

## Flavored E-Cigarettes and Public Health

### Executive Summary

This paper details the extraordinary rise in e-cigarette use among our nation's young people and the ongoing threat to youth posed by high nicotine, flavored e-cigarettes. Since e-cigarettes were introduced into the market, youth e-cigarette use has increased dramatically and rapidly and pediatricians have raised alarms about the impact on our young patients.

Children who use e-cigarettes are becoming addicted because many e-cigarettes sold in the United States today contain very high levels of nicotine. High dose nicotine products were ushered into the marketplace by JUUL, allowing for higher levels of nicotine delivered more effectively to the alveoli and causing self-reinforcing blood nicotine concentrations. Many more products with similarly high levels of nicotine followed suit. In addition to high nicotine concentrations, these newer models of e-cigarettes come in a wide variety of flavors, are sleek, small and discreet. By combining highly concentrated nicotine with a sleek design and appealing flavors, the tobacco industry has created a more addictive product with a much easier on ramp to heavy use and addiction.

The evidence clearly demonstrates that flavored e-cigarettes appeal to youth and are extremely popular among youth. Flavors decrease youth perceptions of harm, help mask the harsh taste of tobacco and play an important role in the initiation and uptake of tobacco products. Flavors also increase the likelihood of developing addiction. The growth in the popularity and market share of menthol-flavored e-cigarettes, in particular, raise serious concerns because menthol acts as both a flavor and an anesthetic. Menthol e-cigarettes present a high risk to youth. Removing all flavored e-cigarettes from the market will help to reduce youth use.

Along with new product designs and appealing flavors, e-cigarette companies market their products in ways that appeal to children and adolescents by using a wide variety of media channels, approaches also used by the tobacco industry to successfully market conventional tobacco products to youth.

Pediatricians are very concerned about youth use of any products that contain nicotine, particularly those with high levels of nicotine since the dangers to the developing brain are well documented. Further, a growing body of research indicates a wide range of negative health effects for inhalation of fine particulate aerosols on young e-cigarette users. Taken together nicotine e-cigarette use can impact a young person's respiratory health, brain development, mood, sleep, and immune function. Youth e-cigarette users are also at an increased risk of starting to smoke combustible tobacco products including cigarettes.

While there has been much discussion as to whether e-cigarettes can be an effective smoking cessation aid, the current evidence is inadequate to conclude that e-cigarettes as an open market product are effective at helping smokers quit. Every major agency and scientific

organization in the U.S. that have examined the evidence report that current research is inadequate to conclude that e-cigarettes are effective at helping smokers quit. The need for open market, flavored, high dose and highly addictive nicotine products just cannot be justified given the evidence of real harm to youth.

Despite the limited evidence from several studies in clinical settings suggesting e-cigarettes could be helpful for adults who want to quit, many studies that evaluated the impact of e-cigarette use on smoking cessation under real world conditions found that e-cigarettes are not associated with smoking cessation. In examining this evidence, it is important to distinguish between studies that examine the impact of specific e-cigarettes when provided as part of a supervised smoking cessation program and the use of e-cigarettes when sold as a commercial product and used without medical supervision or guidance.

More action is needed to address e-cigarette use among young people. To protect our nation's children, AAP recommends that e-cigarette product advertising and promotion accessible to children and youth be prohibited. However, marketing restrictions alone will not be enough to address this serious public health problem. Other policies, such as prohibiting the sale of flavored tobacco products, including menthol products, and addressing the problem posed by the marketing of products that deliver high levels of nicotine, are necessary to further prevent youth initiation. These actions are critical to helping all children live tobacco-free and addiction-free lives.

## **I. Introduction**

Modern e-cigarettes are highly engineered, efficient nicotine delivery devices capable of delivering high doses of concentrated nicotine very rapidly, without the aversive response typical of combustible tobacco products. The usual societal tobacco control measures like smoke-free workplaces, housing, and schools, are not as effective in limiting e-cigarette use throughout the day and night. Even nicotine naïve youth may vape over a pack of cigarettes worth of nicotine anywhere and anytime during sessions without limit. Youth are attracted to e-cigarettes not just by direct-to-consumer promotions, social media marketing, and point of sale advertising but by product design features such as their sleek appearance, concealability, ease of sharing, and concentrations of nicotine that yield self-reinforcing behavior from the very first hit. High dose nicotine e-cigarettes come in enticing flavors such as mint and menthol to which youth can become addicted even more rapidly and strongly, making it harder to quit. Today, more youth initiate tobacco use with e-cigarettes than all other tobacco products combined, subjecting these young Americans to the immediate and long-term harms of nicotine addiction and tobacco product use. For the nicotine naïve, the correct comparator for the safety of these products is breathing clean air. In 1995, David Kessler, then Commissioner of the Food and Drug Administration (FDA), called tobacco use a pediatric disease because most nicotine addiction begins before the age of 21. As pediatricians, we witness the harms that flavored high-dose nicotine e-cigarettes inflict on our patients every day. In this carefully researched report, endorsed by experienced pediatricians from every state in our country, we present the overwhelming evidence that flavored e-cigarettes present to the public's health.

## **II. E-cigarettes present a serious, continued threat to youth and to the progress that has been made in reducing tobacco use among youth.**

Since e-cigarettes were introduced into the market, youth e-cigarette use has increased dramatically and rapidly. Data from the Monitoring the Future (MTF) survey demonstrate the unprecedented nature of the youth e-cigarette epidemic: The increase in youth vaping of nicotine from 2017 to 2018 was the single largest one-year increase in youth use of *any substance* in the survey's 43-year history.<sup>1</sup> This historic increase was followed by another increase in 2019. From 2017 to 2019, youth nicotine vaping more than doubled among 8<sup>th</sup>, 10<sup>th</sup> and 12<sup>th</sup> graders to 9.6%, 19.9% and 25.5%, respectively.<sup>2</sup> Similar trends were seen in the National Youth Tobacco Survey (NYTS) which demonstrated that e-cigarette use among high school students more than doubled from 2017 to 2019, from 11.7% to 27.5% of students, or more than one-in-four high schoolers. Among middle school students, e-cigarette use more than tripled from 2017 to 2019, increasing from 3.3% to 10.5%. Altogether, over 5.3 million middle and high school students used e-cigarettes in 2019 – an increase of over three million users in just two years.<sup>3</sup>

Youth use of e-cigarettes has declined since 2019, however much of this dip is due to the COVID-19 pandemic, and may represent a temporary decrease. E-cigarettes remain at least as popular as when the Surgeon General sounded the alarm about their dangers. Several recent national surveys confirm that today, an alarming number of youth are using e-cigarettes, which places them at risk for nicotine addiction and potentially serious current and future adverse health consequences. Since 2014, e-cigarettes have been the most widely used tobacco product among youth.<sup>4</sup> According to the CDC's Adolescent Behavior and Experiences Survey, conducted from January to June 2021, 15.4% of high school students are current e-cigarette users.<sup>5</sup> The 2021 NYTS found that 11.3% of high school students are current e-cigarette users. Of great concern, both surveys found that students who attended school in person and completed the survey in-school had significantly higher use rates compared to students who attended school virtually and completed the survey virtually. For example, in the Adolescent Behavior and Experiences Survey, 25.2% of high school students who were attending in-person schools reported current use of e-cigarettes compared to 9.1% of those attending school virtually.<sup>6</sup> In the NYTS, 15% of students who took the survey in school reported current use compared to 8.1% among those who were attending school virtually.<sup>7</sup> These differences suggest that youth e-cigarette use may increase as students return fully to in-person school and resume pre-pandemic social interactions. Data from the MTF confirms that e-cigarette use remains high, with approximately 1 in 5 (19.6%) 12<sup>th</sup> graders reporting past 30-day use in 2021.<sup>8</sup> Unfortunately, survey data show that youth are initiating at younger ages. In 2018, 28.6% of high schoolers who had tried e-cigarettes initiated prior to age 14, compared to just 8.8% in 2014.<sup>9</sup>

Methodological changes in data collection due to the COVID-19 pandemic make comparisons between the most recent data and previous years difficult.<sup>10</sup> In addition to the pandemic, a 2019 outbreak of lung injury associated with vaping likely caused youth to perceive

e-cigarettes as more risky<sup>11</sup> and may have contributed to the apparent decline. However, it is clear that given the rates of youth vaping among in-person high school students from recent surveys, youth remain at increased risk as social interactions and schooling continue to re-normalize.

### **III. High levels of e-cigarette use among young people is potentially undermining decades of progress in reducing tobacco use in the United States.**

While the nation has made tremendous progress over the past two decades in reducing adolescent tobacco use, e-cigarettes are eroding progress and may be reversing that trend. The unprecedented increase in the number of youth who use e-cigarettes has increased the total number of youth who use tobacco products. The evidence demonstrates that e-cigarettes are attracting a large percentage of youth who would not have smoked cigarettes while at the same time there is no reliable evidence that the marketing of e-cigarettes has reduced the number of children who currently smoke cigarettes. For example, a study examining data from the 2004-2014 NYTS found that the introduction of e-cigarettes was not associated with a change in the declining trajectory of cigarette smoking among youth. Based on psychosocial risk factors, it also found that e-cigarette-only users would be unlikely to have initiated tobacco product use with cigarettes.<sup>12</sup> A more recent study using data from the 2014-2018 NYTS found that "The introduction of e-cigarettes was followed by a slowing decline in current cigarette smoking, a stall in combined cigarette and e-cigarette use...Traditional psychosocial risk factors for cigarette smoking suggest that e-cigarette users do not fit the traditional risk profile of cigarette smokers."<sup>13</sup> Similarly, according to the American Academy of Pediatrics, "Adolescents who use e-cigarettes appear to have fewer social and behavioral risk factors than conventional cigarette users."<sup>14</sup>

### **IV. An increasing percentage of youth who use e-cigarettes are becoming addicted to nicotine.**

The percentage of children who use e-cigarettes frequently is high and has grown every year since the introduction of JUUL and products that deliver nicotine using similar technology. In 2021, 43.6% of high school e-cigarette users reported vaping on 20 or more days/month, and 27.6% reported daily use.<sup>15</sup> The proportion of high school users who use e-cigarettes on a frequent basis has grown steadily, from 15.5% of users in 2014,<sup>16</sup> to 17.4% in 2015-2017,<sup>17</sup> 27.7% in 2018,<sup>18</sup> 34.2% in 2019<sup>19</sup> and 38.9% in 2020.<sup>20</sup> The percentage of children who use e-cigarettes frequently is significantly higher than those who use cigarettes frequently. According to the 2021 NYTS, 43.6% (n=750,000) of high school e-cigarette users are frequent users, compared to 19.6% (n=50,000) of high school cigarette smokers.<sup>21</sup>

Many children who use these products are becoming addicted. Data from the International Tobacco Control Policy Evaluation Project (ITC) Youth Tobacco and Vaping Survey found that between 2017 and 2019, there was an increase in the proportion of current youth e-cigarette users reporting strong urges to use e-cigarettes on most days or more often. In 2019, 53.1% of youth e-cigarette users reported they were either 'a little' or 'very addicted' to e-

cigarettes.<sup>22</sup> The survey also found that youth who use higher nicotine concentrations report more intensive vaping behavior, including the number of days vaped in the past 30 days, the average number of times vaping per day, the number of days ever vaped, experiencing frequent strong urges to vape, and feeling ‘a little’ or ‘very addicted’ to vaping.<sup>23</sup>

These measures of addiction correlate with nicotine levels. A study of adolescent e-cigarette users in San Francisco found that reports of frequency of e-cigarette use and degree of addiction correlated significantly with cotinine as a biomarker of nicotine exposure.<sup>24</sup> Among this same sample, another study found that e-cigarette use persisted over a 12-month period with significant increases in frequency of use, nicotine exposure, and e-cigarette dependence.<sup>25</sup>

#### **V. E-cigarette products on the market today contain very high levels of nicotine.**

Many e-cigarettes sold in the United States today contain high levels of nicotine. Given the speed with which aerosolized nicotine is delivered to the brain and the high nicotine content, it is no wonder that the abuse liability and rates of addiction to these products have increased so dramatically. Pediatricians have been sounding the alarm about these products for over 10 years due to what we have been and continue to see in our patient population. The U.S. Surgeon General also sounded the alarm with the 2016 report, *E-Cigarette Use Among Youth and Young Adults: A Report of the Surgeon General*,<sup>26</sup> and then again with an advisory on e-cigarette use in 2018.<sup>27</sup>

The concentration of nicotine in e-cigarettes has increased dramatically over the past decade as has the efficiency with which e-cigarettes deliver nicotine. Overall, products with 5% or more nicotine (50 mg/mL) went from less than 1% of the share of the market in 2015 to more than two-thirds of the market in 2018.<sup>28</sup> High nicotine products were ushered into the marketplace by JUUL, who developed nicotine salt solutions which allow higher levels of nicotine to be delivered more effectively and with less irritation than the earlier e-cigarette models that use freebase nicotine.<sup>29</sup> JUUL has reported that one JUUL pod contains as much nicotine as a pack of cigarettes. Freebase nicotine solutions contain a lower concentration of nicotine because they become too irritating and unpalatable for the user at higher concentrations.<sup>30</sup> According to a 2018 Surgeon General advisory on e-cigarette use among youth, because nicotine salts allow users to inhale high levels of nicotine more easily and with less irritation, it could be easier for young people to initiate the use of nicotine with these products.<sup>31</sup> Pediatricians and other health experts saw an increase in youth use of these new types of e-cigarettes, and CDC issued warnings to parents and educators to be aware of the new shapes and types of e-cigarettes.<sup>32, 33</sup>

Since JUUL introduced the high nicotine products to the market, many more products with similarly high levels of nicotine have followed suit. One research study found that “as of September 2018, there were at least 39 JUUL knock off devices on the market.”<sup>34</sup> More recently, several companies have taken advantage of the gap in the FDA’s 2020 enforcement policy limiting the flavors of cartridge and pod products to introduce disposable e-cigarettes in a wide variety of flavors, high nicotine levels, and in designs that echo the sleekness and

concealability of JUUL.<sup>35, 36</sup> There are now many e-cigarette disposable products with over 2000 puffs of nicotine. These inexpensive products, readily available to youth, have over 10 packs worth of nicotine. One product called Elf Bar has 5000 hits—more nicotine than two cartons of cigarettes.

In addition to high nicotine concentrations, these newer models of e-cigarettes are sleek, small and discreet, which allows them to be easily concealed.<sup>37</sup> JUUL, for example, resembles a USB flash drive in size and shape. This type of device also generally emits less visible aerosol than some previous devices, so many adolescents have found ways to vape without detection at home or even in classrooms and locker rooms. Increased concealability of products helped to promote “stealth vaping.”<sup>38, 39</sup> Subsequent devices from companies looking to further conceal vaping activity included sweatshirts that enabled vaping, watches, remote controls, fake car fobs, and coffee cups.<sup>40</sup>

The characteristics of JUUL and other new e-cigarette models have removed many of the traditional barriers to tobacco use, allowing adolescents and young adults to use them as often as they wish.<sup>41</sup> Further, these products do not have a natural shut off mechanism. Unlike traditional cigarettes, with e-cigarettes, youth are able to self-administer nicotine anywhere and at every time of day, increasing the concentration of nicotine in their blood and increasing the chances of nicotine addiction. By combining highly concentrated nicotine with a sleek design, the tobacco industry has created a more addictive product with a much easier on ramp to heavy use and addiction.

Not surprisingly, adolescents who use nicotine salt-based products such as JUUL have higher concentrations of nicotine biomarkers and other indicators of addiction. One study found that adolescents and young adults who use nicotine salt pod-based e-cigarettes such as JUUL have higher concentrations of nicotine biomarkers in their body than adolescents who smoke cigarettes.<sup>42</sup> Another study estimated that youth could meet the threshold for nicotine addiction by consuming just one quarter of a JUUL pod per day.<sup>43</sup> A study of youth and young adult e-cigarette users found that pod users were more likely than non-pod users to report daily use and showed more signs of nicotine dependence.<sup>44</sup> JUUL users demonstrate nicotine dependence symptoms. According to data from the MTF study, 41.3% of adolescent JUUL users report at least one symptom of nicotine dependence.<sup>45</sup> Recently, more non-pod disposable e-cigarettes have copied JUUL’s high nicotine formulation, raising abuse liability for the flavored disposable e-cigarette category as well.<sup>37</sup>

## **VI. Youth exposure to nicotine is a serious concern.**

The dangers of youth exposure to nicotine are well documented. Biologically, the brain is more susceptible to addiction during adolescence, and addiction in youth happens faster and earlier than it does in adults.<sup>46</sup> Because young people are more susceptible and sensitive to the effects of nicotine, they can often feel dependent earlier than adults.<sup>47</sup> According to the 2016 Surgeon General Report, *Health Effects of E-Cigarette Use Among U.S. Youth and Young Adults*, “Because the adolescent brain is still developing, nicotine use during adolescence can disrupt

the formation of brain circuits that control attention, learning, and susceptibility to addiction.”<sup>48</sup> A 2021 study found that the levels of nicotine delivered by modern e-cigarettes are enough to produce consistent nicotine reinforcement in non-nicotine dependent youth.<sup>49</sup> There is no safe level of tobacco use for adolescents and for these reasons, the U.S. Surgeon General has concluded that “the use of e-cigarettes by youth should be avoided and actively discouraged.”<sup>50</sup>

Adding to the problem, many youth who use e-cigarettes do not know they are unsafe or addictive and routinely underestimate their risk. According to the 2021 MTF study, only about half of 10<sup>th</sup> grade students think there is great risk from regularly vaping e-liquids or using JUUL.<sup>51</sup> A 2017 study from Truth Initiative found that 63% of 15-24-year-old JUUL users did not know the product always contains nicotine, even though all pods sold from JUUL do contain nicotine.<sup>52</sup> These misperceptions are due to intentional actions by e-cigarette manufacturers. A lawsuit against JUUL from the state of North Carolina asserted that JUUL deceived consumers by understating the nicotine levels of its product and its addiction potential. The lawsuit claims that “JUUL entered the e-cigarette market with among the highest nicotine potency of any product, a nicotine level so high that, in some countries, it is illegal for consumers of any age. JUUL has deceived consumers about that nicotine strength, has misrepresented the nicotine equivalency of its products to traditional cigarettes, and has understated the risks of addiction that occur with such powerful levels of nicotine.”<sup>53</sup>

Survey data show that large numbers of youth and young adult e-cigarette users want to quit and have even made an attempt to quit. According to the Truth Longitudinal Cohort (TLC) survey, in 2019, over half of young current e-cigarette users (15-24 years old) intended to quit using e-cigarettes and one-third (33.3%) actually made a quit attempt in the past year.<sup>54</sup> Unfortunately, the percentage of adolescents who were unable to quit e-cigarettes was nearly twice that of adolescents who were unable to successfully quit combustible cigarettes. Using data from the MTF survey, a study published in JAMA found that 4.12% of adolescents reported an unsuccessful quit attempt for e-cigarettes, compared to 2.23% for cigarettes. Adolescent e-cigarette use is undermining progress that has been made in reducing youth addiction. In 2020, the prevalence of unsuccessful quit attempts among adolescents who had used either e-cigarettes or cigarettes was higher than the prevalence of unsuccessful cigarette quit attempts in each of the previous 13 years.<sup>55</sup> Other research demonstrates that long-term tobacco cessation is extremely difficult for those who start using tobacco products during adolescence. In one long term study, among adolescent users at baseline who had subsequently quit all tobacco use at the one-year mark, approximately 64% were still current tobacco users at 7-year follow-up.<sup>56</sup>

**VII. The actions of the tobacco industry, including product design and marketing, led to products that are appealing to youth and have increased e-cigarette use among young people.**

The behavior of the tobacco industry has never prioritized public health; this pattern has continued with the design and marketing of the modern e-cigarette. E-cigarettes have been

carefully designed so that they are available in a variety of models and colors, with characteristics that make them appealing to adolescents. Most notably, the popularity of JUUL led to transformational changes in the e-cigarette market. As previously noted, JUUL was the first mainstream product to use nicotine salts in e-liquids and also introduced a “sleek, modern design”<sup>57</sup> that was quickly emulated by other companies.<sup>58, 59</sup> Other features of JUUL attractive to youth include the “party mode” light tricks.<sup>60</sup> The light show telegraphs use to other teens in situations where high visibility enhances social spread whereas the small size, concealability, and small plume allows for use in other situations where use is prohibited such as in school or inside an adolescent’s home.

Along with new product designs, e-cigarette companies market their products in ways that appeal to children and adolescents by using a wide variety of media channels, approaches used by the tobacco industry to successfully market conventional tobacco products to youth.<sup>61</sup> Data collected by the U.S. Federal Trade Commission (FTC) showed large increases in e-cigarette marketing expenditures from 2015 to 2018.<sup>62</sup> Previous studies also demonstrated large increases in spending on e-cigarette marketing in the years leading up to those documented by the FTC.<sup>63</sup> The FTC data are the most recent comprehensive data available, but other research documented an increase in spending on e-cigarette television advertising in 2019.<sup>64</sup>

According to data collected from the top six e-cigarette manufacturers by the FTC, overall advertising and promotion spending increased from \$197.8 million in 2015 to \$643.6 million in 2018. E-cigarette companies use promotional tactics including television advertisements targeted to stations with clear youth appeal;<sup>65</sup> advertisements at the point of sale at retail stores;<sup>66</sup> product Web sites and social media;<sup>67</sup> targeted advertisements through search engines and Web sites that are focused on music, entertainment, and sports;<sup>68</sup> celebrity endorsements; and sponsorships and free samples at youth-oriented events.<sup>69</sup> The majority of these e-cigarette methods of advertising are illegal for conventional cigarettes precisely because such tactics promote youth initiation and progression to traditional tobacco product use.<sup>70, 71</sup>

E-cigarettes have also been promoted with a variety of messages that are appealing to youth, including freedom, rebellion, and independence.<sup>72</sup> The 2016 Surgeon General’s report concluded, “Themes in e-cigarette marketing, including sexual content and customer satisfaction, are parallel to themes and techniques that have been found to be appealing to youth and young adults in conventional cigarette advertising and promotion.”<sup>73</sup> For instance, early magazine ads for blu e-cigarettes featured the headline, “take back your freedom”<sup>74</sup> and more recently, Twist e-liquids posted on its Instagram an image with the statement, “crash your neighbor’s pool” and tagged with “#TwistDare.”<sup>75</sup> A study on JUUL’s early marketing practices described its tactics using channels and themes accessible and appealing to young audiences as “patently youth oriented.”<sup>76</sup>

**VIII. The role of traditional tobacco companies in the e-cigarette industry has led to increased sales and higher exposure to retail outlet advertising of adolescents who frequent convenience stores.**

Marketing and promotional activities by tobacco companies increase youth and young adult tobacco initiation and usage.<sup>77</sup> The tobacco industry has long been known to use deceptive marketing and advertising to target certain populations, including youth, minorities, and the LGBTQ+ community.<sup>78</sup> The FTC spending data, based on the top six e-cigarette companies, five of which are owned by or heavily invested in by the big tobacco companies, reflect spending in many of the same categories that these companies have traditionally relied on, which are effective at targeting youth. For instance, in 2018 (the most recent year available), these companies spent 72.1% of its total advertising expenditures on point of sale and price promotion strategies.<sup>79</sup> The Surgeon General has “concluded that the industry’s extensive use of price-reducing promotions has led to higher rates of tobacco use among young people than would have occurred in the absence of these promotions.”<sup>80</sup>

The tobacco industry’s strategy of targeting certain neighborhoods with greater product access and advertising extends to e-cigarettes as well. A study using in-store surveys found that “E-cigarette point-of-sale availability and marketing increased between 2014 and 2015 and expanded to neighborhoods with a higher proportion of Black residents between 2012 and 2015.” It also found that “E-cigarette price promotions were more prevalent in neighborhoods with more Hispanic residents, while exterior e-cigarette marketing was more prevalent in neighborhoods with more Black residents.”<sup>81</sup>

The introduction of e-cigarettes has also led to the rise of vape shops, a new type of specialty store that adds to the availability and accessibility of tobacco products. Data demonstrate that youth are able to purchase e-cigarettes from vape shops. In 2021, more than one in five middle or high school students who used e-cigarettes bought them from a vape shop.<sup>82</sup> A study in *JAMA Pediatrics* found that in California, 44.7% of tobacco and vape shops sold e-cigarettes to underage buyers.<sup>83</sup> While most of the proprietors are independent from the major tobacco companies, many seem to follow traditional point-of-sale marketing strategies, including price promotions and targeting of specific populations. For instance, an audit of vape shops in six major metropolitan areas found that the large majority offered price promotions and other incentives to encourage brand and store loyalty.<sup>84</sup> More recently, studies have documented higher density of vape shops in socially disadvantaged neighborhoods, including closer proximity to schools.<sup>85, 86, 87</sup>

**IX. E-cigarette companies have moved beyond the traditional forms of marketing that increase the risk to youth.**

JUUL was one of the first companies to have an extensive presence on social media, including effectively using its own accounts on the major platforms, hiring influencers, recruiting affiliates, and inspiring hashtags, all of which led to viral content that fueled youth interest and use.<sup>88</sup> One study found the quantity of JUUL’s tweets were highly correlated with

quarterly retail sales.<sup>89</sup> While other e-cigarette companies primarily participated in traditional media channels – TV and retail promotions – JUUL’s “innovative marketing across a variety of new media platforms” led to its successful growth in sales.<sup>90</sup>

Most e-cigarette brands are present on the major social media platforms (i.e., Facebook, Instagram, Twitter, YouTube), and feature links directly to stores and minimal age-gating. Posts include hashtags unrelated to tobacco/e-cigarettes, which widen the accessibility to the content, and do not include warnings.<sup>91</sup> E-cigarette content is appearing on additional online platforms popular with youth and young people, including TikTok<sup>92</sup> and Twitch.<sup>93</sup> Vape shops have also taken to social media to promote their product offerings and discounts. This channel has the potential for much wider exposure to product marketing than people just passing or going inside the store.

E-cigarette companies also recruit and utilize influencers on a variety of social media platforms. FTC data documented a nearly 15-fold increase in spending on endorsements from celebrities, influencers, brand ambassadors, and others between 2015 and 2018, up to \$4.3 million.<sup>94</sup>

#### **X. Youth exposure to any e-cigarette marketing increases youth e-cigarette use.**

The 2014 Surgeon General’s report stated: “The evidence is sufficient to conclude that advertising and promotional activities by the tobacco companies cause the onset and continuation of smoking among adolescents and young adults.”<sup>95</sup> In spite of this, there remain few controls on the magnetic advertising appeal and exposure of e-cigarettes to youth audiences. Indeed, numerous reports in recent years have shown significant penetration of e-cigarette marketing into the adolescent market.<sup>96, 97</sup>

In 2021, 70.3% of middle and high school students had been exposed to e-cigarette advertisements from at least one source.<sup>96</sup> The channels of exposure to promotions differ between products, with more youth reporting contact with e-cigarette promotions through social media and other online interactions (i.e., emails, texts), compared to movies, retail stores, TV, and digital/video games for cigarettes.<sup>97</sup>

In 2021, 3.1 million youth who used social media reporting seeing e-cigarette-related content daily, and 4.5 million reported seeing that type of content weekly.<sup>98</sup> A small study from California found that “Even brief exposure to e-cigarette content on social media was associated with greater intention to use and more positive attitudes toward e-cigarettes.”<sup>99</sup> Another study found a statistically significant association between social media advertising for e-cigarettes and lower harm perceptions among adolescents.<sup>100</sup>

Similar to the experience with cigarette marketing, studies have revealed that youth who are exposed to advertisements are more likely to use e-cigarettes.<sup>101, 102, 103, 104</sup> Exposure to these advertisements increases intention to use e-cigarettes among adolescent nonusers.<sup>105</sup> It is associated with current e-cigarette use,<sup>106</sup> with increasing exposure being associated with

increased odds of use.<sup>107,108</sup> The increased use of and exposure to e-cigarettes among youth, combined with dramatic increases in advertising,<sup>109</sup> have serious potential to undermine successful efforts to deglamorize, restrict, and decrease the use of tobacco products.

More action is needed to address e-cigarette marketing. AAP's policy recommendation is to ban all e-cigarette product advertising and promotion in forms that are accessible to children and youth.<sup>110</sup> Other policies, such as restricting the sale of flavored tobacco products, can also serve to reduce both the availability of tobacco and exposure to tobacco advertising, which can further prevent youth initiation.<sup>111</sup>

## **XI. Flavored e-cigarettes appeal to youth and are extremely popular among youth.**

The evidence is overwhelming – flavors in e-cigarettes attract youth and increase the number of youth who use these products. It is well documented that flavors decrease the perception of harm,<sup>131</sup> help mask the harsh taste of tobacco and play an important role in the initiation and uptake of tobacco products. As the 2020 Surgeon General Report on Smoking Cessation succinctly stated, “the role of flavors in promoting initiation of tobacco product use among youth is well established.”<sup>112</sup> By masking tobacco's harsh taste, flavors help make repeated use more likely, thereby increasing the likelihood of developing addiction. The 2016 Surgeon General report, *E-Cigarettes Among Youth and Young Adults* concluded that flavors are among the most commonly cited reasons for using e-cigarettes among youth and young adults.<sup>113</sup>

Today, there are currently thousands of flavored e-cigarettes on the market. These products are widely available in stores and online. A 2018 study identified more than 15,500 unique e-cigarette flavors available online.<sup>114</sup> The introduction of these products largely coincided with the rapid and dramatic increase in youth e-cigarette use.

Survey data demonstrate just how popular flavored e-cigarettes are among youth. According to the 2021 NYTS, 84.7% current youth e-cigarette users use flavored e-cigarettes.<sup>115</sup> Earlier data from FDA's PATH survey found that nearly all (97%) youth e-cigarette users used flavored e-cigarettes. The same PATH survey found that 70.3% of e-cigarette users reported using e-cigarettes “because they come in flavors I like.”<sup>116</sup> Survey data demonstrate that youth use a variety of flavors and fruit (72.3%), candy/desserts/other sweets (33%), mint (30.5%) and menthol (29.8%) are the most commonly reported flavors used.<sup>117</sup>

Disposable e-cigarettes, also exempted from FDA's 2020 flavors policy, are available in a wide variety of flavors not permitted in pre-filled cartridge products. The popularity of flavored disposable products soared following FDA's February 2020 e-cigarette policy that removed flavored, cartridge-based products from the market, but explicitly excluded disposable e-cigarettes.<sup>118</sup> From February 2020 to December 26, 2021, sales of disposable e-cigarettes increased from 2.8 million units to 7.6 million units.<sup>119</sup> Between 2019 and 2020, use of disposables among high school e-cigarette users increased from 2.4% to 26.5%.<sup>120</sup> In 2021,

55.8% of high school e-cigarette users reported using disposable e-cigarettes; Puff Bar, a disposable e-cigarette, was the most popular brand among youth.<sup>121</sup>

Adding to the concern about flavored e-cigarettes is the fact that many youth underestimate the risks of e-cigarettes because of the sweet flavors. Adolescents perceive that e-cigarettes with flavors are less harmful than those with tobacco flavors,<sup>122</sup> creating a potential misperception that e-cigarettes with flavors do not contain nicotine.<sup>123</sup> While youth generally believe that e-cigarettes are safer than combustible cigarettes, some studies have found that youth also believe that flavored e-cigarettes are safer than non-flavored products.<sup>124</sup> One study conducted in 2018 concluded that, “youths perceive fruit flavours to be less likely to lead to lung cancer and less likely to produce harmful second-hand vapour and to be healthier.”<sup>125</sup> A 2019 systematic review examined questions around the perceptions of youth and adults of e-cigarettes. It concluded that the presence of flavors increased the appeal of e-cigarettes among children, and that youth believed flavored products to be safer than non-flavored e-cigarettes, stating that, “Among youth, flavours increase not only preferences for e-cigarettes but they also increase e-cigarette product appeal, willingness to use, susceptibility to use and initiation, as well as decrease e-cigarette product harm perceptions.”<sup>126</sup> Other studies have found that many youth believe that flavored cigarettes are easier to use than non-flavored products. One study in this area found that 20% of youth who had never used a tobacco product believed that flavored products were easier to use than non-flavored ones; those with that belief were more likely to begin using e-cigarettes.<sup>127</sup> This perception may exist because flavors can mask the harsh taste of nicotine, which irritates the airways.<sup>128</sup>

## **XII. Menthol flavor poses an unreasonable danger to youth**

Many flavors are popular with youth, and research demonstrates that youth will use whatever flavored e-cigarette products remain available. Over the past few years, actions by FDA have resulted in the removal of some flavors from the market; however, youth adapted by switching to whatever flavors remained. For example, JUUL removed all of its flavors except tobacco, mint and menthol from retail shelves in November 2018 amid pressure from regulators.<sup>129</sup> Subsequently, youth use of mint and menthol flavors increased while youth use of fruit flavors declined by 50%.<sup>130</sup> Among 10<sup>th</sup> and 12<sup>th</sup> grade JUUL users, mint was the most popular flavor in 2019.<sup>131</sup> Market data show that following FDA’s action in 2020 that prohibited all flavors in cartridge-based e-cigarettes except for menthol and tobacco, the market share for menthol flavored e-cigarettes increased significantly. In May 2020, menthol-flavored products accounted for more than half (51.6%) of total e-cigarette sales, an increase from 11.4% in August 2019. Among pre-filled cartridge products like JUUL, the proportion of sales that were menthol increased dramatically during this time period, from 10.7% to 61.8%.<sup>132</sup> According to the 2021 NYTS, among youth who use flavored e-cigarettes or flavored cartridge-based products, approximately 30% and 46% use menthol-flavored products, respectively.<sup>133</sup>

The growth in the popularity and market share of menthol-flavored e-cigarettes raises serious concerns. Menthol could be considered the emperor of all flavors because it acts as

both a flavor and an anesthetic. Menthol's anesthetic properties cool the throat, mask the harshness of nicotine, and make it easier for children to start and continue using tobacco products. According to the FDA's Tobacco Products Scientific Advisory Committee report on menthol cigarettes, released in 2013, menthol cigarettes increase smoking initiation among youth and young adults, enhance addiction, and make it harder to quit.<sup>134</sup> More recently, the FDA summarized the evidence regarding the interaction between menthol and nicotine in its proposed rule to prohibit menthol as a characterizing flavor in cigarettes. Importantly, FDA found that the interaction of menthol and nicotine in the brain enhances nicotine addiction, particularly among young people, and makes it more difficult for menthol users to stop using these products. FDA also noted that the combination of menthol and nicotine is particularly damaging to young people.<sup>135</sup> FDA's conclusions regarding menthol apply to not only cigarettes but any product that combines nicotine and menthol, such as e-cigarettes. A study of young adult e-cigarette users in the Los Angeles area found that e-cigarette initiation with mint or menthol flavors, compared to other flavors, may be associated with more frequent e-cigarette use and nicotine dependence symptoms in young adulthood.<sup>136</sup> These findings, taken together, clearly indicate that menthol e-cigarettes present a high risk to youth.

In addition, data suggest that young people often combine menthol with other flavors, including tobacco flavor. For example, 'Ice' e-cigarette flavors—marketed as a combination of fruity/sweet and cooling flavors—have also become popular among young people. One study found that among a sample of young adult past 30-day e-cigarette users in Los Angeles, ice flavors were the most popular e-cigarette flavor.<sup>137</sup> Flavors with both sweet and cooling sensory attributes may increase the youth appeal and addictiveness of the products.

### **XIII. Removing flavored e-cigarettes from the market will help to reduce youth use.**

Evidence is emerging demonstrating that eliminating flavored e-cigarettes will reduce the number of youth who use these products. A 2021 Massachusetts study found that counties with greater implementation of flavored tobacco product restrictions were associated with reductions in the likelihood of current e-cigarette use and a decrease in the frequency of cigarette use among users.<sup>138</sup> Several local communities in Minnesota, including Minneapolis and St. Paul, have implemented flavor bans. Research shows that these policies helped to buffer these communities from the impact of the national e-cigarette epidemic. From 2016 to 2019, e-cigarette use and any tobacco use increased by a lesser extent in the Twin Cities area than the rest of Minnesota, and cigarette, cigar, and hookah use prevalence decreased to a greater extent in the Twin Cities than the rest of the state.<sup>139</sup> A study that examined youth behaviors in Oakland, CA after the city restricted the sale of flavored products found a decrease in both e-cigarette use and smoking by youth, although the decreases were not statistically significant.<sup>140</sup>

One recently debunked study has suggested that the flavor ban in San Francisco increased the odds of cigarette smoking among San Francisco high school students compared to students in other school districts.<sup>141</sup> Many researchers have identified flaws with the analysis and the author's conclusions, chief among them the fact that the study relied on data that was

collected *before* enforcement of the policy began.<sup>142</sup> As a result, conclusions about the impact of the policy cannot be drawn from this study. Of note, other surveys have not shown an increase in youth smoking in San Francisco. The 2019-2020 California Student Tobacco Survey found that cigarette smoking among San Francisco high schoolers is at a historic low of 1.6%.<sup>143</sup>

#### **XIV. E-Cigarettes contain toxins and other harmful chemicals.**

According to the CDC, “e-cigarette aerosol is NOT harmless ‘water vapor.’”<sup>144</sup> Numerous studies analyzing e-liquids and the aerosol generated from e-cigarettes have identified not only nicotine, but a number of other toxic chemicals.<sup>145</sup> While some these known chemicals may be present at lower levels than in cigarette smoke, e-cigarette aerosol still contains heavy metals such as nickel, tin and lead, aldehydes, volatile organic compounds and carcinogens including tobacco specific nitrosamines.<sup>146, 147, 148</sup>

Studies have also shown that these chemicals are absorbed by e-cigarette users. A population-based adult cohort study revealed that exclusive e-cigarette users had higher urine concentrations of nicotine, metals, volatile organic compounds (VOCs), and tobacco-specific nitrosamines compared with nontobacco users.<sup>149, 150</sup> In addition, this same study showed that e-cigarette users had concentrations of metals and VOCs (toluene, benzene, and carbon disulfide) comparable with those of cigarette smokers, with dual users having the highest levels of nicotine and other tobacco biomarkers, metals, and VOCs.<sup>151, 152</sup>

Flavored e-cigarettes may pose unique harms due to the chemical mix needed to create the wide array of flavored products, which are then heated and inhaled in e-cigarette aerosol. The aerosolization process can also create new toxicants.

The Surgeon General found that, “while some of the flavorings used in e-cigarettes are generally recognized as safe for ingestion as food, the health effects of their inhalation are generally unknown and noted that some of the flavorings found in e-cigarettes have been shown to cause serious lung disease when inhaled.<sup>153</sup> For example, diacetyl, known primarily for causing bronchiolitis obliterans or “popcorn lung,” when inhaled in significant quantities, has been used to impart a buttery taste in e-liquids.<sup>154</sup> FDA has expressed similar concerns about flavoring chemicals in e-cigarettes, noting that “Flavorings that are safe for use in food may become toxic when these chemicals are heated and inhaled. Some have been shown to be harmful to the lungs.”<sup>155</sup>

Inhaling the chemicals found in e-cigarettes can cause inflammation or thickening of the delicate structures in the lung, inhibiting the exchange of oxygen in the bloodstream.<sup>156</sup> Some flavor chemicals, when aerosolized by e-cigarettes, were present at levels high enough to be cytotoxic to humans. Many of the flavoring chemicals in e-cigarettes contain aldehydes, which are known to be respiratory irritants, in sufficient concentrations to be of toxicologic concern.<sup>157, 158</sup>

Studies have also found that e-liquid flavorings can alter endothelial function, raising concerns about potential cardiovascular toxicity.<sup>159</sup> Direct cytotoxicity (cell damage) has been shown in cell experiments from flavoring chemicals, which can be present in high concentrations in e-cigarette liquids.<sup>160, 161</sup> Other experiments found that the level of emissions of carbonyl compounds in e-cigarette aerosol increased with higher concentrations of flavor chemicals mixed into e-liquids.<sup>162</sup>

Many studies have compared the chemicals found in e-cigarette aerosol against a known list of chemicals found in smoke from combustible tobacco products, finding the presence of chemicals such as formaldehyde and tobacco specific nitrosamines.<sup>163</sup> Using a different approach, researchers at Johns Hopkins University conducted a broader analysis of four e-cigarette brands and identified a mixture of approximately 2,000 chemicals, the vast majority of which have yet to be characterized.<sup>164</sup> With so much unknown about the thousands of chemicals in e-cigarettes, the researchers caution that e-cigarette users could be exposing themselves to chemicals with adverse health effects in the future. A critical point is that e-cigarettes have a very different chemical and toxin profile from cigarettes, one that may have different implications for health across life stages.

**XV. A growing body of research points to a wide range of negative health effects for young e-cigarette users.**

The potential long-term effects on the health of adolescent users of e-cigarettes is a significant concern among pediatricians. The lungs are designed to do one thing: breath clean air. Even though there is much to learn about the long-term effects of e-cigarettes on health, there is sufficient information to be clear that youth should not be using any e-cigarette products, as these products pose a threat to the health of young users, impacting their respiratory health, brain development, mood, sleep and immune function. Early e-cigarette use puts youth at risk for the sequelae of nicotine addiction, including all the dangers associated with progression to combusted tobacco use.<sup>165</sup>

First, e-cigarettes contain particulates that can have a significant impact on lungs. The National Academies of Science, Engineering and Medicine (NASEM) Report found evidence for increased cough and wheeze in adolescents who use e-cigarettes.<sup>166</sup> In addition, there is also a growing body of evidence of respiratory effects of e-cigarette use for users.<sup>167, 168, 169</sup>

E-cigarettes can be particularly bad for children with asthma, as there is an association with e-cigarette use and an increase in asthma exacerbations.<sup>170</sup> There are also case reports of a rare side effect for young e-cigarette users: hypersensitivity pneumonitis. This serious condition causes acute respiratory distress and requires hospitalization for intensive care and treatment with steroids.<sup>171, 172</sup>

Further, doctors warn against using e-cigarettes during pregnancy due to risks to developing babies. CDC indicates that nicotine in e-cigarettes is “a health danger for pregnant women and developing babies and can damage a developing baby’s brain and lungs.”<sup>173</sup> A

review of additional research indicates that e-cigarettes may be harmful to early life development.<sup>174</sup>

Nicotine uniquely impacts developing adolescent brains compared to fully developed adult brains<sup>175</sup> and can have lasting adverse effects for brain development.<sup>176, 177</sup> Some impacts include an association with mood and anxiety disorders, suicidal ideation,<sup>178</sup> and depressive symptoms, and long-term mental health effects.<sup>179, 180</sup> These associations have been noted for e-cigarettes specifically.<sup>181, 182</sup> E-cigarette use during adolescence has been strongly associated with serious difficulty concentrating, remembering, and making decisions.<sup>183</sup> Earlier exposure to e-cigarettes was associated with larger effect sizes.<sup>184</sup> E-cigarette use has also been associated with subjective cognitive complaints among adults.<sup>185</sup>

E-cigarette use has also been associated with sleep deprivation. In one study, researchers analyzed data from the 2017-2018 BRFSS and found that young adults (age 18-24) using e-cigarettes every day were more likely to self-report sleep deprivation compared to never users. The authors note that their findings “suggest that e-cigarette use might be related to sleep deprivation in young adults.”<sup>186</sup>

There is also significant reason for concern about the impact of nicotine and e-cigarette use on the immune system of young users. It is well established that smoking increases risk of bacterial and viral infections.<sup>187, 188</sup> Nicotine is also known to suppress immune function throughout the body.<sup>189</sup> Emerging research suggests that e-cigarette aerosol can work to inhibit several types of immune cells in the lungs, which impedes the body’s ability to fight infection.<sup>190</sup>

Since coronavirus attacks the lungs, health experts are concerned that COVID-19 could be an especially serious threat to those who smoke tobacco or who use e-cigarettes.<sup>191</sup> One study found that US youth and young adults who use e-cigarettes are more likely to report having been diagnosed with COVID-19.<sup>192</sup>

While we have enough short-term data to be seriously concerned about adolescent use of e-cigarettes, we of course have no long-term data on its health impacts on children because e-cigarette use is a relatively new phenomenon. NASEM, for instance, found “substantial evidence” that some of the chemicals in e-cigarette aerosols (such as formaldehyde and acrolein) are capable of causing DNA damage and mutagenesis.<sup>193</sup> The report concluded that, this “supports the biological plausibility that long-term exposure to e-cigarette aerosols could increase risk of cancer and adverse reproductive outcomes.”

A preliminary study published after the release of the NASEM report found that exposure to e-cigarette aerosol caused mice to develop lung cancer.<sup>194</sup> In the experiment, 22.5% of mice exposed to e-cigarette aerosol for 54 weeks developed lung cancer. In addition, more than half of the mice exposed to e-cigarette aerosol developed precancerous growth in the bladder. The causal effects of e-cigarettes on human cancer are not yet known, and likely will not be known for decades because human cancers take a long time to develop.<sup>195</sup> In the

case of cigarettes, the public found out how damaging they were to health many years too late. Pediatricians worry about what we will learn about e-cigarettes after it's too late.<sup>196</sup>

#### **XVI. Youth e-cigarette users have an increased risk of starting to smoke cigarettes.**

Studies of US young people who use e-cigarettes identify consistent findings: adolescents and young adults who use e-cigarettes, compared with those who do not, are at higher risk of transitioning to traditional cigarettes.<sup>197</sup>

In 2016, the Surgeon General initially concluded that e-cigarette use is “strongly associated” with the use of other tobacco products among youth and young adults.<sup>198</sup> The 2018 NASEM report found the effect of e-cigarette use on cigarette smoking initiation to be causal, concluding that “There is substantial evidence that e-cigarette use increases risk of ever using combustible tobacco cigarettes among youth and young adults.” The NASEM report also concluded, “There is moderate evidence that e-cigarette use increases the frequency of subsequent combustible tobacco cigarette use” among youth and young adults.<sup>199</sup>

More recently, the World Health Organization (WHO)'s 2021 Report on the Global Tobacco Epidemic concluded that “ENDS use among children and adolescents increases the chances they will use conventional cigarettes and other tobacco products”<sup>200</sup> based on findings from a systematic review and meta-analysis of 25 studies published through 2020, which found that youth who had used e-cigarettes had three times the risk of ever trying cigarettes and more than two times the risk of current smoking.<sup>201</sup>

An analysis of data from the FDA's nationally representative Population Assessment of Tobacco and Health (PATH) study found that from 2013 to 2016, youth (ages 12-15) e-cigarette use was associated with more than four times the odds of trying cigarettes and nearly three times the odds of current cigarette use. The researchers estimated that this translates to over 43,000 current youth cigarette smokers who might not have become smokers if they had not initiated e-cigarette use.<sup>202</sup>

Several studies have also found that the link between e-cigarette use and smoking initiation is actually stronger for those who have *lower* risk factors for smoking at baseline.<sup>203</sup> E-cigarettes may also facilitate the transition to more established smoking behavior among youth who *have* experimented with cigarettes.<sup>204</sup>

Taken together, these findings raise significant concern among pediatricians that e-cigarettes have the potential to addict a new generation to nicotine and tobacco, which could slow the decline in adolescent cigarette smoking that has occurred in recent decades.<sup>205</sup>

Of further concern, we know from the experience with cigarettes that addiction to nicotine by an adolescent increases the risk of addiction in adulthood. The 1994 Surgeon General's report concluded, “People who begin to smoke at an early age are more likely to develop severe levels of nicotine addiction than those who start at a later age.”<sup>206</sup> Ninety

percent of adult cigarette smokers began smoking during their teenage years, and the adolescent brain is more susceptible to nicotine addiction even with intermittent exposure.<sup>207</sup>

**XVII. There is inadequate evidence that the use of flavored e-cigarettes is necessary or even effective at helping smokers quit.**

There has been much to discussion as to whether e-cigarettes can be an effective smoking cessation aid. Some research suggests that e-cigarettes used under certain conditions may help smokers quit. Other studies have found that e-cigarettes used in the real world are often not associated with successful quitting and have not resulted in increased rates of quitting smoking cigarettes on a population level. However, the current evidence is inadequate to conclude that e-cigarettes as an open market product are effective at helping smokers quit. Adults who are addicted to tobacco cigarettes continue to smoke for the nicotine and resulting avoidance of withdrawal symptoms, both of which are realized with use of tobacco flavored e-cigarettes. In fact, there is no conclusive evidence to demonstrate that in the real-world smokers who use flavored e-cigarettes quit at a higher rate than those who use non-flavored e-cigarettes.<sup>208</sup> In examining this evidence, it is important to distinguish between studies that examine the impact of specific e-cigarettes when provided as part of a supervised smoking cessation program and the use of e-cigarettes when sold as a commercial product and used without medical supervision or guidance.

Every major agency and scientific organization in the U.S. that have examined the evidence report that current research is inadequate to conclude that e-cigarettes are effective at helping smokers quit.<sup>209</sup> The 2020 U.S. Surgeon General's Report on Smoking Cessation included the following key finding: "E-cigarettes, a continually changing and heterogeneous group of products, are used in a variety of ways. Consequently, it is difficult to make generalizations about efficacy for cessation based on clinical trials involving a particular e-cigarette, and there is presently inadequate evidence to conclude that e-cigarettes, in general, increase smoking cessation."<sup>210</sup> In the recent U.S. Preventive Services Task Force (USPSTF) Final Recommendation Statement for Tobacco Cessation in Adults they also concluded that, "the current evidence is insufficient to assess the balance of benefits and harms of electronic cigarettes for tobacco cessation in adults, including pregnant persons."<sup>211</sup> Reports from other agencies, including the NASEM and the WHO, have echoed these concerns; there is no conclusive evidence to demonstrate that smokers who use e-cigarettes quit at a higher rate than those who do not.<sup>212</sup> In addition to these major reports, recent meta-analyses have examined whether use of e cigarettes help adults quit the use of combustible cigarettes. A 2020 meta-analysis of 55 studies also found that e-cigarette use was not statistically significantly associated with smoking cessation.<sup>213</sup> An earlier meta-analysis published in 2016 that included 38 studies found that the odds of quitting were less among smokers using e-cigarettes.<sup>214</sup>

Some research studies that evaluated the effectiveness of e-cigarettes for smoking cessation have shown that smokers are more likely to have success with quitting smoking if they use e-cigarettes daily.<sup>215</sup> Two 2021 studies that analyzed nationally representative surveys in the U.S. and Australia, respectively, found daily use of e-cigarettes to be significantly

associated with reductions in, and cessation from cigarette smoking as compared to non-daily or occasional use.<sup>216</sup> A 2020 meta-analysis found that daily e-cigarette use was associated with increased smoking cessation while less than daily e-cigarette use was associated with significantly less smoking cessation.<sup>217</sup> Of concern, research has shown that non-daily e-cigarette use and dual use of e-cigarettes and cigarettes have been found to reduce a smoker's chances of cessation compared to not using e-cigarettes at all.<sup>218</sup> While the 2021 study cited above by McDermott et al, found that frequent use of e-cigarettes can be effective for cessation, it found that if e-cigarettes are not used daily, they may hinder successful cessation as the study reported decreased odds of cessation for non-daily users.<sup>219</sup>

Research also suggests that e-cigarettes may be effective at helping smokers quit traditional cigarettes when combined with behavioral support or other appropriate clinical supports. For example, a 2020 study in *Lancet Respiratory Medicine* found that combining NRT with nicotine e-cigarettes can lead to modest improvement in smoking cessation.<sup>220</sup> A study published in the *New England Journal of Medicine* (NEJM) found that e-cigarette products with refillable tanks were more effective for smoking cessation than nicotine-replacement therapy (NRT), among smokers attending stop smoking services through the U.K. National Health Service.<sup>221</sup> In this study, NRT was 2.5 times as likely to lead to complete abstinence from all tobacco products. The vast majority of those who quit cigarettes using e-cigarettes were still using them at end of study, subjecting them to additional harm as well as increased risk of relapse. However, the study's findings are limited and not generalizable to all smokers. Importantly, this research does not reflect how most e-cigarette users use the product. Many e-cigarette users do not use the product daily and most e-cigarette users do not receive behavioral or clinical cessation support. Further, in the NEJM study – along with three other randomized controlled trial studies utilized by the Cochrane review on e-cigarettes for cessation, which concluded that e-cigarettes can “probably” help people stop smoking – smokers were part of a highly controlled environment, and as a result, are not able to provide information as to whether e-cigarettes are beneficial based on how these products are used among the general population.<sup>222</sup>

Despite the limited evidence suggesting e-cigarettes could be helpful for adults who want to quit, many studies that evaluated the impact of e-cigarette use on smoking cessation under real world conditions found that e-cigarettes are not associated with smoking cessation. For example, an early study from 2018 found no evidence that e-cigarettes help adult smokers quit at a higher rate than smokers who did not use e-cigarettes, despite e-cigarette users in the study being more likely to make a quit attempt.<sup>223</sup> Another study, published in 2020, analyzing ITC Four Country Smoking and Vaping data on cohorts from Australia, Canada, England, and the US examined changes in smoking and vaping behaviors over 18 months and found that the vast majority of cigarette smokers were still smoking cigarettes 18 months later.<sup>224</sup>

In addition, studies that analyzed data from the Population Assessment of Tobacco and Health (PATH) survey have found that the majority of smokers who use e-cigarettes to try to quit smoking are less likely to quit, and instead, end up using both combustible cigarettes and e-cigarettes. One study found that nearly 90% of dual users at PATH Wave 1 (2013-2014) were

still smoking cigarettes at Wave 2 (2014-2015).<sup>225</sup> Another, analyzing the same baseline PATH data (Wave 1), also found that three years later (Wave 4, 2016-2018) adult dual users were less likely to completely quit smoking cigarettes compared to those who hadn't used e-cigarettes.<sup>226</sup> Rates for dual use of combustible cigarettes and e-cigarettes among adults who use e-cigarettes are high. According to 2019 data, 37% of adults who used e-cigarettes also smoked cigarettes.<sup>227</sup> When e-cigarettes are used in conjunction with cigarettes, or in a non-daily manner, the overall impact on the chances of a smoker quitting are negative, not neutral. Further, research shows that dual users have higher exposures to some toxins<sup>228</sup> and emerging studies suggest that dual use can be associated with greater odds of poor health outcomes.<sup>229</sup>

Those who do manage to quit will likely be long term users of e-cigarettes. Many smokers who use e-cigarettes to quit smoking combustible cigarettes continue using e-cigarettes after they have quit smoking. Two studies released in 2020, that analyze data from FDA's PATH survey showed that the majority of participants who either tried or successfully used e-cigarettes to quit smoking were still using e-cigarettes at follow-up, suggesting that e-cigarettes may contribute to ongoing nicotine dependence.<sup>230</sup> Similarly, a 2022 meta-analysis of randomized controlled trials that assessed e-cigarette and nicotine replacement therapy for smoking cessation as well as complete nicotine cessation found that at follow-up, e-cigarette users were much less likely to have stopped all nicotine use compared to NRT users.<sup>231</sup>

Emerging evidence suggests that there should also be concern for former smokers who use e-cigarettes. A 2022 study using PATH data (Waves 3-5, 2016-2019) found that recent former smokers who had used e-cigarettes to quit had a significantly lower rate of staying quit from cigarette smoking compared to those who had used either no e-cigarette products or specifically, used any NRT/pharmaceutical aid.<sup>232</sup> Moreover, a 2022 meta-analysis that examined smoking relapse among former smokers found that the risk of smoking relapse was double among those who used e-cigarettes compared to those who did not.<sup>233</sup>

On a population level, the marketing and growth of e-cigarettes in the US has not had an impact on adult smoking rates. A recent 2022 study published in Tobacco Control examined PATH survey data between 2017 and 2019.<sup>234</sup> The study did not find a cessation benefit from the use of e-cigarettes, and the authors concluded that, "Sales increases in high nicotine e-cigarettes in 2017 did not translate to more smokers using these e-cigarettes to quit smoking. On average, using e-cigarettes for cessation in 2017 did not improve successful quitting or prevent relapse." The authors went on to note that, "[their] analysis suggests that the 2017 JUUL marketing campaigns were not effective in encouraging smokers to use JUUL products to help with quit attempts, unlike their effectiveness in encouraging young people to initiate nicotine use with their products." Another study, using ITC 4CV survey data showed that there was no noticeable increase in adult use of JUUL or other e-cigarette products, while at the same time there was a significant and rapid rise in use of these products among youth.<sup>235</sup> In fact, adult e-cigarette use has remained low and stable, never rising above its highest use rate of 4.5% from 2019. In 2020, the adult e-cigarette use rate went down to 3.7%, just slightly higher than the 2018 rate of 3.2%.<sup>236</sup> Comparatively, a far greater percentage of youth use e-cigarettes

than adults – meaning that the negative impact on youth is a major consideration in evaluating the overall impact of e-cigarettes on our society.<sup>237</sup>

## **XVIII. Conclusion**

The combination of flavors with high dose nicotine delivered in highly engineered concealable modern e-cigarettes has transformed what used to be a road to nicotine addiction into a high-speed interstate highway. As Pediatricians, we see firsthand teenagers who start using e-cigarettes and have extreme difficulty quitting. We have watched many of them become dual and poly users of combustible tobacco products. All children deserve the best chance to live tobacco-free and addiction-free lives. The current e-cigarette products are too appealing to youth, the product placements too numerous, and the nicotine concentrations too high to be allowed on the open market. While cigarettes have become denormalized and more difficult to use in social settings, the heavily marketed to youth e-cigarette remains “cool” and can be used at school, at home, at parties, indoors, and anywhere. In medicine, a fundamental principal taught to all doctors and medical professionals applies to the youth e-cigarette problem, *primum non nocere*. When faced with a known harm to a vulnerable and protected class of people, weighted against uncertain and unproven benefit, the central bioethical precept of non-maleficence dictates, “first, do no harm.” Remove flavored nicotine from the market.

Respectfully Submitted,

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