Vaping Cessation Interventions: A Review of Randomized Controlled Trials

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Abstract

Background: The increasing prevalence of electronic cigarette (e-cigarette) use, particularly among young individuals, has led to a pressing need for effective vaping cessation interventions.

Objective: To summarize the available evidence on vaping cessation interventions, identify key challenges, and highlight future research directions

Methods: We searched PubMed, Google Scholar, and clinicaltrials.gov. for randomized controlled trials (RCTs) evaluating behavioral, pharmacological, and combination interventions aimed at vaping cessation. The search period spanned from 2004 (year of first e-cigarette patent) to April 27, 2025. The outcome of interest was abstinence from vaping at a maximum follow-up.

Results: A total of 11 RCTs, involving 8,182 participants, were identified. These trials investigated behavioral therapy, including tailored text messaging support (n=4), nicotine replacement therapy (NRT; n=3), varenicline (n=3), and cytisine (n=1). Studies were published between 2021 and 2025, with follow-up periods ranging from 1 to 24 months. Most RCTs focused on adults or young adults. Behavioral interventions showed potential to support quitting at follow-up beyond 6 months; however, results were not consistent across trials. While varenicline demonstrated promise as a pharmacological aid for vaping cessation, available RCTs had small sample sizes and short follow-up periods, limiting the strength of the evidence. None of the RCTs investigating the efficacy of NRT (567 participants) or cytisine (160 participants) for vaping cessation showed superiority over the control after treatment discontinuation

Conclusions: With millions of people using e-cigarettes daily and limited data on their long-term safety, stronger evidence is needed to guide vaping cessation strategies.

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STRUCTURED ABSTRACT

Background: The increasing prevalence of electronic cigarette (e-cigarette) use, particularly among young individuals, has led to a pressing need for effective vaping cessation interventions.

Objective: To summarize the available evidence on vaping cessation interventions, identify key challenges, and highlight future research directions.

Methods: We searched PubMed, Google Scholar, and clinicaltrials.gov. for randomized controlled trials (RCTs) evaluating behavioral, pharmacological, and combination interventions aimed at vaping cessation. The search period spanned from 2004 (year of first e-cigarette patent) to April 27, 2025. The outcome of interest was abstinence from vaping at a maximum follow-up.

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Conclusions: With millions of people using e-cigarettes daily and limited data on their long-term safety, stronger evidence is needed to guide vaping cessation strategies.

Key words: vaping cessation, e-cigarettes, young adults, behavioral interventions, pharmacotherapy.

IMPLICATIONS

- This review provides a comprehensive summary of 11 randomized controlled trials (n=8,182 participants) assessing behavioral and pharmacological interventions for vaping cessation across a range of populations.
- In contrast to prior systematic reviews, this narrative review presents a study-by-study evaluation, detailing trial design, key outcomes, and methodological limitations.
- Our approach enables a clearer understanding of the strengths and gaps in current evidence, particularly in areas such as follow-up duration, sample size, use of biochemical verification, and the generalizability of findings.

ABBREVIATIONS

E-cigarette	Electronic Cigarette
FDA	U.S. Food and Drug Administration
NRT	Nicotine Replacement Therapy
PPA	Point-Prevalence Abstinence
RCT	Randomized Controlled Trials

INTRODUCTION

The use of electronic cigarettes (e-cigarettes), or “vaping,” has increased in recent years, with over 14 million adults in the United States now reporting daily use.[1] Use is highest among young adults aged 18–24 (15.3%), over 65% of whom have never smoked combustible cigarettes.[1] In contrast, among individuals aged 65 and older, over 95% who vape are current or former cigarette smokers.[1] In 2024, e-cigarettes became the most used tobacco product, with 1.6 million adolescents reporting daily use.[2] The US e-cigarette market has reached a value of $12.4 billion in 2023, with global projections expected to hit $77.9 billion by 2030.[3] With the increasing use, over half of individuals who use e-cigarettes daily report a desire to quit.[4] Our review provides insights by presenting a cohesive summary of the strengths and limitations of individual trials on vaping cessation interventions. It also offers an overview of ongoing studies, delivering a more comprehensive and up-to-date assessment of the available evidence.

METHODS

A literature search was conducted to identify relevant randomized controlled trials (RCTs) reporting on vaping cessation interventions among individuals using e-cigarettes (or other vaping devices) daily. The databases searched to identify trials were PubMed, Google Scholar, and clinicaltrials.gov. The search period from January 2004 (year of first e-cigarette patent in any language) to April 27, 2025. Medical subject heading terms were used when relevant for the following key words: “vaping cessation,” “e-cigarette cessation,” “electronic cigarettes,” “electronic nicotine delivery systems,” “intervention,” and “randomized controlled trial.” Relevant search results were identified through title screening or snowballing references of included articles. The outcome of interest was abstinence from vaping at a maximum follow-up.

RESULTS

We identified 11 RCTs published between 2021 and 2025, evaluating a range of vaping cessation interventions. These included four trials of behavioral therapies,[5-8] three nicotine replacement therapy (NRT) trials,[9-11] and three pharmacotherapy trials – tree with varenicline, [12-14] and one with cytisine.[15] Collectively, the studies enrolled 8,182 participants, with follow-up durations ranging from 1 to 24 months (**Tables 1-3**). Most trials targeted adults or young adults (aged 18-25 years), with one trial exclusively enrolling adolescents.[8] The most frequently reported primary outcome was 7-day point-prevalence abstinence (PPA) from vaping, defined as self-reported nicotine e-cigarette abstinence within the past 7 days. Four studies incorporated biochemical verification using salivary cotinine testing, with cut-off thresholds ranging from 10 or 30 ng/mL.

Adults

Behavioral interventions

Behavioral interventions may play an important role in vaping cessation by providing psychological support, motivation, and structured guidance.[16] We identified three RCTs (n=5,511 participants) investigating the effects of behavioral interventions for e-cigarette cessation (**Table 1**).[5-7] The trials varied in population and intervention delivery approaches.

Martinez et al. (2021)[6] conducted the largest RCT (n=2,896 participants) in vaping cessation using behavioral intervention, which included three study arms: one control group and two self-help intervention groups. One intervention arm received targeted cessation materials (brochures, booklets, etc) designed specifically for individuals who exclusively use e-cigarettes, while the other received materials tailored for dual users - individuals who smoke both conventional cigarettes and nicotine e-cigarettes. Both intervention arms received self-guided behavioral therapy materials by mail for up to 18 months. As part of the retention strategy,

participants received $10 to $40 for follow-up assessments, with additional bonuses and appreciation gifts for timely and consistent participation. At 24 months, no significant differences were observed based on 7-day PPA from vaping across groups (**Table 4**). Methodological limitations included substantial loss to follow up (53% at 24 months), potentially introducing bias despite the imputation approach. While biochemical validation was conducted, it was limited to a small subset of participants (n=47) living within 100 miles of the research site, leaving most abstinence outcomes based on self-report. The intervention itself largely relied on self-guided cognitive behavioral therapy delivered via printed materials, with no in-person or digital support, which may limit engagement.

Graham et al. (2021)[5] conducted a parallel, two-group, double-blind RCT (n=2,588) to evaluate the efficacy of *This is Quitting*, a fully automated, interactive text message program. The program was designed to support vaping cessation in young adults. A distinctive feature of the program was the inclusion of peer-contributed messages from other individuals who vape. The intervention group received daily supportive and skill-building messages for up to 9 weeks. All participants received incentivized text message assessments about e-cigarette use and abstinence at 14 days post-randomization and monthly for 6 months. The control group did not receive any additional support. Participants received up to $35 for follow-up assessments, $20 for each follow-up survey, and a $10 bonus for responding within 24 hours. At the 7-month follow-up, a higher proportion of participants in the intervention group reported 30-day vaping abstinence compared to the control group (**Table 4**). The study had several strengths, including a large, diverse sample, high retention, and rigorous design. However, it relied on self-reported abstinence without biochemical verification, and online recruitment may have introduced selection bias. The timing during the early COVID-19 pandemic may also have influenced

vaping behaviors.

Palmer et al. (2022)[7] conducted a pilot feasibility study evaluating the use of financial incentives, also known as contingency management, for vaping cessation. Participants (n=27) were randomized in a 4:1 ratio to intervention or a control group. Participants in the intervention group received $20 for each submitted sample that was biochemically verified as abstinent. The control group received $20 for each submitted sample, regardless of the result. Participants could earn up to $310, including abstinence or submission incentives ($200), pre-quit saliva submissions ($15), and compensation for study visits ($95). The intervention was delivered via a smartphone app over a 4-week period. All participants were encouraged to use *This is Quitting* text message program. No significant difference in vaping abstinence at 56 days was found between financial incentive and the control groups (**Table 4**). Although participants in the intervention arm submitted a higher proportion of negative samples during treatment (55% vs. 8%), the small sample size limits the reliability of these findings. A short-term intervention period and follow-up further constrained the relevance of these findings.

Summary

Across three RCTs, behavioral interventions for vaping cessation showed feasibility and acceptability among adolescents and young adults. Low-intensity approaches - such as self-help materials and digital text programs - demonstrated potential to support quitting, particularly among motivated individuals. For clinicians, these tools may offer accessible options for integrating cessation support into routine care. However, small sample sizes, short follow-up periods, and reliance on self-reported outcomes highlight the need for more robust evidence. Limited population heterogeneity further emphasizes the importance of exploring long-term support strategies and integrating pharmacological interventions.

NRT

NRT is historically the most widely used pharmacotherapy for conventional smoking cessation.[17] It aims to reduce motivation to smoke and the physiological withdrawal symptoms without addressing the behavioral rituals of smoking.[18] Three RCTs (n=567 participants) assessed the efficacy of NRT for nicotine e-cigarette cessation (**Table 2**).[9, 10, 19] All studies combined NRT with behavioral interventions, with treatment durations ranging from 28 days to 12 weeks.

Klein et al. (2025)[11, 19] conducted an RCT (n=508) to evaluate the efficacy of NRT and a text-messaging program for vaping cessation among young adults aged 18-24 years. A 2×2 factorial design was used to create the study groups: (1) coaching calls + text-messaging support + NRT, (2) coaching calls + NRT, (3) coaching calls + text-messaging support, (4) coaching calls only. NRT was delivered by mail and included an 8-week supply of nicotine patches and gum or lozenges. All participants received $40 electronic gift cards for baseline and 3-month survey completion. At the 3-month follow-up, 45% of participants reported vaping abstinence, with NRT associated with a 6.5% increase in abstinence compared to non-NRT groups, though the effect was inconclusive (**Table 4**). The study had several strengths, including multisite recruitment, a relatively large sample for vaping cessation research, and a fully remote delivery model. However, the abstinence was self-reported, and the follow-up period was short-term. Notably, NRT was provided for only 8 weeks, whereas most conventional smoking cessation trials use a 12-week course, which may have reduced its efficacy. NRT use was also reported among participants not assigned to receive it. The sample had a higher proportion of female participants (71.3%), which may be attributed to social media recruitment.

Palmer et al. (2023)[10] conducted a mixed-methods preliminary study (n=30) to evaluate the feasibility and acceptability of NRT for vaping cessation among adults who exclusively used

e-cigarettes and dual users. Participants were randomized to receive either a 28-day supply of combination NRT (patches and lozenges) or a referral to telephone-based cessation services (control group). All participants received $20 per assessment (up to $60), while those randomized to the intervention group could earn an additional $60 for completing daily surveys. All payments were electronic gift cards. At 1 month's follow-up, among participants who exclusively used e-cigarettes, one-third in the NRT group reported vaping abstinence, compared to none in the control group. Overall, abstinence rates in the NRT group (33.3%) showed a trend toward being higher than in the control group (0%), though the difference was inconclusive (**Table 4**). The main limitations were small sample size, short follow-up, and reliance on self-reported abstinence without biochemical validation. Moreover, NRT therapy was limited to 28 days, and delivered in fixed doses rather than tailored to individual dependence levels.

Sahr et al. (2021)[9] conducted a pilot RCT (n=24) comparing three vaping cessation methods: (1) NRT, (2) vape-taper, and (3) control (self-guided vaping cessation). Individuals in the vape-taper arm were encouraged to reduce nicotine intake by lowering the vape liquid concentration and decreasing session frequency or duration, aiming to eliminate one session daily. Participants received a $20 gift card at follow-up visits, with a maximum of $60. Those in the self-guided and vape-taper groups received an additional $120 to cover vaping supply costs. At 6 months, the vape-taper group had the highest self-reported abstinence rates, followed by the self-guided and NRT groups (**Table 4**). However, the trial was underpowered and had limited generalizability, as all participants were college students from a single campus, introducing potential sampling bias. A high number of participants were lost to follow-up, particularly in the NRT group, which may have impacted on the reliability of outcomes. Additionally, many individuals in the NRT arm used the products at lower intensity than recommended, potentially

reducing treatment efficacy. Frequent interactions with the self-guided group (assessments) may also have unintentionally influenced behavior and quit attempts.

Summary

Three small RCTs explored NRT for vaping cessation in adults, but none provided clear evidence of superiority compared to control interventions. NRT may be useful, especially with longer treatment periods (12-14 weeks) and concomitant behavioral support. The key limitations were small samples and reliance on self-reported outcomes. More research is needed to determine its effectiveness.

Varenicline

Varenicline, a partial nicotinic agonist selective for α4β2 nicotinic acetylcholine receptors,[20] is the most effective U.S. Food and Drug Administration (FDA) - approved pharmacological agent for conventional tobacco smoking cessation.[21] It relieves withdrawal symptoms and reduces the rewarding effects of tobacco smoking.[22] Most evidence indicates that varenicline is well-tolerated, with the rates of adverse events comparable to other pharmacological interventions.[21, 23] To date, three trials (n=441 participants) have evaluated efficacy and safety of varenicline for vaping cessation in the general population **(Table 3**).

Evins et al. (2025)[12] conducted a three-arm, double-blind, placebo-controlled RCT (n=261) to evaluate the efficacy of varenicline for vaping cessation among youth aged 16–25 years. Participants were randomized to receive 12 weeks of varenicline or placebo with weekly counseling, or to enhanced usual care (text message support via *This is Quitting*). Participants received up to $570 for completing assessments, with those in the varenicline and placebo arms additionally incentivized $1 per video-confirmed medication dose via a reminder app. At 6-months follow-up, varenicline arm had higher continuous abstinence rate compared to placebo. It

also outperformed enhanced usual care. Adverse events were mild and similar between groups. The trial's strengths include its rigorous design, high adherence and retention, and robust biochemical verification. However, limitations include a single-site design and lack of generalizability to dual users. This was the first pharmacotherapy RCT for vaping cessation in youth.

Caponnetto et al. (2023)[13] conducted a double-blind, placebo-controlled RCT (n=140) to evaluate the efficacy of varenicline combined with behavioral counseling for vaping cessation among adults who exclusively used e-cigarettes. Participants received varenicline or placebo for 12 weeks alongside structured counseling. Both groups also received instructions to gradually reduce their vaping product use at their own pace as an additional intervention. At the 6-month follow-up, varenicline more than doubled the odds of biochemically verified abstinence from vaping compared to placebo (**Table 4**). The continuous vaping abstinence indicated similar results. The key limitations included relatively small sample size and short-term follow-up. The study was funded by Pfizer Inc. (USA) and partially supported by ECLAT Srl., a research-based company specializing in combustion-free devices. However, the investigators stated that neither funder had any influence on the study design or conduct.

Fucito et al. (2024)[14] reported the results of double-blind, placebo-controlled RCT evaluating an effect of 8-week varenicline regimen among 40 enrolled participants. All participants received a single low-intensity counseling session and self-guided booklet. At 3 months the differences in abstinence rates between the varenicline and placebo groups were inconclusive (**Table 4**). Strengths of the study included its primary care-based setting and inclusion of participants with psychiatric comorbidities, reflecting a real-world population. However, the study was underpowered, with a short follow-up and a lack of biochemical

verification. Notably, the varenicline treatment course was shorter than a standard 12-week regimen used in smoking cessation, which may have reduced intervention efficacy.

Summary

Varenicline showed potential as a pharmacological aid for vaping cessation when combined with behavioral support. Evidence suggests it may help adults motivated to quit vaping and could inform future recommendations by health authorities and clinicians. However, available RCTs had small sample sizes, and relatively short follow-up periods, reducing the strength of the evidence. Longer-term studies with extended treatment regimens are needed to evaluate its sustained efficacy.

Cytisine

Cytisine, also known as cytisinicline, is a plant-derived alkaloid and a partial agonist of the α4β2 nicotinic acetylcholine receptor, similar to varenicline.[24] It has been used for smoking cessation in Central and Eastern European countries for several decades.[25, 26] In 2016, Health Canada approved it as a natural health product under the brand name Cravv®,[27] though it has not yet received approval from the U.S. Food and Drug Administration. Cytisine has demonstrated greater efficacy for combustible smoking cessation compared to NRT or behavioral interventions, with sustained results for at least six months.[21] One challenge of cytisine-assisted cessation is its complex dosing regimen. It starts with 1 capsule every 2 hours (up to 6 capsules daily) for the first 3 days. The dosage then decreases gradually, with longer intervals and fewer capsules per day. By the days 21-25, the dosage is reduced to 1-2 capsules daily.

Rigotti et al. (2024)[15] conducted a double-blind, placebo-controlled RCT (n=160) to evaluate the efficacy of cytisinicline for vaping cessation in adults who exclusively used nicotine e-cigarettes. Participants followed a simplified dosing regimen of 3 mg cytisinicline, taken 3

times daily for 12 weeks, combined with weekly brief behavioral counseling (**Table 3**). Study participants were compensated for their time spent attending study visits, but no further details were provided by the authors. Cytisinicline more than doubled the likelihood of biochemically validated continuous abstinence compared to placebo from week 9 to 12. However, the effect was inconclusive after medication discontinuation (**Table 4**). Although the study reported 7-day PPA from vaping at 4 months, no numerical values were provided, limiting the ability to compare this outcome across RCTs. The study was partially funded by Achieve Life Sciences, a pharmaceutical company that developed and commercializes cytisinicline for smoking cessation and nicotine addiction.

Summary

Cytisine may be equally effective for vaping cessation as it is for conventional smoking cessation. It could be a useful option for those who did not achieve sustained abstinence with behavioral interventions or cannot tolerate varenicline. However, current evidence is based on a single small study with short-term follow-up.

Adolescents

Since 2017, e-cigarettes have become the most common first nicotine-containing product used by adolescents (12-17 years) in US.[1, 28] More than 70% of teens who try any tobacco product begin with e-cigarettes.[28] The time to first cigarette after waking is considered a key clinical indicator of tobacco dependence.[29] Among teenagers, the proportion using e-cigarettes within five minutes of waking increased from under 2% to over 10%, signaling rising addiction levels.[28] These patterns point to escalating levels of nicotine addiction at increasingly younger ages, underscoring the urgent need for targeted cessation strategies in this vulnerable population.

We identified a single RCT (n=1,503) on vaping cessation that evaluated the efficacy of a

behavioral intervention among adolescents. Graham et al. (2024)[8] conducted a parallel, two-group, double-blind RCT comparing text messaging support through *This is Quitting* to a control. Participants were recruited via social media advertisements (Instagram, Facebook, and Snapchat). To optimize follow-up rates, all participants received $5 for completing text message assessments about e-cigarette use monthly for 6 months. At 7 months, a higher proportion of participants in the intervention group reported 30-day vaping abstinence compared to the control group (**Table 4)**. The study's strengths included its large sample, diverse population, and rigorous design. However, reliance on self-reported abstinence without biochemical verification, along with a loss to follow-up rate exceeding 25%, may introduce misclassification bias.

Summary

The Graham et al. (2024) trial provides the first randomized evidence supporting behavioral, primarily digital, vaping cessation intervention among adolescents. The program was associated with higher abstinence compared to control. Given limited evidence on the safety of pharmacological interventions in this subgroup, applications tailored to youth might be a practical option for vaping cessation support.

Ongoing clinical trials

Our search identified 14 ongoing RCTs at different stages of completion on clinicaltrials.gov, assessing interventions for achieving abstinence from vaping (**Table 5**). Some are in the early stages of recruitment, while others have completed follow-up, but the results are pending. Two-thirds of these trials are investigating the effects of behavioral interventions, such as mobile vaping apps and virtual reality programs on vaping cessation. Half of the trials primarily target younger populations (ages 13-21).

One notable trial, the Avenue Study (NCT06474299),[30] aims to identify the most effective

strategies for helping dual users of cigarettes and e-cigarettes quit smoking. This RCT evaluates four arms, combining pharmacotherapy (varenicline or NRT) with behavioral counseling of varying intensity (1 or 4 sessions). The interventions either address both cigarette and e-cigarette cessation or focus solely on cigarette cessation. With a target enrollment of 500 participants, the study is expected to be completed in 2028. The primary outcome is 7-day PPA from cigarette smoking at 52 weeks, biochemically validated with exhaled carbon monoxide measurement (<6 parts per million) for smoking abstinence. Abstinence from e-cigarette use will be verified using saliva cotinine measurement (<30 ng/mL). This extended follow-up duration is crucial for smoking cessation trials, particularly given the challenges posed by an average loss-to-follow-up rate of approximately 20%.

DISCUSSION

With millions of people now using e-cigarettes, including those who transitioned from conventional smoking, there is a growing need for clear guidance to support vaping cessation after quitting smoking. Among the 11 published RCTs, no definitive conclusions can be made, although available data suggest that interventions used for conventional smoking cessation may be effective for vaping cessation. However, the studies varied widely in design – even within the same intervention category (e.g., behavioral or pharmacological strategies) – as well as in follow-up duration. More than half of the trials were underpowered and did not include biochemical verification of vaping abstinence. A 2025 Cochrane review, which included nine trials, suggested that message-based interventions and varenicline may aid vaping cessation.[31] However, the pooled results for each intervention were drawn from only one-two RCTs, highlighting the lack of evidence. This gap underscores the need for well-designed, adequately powered trials directly comparing interventions for vaping cessation to provide reliable guidance

for clinical practice.

E-cigarette safety concerns

While available evidence indicates that e-cigarette use may be less harmful than conventional tobacco smoking, this does not imply they are without risk. The potential long-term effects of e-cigarette use remain largely unexplored.[32] Most RCTs limit e-cigarette use for smoking cessation to a maximum of 14 weeks, with follow-up rarely extending beyond one year.[33] The 2025 Cochrane review concluded that safety data remain inconclusive.[33] Chronic nicotine exposure during adolescence is linked to cognitive deficits and increased risk of lifelong dependence.[34, 35] Modern devices using nicotine salts deliver higher doses more efficiently, and their modifiability allows users to bypass regulatory limits in countries like Canada and United Kingdom.[36, 37] A 2025 multinational study found that adolescents who vape had nicotine exposure levels comparable to those who smoke, with over one-third using the highest allowed concentration (20 mg/mL).[38] A separate meta-analysis of cross-sectional studies found that e-cigarette use was associated with a 1.5-fold increase in suicidal ideation and more than twice the risk of suicidal planning and attempts.[39] A meta-analysis of over 3.5 million participants found a 1.5-fold increased risk of chronic obstructive pulmonary disease among never-smoking e-cigarette users.[40] These findings highlight the poorly understood risks of e-cigarette use among youth and young adults.

Dual users of e-cigarettes and conventional cigarettes

Many individuals who attempt to switch from conventional smoking to e-cigarettes as a safer alternative often become dual users, a pattern associated with the highest health risks. A 2024 meta-analysis published in NEJM Evidence,[41] synthesized data from 107 studies. The authors reported that dual use was associated with a 20-41% increased risk of asthma, chronic

obstructive pulmonary disease (COPD), stroke, metabolic dysfunction, and oral disease when compared to exclusive cigarette smoking. Compared to no nicotine products use, dual use was linked to higher odds of cardiovascular disease, stroke, metabolic dysfunction, asthma, COPD, and oral disease, with risks ranging from 0.5- to over 3-fold.[41] Flacco et al.[42] reported that the six-year prevalence of smoking-related disorders was higher among dual users (12.1%) compared to exclusive smokers (8.1%). There is a risk that individuals attempting to quit vaping may transition to dual use, which significantly increases health risks. This underscores the need for greater efforts to develop effective vaping cessation interventions to prevent dual use and reduce associated harm.

E-cigarette brand strategies

Major tobacco companies continue to expand the e-cigarette market and increase use, while showing little interest in supporting independent research on vaping cessation. Between January 2020 and December 2022, U.S. e-cigarette unit sales surged from 15.5 million to 22.6 million per month – a 46.6% increase – despite increasing regulatory pressure.[43] Following the FDA's enforcement against flavored prefilled cartridges,[44] sales of refillable disposable e-cigarettes rose by 132.7%.[43] These devices let users alter nicotine and flavor content. The number of unique brands expanded from 184 to 269, drowning the market with modifiable devices. Most of the leading e-cigarette brands are owned or financially supported by major tobacco companies. JUUL®, one of the leading e-cigarette brands in the U.S., became closely tied to Big Tobacco after Altria Group[45] – parent company of Philip Morris USA Inc. – acquired a 35% stake in 2018 for $12.8 billion.[46] This underscores that tobacco companies have shifted toward vaping not to support cessation, but to sustain and even increase nicotine dependence.

Marketing trends

Vaping device brands have employed marketing strategies traditionally used by tobacco companies to increase the number of e-cigarette users. They often target vulnerable populations, particularly adolescents and young adults, who are more easily influenced by social factors. Published in 2024, the Federal Trade Commission E-Cigarette Report for 2021 revealed that e-cigarette manufacturers spent over $850 million on advertising and promotional activities in the United States.[47] On August 23, 2023, the FDA issued warning letters to 15 online retailers for selling unauthorized e-cigarette products designed to resemble youth-oriented items. These included cartoon characters (e.g., SpongeBob), school supplies (e.g., markers), toys, and beverages.[48, 49] Additionally, multiple companies produce vape covers that wrap around devices, allowing individuals to personalize them with unique colors and patterns.[48, 49] This aggressive marketing underscores the urgent need for effective interventions to support vaping cessation, especially among vulnerable populations such as adolescents.

Biochemical validation in trials

Biochemical verification is essential for maintaining accuracy and scientific rigor in vaping cessation trials, yet fewer than half of the reviewed trials incorporated it into their study design. As highlighted in 2019 by Benowitz et al.,[50] reliance solely on self-reported abstinence can lead to significant misclassification, with studies showing that approximately one out of every nine individuals who report quitting fail biochemical validation. This issue is particularly pronounced in populations prone to underreporting - such as adolescents,[51] female individuals,[52] and hospitalized patients.[53] Furthermore, quit rates may be overestimated by as much as half when relying on self-report alone. In the context of vaping, biochemical markers such as cotinine offers objective evidence of nicotine exposure and can differentiate between e-cigarette and combustible tobacco use. Exhaled carbon monoxide measurement, a byproduct of combustion, is

unsuitable for verifying vaping abstinence since vaping does not involve burning. Cotinine, a major nicotine metabolite detected in serum, urine and saliva, has a prolonged half-life, providing a 5-7-day detection window for assessing nicotine exposure.[54] Despite added costs and logistical challenges, incorporating biochemical verification enhances validity and helps avoid inflated efficacy claims in cessation trials.

Financial incentives and their role in cessation outcomes

Most of the reviewed RCTs provided participant compensation to promote retention and optimize follow-up rates, raising concerns about the generalizability of study outcomes. A Cochrane review on incentives for smoking cessation, encompassing 33 mixed-population studies (n=21,600 participants), provided high-certainty evidence that incentives improve smoking cessation rates at long-term follow-up.[55] In 2024, Kendzor et al. reported results from an RCT in which participants (n=320 participants) with low socioeconomic status were randomized to either usual care (counseling plus pharmacotherapy) or usual care combined with abstinence-contingent financial incentives. No significant differences were observed in rates of 7-day PPA, 30-day PPA, or continuous abstinence at 26 weeks (8.7% vs. 13.8%).[56] Instead, compensation was likely effective in improving recruitment and retention rates, which are critical for the robustness of trial findings.

Future research directions

Future research should focus on developing targeted interventions for high-risk populations, including adolescents, gender minorities, and racially and ethnically diverse groups.[57] Interventions specifically designed for dual users are also needed to address their unique patterns, motivations, and barriers to quitting.[58] Optimizing pharmacotherapy requires comparing different dosing strategies and extended treatment durations beyond 12 weeks. Vape-

tapering strategies should be further explored to identify optimal protocols, including pacing, duration, and integration with behavioral counseling or pharmacotherapy. Advancing digital cessation tools, such as mobile apps, chatbots, and text-based programs, could enhance effectiveness through AI-driven personalization, gamification (e.g. competition with others, point scoring), and real-time feedback. Financial incentives could be incorporated not only to promote cessation but also to improve biochemical verification rates, participant retention, and the accuracy of self-reported abstinence. Finally, policy-relevant research should examine how perceptions of harm and regulatory changes affect the willingness to quit and engage in cessation programs.

CONCLUSIONS

With millions developing nicotine dependence through e-cigarettes and minimal data on their long-term safety, stronger evidence is needed to develop vaping cessation strategies. More than half of the available RCTs on vaping cessation had small sample sizes and short follow-up periods, limiting the reliability of their findings. Larger, well-powered trials are necessary to evaluate tailored behavioral interventions and optimize pharmacological treatment protocols for sustained vaping cessation.

Declarations

Clinical Trial Number

Not applicable

Ethical Approval and Consent to Participate

Ethical approval was not required as per the TriCouncil Policy Statement (2022), article 2.2, which exempts research that relies exclusively on publicly available information. Human Ethics

and Consent to Participate declarations: not applicable.

Consent for Publication

Not applicable

Availability of Data and Materials

No original data was generated or analyzed for or in support of this paper.

Competing Interests

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Nothing to declare. The authors declare no relationship with industry.

Authors' Contributors

All authors have made substantial contributions to this study and agreed to publish these data. TZ, AM, AL, and MJE conceptualized and designed the review. TZ, AM, and AL drafted the manuscript. MJE critically revised the manuscript and approved the final manuscript. All authors had final responsibility for the decision to submit for publication.

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Table 1. Characteristics of Randomized Controlled Trials on Behavioral Interventions for Vaping Cessation

Study	Sample size (n)	Inclusion criteria	Interventions	Outcome measure	Biochemical validation of abstinence	Maximum follow-up, months
Martinez, 2021	2,896	Age ≥18 years Current 30-day EC use Combustible cigarettes use	Cessation materials (booklets, links) vs Cessation materials designed for dual users vs Control*	7-day PPA	Exhaled CO (<8 ppm) Saliva cotinine test (who lived <100 miles from the research site [n=47])	24
Graham, 2021	2,588	Age 18-24 years Current 30-day EC use	Text messaging support vs Control*	30-day PPA	-	7
Palmer, 2022	27	Age 12-21 years Current (>25 days/month) EC use	Financial incentives vs Control*	Vaping abstinence	Saliva cotinine test (<30 ng/mL)	1
Adolescents only						
Graham, 2024	1,503	Age 13-17 years Current 30-day EC use	Text messaging support vs Control*	30-day PPA	-	7

Abbreviations: CO - carbon monoxide; EC - electronic cigarette; OR - odds ratio; PPA - point prevalence abstinence; ppm - parts per million.
*The control group did not receive any active intervention and, at most, was referred to publicly available self-guided behavioral resources

Table 2. Characteristics of Randomized Controlled Trials on Nicotine Replacement Therapy for Vaping Cessation

Study	Sample size (n)	Inclusion criteria	Interventions	Outcome measure	Biochemical validation of abstinence	Maximum follow-up, months
Klein, 2025	508	Age 18-24 years Current 30-day EC use	Coaching + Text messaging support + NRT[a] vs Coaching + NRT[a] vs Coaching + Text messaging support vs Coaching only	7-day PPA	-	3
Palmer, 2023	30	Age ≥18 years Current (>25 days/month) EC use Dual users were permitted	NRT[b] vs Control*	7-day PPA	-	1
Sahr, 2021	29	Age 18-24 years Current (≥16 days/months) EC use	NRT[c] vs. Vape-taper vs. Control*	Self-report being vape-free	-	6

Abbreviations: EC - electronic cigarette; PPA - point prevalence abstinence; NRT - nicotine replacement therapy.
[a]NRT: up to an 8-week supply of nicotine patch, gum, and/or lozenge.
[b]NRT was supplied for 28 days.
[c]NRT was supplied for 12 weeks.
*The control group did not receive any active intervention and, at most, was referred to publicly available self-guided behavioral resources.

Table 3. Characteristics of Randomized Controlled Trials on Varenicline and Cytisine for Vaping Cessation

Study	Sample size (n)	Inclusion criteria	Interventions	Outcome measure	Biochemical validation of abstinence	Maximum follow-up, months
Varenicline						
Evins, 2025	261	Age 16-25 years Daily EC use	Varenicline[a] vs Placebo[a] vs Text messaging support	CAR (weeks 9-24)	Saliva cotinine test (cut-off <30 ng/mL)	6
Caponetto, 2023	140	Age ≥18 years Daily EC use	Varenicline[a] vs Placebo[a]	CAR (weeks 4-24) 7-day PPA	Saliva cotinine test (cut-off <10 ng/mL)	6
Fucito, 2024	40	Age ≥18 years Daily EC use >6 months	Varenicline[b] vs Placebo[b]	7-day PPA	-	3
Cytisine						
Rigotti, 2024	160	Age ≥18 years Daily EC use Positive (≥30 ng/mL) saliva cotinine test result	Cytisinicline[a] vs Placebo[a]	CAR (weeks 9-12, 9-16) 7-day PPA	Saliva cotinine test (cut-off<10 ng/mL)	4

Abbreviations: CAR - continuous abstinence rate; EC - electronic cigarette; OR - odds ratio; PPA - point prevalence abstinence.
*The results were reported via figure; no numerical values were provided.
[a]Was supplied for 12 weeks.
[b]Was supplied for 8 weeks.

Table 4. Reported Outcomes of Randomized Controlled Trials on Vaping Cessation Interventions

Interventions	Sample size, n	7-day or 30-day[§] PPA from vaping at maximum follow-up, %	Effect estimates and significance (95% CI)	Continuous abstinence from vaping, %	Effect estimates and significance (95% CI)
Behavioral interventions					
Martinez, 2021					
Cessation materials (booklets, links)	1,154	34.0	OR 1.07 (0.82-1.41)**		
Cessation materials designed for dual users	1,167	35.9	OR 1.17 (0.88-1.54)[a]	NA	NA
Control*	575	32.4	NA		
Graham, 2021					
Text messaging support	1,304	24.1[§]	OR 1.17 (0.88-1.54) RR 1.35 (1.17-1.57)	NA	NA
Control*	1,284	18.6[§]			
Palmer, 2022					
Financial incentives	22	27.0[§]	p=0.74	NA	NA
Control*	55	20.0[§]			
Graham, 2024					
Text messaging support	759	38.7[§]	OR 1.57 (1.26-1.95) RR 1.35 (1.17-1.57)	NA	NA
Control*	744	28.0[§]			
NRT					
Klein, 2025					
Coaching + Text messaging support + NRT[a]	122	48.0	NRT arms vs non-NRT arms OR 1.30 (0.91-1.84)	NA	NA
Coaching + NRT[a]	126	48.0			
Coaching + Text-messaging support	126	43.0			
Coaching only	134	41.0			
Palmer, 2023					
NRT[b]	18	27.8	p=0.67	NA	NA
Control*	12	16.7			

Sahr, 2021					
NRT[c]	7	42.9		28.6	
Vape-taper	8	75.0	p=0.35	37.5	p=0.44
Control*	9	44.4		11.5	
Varenicline					
Evins, 2025					
Varenicline	88			28	aOR 6.0 (2.1-16.9)[b]
Placebo	87	NA	NA	7	
Text messaging support	86			4	aOR 11.0 (3.1-38.8)[c]
Caponetto, 2023					
Varenicline	70	34.3	OR 2.52 (1.14-5.58) p=0.02	34.3	OR 2.52 (1.14-5.58) p=0.02
Placebo	70	17.1		17.1	
Fucito, 2024					
Varenicline	20	40.0	RR 1.36 (0.59-3.13)	NA	NA
Placebo	20	30.0			
Cytisine					
Rigotti, 2024					
Cytisinicline	107	NA	NA	23.4	OR 2.00 (0.82-5.32)
Placebo	53	NA	NA	13.2	

Abbreviations: aOR – adjusted odds ratio; NA - not appliable; NRT - nicotine replacement therapy; OR - odds ratio; PPA - point prevalence abstinence; RR - relative risk.
*The control group did not receive any active intervention and, at most, was referred to publicly available self-guided behavioral resources.
[a]Compared to control arm.
[b]Varenicline vs text messaging support arm.
[c]Varenicline vs text messaging support arm.

Table. 5. Characteristics of Identified Ongoing Randomized Controlled Trials

Title	ID	Target sample size	Age, years	Interventions	Main outcome	Status, date
Behavioral interventions						
Kick-Nic! Youth Quit Vaping App	NCT06662305	306	13-19	Vaping cessation app vs Control	Cotinine-confirmed 7-day PPA	Ongoing, 2029-08-31
Testing the Feasibility and Acceptability of Social Media and Digital Therapeutics To Decrease Vaping Behaviors	NCT05994209	189	15-25	Vaping cessation app + Chatbot feature vs Vaping cessation app vs Usual care	7-day PPA from vaping at 3 months	Ongoing, 2025-03-01
Adolescent Inpatient Tobacco and Ends Intervention	NCT05936099	144	14-21	Counseling (cigarettes and EC focused) vs Control	Cotinine-confirmed 7-day PPA at 3 months	Ongoing, 2025-12-20
Vaping Prevention and Vaping in Youth (Vapechat)	NCT06003439	119 (actual)	13-19	Virtual reality program vs Control	Past 30- and 7-days vaping frequency	Completed, 2024-06-07
Goal2quitvaping For Nicotine Vaping Cessation Among Adolescents	NCT04951193	106 (actual)	16-20	Behavioral activation therapy app vs Usual care	7-day vaping PPA	Completed, 2023-06-21
Quit Nicotine: E-Cig Cessation Intervention	NCT04898075	100	13-20	Financial incentives vs Control	Cotinine-confirmed change in 7-day PPA at 6 and 12 months	Ongoing, 2025-01-05
Incentive-Based and Media Literacy Informed Approaches to Improve Vaping Cessation	NCT05586308	80	19-29	Financial incentive + Text-messaging support + E-learning lessons vs Financial incentive + Text-messaging support vs Text-messaging support + E-learning lessons vs Text-messaging support	Cotinine-confirmed 7-day PPA at 3 months	Ongoing, 2025-06-01
A Smartphone Application (Act on Vaping) For Vaping Cessation in Young Adults	NCT05897242	61 (actual)	18-30	Vaping cessation app vs Text-messaging support vs Control	Cotinine-confirmed 30-day PPA	Completed, 2024-04-26

Vape-Free Text-Messaging: Pilot Study	NCT05906082	50	18-24	Text-messaging support vs Usual care	Cotinine-confirmed 7-day PPA at 1 months	Ongoing, 2024-12-31
Adapting An Intervention for Vaping in Young Veterans	NCT06196489	20	18-30	Vaping cessation video vs Counseling	7-day PPA at 30 days	Ongoing, 2024-06-01
Pharmacotherapy						
The Avenues Study: Dual Use Cessation	NCT06474299	500	>21	Varenicline + Counseling (1 or 4 sessions) (cigarettes and EC cessation focused) vs Varenicline + Counseling (1 or 4 sessions) (cigarettes cessation focused) vs NRT + Counseling (1 or 4 sessions) (cigarettes and EC cessation focused) vs NRT + Counseling (1 or 4 sessions) (cigarettes cessation focused)	ECO-confirmed 7-day PPA from cigarettes at 52 weeks Cotinine-confirmed 7-day PPA from vaping at 52 weeks	Ongoing, 2028-07-01
Vaping Cessation Using the Ottawa Model for Smoking Cessation Among E-Cigarette Users (VC-OMSC)	NCT06164678	180	>18	Counseling +/-NRT vs Usual care	Continuous abstinence at 6- and 12-month follow ups	Ongoing, 2025-12-31
Concurrent vs. Sequential Cessation of Dual Cigarette and E-Cigarette Use	NCT06027840	40	>18	Varenicline (12 weeks) + Counseling + Cessation materials (concurrent cessation of cigarettes and EC) vs Varenicline (12 weeks) + Counseling + Cessation materials (cessation of cigarettes followed sequentially by cessation of e-cigarettes)	Cotinine-confirmed 7-day PPA at 12 weeks	Ongoing, 2025-06-01
Varenicline ror Nicotine Vaping Cessation in Non-Smoker Vaper Adolescents (Pilot)	NCT04602494	5 (actual)	18-25	Varenicline (12 weeks) vs Placebo vs Control	Continuous nicotine vaping abstinence from week 9 to 12	Terminated, 2022-06-27

Abbreviations: EC - electronic cigarette; ECO - exhaled carbon monoxide; PPA - point prevalence abstinence.

References

1. U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION. TOBACCO PRODUCT USE AMONG ADULTS—United States, 2022. 2022. p. 1-12.
2. Jamal A, Park-Lee E, Birdsey J et al. Tobacco Product Use Among Middle and High School Students - National Youth Tobacco Survey, United States, 2024. *MMWR Morb Mortal Wkly Rep*. 2024;**73(41)**:917-24. doi: 10.15585/mmwr.mm7341a2.
3. North America E-cigarette and Vape Market size and Outlook: Horizon Grand View Research; 2023 [Available from: https://www.grandviewresearch.com/horizon/outlook/e-cigarette-and-vape-market/north-america.
4. Truth Initiative. Quitting Tobacco: Facts and Stats 2024 [Available from: https://truthinitiative.org/research-resources/quitting-smoking-vaping/quitting-tobacco-facts-and-stats.
5. Graham AL, Amato MS, Cha S, Jacobs MA, Bottcher MM, Papandonatos GD. Effectiveness of a Vaping Cessation Text Message Program Among Young Adult e-Cigarette Users: A Randomized Clinical Trial. *JAMA Intern Med*. 2021;**181(7)**:923-30. doi: 10.1001/jamainternmed.2021.1793.
6. Martinez U, Simmons VN, Sutton SK et al. Targeted smoking cessation for dual users of combustible and electronic cigarettes: a randomised controlled trial. *Lancet Public Health*. 2021;**6(7)**:e500-e9. doi: 10.1016/S2468-2667(20)30307-8.
7. Palmer AM, Tomko RL, Squeglia LM et al. A pilot feasibility study of a behavioral intervention for nicotine vaping cessation among young adults delivered via telehealth. *Drug Alcohol Depend*. 2022;**232**:109311. doi: 10.1016/j.drugalcdep.2022.109311.
8. Graham AL, Cha S, Jacobs MA et al. A Vaping Cessation Text Message Program for Adolescent E-Cigarette Users: A Randomized Clinical Trial. *JAMA*. 2024;**332(9)**:713-21. doi: 10.1001/jama.2024.11057.
9. Sahr M, Kelsh S, Blower N, Sohn M. Pilot Study of Electronic Nicotine Delivery Systems (ENDS) Cessation Methods. *Pharmacy (Basel)*. 2021;**9(1)**. doi: 10.3390/pharmacy9010021.
10. Palmer AM, Carpenter MJ, Rojewski AM, Haire K, Baker NL, Toll BA. Nicotine replacement therapy for vaping cessation among mono and dual users: A mixed methods preliminary study. *Addict Behav*. 2023;**139**:107579. doi: 10.1016/j.addbeh.2022.107579.
11. Vickerman KA, Carpenter KM, Mullis K et al. Quitline-Based Young Adult Vaping Cessation: A Randomized Clinical Trial Examining NRT and mHealth. *Am J Prev Med*. 2025;**68(2)**:366-76. doi: 10.1016/j.amepre.2024.10.019.
12. Evins AE, Cather C, Reeder HT et al. Varenicline for Youth Nicotine Vaping Cessation: A Randomized Clinical Trial. *JAMA*. 2025. doi: 10.1001/jama.2025.3810.
13. Caponnetto P, Campagna D, Ahluwalia JS et al. Varenicline and counseling for vaping cessation: a double-blind, randomized, parallel-group, placebo-controlled trial. *BMC Med*. 2023;**21(1)**:220. doi: 10.1186/s12916-023-02919-2.
14. Fucito LM, Baldassarri SR, Baker NL et al. Varenicline for E-Cigarette Cessation in Adults: A Preliminary Placebo-Controlled Randomized Trial. *Am J Prev Med*. 2024;**67(2)**:296-8. doi: 10.1016/j.amepre.2024.04.007.
15. Rigotti NA, Benowitz NL, Prochaska JJ et al. Cytisinicline for Vaping Cessation in Adults Using Nicotine E-Cigarettes: The ORCA-V1 Randomized Clinical Trial. *JAMA Intern Med*. 2024;**184(8)**:922-30. doi: 10.1001/jamainternmed.2024.1313.
16. Berg CJ, Krishnan N, Graham AL, Abroms LC. A synthesis of the literature to

inform vaping cessation interventions for young adults. *Addict Behav*. 2021;**119**:106898. doi: 10.1016/j.addbeh.2021.106898.
17. World Health Organization. WHO report on the global tobacco epidemic, 2023: protect people from tobacco smoke.: Geneva: World Health Organization; 2023.
18. West R, Shiffman S. Effect of oral nicotine dosing forms on cigarette withdrawal symptoms and craving: a systematic review. *Psychopharmacology (Berl)*. 2001;**155(2)**:115-22. doi: 10.1007/s002130100712.
19. Klein EG, Shoben AB, Carpenter KM et al. A Randomized Clinical Trial of a Quitline Vaping Cessation Intervention: Baseline Characteristics of Young Adult Exclusive E-Cigarette Users Seeking Treatment. *Int J Environ Res Public Health*. 2024;**21(6)**. doi: 10.3390/ijerph21060809.
20. RxList. Chantix 2022 [Available from: https://www.rxlist.com/chantix-drug.htm.
21. Lindson N, Theodoulou A, Ordonez-Mena JM et al. Pharmacological and electronic cigarette interventions for smoking cessation in adults: component network meta-analyses. *Cochrane Database Syst Rev*. 2023;**9(9)**:CD015226. doi: 10.1002/14651858.CD015226.pub2.
22. Johnstone S, Sorkhou M, Rabin RA, George TP. Dose-dependent effects of Varenicline on tobacco craving and withdrawal in tobacco smokers with and without schizophrenia. *Drug Alcohol Depend*. 2022;**234**:109412. doi: 10.1016/j.drugalcdep.2022.109412.
23. Azuara-Blanco A, Burr J, Ramsay C et al. Effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma (EAGLE): a randomised controlled trial. *Lancet*. 2016;**388(10052)**:1389-97. doi: 10.1016/S0140-6736(16)30956-4.
24. Karnieg T, Wang X. Cytisine for smoking cessation. *CMAJ*. 2018;**190(19)**:E596. doi: 10.1503/cmaj.171371.
25. Zatonski W, Cedzynska M, Tutka P, West R. An uncontrolled trial of cytisine (Tabex) for smoking cessation. *Tob Control*. 2006;**15(6)**:481-4. doi: 10.1136/tc.2006.016097.
26. Paduszynska A, Banach M, Rysz J, Dabrowa M, Gasiorek P, Bielecka-Dabrowa A. Cytisine - From the Past to the Future. *Curr Pharm Des*. 2018;**24(37)**:4413-23. doi: 10.2174/1381612825666181123124733.
27. Health Canada. Product information 2024 [Available from: https://health-products.canada.ca/lnhpd-bdpsnh/info?licence=80072525.
28. Glantz S, Jeffers A, Winickoff JP. Nicotine Addiction and Intensity of e-Cigarette Use by Adolescents in the US, 2014 to 2021. *JAMA Netw Open*. 2022;**5(11)**:e2240671. doi: 10.1001/jamanetworkopen.2022.40671.
29. Xue W, Lopez-Quintero C, Anthony JC. 'Time to first tobacco cigarette soon after waking' occurs more often among underage newly incident smokers in the United States, 2004-2017. *Addict Behav*. 2020;**111**:106535. doi: 10.1016/j.addbeh.2020.106535.
30. ClinivalTrials.gov. The Avenues Study: Dual Use Cessation 2024 [Available from: https://www.clinicaltrials.gov/study/NCT06474299?intr=NCT06474299&rank=1.
31. Butler AR, Lindson N, Livingstone-Banks J et al. Interventions for quitting vaping. *Cochrane Database Syst Rev*. 2025;**1(1)**:CD016058. doi: 10.1002/14651858.CD016058.pub2.
32. Marques P, Piqueras L, Sanz MJ. An updated overview of e-cigarette impact on human health. *Respir Res*. 2021;**22(1)**:151. doi: 10.1186/s12931-021-01737-5.

33. Lindson N, Butler AR, McRobbie H et al. Electronic cigarettes for smoking cessation. *Cochrane Database Syst Rev*. 2025;**1(1)**:CD010216. doi: 10.1002/14651858.CD010216.pub9.
34. Christensen MH, Ishibashi M, Nielsen ML, Leonard CS, Kohlmeier KA. Age-related changes in nicotine response of cholinergic and non-cholinergic laterodorsal tegmental neurons: implications for the heightened adolescent susceptibility to nicotine addiction. *Neuropharmacology*. 2014;**85**:263-83. doi: 10.1016/j.neuropharm.2014.05.010.
35. Holliday ED, Nucero P, Kutlu MG et al. Long-term effects of chronic nicotine on emotional and cognitive behaviors and hippocampus cell morphology in mice: comparisons of adult and adolescent nicotine exposure. *Eur J Neurosci*. 2016;**44(10)**:2818-28. doi: 10.1111/ejn.13398.
36. Government of Canada. Nicotine Concentration in Vaping Products Regulations. Minister of Justice; 2021.
37. Medicines and Healthcare products Regulatory Agency. E-cigarettes: regulations for consumer products 2024 [Available from: https://www.gov.uk/guidance/e-cigarettes-regulations-for-consumer-products#:~:text=The%20requirements%3A,no%20more%20than%2020mg%2Fml.
38. Hammond D, Reid JL, Goniewicz ML et al. Nicotine Exposure From Smoking Tobacco and Vaping Among Adolescents. *JAMA Netw Open*. 2025;**8(3)**:e2462544. doi: 10.1001/jamanetworkopen.2024.62544.
39. Awad AA, Itumalla R, Gaidhane AM et al. Association of electronic cigarette use and suicidal behaviors: a systematic review and meta-analysis. *BMC Psychiatry*. 2024;**24(1)**:608. doi: 10.1186/s12888-024-06012-7.
40. Song C, Hao X, Critselis E, Panagiotakos D. The impact of electronic cigarette use on chronic obstructive pulmonary disease: A systematic review and meta-analysis. *Respir Med*. 2025;**239**:107985. doi: 10.1016/j.rmed.2025.107985.
41. Glantz SA, Nguyen N, Oliveira da Silva AL. Population-Based Disease Odds for E-Cigarettes and Dual Use versus Cigarettes. *NEJM Evid*. 2024;**3(3)**:EVIDoa2300229. doi: 10.1056/EVIDoa2300229.
42. Flacco ME, Fiore M, Acuti Martellucci C et al. Tobacco vs. electronic cigarettes: absence of harm reduction after six years of follow-up. *Eur Rev Med Pharmacol Sci*. 2020;**24(7)**:3923-34. doi: 10.26355/eurrev_202004_20859.
43. Centers for Disease Control and Prevention. E-cigarette Unit Sales by Product and Flavor Type, and Top-Selling Brands, United States, 2020-2022. Morbidity and Mortality Weekly Report; 2023. p. 672-7.
44. U.S. Food and Frug Administration. FDA finalizes enforcement policy on unauthorized flavored cartridge-based e-cigarettes that appeal to children, including fruit and mint 2020 [Available from: https://www.fda.gov/news-events/press-announcements/fda-finalizes-enforcement-policy-unauthorized-flavored-cartridge-based-e-cigarettes-appeal-children.
45. Inc AG. 2022 Annual Report. 2022.
46. Chaykowski K. New Altria Deal Makes Juul Cofounders Billionaires. *Forbs*. 2018.
47. Federal Trade Comission. Federal Trade Commission E-Cigarette Report for 2021. 2024.
48. Campaign for Tobacco-Free Kids. JUUL and Youth: Rising E-Cigarette Popularity 2019 [Available from: https://assets.tobaccofreekids.org/factsheets/0394.pdf.
49. Struik LL, Dow-Fleisner S, Belliveau M, Thompson D, Janke R. Tactics for Drawing Youth to Vaping: Content Analysis of Electronic Cigarette Advertisements. *J*

Med Internet Res. 2020;**22(8)**:e18943. doi: 10.2196/18943.
50. Benowitz NL, Bernert JT, Foulds J et al. Biochemical Verification of Tobacco Use and Abstinence: 2019 Update. *Nicotine Tob Res*. 2020;**22(7)**:1086-97. doi: 10.1093/ntr/ntz132.
51. Meadows AL, Guenthner G, Broster LS, Luo AY, Martin CA. Assessing adolescent tobacco use in a substance use treatment program with self-report and biological measures. *Addict Behav*. 2020;**107**:106424. doi: 10.1016/j.addbeh.2020.106424.
52. Williams J, Rakovac I, Loyola E et al. A comparison of self-reported to cotinine-detected smoking status among adults in Georgia. *Eur J Public Health*. 2020;**30(5)**:1007-12. doi: 10.1093/eurpub/ckaa093.
53. Scheuermann TS, Richter KP, Rigotti NA et al. Accuracy of self-reported smoking abstinence in clinical trials of hospital-initiated smoking interventions. *Addiction*. 2017;**112(12)**:2227-36. doi: 10.1111/add.13913.
54. Tan X, Vrana K, Ding ZM. Cotinine: Pharmacologically Active Metabolite of Nicotine and Neural Mechanisms for Its Actions. *Front Behav Neurosci*. 2021;**15**:758252. doi: 10.3389/fnbeh.2021.758252.
55. Notley C, Gentry S, Livingstone-Banks J, Bauld L, Perera R, Hartmann-Boyce J. Incentives for smoking cessation. *Cochrane Database Syst Rev*. 2019;**7(7)**:CD004307. doi: 10.1002/14651858.CD004307.pub6.
56. Kendzor DE, Businelle MS, Frank-Pearce SG et al. Financial Incentives for Smoking Cessation Among Socioeconomically Disadvantaged Adults: A Randomized Clinical Trial. *JAMA Netw Open*. 2024;**7(7)**:e2418821. doi: 10.1001/jamanetworkopen.2024.18821.
57. Erhabor J, Boakye E, Obisesan O et al. E-Cigarette Use Among US Adults in the 2021 Behavioral Risk Factor Surveillance System Survey. *JAMA Netw Open*. 2023;**6(11)**:e2340859. doi: 10.1001/jamanetworkopen.2023.40859.
58. Jackson SE, Cox S, Shahab L, Brown J. Trends and patterns of dual use of combustible tobacco and e-cigarettes among adults in England: A population study, 2016-2024. *Addiction*. 2025;**120(4)**:608-19. doi: 10.1111/add.16734.