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Impact of Nicotine Messaging on Nicotine Beliefs and Tobacco Use Behavior

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Study Protocol

The current study tests the impact of multiple exposures to a brief nicotine corrective messaging intervention on beliefs about nicotine and on intention and use of tobacco and nicotine products in a 12-week population-based study of 794 adult smokers and non-smokers who are registered Amerispeak national consumer market research panel members. Data were collected by National Opinion Research Center (NORC) at the University of Chicago and sent de-identified to the PI and study team. A parallel lab-based study will be conducted in adult smokers followed for 4 weeks (NCT05108649) who also receive normal nicotine content or reduced nicotine content cigarettes and are explicitly told which product they have been given (i.e., unblinded).

For the population-based study, AmeriSpeak panel members received a standard email invitation describing the study. NORC obtains and documents participants' informed consent at the time of registration in the Amerispeak panel. Potential participants are identified by randomly selecting households within the panel with an adult within the study age range, and targeting study invitations based on recent study participation, and other demographic characteristics as needed to ensure a representative sample. This email invitation introduced study procedures and eligibility criteria, and directed interested panel members to the eligibility screener with items to confirm eligibility. Procedures ensured that potential participants are adults ages 18 and older through two steps: 1) targeting study invitations only to those panel members whose age was within this range; and 2) re-assessing age at eligibility screening and excluding those who provide inconsistent information. Panel members who were confirmed to meet study eligibility criteria proceeded to the online experiment. AmeriSpeak panel members who did not meet study eligibility criteria were redirected to a concluding thank-you screen.

The Nicotine Corrective Messaging (NCM) intervention condition was based on messages tested in our team's pilot study.[1] It included the following six original messages and two new messages addressing nicotine in cigarette and e-cigarette products that were adapted from several evidence-based sources to be more accessible to a lay audience. The sources consisted of FDA's 2017 comprehensive plan for tobacco and nicotine regulation,[2] FDA's 2013 modifications to labeling of NRT products for over-the-counter human use,[3] the 2014 U.S. Surgeon General's Report on the Health Consequences of Smoking,[4] reports on carcinogens from the International Agency for Research on Cancer,[5-7] and the NASEM report on the "Public Health Consequences of E-cigarettes.[8] Participants in the NCM condition were exposed to all eight messages in the same order at each exposure.

Upon study enrollment, participants completed baseline questions about tobacco use behavior, nicotine beliefs, and other measures (see Study Measures). After completing the baseline survey, participants were randomly assigned in equal numbers to the Nicotine Corrective Messaging (NCM) intervention condition or the delayed message control condition. Participants in the NCM condition then received their first exposure to the study messages. Participants viewed each image in the NCM condition for at least 5 seconds, and we assessed self-reported visual attention using a heatmapping task. We allowed for three weeks to maximize the collection of Wave 1 (Weeks 1-3) and Wave 4 (Weeks 10-12) data and two weeks for Wave 2 (Weeks 4-5) and Wave 3 (Weeks 7-8). In the Wave 2 survey (Weeks 4-5), all participants completed measures of nicotine beliefs and intentions/use of nicotine and tobacco products; this provided the first post-exposure measures of the key outcomes. Participants in the NCM condition then received their second exposure to study messages and completed the heatmapping task. Only participants in the NCM condition received the Wave 3 survey (Weeks 7-8), which comprised the third exposure to study messages and the heatmapping task. The Wave 4 survey (Weeks 10-12) included the final survey assessment of key measures, followed by exposure to NCM messages and heatmapping task for all participants.

Study Measures

	Aim 1: Population study	Aim 2: Lab study
Intervention/Exposure		
Nicotine messaging vs. control	Wave 1	Week 1
Normal nicotine vs. RNC cigarette		Week 1
Heatmapping	Waves 1-4	
Perceived message effectiveness	Wave 4	Week 5
Message credibility	Wave 4	Week 5
Eye-tracking		Weeks 1-4
Biomarkers		Weeks 0, 5
Outcomes		
Nicotine beliefs	Waves 1, 2, 4	Weeks 0, 2, 5
Intention to use nicotine/tobacco products	Waves 1, 2, 4	Weeks 0, 2, 5
Nicotine/tobacco use and behavior	Waves 1, 2, 4	Weeks 0, 2, 5
Subjective rating of study cigarette		Weeks 1-5
Manipulation check	Waves 1, 2, 4	Weeks 0, 2, 5
Moderators		
Sociodemographics	Wave 1	Week 0
Literacy	Wave 1	Week 0
Cancer risk beliefs	Wave 1	Week 0
Cancer risk behaviors	Wave 1	Week 0
Fagerstrom test for nicotine dependence	Wave 1	Week 0
Other key constructs		
Attitudes about nicotine	Waves 1, 2, 4	Weeks 0, 2, 5
Nicotine-related norms	Waves 1, 2, 4	Weeks 0, 2, 5
Behavioral control	Waves 1, 2, 4	Weeks 0, 2, 5
Stages of change	Wave 1, 4	Week 0, 5
Policy support	Wave 4	Week 5

Statistical Analysis Plan

Sample Size. Power for Aim 1 was calculated for 715 adults with 70% retention at 12-weeks follow-up. Our pilot data provide estimates of the magnitude of the effect of the Nicotine Corrective Messaging (NCM) intervention on the primary outcome of nicotine beliefs, including four continuous scales on nicotine false beliefs, NRT false beliefs, e-cigarette false beliefs, and reduced nicotine content (RNC) cigarette false beliefs.[1] With an expected final sample size of 500 and ignoring repeated measures, we will have 80% power to detect differences of <1 unit between the intervention and control group means for the nicotine, NRT, and e-cigarette false belief scales and a 1.64 difference in the group means for the RNC cigarette false beliefs scale. These equate to small-to-medium effect sizes (Cohen's *d* ranging from 0.25 to 0.27), which are smaller than the effects observed for nicotine and NRT false beliefs outcomes in the pilot study.[1]

Data Preparation. Prior to performing all analyses, standard data screening/cleaning procedures will be applied. These procedures will (1) screen the data for data recording errors, (2) check for outliers, (3) assess the extent and pattern of missing data, and (4) check that appropriate assumptions of normality are met whenever necessary. In all analyses, the assumptions underlying the application of all the statistical methods that are used will be examined, principally using standardized residuals, influence diagnostics, and graphical displays. Where needed, appropriate transformations will be applied to ensure that data meet model assumptions. Descriptive analyses will characterize participants overall and by study condition. Bivariate tests will assess for differences in participant characteristics by intervention condition (NCM vs. control) and examine if any baseline variables that are imbalanced between study groups are associated with primary and secondary outcomes (p <.10). Any such variables will be accounted for in analyses as covariates.

Analytic Approach.

Aim 1: Test the impact of nicotine corrective messaging (NCM) on nicotine beliefs and the subsequent impact on intention and use of tobacco and nicotine products in a national sample of 715 adult smokers and non-smokers followed for 12 weeks.

Hypothesis 1a: Adults in the NCM condition will report fewer false beliefs about nicotine, NRT, e-cigarettes and RNC cigarettes and lower intentions to use tobacco and nicotine products at follow-up compared to those in the control condition.

Hypothesis 1b: Current smoking will moderate the effect of NCM on false beliefs of nicotine, NRT, e-cigarettes, and RNC cigarettes and intended use of tobacco and nicotine products at follow-up. The effect of NCM on these outcomes will be attenuated in adult smokers compared to non-smokers.

Analyses for Aims 1 and 2 employ common measures and a common analytic framework to test the impact of nicotine education on nicotine beliefs and behavior. Primary analyses will use an intention-to-treat approach. We will conduct sensitivity analyses with different assumptions for the missing data mechanism including analyzing complete data only[9] and last observation carried forward. Outcomes for Aim 1 focus on continuous measures (*primary outcome*: nicotine beliefs; *secondary outcomes*: frequency of nicotine/tobacco use), with the primary hypotheses (**Hypotheses 1a**) focused on the effect of the intervention on these outcomes. Preliminary analyses will examine differences in these outcomes across study conditions at the first post-exposure time point (Wave 2) and at the final timepoint (Wave 4) controlling for covariates that are differentially distributed between study groups. In Aim 1, we will also use multiple logistic regression models to examine effects of the NCM intervention on the proportion of participants reporting specific nicotine beliefs (i.e., "nicotine is a cause of cancer"), intentions to use cigarettes, e-cigarettes, NRT, and low nicotine cigarettes in the next 12 months, and

tobacco/nicotine use (e.g., any new use/trial, any past 30-day use, product-specific past 30-day use).

For **Hypothesis 1b**, we will evaluate whether current smoking moderates the effect of NCM on our primary and secondary outcomes by incorporating an interaction between study condition (NCM/control) and current smoking status (smoker/non-smoker) through the following steps: 1) bivariate analyses, to determine if outcomes vary by these variables; 2) testing whether current cigarette smoking moderates ($p < .05$) experimental effects in the models above by the addition of a study condition-by-smoking status interaction term into the model; 3) if no evidence of moderation exists, including cigarette smoking as a covariate.

Exploratory analyses will focus on three areas: 1) potential moderators of the relationship between intervention condition and the study outcomes; 2) nicotine beliefs as a potential mediator of the relationship between intervention condition and constructs identified in the Theory of Planned Behavior (i.e., nicotine-related attitudes, norms, behavioral control, and nicotine/tobacco intentions and use); and 3) the relationship between visual attention to nicotine education messages and nicotine beliefs in the participants exposed to the NCM intervention.

For the first area (*moderation*), we will conduct exploratory analyses using the same steps described for Hypothesis 1b to determine whether there are potential moderators of the relationship between the intervention(s) and outcomes, specifically age, gender, literacy, baseline cancer beliefs and cancer risk behaviors.

For the second area (*mediation*), we will draw from traditional mediation frameworks and use robust methods to explore the relationships outlined in our theoretical framework, specifically whether changes in nicotine beliefs post-exposure (Wave 2) influence nicotine-related attitudes, norms, behavioral control, intention, and behavior at the final assessment (Wave 4). We will examine whether nicotine beliefs at Wave 2 are associated with these outcomes using bivariate statistics and regression-based analysis accounting for any covariates as described above. Where these preliminary steps indicate potential correlation between nicotine beliefs and study outcomes ($p < .05$), we will test for mediation by estimating the indirect effects of nicotine beliefs on follow-up outcomes via the intervention condition using a bias-corrected bootstrapping method with 1,000 resamples. This approach estimates indirect (i.e., mediation) effects and produces bias-corrected asymmetric 95% CIs correcting for non-normality of the distribution of indirect effects and providing higher power and better control over the Type I error rate versus traditional approaches to test mediation. Asymmetric 95% confidence intervals around indirect effect estimates for nicotine beliefs that do not include zero will be interpreted to indicate significant mediation.

For the third area (*visual attention*), we will use data from the Wave 1 heatmapping task among participants in the NCM condition to identify regions of interest (ROIs) on each of the nicotine education messages and code these as ROIs across all Waves. We will explore whether attention to (i.e., clicking on) the ROIs is correlated with scores on the nicotine beliefs scales (i.e., nicotine, NRT, e-cigarette, RNC cigarette beliefs) at the same assessment (Wave 4). Given the content of messages in the nicotine education condition, we will be able to assess whether attention to specific ROIs is correlated with specific beliefs (i.e., whether clicking on a specific ROI within the “Nicotine does not cause cancer” is correlated with response to the nicotine belief item regarding nicotine causing cancer). We will also be able to explore the prospective relationship between visual attention to the nicotine education messages (e.g., duration spent viewing messages, attention to ROIs) and nicotine beliefs and whether there are differences in visual attention in the NCM intervention condition over the four waves of data collection. These data will inform potential refinements to nicotine education messages for future studies.

Missing data: The most effective approach to eliminating biases and inefficiency caused by missing data is to collect complete data. In both aims of our study, we will use several tools available to maintain contact and verify that forms are complete. Use of computerized survey platforms in this study will provide additional mechanisms to improve completeness of survey responses, but even so, some participants may refuse to answer certain questions. We anticipate that one cause of missing data will be item non-response on self-report questionnaires; another will be missing assessments. When practical, missing items will be imputed using conditional means, estimated with an iterated version of Buck's method.[10] Another cause of missing data is attrition, and we will pursue a range of model-based analyses that account for dropouts assuming data are missing at random (MAR), including multiple imputation methods (MI).[11,12] We will also conduct sensitivity analyses with different assumptions for the missing data mechanism including analyzing complete data only[9] (missing completely at random, MCAR) and last observation carried forward, in which subjects without self-report follow-up data will be considered to have no change.

References

1. Villanti AC, West JC, Mays D, Donny EC, Cappella JN, Strasser AA. Impact of Brief Nicotine Messaging on Nicotine-Related Beliefs in a U.S. Sample. *Am J Prev Med.* 2019;57(4):e135-e142. PubMed PMID: 31542145. PubMed Central PMCID: PMC6756180.

2. U.S. Food and Drug Administration. FDA's Comprehensive Plan for Tobacco and Nicotine Regulation. https://www.fda.gov/TobaccoProducts/NewsEvents/ucm568425.htm. Published 2017. Updated July 31, 2019. Accessed August 26, 2019.

3. U.S. Food and Drug Administration. Modifications To Labeling of Nicotine Replacement Therapy Products for Over-the-Counter Human Use. Federal Register. https://www.federalregister.gov/documents/2013/04/02/2013-07528/modifications-to-labeling-of-nicotine-replacement-therapy-products-for-over-the-counter-human-use. Published 2013. Updated April 2. Accessed July 3, 2018.

4. U.S. Department of Health and Human Services. *The Health Consequences of Smoking—50 Years of Progress. A Report of the Surgeon General.* Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; January 2014.

5. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Smokeless Tobacco and Some Tobacco-specific N-Nitrosamines. 2007;89. http://monographs.iarc.fr/ENG/recentpub/mono89.pdf. Accessed Feb 16, 2016.

6. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Tobacco Smoking. 2012;100-E. http://monographs.iarc.fr/ENG/Monographs/vol100E/mono100E-6.pdf. Accessed Feb 16, 2016.

7. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Smokeless Tobacco. 2012;100-E. http://monographs.iarc.fr/ENG/Monographs/vol100E/mono100E-8.pdf. Accessed Feb 16, 2016.

8. National Academies of Sciences, Engineering, and Medicine. *Public health consequences of e-cigarettes.* Washington, D.C.: The National Academies Press;2018.

9. Little RJA, Rubin DB. *Statistical analysis with missing data.* 2nd ed. Hoboken, NJ: J Wiley & Sons; 2002.

10. Gleason TC, Staelin R. A proposal for handling missing data. *Psychometrika.* 1975;40(2):229-252.

11. Schafer JL. *Analysis of incomplete multivariate data.* New York: Chapman & Hall/CRC; 2002.

12. Siddique J, Harel O, Crespi CM, Hedeker D. Binary variable multiple-model multiple imputation to address missing data mechanism uncertainty: application to a smoking cessation trial. *Stat Med.* 2014;33(17):3013-3028. PubMed PMID: 24634315. PubMed Central PMCID: 4082461.