# **UC San Diego**

### **UC San Diego Previously Published Works**

### Title

The interacting effects of depression symptoms and sweet flavoring on the rewarding and reinforcing value of cigarillo use among young adults.

### **Permalink**

https://escholarship.org/uc/item/3h69q1h6

### **Authors**

Audrain-McGovern, Janet Klapec, Olivia Koita, Fodie et al.

### **Publication Date**

2024-06-01

### DOI

10.1016/j.dadr.2024.100234

### **Copyright Information**

This work is made available under the terms of a Creative Commons Attribution-NonCommercial-NoDerivatives License, available at <a href="https://creativecommons.org/licenses/by-nc-nd/4.0/">https://creativecommons.org/licenses/by-nc-nd/4.0/</a>

Peer reviewed

ELSEVIER

Contents lists available at ScienceDirect

### Drug and Alcohol Dependence Reports

journal homepage: www.elsevier.com/locate/dadr



# The interacting effects of depression symptoms and sweet flavoring on the rewarding and reinforcing value of cigarillo use among young adults<sup>†</sup>

Janet Audrain-McGovern <sup>a,\*</sup>, Olivia Klapec <sup>a</sup>, Fodie Koita <sup>a</sup>, Divya Manikandan <sup>a</sup>, Matthew D. Stone <sup>b</sup>

### HIGHLIGHTS

- First to evaluate depression and flavoring interactions on cigarillo addiction liability.
- Depression was associated with greater cigarillo reward, regardless of flavor.
- Depression was not associated with the relative reinforcing value of sweet flavor.
- Cigarillo consumption, overall and by flavor, did not differ by depression.

### ARTICLE INFO

### Keywords: cigarillos flavoring, young adults abuse liability reward reinforcement

### ABSTRACT

Background: Young adults 18–24 years old have the highest prevalence of cigarillo use, exposing young adults to comparable or higher nicotine levels and many of the same toxicants as combustible cigarettes. Identifying individual and product characteristics that increase the potential for persistent use is warranted. We sought to examine the interacting effects of depression symptoms and sweet flavoring on the rewarding and reinforcing value of cigarillo use.

*Methods*: 86 young adults (18–24 years old, 73.3 % male, 38.4 % White, 33.7 % Black, and 27.9 % Other) completed three laboratory visits assessing the subjective rewarding value (exposure paradigm), relative reinforcing value (computerized choice task), and absolute reinforcing value (ad libitum cigarillo smoking session) of sweet-flavored versus non-flavored cigarillos. Depression symptoms were measured with the 20-item Center for Epidemiologic Studies of Depression Scale and treated as a continuous variable.

Results: General linear models with the appropriate family link tested differences in depressive symptomology for each outcome. Irrespective of flavor, greater cigarillo subjective reward was reported across increasing depressive symptomology (B=0.03 [95%CI=0.00, 0.05], p=0.017). Across symptom levels, no significant differences were observed in the subjective reward and relative and absolute reinforcing values of sweet-flavored versus non-flavored cigarillos (p's >.05).

Conclusions: Young adults with elevated depression find cigarillos more rewarding but not more reinforcing. They are not more vulnerable than young adults with lower symptom levels to sweet cigarillo flavoring. Public health prevention campaigns and tobacco product regulations aimed at preventing the initiation and escalation of young adult cigarillo use may impact young adults broadly.

E-mail address: audrain@pennmedicine.upenn.edu (J. Audrain-McGovern).

<sup>&</sup>lt;sup>a</sup> Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

<sup>&</sup>lt;sup>b</sup> Herbert Wertheim School of Public Health and Human Longevity Science, University of California, San Diego, CA, USA

Abbreviations: CO, carbon monoxide; FR, fixed interval; PR, progressive interval; RRVF, relative reinforcing value of cigarillo flavoring; EMM, estimated marginal mean; CI, confidence interval; OR, odds ratio.

<sup>&</sup>lt;sup>★</sup> Trial Registration: The trial is registered as NCT05092919 at www.clinicaltrials.gov.

<sup>\*</sup> Correspondence to: Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, 3535 Market St., Suite 4100, Philadelphia, PA 19104, USA.

#### 1. Introduction

Young adults 18–24 years old have the highest prevalence of cigarillo use, up to four times that of adults 25 years and older (Corey et al., 2014b; Phan et al., 2021; Rostron et al., 2020). Cigarillos expose young adults to comparable nicotine levels and similar toxicants as combustible cigarettes (Koszowski et al., 2015; Pickworth et al., 2017). Identifying individual and product characteristics that increase the potential for persistent use is warranted.

Depression is one individual characteristic that places young adults at risk for combustible cigarette smoking (Audrain-McGovern et al., 2011) and e-cigarette use (Bandiera et al., 2017). Initial cross-sectional research suggests a similar relationship between depression symptoms and cigarillo smoking among young adults (Bierhoff et al., 2019; Sterling et al., 2013). Explanations for the link between depression and tobacco use are derived from cigarette smoking research, pointing to the phenomenology of depression and the potentially normalizing effects of nicotine on disrupted reward processing (Audrain-McGovern et al., 2014; Forbes, 2009). For example, individuals who are prone to depression find smoking twice as rewarding as other activities (Audrain-McGovern et al., 2014; Spring et al., 2003), more reinforcing than other available reinforcers (Audrain-McGovern et al., 2014), and experience greater smoking-induced dopamine release (Brody et al., 2009). In addition, they derive greater subjective reward from alternative reinforcers when smoking than abstinent (Audrain-McGovern et al., 2014; Klemperer et al., 2021).

Young adults with elevated depression may also find cigarillo smoking more rewarding and reinforcing than young adults without depression symptoms, especially since they come in appealing flavors. Estimates suggest that 51–80 % of young adults who use cigarillos typically smoke flavored cigarillos (Glasser et al., 2023; Rostron et al., 2020) and have a preference for cigarillos flavored to taste like fruit or other sweets (Bansal-Travers et al., 2022; Rose et al., 2020). Indeed, our recent research documented that young adults rate sweet-flavored cigarillos 20 % more rewarding than non-flavored cigarillos, "work" harder for the opportunity to self-administer sweet versus non-flavored cigarillo puffs, and consume sweet-flavored cigarillos at twice the rate of non-flavored cigarillos (Audrain-McGovern et al., 2023). Young adults with elevated depression may be especially vulnerable to the enhanced reward and reinforcement that accompanies the use of sweet-flavored cigarillos.

We sought to determine whether young adults with elevated depression symptoms experience greater rewarding and reinforcing effects from cigarillo use than young adults without depression and if these effects are enhanced for sweet-flavored compared to non-flavored cigarillos. These data will inform public health campaigns to prevent cigarillo initiation and escalation among young adults and tobacco regulatory actions surrounding cigar flavoring. Such efforts are critical to reducing combustible tobacco use disparities among affectively vulnerable populations (Tam et al., 2020).

### 2. Methods

### 2.1. Study sample

Participants were 86 young adults between 18 and 24 years old who reported smoking ≥ 10- lifetime cigarillos, excluding cigarillos modified for blunting with marijuana. A cutoff of 10 cigarillos/lifetime was chosen to ensure that cigarillo naïve young adults were not exposed, and study-related cigarillo exposure did not exceed lifetime exposure. Exclusion criteria included current enrollment in a tobacco cessation program, current use of smoking cessation medication or use of specific medications (e.g., prescription stimulants, opiate medications), regular recreational substance use (e.g., methamphetamine, cocaine, heroin), treatment for substance use in the past 12 months, alcohol consumption exceeding 25 standard drinks per week (Wall et al., 2018), use of

e-cigarettes on more than 15 days in the past 30 days, pregnancy or lactation, serious or unstable medical condition within the past year (e. g., cancer, asthma), and self-reported psychiatric conditions involving psychosis (Audrain-McGovern et al., 2015; Audrain-McGovern et al., 2014). Young adults who smoked combustible cigarettes or used cannabis were not excluded, given the prevalent co-use with cigarillos (Butler et al., 2016; Cohn et al., 2015; Cohn and Chen, 2022; Sterling et al., 2016b). Excluding these young adults would have resulted in a lower-risk and potentially biased sample.

The study was located at the University of Pennsylvania and approved by the Institutional Review Board. Recruitment was initiated in September 2021, and the first participant enrolled on September 14, 2021. The accrual was completed on February 16, 2023. Of the 102 young adults who attended in-person study screening, 95 were eligible and enrolled in the study. Analyses were conducted on the 86 participants who completed all three laboratory visits. The study is registered at CT.gov (NCT05092919).

### 2.2. Procedure

Participants were recruited from the Philadelphia area through social media-based advertisements. Young adults who responded to the ads were prescreened for inclusion and exclusion criteria over the telephone. Cigarillo, large cigar and little cigar use were measured and differentiated through product descriptions and brand examples (Corey et al., 2014a; Giovenco et al., 2018). Respondents self-reported whether cigarillos and other cigar products were used as intended or modified for blunting. Those eligible at the telephone screening provided written informed consent and completed a final eligibility screening to document a negative urine drug screen, a negative urine pregnancy test (females only), and a breath alcohol test = 0.000. Expired alveolar air was used to measure breath carbon monoxide (CO) to document cigarette smoking status.

The three laboratory-based assessments are described below. Participants were compensated \$55, \$65, and \$80 USD for visits 1–3, respectively, and received a \$40 USD bonus for the completion of all three visits. Black and Mild plastic-tipped cigarillos were used in this study since they are the most popular brand among young adults (Delnevo et al., 2015), and rarely used for blunting (Koopman Gonzalez et al., 2017; Mead et al., 2018). The non-flavored cigarillo constituted tobacco without any characterizing flavors. The sweet-flavored cigarillos included citrus fruit ("Jazz") and Cream, two of the most popular sweet flavors. During all three laboratory visits, Black and Mild brandings were obscured with colored tape.

2.2.1. Laboratory visit 1: subjective rewarding value of Cigarillo flavoring Participants completed measures of their tobacco usage and history (number, time, type), lifetime and recent cigarillo use (flavored, non-flavored, preference), cannabis use, and demographics. The subjective rewarding value of sweet-flavored cigarillos was measured with a frequently used exposure paradigm.

During laboratory visit 1, participants were exposed to three Black and Mild cigarillos. One was non-flavored (no characterizing flavors added to the tobacco) and two contained sweet flavoring (citrus "Jazz" and Cream). Participants initiated two puffs from each cigarillo. Exposure to each cigarillo was separated by 20 min. The ordering of the exposures was counterbalanced (Audrain-McGovern et al., 2016b) and randomized by participants' self-reported sex at birth and cigarette smoking status. Following each cigarillo exposure, participants completed the Cigarette Evaluation Scale, adapted to measure cigarillo subjective reward. Participants waited in the lab in between cigarillo exposures. Visit 1 occurred in the afternoon versus the morning to increase the likelihood that participants who smoked cigarettes would smoke normally throughout the day and would rate their experience with the cigarillos in the absence of significant withdrawal symptoms.

# 2.2.2. Laboratory visit 2: relative reinforcing value of Cigarillo flavoring (RRVF)

Prior to laboratory visit 2, participants were instructed to abstain for 10 h from any combustible tobacco or combustible cannabis (CO-verified <10 ppm or half of Visit 1 CO) (Audrain-McGovern et al., 2015) and e-cigarettes (assessed by a reduction in urine cotinine level). Participants arrived at the lab at 1 pm. Participants were introduced to a validated behavioral choice task, which assessed the reinforcing value of a sweet-flavored cigarillo (the cigarillo with the highest rewarding value measured in visit 1) relative to the non-flavored cigarillo (Audrain-Mc-Govern et al., 2016b). Participants completed the task by moving a computer mouse to hit targets on one of two computer screens to earn points toward either the sweet-flavored or the non-flavored cigarillo. Using a concurrent schedule (Audrain-McGovern et al., 2016b; Audrain-McGovern et al., 2014), participants were told that they could switch from working on one screen to the other as often as they wish by moving the computer mouse to have the cursor hit the targets (e.g., either a fruit/cream labeled cigarillo or a cigarillo labeled as tobacco). The reinforcement schedule in the non-flavored cigarillo earning screen remained constant at a fixed ratio FR-25 (25 targets achieved to earn a point), while the reinforcement schedule for the sweet-flavored cigarillo increased (requiring more effort) with a progressive ratio schedule of PR-25x over 10 trials; such that 25, 50, 75, 100, 125, 150, 175, 200, 225, and 250 targets had to be achieved to earn a flavored point (Audrain-McGovern et al., 2015; Audrain-McGovern et al., 2014).

Following a practice session, the computerized task was performed until a participant completed 10 trials and accumulated a total of 10 points from which they could have earned either one puff of a non-flavored or sweet-flavored cigarillo for each point collected (i.e., up to 10 puffs of a non-flavored cigarillo or up to 10 puffs of a flavored cigarillo). Cigarillo puffs were redeemed at the end of the procedure to prevent satiation from influencing responses in subsequent trials. RRVF was defined by the breakpoint, which is the highest trial completed across 10 trials to earn puffs for sweet-flavored versus non-flavored cigarillo puffs (Audrain-McGovern et al., 2015; Audrain-McGovern et al., 2014). To ensure that responding to the choice task was based on reinforcer preference rather than desire to depart from the lab, the choice procedure was followed by a 1 h wait in the laboratory.

# 2.2.3. Laboratory Visit 3: absolute reinforcing value of Cigarillo flavoring Participants arrived at the lab for visit 3 at 1 pm after 10 h of

abstinence from tobacco and cannabis, as noted above. Participants then began a 90 min ad-libitum cigarillo smoking paradigm to assess the absolute reinforcing value of a sweet-flavored cigarillo. The absolute reinforcing value of a sweet-flavored cigarillo was measured by comparing the number of puffs taken from the non-flavored cigarillo or their preferred sweet-flavored cigarillo (determined at visit 1) (Audrain-McGovern et al., 2015; Audrain-McGovern et al., 2016b).

Participants completed the session in a specially ventilated smoking research room equipped with comfortable seating and paper-based puzzles (e.g., wordsearch, crossword). Participants were instructed that they had a 90-minute laboratory smoking session where they could smoke non-flavored or chosen flavored cigarillos ad-libitum. Additional instruction included 30 minutes of enforced abstinence from tobacco use following the completion of the ad-libitum smoking session (Audrain-McGovern et al., 2016b). A clock was placed on the table showing minutes elapsed from 90 minutes. Participants were observed via an observation window by a trained research assistant who monitored and counted the number of cigarillo puffs taken (from each cigarillo) during the 90 minutes (Audrain-McGovern et al., 2015; Audrain-McGovern et al., 2016b).

### 2.3. Measures

### 2.3.1. Outcome variables

The subjective rewarding value of cigarillo flavoring was measured

with the Satisfaction Subscale of the Cigarette Evaluation Scale adapted for cigarillo use. The Satisfaction Subscale has two items with a Likertstyle response option (1=not at all to 7=extremely) (Audrain-McGovern et al., 2016a; Westman et al., 1992).

The relative reinforcing value of cigarillo flavoring (RRVF) was assessed with a validated choice task, evaluating the preference for sweet-flavored versus non-flavored cigarillos (Audrain-McGovern et al., 2016b). RRVF was determined by the breakpoint, which is the highest trial completed across 10 trials to earn puffs for sweet-flavored versus non-flavored cigarillos (Bickel et al., 2000; Epstein et al., 2007).

The absolute reinforcing value of cigarillo flavoring was operationalized as the number of sweet-flavored versus non-flavored cigarillo puffs consumed during the 90-minute ad-libitum smoking session (Audrain-McGovern et al., 2015; Audrain-McGovern et al., 2016b). A research assistant monitored and counted the number of cigarillo puffs taken during the 90-minute period.

### 2.3.2. Covariates and predictor variables

Sex, age, and race were measured via a self-report demographic questionnaire at baseline. Depression symptoms were measured with the 20-item Center for Epidemiologic Studies Depression Scale (CES-D) (Audrain-McGovern et al., 2011; Radloff, 1977). The Likert-style response options, ranging from 0 = 'rarely or none of the time' to 3 ='most or all of the time', were summed for a total score. The CES-D has high internal consistency (sample  $\alpha$ =.90) and correlates with clinical ratings of depression severity (Radloff, 1977). Cigarillo flavor preference was ascertained by asking 'During the day(s) that you smoked cigarillos, how often were they flavored?' with response options dichotomized into a flavor ('Most of the time/Always') and non-flavored ('Sometimes/Rarely/Never') binary indicator. Cigarillo dependence was measured by summating the 10-item, modified Hooked on Nicotine Checklist (HONC) adapted for cigarillo use ( $\alpha$ =.83) (Wellman et al., 2005; Wellman et al., 2008). Past 30-day use of cigarillos, combustible cigarettes, e-cigarettes, and use of cigarillos for blunts was assessed via separate binary indicators (Cornelius et al., 2022; Kasza et al., 2017). The use of cigarillos for blunts was measured and differentiated from cigarillo use as intended.

### 2.4. Statistical analyses

To determine if there are differences in depression symptomatology across cigarillo-related subjective reward, and the relative and absolute reinforcing values of sweet-flavored versus non-flavored cigarillos, general linear models were fit with the applicable family and link respective to each outcome. To examine whether the subjective rewarding value of cigarillos differed by CES-D score, a Gaussian conditional mixed effects model was fit with cigarillo-related subjective reward as the outcome. To test whether subjective reward of flavor differed by CES-D score, a cigarillo flavor × CES-D interaction term was included in a second model. To examine whether the relative reinforcing value of flavor differed by depression, a linear regression was fit with the breakpoint as the outcome. To examine whether CES-D scores differed in the number of cigarillo puffs taken during the ad-libitum smoking session, a negative binomial conditional mixed effects model was fit to estimate the rate-ratio of the puffs taken. To test whether the cigarillo flavor-related absolute reinforcement differed by depression, a cigarillo flavor × CES-D score interaction was fit in a second model.

Models were adjusted for participant age, sex, race, cigarillo flavor preference, and past 30-day use of cigarillos, cigarettes, e-cigarettes, and blunts. Cigarillo dependence was not included as a covariate given its high correlation with cigarillo use. Analyses were 2-tailed ( $\alpha$ <.05) and conducted in R (version 4.3.1) (R Core Team, 2013) using the "lme4" (Bates et al., 2014), "lmerTest" (Kuznetsova et al., 2017), "glmmTMB" (Brooks et al., 2017), and "emmeans" (Lenth et al., 2019) packages.

#### 3. Results

### 3.1. Sample characteristics

A total of 95 adults reporting cigarillo use attended the baseline visit and enrolled into the study. Among these, 9 participants were excluded from the analysis; 2 participants withdrew from the study due to lack of interest and time commitment issues while 7 did not attend all three visits, leaving 86 participants to comprise the analytic sample (Table 1). On average, the sample was predominantly Male (73.3%) with a mean age of 22.2 years (SD=1.57) with self-reported race generally split among White (38.4 %), Black (33.7 %), and Other (27.9 %) races. Included in the Other race category were participants who identified as Multi-racial (n=8, 9.3 %), Hispanic (n=7, 8.1 %), Asian (n=6, 7.0 %), Pacific Islander (n=2, 2.3 %), and American Indian (n=1, 1.2 %). Overall, 61.5 % of the sample reported using cigarillos in the past 30days, but use did not differ by CES-D classifications (past 30-day use by depression = 46.5 % versus no depression = 53.5 % indicator). In general, participants preferred flavored cigarillos with 73.3 % reporting their use either "always" (n=39) or "most of the time" (n=24). Cigarillo dependence in the sample was low (mHONC Mean=1.17, SD=2.26). Regarding past 30-day use of other combusted products, most reported use of blunts (55.8 %) with slightly less use of cigarettes (41.9 %) and ecigarettes (39.5 %).

On average, depression symptomology in the sample was close to the clinical cutoff of 16 (CES-D Mean=15.88, SD=10.29) with corresponding scores for depression (CES-D  $\geq$  16; Mean=24.38, SD=8.71) and no depression (CES-D < 16; Mean=8.50, SD=3.79). However, for cigarillo dependence, those indicating depression reported higher levels of dependence (Mean= 2.48, SD=2.49) versus those indicating no depression (Mean=1.04, SD=1.81).

**Table 1**Sample Characteristics.

		CES-D Indicat		
	Overall	Depression	No Depression	
Characteristic	N = 86	N = 40	N = 46	P-
				value <sup>c</sup>
Depression Symptoms	15.88	24.38	8.50 (3.79)	<.001
(CES-D)	(10.29)	(8.71)		
Age (in years)	22.23	22.63	21.89 (1.62)	.028
	(1.57)	(1.43)		
Sex				.52
Male	63 (73.3 %)	28 (70.0%)	35 (76.1 %)	
Female	23 (26.7 %)	12 (30.0%)	11 (23.9 %)	
Race				.56
White	33 (38.4 %)	16 (40.0%)	17 (37.0 %)	
Black	29 (33.7 %)	15 (37.5%)	14 (30.4 %)	
Other <sup>b</sup>	24 (27.9 %)	9 (22.5%)	15 (32.6 %)	
Cigarillo Flavor				.41
Preference				
Non-flavored	23 (26.7 %)	9 (22.5%)	14 (30.4 %)	
Flavored	63 (73.3 %)	31 (77.5%)	32 (69.6 %)	
Past 30-day Use				
Cigarillos	53 (61.6 %)	16 (40.0%)	17 (37.0 %)	.77
Cigarettes	36 (41.9 %)	22 (55.0%)	28 (60.9 %)	.58
E-Cigarettes	34 (39.5 %)	16 (40.0%)	18 (39.1 %)	.93
Blunts	48 (55.8 %)	17 (42.5%)	21 (45.7 %)	.77
Cigarillo Dependence	1.71 (2.26)	2.48 (2.49)	1.04 (1.81)	<.001

Note. Data expressed as N (%) or Mean (SD).

### 3.2. Subjective reward

Overall, a significant main effect of CES-D score on subjective reward for cigarillos regardless of flavor type was observed (Table 2) such that higher levels of depression was associated with greater levels of subjective reward (B=0.03 [95%CI=0.00, 0.05], p=.017). For example, those classified with depression (mean CES-D score=24.38) were estimated to report higher levels of subjective reward (Estimated Marginal Mean [EMM]=4.40 [95%CI=4.05, 4.75]) versus those classified as having no depression (mean CES-D score=8.50; EMM=3.97 [95% CI=3.62, 4.32]). However, there was no significant cigarillo flavor × CES-D score interaction (F [1,84]=0.46, p=.91). On average, across all levels of CES-D scores, non-flavored cigarillos were observed to have lower rewarding properties (EMMs range=3.14–4.38) compared to the higher rewarding properties of sweet-flavored cigarillos (EMMs range=4.34–5.58; cigarillo flavor main effect B=1.20 [95%CI=0.80, 1.60], p<.001).

### 3.3. Relative reinforcing value of flavor

Participants worked for sweet-flavored cigarillo puffs similarly across depression (Mean clicks=706.4 [SD=485.6]; Mean Puffs Earned=6.16 [SD=3.04]) and no depression (Mean clicks=817.5 [SD=544.3]; Mean Puffs Earned=6.50 [SD=3.59]) CES-D groups (p's>.05). Correspondingly, CES-D scores were not significantly associated with the breakpoint representing the highest level of work performed for a puff of a sweet-flavored cigarillo (Depression EMM=8.23 [95%CI=7.42, 9.03]; No Depression EMM=8.32 [95%CI=7.51, 9.13]; B=0.01 [95%CI=-0.04, 0.06], p=0.81 Table 2).

### 3.4. Absolute reinforcement

During the ad-libitum smoking task, participants took an average of 23.1 puffs (95%CI=20.3, 26.0) of the non-flavored cigarillo and 40.9 puffs (95%CI=37.7, 44.0) of their preferred sweet-flavored cigarillo. However, these puffing behaviors did not differ across CES-D groups (Range of sweet-flavored cigarillo puffs=38.2–43.2, p=.34; Range of non-flavored cigarillo puffs=22.5–23.7, p=.82). Covariate-adjusted models revealed no significant difference in the number of cigarillo puffs taken by CES-D score (p=.83; Table 2). Similarly, there was no significant cigarillo flavor × CES-D interaction on the rate ratio of cigarillo puffs (p=.88; Table 2).

### 4. Discussion

This study adds to the limited research on young adult cigarillo use by documenting the role of depression and its interactions with sweet flavoring on three indices of cigarillo addiction liability. Young adults with elevated depression symptoms reported greater subjective reward from cigarillo use than young adults with low depression symptoms, irrespective of flavor. The reinforcing value of sweet-flavored cigarillos relative to non-flavored cigarillos was comparable among young adults with and without elevated depression symptoms. Finally, depression did not enhance the overall amount of cigarillo use or use of sweet-flavored versus non-flavored cigarillos. Taken together, these findings suggest that young adults with elevated depression are not differentially more vulnerable than young adults with lower symptom levels to sweet cigarillo flavoring.

Two observational studies noted that college students who had higher depression symptoms were more likely to report cigarillo use (Bierhoff et al., 2019; Sterling et al., 2013). Shedding light on this association, young adults with depression symptoms reported greater rewarding value (e.g., good taste and satisfying) immediately after smoking a cigarillo than young adults without depression symptoms. The subjective rewarding value was higher irrespective of cigarillo flavoring, suggesting that the hedonic value is not dependent on sweet

 $<sup>^{\</sup>rm a}$  CESD = Center for Epidemiologic Studies Depression Scale presented as a continuous score and as a  $>\!16$  clinical cutoff.

<sup>&</sup>lt;sup>b</sup> Other race category includes participants who identified as Multi-racial  $(n=8,\ 9.3\ \%)$ , Hispanic  $(n=7,\ 8.1\ \%)$ , Asian  $(n=6,\ 7.0\ \%)$ , Pacific Islander  $(n=2,\ 2.3\ \%)$ , and American Indian  $(n=1,\ 1.2\ \%)$ .

<sup>&</sup>lt;sup>c</sup> Kruskal-Wallis rank sum test; Pearson's Chi-squared test; Fisher's exact test.

**Table 2**Association between depression and subjective reward, relative reinforcing value, and absolute reinforcing value of sweet-flavored and non-flavored cigarillos.

	Subjective Reward		Relative Reinforcement <sup>c</sup>		Absolute Reinforcement	
Regressor	B (95% CI)	<i>P</i> -value	B (95% CI)	<i>P</i> -value	B (95% CI)	<i>P</i> -value
Main Effects Cigarillo Flavor						
Non- flavored	Ref		-		Ref	
Sweet- flavored	1.20 (0.80, 1.60)	<.001	-		1.79 (1.20, 2.67)	.004
CES-D	0.03 (0.00, 0.05)	.017	0.01 (-0.04, 0.06)	.81	1.00 (0.98, 1.02)	.83
Sex	0.03)		0.00)		1.02)	
Male Female	Ref 0.37 (-0.16, 0.91)	.17	Ref 0.73 (-0.51, 1.96)	.25	Ref 0.77 (0.47, 1.26)	.30
Race	,				,	
White Black	Ref -0.40 (-0.95,	.16	Ref 0.04 (-1.25,	.95	Ref 0.76 (0.46,	.29
Other	0.16) -0.26 (-0.81, 0.29)	.35	1.32) 0.22 (-1.06, 1.50)	.73	1.26) 0.98 (0.59, 1.61)	.93
Cigarillo Use <sup>1</sup>						
No Yes	Ref 0.04 (-0.44, 0.52)	.87	Ref -0.13 (-1.24, 0.98)	.82	Ref 1.00 (0.65, 1.56)	.98
Flavor	,		,		,	
Preference Non- flavored	Ref		Ref		Ref	
Flavored	-0.58 (-1.10, -0.06)	.029	1.95 (0.75, 3.14)	.002	1.24 (0.77, 2.00)	.38
Cigarette Use <sup>1</sup>						
No Yes	Ref 0.77 (0.28, 1.27)	.003	Ref 0.17 (-0.98, 1.32)	.77	Ref 1.05 (0.68, 1.61)	.84
E-cigarette Use <sup>1</sup>			,		,	
No Yes	Ref 0.04 (-0.44, 0.53)	.85	Ref 0.06 (-1.05, 1.18)	.91	Ref 1.05 (0.68, 1.62)	.83
Blunt Use <sup>a</sup>	0.00)		1110)		1.02)	
No Yes	Ref 0.03 (-0.42, 0.49)	.89	Ref 0.66 (-0.40, 1.72)	.22	Ref 0.84 (0.55, 1.27)	.40
Interaction <sup>b</sup> Flavor × CES- D Score	0.00 (-0.04, 0.04)	.91	,		0.00 (-0.04, 0.04)	.88

**Note:** Depression is modeled as a continuous variable based on summed CES-D score.

flavoring and may be more reflective of nicotine delivery. Although inconsistent with our hypothesis regarding sweet-flavoring, the findings are in-line with associations between subjective reward and cigarette smoking among those prone to depression (Audrain-McGovern et al., 2014; Spring et al., 2003).

Young adults with elevated depression were not more vulnerable to the reinforcing effects of sweet flavoring compared to young adults with low symptom levels. Indeed, young adults with and without elevated depression symptoms evidenced greater reinforcing value for sweet-flavored cigarillos relative to non-flavored cigarillos. Public health prevention campaigns and tobacco product regulations aimed at preventing initiation and escalation of young adult cigarillo use have the potential to reach young adults broadly. Young adults often downplay the addictive potential and health harms associated with cigarillo use, especially when they are flavored (Antognoli et al., 2018; Sterling et al., 2016a). Regulatory action banning sweet-flavoring may go hand-in-hand with public health efforts targeting such health misbeliefs.

Similarly, young adults smoked more sweet-flavored than non-flavored cigarillo puffs, irrespective of their level of depression symptoms. A recent cross-sectional survey study documented that past 30-day flavored cigarillo use (any flavor other than tobacco) was more prevalent among adults 18–65 years old with severe internalizing symptomology (Ganz et al., 2022). Whether such associations exist among young adults and specific flavor categories warrants attention. Research on e-cigarette flavoring suggests that young adults with depression and/or anxiety were not more likely to use flavored e-cigarettes than tobacco or menthol e-cigarettes (Chen et al., 2018).

As the first study to assess the main and interacting effects of depression on the addiction abuse liability of sweet-flavored compared to non-flavored cigarillos, the study has strengths as well as potential weaknesses. Strengths include a diverse sample, the use of validated tasks in a within-subjects design, and the measurement of other variables that could account for the association of depression and flavor with the outcome variables. The sex and racial composition of the sample mirrored those of people who use cigarillos in large surveillance studies (Azagba et al., 2021; Corey et al., 2018). Our assessment of cigarillo use history allowed us to distinguish between cigarillo use as intended and modified for blunt use. We also included participants with a range of prior cigarillo exposure, albeit above 10, to generalize broadly to young adults who use cigarillos. This is a strength as well as a potential limitation. As a sample with previous cigarillo exposure, over 70 % self-reported a preference for flavored cigarillos, which was controlled for in the models. Further, we did not examine how these indices of cigarillo-related reward and reinforcement prospectively predicted subsequent and persistent cigarillo use among young adults with high levels of depression symptoms. In addition, we did not examine these relationships by sex or race. These topics warrant attention in future research. Finally, this study is potentially underpowered to show a statistically significant interaction between depressive symptoms and cigarillo flavoring on cigarillo-related reward and reinforcement.

### 5. Conclusion

Young adults with elevated depression symptoms find cigarillos more rewarding but not more reinforcing than young adults with low depression symptoms. While our research indicates that sweet-flavoring increases the rewarding and reinforcing effects of cigarillo use among young adults (Audrain-McGovern et al., 2023), young adults with higher levels of depression are not more vulnerable to these effects. Removing sweet-flavored cigarillos from the market will likely lessen cigarillo use among young adults in general.

### Role of funding source

Research reported in this publication was supported in part by the National Institute on Drug Abuse (NIDA) of the National Institutes of

a Past 30-day use;

<sup>&</sup>lt;sup>b</sup> From a separate model including all regressors plus a CES-D score by cigarillo flavor interaction term:

<sup>&</sup>lt;sup>c</sup> Relative reinforcement accounts for the main effect of cigarillo flavor via the breakpoint outcome's measurement of the highest trial completed to earn puffs for sweet-flavored versus non-flavored cigarillo puffs.

Health (NIH) and the US Food and Drug Administration (FDA) Center for Tobacco Products under Award Number R21DA050789.

### CRediT authorship contribution statement

Matthew D. Stone: Writing – review & editing, Writing – original draft, Formal analysis. Fodie Koita: Writing – review & editing, Writing – original draft. Divya Manikandan: Writing – review & editing, Writing – original draft, Project administration. Janet Audrain-McGovern: Writing – review & editing, Writing – original draft, Supervision, Methodology, Funding acquisition, Conceptualization. Olivia Klapec: Writing – review & editing, Writing – original draft.

### **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### References

- Antognoli, E., Cavallo, D., Trapl, E., Step, M., Koopman Gonzalez, S., Perez, R., Flocke, S., 2018. Understanding nicotine dependence and addiction among young adults who smoke cigarillos: a qualitative study. Nicotine Tob. Res 20 (3), 377–38210, 1093/ntr/ntx008.
- Audrain-McGovern, J., Manikandan, D., Koita, F., Klapec, O., Pickworth, W.B., Stone, M. D., 2023. The effect of sweet flavoring on the rewarding and reinforcing value of cigarillo use among young adults. Tob. Control. https://doi.org/10.1136/tc-2023-058307.
- Audrain-McGovern, J., Rodriguez, D., Rodgers, K., Cuevas, J., 2011. Declining alternative reinforcers link depression to young adult smoking. Addiction 106 (1), 178–18710, 1111/j.1360-0443.2010.03113.x.
- Audrain-McGovern, J., Strasser, A.A., Ashare, R., Wileyto, E.P., 2015. Reinforcing value of smoking relative to physical activity and the effects of physical activity on smoking abstinence symptoms among young adults. Exp. Clin. Psychopharmacol. 23 (6), 477–48510, 1037/pha0000051.
- Audrain-McGovern, J., Strasser, A.A., Wileyto, E.P., 2016a. Can repetitive mental simulation of smoking engender habituation? Exp. Clin. Psychopharmacol. 24 (6), 415–42210, 1037/pha0000099.
- Audrain-McGovern, J., Strasser, A.A., Wileyto, E.P., 2016b. The impact of flavoring on the rewarding and reinforcing value of e-cigarettes with nicotine among young adult smokers. Drug Alcohol Depend. 166, 263–26710, 1016/j.drugalcdep.2016.06.030.
- Audrain-McGovern, J., Wileyto, E.P., Ashare, R., Cuevas, J., Strasser, A.A., 2014. Reward and affective regulation in depression-prone smokers. Biol. Psychiatry 76 (9), 689–69710, 1016/j.biopsych.2014.04.018.
- Azagba, S., King, J.L., Shan, L., 2021. Characteristics differ based on usual cigar-type use among U.S. adults: Analysis from the tobacco use supplement to the current population survey. Prev. Med Rep. 24, 10156010. .1016/j.pmedr.2021.101560.
- Bandiera, F.C., Loukas, A., Li, X., Wilkinson, A.V., Perry, C.L., 2017. Depressive Symptoms Predict Current E-Cigarette Use Among College Students in Texas. Nicotine Tob. Res 19 (9), 1102–110610, 1093/ntr/ntx014.
- Bansal-Travers, M., Rivard, C., Silveira, M.L., Kimmel, H., Poonai, K., Bernat, J.K., Jackson, K., Rudy, S., Johnson, A., Cullen, K.A., Goniewicz, M., Travers, M., Hyland, A., Villanti, A., Hrywna, M., Abrams, D., Fong, G., Elton-Marshall, T., Stanton, C., Sharma, E., 2022. Factors associated with changes in flavored tobacco products used: Findings from wave 2 and wave 3 (2014-2016) of the population assessment of tobacco and health (PATH) study. Addict. Behav. 130, 10729010.1016/j.addbeh.2022.107290.
- Bates, D., Mächler, M., Bolker, B., Walker, S., (2014). Fitting linear mixed-effects models using lme4. arXiv preprint arXiv:1406.5823
- Bickel, W.K., Marsch, L.A., Carroll, M.E., 2000. Deconstructing relative reinforcing efficacy and situating the measures of pharmacological reinforcement with behavioral economics: a theoretical proposal. Psychopharmacol. (Berl.) 153 (1), 44–56.
- Bierhoff, J., Haardorfer, R., Windle, M., Berg, C.J., 2019. Psychological Risk Factors for Alcohol, Cannabis, and Various Tobacco Use among Young Adults: A Longitudinal Analysis. Subst. Use Misuse 54 (8), 1365–137510, 1080/10826084.2019.1581220.
- Brody, A.L., Olmstead, R.E., Abrams, A.L., Costello, M.R., Khan, A., Kozman, D., Saxena, S., Farahi, J., London, E.D., Mandelkern, M.A., 2009. Effect of a history of major depressive disorder on smoking-induced dopamine release. Biol. Psychiatry 66 (9), 898–90110, 1016/j.biopsych.2009.06.011.
- Brooks, M., Kristensen, K., van Benthem, K., Magnusson, A., Berg, C., Nielsen, A., Skaug, H., Mächler, M., Bolker, B., 2017. glmmTMB Balances Speed and Flexibility Among Packages for Zero-inflated Generalized Linear Mixed Modeling. R. J. 9, 378–400, 10.32614/RJ-2017-066.
- Butler, K.M., Ickes, M.J., Rayens, M.K., Wiggins, A.T., Hahn, E.J., 2016. Polytobacco use among college students. Nicotine Tob. Res 18 (2), 163–16910, 1093/ntr/ntv056.
- Chen, J.C., Green, K.M., Arria, A.M., Borzekowski, D.L.G., 2018. Prospective predictors of flavored e-cigarette use: A one-year longitudinal study of young adults in the U.S. Drug Alcohol Depend. 191, 279–28510, 1016/j.drugalcdep.2018.07.020.

- Cohn, A.M., Chen, S., 2022. Age groups differences in the prevalence and popularity of individual tobacco product use in young adult and adult marijuana and tobacco cousers and tobacco-only users: Findings from Wave 4 of the population assessment of tobacco and health study. Drug Alcohol Depend. 233, 109278 https://doi.org/ 10.1016/j.drugalcdep.2022.109278.
- Cohn, A., Cobb, C.O., Niaura, R.S., Richardson, A., 2015. The other combustible products: prevalence and correlates of little cigar/cigarillo use among cigarette smokers. Nicotine Tob. Res 17 (12), 1473–148110, 1093/ntr/ntv022.
- Corey, C.G., Dube, S.R., Ambrose, B.K., King, B.A., Apelberg, B.J., Husten, C.G., 2014a. Cigar smoking among U.S. students: reported use after adding brands to survey items. Am. J. Prev. Med 47 (2 Suppl 1), S28–3510, 1016/j.amepre.2014.05.004.
- Corey, C.G., Holder-Hayes, E., Nguyen, A.B., Delnevo, C.D., Rostron, B.L., Bansal-Travers, M., Kimmel, H.L., Koblitz, A., Lambert, E., Pearson, J.L., Sharma, E., Tworek, C., Hyland, A.J., Conway, K.P., Ambrose, B.K., Borek, N., 2018. US Adult Cigar Smoking Patterns, Purchasing Behaviors, and Reasons for Use According Cigar Type: Findings From the Population Assessment of Tobacco and Health (PATH) Study, 2013-2014. Nicotine Tob. Res 20 (12), 1457–146610, 1093/ntr/ntx209.
- Corey, C.G., King, B.A., Coleman, B.N., Delnevo, C.D., Husten, C.G., Ambrose, B.K., Apelberg, B.J., 2014b. Little filtered cigar, cigarillo, and premium cigar smoking among adults — United States, 2012–2013. Morb. Mortal. Wkly Rep. 63 (30), 650, 654
- Cornelius, M.E., Loretan, C.G., Wang, T.W., Jamal, A., Homa, D.M., 2022. Tobacco Product Use Among Adults - United States, 2020. Morb. Mortal. Wkly Rep. 71 (11), 397–405, 10.15585/mmwr.mm7111a1.
- Delnevo, C.D., Giovenco, D.P., Ambrose, B.K., Corey, C.G., Conway, K.P., 2015.

  Preference for flavoured cigar brands among youth, young adults and adults in the USA. Tob. Control 24 (4), 389.
- Epstein, L.H., Temple, J.L., Neaderhiser, B.J., Salis, R.J., Erbe, R.W., Leddy, J.J., 2007. Food reinforcement, the dopamine D2 receptor genotype, and energy intake in obese and nonobese humans. Behav. Neurosci. 121 (5), 877–886.
- Forbes, E., 2009. Where's the fun in that? Broadening the focus on reward function in depression. Biol. Psychiatry 66 (3), 199–20010, 1016/j.biopsych.2009.05.001.
- Ganz, O., Cohn, A.M., Goodwin, R.D., Giovenco, D.P., Wackowski, O.A., Talbot, E.M., Delnevo, C.D., 2022. Internalizing problems are associated with initiation and past 30-Day use of flavored tobacco products. Addict. Behav. 125, 107162 https://doi. org/10.1016/j.addbeh.2021.107162.
- Giovenco, D.P., Spillane, T.E., Merizier, J.M., 2018. Neighborhood differences in alternative tobacco product availability and advertising in New York City: implications for health disparities. Nicotine Tob. Res, 10.1093/ntr/nty244.
- Glasser, A.M., Nemeth, J.M., Quisenberry, A.J., Shoben, A.B., Trapl, E.S., Klein, E.G., 2023. The Role of Cigarillo Flavor in the Co-Use of Cigarillos and Cannabis among Young Adults. Subst. Use Misuse 58 (5), 717–727. https://doi.org/10.1080/ 10826084.2023.2184206.
- Kasza, K.A., Ambrose, B.K., Conway, K.P., Borek, N., Taylor, K., Goniewicz, M.L., Cummings, K.M., Sharma, E., Pearson, J.L., Green, V.R., Kaufman, A.R., Bansal-Travers, M., Travers, M.J., Kwan, J., Tworek, C., Cheng, Y.C., Yang, L., Pharris-Ciurej, N., van Bemmel, D.M., Backinger, C.L., Compton, W.M., Hyland, A.J., 2017. Tobacco-product use by adults and youths in the United States in 2013 and 2014. N. Engl. J. Med 376 (4), 342–353. https://doi.org/10.1056/NEJMsa1607538.
- Klemperer, E.M., Hughes, J.R., Peasley-Miklus, C.E., Callas, P.W., Cook, J.W., Streck, J. M., Morley, N.E., 2021. Possible new symptoms of tobacco withdrawal III: reduced positive affect-a review and meta-analysis. Nicotine Tob. Res 23 (2), 259–266. https://doi.org/10.1093/ntr/ntaa044.
- Koopman Gonzalez, S.J., Cofie, L.E., Trapl, E.S., 2017. "I just use it for weed": the modification of little cigars and cigarillos by young adult African American male users. J. Ethn. Subst. Abus. 1–14. https://doi.org/10.1080/ 15332640.2015.1081117.
- Koszowski, B., Rosenberry, Z.R., Kanu, A., Viray, L.C., Potts, J.L., Pickworth, W.B., 2015. Nicotine and carbon monoxide exposure from inhalation of cigarillo smoke. Pharm. Biochem Behav. 139 (Pt A), 7–1410, 1016/j.pbb.2015.10.007.
- Kuznetsova, A., Brockhoff, P.B., Christensen, R.H.B., 2017. lmerTest Package: Tests in Linear Mixed Effects Models. J. Stat. Softw. 82, 1–26.
- Lenth, R., Singmann, H., Love, J., Buerkner, P., Herve, M., 2019. Package 'emmeans'. R. Package Version 1 (3.2).
- Mead, E.L., Johnson, S.L., Siddiqui, J., Butler 3rd, J., Kirchner, T., Feldman, R.H., 2018. Beyond blunts: reasons for cigarette and cigar use among African American young adult dual users. Addict. Res Theory 26 (5), 349–360. https://doi.org/10.1080/ 16066359.2017.1366456.
- Phan, L., McNeel, T.S., Choi, K., 2021. Prevalence of current large cigar versus little cigar/cigarillo smoking among U.S. adults, 2018–2019. Prev. Med. Rep. 24, 101534 https://doi.org/10.1016/j.pmedr.2021.101534.
- Pickworth, W.B., Rosenberry, Z.R., O'Grady, K.E., Koszowski, B., 2017. Dual Use of Cigarettes, Little Cigars, Cigarillos, and Large Cigars: Smoking Topography and Toxicant Exposure. Tob. Regul. Sci. 3 (Suppl 1), S72–s83. https://doi.org/10.18001/ trs.3.2(suppl 1).8.
- R Core Team, 2013. R: A Language and Environent for Statistical Computing. R Foundation for Statistical Computing.
- Radloff, L.S., 1977. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. Appl. Psychol. Meas. 1 (3), 385–401. https://doi.org/10.1177/ 014662167700100306.
- Rose, S.W., Johnson, A.L., Glasser, A.M., Villanti, A.C., Ambrose, B.K., Conway, K., Cummings, K.M., Stanton, C.A., Delnevo, C., Wackowski, O.A., Edwards, K.C., Feirman, S.P., Bansal-Travers, M., Bernat, J., Holder-Hayes, E., Green, V., Silveira, M.L., Zhou, Y., Abudayyeh, H., Hyland, A., 2020. Flavour types used by youth and adult tobacco users in wave 2 of the Population Assessment of Tobacco

- and Health (PATH) Study 2014-2015. Tob. Control 29 (4), 432–446. https://doi.org/10.1136/tobaccocontrol-2018-054852.
- Rostron, B.L., Cheng, Y.C., Gardner, L.D., Ambrose, B.K., 2020. Prevalence and Reasons for Use of Flavored Cigars and ENDS among US Youth and Adults: Estimates from Wave 4 of the PATH Study, 2016-2017. Am. J. Health Behav. 44 (1), 76–81. https://doi.org/10.5993/ajhb.44.1.8.
- Spring, B., Pingitore, R., McChargue, D.E., 2003. Reward value of cigarette smoking for comparably heavy smoking schizophrenic, depressed, and nonpatient smokers. Am. J. Psychiatry 160 (2), 316–322. https://doi.org/10.1176/appi.ajp.160.2.316.
- Sterling, K.L., Berg, C.J., Thomas, A.N., Glantz, S.A., Ahluwalia, J.S., 2013. Factors associated with small cigar use among college students. Am. J. Health Behav. 37 (3), 325–333. https://doi.org/10.5993/ajhb.37.3.5.
- Sterling, K.L., Fryer, C.S., Pagano, I., Fagan, P., 2016b. Little cigars and cigarillos use among young adult cigarette smokers in the United States: understanding risk of concomitant use subtypes. Nicotine Tob. Res 18 (12), 2234–2242. https://doi.org/ 10.1093/htr/ntw170.
- Sterling, K., Fryer, C., Pagano, I., Jones, D., Fagan, P., 2016a. Association between menthol-flavoured cigarette smoking and flavoured little cigar and cigarillo use

- among African-American, Hispanic, and white young and middle-aged adult smokers. Tob. Control 25 (Suppl 2), ii21–ii31.
- Tam, J., Taylor, G.M.J., Zivin, K., Warner, K.E., Meza, R., 2020. Modeling smokingattributable mortality among adults with major depression in the United States. Prev. Med 140, 106241. https://doi.org/10.1016/j.ypmed.2020.106241.
- Wall, C.S., Bono, R.S., Lester, R.C., Hoetger, C., Lipato, T., Guy, M.C., Eissenberg, T.E., Bickel, W.K., Barnes, A.J., Cobb, C.O., 2018. Triangulating abuse liability assessment for flavoured cigar products using physiological, behavioural economic and subjective assessments: a within-subjects clinical laboratory protocol. BMJ Open 8 (10), e023850. https://doi.org/10.1136/bmjopen-2018-023850.
- Wellman, R.J., DiFranza, J.R., Savageau, J.A., Godiwala, S., Friedman, K., Hazelton, J., 2005. Measuring adults' loss of autonomy over nicotine use: the Hooked on Nicotine Checklist. Nicotine Tob. Res 7 (1), 157–161. https://doi.org/10.1080/ 14622200412331328394.
- Wellman, R.J., McMillen, R., Difranza, J., 2008. Assessing college students' autonomy over smoking with the Hooked On Nicotine Checklist. J. Am. Coll. Health 56 (5), 549–553. https://doi.org/10.3200/jach.56.5.549-554.
- Westman, E.C., Levin, E.D., Rose, J.E., 1992. Smoking while wearing the nicotine patch: is smoking satisfying or harmful. Clin. Res. 10 (11a).