waterpipe cafes. *Tobacco Control, 24*(2), 175-181.
Zhou, S., Weitzman, M., Vilcassim, R., Wilson, J., Legrand, N., Saunders, E., et al. (2014). Air quality in New York City hookah bars. *Tobacco Control, 24*(e3), e193-e198. doi:10.1136/tobaccocontrol-2014-051763.
[106] Eissenberg, T., & Shihadeh, A. (2009). Waterpipe tobacco and cigarette smoking: Direct comparison of toxicant exposure. *American Journal of Preventive Medicine, 37*(6), 518-523.
Jacob, P., Abu Raddaha, A. H., Dempsey, D., Havel, C., Peng, M., Yu, L., et al. (2011). Nicotine, carbon monoxide, and carcinogen exposure after a single use of a water pipe. *Cancer Epidemiology Biomarkers and Prevention, 20*(11), 2345-2353.
Maziak, W., Rastam, S., Ibrahim, I., Ward, K. D., Shihadeh, A., & Eissenberg, T. (2009). CO exposure, puff topography, and subjective effects in waterpipe tobacco smokers. *Nicotine and Tobacco Research, 11*(7), 806-811.
Primack, B. A., Carroll, M. V., Weiss, P. M., Shihadeh, A. L., Shensa, A., Farley, S. T., et al. (2016). Systematic review and meta-analysis of inhaled toxicants from waterpipe and cigarette smoking. *Public Health Reports, 131*(1), 76-85.

[107] World Health Organization. (2005). *Advisory note: Waterpipe tobacco smoking: Health effects, research needs and recommended actions by regulators*. Geneva, Switzerland: WHO Study Group on Tobacco Product Regulation (TobReg).
[108] Eissenberg, T., & Shihadeh, A. (2009). Waterpipe tobacco and cigarette smoking: Direct comparison of toxicant exposure. *American Journal of Preventive Medicine, 37*(6), 518-523.
Shihadeh, A., Schubert, J., Klaiany, J., El, S. M., Luch, A., & Saliba, N. A. (2015). Toxicant content, physical properties and biological activity of waterpipe tobacco smoke and its tobacco-free alternatives. *Tobacco Control, 24*(Suppl 1), i22-i30.
[109] SalloumRG2016_10688
[110] Neergaard, J., Singh, P., Job, J., & Montgomery, S. (2007). Waterpipe smoking and nicotine exposure: A review of the current evidence. *Nicotine and Tobacco Research, 9*(10), 987-994.
Nuwayhid, I. A., Yamout, B., Azar, G., & Kambris, M. A. (1998). Narghile (hubble-bubble) smoking, low birth weight, and other pregnancy outcomes. *American Journal of Epidemiology, 148*(4), 375-383.
[111] Hadidi, K. A., & Mohammed, F. I. (2004). Nicotine content in tobacco used in hubble-bubble smoking. *Saudi Medical Journal, 25*(7), 912-917.
Neergaard, J., Singh, P., Job, J., & Montgomery, S. (2007). Waterpipe smoking and nicotine exposure: A review of the current evidence. *Nicotine and Tobacco Research, 9*(10), 987-994.
[112] Aslam, H. M., Saleem, S., German, S., & Qureshi, W. A. (2014). Harmful effects of shisha: Literature review. *International Archives of Medicine, 7*, 16. doi:10.1186/1755-7682-7-16.
Neergaard, J., Singh, P., Job, J., & Montgomery, S. (2007). Waterpipe smoking and nicotine exposure: A review of the current evidence. *Nicotine and Tobacco Research, 9*(10), 987-994.
[113] Neergaard, J., Singh, P., Job, J., & Montgomery, S. (2007). Waterpipe smoking and nicotine exposure: A review of the current evidence. *Nicotine and Tobacco Research, 9*(10), 987-994.
[114] Neergaard, J., Singh, P., Job, J., & Montgomery, S. (2007). Waterpipe smoking and nicotine exposure: A review of the current evidence. *Nicotine and Tobacco Research, 9*(10), 987-994.
[115] Sibai, A. M., Tohme, R. A., Almedawar, M. M., Itani, T., Yassine, S. I., Nohra, E. A., et al. (2014). Lifetime cumulative exposure to waterpipe smoking is associated with coronary artery disease. *Atherosclerosis, 234*(2), 454-460.
[116] Aslam, H. M., Saleem, S., German, S., & Qureshi, W. A. (2014). Harmful effects of shisha: Literature review. *International Archives of Medicine, 7*, 16. doi:10.1186/1755-7682-7-16.
Blank, M. D., Cobb, C. O., Kilgalen, B., Austin, J., Weaver, M. F., Shihadeh, A., et al. (2011). Acute effects of waterpipe tobacco smoking: A double-blind, placebo-control study. *Drug and Alcohol Dependence, 116*(1-3), 102-109.
[117] Akl, E. A., Gaddam, S., Gunukula, S. K., Honeine, R., Jaoude, P. A., & Irani, J. (2010). The effects of waterpipe tobacco smoking on health outcomes: A systematic review. *International Journal of Epidemiology, 39*(3), 834-857.
Daher, N., Saleh, R., Jaroudi, E., Sheheitli, H., Badr, T., Sepetdjian, E., et al. (2010). Comparison of carcinogen, carbon monoxide, and ultrafine particle emissions from narghile waterpipe and cigarette smoking: Sidestream smoke measurements and assessment of second-hand smoke emission factors. *Atmospheric Environment (1994), 44*(1), 8-14.
El-Zaatari, Z. M., Chami, H. A., & Zaatari, G. S. (2015). Health effects associated with waterpipe smoking. *Tobacco Control, 24 Suppl 1*, i31-i43.
Kumar, S. R., Davies, S., Weitzman, M., & Sherman, S. (2015). A review of air quality, biological indicators and health effects of second-hand waterpipe smoke exposure. *Tobacco Control, 24*(Suppl 1), i54-i59.
Shihadeh, A., Eissenberg, T., Rammah, M., Salman, R., Jaroudi, E., & El-Sabban, M. (2014). Comparison of tobacco-containing and tobacco-free waterpipe products: Effects on human alveolar cells. *Nicotine and Tobacco Research, 16*(4), 496-499.
Shihadeh, A., Schubert, J., Klaiany, J., El, S. M., Luch, A., & Saliba, N. A. (2015). Toxicant content, physical properties and biological activity of waterpipe tobacco smoke and its tobacco-free alternatives. *Tobacco Control, 24*(Suppl 1), i22-i30.
Sepetdjian, E., Saliba, N., & Shihadeh, A. (2010). Carcinogenic PAH in waterpipe charcoal products. *Food and Chemical Toxicology, 48*(11), 3242-3245.
Shihadeh, A., Salman, R., Jaroudi, E., Saliba, N., Sepetdjian, E., Blank, M. D., et al. (2012). Does switching to a tobacco-free waterpipe product reduce toxicant intake? A crossover study comparing CO, NO, PAH, volatile aldehydes, "tar" and nicotine yields. *Food and Chemical Toxicology, 50*(5), 1494-1498.

Zhou, S., Weitzman, M., Vilcassim, R., Wilson, J., Legrand, N., Saunders, E., et al. (2014). Air quality in New York City hookah bars. *Tobacco Control, 24*(e3), e193-e198. doi:10.1136/tobaccocontrol-2014-051763.
[118] El-Zaatari, Z. M., Chami, H. A., & Zaatari, G. S. (2015). Health effects associated with waterpipe smoking. *Tobacco Control, 24*(Suppl 1), i31-i43.
Shihadeh, A., Eissenberg, T., Rammah, M., Salman, R., Jaroudi, E., & El-Sabban, M. (2014). Comparison of tobacco-containing and tobacco-free waterpipe products: Effects on human alveolar cells. *Nicotine and Tobacco Research, 16*(4), 496-499.
[119] El-Zaatari, Z. M., Chami, H. A., & Zaatari, G. S. (2015). Health effects associated with waterpipe smoking. *Tobacco Control, 24*(Suppl 1), i31-i43.
[120] Aslam, H. M., Saleem, S., German, S., & Qureshi, W. A. (2014). Harmful effects of shisha: literature review. *International Archives of Medicine, 7*, 16. doi:10.1186/1755-7682-7-16.
Nuwayhid, I. A., Yamout, B., Azar, G., & Kambris, M. A. (1998). Narghile (hubble-bubble) smoking, low birth weight, and other pregnancy outcomes. *American Journal of Epidemiology, 148*(4), 375-383.
[121] El-Zaatari, Z. M., Chami, H. A., & Zaatari, G. S. (2015). Health effects associated with waterpipe smoking. *Tobacco Control, 24*(Suppl 1), i31-i43.
La, F. G., Weiser, G., Steiner, I. P., & Shavit, I. (2012). Carbon monoxide poisoning in narghile (water pipe) tobacco smokers. *Canadian Journal of Emergency Medicine, 14*(1), 57-59.
Monzer, B., Sepetdjian, E., Saliba, N., & Shihadeh, A. (2008). Charcoal emissions as a source of CO and carcinogenic PAH in mainstream narghile waterpipe smoke. *Food and Chemical Toxicology, 46*(9), 2991-2995.
von, R. J., Schonenberger, M., & Barlocher, L. (2014). Carbon monoxide poisoning following use of a water pipe/hookah. *Deutsches Ärzteblatt International, 111*(40), 674-679.
[122] Zhang, B., Haji, F., Kaufman, P., Muir, S., & Ferrence, R. (2015). 'Enter at your own risk': A multimethod study of air quality and biological measures in Canadian waterpipe cafes. *Tobacco Control, 24*(2), 175-181.
[123] Centers for Disease Control and Prevention. (2016). *Smokeless tobacco: Products and marketing.* Retrieved from https://www.cdc.gov.
[124] Centers for Disease Control and Prevention. (2016). *Smokeless tobacco: Products and marketing.* Retrieved from https://www.cdc.gov.
World Health Organization. (2007). *IARC monographs on the evaluation of carcinogenic risks to humans: Volume 89: Smokeless tobacco and some tobacco-specific N-nitrosamines.* France: International Agency for Research on Cancer.
[125] Centers for Disease Control and Prevention. (2016). *Smokeless tobacco: Products and marketing.* Retrieved from https://www.cdc.gov.
World Health Organization. (2007). *IARC monographs on the evaluation of carcinogenic risks to humans: Volume 89: Smokeless tobacco and some tobacco-specific N-nitrosamines.* France: International Agency for Research on Cancer.
[126] Centers for Disease Control and Prevention. (2016). *Smokeless tobacco: Products and marketing.* Retrieved from https://www.cdc.gov.
[127] Centers for Disease Control and Prevention. (2016). *Smokeless tobacco: Products and marketing.* Retrieved from https://www.cdc.gov.
[128] Hatsukami, D. K., Stepanov, I., Severson, H., Jensen, J. A., Lindgren, B. R., Horn, K., et al. (2015). Evidence supporting product standards for carcinogens in smokeless tobacco products. *Cancer Prevention Research, 8*(1), 20-26.
World Health Organization. (2007). *IARC monographs on the evaluation of carcinogenic risks to humans: Volume 89: Smokeless tobacco and some tobacco-specific N-nitrosamines.* France: International Agency for Research on Cancer.
[129] Mayo Clinic. (2016). *Chewing tobacco: Not a safe product.* Retrieved from http://www.mayoclinic.org.
[130] Centers for Disease Control and Prevention. (2016). *Smokeless tobacco: Products and marketing.* Retrieved from https://www.cdc.gov.
World Health Organization. (2007). *IARC monographs on the evaluation of carcinogenic risks to humans: Volume 89: Smokeless tobacco and some tobacco-specific N-nitrosamines.* France: International Agency for Research on Cancer.
[131] Centers for Disease Control and Prevention. (2016). *Smokeless tobacco: Products and marketing.* Retrieved from https://www.cdc.gov.
[132] Centers for Disease Control and Prevention. (2016). *Smokeless tobacco: Products and marketing.* Retrieved from https://www.cdc.gov.

[133] Lawler, T. S., Stanfill, S. B., Zhang, L., Ashley, D. L., & Watson, C. H. (2013). Chemical characterization of domestic oral tobacco products: Total nicotine, pH, unprotonated nicotine and tobacco-specific N-nitrosamines. *Food and Chemical Toxicology, 57*, 380-386.

Pickworth, W. B., Rosenberry, Z. R., Gold, W., & Koszowski, B. (2014). Nicotine absorption from smokeless tobacco modified to adjust pH. *Journal of Addiction Research and Therapy, 5*(3), 1000184. doi:10.4172/2155-6105.1000184.

Richter, P., Hodge, K., Stanfill, S., Zhang, L., & Watson, C. (2008). Surveillance of moist snuff: Total nicotine, moisture, pH, un-ionized nicotine, and tobacco-specific nitrosamines. *Nicotine and Tobacco Research, 10*(11), 1645-1652.

Stepanov, I., Jensen, J., Biener, L., Bliss, R. L., Hecht, S. S., & Hatsukami, D. K. (2012). Increased pouch sizes and resulting changes in the amounts of nicotine and tobacco-specific N-nitrosamines in single pouches of Camel Snus and Marlboro Snus. *Nicotine and Tobacco Research, 14*(10), 1241-1245.

[134] Stanfill, S. B., Connolly, G. N., Zhang, L., Jia, L. T., Henningfield, J. E., Richter, P., et al. (2011). Global surveillance of oral tobacco products: Total nicotine, unionised nicotine and tobacco-specific N-nitrosamines. *Tobacco Control, 20*(3), e2. doi:10.1136/tc.2010.037465.

[135] Stanfill, S. B., Connolly, G. N., Zhang, L., Jia, L. T., Henningfield, J. E., Richter, P., et al. (2011). Global surveillance of oral tobacco products: total nicotine, unionised nicotine and tobacco-specific N-nitrosamines. *Tobacco Control, 20*(3), e2. doi:10.1136/tc.2010.037465.

[136] Lawler, T. S., Stanfill, S. B., Zhang, L., Ashley, D. L., & Watson, C. H. (2013). Chemical characterization of domestic oral tobacco products: Total nicotine, pH, unprotonated nicotine and tobacco-specific N-nitrosamines. *Food and Chemical Toxicology, 57*, 380-386.

[137] Alguacil, J., & Silverman, D. T. (2004). Smokeless and other noncigarette tobacco use and pancreatic cancer: A case-control study based on direct interviews. *Cancer Epidemiology, Biomarkers and Prevention, 13*(1), 55-58.

Bertuccio, P., La, V. C., Silverman, D. T., Petersen, G. M., Bracci, P. M., Negri, E., et al. (2011). Cigar and pipe smoking, smokeless tobacco use and pancreatic cancer: An analysis from the International Pancreatic Cancer Case-Control Consortium (PanC4). *Annals of Oncology, 22*(6), 1420-1426.

Boffetta, P., Aagnes, B., Weiderpass, E., & Andersen, A. (2005). Smokeless tobacco use and risk of cancer of the pancreas and other organs. *International Journal of Cancer, 114*(6), 992-995.

Boffetta, P., Hecht, S., Gray, N., Gupta, P., & Straif, K. (2008). Smokeless tobacco and cancer. *Lancet Oncology, 9*(7), 667-675.

Burkey, M. D., Feirman, S., Wang, H., Choudhury, S. R., Grover, S., & Johnston, F. M. (2014). The association between smokeless tobacco use and pancreatic adenocarcinoma: A systematic review. *Cancer Epidemiology, 38*(6), 647-653.

Colilla, S. A. (2010). An epidemiologic review of smokeless tobacco health effects and harm reduction potential. *Regulatory Toxicology and Pharmacology, 56*(2), 197-211.

Hoffmann, D., & Djordjevic, M. V. (1997). Chemical composition and carcinogenicity of smokeless tobacco. *Advances in Dental Research, 11*(3), 322-329.

Janbaz, K. H., Qadir, M. I., Basser, H. T., Bokhari, T. H., & Ahmad, B. (2014). Risk for oral cancer from smokeless tobacco. *Contemporary Oncology, 18*(3), 160-164.

Khan, Z., Tonnies, J., & Muller, S. (2014). Smokeless tobacco and oral cancer in South Asia: A systematic review with meta-analysis. *Journal of Cancer Epidemiology, 2014*, 394696.

Winn, D. M., Blot, W. J., Shy, C. M., Pickle, L. W., Toledo, A., & Fraumeni, J. F. (1981). Snuff dipping and oral cancer among women in the southern United States. *New England Journal of Medicine, 304*(13), 745-749.

Lee, P. N., & Hamling, J. (2009). Systematic review of the relation between smokeless tobacco and cancer in Europe and North America. *BMC Medicine, 7*, 36.

Siddiqi, K., Shah, S., Abbas, S. M., Vidyasagaran, A., Jawad, M., Dogar, O., et al. (2015). Global burden of disease due to smokeless tobacco consumption in adults: Analysis of data from 113 countries. *BMC Medicine, 13*, 194.

Weitkunat, R., Sanders, E., & Lee, P. N. (2007). Meta-analysis of the relation between European and American smokeless tobacco and oral cancer. *BMC Public Health, 7*, 334. doi:10.1186/1471-2458-7-334.

Rodu, B., & Jansson, C. (2004). Smokeless tobacco and oral cancer: a review of the risks and determinants. *Critical Reviews in Oral Biology and Medicine, 15*(5), 252-263.

Zhou, J., Michaud, D. S., Langevin, S. M., McClean, M. D., Eliot, M., & Kelsey, K. T. (2013). Smokeless tobacco and risk of head and neck cancer: Evidence from a case-control study in New England. *International Journal of Cancer, 132*(8), 1911-1917.

Lee, P. N. (2011). Summary of the epidemiological evidence relating snus to health. *Regulatory Toxicology and Pharmacology, 59*(2), 197-214.
Luo, J., Ye, W., Zendehdel, K., Adami, J., Adami, H. O., Boffetta, P., et al. (2007). Oral use of Swedish moist snuff (snus) and risk for cancer of the mouth, lung, and pancreas in male construction workers: A retrospective cohort study. *Lancet, 369*(9578), 2015-2020.
Sponsiello-Wang, Z., Weitkunat, R., & Lee, P. N. (2008). Systematic review of the relation between smokeless tobacco and cancer of the pancreas in Europe and North America. *BMC Cancer, 8*, 356. doi:10.1186/1471-2407-8-356.
[138] Boffetta, P., Hecht, S., Gray, N., Gupta, P., & Straif, K. (2008). Smokeless tobacco and cancer. *Lancet Oncology, 9*(7), 667-675.
Hatsukami, D. K., Stepanov, I., Severson, H., Jensen, J. A., Lindgren, B. R., Horn, K., et al. (2015). Evidence supporting product standards for carcinogens in smokeless tobacco products. *Cancer Prevention Research, 8*(1), 20-26.
Janbaz, K. H., Qadir, M. I., Basser, H. T., Bokhari, T. H., & Ahmad, B. (2014). Risk for oral cancer from smokeless tobacco. *Contemporary Oncology, 18*(3), 160-164.
Lawler, T. S., Stanfill, S. B., Zhang, L., Ashley, D. L., & Watson, C. H. (2013). Chemical characterization of domestic oral tobacco products: Total nicotine, pH, unprotonated nicotine and tobacco-specific N-nitrosamines. *Food and Chemical Toxicology, 57*, 380-386.
Rodu, B., & Jansson, C. (2004). Smokeless tobacco and oral cancer: A review of the risks and determinants. *Critical Reviews in Oral Biology and Medicine, 15*(5), 252-263.
[139] Borgerding, M. F., Bodnar, J. A., Curtin, G. M., & Swauger, J. E. (2012). The chemical composition of smokeless tobacco: A survey of products sold in the United States in 2006 and 2007. *Regulatory Toxicology and Pharmacology, 64*(3), 367-387.
Centers for Disease Control and Prevention. (2015). *NNAL (4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol)* . Retrieved from https://www.cdc.gov.
Hecht, S. S., & Hoffmann, D. (1988). Tobacco-specific nitrosamines, an important group of carcinogens in tobacco and tobacco smoke. *Carcinogenesis, 9*(6), 875-884.
Hoffmann, D., Djordjevic, M. V., Fan, J., Zang, E., Glynn, T., & Connolly, G. N. (1995). Five leading U.S. commercial brands of moist snuff in 1994: Assessment of carcinogenic N-nitrosamines. *Journal of the National Cancer Institute, 87*(24), 1862-1869.
Hoffmann, D., & Djordjevic, M. V. (1997). Chemical composition and carcinogenicity of smokeless tobacco. *Advances in Dental Research, 11*(3), 322-329.
International Agency for Research on Cancer. (2016). *Agents classified by the IARC monographs, Volumes 1-112.* Retrieved from https://monographs.iarc.fr.
Lawler, T. S., Stanfill, S. B., Zhang, L., Ashley, D. L., & Watson, C. H. (2013). Chemical characterization of domestic oral tobacco products: Total nicotine, pH, unprotonated nicotine and tobacco-specific N-nitrosamines. *Food and Chemical Toxicology, 57*, 380-386.
McAdam, K. G., Faizi, A., Kimpton, H., Porter, A., & Rodu, B. (2013). Polycyclic aromatic hydrocarbons in U.S. and Swedish smokeless tobacco products. *Chemistry Central Journal, 7*(1), 151.
Rodu, B., & Jansson, C. (2004). Smokeless tobacco and oral cancer: A review of the risks and determinants. *Critical Reviews in Oral Biology and Medicine, 15*(5), 252-263.
Rostron, B. L., Chang, C. M., van Bemmel, D. M., Xia, Y., & Blount, B. C. (2015). Nicotine and toxicant exposure among U.S. smokeless tobacco users: Results from 1999 to 2012 National Health and Nutrition Examination Survey data. *Cancer Epidemiology, Biomarkers and Prevention, 24*(12), 1829-1837.
Stepanov, I., Villalta, P. W., Knezevich, A., Jensen, J., Hatsukami, D., & Hecht, S. S. (2010). Analysis of 23 polycyclic aromatic hydrocarbons in smokeless tobacco by gas chromatography-mass spectrometry. *Chemical Research in Toxicology, 23*(1), 66-73.
Stepanov, I., Biener, L., Yershova, K., Nyman, A. L., Bliss, R., Parascandola, M., et al. (2014). Monitoring tobacco-specific N-nitrosamines and nicotine in novel smokeless tobacco products: Findings from round II of the new product watch. *Nicotine and Tobacco Research, 16*(8), 1070-1078.
[140] Brunnemann, K. D., Qi, J., & Hoffmann, D. (2002). Chemical profile of two types of oral snuff tobacco. *Food and Chemical Toxicology, 40*(11), 1699-1703.
Lawler, T. S., Stanfill, S. B., Zhang, L., Ashley, D. L., & Watson, C. H. (2013). Chemical characterization of domestic oral tobacco products: Total nicotine, pH, unprotonated nicotine and tobacco-specific N-nitrosamines. *Food and Chemical Toxicology, 57*, 380-386.

Richter, P., Hodge, K., Stanfill, S., Zhang, L., & Watson, C. (2008). Surveillance of moist snuff: Total nicotine, moisture, pH, un-ionized nicotine, and tobacco-specific nitrosamines. *Nicotine and Tobacco Research, 10*(11), 1645-1652.
[141] Richter, P., Hodge, K., Stanfill, S., Zhang, L., & Watson, C. (2008). Surveillance of moist snuff: Total nicotine, moisture, pH, un-ionized nicotine, and tobacco-specific nitrosamines. *Nicotine and Tobacco Research, 10*(11), 1645-1652.
[142] Brunnemann, K. D., Qi, J., & Hoffmann, D. (2002). Chemical profile of two types of oral snuff tobacco. *Food and Chemical Toxicology, 40*(11), 1699-1703.
Lawler, T. S., Stanfill, S. B., Zhang, L., Ashley, D. L., & Watson, C. H. (2013). Chemical characterization of domestic oral tobacco products: Total nicotine, pH, unprotonated nicotine and tobacco-specific N-nitrosamines. *Food and Chemical Toxicology, 57*, 380-386.
Richter, P., Hodge, K., Stanfill, S., Zhang, L., & Watson, C. (2008). Surveillance of moist snuff: Total nicotine, moisture, pH, un-ionized nicotine, and tobacco-specific nitrosamines. *Nicotine and Tobacco Research, 10*(11), 1645-1652.
Pickworth, W. B., Rosenberry, Z. R., Gold, W., & Koszowski, B. (2014). Nicotine absorption from smokeless tobacco modified to adjust pH. *Journal of Addiction Research and Therapy, 5*(3), 1000184. doi:10.4172/2155-6105.1000184.
[143] Stepanov, I., Jensen, J., Biener, L., Bliss, R. L., Hecht, S. S., & Hatsukami, D. K. (2012). Increased pouch sizes and resulting changes in the amounts of nicotine and tobacco-specific N-nitrosamines in single pouches of Camel Snus and Marlboro Snus. *Nicotine and Tobacco Research, 14*(10), 1241-1245.
[144] Richter, P., Hodge, K., Stanfill, S., Zhang, L., & Watson, C. (2008). Surveillance of moist snuff: Total nicotine, moisture, pH, un-ionized nicotine, and tobacco-specific nitrosamines. *Nicotine and Tobacco Research, 10*(11), 1645-1652.
[145] Richter, P., Hodge, K., Stanfill, S., Zhang, L., & Watson, C. (2008). Surveillance of moist snuff: Total nicotine, moisture, pH, un-ionized nicotine, and tobacco-specific nitrosamines. *Nicotine and Tobacco Research, 10*(11), 1645-1652.
[146] DiFranza, J. R., Sweet, M., Savageau, J. A., & Ursprung, W. W. (2012). The assessment of tobacco dependence in young users of smokeless tobacco. *Tobacco Control, 21*(5), 471-476.
[147] Asplund, K. (2003). Smokeless tobacco and cardiovascular disease. *Progress in Cardiovascular Diseases, 45*(5), 383-394.
[148] Boffetta, P., & Straif, K. (2009). Use of smokeless tobacco and risk of myocardial infarction and stroke: Systematic review with meta-analysis. *BMJ, 339*, b3060.
Colilla, S. A. (2010). An epidemiologic review of smokeless tobacco health effects and harm reduction potential. *Regulatory Toxicology and Pharmacology, 56*(2), 197-211.
Hergens, M. P., Alfredsson, L., Bolinder, G., Lambe, M., Pershagen, G., & Ye, W. (2007). Long-term use of Swedish moist snuff and the risk of myocardial infarction amongst men. *Journal of Internal Medicine, 262*(3), 351-359.
Siegel, D., Benowitz, N., Ernster, V. L., Grady, D. G., & Hauck, W. W. (1992). Smokeless tobacco, cardiovascular risk factors, and nicotine and cotinine levels in professional baseball players. *American Journal of Public Health, 82*(3), 417-421.
[149] Gupta, R., Gupta, N., & Khedar, R. S. (2013). Smokeless tobacco and cardiovascular disease in low and middle income countries. *Indian Heart Journal, 65*(4), 369-377.
[150] Rostron, B. L., Chang, C. M., van Bemmel, D. M., Xia, Y., & Blount, B. C. (2015). Nicotine and toxicant exposure among U.S. smokeless tobacco users: Results from 1999 to 2012 National Health and Nutrition Examination Survey data. *Cancer Epidemiology, Biomarkers and Prevention, 24*(12), 1829-1837.
[151] Boffetta, P., Hecht, S., Gray, N., Gupta, P., & Straif, K. (2008). Smokeless tobacco and cancer. *Lancet Oncology, 9*(7), 667-675.
Hoffmann, D., & Djordjevic, M. V. (1997). Chemical composition and carcinogenicity of smokeless tobacco. *Advances in Dental Research, 11*(3), 322-329.
Janbaz, K. H., Qadir, M. I., Basser, H. T., Bokhari, T. H., & Ahmad, B. (2014). Risk for oral cancer from smokeless tobacco. *Contemporary Oncology, 18*(3), 160-164.
Khan, Z., Tonnies, J., & Muller, S. (2014). Smokeless tobacco and oral cancer in South Asia: A systematic review with meta-analysis. *Journal of Cancer Epidemiology*. doi:10.1155/2014/394696.
Lee, P. N., & Hamling, J. (2009). Systematic review of the relation between smokeless tobacco and cancer in Europe and North America. *BMC Medicine, 7*, 36. doi:10.1186/1741-7015-7-36.

Siddiqi, K., Shah, S., Abbas, S. M., Vidyasagaran, A., Jawad, M., Dogar, O., et al. (2015). Global burden of disease due to smokeless tobacco consumption in adults: Analysis of data from 113 countries. *BMC Medicine, 13*, 194.
Weitkunat, R., Sanders, E., & Lee, P. N. (2007). Meta-analysis of the relation between European and American smokeless tobacco and oral cancer. *BMC Public Health, 7*, 334. doi:10.1186/1471-2458-7-334.
Winn, D. M., Blot, W. J., Shy, C. M., Pickle, L. W., Toledo, A., & Fraumeni, J. F. (1981). Snuff dipping and oral cancer among women in the southern United States. *New England Journal of Medicine, 304*(13), 745-749.
Zhou, J., Michaud, D. S., Langevin, S. M., McClean, M. D., Eliot, M., & Kelsey, K. T. (2013). Smokeless tobacco and risk of head and neck cancer: Evidence from a case-control study in New England. *International Journal of Cancer, 132*(8), 1911-1917.
[152] Rodu, B., & Jansson, C. (2004). Smokeless tobacco and oral cancer: A review of the risks and determinants. *Critical Reviews in Oral Biology and Medicine, 15*(5), 252-263.
[153] Alguacil, J., & Silverman, D. T. (2004). Smokeless and other noncigarette tobacco use and pancreatic cancer: A case-control study based on direct interviews. *Cancer Epidemiology, Biomarkers and Prevention, 13*(1), 55-58.
Boffetta, P., Aagnes, B., Weiderpass, E., & Andersen, A. (2005). Smokeless tobacco use and risk of cancer of the pancreas and other organs. *International Journal of Cancer, 114*(6), 992-995.
Luo, J., Ye, W., Zendehdel, K., Adami, J., Adami, H. O., Boffetta, P., et al. (2007). Oral use of Swedish moist snuff (snus) and risk for cancer of the mouth, lung, and pancreas in male construction workers: A retrospective cohort study. *Lancet, 369*(9578), 2015-2020.
[154] Bertuccio, P., La, V. C., Silverman, D. T., Petersen, G. M., Bracci, P. M., Negri, E., et al. (2011). Cigar and pipe smoking, smokeless tobacco use and pancreatic cancer: An analysis from the International Pancreatic Cancer Case-Control Consortium (PanC4). *Annals of Oncology, 22*(6), 1420-1426.
Boffetta, P., Hecht, S., Gray, N., Gupta, P., & Straif, K. (2008). Smokeless tobacco and cancer. *Lancet Oncology, 9*(7), 667-675.
Burkey, M. D., Feirman, S., Wang, H., Choudhury, S. R., Grover, S., & Johnston, F. M. (2014). The association between smokeless tobacco use and pancreatic adenocarcinoma: A systematic review. *Cancer Epidemiology, 38*(6), 647-653.
Colilla, S. A. (2010). An epidemiologic review of smokeless tobacco health effects and harm reduction potential. *Regulatory Toxicology and Pharmacology, 56*(2), 197-211.
Lee, P. N., & Hamling, J. (2009). Systematic review of the relation between smokeless tobacco and cancer in Europe and North America. *BMC Medicine, 7*, 36.
Lee, P. N. (2011). Summary of the epidemiological evidence relating snus to health. *Regulatory Toxicology and Pharmacology, 59*(2), 197-214.
Sponsiello-Wang, Z., Weitkunat, R., & Lee, P. N. (2008). Systematic review of the relation between smokeless tobacco and cancer of the pancreas in Europe and North America. *BMC Cancer, 8*, 356. doi:10.1186/1471-2407-8-356.
[155] England, L. J., Kim, S. Y., Shapiro-Mendoza, C. K., Wilson, H. G., Kendrick, J. S., Satten, G. A., et al. (2013). Effects of maternal smokeless tobacco use on selected pregnancy outcomes in Alaska Native women: A case-control study. *Acta Obstetricia et Gynecologica Scandinavica, 92*(6), 648-655.
[156] Cheng, T. (2014). Chemical evaluation of electronic cigarettes. *Tobacco Control, 23*(Suppl 2), ii11-ii17.
McAuley, T. R., Hopke, P. K., Zhao, J., & Babaian, S. (2012). Comparison of the effects of e-cigarette vapor and cigarette smoke on indoor air quality. *Inhalation Toxicology, 24*(12), 850-857.
[157] Cheng, T. (2014). Chemical evaluation of electronic cigarettes. *Tobacco Control, 23*(Suppl 2), ii11-ii17.
Schripp, T., Markewitz, D., Uhde, E., & Salthammer, T. (2013). Does e-cigarette consumption cause passive vaping? *Indoor Air, 23*(1), 25-31.
[158] Brown, C. J., & Cheng, J. M. (2014). Electronic cigarettes: Product characterisation and design considerations. *Tobacco Control, 23*(Suppl 2), ii4-10.
Pearson, J. L., Amato, M. S., Wang, X., Zhao, K., Cha, S., Cohn, A. M., et al. (2017). How U.S. smokers refer to e-cigarettes: An examination of user-generated posts from a web-based smoking cessation intervention, 2008-2015. *Nicotine and Tobacco Research, 19*(2), 253-257.
[159] Breland, A. B., Spindle, T., Weaver, M., & Eissenberg, T. (2014). Science and electronic cigarettes: Current data, future needs. *Journal of Addiction Medicine, 8*(4), 223-233.
[160] Breland, A. B., Spindle, T., Weaver, M., & Eissenberg, T. (2014). Science and electronic cigarettes: Current data, future needs. *Journal of Addiction Medicine, 8*(4), 223-233.
Brown, C. J., & Cheng, J. M. (2014). Electronic cigarettes: Product characterisation and design considerations. *Tobacco Control, 23*(Suppl 2), ii4-10.

[161] Brown, C. J., & Cheng, J. M. (2014). Electronic cigarettes: Product characterisation and design considerations. *Tobacco Control, 23*(Suppl 2), ii4-10.
[162] NJOY.com. (2016). *NJOY daily.* Retrieved from https://www.njoy.com.
[163] Yingst, J. M., Veldheer, S., Hrabovsky, S., Nichols, T. T., Wilson, S. J., & Foulds, J. (2015). Factors associated with electronic cigarette users' device preferences and transition from first generation to advanced generation devices. *Nicotine and Tobacco Research, 17*(10), 1242-1246.
[164] Brown, C. J., & Cheng, J. M. (2014). Electronic cigarettes: Product characterisation and design considerations. *Tobacco Control, 23*(Suppl 2), ii4-10.
[165] Yingst, J. M., Veldheer, S., Hrabovsky, S., Nichols, T. T., Wilson, S. J., & Foulds, J. (2015). Factors associated with electronic cigarette users' device preferences and transition from first generation to advanced generation devices. *Nicotine and Tobacco Research, 17*(10), 1242-1246.
[166] Williams, M., Ghai, S., & Talbot, P. (2015). Disposable electronic cigarettes and electronic hookahs: Evaluation of performance. *Nicotine and Tobacco Research, 17*(2), 201-208.
[167] Cheng, T. (2014). Chemical evaluation of electronic cigarettes. *Tobacco Control, 23*(Suppl 2), ii11-ii17.
McAuley, T. R., Hopke, P. K., Zhao, J., & Babaian, S. (2012). Comparison of the effects of e-cigarette vapor and cigarette smoke on indoor air quality. *Inhalation Toxicology, 24*(12), 850-857.
Williams, M., Ghai, S., & Talbot, P. (2015). Disposable electronic cigarettes and electronic hookahs: Evaluation of performance. *Nicotine and Tobacco Research, 17*(2), 201-208.
[168] Breland, A. B., Spindle, T., Weaver, M., & Eissenberg, T. (2014). Science and electronic cigarettes: Current data, future needs. *Journal of Addiction Medicine, 8*(4), 223-233.
Brown, C. J., & Cheng, J. M. (2014). Electronic cigarettes: Product characterisation and design considerations. *Tobacco Control, 23*(Suppl 2), ii4-10.
[169] Behar, R. Z., Hua, M., & Talbot, P. (2015). Puffing topography and nicotine intake of electronic cigarette users. *PLoS One, 10*(2), e0117222. doi:10.1371/journal.pone.0117222.
Breland, A. B., Spindle, T., Weaver, M., & Eissenberg, T. (2014). Science and electronic cigarettes: Current data, future needs. *Journal of Addiction Medicine, 8*(4), 223-233.
Oh, A. Y., & Kacker, A. (2014). Do electronic cigarettes impart a lower potential disease burden than conventional tobacco cigarettes? Review on e-cigarette vapor versus tobacco smoke. *Laryngoscope, 124*(12), 2702-2706.
Tayyarah, R., & Long, G. A. (2014). Comparison of select analytes in aerosol from e-cigarettes with smoke from conventional cigarettes and with ambient air. *Regulatory Toxicology and Pharmacology, 70*, 704-710.
[170] McAuley, T. R., Hopke, P. K., Zhao, J., & Babaian, S. (2012). Comparison of the effects of e-cigarette vapor and cigarette smoke on indoor air quality. *Inhalation Toxicology, 24*(12), 850-857.
Trtchounian, A., & Talbot, P. (2011). Electronic nicotine delivery systems: is there a need for regulation? *Tobacco Control, 20*(1), 47-52.
Williams, M., Villarreal, A., Bozhilov, K., Lin, S., & Talbot, P. (2013). Metal and silicate particles including nanoparticles are present in electronic cigarette cartomizer fluid and aerosol. *PLoS One, 8*(3), e57987. doi:10.1371/journal.pone.0057987.
[171] Bahl, V., Lin, S., Xu, N., Davis, B., Wang, Y. H., & Talbot, P. (2012). Comparison of electronic cigarette refill fluid cytotoxicity using embryonic and adult models. *Reproductive Toxicology, 34*(4), 529-537.
McAuley, T. R., Hopke, P. K., Zhao, J., & Babaian, S. (2012). Comparison of the effects of e-cigarette vapor and cigarette smoke on indoor air quality. *Inhalation Toxicology, 24*(12), 850-857.
Williams, M., Villarreal, A., Bozhilov, K., Lin, S., & Talbot, P. (2013). Metal and silicate particles including nanoparticles are present in electronic cigarette cartomizer fluid and aerosol. *PLoS One, 8*(3), e57987. doi:10.1371/journal.pone.0057987.
[172] Centers for Disease Control and Prevention. (2015). *E-cigarettes: An emerging public health challenge.* Retrieved from https://www.cdc.gov.
[173] El-Hellani, A., El-Hage, R., Baalbaki, R., Salman, R., Talih, S., Shihadeh, A., et al. (2015). Free-base and protonated nicotine in electronic cigarette liquids and aerosols. *Chemical Research in Toxicology, 28*(8), 1532-1537.
Stepanov, I., & Fujioka, N. (2015). Bringing attention to e-cigarette pH as an important element for research and regulation. *Tobacco Control, 24*, 413-414.
[174] Farsalinos, K. E., Romagna, G., & Voudris, V. (2015). Factors associated with dual use of tobacco and electronic cigarettes: A case control study. *International Journal of Drug Policy*.
Hajek, P., Przulj, D., Phillips, A., Anderson, R., & McRobbie, H. (2017). Nicotine delivery to users from cigarettes and from different types of e-cigarettes. *Psychopharmacology*. doi:10.1007/s00213-016-4512-6.
[175] Etter, J. F. (2014). Levels of saliva cotinine in electronic cigarette users. *Addiction, 109*(5), 825-829.

Lopez, A. A., Hiler, M. M., Soule, E. K., Ramoa, C. P., Karaoghlanian, N. V., Lipato, T., et al. (2016). Effects of Electronic Cigarette Liquid Nicotine Concentration on Plasma Nicotine and Puff Topography in Tobacco Cigarette Smokers: A Preliminary Report. *Nicotine and Tobacco Research, 18*(5), 720-723.
Ramoa, C. P., Hiler, M. M., Spindle, T. R., Lopez, A. A., Karaoghlanian, N., Lipato, T., et al. (2016). Electronic cigarette nicotine delivery can exceed that of combustible cigarettes: a preliminary report. *Tobacco Control, 25*(e1), e6-e9.
St. Helen G., Havel, C., Dempsey, D. A., Jacob, P., & Benowitz, N. L. (2016). Nicotine delivery, retention and pharmacokinetics from various electronic cigarettes. *Addiction, 111*(3), 535-544.
Wagener, T. L., Floyd, E. L., Stpanov, I., Driskill, L. M., Frank, S. G., Meier, E., et al. (2016). Have combustible cigarettes met their match? The nicotine delivery profiles and harmful constituent exposures of second-generationa and third-generation electronic cigarette users. *Tobacco Control*.
[176] Bahl, V., Lin, S., Xu, N., Davis, B., Wang, Y. H., & Talbot, P. (2012). Comparison of electronic cigarette refill fluid cytotoxicity using embryonic and adult models. *Reproductive Toxicology, 34*(4), 529-537.
Etter, J. F., Zather, E., & Svensson, S. (2013). Analysis of refill liquids for electronic cigarettes. *Addiction, 108*(9), 1671-1679.
Farsalinos, K. E., Romagna, G., & Voudris, V. (2015). Factors associated with dual use of tobacco and electronic cigarettes: A case control study. *International Journal of Drug Policy*.
Kosmider, L., Sobczak, A., Fik, M., Knysak, J., Zaciera, M., Kurek, J., et al. (2014). Carbonyl compounds in electronic cigarette vapors: effects of nicotine solvent and battery output voltage. *Nicotine and Tobacco Research, 16*(10), 1319-1326.
Lerner, C. A., Sundar, I. K., Watson, R. M., Elder, A., Jones, R., Done, D., et al. (2015). Environmental health hazards of e-cigarettes and their components: Oxidants and copper in e-cigarette aerosols. *Environmental Pollution, 198*, 100-107.
Lisko, J. G., Tran, H., Stanfill, S. B., Blount, B. C., & Watson, C. H. (2015). Chemical composition and evaluation of nicotine, tobacco alkaloids, pH, and selected flavors in e-cigarette cartridges and refill solutions. *Nicotine and Tobacco Research, 17*(10), 1270-1278.
Schroeder, M. J., & Hoffman, A. C. (2014). Electronic cigarettes and nicotine clinical pharmacology. *Tobacco Control, 23*(Suppl 2), ii30-ii35. doi:10.1136/tobaccocontrol-2013-051469.
[177] Etter, J. F., Zather, E., & Svensson, S. (2013). Analysis of refill liquids for electronic cigarettes. *Addiction, 108*(9), 1671-1679.
[178] Han, S., Chen, H., Zhang, X., Liu, T., & Fu, Y. (2016). Levels of selected groups of compounds in refill solutions for electronic cigarettes. *Nicotine and Tobacco Research, 18*(5), 708-714.
[179] Cheng, T. (2014). Chemical evaluation of electronic cigarettes. *Tobacco Control, 23*(Suppl 2), ii11-ii17.
Etter, J. F., Zather, E., & Svensson, S. (2013). Analysis of refill liquids for electronic cigarettes. *Addiction, 108*(9), 1671-1679.
Farsalinos, K. E., Gillman, I. G., Melvin, M. S., Paolantonio, A. R., Gardow, W. J., Humphries, K. E., et al. (2015). Nicotine levels and presence of selected tobacco-derived toxins in tobacco flavoured electronic cigarette refill liquids. *International Journal of Environmental Research and Public Health, 12*(4), 3439-3452.
Goniewicz, M. L., Kuma, T., Gawron, M., Knysak, J., & Kosmider, L. (2013). Nicotine levels in electronic cigarettes. *Nicotine and Tobacco Research, 15*(1), 158-166.
Goniewicz, M. L., Gupta, R., Lee, Y. H., Reinhardt, S., Kim, S., Kim, B., et al. (2015). Nicotine levels in electronic cigarette refill solutions: A comparative analysis of products from the U.S., Korea, and Poland. *International Journal of Drug Policy, 26*(6), 583-588.
Hahn, J., Monakhova, Y. B., Hengen, J., Kohl-Himmelseher, M., Schussler, J., Hahn, H., et al. (2014). Electronic cigarettes: overview of chemical composition and exposure estimation. *Tobacco Induced Diseases, 12*(1), 23.
Han, S., Chen, H., Zhang, X., Liu, T., & Fu, Y. (2016). Levels of selected groups of compounds in refill solutions for electronic cigarettes. *Nicotine and Tobacco Research, 18*(5), 708-714.
Hutzler, C., Paschke, M., Kruschinski, S., Henkler, F., Hahn, J., & Luch, A. (2014). Chemical hazards present in liquids and vapors of electronic cigarettes. *Archives of Toxicology, 88*(7), 1295-1308.
Kim, J. W., & Baum, C. R. (2015). Liquid Nicotine Toxicity. *Pediatric Emergency Care, 31*(7), 517-521.
Schroeder, M. J., & Hoffman, A. C. (2014). Electronic cigarettes and nicotine clinical pharmacology. *Tobacco Control, 23*(Suppl 2), ii30-ii35. doi:10.1136/tobaccocontrol-2013-051469.
Pagano, T., DiFrancesco, A. G., Smith, S. B., George, J., Wink, G., Rahman, I., et al. (2016). Determination of Nicotine Content and Delivery in Disposable Electronic Cigarettes Available in the United States by Gas Chromatography-Mass Spectrometry. *Nicotine and Tobacco Research, 18*(5), 700-707.

Schober, W., Szendrei, K., Matzen, W., Osiander-Fuchs, H., Heitmann, D., Schettgen, T., et al. (2014). Use of electronic cigarettes (e-cigarettes) impairs indoor air quality and increases FeNO levels of e-cigarette consumers. *International Journal of Hygiene and Environmental Health, 217*(6), 628-637.
Trehy, M. L., Ye, W., Hadwiger, M. E., Moore, T. W., Allgire, J. F., Woodruff, J. T., et al. (2011). Analysis of electronic cigarette cartridges, refill solutions, and smoke for nicotine and nicotine related impurities. *Journal of Liquid Chromatography and Related Technologies, 374*, 1442-1458.
[180] Behar, R. Z., Hua, M., & Talbot, P. (2015). Puffing topography and nicotine intake of electronic cigarette users. *PLoS One, 10*(2), e0117222. doi:10.1371/journal.pone.0117222.
Farsalinos, K. E., Spyrou, A., Stefopoulos, C., Tsimopoulou, K., Kourkoveli, P., Tsiapras, D., et al. (2015). Nicotine absorbption from electronic cigarette use: Comparison between experienced consumers (vapers) and naive users (smokers). *Scientific Reports, 17*(5), 11269.
Norton, K. J., June, K. M., & O'Connor, R. J. (2016). Initial puffing behaviors and subjective responses differ between an electronic nicotine delivery system and traditional cigarettes. *Tobacco Induced Diseases, 12*, 17-25.
Robinson, R. J., Hensel, E. C., & Morabito, P. N. (2015). Electronic cigarette topography in the natural environment. *PLoS One, 10*(6), e0129296.
Talih, S., Balhas, Z., Eissenberg, T., Salman, R., Karaoghlanian, N., El-Hellani A., et al. (2015). Effects of user puff topography, device voltage, and liquid nicotine concentration on electronic cigarette nicotine yield: Measurements and model predictions. *Nicotine and Tobacco Research, 17*(2), 150-157.
[181] Farsalinos, K. E., Spyrou, A., Stefopoulos, C., Tsimopoulou, K., Kourkoveli, P., Tsiapras, D., et al. (2015). Nicotine absorbption from electronic cigarette use: Comparison between experienced consumers (vapers) and naive users (smokers). *Scientific Reports, 17*(5), 11269.
Lee, Y. O., Hebert, C. J., Nonnemaker, J. M., & Kim, A. E. (2015). Youth tobacco product use in the United States. *Pediatrics, 135*(3), 409-415.
Schroeder, M. J., & Hoffman, A. C. (2014). Electronic cigarettes and nicotine clinical pharmacology. *Tobacco Control, 23*(Suppl 2), ii30-ii35. doi:10.1136/tobaccocontrol-2013-051469.
[182] Antoniewicz, L., Bosson, J. A., Kuhl, J., Abdel-Halim, S. M., Kiessling, A., Mobarrez, F., et al. (2016). Electronic cigarettes increase endothelial progenitor cells in the blood of healthy volunteers. *Atherosclerosis, 255*, 179-185.
Bekki, K., Uchiyama, S., Ohta, K., Inaba, Y., Nakagome, H., & Kunugita, N. (2014). Carbonyl compounds generated from electronic cigarettes. *International Journal of Environmental Research and Public Health, 11*(11), 11192-11200.
Burstyn, I. (2014). Peering through the mist: Systematic review of what the chemistry of contaminants in electronic cigarettes tells us about health risks. *BMC Public Health, 14*, 18.
Carnevale, R., Sciarretta, S., Violi, F., Nocella, C., Loffredo, L., Perri, L., et al. (2016). Acute impact of tobacco versus electronic cigarette smoking on oxidative stress and vascular function. *Chest*, 150(3), 606-612.
Dawkins, L., & Corcoran, O. (2014). Acute electronic cigarette use: nicotine delivery and subjective effects in regular users. *Psychopharmacology, 231*(2), 401-407.
Dinakar, C., & O'Connor, G. T. (2016). The health effects of electronic cigarettes. *New England Journal of Medicine, 375*(14), 1372-1381.
Goniewicz, M. L., Knysak, J., Gawron, M., Kosmider, L., Sobczak, A., Kurek, J., et al. (2014). Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tobacco Control, 23*(2), 133-139.
Herrington, J. S., & Myers, C. (2015). Electronic cigarette solutions and resultant aerosol profiles. *Journal of Chromatography, 1418*, 192-199.
Hiemstra, P. S., & Bals, R. (2016). Basic science of electronic cigarettes: Assessment in cell culture and in vivo models. *Respiratory Research, 17*(1), 127. doi:10.1186/s12931-016-0447-z.
Hutzler, C., Paschke, M., Kruschinski, S., Henkler, F., Hahn, J., & Luch, A. (2014). Chemical hazards present in liquids and vapors of electronic cigarettes. *Archives of Toxicology, 88*(7), 1295-1308.
Jo, S. H., & Kim, K. H. (2016). Development of a sampling method for carbonyl compounds released due to the use of electronic cigarettes and quantitation of their conversion from liquid to aerosol. *Journal of Chromatography, 1429*, 369-373.
Kaisar, M. A., Prasad, S., Liles, T., & Cucullo, L. (2016). A decade of e-cigarettes: Limited research and unresolved sefety concerns. *Toxicology, 365*, 67-75.
Kosmider, L., Sobczak, A., Fik, M., Knysak, J., Zaciera, M., Kurek, J., et al. (2014). Carbonyl compounds in electronic cigarette vapors: effects of nicotine solvent and battery output voltage. *Nicotine and Tobacco Research, 16*(10), 1319-1326.

Maridet, C., Atge, B., Amici, J. M., Taieb, A., & Milpied, B. (2015). The electronic cigarette: the new source of nickel contact allergy of the 21st century? *Contact Dermatitis, 73*(1), 49-50.
Sundar, I. K., Javed, F., Romanos, G. E., & Rahman, I. (2016). E-cigarettes and flavorings induce inflammatory and pro-senescence responses in oral epithelial cells and periodontal fibroblasts. *Oncotarget, 7*(47), 77196-77204.
Uchiyama, S., Ohta, K., Inaba, Y., & Kunugita, N. (2013). Determination of carbonyl compounds generated from the E-cigarette using coupled silica cartridges impregnated with hydroquinone and 2,4-dinitrophenylhydrazine, followed by high-performance liquid chromatography. *Analytical Sciences, 29*(12), 1219-1222.
Vansickel, A. R., Cobb, C. O., Weaver, M. F., & Eissenberg, T. (2011). A clinical laboratory model for evaluating the acute effects of electronic "cigarettes": Nicotine delivery profile and cardiovascular and subjective effects. *Cancer Epidemiology Biomarkers and Prevention, 19*(8), 1945-1953.
Wang, M. P., Ho, S. Y., Leung, L. T., & Lam, T. H. (2016). Electronic cigarette use and respiratory symptoms in Chinese adolescents in Hong Kong. *JAMA Pediatrics, 170*(1), 89-91.
[183] Cheng, T. (2014). Chemical evaluation of electronic cigarettes. *Tobacco Control, 23*(Suppl 2), ii11-ii17.
Hutzler, C., Paschke, M., Kruschinski, S., Henkler, F., Hahn, J., & Luch, A. (2014). Chemical hazards present in liquids and vapors of electronic cigarettes. *Archives of Toxicology, 88*(7), 1295-1308.
[184] Dawkins, L., & Corcoran, O. (2014). Acute electronic cigarette use: nicotine delivery and subjective effects in regular users. *Psychopharmacology, 231*(2), 401-407.
Vansickel, A. R., Cobb, C. O., Weaver, M. F., & Eissenberg, T. (2011). A clinical laboratory model for evaluating the acute effects of electronic "cigarettes": Nicotine delivery profile and cardiovascular and subjective effects. *Cancer Epidemiology Biomarkers and Prevention, 19*(8), 1945-1953.
[185] Carnevale, R., Sciarretta, S., Violi, F., Nocella, C., Loffredo, L., Perri, L., et al. (2016). Acute impact of tobacco versus electronic cigarette smoking on oxidative stress and vascular function. *Chest*, 150(3), 606-612.
Kaisar, M. A., Prasad, S., Liles, T., & Cucullo, L. (2016). A decade of e-cigarettes: Limited research and unresolved sefety concerns. *Toxicology, 365*, 67-75.
Sundar, I. K., Javed, F., Romanos, G. E., & Rahman, I. (2016). E-cigarettes and flavorings induce inflammatory and pro-senescence responses in oral epithelial cells and periodontal fibroblasts. *Oncotarget, 7*(47), 77196-77204.
Wang, M. P., Ho, S. Y., Leung, L. T., & Lam, T. H. (2016). Electronic cigarette use and respiratory symptoms in Chinese adolescents in Hong Kong. *JAMA Pediatrics, 170*(1), 89-91.
[186] Allen, J. G., Flanigan, S. S., LeBlanc, M., Vallarino, J., MacNaughton, P., Stewart, J. H., et al. (2016). Flavoring chemicals in e-cigarettes: Diacetyl, 2,3-pentanedione, and acetoin in a sample of 51 products, including fruit-, candy-, and cocktail-flavored e-cigarettes. *Environmental Health Perspectives, 124*(6), 733-739.
Cheng, T. (2014). Chemical evaluation of electronic cigarettes. *Tobacco Control, 23*(Suppl 2), ii11-ii17.
Costigan, S., & Meredith, C. (2015). An approach to ingredient screening and toxicological risk assessment of flavours in e-liquids. *Regulatory Toxicology and Pharmacology, 72*(2), 361-369.
Fernandez, E., Ballbe, M., Sureda, X., Fu, M., Salto, E., & Martinez-Sanchez, J. M. (2015). Particulate matter from electronic cigarettes and conventional cigarettes: A systematic review and observational study. *Current Environmental Health Reports, 2*(4), 423-429.
Flora, J. W., Meruva, N., Huang, C. B., Wilkinson, C. T., Ballentine, R., Smith, D. C., et al. (2016). Characterization of potential impurities and degradation products in electronic cigarette formulations and aerosols. *Regulatory Toxicology and Pharmacology, 74*, 1-11.
Geiss, O., Bianchi, I., & Barrero-Moreno, J. (2016). Correlation of volatile carbonyl yields emitted by e-cigarettes with the temperature of the heating coil and the perceived sensorial quality of the generated vapours. *International Journal of Hygiene and Environmental Health, 219*(3), 268-277.
Gillman, I. G., Kistler, K. A., Stewart, E. W., & Paolantonio, A. R. (2016). Effect of variable power levels on the yield of total aerosol mass and formation of aldehydes in e-cigarette aerosols. *Regulatory Toxicology and Pharmacology, 75*, 58-65.
Goniewicz, M. L., Knysak, J., Gawron, M., Kosmider, L., Sobczak, A., Kurek, J., et al. (2014). Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tobacco Control, 23*(2), 133-139.
Han, S., Chen, H., Zhang, X., Liu, T., & Fu, Y. (2016). Levels of selected groups of compounds in refill solutions for electronic cigarettes. *Nicotine and Tobacco Research, 18*(5), 708-714.
Herrington, J. S., & Myers, C. (2015). Electronic cigarette solutions and resultant aerosol profiles. *Journal of Chromatography, 1418*, 192-199.
Hutzler, C., Paschke, M., Kruschinski, S., Henkler, F., Hahn, J., & Luch, A. (2014). Chemical hazards present in liquids and vapors of electronic cigarettes. *Archives of Toxicology, 88*(7), 1295-1308.

Jo, S. H., & Kim, K. H. (2016). Development of a sampling method for carbonyl compounds released due to the use of electronic cigarettes and quantitation of their conversion from liquid to aerosol. *Journal of Chromatography, 1429*, 369-373.
Kaisar, M. A., Prasad, S., Liles, T., & Cucullo, L. (2016). A decade of e-cigarettes: Limited research and unresolved sefety concerns. *Toxicology, 365*, 67-75.
Kim, H. J., & Shin, H. S. (2013). Determination of tobacco-specific nitrosamines in replacement liquids of electronic cigarettes by liquid chromatography-tandem mass spectrometry. *Journal of Chromatography, 1291*, 48-55.
Kosmider, L., Sobczak, A., Fik, M., Knysak, J., Zaciera, M., Kurek, J., et al. (2014). Carbonyl compounds in electronic cigarette vapors: effects of nicotine solvent and battery output voltage. *Nicotine and Tobacco Research, 16*(10), 1319-1326.
Kosmider, L., Sobczak, A., Prokopowicz, A., Kurek, J., Zaciera, M., Knysak, J., et al. (2016). Cherry-flavoured electronic cigarettes expose users to the inhalation irritant, benzaldehyde. *Thorax, 71*(4), 376-377.
Lerner, C. A., Sundar, I. K., Watson, R. M., Elder, A., Jones, R., Done, D., et al. (2015). Environmental health hazards of e-cigarettes and their components: Oxidants and copper in e-cigarette aerosols. *Environmental Pollution, 198*, 100-107.
Saffari, A., Daher, N., Ruprecht, A., De, M. C., Pozzi, P., Boffi, R., et al. (2014). Particulate metals and organic compounds from electronic and tobacco-containing cigarettes: comparison of emission rates and secondhand exposure. *Enviromental Science Processes and Impacts, 16*(10), 2259-2267.
Schober, W., Szendrei, K., Matzen, W., Osiander-Fuchs, H., Heitmann, D., Schettgen, T., et al. (2014). Use of electronic cigarettes (e-cigarettes) impairs indoor air quality and increases FeNO levels of e-cigarette consumers. *International Journal of Hygiene and Environmental Health, 217*(6), 628-637.
Tierney, P. A., Karpinski, C. D., Brown, J. E., Luo, W., & Pankow, J. F. (2016). Flavour chemicals in electronic cigarette fluids. *Tobacco Control, 25*(e1), e10-e15.
Uchiyama, S., Ohta, K., Inaba, Y., & Kunugita, N. (2013). Determination of carbonyl compounds generated from the E-cigarette using coupled silica cartridges impregnated with hydroquinone and 2,4-dinitrophenylhydrazine, followed by high-performance liquid chromatography. *Analytical Sciences, 29*(12), 1219-1222.
Varlet, V., Farsalinos, K., Augsburger, M., Thomas, A., & Etter, J. F. (2015). Toxicity assessment of refill liquids for electronic cigarettes. *International Journal of Environmental Research and Public Health, 12*(5), 4796-4815.
Williams, M., Villarreal, A., Bozhilov, K., Lin, S., & Talbot, P. (2013). Metal and silicate particles including nanoparticles are present in electronic cigarette cartomizer fluid and aerosol. *PLoS One, 8*(3), e57987. doi:10.1371/journal.pone.0057987.
Williams, M., To, A., Bozhilov, K., & Talbot, P. (2015). Strategies to reduce tin and other metals in electronic cigarette aerosol. *PLoS One, 10*(9), e0138933. doi:10.1371/journal.pone.0138933.
[187] Cheng, T. (2014). Chemical evaluation of electronic cigarettes. *Tobacco Control, 23*(Suppl 2), ii11-ii17.
International Agency for Research on Cancer. (2016). *Agents classified by the IARC monographs, Volumes 1-112*. Retrieved from https://monographs.iarc.fr.
[188] Herrington, J. S., & Myers, C. (2015). Electronic cigarette solutions and resultant aerosol profiles. *Journal of Chromatography, 1418*, 192-199.
[189] Dunbar, M. S., Tucker, J. S., Ewing, B. A., Pedersen, E. R., Miles, J. N., Shih, R. A., et al. (2016). Frequency of e-cigarette use, health status, and risk and protective health behaviors in adolescents. *Journal of Addiction Medicine, 11*(1), 55-62.
[190] Lechner, W. V., Janssen , T., Kahler, C. W., Audrain-McGovern, J., & Leventhal, A. M. (2017). Bi-directional associations of electronic and combustible cigarette use onset patterns with depressive symptoms in adolescents. *Preventive Medicine, 96*, 73-78.
[191] McConnell, R., Barrington-Trimis, J. L., Wang, K., Urman, R., Hong, H., Unger, J., et al. (2016). Electronic-cigarette use and respiratory symptoms in adolescents. *American Journal of Respiratory and Critical Care Medicine*.
[192] Krishnan-Sarin, S., Morean, M., Kong, G., Bold, K. W., Camenga, D. R., Cavallo, D. A., et al. (2017). E-cigarettes and "dripping" among high-school youth. *Pediatrics, 139*(3). doi:10.1542/peds.2016.3224.
[193] Talih, S., Balhas, Z., Salman, R., Karaoghlanian, N., & Shihadeh, A. (2016). "Direct dripping": A high-temperature, high-formaldehyde emission electronic cigarette use method. *Nicotine and Tobacco Research, 18*(4), 453-459.
[194] Burstyn, I. (2014). Peering through the mist: Systematic review of what the chemistry of contaminants in electronic cigarettes tells us about health risks. *BMC Public Health, 14*, 18.

Cheng, T. (2014). Chemical evaluation of electronic cigarettes. *Tobacco Control, 23*(Suppl 2), ii11-ii17.
Han, S., Chen, H., Zhang, X., Liu, T., & Fu, Y. (2016). Levels of selected groups of compounds in refill solutions for electronic cigarettes. *Nicotine and Tobacco Research, 18*(5), 708-714.
Hutzler, C., Paschke, M., Kruschinski, S., Henkler, F., Hahn, J., & Luch, A. (2014). Chemical hazards present in liquids and vapors of electronic cigarettes. *Archives of Toxicology, 88*(7), 1295-1308.
Varlet, V., Farsalinos, K., Augsburger, M., Thomas, A., & Etter, J. F. (2015). Toxicity assessment of refill liquids for electronic cigarettes. *International Journal of Environmental Research and Public Health, 12*(5), 4796-4815.
[195] Burstyn, I. (2014). Peering through the mist: Systematic review of what the chemistry of contaminants in electronic cigarettes tells us about health risks. *BMC Public Health, 14*, 18.
Callahan-Lyon, P. (2014). Electronic cigarettes: Human health effects. *Tobacco Control, 23*(Suppl 2), ii36-ii40.
Kienhuis, A. S., Soeteman-Hernandez, L. G., Bos, P. M., Cremers, H. W., Klerx, W. N., & Talhout, R. (2015). Potential harmful health effects of inhaling nicotine-free shisha-pen vapor: a chemical risk assessment of the main components propylene glycol and glycerol. *Tobacco Induced Diseases, 13*(1), 15.
[196] Flora, J. W., Meruva, N., Huang, C. B., Wilkinson, C. T., Ballentine, R., Smith, D. C., et al. (2016). Characterization of potential impurities and degradation products in electronic cigarette formulations and aerosols. *Regulatory Toxicology and Pharmacology, 74*, 1-11.
Geiss, O., Bianchi, I., & Barrero-Moreno, J. (2016). Correlation of volatile carbonyl yields emitted by e-cigarettes with the temperature of the heating coil and the perceived sensorial quality of the generated vapours. *International Journal of Hygiene and Environmental Health, 219*(3), 268-277.
Gillman, I. G., Kistler, K. A., Stewart, E. W., & Paolantonio, A. R. (2016). Effect of variable power levels on the yield of total aerosol mass and formation of aldehydes in e-cigarette aerosols. *Regulatory Toxicology and Pharmacology, 75*, 58-65.
Goniewicz, M. L., Knysak, J., Gawron, M., Kosmider, L., Sobczak, A., Kurek, J., et al. (2014). Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tobacco Control, 23*(2), 133-139.
Han, S., Chen, H., Zhang, X., Liu, T., & Fu, Y. (2016). Levels of selected groups of compounds in refill solutions for electronic cigarettes. *Nicotine and Tobacco Research, 18*(5), 708-714.
Herrington, J. S., & Myers, C. (2015). Electronic cigarette solutions and resultant aerosol profiles. *Journal of Chromatography, 1418*, 192-199.
Hutzler, C., Paschke, M., Kruschinski, S., Henkler, F., Hahn, J., & Luch, A. (2014). Chemical hazards present in liquids and vapors of electronic cigarettes. *Archives of Toxicology, 88*(7), 1295-1308.
Jo, S. H., & Kim, K. H. (2016). Development of a sampling method for carbonyl compounds released due to the use of electronic cigarettes and quantitation of their conversion from liquid to aerosol. *Journal of Chromatography, 1429*, 369-373.
Kosmider, L., Sobczak, A., Fik, M., Knysak, J., Zaciera, M., Kurek, J., et al. (2014). Carbonyl compounds in electronic cigarette vapors: effects of nicotine solvent and battery output voltage. *Nicotine and Tobacco Research, 16*(10), 1319-1326.
Uchiyama, S., Ohta, K., Inaba, Y., & Kunugita, N. (2013). Determination of carbonyl compounds generated from the E-cigarette using coupled silica cartridges impregnated with hydroquinone and 2,4-dinitrophenylhydrazine, followed by high-performance liquid chromatography. *Analytical Sciences, 29*(12), 1219-1222.
Varlet, V., Farsalinos, K., Augsburger, M., Thomas, A., & Etter, J. F. (2015). Toxicity assessment of refill liquids for electronic cigarettes. *International Journal of Environmental Research and Public Health, 12*(5), 4796-4815.
[197] Flora, J. W., Meruva, N., Huang, C. B., Wilkinson, C. T., Ballentine, R., Smith, D. C., et al. (2016). Characterization of potential impurities and degradation products in electronic cigarette formulations and aerosols. *Regulatory Toxicology and Pharmacology, 74*, 1-11.
Geiss, O., Bianchi, I., & Barrero-Moreno, J. (2016). Correlation of volatile carbonyl yields emitted by e-cigarettes with the temperature of the heating coil and the perceived sensorial quality of the generated vapours. *International Journal of Hygiene and Environmental Health, 219*(3), 268-277.
Gillman, I. G., Kistler, K. A., Stewart, E. W., & Paolantonio, A. R. (2016). Effect of variable power levels on the yield of total aerosol mass and formation of aldehydes in e-cigarette aerosols. *Regulatory Toxicology and Pharmacology, 75*, 58-65.
Goniewicz, M. L., Knysak, J., Gawron, M., Kosmider, L., Sobczak, A., Kurek, J., et al. (2014). Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tobacco Control, 23*(2), 133-139.
Han, S., Chen, H., Zhang, X., Liu, T., & Fu, Y. (2016). Levels of selected groups of compounds in refill solutions for electronic cigarettes. *Nicotine and Tobacco Research, 18*(5), 708-714.

Herrington, J. S., & Myers, C. (2015). Electronic cigarette solutions and resultant aerosol profiles. *Journal of Chromatography, 1418*, 192-199.
Hutzler, C., Paschke, M., Kruschinski, S., Henkler, F., Hahn, J., & Luch, A. (2014). Chemical hazards present in liquids and vapors of electronic cigarettes. *Archives of Toxicology, 88*(7), 1295-1308.
Jo, S. H., & Kim, K. H. (2016). Development of a sampling method for carbonyl compounds released due to the use of electronic cigarettes and quantitation of their conversion from liquid to aerosol. *Journal of Chromatography, 1429*, 369-373.
Kosmider, L., Sobczak, A., Fik, M., Knysak, J., Zaciera, M., Kurek, J., et al. (2014). Carbonyl compounds in electronic cigarette vapors: effects of nicotine solvent and battery output voltage. *Nicotine and Tobacco Research, 16*(10), 1319-1326.
Uchiyama, S., Ohta, K., Inaba, Y., & Kunugita, N. (2013). Determination of carbonyl compounds generated from the E-cigarette using coupled silica cartridges impregnated with hydroquinone and 2,4-dinitrophenylhydrazine, followed by high-performance liquid chromatography. *Analytical Sciences, 29*(12), 1219-1222.
Varlet, V., Farsalinos, K., Augsburger, M., Thomas, A., & Etter, J. F. (2015). Toxicity assessment of refill liquids for electronic cigarettes. *International Journal of Environmental Research and Public Health, 12*(5), 4796-4815.
[198] Flora, J. W., Meruva, N., Huang, C. B., Wilkinson, C. T., Ballentine, R., Smith, D. C., et al. (2016). Characterization of potential impurities and degradation products in electronic cigarette formulations and aerosols. *Regulatory Toxicology and Pharmacology, 74*, 1-11.
Gillman, I. G., Kistler, K. A., Stewart, E. W., & Paolantonio, A. R. (2016). Effect of variable power levels on the yield of total aerosol mass and formation of aldehydes in e-cigarette aerosols. *Regulatory Toxicology and Pharmacology, 75*, 58-65.
Herrington, J. S., & Myers, C. (2015). Electronic cigarette solutions and resultant aerosol profiles. *Journal of Chromatography, 1418*, 192-199.
[199] Gillman, I. G., Kistler, K. A., Stewart, E. W., & Paolantonio, A. R. (2016). Effect of variable power levels on the yield of total aerosol mass and formation of aldehydes in e-cigarette aerosols. *Regulatory Toxicology and Pharmacology, 75*, 58-65.
Geiss, O., Bianchi, I., & Barrero-Moreno, J. (2016). Correlation of volatile carbonyl yields emitted by e-cigarettes with the temperature of the heating coil and the perceived sensorial quality of the generated vapours. *International Journal of Hygiene and Environmental Health, 219*(3), 268-277.
Kosmider, L., Sobczak, A., Fik, M., Knysak, J., Zaciera, M., Kurek, J., et al. (2014). Carbonyl compounds in electronic cigarette vapors: effects of nicotine solvent and battery output voltage. *Nicotine and Tobacco Research, 16*(10), 1319-1326.
[200] Goniewicz, M. L., Knysak, J., Gawron, M., Kosmider, L., Sobczak, A., Kurek, J., et al. (2014). Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tobacco Control, 23*(2), 133-139.
International Agency for Research on Cancer. (2016). *Agents classified by the IARC monographs, Volumes 1-112*. Retrieved from https://monographs.iarc.fr.
World Health Organization. (2016). *IARC monographs on the evaluation of carcinogenic risks to humans.* Retrieved from http://monographs.iarc.fr.
[201] Moghe, A., Ghare, S., Lamoreau, B., Mohammad, M., Barve, S., McClain, C., et al. (2015). Molecular mechanisms of acrolein toxicity: Relevance to human disease. *Toxicological Sciences, 143*(2), 242-255.
[202] Moghe, A., Ghare, S., Lamoreau, B., Mohammad, M., Barve, S., McClain, C., et al. (2015). Molecular mechanisms of acrolein toxicity: Relevance to human disease. *Toxicological Sciences, 143*(2), 242-255.
[203] Farsalinos, K. E., Voudris, V., & Poulas, K. (2015). E-cigarettes generate high levels of aldehydes only in 'dry puff' conditions. *Addiction, 110*(8), 1352-1356.
Kosmider, L., Sobczak, A., Fik, M., Knysak, J., Zaciera, M., Kurek, J., et al. (2014). Carbonyl compounds in electronic cigarette vapors: effects of nicotine solvent and battery output voltage. *Nicotine and Tobacco Research, 16*(10), 1319-1326.
Lerner, C. A., Sundar, I. K., Watson, R. M., Elder, A., Jones, R., Done, D., et al. (2015). Environmental health hazards of e-cigarettes and their components: Oxidants and copper in e-cigarette aerosols. *Environmental Pollution, 198*, 100-107.
McAuley, T. R., Hopke, P. K., Zhao, J., & Babaian, S. (2012). Comparison of the effects of e-cigarette vapor and cigarette smoke on indoor air quality. *Inhalation Toxicology, 24*(12), 850-857.
[204] Burstyn, I. (2014). Peering through the mist: Systematic review of what the chemistry of contaminants in electronic cigarettes tells us about health risks. *BMC Public Health, 14*, 18.
Cheng, T. (2014). Chemical evaluation of electronic cigarettes. *Tobacco Control, 23*(Suppl 2), ii11-ii17.

Flora, J. W., Meruva, N., Huang, C. B., Wilkinson, C. T., Ballentine, R., Smith, D. C., et al. (2016). Characterization of potential impurities and degradation products in electronic cigarette formulations and aerosols. *Regulatory Toxicology and Pharmacology, 74*, 1-11.
Goniewicz, M. L., Knysak, J., Gawron, M., Kosmider, L., Sobczak, A., Kurek, J., et al. (2014). Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tobacco Control, 23*(2), 133-139.
Han, S., Chen, H., Zhang, X., Liu, T., & Fu, Y. (2016). Levels of selected groups of compounds in refill solutions for electronic cigarettes. *Nicotine and Tobacco Research, 18*(5), 708-714.
International Agency for Research on Cancer. (2016). *Agents classified by the IARC monographs, Volumes 1-112.* Retrieved from https://monographs.iarc.fr.
Kim, H. J., & Shin, H. S. (2013). Determination of tobacco-specific nitrosamines in replacement liquids of electronic cigarettes by liquid chromatography-tandem mass spectrometry. *Journal of Chromatography, 1291*, 48-55.
[205] Fernandez, E., Ballbe, M., Sureda, X., Fu, M., Salto, E., & Martinez-Sanchez, J. M. (2015). Particulate matter from electronic cigarettes and conventional cigarettes: A systematic review and observational study. *Current Environmental Health Reports, 2*(4), 423-429.
Goniewicz, M. L., Knysak, J., Gawron, M., Kosmider, L., Sobczak, A., Kurek, J., et al. (2014). Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tobacco Control, 23*(2), 133-139.
Lerner, C. A., Sundar, I. K., Watson, R. M., Elder, A., Jones, R., Done, D., et al. (2015). Environmental health hazards of e-cigarettes and their components: Oxidants and copper in e-cigarette aerosols. *Environmental Pollution, 198*, 100-107.
Saffari, A., Daher, N., Ruprecht, A., De, M. C., Pozzi, P., Boffi, R., et al. (2014). Particulate metals and organic compounds from electronic and tobacco-containing cigarettes: comparison of emission rates and secondhand exposure. *Enviromental Science Processes and Impacts, 16*(10), 2259-2267.
Schober, W., Szendrei, K., Matzen, W., Osiander-Fuchs, H., Heitmann, D., Schettgen, T., et al. (2014). Use of electronic cigarettes (e-cigarettes) impairs indoor air quality and increases FeNO levels of e-cigarette consumers. *International Journal of Hygiene and Environmental Health, 217*(6), 628-637.
Williams, M., Villarreal, A., Bozhilov, K., Lin, S., & Talbot, P. (2013). Metal and silicate particles including nanoparticles are present in electronic cigarette cartomizer fluid and aerosol. *PLoS One, 8*(3), e57987. doi:10.1371/journal.pone.0057987.
Williams, M., To, A., Bozhilov, K., & Talbot, P. (2015). Strategies to reduce tin and other metals in electronic cigarette aerosol. *PLoS One, 10*(9), e0138933. doi:10.1371/journal.pone.0138933.
[206] Saffari, A., Daher, N., Ruprecht, A., De, M. C., Pozzi, P., Boffi, R., et al. (2014). Particulate metals and organic compounds from electronic and tobacco-containing cigarettes: comparison of emission rates and secondhand exposure. *Enviromental Science Processes and Impacts, 16*(10), 2259-2267.
[207] Williams, M., Villarreal, A., Bozhilov, K., Lin, S., & Talbot, P. (2013). Metal and silicate particles including nanoparticles are present in electronic cigarette cartomizer fluid and aerosol. *PLoS One, 8*(3), e57987. doi:10.1371/journal.pone.0057987.
U.S. Department of Health and Human Services. (2008). *Toxicological profile for aluminum*. Atlanta, GA: Agency for Toxic Substances and Disease Registry.
[208] Allen, J. G., Flanigan, S. S., LeBlanc, M., Vallarino, J., MacNaughton, P., Stewart, J. H., et al. (2016). Flavoring chemicals in e-cigarettes: Diacetyl, 2,3-pentanedione, and acetoin in a sample of 51 products, including fruit-, candy-, and cocktail-flavored e-cigarettes. *Environmental Health Perspectives, 124*(6), 733-739.
Bahl, V., Lin, S., Xu, N., Davis, B., Wang, Y. H., & Talbot, P. (2012). Comparison of electronic cigarette refill fluid cytotoxicity using embryonic and adult models. *Reproductive Toxicology, 34*(4), 529-537.
Costigan, S., & Meredith, C. (2015). An approach to ingredient screening and toxicological risk assessment of flavours in e-liquids. *Regulatory Toxicology and Pharmacology, 72*(2), 361-369.
Farsalinos, K. E., Kistler, K. A., Gillman, G., & Voudris, V. (2015). Evaluation of electronic cigarette liquids and aerosol for the presence of selected inhalation toxins. *Nicotine and Tobacco Research, 17*(2), 168-174.
U.S. Food and Drug Administration. (1980). *Select committee on GRAS Substances (SCOGS) opinion: Diacetyl and starter distillate.* Retrieved from http://www.fda.gov.
Synthetic flavoring substances and adjuvants. 21 C.F.R. § 172.515 (2015).
Kosmider, L., Sobczak, A., Prokopowicz, A., Kurek, J., Zaciera, M., Knysak, J., et al. (2016). Cherry-flavoured electronic cigarettes expose users to the inhalation irritant, benzaldehyde. *Thorax, 71*(4), 376-377.
Tierney, P. A., Karpinski, C. D., Brown, J. E., Luo, W., & Pankow, J. F. (2016). Flavour chemicals in electronic cigarette fluids. *Tobacco Control, 25*(e1), e10-e15.

[209] Bahl, V., Lin, S., Xu, N., Davis, B., Wang, Y. H., & Talbot, P. (2012). Comparison of electronic cigarette refill fluid cytotoxicity using embryonic and adult models. *Reproductive Toxicology, 34*(4), 529-537.
Behar, R. Z., Davis, B., Wang, Y., Bahl, V., Lin, S., & Talbot, P. (2014). Identification of toxicants in cinnamon-flavored electronic cigarette refill fluids. *Toxicology in Vitro, 28*(2), 198-208.
Farsalinos, K. E., Romagna, G., Tsiapras, D., Kyrzopoulos, S., Spyrou, A., & Voudris, V. (2013). Impact of flavour variability on electronic cigarette use experience: an internet survey. *International Journal of Environmental Research and Public Health, 10*(12), 7272-7282.
Lerner, C. A., Sundar, I. K., Yao, H., Gerloff, J., Ossip, D. J., McIntosh, S., et al. (2015). Vapors produced by electronic cigarettes and e-juices with flavorings induce toxicity, oxidative stress, and inflammatory response in lung epithelial cells and in mouse lung. *PLoS.One., 10*(2), e0116732.
[210] Cantrell, F. L. (2014). Adverse effects of e-cigarette exposures. *Journal of Community Health, 39*(3), 614-616.
[211] Chatham-Stephens, K., Law, R., Taylor, E., Melstrom, P., Bunnell, R., Wang, B., et al. (2014). Notes from the field: Calls to poison centers for exposures to electronic cigarettes - United States, September 2010-February 2014. *Morbidity Mortality Weekly Report, 63*(13), 292-293.
[212] Kamboj, A., Spiller, H. A., Csavant, M. J., Chounthirath, T., & Smith, G. A. (2016). Pediatric exposure to e-cigarettes, nicotine and tobacco products in the United States. *Pediatrics, 137*(6), e20160041. doi:10.1542/peds.2016-0041.
[213] Brownson, E. G., Thompson, C. M., Goldsberry, S., Chong, H. J., Friedrich, J. B., Pham, T. N., et al. (2016). Explosion injuries from e-cigarettes. *New England Journal of Medicine, 375*(14), 1400-1402.
Colaianni, C. A., Tapias, L. F., Cauley, R., Sheridan, R., Schulz, J. T., & Goverman, J. (2016). Injuries caused by explosion of electronic cigarette devices. *Eplasty, 16*, ic9.
[214] Brown, C. J., & Cheng, J. M. (2014). Electronic cigarettes: Product characterisation and design considerations. *Tobacco Control, 23*(Suppl 2), ii4-10.
Roger, J. M., Abayon, M., Elad, S., & Kolokythas, A. (2016). Oral trauma and tooth avulsion following explosion of e-cigarette. *Journal of Oral and Maxillofacial Surgeons, 74*(6), 1181-1185.
Nicoll, K. J., Rose, A. M., Khan, M. A., Quaba, O., & Lowrie, A. G. (2016). Thigh burns from exploding e-cigarette lithium ion batteries: First case series. *Burns, 42*(4), e42-e46.
U.S. Fire Administration. (2014). *Electronic cigarette fires and explosions*. Emmitsburg, MD: FEMA.
[215] Etter, J. F. (2014). Levels of saliva cotinine in electronic cigarette users. *Addiction, 109*(5), 825-829.
Lopez, A. A., Hiler, M. M., Soule, E. K., Ramoa, C. P., Karaoghlanian, N. V., Lipato, T., et al. (2016). Effects of Electronic Cigarette Liquid Nicotine Concentration on Plasma Nicotine and Puff Topography in Tobacco Cigarette Smokers: A Preliminary Report. *Nicotine and Tobacco Research, 18*(5), 720-723.
Ramoa, C. P., Hiler, M. M., Spindle, T. R., Lopez, A. A., Karaoghlanian, N., Lipato, T., et al. (2016). Electronic cigarette nicotine delivery can exceed that of combustible cigarettes: a preliminary report. *Tobacco Control, 25*(e1), e6-e9.
St. Helen G., Havel, C., Dempsey, D. A., Jacob, P., & Benowitz, N. L. (2016). Nicotine delivery, retention and pharmacokinetics from various electronic cigarettes. *Addiction, 111*(3), 535-544.
[216] Farsalinos, K. E., Romagna, G., & Voudris, V. (2015). Factors associated with dual use of tobacco and electronic cigarettes: A case control study. *International Journal of Drug Policy*.
[217] Bahl, V., Lin, S., Xu, N., Davis, B., Wang, Y. H., & Talbot, P. (2012). Comparison of electronic cigarette refill fluid cytotoxicity using embryonic and adult models. *Reproductive Toxicology, 34*(4), 529-537.
Etter, J. F., Zather, E., & Svensson, S. (2013). Analysis of refill liquids for electronic cigarettes. *Addiction, 108*(9), 1671-1679.
Farsalinos, K. E., Kistler, K. A., Gillman, G., & Voudris, V. (2015). Evaluation of electronic cigarette liquids and aerosol for the presence of selected inhalation toxins. *Nicotine and Tobacco Research, 17*(2), 168-174.
Kosmider, L., Sobczak, A., Fik, M., Knysak, J., Zaciera, M., Kurek, J., et al. (2014). Carbonyl compounds in electronic cigarette vapors: effects of nicotine solvent and battery output voltage. *Nicotine and Tobacco Research, 16*(10), 1319-1326.
[218] Goniewicz, M. L., Kuma, T., Gawron, M., Knysak, J., & Kosmider, L. (2013). Nicotine levels in electronic cigarettes. *Nicotine and Tobacco Research, 15*(1), 158-166.
[219] Schroeder, M. J., & Hoffman, A. C. (2014). Electronic cigarettes and nicotine clinical pharmacology. *Tobacco Control, 23*(Suppl 2), ii30-ii35. doi:10.1136/tobaccocontrol-2013-051469.
Farsalinos, K. E., Spyrou, A., Stefopoulos, C., Tsimopoulou, K., Kourkoveli, P., Tsiapras, D., et al. (2015). Nicotine absorbption from electronic cigarette use: Comparison between experienced consumers (vapers) and naive users (smokers). *Scientific Reports, 17*(5), 11269.

Lee, Y. O., Hebert, C. J., Nonnemaker, J. M., & Kim, A. E. (2015). Youth tobacco product use in the United States. *Pediatrics, 135*(3), 409-415.
[220] El-Hellani, A., El-Hage, R., Baalbaki, R., Salman, R., Talih, S., Shihadeh, A., et al. (2015). Free-base and protonated nicotine in electronic cigarette liquids and aerosols. *Chemical Research in Toxicology, 28*(8), 1532-1537.
[221] Stepanov, I., & Fujioka, N. (2015). Bringing attention to e-cigarette pH as an important element for research and regulation. *Tobacco Control, 24*, 413-414.
[222] Dawkins, L., & Corcoran, O. (2014). Acute electronic cigarette use: nicotine delivery and subjective effects in regular users. *Psychopharmacology, 231*(2), 401-407.
Vansickel, A. R., Cobb, C. O., Weaver, M. F., & Eissenberg, T. (2011). A clinical laboratory model for evaluating the acute effects of electronic "cigarettes": Nicotine delivery profile and cardiovascular and subjective effects. *Cancer Epidemiology Biomarkers and Prevention, 19*(8), 1945-1953.
[223] Cheng, T. (2014). Chemical evaluation of electronic cigarettes. *Tobacco Control, 23*(Suppl 2), ii11-ii17.
[224] Cheng, T. (2014). Chemical evaluation of electronic cigarettes. *Tobacco Control, 23*(Suppl 2), ii11-ii17.
Fernandez, E., Ballbe, M., Sureda, X., Fu, M., Salto, E., & Martinez-Sanchez, J. M. (2015). Particulate matter from electronic cigarettes and conventional cigarettes: A systematic review and observational study. *Current Environmental Health Reports, 2*(4), 423-429.
Flora, J. W., Meruva, N., Huang, C. B., Wilkinson, C. T., Ballentine, R., Smith, D. C., et al. (2016). Characterization of potential impurities and degradation products in electronic cigarette formulations and aerosols. *Regulatory Toxicology and Pharmacology, 74*, 1-11.
Goniewicz, M. L., Knysak, J., Gawron, M., Kosmider, L., Sobczak, A., Kurek, J., et al. (2014). Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tobacco Control, 23*(2), 133-139.
Han, S., Chen, H., Zhang, X., Liu, T., & Fu, Y. (2016). Levels of selected groups of compounds in refill solutions for electronic cigarettes. *Nicotine and Tobacco Research, 18*(5), 708-714.
International Agency for Research on Cancer. (2016). *Agents classified by the IARC monographs, Volumes 1-112*. Retrieved from https://monographs.iarc.fr.
Kim, H. J., & Shin, H. S. (2013). Determination of tobacco-specific nitrosamines in replacement liquids of electronic cigarettes by liquid chromatography-tandem mass spectrometry. *Journal of Chromatography, 1291*, 48-55.
Lerner, C. A., Sundar, I. K., Watson, R. M., Elder, A., Jones, R., Done, D., et al. (2015). Environmental health hazards of e-cigarettes and their components: Oxidants and copper in e-cigarette aerosols. *Environmental Pollution, 198*, 100-107.
Saffari, A., Daher, N., Ruprecht, A., De, M. C., Pozzi, P., Boffi, R., et al. (2014). Particulate metals and organic compounds from electronic and tobacco-containing cigarettes: Comparison of emission rates and secondhand exposure. *Enviromental Science Processes and Impacts, 16*(10), 2259-2267.
Williams, M., Villarreal, A., Bozhilov, K., Lin, S., & Talbot, P. (2013). Metal and silicate particles including nanoparticles are present in electronic cigarette cartomizer fluid and aerosol. *PLoS One, 8*(3), e57987. doi:10.1371/journal.pone.0057987.
Williams, M., To, A., Bozhilov, K., & Talbot, P. (2015). Strategies to reduce tin and other metals in electronic cigarette aerosol. *PLoS One, 10*(9), e0138933. doi:10.1371/journal.pone.0138933.
[225] Cheng, T. (2014). Chemical evaluation of electronic cigarettes. *Tobacco Control, 23*(Suppl 2), ii11-ii17.
[226] Burstyn, I. (2014). Peering through the mist: Systematic review of what the chemistry of contaminants in electronic cigarettes tells us about health risks. *BMC Public Health, 14*, 18.
Callahan-Lyon, P. (2014). Electronic cigarettes: Human health effects. *Tobacco Control, 23*(Suppl 2), ii36-ii40.
Kienhuis, A. S., Soeteman-Hernandez, L. G., Bos, P. M., Cremers, H. W., Klerx, W. N., & Talhout, R. (2015). Potential harmful health effects of inhaling nicotine-free shisha-pen vapor: A chemical risk assessment of the main components propylene glycol and glycerol. *Tobacco Induced Diseases, 13*(1), 15. doi:10.1186/s12971-015-0038-7.
[227] Allen, J. G., Flanigan, S. S., LeBlanc, M., Vallarino, J., MacNaughton, P., Stewart, J. H., et al. (2016). Flavoring chemicals in e-cigarettes: Diacetyl, 2,3-pentanedione, and acetoin in a sample of 51 products, including fruit-, candy-, and cocktail-flavored e-cigarettes. *Environmental Health Perspectives, 124*(6), 733-739.
Costigan, S., & Meredith, C. (2015). An approach to ingredient screening and toxicological risk assessment of flavours in e-liquids. *Regulatory Toxicology and Pharmacology, 72*(2), 361-369.
Farsalinos, K. E., Kistler, K. A., Gillman, G., & Voudris, V. (2015). Evaluation of electronic cigarette liquids and aerosol for the presence of selected inhalation toxins. *Nicotine and Tobacco Research, 17*(2), 168-174.
Kosmider, L., Sobczak, A., Prokopowicz, A., Kurek, J., Zaciera, M., Knysak, J., et al. (2016). Cherry-flavoured electronic cigarettes expose users to the inhalation irritant, benzaldehyde. *Thorax, 71*(4), 376-377.

Tierney, P. A., Karpinski, C. D., Brown, J. E., Luo, W., & Pankow, J. F. (2016). Flavour chemicals in electronic cigarette fluids. *Tobacco Control, 25*(e1), e10-e15.
[228] Suter, M. A., Mastrobattista, J., Sachs, M., & Aagaard, K. (2014). Is there evidence for potential harm of electronic cigarette use in pregnancy? *Birth Defects Research: Part A, Clinical and Molecular Teratology, 103*(3), 186-95.
[229] Suter, M. A., Mastrobattista, J., Sachs, M., & Aagaard, K. (2014). Is there evidence for potential harm of electronic cigarette use in pregnancy? *Birth Defects Research: Part A, Clinical and Molecular Teratology, 103*(3), 186-95.
[230] Soule, E. K., Maloney, S. F., Spindle, T. R., Rudy, A. K., Hiler, M. M., & Cobb, C. O. (2017). Electronic cigarette use and indoor air quality in a natural setting. *Tobacco Control, 26*(1), 109-112.
[231] Bertholon, J. F., Becquemin, M. H., Annesi-Maesano, I., & Dautzenberg, B. (2013). Electronic cigarettes: A short review. *Respiration, 86*(5), 433-438.
[232] King, A. C., Smith, L. J., McNamara, P. J., & Cao, D. (2017). Second generation electronic nicotine delivery system vape pen exposure generalizes as a smoking cue. *Nicotine and Tobacco Research*. doi: 10.1093/ntr/ntw327.
[233] Chatham-Stephens, K., Law, R., Taylor, E., Melstrom, P., Bunnell, R., Wang, B., et al. (2014). Notes from the field: Calls to poison centers for exposures to electronic cigarettes - United States, September 2010-February 2014. *Morbidity Mortality Weekly Report, 63*(13), 292-293.
[234] Cantrell, F. L. (2014). Adverse effects of e-cigarette exposures. *Journal of Community Health, 39*(3), 614-616.
[235] Colaianni, C. A., Tapias, L. F., Cauley, R., Sheridan, R., Schulz, J. T., & Goverman, J. (2016). Injuries caused by explosion of electronic cigarette devices. *Eplasty, 16*, ic9.
U.S. Fire Administration. (2014). *Electronic cigarette fires and explosions*. Emmitsburg, MD: FEMA.

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Notes

[1] U.S. Department of Health and Human Services. (2016). *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, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

[2] England, L. J., Bunnell, R. E., Pechacek, T. F., Tong, V. T., & McAfee, T. A. (2015). Nicotine and the developing human: A neglected element in the electronic cigarette debate. *American Journal of Preventive Medicine, 49*(2), 286-293.

[3] Centers for Disease Control and Prevention. (2015). *E-cigarettes: An emerging public health challenge.* Retrieved from https://www.cdc.gov.

[4] U.S. Department of Health and Human Services. (2016). *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, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

[5] Singh, T., Arrazola, R. A., Corey, C. G., Husten, C. G., Neff, L. J., Homa, D. M., et al. (2016). Tobacco use among middle and high school students - United States, 2011-2015. *Morbidity and Mortality Weekly Report, 65*(14), 361-367.

[6] Johnston, L. D., Miech, R. A., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E. (2016). *Teen use of any illicit drug other than marijuana at new low, same true for alcohol: Data tables.* Retrieved from http://monitoringthefuture.org.

University of Michigan. (2017). *Press release: Vaping, hookah use by U.S. teens declines for first time.* Retrieved from http://ns.umich.edu.

[7] Schoenborn, C. A., & Gindi, R. M. (2015). Electronic cigarette use among adults: United States, 2014. *NCHS Data Brief, 217*, 1-8.

[8] Kasza, K. A., Ambrose, B. K., Conway, K. P., Borek, N., Taylor, K., Goniewicz, M. L., et al. (2017). Tobacco-product use by adults and youths in the United States in 2013 and 2014. *New England Journal of Medicine, 376*(4), 342-353.

[9] Centers for Disease Control and Prevention. (2013). *Electronic cigarette use among middle and high school students - United States, 2011-2012.* Retrieved from https://www.cdc.gov.

[10] King, B. A., Patel, R., Nguyen, K. H., & Dube, S. R. (2015). Trends in awareness and use of electronic cigarettes among U.S. adults, 2010-2013. *Nicotine and Tobacco Research, 17*(2), 219-227.

[11] Barrington-Trimis, J. L., Berhane, K., Unger, J. B., Cruz, T. B., Huh, J., Leventhal, A. M., et al. (2015). Psychosocial factors associated with adolescent electronic cigarette and cigarette use. *Pediatrics, 136*(2), 308-317.

Bostean, G., Trinidad, D. R., & McCarthy, W. J. (2015). E-cigarette use among never-smoking California students. *American Journal of Public Health, 105*(12), 2423-2425.

Bunnell, R. E., Agaku, I. T., Arrazola, R. A., Apelberg, B. J., Caraballo, R. S., Corey, C. G., et al. (2015). Intentions to smoke cigarettes among never-smoking U.S. middle and high school electronic cigarette users: National Youth Tobacco Survey, 2011-2013. *Nicotine and Tobacco Research, 17*(2), 228-235.

Camenga, D. R., Kong, G., Cavallo, D. A., Liss, A., Hyland, A., Delmerico, J., et al. (2014). Alternate tobacco product and drug use among adolescents who use electronic cigarettes, cigarettes only, and never smokers. *Journal of Adolescent Health, 55*(4), 588-591.

Grana, R., Benowitz, N., & Glantz, S. A. (2014). E-cigarettes: A scientific review. *Circulation, 129*(19), 1972-1986.

Krishnan-Sarin, S., Morean, M., Camenga, D., Cavallo, D. A., & Kong, G. (2015). E-cigarette use among high school and middle school adolescents in Connecticut. *Nicotine and Tobacco Research, 17*(7), 810-818.

Schoenborn, C. A., & Gindi, R. M. (2015). Electronic cigarette use among adults: United States, 2014. *NCHS Data Brief, 217*, 1-8.

Wills, T. A., Sargent, J. D., Knight, R., Pagano, I., & Gibbons, F. X. (2016). E-cigarette use and willingness to smoke: A sample of adolescent non-smokers. *Tobacco Control, 25*(e1), e52-e59.

[12] Bunnell, R. E., Agaku, I. T., Arrazola, R. A., Apelberg, B. J., Caraballo, R. S., Corey, C. G., et al. (2015). Intentions to smoke cigarettes among never-smoking U.S. middle and high school electronic cigarette users: National Youth Tobacco Survey, 2011-2013. *Nicotine and Tobacco Research, 17*(2), 228-235.

[13] Krishnan-Sarin, S., Morean, M., Camenga, D., Cavallo, D. A., & Kong, G. (2015). E-cigarette use among high school and middle school adolescents in Connecticut. *Nicotine and Tobacco Research, 17*(7), 810-818.

[14] Schoenborn, C. A., & Gindi, R. M. (2015). Electronic cigarette use among adults: United States, 2014. *NCHS Data Brief, 217*, 1-8.
[15] Dutra, L. M., & Glantz, S. A. (2017). E-cigarettes and national adolescent cigarette use: 2004-2014. *Pediatrics, 139*(2), e20162450. doi:10.1542/peds.2016-2450.
[16] McMillen, R. C., Gottlieb, M. A., Shaefer, R. M., Winickoff, J. P., & Klein, J. D. (2014). Trends in electronic cigarette use among U.S. adults: Use is increasing in both smokers and nonsmokers. *Nicotine and Tobacco Research*. *17*(10), 1195-1202.
[17] Bunnell, R. E., Agaku, I. T., Arrazola, R. A., Apelberg, B. J., Caraballo, R. S., Corey, C. G., et al. (2015). Intentions to smoke cigarettes among never-smoking U.S. middle and high school electronic cigarette users: National Youth Tobacco Survey, 2011-2013. *Nicotine and Tobacco Research, 17*(2), 228-235.
Coleman, B. N., Apelberg, B. J., Ambrose, B. K., Green, K. M., Choiniere, C. J., Bunnell, R., et al. (2014). Association between electronic cigarette use and openness to cigarette smoking among U.S. young adults. *Nicotine and Tobacco Research*. doi:10.1093/ntr/ntu211.
Miech, R., Patrick, M. E., O'Malley, P. M., & Johnston, L. D. (2017). E-cigarette use as a predictor of cigarette smoking: Results from a 1-year follow-up of a national sample of 12th grade students. *Tobacco Control*, doi: 10.1136/tobaccocontrol-2016-053291.
Wills, T. A., Sargent, J. D., Knight, R., Pagano, I., & Gibbons, F. X. (2016). E-cigarette use and willingness to smoke: A sample of adolescent non-smokers. *Tobacco Control, 25*(e1), e52-e59.
Zhong, J., Cao, S., Gong, W., Fei, F., & Wang, M. (2016). Electronic cigarettes use and intention to cigarette smoking among never-smoking adolescents and young adults: A meta-analysis. *International Journal of Environmental Research and Public Health, 13*(5), 465. doi:10.3390/ijerph13050465.
[18] Bunnell, R. E., Agaku, I. T., Arrazola, R. A., Apelberg, B. J., Caraballo, R. S., Corey, C. G., et al. (2015). Intentions to smoke cigarettes among never-smoking U.S. middle and high school electronic cigarette users: National Youth Tobacco Survey, 2011-2013. *Nicotine and Tobacco Research, 17*(2), 228-235.
[19] Miech, R., Patrick, M. E., O'Malley, P. M., & Johnston, L. D. (2017). E-cigarette use as a predictor of cigarette smoking: Results from a 1-year follow-up of a national sample of 12th grade students. *Tobacco Control*, doi: 10.1136/tobaccocontrol-2016-053291.
[20] Wills, T. A., Sargent, J. D., Knight, R., Pagano, I., & Gibbons, F. X. (2016). E-cigarette use and willingness to smoke: A sample of adolescent non-smokers. *Tobacco Control, 25*(e1), e52-e59.
[21] Wills, T. A., Knight, R., Sargent, J. D., Gibbons, F. X., Pagano, I., & Williams, R. J. (2016). Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. *Tobacco Control*. doi:10.1136/tobaccocontrol-2015-052705.
[22] Barrington-Trimis, J. L., Berhane, K., Unger, J. B., Cruz, T. B., Urman, R., Chou, C. P., et al. (2016). The e-cigarette social environment, e-cigarette use, and susceptibility to cigarette smoking. *Journal of Adolescent Health, 59*(1), 75-80.
[23] Barrington-Trimis, J. L., Urman, R., Berhane, K., Unger, J. B., Cruz, T. B., Pentz, M. A., et al. (2016). E-cigarettes and future cigarette use. *Pediatrics, 138*(1), e20160379. doi:10.1542/peds.2016-0379.
[24] Leventhal, A. M., Stone, M. D., Andrabi, N., Barrington-Trimis, J., Strong, D. R., Sussman, S., et al. (2016). Association of e-cigarette vaping and progression to heavier patterns of cigarette smoking. *JAMA, 316*(18), 1918-1920.
[25] Coleman, B. N., Apelberg, B. J., Ambrose, B. K., Green, K. M., Choiniere, C. J., Bunnell, R., et al. (2014). Association between electronic cigarette use and openness to cigarette smoking among U.S. young adults. *Nicotine and Tobacco Research*. doi:10.1093/ntr/ntu211.
[26] Spindle, T., Hiler, M. M., Cooke, M. E., Eissenberg, T., Kendler, K. S., & Dick, D. M. (2017). Electronic cigarette use and uptake of cigarette smoking: A longitudinal examination of U.S. college students. *Addictive Behaviors, 67*, 66-72.
[27] Barrington-Trimis, J. L., Urman, R., Berhane, K., Unger, J. B., Cruz, T. B., Pentz, M. A., et al. (2016). E-cigarettes and future cigarette use. *Pediatrics, 138*(1), e20160379. doi:10.1542/peds.2016-0379.
Dutra, L. M., & Glantz, S. A. (2017). E-cigarettes and national adolescent cigarette use: 2004-2014. *Pediatrics, 139*(2), e20162450. doi:10.1542/peds.2016-2450.
Leventhal, A. M., Strong, D. R., Kirkpatrick, M. G., Unger, J. B., Sussman, S., Riggs, N. R., et al. (2015). Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. *JAMA, 314*(7), 700-707.
Primack, B. A., Soneji, S., Stoolmiller, M., Fine, M. J., & Sargent, J. D. (2015). Progression to cigarette smoking after electronic cigarette use among U.S. adolescents and young adults. *JAMA Pediatrics, 169*(11), 1018-1023.

Wills, T. A., Knight, R., Sargent, J. D., Gibbons, F. X., Pagano, I., & Williams, R. J. (2016). Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. *Tobacco Control*. doi:10.1136/tobaccocontrol-2015-052705.
[28] Primack, B. A., Soneji, S., Stoolmiller, M., Fine, M. J., & Sargent, J. D. (2015). Progression to cigarette smoking after electronic cigarette use among U.S. adolescents and young adults. *JAMA Pediatrics, 169*(11), 1018-1023.
[29] Leventhal, A. M., Strong, D. R., Kirkpatrick, M. G., Unger, J. B., Sussman, S., Riggs, N. R., et al. (2015). Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. *JAMA, 314*(7), 700-707.
[30] Wills, T. A., Gibbons, F. X., Sargent, J., & Schweitzer, R. J. (2016). How is the effect of adolescent e-cigarette use on smoking onset mediated: A longitudinal analysis. *Psychology of Addictive Behaviors, 30*(8), 876-886.
[31] Miech, R., Patrick, M. E., O'Malley, P. M., & Johnston, L. D. (2017). E-cigarette use as a predictor of cigarette smoking: Results from a 1-year follow-up of a national sample of 12th grade students. *Tobacco Control*, doi: 10.1136/tobaccocontrol-2016-053291.
[32] Choi, K., Grana, R., & Bernat, D. (2017). Electronic nicotine delivery systems and acceptability of adult smoking among Florida youth: Renormalization of smoking? *Journal of Adolescent Health.* doi: 10.1016/j.jadohealth.2016.12.001.
[33] Bullen, C., Howe, C., Laugesen, M., McRobbie, H., Parag, V., Williman, J., et al. (2013). Electronic cigarettes for smoking cessation: A randomised controlled trial. *Lancet, 382*(9905), 1629-1637.
Bullen, C. (2014). Electronic cigarettes for smoking cessation. *Current Cardiology Reports, 16*(11), 538.
Centers for Disease Control and Prevention. (2015). *E-cigarettes: An emerging public health challenge.* Retrieved from https://www.cdc.gov.
Dinakar, C., & O'Connor, G. T. (2016). The health effects of electronic cigarettes. *New England Journal of Medicine, 375*(14), 1372-1381.
Kaisar, M. A., Prasad, S., Liles, T., & Cucullo, L. (2016). A decade of e-cigarettes: Limited research and unresolved safety concerns. *Toxicology, 365*, 67-75.
McRobbie, H., Bullen, C., Hartmann-Boyce, J., & Hajek, P. (2014). Electronic cigarettes for smoking cessation and reduction. *Cochrane Database of Systematic Reviews.* doi:10.1002/14651858.CD010216.pub2.
[34] Beard, E., West, R., Michie, S., & Brown, J. (2016). Association between electronic cigarette use and changes in quit attempts, success of quit attempts, use of smoking cessation pharmacotherapy, and use of stop smoking services in England: Time series analysis of population trends. *BMJ, 354*. doi:10.1136/bmj.i4645.
Hartmann-Boyce, J., McRobbie, H., Bullen, C., Begh, R., Stead, L. F., & Hajek, P. (2016). Electronic cigarettes for smoking cessation. *Cochrane Database of Systematic Reviews, 9*, doi:10.1002/14651858.CD010216.pub3.
[35] Tseng, T. Y., Ostroff, J. S., Campo, A., Gerard, M., Kirchner, T., Rotrosen, J., et al. (2016). A randomized trial comparing the effect of nicotine versus placebo electronic cigarettes on smoking reduction among young adult smokers. *Nicotine and Tobacco Research, 18*(10), 1937-1943.
[36] Kalkhoran, S., & Glantz, S. A. (2016). E-cigarettes and smoking cessation in real-world and clinical settings: A systematic review and meta-analysis. *Lancet Respiratory Medicine, 4*(2), 116-128.
[37] Dutra, L. M., & Glantz, S. A. (2014). Electronic cigarettes and conventional cigarette use among U.S. adolescents: A cross-sectional study. *JAMA Pediatrics, 168*(7), 610-617.
[38] Lippert, A. M. (2016). Temporal changes in the correlates of U.S. adolescent electronic cigarette use and utilization in tobacco cessation, 2011 to 2013. *Health Education and Behavior*. doi:10.1177/1090198116650150.
[39] Miech, R., Patrick, M. E., O'Malley, P. M., & Johnston, L. D. (2017). E-cigarette use as a predictor of cigarette smoking: Results from a 1-year follow-up of a national sample of 12th grade students. *Tobacco Control*, doi: 10.1136/tobaccocontrol-2016-053291.
[40] Sutfin, E. L., Reboussin, B. A., Debinski, B., Wagoner, K. G., Spangler, J., & Wolfson, M. (2015). The impact of trying electronic cigarettes on cigarette smoking by college students: A prospective analysis. *American Journal of Public Health, 105*(8), e83-e89. doi:10.2105/AJPH.2015.302707.
[41] Tseng, T. Y., Ostroff, J. S., Campo, A., Gerard, M., Kirchner, T., Rotrosen, J., et al. (2016). A randomized trial comparing the effect of nicotine versus placebo electronic cigarettes on smoking reduction among young adult smokers. *Nicotine and Tobacco Research, 18*(10), 1937-1943.
[42] Al-Delaimy, W. K., Myers, M. G., Leas, E. C., Strong, D. R., & Hofstetter, C. R. (2015). E-cigarette use in the past and quitting behavior in the future: A population-based study. *American Journal of Public Health, 105*(6), 1213-1219.

[43] Brose, L. S., Hitchman, S. C., Brown, J., West, R., & McNeill, A. (2015). Is the use of electronic cigarettes while smoking associated with smoking cessation attempts, cessation and reduced cigarette consumption? A survey with a 1-year follow-up. *Addiction, 110*(7), 1160-1168.

[44] Grana, R. A., Popova, L., & Ling, P. M. (2014). A longitudinal analysis of electronic cigarette use and smoking cessation. *JAMA Internal Medicine, 174*(5), 812-813.

[45] Shi, Y., Pierce, J. P., White, M., Vijayaraghavan, M., Compton, W., Conway, K., et al. (2016). E-cigarette use and smoking reduction or cessation in the 2010/2011 TUS-CPS longitudinal cohort. *BMC Public Health, 16*(1), 1105.

[46] Adkison, S. E., O'Connor, R. J., Bansal-Travers, M., Hyland, A., Borland, R., Yong, H. H., et al. (2013). Electronic nicotine delivery systems: International tobacco control four-country survey. *American Journal of Preventive Medicine, 44*(3), 207-215.

Grana, R., Benowitz, N., & Glantz, S. A. (2014). E-cigarettes: A scientific review. *Circulation, 129*(19), 1972-1986.

[47] Pisinger, C. (2014). Why public health people are more worried than excited over e-cigarettes. *BMC Medicine, 12*, 226. doi:10.1186/s12916-014-0226-y.

Yeh, J. S., Bullen, C., & Glantz, S. A. (2016). E-cigarettes and smoking cessation. *New England Journal of Medicine, 374*(22), 2172-2174.

[48] Bjartveit, K., & Tverdal, A. (2005). Health consequences of smoking 1-4 cigarettes per day. *Tobacco Control, 14*(5), 315-320.

Inoue-Choi, M., Liao, L. M., Reyes-Guzman, C., Hartge, P., Caporaso, N., & Freedman, N. D. (201&). Association of long-term, low-intensity smoking with all-cause and cause-specific mortality in the National Institutes of Health-AARP diet and health study. *JAMA Internal Medicine, 177*(1), 87-95.

Schane, R. E., Ling, P. M., & Glantz, S. A. (2010). Health effects of light and intermittent smoking: A review. *Circulation, 121*(13), 1518-1522.

U.S. Department of Health and Human Services. (2014). *The health consequences of smoking-50 years of progress. A report of the Surgeon General* (January 2014. Printed with corrections). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

Chapter III
Notes

[1] Harrell, P. T., Naqvi, S. M. H., Plunk, A. D., Ji, M., & Martins, S. S. (2016). Patterns of youth tobacco and polytobacco usage: The shift to alternative tobacco products. *American Journal of Drugand Alcohol Abuse.* doi:10.1080/00952990.2016.1225072.

Jamal, A., Homa, D. M., O'Connor, E., Babb, S. D., Caraballo, R. S., Singh, T., et al. (2015). Current cigarette smoking among adults - United States, 2005-2014. *Morbidity and Mortality Weekly Report, 64*(44), 1233-1240.

Kasza, K. A., Ambrose, B. K., Conway, K. P., Borek, N., Taylor, K., Goniewicz, M. L., et al. (2017). Tobacco-product use by adults and youths in the United States in 2013 and 2014. *New England Journal of Medicine, 376*(4), 342-353.

Singh, T., Arrazola, R. A., Corey, C. G., Husten, C. G., Neff, L. J., Homa, D. M., et al. (2016). Tobacco use among middle and high school students - United States, 2011-2015. *Morbidity and Mortality Weekly Report, 65*(14), 361-367.

[2] Singh, T., Arrazola, R. A., Corey, C. G., Husten, C. G., Neff, L. J., Homa, D. M., et al. (2016). Tobacco use among middle and high school students - United States, 2011-2015. *Morbidity and Mortality Weekly Report, 65*(14), 361-367.

[3] Dutra, L. M., & Glantz, S. A. (2017). E-cigarettes and national adolescent cigarette use: 2004-2014. *Pediatrics, 139*(2), e20162450. doi:10.1542/peds.2016-2450.

[4] Johnston, L. D., Miech, R. A., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E. (2016). *Teen use of any illicit drug other than marijuana at new low, same true for alcohol: Data tables.* Retrieved from http://monitoringthefuture.org.

University of Michigan. (2017). *Press release: Vaping, hookah use by U.S. teens declines for first time.* Retrieved from http://ns.umich.edu.

[5] Ali, M., Gray, T. R., Martinez, D. J., Curry, L. E., & Horn, K. A. (2016). Risk profiles of youth single, dual, and poly tobacco users. *Nicotine and Tobacco Research, 18*(7), 1614-1621.

Kasza, K. A., Ambrose, B. K., Conway, K. P., Borek, N., Taylor, K., Goniewicz, M. L., et al. (2017). Tobacco-product use by adults and youths in the United States in 2013 and 2014. *New England Journal of Medicine, 376*(4), 342-353.

Lee, Y. O., Hebert, C. J., Nonnemaker, J. M., & Kim, A. E. (2014). Multiple tobacco product use among adults in the United States: Cigarettes, cigars, electronic cigarettes, hookah, smokeless tobacco, and snus. *Preventive Medicine, 62*, 14-19.

Lee, Y. O., Hebert, C. J., Nonnemaker, J. M., & Kim, A. E. (2015). Youth tobacco product use in the United States. *Pediatrics, 135*(3), 409-415.

Singh, T., Arrazola, R. A., Corey, C. G., Husten, C. G., Neff, L. J., Homa, D. M., et al. (2016). Tobacco use among middle and high school students - United States, 2011-2015. *Morbidity and Mortality Weekly Report, 65*(14), 361-367.

Villanti, A. C., Pearson, J. L., Glasser, A. M., Johnson, A. L., Collins, L. K., Niaura, R. S., et al. (2017). Frequency of youth e-cigarette and tobacco use patterns in the United States: Measurement precision is critical to inform public health. *Nicotine and Tobacco Research*. doi:10.1093/ntr/ntw388.

[6] CASAColumbia. (2011). *Adolescent substance use: America's #1 public health problem*. New York: Author.

CASAColumbia. (2012). *Addiction medicine: Closing the gap between science and practice*. New York: Author.

CASAColumbia. (2015). *Understanding and addressing nicotine addiction: A science-based approach to policy and practice*. New York: Author.

Creamer, M. R., Portillo, G. V., Clendennen, S. L., & Perry, C. L. (2016). Is adolescent poly-tobacco use associated with alcohol and other drug use? *American Journal of Health Behaviors, 40*(1), 117-122.

Cross, S. J., Lotfipour, S., & Leslie, F. M. (2017). Mechanisms and genetic factors underlying co-use of nicotine and alcohol or other drugs of abuse. *American Journal of Drug and Alcohol Abuse*. doi:10.1080/00952990.2016.1209512.

Fillon, M. (2015). Electronic cigarettes may lead to nicotine addiction. *Journal of the National Cancer Institute, 107*(3). doi:10.1093/jnci/djv070.

Kandel, D. B., & Kandel, E. R. (2014). A molecular basis for nicotine as a gateway drug. *New England Journal of Medicine, 371*(21), 2038-2039.

Lanza, S. T., & Vasilenko, S. A. (2015). New methods shed light on age of onset as a risk factor for nicotine dependence. *Addictive Behaviors, 50*, 161-164.
Richter, L., Pugh, B. S., & Ball, S. A. (2016). Assessing the risk of marijuana use disorder among adolescents and adults who use marijuana. *American Journal of Drug and Alcohol Abuse*. doi:10.3109/00952990.2016.1164711.
Richter, L., Pugh, B. S., Peters, E. A., Vaughan, R. D., & Foster, S. E. (2016). Underage drinking: Prevalence and correlates of risky drinking measures among youth aged 12–20. *American Journal of Drug and Alcohol Abuse, 42*(4), 385-94.
Richter, L., Pugh, B. S., Smith, P. H., & Ball, S. A. (2016). The co-occurrence of nicotine and other substance use and addiction among youth and adults in the United States: Implications for research, practice, and policy. *American Journal of Drug and Alcohol Abuse, 43*(2), 132-145.
Weissman, D. G., Schriber, R. A., Fassbender, C., Atherton, O., Krafft, C., Robins, R. W., et al. (2015). Earlier adolescent substance use onset predicts stronger connectivity between reward and cognitive control brain networks. *Developmental Cognitive Neuroscience, 16*, 121-129.
[7] Kasza, K. A., Ambrose, B. K., Conway, K. P., Borek, N., Taylor, K., Goniewicz, M. L., et al. (2017). Tobacco-product use by adults and youths in the United States in 2013 and 2014. *New England Journal of Medicine, 376*(4), 342-353.
[8] King, B. A., Dube, S. R., & Tynan, M. A. (2012). Current tobacco use among adults in the United States: Findings from the National Adult Tobacco Survey. *American Journal of Public Health, 102*(11), e93-e100.
[9] Hu, S. S., Neff, L., Agaku, I. T., Cox, S., Day, H. R., Holder-Hayes, E., et al. (2016). Tobacco product use among adults - United States, 2013-2014. *Morbidity and Mortality Weekly Report, 65*(27), 686-691.
[10] King, B. A., Dube, S. R., & Tynan, M. A. (2012). Current tobacco use among adults in the United States: Findings from the National Adult Tobacco Survey. *American Journal of Public Health, 102*(11), e93-e100.
Singh, T., Arrazola, R. A., Corey, C. G., Husten, C. G., Neff, L. J., Homa, D. M., et al. (2016). Tobacco use among middle and high school students - United States, 2011-2015. *Morbidity and Mortality Weekly Report, 65*(14), 361-367.
[11] Strong, D. R., Messer, K., Hartman, S. J., Conway, K. P., Hoffman, A. C., Pharris-Ciurej, N., et al. (2015). Measurement of multiple nicotine dependence domains among cigarette, non-cigarette and poly-tobacco users: Insights from item response theory. *Drug and Alcohol Dependence, 152*, 185-193.
[12] CASAColumbia. (2011). *Adolescent substance use: America's #1 public health problem*. New York: Author.
Lanza, S. T., & Vasilenko, S. A. (2015). New methods shed light on age of onset as a risk factor for nicotine dependence. *Addictive Behaviors, 50*, 161-164.
Weissman, D. G., Schriber, R. A., Fassbender, C., Atherton, O., Krafft, C., Robins, R. W., et al. (2015). Earlier adolescent substance use onset predicts stronger connectivity between reward and cognitive control brain networks. *Developmental Cognitive Neuroscience, 16*, 121-129.
[13] Smith, R. F., McDonald, C. G., Bergstrom, H. C., Ehlinger, D. G., & Brielmaier, J. M. (2015). Adolescent nicotine induces persisting changes in development of neural connectivity. *Neuroscience and Biobehavioral Reviews, 55*, 432-443.
Yuan, M., Cross, S. J., Loughlin, S. E., & Leslie, F. M. (2015). Nicotine and the adolescent brain. *Journal of Physiology, 593*(16), 3397-3412.
[14] CASAColumbia. (2011). *Adolescent substance use: America's #1 public health problem*. New York: Author.
Gipson, C. D., Kupchik, Y. M., & Kalivas, P. W. (2014). Rapid, transient synaptic plasticity in addiction. *Neuropharmacology, 76*(Pt B), 276-286.
Smith, R. F., McDonald, C. G., Bergstrom, H. C., Ehlinger, D. G., & Brielmaier, J. M. (2015). Adolescent nicotine induces persisting changes in development of neural connectivity. *Neuroscience and Biobehavioral Reviews, 55*, 432-443.
Yuan, M., Cross, S. J., Loughlin, S. E., & Leslie, F. M. (2015). Nicotine and the adolescent brain. *Journal of Physiology, 593*(16), 3397-3412.
[15] DiFranza, J. R., Rigotti, N. A., McNeill, A. D., Ockene, J. K., Savageau, J. A., St, C. D., et al. (2000). Initial symptoms of nicotine dependence in adolescents. *Tobacco Control, 9*(3), 313-319.
[16] Ali, M., Gray, T. R., Martinez, D. J., Curry, L. E., & Horn, K. A. (2016). Risk profiles of youth single, dual, and poly tobacco users. *Nicotine and Tobacco Research, 18*(7), 1614-1621.

Kasza, K. A., Ambrose, B. K., Conway, K. P., Borek, N., Taylor, K., Goniewicz, M. L., et al. (2017). Tobacco-product use by adults and youths in the United States in 2013 and 2014. *New England Journal of Medicine, 376*(4), 342-353.
Lee, Y. O., Hebert, C. J., Nonnemaker, J. M., & Kim, A. E. (2014). Multiple tobacco product use among adults in the United States: Cigarettes, cigars, electronic cigarettes, hookah, smokeless tobacco, and snus. *Preventive Medicine, 62*, 14-19.
Lee, Y. O., Hebert, C. J., Nonnemaker, J. M., & Kim, A. E. (2015). Youth tobacco product use in the United States. *Pediatrics, 135*(3), 409-415.
Singh, T., Arrazola, R. A., Corey, C. G., Husten, C. G., Neff, L. J., Homa, D. M., et al. (2016). Tobacco use among middle and high school students - United States, 2011-2015. *Morbidity and Mortality Weekly Report, 65*(14), 361-367.
Villanti, A. C., Pearson, J. L., Glasser, A. M., Johnson, A. L., Collins, L. K., Niaura, R. S., et al. (2017). Frequency of youth e-cigarette and tobacco use patterns in the United States: Measurement precision is critical to inform public health. *Nicotine and Tobacco Research*. doi:10.1093/ntr/ntw388.
[17] CASAColumbia. (2015). *Understanding and addressing nicotine addiction: A science-based approach to policy and practice*. New York: Author.
Dunbar, M. S., Shadel, W. G., Tucker, J. S., & Edelen, M. O. (2016). Use of and reasons for using multiple other tobacco products in daily and nondaily smokers: Associations with cigarette consumption and nicotine dependence. *Drug and Alcohol Dependence, 168*, 156-163.
Harrell, P. T., Naqvi, S. M. H., Plunk, A. D., Ji, M., & Martins, S. S. (2016). Patterns of youth tobacco and polytobacco usage: The shift to alternative tobacco products. *American Journal of Drug and Alcohol Abuse.* doi:10.1080/00952990.2016.1225072.
Timberlake, D. S. (2008). A latent class analysis of nicotine-dependence criteria and use of alternate tobacco. *Journal of Studies on Alcohol and Drugs, 69*(5), 709-717.
[18] Kasza, K. A., Ambrose, B. K., Conway, K. P., Borek, N., Taylor, K., Goniewicz, M. L., et al. (2017). Tobacco-product use by adults and youths in the United States in 2013 and 2014. *New England Journal of Medicine, 376*(4), 342-353.
Lee, Y. O., Hebert, C. J., Nonnemaker, J. M., & Kim, A. E. (2014). Multiple tobacco product use among adults in the United States: Cigarettes, cigars, electronic cigarettes, hookah, smokeless tobacco, and snus. *Preventive Medicine, 62*, 14-19.
[19] Timberlake, D. S. (2008). A latent class analysis of nicotine-dependence criteria and use of alternate tobacco. *Journal of Studies on Alcohol and Drugs, 69*(5), 709-717.
[20] Timberlake, D. S. (2008). A latent class analysis of nicotine-dependence criteria and use of alternate tobacco. *Journal of Studies on Alcohol and Drugs, 69*(5), 709-717.
[21] Carroll Chapman, S. L., & Wu, L. T. (2014). E-cigarette prevalence and correlates of use among adolescents versus adults: A review and comparison. *Journal of Psychiatric Research, 54*, 43-54.
Cohn, A., Cobb, C. O., Niaura, R. S., & Richardson, A. (2015). The other combustible products: Prevalence and correlates of little cigar/cigarillo use among cigarette smokers. *Nicotine and Tobacco Research*, *17*(12), 1473-1481.
Coleman, B. N., Johnson, S. E., Tessman, G. K., Tworek, C., Alexander, J., Dickinson, D. M., et al. (2016). "It's not smoke. It's not tar. It's not 4000 chemicals. Case closed": Exploring attitudes, beliefs, and perceived social norms of e-cigarette use among adult users. *Drug and Alcohol Dependence, 159*, 80-85.
Cooper, M., Harrell, M. B., Perez, A., Delk, J., & Perry, C. L. (2016). Flavorings and perceived harm and addictiveness of e-cigarettes among youth. *Tobacco Regulatory Science, 2*(3), 278-289.
Harrell, P. T., Marquinez, N. S., Correa, J. B., Meltzer, L. R., Unrod, M., Sutton, S. K., et al. (2015). Expectancies for cigarettes, e-cigarettes, and nicotine replacement therapies among e-cigarette users ("Vapers"). *Nicotine and Tobacco Research*, *17*(2), 193-200.
Heinz, A. J., Giedgowd, G. E., Crane, N. A., Veilleux, J. C., Conrad, M., Braun, A. R., et al. (2013). A comprehensive examination of hookah smoking in college students: Use patterns and contexts, social norms and attitudes, harm perception, psychological correlates and co-occurring substance use. *Addictive Behaviors, 38*(11), 2751-2760.
Payne, J. D., Orellana-Barrios, M., Medrano-Juarez, R., Buscemi, D., & Nugent, K. (2016). Electronic cigarettes in the media. *Proceedings (Baylor University Medical Center), 29*(3), 280-283.

Richardson, A., Pearson, J., Xiao, H., Stalgaitis, C., & Vallone, D. (2014). Prevalence, harm perceptions, and reasons for using noncombustible tobacco products among current and former smokers. *American Journal of Public Health, 104*(8), 1437-1444.
Smith, S. Y., Curbow, B., & Stillman, F. A. (2007). Harm perception of nicotine products in college freshmen. *Nicotine and Tobacco Research, 9*(9), 977-982.
Wagoner, K. G., Cornacchione, J., Wiseman, K. D., Teal, R., Moracco, K. E., & Sutfin, E. L. (2016). E-cigarettes, hookah pens and vapes: Adolescent and young adult perceptions of electronic nicotine delivery systems. *Nicotine and Tobacco Research*, *18*(10), 2006-2012.
[22] Al-Delaimy, W. K., Myers, M. G., Leas, E. C., Strong, D. R., & Hofstetter, C. R. (2015). E-cigarette use in the past and quitting behavior in the future: A population-based study. *American Journal of Public Health, 105*(6), 1213-1219.
Messer, K., Vijayaraghavan, M., White, M. M., Shi, Y., Chang, C., Conway, K. P., et al. (2015). Cigarette smoking cessation attempts among current U.S. smokers who also use smokeless tobacco. *Addictive Behaviors, 51*, 113-119.
[23] Arnett, J. J. (2000). Emerging adulthood. A theory of development from the late teens through the twenties. *American Psychologist, 55*(5), 469-480.
[24] Ambrose, B. K., Rostron, B. L., Johnson, S. E., Portnoy, D. B., Apelberg, B. J., Kaufman, A. R., et al. (2014). Perceptions of the relative harm of cigarettes and e-cigarettes among U.S. youth. *American Journal of Preventive Medicine, 47*(Suppl 1), S53-S60.
Amrock, S. M., Lee, L., & Weitzman, M. (2016). Perceptions of e-cigarettes and noncigarette tobacco products among U.S. youth. *Pediatrics, 138*(5), 1-10.
Roditis, M., Delucchi, K., Cash, D., & Halpern-Felsher, B. (2016). Adolescents' perceptions of health risks, social risks, and benefits differ across tobacco products. *Journal of Adolescent Health, 58*(5), 558-566.
Wagoner, K. G., Cornacchione, J., Wiseman, K. D., Teal, R., Moracco, K. E., & Sutfin, E. L. (2016). E-cigarettes, hookah pens and vapes: Adolescent and young adult perceptions of electronic nicotine delivery systems. *Nicotine and Tobacco Research*, *18*(10), 2006-2012.
[25] Cummins, S. E., Zhu, S. H., Tedeschi, G. J., Gamst, A. C., & Myers, M. G. (2014). Use of e-cigarettes by individuals with mental health conditions. *Tobacco Control, 23*(Suppl 3), iii48-iii53.
Redner, R., White, T. J., Harder, V. S., & Higgins, S. T. (2014). Examining vulnerability to smokeless tobacco use among adolescents and adults meeting diagnostic criteria for major depressive disorder. *Experimental and Clinical Psychopharmacology, 22*(4), 316-322.
Stanton, C. A., Keith, D. R., Gaalema, D. E., Bunn, J. Y., Doogan, N. J., Redner, R., et al. (2016). Trends in tobacco use among U.S. adults with chronic health conditions: National Survey on Drug Use and Health 2005-2013. *Preventive Medicine, 92,* 160-168.
[26] Benowitz, N. L. (2009). Pharmacology of nicotine: Addiction, smoking-induced disease, and therapeutics. *Annual Review of Pharmacology and Toxicology, 49*, 57-71.
England, L. J., Bunnell, R. E., Pechacek, T. F., Tong, V. T., & McAfee, T. A. (2015). Nicotine and the developing human: A neglected element in the electronic cigarette debate. *American Journal of Preventive Medicine, 49*(2), 286-293.
Kohlmeier, K. A. (2015). Nicotine during pregnancy: Changes induced in neurotransmission, which could heighten proclivity to addict and induce maladaptive control of attention. *Journal of Developmental Origins of Health and Disease, 6*(3), 169-181.
U.S. Department of Health and Human Services. (1988). *The health consequences of smoking: Nicotine addiction: A report of the Surgeon General*. Rockville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[27] Cummins, S. E., Zhu, S. H., Tedeschi, G. J., Gamst, A. C., & Myers, M. G. (2014). Use of e-cigarettes by individuals with mental health conditions. *Tobacco Control, 23*(Suppl 3), iii48-iii53.
Redner, R., White, T. J., Harder, V. S., & Higgins, S. T. (2014). Examining vulnerability to smokeless tobacco use among adolescents and adults meeting diagnostic criteria for major depressive disorder. *Experimental and Clinical Psychopharmacology, 22*(4), 316-322.
Stanton, C. A., Keith, D. R., Gaalema, D. E., Bunn, J. Y., Doogan, N. J., Redner, R., et al. (2016). Trends in tobacco use among U.S. adults with chronic health conditions: National Survey on Drug Use and Health 2005-2013. *Preventive Medicine, 92,* 160-168.

[28] Cummins, S. E., Zhu, S. H., Tedeschi, G. J., Gamst, A. C., & Myers, M. G. (2014). Use of e-cigarettes by individuals with mental health conditions. *Tobacco Control, 23*(Suppl 3), iii48-iii53.
[29] Redner, R., White, T. J., Harder, V. S., & Higgins, S. T. (2014). Examining vulnerability to smokeless tobacco use among adolescents and adults meeting diagnostic criteria for major depressive disorder. *Experimental and Clinical Psychopharmacology, 22*(4), 316-322.
Stanton, C. A., Keith, D. R., Gaalema, D. E., Bunn, J. Y., Doogan, N. J., Redner, R., et al. (2016). Trends in tobacco use among U.S. adults with chronic health conditions: National Survey on Drug Use and Health 2005-2013. *Preventive Medicine*, *92,* 160-168.
[30] Benowitz, N. L. (2009). Pharmacology of nicotine: Addiction, smoking-induced disease, and therapeutics. *Annual Review of Pharmacology and Toxicology, 49*, 57-71.
England, L. J., Bunnell, R. E., Pechacek, T. F., Tong, V. T., & McAfee, T. A. (2015). Nicotine and the developing human: A neglected element in the electronic cigarette debate. *American Journal of Preventive Medicine, 49*(2), 286-293.
Kohlmeier, K. A. (2015). Nicotine during pregnancy: Changes induced in neurotransmission, which could heighten proclivity to addict and induce maladaptive control of attention. *Journal of Developmental Origins of Health and Disease, 6*(3), 169-181
U.S. Department of Health and Human Services. (1988). *The health consequences of smoking: Nicotine addiction: A report of the Surgeon General*. Rockville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[31] Siu, A. L. (2015). Behavioral and pharmacotherapy interventions for tobacco smoking cessation in adults, including pregnant women: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine, 163*(8), 622-634.

Chapter IV
Notes

[1] Kozlowski, L. T., & Abrams, D. B. (2016). Obsolete tobacco control themes can be hazardous to public health: The need for updating views on absolute product risks and harm reduction. *BMC Public Health, 16*, 432. doi:10.1186/s12889-016-3079-9.
U.S. Department of Health, Education, and Welfare. (1964). *Smoking and health: Report of the advisory committee to the Surgeon General of the public health service* (PHS Publication No. 1103). Washington, DC: U.S. Government Printing Office.
[2] U.S. Department of Health, Education, and Welfare. (1964). *Smoking and health: Report of the advisory committee to the Surgeon General of the public health service* (PHS Publication No. 1103). Washington, DC: U.S. Government Printing Office.
U.S. Department of Health and Human Services. (2014). *The health consequences of smoking-50 years of progress. A report of the Surgeon General* (January 2014. Printed with corrections). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[3] Kozlowski, L. T., & Abrams, D. B. (2016). Obsolete tobacco control themes can be hazardous to public health: The need for updating views on absolute product risks and harm reduction. *BMC Public Health, 16*, 432. doi:10.1186/s12889-016-3079-9.
U.S. Department of Health and Human Services. (2014). *The health consequences of smoking-50 years of progress. A report of the Surgeon General* (January 2014. Printed with corrections). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[4] U.S. Department of Health, Education, and Welfare. (1964). *Smoking and health: Report of the advisory committee to the Surgeon General of the public health service* (PHS Publication No. 1103). Washington, DC: U.S. Government Printing Office.
[5] U.S. Department of Health and Human Services. (1988). *The health consequences of smoking: Nicotine addiction: A report of the Surgeon General*. Rockville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[6] Warner, K. E. (2006). Tobacco control policy. San Francisco, CA: Jossey-Bass.
[7] Centers for Disease Control and Prevention. (2013). *The Federal Cigarette Labeling and Advertising Act (FCLAA) and Comprehensive Smokeless Tobacco Health Education Act (CSTHEA).* Retrieved from http://www.cdc.gov.
Centers for Disease Control and Prevention. (2013). *Tobacco ingredient and nicotine reporting.* Retrieved from http://www.cdc.gov.
Pub. L. No. 89-92, 79 Stat. 282 (1965) (codified as amended at 15 U.S.C. §§ 1331-1341 (2012)).
[8] Public Health Cigarette Smoking Act of 1969, Pub. L. No. 91-222, 84 Stat. 87 (1970) (codified as amended at 15 U.S.C. §§ 1331-1341 (2012)).
[9] GovTrack.us. (1973). *S. 1165 - 93rd Congress: Little Cigar Act.* Retrieved from https://www.govtrack.us.
Pub. L. 93-109, 87 Stat. 352 (1973) (codified as amended at 15 U.S.C. §§ 1331-1341).
Unlawful advertisements on medium of electronic communication. 15 U.S.C. § 1335 (2010).
[10] GovTrack.us. (2016). *S. 1574 - 99th Congress: Comprehensive Smokeless Tobacco Health Education Act of 1986.* Retrieved from https://www.govtrack.us.
[11] Federal Cigarette Labeling and Advertising Act, Pub. L. No. 89-92, 79 Stat. 282 (1965).
Pub. L. No. 89-92, 79 Stat. 282 (1965) (codified as amended at 15 U.S.C. §§ 1331-1341 (2012)).
Public Health Cigarette Smoking Act of 1969, Pub. L. No. 91-222, 84 Stat. 87 (1970) (codified as amended at 15 U.S.C. §§ 1331-1341 (2012)).
[12] Centers for Disease Control and Prevention. (2016). *Selected actions of the U.S. government regarding the regulation of tobacco sales, marketing, and use.* Retrieved from http://www.cdc.gov.
[13] U.S. Department of Health and Human Services. (1994). *Youth and tobacco: Preventing tobacco use among young people: A report of the Surgeon General.* Washington, DC: U.S. Department of Health and Human Services, U.S. Department of Education.
[14] Warner, K. E. (06). Tobacco control policy. San Francisco, CA: Jossey-Bass.

[15] GovTrack.us. (1973). *S. 1306 - 102nd Congress: ADAMHA Reorganization Act.* Retrieved from https://www.govtrack.us.
[16] Apollonio, D. E., & Glantz, S. A. (2016). Minimum ages of legal access for tobacco in the United States from 1863 to 2015. *American Journal of Public Health, 106*(7), 1200-1207.
Grucza, R. A., Plunk, A. D., Hipp, P. R., Cavazos-Rehg, P., Krauss, M. J., Brownson, R. C., et al. (2013). Long-term effects of laws governing youth access to tobacco. *American Journal of Public Health, 103*(8), 1493-1499.
[17] Tobacco Control Legal Consortium. (2016). *U.S. e-cigarette regulation: A 50-state review.* Retrieved from http://publichealthlawcenter.org.
[18] Family Smoking Prevention and Tobacco Control Act. 21 U.S.C. §§ 387 - 387u (2011).
IOM (Institute of Medicine). (2015). *Report brief: Public health implications of raising the minimum age of legal access to tobacco products*. Washington, DC: The National Academies Press.
[19] U.S. Food and Drug Administration. (2016). *Family Smoking Prevention and Tobacco Control Act: 21 CFR parts 1100, 1140, and 1143.* Retrieved from http://federalregister.gov.
[20] IOM (Institute of Medicine). (2015). *Report brief: Public health implications of raising the minimum age of legal access to tobacco products*. Washington, DC: The National Academies Press.
[21] IOM (Institute of Medicine). (2015). *Report brief: Public health implications of raising the minimum age of legal access to tobacco products*. Washington, DC: The National Academies Press.
[22] Family Smoking Prevention and Tobacco Control Act. 21 U.S.C. §§ 387 - 387u (2011).
[23] IOM (Institute of Medicine). (2015). *Report brief: Public health implications of raising the minimum age of legal access to tobacco products*. Washington, DC: The National Academies Press.
[24] U.S. Food and Drug Administration. (2016). *Family Smoking Prevention and Tobacco Control Act: 21 CFR parts 1100, 1140, and 1143.* Retrieved from http://federalregister.gov.
[25] Lee, J. G., Boynton, M. H., Richardson, A., Jarman, K., Ranney, L. M., & Goldstein, A. O. (2016). Raising the legal age of tobacco sales: Policy support and trust in government, 2014-2015, U.S. *American Journal of Preventive Medicine, 51*(6), 910-915..
[26] Campaign for Tobacco-Free Kids. (2016). *States and localities that have raised the minimum legal sale age for tobacco products to 21.* Retrieved from http://www.tobaccofreekids.org.
[27] Friedman, A. S. (2015). How does electronic cigarette access affect adolescent smoking? *Journal of Health Economics*, 44, 300-308.
Pesko, M. F., Hughes, J. M., & Faisal, F. S. (2016). The influence of electronic cigarette age purchasing restrictions on adolescent tobacco and marijuana use. *Preventive Medicine, 87*, 207-212.
[28] Pesko, M. F., Hughes, J. M., & Faisal, F. S. (2016). The influence of electronic cigarette age purchasing restrictions on adolescent tobacco and marijuana use. *Preventive Medicine, 87*, 207-212.
[29] National Association of Attorneys General. (1998). *Master settlement agreement.* Retrieved from http://web.archive.org.
[30] National Association of Attorneys General. (1998). *Master settlement agreement.* Retrieved from http://web.archive.org.
U.S. Department of Health and Human Services. (2014). *The health consequences of smoking-50 years of progress. A report of the Surgeon General* (January 2014. Printed with corrections). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[31] National Association of Attorneys General. (1998). *Master settlement agreement.* Retrieved from http://web.archive.org.
U.S. Department of Health and Human Services. (2014). *The health consequences of smoking-50 years of progress. A report of the Surgeon General* (January 2014. Printed with corrections). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[32] Richtel, M. (2013). *The e-cigarette industry: Waiting to exhale.* Retrieved from http://www.nytimes.com.
[33] Singh, T., Marynak, K., Arrazola, R. A., Cox, S., Rolle, I. V., & King, B. A. (2016). Vital signs: Exposure to electronic cigarette advertising among middle school and high school students - United States, 2014. *Morbidity and Mortality Weekly Report, 64*(52), 1403-1408.
[34] Truth Initiative. (2015). *Vaporized: Youth and young adult exposure to e-cigarette marketing* . Washington, DC: Truth Initiative.

[35] U.S. Department of Health and Human Services. (2014). *The health consequences of smoking-50 years of progress. A report of the Surgeon General* (January 2014. Printed with corrections). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[36] Family Smoking Prevention and Tobacco Control Act. 21 U.S.C. §§ 387 - 387u (2011)
[37] Complaint, American Academy of Pediatrics v. FDA, No. 16-cv-11985 (D. Mass. filed Oct. 4, 2016). (2016). *Complaint, American Academy of Pediatrics v. FDA, No. 16-cv-11985 (D. Mass. filed Oct. 4, 2016).* Available at http://www.acscan.org.
[38] U.S. Food and Drug Administration. (2014). *FDA proposes to extend its tobacco authority to additional tobacco products, including e-cigarettes.* Retrieved from http://www.fda.gov.
[39] U.S. Food and Drug Administration. (2016). *Family Smoking Prevention and Tobacco Control Act: 21 CFR parts 1100, 1140, and 1143.* Retrieved from http://federalregister.gov.
[40] U.S. Department of Health and Human Services. (2016). 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: Final rule. *Federal Register, 81*(90), 28974-29106.
[41] Tobacco Control Legal Consortium. (2016). *The deeming regulation: FDA authority over e-cigarettes, cigars, and other tobacco products*. Saint Paul, MN: Public Health Law Center.
[42] Tobacco Control Legal Consortium. (2012). *Regulating tobacco products based on pack size*. Saint Paul, MN: Public Health Law Center.
[43] Tobacco Control Legal Consortium. (2016). *The FDA's premarket review of tobacco products fails to fully protect public health.* Saint Paul, MN: Public Health Law Center.
[44] www.GovTrack.us. (2009). *H.R. 1256 - 111th Congress: Family Smoking Prevention and Tobacco Control Act.* Retrieved from https://www.govtrack.us.
[45] Family Smoking Prevention and Tobacco Control Act. 21 U.S.C. § 387j(c) (2011).
Tobacco Control Legal Consortium. (2016). *The FDA's premarket review of tobacco products fails to fully protect public health.* Saint Paul, MN: Public Health Law Center.
[46] U.S. Department of Health and Human Services. (2016). *Premarket tobacco product applications for electronic nicotine delivery systems: Guidance for industry.* Retrieved from http://tveca.com.
[47] Tobacco Control Legal Consortium. (2016). *The deeming regulation: FDA authority over e-cigarettes, cigars, and other tobacco products*. Saint Paul, MN: Public Health Law Center.
[48] Siegel, M. (2016). *FDA e-cigarette deeming regulations are a disaster for public health.* Retrieved from http://tobaccoanalysis.blogspot.com.
[49] Jenson, D., Lester, J., & Berman, M. L. (2016). FDA's misplaced priorities: Premarket review under the Family Smoking Prevention and Tobacco Control Act. *Tobacco Control, 25*(3), 246-253.
[50] Family Smoking Prevention and Tobacco Control Act. 21 U.S.C. § 387j(c) (2011).
Tobacco Control Legal Consortium. (2016). *The FDA's premarket review of tobacco products fails to fully protect public health.* Saint Paul, MN: Public Health Law Center.
[51] Family Smoking Prevention and Tobacco Control Act. 21 U.S.C. § 387j(c) (2011).
Tobacco Control Legal Consortium. (2016). *The FDA's premarket review of tobacco products fails to fully protect public health.* Saint Paul, MN: Public Health Law Center.
[52] Tobacco Control Legal Consortium. (2016). *The deeming regulation: FDA authority over e-cigarettes, cigars, and other tobacco products*. Saint Paul, MN: Public Health Law Center.
[53] U.S. Department of Health and Human Services. (2016). 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: Final rule. *Federal Register, 81*(90), 28974-29106.
[54] U.S. Department of Health and Human Services. (2016). 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: Final rule. *Federal Register, 81*(90), 28974-29106.

[55] Center for Tobacco Control Research and Education. (2016). *Tobacco product standard for N-nitrosonornicotine level in finished smokeless tobacco products [Docket No. FDA-2016-N-2527]*. Retrieved from http://tobacco.ucsf.edu.
[56] Tobacco Control Legal Consortium. (2014). *Preemption: The biggest challenge to tobacco control.* Retrieved from http://publichealthlawcenter.org.
[57] Americans for Nonsmokers' Rights. (2016). *The evolving face of preemption: New tactics to limit local control.* Retrieved from http://www.protectlocalcontrol.org.
Siegel, M., Carol, J., Jordan, J., Hobart, R., Schoenmarklin, S., DuMelle, F., et al. (1997). Preemption in tobacco control. Review of an emerging public health problem. *JAMA, 278*(10), 858-863.
[58] www.GovTrack.us. (2009). *H.R. 1256 - 111th Congress: Family Smoking Prevention and Tobacco Control Act.* Retrieved from https://www.govtrack.us.
Tobacco Control Legal Consortium. (2014). *Preemption: The biggest challenge to tobacco control.* Retrieved from http://publichealthlawcenter.org.
[59] Tobacco Control Legal Consortium. (2014). *Preemption: The biggest challenge to tobacco control.* Retrieved from http://publichealthlawcenter.org.
[60] Siegel, M., Carol, J., Jordan, J., Hobart, R., Schoenmarklin, S., DuMelle, F., et al. (1997). Preemption in tobacco control. Review of an emerging public health problem. *JAMA, 278*(10), 858-863.
Tobacco Control Legal Consortium. (2014). *Preemption: The biggest challenge to tobacco control.* Retrieved from http://publichealthlawcenter.org.
[61] Americans for Nonsmokers' Rights. (2016). *The evolving face of preemption: New tactics to limit local control.* Retrieved from http://www.protectlocalcontrol.org.
Siegel, M., Carol, J., Jordan, J., Hobart, R., Schoenmarklin, S., DuMelle, F., et al. (1997). Preemption in tobacco control. Review of an emerging public health problem. *JAMA, 278*(10), 858-863.
[62] Americans for Nonsmokers' Rights. (2016). *States with any type of preemption of smokefree air laws.* Retrieved from http://no-smoke.org.
Americans for Nonsmokers' Rights. (2016). *The evolving face of preemption: New tactics to limit local control.* Retrieved from http://www.protectlocalcontrol.org.
[63] Americans for Nonsmokers' Rights. (2016). *States with any type of preemption of smokefree air laws.* Retrieved from http://no-smoke.org.
[64] U.S. Department of Health and Human Services. (2014). *The health consequences of smoking-50 years of progress. A report of the Surgeon General* (January 2014. Printed with corrections). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[65] U.S. Department of Health and Human Services. (2014). *The health consequences of smoking-50 years of progress. A report of the Surgeon General* (January 2014. Printed with corrections). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
U.S. Department of Health, Education, and Welfare. (1986). *The health consequences of involuntary smoking: A report of the Surgeon General* (PHS Publication No. 1103). Washington, DC: U.S. Government Printing Office.
[66] National Research Council. (1986). *Environmental tobacco smoke: Measuring exposures and assessing health effects*. Washington, DC: The National Academies Press.
[67] U.S. Department of Health and Human Services. (2014). *The health consequences of smoking-50 years of progress. A report of the Surgeon General* (January 2014. Printed with corrections). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[68] U.S. Department of Health and Human Services. (2014). *The health consequences of smoking-50 years of progress. A report of the Surgeon General* (January 2014. Printed with corrections). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[69] U.S. Department of Health and Human Services. (2014). *The health consequences of smoking-50 years of progress. A report of the Surgeon General* (January 2014. Printed with corrections). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

[70] Federal Aviation Administration. (2013). *Pack safe: Electronic cigarettes, vaping devices.* Retrieved from https://www.faa.gov.
[71] Tynan, M., Babb, S., MacNeil, A., & Griffin, M. (2011). State smoke-free laws for worksites, restaurants, and bars - United States, 2000-2010. *Morbidity and Mortality Weekly Report, 60*(15), 472-475.
[72] Americans for Nonsmokers' Rights. (2016). *Overview list: How many smokefree laws?* Retrieved from http://www.no-smoke.org.
[73] Americans for Nonsmokers' Rights. (2016). *U.S. 100% smokefree laws in non-hospitality workplaces and restaurants and bars.* Retrieved from http://www.no-smoke.org.
[74] Americans for Nonsmokers' Rights. (2016). *States and municipalities with laws regulating use of electronic cigarettes.* Retrieved from http://www.no-smoke.org.
[75] Warner, K. E. (06). *Tobacco control policy*. San Francisco, CA: Jossey-Bass.
[76] Simmons, R. (2016). *Tobacco use: Prevention, cessation and policy.* Association for Prevention Teaching and Research. Retrieved from http://www.aptrweb.org.
[77] Iowa Department of Revenue. (2016). *History of tax legislation.* Retrieved from https://tax.iowa.gov.
[78] Emanual, L. (2014). *When did your state adopt its cigarette tax?* Retrieved from http://taxfoundation.org.
[79] Federation of Tax Administrators. (2016). *State excise tax rates on cigarettes.* Retrieved from http://www.taxadmin.org.
[80] Chaloupka, F. J., Warner, K. E., Acemoglu, D., Gruber, J., Laux, F., Max, W., et al. (2015). An evaluation of the FDA's analysis of the costs and benefits of the graphic warning label regulation. *Tobacco Control, 24*(2), 112-119.
[81] Campaign for Tobacco-Free Kids. (2016). *State excise tax rates for non-cigarette tobacco products.* Retrieved from http://www.tobaccofreekids.org.
[82] Campaign for Tobacco-Free Kids. (2016). *State excise tax rates for non-cigarette tobacco products.* Retrieved from http://www.tobaccofreekids.org.
[83] Drenkard, S. (2016). *Vapor products and tax policy.* Retrieved from http://taxfoundation.org.
Tobacco Control Legal Consortium. (2016). *U.S. e-cigarette regulation: A 50-state review.* Retrieved from http://publichealthlawcenter.org.
[84] Centers for Disease Control and Prevention. (2014). *Best practices for comprehensive tobacco control programs*: *Cessation interventions.* Retrieved from https://www.cdc.gov.
[85] Hawkins, S. S., Bach, N., & Baum, C. F. (2016). Impact of tobacco control policies on adolescent smoking. *Journal of Adolescent Health, 58*, 679-685.
[86] Chaloupka, F. J., Sweanor, D., & Warner, K. E. (2015). Differential taxes for differential risks: Toward reduced harm from nicotine-yielding products. *New England Journal of Medicine, 373*(7), 594-597.
Mainous, A. G., Tanner, R. J., Mainous, R. W., & Talbert, J. (2015). Health considerations in regulation and taxation of electronic cigarettes. *Journal of American Board of Family Medicine, 28*, 802-806.
Stoklosa, M., Drope, J., & Chaloupka, F. J. (2016). Prices and e-cigarette demand: Evidence from the European Union. *Nicotine and Tobacco Research, 18*(10), 1973-1980.
[87] Friedman, A. S. (2015). How does electronic cigarette access affect adolescent smoking? *Journal of Health Economics*, 44, 300-308.
Stoklosa, M., Drope, J., & Chaloupka, F. J. (2016). Prices and e-cigarette demand: Evidence from the European Union. *Nicotine and Tobacco Research, 18*(10), 1973-1980.
Huang, J., Tauras, J., & Chaloupka, F. J. (2014). The impact of price and tobacco control policies on the demand for electronic nicotine delivery systems. *Tobacco Control, 23*(Suppl 3), iii41-iii47.
Liber, A. C., Drope, J. M., & Stoklosa, M. (2016). Combustible cigarettes cost less to use than e-cigarettes: Global evidence and tax policy implications. *Tobacco Control*. doi:10.1136/tobaccocontrol-2015-052874.
[88] Mainous, A. G., Tanner, R. J., Mainous, R. W., & Talbert, J. (2015). Health considerations in regulation and taxation of electronic cigarettes. *Journal of American Board of Family Medicine, 28*, 802-806.
[89] www.GovTrack.us. (2009). *H.R. 1256 - 111th Congress: Family Smoking Prevention and Tobacco Control Act.* Retrieved from https://www.govtrack.us.
[90] Legislative Counsel of California. (2016). *An act to amend sections 17537.3, 22951, 22952, 22956, 22958, and 22963 of, and to add Section 22964 to, the Business and Professions Code, and to amend Section 308 of the Penal Code, relating to tobacco* . Retrieved from http://leginfo.legislature.ca.gov.
Tobacco Control Legal Consortium. (2016). *U.S. e-cigarette regulation: A 50-state review.* Retrieved from http://publichealthlawcenter.org.

[91] Campaign for Tobacco-Free Kids. (2016). *States and localities that have raised the minimum legal sale age for tobacco products to 21.* Retrieved from http://www.tobaccofreekids.org.
[92] Tobacco Control Legal Consortium. (2016). *U.S. e-cigarette regulation: A 50-state review.* Retrieved from http://publichealthlawcenter.org.
[93] Tobacco Control Legal Consortium. (2016). *U.S. e-cigarette regulation: A 50-state review.* Retrieved from http://publichealthlawcenter.org.
[94] Centers for Disease Control and Prevention. (2014). *Best practices for comprehensive tobacco control programs*: *Cessation interventions.* Retrieved from https://www.cdc.gov.
[95] 111th Cong. (2010). *Compilation of Patient Protection and Affordable Care Act.* Retrieved from http://housedocs.house.gov.
Kofman, M., Dunton, K., & Senkewicz, M. B. (2012). *Implementation of tobacco cessation coverage under the Affordable Care Act: Understanding how private health insurance policies cover tobacco cessation treatments*. Washington, DC: Georgetown University.
[96] Centers for Disease Control and Prevention. (2014). Centers for Disease Control and Prevention. (2014). *Best practices for comprehensive tobacco control programs*: *Cessation interventions.* Retrieved from https://www.cdc.gov.
[97] Essential health benefits package. 42 U.S.C. § 300gg-6(a) (2010). Establishment of qualified health plans. Essential health benefits requirement. 42 U.S.C. § 18022 (2010).
[98] Siu, A. L. (2015). Behavioral and pharmacotherapy interventions for tobacco smoking cessation in adults, including pregnant women: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*, *163*(8), 622-634.
U.S. Preventive Services Task Force. (2015). *Behavioral and pharmacotherapy interventions for tobacco smoking cessation in adults, including pregnant women: Clinical summary.* Retrieved from http://annals.org.
[99] Tobacco Control Legal Consortium. (2014). *How the Affordable Care Act affects tobacco use and control.* Retrieved from http://publichealthlawcenter.org.
[100] HealthyAmericans.org. (2015). *The prevention and public health fund: Preventing chronic disease and reducing long-term health costs.* Retrieved from http://healthyamericans.org.
[101] National Prevention Council. (2011). *National prevention strategy: America's plan for better health and wellness*. Washington, DC: U.S. Department of Health and Human Services, Office of the Surgeon General.
[102] Centers for Medicare & Medicaid Services. (2016). *Medicaid incentives for the prevention of chronic diseases model.* Retrieved from https://innovation.cms.gov.
[103] National Conference of State Legislatures. (2010). *Summary of the health workforce provisions in the Patient Protection and Affordable Care Act: H.R. 3590*. Washington, DC: Author.
[104] Keith, K., & Lucia, K. W. (2014). *Implementing the Affordable Care Act: The state of the states.* Washington, DC: The Commonwealth Fund.
[105] The National Center on Addiction and Substance Abuse. (2016). *Uncovering coverage gaps: A review of addiction benefits in ACA plans*. New York: Author.
[106] U.S. Department of Labor. (2014). *FAQS about Affordable Care Act implementation (Part XIX).* Retrieved from https://www.dol.gov.
[107] Health Care and Education Reconciliation Act of 2010, Pub. L. No. 111-152, 124 Stat. 1029 (2010) (codified as amended at 42 U.S.C. § 1305 (2010)).
Patient Protection and Affordable Care Act, Pub. L. No. 111-148, 124 Stat. 119 (2010) (codified as amended at 42 U.S.C. §§ 18001–18121 (2010)).
Prohibiting discriminatory premium rates. 42 U.S.C. § 300gg(a)(1) (2010).
Tobacco Control Legal Consortium. (2014). *How the Affordable Care Act affects tobacco use and control.* Retrieved from http://publichealthlawcenter.org.
[108] U.S. Food and Drug Administration. (2016). *Family Smoking Prevention and Tobacco Control Act: 21 CFR parts 1100, 1140, and 1143.* Retrieved from http://federalregister.gov.
[109] Tobacco Control Legal Consortium. (2014). *How the Affordable Care Act affects tobacco use and control.* Retrieved from http://publichealthlawcenter.org.
[110] Friedman, A. S., Schpero, W. L., & Busch, S. H. (2016). Evidence suggests that the aca's tobacco surcharges reduced insurance take-up and did not increase smoking cessation. *Health Affairs*, *35*(7), 1176-1183.
[111] Fair health insurance premiums 45 C.F.R. § 147.102 (a)(i), (iv) (2016)).

[112] Centers for Medicare & Medicaid Services. (2016). *The Center For Consumer Information and Insurance Oversight: Market rating reforms: State specific rating variations.* Retrieved from www.cms.gov.
Kansas Health Institute. (2015). *States vary on higher premiums paid by tobacco users under the ACA: Kansas insurers applying up to 44 percent surcharge for tobacco users in 2015*. Retrieved from http://www.khi.org.

Chapter V
Notes

[1] U.S. Department of Health and Human Services. (2014). *The health consequences of smoking-50 years of progress. A report of the Surgeon General* (January 2014. Printed with corrections). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

[2] Cooper, M., Harrell, M. B., Perez, A., Delk, J., & Perry, C. L. (2016). Flavorings and perceived harm and addictiveness of e-cigarettes among youth. *Tobacco Regulatory Science, 2*(3), 278-289.

Pearson, J. L., Stanton, C. A., Cha, S., Niaura, R. S., Luta, G., & Graham, A. L. (2015). E-cigarettes and smoking cessation: Insights and cautions from a secondary analysis of data from a study of online treatment-seeking smokers. *Nicotine and Tobacco Research, 17*(10), 1219-1227.

Popova, L., & Ling, P. M. (2013). Perceptions of relative risk of snus and cigarettes among U.S. smokers. *American Journal of Public Health, 103*(11), e21-e23.

Richardson, A., Pearson, J., Xiao, H., Stalgaitis, C., & Vallone, D. (2014). Prevalence, harm perceptions, and reasons for using noncombustible tobacco products among current and former smokers. *American Journal of Public Health, 104*(8), 1437-1444.

Wagoner, K. G., Cornacchione, J., Wiseman, K. D., Teal, R., Moracco, K. E., & Sutfin, E. L. (2016). E-cigarettes, hookah pens and vapes: Adolescent and young adult perceptions of electronic nicotine delivery systems. *Nicotine and Tobacco Research, 18*(10), 2006-2012.

[3] U.S. Department of Health and Human Services. (2014). *The health consequences of smoking-50 years of progress. A report of the Surgeon General* (January 2014. Printed with corrections). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

[4] Carroll Chapman, S. L., & Wu, L. T. (2014). E-cigarette prevalence and correlates of use among adolescents versus adults: A review and comparison. *Journal of Psychiatric Research, 54*, 43-54.

Payne, J. D., Orellana-Barrios, M., Medrano-Juarez, R., Buscemi, D., & Nugent, K. (2016). Electronic cigarettes in the media. *Proceedings (Baylor University Medical Center), 29*(3), 280-283.

[5] Amrock, S. M., Lee, L., & Weitzman, M. (2016). Perceptions of e-cigarettes and noncigarette tobacco products among U.S. youth. *Pediatrics, 138*(5), 1-10.

Ambrose, B. K., Rostron, B. L., Johnson, S. E., Portnoy, D. B., Apelberg, B. J., Kaufman, A. R., et al. (2014). Perceptions of the relative harm of cigarettes and e-cigarettes among U.S. youth. *American Journal of Preventive Medicine, 47*(Suppl 1), S53-S60.

Cohn, A., Cobb, C. O., Niaura, R. S., & Richardson, A. (2015). The other combustible products: Prevalence and correlates of little cigar/cigarillo use among cigarette smokers. *Nicotine and Tobacco Research, 17*(12), 1473-1481.

Coleman, B. N., Johnson, S. E., Tessman, G. K., Tworek, C., Alexander, J., Dickinson, D. M., et al. (2016). "It's not smoke. It's not tar. It's not 4000 chemicals. Case closed": Exploring attitudes, beliefs, and perceived social norms of e-cigarette use among adult users. *Drug and Alcohol Dependence, 159*, 80-85.

Cooper, M., Harrell, M. B., Perez, A., Delk, J., & Perry, C. L. (2016). Flavorings and perceived harm and addictiveness of e-cigarettes among youth. *Tobacco Regulatory Science, 2*(3), 278-289.

Harrell, P. T., Marquinez, N. S., Correa, J. B., Meltzer, L. R., Unrod, M., Sutton, S. K., et al. (2015). Expectancies for cigarettes, e-cigarettes, and nicotine replacement therapies among e-cigarette users ("Vapers"). *Nicotine and Tobacco Research, 17*(2), 193-200.

Heinz, A. J., Giedgowd, G. E., Crane, N. A., Veilleux, J. C., Conrad, M., Braun, A. R., et al. (2013). A comprehensive examination of hookah smoking in college students: Use patterns and contexts, social norms and attitudes, harm perception, psychological correlates and co-occurring substance use. *Addictive Behaviors, 38*(11), 2751-2760.

Martinasek, M. P., Gibson-Young, L., & Forrest, J. (2014). Hookah smoking and harm perception among asthmatic adolescents: findings from the Florida youth tobacco survey. *Journal of School Health, 84*(5), 334-341.

Richardson, A., Pearson, J., Xiao, H., Stalgaitis, C., & Vallone, D. (2014). Prevalence, harm perceptions, and reasons for using noncombustible tobacco products among current and former smokers. *American Journal of Public Health, 104*(8), 1437-1444.

Roditis, M., Delucchi, K., Cash, D., & Halpern-Felsher, B. (2016). Adolescents' perceptions of health risks, social risks, and benefits differ across tobacco products. *Journal of Adolescent Health, 58*(5), 558-566.

Smith, S. Y., Curbow, B., & Stillman, F. A. (2007). Harm perception of nicotine products in college freshmen. *Nicotine and Tobacco Research, 9*(9), 977-982.
Wagoner, K. G., Cornacchione, J., Wiseman, K. D., Teal, R., Moracco, K. E., & Sutfin, E. L. (2016). E-cigarettes, hookah pens and vapes: Adolescent and young adult perceptions of electronic nicotine delivery systems. *Nicotine and Tobacco Research, 18*(10), 2006-2012.
[6] Coleman, B. N., Johnson, S. E., Tessman, G. K., Tworek, C., Alexander, J., Dickinson, D. M., et al. (2016). "It's not smoke. It's not tar. It's not 4000 chemicals. Case closed": Exploring attitudes, beliefs, and perceived social norms of e-cigarette use among adult users. *Drug and Alcohol Dependence, 159*, 80-85.
Heinz, A. J., Giedgowd, G. E., Crane, N. A., Veilleux, J. C., Conrad, M., Braun, A. R., et al. (2013). A comprehensive examination of hookah smoking in college students: Use patterns and contexts, social norms and attitudes, harm perception, psychological correlates and co-occurring substance use. *Addictive Behaviors, 38*(11), 2751-2760.
Milam, A. J., Bone, L. R., Byron, M. J., Hoke, K., Williams, C. D., Furr-Holden, C. D., et al. (2013). Cigarillo use among high-risk urban young adults. *Journal of Health Care for the Poor and Underserved, 24*(4), 1657-1665.
Nuzzo, E., Shensa, A., Kim, K. H., Fine, M. J., Barnett, T. E., Cook, R., et al. (2013). Associations between hookah tobacco smoking knowledge and hookah smoking behavior among U.S. college students. *Health Education Research, 28*(1), 92-100.
Rezk-Hanna, M., Macabasco-O'Connell, A., & Woo, M. (2014). Hookah smoking among young adults in southern California. *Nursing Research, 63*(4), 300-306.
Sanders-Jackson, A. N., Tan, A. S., Bigman, C. A., & Henriksen, L. (2015). Knowledge about e-cigarette constituents and regulation: Results from a national survey of U.S. young adults. *Nicotine and Tobacco Research, 17*(10), 1247-1254.
Wray, R. J., Jupka, K., Berman, S., Zellin, S., & Vijaykumar, S. (2012). Young adults' perceptions about established and emerging tobacco products: Results from eight focus groups. *Nicotine and Tobacco Research, 14*(2), 184-190.
[7] Akl, E. A., Jawad, M., Lam, W. Y., Co, C. N., Obeid, R., & Irani, J. (2013). Motives, beliefs and attitudes towards waterpipe tobacco smoking: A systematic review. *Harm Reduction Journal, 10*, 12.
Aljarrah, K., Ababneh, Z. Q., & Al-Delaimy, W. K. (2009). Perceptions of hookah smoking harmfulness: Predictors and characteristics among current hookah users. *Tobacco Induced Diseases, 5*(1), 16.
Amrock, S. M., Lee, L., & Weitzman, M. (2016). Perceptions of e-cigarettes and noncigarette tobacco products among U.S. youth. *Pediatrics, 138*(5), 1-10.
Berg, C. J., Stratton, E., Schauer, G. L., Lewis, M., Wang, Y., Windle, M., et al. (2015). Perceived harm, addictiveness, and social acceptability of tobacco products and marijuana among young adults: Marijuana, hookah, and electronic cigarettes win. *Substance Use and Misuse, 50*(1), 79-89.
Cohn, A., Cobb, C. O., Niaura, R. S., & Richardson, A. (2015). The other combustible products: Prevalence and correlates of little cigar/cigarillo use among cigarette smokers. *Nicotine and Tobacco Research, 17*(12), 1473-1481.
Gorukanti, A., Delucchi, K., Ling, P., Fisher-Travis, R., & Halpern-Felsher, B. (2017). Adolescents' attitudes towards e-cigarette ingredients, safety, addictive properties, social norms, and regulation. *Preventive Medicine, 94*, 65-71.
Heinz, A. J., Giedgowd, G. E., Crane, N. A., Veilleux, J. C., Conrad, M., Braun, A. R., et al. (2013). A comprehensive examination of hookah smoking in college students: Use patterns and contexts, social norms and attitudes, harm perception, psychological correlates and co-occurring substance use. *Addictive Behaviors, 38*(11), 2751-2760.
Martinasek, M. P., Gibson-Young, L., & Forrest, J. (2014). Hookah smoking and harm perception among asthmatic adolescents: Findings from the Florida youth tobacco survey. *Journal of School Health, 84*(5), 334-341.
Rezk-Hanna, M., Macabasco-O'Connell, A., & Woo, M. (2014). Hookah smoking among young adults in southern California. *Nursing Research, 63*(4), 300-306.
Richardson, A., Pearson, J., Xiao, H., Stalgaitis, C., & Vallone, D. (2014). Prevalence, harm perceptions, and reasons for using noncombustible tobacco products among current and former smokers. *American Journal of Public Health, 104*(8), 1437-1444.
Roditis, M., Delucchi, K., Cash, D., & Halpern-Felsher, B. (2016). Adolescents' perceptions of health risks, social risks, and benefits differ across tobacco products. *Journal of Adolescent Health, 58*(5), 558-566.
Saddleson, M. L., Kozlowski, L. T., Giovino, G. A., Hawk, L. W., Murphy, J. M., MacLean, M. G., et al. (2015). Risky behaviors, e-cigarette use and susceptibility of use among college students. *Drug and Alcohol Dependence, 149*, 25-30.
Truth Initiative. (2015). *Hookah: Background.* Retrieved from http://truthinitiative.org.

Villanti, A. C., Cobb, C. O., Cohn, A. M., Williams, V. F., & Rath, J. M. (2015). Correlates of hookah use and predictors of hookah trial in U.S. young adults. *American Journal of Preventive Medicine, 48*(6), 742-746.
Wackowski, O. A., & Delnevo, C. D. (2016). Young adults' risk perceptions of various tobacco products relative to cigarettes: Results from the National Young Adult Health Survey. *Health Education and Behavior, 43*(3), 328-336.
[8] Rezk-Hanna, M., Macabasco-O'Connell, A., & Woo, M. (2014). Hookah smoking among young adults in southern California. *Nursing Research, 63*(4), 300-306.
[9] Berg, C. J., Stratton, E., Schauer, G. L., Lewis, M., Wang, Y., Windle, M., et al. (2015). Perceived harm, addictiveness, and social acceptability of tobacco products and marijuana among young adults: Marijuana, hookah, and electronic cigarettes win. *Substance Use and Misuse, 50*(1), 79-89.
Primack, B. A., Sidana, J., Shadel, W. G., & Eissenberg, T. E. (2008). Prevalence of and associations with waterpipe tobacco smoking among U.S. university students. *Annals of Behavioral Medicine, 36*, 81-82.
[10] Al, A. R., Rastam, S., Ibrahim, I., Bazzi, A., Fayad, S., Shihadeh, A. L., et al. (2015). A comparative study of systemic carcinogen exposure in waterpipe smokers, cigarette smokers and non-smokers. *Tobacco Control, 24*(2), 125-127.
Al-Kazwini, A. T., Said, A. J., & Sdepanian, S. (2015). Compartmental analysis of metals in waterpipe smoking technique. *BMC Public Health, 15*, 153.
Al, R. M., Shihadeh, A., & Saliba, N. A. (2008). Volatile aldehydes in the mainstream smoke of the narghile waterpipe. *Food and Chemical Toxicology, 46*(11), 3546-3549.
Daher, N., Saleh, R., Jaroudi, E., Sheheitli, H., Badr, T., Sepetdjian, E., et al. (2010). Comparison of carcinogen, carbon monoxide, and ultrafine particle emissions from narghile waterpipe and cigarette smoking: Sidestream smoke measurements and assessment of second-hand smoke emission factors. *Atmospheric Environment (1994), 44*(1), 8-14.
Hammal, F., Chappell, A., Wild, T. C., Kindzierski, W., Shihadeh, A., Vanderhoek, A., et al. (2015). 'Herbal' but potentially hazardous: An analysis of the constituents and smoke emissions of tobacco-free waterpipe products and the air quality in the cafes where they are served. *Tobacco Control, 24*(3), 290-297.
Kadhum, M., Sweidan, A., Jaffery, A. E., Al-Saadi, A., & Madden, B. (2015). A review of the health effects of smoking shisha. *Clinical Medicine, 15*(3), 263-266.
Kumar, S. R., Davies, S., Weitzman, M., & Sherman, S. (2015). A review of air quality, biological indicators and health effects of second-hand waterpipe smoke exposure. *Tobacco Control, 24* (Suppl 1), i54-i59.
Monzer, B., Sepetdjian, E., Saliba, N., & Shihadeh, A. (2008). Charcoal emissions as a source of CO and carcinogenic PAH in mainstream narghile waterpipe smoke. *Food and Chemical Toxicology, 46*(9), 2991-2995.
Primack, B. A., Carroll, M. V., Weiss, P. M., Shihadeh, A. L., Shensa, A., Farley, S. T., et al. (2016). Systematic review and meta-analysis of inhaled toxicants from waterpipe and cigarette smoking. *Public Health Reports, 131*(1), 76-85.
Sepetdjian, E., Abdul, H. R., Salman, R., Jaroudi, E., Shihadeh, A., & Saliba, N. A. (2013). Phenolic compounds in particles of mainstream waterpipe smoke. *Nicotine and Tobacco Research, 15*(6), 1107-1112.
Sepetdjian, E., Saliba, N., & Shihadeh, A. (2010). Carcinogenic PAH in waterpipe charcoal products. *Food and Chemical Toxicology, 48*(11), 3242-3245.
Shihadeh, A. (2003). Investigation of mainstream smoke aerosol of the argileh water pipe. *Food and Chemical Toxicology, 41*(1), 143-152.
Shihadeh, A., Eissenberg, T., Rammah, M., Salman, R., Jaroudi, E., & El-Sabban, M. (2014). Comparison of tobacco-containing and tobacco-free waterpipe products: Effects on human alveolar cells. *Nicotine and Tobacco Research, 16*(4), 496-499.
Shihadeh, A., Salman, R., Jaroudi, E., Saliba, N., Sepetdjian, E., Blank, M. D., et al. (2012). Does switching to a tobacco-free waterpipe product reduce toxicant intake? A crossover study comparing CO, NO, PAH, volatile aldehydes, "tar" and nicotine yields. *Food and Chemical Toxicology, 50*(5), 1494-1498.
Shihadeh, A., Schubert, J., Klaiany, J., El, S. M., Luch, A., & Saliba, N. A. (2015). Toxicant content, physical properties and biological activity of waterpipe tobacco smoke and its tobacco-free alternatives. *Tobacco Control, 24* (Suppl 1), i22-i30.
St. Helen G., Benowitz, N. L., Dains, K. M., Havel, C., Peng, M., & Jacob, P. (2014). Nicotine and carcinogen exposure after water pipe smoking in hookah bars. *Cancer Epidemiology, Biomarkers and Prevention, 23*(6), 1055-1066.
Zhou, S., Weitzman, M., Vilcassim, R., Wilson, J., Legrand, N., Saunders, E., et al. (2014). Air quality in New York City hookah bars. *Tobacco Control, 24*(e3), e193-e198. doi:10.1136/tobaccocontrol-2014-051763.

[11] Gorukanti, A., Delucchi, K., Ling, P., Fisher-Travis, R., & Halpern-Felsher, B. (2017). Adolescents' attitudes towards e-cigarette ingredients, safety, addictive properties, social norms, and regulation. *Preventive Medicine, 94*, 65-71.
[12] Johnston, L. D., Miech, R. A., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E. (2016). *Teen use of any illicit drug other than marijuana at new low, same true for alcohol: Data tables.* Retrieved from http://monitoringthefuture.org.
[13] Berg, C. J., Haardoerfer, R., Escoffery, C., Zheng, P., & Kegler, M. (2014). Cigarette users' interest in using or switching to electronic nicotine delivery systems or smokeless tobacco for harm reduction, cessation, or novelty: A cross-sectional survey of U.S. adults. *Nicotine and Tobacco Research,17*(2), 245-55.
Biener, L., & Hargraves, J. L. (2015). A longitudinal study of electronic cigarette use among a population-based sample of adult smokers: Association with smoking cessation and motivation to quit. *Nicotine and Tobacco Research, 17*(2), 127-133.
Cohn, A., Cobb, C. O., Niaura, R. S., & Richardson, A. (2015). The other combustible products: Prevalence and correlates of little cigar/cigarillo use among cigarette smokers. *Nicotine and Tobacco Research, 17*(12), 1473-1481.
Coleman, B. N., Johnson, S. E., Tessman, G. K., Tworek, C., Alexander, J., Dickinson, D. M., et al. (2016). "It's not smoke. It's not tar. It's not 4000 chemicals. Case closed": Exploring attitudes, beliefs, and perceived social norms of e-cigarette use among adult users. *Drug and Alcohol Dependence, 159*, 80-85.
Kim, H., Davis, A. H., Dohack, J. L., & Clark, P. I. (2017). E-cigarettes use behavior and experience of adults: Qualitative research findings to inform e-cigarette use measure development. *Nicotine and Tobacco Research, 19*(2), 190-196.
Patel, D., Davis, K. C., Cox, S., Bradfield, B., King, B. A., Shafer, P., et al. (2016). Reasons for current e-cigarette use among U.S. adults. *Preventive Medicine, 93*, 14-20.
Popova, L., & Ling, P. M. (2013). Alternative tobacco product use and smoking cessation: A national study. *American Journal of Public Health, 103*(5), 923-930.
Rass, O., Pacek, L. R., Johnson, P. S., & Johnson, M. W. (2015). Characterizing use patterns and perceptions of relative harm in dual users of electronic and tobacco cigarettes. *Experimental and Clinical Psychopharmacology, 23*(6), 494-503.
[14] Berg, C. J., Haardoerfer, R., Escoffery, C., Zheng, P., & Kegler, M. (2014). Cigarette users' interest in using or switching to electronic nicotine delivery systems or smokeless tobacco for harm reduction, cessation, or novelty: A cross-sectional survey of U.S. adults. *Nicotine and Tobacco Research,17*(2), 245-55.
Biener, L., & Hargraves, J. L. (2015). A longitudinal study of electronic cigarette use among a population-based sample of adult smokers: Association with smoking cessation and motivation to quit. *Nicotine and Tobacco Research, 17*(2), 127-133.
Biener, L., Song, E., Sutfin, E. L., Spangler, J., & Wolfson, M. (2015). Electronic cigarette trial and use among young adults: Reasons for trial and cessation of vaping. *International Journal of Environmental Research and Public Health, 12*(12), 16019-16026.
Carroll Chapman, S. L., & Wu, L. T. (2014). E-cigarette prevalence and correlates of use among adolescents versus adults: A review and comparison. *Journal of Psychiatric Research, 54*, 43-54.
Jolly, D. H. (2008). Exploring the use of little cigars by students at a historically black university. *Preventing Chronic Disease, 5*(3), A82.
Rass, O., Pacek, L. R., Johnson, P. S., & Johnson, M. W. (2015). Characterizing use patterns and perceptions of relative harm in dual users of electronic and tobacco cigarettes. *Experimental and Clinical Psychopharmacology, 23*(6), 494-503.
Richardson, A., Pearson, J., Xiao, H., Stalgaitis, C., & Vallone, D. (2014). Prevalence, harm perceptions, and reasons for using noncombustible tobacco products among current and former smokers. *American Journal of Public Health, 104*(8), 1437-1444.
Rutten, L. J., Blake, K. D., Agunwamba, A. A., Grana, R. A., Wilson, P. M., Ebbert, J. O., et al. (2015). Use of e-cigarettes among current smokers: Associations among reasons for use, quit intentions, and current tobacco use. *Nicotine and Tobacco Research, 17*(10), 1228-1234.
Wackowski, O. A., Bover Manderski, M. T., Delnevo, C. D., Giovenco, D. P., & Lewis, M. J. (2016). Smokers' early e-cigarette experiences, reasons for use, and use intentions. *Tobacco Regulatory Science, 2*(2), 133-145.
[15] Choi, K., Fabian, L., Mottey, N., Corbett, A., & Forster, J. (2012). Young adults' favorable perceptions of snus, dissolvable tobacco products, and electronic cigarettes: Findings from a focus group study. *American Journal of Public Health, 102*(11), 2088-2093.

Coleman, B. N., Johnson, S. E., Tessman, G. K., Tworek, C., Alexander, J., Dickinson, D. M., et al. (2016). "It's not smoke. It's not tar. It's not 4000 chemicals. Case closed": Exploring attitudes, beliefs, and perceived social norms of e-cigarette use among adult users. *Drug and Alcohol Dependence, 159*, 80-85.
Cornacchione, J., Wagoner, K. G., Wiseman, K. D., Kelley, D., Noar, S. M., Smith, M. H., et al. (2016). Adolescent and young adult perceptions of hookah and little cigars/cigarillos: Implications for risk messages. *Journal of Health Communication, 21*(7), 818-825.
Kim, H., Davis, A. H., Dohack, J. L., & Clark, P. I. (2016). E-cigarettes use behavior and experience of adults: Qualitative research findings to inform e-cigarette use measure development. *Nicotine and Tobacco Research, 19*(2), 190-196.
Kong, G., Morean, M. E., Cavallo, D. A., Camenga, D. R., & Krishnan-Sarin, S. (2015). Reasons for electronic cigarette experimentation and discontinuation among adolescents and young adults. *Nicotine and Tobacco Research, 17*(7), 847-854.
Nyman, A. L., Sterling, K. L., Weaver, S. R., Majeed, B. A., & Eriksen, M. P. (2016). Little cigars and cigarillos: Users, perceptions, and reasons for use. *Tobacco Regulatory Science, 2*(3), 239-251.
Patel, D., Davis, K. C., Cox, S., Bradfield, B., King, B. A., Shafer, P., et al. (2016). Reasons for current e-cigarette use among U.S. adults. *Preventive Medicine, 93*, 14-20.
[16] Bahreinifar, S., Sheon, N. M., & Ling, P. M. (2013). Is snus the same as dip? Smokers' perceptions of new smokeless tobacco advertising. *Tobacco Control, 22*(2), 84-90.
Choi, K., Fabian, L., Mottey, N., Corbett, A., & Forster, J. (2012). Young adults' favorable perceptions of snus, dissolvable tobacco products, and electronic cigarettes: Findings from a focus group study. *American Journal of Public Health, 102*(11), 2088-2093.
Coleman, B. N., Johnson, S. E., Tessman, G. K., Tworek, C., Alexander, J., Dickinson, D. M., et al. (2016). "It's not smoke. It's not tar. It's not 4000 chemicals. Case closed": Exploring attitudes, beliefs, and perceived social norms of e-cigarette use among adult users. *Drug and Alcohol Dependence, 159*, 80-85.
Kim, H., Davis, A. H., Dohack, J. L., & Clark, P. I. (2016). E-cigarettes use behavior and experience of adults: Qualitative research findings to inform e-cigarette use measure development. *Nicotine and Tobacco Research, 19*(2), 190-196.
Liu, S. T., Nemeth, J. M., Klein, E. G., Ferketich, A. K., Kwan, M. P., & Wewers, M. E. (2014). Adolescent and adult perceptions of traditional and novel smokeless tobacco products and packaging in rural Ohio. *Tobacco Control, 23*(3), 209-214.
Richardson, A., Pearson, J., Xiao, H., Stalgaitis, C., & Vallone, D. (2014). Prevalence, harm perceptions, and reasons for using noncombustible tobacco products among current and former smokers. *American Journal of Public Health, 104*(8), 1437-1444.
[17] Akl, E. A., Jawad, M., Lam, W. Y., Co, C. N., Obeid, R., & Irani, J. (2013). Motives, beliefs and attitudes towards waterpipe tobacco smoking: a systematic review. *Harm Reduction Journal, 10*, 12.
Akl, E. A., Ward, K. D., Bteddini, D., Khaliel, R., Alexander, A. C., Lotfi, T., et al. (2015). The allure of the waterpipe: a narrative review of factors affecting the epidemic rise in waterpipe smoking among young persons globally. *Tobacco Control, 24* (Suppl 1), i13-i21.
Barnett, T. E., Smith, T., He, Y., Soule, E. K., Curbow, B. A., Tomar, S. L., et al. (2013). Evidence of emerging hookah use among university students: a cross-sectional comparison between hookah and cigarette use. *BMC Public Health, 13*, 302. doi:1471-2458-13-302.
Braun, R. E., Glassman, T., Wohlwend, J., Whewell, A., & Reindl, D. M. (2012). Hookah use among college students from a Midwest University. *Journal of Community Health, 37*(2), 294-298.
Cornacchione, J., Wagoner, K. G., Wiseman, K. D., Kelley, D., Noar, S. M., Smith, M. H., et al. (2016). Adolescent and young adult perceptions of hookah and little cigars/cigarillos: Implications for risk messages. *Journal of Health Communication, 21*(7), 818-825.
Heinz, A. J., Giedgowd, G. E., Crane, N. A., Veilleux, J. C., Conrad, M., Braun, A. R., et al. (2013). A comprehensive examination of hookah smoking in college students: Use patterns and contexts, social norms and attitudes, harm perception, psychological correlates and co-occurring substance use. *Addictive Behaviors, 38*(11), 2751-2760.
Jolly, D. H. (2008). Exploring the use of little cigars by students at a historically black university. *Preventing Chronic Disease, 5*(3), A82.
Rezk-Hanna, M., Macabasco-O'Connell, A., & Woo, M. (2014). Hookah smoking among young adults in southern California. *Nursing Research, 63*(4), 300-306.

Sharma, E., Clark, P. I., & Sharp, K. E. (2014). Understanding psychosocial aspects of waterpipe smoking among college students. *American Journal of Health Behavior, 38*(3), 440-447.
[18] Biener, L., Song, E., Sutfin, E. L., Spangler, J., & Wolfson, M. (2015). Electronic cigarette trial and use among young adults: Reasons for trial and cessation of vaping. *International Journal of Environmental Research and Public Health, 12*(12), 16019-16026.
Pepper, J. K., Ribisl, K. M., Emery, S. L., & Brewer, N. T. (2014). Reasons for starting and stopping electronic cigarette use. *International Journal of Environmental Research and Public Health, 11*(10), 10345-10361.
[19] Berg, C. J., Haardoerfer, R., Escoffery, C., Zheng, P., & Kegler, M. (2014). Cigarette users' interest in using or switching to electronic nicotine delivery systems or smokeless tobacco for harm reduction, cessation, or novelty: A cross-sectional survey of U.S. adults. *Nicotine and Tobacco Research,17*(2), 245-55.
Biener, L., & Hargraves, J. L. (2015). A longitudinal study of electronic cigarette use among a population-based sample of adult smokers: Association with smoking cessation and motivation to quit. *Nicotine and Tobacco Research, 17*(2), 127-133.
Patel, D., Davis, K. C., Cox, S., Bradfield, B., King, B. A., Shafer, P., et al. (2016). Reasons for current e-cigarette use among U.S. adults. *Preventive Medicine, 93*, 14-20.
Pokhrel, P., Herzog, T. A., Muranaka, N., & Fagan, P. (2015). Young adult e-cigarette users' reasons for liking and not liking e-cigarettes: A qualitative study. *Psychology and Health, 30*(12), 1450-1469.
Rass, O., Pacek, L. R., Johnson, P. S., & Johnson, M. W. (2015). Characterizing use patterns and perceptions of relative harm in dual users of electronic and tobacco cigarettes. *Experimental and Clinical Psychopharmacology, 23*(6), 494-503.
[20] Kong, G., Morean, M. E., Cavallo, D. A., Camenga, D. R., & Krishnan-Sarin, S. (2015). Reasons for electronic cigarette experimentation and discontinuation among adolescents and young adults. *Nicotine and Tobacco Research, 17*(7), 847-854.
Wagoner, K. G., Cornacchione, J., Wiseman, K. D., Teal, R., Moracco, K. E., & Sutfin, E. L. (2016). E-cigarettes, hookah pens and vapes: Adolescent and young adult perceptions of electronic nicotine delivery systems. *Nicotine and Tobacco Research, 18*(10), 2006-2012.
[21] Coleman, B. N., Johnson, S. E., Tessman, G. K., Tworek, C., Alexander, J., Dickinson, D. M., et al. (2016). "It's not smoke. It's not tar. It's not 4000 chemicals. Case closed": Exploring attitudes, beliefs, and perceived social norms of e-cigarette use among adult users. *Drug and Alcohol Dependence, 159*, 80-85.
Saddleson, M. L., Kozlowski, L. T., Giovino, G. A., Goniewicz, M. L., Mahoney, M. C., Homish, G. G., et al. (2016). Enjoyment and other reasons for electronic cigarette use: Results from college students in New York. *Addictive Behaviors, 54*, 33-39.
[22] Benowitz, N. L. (2010). Nicotine addiction. *New England Journal of Medicine, 362*(24), 2295-2303.
Caraballo, R. S., Novak, S. P., & Asman, K. (2009). Linking quantity and frequency profiles of cigarette smoking to the presence of nicotine dependence symptoms among adolescent smokers: Findings from the 2004 National Youth Tobacco Survey. *Nicotine and Tobacco Research, 11*(1), 49-57.
National Institute on Drug Abuse. (2012). *Research report series: Tobacco addiction* (NIH Pub No. 12-4342). Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Institute on Drug Abuse.
U.S. Department of Health and Human Services. (2010). *How tobacco smoke causes disease: The biology and behavioral basis for smoking-attributable disease: A report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
Zhu, A. Z. X. & Tyndale, R. F. (2012). Nicotine metabolism and its implications. In P. Anzenbacher & U. M. Zanger (Eds.), *Metabolism of drugs and other xenobiotics*. Weinheim, Germany: Wiley-VCH Verlag GmbH & Co. KGaA.
[23] Koob, G. F., & Volkow, N. D. (2010). Neurocircuitry of addiction. *Neuropsychopharmacology, 35*(1), 217-238.
[24] Siqueira, L. M. (2016). Nicotine and tobacco as substances of abuse in children and adolescents. *American Academy of Pediatrics, 139*(1). doi:10.1542/peds.2016-3436.
Schroeder, S. A., & Morris, C. D. (2010). Confronting a neglected epidemic: Tobacco cessation for persons with mental illnesses and substance abuse problems. *Annual Review of Public Health, 31*, 297-314.
The National Center on Addiction and Substance Abuse. (2015). *Understanding and addressing nicotine addiction: A science-based approach to policy and practice*. New York: Author.

[25] National Institute on Drug Abuse. (2016). *Research report series: Tobacco/nicotine* (NIH Pub No. 16-4342). Bethesda, MD: U.S. Department of Healtha nd Human Services, National Institutes of Health, National Institute on Drug Abuse.
[26] DiFranza, J. R., Rigotti, N. A., McNeill, A. D., Ockene, J. K., Savageau, J. A., St, C. D., et al. (2000). Initial symptoms of nicotine dependence in adolescents. *Tobacco Control, 9*(3), 313-319.
Dierker, L., Swendsen, J., Rose, J., He, J., & Merikangas, K. (2012). Transitions to regular smoking and nicotine dependence in the Adolescent National Comorbidity Survey (NCS-A). *Annals of Behavioral Medicine, 43*(3), 394-401.
DiFranza, J. R. (2015). A 2015 update on the natural history and diagnosis of nicotine addiction. *Current Pediatric Review, 11*(1), 43-55.
Scragg, R., Wellman, R. J., Laugesen, M., & DiFranza, J. R. (2008). Diminished autonomy over tobacco can appear with the first cigarettes. *Addictive Behaviors, 33*, 689-698.
Siqueira, L. M. (2016). Nicotine and tobacco as substances of abuse in children and adolescents. *American Academy of Pediatrics, 139*(1). doi:10.1542/peds.2016-3436.
[27] Siqueira, L. M. (2016). Nicotine and tobacco as substances of abuse in children and adolescents. *American Academy of Pediatrics, 139*(1). doi:10.1542/peds.2016-3436.
[28] Siqueira, L. M. (2016). Nicotine and tobacco as substances of abuse in children and adolescents. *American Academy of Pediatrics, 139*(1). doi:10.1542/peds.2016-3436.
[29] National Institute on Drug Abuse. (2016). *Research report series: Tobacco/nicotine* (NIH Pub No. 16-4342). Bethesda, MD: U.S. Department of Healtha nd Human Services, National Institutes of Health, National Institute on Drug Abuse.
[30] Fagerstrom, K., & Eissenberg, T. (2012). Dependence on tobacco and nicotine products: A case for product-specific assessment. *Nicotine and Tobacco Research, 14*(11), 1382-1390.
Luty, J. (2002). Nicotine addiction and smoking cessation treatments. *Advances in Psychiatric Treatment, 8*, 42-48.
Niaura, R. (2016). *Re-thinking nicotine and its effects*. Washington, DC: Truth Initiative.
[31] Fagerstrom, K., & Eissenberg, T. (2012). Dependence on tobacco and nicotine products: A case for product-specific assessment. *Nicotine and Tobacco Research, 14*(11), 1382-1390.
U.S. Food and Drug Administration. (2013). *Nicotine replacement therapy labels may change.* Retrieved from http://www.fda.gov.
Pickworth, W. B., Bunker, E. B., & Henningfield, J. E. (1994). Transdermal nicotine: Reduction of smoking with minimal abuse liability. *Psychopharmacology, 115*, 9-14.
[32] The Clinical Practice Guideline Treating Tobacco Use and Dependence 2008 Update Panel, Liaisons, and Staff. (2008). A clinical practice guideline for treating tobacco use and dependence: 2008 update: A U.S. Public Health Service report. *American Journal of Preventive Medicine, 35*(2), 158-176.
Stead, L. F., Perera, R., Bullen, C., Mant, D., Hartmann-Boyce, J., Cahill, K., et al. (2012). Nicotine replacement therapy for smoking cessation. *Cochrane Database of Systematic Reviews, 11*, CD000146.
[33] Stead, L. F., Perera, R., Bullen, C., Mant, D., Hartmann-Boyce, J., Cahill, K., et al. (2012). Nicotine replacement therapy for smoking cessation. *Cochrane Database of Systematic Reviews, 11*, CD000146.
[34] The Clinical Practice Guideline Treating Tobacco Use and Dependence 2008 Update Panel, Liaisons, and Staff. (2008). A clinical practice guideline for treating tobacco use and dependence: 2008 update: A U.S. Public Health Service report. *American Journal of Preventive Medicine, 35*(2), 158-176.
[35] Grana, R. A., Popova, L., & Ling, P. M. (2014). A longitudinal analysis of electronic cigarette use and smoking cessation. *JAMA Internal Medicine, 174*(5), 812-813.
U.S. Preventive Services Task Force. (2015). *Behavioral and pharmacotherapy interventions for tobacco smoking cessation in adults, including pregnant women: Clinical summary.* Retrieved from http://annals.org.
[36] U.S. Department of Health and Human Services. (2016). *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, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[37] Family Smoking Prevention and Tobacco Control Act. H.R. 1256, 111th Cong. (2010).
[38] Ganz, O., Cantrell, J., Moon-Howard, J., Aidala, A., Kirchner, T. R., & Vallone, D. (2015). Electronic cigarette advertising at the point-of-sale: a gap in tobacco control research. *Tobacco Control, 24*(e1), e110-e112.
Portnoy, D. B., Wu, C. C., Tworek, C., Chen, J., & Borek, N. (2014). Youth curiosity about cigarettes, smokeless tobacco, and cigars: Prevalence and associations with advertising. *American Journal of Preventive Medicine, 47*(Suppl 1), S76-S86.

Richardson, A., Ganz, O., & Vallone, D. (2015). Tobacco on the web: Surveillance and characterisation of online tobacco and e-cigarette advertising. *Tobacco Control, 24*(4), 341-347.
[39] Basch, C. H., Mongiovi, J., Hillyer, G. C., MacDonald, Z., & Basch, C. E. (2016). YouTube videos related to e-cigarette safety and related health risks: Implications for preventing and emerging epidemic. *Public Health, 132*, 57-59. doi:10.1016/j.puhe.2015.12.003.
Chu, K. H., Unger, J. B., Allem, J. P., Pattarroyo, M., Soto, D., Cruz, T. B., et al. (2015). Diffusion of messages from an electronic cigarette brand to potential users through Twitter. *PLoS One, 10*(12), doi.org/10.1371/journal.pone.0145387.
Huang, J., Kornfield, R., Szczypka, G., & Emergy, S. L. (2014). A cross-sectional examination of marketing of electronic cigarettes on Twitter. *Tobacco Control,* (23), iii26-iii30. doi:10.1136/tobaccocontrol-2014-051551.
Kim, A. E., Hopper, T., Simpson, S., Nonnemaker, J., Lieberman, A. J., Hansen, H., et al. (2015). Using Twitter data to gain insights into e-cigarette marketing and locations of use: An infoveillance study. *Journal of Medical Internet Research, 17*(11), e251. doi:10.2196/jmir.4466.
Klein, E. G., Berman, M., Hemmerich, N., Carlson, C., Htut, S., & Slater, M. (2016). Online e-cigarette marketing claims: A systematic content and legal analysis. *Tobacco Regulatory Science, 2*(3), 252-262.
Singh, T., Marynak, K., Arrazola, R. A., Cox, S., Rolle, I. V., & King, B. A. (2016). Vital signs: Exposure to electronic cigarette advertising among middle school and high school students - United States, 2014. *Morbidity Mortality Weekly Report, 64*(52), 1403-1408.
Wang, L., Zhan, Y., Li, Q., Zeng, D. D., Leischow, S. J., & Okamoto, J. (2015). An examination of electronic cigarette content on social media: Analysis of e-cigarette flavor content on Reddit. *International Journal of Environmental Research and Public Health, 12*(11), 14916-14935.
[40] Klein, E. G., Berman, M., Hemmerich, N., Carlson, C., Htut, S., & Slater, M. (2016). Online e-cigarette marketing claims: A systematic content and legal analysis. *Tobacco Regulatory Science, 2*(3), 252-262.
Sterling, K. L., Fryer, C. S., Majeed, B., & Duong, M. M. (2015). Promotion of waterpipe tobacco use, its variants and accessories in young adult newspapers: A content analysis of message portrayal. *Health Education Research, 30*(1), 152-161.
Willis, E., Haught, M. J., & Morris Ii, D. L. (2017). Up in vapor: Exploring the health messages of e-cigarette advertisements. *Health Communication, 32*(3), 372-380.
[41] Grana, R., Benowitz, N., & Glantz, S. A. (2014). E-cigarettes: A scientific review. *Circulation, 129*(19), 1972-1986.
Mejia, A. B., Ling, P. M., & Glantz, S. A. (2010). Quantifying the effects of promoting smokeless tobacco as a harm reduction strategy in the USA. *Tobacco Control, 19*(4), 297-305.
Payne, J. D., Orellana-Barrios, M., Medrano-Juarez, R., Buscemi, D., & Nugent, K. (2016). Electronic cigarettes in the media. *Proceedings (Baylor University Medical Center), 29*(3), 280-283.
Willis, E., Haught, M. J., & Morris Ii, D. L. (2017). Up in vapor: Exploring the health messages of e-cigarette advertisements. *Health Communication, 32*(3), 372-380.
[42] Timberlake, D. S. (2016). Advertising Receptivity and Youth Initiation of Smokeless Tobacco. *Subst.Use.Misuse., 51*(9), 1077-1082.
U.S. Department of Health and Human Services. (2012). *Preventing tobacco use among youth and young adults: A report of the Surgeon General.* Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
[43] Mejia, A. B., & Ling, P. M. (2010). Tobacco industry consumer research on smokeless tobacco users and product development. *American Journal of Public Health, 100*(1), 78-87.
[44] Mejia, A. B., & Ling, P. M. (2010). Tobacco industry consumer research on smokeless tobacco users and product development. *American Journal of Public Health, 100*(1), 78-87.
[45] VapeRanks. (2014). *Imperial tobacco acquires Blu e-cigarettes following R. J. Reynolds-Lorillard merger.* Retrieved from http://vaperanks.com.
[46] R. J. Reynolds Vapor. (2016). *What is R.J. Reynolds vapor company?* Retrieved from http://rjrvapor.com.
[47] Altria.com. (2014). *Press release: Altria announces agreement to acquire e-vapor business of Green Smoke, Inc.* Retrieved from http://investor.altria.com.
[48] Altria.com. (2014). *Press release: Altria announces agreement to acquire e-vapor business of Green Smoke, Inc.* Retrieved from http://investor.altria.com.
[49] Cantrell, J., Pearson, J. L., Anesetti-Rothermel, A., Xiao, H., Kirchner, T. R., & Vallone, D. (2016). Tobacco retail outlet density and young adult tobacco initiation. *Nicotine and Tobacco Research, 18*(2), 130-137.

Truth Initiative. (2015). *Vaporized: Youth and young adult exposure to e-cigarette marketing*. Washington, DC: Truth Initiative.

[50] Kim, A. E., Arnold, K. Y., & Makarenko, O. (2014). E-cigarette advertising expenditures in the U.S., 2011-2012. *American Journal of Preventive Medicine, 46*(4), 409-412.

[51]Cantrell, J., Pearson, J. L., Anesetti-Rothermel, A., Xiao, H., Kirchner, T. R., & Vallone, D. (2016). Tobacco retail outlet density and young adult tobacco initiation. *Nicotine and Tobacco Research, 18*(2), 130-137.

Truth Initiative. (2015). *Vaporized: Youth and young adult exposure to e-cigarette marketing*. Washington, DC: Truth Initiative.

[52] Singh, T., Marynak, K., Arrazola, R. A., Cox, S., Rolle, I. V., & King, B. A. (2016). Vital signs: Exposure to electronic cigarette advertising among middle school and high school students - United States, 2014. *Morbidity Mortality Weekly Report, 64*(52), 1403-1408.

[53] Truth Initiative. (2015). *Vaporized: Youth and young adult exposure to e-cigarette marketing*. Washington, DC: Truth Initiative.

[54] Bogdanovica, I., Szatkowski, L., McNeill, A., Spanopoulos, D., & Britton, J. (2015). Exposure to point-of-sale displays and changes in susceptibility to smoking: Findings from a cohort study of school students. *Addiction, 110*(4), 693-702.

Cantrell, J., Pearson, J. L., Anesetti-Rothermel, A., Xiao, H., Kirchner, T. R., & Vallone, D. (2016). Tobacco retail outlet density and young adult tobacco initiation. *Nicotine and Tobacco Research, 18*(2), 130-137.

Johns, M., Sacks, R., Rane, M., & Kansagra, S. M. (2013). Exposure to tobacco retail outlets and smoking initiation among New York City adolescents. *Journal of Urban Health, 90*(6), 1091-1101.

Mantey, D. S., Cooper, M. R., Clendennen, S. L., Pasch, K. E., & Perry, C. L. (2016). E-cigarette marketing exposure is associated with e-cigarette use among U.S. youth. *Journal of Adolescent Health, 58*(6), 686-690.

Portnoy, D. B., Wu, C. C., Tworek, C., Chen, J., & Borek, N. (2014). Youth curiosity about cigarettes, smokeless tobacco, and cigars: Prevalence and associations with advertising. *American Journal of Preventive Medicine, 47*(2 Suppl 1), S76-S86.

[55] Duke, J. C., Allen, J. A., Eggers, M. E., Nonnemaker, J., & Farrelly, M. C. (2016). Exploring differences in youth perceptions of the effectiveness of electronic cigarette television advertisements. *Nicotine and Tobacco Research, 18*(5), 1382-1386.

Farrelly, M. C., Duke, J. C., Crankshaw, E. C., Eggers, M. E., Lee, Y. O., Nonnemaker, J. M., et al. (2015). A randomized trial of the effect of e-cigarette TV advertisements on intentions to use e-cigarettes. *American Journal of Preventive Medicine, 49*(5), 686-693.

Pepper, J. K., Emery, S. L., Ribisl, K. M., Southwell, B. G., & Brewer, N. T. (2014). Effects of advertisements on smokers' interest in trying e-cigarettes: The roles of product comparison and visual cues. *Tobacco Control, 23 (Suppl 3)*, iii31-iii36.

Pokhrel, P., Fagan, P., Kehl, L., & Herzog, T. A. (2015). Receptivity to e-cigarette marketing, harm perceptions, and e-cigarette Use. *American Journal of Health Behavior, 39*(1), 121-131.

Pokhrel, P., Fagan, P., Herzog, T. A., Chen, Q., Muranaka, N., Kehl, L., et al. (2016). E-cigarette advertising exposure and implicit attitudes among young adult non-smokers. *Drug and Alcohol Dependence, 163*, 134-140.

Tan, A. S., Bigman, C. A., Mello, S., & Sanders-Jackson, A. (2015). Is exposure to e-cigarette communication associated with perceived harms of e-cigarette secondhand vapour? Results from a national survey of U.S. adults. *BMJ Open., 5*(3). doi:10.1136/bmjopen-2014-007134.

Villanti, A. C., Rath, J. M., Williams, V. F., Pearson, J. L., Richardson, A., Abrams, D. B., et al. (2016). Impact of exposure to electronic cigarette advertising on susceptibility and trial of electronic cigarettes and cigarettes in U.S. young adults: A randomized controlled trial. *Nicotine and Tobacco Research, 18*(5), 1331-1339.

[56] Singh, T., Agaku, I. T., Arrazola, R. A., Marynak, K. L., Neff, L. J., Rolle, I. T., et al. (2016). Exposure to advertisements and electronic cigarette use among U.S. middle and high school students. *Pediatrics, 137*(5). doi:10.1542/peds.2015-4155.

[57] Ganz, O., Cantrell, J., Moon-Howard, J., Aidala, A., Kirchner, T. R., & Vallone, D. (2015). Electronic cigarette advertising at the point-of-sale: A gap in tobacco control research. *Tobacco Control, 24*(e1), e110-e112.

Willis, E., Haught, M. J., & Morris Ii, D. L. (2017). Up in vapor: Exploring the health messages of e-cigarette advertisements. *Health Communication, 32*(3), 372-380.

[58] Ganz, O., Cantrell, J., Moon-Howard, J., Aidala, A., Kirchner, T. R., & Vallone, D. (2015). Electronic cigarette advertising at the point-of-sale: A gap in tobacco control research. *Tobacco Control, 24*(e1), e110-e112.

Liu, S. T., Nemeth, J. M., Klein, E. G., Ferketich, A. K., Kwan, M. P., & Wewers, M. E. (2014). Adolescent and adult perceptions of traditional and novel smokeless tobacco products and packaging in rural Ohio. *Tobacco Control, 23*(3), 209-214.
Villanti, A. C., Richardson, A., Vallone, D. M., & Rath, J. M. (2013). Flavored tobacco product use among U.S. young adults. *American Journal of Preventive Medicine,* 44(4), 388-391.
[59] Amrock, S. M., Gordon, T., Zelikoff, J. T., & Weitzman, M. (2014). Hookah use among adolescents in the United States: Results of a national survey. *Nicotine and Tobacco Research, 16*(2), 231-237.
Cardenas, V. M., Breen, P. J., Compadre, C. M., Delongchamp, R. R., Barone, C. P., Phillips, M. M., et al. (2015). The smoking habits of the family influence the uptake of e-cigarettes in U.S. children. *Annals of Epidemiology, 25*(1), 60-62.
Kassem, N. O., Jackson, S. R., Boman-Davis, M., Kassem, N. O., Liles, S., Daffa, R. M., et al. (2015). Hookah smoking and facilitators/barriers to lounge use among students at a U.S. university. *American Journal of Health Behavior, 39*(6), 832-848.
[60] Johns, M., Sacks, R., Rane, M., & Kansagra, S. M. (2013). Exposure to tobacco retail outlets and smoking initiation among New York City adolescents. *Journal of Urban Health, 90*(6), 1091-1101.
Mennis, J., & Mason, M. (2016). Tobacco outlet density and attitudes towards smoking among urban adolescent smokers. *Substance Abuse, 37*(4), 521-525.
[61] Kirchner, T. R., Villanti, A. C., Cantrell, J., Anesetti-Rothermel, A., Ganz, O., Conway, K. P., et al. (2015). Tobacco retail outlet advertising practices and proximity to schools, parks and public housing affect Synar underage sales violations in Washington, DC. *Tobacco Control, 24*(e1), e52-e58.
Tucker-Seeley, R. D., Bezold, C. P., James, P., Miller, M., & Wallington, S. F. (2016). Retail pharmacy policy to end the sale of tobacco products: What is the impact on disparity in neighborhood density of tobacco outlets? *Cancer Epidemiology, Biomarkers and Prevention, 25*(9), 1305-1310.
[62] Cantrell, J., Anesetti-Rothermel, A., Pearson, J. L., Xiao, H., Vallone, D., & Kirchner, T. R. (2015). The impact of the tobacco retail outlet environment on adult cessation and differences by neighborhood poverty. *Addiction, 110*(1), 152-161.
[63] Kassem, N. O., Jackson, S. R., Boman-Davis, M., Kassem, N. O., Liles, S., Daffa, R. M., et al. (2015). Hookah smoking and facilitators/barriers to lounge use among students at a U.S. university. *American Journal of Health Behavior, 39*(6), 832-848.
[64] Giovenco, D. P., Casseus, M., Duncan, D. T., Coups, E. J., Lewis, M. J., & Delnevo, C. D. (2016). Association between electronic cigarette marketing near schools and e-cigarette use among youth. *Journal of Adolescent Health, 59*(6), 627-634.
[65] Akl, E. A., Ward, K. D., Bteddini, D., Khaliel, R., Alexander, A. C., Lotfi, T., et al. (2015). The allure of the waterpipe: a narrative review of factors affecting the epidemic rise in waterpipe smoking among young persons globally. *Tobacco Control, 24 (Suppl 1)*, i13-i21.
Chu, K. H., Unger, J. B., Allem, J. P., Pattarroyo, M., Soto, D., Cruz, T. B., et al. (2015). Diffusion of messages from an electronic cigarette brand to potential users through Twitter. *PLoS One, 10*(12), doi.org/10.1371/journal.pone.0145387.
Huang, J., Kornfield, R., Szczypka, G., & Emergy, S. L. (2014). A cross-sectional examination of marketing of electronic cigarettes on Twitter. *Tobacco Control,* (23), iii26-iii30. doi:10.1136/tobaccocontrol-2014-051551.
Huang, J., Kornfield, R., & Emery, S. L. (2016). 100 million views of electronic cigarette YouTube videos and counting: Quantification, content evaluation, and engagement levels of videos. *Journal of Medical Internet Research, 18*(3), e67. doi:10.2196/jmir.4265.
Klein, E. G., Berman, M., Hemmerich, N., Carlson, C., Htut, S., & Slater, M. (2016). Online e-cigarette marketing claims: A systematic content and legal analysis. *Tobacco Regulatory Science, 2*(3), 252-262.
Link, A. R., Cawkwell, P. B., Shelley, D. R., & Sherman, S. E. (2015). An exploration of online behaviors and social media use among hookah and electronic-cigarette users. *Addictive Behaviors Report, 2*, 37-40.
Luo, C., Zheng, X., Zeng, D. D., & Leischow, S. (2014). Portrayal of electronic cigarettes on YouTube. *BMC Public Health, 14*, 1028. doi:10.1186/1471-2458-14-1028.
Paek, H. J., Kim, S., Hove, T., & Huh, J. Y. (2014). Reduced harm or another gateway to smoking? Source, message, and information characteristics of e-cigarette videos on YouTube. *Journal of Health Communication, 19*(5), 545-560.
Richardson, A., Ganz, O., & Vallone, D. (2015). Tobacco on the web: Surveillance and characterisation of online tobacco and e-cigarette advertising. *Tobacco Control, 24*(4), 341-347.

Salloum, R. G., Osman, A., Maziak, W., & Thrasher, J. F. (2015). How popular is waterpipe tobacco smoking? Findings from internet search queries. *Tobacco Control, 24*, 509-513.
van der Tempel, J., Noormohamed, A., Schwartz, R., Norman, C., Malas, M., & Zawertailo, L. (2016). Vape, quit, tweet? Electronic cigarettes and smoking cessation on Twitter. *International Journal of Public Health, 61*(2), 249-256.
[66] Basch, C. H., Mongiovi, J., Hillyer, G. C., MacDonald, Z., & Basch, C. E. (2016). YouTube videos related to e-cigarette safety and related health risks: Implications for preventing and emerging epidemic. *Public Health, 132*, 57-59. doi:10.1016/j.puhe.2015.12.003.
Link, A. R., Cawkwell, P. B., Shelley, D. R., & Sherman, S. E. (2015). An exploration of online behaviors and social media use among hookah and electronic-cigarette users. *Addictive Behaviors Report, 2*, 37-40.
van der Tempel, J., Noormohamed, A., Schwartz, R., Norman, C., Malas, M., & Zawertailo, L. (2016). Vape, quit, tweet? Electronic cigarettes and smoking cessation on Twitter. *International Journal of Public Health, 61*(2), 249-256.
[67] Richardson, A., Ganz, O., & Vallone, D. (2015). Tobacco on the web: Surveillance and characterisation of online tobacco and e-cigarette advertising. *Tobacco Control, 24*(4), 341-347.
[68] Sowles, S. J., Krauss, M. J., Connolly, S., & Cavazos-Rehg, P. A. (2016). A content analysis of vaping advertisements on Twitter. *Preventing Chronic Disease, 13*, E139. doi:10.5888/pcd13.160274.
Wang, L., Zhan, Y., Li, Q., Zeng, D. D., Leischow, S. J., & Okamoto, J. (2015). An examination of electronic cigarette content on social media: Analysis of e-cigarette flavor content on Reddit. *International Journal of Environmental Research and Public Health, 12*(11), 14916-14935.
[69] Chu, K. H., Unger, J. B., Allem, J. P., Pattarroyo, M., Soto, D., Cruz, T. B., et al. (2015). Diffusion of messages from an electronic cigarette brand to potential users through Twitter. *PLoS One, 10*(12), doi.org/10.1371/journal.pone.0145387.
Huang, J., Kornfield, R., & Emery, S. L. (2016). 100 million views of electronic cigarette YouTube videos and counting: Quantification, content evaluation, and engagement levels of videos. *Journal of Medical Internet Research, 18*(3), e67. doi:10.2196/jmir.4265.
Kim, A. E., Hopper, T., Simpson, S., Nonnemaker, J., Lieberman, A. J., Hansen, H., et al. (2015). Using Twitter data to gain insights into e-cigarette marketing and locations of use: An infoveillance study. *Journal of Medical Internet Research, 17*(11), e251. doi:10.2196/jmir.4466.
Liang, Y., Zheng, X., Zeng, D. D., Zhou, X., Leischow, S. J., & Chung, W. (2015). Exploring how the tobacco industry presents and promotes itself in social media. *Journal of Medical Internet Research, 17*(1), e24. doi:10.2196/jmir.3665.
[70] Huang, J., Kornfield, R., Szczypka, G., & Emergy, S. L. (2014). A cross-sectional examination of marketing of electronic cigarettes on Twitter. *Tobacco Control,* (23), iii26-iii30. doi:10.1136/tobaccocontrol-2014-051551.
[71] van der Tempel, J., Noormohamed, A., Schwartz, R., Norman, C., Malas, M., & Zawertailo, L. (2016). Vape, quit, tweet? Electronic cigarettes and smoking cessation on Twitter. *International Journal of Public Health, 61*(2), 249-256.
[72] Seidenberg, A. B., Rodgers, E. J., Rees, V. W., & Connolly, G. N. (2012). Youth access, creation, and content of smokeless tobacco ("dip") videos in social media. *Journal of Adolescent Health, 50*(4), 334-338.
[73] Basch, C. H., Mongiovi, J., Hillyer, G. C., MacDonald, Z., & Basch, C. E. (2016). YouTube videos related to e-cigarette safety and related health risks: Implications for preventing and emerging epidemic. *Public Health, 132*, 57-59. doi:10.1016/j.puhe.2015.12.003.
[74] Ramamurthi, D., Gall, P. A., Ayoub, N., & Jackler, R. K. (2016). Leading-brand advertisement of quitting smoking benefits for e-cigarettes. *American Journal of Public Health, 106*(11), 2057-2063.
[75] Wang, L., Zhan, Y., Li, Q., Zeng, D. D., Leischow, S. J., & Okamoto, J. (2015). An examination of electronic cigarette content on social media: Analysis of e-cigarette flavor content on Reddit. *International Journal of Environmental Research and Public Health, 12*(11), 14916-14935.
[76] Wang, L., Zhan, Y., Li, Q., Zeng, D. D., Leischow, S. J., & Okamoto, J. (2015). An examination of electronic cigarette content on social media: Analysis of e-cigarette flavor content on Reddit. *International Journal of Environmental Research and Public Health, 12*(11), 14916-14935.
[77] Kostygina, G., Glantz, S. A., & Ling, P. M. (2016). Tobacco industry use of flavours to recruit new users of little cigars and cigarillos. *Tobacco Control, 25*(1), 66-74.
Liu, S. T., Nemeth, J. M., Klein, E. G., Ferketich, A. K., Kwan, M. P., & Wewers, M. E. (2014). Adolescent and adult perceptions of traditional and novel smokeless tobacco products and packaging in rural Ohio. *Tobacco Control, 23*(3), 209-214.

Villanti, A. C., Richardson, A., Vallone, D. M., & Rath, J. M. (2013). Flavored tobacco product use among U.S. young adults. *American Journal of Preventive Medicine,* 44(4), 388-391.
[78] Yingst, J. M., Veldheer, S., Hrabovsky, S., Nichols, T. T., Wilson, S. J., & Foulds, J. (2015). Factors associated with electronic cigarette users' device preferences and transition from first generation to advanced generation devices. *Nicotine and Tobacco Research, 17*(10), 1242-1246.
[79] Yingst, J. M., Veldheer, S., Hrabovsky, S., Nichols, T. T., Wilson, S. J., & Foulds, J. (2015). Factors associated with electronic cigarette users' device preferences and transition from first generation to advanced generation devices. *Nicotine and Tobacco Research, 17*(10), 1242-1246.
[80] Chen, C., Zhuang, Y. L., & Zhu, S. H. (2016). E-Cigarette design preference and smoking cessation: A U.S. population study. *American Journal of Preventive Medicine, 51*(3), 356-363.
Yingst, J. M., Veldheer, S., Hrabovsky, S., Nichols, T. T., Wilson, S. J., & Foulds, J. (2015). Factors associated with electronic cigarette users' device preferences and transition from first generation to advanced generation devices. *Nicotine and Tobacco Research, 17*(10), 1242-1246.
[81] Delnevo, C. D., & Hrywna, M. (2007). "A whole 'nother smoke" or a cigarette in disguise: How RJ Reynolds reframed the image of little cigars. *American Journal of Public Health, 97*(8), 1368-1375.
[82] Delnevo, C. D., & Hrywna, M. (2007). "A whole 'nother smoke" or a cigarette in disguise: How RJ Reynolds reframed the image of little cigars. *American Journal of Public Health, 97*(8), 1368-1375.
[83] Delnevo, C. D. (2006). Smokers' choice: What explains the steady growth of cigar use in the U.S.? *Public Health Reports, 121*(2), 116-119.
Truth Tobacco Industry Documents. (1971). *Cigarette industry new products review.* Retrieved from https://www.industrydocumentslibrary.ucsf.edu.
[84] U.S. Food and Drug Administration. (2016). *News release: FDA takes action against four tobacco manufacturers for illegal sales of flavored cigarettes labeled as little cigars or cigars.* Retrieved from http://www.fda.gov.
[85] U.S. Department of Health and Human Services. (2016). 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: Final rule. *Federal Register, 81*(90), 28974-29106.
[86] Tobacco Control Legal Consortium. (2016). *The deeming regulation: FDA authority over e-cigarettes, cigars, and other tobacco products*. Saint Paul, MN: Public Health Law Center.
[87] Allen, J. G., Flanigan, S. S., LeBlanc, M., Vallarino, J., MacNaughton, P., Stewart, J. H., et al. (2016). Flavoring chemicals in e-cigarettes: Diacetyl, 2,3-pentanedione, and acetoin in a sample of 51 products, including fruit-, candy-, and cocktail-flavored e-cigarettes. *Environmental Health Perspectives, 124*(6), 733-739.
Costigan, S., & Meredith, C. (2015). An approach to ingredient screening and toxicological risk assessment of flavours in e-liquids. *Regulatory Toxicology and Pharmacology, 72*(2), 361-369.
Flora, J. W., Meruva, N., Huang, C. B., Wilkinson, C. T., Ballentine, R., Smith, D. C., et al. (2016). Characterization of potential impurities and degradation products in electronic cigarette formulations and aerosols. *Regulatory Toxicology and Pharmacology, 74*, 1-11.
Geiss, O., Bianchi, I., & Barrero-Moreno, J. (2016). Correlation of volatile carbonyl yields emitted by e-cigarettes with the temperature of the heating coil and the perceived sensorial quality of the generated vapours. *International Journal of Hygiene and Environmental Health, 219*(3), 268-277.
Gillman, I. G., Kistler, K. A., Stewart, E. W., & Paolantonio, A. R. (2016). Effect of variable power levels on the yield of total aerosol mass and formation of aldehydes in e-cigarette aerosols. *Regulatory Toxicology and Pharmacology, 75*, 58-65.
Goniewicz, M. L., Knysak, J., Gawron, M., Kosmider, L., Sobczak, A., Kurek, J., et al. (2014). Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tobacco Control, 23*(2), 133-139.
Han, S., Chen, H., Zhang, X., Liu, T., & Fu, Y. (2016). Levels of selected groups of compounds in refill solutions for electronic cigarettes. *Nicotine and Tobacco Research, 18*(5), 708-714.
Hutzler, C., Paschke, M., Kruschinski, S., Henkler, F., Hahn, J., & Luch, A. (2014). Chemical hazards present in liquids and vapors of electronic cigarettes. *Archives of Toxicology, 88*(7), 1295-1308.
Herrington, J. S., & Myers, C. (2015). Electronic cigarette solutions and resultant aerosol profiles. *Journal of Chromatography, 1418*, 192-199.
Jo, S. H., & Kim, K. H. (2016). Development of a sampling method for carbonyl compounds released due to the use of electronic cigarettes and quantitation of their conversion from liquid to aerosol. *Journal of Chromatography, 1429*, 369-373.

Kosmider, L., Sobczak, A., Fik, M., Knysak, J., Zaciera, M., Kurek, J., et al. (2014). Carbonyl compounds in electronic cigarette vapors: Effects of nicotine solvent and battery output voltage. *Nicotine and Tobacco Research, 16*(10), 1319-1326.
Kosmider, L., Sobczak, A., Prokopowicz, A., Kurek, J., Zaciera, M., Knysak, J., et al. (2016). Cherry-flavoured electronic cigarettes expose users to the inhalation irritant, benzaldehyde. *Thorax, 71*(4), 376-377.
Sleiman, M., Logue, J. M., Montesinos, V. N., Russell, M. L., Litter, M. I., Gundel, L. A., et al. (2016). Emissions from electronic cigarettes: Key parameters affecting the release of harmful chemicals. *Environmental Science and Technology, 50*(17), 9644-9651.
Tierney, P. A., Karpinski, C. D., Brown, J. E., Luo, W., & Pankow, J. F. (2016). Flavour chemicals in electronic cigarette fluids. *Tobacco Control, 25*(e1), e10-e15.
Uchiyama, S., Ohta, K., Inaba, Y., & Kunugita, N. (2013). Determination of carbonyl compounds generated from the e-cigarette using coupled silica cartridges impregnated with hydroquinone and 2,4-dinitrophenylhydrazine, followed by high-performance liquid chromatography. *Analytical Sciences, 29*(12), 1219-1222.
Varlet, V., Farsalinos, K., Augsburger, M., Thomas, A., & Etter, J. F. (2015). Toxicity assessment of refill liquids for electronic cigarettes. *International Journal of Environmental Research and Public Health, 12*(5), 4796-4815.
[88] Choi, K., Fabian, L., Mottey, N., Corbett, A., & Forster, J. (2012). Young adults' favorable perceptions of snus, dissolvable tobacco products, and electronic cigarettes: Findings from a focus group study. *American Journal of Public Health, 102*(11), 2088-2093.
Cornacchione, J., Wagoner, K. G., Wiseman, K. D., Kelley, D., Noar, S. M., Smith, M. H., et al. (2016). Adolescent and young adult perceptions of hookah and little cigars/cigarillos: Implications for risk messages. *Journal of Health Communication, 21*(7), 818-825.
Courtemanche, C. J., Palmer, M. K., & Pesko, M. F. (2016). Influence of the flavored cigarette ban on adolescent tobacco use. *American Journal of Preventive Medicine*. doi:10.1016/j.amepre.2016.11.019.
Kong, G., Morean, M. E., Cavallo, D. A., Camenga, D. R., & Krishnan-Sarin, S. (2015). Reasons for electronic cigarette experimentation and discontinuation among adolescents and young adults. *Nicotine and Tobacco Research, 17*(7), 847-854.
Wagoner, K. G., Cornacchione, J., Wiseman, K. D., Teal, R., Moracco, K. E., & Sutfin, E. L. (2016). E-cigarettes, hookah pens and vapes: Adolescent and young adult perceptions of electronic nicotine delivery systems. *Nicotine and Tobacco Research, 18*(10), 2006-2012.
[89] Family Smoking Prevention and Tobacco Control Act. H.R. 1256, 111th Cong. (2010).
[90] Courtemanche, C. J., Palmer, M. K., & Pesko, M. F. (2016). Influence of the flavored cigarette ban on adolescent tobacco use. *American Journal of Preventive Medicine*. doi:10.1016/j.amepre.2016.11.019.
[91] Anderson, S. J. (2011). Menthol cigarettes and smoking cessation behaviour: A review of tobacco industry documents. *Tobacco Control, 20*(Suppl 2), ii49-ii56.
Fagan, P., Moolchan, E. T., Hart, A., Rose, l. A., Lawrence, D., Shavers, V. L., et al. (2010). Nicotine dependence and quitting behaviors among menthol and non-menthol smokers with similar consumptive patterns. *Addiction, 105*(Suppl 1), 55-74.
Kreslake, J. M., Wayne, G. F., Alpert, H. R., Koh, H. K., & Connolly, G. N. (2008). Tobacco industry control of menthol in cigarettes and targeting of adolescents and young adults. *American Journal of Public Health, 98*(9), 1685-1692.
Wickham, R. J. (2015). How menthol alters tobacco-smoking behavior: A biological perspective. *Yale Journal of Biology and Medicine, 88*, 279-287.
Yerger, V. B. (2011). Menthol's potential effects on nicotine dependence: A tobacco industry perspective. *Tobacco Control, 20*(Suppl 2), ii29-ii36.
[92] The National Center on Addiction and Substance Abuse. (2014). *Time to ban menthol*. New York: Author.
[93] Villanti, A. C., Richardson, A., Vallone, D. M., & Rath, J. M. (2013). Flavored tobacco product use among U.S. young adults. *American Journal of Preventive Medicine, 44*(4), 388-391.
[94] Delnevo, C. D., Giovenco, D. P., Ambrose, B. K., Corey, C. G., & Conway, K. P. (2014). Preference for flavoured cigar brands among youth, young adults and adults in the USA. *Tobacco Control*, 24(4), 389-394.
King, B. A., Tynan, M. A., Dube, S. R., & Arrazola, R. (2014). Flavored-little-cigar and flavored-cigarette use among U.S. middle and high school students. *Journal of Adolescent Health, 54*(1), 40-46.
[95] Jo, C. L., Williams, R. S., & Ribisl, K. M. (2015). Tobacco products sold by internet vendors following restrictions on flavors and light descriptors. *Nicotine and Tobacco Research, 17*(3), 344-349.
[96] Miao, S., Beach, E. S., Sommer, T. J., Zimmerman, J. B., & Jordt, S.-E. (2016). High-intensity sweeteners in alternative tobacco products. *Nicotine and Tobacco Research*, 18(11), 2169-2173.

[97] Kostygina, G., Glantz, S. A., & Ling, P. M. (2016). Tobacco industry use of flavours to recruit new users of little cigars and cigarillos. *Tobacco Control, 25*(1), 66-74.
Pepper, J. K., Ribisl, K. M., & Brewer, N. T. (2016). Adolescents' interest in trying flavoured e-cigarettes. *Tobacco Control, 25*(Suppl 2), ii62-ii66. doi:10.1136/tobaccocontrol-2016-053174.
Wagoner, K. G., Cornacchione, J., Wiseman, K. D., Teal, R., Moracco, K. E., & Sutfin, E. L. (2016). E-cigarettes, hookah pens and vapes: Adolescent and young adult perceptions of electronic nicotine delivery systems. *Nicotine and Tobacco Research, 18*(10), 2006-2012.
[98] Ambrose, B. K., Day, H. R., Rostron, B., Conway, K. P., Borek, N., Hyland, A., et al. (2015). Flavored tobacco products use among U.S. youth aged 12-17 years, 2013-2014. *JAMA, 314*(17), 1871-1873.
[99] Ambrose, B. K., Day, H. R., Rostron, B., Conway, K. P., Borek, N., Hyland, A., et al. (2015). Flavored tobacco products use among U.S. youth aged 12-17 years, 2013-2014. *JAMA, 314*(17), 1871-1873.
[100] Corey, C. G., Ambrose, B. K., Apelberg, B. J., & King, B. A. (2015). Flavored tobacco product use among middle and high school students - United States, 2014. *Morbidity Mortality Weekly Report, 64*(38), 1066-1070.
[101] Bonhomme, M. G., Holder-Hayes, E., Ambrose, B. K., Tworek, C., Feirman, S. P., King, B. A., et al. (2016). Flavoured non-cigarette tobacco product use among U.S. adults: 2013-2014. *Tobacco Control, 25*(Suppl 2), ii4-ii13.
[102] Allen, J. G., Flanigan, S. S., LeBlanc, M., Vallarino, J., MacNaughton, P., Stewart, J. H., et al. (2016). Flavoring chemicals in e-cigarettes: Diacetyl, 2,3-pentanedione, and acetoin in a sample of 51 products, including fruit-, candy-, and cocktail-flavored e-cigarettes. *Environmental Health Perspectives, 124*(6), 733-739.
Zhu, S. H., Sun, J. Y., Bonnevie, E., Cummins, S. E., Gamst, A., Yin, L., et al. (2014). Four hundred and sixty brands of e-cigarettes and counting: implications for product regulation. *Tobacco Control, 23*(Suppl 3), iii3-iii9.
[103] Harrell, M. B., Weaver, S. R., Loukas, A., Creamer, M., Marti, C. N., Jackson, C. D., et al. (2017). Flavored e-cigarette use: Characterizing youth, young adult, and adult users. *Preventive Medicine Reports, 5*, 33-40.
[104] Cooper, M., Harrell, M. B., Perez, A., Delk, J., & Perry, C. L. (2016). Flavorings and perceived harm and addictiveness of e-cigarettes among youth. *Tobacco Regulatory Science, 2*(3), 278-289.
Pepper, J. K., Ribisl, K. M., & Brewer, N. T. (2016). Adolescents' interest in trying flavoured e-cigarettes. *Tobacco Control, 25*(Suppl 2), ii62-ii66. doi:10.1136/tobaccocontrol-2016-053174.
[105] Vasiljevic, M., Petrescu, D. C., & Marteau, T. M. (2016). Impact of advertisements promoting candy-like flavoured e-cigarettes on appeal of tobacco smoking among children: An experimental study. *Tobacco Control*, 25(e2), e107-e112. doi:10.1136/tobaccocontrol-2015-052593.
[106] Pepper, J. K., Ribisl, K. M., & Brewer, N. T. (2016). Adolescents' interest in trying flavoured e-cigarettes. *Tobacco Control, 25*(Suppl 2), ii62-ii66. doi:10.1136/tobaccocontrol-2016-053174.
[107] Goldenson, N. I., Kirkpatrick, M. G., Barrington-Trimis, J. L., Pang, R. D., McBeth, J. F., Pentz, M. A., et al. (2016). 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 and Alcohol Dependence, 168*, 176-180.
[108] Audrain-McGovern, J., Strasser, A. A., & Wileyto, E. P. (2016). The impact of flavoring on the rewarding and reinforcing value of e-cigarettes with nicotine among young adult smokers. *Drug and Alcohol Dependence, 166*, 263-267.
[109] U.S. Department of Health and Human Services. (2016). *Food and Drug Administration: 21 CFR Parts 1100, 1140, and 1143. Docket No. FDA-2014-N-0189.* Retrieved from https://s3.amazonaws.com.
[110] U.S. Department of Health and Human Services. (2016). *Food and Drug Administration: 21 CFR Parts 1100, 1140, and 1143. Docket No. FDA-2014-N-0189.* Retrieved from https://s3.amazonaws.com.
[111] Farsalinos, K. E., Romagna, G., Tsiapras, D., Kyrzopoulos, S., Spyrou, A., & Voudris, V. (2013). Impact of flavour variability on electronic cigarette use experience: an internet survey. *International Journal of Environmental Research and Public Health, 10*(12), 7272-7282.
Litt, M. D., Duffy, V., & Onchen, C. (2016). Cigarette smoking and electronic cigarette vaping patterns as a function of e-cigarette flavourings. *Tobacco Control, 25*(Suppl 2),: ii67-ii72. doi:10.1136/tobaccocontrol-2016-053223.
[112] Proctor, R. N. (2015). The cigarette catastrophe continues. *Lancet, 385*(9972), 938-939.
[113] Center for Responsive Politics. (2016). *Industry profile: Summary, 2015.* Retrieved from https://www.opensecrets.org.
[114] Kusnetz, N. (2016). *Who's calling the shots in state politics? How big tobacco lobbies to safeguard e-cigarettes: California takes center stage in fight between health groups and tobacco firms.* Retrieved from Center for Public Integrity: https://www.publicintegrity.org.

[115] Kusnetz, N. (2016). *Who's calling the shots in state politics? How big tobacco lobbies to safeguard e-cigarettes: California takes center stage in fight between health groups and tobacco firms.* Retrieved from Center for Public Integrity: https://www.publicintegrity.org.
[116] Tobacco Products Scientific Advisory Committee. (2011). *Menthol cigarettes and public health: Review of the scientific evidence and recommendations.* Retrieved from http://www.fda.gov.
[117] Vanderford, R. (2011). *Tobacco cos. sue FDA over 'biased' advisory board.* Retrieved from http://www.law360.com.
CNN. (2011). *Tobacco companies sue to thwart federal panel, claiming bias.* Retrieved from http://www.cnn.com.
[118] Lammi, G. G. (2014). *FDA advisory committee not rife with conflicts of interest? "Please!" quips federal judge.* Retrieved from http://www.forbes.com.
[119] Glantz, S. (2016). *The White House told FDA that Black lives don't matter.* Retrieved from http://tobacco.ucsf.edu.
[120] Cox, E., Barry, R. A., & Glantz, S. (2016). E-cigarette policymaking by local and state governments: 2009-2014. *Milbank Quarterly, 94*(3), 520-596.
[121] Kaplan, S. (2017). *Lawmakers seek to help e-cigarette makers escape new regulations.* Retrieved from https://www.statnews.com.
Lipton, E. (2016, September 11). *A lobbyist wrote the Bill. Will the tobacco industry win its e-cigarette fight? The New York Times.* Retrieved from http://www.nytimes.com.
[122] U.S. Food and Drug Administration. (2016). *Family Smoking Prevention and Tobacco Control Act: 21 CFR parts 1100, 1140, and 1143.* Retrieved from http://federalregister.gov.
[123] Popova, L., & Ling, P. M. (2014). Nonsmokers' responses to new warning labels on smokeless tobacco and electronic cigarettes: An experimental study. *BMC Public Health, 14*, 997. doi:10.1186/1471-2458-14-997.
[124] Morgenstein, M. (2011). *Tobacco giants suing FDA over warning labels mandate.* CNN. Retrieved from http://www.cnn.com.
U.S. Food and Drug Administration. (2013). *Frequently asked questions: Final rule "Required warnings for cigarette packages and advertisements.* Retrieved from http://www.fda.gov.
[125] U.S. Food and Drug Administration. (2015). *Issue snapshot: Modified Risk Tobacco Products (MRTPs).* Retrieved from http://www.fda.gov.
[126] Popova, L., & Ling, P. M. (2014). Nonsmokers' responses to new warning labels on smokeless tobacco and electronic cigarettes: An experimental study. *BMC Public Health, 14*, 997. doi:10.1186/1471-2458-14-997.
[127] Kong, G., Morean, M. E., Cavallo, D. A., Camenga, D. R., & Krishnan-Sarin, S. (2015). Reasons for electronic cigarette experimentation and discontinuation among adolescents and young adults. *Nicotine and Tobacco Research, 17*(7), 847-854.
Margolis, K. A., Nguyen, A. B., Slavit, W. I., & King, B. A. (2016). E-cigarette curiosity among U.S. middle and high school students: Findings from the 2014 national youth tobacco survey. *Preventive Medicine, 89*, 1-6. doi:10.1016/j.ypmed.2016.05.001.
[128] Mejia, A. B., Ling, P. M., & Glantz, S. A. (2010). Quantifying the effects of promoting smokeless tobacco as a harm reduction strategy in the USA. *Tobacco Control, 19*(4), 297-305.
[129] Fooks, G. J., Gilmore, A. B., Smith, K. E., Collin, J., Holden, C., & Lee, K. (2011). Corporate social responsibility and access to policy elites: An analysis of tobacco industry documents. *PLoS Medicine, 8*(8), e1001076. doi:org/10.1371/journal.pmed.1001076.
Peeters, S., & Gilmore, A. B. (2015). Understanding the emergence of the tobacco industry's use of the term tobacco harm reduction in order to inform public health policy. *Tobacco Control, 24*, 182-189.
[130] Peeters, S., & Gilmore, A. B. (2013). Transnational tobacco company interests in smokeless tobacco in Europe: Analysis of internal industry documents and contemporary industry materials. *PLoS Medicine, 10*(9), e1001506. doi:10.1371/journal.pmed.1001506.
[131] Bansal-Travers, M., Hammond, D., Smith, P., & Cummings, K. M. (2011). The impact of cigarette pack design, descriptors, and warning labels on risk perception in the U.S. *American Journal of Preventive Medicine, 40*(6), 674-682.
Germain, D., Hons, B. P., Wakefield, M. A., & Durkin, S. J. (2010). Adolescents' perceptions of cigarette brand image: Dose plain packaging make a difference? *Journal of Adolescent Health, 46*, 385-392.
[132] Adkison, S. E., Bansal-Travers, M., Smith, D. M., O'Connor, R. J., & Hyland, A. J. (2014). Impact of smokeless tobacco packaging on perceptions and beliefs among youth, young adults, and adults in the U.S.: Findings from an internet-based cross-sectional survey. *Harm Reduction Journal, 11*, 2. doi:10.1186/1477-7517-11-2.

Liu, S. T., Nemeth, J. M., Klein, E. G., Ferketich, A. K., Kwan, M. P., & Wewers, M. E. (2014). Adolescent and adult perceptions of traditional and novel smokeless tobacco products and packaging in rural Ohio. *Tobacco Control, 23*(3), 209-214.
[133] Adkison, S. E., Bansal-Travers, M., Smith, D. M., O'Connor, R. J., & Hyland, A. J. (2014). Impact of smokeless tobacco packaging on perceptions and beliefs among youth, young adults, and adults in the U.S.: Findings from an internet-based cross-sectional survey. *Harm Reduction Journal, 11*, 2. doi:10.1186/1477-7517-11-2.
[134] Popova, L., & Ling, P. M. (2014). Nonsmokers' responses to new warning labels on smokeless tobacco and electronic cigarettes: An experimental study. *BMC Public Health, 14*, 997. doi:10.1186/1471-2458-14-997.
[135] Clarke, T. (2015). *FDA panel votes against label change to Swedish Match snus.* Retrieved from http://www.reuters.com.
Perrone, M. (2015). *FDA experts reject evidence from Swedish company seeking to drop warnings from tobacco snus.* Retrieved from http://www.usnews.com.
Swedish Match. (2014). *Swedish Match submits a Modified Risk Tobacco Product (MRTP) application.* Retrieved from https://www.swedishmatch.com.
Tavernise, S. (2015). *Swedish company asks FDA to remove warnings from smokeless tobacco product.* Retrieved from http://www.nytimes.com.
[136] Swedish Match. (2014). *Swedish Match submits a Modified Risk Tobacco Product (MRTP) application.* Retrieved from https://www.swedishmatch.com/.
[137] Tavernise, S. (2015). *Milder warning opposed for Swedish tobacco item.* Retrieved from http://www.nytimes.com.
[138] Popova, L., & Ling, P. M. (2014). Nonsmokers' responses to new warning labels on smokeless tobacco and electronic cigarettes: An experimental study. *BMC Public Health, 14*, 997. doi:10.1186/1471-2458-14-997.
[139] University of Louisville. (2016). *Bucks for brains.* Retrieved from http://louisville.edu.
University of Louisville. (2005). *Endowed chair in tobacco harm reduction research.* Retrieved from http://louisville.edu.
Glantz, S. (2011). *Two high profile uncritical media stories on industry-supported "harm reduction."* Retrieved from https://tobacco.ucsf.edu.
[140] Lencucha, R., Drope, J., & Labonte, R. (2016). Rhetoric and the law, or the law of rhetoric: How countries oppose novel tobacco control measures at the World Trade Organization. *Social Science and Medicine, 164*, 100-107.
[141] Hammond, D. (2010). "Plain packaging" regulations for tobacco products: The impact of standardizing the color and design of cigarette packs. *Salud Pública de México, 52*(Suppl 2), s226-s232.
[142] Australian Department of Health. (2016). *Introduction of tobacco plain packaging in Australia*. Retrieved from http://www.health.gov.au.
Scollo, M., Lindorff, K., Coomber, K., Bayly, M., & Wakefield, M. (2015). Standardised packaging and new enlarged graphic health warnings for tobacco products in Australia: Legislative requirements and implementation of the Tobacco Plain Packaging Act 2011 and the Competition and Consumer (Tobacco) Information Standard, 2011. *Tobacco Control, 24*, ii9-ii16.
[143] Lencucha, R., Drope, J., & Labonte, R. (2016). Rhetoric and the law, or the law of rhetoric: How countries oppose novel tobacco control measures at the World Trade Organization. *Social Science and Medicine, 164*, 100-107.
[144] Wise, J. (2015). No increase in Australia's illicit tobacco trade after plain packs are introduced. *BMJ, 350*, h1781. doi:10.1136/bmj.h1781.
Nonnemaker, J., Kim, A., Shafer, P., Loomis, B., Hill, E., Holloway, J., et al. (2016). Influence of point-of-sale tobacco displays and plain black and white cigarette packaging and advertisements on adults: Evidence from a virtual store experimental study. *Addictive Behaviors, 56*, 15-22.
Hammond, D., Daniel, S., & White, C. M. (2013). The effect of cigarette branding and plain packaging on female youth in the United Kingdom. *Journal of Adolescent Health, 52*, 151-157.
Thrasher, J. F., Rousu, M. C., Hammond, D., Navarro, A., & Corrigan, J. R. (2011). Estimating the impact of pictorial health warnings and "plain" cigarette packaging: Evidence from experimental auctions among adult smokers in the United States. *Health Policy, 102*, 41-48.
Wakefield, M. A., Hayes, L., Durkin, S., & Borland, R. (2013). Introduction effects of the Australian plain packaging policy on adult smokers: A cross-sectional study. *BMJ Open, 3*(7). doi:10.1136/bmjopen-2013-003175.

[145] Action on Smoking and Health New Zealand. (2016). *Standardised packaging: Latest news: Smoke-free Environments (Tobacco Plain Packaging) Amendment Bill passes second reading.* Retrieved from http://www.ash.org.nz.
[146] Canadian Cancer Society. (2016). *Plain packaging: International overview.* Retrieved from http://www.ash.org.uk.
[147] Action on Smoking and Health New Zealand. (2015). *Plain packaging for tobacco will become the global norm.* Retrieved from http://ash.org.
CSP Magazine. (2015). *Could plain tobacco packaging come to U.S.?* Retrieved from http://www.cspdailynews.com.
[148] Barrington-Trimis, J. L., Berhane, K., Unger, J. B., Cruz, T. B., Huh, J., Leventhal, A. M., et al. (2015). Psychosocial factors associated with adolescent electronic cigarette and cigarette use. *Pediatrics, 136*(2), 308-317.
Choi, K., Fabian, L., Mottey, N., Corbett, A., & Forster, J. (2012). Young adults' favorable perceptions of snus, dissolvable tobacco products, and electronic cigarettes: Findings from a focus group study. *American Journal of Public Health, 102*(11), 2088-2093.
Fielder, R. L., Carey, K. B., & Carey, M. P. (2012). Predictors of initiation of hookah tobacco smoking: A one-year prospective study of first-year college women. *Psychology of Addictive Behaviors, 26*(4), 963-968.
Holman, L. R., Bricker, J. B., & Comstock, B. A. (2013). Psychological predictors of male smokeless tobacco use initiation and cessation: a 16-year longitudinal study. *Addiction, 108*(7), 1327-1335.
Noland, M., Ickes, M. J., Rayens, M. K., Butler, K., Wiggins, A. T., & Hahn, E. J. (2016). Social influences on use of cigarettes, e-cigarettes, and hookah by college students. *Journal of American College Health, 64*(4), 319-328.
Roditis, M., Delucchi, K., Cash, D., & Halpern-Felsher, B. (2016). Adolescents' perceptions of health risks, social risks, and benefits differ across tobacco products. *Journal of Adolescent Health, 58*(5), 558-566.
Smith, M. L., Colwell, B., Forte, C. A., Pulczinski, J. C., & McKyer, E. L. (2014). Psychosocial correlates of smokeless tobacco use among Indiana adolescents. *Journal of Community Health, 40*(2), 208-14.
[149] Miech, R. A., Johnston, L. D., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E. (2016). *Monitoring the Future national survey results on drug use, 1975–2015: Volume I, secondary school students*. Ann Arbor, MI: Institute for Social Research, The University of Michigan.
[150] Johnston, L. D., O'Malley, P. M., Bachman, J. G., Schulenberg, J. E., & Miech, R. A. (2016). *Monitoring the Future national survey results on drug use, 1975–2015: Volume 2, college students and adults ages 19–55*. Ann Arbor, MI: Institute for Social Research, The University of Michigan.
[151] Roditis, M., Delucchi, K., Cash, D., & Halpern-Felsher, B. (2016). Adolescents' perceptions of health risks, social risks, and benefits differ across tobacco products. *Journal of Adolescent Health, 58*(5), 558-566.
[152] Roditis, M., Delucchi, K., Cash, D., & Halpern-Felsher, B. (2016). Adolescents' perceptions of health risks, social risks, and benefits differ across tobacco products. *Journal of Adolescent Health, 58*(5), 558-566.
[153] Noland, M., Ickes, M. J., Rayens, M. K., Butler, K., Wiggins, A. T., & Hahn, E. J. (2016). Social influences on use of cigarettes, e-cigarettes, and hookah by college students. *Journal of American College Health, 64*(4), 319-328.
[154] Amrock, S. M., Gordon, T., Zelikoff, J. T., & Weitzman, M. (2014). Hookah use among adolescents in the United States: Results of a national survey. *Nicotine and Tobacco Research, 16*(2), 231-237.
Braun, R. E., Glassman, T., Wohlwend, J., Whewell, A., & Reindl, D. M. (2012). Hookah use among college students from a Midwest University. *Journal of Community Health, 37*(2), 294-298.
Heinz, A. J., Giedgowd, G. E., Crane, N. A., Veilleux, J. C., Conrad, M., Braun, A. R., et al. (2013). A comprehensive examination of hookah smoking in college students: Use patterns and contexts, social norms and attitudes, harm perception, psychological correlates and co-occurring substance use. *Addictive Behaviors, 38*(11), 2751-2760.
Noland, M., Ickes, M. J., Rayens, M. K., Butler, K., Wiggins, A. T., & Hahn, E. J. (2016). Social influences on use of cigarettes, e-cigarettes, and hookah by college students. *Journal of American College Health, 64*(4), 319-328.
[155] Akl, E. A., Jawad, M., Lam, W. Y., Co, C. N., Obeid, R., & Irani, J. (2013). Motives, beliefs and attitudes towards waterpipe tobacco smoking: A systematic review. *Harm Reduction Journal, 10*, 12.
Braun, R. E., Glassman, T., Wohlwend, J., Whewell, A., & Reindl, D. M. (2012). Hookah use among college students from a Midwest University. *Journal of Community Health, 37*(2), 294-298.
Cornacchione, J., Wagoner, K. G., Wiseman, K. D., Kelley, D., Noar, S. M., Smith, M. H., et al. (2016). Adolescent and young adult perceptions of hookah and little cigars/cigarillos: Implications for risk messages. *Journal of Health Communication, 21*(7), 818-825.
Heinz, A. J., Giedgowd, G. E., Crane, N. A., Veilleux, J. C., Conrad, M., Braun, A. R., et al. (2013). A comprehensive examination of hookah smoking in college students: use patterns and contexts, social norms and

attitudes, harm perception, psychological correlates and co-occurring substance use. *Addictive Behaviors, 38*(11), 2751-2760.
Sharma, E., Clark, P. I., & Sharp, K. E. (2014). Understanding psychosocial aspects of waterpipe smoking among college students. *American Journal of Health Behavior, 38*(3), 440-447.
[156] Amrock, S. M., Gordon, T., Zelikoff, J. T., & Weitzman, M. (2014). Hookah use among adolescents in the United States: Results of a national survey. *Nicotine and Tobacco Research, 16*(2), 231-237.
Barnett, T. E., Smith, T., He, Y., Soule, E. K., Curbow, B. A., Tomar, S. L., et al. (2013). Evidence of emerging hookah use among university students: A cross-sectional comparison between hookah and cigarette use. *BMC Public Health, 13*, 302.
Braun, R. E., Glassman, T., Wohlwend, J., Whewell, A., & Reindl, D. M. (2012). Hookah use among college students from a Midwest University. *Journal of Community Health, 37*(2), 294-298.
Heinz, A. J., Giedgowd, G. E., Crane, N. A., Veilleux, J. C., Conrad, M., Braun, A. R., et al. (2013). A comprehensive examination of hookah smoking in college students: Use patterns and contexts, social norms and attitudes, harm perception, psychological correlates and co-occurring substance use. *Addictive Behaviors, 38*(11), 2751-2760.
[157] Holman, L. R., Bricker, J. B., & Comstock, B. A. (2013). Psychological predictors of male smokeless tobacco use initiation and cessation: A 16-year longitudinal study. *Addiction, 108*(7), 1327-1335.
Smith, M. L., Colwell, B., Forte, C. A., Pulczinski, J. C., & McKyer, E. L. (2014). Psychosocial correlates of smokeless tobacco use among Indiana adolescents. *Journal of Community Health, 40*(2), 208-14.
Tercyak, K. P., & Audrain, J. (2002). Psychosocial correlates of alternate tobacco product use during early adolescence. *Preventive Medicine, 35*(2), 193-198.
[158] Biener, L., Song, E., Sutfin, E. L., Spangler, J., & Wolfson, M. (2015). Electronic cigarette trial and use among young adults: Reasons for trial and cessation of vaping. *International Journal of Environmental Research and Public Health, 12*(12), 16019-16026.
Kong, G., Morean, M. E., Cavallo, D. A., Camenga, D. R., & Krishnan-Sarin, S. (2015). Reasons for electronic cigarette experimentation and discontinuation among adolescents and young adults. *Nicotine and Tobacco Research, 17*(7), 847-854.
Patel, D., Davis, K. C., Cox, S., Bradfield, B., King, B. A., Shafer, P., et al. (2016). Reasons for current E-cigarette use among U.S. adults. *Preventive Medicine, 93*, 14-20.
[159] Barrington-Trimis, J. L., Berhane, K., Unger, J. B., Cruz, T. B., Huh, J., Leventhal, A. M., et al. (2015). Psychosocial factors associated with adolescent electronic cigarette and cigarette use. *Pediatrics, 136*(2), 308-317.
[160] Cardenas, V. M., Breen, P. J., Compadre, C. M., Delongchamp, R. R., Barone, C. P., Phillips, M. M., et al. (2015). The smoking habits of the family influence the uptake of e-cigarettes in U.S. children. *Annals of Epidemiology, 25*(1), 60-62.
Barrington-Trimis, J. L., Berhane, K., Unger, J. B., Cruz, T. B., Huh, J., Leventhal, A. M., et al. (2015). Psychosocial factors associated with adolescent electronic cigarette and cigarette use. *Pediatrics, 136*(2), 308-317.
Haardorfer, R., Berg, C. J., Lewis, M., Payne, J., Pillai, D., McDonald, B., et al. (2016). Polytobacco, marijuana, and alcohol use patterns in college students: A latent class analysis. *Addictive Behaviors, 59*, 58-64.
Zhang, X., & Pu, J. (2016). E-cigarette use among U.S. adolescents: Secondhand smoke at home matters. *International Journal of Public Health, 61*(2), 209-213.
[161] Barrington-Trimis, J. L., Berhane, K., Unger, J. B., Cruz, T. B., Huh, J., Leventhal, A. M., et al. (2015). Psychosocial factors associated with adolescent electronic cigarette and cigarette use. *Pediatrics, 136*(2), 308-317.
Cardenas, V. M., Breen, P. J., Compadre, C. M., Delongchamp, R. R., Barone, C. P., Phillips, M. M., et al. (2015). The smoking habits of the family influence the uptake of e-cigarettes in U.S. children. *Annals of Epidemiology, 25*(1), 60-62.
Hanewinkel, R., & Isensee, B. (2015). Risk factors for e-cigarette, conventional cigarette, and dual use in German adolescents: A cohort study. *Preventive Medicine, 74*, 59-62.
Hughes, K., Bellis, M. A., Hardcastle, K. A., McHale, P., Bennett, A., Ireland, R., et al. (2015). Associations between e-cigarette access and smoking and drinking behaviours in teenagers. *BMC Public Health, 15*, 244.
Pentz, M. A., Shin, H., Riggs, N., Unger, J. B., Collison, K. L., & Chou, C. P. (2015). Parent, peer, and executive function relationships to early adolescent e-cigarette use: A substance use pathway? *Addictive Behaviors, 42C*, 73-78.
Zhang, X., & Pu, J. (2016). E-cigarette use among U.S. adolescents: Secondhand smoke at home matters. *International Journal of Public Health, 61*(2), 209-213.

[162] Amrock, S. M., Gordon, T., Zelikoff, J. T., & Weitzman, M. (2014). Hookah use among adolescents in the United States: Results of a national survey. *Nicotine and Tobacco Research, 16*(2), 231-237.
Jamil, H., Elsouhag, D., Hiller, S., Arnetz, J. E., & Arnetz, B. B. (2010). Sociodemographic risk indicators of hookah smoking among White Americans: A pilot study. *Nicotine and Tobacco Research, 12*(5), 525-529.
[163] Nemeth, J. M., Liu, S. T., Klein, E. G., Ferketich, A. K., Kwan, M. P., & Wewers, M. E. (2012). Factors influencing smokeless tobacco use in rural Ohio Appalachia. *Journal of Community Health, 37*(6), 1208-1217.
[164] Nemeth, J. M., Liu, S. T., Klein, E. G., Ferketich, A. K., Kwan, M. P., & Wewers, M. E. (2012). Factors influencing smokeless tobacco use in rural Ohio Appalachia. *Journal of Community Health, 37*(6), 1208-1217.
[165] Lessard, J., Henrie, J., Livingston, J. A., Leonard, K. E., Colder, C. R., & Eiden, R. D. (2014). Correlates of ever having used electronic cigarettes among older adolescent children of alcoholic fathers. *Nicotine and Tobacco Research, 16*(12), 1656-1660.
Trapl, E. S., Yoder, L. D., Frank, J. L., Borawski, E. A., & Sattar, A. (2016). Individual, parental, and environmental correlates of cigar, cigarillo, and little cigar use among middle school adolescents. *Nicotine and Tobacco Research, 18*(5), 834-841.
[166] Ayers, J. W., Althouse, B. M., Allem, J. P., Leas, E. C., Dredze, M., & Williams, R. S. (2016). Revisiting the rise of electronic nicotine delivery systems using search query surveillance. *American Journal of Preventive Medicine,* 50(6), e173-e181. doi:10.1016/j.amepre.2015.12.008.
Colilla, S. A. (2010). An epidemiologic review of smokeless tobacco health effects and harm reduction potential. *Regulatory Toxicology and Pharmacology, 56*(2), 197-211.
Kaisar, M. A., Prasad, S., Liles, T., & Cucullo, L. (2016). A decade of e-cigarettes: Limited research and unresolved safety concerns. *Toxicology, 365*, 67-75.
Lee, P. N. (2011). Summary of the epidemiological evidence relating snus to health. *Regulatory Toxicology and Pharmacology, 59*(2), 197-214.
Rodu, B., & Jansson, C. (2004). Smokeless tobacco and oral cancer: A review of the risks and determinants. *Critical Reviews in Oral Biology and Medicine, 15*(5), 252-263.
Sponsiello-Wang, Z., Weitkunat, R., & Lee, P. N. (2008). Systematic review of the relation between smokeless tobacco and cancer of the pancreas in Europe and North America. *BMC Cancer, 8*, 356.
[167] Fairchild, A. L., & Bayer, R. (2015). Public health. Smoke and fire over e-cigarettes. *Science, 347*(6220), 375-376.
Kadowaki, J., Vuolo, M., & Kelly, B. C. (2015). A review of the current geographic distribution of and debate surrounding electronic cigarette clean air regulations in the United States. *Health Place, 31*, 75-82.
[168] Chaloupka, F. J., Sweanor, D., & Warner, K. E. (2015). Differential taxes for differential risks: Toward reduced harm from nicotine-yielding products. *New England Journal of Medicine, 373*(7), 594-597.
Fairchild, A. L., & Bayer, R. (2015). Public health. Smoke and fire over e-cigarettes. *Science, 347*(6220), 375-376.
Pesko, M. F., Kenkel, D. S., Wang, H., & Hughes, J. M. (2016). The effect of potential electronic nicotine delivery system regulations on nicotine product selection. *Addiction, 111*(4), 734-744.
[169] Friedman, A. S. (2015). How does electronic cigarette access affect adolescent smoking? *Journal of Health Economics, 44*, 300-308.
Pesko, M. F., Hughes, J. M., & Faisal, F. S. (2016). The influence of electronic cigarette age purchasing restrictions on adolescent tobacco and marijuana use. *Preventive Medicine, 87*, 207-212.
[170] Chaloupka, F. J., Sweanor, D., & Warner, K. E. (2015). Differential taxes for differential risks: Toward reduced harm from nicotine-yielding products. *New England Journal of Medicine, 373*(7), 594-597.
[171] Gorzkowski, J. A., Whitmore, R. M., Kaseeska, K. R., Brishke, J. K., & Klein, J. D. (2016). Pediatrician knowledge, attitudes, and practice related to electronic cigarettes. *Journal of Adolescent Health, 59*(1), 81-86.
[172] Brown-Johnson, C. G., Burbank, A., Daza, E. J., Wassmann, A., Chieng, A., Rutledge, G. W., et al. (2016). Online patient-provider e-cigarette consultations: Perceptions of safety and harm. *American Journal of Preventive Medicine, 51*(6), 882-889.
[173] Pepper, J. K., Gilkey, M. B., & Brewer, N. T. (2015). Physicians' counseling of adolescents regarding e-cigarette use. *Journal of Adolescent Health, 57*(6), 580-586.
[174] Kollath-Cattano, C., Thrasher, J. F., Osman, A., Andrews, J. O., & Strayer, S. M. (2016). Physician advice for e-cigarette use. *Journal of the American Board of Family Medicine, 29*(6), 741-747.
[175] U.S. Preventive Services Task Force. (2015). *Behavioral and pharmacotherapy interventions for tobacco smoking cessation in adults, including pregnant women: Clinical summary.* Retrieved from http://annals.org.

Chapter VI
Notes

[1] CASAColumbia. (2015). *Understanding and addressing nicotine addiction: A science-based approach to policy and practice*. New York: Author.
Richter, L., & Foster, S. E. (2013). The exclusion of nicotine: Closing the gap in addiction policy and practice. *American Journal of Public Health, 103*(8), e14-e16.
[2] U.S. Food and Drug Administration. (2016). *Family Smoking Prevention and Tobacco Control Act: 21 CFR parts 1100, 1140, and 1143.* Retrieved from http://federalregister.gov.
[3] Tobacco Control Legal Consortium. (2016). *State and local tobacco regulation in a post-deeming world*. Saint Paul, MN: Public Health Law Center.
[4] Jenson, D., Lester, J., & Berman, M. L. (2016). FDA's misplaced priorities: Premarket review under the Family Smoking Prevention and Tobacco Control Act. *Tobacco Control, 25*(3), 246-253.
Tobacco Control Legal Consortium. (2016). *The FDA's premarket review of tobacco products fails to fully protect public health*. Saint Paul, MN: Public Health Law Center.
[5] Center for Tobacco Control Research and Education. (2016). *Child resistant packaging of electronic cigarette devices and refill liquid containers containing nicotine to prevent childhood poisoning: Docket No. FDA-2014-N-0189.* Retrieved from https://tobacco.ucsf.edu.
[6] CASAColumbia. (2015). *Understanding and addressing nicotine addiction: A science-based approach to policy and practice*. New York: Author.
Truth Initiative. (2015). *The truth about: Electronic nicotine delivery systems.* Retrieved from http://truthinitiative.org.
[7] Center for Tobacco Control Research and Education. (2016). *FDA should regulate the manufacturing and marketing of hookah tobacco to prevent misperceptions of harm and widespread use among youth and young adults.* Retrieved from https://tobacco.ucsf.edu.
[8] Harrison, T. A., Adams, D. G., Tyler, R. S., Craig, A. W., Moore, J. G., & Havens, J. A. (2016). *House appropriations committee approves new e-cigarette "Grandfather Date": Currently marketed products would be spared.* Retrieved from https://www.venable.com.
[9] Lee, J. G., Boynton, M. H., Richardson, A., Jarman, K., Ranney, L. M., & Goldstein, A. O. (2016). Raising the legal age of tobacco sales: Policy support and trust in government, 2014-2015, U.S. *American Journal of Preventive Medicine, 51*(6), 910-915.
[10] Chaloupka, F. J., Sweanor, D., & Warner, K. E. (2015). Differential taxes for differential risks: Toward reduced harm from nicotine-yielding products. *New England Journal of Medicine, 373*(7), 594-597.
Pesko, M. F., Kenkel, D. S., Wang, H., & Hughes, J. M. (2016). The effect of potential electronic nicotine delivery system regulations on nicotine product selection. *Addiction, 111*(4), 734-744.
Truth Initiative. (2015). *Hookah: Background.* Retrieved from http://truthinitiative.org.
[11] Centers for Disease Control and Prevention. (2014). *Best practices for comprehensive tobacco control programs*: *Cessation interventions.* Retrieved from https://www.cdc.gov.
[12] Farber, H. J., Walley, S. C., Groner, J. A., & Nelson, K. E. (2015). Clinical practice policy to protect children from tobacco, nicotine, and tobacco smoke. *Pediatrics, 136*(5), 1008-1017.
[13] Farber, H. J., Walley, S. C., Groner, J. A., & Nelson, K. E. (2015). Clinical practice policy to protect children from tobacco, nicotine, and tobacco smoke. *Pediatrics, 136*(5), 1008-1017.
Hildick-Smith, G. J., Pesko, M. F., Shearer, L., Hughes, J. M., Chang, J., Loughlin, G. M., et al. (2015). A practitioner's guide to electronic cigarettes in the adolescent population. *Journal of Adolescent Health, 57*(6), 574-579.
U.S. Preventive Services Task Force. (2009). Counseling and interventions to prevent tobacco use and tobacco-caused disease in adults and pregnant women: U.S. Preventive Services Task Force reaffirmation recommendation statement. *Annals of Internal Medicine, 150*(8), 551-555.
[14] U.S. Preventive Services Task Force. (2015). *Behavioral and pharmacotherapy interventions for tobacco smoking cessation in adults, including pregnant women: Clinical summary.* Retrieved from http://annals.org.
[15] U.S. Preventive Services Task Force. (2013). *Tobacco use in children and adolescents: Primary care interventions.* Retrieved from http://www.uspreventiveservicestaskforce.org.
[16] CASAColumbia. (2015). *Understanding and addressing nicotine addiction: A science-based approach to policy and practice*. New York: Author.

Richter, L., Pugh, B. S., Smith, P. H., & Ball, S. A. (2016). The co-occurrence of nicotine and other substance use and addiction among youth and adults in the United States: Implications for research, practice, and policy. *American Journal of Drug and Alcohol Abuse, 43*(2), 132-145.
[17] Campaign for Tobacco-Free Kids. (2016). *How schools can help students stay tobacco-free.* Retrieved from https://www.tobaccofreekids.org.
[18] England, L. J., Bunnell, R. E., Pechacek, T. F., Tong, V. T., & McAfee, T. A. (2015). Nicotine and the developing human: A neglected element in the electronic cigarette debate. *American Journal of Preventive Medicine, 49*(2), 286-293.
Richter, L., & Foster, S. E. (2013). The exclusion of nicotine: Closing the gap in addiction policy and practice. *American Journal of Public Health, 103*(8), e14-e16.
[19] Campaign for Tobacco-Free Kids. (2015). *How parents can protect their kids from becoming addicted smokers.* Retrieved from https://www.tobaccofreekids.org.
[20] Truth Initiative. (2015). *Vaporized: Youth and young adult exposure to e-cigarette marketing* . Washington, DC: Truth Initiative.
[21] Truth Initiative. (2015). *Played: Smoking and video games.* Retrieved from http://truthinitiative.org.
World Health Organization. (2009). *Guidelines for implementation of Article 13 of the WHO Framework Convention on Tobacco Control (Tobacco advertising, promotion and sponsorship).* Retrieved from http://www.who.int.
[22] Etter, J. F. (2015). Explaining the effects of electronic cigarettes on craving for tobacco in recent quitters. *Drug and Alcohol Dependence, 148*, 102-108.
Kaisar, M. A., Prasad, S., Liles, T., & Cucullo, L. (2016). A decade of e-cigarettes: Limited research and unresolved safety concerns. *Toxicology, 365*, 67-75.
[23] Hyland, A., Ambrose, B. K., Conway, K. P., Borek, N., Lambert, E., Carusi, C., et al. (2016). Design and methods of the Population Assessment of Tobacco and Health (PATH) Study. *Tobacco Control*. doi:10.1136/tobaccocontrol-2016-052934.
[24] Heatherton, T. F., Kozlowski, L. T., Frecker, R. C., & Fagerstrom, K. O. (1991). The Fagerstrom test for nicotine dependence: A revision of the Fagerstrom tolerance questionnaire. *British Journal of Addiction, 86*(9), 1119-1127.
[25] De, L. E., Smith, K. C., & Cohen, J. E. (2014). Dependence measures for non-cigarette tobacco products within the context of the global epidemic: A systematic review. *Tobacco Control, 23*(3), 197-203.
Foulds, J., Veldheer, S., Yingst, J., Hrabovsky, S., Wilson, S. J., Nichols, T. T., et al. (2015). Development of a questionnaire for assessing dependence on electronic cigarettes among a large sample of ex-smoking e-cigarette users. *Nicotine and Tobacco Research, 17*(2), 186-192.
Strong, D. R., Messer, K., Hartman, S. J., Conway, K. P., Hoffman, A. C., Pharris-Ciurej, N., et al. (2015). Measurement of multiple nicotine dependence domains among cigarette, non-cigarette and poly-tobacco users: Insights from item response theory. *Drug and Alcohol Dependence, 152*, 185-193.
[26] Fagerstrom, K., & Eissenberg, T. (2012). Dependence on tobacco and nicotine products: A case for product-specific assessment. *Nicotine and Tobacco Research, 14*(11), 1382-1390.
[27] Winden, T. J., Chen, E. S., Wang, Y., Sarkar, I. N., Carter, E. W., & Melton, G. B. (2015). Towards the standardized documentation of e-cigarette use in the electronic health record for population health surveillance and research. *AMIA Joint Summits on Translational Science proceedings, 2015*, 199-203.
[28] Winden, T. J., Chen, E. S., Wang, Y., Sarkar, I. N., Carter, E. W., & Melton, G. B. (2015). Towards the standardized documentation of e-cigarette use in the electronic health record for population health surveillance and research. *AMIA Joint Summits on Translational Science proceedings, 2015*, 199-203.
[29] Cobb, C. O., Hendricks, P. S., & Eissenberg, T. (2015). Electronic cigarettes and nicotine dependence: Evolving products, evolving problems. *BMC Medicine, 13*, 119. doi:10.1186/s12916-015-0355-y.
Grana, R., Benowitz, N., & Glantz, S. A. (2014). E-cigarettes: A scientific review. *Circulation, 129*(19), 1972-1986.
[30] Lempert, L. K., Popova, L., Halpern-Felsher, B., Chaffee, B., Benowitz, N., St. Helen, G., et al. (2016). *Listing of ingredients in tobacco products: Revised guidance for industry (Docket No. FDA-2009-D-0524).* Retrieved from http://www.fda.gov.
[31] Family Smoking Prevention and Tobacco Control Act. 21 U.S.C. §§ 387 - 387u (2011).

Appendix
Notes

[1] Singh, T., Arrazola, R. A., Corey, C. G., Husten, C. G., Neff, L. J., Homa, D. M., et al. (2016). Tobacco use among middle and high school students - United States, 2011-2015. *Morbidity and Mortality Weekly Report, 65*(14), 361-367.
[2] Singh, T., Arrazola, R. A., Corey, C. G., Husten, C. G., Neff, L. J., Homa, D. M., et al. (2016). Tobacco use among middle and high school students - United States, 2011-2015. *Morbidity and Mortality Weekly Report, 65*(14), 361-367.
[3] Hu, S. S., Neff, L., Agaku, I. T., Cox, S., Day, H. R., Holder-Hayes, E., et al. (2016). Tobacco product use among adults - United States, 2013-2014. *Morbidity and Mortality Weekly Report, 65*(27), 686-691.
[4] Singh, T., Arrazola, R. A., Corey, C. G., Husten, C. G., Neff, L. J., Homa, D. M., et al. (2016). Tobacco use among middle and high school students - United States, 2011-2015. *Morbidity and Mortality Weekly Report, 65*(14), 361-367.
[5] Strong, D. R., Messer, K., Hartman, S. J., Conway, K. P., Hoffman, A. C., Pharris-Ciurej, N., et al. (2015). Measurement of multiple nicotine dependence domains among cigarette, non-cigarette and poly-tobacco users: Insights from item response theory. *Drug and Alcohol Dependence, 152*, 185-193.
[6] Strong, D. R., Messer, K., Hartman, S. J., Conway, K. P., Hoffman, A. C., Pharris-Ciurej, N., et al. (2015). Measurement of multiple nicotine dependence domains among cigarette, non-cigarette and poly-tobacco users: Insights from item response theory. *Drug and Alcohol Dependence, 152*, 185-193.

Bibliography

111th Cong. (2010). *Compilation of Patient Protection and Affordable Care Act.* Retrieved from http://housedocs.house.gov.

Action on Smoking and Health New Zealand. (2015). *Plain packaging for tobacco will become the global norm.* Retrieved from http://ash.org.

Action on Smoking and Health New Zealand. (2016). *Standardised packaging: Latest news: Smoke-free Environments (Tobacco Plain Packaging) Amendment Bill passes second reading.* Retrieved from http://www.ash.org.

Adkison, S. E., Bansal-Travers, M., Smith, D. M., O'Connor, R. J., & Hyland, A. J. (2014). Impact of smokeless tobacco packaging on perceptions and beliefs among youth, young adults, and adults in the U.S.: Findings from an internet-based cross-sectional survey. *Harm Reduction Journal, 11*, 2. doi:10.1186/1477-7517-11-2.

Adkison, S. E., O'Connor, R. J., Bansal-Travers, M., Hyland, A., Borland, R., Yong, H. H., et al. (2013). Electronic nicotine delivery systems: International tobacco control four-country survey. *American Journal of Preventive Medicine, 44*(3), 207-215.

Agaku, I. T., King, B. A., Husten, C. G., Bunnell, R., Ambrose, B. K., Hu, S. S., et al. (2014). Tobacco product use among adults - United States, 2012-2013. *Morbidity and Mortality Weekly Report, 63*(25), 542-547.

Akl, E. A., Gaddam, S., Gunukula, S. K., Honeine, R., Jaoude, P. A., & Irani, J. (2010). The effects of waterpipe tobacco smoking on health outcomes: A systematic review. *International Journal of Epidemiology, 39*(3), 834-857.

Akl, E. A., Jawad, M., Lam, W. Y., Co, C. N., Obeid, R., & Irani, J. (2013). Motives, beliefs and attitudes towards waterpipe tobacco smoking: A systematic review. *Harm Reduction Journal*, 10, 12.

Akl, E. A., Ward, K. D., Bteddini, D., Khaliel, R., Alexander, A. C., Lotfi, T., et al. (2015). The allure of the waterpipe: A narrative review of factors affecting the epidemic rise in waterpipe smoking among young persons globally. *Tobacco Control, 24* (Suppl 1), i13-i21.

Al, A. R., Rastam, S., Ibrahim, I., Bazzi, A., Fayad, S., Shihadeh, A. L., et al. (2015). A comparative study of systemic carcinogen exposure in waterpipe smokers, cigarette smokers and non-smokers. *Tobacco Control, 24*(2), 125-127.

Al, R. M., Shihadeh, A., & Saliba, N. A. (2008). Volatile aldehydes in the mainstream smoke of the narghile waterpipe. *Food and Chemical Toxicology, 46*(11), 3546-3549.

Albandar, J. M., Streckfus, C. F., Adesanya, M. R., & Winn, D. M. (2000). Cigar, pipe, and cigarette smoking as risk factors for periodontal disease and tooth loss. *Journal of Periodontology, 71*(12), 1874-1881.

Al-Delaimy, W. K., Myers, M. G., Leas, E. C., Strong, D. R., & Hofstetter, C. R. (2015). E-cigarette use in the past and quitting behavior in the future: A population-based study. *American Journal of Public Health, 105*(6), 1213-1219.

Alguacil, J., & Silverman, D. T. (2004). Smokeless and other noncigarette tobacco use and pancreatic cancer: A case-control study based on direct interviews. *Cancer Epidemiology, Biomarkers and Prevention, 13*(1), 55-58.

Ali, M., Gray, T. R., Martinez, D. J., Curry, L. E., & Horn, K. A. (2016). Risk profiles of youth single, dual, and poly tobacco users. *Nicotine and Tobacco Research, 18*(7), 1614-1621.

Aljarrah, K., Ababneh, Z. Q., & Al-Delaimy, W. K. (2009). Perceptions of hookah smoking harmfulness: Predictors and characteristics among current hookah users. *Tobacco Induced Diseases, 5*(1), 16.

Al-Kazwini, A. T., Said, A. J., & Sdepanian, S. (2015). Compartmental analysis of metals in waterpipe smoking technique. *BMC Public Health, 15*, 153. doi:10.1186/s12889-015-1373-6.

Allen, J. G., Flanigan, S. S., LeBlanc, M., Vallarino, J., MacNaughton, P., Stewart, J. H., et al. (2016). Flavoring chemicals in e-cigarettes: Diacetyl, 2,3-pentanedione, and acetoin in a sample of 51 products, including fruit-, candy-, and cocktail-flavored e-cigarettes. *Environmental Health Perspectives, 124*(6), 733-739.

Altria.com. (2014). *Press release: Altria announces agreement to acquire e-vapor business of Green Smoke, Inc.* Retrieved from http://investor.altria.com.

Ambrose, B. K., Day, H. R., Rostron, B., Conway, K. P., Borek, N., Hyland, A., et al. (2015). Flavored tobacco products use among U.S. youth aged 12-17 years, 2013-2014. *JAMA, 314*(17), 1871-1873.

Ambrose, B. K., Rostron, B. L., Johnson, S. E., Portnoy, D. B., Apelberg, B. J., Kaufman, A. R., et al. (2014). Perceptions of the relative harm of cigarettes and e-cigarettes among U.S. youth. *American Journal of Preventive Medicine, 47*(Suppl 1), S53-S60.

American Cancer Society. (2015). *Is any type of smoking safe?* Retrieved from http://www.cancer.org.

American Lung Association. (2007). *An emerging deadly trend: Waterpipe tobacco use.* Retrieved from http://www.lungusa2.org.

American Lung Association. (2007). *Hookah smoking: A growing threat to public health.* Retrieved from http://www.lung.org.

American Lung Association. (2012). *Cutting tobacco's rural roots: Tobacco use in rural communities*. Washington, DC: American Lung Association National Headquarters.

Americans for Nonsmokers' Rights. (2016). *Overview list: How many smokefree laws?* Retrieved from http://www.no-smoke.org.

Americans for Nonsmokers' Rights. (2016). *States and municipalities with laws regulating use of electronic cigarettes.* Retrieved from http://www.no-smoke.org.

Americans for Nonsmokers' Rights. (2016). *States with any type of preemption of smokefree air laws.* Retrieved from http://no-smoke.org.

Americans for Nonsmokers' Rights. (2016). *The evolving face of preemption: New tactics to limit local control.* Retrieved from http://www.protectlocalcontrol.org.

Americans for Nonsmokers' Rights. (2016). *U.S. 100% smokefree laws in non-hospitality workplaces and restaurants and bars.* Retrieved from http://www.no-smoke.org.

Amrock, S. M., Gordon, T., Zelikoff, J. T., & Weitzman, M. (2014). Hookah use among adolescents in the United States: Results of a national survey. *Nicotine and Tobacco Research, 16*(2), 231-237.

Amrock, S. M., Lee, L., & Weitzman, M. (2016). Perceptions of e-cigarettes and noncigarette tobacco products among U.S. youth. *Pediatrics, 138*(5), 1-10.

Anderson, S. J. (2011). Menthol cigarettes and smoking cessation behaviour: A review of tobacco industry documents. *Tobacco Control, 20*(Suppl 2), ii49-ii56.

Antoniewicz, L., Bosson, J. A., Kuhl, J., Abdel-Halim, S. M., Kiessling, A., Mobarrez, F., et al. (2016). Electronic cigarettes increase endothelial progenitor cells in the blood of healthy volunteers. *Atherosclerosis, 255*, 179-185.

Apollonio, D. E., & Glantz, S. A. (2016). Minimum ages of legal access for tobacco in the United States from 1863 to 2015. *American Journal of Public Health, 106*(7), 1200-1207.

Armitage, A. K., & Turner, D. M. (1970). Absorption of nicotine in cigarette and cigar smoke through the oral mucosa. *Nature, 226*(5252), 1231-1232.

Armitage, A. K., Dollery, C. T., Houseman, T. H., Kohner, E. M., Lewis, P. J., & Turner, D. M. (1977). Absorption of nicotine by man during cigar smoking [proceedings]. *British Journal of Pharmacology, 59*(3), 493P.

Arnett, J. J. (2000). Emerging adulthood. A theory of development from the late teens through the twenties. *American Psychologist, 55*(5), 469-480.

Aslam, H. M., Saleem, S., German, S., & Qureshi, W. A. (2014). Harmful effects of shisha: Literature review. *International Archives of Medicine, 7*, 16. doi:10.1186/1755-7682-7-16.

Asplund, K. (2003). Smokeless tobacco and cardiovascular disease. *Progress in Cardiovascular Diseases, 45*(5), 383-394.

Audrain-McGovern, J., Strasser, A. A., & Wileyto, E. P. (2016). The impact of flavoring on the rewarding and reinforcing value of e-cigarettes with nicotine among young adult smokers. *Drug and Alcohol Dependence, 166*, 263-267.

Australian Department of Health. (2016). *Introduction of tobacco plain packaging in Australia.* Retrieved from http://www.health.gov.au.

Ayers, J. W., Althouse, B. M., Allem, J. P., Leas, E. C., Dredze, M., & Williams, R. S. (2016). Revisiting the rise of electronic nicotine delivery systems using search query surveillance. *American Journal of Preventive Medicine,* 50(6), e173-e181. doi:10.1016/j.amepre.2015.12.008.

Bahl, V., Lin, S., Xu, N., Davis, B., Wang, Y. H., & Talbot, P. (2012). Comparison of electronic cigarette refill fluid cytotoxicity using embryonic and adult models. *Reproductive Toxicology, 34*(4), 529-537.

Bahreinifar, S., Sheon, N. M., & Ling, P. M. (2013). Is snus the same as dip? Smokers' perceptions of new smokeless tobacco advertising. *Tobacco Control, 22*(2), 84-90.

Baker, F., Ainsworth, S. R., Dye, J. T., Crammer, C., Thun, M. J., Hoffmann, D., et al. (2000). Health risks associated with cigar smoking. *JAMA, 284*(6), 735-740.

Bansal-Travers, M., Hammond, D., Smith, P., & Cummings, K. M. (2011). The impact of cigarette pack design, descriptors, and warning labels on risk perception in the U.S. *American Journal of Preventive Medicine, 40*(6), 674-682.

Barnett, T. E., Smith, T., He, Y., Soule, E. K., Curbow, B. A., Tomar, S. L., et al. (2013). Evidence of emerging hookah use among university students: A cross-sectional comparison between hookah and cigarette use. *BMC Public Health, 13*, 302. doi:1471-2458-13-302.

Barrington-Trimis, J. L., Berhane, K., Unger, J. B., Cruz, T. B., Huh, J., Leventhal, A. M., et al. (2015). Psychosocial factors associated with adolescent electronic cigarette and cigarette use. *Pediatrics, 136*(2), 308-317.

Barrington-Trimis, J. L., Berhane, K., Unger, J. B., Cruz, T. B., Urman, R., Chou, C. P., et al. (2016). The e-cigarette social environment, e-cigarette use, and susceptibility to cigarette smoking. *Journal of Adolescent Health, 59*(1), 75-80.

Barrington-Trimis, J. L., Urman, R., Berhane, K., Unger, J. B., Cruz, T. B., Pentz, M. A., et al. (2016). E-cigarettes and future cigarette use. *Pediatrics, 138*(1), e20160379. doi:10.1542/peds.2016-0379.

Basch, C. H., Mongiovi, J., Hillyer, G. C., MacDonald, Z., & Basch, C. E. (2016). YouTube videos related to e-cigarette safety and related health risks: Implications for preventing and emerging epidemic. *Public Health, 132*, 57-59. doi:10.1016/j.puhe.2015.12.003.

Beard, E., West, R., Michie, S., & Brown, J. (2016). Association between electronic cigarette use and changes in quit attempts, success of quit attempts, use of smoking cessation pharmacotherapy, and use of stop smoking services in England: Time series analysis of population trends. *BMJ, 354*. doi:10.1136/bmj.i4645.

Behar, R. Z., Davis, B., Wang, Y., Bahl, V., Lin, S., & Talbot, P. (2014). Identification of toxicants in cinnamon-flavored electronic cigarette refill fluids. *Toxicology in Vitro, 28*(2), 198-208.

Behar, R. Z., Hua, M., & Talbot, P. (2015). Puffing topography and nicotine intake of electronic cigarette users. *PLoS One, 10*(2). doi:10.1371/journal.pone.0117222.

Bekki, K., Uchiyama, S., Ohta, K., Inaba, Y., Nakagome, H., & Kunugita, N. (2014). Carbonyl compounds generated from electronic cigarettes. *International Journal of Environmental Research and Public Health, 11*(11), 11192-11200.

Benowitz, N. L. (2009). Pharmacology of nicotine: Addiction, smoking-induced disease, and therapeutics. *Annual Review of Pharmacology and Toxicology, 49*, 57-71.

Benowitz, N. L. (2010). Nicotine addiction. *New England Journal of Medicine, 362*(24), 2295-2303.

Benowitz, N. L., & Burbank, A. D. (2016). Cardiovascular toxicity of nicotine: Implications for electronic cigarette use. *Trends in Cardiovascular Medicine, 26*(6), 515-523.

Berg, C. J., Haardoerfer, R., Escoffery, C., Zheng, P., & Kegler, M. (2014). Cigarette users' interest in using or switching to electronic nicotine delivery systems or smokeless tobacco for harm reduction, cessation, or novelty: A cross-sectional survey of U.S. adults. *Nicotine and Tobacco Research,17*(2), 245-55.

Berg, C. J., Stratton, E., Schauer, G. L., Lewis, M., Wang, Y., Windle, M., et al. (2015). Perceived harm, addictiveness, and social acceptability of tobacco products and marijuana among young adults: Marijuana, hookah, and electronic cigarettes win. *Substance Use and Misuse, 50*(1), 79-89.

Bertholon, J. F., Becquemin, M. H., Annesi-Maesano, I., & Dautzenberg, B. (2013). Electronic cigarettes: A short review. *Respiration, 86*(5), 433-438.

Bertuccio, P., La, V. C., Silverman, D. T., Petersen, G. M., Bracci, P. M., Negri, E., et al. (2011). Cigar and pipe smoking, smokeless tobacco use and pancreatic cancer: An analysis from the International Pancreatic Cancer Case-Control Consortium (PanC4). *Annals of Oncology, 22*(6), 1420-1426.

Biener, L., & Hargraves, J. L. (2015). A longitudinal study of electronic cigarette use among a population-based sample of adult smokers: Association with smoking cessation and motivation to quit. *Nicotine and Tobacco Research, 17*(2), 127-133.

Biener, L., Song, E., Sutfin, E. L., Spangler, J., & Wolfson, M. (2015). Electronic cigarette trial and use among young adults: Reasons for trial and cessation of vaping. *International Journal of Environmental Research and Public Health, 12*(12), 16019-16026.

Bjartveit, K., & Tverdal, A. (2005). Health consequences of smoking 1-4 cigarettes per day. *Tobacco Control, 14*(5), 315-320.

Blank, M. D., Cobb, C. O., Kilgalen, B., Austin, J., Weaver, M. F., Shihadeh, A., et al. (2011). Acute effects of waterpipe tobacco smoking: A double-blind, placebo-control study. *Drug and Alcohol Dependence, 116*(1-3), 102-109.

Boffetta, P., Aagnes, B., Weiderpass, E., & Andersen, A. (2005). Smokeless tobacco use and risk of cancer of the pancreas and other organs. *International Journal of Cancer, 114*(6), 992-995.

Boffetta, P., Hecht, S., Gray, N., Gupta, P., & Straif, K. (2008). Smokeless tobacco and cancer. *Lancet Oncology, 9*(7), 667-675.

Boffetta, P., & Straif, K. (2009). Use of smokeless tobacco and risk of myocardial infarction and stroke: Systematic review with meta-analysis. *BMJ, 339*, b3060.

Bogdanovica, I., Szatkowski, L., McNeill, A., Spanopoulos, D., & Britton, J. (2015). Exposure to point-of-sale displays and changes in susceptibility to smoking: Findings from a cohort study of school students. *Addiction, 110*(4), 693-702.

Bonhomme, M. G., Holder-Hayes, E., Ambrose, B. K., Tworek, C., Feirman, S. P., King, B. A., et al. (2016). Flavoured non-cigarette tobacco product use among U.S. adults: 2013-2014. *Tobacco Control, 25*(Suppl 2), ii4-ii13.

Borgerding, M. F., Bodnar, J. A., Curtin, G. M., & Swauger, J. E. (2012). The chemical composition of smokeless tobacco: A survey of products sold in the United States in 2006 and 2007. *Regulatory Toxicology and Pharmacology, 64*(3), 367-387.

Bostean, G., Trinidad, D. R., & McCarthy, W. J. (2015). E-cigarette use among never-smoking California students. *American Journal of Public Health, 105*(12), 2423-2425.

Braun, R. E., Glassman, T., Wohlwend, J., Whewell, A., & Reindl, D. M. (2012). Hookah use among college students from a Midwest University. *Journal of Community Health, 37*(2), 294-298.

Breland, A. B., Spindle, T., Weaver, M., & Eissenberg, T. (2014). Science and electronic cigarettes: Current data, future needs. *Journal of Addiction Medicine, 8*(4), 223-233.

Breuss, J. M., Froehlich, J. F., Steurer, S., Kaun, C., Binder, B. R., Huber, K., et al. (2004). Inhibition of smooth muscle cell migration by eptifibatide in vitro. Eptifibatide inhibits localization of integrin - Subunit to focal adhesions. *Poster Abstracts: Cardiovascular Pathology, 13*, s80-s138.

Brose, L. S., Hitchman, S. C., Brown, J., West, R., & McNeill, A. (2015). Is the use of electronic cigarettes while smoking associated with smoking cessation attempts, cessation and reduced cigarette consumption? A survey with a 1-year follow-up. *Addiction, 110*(7), 1160-1168.

Brown, C. J., & Cheng, J. M. (2014). Electronic cigarettes: Product characterisation and design considerations. *Tobacco Control, 23*(Suppl 2), ii4-10.

Brown-Johnson, C. G., Burbank, A., Daza, E. J., Wassmann, A., Chieng, A., Rutledge, G. W., et al. (2016). Online patient-provider e-cigarette consultations: Perceptions of safety and harm. *American Journal of Preventive Medicine, 51*(6), 882-889.

Brownson, E. G., Thompson, C. M., Goldsberry, S., Chong, H. J., Friedrich, J. B., Pham, T. N., et al. (2016). Explosion injuries from e-cigarettes. *New England Journal of Medicine, 375*(14), 1400-1402.

Brunnemann, K. D., Qi, J., & Hoffmann, D. (2002). Chemical profile of two types of oral snuff tobacco. *Food and Chemical Toxicology, 40*(11), 1699-1703.

Bullen, C. (2014). Electronic cigarettes for smoking cessation. *Current Cardiology Reports, 16*(11), 538.

Bullen, C., Howe, C., Laugesen, M., McRobbie, H., Parag, V., Williman, J., et al. (2013). Electronic cigarettes for smoking cessation: A randomised controlled trial. *Lancet, 382*(9905), 1629-1637.

Bunnell, R. E., Agaku, I. T., Arrazola, R. A., Apelberg, B. J., Caraballo, R. S., Corey, C. G., et al. (2015). Intentions to smoke cigarettes among never-smoking U.S. middle and high school electronic cigarette users: National Youth Tobacco Survey, 2011-2013. *Nicotine and Tobacco Research, 17*(2), 228-235.

Burkey, M. D., Feirman, S., Wang, H., Choudhury, S. R., Grover, S., & Johnston, F. M. (2014). The association between smokeless tobacco use and pancreatic adenocarcinoma: A systematic review. *Cancer Epidemiology, 38*(6), 647-653.

Burstyn, I. (2014). Peering through the mist: Systematic review of what the chemistry of contaminants in electronic cigarettes tells us about health risks. *BMC Public Health, 14*, 18. doi:10.1186/1471-2458-14-18.

Callahan-Lyon, P. (2014). Electronic cigarettes: Human health effects. *Tobacco Control, 23*(Suppl 2), ii36-ii40.

Camenga, D. R., Kong, G., Cavallo, D. A., Liss, A., Hyland, A., Delmerico, J., et al. (2014). Alternate tobacco product and drug use among adolescents who use electronic cigarettes, cigarettes only, and never smokers. *Journal of Adolescent Health, 55*(4), 588-591.

Campaign for Tobacco-Free Kids. (2015). *How parents can protect their kids from becoming addicted smokers.* Retrieved from https://www.tobaccofreekids.org.

Campaign for Tobacco-Free Kids. (2016). *How schools can help students stay tobacco-free.* Retrieved from https://www.tobaccofreekids.org.

Campaign for Tobacco-Free Kids. (2016). *State excise tax rates for non-cigarette tobacco products.* Retrieved from http://www.tobaccofreekids.org.

Campaign for Tobacco-Free Kids. (2016). *States and localities that have raised the minimum legal sale age for tobacco products to 21.* Retrieved from http://www.tobaccofreekids.org.

Canadian Cancer Society. (2016). *Plain packaging: International overview.* Retrieved from http://www.ash.org.uk.

Cantrell, F. L. (2014). Adverse effects of e-cigarette exposures. *Journal of Community Health, 39*(3), 614-616.

Cantrell, J., Anesetti-Rothermel, A., Pearson, J. L., Xiao, H., Vallone, D., & Kirchner, T. R. (2015). The impact of the tobacco retail outlet environment on adult cessation and differences by neighborhood poverty. *Addiction, 110*(1), 152-161.

Cantrell, J., Pearson, J. L., Anesetti-Rothermel, A., Xiao, H., Kirchner, T. R., & Vallone, D. (2016). Tobacco retail outlet density and young adult tobacco initiation. *Nicotine and Tobacco Research, 18*(2), 130-137.

Caraballo, R. S., Novak, S. P., & Asman, K. (2009). Linking quantity and frequency profiles of cigarette smoking to the presence of nicotine dependence symptoms among adolescent smokers: Findings from the 2004 National Youth Tobacco Survey. *Nicotine and Tobacco Research, 11*(1), 49-57.

Cardenas, V. M., Breen, P. J., Compadre, C. M., Delongchamp, R. R., Barone, C. P., Phillips, M. M., et al. (2015). The smoking habits of the family influence the uptake of e-cigarettes in U.S. children. *Annals of Epidemiology, 25*(1), 60-62.

Carnevale, R., Sciarretta, S., Violi, F., Nocella, C., Loffredo, L., Perri, L., et al. (2016). Acute impact of tobacco versus electronic cigarette smoking on oxidative stress and vascular function. *Chest, 150*(3), 606-612.

Carroll Chapman, S. L., & Wu, L. T. (2014). E-cigarette prevalence and correlates of use among adolescents versus adults: A review and comparison. *Journal of Psychiatric Research, 54*, 43-54.

Carstensen, J. M., Pershagen, G., & Eklund, G. (1987). Mortality in relation to cigarette and pipe smoking: 16 years' observation of 25,000 Swedish men. *Journal of Epidemiology and Community Health, 41*(2), 166-172.

CASAColumbia. (2011). *Adolescent substance use: America's #1 public health problem*. New York: Author.

CASAColumbia. (2012). *Addiction medicine: Closing the gap between science and practice*. New York: Author.

CASAColumbia. (2014). *Time to ban menthol*. New York: Author.

CASAColumbia. (2015). U*nderstanding and addressing nicotine addiction: A science-based approach to policy and practice*. New York: Author.

Castleden, C. M., & Cole, P. V. (1973). Inhalation of tobacco smoke by pipe and cigar smokers. *Lancet, 2*(7819), 21-22.

Center for Responsive Politics. (2016). *Industry profile: Summary, 2015.* Retrieved from https://www.opensecrets.org.

Center for Tobacco Control Research and Education. (2016). *Child resistant packaging of electronic cigarette devices and refill liquid containers containing nicotine to prevent childhood poisoning* (Docket No. FDA-2014-N-0189). Retrieved from https://tobacco.ucsf.edu.

Center for Tobacco Control Research and Education. (2016). *FDA should regulate the manufacturing and marketing of hookah tobacco to prevent misperceptions of harm and widespread use among youth and young adults.* Retrieved from https://tobacco.ucsf.edu.

Center for Tobacco Control Research and Education. (2016). *Tobacco product standard for N-nitrosonornicotine level in finished smokeless tobacco products [Docket No. FDA-2016-N-2527]*. Retrieved from http://tobacco.ucsf.edu.

Centers for Disease Control and Prevention. (2013). *Electronic cigarette use among middle and high school students - United States, 2011-2012.* Retrieved from https://www.cdc.gov.

Centers for Disease Control and Prevention. (2013). *The Federal Cigarette Labeling and Advertising Act (FCLAA) and Comprehensive Smokeless Tobacco Health Education Act (CSTHEA).* Retrieved from http://www.cdc.gov.

Centers for Disease Control and Prevention. (2013). *Tobacco ingredient and nicotine reporting.* Retrieved from http://www.cdc.gov.

Centers for Disease Control and Prevention. (2014). *Best practices for comprehensive tobacco control programs*: *Cessation interventions.* Retrieved from https://www.cdc.gov.

Centers for Disease Control and Prevention. (2015). *E-cigarettes: An emerging public health challenge.* Retrieved from https://www.cdc.gov.

Centers for Disease Control and Prevention. (2015). *Hookahs.* Retrieved from http://www.cdc.gov.

Centers for Disease Control and Prevention. (2015). *NNAL (4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol)* . Retrieved from https://www.cdc.gov.

Centers for Disease Control and Prevention. (2016). *Cigars.* Retrieved from http://www.cdc.gov.

Centers for Disease Control and Prevention. (2016). *Selected actions of the U.S. government regarding the regulation of tobacco sales, marketing, and use.* Retrieved from http://www.cdc.gov.

Centers for Disease Control and Prevention. (2016). *Smokeless tobacco: Products and marketing.* Retrieved from https://www.cdc.gov.

Centers for Disease Control and Prevention. (2016). *Trends in current cigarette smoking by high school students and adults: United States, 1965-2014.* Retrieved from http://www.cdc.gov.

Centers for Medicare & Medicaid Services. (2016). *Medicaid incentives for the prevention of chronic diseases model.* Retrieved from https://innovation.cms.gov.

Centers for Medicare & Medicaid Services. (2016). *The Center for Consumer Information and Insurance Oversight: Market rating reforms: State specific rating variations.* Retrieved from http://www.cms.gov.

Chaloupka, F. J. (2015). *Taxing e-cigarettes: Options and potential public health impact.* Retrieved from http://www.trdrp.org/files/e-cigarettes/frank-e-cigs.pdf.

Chaloupka, F. J., Sweanor, D., & Warner, K. E. (2015). Differential taxes for differential risks: Toward reduced harm from nicotine-yielding products. *New England Journal of Medicine, 373*(7), 594-597.

Chaloupka, F. J., Warner, K. E., Acemoglu, D., Gruber, J., Laux, F., Max, W., et al. (2015). An evaluation of the FDA's analysis of the costs and benefits of the graphic warning label regulation. *Tobacco Control, 24*(2), 112-119.

Chang, C. M., Corey, C. G., Rostron, B. L., & Apelberg, B. J. (2015). Systematic review of cigar smoking and all cause and smoking related mortality. *BMC Public Health, 15*, 390. doi:10.1186/s12889-015-1617-5.

Chatham-Stephens, K., Law, R., Taylor, E., Melstrom, P., Bunnell, R., Wang, B., et al. (2014). Notes from the field: Calls to poison centers for exposures to electronic cigarettes - United States, September 2010-February 2014. *Morbidity and Mortality Weekly Report, 63*(13), 292-293.

Chen, C., Zhuang, Y. L., & Zhu, S. H. (2016). E-Cigarette design preference and smoking cessation: A U.S. population study. *American Journal of Preventive Medicine, 51*(3), 356-363.

Cheng, T. (2014). Chemical evaluation of electronic cigarettes. *Tobacco Control, 23*(Suppl 2), ii11-ii17.

Chernyavsky, A. I., Shchepotin, I. B., Galitovkiy, V., & Grando, S. A. (2015). Mechanisms of tumor-promoting activities of nicotine in lung cancer: Synergistic effects of cell membrane and mitochondrial nicotinic acetylcholine receptors. *BMC Cancer, 15*, 152. doi:10.1186/s12885-015-1158-4.

Choi, K., Fabian, L., Mottey, N., Corbett, A., & Forster, J. (2012). Young adults' favorable perceptions of snus, dissolvable tobacco products, and electronic cigarettes: Findings from a focus group study. *American Journal of Public Health, 102*(11), 2088-2093.

Choi, K., Grana, R., & Bernat, D. (2017). Electronic nicotine delivery systems and acceptability of adult smoking among Florida youth: Renormalization of smoking? *Journal of Adolescent Health.* doi:10.1016/j.jadohealth.2016.12.001.

Chu, K. H., Unger, J. B., Allem, J. P., Pattarroyo, M., Soto, D., Cruz, T. B., et al. (2015). Diffusion of messages from an electronic cigarette brand to potential users through Twitter. *PLoS One, 10*(12), doi.org/10.1371/journal.pone.0145387.

Clarke, T. (2015). *FDA panel votes against label change to Swedish Match snus.* Retrieved from http://www.reuters.com.

CNN. (2011). *Tobacco companies sue to thwart federal panel, claiming bias.* Retrieved from http://www.cnn.com.

Cobb, C. O., Hendricks, P. S., & Eissenberg, T. (2015). Electronic cigarettes and nicotine dependence: Evolving products, evolving problems. *BMC Medicine, 13*, 119. doi:10.1186/s12916-015-0355-y.

Cobb, C. O., Shihadeh, A., Weaver, M. F., & Eissenberg, T. (2011). Waterpipe tobacco smoking and cigarette smoking: A direct comparison of toxicant exposure and subjective effects. *Nicotine and Tobacco Research, 13*(2), 78-87.

Cobb, C. O., Vansickel, A. R., Blank, M. D., Jentink, K., Travers, M. J., & Eissenberg, T. (2013). Indoor air quality in Virginia waterpipe cafes. *Tobacco Control, 22*(5), 338-343.

Cohn, A., Cobb, C. O., Niaura, R. S., & Richardson, A. (2015). The other combustible products: Prevalence and correlates of little cigar/cigarillo use among cigarette smokers. *Nicotine and Tobacco Research, 17*(12), 1473-1481.

Colaianni, C. A., Tapias, L. F., Cauley, R., Sheridan, R., Schulz, J. T., & Goverman, J. (2016). Injuries caused by explosion of electronic cigarette devices. *Eplasty, 16*, ic9.

Coleman, B. N., Apelberg, B. J., Ambrose, B. K., Green, K. M., Choiniere, C. J., Bunnell, R., et al. (2014). Association between electronic cigarette use and openness to cigarette smoking among U.S. young adults. *Nicotine and Tobacco Research, 17*(2), 212-218.

Coleman, B. N., Johnson, S. E., Tessman, G. K., Tworek, C., Alexander, J., Dickinson, D. M., et al. (2016). "It's not smoke. It's not tar. It's not 4000 chemicals. Case closed": Exploring attitudes, beliefs, and perceived social norms of e-cigarette use among adult users. *Drug and Alcohol Dependence, 159*, 80-85.

Colilla, S. A. (2010). An epidemiologic review of smokeless tobacco health effects and harm reduction potential. *Regulatory Toxicology and Pharmacology, 56*(2), 197-211.

Complaint, American Academy of Pediatrics v. FDA, No. 16-cv-11985 (D. Mass. filed Oct. 4, 2016). (2016). Available at http://www.acscan.org.

Cooper, M., Harrell, M. B., Perez, A., Delk, J., & Perry, C. L. (2016). Flavorings and perceived harm and addictiveness of e-cigarettes among youth. *Tobacco Regulatory Science, 2*(3), 278-289.

Corey, C. G., Ambrose, B. K., Apelberg, B. J., & King, B. A. (2015). Flavored tobacco product use among middle and high school students - United States, 2014. *Morbidity and Mortality Weekly Report, 64*(38), 1066-1070.

Cornacchione, J., Wagoner, K. G., Wiseman, K. D., Kelley, D., Noar, S. M., Smith, M. H., et al. (2016). Adolescent and young adult perceptions of hookah and little cigars/cigarillos: Implications for risk messages. *Journal of Health Communication, 21*(7), 818-825.

Costigan, S., & Meredith, C. (2015). An approach to ingredient screening and toxicological risk assessment of flavours in e-liquids. *Regulatory Toxicology and Pharmacology, 72*(2), 361-369.

Courtemanche, C. J., Palmer, M. K., & Pesko, M. F. (2016). Influence of the flavored cigarette ban on adolescent tobacco use. *American Journal of Preventive Medicine*. doi:10.1016/j.amepre.2016.11.019.

Cox, E., Barry, R. A., & Glantz, S. (2016). E-cigarette policymaking by local and state governments: 2009-2014. *Milbank Quarterly, 94*(3), 520-596.

Creamer, M. R., Portillo, G. V., Clendennen, S. L., & Perry, C. L. (2016). Is adolescent poly-tobacco use associated with alcohol and other drug use? *American Journal of Health Behaviors, 40*(1), 117-122.

Cross, S. J., Lotfipour, S., & Leslie, F. M. (2017). Mechanisms and genetic factors underlying co-use of nicotine and alcohol or other drugs of abuse. *American Journal of Drug and Alcohol Abuse*. doi:10.1080/00952990.2016.1209512.

CSP Magazine. (2015). *Could plain tobacco packaging come to U.S.?* Retrieved from http://www.cspdailynews.com.

Cummins, S. E., Zhu, S. H., Tedeschi, G. J., Gamst, A. C., & Myers, M. G. (2014). Use of e-cigarettes by individuals with mental health conditions. *Tobacco Control, 23*(Suppl 3), iii48-iii53.

Daher, N., Saleh, R., Jaroudi, E., Sheheitli, H., Badr, T., Sepetdjian, E., et al. (2010). Comparison of carcinogen, carbon monoxide, and ultrafine particle emissions from narghile waterpipe and cigarette smoking: Sidestream smoke measurements and assessment of second-hand smoke emission factors. *Atmospheric Environment (1994), 44*(1), 8-14.

Dani, J. A., Kosten, T. R., & Benowitz, N. L. (2014). The pharmacology of nicotine and tobacco. In C. A. Cavacuiti (Ed.), *Principles of addiction medicine: The essentials.* (pp. 55-59). Philadelphia, PA: Lippincott Williams & Wilkins.

Dasgupta, P., Rizwani, W., Pillai, S., Kinkade, R., Kovacs, M., Rastogi, S., et al. (2009). Nicotine induces cell proliferation, invasion and epithelial-mesenchymal transition in a variety of human cancer cell lines. *International Journal of Cancer, 124*(1), 36-45.

Dawkins, L., & Corcoran, O. (2014). Acute electronic cigarette use: Nicotine delivery and subjective effects in regular users. *Psychopharmacology, 231*(2), 401-407.

De, L. E., Smith, K. C., & Cohen, J. E. (2014). Dependence measures for non-cigarette tobacco products within the context of the global epidemic: A systematic review. *Tobacco Control, 23*(3), 197-203.

Delnevo, C. D. (2006). Smokers' choice: What explains the steady growth of cigar use in the U.S.? *Public Health Reports, 121*(2), 116-119.

Delnevo, C. D., Giovenco, D. P., Ambrose, B. K., Corey, C. G., & Conway, K. P. (2014). Preference for flavoured cigar brands among youth, young adults and adults in the USA. *Tobacco Control, 24*(4), 389-394.

Delnevo, C. D., & Hrywna, M. (2007). "A whole 'nother smoke" or a cigarette in disguise: How RJ Reynolds reframed the image of little cigars. *American Journal of Public Health, 97*(8), 1368-1375.

Dierker, L., Swendsen, J., Rose, J., He, J., & Merikangas, K. (2012). Transitions to regular smoking and nicotine dependence in the Adolescent National Comorbidity Survey (NCS-A). *Annals of Behavioral Medicine, 43*(3), 394-401.

DiFranza, J. R. (2015). A 2015 update on the natural history and diagnosis of nicotine addiction. *Current Pediatric Reviews, 11*(1), 43-55.

DiFranza, J. R., Rigotti, N. A., McNeill, A. D., Ockene, J. K., Savageau, J. A., St, C. D., et al. (2000). Initial symptoms of nicotine dependence in adolescents. *Tobacco Control, 9*(3), 313-319.

DiFranza, J. R., Sweet, M., Savageau, J. A., & Ursprung, W. W. (2012). The assessment of tobacco dependence in young users of smokeless tobacco. *Tobacco Control, 21*(5), 471-476.

Dinakar, C., & O'Connor, G. T. (2016). The health effects of electronic cigarettes. *New England Journal of Medicine, 375*(14), 1372-1381.

Drenkard, S. (2016). *Vapor products and tax policy.* Retrieved from http://taxfoundation.org.

D'Souza, M. S., & Markou, A. (2013). The "stop" and "go" of nicotine dependence: Role of GABA and glutamate. *Cold Spring Harbor Perspectives in Medicine, 3*(6). doi:10.1101/cshperspect.a012146.

Duke, J. C., Allen, J. A., Eggers, M. E., Nonnemaker, J., & Farrelly, M. C. (2016). Exploring differences in youth perceptions of the effectiveness of electronic cigarette television advertisements. *Nicotine and Tobacco Research, 18*(5), 1382-1386.

Dunbar, M. S., Shadel, W. G., Tucker, J. S., & Edelen, M. O. (2016). Use of and reasons for using multiple other tobacco products in daily and nondaily smokers: Associations with cigarette consumption and nicotine dependence. *Drug and Alcohol Dependence, 168*, 156-163.

Dunbar, M. S., Tucker, J. S., Ewing, B. A., Pedersen, E. R., Miles, J. N., Shih, R. A., et al. (2016). Frequency of e-cigarette use, health status, and risk and protective health behaviors in adolescents. *Journal of Addiction Medicine, 11*(1), 55-62.

Dutra, L. M., & Glantz, S. A. (2014). Electronic cigarettes and conventional cigarette use among U.S. adolescents: A cross-sectional study. *JAMA Pediatrics, 168*(7), 610-617.

Dutra, L. M., & Glantz, S. A. (2017). E-cigarettes and national adolescent cigarette use: 2004-2014. *Pediatrics, 139*(2), e20162450. doi:10.1542/peds.2016-2450.

Dwyer, J. B., McQuown, S. C., & Leslie, F. M. (2009). The dynamic effects of nicotine on the developing brain. *Pharmacology and Therapeutics, 122*(2), 125-139.

Eissenberg, T., & Shihadeh, A. (2009). Waterpipe tobacco and cigarette smoking: Direct comparison of toxicant exposure. *American Journal of Preventive Medicine, 37*(6), 518-523.

El-Hellani, A., El-Hage, R., Baalbaki, R., Salman, R., Talih, S., Shihadeh, A., et al. (2015). Free-base and protonated nicotine in electronic cigarette liquids and aerosols. *Chemical Research in Toxicology, 28*(8), 1532-1537.

El-Zaatari, Z. M., Chami, H. A., & Zaatari, G. S. (2015). Health effects associated with waterpipe smoking. *Tobacco Control, 24* (Suppl 1), i31-i43.

Emanual, L. (2014). *When did your state adopt its cigarette tax?* Retrieved from http://taxfoundation.org.

England, L. J., Aagaard, K., Bloch, M., Conway, K., Cosgrove, K., Grana, R., et al. (2017). Developmental toxicity of nicotine: A transdisciplinary synthesis and implications for emerging tobacco products. *Neuroscience and Biobehavioral Reviews, 72*, 176-189.

England, L. J., Bunnell, R. E., Pechacek, T. F., Tong, V. T., & McAfee, T. A. (2015). Nicotine and the developing human: A neglected element in the electronic cigarette debate. *American Journal of Preventive Medicine, 49*(2), 286-293.

England, L. J., Kim, S. Y., Shapiro-Mendoza, C. K., Wilson, H. G., Kendrick, J. S., Satten, G. A., et al. (2013). Effects of maternal smokeless tobacco use on selected pregnancy outcomes in Alaska Native women: A case-control study. *Acta Obstetricia et Gynecologica Scandinavica, 92*(6), 648-655.

Essential health benefits package. 42 U.S.C. § 300gg-6(a) (2010). Establishment of qualified health plans. Essential health benefits requirement. 42 U.S.C. § 18022 (2010).

Etter, J. F. (2014). Levels of saliva cotinine in electronic cigarette users. *Addiction, 109*(5), 825-829.

Etter, J. F. (2015). Explaining the effects of electronic cigarettes on craving for tobacco in recent quitters. *Drug and Alcohol Dependence, 148*, 102-108.

Etter, J. F., Zather, E., & Svensson, S. (2013). Analysis of refill liquids for electronic cigarettes. *Addiction, 108*(9), 1671-1679.

Fagan, P., Moolchan, E. T., Hart, A., Rose, l. A., Lawrence, D., Shavers, V. L., et al. (2010). Nicotine dependence and quitting behaviors among menthol and non-menthol smokers with similar consumptive patterns. *Addiction, 105*(Suppl 1), 55-74.

Fagerstrom, K., & Eissenberg, T. (2012). Dependence on tobacco and nicotine products: A case for product-specific assessment. *Nicotine and Tobacco Research, 14*(11), 1382-1390.

Fair health insurance premiums 45 C.F.R. § 147.102 (a)(i), (iv) (2016).

Fairchild, A. L., & Bayer, R. (2015). Public health. Smoke and fire over e-cigarettes. *Science, 347*(6220), 375-376.

Family Smoking Prevention and Tobacco Control Act. 21 U.S.C. § 387j(c) (2011).

Family Smoking Prevention and Tobacco Control Act. 21 U.S.C. §§ 387 - 387u (2011).

Family Smoking Prevention and Tobacco Control Act. H.R. 1256, 111th Cong. (2010).

Farber, H. J., Walley, S. C., Groner, J. A., & Nelson, K. E. (2015). Clinical practice policy to protect children from tobacco, nicotine, and tobacco smoke. *Pediatrics, 136*(5), 1008-1017.

Farrelly, M. C., Duke, J. C., Crankshaw, E. C., Eggers, M. E., Lee, Y. O., Nonnemaker, J. M., et al. (2015). A randomized trial of the effect of e-cigarette TV advertisements on intentions to use e-cigarettes. *American Journal of Preventive Medicine, 49*(5), 686-693.

Farsalinos, K. E., Gillman, I. G., Melvin, M. S., Paolantonio, A. R., Gardow, W. J., Humphries, K. E., et al. (2015). Nicotine levels and presence of selected tobacco-derived toxins in tobacco flavoured electronic cigarette refill liquids. *International Journal of Environmental Research and Public Health, 12*(4), 3439-3452.

Farsalinos, K. E., Kistler, K. A., Gillman, G., & Voudris, V. (2015). Evaluation of electronic cigarette liquids and aerosol for the presence of selected inhalation toxins. *Nicotine and Tobacco Research, 17*(2), 168-174.

Farsalinos, K. E., Romagna, G., Tsiapras, D., Kyrzopoulos, S., Spyrou, A., & Voudris, V. (2013). Impact of flavour variability on electronic cigarette use experience: An internet survey. *International Journal of Environmental Research and Public Health, 10*(12), 7272-7282.

Farsalinos, K. E., Romagna, G., & Voudris, V. (2015). Factors associated with dual use of tobacco and electronic cigarettes: A case control study. *International Journal of Drug Policy, 26*(6), 595-600.

Farsalinos, K. E., Spyrou, A., Stefopoulos, C., Tsimopoulou, K., Kourkoveli, P., Tsiapras, D., et al. (2015). Nicotine absorption from electronic cigarette use: Comparison between experienced consumers (vapers) and naive users (smokers). *Scientific Reports, 17*(5), 11269. doi:10.1038/srep11269.

Farsalinos, K. E., Voudris, V., & Poulas, K. (2015). E-cigarettes generate high levels of aldehydes only in 'dry puff' conditions. *Addiction, 110*(8), 1352-1356.

Federal Aviation Administration. (2013). *Pack safe: Electronic cigarettes, vaping devices.* Retrieved from https://www.faa.gov.

Federal Cigarette Labeling and Advertising Act, Pub. L. No. 89-92, 79 Stat. 282 (1965).

Federation of Tax Administrators. (2016). *State excise tax rates on cigarettes.* Retrieved from http://www.taxadmin.org.

Fernandez, E., Ballbe, M., Sureda, X., Fu, M., Salto, E., & Martinez-Sanchez, J. M. (2015). Particulate matter from electronic cigarettes and conventional cigarettes: A systematic review and observational study. *Current Environmental Health Reports, 2*(4), 423-429.

Fielder, R. L., Carey, K. B., & Carey, M. P. (2012). Predictors of initiation of hookah tobacco smoking: A one-year prospective study of first-year college women. *Psychology of Addictive Behaviors, 26*(4), 963-968.

Fillon, M. (2015). Electronic cigarettes may lead to nicotine addiction. *Journal of the National Cancer Institute, 107*(3). doi:10.1093/jnci/djv070.

Flora, J. W., Meruva, N., Huang, C. B., Wilkinson, C. T., Ballentine, R., Smith, D. C., et al. (2016). Characterization of potential impurities and degradation products in electronic cigarette formulations and aerosols. *Regulatory Toxicology and Pharmacology, 74*, 1-11. doi:10.1016/j.yrtph.2015.11.009.

Fooks, G. J., Gilmore, A. B., Smith, K. E., Collin, J., Holden, C., & Lee, K. (2011). Corporate social responsibility and access to policy elites: An analysis of tobacco industry documents. *PLoS Medicine, 8*(8), doi:org/10.1371/journal.pmed.1001076.

Foulds, J., Veldheer, S., Yingst, J., Hrabovsky, S., Wilson, S. J., Nichols, T. T., et al. (2015). Development of a questionnaire for assessing dependence on electronic cigarettes among a large sample of ex-smoking e-cigarette users. *Nicotine and Tobacco Research, 17*(2), 186-192.

Friedman, A. S. (2015). How does electronic cigarette access affect adolescent smoking? *Journal of Health Economics, 44*, 300-308.

Friedman, A. S., Schpero, W. L., & Busch, S. H. (2016). Evidence suggests that the ACA's tobacco surcharges reduced insurance take-up and did not increase smoking cessation. *Health Affairs, 35*(7), 1176-1183.

Funck-Brentano, C., Raphael, M., Lafontaine, M., Arnould, J. P., Verstuyft, C., Lebot, M., et al. (2006). Effects of type of smoking (pipe, cigars or cigarettes) on biological indices of tobacco exposure and toxicity. *Lung Cancer, 54*(1), 11-18.

Ganz, O., Cantrell, J., Moon-Howard, J., Aidala, A., Kirchner, T. R., & Vallone, D. (2015). Electronic cigarette advertising at the point-of-sale: A gap in tobacco control research. *Tobacco Control, 24*(e1), e110-e112.

Geiss, O., Bianchi, I., & Barrero-Moreno, J. (2016). Correlation of volatile carbonyl yields emitted by e-cigarettes with the temperature of the heating coil and the perceived sensorial quality of the generated vapours. *International Journal of Hygiene and Environmental Health, 219*(3), 268-277.

Germain, D., Hons, B. P., Wakefield, M. A., & Durkin, S. J. (2010). Adolescents' perceptions of cigarette brand image: Dose plain packaging make a difference? *Journal of Adolescent Health, 46*, 385-392.

Gillman, I. G., Kistler, K. A., Stewart, E. W., & Paolantonio, A. R. (2016). Effect of variable power levels on the yield of total aerosol mass and formation of aldehydes in e-cigarette aerosols. *Regulatory Toxicology and Pharmacology, 75*, 58-65.

Giovenco, D. P., Casseus, M., Duncan, D. T., Coups, E. J., Lewis, M. J., & Delnevo, C. D. (2016). Association between electronic cigarette marketing near schools and e-cigarette use among youth. *Journal of Adolescent Health, 59*(6), 627-634.

Gipson, C. D., Kupchik, Y. M., & Kalivas, P. W. (2014). Rapid, transient synaptic plasticity in addiction. *Neuropharmacology, 76*(Pt B), 276-286.

Glantz, S. (2011). *Two high profile uncritical media stories on industry-supported "harm reduction."* Retrieved from https://tobacco.ucsf.edu.

Glantz, S. (2016). *The White House told FDA that black lives don't matter.* Retrieved from http://tobacco.ucsf.edu.

Goldenson, N. I., Kirkpatrick, M. G., Barrington-Trimis, J. L., Pang, R. D., McBeth, J. F., Pentz, M. A., et al. (2016). 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 and Alcohol Dependence, 168*, 176-180.

Goniewicz, M. L., Gupta, R., Lee, Y. H., Reinhardt, S., Kim, S., Kim, B., et al. (2015). Nicotine levels in electronic cigarette refill solutions: A comparative analysis of products from the U.S., Korea, and Poland. *International Journal of Drug Policy, 26*(6), 583-588.

Goniewicz, M. L., Knysak, J., Gawron, M., Kosmider, L., Sobczak, A., Kurek, J., et al. (2014). Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tobacco Control, 23*(2), 133-139.

Goniewicz, M. L., Kuma, T., Gawron, M., Knysak, J., & Kosmider, L. (2013). Nicotine levels in electronic cigarettes. *Nicotine and Tobacco Research, 15*(1), 158-166.

Gorukanti, A., Delucchi, K., Ling, P., Fisher-Travis, R., & Halpern-Felsher, B. (2017). Adolescents' attitudes towards e-cigarette ingredients, safety, addictive properties, social norms, and regulation. *Preventive Medicine, 94*, 65-71.

Gorzkowski, J. A., Whitmore, R. M., Kaseeska, K. R., Brishke, J. K., & Klein, J. D. (2016). Pediatrician knowledge, attitudes, and practice related to electronic cigarettes. *Journal of Adolescent Health, 59*(1), 81-86.

GovTrack.us. (1973). *S. 1165 - 93rd Congress: Little Cigar Act.* Retrieved from https://www.govtrack.us.

GovTrack.us. (1973). *S. 1306 - 102nd Congress: ADAMHA Reorganization Act.* Retrieved from https://www.govtrack.us.

GovTrack.us. (2016). *S. 1574 - 99th Congress: Comprehensive Smokeless Tobacco Health Education Act of 1986.* Retrieved from https://www.govtrack.us.

Grana, R., Benowitz, N., & Glantz, S. A. (2014). E-cigarettes: A scientific review. *Circulation, 129*(19), 1972-1986.

Grana, R. A., Popova, L., & Ling, P. M. (2014). A longitudinal analysis of electronic cigarette use and smoking cessation. *JAMA Internal Medicine, 174*(5), 812-813.

Grando, S. A. (2014). Connections of nicotine to cancer. *Nature Reviews. Cancer, 14*(6), 419-429.

Grucza, R. A., Plunk, A. D., Hipp, P. R., Cavazos-Rehg, P., Krauss, M. J., Brownson, R. C., et al. (2013). Long-term effects of laws governing youth access to tobacco. *American Journal of Public Health, 103*(8), 1493-1499.

Gupta, R., Gupta, N., & Khedar, R. S. (2013). Smokeless tobacco and cardiovascular disease in low and middle income countries. *Indian Heart Journal, 65*(4), 369-377.

Haardorfer, R., Berg, C. J., Lewis, M., Payne, J., Pillai, D., McDonald, B., et al. (2016). Polytobacco, marijuana, and alcohol use patterns in college students: A latent class analysis. *Addictive Behaviors, 59*, 58-64.

Hadidi, K. A., & Mohammed, F. I. (2004). Nicotine content in tobacco used in hubble-bubble smoking. *Saudi Medical Journal, 25*(7), 912-917.

Hahn, J., Monakhova, Y. B., Hengen, J., Kohl-Himmelseher, M., Schussler, J., Hahn, H., et al. (2014). Electronic cigarettes: Overview of chemical composition and exposure estimation. *Tobacco Induced Diseases, 12*(1), 23.

Hammal, F., Chappell, A., Wild, T. C., Kindzierski, W., Shihadeh, A., Vanderhoek, A., et al. (2015). 'Herbal' but potentially hazardous: An analysis of the constituents and smoke emissions of tobacco-free waterpipe products and the air quality in the cafes where they are served. *Tobacco Control, 24*(3), 290-297.

Hammond, D. (2010). "Plain packaging" regulations for tobacco products: The impact of standardizing the color and design of cigarette packs. *Salud Pública de México, 52*(Suppl 2), s226-s232.

Hammond, D., Daniel, S., & White, C. M. (2013). The effect of cigarette branding and plain packaging on female youth in the United Kingdom. *Journal of Adolescent Health, 52*, 151-157.

Han, S., Chen, H., Zhang, X., Liu, T., & Fu, Y. (2016). Levels of selected groups of compounds in refill solutions for electronic cigarettes. *Nicotine and Tobacco Research, 18*(5), 708-714.

Hanewinkel, R., & Isensee, B. (2015). Risk factors for e-cigarette, conventional cigarette, and dual use in German adolescents: A cohort study. *Preventive Medicine, 74*, 59-62.

Harrell, M. B., Weaver, S. R., Loukas, A., Creamer, M., Marti, C. N., Jackson, C. D., et al. (2017). Flavored e-cigarette use: Characterizing youth, young adult, and adult users. *Preventive Medicine Reports, 5*, 33-40.

Harrell, P. T., Marquinez, N. S., Correa, J. B., Meltzer, L. R., Unrod, M., Sutton, S. K., et al. (2015). Expectancies for cigarettes, e-cigarettes, and nicotine replacement therapies among e-cigarette users ("Vapers"). *Nicotine and Tobacco Research*, *17*(2), 193-200.

Harrell, P. T., Naqvi, S. M. H., Plunk, A. D., Ji, M., & Martins, S. S. (2016). Patterns of youth tobacco and polytobacco usage: The shift to alternative tobacco products. *American Journal of Drug and Alcohol Abuse*. doi:10.1080/00952990.2016.1225072.

Harrison, T. A., Adams, D. G., Tyler, R. S., Craig, A. W., Moore, J. G., & Havens, J. A. (2016). *House appropriations committee approves new e-cigarette "Grandfather Date": Currently marketed products would be spared.* Retrieved from https://www.venable.com.

Hartmann-Boyce, J., McRobbie, H., Bullen, C., Begh, R., Stead, L. F., & Hajek, P. (2016). Electronic cigarettes for smoking cessation. *Cochrane Database of Systematic Reviews, 9*, doi:10.1002/14651858.CD010216.pub3.

Hatsukami, D. K., Stepanov, I., Severson, H., Jensen, J. A., Lindgren, B. R., Horn, K., et al. (2015). Evidence supporting product standards for carcinogens in smokeless tobacco products. *Cancer Prevention Research, 8*(1), 20-26.

Hawkins, S. S., Bach, N., & Baum, C. F. (2016). Impact of tobacco control policies on adolescent smoking. *Journal of Adolescent Health, 58*, 679-685.

Health Care and Education Reconciliation Act of 2010, Pub. L. No. 111-152, 124 Stat. 1029 (2010) (codified as amended at 42 U.S.C. § 1305 (2010)).

HealthyAmericans.org. (2015). *The prevention and public health fund: Preventing chronic disease and reducing long-term health costs.* Retrieved from http://healthyamericans.org.

Heatherton, T. F., Kozlowski, L. T., Frecker, R. C., & Fagerstrom, K. O. (1991). The Fagerstrom test for nicotine dependence: A revision of the Fagerstrom tolerance questionnaire. *British Journal of Addiction, 86*(9), 1119-1127.

Hecht, S. S., & Hoffmann, D. (1988). Tobacco-specific nitrosamines, an important group of carcinogens in tobacco and tobacco smoke. *Carcinogenesis, 9*(6), 875-884.

Heinz, A. J., Giedgowd, G. E., Crane, N. A., Veilleux, J. C., Conrad, M., Braun, A. R., et al. (2013). A comprehensive examination of hookah smoking in college students: Use patterns and contexts, social norms and attitudes, harm perception, psychological correlates and co-occurring substance use. *Addictive Behaviors, 38*(11), 2751-2760.

Henley, S. J., Thun, M. J., Chao, A., & Calle, E. E. (2004). Association between exclusive pipe smoking and mortality from cancer and other diseases. *Journal of the National Cancer Institute, 96*(11), 853-861.

Henningfield, J. E., Fant, R. V., Radzius, A., & Frost, S. (1999). Nicotine concentration, smoke pH and whole tobacco aqueous pH of some cigar brands and types popular in the United States. *Nicotine and Tobacco Research, 1*(2), 163-168.

Hergens, M. P., Alfredsson, L., Bolinder, G., Lambe, M., Pershagen, G., & Ye, W. (2007). Long-term use of Swedish moist snuff and the risk of myocardial infarction amongst men. *Journal of Internal Medicine, 262*(3), 351-359.

Herling, S., & Kozlowski, L. T. (1988). The importance of direct questions about inhalation and daily intake in the evaluation of pipe and cigar smokers. *Preventive Medicine, 17*(1), 73-78.

Herrington, J. S., & Myers, C. (2015). Electronic cigarette solutions and resultant aerosol profiles. *Journal of Chromatography, 1418*, 192-199.

Hiemstra, P. S., & Bals, R. (2016). Basic science of electronic cigarettes: Assessment in cell culture and in vivo models. *Respiratory Research, 17*(1), 127. doi:10.1186/s12931-016-0447-z.

Higgins, I. T., Mahan, C. M., & Wynder, E. L. (1988). Lung cancer among cigar and pipe smokers. *Preventive Medicine, 17*(1), 116-128.

Hildick-Smith, G. J., Pesko, M. F., Shearer, L., Hughes, J. M., Chang, J., Loughlin, G. M., et al. (2015). A practitioner's guide to electronic cigarettes in the adolescent population. *Journal of Adolescent Health, 57*(6), 574-579.

Hoffmann, D., & Djordjevic, M. V. (1997). Chemical composition and carcinogenicity of smokeless tobacco. *Advances in Dental Research, 11*(3), 322-329.

Hoffmann, D., Djordjevic, M. V., Fan, J., Zang, E., Glynn, T., & Connolly, G. N. (1995). Five leading U.S. commercial brands of moist snuff in 1994: Assessment of carcinogenic N-nitrosamines. *Journal of the National Cancer Institute, 87*(24), 1862-1869.

Hoffmann, D., & Wynder, E. L. (1972). Smoke of cigarettes and little cigars: An analytical comparison. *Science, 178*(4066), 1197-1199.

Holman, L. R., Bricker, J. B., & Comstock, B. A. (2013). Psychological predictors of male smokeless tobacco use initiation and cessation: A 16-year longitudinal study. *Addiction, 108*(7), 1327-1335.

Hu, S. S., Neff, L., Agaku, I. T., Cox, S., Day, H. R., Holder-Hayes, E., et al. (2016). Tobacco product use among adults - United States, 2013-2014. *Morbidity and Mortality Weekly Report, 65*(27), 686-691.

Huang, J., Kornfield, R., & Emery, S. L. (2016). 100 million views of electronic cigarette YouTube videos and counting: Quantification, content evaluation, and engagement levels of videos. *Journal of Medical Internet Research, 18*(3), e67. doi:10.2196/jmir.4265.

Huang, J., Kornfield, R., Szczypka, G., & Emergy, S. L. (2014). A cross-sectional examination of marketing of electronic cigarettes on Twitter. *Tobacco Control,* (23), iii26-iii30. doi:10.1136/tobaccocontrol-2014-051551.

Huang, J., Tauras, J., & Chaloupka, F. J. (2014). The impact of price and tobacco control policies on the demand for electronic nicotine delivery systems. *Tobacco Control, 23*(Suppl 3), iii41-iii47.

Hughes, K., Bellis, M. A., Hardcastle, K. A., McHale, P., Bennett, A., Ireland, R., et al. (2015). Associations between e-cigarette access and smoking and drinking behaviours in teenagers. *BMC Public Health, 15*, 244.

Hutzler, C., Paschke, M., Kruschinski, S., Henkler, F., Hahn, J., & Luch, A. (2014). Chemical hazards present in liquids and vapors of electronic cigarettes. *Archives of Toxicology, 88*(7), 1295-1308.

Hyland, A., Ambrose, B. K., Conway, K. P., Borek, N., Lambert, E., Carusi, C., et al. (2016). Design and methods of the Population Assessment of Tobacco and Health (PATH) Study. *Tobacco Control*. doi:10.1136/tobaccocontrol-2016-052934.

Inoue-Choi, M., Liao, L. M., Reyes-Guzman, C., Hartge, P., Caporaso, N., & Freedman, N. D. (2017). Association of long-term, low-intensity smoking with all-cause and cause-specific mortality in the National Institutes of Health-AARP diet and health study. *JAMA Internal Medicine, 177*(1), 87-95.

International Agency for Research on Cancer. (2016). *Agents classified by the IARC monographs, Volumes 1-112.* Retrieved from https://monographs.iarc.fr.

IOM (Institute of Medicine). (2015). *Report brief: Public health implications of raising the minimum age of legal access to tobacco products*. Washington, DC: The National Academies Press.

Iowa Department of Revenue. (2016). *History of tax legislation.* Retrieved from https://tax.iowa.gov.

Jacob, P., Abu Raddaha, A. H., Dempsey, D., Havel, C., Peng, M., Yu, L., et al. (2011). Nicotine, carbon monoxide, and carcinogen exposure after a single use of a water pipe. *Cancer Epidemiology, Biomarkers and Prevention, 20*(11), 2345-2353.

Jacob, P., Abu Raddaha, A. H., Dempsey, D., Havel, C., Peng, M., Yu, L., et al. (2013). Comparison of nicotine and carcinogen exposure with water pipe and cigarette smoking. *Cancer Epidemiology, Biomarkers amd Prevention, 22*(5), 765-772.

Jamal, A., Homa, D. M., O'Connor, E., Babb, S. D., Caraballo, R. S., Singh, T., et al. (2015). Current cigarette smoking among adults - United States, 2005-2014. *Morbidity and Mortality Weekly Report, 64*(44), 1233-1240.

Jamil, H., Elsouhag, D., Hiller, S., Arnetz, J. E., & Arnetz, B. B. (2010). Sociodemographic risk indicators of hookah smoking among white Americans: A pilot study. *Nicotine and Tobacco Research, 12*(5), 525-529.

Janbaz, K. H., Qadir, M. I., Basser, H. T., Bokhari, T. H., & Ahmad, B. (2014). Risk for oral cancer from smokeless tobacco. *Contemporary Oncology, 18*(3), 160-164.

Jenson, D., Lester, J., & Berman, M. L. (2016). FDA's misplaced priorities: Premarket review under the Family Smoking Prevention and Tobacco Control Act. *Tobacco Control, 25*(3), 246-253.

Jerry, J. M., Collins, G. B., & Streem, D. (2015). E-cigarettes: Safe to recommend to patients? *Cleaveland Clinic Journal of Medicine, 82*(8), 521-526.

Jo, C. L., Williams, R. S., & Ribisl, K. M. (2015). Tobacco products sold by internet vendors following restrictions on flavors and light descriptors. *Nicotine and Tobacco Research, 17*(3), 344-349.

Jo, S. H., & Kim, K. H. (2016). Development of a sampling method for carbonyl compounds released due to the use of electronic cigarettes and quantitation of their conversion from liquid to aerosol. *Journal of Chromatography, 1429*, 369-373.

Johns, M., Sacks, R., Rane, M., & Kansagra, S. M. (2013). Exposure to tobacco retail outlets and smoking initiation among New York City adolescents. *Journal of Urban Health, 90*(6), 1091-1101.

Johnston, L. D., Miech, R. A., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E. (2016). *Teen use of any illicit drug other than marijuana at new low, same true for alcohol: Data tables*. Retrieved from http://monitoringthefuture.org.

Johnston, L. D., O'Malley, P. M., Bachman, J. G., Schulenberg, J. E., & Miech, R. A. (2016). *Monitoring the Future national survey results on drug use, 1975–2015: Volume 2, college students and adults ages 19–55*. Ann Arbor, MI: Institute for Social Research, The University of Michigan.

Jolly, D. H. (2008). Exploring the use of little cigars by students at a historically black university. *Preventing Chronic Disease, 5*(3), A82.

Kadhum, M., Sweidan, A., Jaffery, A. E., Al-Saadi, A., & Madden, B. (2015). A review of the health effects of smoking shisha. *Clinical Medicine, 15*(3), 263-266.

Kadowaki, J., Vuolo, M., & Kelly, B. C. (2015). A review of the current geographic distribution of and debate surrounding electronic cigarette clean air regulations in the United States. *Health Place, 31*, 75-82.

Kaisar, M. A., Prasad, S., Liles, T., & Cucullo, L. (2016). A decade of e-cigarettes: Limited research and unresolved safety concerns. *Toxicology, 365*, 67-75.

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

Kamboj, A., Spiller, H. A., Csavant, M. J., Chounthirath, T., & Smith, G. A. (2016). Pediatric exposure to e-cigarettes, nicotine, and tobacco products in the United States. *Pediatrics, 137*(6), e20160041. doi: 10.1542/peds.2016-0041.

Kandel, D. B., & Kandel, E. R. (2014). A molecular basis for nicotine as a gateway drug. *New England Journal of Medicine, 371*(21), 2038-2039.

Kansas Health Institute. (2015). *States vary on higher premiums paid by tobacco users under the ACA: Kansas insurers applying up to 44 percent surcharge for tobacco users in 2015*. Retrieved from http://www.khi.org.

Kaplan, S. (2017). *Lawmakers seek to help e-cigarette makers escape new regulations*. Retrieved from https://www.statnews.com.

Kassem, N. O., Jackson, S. R., Boman-Davis, M., Kassem, N. O., Liles, S., Daffa, R. M., et al. (2015). Hookah smoking and facilitators/barriers to lounge use among students at a U.S. university. *American Journal of Health Behavior, 39*(6), 832-848.

Kasza, K. A., Ambrose, B. K., Conway, K. P., Borek, N., Taylor, K., Goniewicz, M. L., et al. (2017). Tobacco-product use by adults and youths in the United States in 2013 and 2014. *New England Journal of Medicine, 376*(4), 342-353.

Keith, K., & Lucia, K. W. (2014). *Implementing the Affordable Care Act: The state of the states*. Washington, DC: The Commonwealth Fund.

Khan, Z., Tonnies, J., & Muller, S. (2014). Smokeless tobacco and oral cancer in South Asia: A systematic review with meta-analysis. *Journal of Cancer Epidemiology*. doi:10.1155/2014/394696.

Kienhuis, A. S., Soeteman-Hernandez, L. G., Bos, P. M., Cremers, H. W., Klerx, W. N., & Talhout, R. (2015). Potential harmful health effects of inhaling nicotine-free shisha-pen vapor: A chemical risk assessment of the main components propylene glycol and glycerol. *Tobacco Induced Diseases, 13*(1), 15. doi:10.1186/s12971-015-0038-7.

Kim, A. E., Arnold, K. Y., & Makarenko, O. (2014). E-cigarette advertising expenditures in the U.S., 2011-2012. *American Journal of Preventive Medicine, 46*(4), 409-412.

Kim, A. E., Hopper, T., Simpson, S., Nonnemaker, J., Lieberman, A. J., Hansen, H., et al. (2015). Using Twitter data to gain insights into e-cigarette marketing and locations of use: An infoveillance study. *Journal of Medical Internet Research, 17*(11), e251. doi:10.2196/jmir.4466.

Kim, H. J., & Shin, H. S. (2013). Determination of tobacco-specific nitrosamines in replacement liquids of electronic cigarettes by liquid chromatography-tandem mass spectrometry. *Journal of Chromatography, 1291*, 48-55.

Kim, H., Davis, A. H., Dohack, J. L., & Clark, P. I. (2017). E-cigarettes use behavior and experience of adults: Qualitative research findings to inform e-cigarette use measure development. *Nicotine and Tobacco Research, 19*(2), 190-196.

Kim, J. W., & Baum, C. R. (2015). Liquid nicotine toxicity. *Pediatric Emergency Care, 31*(7), 517-521.

King, B. A., Dube, S. R., & Tynan, M. A. (2012). Current tobacco use among adults in the United States: Findings from the National Adult Tobacco Survey. *American Journal of Public Health, 102*(11), e93-e100.

King, B. A., Patel, R., Nguyen, K. H., & Dube, S. R. (2015). Trends in awareness and use of electronic cigarettes among U.S. adults, 2010-2013. *Nicotine and Tobacco Research, 17*(2), 219-227.

King, A. C., Smith, L. J., McNamara, P. J., & Cao, D. (2017). Second generation electronic nicotine delivery system vape pen exposure generalizes as a smoking cue. *Nicotine and Tobacco Research*. doi: 10.1093/ntr/ntw327.

King, B. A., Tynan, M. A., Dube, S. R., & Arrazola, R. (2014). Flavored-little-cigar and flavored-cigarette use among U.S. middle and high school students. *Journal of Adolescent Health, 54*(1), 40-46.

Kirchner, T. R., Villanti, A. C., Cantrell, J., Anesetti-Rothermel, A., Ganz, O., Conway, K. P., et al. (2015). Tobacco retail outlet advertising practices and proximity to schools, parks and public housing affect Synar underage sales violations in Washington, DC. *Tobacco Control, 24*(e1), e52-e58.

Klein, E. G., Berman, M., Hemmerich, N., Carlson, C., Htut, S., & Slater, M. (2016). Online e-cigarette marketing claims: A systematic content and legal analysis. *Tobacco Regulatory Science, 2*(3), 252-262.

Klein, J. D. (2015). Electronic cigarettes are another route to nicotine addiction for youth. *JAMA Pediatrics, 169*(11), 993-994.

Klepeis, N. E., Ott, W. R., & Repace, J. L. (1999). The effect of cigar smoking on indoor levels of carbon monoxide and particles. *Journal of Exposure Analysis and Environmental Epidemiology, 9*(6), 622-635.

Kofman, M., Dunton, K., & Senkewicz, M. B. (2012). *Implementation of tobacco cessation coverage under the Affordable Care Act: Understanding how private health insurance policies cover tobacco cessation treatments*. Washington, DC: Georgetown University.

Kohlmeier, K. A. (2015). Nicotine during pregnancy: Changes induced in neurotransmission, which could heighten proclivity to addict and induce maladaptive control of attention. *Journal of Developmental Origins of Health and Disease, 6*(3), 169-181.

Kollath-Cattano, C., Thrasher, J. F., Osman, A., Andrews, J. O., & Strayer, S. M. (2016). Physician advice for e-cigarette use. *Journal of the American Board of Family Medicine, 29*(6), 741-747.

Kong, G., Morean, M. E., Cavallo, D. A., Camenga, D. R., & Krishnan-Sarin, S. (2015). Reasons for electronic cigarette experimentation and discontinuation among adolescents and young adults. *Nicotine and Tobacco Research, 17*(7), 847-854.

Koob, G. F., & Volkow, N. D. (2010). Neurocircuitry of addiction. *Neuropsychopharmacology, 35*(1), 217-238.

Kosmider, L., Sobczak, A., Fik, M., Knysak, J., Zaciera, M., Kurek, J., et al. (2014). Carbonyl compounds in electronic cigarette vapors: Effects of nicotine solvent and battery output voltage. *Nicotine and Tobacco Research, 16*(10), 1319-1326.

Kosmider, L., Sobczak, A., Prokopowicz, A., Kurek, J., Zaciera, M., Knysak, J., et al. (2016). Cherry-flavoured electronic cigarettes expose users to the inhalation irritant, benzaldehyde. *Thorax, 71*(4), 376-377.

Kostygina, G., Glantz, S. A., & Ling, P. M. (2016). Tobacco industry use of flavours to recruit new users of little cigars and cigarillos. *Tobacco Control, 25*(1), 66-74.

Koszowski, B., Rosenberry, Z. R., Kanu, A., Viray, L. C., Potts, J. L., & Pickworth, W. B. (2015). Nicotine and carbon monoxide exposure from inhalation of cigarillo smoke. *Pharmacology, Biochemistry, and Behavior, 139*(Pt A), 7-14.

Kozlowski, L. T., & Abrams, D. B. (2016). Obsolete tobacco control themes can be hazardous to public health: The need for updating views on absolute product risks and harm reduction. *BMC Public Health, 16*, 432. doi:10.1186/s12889-016-3079-9.

Kreslake, J. M., Wayne, G. F., Alpert, H. R., Koh, H. K., & Connolly, G. N. (2008). Tobacco industry control of menthol in cigarettes and targeting of adolescents and young adults. *American Journal of Public Health, 98*(9), 1685-1692.

Krishnan-Sarin, S., Morean, M., Camenga, D., Cavallo, D. A., & Kong, G. (2015). E-cigarette use among high school and middle school adolescents in Connecticut. *Nicotine and Tobacco Research, 17*(7), 810-818.

Krishnan-Sarin, S., Morean, M., Kong, G., Bold, K. W., Camenga, D. R., Cavallo, D. A., et al. (2017). E-cigarettes and "dripping" among high-school youth. *Pediatrics, 139*(3). doi:10.1542/peds.2016.3224.

Kumar, S. R., Davies, S., Weitzman, M., & Sherman, S. (2015). A review of air quality, biological indicators and health effects of second-hand waterpipe smoke exposure. *Tobacco Control, 24*(Suppl 1), i54-i59.

Kusnetz, N. (2016). *Who's calling the shots in state politics? How big tobacco lobbies to safeguard e-cigarettes: California takes center stage in fight between health groups and tobacco firms.* Retrieved from Center for Public Integrity: https://www.publicintegrity.org.

Kutlu, M. G., Parikh, V., & Gould, T. J. (2015). Nicotine addiction and psychiatric disorders. *International Review of Neurobiology, 124*, 171-208.

La, F. G., Weiser, G., Steiner, I. P., & Shavit, I. (2012). Carbon monoxide poisoning in narghile (water pipe) tobacco smokers. *Canadian Journal of Emergency Medicine, 14*(1), 57-59.

Lammi, G. G. (2014). *FDA advisory committee not rife with conflicts of interest? "Please!" quips federal judge.* Retrieved from http://www.forbes.com.

Lange, P., Groth, S., Nyboe, J., Mortensen, J., Appleyard, M., Jensen, G., et al. (1990). Decline of the lung function related to the type of tobacco smoked and inhalation. *Thorax, 45*(1), 22-26.

Lanza, S. T., & Vasilenko, S. A. (2015). New methods shed light on age of onset as a risk factor for nicotine dependence. *Addictive Behaviors, 50*, 161-164.

Lawler, T. S., Stanfill, S. B., Zhang, L., Ashley, D. L., & Watson, C. H. (2013). Chemical characterization of domestic oral tobacco products: Total nicotine, pH, unprotonated nicotine and tobacco-specific N-nitrosamines. *Food and Chemical Toxicology, 57*, 380-386.

Lechner, W. V., Janssen , T., Kahler, C. W., Audrain-McGovern, J., & Leventhal, A. M. (2017). Bi-directional associations of electronic and combustible cigarette use onset patterns with depressive symptoms in adolescents. *Preventive Medicine, 96*, 73-78.

Lee, J. G., Boynton, M. H., Richardson, A., Jarman, K., Ranney, L. M., & Goldstein, A. O. (2016). Raising the legal age of tobacco sales: Policy support and trust in government, 2014-2015, U.S. *American Journal of Preventive Medicine, 51*(6), 910-915.

Lee, P. N. (2011). Summary of the epidemiological evidence relating snus to health. *Regulatory Toxicology and Pharmacology, 59*(2), 197-214.

Lee, P. N., & Hamling, J. (2009). Systematic review of the relation between smokeless tobacco and cancer in Europe and North America. *BMC Medicine, 7*, 36. doi:10.1186/1741-7015-7-36.

Lee, Y. O., Hebert, C. J., Nonnemaker, J. M., & Kim, A. E. (2014). Multiple tobacco product use among adults in the United States: Cigarettes, cigars, electronic cigarettes, hookah, smokeless tobacco, and snus. *Preventive Medicine, 62*, 14-19.

Lee, Y. O., Hebert, C. J., Nonnemaker, J. M., & Kim, A. E. (2015). Youth tobacco product use in the United States. *Pediatrics, 135*(3), 409-415.

Legislative Counsel of California. (2016). *An act to amend sections 17537.3, 22951, 22952, 22956, 22958, and 22963 of, and to add Section 22964 to, the Business and Professions Code, and to amend Section 308 of the Penal Code, relating to tobacco.* Retrieved from http://leginfo.legislature.ca.gov.

Lempert, L. K., Popova, L., Halpern-Felsher, B., Chaffee, B., Benowitz, N., St. Helen, G., et al. (2016). *Listing of ingredients in tobacco products: Revised guidance for industry (Docket No. FDA-2009-D-0524).* Retrieved from http://www.fda.gov.

Lencucha, R., Drope, J., & Labonte, R. (2016). Rhetoric and the law, or the law of rhetoric: How countries oppose novel tobacco control measures at the World Trade Organization. *Social Science and Medicine, 164*, 100-107.

Lerner, C. A., Sundar, I. K., Watson, R. M., Elder, A., Jones, R., Done, D., et al. (2015). Environmental health hazards of e-cigarettes and their components: Oxidants and copper in e-cigarette aerosols. *Environmental Pollution, 198*, 100-107.

Lerner, C. A., Sundar, I. K., Yao, H., Gerloff, J., Ossip, D. J., McIntosh, S., et al. (2015). Vapors produced by electronic cigarettes and e-juices with flavorings induce toxicity, oxidative stress, and inflammatory response in lung epithelial cells and in mouse lung. *PLoS One, 10*(2), e0116732. doi:10.1371/journal.pone.0116732.

Lessard, J., Henrie, J., Livingston, J. A., Leonard, K. E., Colder, C. R., & Eiden, R. D. (2014). Correlates of ever having used electronic cigarettes among older adolescent children of alcoholic fathers. *Nicotine and Tobacco Research, 16*(12), 1656-1660.

Leventhal, A. M., Stone, M. D., Andrabi, N., Barrington-Trimis, J., Strong, D. R., Sussman, S., et al. (2016). Association of e-cigarette vaping and progression to heavier patterns of cigarette smoking. *JAMA, 316*(18), 1918-1920.

Leventhal, A. M., Strong, D. R., Kirkpatrick, M. G., Unger, J. B., Sussman, S., Riggs, N. R., et al. (2015). Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. *JAMA, 314*(7), 700-707.

Liang, Y., Zheng, X., Zeng, D. D., Zhou, X., Leischow, S. J., & Chung, W. (2015). Exploring how the tobacco industry presents and promotes itself in social media. *Journal of Medical Internet Research, 17*(1), e24. doi:10.2196/jmir.3665.

Liber, A. C., Drope, J. M., & Stoklosa, M. (2016). Combustible cigarettes cost less to use than e-cigarettes: Global evidence and tax policy implications. *Tobacco Control*. doi:10.1136/tobaccocontrol-2015-052874.

Link, A. R., Cawkwell, P. B., Shelley, D. R., & Sherman, S. E. (2015). An exploration of online behaviors and social media use among hookah and electronic-cigarette users. *Addictive Behaviors Report, 2*, 37-40.

Lippert, A. M. (2016). Temporal changes in the correlates of U.S. adolescent electronic cigarette use and utilization in tobacco cessation, 2011 to 2013. *Health Education and Behavior*. doi:10.1177/1090198116650150.

Lipton, E. (2016, September 11). *A lobbyist wrote the Bill. Will the tobacco industry win its e-cigarette fight? The New York Times*. Retrieved from http://www.nytimes.com.

Lisko, J. G., Tran, H., Stanfill, S. B., Blount, B. C., & Watson, C. H. (2015). Chemical composition and evaluation of nicotine, tobacco alkaloids, pH, and selected flavors in e-cigarette cartridges and refill solutions. *Nicotine and Tobacco Research, 17*(10), 1270-1278.

Litt, M. D., Duffy, V., & Onchen, C. (2016). Cigarette smoking and electronic cigarette vaping patterns as a function of e-cigarette flavourings. Tobacco Control, *25*(Suppl 2),: ii67-ii72. doi:10.1136/tobaccocontrol-2016-053223.

Liu, J., Wang, X., Narayan, S., Glantz, S. A., Schick, S. F., & Springer, M. L. (2016). Impairment of endothelial function by little cigar secondhand smoke. *Tobacco Regulatory Science, 2*(1), 56-63.

Liu, S. T., Nemeth, J. M., Klein, E. G., Ferketich, A. K., Kwan, M. P., & Wewers, M. E. (2014). Adolescent and adult perceptions of traditional and novel smokeless tobacco products and packaging in rural Ohio. *Tobacco Control, 23*(3), 209-214.

Lopez, A. A., Hiler, M. M., Soule, E. K., Ramoa, C. P., Karaoghlanian, N. V., Lipato, T., et al. (2016). Effects of electronic cigarette liquid nicotine concentration on plasma nicotine and puff topography in tobacco cigarette smokers: A preliminary report. *Nicotine and Tobacco Research, 18*(5), 720-723.

Loukas, A., Batanova, M., Fernandez, A., & Agarwal, D. (2015). Changes in use of cigarettes and non-cigarette alternative products among college students. *Addictive Behaviors, 49*, 46-51.

Luo, C., Zheng, X., Zeng, D. D., & Leischow, S. (2014). Portrayal of electronic cigarettes on YouTube. *BMC Public Health, 14*, 1028. doi:10.1186/1471-2458-14-1028.

Luo, J., Ye, W., Zendehdel, K., Adami, J., Adami, H. O., Boffetta, P., et al. (2007). Oral use of Swedish moist snuff (snus) and risk for cancer of the mouth, lung, and pancreas in male construction workers: A retrospective cohort study. *Lancet, 369*(9578), 2015-2020.

Luty, J. (2002). Nicotine addiction and smoking cessation treatments. *Advances in Psychiatric Treatment, 8*, 42-48.

Mainous, A. G., Tanner, R. J., Mainous, R. W., & Talbert, J. (2015). Health considerations in regulation and taxation of electronic cigarettes. *Journal of American Board of Family Medicine, 28*, 802-806.

Malson, J. L., Sims, K., Murty, R., & Pickworth, W. B. (2001). Comparison of the nicotine content of tobacco used in bidis and conventional cigarettes. *Tobacco Control, 10*(2), 181-183.

Mansvelder, H. D., Keath, J. R., & McGehee, D. S. (2002). Synaptic mechanisms underlie nicotine-induced excitability of brain reward areas. *Neuron, 33*(6), 905-919.

Mantey, D. S., Cooper, M. R., Clendennen, S. L., Pasch, K. E., & Perry, C. L. (2016). E-cigarette marketing exposure is associated with e-cigarette use among U.S. youth. *Journal of Adolescent Health, 58*(6), 686-690.

Margolis, K. A., Nguyen, A. B., Slavit, W. I., & King, B. A. (2016). E-cigarette curiosity among U.S. middle and high school students: Findings from the 2014 National Youth Tobacco Survey. *Preventive Medicine, 89*, 1-6. doi:10.1016/j.ypmed.2016.05.001.

Maridet, C., Atge, B., Amici, J. M., Taieb, A., & Milpied, B. (2015). The electronic cigarette: The new source of nickel contact allergy of the 21st century? *Contact Dermatitis, 73*(1), 49-50.

Martinasek, M. P., Gibson-Young, L., & Forrest, J. (2014). Hookah smoking and harm perception among asthmatic adolescents: Findings from the Florida youth tobacco survey. *Journal of School Health, 84*(5), 334-341.

Martinasek, M. P., Ward, K. D., & Calvanese, A. V. (2014). Change in carbon monoxide exposure among waterpipe bar patrons. *Nicotine and Tobacco Research, 16*(7), 1014-1019.

Mayer, B. (2014). How much nicotine kills a human? Tracing back the generally accepted lethal dose to dubious self-experiments in the nineteenth century. *Archives of Toxicology, 88*(1), 5-7.

Mayo Clinic. (2016). *Chewing tobacco: Not a safe product.* Retrieved from http://www.mayoclinic.org.

Maziak, W., Rastam, S., Ibrahim, I., Ward, K. D., Shihadeh, A., & Eissenberg, T. (2009). CO exposure, puff topography, and subjective effects in waterpipe tobacco smokers. *Nicotine and Tobacco Research, 11*(7), 806-811.

Maziak, W., Rastam, S., Shihadeh, A. L., Bazzi, A., Ibrahim, I., Zaatari, G. S., et al. (2011). Nicotine exposure in daily waterpipe smokers and its relation to puff topography. *Addictive Behaviors, 36*(4), 397-399.

McAdam, K. G., Faizi, A., Kimpton, H., Porter, A., & Rodu, B. (2013). Polycyclic aromatic hydrocarbons in U.S. and Swedish smokeless tobacco products. *Chemistry Central Journal, 7*(1), 151.

McAuley, T. R., Hopke, P. K., Zhao, J., & Babaian, S. (2012). Comparison of the effects of e-cigarette vapor and cigarette smoke on indoor air quality. *Inhalation Toxicology, 24*(12), 850-857.

McConnell, R., Barrington-Trimis, J. L., Wang, K., Urman, R., Hong, H., Unger, J., et al. (2016). Electronic-cigarette use and respiratory symptoms in adolescents. *American Journal of Respiratory and Critical Care Medicine*. doi:10.1164/rccm.201604-0804OC.

McCormack, V. A., Agudo, A., Dahm, C. C., Overvad, K., Olsen, A., Tjonneland, A., et al. (2010). Cigar and pipe smoking and cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC). *International Journal of Cancer, 127*(10), 2402-2411.

McCusker, K., McNabb, E., & Bone, R. (1982). Plasma nicotine levels in pipe smokers. *JAMA, 248*(5), 577-578.

McDonald, L. J., Bhatia, R. S., & Hollett, P. D. (2002). Deposition of cigar smoke particles in the lung: Evaluation with ventilation scan using (99m)Tc-labeled sulfur colloid particles. *Journal of Nuclear Medicine, 43*(12), 1591-1595.

McMillen, R. C., Gottlieb, M. A., Shaefer, R. M., Winickoff, J. P., & Klein, J. D. (2014). Trends in electronic cigarette use among U.S. adults: Use is increasing in both smokers and nonsmokers. *Nicotine and Tobacco Research. 17*(10), 1195-1202.

McRobbie, H., Bullen, C., Hartmann-Boyce, J., & Hajek, P. (2014). Electronic cigarettes for smoking cessation and reduction. *Cochrane Database of Systematic Reviews.* doi:10.1002/14651858.CD010216.pub2.

Mejia, A. B., & Ling, P. M. (2010). Tobacco industry consumer research on smokeless tobacco users and product development. *American Journal of Public Health, 100*(1), 78-87.

Mejia, A. B., Ling, P. M., & Glantz, S. A. (2010). Quantifying the effects of promoting smokeless tobacco as a harm reduction strategy in the USA. *Tobacco Control, 19*(4), 297-305.

Mennis, J., & Mason, M. (2016). Tobacco outlet density and attitudes towards smoking among urban adolescent smokers. *Substance Abuse, 37*(4), 521-525.

Messer, K., Vijayaraghavan, M., White, M. M., Shi, Y., Chang, C., Conway, K. P., et al. (2015). Cigarette smoking cessation attempts among current U.S. smokers who also use smokeless tobacco. *Addictive Behaviors, 51*, 113-119.

Miao, S., Beach, E. S., Sommer, T. J., Zimmerman, J. B., & Jordt, S.-E. (2016). High-intensity sweeteners in alternative tobacco products. *Nicotine and Tobacco Research, 18*(11), 2169-2173.

Middlekauff, H. R., Park, J., & Moheimani, R. S. (2014). Adverse effects of cigarette and noncigarette smoke exposure on the autonomic nervous system: Mechanisms and implications for cardiovascular risk. *Journal of the American College of Cardiology, 64*(16), 1740-1750.

Miech, R. A., Johnston, L. D., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E. (2016). *Monitoring the Future national survey results on drug use, 1975–2015: Volume I, secondary school students*. Ann Arbor, MI: The University of Michigan, Institute for Social Research.

Miech, R., Patrick, M. E., O'Malley, P. M., & Johnston, L. D. (2017). E-cigarette use as a predictor of cigarette smoking: Results from a 1-year follow-up of a national sample of 12th grade students. *Tobacco Control*. doi:10.1136/tobaccocontrol-2016-053291.

Milam, A. J., Bone, L. R., Byron, M. J., Hoke, K., Williams, C. D., Furr-Holden, C. D., et al. (2013). Cigarillo use among high-risk urban young adults. *Journal of Health Care for the Poor and Underserved, 24*(4), 1657-1665.

Mishra, A., Chaturvedi, P., Datta, S., Sinukumar, S., Joshi, P., & Garg, A. (2015). Harmful effects of nicotine. *Indian Society of Medical and Paediatric Oncology, 36*(1), 24-31.

Moghe, A., Ghare, S., Lamoreau, B., Mohammad, M., Barve, S., McClain, C., et al. (2015). Molecular mechanisms of acrolein toxicity: Relevance to human disease. *Toxicological Sciences, 143*(2), 242-255.

Monzer, B., Sepetdjian, E., Saliba, N., & Shihadeh, A. (2008). Charcoal emissions as a source of CO and carcinogenic PAH in mainstream narghile waterpipe smoke. *Food and Chemical Toxicology, 46*(9), 2991-2995.

Morgenstein, M. (2011). *Tobacco giants suing FDA over warning labels mandate.* CNN. Retrieved from http://www.cnn.com.

National Association of Attorneys General. (1998). *Master settlement agreement.* Retrieved from http://web.archive.org.

National Cancer Institute. (1998). *Cigars: Health effects and trends.* Retrieved from http://cancercontrol.cancer.gov.

National Conference of State Legislatures. (2010). *Summary of the health workforce provisions in the Patient Protection and Affordable Care Act: H.R. 3590*. Washington, DC: Author.

National Institute on Drug Abuse. (2012). *Research report series: Tobacco addiction* (NIH Pub No. 12-4342). Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Institute on Drug Abuse.

National Prevention Council. (2011). *National prevention strategy: America's plan for better health and wellness*. Washington, DC: U.S. Department of Health and Human Services, Office of the Surgeon General.

National Research Council. (1986). *Environmental tobacco smoke: Measuring exposures and assessing health effects*. Washington, DC: The National Academies Press.

Neergaard, J., Singh, P., Job, J., & Montgomery, S. (2007). Waterpipe smoking and nicotine exposure: A review of the current evidence. *Nicotine and Tobacco Research, 9*(10), 987-994.

Nemeth, J. M., Liu, S. T., Klein, E. G., Ferketich, A. K., Kwan, M. P., & Wewers, M. E. (2012). Factors influencing smokeless tobacco use in rural Ohio Appalachia. *Journal of Community Health, 37*(6), 1208-1217.

Niaura, R. (2016). *Re-thinking nicotine and its effects*. Washington, DC: Truth Initiative.

Nicoll, K. J., Rose, A. M., Khan, M. A., Quaba, O., & Lowrie, A. G. (2016). Thigh burns from exploding e-cigarette lithium ion batteries: First case series. *Burns, 42*(4), e42-e46.

NJOY.com. (2016). *NJOY daily.* Retrieved from https://www.njoy.com.

Noland, M., Ickes, M. J., Rayens, M. K., Butler, K., Wiggins, A. T., & Hahn, E. J. (2016). Social influences on use of cigarettes, e-cigarettes, and hookah by college students. *Journal of American College Health, 64*(4), 319-328.

Nonnemaker, J., Kim, A., Shafer, P., Loomis, B., Hill, E., Holloway, J., et al. (2016). Influence of point-of-sale tobacco displays and plain black and white cigarette packaging and advertisements on adults: Evidence from a virtual store experimental study. *Addictive Behaviors, 56*, 15-22.

Norton, K. J., June, K. M., & O'Connor, R. J. (2016). Initial puffing behaviors and subjective responses differ between an electronic nicotine delivery system and traditional cigarettes. *Tobacco Induced Diseases, 12*, 17-25.

Nuwayhid, I. A., Yamout, B., Azar, G., & Kambris, M. A. (1998). Narghile (hubble-bubble) smoking, low birth weight, and other pregnancy outcomes. *American Journal of Epidemiology, 148*(4), 375-383.

Nuzzo, E., Shensa, A., Kim, K. H., Fine, M. J., Barnett, T. E., Cook, R., et al. (2013). Associations between hookah tobacco smoking knowledge and hookah smoking behavior among U.S. college students. *Health Education Research, 28*(1), 92-100.

Nyman, A. L., Sterling, K. L., Weaver, S. R., Majeed, B. A., & Eriksen, M. P. (2016). Little cigars and cigarillos: Users, perceptions, and reasons for use. *Tobacco Regulatory Science, 2*(3), 239-251.

Ockene, J. K., Pechacek, T. F., Vogt, T., & Svendsen, K. (1987). Does switching from cigarettes to pipes or cigars reduce tobacco smoke exposure? *American Journal of Public Health, 77*(11), 1412-1416.

O'Connor, R. J. (2012). Non-cigarette tobacco products: What have we learnt and where are we headed? *Tobacco Control, 21*(2), 181-190.

Oh, A. Y., & Kacker, A. (2014). Do electronic cigarettes impart a lower potential disease burden than conventional tobacco cigarettes? Review on e-cigarette vapor versus tobacco smoke. *Laryngoscope, 124*(12), 2702-2706.

Owusu, D., Aibangbee, J., Collins, C., Robertson, C., Wang, L., Littleton, M. A., et al. (2016). The use of e-cigarettes among school-going adolescents in a predominantly rural environment of Central Appalachia. *Journal of Community Health*. doi:10.1007/s10900-016-0297-0.

Paek, H. J., Kim, S., Hove, T., & Huh, J. Y. (2014). Reduced harm or another gateway to smoking? Source, message, and information characteristics of e-cigarette videos on YouTube. *Journal of Health Communication, 19*(5), 545-560.

Pagano, T., DiFrancesco, A. G., Smith, S. B., George, J., Wink, G., Rahman, I., et al. (2016). Determination of nicotine content and delivery in disposable electronic cigarettes available in the United States by gas chromatography-mass spectrometry. *Nicotine and Tobacco Research, 18*(5), 700-707.

Patel, D., Davis, K. C., Cox, S., Bradfield, B., King, B. A., Shafer, P., et al. (2016). Reasons for current e-cigarette use among U.S. adults. *Preventive Medicine, 93*, 14-20.

Patient Protection and Affordable Care Act, Pub. L. No. 111-148, 124 Stat. 119 (2010) (codified as amended at 42 U.S.C. §§ 18001–18121 (2010)).

Payne, J. D., Orellana-Barrios, M., Medrano-Juarez, R., Buscemi, D., & Nugent, K. (2016). Electronic cigarettes in the media. *Proceedings (Baylor University Medical Center), 29*(3), 280-283.

Pearson, J. L., Amato, M. S., Wang, X., Zhao, K., Cha, S., Cohn, A. M., et al. (2017). How U.S. smokers refer to e-cigarettes: An examination of user-generated posts from a web-based smoking cessation intervention, 2008-2015. *Nicotine and Tobacco Research, 19*(2), 253-257.

Pearson, J. L., Stanton, C. A., Cha, S., Niaura, R. S., Luta, G., & Graham, A. L. (2015). E-cigarettes and smoking cessation: Insights and cautions from a secondary analysis of data from a study of online treatment-seeking smokers. *Nicotine and Tobacco Research, 17*(10), 1219-1227.

Peeters, S., & Gilmore, A. B. (2013). Transnational tobacco company interests in smokeless tobacco in Europe: Analysis of internal industry documents and contemporary industry materials. *PLoS Medicine, 10*(9), e1001506. doi:10.1371/journal.pmed.1001506.

Peeters, S., & Gilmore, A. B. (2015). Understanding the emergence of the tobacco industry's use of the term tobacco harm reduction in order to inform public health policy. *Tobacco Control, 24*, 182-189.

Pentz, M. A., Shin, H., Riggs, N., Unger, J. B., Collison, K. L., & Chou, C. P. (2015). Parent, peer, and executive function relationships to early adolescent e-cigarette use: A substance use pathway? *Addictive Behaviors, 42*, 73-78.

Pepper, J. K., Emery, S. L., Ribisl, K. M., Southwell, B. G., & Brewer, N. T. (2014). Effects of advertisements on smokers' interest in trying e-cigarettes: The roles of product comparison and visual cues. *Tobacco Control, 23* (Suppl 3), iii31-iii36.

Pepper, J. K., Gilkey, M. B., & Brewer, N. T. (2015). Physicians' counseling of adolescents regarding e-cigarette use. *Journal of Adolescent Health, 57*(6), 580-586.

Pepper, J. K., Ribisl, K. M., & Brewer, N. T. (2016). Adolescents' interest in trying flavoured e-cigarettes. *Tobacco Control, 25*(Suppl 2), ii62-ii66. doi:10.1136/tobaccocontrol-2016-053174.

Pepper, J. K., Ribisl, K. M., Emery, S. L., & Brewer, N. T. (2014). Reasons for starting and stopping electronic cigarette use. *International Journal of Environmental Research and Public Health, 11*(10), 10345-10361.

Perrone, M. (2015). *FDA experts reject evidence from Swedish company seeking to drop warnings from tobacco snus.* Retrieved from http://www.usnews.com.

Pesko, M. F. (2016, May). *E-cigarette regulations: Evaluating intended and unintended effects. Presented at The National Center on Addiction and Substance Abuse's speaker addiction series.* New York.

Pesko, M. F., Hughes, J. M., & Faisal, F. S. (2016). The influence of electronic cigarette age purchasing restrictions on adolescent tobacco and marijuana use. *Preventive Medicine, 87*, 207-212.

Pesko, M. F., Kenkel, D. S., Wang, H., & Hughes, J. M. (2016). The effect of potential electronic nicotine delivery system regulations on nicotine product selection. *Addiction, 111*(4), 734-744.

Pickworth, W. B., Bunker, E. B., & Henningfield, J. E. (1994). Transdermal nicotine: Reduction of smoking with minimal abuse liability. *Psychopharmacology, 115*, 9-14.

Pickworth, W. B., Rosenberry, Z. R., Gold, W., & Koszowski, B. (2014). Nicotine absorption from smokeless tobacco modified to adjust pH. *Journal of Addiction Research and Therapy, 5*(3), 1000184. doi:10.4172/2155-6105.1000184.

Pisinger, C. (2014). Why public health people are more worried than excited over e-cigarettes. *BMC Medicine, 12*, 226. doi:10.1186/s12916-014-0226-y.

Pokhrel, P., Fagan, P., Herzog, T. A., Chen, Q., Muranaka, N., Kehl, L., et al. (2016). E-cigarette advertising exposure and implicit attitudes among young adult non-smokers. *Drug and Alcohol Dependence, 163*, 134-140.

Pokhrel, P., Fagan, P., Kehl, L., & Herzog, T. A. (2015). Receptivity to e-cigarette marketing, harm perceptions, and e-cigarette use. *American Journal of Health Behavior, 39*(1), 121-131.

Pokhrel, P., Herzog, T. A., Muranaka, N., & Fagan, P. (2015). Young adult e-cigarette users' reasons for liking and not liking e-cigarettes: A qualitative study. *Psychology and Health, 30*(12), 1450-1469.

Popova, L., & Ling, P. M. (2013). Alternative tobacco product use and smoking cessation: A national study. *American Journal of Public Health, 103*(5), 923-930.

Popova, L., & Ling, P. M. (2013). Perceptions of relative risk of snus and cigarettes among U.S. smokers. *American Journal of Public Health, 103*(11), e21-e23.

Popova, L., & Ling, P. M. (2014). Nonsmokers' responses to new warning labels on smokeless tobacco and electronic cigarettes: An experimental study. *BMC Public Health, 14*, 997. doi:10.1186/1471-2458-14-997.

Portnoy, D. B., Wu, C. C., Tworek, C., Chen, J., & Borek, N. (2014). Youth curiosity about cigarettes, smokeless tobacco, and cigars: Prevalence and associations with advertising. *American Journal of Preventive Medicine, 47*(Suppl 1), S76-S86.

Primack, B. A., Carroll, M. V., Weiss, P. M., Shihadeh, A. L., Shensa, A., Farley, S. T., et al. (2016). Systematic review and meta-analysis of inhaled toxicants from waterpipe and cigarette smoking. *Public Health Reports, 131*(1), 76-85.

Primack, B. A., Sidana, J., Shadel, W. G., & Eissenberg, T. E. (2008). Prevalence of and associations with waterpipe tobacco smoking among U.S. university students. *Annals of Behavioral Medicine, 36*, 81-82.

Primack, B. A., Soneji, S., Stoolmiller, M., Fine, M. J., & Sargent, J. D. (2015). Progression to cigarette smoking after electronic cigarette use among U.S. adolescents and young adults. *JAMA Pediatrics, 169*(11), 1018-1023.

Proctor, R. N. (2015). The cigarette catastrophe continues. *Lancet, 385*(9972), 938-939.

Prohibiting discriminatory premium rates. 42 U.S.C. § 300gg(a)(1) (2010).

Pub. L. 93-109, 87 Stat. 352 (1973) (codified as amended at 15 U.S.C. §§ 1331-1341).

Pub. L. No. 89-92, 79 Stat. 282 (1965) (codified as amended at 15 U.S.C. §§ 1331-1341 (2012)).

Public Health Cigarette Smoking Act of 1969, Pub. L. No. 91-222, 84 Stat. 87 (1970) (codified as amended at 15 U.S.C. §§ 1331-1341 (2012)).

R. J. Reynolds Vapor. (2016). *What is R.J. Reynolds vapor company?* Retrieved from http://rjrvapor.com.

Ramamurthi, D., Gall, P. A., Ayoub, N., & Jackler, R. K. (2016). Leading-brand advertisement of quitting smoking benefits for e-cigarettes. *American Journal of Public Health, 106*(11), 2057-2063.

Ramoa, C. P., Hiler, M. M., Spindle, T. R., Lopez, A. A., Karaoghlanian, N., Lipato, T., et al. (2016). Electronic cigarette nicotine delivery can exceed that of combustible cigarettes: A preliminary report. *Tobacco Control, 25*(e1), e6-e9.

Rass, O., Pacek, L. R., Johnson, P. S., & Johnson, M. W. (2015). Characterizing use patterns and perceptions of relative harm in dual users of electronic and tobacco cigarettes. *Experimental and Clinical Psychopharmacology, 23*(6), 494-503.

Redner, R., White, T. J., Harder, V. S., & Higgins, S. T. (2014). Examining vulnerability to smokeless tobacco use among adolescents and adults meeting diagnostic criteria for major depressive disorder. *Experimental and Clinical Psychopharmacology, 22*(4), 316-322.

Rezk-Hanna, M., Macabasco-O'Connell, A., & Woo, M. (2014). Hookah smoking among young adults in southern California. *Nursing Research, 63*(4), 300-306.

Richardson, A., Ganz, O., & Vallone, D. (2015). Tobacco on the web: Surveillance and characterisation of online tobacco and e-cigarette advertising. *Tobacco Control, 24*(4), 341-347.

Richardson, A., Pearson, J., Xiao, H., Stalgaitis, C., & Vallone, D. (2014). Prevalence, harm perceptions, and reasons for using noncombustible tobacco products among current and former smokers. *American Journal of Public Health, 104*(8), 1437-1444.

Richardson, A., Xiao, H., & Vallone, D. M. (2012). Primary and dual users of cigars and cigarettes: Profiles, tobacco use patterns and relevance to policy. *Nicotine and Tobacco Research, 14*(8), 927-932.

Richtel, M. (2013). *The e-cigarette industry: Waiting to exhale.* Retrieved from http://www.nytimes.com.

Richter, L., & Foster, S. E. (2013). The exclusion of nicotine: Closing the gap in addiction policy and practice. *American Journal of Public Health, 103*(8), e14-e16.

Richter, L., Pugh, B. S., & Ball, S. A. (2016). Assessing the risk of marijuana use disorder among adolescents and adults who use marijuana. *American Journal of Drug and Alcohol Abuse*. doi:10.3109/00952990.2016.1164711.

Richter, L., Pugh, B. S., Peters, E. A., Vaughan, R. D., & Foster, S. E. (2016). Underage drinking: Prevalence and correlates of risky drinking measures among youth aged 12–20. *American Journal of Drug and Alcohol Abuse, 42*(4), 385-94.

Richter, L., Pugh, B. S., Smith, P. H., & Ball, S. A. (2016). The co-occurrence of nicotine and other substance use and addiction among youth and adults in the United States: Implications for research, practice, and policy. *American Journal of Drug and Alcohol Abuse, 43*(2), 132-145.

Richter, P., Hodge, K., Stanfill, S., Zhang, L., & Watson, C. (2008). Surveillance of moist snuff: Total nicotine, moisture, pH, un-ionized nicotine, and tobacco-specific nitrosamines. *Nicotine and Tobacco Research, 10*(11), 1645-1652.

Rickert, W. S., Trivedi, A. H., Momin, R. A., Wagstaff, W. G., & Lauterbach, J. H. (2011). Mutagenic, cytotoxic, and genotoxic properties of tobacco smoke produced by cigarillos available on the Canadian market. *Regulatory Toxicology and Pharmacology, 61*(2), 199-209.

Robinson, R. J., Hensel, E. C., & Morabito, P. N. (2015). Electronic cigarette topography in the natural environment. *PLoS One, 10*(6), e0129296.

Roditis, M., Delucchi, K., Cash, D., & Halpern-Felsher, B. (2016). Adolescents' perceptions of health risks, social risks, and benefits differ across tobacco products. *Journal of Adolescent Health, 58*(5), 558-566.

Rodriguez, J., Jiang, R., Johnson, W. C., MacKenzie, B. A., Smith, L. J., & Barr, R. G. (2010). The association of pipe and cigar use with cotinine levels, lung function, and airflow obstruction: A cross-sectional study. *Annals of Internal Medicine, 152*(4), 201-210.

Rodu, B., & Jansson, C. (2004). Smokeless tobacco and oral cancer: A review of the risks and determinants. *Critical Reviews in Oral Biology and Medicine, 15*(5), 252-263.

Roger, J. M., Abayon, M., Elad, S., & Kolokythas, A. (2016). Oral trauma and tooth avulsion following explosion of e-cigarette. *Journal of Oral and Maxillofacial Surgeons, 74*(6), 1181-1185.

Rom, O., Pecorelli, A., Valacchi, G., & Reznick, A. Z. (2015). Are e-cigarettes a safe and good alternative to cigarette smoking? *Annals of the New York Academy of Sciences*. 1340, 65-74.

Rostron, B. L., Chang, C. M., van Bemmel, D. M., Xia, Y., & Blount, B. C. (2015). Nicotine and toxicant exposure among U.S. smokeless tobacco users: Results from 1999 to 2012 National Health and Nutrition Examination Survey data. *Cancer Epidemiology, Biomarkers and Prevention, 24*(12), 1829-1837.

Rutten, L. J., Blake, K. D., Agunwamba, A. A., Grana, R. A., Wilson, P. M., Ebbert, J. O., et al. (2015). Use of e-cigarettes among current smokers: Associations among reasons for use, quit intentions, and current tobacco use. *Nicotine and Tobacco Research, 17*(10), 1228-1234.

Saddleson, M. L., Kozlowski, L. T., Giovino, G. A., Goniewicz, M. L., Mahoney, M. C., Homish, G. G., et al. (2016). Enjoyment and other reasons for electronic cigarette use: Results from college students in New York. *Addictive Behaviors, 54*, 33-39.

Saddleson, M. L., Kozlowski, L. T., Giovino, G. A., Hawk, L. W., Murphy, J. M., MacLean, M. G., et al. (2015). Risky behaviors, e-cigarette use and susceptibility of use among college students. *Drug and Alcohol Dependence, 149*, 25-30.

Saffari, A., Daher, N., Ruprecht, A., De, M. C., Pozzi, P., Boffi, R., et al. (2014). Particulate metals and organic compounds from electronic and tobacco-containing cigarettes: Comparison of emission rates and secondhand exposure. *Environmental Science Processes and Impacts, 16*(10), 2259-2267.

Salloum, R. G., Osman, A., Maziak, W., & Thrasher, J. F. (2015). How popular is waterpipe tobacco smoking? Findings from internet search queries. *Tobacco Control, 24*, 509-513.

Sanders-Jackson, A. N., Tan, A. S., Bigman, C. A., & Henriksen, L. (2015). Knowledge about e-cigarette constituents and regulation: Results from a national survey of U.S. young adults. *Nicotine and Tobacco Research, 17*(10), 1247-1254.

Schane, R. E., Ling, P. M., & Glantz, S. A. (2010). Health effects of light and intermittent smoking: A review. *Circulation, 121*(13), 1518-1522.

Schober, W., Szendrei, K., Matzen, W., Osiander-Fuchs, H., Heitmann, D., Schettgen, T., et al. (2014). Use of electronic cigarettes (e-cigarettes) impairs indoor air quality and increases FeNO levels of e-cigarette consumers. *International Journal of Hygiene and Environmental Health, 217*(6), 628-637.

Schoenborn, C. A., & Gindi, R. M. (2015). Electronic cigarette use among adults: United States, 2014. *NCHS Data Brief, 217*, 1-8.

Schripp, T., Markewitz, D., Uhde, E., & Salthammer, T. (2013). Does e-cigarette consumption cause passive vaping? *Indoor Air, 23*(1), 25-31.

Schroeder, M. J., & Hoffman, A. C. (2014). Electronic cigarettes and nicotine clinical pharmacology. *Tobacco Control, 23*(Suppl 2), ii30-ii35. doi:10.1136/tobaccocontrol-2013-051469.

Schroeder, S. A., & Morris, C. D. (2010). Confronting a neglected epidemic: Tobacco cessation for persons with mental illnesses and substance abuse problems. *Annual Review of Public Health, 31*, 297-314.

Schweitzer, K. S., Chen, S. X., Law, S., Van Demark, M. J., Poirier, C., Justice, M. J., et al. (2015). Endothelial disruptive pro-inflammatory effects of nicotine and e-cigarette vapor exposures. *American Journal of Physiology - Lung Cellular and Molecular Physiology, 309*(2), L175-L187. doi:ajplung.00411.2014.

Scollo, M., Lindorff, K., Coomber, K., Bayly, M., & Wakefield, M. (2015). Standardised packaging and new enlarged graphic health warnings for tobacco products in Australia: Legislative requirements and implementation of the Tobacco Plain Packaging Act 2011 and the Competition and Consumer (Tobacco) Information Standard, 2011. *Tobacco Control, 24*, ii9-ii16. doi:10.1136/tobaccocontrol-2014-052073.

Scragg, R., Wellman, R. J., Laugesen, M., & DiFranza, J. R. (2008). Diminished autonomy over tobacco can appear with the first cigarettes. *Addictive Behaviors, 33*, 689-698.

Seidenberg, A. B., Rodgers, E. J., Rees, V. W., & Connolly, G. N. (2012). Youth access, creation, and content of smokeless tobacco ("dip") videos in social media. *Journal of Adolescent Health, 50*(4), 334-338.

Sepetdjian, E., Abdul, H. R., Salman, R., Jaroudi, E., Shihadeh, A., & Saliba, N. A. (2013). Phenolic compounds in particles of mainstream waterpipe smoke. *Nicotine and Tobacco Research, 15*(6), 1107-1112.

Sepetdjian, E., Saliba, N., & Shihadeh, A. (2010). Carcinogenic PAH in waterpipe charcoal products. *Food and Chemical Toxicology, 48*(11), 3242-3245.

Shafagoj, Y. A., Mohammed, F. I., & Hadidi, K. A. (2002). Hubble-bubble (water pipe) smoking: Levels of nicotine and cotinine in plasma, saliva and urine. *International Journal of Clinical Pharmacology and Therapeutics, 40*(6), 249-255.

Shanks, T. G., & Burns, D. M. (1998). *Disease consequences of cigar smoking.* Retrieved from http://cancercontrol.cancer.gov.

Sharma, E., Clark, P. I., & Sharp, K. E. (2014). Understanding psychosocial aspects of waterpipe smoking among college students. *American Journal of Health Behavior, 38*(3), 440-447.

Shi, Y., Pierce, J. P., White, M., Vijayaraghavan, M., Compton, W., Conway, K., et al. (2016). E-cigarette use and smoking reduction or cessation in the 2010/2011 TUS-CPS longitudinal cohort. *BMC Public Health, 16*(1), 1105.

Shihadeh, A. (2003). Investigation of mainstream smoke aerosol of the argileh water pipe. *Food and Chemical Toxicology, 41*(1), 143-152.

Shihadeh, A., & Saleh, R. (2005). Polycyclic aromatic hydrocarbons, carbon monoxide, "tar", and nicotine in the mainstream smoke aerosol of the narghile water pipe. *Food and Chemical Toxicology, 43*(5), 655-661.

Shihadeh, A., Eissenberg, T., Rammah, M., Salman, R., Jaroudi, E., & El-Sabban, M. (2014). Comparison of tobacco-containing and tobacco-free waterpipe products: Effects on human alveolar cells. *Nicotine and Tobacco Research, 16*(4), 496-499.

Shihadeh, A., Salman, R., Jaroudi, E., Saliba, N., Sepetdjian, E., Blank, M. D., et al. (2012). Does switching to a tobacco-free waterpipe product reduce toxicant intake? A crossover study comparing CO, NO, PAH, volatile aldehydes, "tar" and nicotine yields. *Food and Chemical Toxicology, 50*(5), 1494-1498.

Shihadeh, A., Schubert, J., Klaiany, J., El, S. M., Luch, A., & Saliba, N. A. (2015). Toxicant content, physical properties and biological activity of waterpipe tobacco smoke and its tobacco-free alternatives. *Tobacco Control, 24*(Suppl 1), i22-i30.

Sibai, A. M., Tohme, R. A., Almedawar, M. M., Itani, T., Yassine, S. I., Nohra, E. A., et al. (2014). Lifetime cumulative exposure to waterpipe smoking is associated with coronary artery disease. *Atherosclerosis, 234*(2), 454-460.

Siddiqi, K., Shah, S., Abbas, S. M., Vidyasagaran, A., Jawad, M., Dogar, O., et al. (2015). Global burden of disease due to smokeless tobacco consumption in adults: Analysis of data from 113 countries. *BMC Medicine, 13*, 194.

Siegel, D., Benowitz, N., Ernster, V. L., Grady, D. G., & Hauck, W. W. (1992). Smokeless tobacco, cardiovascular risk factors, and nicotine and cotinine levels in professional baseball players. *American Journal of Public Health, 82*(3), 417-421.

Siegel, M. (2016). *FDA e-cigarette deeming regulations are a disaster for public health.* Retrieved from http://tobaccoanalysis.blogspot.com.

Siegel, M., Carol, J., Jordan, J., Hobart, R., Schoenmarklin, S., DuMelle, F., et al. (1997). Preemption in tobacco control. Review of an emerging public health problem. *JAMA, 278*(10), 858-863.

Simmons, R. (2016). *Tobacco use: Prevention, cessation and policy.* Association for Prevention Teaching and Research. Retrieved from http://www.aptrweb.org.

Singh, T., Agaku, I. T., Arrazola, R. A., Marynak, K. L., Neff, L. J., Rolle, I. T., et al. (2016). Exposure to advertisements and electronic cigarette use among U.S. middle and high school students. *Pediatrics, 137*(5). doi:10.1542/peds.2015-4155.

Singh, T., Arrazola, R. A., Corey, C. G., Husten, C. G., Neff, L. J., Homa, D. M., et al. (2016). Tobacco use among middle and high school students - United States, 2011-2015. *Morbidity and Mortality Weekly Report, 65*(14), 361-367.

Singh, T., Marynak, K., Arrazola, R. A., Cox, S., Rolle, I. V., & King, B. A. (2016). Vital signs: Exposure to electronic cigarette advertising among middle school and high school students - United States, 2014. *Morbidity and Mortality Weekly Report, 64*(52), 1403-1408.

Siqueira, L. M. (2016). Nicotine and tobacco as substances of abuse in children and adolescents. *American Academy of Pediatrics, 139*(1). doi:10.1542/peds.2016-3436.

Siu, A. L. (2015). Behavioral and pharmacotherapy interventions for tobacco smoking cessation in adults, including pregnant women: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine, 163*(8), 622-634.

Sleiman, M., Logue, J. M., Montesinos, V. N., Russell, M. L., Litter, M. I., Gundel, L. A., et al. (2016). Emissions from electronic cigarettes: Key parameters affecting the release of harmful chemicals. *Environmental Science and Technology, 50*(17), 9644-9651.

Smith, M. L., Colwell, B., Forte, C. A., Pulczinski, J. C., & McKyer, E. L. (2014). Psychosocial correlates of smokeless tobacco use among Indiana adolescents. *Journal of Community Health, 40*(2), 208-14.

Smith, R. F., McDonald, C. G., Bergstrom, H. C., Ehlinger, D. G., & Brielmaier, J. M. (2015). Adolescent nicotine induces persisting changes in development of neural connectivity. *Neuroscience and Biobehavioral Reviews, 55*, 432-443.

Smith, S. Y., Curbow, B., & Stillman, F. A. (2007). Harm perception of nicotine products in college freshmen. *Nicotine and Tobacco Research, 9*(9), 977-982.

Soule, E. K., Maloney, S. F., Spindle, T. R., Rudy, A. K., Hiler, M. M., & Cobb, C. O. (2017). Electronic cigarette use and indoor air quality in a natural setting. *Tobacco Control, 26*(1), 109-112.

Sowles, S. J., Krauss, M. J., Connolly, S., & Cavazos-Rehg, P. A. (2016). A content analysis of vaping advertisements on Twitter. *Preventing Chronic Disease, 13*, E139. doi:10.5888/pcd13.160274.

Spindle, T., Hiler, M. M., Cooke, M. E., Eissenberg, T., Kendler, K. S., & Dick, D. M. (2017). Electronic cigarette use and uptake of cigarette smoking: A longitudinal examination of U.S. college students. *Addictive Behaviors, 67*, 66-72.

Sponsiello-Wang, Z., Weitkunat, R., & Lee, P. N. (2008). Systematic review of the relation between smokeless tobacco and cancer of the pancreas in Europe and North America. *BMC Cancer, 8*, 356. doi:10.1186/1471-2407-8-356.

St. Helen G., Benowitz, N. L., Dains, K. M., Havel, C., Peng, M., & Jacob, P. (2014). Nicotine and carcinogen exposure after water pipe smoking in hookah bars. *Cancer Epidemiology, Biomarkers and Prevention, 23*(6), 1055-1066.

St. Helen G., Havel, C., Dempsey, D. A., Jacob, P., III, & Benowitz, N. L. (2016). Nicotine delivery, retention and pharmacokinetics from various electronic cigarettes. *Addiction, 111*(3), 535-544.

Stanfill, S. B., Connolly, G. N., Zhang, L., Jia, L. T., Henningfield, J. E., Richter, P., et al. (2011). Global surveillance of oral tobacco products: Total nicotine, unionised nicotine and tobacco-specific N-nitrosamines. *Tobacco Control, 20*(3), e2. doi:10.1136/tc.2010.037465.

Stanton, C. A., Keith, D. R., Gaalema, D. E., Bunn, J. Y., Doogan, N. J., Redner, R., et al. (2016). Trends in tobacco use among U.S. adults with chronic health conditions: National Survey on Drug Use and Health 2005-2013. *Preventive Medicine, 92*, 160-168.

Stead, L. F., Perera, R., Bullen, C., Mant, D., Hartmann-Boyce, J., Cahill, K., et al. (2012). Nicotine replacement therapy for smoking cessation. *Cochrane Database of Systematic Reviews, 11*. doi:10.1002/14651858.

Stepanov, I., & Fujioka, N. (2015). Bringing attention to e-cigarette pH as an important element for research and regulation. *Tobacco Control, 24*(4), 413-414.

Stepanov, I., Biener, L., Yershova, K., Nyman, A. L., Bliss, R., Parascandola, M., et al. (2014). Monitoring tobacco-specific N-nitrosamines and nicotine in novel smokeless tobacco products: Findings from round II of the new product watch. *Nicotine and Tobacco Research, 16*(8), 1070-1078.

Stepanov, I., Jensen, J., Biener, L., Bliss, R. L., Hecht, S. S., & Hatsukami, D. K. (2012). Increased pouch sizes and resulting changes in the amounts of nicotine and tobacco-specific N-nitrosamines in single pouches of Camel Snus and Marlboro Snus. *Nicotine and Tobacco Research, 14*(10), 1241-1245.

Stepanov, I., Villalta, P. W., Knezevich, A., Jensen, J., Hatsukami, D., & Hecht, S. S. (2010). Analysis of 23 polycyclic aromatic hydrocarbons in smokeless tobacco by gas chromatography-mass spectrometry. *Chemical Research in Toxicology, 23*(1), 66-73.

Sterling, K. L., Fryer, C. S., Majeed, B., & Duong, M. M. (2015). Promotion of waterpipe tobacco use, its variants and accessories in young adult newspapers: A content analysis of message portrayal. *Health Education Research, 30*(1), 152-161.

Stoklosa, M., Drope, J., & Chaloupka, F. J. (2016). Prices and e-cigarette demand: Evidence from the European Union. *Nicotine and Tobacco Research, 18*(10), 1973-1980.

Strong, D. R., Messer, K., Hartman, S. J., Conway, K. P., Hoffman, A. C., Pharris-Ciurej, N., et al. (2015). Measurement of multiple nicotine dependence domains among cigarette, non-cigarette and poly-tobacco users: Insights from item response theory. *Drug and Alcohol Dependence, 152*, 185-193.

Sundar, I. K., Javed, F., Romanos, G. E., & Rahman, I. (2016). E-cigarettes and flavorings induce inflammatory and pro-senescence responses in oral epithelial cells and periodontal fibroblasts. *Oncotarget, 7*(47), 77196-77204.

Suter, M. A., Mastrobattista, J., Sachs, M., & Aagaard, K. (2015). Is there evidence for potential harm of electronic cigarette use in pregnancy? *Birth Defects Research: Part A, Clinical and Molecular Teratology, 103*(3), 186-95.

Sutfin, E. L., Reboussin, B. A., Debinski, B., Wagoner, K. G., Spangler, J., & Wolfson, M. (2015). The impact of trying electronic cigarettes on cigarette smoking by college students: A prospective analysis. *American Journal of Public Health, 105*(8), e83-e89. doi:10.2105/AJPH.2015.302707.

Swedish Match. (2014). *Swedish match submits a Modified Risk Tobacco Product (MRTP) application.* Retrieved from https://www.swedishmatch.com.

Synthetic flavoring substances and adjuvants. 21 C.F.R. § 172.515 (2015).

Taghavi, S., Khashyarmanesh, Z., Moalemzadeh-Haghighi, H., Nassirli, H., Eshraghi, P., Jalali, N., et al. (2012). Nicotine content of domestic cigarettes, imported cigarettes and pipe tobacco in Iran. *Addiction & Health, 4*(1-2), 28-35.

Talih, S., Balhas, Z., Eissenberg, T., Salman, R., Karaoghlanian, N., El-Hellani A., et al. (2015). Effects of user puff topography, device voltage, and liquid nicotine concentration on electronic cigarette nicotine yield: Measurements and model predictions. *Nicotine and Tobacco Research, 17*(2), 150-157.

Talih, S., Balhas, Z., Salman, R., Karaoghlanian, N., & Shihadeh, A. (2016). "Direct dripping": A high-temperature, high-formaldehyde emission electronic cigarette use method. *Nicotine and Tobacco Research, 18*(4), 453-459.

Tan, A. S., Bigman, C. A., Mello, S., & Sanders-Jackson, A. (2015). Is exposure to e-cigarette communication associated with perceived harms of e-cigarette secondhand vapour? Results from a national survey of U.S. adults. *BMJ Open., 5*(3). doi:10.1136/bmjopen-2014-007134.

Tavernise, S. (2015, April 10). *Milder warning opposed for Swedish tobacco item.* New York Times. Retrieved from http://www.nytimes.com.

Tavernise, S. (2015, April 8). *Swedish company asks FDA to remove warnings from smokeless tobacco product.* New York Times. Retrieved from http://www.nytimes.com.

Tayyarah, R., & Long, G. A. (2014). Comparison of select analytes in aerosol from e-cigarettes with smoke from conventional cigarettes and with ambient air. *Regulatory Toxicology and Pharmacology, 70*, 704-710.

Tercyak, K. P., & Audrain, J. (2002). Psychosocial correlates of alternate tobacco product use during early adolescence. *Preventive Medicine, 35*(2), 193-198.

The Clinical Practice Guideline Treating Tobacco Use and Dependence 2008 Update Panel, Liaisons, and Staff. (2008). A clinical practice guideline for treating tobacco use and dependence: 2008 update: A U.S. Public Health Service report. *American Journal of Preventive Medicine, 35*(2), 158-76.

The National Center on Addiction and Substance Abuse. (2016). *Uncovering coverage gaps: A review of addiction benefits in ACA plans*. New York: Author.

Thrasher, J. F., Rousu, M. C., Hammond, D., Navarro, A., & Corrigan, J. R. (2011). Estimating the impact of pictorial health warnings and "plain" cigarette packaging: Evidence from experimental auctions among adult smokers in the United States. *Health Policy, 102*, 41-48.

Tierney, P. A., Karpinski, C. D., Brown, J. E., Luo, W., & Pankow, J. F. (2016). Flavour chemicals in electronic cigarette fluids. *Tobacco Control, 25*(e1), e10-e15.

Timberlake, D. S. (2008). A latent class analysis of nicotine-dependence criteria and use of alternate tobacco. *Journal of Studies on Alcohol and Drugs, 69*(5), 709-717.

Timberlake, D. S. (2016). Advertising receptivity and youth initiation of smokeless tobacco. *Substance Use and Misuse, 51*(9), 1077-1082.

Tobacco Control Legal Consortium. (2012). *Regulating tobacco products based on pack size.* Saint Paul, MN: Public Health Law Center.

Tobacco Control Legal Consortium. (2014). *How the Affordable Care Act affects tobacco use and control.* Retrieved from http://publichealthlawcenter.org.

Tobacco Control Legal Consortium. (2014). *Preemption: The biggest challenge to tobacco control.* Retrieved from http://publichealthlawcenter.org.

Tobacco Control Legal Consortium. (2016). *State and local tobacco regulation in a post-deeming world*. Saint Paul, MN: Public Health Law Center.

Tobacco Control Legal Consortium. (2016). *The deeming regulation: FDA authority over e-cigarettes, cigars, and other tobacco products.* Saint Paul, MN: Public Health Law Center.

Tobacco Control Legal Consortium. (2016). *The FDA's premarket review of tobacco products fails to fully protect public health*. Saint Paul, MN: Public Health Law Center.

Tobacco Control Legal Consortium. (2016). *U.S. e-cigarette regulation: A 50-state review.* Retrieved from http://publichealthlawcenter.org.

Tobacco Products Scientific Advisory Committee. (2011). *Menthol cigarettes and public health: Review of the scientific evidence and recommendations.* Retrieved from http://www.fda.gov.

Trapl, E. S., Yoder, L. D., Frank, J. L., Borawski, E. A., & Sattar, A. (2016). Individual, parental, and environmental correlates of cigar, cigarillo, and little cigar use among middle school adolescents. *Nicotine and Tobacco Research, 18*(5), 834-841.

Trehy, M. L., Ye, W., Hadwiger, M. E., Moore, T. W., Allgire, J. F., Woodruff, J. T., et al. (2011). Analysis of electronic cigarette cartridges, refill solutions, and smoke for nicotine and nicotine related impurities. *Journal of Liquid Chromatography and Related Technologies, 374*, 1442-1458.

Trtchounian, A., & Talbot, P. (2011). Electronic nicotine delivery systems: Is there a need for regulation? *Tobacco Control, 20*(1), 47-52.

Truth Initiative. (2015). *Hookah: Background.* Retrieved from http://truthinitiative.org.

Truth Initiative. (2015). *Played: Smoking and video games.* Retrieved from http://truthinitiative.org.

Truth Initiative. (2015). *The truth about: Electronic nicotine delivery systems.* Retrieved from http://truthinitiative.org.

Truth Initiative. (2015). *Vaporized: Youth and young adult exposure to e-cigarette marketing* . Washington, DC: Truth Initiative.

Truth Tobacco Industry Documents. (1971). *Cigarette industry new products review.* Retrieved from https://www.industrydocumentslibrary.ucsf.edu.

Tseng, T. Y., Ostroff, J. S., Campo, A., Gerard, M., Kirchner, T., Rotrosen, J., et al. (2016). A randomized trial comparing the effect of nicotine versus placebo electronic cigarettes on smoking reduction among young adult smokers. *Nicotine and Tobacco Research, 18*(10), 1937-1943.

Tucker-Seeley, R. D., Bezold, C. P., James, P., Miller, M., & Wallington, S. F. (2016). Retail pharmacy policy to end the sale of tobacco products: What is the impact on disparity in neighborhood density of tobacco outlets? *Cancer Epidemiology, Biomarkers and Prevention, 25*(9), 1305-1310.

Tverdal, A., & Bjartveit, K. (2011). Health consequences of pipe versus cigarette smoking. *Tobacco Control, 20*(2), 123-130.

Tynan, M., Babb, S., MacNeil, A., & Griffin, M. (2011). State smoke-free laws for worksites, restaurants, and bars - United States, 2000-2010. *Morbidity and Mortality Weekly Report, 60*(15), 472-475.

U.S. Department of Health and Human Services. (1983). *The health consequences of smoking: Cardiovascular disease: A report of the Surgeon General*. Rockville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

U.S. Department of Health and Human Services. (1988). *The health consequences of smoking: Nicotine addiction: A report of the Surgeon General*. Rockville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

U.S. Department of Health and Human Services. (1994). *Youth and tobacco: Preventing tobacco use among young people: A report of the Surgeon General*. Washington, DC: U.S. Department of Health and Human Services, U.S. Department of Education.

U.S. Department of Health and Human Services. (2008). *Toxicological profile for aluminum*. Atlanta, GA: Agency for Toxic Substances and Disease Registry.

U.S. Department of Health and Human Services. (2010). *How tobacco smoke causes disease: The biology and behavioral basis for smoking-attributable disease: A report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

U.S. Department of Health and Human Services. (2012). *Preventing tobacco use among youth and young adults: A report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

U.S. Department of Health and Human Services. (2014). *The health consequences of smoking-50 years of progress. A report of the Surgeon General* (January 2014. Printed with corrections). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

U.S. Department of Health and Human Services. (2016). 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: Final rule. *Federal Register, 81*(90), 28974-29106.

U.S. Department of Health and Human Services. (2016). *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, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

U.S. Department of Health and Human Services. (2016). *Food and Drug Administration: 21 CFR Parts 1100, 1140, and 1143. Docket No. FDA-2014-N-0189*. Retrieved from https://s3.amazonaws.com.

U.S. Department of Health and Human Services. (2016). *Premarket tobacco product applications for electronic nicotine delivery systems: Guidance for industry.* Retrieved from http://tveca.com.

U.S. Department of Health, Education, and Welfare. (1964). *Smoking and health: Report of the advisory committee to the Surgeon General of the public health service* (PHS Publication No. 1103). Washington, DC: U.S. Government Printing Office.

U.S. Department of Health, Education, and Welfare. (1986). *The health consequences of involuntary smoking: A report of the Surgeon General* (PHS Publication No. 1103). Washington, DC: U.S. Government Printing Office.

U.S. Department of Labor. (2014). *FAQS about Affordable Care Act implementation (Part XIX).* Retrieved from https://www.dol.gov.

U.S. Fire Administration. (2014). *Electronic cigarette fires and explosions*. Emmitsburg, MD: FEMA.

U.S. Food and Drug Administration. (1980). *Select Committee on GRAS Substances (SCOGS) opinion: Diacetyl and starter distillate.* Retrieved from http://www.fda.gov.

U.S. Food and Drug Administration. (2013). *Frequently asked questions: Required warnings for cigarette packages and advertisements.* Retrieved from http://www.fda.gov.

U.S. Food and Drug Administration. (2013). *Nicotine replacement therapy labels may change.* Retrieved from http://www.fda.gov.

U.S. Food and Drug Administration. (2014). *FDA proposes to extend its tobacco authority to additional tobacco products, including e-cigarettes.* Retrieved from http://www.fda.gov.

U.S. Food and Drug Administration. (2015). *Issue snapshot: Modified Risk Tobacco Products (MRTPs).* Retrieved from http://www.fda.gov.

U.S. Food and Drug Administration. (2016). *Family Smoking Prevention and Tobacco Control Act: 21 CFR parts 1100, 1140, and 1143.* Retrieved from http://federalregister.gov.

U.S. Food and Drug Administration. (2016). *News release: FDA takes action against four tobacco manufacturers for illegal sales of flavored cigarettes labeled as little cigars or cigars.* Retrieved from http://www.fda.gov.

U.S. Preventive Services Task Force. (2009). Counseling and interventions to prevent tobacco use and tobacco-caused disease in adults and pregnant women: U.S. Preventive Services Task Force reaffirmation recommendation statement. *Annals of Internal Medicine, 150*(8), 551-555.

U.S. Preventive Services Task Force. (2013). *Tobacco use in children and adolescents: Primary care interventions.* Retrieved from http://www.uspreventiveservicestaskforce.org.

U.S. Preventive Services Task Force. (2015). *Behavioral and pharmacotherapy interventions for tobacco smoking cessation in adults, including pregnant women: Clinical summary.* Retrieved from http://annals.org.

Uchiyama, S., Ohta, K., Inaba, Y., & Kunugita, N. (2013). Determination of carbonyl compounds generated from the E-cigarette using coupled silica cartridges impregnated with hydroquinone and 2,4-dinitrophenylhydrazine, followed by high-performance liquid chromatography. *Analytical Sciences, 29*(12), 1219-1222.

University of Louisville. (2005). *Endowed chair in tobacco harm reduction research.* Retrieved from http://louisville.edu.

University of Louisville. (2016). *Bucks for brains.* Retrieved from http://louisville.edu.

University of Michigan. (2017). *Press release: Vaping, hookah use by U.S. teens declines for first time*. Retrieved from http://ns.umich.edu.

Unlawful advertisements on medium of electronic communication. 15 U.S.C. § 1335 (2010).

van der Tempel, J., Noormohamed, A., Schwartz, R., Norman, C., Malas, M., & Zawertailo, L. (2016). Vape, quit, tweet? Electronic cigarettes and smoking cessation on Twitter. *International Journal of Public Health, 61*(2), 249-256.

Vanderford, R. (2011). *Tobacco cos. sue FDA over 'biased' advisory board.* Retrieved from http://www.law360.com.

Vansickel, A. R., Cobb, C. O., Weaver, M. F., & Eissenberg, T. (2011). A clinical laboratory model for evaluating the acute effects of electronic "cigarettes": Nicotine delivery profile and cardiovascular and subjective effects. *Cancer Epidemiology, Biomarkers and Prevention, 19*(8), 1945-1953.

VapeRanks. (2014). *Imperial tobacco acquires Blu e-cigarettes following R. J. Reynolds-Lorillard merger.* Retrieved from http://vaperanks.com.

Varlet, V., Farsalinos, K., Augsburger, M., Thomas, A., & Etter, J. F. (2015). Toxicity assessment of refill liquids for electronic cigarettes. *International Journal of Environmental Research and Public Health, 12*(5), 4796-4815.

Vasiljevic, M., Petrescu, D. C., & Marteau, T. M. (2016). Impact of advertisements promoting candy-like flavoured e-cigarettes on appeal of tobacco smoking among children: An experimental study. *Tobacco Control, 25*(e2), e107-e112. doi:10.1136/tobaccocontrol-2015-052593.

Villanti, A. C., Cobb, C. O., Cohn, A. M., Williams, V. F., & Rath, J. M. (2015). Correlates of hookah use and predictors of hookah trial in U.S. young adults. *American Journal of Preventive Medicine, 48*(6), 742-746.

Villanti, A. C., Pearson, J. L., Glasser, A. M., Johnson, A. L., Collins, L. K., Niaura, R. S., et al. (2017). Frequency of youth e-cigarette and tobacco use patterns in the United States: Measurement precision is critical to inform public health. *Nicotine and Tobacco Research*. doi:10.1093/ntr/ntw388.

Villanti, A. C., Rath, J. M., Williams, V. F., Pearson, J. L., Richardson, A., Abrams, D. B., et al. (2016). Impact of exposure to electronic cigarette advertising on susceptibility and trial of electronic cigarettes and cigarettes in U.S. young adults: A randomized controlled trial. *Nicotine and Tobacco Research, 18*(5), 1331-1339.

Villanti, A. C., Richardson, A., Vallone, D. M., & Rath, J. M. (2013). Flavored tobacco product use among U.S. young adults. *American Journal of Preventive Medicine, 44*(4), 388-391.

von, R. J., Schonenberger, M., & Barlocher, L. (2014). Carbon monoxide poisoning following use of a water pipe/hookah. *Deutsches Ärzteblatt International, 111*(40), 674-679.

Wackowski, O. A., & Delnevo, C. D. (2016). Young adults' risk perceptions of various tobacco products relative to cigarettes: Results from the National Young Adult Health Survey. *Health Education and Behavior, 43*(3), 328-336.

Wackowski, O. A., Bover Manderski, M. T., Delnevo, C. D., Giovenco, D. P., & Lewis, M. J. (2016). Smokers' early e-cigarette experiences, reasons for use, and use intentions. *Tobacco Regulatory Science, 2*(2), 133-145.

Wagener, T. L., Floyd, E. L., Stpanov, I., Driskill, L. M., Frank, S. G., Meier, E., et al. (2016). Have combustible cigarettes met their match? The nicotine delivery profiles and harmful constituent exposures of second-generation and third-generation electronic cigarette users. *Tobacco Control*. doi:10.1136/tobaccocontrol-2016-053041.

Wagoner, K. G., Cornacchione, J., Wiseman, K. D., Teal, R., Moracco, K. E., & Sutfin, E. L. (2016). E-cigarettes, hookah pens and vapes: Adolescent and young adult perceptions of electronic nicotine delivery systems. *Nicotine and Tobacco Research, 18*(10), 2006-2012.

Wakefield, M. A., Hayes, L., Durkin, S., & Borland, R. (2013). Introduction effects of the Australian plain packaging policy on adult smokers: A cross-sectional study. *BMJ Open, 3*(7). doi:10.1136/bmjopen-2013-003175.

Wald, N. J., & Watt, H. C. (1997). Prospective study of effect of switching from cigarettes to pipes or cigars on mortality from three smoking related diseases. *BMJ, 314*(7098), 1860-1863.

Wang, L., Zhan, Y., Li, Q., Zeng, D. D., Leischow, S. J., & Okamoto, J. (2015). An examination of electronic cigarette content on social media: Analysis of e-cigarette flavor content on Reddit. *International Journal of Environmental Research and Public Health, 12*(11), 14916-14935.

Wang, M. P., Ho, S. Y., Leung, L. T., & Lam, T. H. (2016). Electronic cigarette use and respiratory symptoms in Chinese adolescents in Hong Kong. *JAMA Pediatrics, 170*(1), 89-91.

Warner, K. E. (Eds.). (2006). *Tobacco control policy*. San Francisco, CA: Jossey-Bass.

Weissman, D. G., Schriber, R. A., Fassbender, C., Atherton, O., Krafft, C., Robins, R. W., et al. (2015). Earlier adolescent substance use onset predicts stronger connectivity between reward and cognitive control brain networks. *Developmental Cognitive Neuroscience, 16*, 121-129.

Weitkunat, R., Sanders, E., & Lee, P. N. (2007). Meta-analysis of the relation between European and American smokeless tobacco and oral cancer. *BMC Public Health, 7*, 334. doi:10.1186/1471-2458-7-334.

Wickham, R. J. (2015). How menthol alters tobacco-smoking behavior: A biological perspective. *Yale Journal of Biology and Medicine, 88*, 279-287.

Williams, M., Ghai, S., & Talbot, P. (2015). Disposable electronic cigarettes and electronic hookahs: Evaluation of performance. *Nicotine and Tobacco Research, 17*(2), 201-208.

Williams, M., To, A., Bozhilov, K., & Talbot, P. (2015). Strategies to reduce tin and other metals in electronic cigarette aerosol. *PLoS One, 10*(9), e0138933. doi:10.1371/journal.pone.0138933.

Williams, M., Villarreal, A., Bozhilov, K., Lin, S., & Talbot, P. (2013). Metal and silicate particles including nanoparticles are present in electronic cigarette cartomizer fluid and aerosol. *PLoS One, 8*(3), e57987. doi:10.1371/journal.pone.0057987.

Willis, E., Haught, M. J., & Morris Ii, D. L. (2017). Up in vapor: Exploring the health messages of e-cigarette advertisements. *Health Communication, 32*(3), 372-380..

Wills, T. A., Gibbons, F. X., Sargent, J., & Schweitzer, R. J. (2016). How is the effect of adolescent e-cigarette use on smoking onset mediated: A longitudinal analysis. *Psychology of Addictive Behaviors, 30*(8), 876-886.

Wills, T. A., Knight, R., Sargent, J. D., Gibbons, F. X., Pagano, I., & Williams, R. J. (2017). Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. *Tobacco Control, 26*(1), 34-39.

Wills, T. A., Sargent, J. D., Knight, R., Pagano, I., & Gibbons, F. X. (2016). E-cigarette use and willingness to smoke: A sample of adolescent non-smokers. *Tobacco Control, 25*(e1), e52-e59.

Winden, T. J., Chen, E. S., Wang, Y., Sarkar, I. N., Carter, E. W., & Melton, G. B. (2015). Towards the standardized documentation of e-cigarette use in the electronic health record for population health surveillance and research. *AMIA Joint Summits on Translational Science proceedings, 2015*, 199-203.

Winn, D. M., Blot, W. J., Shy, C. M., Pickle, L. W., Toledo, A., & Fraumeni, J. F. (1981). Snuff dipping and oral cancer among women in the southern United States. *New England Journal of Medicine, 304*(13), 745-749.

Wise, J. (2015). No increase in Australia's illicit tobacco trade after plain packs are introduced. *BMJ, 350*, h1781. doi:10.1136/bmj.h1781.

World Health Organization. (2005). *Advisory note: Waterpipe tobacco smoking: Health effects, research needs and recommended actions by regulators*. Geneva, Switzerland: WHO Study Group on Tobacco Product Regulation (TobReg).

World Health Organization. (2007). *IARC monographs on the evaluation of carcinogenic risks to humans: Volume 89: Smokeless tobacco and some tobacco-specific N-nitrosamines*. France: International Agency for Research on Cancer.

World Health Organization. (2009). *Guidelines for implementation of Article 13 of the WHO Framework Convention on Tobacco Control (Tobacco advertising, promotion and sponsorship).* Retrieved from http://www.who.int.

World Health Organization. (2016). *IARC monographs on the evaluation of carcinogenic risks to humans.* Retrieved from http://monographs.iarc.fr.

Wray, R. J., Jupka, K., Berman, S., Zellin, S., & Vijaykumar, S. (2012). Young adults' perceptions about established and emerging tobacco products: Results from eight focus groups. *Nicotine and Tobacco Research, 14*(2), 184-190.

www.GovTrack.us. (2009). *H.R. 1256 - 111th Congress: Family Smoking Prevention and Tobacco Control Act.* Retrieved from https://www.govtrack.us.

Wyss, A., Hashibe, M., Chuang, S. C., Lee, Y. C., Zhang, Z. F., Yu, G. P., et al. (2013). Cigarette, cigar, and pipe smoking and the risk of head and neck cancers: Pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. *American Journal of Epidemiology, 178*(5), 679-690.

Yeh, J. S., Bullen, C., & Glantz, S. A. (2016). E-cigarettes and smoking cessation. *New England Journal of Medicine, 374*(22), 2172-2174.

Yerger, V. B. (2011). Menthol's potential effects on nicotine dependence: A tobacco industry perspective. *Tobacco Control, 20*(Suppl 2), ii29-ii36.

Yingst, J. M., Veldheer, S., Hrabovsky, S., Nichols, T. T., Wilson, S. J., & Foulds, J. (2015). Factors associated with electronic cigarette users' device preferences and transition from first generation to advanced generation devices. *Nicotine and Tobacco Research, 17*(10), 1242-1246.

Yuan, M., Cross, S. J., Loughlin, S. E., & Leslie, F. M. (2015). Nicotine and the adolescent brain. *Journal of Physiology, 593*(16), 3397-3412.

Zeidler, R., Albermann, K., & Lang, S. (2007). Nicotine and apoptosis. *Apoptosis, 12*(11), 1927-1943.

Zhang, B., Haji, F., Kaufman, P., Muir, S., & Ferrence, R. (2015). 'Enter at your own risk': A multimethod study of air quality and biological measures in Canadian waterpipe cafes. *Tobacco Control, 24*(2), 175-181.

Zhang, X., & Pu, J. (2016). E-cigarette use among U.S. adolescents: Secondhand smoke at home matters. *International Journal of Public Health, 61*(2), 209-213.

Zhong, J., Cao, S., Gong, W., Fei, F., & Wang, M. (2016). Electronic cigarettes use and intention to cigarette smoking among never-smoking adolescents and young adults: A meta-analysis. *International Journal of Environmental Research and Public Health, 13*(5), 465. doi:10.3390/ijerph13050465.

Zhou, J., Michaud, D. S., Langevin, S. M., McClean, M. D., Eliot, M., & Kelsey, K. T. (2013). Smokeless tobacco and risk of head and neck cancer: Evidence from a case-control study in New England. *International Journal of Cancer, 132*(8), 1911-1917.

Zhou, S., Weitzman, M., Vilcassim, R., Wilson, J., Legrand, N., Saunders, E., et al. (2015). Air quality in New York City hookah bars. *Tobacco Control, 24*(e3), e193-e198. doi:10.1136/tobaccocontrol-2014-051763.

Zhu, A. Z. X., & Tyndale, R. F. (2012). Nicotine metabolism and its implications. In P. Anzenbacher & U. M. Zanger (Eds.), *Metabolism of drugs and other xenobiotics.* Weinheim, Germany: Wiley-VCH Verlag GmbH & Co. KGaA.

Zhu, S. H., Sun, J. Y., Bonnevie, E., Cummins, S. E., Gamst, A., Yin, L., et al. (2014). Four hundred and sixty brands of e-cigarettes and counting: Implications for product regulation. *Tobacco Control, 23*(Suppl 3), iii3-iii9.