

The Role of Flavors in Migrating Adult Smokers to Alternative Nicotine Products

Sarah Baxter, VP-Regulatory Science, RAI Services Co

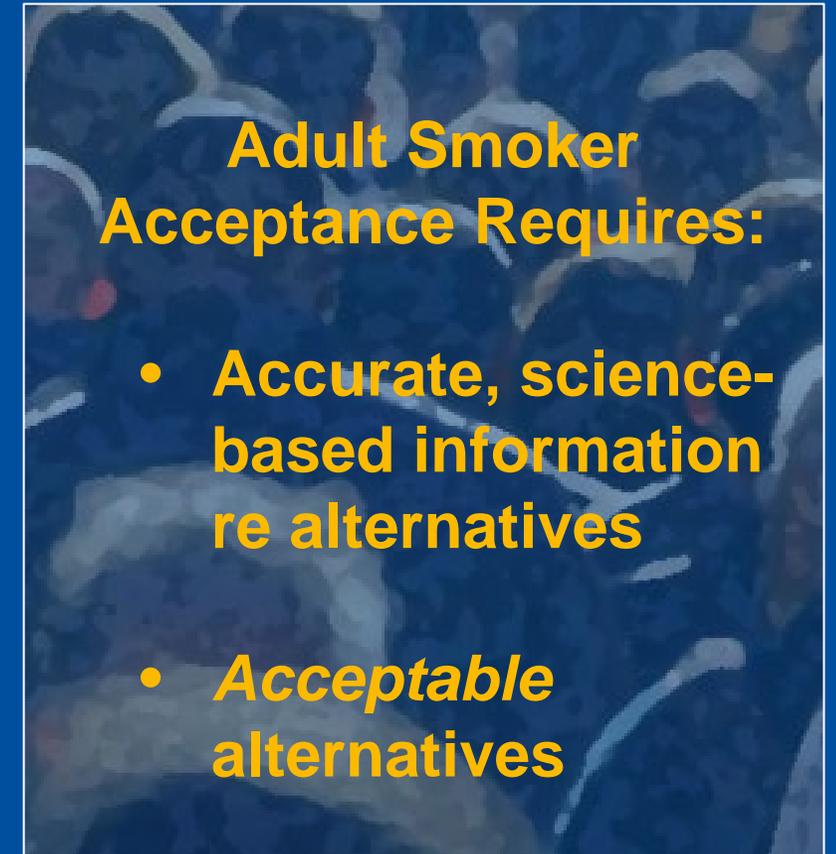
September 11-14, 2022

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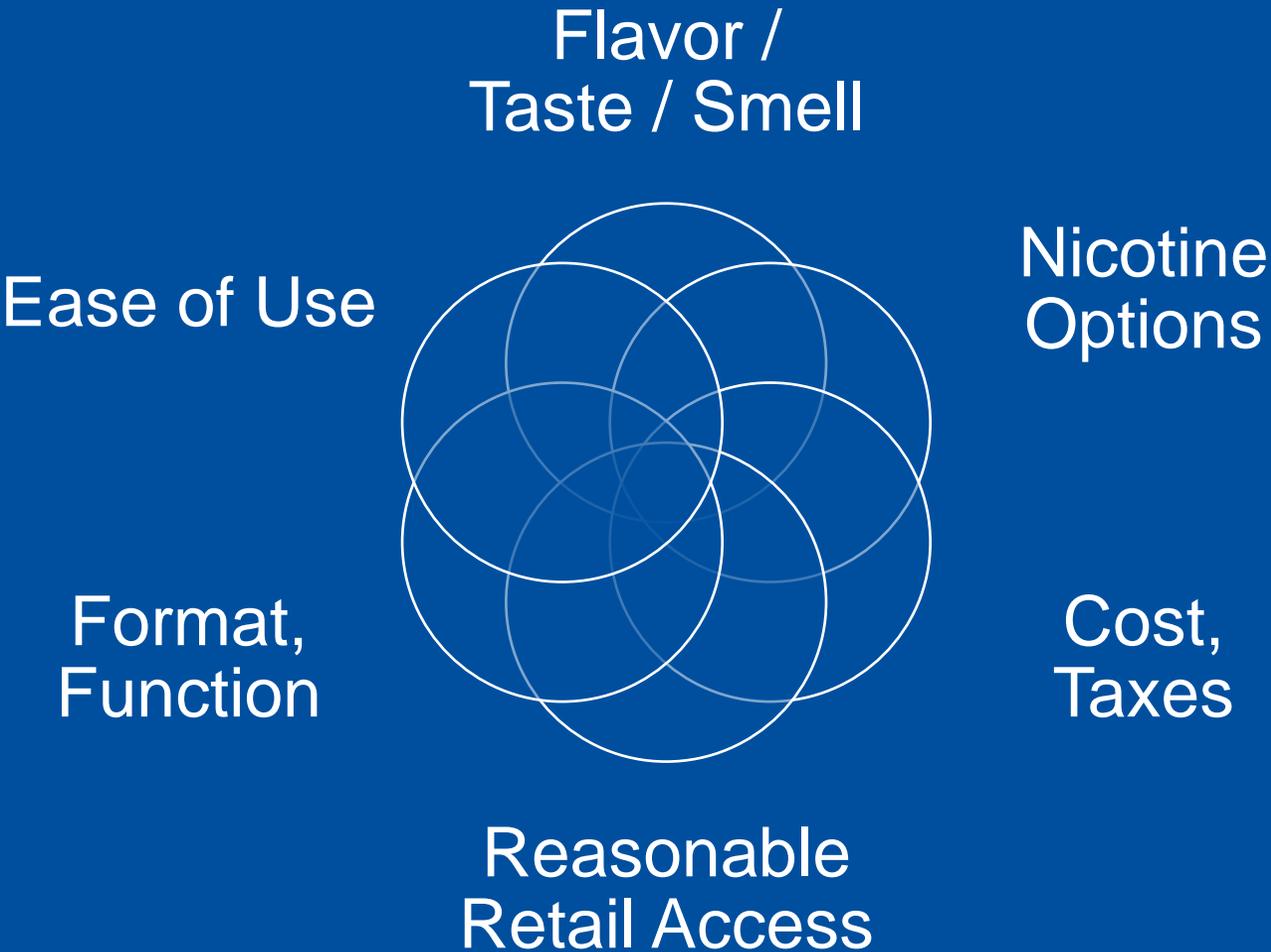
- Reynolds is committed to reducing the health impact of cigarette smoking and A better tomorrow.TM Reynolds supports tobacco harm reduction (“THR”), a policy widely embraced by many in public health. THR counsels that the best way to further reduce the health consequences of cigarette smoking is to provide adult smokers with accurate, science-based information about alternative product choices that may present less risk, and to encourage adult smokers uninterested in quitting tobacco altogether to consider switching to those alternatives.
- The following materials are prepared to facilitate discussion regarding government policy and thr.
- The data reviewed in this presentation is solely for the purpose of addressing public policy issues regarding tobacco products.
- Reynolds is not responsible for the content of referenced sources and the views expressed do not necessarily represent the views of reynolds.
- Reynolds does not make health or cessation claims regarding its brands. Nothing contained in this document should be misconstrued to the contrary.
- No tobacco product is safe, all tobacco products are addictive. Youth should never use tobacco. Smokers who are concerned about their health should quit.
- The views expressed in this presentation are those of the presenter and may not reflect the views of reynolds.

Driving from THR Policy > Acceptance

- Reynolds is committed to reducing the health impact of its business
- THR is an important means of achieving this goal
 - THR counsels that the best way to further reduce the health consequences of cigarette smoking is to provide adult smokers with accurate, science-based information about alternative product choices that may present less risk, and to encourage adult smokers uninterested in quitting tobacco altogether to consider switching to those alternatives.
 - THR is a necessary supplement to existing efforts to reduce smoking (e.g., education, NRTs) because they have not eliminated smoking – **30.8M adults smoke in the US** (NHIS, 2020).



Key Aspects of Product Acceptability



**Acceptability Is
Critical
Unacceptable
Aren't Used**

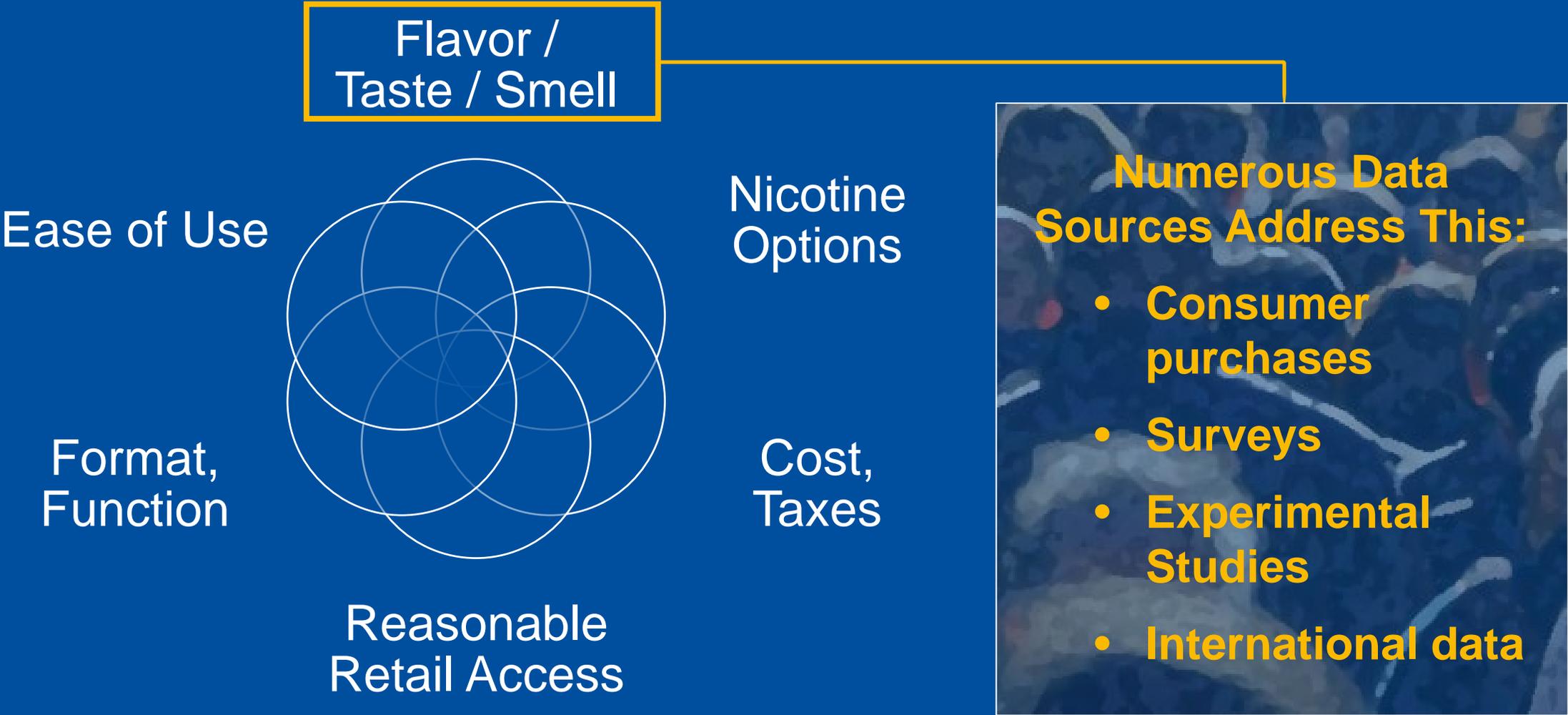


Premier (1989)

“near-perfect
low-tar cigarette”
(Lancet, 1991)

“Tastes like sh*t”

Key Elements of Product Acceptability



When Do Flavor Options Matter?



- Potential Interest
- Purchase Intent
- Initial Experience
- Conversion to Dominant Use
- Switching
- *And adult flavor preferences may not be static*

The *Entire* Journey

Systematic Literature Review Confirms Importance of Flavors to Acceptability

Review of 104 Research Studies:

Nicotine and Tobacco Research, 2022, 24, 1322-1343
https://doi.org/10.1093/ntr/ntab022
Advance access publication 19 March 2022

Review

SRNT OXFORD

The Role of Nicotine and Flavor in the Abuse Potential and Appeal of Electronic Cigarettes for Adult Current and Former Cigarette and Electronic Cigarette Users: A Systematic Review

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Abstract
Introduction: Many adult cigarette smokers use electronic cigarettes (e-cigarettes) to cut down on or quit smoking cigarettes. E-cigarettes with higher abuse potential and appeal might facilitate complete switching. E-liquid nicotine concentration and flavor are two of the characteristics that may affect the abuse potential and appeal of e-cigarettes. The objective of this systematic review was to compile results from surveys, animal, human laboratory, and clinical studies to understand the possible effects of nicotine concentration and flavor on abuse potential and appeal of e-cigarettes in adult current and former cigarette and e-cigarette users.
Aims and Methods: A comprehensive literature search was conducted in Ovid Medline and PsycINFO followed by citation tracking in Web of Science Core Collection. Peer-reviewed studies published in English between 2007 and August 2020 were selected that analyzed differences between e-liquid nicotine concentration and/or flavors, had outcome measures related to abuse potential and/or appeal, and included adult humans (18+) or animals. A total of 104 studies were identified and screened. A qualitative synthesis of results was performed.
Results: Results from 104 studies included in this review suggest that higher nicotine concentration and access to a variety of flavors are likely to be associated with higher abuse potential and appeal of e-cigarettes for adult current and former cigarette and e-cigarette users.
Conclusions: Higher nicotine concentrations and the availability of a variety of flavors in e-cigarettes might facilitate complete substitution for cigarettes. Future e-cigarette regulations should take into account their impact on smokers, for whom e-cigarettes may be a cessation tool or reduced-harm alternative.
Implications: E-cigarettes may provide a reduced-harm alternative to cigarettes for smokers unwilling/unable to quit or serve as a path for quitting all nicotine products. Higher nicotine concentrations and flavor variety are associated with higher abuse potential and appeal of e-cigarettes. Higher abuse potential and appeal products may help facilitate complete switching from cigarettes to e-cigarettes. Regulation of nicotine concentration and flavors aimed at decreasing naive uptake may inadvertently decrease uptake and complete switching among smokers, reducing the harm reduction potential of e-cigarettes. Evidence-based effects of regulating nicotine concentration and flavors must be considered for the population as a whole, including smokers.

Introduction
Electronic cigarettes (e-cigarettes) are a potential “disruptive technology” in the landscape of current tobacco products. They are associated with lower levels of known tobacco-related toxicants compared with cigarettes,^{1,2} making them a potentially less-harmful substitute for combustible tobacco use.³ However, the rising popularity of e-cigarettes has been controversial for several reasons: the high uptake among youth, unknown long-term health consequences, and the potential gateway to and re-normalization of cigarette smoking.⁴

Despite the controversy, there is “moderate-certainty evidence that [e-cigarettes] with nicotine increase quit rates compared to [nicotine replacement therapies].”⁵ According to the CDC, there are 34.1 million smokers in the United States, and 68% of them want to quit smoking. Many current and former cigarette smokers report using e-cigarettes to cut down or quit smoking.⁶ However, concurrent use of e-cigarette and combustible tobacco products (dual use) is a predominant pattern of use, and co-exposure to e-cigarette aerosol and cigarette smoke, as it occurs in dual users, may result in higher nicotine intake and increased exposure to

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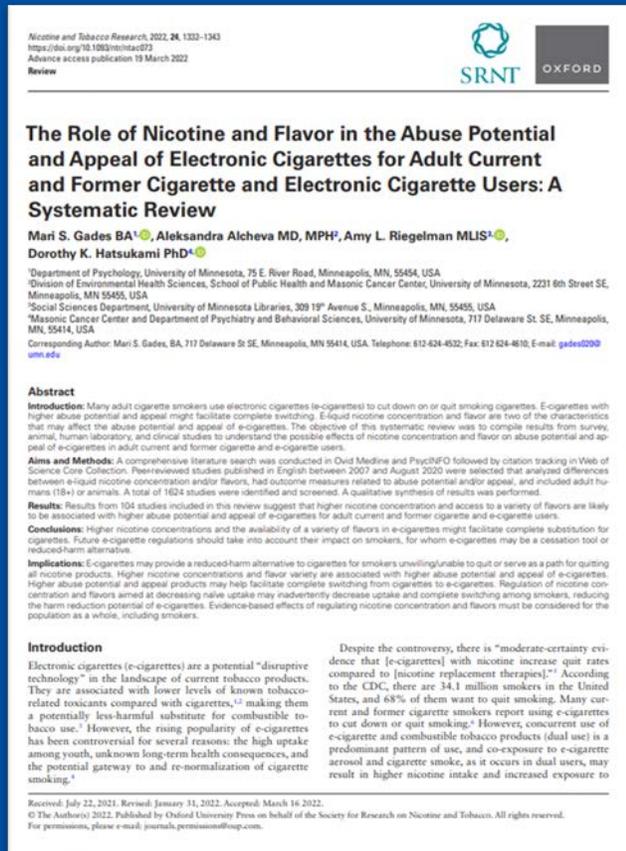
“Availability of a variety of flavors and the ability to switch between flavors was a valued aspect of e-cigarettes and **was often cited as a main reason for use**—behind health and smoking cessation.”

Main Reason for Use

“Compared with using tobacco or unflavored e-liquids alone, cigarette smokers who used one or multiple nontobacco flavored e-liquids were **more likely to have reduced or quit smoking.**”

Reduced Smoking & Quitting

Systematic Literature Review Confirms Importance of Flavors to Acceptability



“In general, the most preferred/used flavors were **fruit, mint/menthol, and candy/dessert flavors.**”

“Compared to former smokers..., dual use and/or increasing age were associated with higher tobacco flavor preference, although **fruit and/or menthol/mint flavors were still generally more preferred than tobacco even in these populations.**”

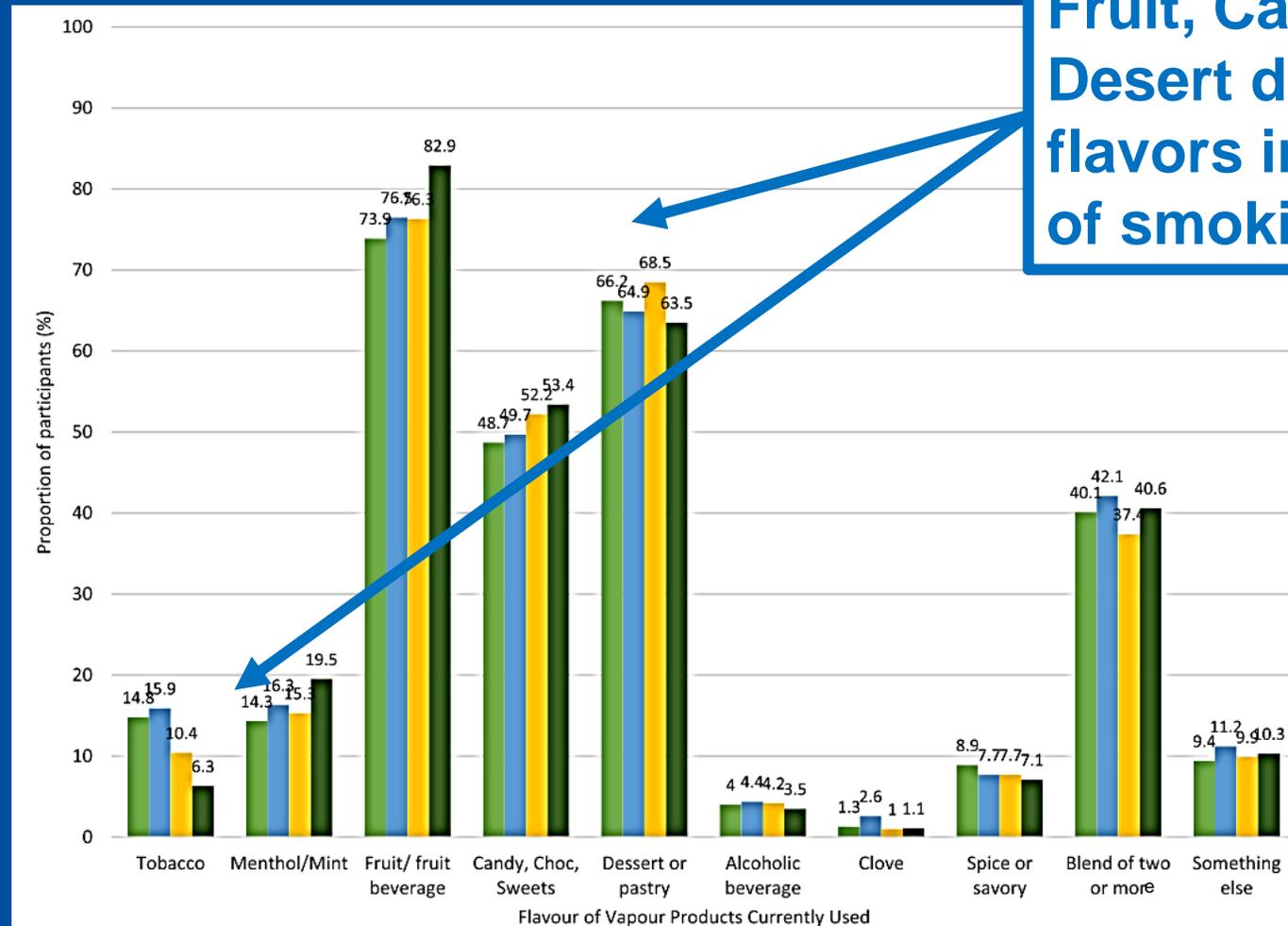
“Regulation of . . . flavors aimed at decreasing naïve uptake may **inadvertently decrease uptake and complete switching among smokers, reducing the harm reduction potential of e-cigarettes.**”

E-Cigarette Flavor Preferences

(Stratified by Smoking Category)

- **Current Use of E-cigarette/e-liquid flavors (2016) (n=20,676 US adults)**
- **75% of respondents had completely switched from CC**

- Switchers (n=15,807)
- Dual users (n=1,330)
- Former-smoker e-cigarette users (n=2,483)
- Never-smoker e-cigarette users (n=1,056)



Fruit, Candy and Desert dominant flavors irrespective of smoking status

E-Cigarette Flavor – 1st Purchase

(Stratified by Smoking Category – By Time)

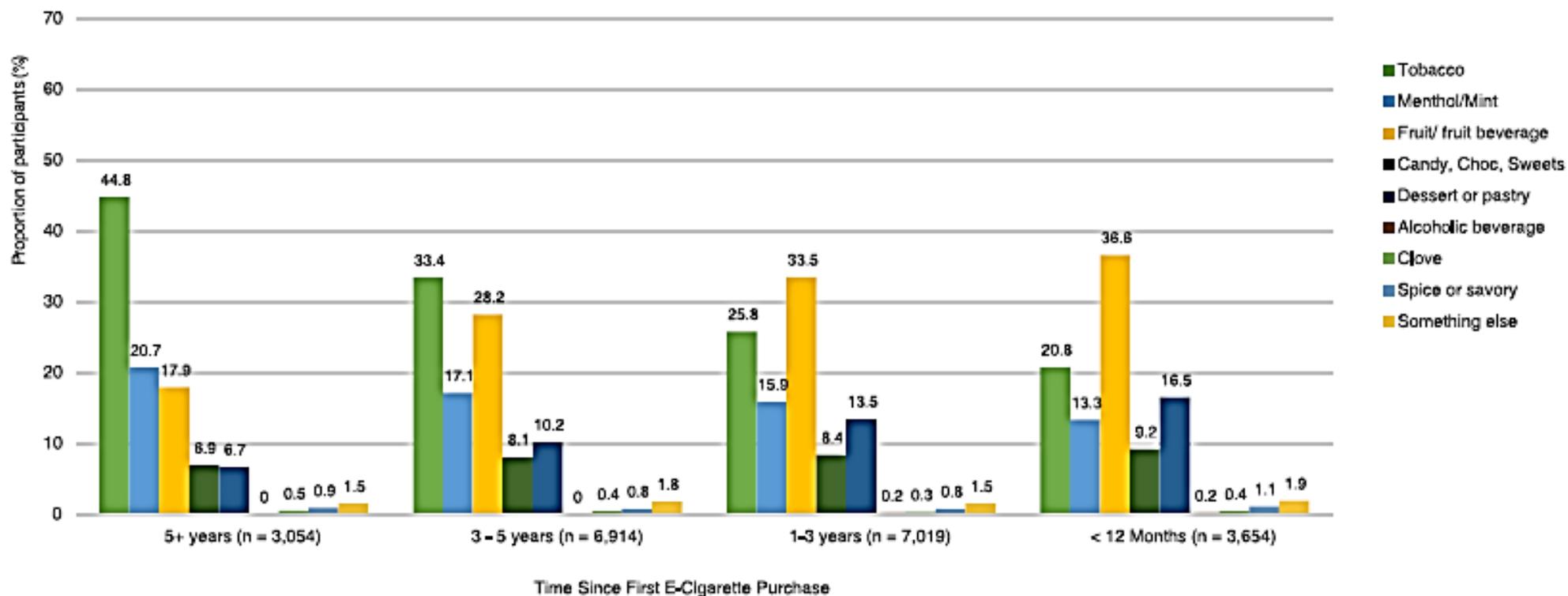


Fig. 1 Flavor of first e-cigarette purchased by time since first e-cigarette purchase: frequent e-cigarette users (n = 20,641/20,676)

Tobacco Declines —————→ **Fruit Increases**

Adult Flavor Preferences Are Complex and Change Over Time

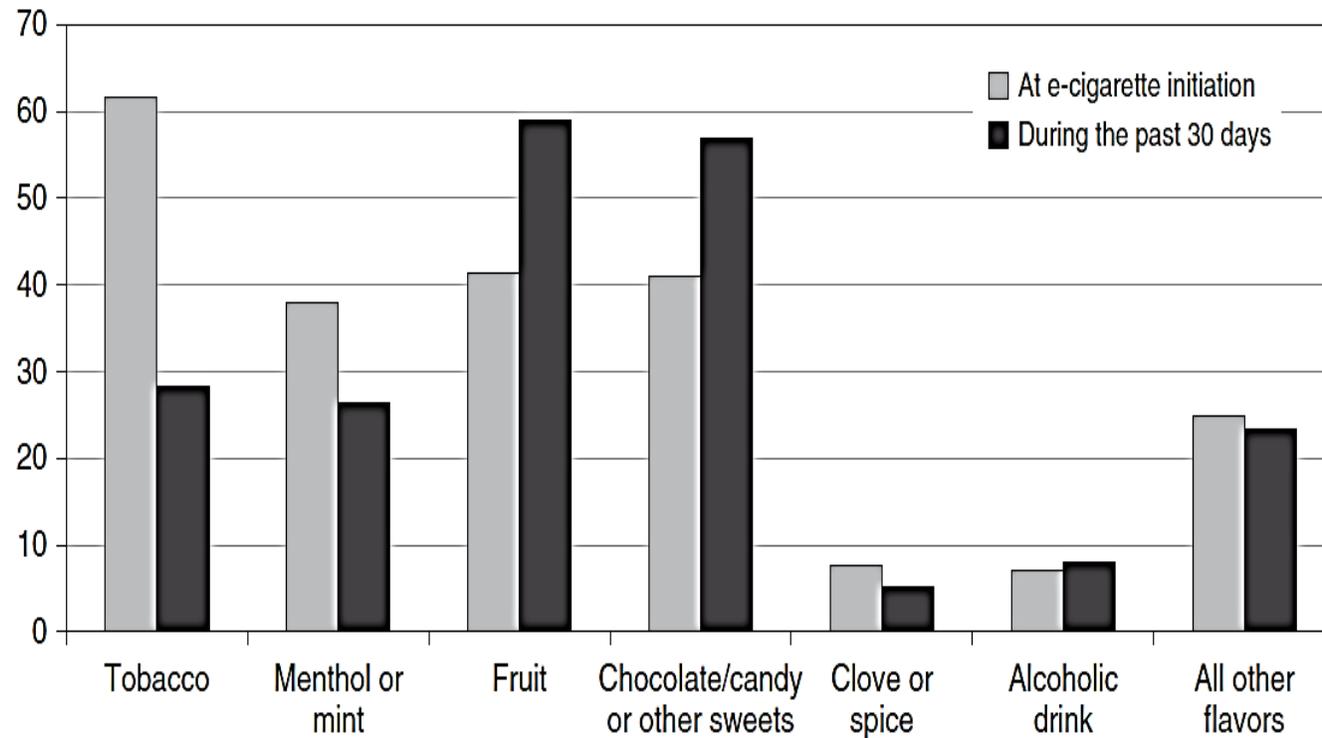
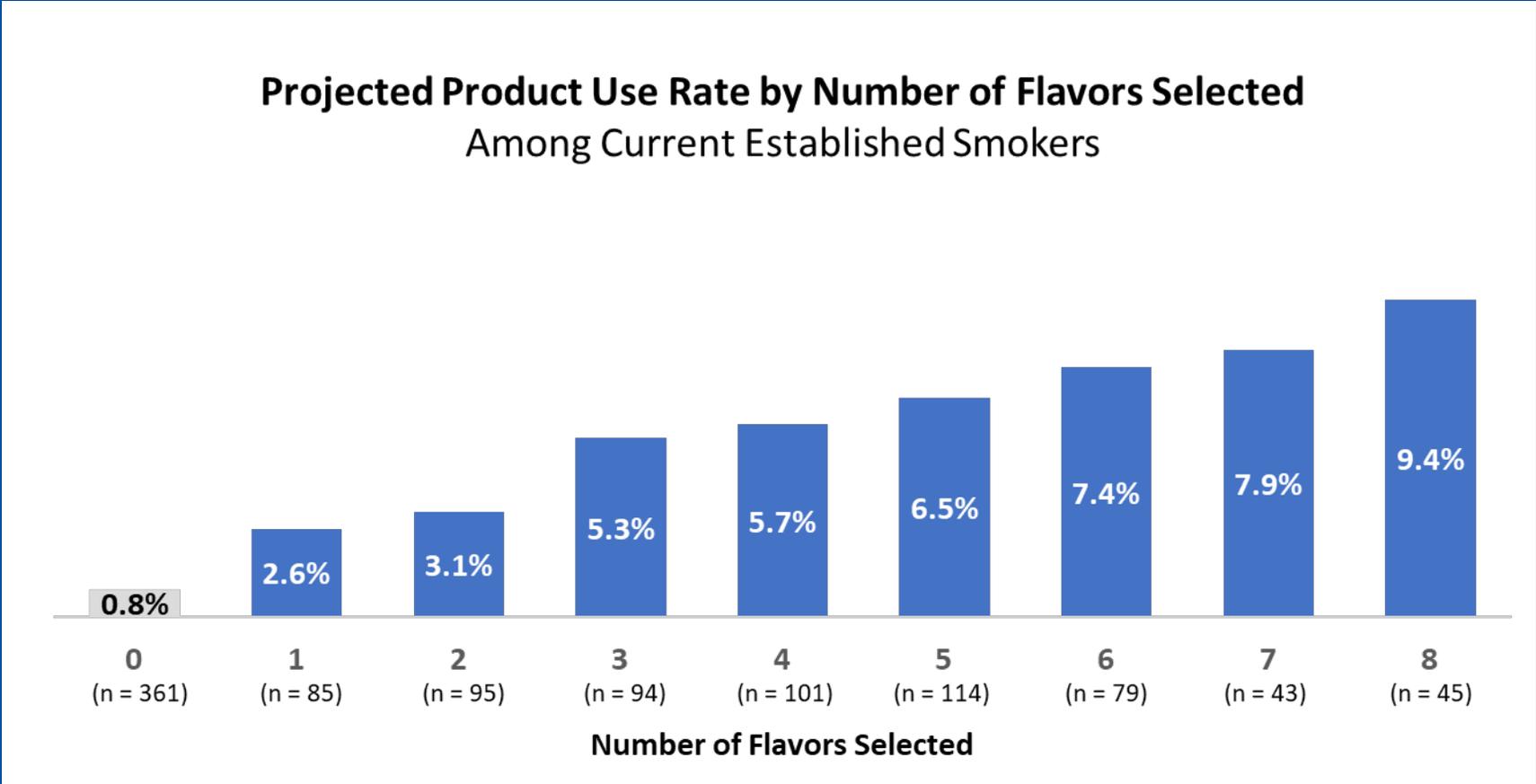


Figure 1. Flavors used at e-cigarette initiation and during the past 30 days. Participants were asked to recall their flavor use at e-cigarette initiation (shown in gray bar) and during the past 30 days at the follow-up survey (shown in black bar) from a list of flavors, including menthol or mint, tobacco, clove or spice, fruit, chocolate, candy or other sweets, alcoholic drink, and other flavor. Participants could report multiple flavor uses, not limited to their preferred flavor.

- Longitudinal study of e-cig adult users (n=7K)
- 60% changed flavors over time
- >75% reported having tried at least 10 flavors
- 98.2% used 2 or more flavors regularly

Interest in Flavors and Projected Use



**Increase Number
of Flavors**



**Increase
Projected Use**

Impact on Smoking Reduction/Cessation

- Majority of concurrent users reported vaping helps them reduce cigarettes smoked
 - - *Highest proportion used candy or fruit*
 - But overall, no significant different between flavors
- Majority of concurrent users reported that vaping may help them quit smoking
 - *Significantly more users using candy or fruit vs tobacco*
- Nearly all exclusive vapors/recent former smokers reported vaping helped them stay quit from smoking
- Smokers using ≥ 1 nontobacco flavors were more likely to have reduced or quit smoking

“Limiting access to flavors may therefore reduce the appeal of e-cigarettes among adults who are trying to quit smoking or stay quit.”

Role of Flavors in Smoking Cessation

(PATH Waves 1 – 4)

Adjusted Odds Ratios for the Relative Association of Flavored vs Unflavored Vaping with Subsequent Smoking Cessation

JAMA Network Open

Original Investigation | Substance Use and Addiction
Associations of Flavored e-Cigarette Uptake With Subsequent Smoking Initiation and Cessation
Abigail S. Friedman, PhD, SiQing Xu, BS

Abstract

IMPORTANCE Several states have banned sales of flavored e-cigarettes, but evidence on the association between vaping flavors and subsequent smoking initiation and cessation is limited.

OBJECTIVE To evaluate whether new uptake of flavored e-cigarettes is more strongly associated with subsequent smoking initiation and cessation than uptake of unflavored e-cigarettes, separately for youths (12-17 years), emerging adults (18-24 years), and prime-age adults (25-54 years).

DESIGN, SETTING, AND PARTICIPANTS This cohort study conducted secondary data analyses of longitudinal survey data from waves 1 to 4 of the Population Assessment of Tobacco and Health Study (collected from 2013 to 2018). The analytic sample was limited to 17 929 respondents aged 12 to 54 years at wave 1 who completed at least 3 consecutive waves of the survey and did not use e-cigarettes at baseline. Data were collected from 2013 to 2018 and analyzed in February 2020.

EXPOSURES Flavored vs unflavored e-cigarette use reported in wave 2 of the Population Assessment of Tobacco and Health Study.

MAIN OUTCOMES AND MEASURES Binary indicators captured wave 3 smoking among 7311 youths and 4634 emerging adults who did not smoke at baseline (ie, initiation) and not smoking at wave 3 among 1503 emerging adults and 4481 prime-age adults who smoked at baseline (ie, cessation). Smoking status was based on having smoked in the past 30 days for youths and established smoking (ie, current smoking among those who smoked at least 100 cigarettes in their lifetime) for emerging and prime-age adults.

RESULTS The youths who did not smoke at baseline, emerging adults who smoked at baseline, and prime-age adults who smoked at baseline consisted of 51.4% to 58.0% male participants and 66.9% to 77.0% white individuals. Vaping uptake was positively associated with smoking initiation in youth (adjusted odds ratio [AOR], 6.75; 95% CI, 3.93-11.57; $P < .001$) and in emerging adults (AOR, 1.34; 95% CI, 1.70-6.02; $P < .001$). Vaping uptake was associated with cessation in adults (AOR, 1.34; 95% CI, 1.02-1.75; $P = .03$). Vaping nontobacco flavors was no more associated with youth smoking initiation than vaping tobacco flavors (AOR in youth, 0.66; 95% CI, 0.16-2.76; $P = .56$) but was associated with increased adult smoking cessation (AOR in adults, 2.28; 95% CI, 1.04-5.01; $P = .04$).

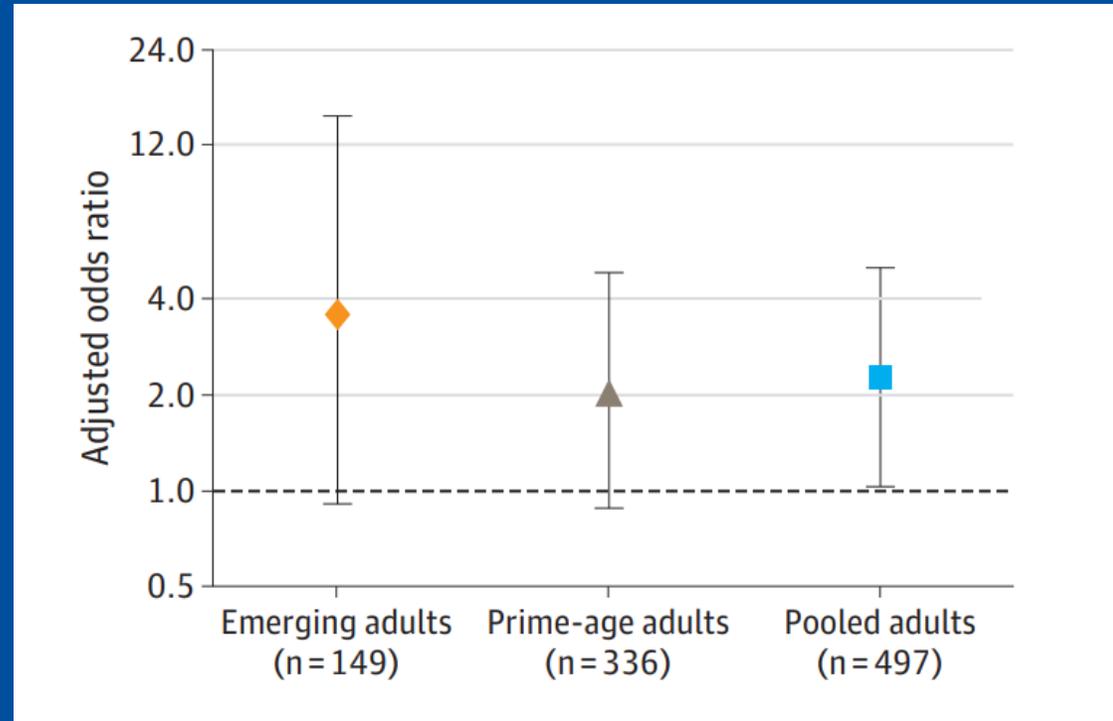
CONCLUSIONS AND RELEVANCE In this study, adults who began vaping nontobacco-flavored e-cigarettes were more likely to quit smoking than those who vaped tobacco flavors. More research is needed to establish the relationship between e-cigarette flavors and smoking and to guide related policy.

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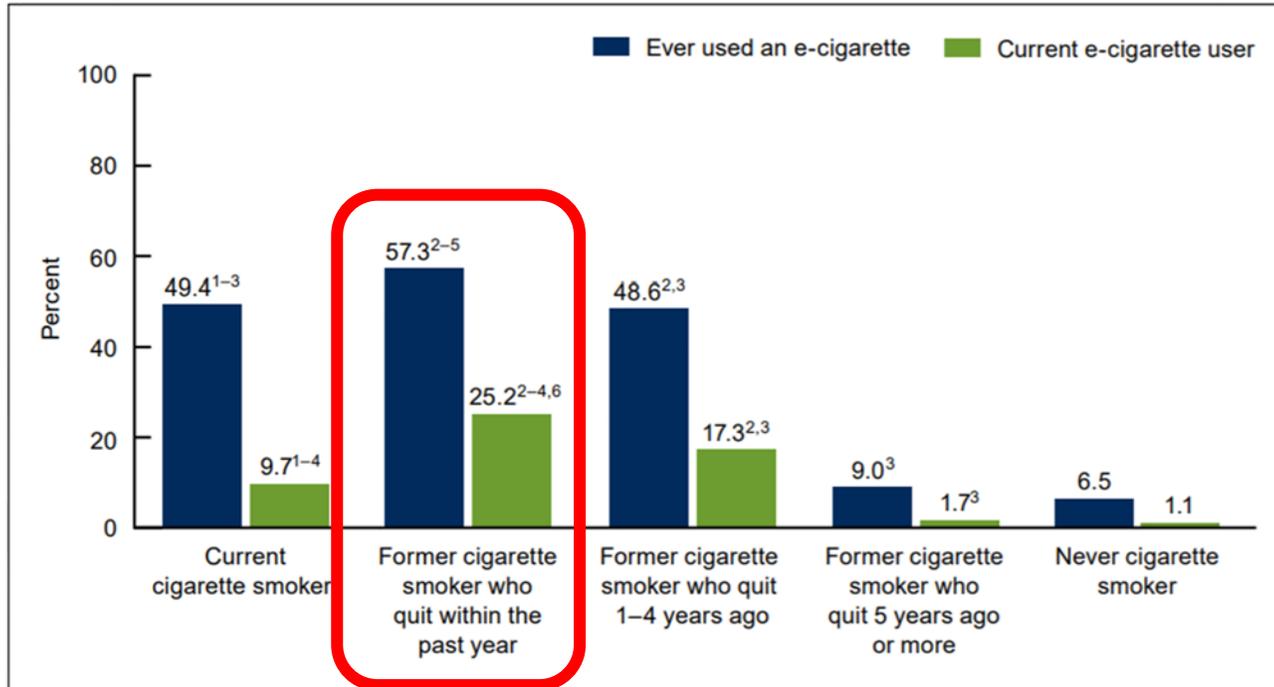
“...among adults who smoked and began vaping, the odds of cessation for those favoring nontobacco flavors were 2.3 times that of those who used tobacco-flavored e-cigarettes.”

Flavor Restriction/Ban Considerations

- Young adult e-cigarette users:
 - If e-cigarettes were restricted to tobacco/menthol → they would decrease e-cigarette use but **maintain or increase their cigarette use** (Pacek et al, 2019)
 - If vape product sales were restricted to tobacco flavors → 39.1% reported being likely to continue using e-cigarettes; **33.2% were likely to switch to cigarettes** (Posner et al., 2021).
- Long-term e-cigarette users:
 - “Nearly 50% of the participants reported that **they would “find a way”** to buy their preferred flavor **or add flavoring agents themselves** if nontobacco flavors were banned.” (Du et al., 2020)
- Data from global markets (The EU Nicotine Users Survey, 2020):
 - Consumers impacted by vape flavor bans/vape taxes (Finland, Estonia, and Hungary) **report using the black market and other alternative sources or buying from abroad.**
 - Also more likely to report lack of availability of vape products for their continued smoking.
 - In response to potential EU regulations: If flavours were banned, **more than 71% of vapers would look for alternative sources to the legal market.**

The THR Opportunity - E-Cigarette Use Among Former Smokers

Figure 3. Percentage of adults who had ever used an e-cigarette and were current e-cigarette users, by cigarette smoking status: United States, 2018



¹Significantly different from former cigarette smokers who quit within the past year ($p < 0.05$).

²Significantly different from former cigarette smokers who quit 5 years ago or more ($p < 0.05$).

³Significantly different from never smokers ($p < 0.05$).

⁴Significantly different from former cigarette smokers who quit 1-4 years ago ($p < 0.05$).

⁵Significant quadratic trend by duration of quitting cigarette smoking among former smokers ($p < 0.05$).

⁶Significant linear trend by duration of quitting cigarette smoking among former smokers ($p < 0.05$).

NOTES: Estimates are based on household interviews of a sample of the civilian noninstitutionalized U.S. population. Access data table for Figure 3 at:

<https://www.cdc.gov/nchs/data/databriefs/db365-tables-508.pdf#3>.

SOURCE: NCHS, National Health Interview Survey, 2018.

- Adult Ever and Current E-cigarette Users by Smoking Status, 2018
- Adults who quit smoking cigarettes within the past year were the most likely to have ever used (57.3%) and to be current (25.2%) e-cigarette users

CDC, Nat'l Ctr. For Health Statistics (2020)

Potential THR Benefit is Profound

“[Modeling] projects that under current patterns of... use and substitution, [US] nicotine vaping product use will translate into:*

1.8 million premature... deaths avoided

38.9 million life-years gained*

Conclusions

- **Non-Tobacco Flavors Appeal to Adult Smokers**
- **Availability of multiple flavors may increase purchase intent and use**
- **Flavor preferences are not static – Most smokers now initiate e-cigarettes with nontobacco flavors**
- **Fruit, candy, and dessert e-cigarette flavors are preferred/used more than tobacco and menthol flavors among current smokers, and those who have switched from cigarette smoking**
- **Nontobacco flavors, and use of multiple flavors, are associated with smoking cessation**
- **Huge potential impact on reducing smoking related morbidity and mortality**
- **There may be unintended consequences of flavor bans and restrictions**
- **Flavored e-cigarettes are an important tool for Tobacco Harm Reduction**

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