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The impact of conventional and nonconventional inhalants on children and adolescents

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Abstract

Aim: Inhalant abuse in the adolescent population is a growing concern for care givers, communities, physicians, and medical providers. The aim of this article is to provide a review of the literature about this new challenge. In addition, it raises awareness about recent health policy rulings.

Methods: Review of the literature was done.

Results: In this review article, the prevalence of different modes of inhalant use and abuse in children and young adults and their potential health implications will be examined: Cigarettes, ENDS (E Cigarettes), Hookah, Marijuana, and Huffing. Additionally, marketing and advertising tactics will be reviewed to understand how they target this population. A review of current health policy recommendations from the FDA, American Thoracic Society, and the American Academy of Pediatrics will also be discussed.

Conclusion: The rapid rise in e-cigarette and hookah use in school aged children should trigger a call to action in the medical and public health communities. Health policy recommendations need to be made to reduce the level of adolescent substance abuse.

KEYWORDS
environmental lung disease, international health, pulmonology (general)

1 | INTRODUCTION

Inhalant abuse in the adolescent population is a growing concern for care givers, communities, physicians, and medical providers alike. Aside from the health implications, addiction to certain inhalant substances most often begins in adolescents.[1] As one of public health's greatest successes, tobacco control has helped mitigate the prevalence of smoking, and many of the adverse health effects associated with it. With the development and introduction of new devices like the electronic cigarettes (e-cigarettes or electronic nicotine delivery system [ENDS]) and hookah, it has become more difficult to monitor and regulate the use of these devices especially in the at risk populations, including adolescents. The use of electronic cigarettes (e-cigarettes) is growing rapidly among American youth and young adults. Although the health implications of some substances, like cigarette and alcohol remain clear, we have yet to understand the risk of others.[2] However, while smoking is not as socially acceptable as it was several years ago, now, much more work in advocacy and increasing awareness needs to be done to address the new devices and other inhalants. Along with traditional cigarette smoking, the increased use

Abbreviations: ENDS, the electronic nicotine delivery system; e-cigarette, electronic cigarette; WPS, water pipe smoking; MMLs, medical marijuana laws; NO, nitrous oxide; VS, volatile solvent; FVC, forced vital capacity; FEV1, forced expiratory volume at 1 second; FEV1/FVC, ratio of forced expiratory volume in one second to forced vital capacity; FEF 25–75%, forced expiratory flow between 25 and 75 percent of FVC; FeNO, Fractional Exhaled Nitric Oxide.

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of alternative forms of tobacco, such as hookah (water-pipes) and e-cigarettes, has led to the development of new research efforts documenting both prevalence of smoking and the health consequences associated with their usage. Marketing campaigns take aim at the youth with their unique colors, designs, and popularity during this social media era. The lack of regulations on the advertisement of these products may lead to increased prevalence of their use.[3] Therefore, specific health policy recommendations need to be made to reduce the level of adolescent substance abuse.[4]

1.1 | Category of inhalants

1.1.1 | Electronic cigarettes (E-cigarettes)

The idea of e-cigarette, a battery-powered nicotine delivery device dates back to 1963 but did not come to fruition until the e-cigarette was created in China by Hon Lik in 2003. The concept underlying the device was to deliver nicotine in a breathable form to provide characteristics of conventional tobacco but with the hope of reducing tobacco-associated diseases. E-cigarettes contain nicotine, propylene glycol, and vegetable glycerin in various combinations and are marketed with various flavors/additives to target various demographic groups.[1–3,5] Driven by worldwide recognition of the inherent dangers associated with smoking and other tobacco product use, and aggressive marketing, the e-cigarette manufacturing has grown rapidly. Although touted as "safer" because of the lack of tar and other combustion products, they are potent vehicles for delivery of nicotine, and little is known about other potential risks associated with e-cigarette delivery mechanisms.[6] E-cigarettes are one of the world's fastest growing products and have overtaken traditional cigarette use among school children as reported in a recent United States government survey.[1] More than 80% of users felt that they were less harmful than combustible cigarettes and three-fourths of individuals started them to reduce smoking or avoid relapsing. Smokers or former smokers often began e-cigarettes to deal with nicotine craving or withdrawal symptoms. Others stated that they used them because they were cheaper than smoking tobacco cigarettes (57%) or could be used in situations where smoking was prohibited (39%).[7,8] In 2015, a total of 25.3% of high school students reported current use of a tobacco product, including 13.0% who reported current use of ≥2 tobacco products. Among all high school students, e-cigarettes (16.0%) were the most common tobacco products used, followed by cigarettes (9.3%), cigars (8.6%), hookahs (7.2%), smokeless tobacco (6.0%), pipe tobacco (1.0%), and bidis (0.6%)[1] (Figure 1). Current use of any tobacco and ≥2 tobacco products among middle school students was 7.4% and 3.3%, respectively. E-cigarettes (5.3%) were the tobacco product used most commonly by middle school students, followed by cigarettes (2.3%), hookahs (2.0%), smokeless tobacco (1.8%), cigars (1.6%), pipe tobacco (0.4%), and bidis (0.2%)[1] (Figure 2).

There is scarce evidence about passive exposure to the vapor released or exhaled from e-cigarettes under real conditions. A study was conducted to characterize passive exposure to nicotine from e-cigarettes' vapor and conventional cigarettes' smoke at home among non-smokers under real-use conditions.[9] The airborne markers were statistically higher in conventional cigarette homes than in e-cigarettes

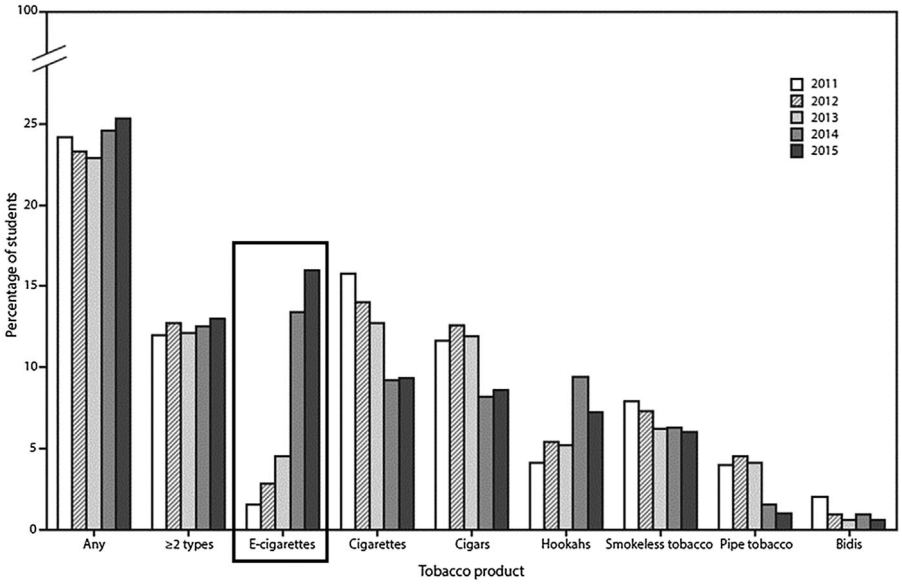

FIGURE 1 Estimated percentage of high school students who currently use any tobacco products, ≥2 tobacco products, —and select tobacco products —National Youth Tobacco Survey 2011-2015. Any tobacco product use is defined as past 30-day use of cigarettes, cigars, smokeless tobacco, e-cigarettes, hookahs, pipe tobacco, and/or bidis. ≥2 tobacco product use is defined as past 30-day use of two or more of the following product types: cigarettes, cigars, smokeless tobacco, e-cigarettes, hookahs, pipe tobacco, and/or bidis. E-cigarettes and hookahs demonstrated a nonlinear increase ($P < 0.05$). Cigarettes and smokeless tobacco demonstrated a linear decrease ($P < 0.05$). Cigars, pipe tobacco, and bidis demonstrated a nonlinear Reproduced from Arrazola et al[1]

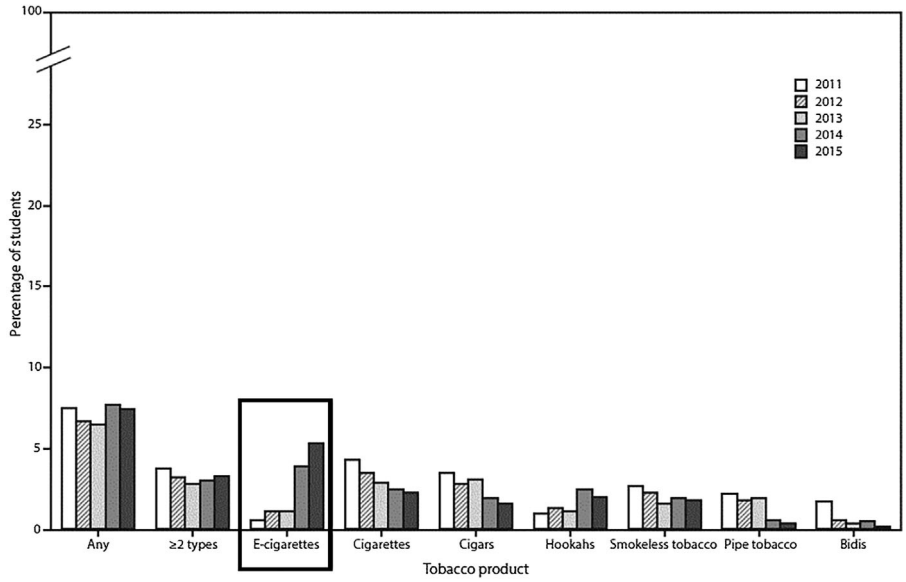

FIGURE 2 Estimated percentage of middle school students who currently use any tobacco products, ≥2 tobacco products, and select tobacco products in the past 30 days — National Youth Tobacco Survey, 2011-2015. Any tobacco product use is defined as past 30-day use of cigarettes, cigars, smokeless tobacco, e-cigarettes, hookahs, pipe tobacco, and/or bidis. ≥2 tobacco product use is defined as past 30-day use of two or more of the following product types: cigarettes, cigars, smokeless tobacco, e-cigarettes, hookahs, pipe tobacco, and/or bidis. ≥2 tobacco product use demonstrated a nonlinear change ($P < 0.05$). E-cigarettes and hookahs demonstrated a linear increase ($P < 0.05$). Cigarettes, cigars, and smokeless tobacco demonstrated a linear decrease ($P < 0.05$). Pipe tobacco and bidis demonstrated a nonlinear decrease ($P < 0.05$). Reproduced from Arrazola et al[1]

homes (5.7 times higher). However, concentrations of both biomarkers (cotinine in saliva and urine) among non-smokers exposed to conventional cigarettes and e-cigarettes' vapor were statistically similar (only 2 and 1.4 times higher, respectively). The levels of airborne nicotine and cotinine concentrations (both in saliva and urine) at the homes with e-cigarette users were significantly higher than at control homes ($P < 0.001$). The results show that non-smokers passively exposed to e-cigarettes absorb nicotine.[9]

As a relatively new and emerging nonconventional tobacco product, e-cigarettes have raised concerns due to limited data regarding long-term effects, the increased use among youth, a lack of government control measures, and the evidence of toxic chemical content. While e-cigarettes do not contain the combustion related toxic substances found in cigarette smoke, e-cigarette aerosols can cause upper respiratory tract irritation, dry cough, and dryness of the mucus membrane.[10] One study also found that five minutes of e-cigarette use was associated with an immediate decrease in fraction of exhaled nitric oxide (FeNO) within the experimental group by 2.14 ppb ($P = 0.005$) but not in the control group ($P = 0.859$). Total respiratory impedance at 5 Hz in the experimental group was found to increase by 0.033 kPa/(L/s) ($P = 0.001$), and flow respiratory resistance at 5 Hz, 10 Hz, and 20 Hz and overall peripheral resistance were also statistically increased ($P = 0.24$), after using an e-cigarette.[11] In considering its cardiovascular effects, e-cigarettes are associated with increased systolic and diastolic blood pressures and heart rate.[12] In another experimental study, it was found that the nicotine concentrations of e-cigarette solutions vary by manufacturer, indicating a need for better regulation and labeling.[13] Aside from the harmful effects of nicotine, propylene glycol, the nicotine solvent used in e-cigarettes, has been shown to irritate the eye and respiratory system.[12,14] E-cigarette aerosol also contains toxic chemicals such as formaldehyde and acetaldehyde, though these levels are lower than those found in conventional cigarettes.[15]

In another study it was found that 39 out of 51 types of flavored e-cigarettes were found to contain a flavoring chemical known as diacetyl.[16] Diacetyl received much attention a few years ago when eight people who had previously worked at a microwave popcorn-processing plant were found to have severe bronchiolitis obliterans. Upon further investigation by the National Institute of Occupational Safety and Health (NIOSH), it was determined that there was a strong association between this lung disease and airborne exposure to butter-flavoring chemicals in the facility, with diacetyl being the most prominent. Due to its occurrence in microwave popcorn manufacturing plants, bronchiolitis obliterans has become known as "popcorn lung."[16]

To protect young people from initiating or continuing the use of e-cigarettes, actions must be taken at the federal, state, and local levels. At the federal level, the U.S. Food and Drug Administration (FDA)—under authority granted to it by Congress under the *Family Smoking Prevention and Tobacco Control Act of 2009*—took a historic step to protect America's youth from the harmful effects of using e-cigarettes by extending its regulatory authority over the manufacturing, distribution, and marketing of e-cigarettes. Through such action, FDA now requires minimum age restrictions to prevent sales to minors and prohibits sales through vending machines (in any facility that

admits youth), and will require products to carry a nicotine warning.[17] Unfortunately, language banning the sale of flavored e-cigarette products was removed from the final version of the rule. In May 2016, the FDA published a Deeming Rule to extend its tobacco regulating authority to currently marketed products such as certain dissolvables, gels, hookah tobacco, electronic cigarettes, cigars, and pipe tobacco. Components and parts of tobacco products, but not their related accessories, are included in the scope of this proposed rule.[4]

1.1.2 | Hookahs (water-pipe)

Though, hookah or water-pipe smoking (WPS) has been in use for centuries, it is only recently that is has gained increased worldwide popularity.[17,18] The prevalence of hookah tobacco smoking has increased worldwide, in part, because of misconceptions that it is safer.[19] Hookah (WPS) has become popular among youth and young adults owing to its social acceptance, novelty, availability in numerous appealing flavors, and its relative low cost.[18,20] Although both the chronic and the acute health consequences of hookah are beginning to surface in the literature, information about the negative short- and long-term health effects is not being conveyed adequately to the general population; rather, health-related information is overshadowed by hookah bar marketing efforts and lack of regulatory involvement of governmental bodies.[20] A systematic review using the approach of the Cochrane Collaboration was performed (comparing six cross-sectional studies) to systematically review the effects of WPS on lung function. The secondary objective was to compare the effects of WPS and cigarette smoking on lung function.[21] Compared with no smoking, WPS was associated with a statistically significant standardized mean difference (SMD) in FEV1 (95%CI, −0.58 to −0.29; equivalent to a 4.04% lower FEV1 % predicted value). Comparing WPS with cigarette smoking, there was no statistically significant difference in FEV1, FVC, and FEV1/FVC.[21] In another cross-sectional study the effects of WPS on lung functions and fractional exhaled nitric oxide (FeNO) was examined. A significant decrease in lung function parameters FEV1, FEV1/FVC Ratio, FEF-25%, FEF-50%, FEF-75% and FEF-75-85% were found among hookah smokers relative to their control group. There was also a significant reduction in FeNO among hookah smokers compared to control group.[22]

Hookah use among adolescents has been increasing over the past few years in the US and worldwide. According to the CDC's analysis of the 2011-2015 National Youth Tobacco Survey, hookah usage was the third most common source of inhalant abuse among students in 2015.[1] The study found a non-linear statistically significant increase noted between the years of 2011-2014 with a change from 4.1% to 9.4% among high school students, dropping to 7.2% of high school students having one or more sessions of hookah within the past 30 days in 2015.[1] The biggest increase was found between the years of 2013-2014. Prevalence nearly doubled for high school with a change of 5.2% (770 000) to 9.4% (1.3 million).[1] Prevalence among middle school students more than doubled from 1.1% (120,000) to 2.5% (280,000).[1] Similar international studies found much higher levels among adolescents. Based on the Global Youth Tobacco Survey that was conducted between 1999 and 2007, and involved more than 90 000 children (13-15 years) in the Eastern Mediterranean Region, the prevalence of WPS has become higher than cigarette smoking among youth in this region.[23]

While research about hookah smoking is still emerging, current findings show that it poses many problems. Hookah has been found to be significantly associated with lung cancer,[24] communicable diseases such as hepatitis C,[25] tuberculosis,[26] respiratory illness (defined as perennial rhinitis and including nasal congestion and wheezing), periodontal disease.[27] Other acute respiratory effects of WPS included increased respiratory rate (RR), carbon monoxide (CO), and carboxyhemoglobin (COHb).[28,29] Chronically, WPS has been associated COPD, chronic bronchitis, emphysema, and asthma.[27] Some proposed mechanisms of WPS-induced respiratory effect include CO exposure, increased airway resistance, lung inflammation, oxidative stress, and damage to the airway ciliary epithelium.[21,30,31]

In another study which looked at the acute effects of WPS on the cardiovascular system, it was found that a 45-90 min session of WPS led to significant increases in systolic and diastolic blood pressure ($P < 0.001$), heart rate ($P < 0.001$), and carbon monoxide levels ($P < 0.001$).[32] Over long-term use, WPS has also been associated with an increased odds of coronary artery disease (CAD) in comparison to individuals who never smoked.[28,29] Mechanisms that have been proposed to explain the association of WPS with cardiovascular issues include endothelial dysfunction, HR variability, and increased oxidative stress.[8] Aside from this, WPS has been associated with a risk for contracting communicable diseases, as the water pipe and water inside can harbor bacteria.[25,26,31]

Another study, examined the effect of smoking on three groups of pregnant women: those who smoked hookah during pregnancy, those who smoked cigarettes during this time, and a third group which did not smoke at all. It was found that the children born to women who smoked hookah weighed about 100 grams less than the children born to non-smokers ($P < 0.1$), and that this finding was less significant than cigarette smoking.[33] It was also found that the adjusted risk of having pulmonary problems, malformations (such as hydrocephalus), and perinatal complications increased among babies that were born to hookah and cigarette users. The risk was highest among hookah users, however, with an odds ratio of 3.65 (95%CI 1.52-8.75).[33] Furthermore, while studies have determined several adverse health effects associated with WPS, one particular study analyzed the air quality of 10 WPS bars. It was found that all had an unhealthy air quality index (AQI) of 151-200, while two were found to reach a dangerous AQI level of 301-500.[31]

1.1.3 | Cigarettes

The epidemic of smoking-caused disease in the twentieth century ranks among the greatest public health catastrophes of the century. The decline of smoking consequent to tobacco control is surely one of public health's greatest successes. However, the current rate of progress in tobacco control is not fast enough and much more needs to be done to end the tobacco epidemic.[34] Tobacco use and addiction

most often begin during youth and young adulthood.[34,35] From the current literature, cigarette smoking harms almost every organ in the body. It was reported that 71% of people in the United States that smoke tried their first cigarette in adolescence. Tobacco use in any form may have lasting adverse consequences on the developing brain.[34] This leads to much concern over the health implications of tobacco exposure in at risk adolescent and youth populations.

The effect of tobacco exposure on adolescent lung development has been found to create significant health implications. Cigarette smoking is associated with evidence of mild airway obstruction and slowed growth of lung function in adolescents. Adolescent girls may be more vulnerable than boys to the effects of smoking on the growth of their lung function.[36] Furthermore, given that allergens and environmental pollutants have long been known to cause or exacerbate asthma, there is accumulating evidence linking cigarette smoking to asthma. In a large population-based sample of young teenagers, it was reported that asthma and allergic diseases were significantly associated with active tobacco smoking even after controlling for passive tobacco smoking exposure, which is known to increase asthma in children.[37] In another study conducted on middle school children, children who currently smoked or reported any tobacco smoke exposure were at an increased risk of reporting active asthma symptoms.[38] This work suggests that active cigarette smoking could be a risk factor for asthma among adolescents as well. Both allergic rhinitis and eczema are more commonly reported by current smokers among adolescents and by former smokers among adults, respectively.[37] The association between smoking and idiopathic pulmonary fibrosis (IPF) has also been investigated. In a case-control study involved subjects diagnosed with IPF, a history of smoking was associated with an increased risk of developing IPF.[39]

In addition, psychiatric comorbidity is common in adolescent cigarette smokers, especially disruptive behavior disorders (such as oppositional defiant disorder, conduct disorder, and attention-deficit/hyperactivity disorder), major depressive disorders, and drug and alcohol use disorders.[40] Anxiety disorders are modestly associated with cigarette smoking. Both early onset (<13 years) cigarette smoking and conduct problems seem to be robust markers of increased psychopathology, including substance abuse, later in life. In spite of the high comorbidity, very few adolescents have nicotine dependence diagnosed or receive smoking cessation treatment in child and adolescent psychiatric treatment settings.[40]

1.1.4 | Other inhalant (Marijuana)

Marijuana (cannabis) is the most commonly used illicit drug in the United States. It is also the most widely used illicit drug on college campuses.[41] Moreover, its use is increasing among adolescents and young adults, partially due to society's changing beliefs about cannabis use and its legal status.[42] As of February 2015, 23 states and the District of Columbia have implemented medical marijuana laws (MMLs), which permit marijuana use for medical purposes. Despite the growing consensus about the relief medical marijuana can bring for a range of serious illnesses, concerns have been voiced that MMLs may give rise to increased marijuana use in the general population and increased use of other substances.[43] A study examined the effect of the implementation of MMLs in 10 states between 2004 and 2012 on a variety of substance use outcomes including marijuana use, alcohol use, pain medication misuse, and hard drug use in both adolescent and adult populations.[43] It was concluded that implementation of an MML led to a relative 14% increase in the probability of past-month marijuana use and a 15% increase in the probability of almost daily/daily marijuana use among adults aged 21 or above. For this age group, MML implementation also resulted in a 10% increase in the probability of marijuana abuse/dependence.[43] Among adolescents and young adults aged 12-20, it was found that a 5% increase in the probability of past-year marijuana use initiation was attributable to MML implementation.[43]

1.1.5 | Huffing

Inhalant use is the deliberate inhalation of volatile substances, via sniffing, snorting, bagging, or huffing, to induce a psychoactive or mind-altering effect. It is a serious drug problem worldwide, particularly in disadvantaged populations and among adolescents.[44] Inhalant abuse is a significant problem affecting many people, particularly youth. The easy availability of products containing volatile substances (eg, aerosol sprays, cleaning products, paint) provides opportunity for mind-altering experiences. Unfortunately, serious complications such as brain, cardiovascular, liver, and renal damage or even death may ensue.[45] Adolescents perceive the risk as low, and parents may be unaware of the risks. Health care providers, particularly psychiatrists, should undertake strategies of prevention, assessment, and treatment of this challenging problem.[46]

Inhalant abuse and dependence among adolescents in the United States age 12-17 years was 0.2% and 0.2%, respectively. The prevalence of inhalant abuse and dependence among one year inhalant users was 6% and 4%, respectively.[44] The most commonly used inhalants were glue/shoe polish and gasoline, which were used by 43% and 36%, respectively, of inhalant users. About one-half (51%) of adolescent inhalant users had used two or more types of inhalants in their lifetime. Most (80%) inhalant users reported their first inhalant use before age 15. Males were more likely to have ever used gasoline and nitrous oxide, whereas females were more likely to have ever used glue/shoe polish, spray paints, correction fluid, and aerosol sprays.[44] According to data from the 2000/2001 National Household Survey on Drug Abuse, approximately 9.0% of U.S. 12- to 17-year-olds had used inhalants and, of these, 21.7% reported lifetime nitrous oxide (NO) use, making NO use the fourth most prevalent specific class of inhalants used nationally among adolescents, with a lifetime prevalence of use estimated at 2.0%.[44]

Few studies have examined the prevalence of NO inhalation or co-occurrence of NO and volatile solvent (VS) use in adolescents. A study was done with the aim of describing the independent and conjoint prevalence of NO and VS use in incarcerated youth, who were ethnically diverse and predominantly male.[47] Lifetime prevalence of NO use was 15.8%. NO and VS users demonstrated greater

impairments compared to NO and VS nonusers. VS-only users demonstrated impairments that were similar in kind but at lower prevalence compared to those displayed by NO and VS users, whereas NO-only youth had profiles that were similar to those of NO/VS nonusers. Psychiatric disorders, polydrug use, and temperamental fearlessness were correlates of NO use. NO and VS users were at high risk for behavioral and emotional problems. Screening and interventions for NO and VS inhalant use should be implemented in juvenile justice facilities.[47]

1.2 | Health implications of inhalants on neurodevelopment

Whereas risk taking during the teenage years may be normative and functionally adaptive as the adolescent strives for independence from adults, such behaviors may also contribute to an incentive to initiate drug use. Given the unique neurodevelopmental processes taking place during adolescence, trying out new experiences and taking risks (including drug use) is more likely among teenagers than among children and adults.[48] The emerging science of neuro-development is providing a new framework for viewing adolescent risk-taking, including decisions made by young people to use tobacco and/or other drugs. This research, aided by sophisticated brain imaging technology, has documented the surprising finding that the human brain is still maturing in significant ways during the adolescent years.[49] The way the brain develops during adolescence may help explain why youth sometimes make decisions that seem to be quite risky. There are several lines of evidence suggesting that adolescents are uniquely susceptible to the short- and long-term effects of drugs. Early drug use may alter brain maturation, contribute to lasting cognitive impairment of certain functions, and significantly increase short- and long-term susceptibility for developing a substance use disorder.[50]

Research into brain development has shown that the maturing brain may be particularly vulnerable to the acute effects of drugs, and that drug use during adolescence may significantly increase a young person's risk for developing a substance use disorder later in life.[51] Nicotine is one substance that has been thought to make children more vulnerable to drug addiction in the future.[52] While there are sociocultural influences, data at preclinical and clinical levels indicate that this adolescent sensitivity has strong neurobiological underpinnings. This may induce epigenetic changes that sensitize the brain to other drugs and prime it for future substance abuse.[52–54] Cannabis use is another drug used in at risk adolescent populations. Cannabis use is associated with impairments of cognitive functions, including learning and memory, attention, and decision-making.[55] A study was done by collecting and analyzing high-resolution MRI scans on young adult recreational marijuana user and non-using controls. Significant shape differences were detected in the left nucleus accumbens and right amygdala. The left nucleus accumbens showed salient exposure dependent alterations across all measures and an altered multimodal relationship across measures in the marijuana group. These data suggest that marijuana exposure, even in young recreational users, is associated with exposure-dependent alterations of the neural matrix of core reward structures and is consistent with animal studies of changes in dendritic arborization.[55]

Taken together, this data makes clear the significant public health implications for pediatric inhalant exposure and underscores the need for targeted efforts to reduce direct or indirect exposures to inhalants in children and adolescents.

1.3 | Marketing/advertising to adolescents and young adults in social media age

Research into exposure to pro-tobacco marketing and media has found an increase in the odds of youth holding positive attitudes toward tobacco use (odds ratio, 1.51; 95% confidence interval, 1.08-2.13) and more than doubles the odds of initiating tobacco use (odds ratio, 2.23; 95% confidence interval, 1.79-2.77). Highly engaging marketing and media are more effective at promoting use (odds ratio, 2.67; 95% confidence interval, 2.19-3.25). These effects are observed across time, in different countries, with different study designs and measures of exposure and outcome.[56]

According to United States Food and Drug Administration documents, marketing of e-cigarettes has been directed at the young adults and children.[57] Sophisticated advertising and internet availability make electronic cigarettes easily accessible to youth. Electronic cigarette manufacturers advertise heavily through social networking systems and avoid using the word cigarette because of its negative connotations. Teenagers may deny using electronic cigarettes, but they state that they are vaping, for example, on a nicotine-containing, e-cigarette, or flavored hookah pen. This may underestimate self-reported electronic cigarette or hookah use in surveys.[7] Flavorings, which appeal to children, have been banned (except menthol) for combustible cigarettes, but not for electronic cigarettes. The various flavorings available for ENDS make them very attractive to young people. There are hundreds of electronic nicotine delivery products; many are poorly regulated and often lack production standards. The lack of regulation affects safety. In many places, the sales of electronic cigarettes are uncontrolled. Until the recent FDA rule they have not been licensed as drug or tobacco products or had regulation of ingredient labeling. This increases the odds that ingredients may vary with products and with different batches of the same product.[7] The lack of child-proof containers for candy-flavored products poses a serious threat to young children. The availability of nicotine and advertised flavors allows anyone to make their own solutions at home.

Increased marketing has contributed to the growing popularity of water-pipe smoking, higher overall sales, particularly through Internet sites, sponsorship at events, distribution of free samples, and direct advertisements.[56,58] Marketing techniques conceal potential dangers associated with water-pipes. For example, in the Eastern Mediterranean Region, the package is labeled as being “100% natural,” making the product seem more acceptable and perhaps even a healthy behavior to consider.[59] Newer marketing strategies are focused on the portability of the hookah device with its carrying case and shoulder strap making the ease of transport seemingly more attractive.[60] These same markets are advocating for the purchase of other products that

claim to decrease the negative health effects of water-pipe smoking, such as filtered mouthpieces. None of these devices has been shown to be efficacious in reducing exposure to toxins or the associated risks of tobacco-related disease and death.[60]

1.4 | Health policy

In May 2016, the FDA published a final rule to extend its tobacco regulating authority to currently marketed products such as certain dissolvables, gels, hookah tobacco, electronic cigarettes, cigars, and pipe tobacco. Components and parts of tobacco products, but not their related accessories, are included in the scope of this rule.[4] The rule restricts sales to minors younger than 18, requires health warnings on packaging, prohibits vending machine sales, and prohibits marketing the products as healthy or safe.[4] These FDA rules do not address the use of candy and fruit flavors which appeal to youth and will not go into effect until at least 2 years after the rule is finalized and challenges to the rule in Congress have already begun. In absence of strong federal regulation, states have been acting to restrict e-cigarette purchases by minors, marketing targeted at children and adolescents, and the use of the devices in public places.[61]

1.5 | Recommendations and conclusions

Professional groups with an interest in child health are actively engages on these issues. The American Academy of Pediatrics' position is:

1. Sales of e-cigarettes to minors younger than 18 years should be prohibited.
2. Candy and fruit flavored e-cigarettes, which encourage youth smoking initiation, should be banned.
3. Federal, state, and local governments should enact and enforce laws that mandate the provision of smoke-free environments, including e-cigarette vapor, in all public places and require employers to provide smoke-free/e-cigarette vapor-free work environments for their employees.[61]

The American Thoracic Society has a long-held position that e-cigarettes need to be subjected to the same marketing and manufacturing restrictions as tobacco products. The alarming increases in e-cigarette and hookah use in children, if left unchecked, will lead to another generation of young people becoming addicted to nicotine and will do tremendous and costly damage to the public's health.[62]

Comprehensive tobacco control and prevention strategies for youth and young adults should address all tobacco products, including e-cigarettes. Further reductions in tobacco use and initiation among youth and young adults are achievable by regulating the manufacturing, distribution, marketing, and sales of all tobacco products—including e-cigarettes, and particularly to children—and combining those approaches with other proven strategies. These strategies include funding tobacco control programs at levels recommended by the Centers for Disease Control and Prevention (CDC); increasing prices of tobacco products; implementing and enforcing comprehensive smoke-free laws; and sustaining hard-hitting media campaigns, such as CDC's *Tips from Former Smokers* that encourages smokers to quit for good, and FDA's *Real Cost* that is aimed at preventing youth from trying tobacco and reducing the number of youth who move from experimenting to regular use.

The rapid rise in e-cigarette and hookah use in school aged children should trigger a call to action in the medical and public health communities lest we repeat the mistakes made with cigarettes. Although the recent FDA final rule extending oversight to e-cigarettes and other ENDS and prohibiting sales to minors is an important step in the right direction it is only a start. We have more to do to help protect people worldwide from the dangers of tobacco and nicotine, especially our youth. As cigarette smoking among those under 18 has fallen, the use of other nicotine products, including e-cigarettes, has taken a drastic leap. The absence of effective regulations preventing aggressive marketing of nicotine products to children is creating a new generation of Americans who are at risk of nicotine addiction.

Better education and awareness of the dangers of inhalants to our youth and their parents are warranted. As it is clear that banning advertisements for cigarettes has led to decrease tobacco use in youth and adults, efforts to place similar restrictions on advertisement of e-cigarette and other inhalants must be pursued. Similarly, pricing/taxation strategies to create financial barriers to youth using these products are worth consideration. Marketing strategies targeting children, including flavored products appealing to children must be banned. Investment in a comprehensive strategy for reducing the impact of ENDS and other inhaled substances on our children has the potential to deliver a significant public health return and prevent public health catastrophe. We can implement these cost-effective, evidence-based, life-saving strategies now. Together with additional effort and support, we can protect the health of our nation's young people.[16]

AUTHORS' CONTRIBUTORS

Samya Nasr: Dr. Nasr did the initial literature review, drafted the initial manuscript, and approved the final manuscript as submitted. Stuart C. Sweet: Dr. Sweet did the literature review, reviewed and revised the manuscript, and approved the final manuscript as submitted. Ali Ibrahim Nasrallah: Mr. Nasrallah participated in the literature search, participated in the initial drafting of the manuscript and critically reviewed the manuscript, and approved the final manuscript as submitted. Mariam Abdulghani: Ms. Abdulghani participated in the literature search, participated in the initial drafting of the manuscript and critically reviewed the manuscript, and approved the final manuscript as submitted. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work

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CLINICAL TRIAL REGISTRATION

None.

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