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Examining the role of menthol cigarettes in progression to established smoking among youth

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HIGHLIGHTS

- Used survival analysis to model the effect of menthol on youth smoking progression
- Menthol use was associated with progression to established current smoking.
- Results suggest menthol puts youth at increased risk for future regular cigarette use.

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ABSTRACT

Background: Menthol, a flavoring compound added to cigarettes, makes cigarettes more appealing to youth and inexperienced smokers and increases cigarettes' abuse liability. However, limited studies are available on menthol's role in smoking progression.

Methods: To assess the association between menthol in cigarettes and progression to established smoking, we used five waves of data from the Evaluation of Public Education Campaign on Teen Tobacco Cohort Study, a nationally representative longitudinal survey of U.S. youth conducted as part of "The Real Cost" evaluation. We used discrete time survival analysis to model the occurrence of two event outcomes—progression to established, current smoking and progression to established, frequent smoking—using a logit model with a menthol use indicator as the key explanatory variable. Based on this framework, we estimated the effect of prior menthol use on the odds of smoking progression.

Results: In the progression to established, current smoking model, prior menthol use was significantly associated with progression [adjusted odds ratio (aOR) = 1.80, $p < .05$, confidence interval (CI) = (1.03–3.16)]. While results were in a similar direction for the model of progression to established, frequent smoking, the association between prior menthol use and this progression model did not reach significance [aOR = 1.56, CI = (0.80–3.03)].

Conclusion: The results suggest a relationship between using menthol cigarettes and progression from experimental to established, current smoking among youth. This study adds to a growing literature base that supports that menthol cigarettes, compared to nonmenthol cigarettes, put youth at increased risk for regular cigarette use.

1. Introduction

Menthol in cigarettes carries particular appeal among new smokers (Giovino et al., 2015; Villanti et al., 2016), and several studies have found an association between continued smoking and nicotine dependence among youth (Hersey et al., 2006, 2010a; Villanti et al., 2017). Menthol is a flavoring compound added to tobacco that enhances the taste, provides a cooling sensation, and reduces the harshness of tobacco smoke, making it easier to smoke and inhale more deeply compared to nonmenthol tobacco products (Healton et al., 2010; Klausner, 2011; Kreslake, Wayne, Alpert, Koh, & Connolly, 2008; Kreslake, Wayne, & Connolly, 2008; Kreslake & Yerger, 2010). New menthol

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smokers also report experiencing less nausea during their first smoking experience compared to new smokers of nonmenthol cigarettes (D'Silva, Cohn, Johnson, & Villanti, 2018), suggesting that menthol reduces aversion associated with initial smoking experiences, which can promote continued use. The taste and smell of menthol can act as a drug cue and reinforce smoking by conditioning smokers to anticipate a hit of nicotine (Ahijevych & Garrett, 2010). Menthol also binds to nicotinic acetylcholine receptors (nAChRs) in the brain which may further contribute to its role in nicotine dependence (Henderson et al., 2016, 2017; Thompson et al., 2018). Together, menthol's chemosensory effects, that make menthol cigarettes more appealing to youth and inexperienced smokers (Anderson, 2011; Hersey, Nonnemaker, & Homsi, 2010b; Kreslake, Wayne, & Connolly, 2008; Wackowski et al., 2018), and its neural effects, that have the potential to enhance dependence, are of particular concern for youth. Specifically, the effects of nicotine on adolescent brain development can have long-term implications for dependence and other health effects (Slotkin, 2002; Yuan, Cross, Loughlin, & Leslie, 2015).

Studies on progression from experimental to regular smoking find that menthol plays a major role. One retrospective study found that established ever-smokers (aged 18–34) had greater odds of increasing smoking behavior (e.g., increased from some-day to daily smoking, relapsed/reinitiated from nonsmoking) over 1 year if they smoked menthol compared to nonmenthol cigarettes (Delnevo, Villanti, Wackowski, Gundersen, & Giovenco, 2016). However, this study relied on recall data regarding menthol use, thereby limiting conclusions about menthol's role in future outcomes. One longitudinal study collected data on menthol use among youth and found evidence linking menthol with progression to established smoking. Using data from the 2000–2003 American Legacy Longitudinal Tobacco Use Reduction Study (ALLTURS), Nonnemaker et al. (2013) found that youth who initiated smoking with menthol cigarettes during the study were more likely to progress to established smoking (defined as having smoked ≥ 100 cigarettes in lifetime and smoking on the past 20 of 30 days) than those who initiated with nonmenthol cigarettes. However, results from this study may not be applicable to youth smokers of today because this study used data from 2000 to 2003 and the sample was not nationally representative.

Youth and young adults are more likely than older smokers to initiate tobacco product use with a flavored tobacco product and are disproportionally more likely to smoke menthol than nonmenthol cigarettes (Giovino et al., 2015; Villanti et al., 2016, 2017). The impact of flavors (including menthol) in tobacco products is a focus for the U.S. Food and Drug Administration (FDA) (Federal Register, 2018). Whereas the sale of flavored cigarettes, including clove, fruit, and candy flavors, was prohibited by the 2009 Family Smoking Prevention and Tobacco Control Act (111th United States Congress, 2009), menthol and natural tobacco flavors were excluded from the prohibition. Nonetheless, the statute allowed for future regulation of menthol in cigarettes, and FDA recently issued an advanced notice of proposed rulemaking requesting information on the role that flavors in tobacco products, including menthol, play in youth tobacco product initiation and progression to regular use (Federal Register, 2018). To address the role of menthol use in progression from experimental to established smoking, we conducted an analysis using longitudinal, nationally representative data in U.S. youth from the 2014–2016 Evaluation of Public Education Campaign on Teen Tobacco (ExPECTT) Cohort Study. Using five waves of data from the ExPECTT Cohort Study, we examined the relationship between menthol use and progression to future smoking outcomes using discrete time survival analysis.

2. Methods

2.1. Data

We conducted analyses using data from the ExPECTT Cohort Study, a longitudinal, nationally representative survey of U.S. youth conducted as part of "The Real Cost" evaluation. "The Real Cost" is an FDA-sponsored, youth-focused tobacco prevention public education campaign (Duke et al., 2015, 2018; Farrelly et al., 2017). The ExPECTT Cohort Study used an address-based sampling frame to randomly select households clustered in U.S. census block groups within 75 media markets and supplemented the frame with market research databases to identify households likely to have at least one eligible youth (approximately 5% of households) aged 11 to 16 years. A lead letter describing the study was mailed to each of the selected addresses; then a field interviewer visited each address to conduct the actual survey. In-person baseline data collection (Wave 1) took place from November 11, 2013 through March 31, 2014. Four subsequent surveys were collected via online or in-person interviews during the following time periods: Wave 2 (July 24–October 27, 2014); Wave 3 (April 6–July 4, 2015); Wave 4 (December 17, 2015–April 5, 2016); and Wave 5 (September 15, 2016–November 22, 2016). Parental permission and youth assent were collected at each interview. The baseline sample size was 6743 youth, and 4210 youth completed all follow-up waves. The study was approved by institutional review boards at FDA and RTI International.

2.2. Measures

2.2.1. Progression to established, current smoking (event 1)

The first outcome event we examined was progression to established, current smoking. The risk pool for this event was current, experimental smokers, defined as those who answered "yes" to "Have you ever smoked?", reported smoking fewer than 100 cigarettes in their lifetime, and reported smoking on one or more days in the past 30 days. For those in the risk pool to experience the event (progression to established, current smoking), respondents had to be in the risk pool and meet the following criteria at the next wave: answered "yes" to "Have you ever smoked?", reported smoking on one or more days in the past 30 days, and reported having smoked at least 100 cigarettes in their lifetime. Progression is thus defined as transitioning from smoking fewer than 100 cigarettes to smoking 100 or more cigarettes.

2.2.2. Progression to established, frequent smoking (event 2)

The second outcome event we examined started with a risk pool of non-established and/or infrequent smokers. Non-established smokers were defined as those who answered "yes" to "Have you ever smoked?" and reported either smoking fewer than 100 cigarettes in their lifetime, not having smoked on 20 or more days in the past 30 days, or both. For those in the risk pool to experience the event (progression to established, frequent smoking), respondents had to be in the risk pool and meet the following criteria at the next wave: answered "yes" to "Have you ever smoked?", reported smoking on 20 or more days in the past 30 days, and reported having smoked at least 100 cigarettes in their lifetime.

2.2.3. Menthol use

We defined menthol use in our models based on the question "During the past 30 days, were the cigarettes that you usually smoked menthol?" (yes = 1, no = 0, missing). Menthol use was measured at the beginning of each period, i.e., we observed event occurrence at the end of each period, time t, and measured menthol status at time t-1.

2.2.4. Covariates

The time variable for the discrete time survival analysis was age. Given the low incidence rate within each age category, we used a continuous measure of age in the models, centered at the mean age of the risk pool. Age is wave-specific and was measured in discrete years when the event variable was recorded. In addition, we included the following baseline covariates in our controlled models: gender (male/female), race/ethnicity (defined as an indicator variable for white, non-Hispanic vs. other, because of sample sizes), lives with a tobacco user

(youth who reported that someone they live with uses one or more of the following products: cigarettes, cigars, hookah, smokeless, or other tobacco product, were considered to live with a tobacco user).

2.2.5. Sensation seeking

We used the Brief Sensation Seeking Scale (BSSS-4) (Stephenson, Hoyle, Palmgreen, & Slater, 2003) to measure sensation seeking: (1) I would like to explore strange places; (2) I like to do frightening things; (3) I like new and exciting experiences, even if I have to break the rules; and (4) I prefer friends who are exciting and unpredictable. Responses ranged from 1 ("disagree strongly") to 5 ("agree strongly") and had a Cronbach's alpha of 0.74.

2.3. Statistical analyses

We modeled the two event outcomes—progression to established, current smoking and progression to established, frequent smoking—using a logit model with a menthol use indicator as the key explanatory variable along with other covariates. Based on this framework, we estimated the effect of prior menthol use on the odds of event occurrence rather than a risk of event occurrence. In our model we have 4 periods: (P1) wave 1 to wave 2, (P2) wave 2 to wave 3, (P3) wave 3 to wave 4, and (P4) wave 4 to wave 5. We observe the event for each period at the end of the period, i.e., observe event for P1 at wave 2 (e2), event for P2 at wave 3 (e3), event for P3 at wave 4 (e4), and event for P4 at wave 5 (e5). We observe menthol status at the beginning of each period, i.e. we examine e2 = f(menthol at wave 1), e3 = f(menthol at wave 2), e4 = f(menthol at wave 3), and e5 = f(menthol at wave 4). That is, we examine e_t = f(menthol $status_{t-1}$).

We examined three model specifications for each event: Model 1 (base model) includes menthol use at a previous wave and age as explanatory variables; Model 2 includes Model 1 variables in addition to gender, race/ethnicity, and a control variable measuring whether the respondent lives with a tobacco user; and Model 3 includes all variables from Models 1 and 2 plus sensation seeking. Observations with missing data were excluded from the models.

We conducted several sensitivity analyses. In Appendix A, we estimated a model to account for youth who progressed to established smoking relatively quickly by progressing from nonsmoking to established smoking within the period between two waves. These respondents experienced the event of progression to established smoking but did not have a measure of menthol use at the beginning of a period because they did not report current smoking at that wave. In this sensitivity analysis, we investigated using same-wave menthol use for these respondents. In Appendix B, we estimated models using two new specifications of menthol use: (1) a set of dummy variables defining never use of menthol, last wave use of menthol, or prior use of menthol that was not last wave use, and (2) a set of indicators measuring never use of menthol, those who switched between menthol and non-menthol (or vice-versa), or those who only used menthol. These analyses assess whether different patterns of menthol use (e.g., for those who use menthol consistently versus who switch between menthol and non-menthol use) are differentially related to progression. All analyses were conducted with Stata version 15.1.

3. Results

3.1. Sample demographics

Table 1 summarizes baseline demographic characteristics for the analytic samples across both event definitions for all unique respondents in the risk pool over time. Unique observations for the first event definition, "Progression to established, current smoking," consist of 307 of 404 total observations in the main analysis model and 343 of 488 observations for the secondary analysis model. The remaining observations are repeated observations for youth who did not experience the event and remained in the risk pool for future waves. Characteristics changed little across the event definitions, aside from the sample for Event 2, "Progression to established, frequent smoking," consisting of more white youth. Both samples skew slightly male and older. The sample size for Event 1 was smaller because more youth already met the criteria for established, current smoking at Wave 1, resulting in fewer youth eligible for the risk pool.

Table 1
Descriptive statistics at baseline (wave 1) for unique youth in the analytic sample for progression to established, Current smoking and progression to established, frequent smoking.

	Progression to established, current smoking (Event 1)		Progression to established, frequent smoking (Event 2)	
	n = 307		n = 343	
Variable	n	%	n	%
Age				
11	8	2.6	8	2.3
12	23	7.5	24	7.0
13	40	13.0	45	13.1
14	58	18.9	65	19.0
15	81	26.4	94	27.4
16	97	31.6	107	31.2
Gender				
Male	156	50.8	172	50.2
Female	151	49.2	171	49.9
Race/Ethnicity				
White, non-Hispanic	150	48.9	180	52.5
Other	157	51.1	163	47.5
Lives with a tobacco user				
Yes	147	47.9	179	52.2
No	159	51.8	162	47.2
Missing	1	0.3	2	0.6
	n	Mean	n	Mean
Sensation seeking scale	289	3.6	323	3.6

3.2. Menthol use and progression (two events)

Table 2 provides life tables for the two progression events that document how youth moved through the model. For example, in Event 2 at Wave 1 to Wave 2, 146 youth were current, but not established, smokers and were not missing data for menthol use. Of these youth, 35 left the sample at Wave 2 because of attrition; 8 became established, frequent smokers; and 103 stayed in the risk pool as non-established smokers. From Wave 2 to Wave 3, the 167 individuals in the starting risk pool include the 103 from the previous cycle and 64 new individuals who joined the risk pool by becoming current, experimental smokers or by reporting menthol use (previously missing). The analytic sample size for Event 1 was 418 and for Event 2 was 503.

3.3. Model results

Table 3 presents the regression results. There was a significant relationship between menthol use and progression to established, current use (Event 1). Menthol use was significantly associated with smoking progression across all three models [Model 1: odds ratio (aOR) = 1.80, $p < .05$, confidence interval (CI) = (1.03–3.16)], with the inclusion of additional covariates strengthening the magnitude of the relationship [Model 2: aOR = 1.91, $p < .05$, CI = (1.07–3.42); Model 3: aOR = 0.85, $p < .05$, CI = (1.03–3.33)]. Gender was the only significant covariate in Models 2 and 3 [Model 2: aOR = 1.83, $p < .05$, CI = (1.02–3.29); Model 3: aOR = 1.84, $p < .05$, CI = (1.01–3.33)], suggesting that males are almost twice as likely as females to progress to established, current smoking. In Model 3, sensation seeking was not statistically significant, and its inclusion did not impact the other

Table 2
Life tables for progression to established, Current smoking and progression to established, frequent smoking.

Event	Period				
	Overall	W1 to W2	W2 to W3	W3 to W4	W4 to W5
Progression to established, current smoking (Event 1)					
Starting risk pool	532	127	134	144	127
Attrition (Missing)	114	30	30	26	28
Stayed in risk pool	359	80	91	103	85
Experienced event	59	17	13	15	14
Used menthol	158	33	41	44	40
Did not use menthol	246	51	63	73	59
Missing menthol status	14	13	0	1	0
Progression to established, frequent smoking (Event 2)					
Starting risk pool	654	146	167	181	160
Attrition (Missing)	151	35	44	36	36
Stayed in risk pool	461	103	114	133	111
Experienced event	42	8	9	12	13
Used menthol	196	41	51	56	48
Did not use menthol	292	56	72	88	76
Missing menthol status	15	14	0	1	0

Note. W1 = Wave 1, W2 = Wave 2, W3 = Wave 3, W4 = Wave 4, W5 = Wave 5. Data collection for the surveys occurred as follows: Wave 1 (November 11, 2013–March 31, 2014); Wave 2 (July 24–October 27, 2014); Wave 3 (April 6–July 4, 2015); Wave 4 (December 17, 2015–April 5, 2016); Wave 5 (September 15, 2016–November 22, 2016), with an average time between survey waves of 8 months.

results.

Menthol use at the previous wave did not significantly predict progression to established, frequent smoking (Event 2) [Model 1: aOR = 1.59, CI = (0.84–3.03)]; however, the results followed a similar direction as Event 1. The inclusion of additional covariates did not have a significant impact on the relationship between menthol use and progression (Model 2: aOR = 1.56, CI = (0.80–3.03); Model 3: aOR = 1.51, CI = (0.76–2.97). However, youth who were older [aOR = 1.36, $p < .05$, CI = (1.05–1.77)] and white [aOR = 2.22, $p < .05$, CI = (1.09–4.51)] were significantly more likely to progress to established, frequent smoking during the period of observation in Model 2. Additionally, males [aOR = 1.91, CI = (0.96–3.80)] and those who live with another tobacco user [aOR = 1.82, CI = (0.91–3.65)] were more likely to progress to established, frequent smoking; however, the odds of this occurring were not statistically significant. In Model 3, sensation seeking was not statistically significant [aOR = 1.47, CI = (0.94–2.29)], and its inclusion did not impact the other results.

In Appendix A, when we used current menthol status in place of prior wave menthol status for those who were missing prior wave menthol status, we found results similar to the models reported in the paper. In Appendix B, we estimated models with alternative definitions of menthol use to differentiate among those who used menthol consistently versus those who switched between menthol to non-menthol use (or vice-versa). These models suggest that last wave use of menthol and/or consistent use of menthol across prior waves is associated with progression to established, current smoking (Event 1).

4. Discussion

This study used data from a nationally representative, longitudinal study of U.S. youth to assess the role of menthol in cigarettes and progression from experimental to established cigarette smoking. Results from this study find that, among youth, menthol cigarette smoking (compared to nonmenthol cigarettes) is associated with progression from experimental to established, current cigarette smoking (defined as progressing from smoking fewer than 100 cigarettes to smoking 100 or more cigarettes while continuing current use). However, menthol use was not significantly associated with progression to established, frequent cigarette smoking (defined as smoking at least 20 of the past 30 days). Although the direction of the relationship was similar across the events, statistical significance was mixed.

A prior longitudinal study analyzed the ALLTURS dataset and reported similar findings of a relationship between youth menthol use and progression to established use (Nonnemaker et al., 2013). The current study provides data from a contemporary, nationally representative sample and finds results similar to the previous study, i.e., that youth menthol use is associated with smoking progression. The results are also consistent with the chemosensory properties of menthol and biological mechanisms for how menthol may facilitate smoking progression.

This study has several limitations. First, our outcomes are based on self-reported measures of smoking and menthol use. Although similar to measures used in other studies, these measures may be subject to recall bias. Second, we have no measure of menthol use prior to Wave 1 and thus have no way to include those who were experimental smokers at or before Wave 1 in our models of progression. Third, the smoking prevalence in our sample is low and thus the number of smokers transitioning from experimental to more established smoking is also low. The ExPECTT Cohort Study was designed with the intention of evaluating a media campaign, not specifically to assess the association of menthol

Table 3
Logistic regression models predicting progression to established, Current smoking and progression to established, frequent smoking.

	Progression to Established, Current Smoking (Event 1)[a]						Progression to Established, Frequent Smoking (Event 2)[b]					
	Model 1		Model 2		Model 3		Model 1		Model 2		Model 3	
	aOR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI
Menthol use at previous wave	1.80*	[1.03–3.16]	1.91*	[1.07–3.42]	1.85*	[1.03–3.33]	1.59	[0.84–3.01]	1.56	[0.80–3.03]	1.51	[0.76–2.97]
Age: mean centered	1.15	[0.94–1.42]	1.15	[0.93–1.42]	1.12	[0.91–1.39]	1.33*	[1.04–1.72]	1.36*	[1.05–1.77]	1.32*	[1.01–1.71]
Male			1.83*	[1.02–3.29]	1.84*	[1.01–3.33]			1.91+	[0.96–3.80]	1.96+	[0.97–3.97]
White, non-Hispanic			1.62	[0.91–2.87]	1.53	[0.85–2.75]			2.22*	[1.09–4.51]	2.24*	[1.08–4.65]
Lives with a tobacco user			1.58	[0.88–2.85]	1.53	[0.84–2.81]			1.82+	[0.91–3.65]	1.83+	[0.89–3.75]
Sensation seeking scale					1.15	[0.81–1.63]					1.47+	[0.94–2.29]
Sample size	404		403		381		488		486		462	

Note: aOR = Adjusted Odds ratio, CI = Confidence interval.

[a] The starting sample size is 418; 14 observations were missing measure of menthol use at the prior wave, 1 observation was missing "lives with tobacco user," and 26 observations were missing sensation seeking scale.

[b] The starting sample size is 503; 15 observations were missing menthol use at the prior wave, 2 observations were missing "lives with tobacco user," and 24 observations were missing sensation seeking scale.

+ $p < .10$,

* $p < .05$,

use and progression to regular smoking and may be underpowered to detect such associations. Fourth, it was not possible to examine racial/ethnic differences in the effect of menthol on progression given the low prevalence of smoking. Because nicotine metabolism (Perez-Stable, Herrera, Jacob, & Benowitz, 1998) and rates of menthol use differ by race/ethnicity (Villanti et al., 2016), it is possible that menthol's effect on progression also differs by race/ethnicity. Fifth, our study does not account for other tobacco product use or polytobacco use. Finally, attrition may have influenced our results, and we have no way to address this in our study.

Despite these limitations, the results suggest a relationship between menthol cigarettes and progression from experimental to more established smoking among youth. This study adds to a growing literature base that suggests that experimentation with menthol cigarettes (vs. nonmenthol) puts non-established smokers at increased risk for regular cigarette smoking (Delnevo et al., 2016; Nonnemaker et al., 2013). Youth progression to regular cigarette smoking represents a significant threat to public health because youth who smoke cigarettes and transition to a lifetime of regular use are at an elevated risk of smoking-associated morbidity and mortality compared to nonsmokers (U.S. Department of Health and Human Services, 2014). Thus, identifying menthol as a predictor of smoking progression or escalation in cigarette smoking is important in developing targeted interventions aimed to disrupt escalating trajectories (D'Silva et al., 2018).

Declaration of interest

None.

Disclosures

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Contributors

OR, MS, KJ developed the study concept with contributions from SF, BA, and AS. All authors contributed to study design. JN, AM, and WR conducted all study analyses and wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Appendices. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.addbeh.2019.106045.

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