Supplement 1
Randomized Controlled Trial Evaluating the Impact of Cigarette Pack Constituent Disclosures
Study Protocol

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Contents

Background

Federal law requires the U.S. Food and Drug Administration (FDA) to disseminate information about tobacco constituents. The 2009 Family Smoking Prevention and Tobacco Control Act grants FDA broad authority to regulate tobacco products, including helping the public to better understand harmful and potentially harmful constituents (HPHCs) present in tobacco products and tobacco smoke. According to Section 206 of the Act, using the appropriate federal rulemaking channels and procedures, FDA may require disclosure of tobacco constituents if the disclosed information benefits public health and increases consumer awareness of the health consequences of tobacco products. This study will assess the impact of constituent disclosures on smokers' cigarette packs in a randomized control trial.

Trial purpose

The purpose of this randomized controlled trial is to determine whether constituent disclosures on cigarette packs increase intentions to quit smoking. Previous studies have been informative, but they have evaluated candidate graphic warnings, not constituent disclosures. Furthermore, they typically expose participants to messages in controlled but artificial experimental settings for a short period of time, using much lower frequency and shorter duration of message exposure than found in the real world. This study addresses these issues by evaluating the impact of constituent disclosures by randomly assigning smokers to have their cigarette packs labeled with constituent disclosure messages or cigarette butt littering messages.

Main hypothesis: Smokers randomized to receive labels with constituent disclosure messages on their cigarette packs will have higher intentions to quit smoking than smokers randomized to receive labels with cigarette butt litter messages.

Trial design

This protocol is for a randomized controlled trial with smokers in San Francisco, California. The trial arms are described below.

Trial arms

1. Experimental: Labels with constituent disclosure messages that include text about chemicals in cigarette smoke and health effects of the chemicals will be applied to participants' cigarette packs on the right side (the Surgeon General's warning is on the left side). At the week 2 visit, participants' packs will be labeled with 1 of 3 disclosures selected at random; at the week 3 visit, they will get one of the 2 remaining disclosures selected at random, and at the week 4 visit they will get the remaining disclosure. Study investigators developed the text and design of these labels:
    - Cigarette smoke contains formaldehyde. This causes throat cancer.
    - Cigarette smoke contains uranium. This causes lung tumors and kidney damage.
    - Cigarette smoke contains arsenic. This causes heart damage.
2. Active Comparator: Labels with litter messages that include text about littering cigarette butts will be applied to participants' cigarette packs on the right side (the Surgeon

General's warning is on the left side). At the week 2 visit, participants' packs will be labeled with 1 of 3 litter messages selected at random; at the week 3 visit, they will get one of the 2 remaining litter message selected at random, and at the week 4 visit they will get the remaining litter message. Study investigators developed the text and design of these labels.

- Cigarette litter requires cleanup. Discard cigarette butts properly.
- Please refrain from littering. Cigarette butts are the most littered item.
- Cigarette butts don't biodegrade. Please do not litter.

Trial location

1. Ewald & Wasserman Research Consultants, LLC. San Francisco, California, United States, 94108

Participants

Participants are adult cigarette smokers in in the Bay Area in California, US. Inclusion and exclusion criteria are described below.

Inclusion criteria:

- Be 21 years or older
- Have smoked at least 100 cigarettes in his or her lifetime
- Currently smoke cigarettes every day or some days
- Currently smoke at least 7 cigarettes per week, on average
- Be able to read and speak English
- Be able to use a computer to take surveys
- Be able to attend 5 weekly appointments
- Be able to bring in 8 days' worth of cigarettes to each of the first 4 weekly appointments

Exclusion criteria:

- Pregnant women
- Smokers who smoke exclusively roll-your-own cigarettes
- Smokers concurrently enrolled in any research studies about smoking or using other tobacco products
- Smokers who live in the same household as someone who has enrolled in the study

Recruitment and screening

Ewald & Wasserman, the study contractor, will use recruitment materials that direct people to a study phone number and a website that gives information about the study in written FAQs. To recruit smokers, staff will use Facebook, Craigslist, in-person recruitment, and newspaper advertisements. Smokers will first undergo screening online or call the study center to complete the screening questionnaire over the phone. Study staff will schedule eligible smokers for 5 in-person visits. For each of their 5 visits, smokers will be asked to bring the number of cigarettes they expect to smoke in an 8 day period. We aim to have 672 smokers complete the trial.

Procedures

Cognitive Interviewing Methods: Staff members from the UNC team will cognitively test new or modified survey items with 8-16 smokers prior to the pilot study. Cognitive interviewing participants will be asked to take a survey that asks questions about their smoking behavior and reactions to health messages. A UNC research assistant will ask them follow up questions to determine whether participants understand the survey questions and if the survey questions include all appropriate response options. This process will take 45-60 minutes to complete and will be conducted in a private UNC study office. The results from the cognitive interviewing will inform the survey that will be used in the pilot study and full RCT. Participants will be given a $40 incentive for their participation. A second round of cognitive testing will also be conducted with ~25 current smokers recruited online through Amazon Mechanical Turk (MTurk), a web-based platform commonly used for social science and experimental research. The process will be similar to the first round with participants completing a survey and then answering follow-up questions to confirm items are interpreted as intended. Compensation will be $1.20 for about a 5-10 minute survey.

Pilot Study: We will conduct a pilot study with 20 smokers to confirm the ability to implement all RCT procedures with fidelity. This pilot study will confirm that smokers will complete a 4-week protocol that requires 5 appointments at the study offices (baseline and 4 follow-up appointments). We will make changes as needed to address any problems the pilot identifies.

RCT: E&W's office is in San Francisco, CA and is accessible by public transportation. The Bay Area has a diverse community.

UNC's project manager and Dr. Brewer will receive weekly updates from E&W about the study. The updates will indicate accrual, number of participants at each study phase, deviations from the study protocol identified during quality checks, and any other problems encountered. The project manager will travel to the site at the beginning of study implementation. A local independent research assistant will regularly visit the site during the study to monitor data collection. E&W will also assign a supervisor who will conduct quality checks using a checklist.

E&W staff will schedule participants' 5 appointments to visit the study office and ask them how much they smoke in a typical day. If a participant does not bring cigarettes to an appointment, staff will ask them to go purchase the necessary cigarettes and, if necessary, reschedule the appointment within the next 24 hours. E&W's office in San Francisco is centrally located within a 5 minute walk of retailers that sell a broad variety of popular cigarette brands.

Prior to consenting smokers, research staff will visually inspect photo identification of all smokers. At the beginning of the first appointment, study personnel will explain the consent form and ask the smoker to read the form. Once the participant has finished reading the form, the study personnel member will ask the participant if he or she has any questions. Then both parties will sign the consent form and the participant will receive a copy of the consent form.

Each week participants will bring in 8 days' worth of cigarettes (one extra day to provide a buffer in case of rescheduled appointments or smoking more than anticipated) for labeling and tracking.

Additionally, they will bring in any unused labeled packs from the previous visit when applicable. While participants are taking the survey, research staff will count participants' cigarette packs. Study staff will mark packs with a code indicating the date of the visit and label them.

Participants will complete 5 computer-based surveys during the study. The first appointment will take around 60 minutes and each subsequent visit will take around 30-45 minutes to complete. At all 5 visits, participants will complete a survey. Research staff will ask participants who miss any of visits 3, 4 or 5 to complete the corresponding computer survey online. At visits 2-4, participants' will have their cigarette packs labeled based on their condition. Cigarette packs will be tracked at all 5 study visits.

At the week 2 visit, study personnel will randomly assign participants to one of the two study arms. The investigators will determine the randomization order a priori. Smokers have an equal chance of being randomized to have labels with constituent disclosure messages or labels with litter messages applied to their cigarette packs.

Participants randomized to the intervention arm will have labels with constituent disclosure messages applied to their cigarette packs during visits for weeks 2-4. Constituent disclosures that include text about chemicals in cigarette smoke and health effects of the chemicals will be applied to participants' cigarette packs as labels on the right side (the Surgeon General's warning is on the left side). At the week 2 visit, participants' packs will be labeled with 1 of 3 disclosures selected at random; at the week 3 visit, they will get one of the 2 remaining disclosures selected at random, and at the week 4 visit they will get the remaining disclosure. Study investigators developed the text and design of these labels. Participants assigned to the control arm will have labels with litter messages applied to the right side of their cigarette packs.

Study staff will then place cigarette packs in sealed bags to preserve freshness. Labeling of cigarettes will take place in person because federal law (Prevent All Cigarette Trafficking Act of 2010) prohibits mailing cigarettes. Study staff will instruct smokers to bring their unsmoked cigarettes to each appointment and conduct this labeling procedure each time (except the final appointment).

Participants will receive no instruction about refraining from covering the labels during the study, because the intention of the study is to assess the real-world impact of the labels. Study staff will instruct participants in both arms to smoke or not smoke as they normally would. Participants who stop smoking will remain in the study, continue to attend study appointments, and receive payment for the surveys they complete.

Participants will receive a total of $300 in incentives ($75 at visit 1; $50 at visit 2; $50 at visit 3; $50 at visit 4; $75 at visit 5). Our previous studies suggest that payments of this size motivate participants. A $50 incentive is enough to pay for 8 days’ worth of cigarettes, assuming less than a pack of cigarettes per day. We wish to give participation incentives that reduce the financial burden that purchasing multiple packs at one time may place on lower-income smokers, but also wish to avoid smokers believing that the study is buying them cigarettes or defraying the cost. Thus, study staff will provide incentives in cash at the appointments, *after* participants

complete each survey and in envelopes labeled "payment for completing survey." At the end of the study, participants will receive a list of cessation resources.

Measures

Primary outcome measure:

- Quit intentions: The primary outcome is quit intentions measured at 4 weeks by survey.

Secondary Outcome Measures:

- Awareness of health effects from smoking cigarettes: Awareness of health effects will be measured at 4 weeks by survey.
- Awareness of cigarette smoke constituents: Awareness of constituents will be measured at 4 weeks by survey.
- Quit attempts: Quit attempt will be measured during the 4 weeks of the study, reported at either 2, 3, or 4 weeks. A quit attempt is defined as 24 hours without smoking.
- Successful Quitting: Successful quitting will be defined as self-reported smoking on 0 of the past 7 days at 4 weeks.
- Forgoing a cigarette: Forgoing a cigarette will be measured at 4 weeks as the frequency of butting out a cigarette or forgoing a cigarette in an effort to smoke less.
- Perceived likelihood: Perceived likelihood of developing smoking-related health outcomes will be measured at 4 weeks by survey.
- Frequency of conversations about health messages: Frequency of conversations with others about the health message on cigarette packs will be measured at 4 weeks by survey.
- Negative affective reactions: Negative affect will be measured at 4 weeks by survey.
- Cognitive elaboration: Cognitive elaboration (how much the participant reports thinking about the label) will be measured at 4 weeks by survey.

Data analysis

Power analyses indicated that the target enrollment of 672 smokers would provide > 80% power to detect a difference in quit intentions of at least $d = .22$ (a small effect) or larger in analyses with $\alpha = .05$. The primary trial outcome is intention to quit smoking in the next month, modeled as a continuous outcome. We hypothesize that smokers randomized to receive labels with constituent disclosure messages on their cigarette packs will have higher intentions to quit smoking than smokers randomized to receive labels with cigarette butt litter messages. To check whether random assignment creates trial arms that are equivalent on demographic and outcome variables at Visit 2 (the randomization visit), we will use χ^2 tests for categorical variables and *t*-tests for continuous variables. We will use logistic regression to assess differential attrition. If conditions differ on any of these variables, main analyses will control for them. We will use linear regression to assess the effect of trial arm on the primary outcome. We will conduct exploratory analyses to assess whether the impact of trial arm differs among demographic subgroups (i.e., income, race, Hispanic ethnicity, sexual orientation, sex, age, education, and smoking frequency). We will also examine the intervention's effects on other secondary study

outcomes, using χ^2 tests for categorical variables and *t*-tests for continuous variables. Analyses will be intent-to-treat, deeming any missing values at follow-up as being equivalent to the last observed value for smokers who drop out during the trial and do not complete the final survey.