Personalized Intervention Program: Tobacco Treatment for Patients at Risk for Lung Cancer

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Abstract

**Background:** Lung cancer screening and tobacco treatment for patients at high-risk for lung cancer may greatly reduce mortality from smoking, and there is an urgent need to improve smoking cessation therapies for this population.

**Aims:** The purpose of this study is to test the efficacy of two separate, sequential interventions to promote tobacco cessation/reduction compared to standard care in smokers considered high-risk for lung cancer.

**Methods:** The study will recruit 276 current smokers attending a lung cancer screening clinic or considered high-risk for lung cancer based on age and smoking history across two sites. Patients first will be randomized to either standard tobacco treatment (8 weeks of nicotine patch and five individual counselling sessions) or standard tobacco treatment plus personalized gain-framed messaging. At the 8-week visit, all patients will be re-randomized to receive biomarker feedback or no biomarker feedback. Repeated assessments during treatment will be used to evaluate changes...
in novel biomarkers: skin carotenoids, lung function, and plasma bilirubin that will be used for biomarker feedback. We hypothesize that personalized gain-framed messages and receiving biomarker feedback related to tobacco cessation/reduction will improve quit rates and prevent relapse compared to standard care. Primary outcomes include 7-day point-prevalence abstinence verified with expired carbon monoxide at 8 weeks and mean cigarettes per day in the past week at 6 months.

**Conclusions:** Study findings will inform the development of novel interventions for patients at risk for lung cancer to improve smoking cessation rates.

**Introduction**

Smoking remains the leading cause of preventable death and illness (World Health Organization, 2012), and lung screening and tobacco treatment may reduce mortality for patients at high-risk for lung cancer (National Lung Screening Trial Research Team, 2011). This study evaluates whether two novel interventions tailored for patients receiving lung screening or considered high-risk for lung cancer (NCCN, 2017; USPSTF, 2013) improve smoking outcomes when added to standard tobacco treatment.

This study builds on research indicating that (1) gain-framed messaging (i.e., focussing on cessation benefits) substantially increases quit intentions, attempts, and success rates in general populations of smokers (McKee et al., 2004; Schneider et al., 2001; Toll et al., 2007, 2010), (2) smoking cessation is associated with improvements in biomarkers (i.e., skin carotenoid, lung function, plasma bilirubin levels (Galan et al., 2005; O’Malley, Wu, Mayne, & Jatlow, 2014; Scanlon et al., 2000)), and (3) biomarker feedback may encourage quitting (Bize et al., 2012; McClure, 2001). The current study is the first to test personalized gain-framed messaging and feedback about biomarker changes among patients eligible for lung cancer screening.

We hypothesize that (1) personalized gain-framed messages will improve quit rates over standard tobacco treatment, and (2) feedback about improvements in biomarkers following initial cessation/reduction efforts will reinforce behaviour change and prevent relapse.

**Methods and Design**

**Study Design**

We will test two separate, sequential interventions to promote tobacco cessation/reduction compared to standard care (SC). Separate randomizations will occur at baseline (week 0) and week 8 (Figure 1). Sequential randomization (rather than a 2 × 2 design) requires fewer subjects and allows us to examine responder status at week 8 as a moderator of the effect of the phase 2 intervention. All participants will receive $120 for study completion.

**Planned Recruitment**

The enrolment target is 276 current smokers across two outpatient hospitals. Inclusion criteria are: (1) receiving lung screening or considered high-risk for lung cancer based on age and smoking history, thereby eligible for lung cancer screening (NCCN, 2017; USPSTF,
2013), (2) current smoker, (3) not known to currently have lung cancer, (4) willing to be randomized; Exclusion criteria are: (1) dementia or current serious psychiatric or unstable medical illnesses, (2) known fat mal-absorption diseases possibly affecting skin carotenoid status, (3) current tobacco treatment. Participants will be identified through the hospital electronic medical records system, lung cancer screening, or lung health visits. Additional recruitment sites such as pulmonology clinics and Veteran Affairs hospitals may be included to meet recruitment goals.

**Intervention 1**

Participants will be randomized to either: (1) SC from a Tobacco Treatment Service provider (i.e., intake, five counselling sessions, 8-week supply of nicotine patch following standard dosing procedures) or (2) SC + personalized gain-framed video and print messaging (SC+P). SC counselling will be based on cognitive behavioural, evidence-based, smoking cessation treatment (Fiore et al., 2008). Participants will begin using nicotine patches following the first counselling session, prior to their scheduled quit date. In addition to the SC procedures, participants receiving the SC+P intervention will view brief (8–10 min) gain-framed videos at four visits (week 0, 2, 4, and 6) and receive personalized gain-framed print media at all five counselling visits. The videos are designed for patients at high-risk for lung cancer based on age and smoking history and address the benefits of quitting smoking. Print media messages will be personalized based on participant demographics and smoking history (Webb, Hendricks, & Brandon, 2007).

**Intervention 2**

All participants will be randomized again at 8 weeks to (1) biomarker feedback or (2) no feedback. Biomarker feedback scripts will use language consistent with a personalized, gain-framed intervention. All participants will complete blood draws and biomarker assessments following the same schedule (Table 1). The biomarker feedback group will receive personalized information at the 8-week and 3-month visits, summarizing changes in their biomarker data from baseline. The control group will be informed that we are evaluating novel biomarkers that may change with tobacco reduction or cessation. They will receive feedback at the 6-month visit.

**Measures**

**Breath Carbon Monoxide (CO)**—Expired breath CO, an objective measure of smoking, will be assessed at every visit.

**Biomarkers**—We will collect measures of carotenoid status, lung function (measured via spirometry), and plasma bilirubin at multiple time-points. While most studies measure plasma/serum carotenoids, our team pioneered non-invasive methods (resonance Raman spectroscopy) to measure skin carotenoids using a brief palm scan (Mayne et al., 2013).

**Primary Outcomes**—Primary outcomes include CO-verified (CO ≤ 6 ppm) 7-day point-prevalence abstinence (week 8, aim 1) and mean cigarettes per day in the past week (6 months, aim 2).
Data Analysis and Management—The protocol was approved by the Institutional Review Board at both sites, and a Data and Safety Monitoring Plan was established. Logistic regressions will test the main effect of SC+P versus SC on smoking cessation in the intent to treat sample. Linear-mixed models will test the effect of providing biomarker feedback on change in cigarette use. We anticipate a 70% follow-up rate, allowing complete data for \( n = 96 \) per group at the end of 8 weeks. We have 80% power (two-tailed alpha = 0.05) to detect a 17% difference in quit rates at 8 weeks (35% vs. 52%, 30% vs. 47%) and a four cigarette mean difference at 6 months (SD = 10) between the two conditions. We attempt to account for potential differences between sites (e.g., patient demographics and therapist effects) by including site as a stratification factor for randomization and including site as a predictor in all data analyses.

Discussion

This is the first randomized trial evaluating personalized, gain-framed messages tailored specifically for high-risk patients who are eligible for lung cancer screening. This project is also the first large, well-powered study examining the effects of smoking cessation on novel biomarkers including skin carotenoids and bilirubin and the effects of feedback about these biomarkers. Results may inform ways to optimize interventions for patients at high-risk for lung cancer including lung screening patients who present to cancer centers or healthcare organizations. Effective interventions to promote cessation among these high-risk patients are greatly needed to reduce lung cancer incidence and mortality.

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Figure 1.
Study Timeline Randomization in Phase 1 will be stratified by recruitment route (e.g.,
electronic medical record) within site and time to first morning cigarette (≤ or > 30 min).
Randomization in Phase 2 will be stratified by site, treatment group, and responder status in
Phase 1.
Table 1
Timeline of assessments

| Study Timeline          | Intake | Week 0 | Week 2 | Week 4 | Week 6 | Week 8 | Month 3 | Month 6 |
|------------------------|--------|--------|--------|--------|--------|--------|---------|---------|
| Consent to Study       | X      |        |        |        |        |        |         |         |
| Screening Visit        | X      |        |        |        |        |        |         |         |
| Randomization 1        | X      |        |        |        |        |        |         |         |
| Blood Draw             | X      |        |        |        | X      | X      | X       |         |
| Breath Carbon Monoxide | X      |        | X      |        | X      | X      | X       |         |
| Spirometer             | X      |        |        |        | X      |        | X       |         |
| Skin Carotenoids       | X      |        |        |        | X      | X      | X       |         |
| Nicotine Patch         | X      | X      | X      | X      |        |        |         |         |
| Counselling            | X      | X      | X      | X      | X      |        |         |         |
| Randomization 2        |        |        |        |        |        |        |         | X       |