



ENDS PMTAs: Learnings & Opportunities to Advance Public Health

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PMTA Progress To-Date

>6.5m

PMTAs
Accepted

~1.2m

MDOs

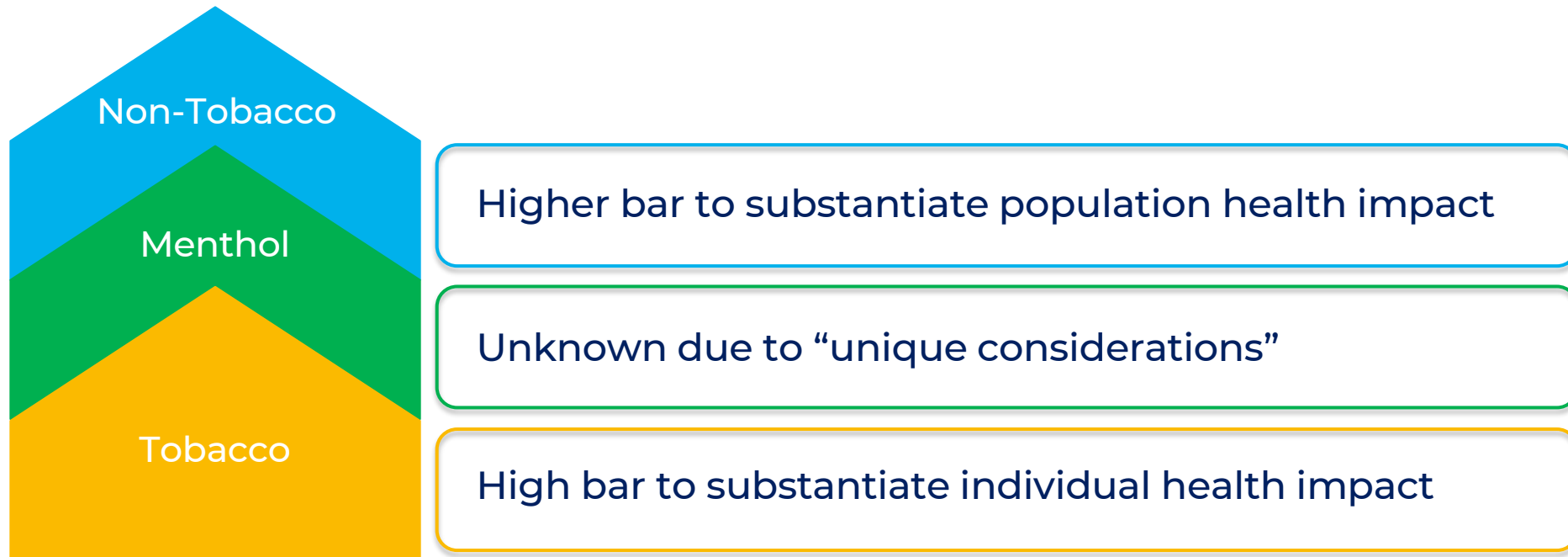
21

MGOs

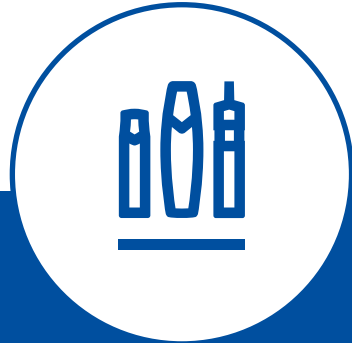
240

“Covered
Applications”

Learnings from FDA Actions or Communications



Implications of Agency Actions



01

De Facto Flavor Ban

Evidence suggests flavor bans may lead to unintended outcomes.

Nicotine and Tobacco Research, 2022, XX, 1–12
<https://doi.org/10.1093/ntn/ntac073>
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Review



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 survey, 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 1624 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 naïve 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. 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.³

Despite the controversy, there is “moderate-certainty evidence that [e-cigarettes] with nicotine increase quit rates compared to [nicotine replacement therapies].”⁴ 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.⁵ 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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“Regulation of nicotine concentration and flavors aimed at decreasing naïve uptake may inadvertently decrease uptake and complete switching among smokers, reducing the harm reduction potential of e-cigarettes.”⁽ⁱ⁾

(i) Gades et al. 2022

Implications of Agency Actions

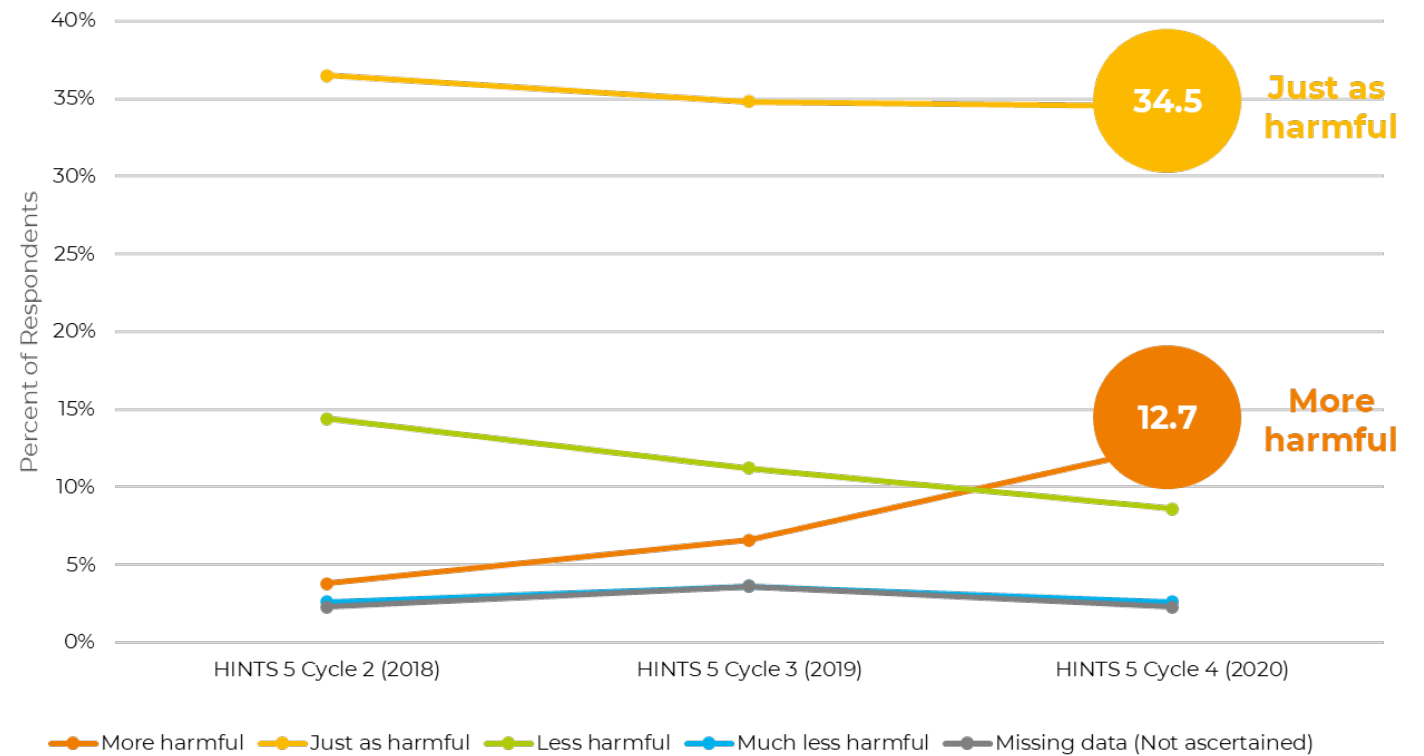


02

Continued Misperceptions

Misperceptions on relative risk of ENDS compared to cigarettes has doubled since 2019.

“Compared to smoking cigarettes, would you say that electronic cigarettes are...”⁽ⁱ⁾



(i) Health Information National Trends Survey (HINTS), 2018-2020

Implications of Agency Actions



03

Barrier to Innovation

Length of review and lack of transparency on timing limits product advancements and diversity of options to transition adult smokers.

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, 3.20; 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.

JAMA Network Open. 2020;3(6):e203826.
Corrected on June 26, 2020. doi:10.1001/jamanetworkopen.2020.3826

Key Points

Question Does the association between vaping uptake and subsequent smoking differ between individuals favoring tobacco- vs nontobacco-flavored e-cigarettes?

Findings In this cohort study with 17 929 participants, multivariable analyses of nationally representative, longitudinal survey data evaluated differences in smoking initiation and cessation subsequent to vaping uptake among those who used flavored vs unflavored e-cigarettes, separately by age group. Relative to vaping tobacco flavors, vaping nontobacco-flavored e-cigarettes was not associated with increased youth smoking initiation but was associated with an increase in the odds of adult smoking cessation.

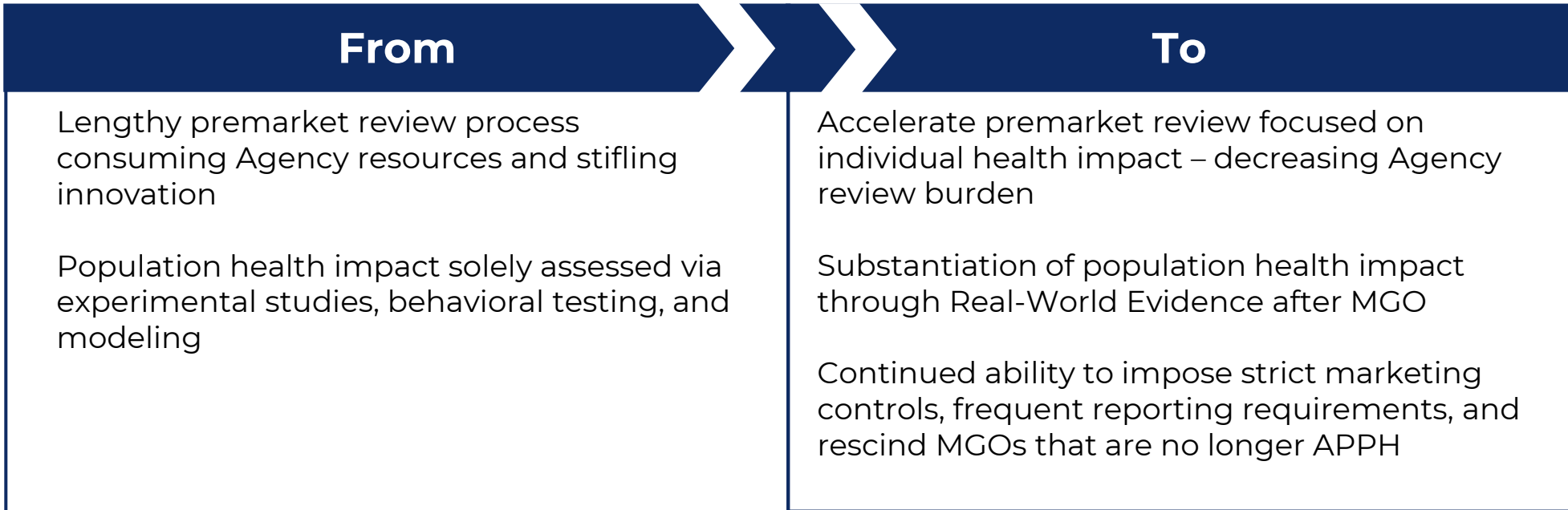
Meaning In this study, adults who vaped flavored e-cigarettes were more likely to subsequently quit smoking than those who used unflavored e-cigarettes.

+ Editorial
+ Supplemental content
Author affiliations and article information are listed at the end of this article.

“ In this study, adults who vaped flavored e-cigarettes were more likely to subsequently quit smoking than those who used unflavored e-cigarettes.⁽ⁱ⁾ ”

(i) Friedman and Xu, 2020

Opportunity to Improve the Process



Greater Reliance on Postmarket Surveillance

Potential THR Benefit for the US is Profound



POPULATION:
330 M



SMOKING
PREVALENCE:
14%⁽ⁱ⁾



VAPING
PREVALENCE:
3%⁽ⁱⁱ⁾

“[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^{”(iii)} from 2013-2060

(i) CDC, 2020; (ii) Villarroel et al., 2020; (iii) Levy et al., 2021