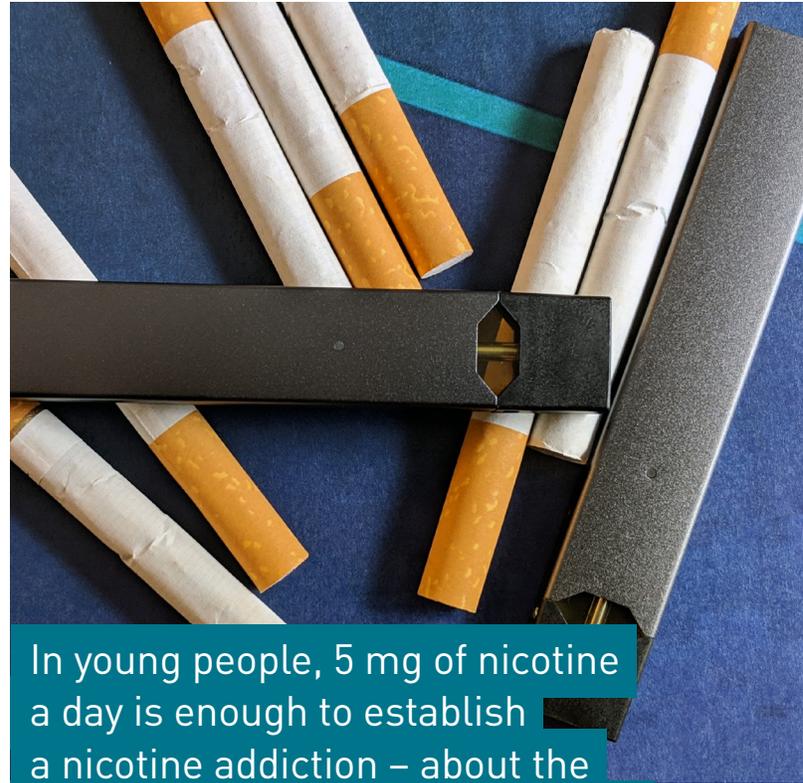


# NICOTINE AND THE YOUNG BRAIN

## WHAT IS NICOTINE?

Nicotine is highly addictive and found in cigarettes, e-cigarettes, and other tobacco products.<sup>1</sup> When users inhale or otherwise use nicotine-containing products, the addictive drug makes its way quickly to the brain where it drives the release of dopamine, a chemical that signals pleasure and keeps users addicted to nicotine.<sup>2</sup> **In young people, 5 mg of nicotine a day is enough to establish a nicotine addiction – about the amount of nicotine in one-quarter of an e-cigarette pod.**<sup>3,4</sup>

Tobacco products have traditionally contained nicotine that is extracted from tobacco leaves. Recently, more products are claiming to contain **synthetic nicotine** that was created in a lab. Newer methods of making synthetic nicotine can produce and isolate the more potent version of nicotine found in tobacco leaves at lower costs, leading to a surplus of new nicotine-containing products like Puff Bar and oral nicotine Bidi Pouches that claim to be “tobacco-free”<sup>5</sup> even though they still contain the addictive chemical nicotine.



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## Do e-cigarettes contain nicotine?

E-cigarettes heat up a liquid solution to a high enough temperature so that it produces an aerosol that can be inhaled.<sup>6</sup> The liquid solution almost always includes nicotine, flavoring and a humectant to retain moisture and create the aerosol when heated.<sup>6</sup> While some e-cigarette brands offer nicotine-free products, 99% of e-cigarette products sold in U.S. convenience stores and mass retail locations in 2015 contained nicotine.<sup>7</sup> Many young e-cigarette users are not aware of the nicotine content in the products. For example, nearly two-thirds of young JUUL users aged 15-21 were not aware the product always contains nicotine.<sup>8</sup>

## HOW DOES NICOTINE AFFECT YOUNG BRAINS?

Nicotine is harmful to developing brains and its use during adolescence can disrupt the formation of brain circuits that control attention, learning, and susceptibility to addiction.<sup>9,10</sup> Research has shown early age of smoking and pleasurable initial experiences are correlated with daily use and lifetime nicotine dependence.<sup>11</sup> Here's what we know about how nicotine exposure in its many forms can adversely affect adolescents:

- > Exposure to nicotine among youth is particularly dangerous since it affects key brain receptors, making young people more susceptible to nicotine addiction.<sup>9</sup>
- > Studies have shown that young people who have never smoked previously and began using e-cigarettes are more likely to smoke cigarettes in the future. One study found that nicotine naïve youth and young adults who had ever used e-cigarettes had seven times higher odds of becoming smokers one year later compared with those who had never vaped.<sup>12</sup>
- > Vaping is significantly associated with higher levels of ADHD symptoms, based on a 2019 study of college students.<sup>14</sup>

There is evidence that the effect of nicotine on developing brains may also prime greater vulnerability to addiction to other drugs.



- > Studies have shown that nicotine can worsen anxiety symptoms and amplify feelings of depression.<sup>15,16</sup> Current e-cigarette users have double the odds of also having a diagnosis of depression compared to those who have never vaped, according to a 2019 cross-sectional study, published in JAMA, of nearly 30,000 current e-cigarette users.<sup>7</sup> Frequent vaping is tied to even higher odds (2.4X) of having a diagnosis of depression compared to never users. (See our report “[Colliding Crises: Youth Mental Health and Nicotine Use](#)” for more details.)
- > Nicotine use — whether through smoking or vaping — can increase stress levels. (See our report on “[Nicotine Use and Stress](#)” and the myth of nicotine as a stress-reliever.)

## HOW IS NICOTINE REGULATED IN THE U.S.?

The FDA regulates all nicotine products. Products containing tobacco or nicotine, regardless of its source (either tobacco-derived or synthetic), must be authorized by the Center for Tobacco Products. Cessation products such as nicotine replacement therapies (NRT) that are expressly for cessation or otherwise make therapeutic claims must be authorized by the Center for Drug Evaluation and Research approval process for safety and effectiveness.

Until recently, many e-cigarette makers used [synthetic nicotine to try to skirt regulation by the FDA](#). For example, Puff Bar, a top vape brand among youth, was told by the FDA in July 2020 to stop selling their flavored, tobacco-derived e-cigarette products. In March 2021, the company returned to the market claiming their product had been reformulated with synthetic “tobacco-free nicotine.” A new law granting FDA authority over synthetic nicotine products has since gone into effect. The new law ensures that any nicotine-containing product, regardless of the nicotine’s origin, is regulated in a consistent way, and closes the loophole that e-cigarette manufacturers were exploiting to keep addictive, youth-appealing nicotine products on the market.

More research is needed on the health effects of synthetic nicotine.

## IS THERE A CAP ON NICOTINE LEVELS?

There is no limit on nicotine levels in the U.S. in e-cigarettes or cigarettes. Popular e-cigarettes contain increasing levels of nicotine and many times match or exceed nicotine levels in cigarettes. A 2019 study found that the average nicotine concentration in e-cigarettes more than doubled from 2.1% in 2013 to 4.34% in 2018.<sup>18</sup> Puff Bar, an e-cigarette brand popular with young people, can have nicotine levels as high as 5%, more than double the highest nicotine concentration allowed in the European Union, the United Kingdom, and Canada — 2%. When the flavored e-cigarette JUUL debuted, it came in concentrations of 5% (or 59 mg/ml) nicotine, with its pods containing 20 cigarettes worth of nicotine. Other e-cigarette competitors claim to have 6-7% nicotine.

The amount of nicotine delivered by tobacco products depends on other factors in addition to nicotine levels, such as the use of nicotine salts, other ingredients, and device features like voltage:

- > Modern e-cigarettes rely on nicotine salts to ensure that they deliver a high level of nicotine that can be inhaled more easily and with less irritation than the free-base nicotine that has traditionally been used in tobacco products, including e-cigarettes<sup>19,20</sup>. Puff Bar, JUUL, Vuse and most other popular e-cigarette brands use nicotine salts.
- > The maker of JUUL claims its nicotine salt formulation increases the rate and amount of nicotine delivered into the blood, compared with other formulations. The company has claimed the product delivers nicotine up to 2.7 times faster than other e-cigarettes.
- > Increasing efficiency in nicotine delivery isn't limited to e-cigarettes. Tobacco manufacturers adjusted their cigarette design so that the nicotine delivered to smokers increased by 14.5% between 1999 and 2011.<sup>20</sup>

Higher nicotine levels are important because they contribute to greater nicotine addiction.



## Lowering nicotine levels to non-addictive levels

In 2018, the FDA announced plans to explore a product standard to lower nicotine in cigarettes to minimally or non-addictive levels. At the same time, they released results from a study published in the New England Journal of Medicine that modeled what would happen after implementing a policy lowering nicotine levels in cigarettes and other combustible tobacco products, including roll-your-own tobacco, pipe tobacco, and non-premium cigars.<sup>22</sup> According to the model, if the policy were put in place by 2020, approximately 5 million additional adult smokers would quit smoking one year after implementation, compared to a scenario where the policy hadn't been enacted. The study estimates that by 2100, more than 33 million people would avoid becoming regular smokers.

Unfortunately, FDA has not yet taken action on reducing nicotine levels in any product to non-addictive levels. Truth Initiative supports restricting nicotine levels in both combustible products and e-cigarettes as well as other factors that affect nicotine delivery, such as nicotine salts, to help reduce the addictiveness of nicotine-containing products.

Young people who vaped fruit-, menthol-, and mint-flavored e-cigarettes with higher nicotine concentrations had greater nicotine dependence compared to those who used e-cigarettes with lower nicotine levels, according to a Truth Initiative study published in Substance Use and Misuse.<sup>21</sup> In the Preamble to the proposed rule, FDA presented

## How do other countries regulate nicotine?

The U.S.'s lack of regulation of nicotine levels is dramatically different from other countries. The highest nicotine concentration allowed in the European Union and the United Kingdom is 20 mg/ml (2%).



evidence that the interaction of menthol and nicotine in the brain enhances nicotine addiction, particularly among young people, resulting in increased nicotine dependence and making it more difficult for users to stop using such products.

### QUITTING NICOTINE

Tapping into supports like medication and counseling to help quit smoking can triple a smoker's chance of quitting.<sup>27</sup> Nicotine replacement therapy (NRT) aims to replace nicotine from cigarettes in smokers who are attempting to quit and suffering from nicotine withdrawal symptoms.<sup>28</sup> The FDA has approved NRT gum, inhalers, lozenges, nasal sprays, and patches, as well as the medications varenicline (Chantix) and bupropion for use in quitting tobacco. These medications have been demonstrated to improve quit rates by 50 to 70%.<sup>27</sup>

There are substantial research gaps in proving the effectiveness of e-cigarettes as quit smoking aids. The 2020 Surgeon General's Report on smoking cessation found that there is "inadequate evidence" to conclude that e-cigarettes increase smoking cessation. Similarly, the 2018 National Academies report found limited evidence on the effectiveness of e-cigarettes to promote quitting. E-cigarettes

## Harm reduction

Harm reduction — the principle of providing evidence-based, lower harm alternatives for those who do not quit harmful substances — is a proven public health strategy. Truth Initiative supports the idea that a genuine harm reduction approach to nicotine requires a measured and careful deployment of regulated nicotine alternatives that are tightly focused on helping smokers who otherwise would not quit smoking cigarettes.

[See our [in-depth statement](#) on harm reduction for more information.]

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are also not approved as quit aids by the FDA or the U.S. Preventative Service Task Force. A 2019 study by the U.K. National Health Service and published in the New England Journal of Medicine did find, however, that e-cigarettes may help adults quit, if they have the right support. A group assigned to e-cigarettes as a combustible tobacco replacement were more likely to remain abstinent one year later compared with a group using nicotine replacement products (18% vs. 9.9%). However, a majority of e-cigarette users were still

using e-cigarettes at the one-year follow-up. Study participants were actively seeking to quit smoking and received at least four weeks of behavioral support. No similar study has replicated these results in the U.S.

More research is needed to determine whether e-cigarettes are appropriate for tobacco cessation. [See “[E-cigarettes: Facts, Stats, and Regulations](#)” and “[What you need to know to quit smoking](#)” for more information.]

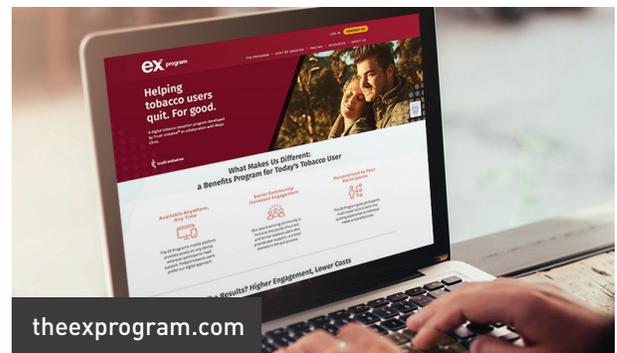
## Resources for quitting

Truth Initiative has resources for young people and adults to support quitting nicotine.

**This is Quitting** is a free and anonymous text messaging program from Truth Initiative designed to help young people quit vaping. The first-of-its-kind, evidence proven quit program has helped nearly 500,000 young people to date. Learn more at [truthinitiative.org/thisisquitting](https://truthinitiative.org/thisisquitting).

**BecomeAnEX**, a free, digital quit-smoking plan and online community of thousands of smokers and ex-smokers developed by Truth Initiative in collaboration with Mayo Clinic has helped more than 910,000 people develop the skills and confidence to successfully quit. Learn more at [becomeanex.org](https://becomeanex.org).

**The EX Program** expands on BecomeAnEX to provide an enterprise-level tobacco cessation program designed for employers and health plans. The EX Program has an active social network of thousands of smokers and ex-smokers and delivers proven quit-smoking treatment via interactive quitting tools and video, live chat, text message, email, and quit medication. Learn more at [theexprogram.com](https://theexprogram.com).



## REFERENCES

- 1 Administration, U.S.F.D. *Nicotine Is Why Tobacco Products Are Addictive*. 8/19/2021 3/7/2022; Available from: <https://www.fda.gov/tobacco-products/health-effects-tobacco-use/nicotine-why-tobacco-products-are-addictive>.
- 2 Benowitz, N.L., *Pharmacology of nicotine: addiction, smoking-induced disease, and therapeutics*. Annual review of pharmacology and toxicology, 2009. 49: p. 57-71.
- 3 Jackler, R.K. and D. Ramamurthi, *Nicotine arms race: JUUL and the high-nicotine product market*. Tobacco Control, 2019. 28(6): p. 623-628.
- 4 Benowitz, N.L. and J.E. Henningfield, *Establishing a nicotine threshold for addiction—the implications for tobacco regulation*. 1994, Massachusetts Medical Society p. 123-125.
- 5 Seidenberg, A.B., *An Introduction to Synthetic Nicotine*. 2021, National Cancer Institute.
- 6 *Public Health Consequences of E-Cigarettes*. 2018, The National Academies of Sciences, Engineering, and Medicine: Washington, DC
- 7 Marynak, K.L., et al., *Sales of nicotine-containing electronic cigarette products: United States, 2015*. American Journal of Public Health, 2017. 107(5): p. 702-705.
- 8 Willett, J.G., et al., *Recognition, use and perceptions of JUUL among youth and young adults*. Tobacco Control, 2019. 28(1): p. 115-116.
- 9 *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General*. 2014, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health: Atlanta, GA.
- 10 England, L.J., et al., *Nicotine and the developing human: a neglected element in the electronic cigarette debate*. American Journal of Preventive Medicine, 2015. 49(2): p. 286-293.
- 11 Hu, M.-C., M. Davies, and D.B. Kandel, *Epidemiology and correlates of daily smoking and nicotine dependence among young adults in the United States*. American Journal of Public Health, 2006. 96(2): p. 299-308.
- 12 Kandel, E.R. and D.B. Kandel, *A molecular basis for nicotine as a gateway drug*. New England Journal of Medicine, 2014. 371(10): p. 932-943.
- 13 Hair, E.C., et al., *Association between e-cigarette use and future combustible cigarette use: Evidence from a prospective cohort of youth and young adults, 2017–2019*. Addictive Behaviors, 2021. 112: p. 106593.
- 14 Bierhoff, J., et al., *Psychological risk factors for alcohol, cannabis, and various tobacco use among young adults: a longitudinal analysis*. Substance Use & Misuse, 2019. 54(8): p. 1365-1375.
- 15 Kutlu, M.G. and T.J. Gould, *Nicotine modulation of fear memories and anxiety: Implications for learning and anxiety disorders*. Biochemical Pharmacology, 2015. 97(4): p. 498-511.
- 16 Lechner, W.V., et al., *Bi-directional associations of electronic and combustible cigarette use onset patterns with depressive symptoms in adolescents*. Preventive Medicine, 2017. 96: p. 73-78.
- 17 Obisesan, O.H., et al., *Association between e-cigarette use and depression in the behavioral risk factor surveillance system, 2016–2017*. JAMA Network Open, 2019. 2(12): p. e1916800-e1916800.
- 18 Romberg, A.R., et al., *Patterns of nicotine concentrations in electronic cigarettes sold in the United States, 2013–2018*. Drug and Alcohol Dependence, 2019. 203: p. 1-7.
- 19 Bowen A, X.C., *Nicotine Salt Formulations for Aerosol Devices and Methods Thereof*. 2014, US Patent and Trademark Office.
- 20 *Designed for Addiction*. 2014, Campaign for Tobacco-Free Kids.
- 21 Do, E.K., et al., *Influence of Flavors and Nicotine Concentration on Nicotine Dependence in Adolescent and Young Adult E-Cigarette Users*. Substance Use & Misuse, 2022: p. 1-8.
- 22 Apelberg, B.J., et al., *Potential public health effects of reducing nicotine levels in cigarettes in the United States*. New England Journal of Medicine, 2018. 378(18): p. 1725-1733.
- 23 Snell, L.M., et al., *Emerging electronic cigarette policies in European member states, Canada, and the United States*. Health Policy, 2021. 125(4): p. 425-435.
- 24 *E-cigarettes: regulations for consumer products*. 2016 2/7/2022 5/11/2022; Available from: <https://www.gov.uk/guidance/e-cigarettes-regulations-for-consumer-products#:~:text=The%20requirements%3A,no%20more%20than%2020mg%2Fml>.
- 25 *Vaping Products – New limits on nicotine concentration and consultation on flavour restrictions*. 2021. 5/11/2022; Available from: <https://www.canada.ca/en/health-canada/news/2021/06/background-vaping-products--new-limits-on-nicotine-concentration-and-consultation-on-flavour-restrictions.html>.
- 26 Menon, P., *New Zealand's smoking ban overlooks worry about growing youth vaping*, in Reuters. <https://www.reuters.com/world/asia-pacific/new-zealands-smoking-ban-overlooks-worry-about-growing-youth-vaping-2021-12-10/>.
- 27 *Treating tobacco use and dependence: 2008 update - Tobacco Use and Dependence Guideline Panel*. 2008, U.S. Dept. of Health and Human Services, Public Health Service: Rockville, MD.
- 28 Hartmann-Boyce, J., et al., *Nicotine replacement therapy versus control for smoking cessation*. Cochrane Database of Systematic Reviews, 2018(5).



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