Randomized Trial of Pictorial Cigarette Pack Warnings' Impact on Smoking Behaviors
Study Protocol

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Contents

Background

The U.S. Food and Drug Administration (FDA) approved 9 new warnings for cigarette packs in June 2011 to better communicate the risks of smoking. A court ruling that struck down the labels criticized FDA for failing to "present any data – much less the substantial evidence required under the federal law – showing that enacting their proposed graphic warnings will accomplish the agency's stated objective of reducing smoking rates." Our project will address this critique head-on by rigorously testing the impact of the text and graphic warnings on risk perception and smoking behavior.

While the randomized experiments on candidate warnings have been informative, one limitation is their use of psychological outcomes, such as attitudes or quit intentions, but not smoking behavior. Another is that they typically expose participants to warnings in artificial experimental settings for a short period of time, using much lower frequency and shorter duration of warning exposure than found in the real world. Finally, previous experiments have largely ignored the impact of warnings on vulnerable populations. Research on the impact of cigarette pack warnings currently in use focuses on population-level observational studies of smoking behavior, but these studies are unable to support strong causal inferences. Our study will address these limitations by measuring the impact of warnings on risk perceptions and cessation behaviors, placing warnings on smokers' actual cigarette packs for 4 weeks, and assessing the impact of the warnings on low-income adults, a group with high rates of smoking and thus high risk for harm.

Study purpose

The purpose of this randomized controlled trial is to determine whether graphic health warnings on cigarette packs are more effective than the existing Surgeon General's warning on cigarette packs at encouraging quit attempts. While previous experiments evaluating candidate graphic warnings have been informative, they have used psychological outcomes, such as attitudes or quit intentions, but not actual cessation behavior (e.g., quit attempts). Furthermore, they typically expose participants to warnings in controlled but artificial experimental settings for a short period of time, using much lower frequency and shorter duration of warning exposure than found in the real world. This study addresses these issues by evaluating the impact of warnings on quit attempts by randomly assigning smokers to have their cigarette packs labeled with either a graphic warning or a Surgeon General's warning for four weeks.

Main hypothesis: Smokers randomized to receive graphic warnings on their cigarette packs will be more likely to report a quit attempt in the 4 weeks of the study than smokers randomized to receive a Surgeon General's label on their cigarette packs.

Secondary hypothesis: Smokers randomized to receive graphic warnings on their cigarette packs will have higher quit intentions at 4 weeks than smokers randomized to receive a Surgeon General's label on their cigarette packs, controlling for baseline quit intentions.

Study design

This protocol is for a parallel-group, randomized, controlled trial with smokers in Chapel Hill, North Carolina and Oakland, California. The study arms and location are described below.

Study arms

1. Experimental: Graphic warnings that include text and an image depicting a health effect of smoking will be applied on labels that cover the top half of the front and back of participants' cigarette packs each week for 4 weeks. The text for these warnings was selected from the 2009 Family Smoking Prevention and Tobacco Control Act and the images were proposed by the FDA. Participants will be randomly assigned to receive one of the following four graphic warnings on their cigarette packs for 4 weeks:
    - Text: "WARNING: Cigarettes are addictive." Image: Man smoking through tracheotomy hole.
    - Text: "WARNING: Cigarettes causes fatal lung disease." Image: Healthy lungs next to diseased lungs.
    - Text: "WARNING: Cigarettes cause cancer." Image: Mouth with cancerous lesion on lip.
    - Text: "WARNING: Smoking can kill you." Image: Woman dying from cancer.
2. Active Comparator: Labels with Surgeon General's Warning text will be applied to the side of participants' cigarette packs each week for 4 weeks, on top of the Surgeon General's Warning printed by the manufacturer. Participants will be randomly assigned to receive warnings with one of the four Surgeon General's Warnings on their cigarette packs for 4 weeks:
    - SURGEON GENERAL'S WARNING: Smoking Causes Lung Cancer, Heart Disease, Emphysema, and May Complicate Pregnancy.
    - SURGEON GENERAL'S WARNING: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health.
    - SURGEON GENERAL'S WARNING: Smoking by Pregnant Women May Result in Fetal Injury, Premature Birth, and Low Birth Weight.
    - SURGEON GENERAL'S WARNING: Cigarette Smoke Contains Carbon Monoxide.

Study locations

1. Prevention Research Center of the Pacific Institute for Research & Evaluation. Oakland, California, United States, 94612
2. Pacific Institute for Research and Evaluation. Chapel Hill, North Carolina, United States, 27514

Participants

Participants are adult cigarette smokers in North Carolina and California. Inclusion and exclusion criteria are described below.

Inclusion criteria:

- Be 18 years or older
- Have smoked at least 100 cigarettes in his or her lifetime
- Currently smoke cigarettes
- Be able to read and speak English

Exclusion criteria:

- Pregnant women
- Smokers who smoke exclusively roll-your-own cigarettes
- Smokers concurrently enrolled in another cessation study

- Smokers who smoke fewer than 7 cigarettes per week, on average
- Smokers who live in the same household as someone who has enrolled in the study

Recruitment and screening

PIRE and Ewald & Wasserman, the study contractors, will use recruitment methods that include a study phone number and a website that gives information about the study in written FAQs. To recruit smokers, staff will use Facebook, Craigslist, e-mail lists, in-person recruitment, referrals from local retailers, flyers, yard signs, bus advertisements, and newspaper advertisements. Staff will use a recruiting script to recruit smokers in person, during which smokers may opt to provide contact information to facilitate follow up from staff regarding the study. Smokers will complete an electronic screener on the study website or over the phone with a staff member. After confirming eligibility, study staff will schedule the baseline appointment for eligible smokers. We aim to enroll 2,250 smokers in the trial.

Procedures

Cognitive Interviewing Methods: Staff members from the UNC team will cognitively test the survey instrument with 12-16 smokers prior to the pilot study. Cognitive interviewing participants will be shown a cigarette pack with a graphic warning label and asked to take a survey that asks questions about their smoking behavior and reactions to the label. 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 $50 cash incentive for their participation. A second round of cognitive testing will be conducted with 10 current smokers and e-cigarette users. The process will be the same as the first round but will also include questions about e-cigarette use. There are two versions of the interview guide that include different exposures to warning labels on cigarette packs. We will use one guide with half the participants and one guide with the other half of participants. Compensation will also be $50 for about a 45-60 minute appointment.

Pilot Study: We will conduct a pilot study with ~50 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: PIRE has offices across the U.S. We chose their offices in Chapel Hill, North Carolina and Oakland, California to be study sites as they represent geographically distinct regions. Both also serve diverse communities with a higher percentage of low-income than the U.S. (Chapel Hill/Durham: 19% low-income, 41% African American, 14% Hispanic; Berkeley/Oakland: 18% low-income, 10% African American; 11% Hispanic). Both offices are accessible by public transportation. Each study site will recruit half of the participants needed for the study.

UNC's project manager and Dr. Brewer will receive weekly updates from PIRE 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 visit each site regularly during the study to monitor data collection. PIRE will assign supervisors for each site who will conduct quality checks using a checklist. The

RCT will first begin at the Chapel Hill site to allow the project manager and PI to closely monitor the initial implementation. The project manager will also travel to Oakland to oversee the initial week of study implementation there.

PIRE staff will schedule participants' 5 appointments to visit our offices 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. PIRE offices in North Carolina and California are centrally located within a 5-10 minute walk of retailers that sell a broad variety of popular cigarette brands.

UNC will randomize smokers at each site, *a priori* by order of enrollment, and provide each site's assignments in a spreadsheet. Each smoker will receive the same warning label on their packs throughout their participation in the study.

At the baseline appointment, to ensure that we do not enroll participants under age 18, we will visually inspect a valid form of photo ID (e.g., driver's license) for participants who appear to be under age 27. Then, study staff will obtain written informed consent from study participants. Participants will complete two computer surveys at the first appointment, and one survey at the subsequent follow-up appointments. Research staff will ask participants who miss visits to complete the computer survey remotely.

At the first four appointments, we will apply the warning labels on participants' cigarette packs (including any currently open packs) using the procedures that we developed in our previous pilot studies. We will remove the top of the cellophane wrapping from the cigarette packs in front of the study participants so that they know that these are fresh cigarette packs that we do not otherwise alter. We will apply self-adhesive labels that have the warnings (printed in color) directly to the packs to prevent smokers from removing the plastic with the label. Graphic labels will go on the top 50% of the front and rear panels of the packs in accordance with the Tobacco Control Act's requirements. Thus, packs will receive 2 (same) labels each – front and back. For hard-pack cigarettes, we will use a utility knife to cut the label horizontally to allow it to separate where the pack opens; this approach was effective in our pilot work. Surgeon General's labels will be applied directly on top of the current Surgeon General's warning.

We 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. We 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 warnings during the trial, because our intention is to assess the real-world impact of the labels. Participants who stop smoking will remain in the study, continue to attend study appointments, and receive payment for the surveys they complete.

Smokers in NC will receive a total of $185 in incentives ($50 at baseline; $30 at week 1; $30 at week 2; $30 at week 3; $45 at week 4). Smokers in CA will receive a total of $200 in incentives ($50 at baseline; $30 at week 1; $30 at week 2; $40 at week 3; $50 at week 4). Our pilot studies suggest that payments of this size motivate participants. A $30 incentive is enough to pay for 8 days' worth of cigarettes, assuming less than a pack of cigarettes per day. Research experts in CA indicated that incentives needed to be greater to account for the increased cost of living. 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, we will provide incentives in cash at the appointments, *after* they complete each survey and in envelopes labeled "payment for completing survey." At the end of the final appointment, each participant will also receive information about local smoking cessation programs.

Measures

Primary outcome measures

- Quit attempts: The primary outcome is a quit attempt during the 4 weeks of the study, reported at either 1, 2, 3, or 4 weeks. A quit attempt is defined as 24 hours without smoking.

Secondary outcome measures

- Quit intentions: Quit intentions will be measured at baseline pretest and posttest, 1, 2, 3, and 4 weeks using the 3-item quit intention scale developed by Klein, Zajac, and Monin (2009).
- 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 baseline pretest, 1, 2, 3, and 4 weeks as the frequency of butting out a cigarette or forgoing a cigarette in an effort to smoke less.
- Positive reinforcement attitudes: Positive reinforcement attitudes smoking attitudes will be measured at baseline prettest and posttest, 1, 2, 3, and 4 weeks using measures adapted from the Smoking Consequences Scale developed by Brandon & Baker (1991).
- Negative reinforcement attitudes: Negative reinforcement attitudes will be measured at baseline prettest and posttest, 1, 2, 3, and 4 weeks using measures adapted from the Smoking Consequences Scale developed by Brandon & Baker (1991).
- Perceived likelihood: Perceived likelihood of developing various smoking-related health outcomes will be measured at baseline pretest and posttest, 1, 2, 3, and 4 weeks using measures adapted from Pepper (2013).
- Conversations about warning labels: Frequency of conversations with other about the warning labels, health effects of smoking and quitting in the past week will be measured at 1, 2, 3, and 4 weeks.
- Fear: Fear will be measured at baseline posttest, 1, 2, 3, and 4 weeks using 12 items developed by the researcher team and adapted from Nonnemaker et al. (2010), Leshner et al. (2011), Watson et al. (1988), and Keller and Block (1996).
- Cognitive elaboration: Cognitive elaboration will be measured at 1, 2, 3, and 4 weeks using the Depth of Cognitive Processing Scale (Hammond, Fong, McDonald, Cameron, and Brown, 2003) and measures adapted from Fathelrahman et al (2010).

Other outcome measures

- Positive and negative smoker prototypes will be measured at baseline pretest and posttest, 1, 2, 3, and 4 weeks using a shortened version of the smoker prototype scale developed by McCool, Cameron, et al. (2010).
- Positive and negative e-cigarette user prototypes will be measured at baseline pretest and posttest, 1, 2, 3, and 4 weeks adapting a shortened version of the smoker prototype scale developed by McCool, Cameron, et al. (2010).

- Quit stage will be measured at baseline pretest and posttest, 1, 2, 3, and 4 weeks using measures adapted from the ITC Quit Intention Scale.
- Smoking quantity will be measured at baseline pretest, 1, 2, 3, and 4 weeks as the self-reported average number of cigarettes smoked per day during the past week.
- Implementation intentions will be measured at baseline pretest and 4 weeks to assess how much participants have planned when to quit, how to quit, and how to deal with cravings after quitting.
- Emotional reactions (i.e., anxiety, disgust, sadness, guilt, anger) will be measured at baseline posttest, 1, 2, 3, and 4 weeks using 12 items developed by the researcher team and adapted from Nonnemaker et al. (2010), Leshner et al. (2011), Watson et al. (1988), and Keller and Block (1996).
- Perceived understandability will be measured at 1, 2, 3, and 4 weeks using a measure adapted from Cameron, Pepper, and Brewer (2013).
- Attention/noticing of labels will be measured at baseline posttest, 1, 2, 3, and 4 weeks using measured adapted from Fathelrahman et al. (2010) and Nonnemaker et al. (2010).
- Pack attitudes will be measured at baseline pretest and 4 weeks using measures adapted from Moodie (2011).
- Avoidance of the warning label will be measured 1, 2, 3, and 4 weeks using measures adapted from the Population Assessment of Tobacco and Health Study (2014) and the Environics Research Group (2008), as well as measures developed by the research team.
- Reactance to the warning label will be measured at baseline posttest, 2, and 4 weeks using a scale developed by the research team.
- Perceived effectiveness of the warning labels will be measured at baseline post-test and 4 weeks using measures adapted from Hitchman, Driezen, Logel, Hammond, and Fong (2013), Thrasher et al. (2012) & Cantrell et al.
- Social reactions to the warning labels will be measured at 1, 2, 3, and 4 weeks using measures developed by the research team to assess the nature, frequency, recipient and mode of communication and regarding conversations about the warning labels, quitting smoking, and the health effects of smoking.
- Perceived severity of developing various smoking-related health outcomes and of developing quitting side effects will be measured at baseline pretest and posttest, 1, 2, 3, and 4 weeks using measures adapted from Lyna (2002).
- Anticipated regret of continuing to smoke and anticipated regret of quitting smoking will be measured at baseline pretest and posttest, 1, 2, 3, and 4 weeks using measures developed by the research team.
- Perceived risks of quitting will be measured at baseline pretest, 1, 2, 3, and 4 weeks using measures adapted from McKee, O'Malley, Salovey, Krishnan-Sarin, and Mazure (2005).
- Perceived benefits of quitting will be measured at baseline pretest, 1, 2, 3, and 4 weeks using measures adapted from McKee, O'Malley, Salovey, Krishnan-Sarin, and Mazure (2005).
- Worry about the consequences of smoking will be measured at baseline pretest and posttest, 1, 2, 3, and 4 weeks using measures adapted from Dijkstra (2003), Ranby (2013) and Magnan (2009 and 2013).
- Subjective norms about smoking cessation will be measured at baseline pretest, 1, 2, 3, and 4 weeks using measures adapted from Armitage (2007) and Von Dras (2004).
- Self-efficacy to quit smoking will be measured at baseline pretest, 1, 2, 3, and 4 weeks using measures adapted from Armitage (2007).

- Participants will be randomly assigned to be assessed unprompted recall of the image and/or text of their assigned warning label at 1, 2, 3 or 4 weeks.
- Participants will be randomly assigned to be assessed recognition of the image and/or text of their assigned warning label at either 1, 2, 3, or 4 weeks.
- Frequency of e-cigarette use will be measured at 1, 2, 3, and 4 weeks as the number of days of use in the last 7 days.
- Among never users of e-cigarettes at baseline pretest, initiation of e-cigarette use will be measured at 4 weeks.
- Use of cessation aids will be measured at baseline pretest, 1, 2, 3, and 4 weeks.
- The response efficacy of quitting smoking will be measured at baseline pretest and posttest, 1, 2, 3, and 4 weeks using measures developed by the research team.
- Cons of smoking will be measured at baseline pretest and posttest, 1, 2, 3, and 4 weeks using measures adapted from the Smoking Consequences Scale developed by Brandon & Baker (1991) and items from Velicer (1985).

Data analysis

Power analyses indicated that the target enrollment of 2,250 smokers would provide 80% power to detect a 3% or larger difference in quit attempts, assuming an alpha of .05. We hypothesize that graphic warnings will lead to more quit attempts than text-only warnings. The primary outcome is making any quit attempt during the trial, modeled as a dichotomous outcome. Preliminary analyses will confirm the success of randomization by examining whether the experimental conditions differ by various characteristics (e.g., study site, income, race, Hispanic ethnicity, sexual orientation, sex, age, and education). If conditions differ on any of these variables, main analyses will control for them. Analyses will be intent-to-treat, deeming any missing values at follow-up as being the same as the last observation for adult smokers who drop out during the study and do not complete the final survey. We will also examine the intervention's effects on other secondary study outcomes including intention to quit smoking, and will examine whether poverty status moderates the relationship between pictorial warning assignment and quit attempts. Finally, exploratory analyses will examine time trends in the outcome during the course of the study.