

# Two-Year Follow-Up of a Randomized Controlled Study of Integrated Smoking Cessation in a Lung Cancer Screening Program



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## ABSTRACT

**Introduction:** Smoking cessation activities incorporated into lung cancer screening programs have been broadly recommended, but studies to date have not exhibited increased quit rates associated with cessation programs in this setting. We aimed to determine the long-term effectiveness of smoking cessation counseling in smokers presenting for lung cancer screening.

**Methods:** This was a randomized control trial of an intensive, telephone-based smoking cessation counseling intervention incorporating lung cancer screening results versus usual care (information pamphlet). This analysis reports on the long-term impact (24-mo) of the intervention on abstinence from smoking.

**Results:** A total of 337 active smokers who participated in the screening study were randomized to active smoking cessation counseling ( $n = 171$ ) or control arm ( $n = 174$ ) and completed a 24-month assessment. The 30-day smoking abstinence rates at 24 months postrandomization was 18.3% and 21.4% in the control and intervention arms, respectively—a 3.1% difference (95% confidence interval:  $-5.4$  to  $11.6$ ,  $p = 0.48$ ). No statistically significant differences in the 7-day abstinence, the use of pharmacologic cessation aids, nicotine replacement therapies, nor intent to quit in the following 30 days were noted ( $p > 0.05$ ). The abstinence rates at 24-months were higher overall than at 12-months (19.9% versus 13.3%,  $p < 0.001$ ), and smoking intensity was lower than at baseline for ongoing smokers.

**Conclusions:** A telephone-based smoking cessation counseling intervention incorporating lung cancer screening results did not result in increased long-term cessation rates versus written information alone in unselected smokers undergoing lung cancer screening. Overall, quit rates were high and continued to improve throughout participation in the screening program. ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02431962) NCT02431962).

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**Keywords:** Mass Screening; Lung neoplasms; Smoking cessation; Counseling; Randomized controlled trial

## Introduction

Participation in lung cancer screening programs has been associated with increased smoking cessation rates,<sup>1</sup> and several guideline documents strongly suggest the incorporation of cessation services alongside screening.<sup>2,3</sup> Such cessation assistance is a prerequisite for reimbursement of lung cancer screening by the Centers for Medicare and Medicaid Services in the United States. Nevertheless, randomized studies, to date, have not exhibited increased quit rates associated with specific smoking cessation programs within the screening environment, and the paucity of data on the efficacy and feasibility of such approaches has been acknowledged.<sup>2,4,5</sup>

We recently published the results of a randomized controlled study of an intensive, telephone-based counseling smoking cessation program to determine its impact on smoking cessation rates in all active smokers participating in a lung cancer screening program.<sup>6</sup> Unfortunately, we did not find an impact of this intervention on the primary study end point of smoking abstinence at 12 months. This brief report aims to present the results of the final 24-month smoking assessment in this trial.

## Materials and Methods

The Alberta Lung Cancer Screening Study is an investigational cohort of 806 individuals screened for lung cancer with three annual low-dose computed tomography (CT) (LDCT) examinations.<sup>7</sup> Eligible participants met either the National Lung Screening Trial criteria (age 55–74 y;  $\geq 30$  pack-year smoking history; quit  $\leq 15$  y before)<sup>8</sup> or were age 55 to 80 years and had an estimated 6-year lung cancer risk greater than or equal to 1.5% using a validated model (PLCO2012).<sup>9</sup> Participants reporting active cigarette smoking at study enrollment were enrolled into the smoking cessation study as an integral part of the screening protocol and randomized on a one-to-one ratio to an intensive counseling-based program versus provision of a cessation information pamphlet only. Additional study methods can be found in the original publication.<sup>6</sup> The study was approved by the Health Research Ethics Board of Alberta Cancer Committee (protocol HREBA.

CC-16-0496) and registered in a clinical trial database (NCT02431962). All participants provided informed consent in writing. No public or funded lung cancer screening program was in place in Alberta or in the whole of Canada at the time of the study.

The active intervention arm comprised an intensive counseling-based (seven telephone sessions) program tailored to the specifics of the smoker (individualized to motivation and addiction levels), including recommendations with regard to nicotine replacement therapy (NRT) and prescription cessation medications and incorporating the screening LDCT results.<sup>10</sup> Subjects randomized to the intervention arm of this trial were mailed a standardized letter informing them that they would be contacted by a smoking cessation counselor. Participant information was then communicated to the smoking cessation program, identifying the individual as a screening study participant and the results of their baseline screen, including the presence of emphysematous changes. No additional efforts were made to contact the individuals, although a reminder of available cessation support programs was included with CT report letters for all participants. The primary study end point was an assessment of self-reported smoking status at 12 months after randomization. This report updated the original findings with the completed 24-month assessment. Smoking rates were assessed through a phone questionnaire by a screening study coordinator independent of the cessation program.

Data analysis was performed with IBM Statistical Package for the Social Sciences Statistics software, version 25 (IBM, Armonk, NY). All analyses were performed and presented on an intent-to-treat basis. The Pearson chi-square test was also used to compare the quit rates and cessation aids/services used by each group at 24 months, and Fisher's exact test for relapse rates. The McNemar and Wilcoxon signed-rank tests were used to compare binary and ordinal data between individuals at different time points, respectively.

## Results

A total of 369 active smokers were enrolled in the screening study and underwent baseline LDCT screening. A randomization module error resulted in the initial 24 participants in the negative CT/positive intent-to-quit strata to all be assigned to the intervention arm and was excluded from further analysis. The remaining 345 participants were randomized to the active smoking cessation arm ( $n = 171$ ) or the control arm ( $n = 174$ ). The final 24-month outcome assessment was done in November 2019, with the remaining 337 participants available for follow-up; three participants died (all in the

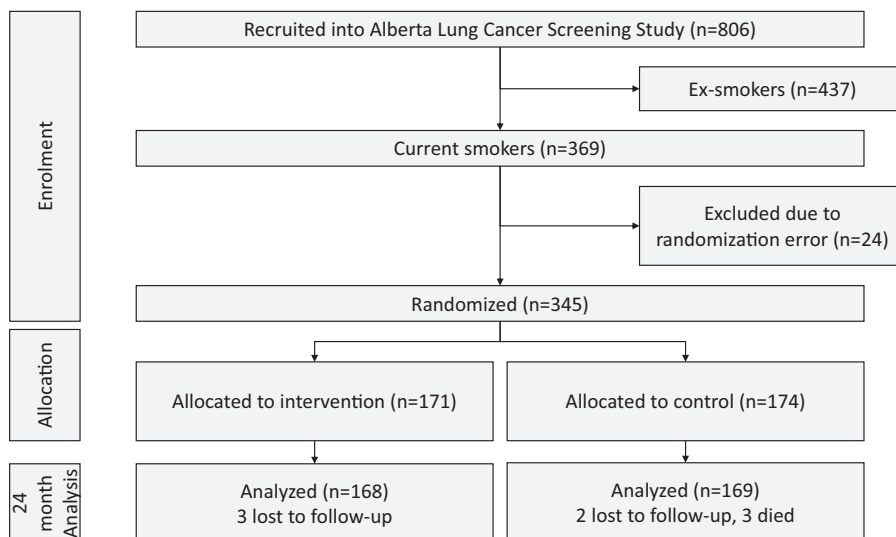


Figure 1. Study flow diagram.

control arm), and five were lost to follow-up (three in the intervention arm, two in control arm) (Fig. 1).

The baseline demographics and details of the intervention provided were reported previously, as were the 6- and 12-month cessation outcomes.<sup>6</sup> The groups were well matched apart from a more frequent history of depression in the intervention arm (29.8% versus 17.2%,  $p < 0.05$ ). At least one phone contact was achieved with a cessation counselor for 126 of 171 (73.7%) participants in the active intervention arm, whereas only 12 of 174 (6.9%) of those in the control arm had contact with the cessation program ( $p < 0.001$ )

### Outcomes After 24 Months

A total of 30-day self-reported smoking abstinence at 24 months after randomization was noted in 31 of 169 (18.3%) and 36 of 168 (21.4%) of participants in the control and intervention arms, respectively—a 3.1% difference (95% confidence interval:  $-5.4$  to  $11.6$ ,  $p = 0.48$ ). No statistically significant differences in the 7-day abstinence or current abstinence were noted (Table 1). Overall, abstinence rates were higher at the 24-month time point than at 12-months (19.9% versus 13.3%, McNemar  $p < 0.001$ ) with this increase also statistically significant for each study arm. In addition, the smoking intensity item of the Fagerström scale for “How many cigarettes a day do you smoke” was lower in active smokers at 24 months versus their baseline (86.2% versus 69.9% smoking 20 or fewer cigarettes/d, respectively).

No differences in the current use of pharmacologic smoking aids, NRT, nor in the intent-to-quit over the next 30 days were noted between groups. Individuals in the intervention arm had a higher reported number of quit

attempts lasting more than 24 hours since randomization than controls (median [interquartile range]: 3 [1–8] versus 2 [0.5–5],  $p = 0.041$ ).

The overall relapse rate at 24 months for individuals reporting abstinence at 12 months was five of 44 (11.4%), with two of 22 (9.1%), and three of 22 (13.6%) relapsing in the control and intervention arms, respectively.

### Discussion

We reported the long-term outcomes of a randomized study of a counseling-based smoking cessation intervention incorporated into a lung cancer screening program. The intervention was initiated in the days after the receipt of baseline results, and the results were also incorporated in the discussion. In keeping with the findings of our primary end point analysis of cessation rates at 12-months, we found no impact of a routine referral to such counseling on smoking cessation rates at 24-months compared with simply providing written information on available smoking cessation resources.

Overall, tobacco abstinence rates increased further from what was noted at 12 months, from 13.3% to 19.9% (+6.6%), such that one of five smokers entering the screening program was able to quit during the 2-year screening study. This incremental increase in cessation rates suggests that ongoing efforts to assist these smokers are important. Such ongoing cessation success was also noted in the Danish Lung Cancer Screening Trial (11.9%), with a consistent annual increase in quitters such that, by year 5, only 1583 of 3124 (51%) of the baseline smokers were still using tobacco.<sup>11</sup> These cessation rates also seem slightly higher than the 5% reported in a general population of older adults.<sup>12</sup>

**Table 1. Smoking Cessation Outcomes**

Cessation Outcomes at 24 mo	Control n = 169, n (%)	Intervention n = 168, n (%)	Difference % (95% CI)	p Value
30-d abstinence	31 (18.3)	36 (21.4)	3.1 (−5.4 to 11.6)	0.48
7-d abstinence	40 (23.7)	44 (26.2)	2.5 (−6.7 to 11.7)	0.6
Current abstinence <sup>a</sup>	44 (26.0)	47 (28.0)	2.0 (−7.4 to 11.4)	0.68
Use of pharmacologic cessation aid <sup>b,c</sup>	6 (3.6)	7 (4.2)	0.6 (−3.9 to 5.2)	0.78
Use of NRT <sup>c</sup>	38 (22.5)	39 (23.2)	0.7 (−8.2 to 805)	0.88
Intent to quit in next 30 d	52/125 (41.6)	60/125 (49.6)	8.0 (−4.3 to 20.0)	0.21
No. of quit attempts (median)	2	3	1	0.04

<sup>a</sup>Assessed by the question “Do you currently smoke?”

<sup>b</sup>Examples include bupropion or varenicline.

<sup>c</sup>Refers to current use.

CI, confidence interval; NRT, nicotine replacement therapy.

Our intervention failed to impact smoking relapse rates for individuals who had quit at the 12-month assessment, although the low number of observations precludes meaningful statistical comparison. These relapse rates were also in keeping with relapse rates of 10% noted in the Danish trial.<sup>11</sup> It should be noted that, although stay-quit support is generally made available through the cessation program used in this trial, no proactive enrollment or counseling follow-up was built into the intervention, and the sample size for this analysis was small. We are not aware of any investigations reporting on the effectiveness of stay-quit support in the lung cancer screening environment, but we suggest that such approaches may offer additional benefits to screening participants.

Other randomized trials of smoking cessation interventions have been performed in this setting, although these have been limited in statistical power or intensity of the interventions.<sup>5,13–15</sup> One preliminary report noted the short-term success of a telephone-based intervention.<sup>16</sup> This approach and others are being investigated in larger trials.<sup>17</sup> The difficulty of exhibiting increased smoking cessation rates in screening programs through the application of interventions otherwise considered effective has been discussed previously.<sup>6,18</sup> It seems that initial and ongoing participation in a lung cancer screening program is associated with increasing abstinence rates overall, but it remains unclear how additional cessation support can further improve on these rates.

The strengths of our study included its randomized design, enrolling all active smokers enrolled in a screening study regardless of their current motivation to quit, and a very high rate of follow-up. Its limitations include the low statistical power of the study and our population being skewed toward white participants and the more highly educated group, which may not be representative of the general population. In addition, the intensity of and participation rates in the counseling programs may not have been high enough to have a

substantial impact on the population as a whole. As reported in our original report, only 42% of individuals in the active intervention arm had two or more contacts with the cessation program.<sup>6</sup>

In conclusion, this randomized trial of an intensive, telephone-based smoking cessation counseling intervention incorporating lung cancer screening results could not exhibit a significant increase in quit rates up to and including 24 months. The routine referral of all current smokers to telephone-based smoking cessation counseling programs may not be effective in long-term heavy smokers above 55 years of age undergoing lung cancer screening. Nevertheless, smokers enrolled in screening continue to make efforts to quit while in the program, and the opportunity remains to support them in these efforts. Future studies are needed to exhibit the effectiveness of smoking cessation approaches in this group of smokers and determine the optimal method(s) of integrating smoking cessation into a lung cancer screening program.

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