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A Pilot Randomized Controlled Trial of a Comprehensive Smoking Cessation Intervention for Upper Aerodigestive Cancer Patients Undergoing Radiation Therapy

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Abstract

Background—Smoking among cancer patients is associated with poor outcomes, however smoking cessation interventions have had limited success.

Methods—This randomized controlled trial compared a novel smoking cessation intervention ('Intervention') with enhanced usual care ('Control'). Participants were smokers with head and neck or thoracic malignancies undergoing radiation. Controls received brief counseling. Intervention participants received intensive counseling, pharmacotherapy, text-messaging, and financial incentives. Biochemically confirmed seven-day abstinence at 8 weeks was compared using Fisher's exact t-test. Smoking abstinence and intensity were also analyzed using time-series panel regression.

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Presentation at Meetings

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Conflict of interest

None declared.

Results—The study population comprised 19 Intervention and 10 Control participants. More Intervention (74%) than Control (30%) participants abstained from smoking at 8 weeks ($p=0.05$). Intervention participants were significantly more likely to abstain (adjusted odds ratio=14.70[95% confidence interval [CI]=3.56–60.76]) and smoked fewer cigarettes (adjusted incidence rate ratio=0.16[95%CI=0.06–0.40]) during weeks 1–8.

Conclusion—This intervention decreased smoking among patients with upper aerodigestive cancers during radiation.

Keywords

Head and neck cancer; lung cancer; tobacco dependence; smoking cessation intervention; radiation therapy

Introduction

Tobacco smoking is the greatest risk factor for upper aerodigestive malignancies.^{1–4} Continued tobacco smoking during and after cancer treatment is associated with poor outcomes including higher risk of recurrence, second primary tumors, death^{5–7} and treatment-related morbidities^{7, 8} and lower quality of life.⁹ Many patients with head and neck or thoracic cancers, however, continue to smoke after diagnosis.^{10–14} Advocating and supporting smoking cessation among these patients is increasingly recognized as an essential component of multidisciplinary cancer care,^{15–18} and successful tobacco smoking cessation, even after diagnosis, is associated with improved outcomes.^{5, 11, 16} Among patients receiving radiation therapy, smoking abstinence during treatment may increase tumor radiosensitivity and therefore enhance response to treatment.^{7, 19–23}

Smoking cessation interventions to date among cancer patients, however, have had only limited success,²⁴ despite evidence that the time around cancer diagnosis is a ‘teachable moment’ during which patients are more likely to quit than at other times in their lives.²⁵ Interventions that show promise in initial research employ combination therapies, e.g. both counseling and pharmacotherapy.^{24, 26–32} Several smoking cessation strategies have shown efficacy in non-cancer populations by utilizing mobile technology,³³ contingency management,^{34, 35} or combination nicotine replacement therapy (NRT),³⁶ but have not yet been evaluated among patients with head and neck or thoracic cancer.

We designed a pilot study to determine whether a novel combination smoking cessation intervention tailored to cancer patients would be both feasible and effective in increasing smoking abstinence for head and neck or thoracic cancer patients during radiation. Long-term smoking cessation was also assessed.

Materials and methods

Participants and Design

This pilot study was a randomized, controlled two-arm trial of a comprehensive smoking cessation intervention compared with enhanced usual care ([ClinicalTrials.gov](https://clinicaltrials.gov) number

NCT02188563). This study was approved by the Johns Hopkins Hospital Institutional Review Board.

Participants were enrolled from May 2014 through March 2015. Eligible patients were 18 years or older, English-speaking, able to provide informed consent, had an incident head and neck or thoracic malignancy and planned radiation therapy for five or more weeks at Johns Hopkins cancer treatment centers, and reported smoking cigarettes within the previous 14 days.

Study Procedures

Participants were randomized to Enhanced Usual Care ('Control') or Intervention groups using 1:1 block randomization with stratification by cancer site (head and neck versus thoracic) and sex. Randomization was generated using SAS® software (Cary, NC, United States [U.S.]) and concealed in sequentially numbered opaque envelopes until study group assignment.

Both groups were followed closely for the first 8 weeks of the study, with study visits at baseline and weekly for 8 weeks, and then had long-term follow up visits at 3, 6 and 12 months (Figure 1). The Control group received a single counseling session at the baseline visit, whereas the Intervention group received intensive counseling, pharmacotherapy support, and other interventions at baseline and throughout weeks 1–8 (Figure 1).

The baseline visit for the Control group comprised four intervention components to constitute 'Enhanced Usual Care': 1) brief counseling by a trained Tobacco Treatment Specialist (TTS) consistent with the "5 A's" recommended by the United States Department of Health and Human Services;³⁷ 2) a smoking cessation workbook tailored to cancer patients; 3) contact information for local and national smoking cessation resources, including some offering free NRT; and 4) mental health screening to evaluate depressive symptoms, whereby individuals scoring ≥ 8 on the Depression subscale of the Hospital Anxiety and Depression Scale (HADS-D)^{38, 39} were offered referral to psychiatric services. At every visit surveys were administered to ascertain smoking behavior and use of smoking cessation resources, and exhaled carbon monoxide (exCO) testing was administered for biochemical confirmation of smoking status (Micro+™ Smokerlyzer®, Bedfont Scientific, Kent, England; cost for device: \$1,398.15). All participants were offered small gift cards for each completed study visit (\$10 baseline and \$5 follow-up). TTSs are professionals who are specially trained to provide treatment for individuals seeking to stop using tobacco (more information at cttp.org).

The Intervention group had the same study visit schedule, surveys, exCO administration and mental health screening as the Control group. However, the components of each study visit were different, and there were up to four additional daily visits during the first week. At baseline, the Intervention group received the smoking cessation workbook and underwent intensive TTS motivational interviewing, with brief follow-up motivational interviewing sessions at subsequent study visits, daily for the first week, then weekly for eight weeks. Other additional interventions received included: Enrollment in the National Cancer Institute's free smokefreetxt text-messaging program (smokefree.gov); contingency

management at each visit, by which participants received \$5 gift cards for biochemically confirmed smoking abstinence; and guided pharmacotherapy. Pharmacotherapeutic options offered were combination NRT (patch/gum, patch/lozenge, or patch/nasal spray), bupropion, and varenicline.

Participants receiving combination NRT were instructed to use the patch daily, and to also use the nicotine gum, lozenges or nasal spray as needed. Medication recommendations were based on mental health screening, comorbidities and allergies, with oversight by a physician with expertise in tobacco cessation (FK; Supplementary Figure 1). Over-the-counter NRT was provided for free (estimated cost per participant: \$240), and prescriptions provided for other medications. Participants were permitted to opt-out of intervention components.

Medical record abstraction was performed to evaluate clinical characteristics of interest. Participants with either former or current illicit injection drug use (IDU) were considered to have ‘history of IDU’. ‘Mucositis’ was considered Common Terminology Criteria for Adverse Events v3.0 (CTC3)⁴⁰ grade 2 or higher mucositis/stomatitis (including esophagitis) at any time during weeks 1–8. This pilot study originally had a target sample size of 60. Enrollment was slower than expected however, and at the interim analysis (once 30 people were enrolled) the decision was made to stop the study.

Outcome measures

The primary outcome for this study was seven-day smoking abstinence at eight weeks from the baseline study visit. Participants were considered abstinent if they both reported not smoking in the previous seven days and had exCO ≤ 8 .⁴¹ Secondary outcomes included smoking abstinence at other time points, smoking intensity (total cigarettes per previous 7 days) and the reduction from baseline thereof, and total cigarettes smoked.

Statistical analysis

Descriptive variables were reported as number and percent, or median and interquartile range (IQR). Characteristics of the Intervention and Control groups were compared using two-sided Fisher’s Exact Tests for categorical variables. Differences in medians were compared using Wilcoxon Rank-Sum Tests. Prevalence of smoking abstinence was compared using Fisher’s Exact Test. Change from baseline in smoking intensity was compared using repeated-measures ANOVA. Characteristics associated with smoking abstinence were analyzed for short-term (weeks 1–8 combined) and long-term (3-, 6- and 12-months combined) study visits separately, using time-series panel data logistic regression models⁴² to account for the repeated visits. Unadjusted and adjusted odds ratios (ORs) were reported with 95% confidence intervals (CI). Characteristics associated with smoking intensity were similarly evaluated with time-series panel data negative binomial regression models, and incidence rate ratios (IRRs) reported. Kappa statistics were calculated to compare agreement between biochemical (exCO) with self-reported smoking status and reported with standard error (SE). Sensitivity and specificity of exCO with a cutoff of 8 parts per million (ppm)⁴¹ for self-reported smoking status, and vice versa, were calculated. Statistical analysis was performed using Stata 11.2 (College Station, TX, U.S.).

Results

Study population

There were 30 participants in this study, 19 randomized to the Intervention group and 11 to the Control group (Figure 1). One participant in the Control group was lost to follow-up after the baseline visit; therefore the analytic cohort comprised 29 participants (19 Intervention and 10 Control) (Supplementary Figure 2).

Baseline demographic and disease-related characteristics of the two study groups are shown in Table 1. Median age was 55 years (IQR 52–62). The majority of participants were male (N=18, 62%) and white (N=18, 62%). Median pack-years of smoking was 48 (IQR 28–64). Nearly all (N=27, 93%) participants reported cutting back on smoking when diagnosed with cancer. Although most participants (N=22, 76%) had been advised by a healthcare worker to quit smoking in the past year, only one reported that a healthcare worker followed up on that recommendation. Most (N=19, 66%) participants had tried electronic cigarettes (e-cigarettes, also called vaping) prior to study enrollment, and the majority of these individuals (N=16, 84%) reported using e-cigarettes to ‘cut down on smoking’. The HADS-D depression screen was positive for 9 patients, of whom 3 accepted psychiatry referral. Baseline characteristics were statistically similar by study group, with the exception that more Intervention participants reported post-high school education (53% vs. 10%, $p=0.04$).

Interventions received & resources used

Overall, 95.1% (292/307) of planned study visits were completed, excluding the 12 study visits among 7 participants not completed due to participants’ death prior to study completion.

As expected, participants in the Intervention group received significantly more cessation support during weeks 1–8 than those in the Control group (Figure 2). During this time, the Intervention group received more motivational interviewing than the Control group (median 87 versus 15 minutes, $p<0.001$). A higher proportion of patients in the Intervention versus Control group used combined NRT (47% versus 10%, $p=0.10$) and text-messaging cessation support (79% versus 0%, $p<0.001$). Although consistent medication use was low in both groups, participants in the Intervention group used smoking cessation medications on more days than the Control group (median 33% versus 11% of days, $p=0.06$). By week 8, only 2 participants used medications; these were both in the Intervention group, and both used a combination of nicotine patch and nicotine gum.

Smoking abstinence

Participants in the Intervention group were significantly more likely to abstain from cigarette smoking than those in the Control group at week 8, the primary study end point (74% versus 30%, $p=0.046$, Figure 3). In fact, Intervention participants were more likely to abstain from smoking at every follow-up study visit during weeks 1–8. Additionally, the proportion of Intervention participants who abstained from smoking increased or was stable each subsequent week of follow-up during weeks 1–8, which was not true of the Controls (Figure 3).

Considering long-term outcomes (3, 6, and 12-months), the proportion of participants who abstained from smoking remained higher in the Intervention compared with the Control group, but was not significantly different at any time point (Figure 2). In both groups, the proportion of participants who abstained from smoking after the intervention ended decreased over time in long-term follow-up (Figure 3). Although smoking abstinence was not maintained by most participants, some in the Intervention group did achieve long-term cessation. At 12 months 31% (4/13) of Intervention participants still in follow-up were abstinent compared to none of the Control participants (0/8).

Smoking intensity

Benefits to the Intervention group were similarly apparent when considering the intensity of cigarette smoking during weeks 1–8 (Figure 4). Compared with the Control group, participants in the Intervention group smoked significantly fewer cigarettes per week at week 8 (median 0 versus 10, $p=0.04$), smoked fewer total cigarettes during weeks 1–8 (median 49 versus 156, $p=0.09$), and had a greater reduction in number of cigarettes smoked per week at week 8 compared with baseline (median -28 versus -14 , $p=0.28$).

Characteristics associated with smoking abstinence and intensity, short-term

Participant characteristics associated with smoking abstinence during weeks 1–8 after the baseline intervention were evaluated (Table 2). Assignment to the Intervention group was associated with nearly five-fold higher odds of smoking abstinence (unadjusted OR=4.83, 95%CI=1.31–17.76). The only other factor associated with improved smoking cessation was being married (OR=4.78, 95%CI=1.46–15.63), while a history of depression (OR=0.16, 95%CI=0.03–0.95) or IDU (OR=0.04, 95%CI=0.005–0.28) were both associated with lower likelihood of smoking abstinence. Current depressive symptoms, as measured by HADS-D 8, was not associated with smoking cessation (OR=1.03, 95%CI=0.85–1.25). In the adjusted model, participants in the Intervention group remained substantially more likely to be abstinent (aOR=14.70, 95%CI=3.56–60.76), whereas those with a history of depression (aOR for abstinence 0.16, 95%CI=0.03–0.97) or IDU (aOR=0.04, 95%CI=0.004–0.29) were less likely to abstain from smoking. As expected, the odds of abstinence increased each successive week that the participants progressed through the study protocol and radiation therapy (aOR per each subsequent study visit 1.52, 95%CI=1.29–1.80). The effect of study group on abstinence was similar across study visits (e.g., there was no interaction between study group and study visit, $p_{\text{interaction}}=0.60$).

Characteristics associated with smoking intensity were also examined. During weeks 1–8, the rate of smoking was 59% lower among participants in the Intervention group compared to the Control group (unadjusted IRR for number of cigarettes smoked per week 0.41, 95%CI=0.17–0.98; Table 3). Other factors associated with smoking fewer cigarettes included older age (IRR=0.32, 95%CI=0.16–0.65 for ≥ 55 versus <55 years), being married (IRR=0.43, 95%CI=0.19–1.00), and e-cigarette use in the previous week (IRR=0.45, 95%CI=0.26–0.79). Participants with a history of IDU (IRR=3.86, 95%CI=1.79–8.30) or depression (IRR=3.61, 95%CI=1.70–7.70) smoked more cigarettes. In adjusted analysis, assignment to the Intervention group continued to be associated with a strong decrease in smoking intensity. Indeed, after adjusting for other factors, the rate of cigarette use was 84%

lower in Intervention than Control participants (aIRR=0.16, 95%CI=0.06–0.40). A history of IDU (aIRR=0.04, 95%CI=0.004–0.29) or depression (aIRR=0.16, 95%CI=0.03–0.97) both remained associated with higher rates of smoking, but e-cigarette use was no longer a predictor of smoking intensity in the adjusted model (Table 3). Similar to smoking abstinence, smoking intensity decreased with each week participants were in the study (aIRR per week 0.76, 95%CI=0.64–0.89), without a significant interaction between study group and visit ($p=0.84$).

Characteristics associated with smoking abstinence and intensity, long-term

During long-term follow-up (3, 6 and 12-month study visits), individuals in the Intervention group remained more likely to be abstinent from smoking compared with those in the Control group, although this difference was only marginally significant (OR=5.60, 95%CI 0.98–32.0, $p=0.05$; Supplementary Table 1). Marriage, no history of IDU, and absence of treatment-related mucositis were significantly associated with long-term abstinence. The odds of long-term smoking cessation were 10 fold higher in married than unmarried participants (OR=10.45, 95%CI=1.78–61.22). Continued smoking was reported at all long-term visits by each participant with a history of IDU (100% of 16 visits total) compared with 22 of 56 (39%) visits among participants without IDU (Fisher's exact $p=0.002$). Participants who experienced mucositis during treatment were significantly less likely to quit in the long term (OR 0.21, 95%CI=0.04–0.96). In contrast to weeks 1–8, the odds of smoking cessation decreased by 38% per visit during these longer-term study visits, during which no study interventions were being given (OR per visit 0.62, 95%CI=0.41–0.93).

Considering smoking intensity during long-term follow-up, individuals in the Intervention group continued to smoke fewer cigarettes than controls, but this difference was not significant (IRR=0.91, 95%CI=0.43–1.89; Supplementary Table 1). Again, married participants smoked fewer cigarettes (IRR=0.32, 95%CI=0.11–0.93) while participants with IDU history smoked more (IRR=4.33, 95%CI=2.23–8.41). In addition, participants with higher pain scores smoked significantly more cigarettes (IRR=1.19, 95%CI=1.11–1.29) in the long term. Interestingly, individuals with thoracic cancers smoked fewer cigarettes than those with head and neck cancers (IRR=0.36, 95%CI=0.16–0.80), while individuals who experienced mucositis during treatment smoked over four times more cigarettes than those who did not develop mucositis (IRR=4.48, 95%CI=1.74–11.58; Supplementary Table 1). Of note, all participants with head and neck cancer experienced mucositis (15 of 15, 100%) compared with only 5 of 13 (38%) thoracic cancer patients ($p<0.001$), which may account for the observed site-specific differences.

Exhaled CO

Overall, 81% (245/301) of smoking status self-reports were accompanied by contemporaneous exCO measurements. There were just two instances in which a participant reported abstinence but had exCO>8ppm (Supplementary Table 2). Using exCO 8ppm as consistent with smoking abstinence,⁴¹ kappa was 0.69 (SE 0.06), indicating substantial agreement. ExCO 8 had 71.3% (95%CI=62.7–78.9%) sensitivity and 98.3% (95%CI=93.9–99.8%) specificity for self-reported abstinence, and self-reported abstinence had 98.3% (95%CI=93.9–99.8%) sensitivity and 70.9% (95%CI=62.2–78.6%) specificity for exCO 8.

Discussion

This comprehensive smoking cessation intervention significantly increased smoking abstinence and decreased smoking intensity among individuals undergoing treatment for upper aerodigestive cancers, with many participants achieving smoking cessation during radiation therapy and some maintaining long-term abstinence. This is the first study to combine counseling, pharmacotherapy including combination NRT, mobile technology, and contingency management in a smoking cessation intervention for cancer patients, and is one of the most intensive interventions described to date for this population. The success of this intervention may inform the design of future smoking cessation programs for cancer patients.

Previous studies of smoking cessation among cancer patients have had limited success, but do suggest that combination therapies are more successful than monotherapies for this challenging population.²⁴ Although it is not possible from our study to determine the relative importance of the various intervention components, the successful short-term reductions in smoking observed may be attributable to its comprehensive nature rather than to any single element. The intensity of our intervention was likely another key factor in increasing abstinence rates, as differences in smoking abstinence and intensity between the Intervention and Control groups paralleled the intensity level over time. These differences were most evident during the first eight weeks of the study, when counseling and other support was provided at least weekly for the Intervention group. Subsequently, the decrease in study visit frequency and the withdrawal of intervention components after eight weeks coincided with an observed decrease in long-term abstinence rates for both groups. It is conceivable that abstinence rates for Intervention participants would have remained high had the intervention continued. More study will be needed to determine the optimal duration of smoking cessation support after cancer treatment. The impact of the stronger educational background amongst Intervention participants is unclear, as education was not associated with smoking-related outcomes.

The efficacy of our intervention during radiation therapy is particularly noteworthy when considering the detrimental effects of cigarette smoking on tumor response to radiation and on survival outcomes after radiation. Radiation-induced cell death is dependent on oxygen present in tumor tissues.⁴³ Carbon monoxide from cigarette smoking leads to carboxyhemoglobin formation, reducing the oxygen-carrying capacity of hemoglobin and resulting in tissue hypoxia that hampers the ability of radiation to kill cancer cells, termed 'hypoxic radioresistance'.^{19, 20, 44} Clinical studies of head and neck cancer patients undergoing radiation who were smokers prior to treatment have demonstrated an association of smoking during radiation with worse survival and locoregional control.^{7, 11, 45, 46} This both supports the hypoxic radioresistance theory and highlights other ill effects of cigarette smoking on tumor biology and patients' ability to tolerate treatment.^{7, 20, 47} It follows, then, that an efficacious smoking cessation intervention delivered throughout radiation therapy such as we describe here may have the potential to improve survival outcomes, possibly even independent of smoking relapse post-radiation, and warrants further study as an additional modality of cancer treatment.

We describe several psychosocial risk factors for persistent smoking, which are useful in identifying patients who may require more intensive resources to achieve abstinence during treatment. IDU history emerged as a risk factor for smoking behaviors. This is not surprising, as tobacco smoking is common but quit rates are low amongst current and former injection drug users.³⁵ Unmarried participants in our study also smoked more cigarettes and were less likely to quit, consistent with previous research.⁴⁸ Patients with history of IDU or who are unmarried should be considered higher risk for continued smoking and may benefit from mobilization of any available social support resources.

Two modifiable risk factors for smoking that were identified during the study, highlighting opportunities to intervene and optimize conditions for smoking cessation, are history of depression and current pain. Depression is frequently comorbid with tobacco smoking^{49, 50} and afflicts many upper aerodigestive cancer patients, with around 40% of head and neck and lung cancer patients screening positive for depressive symptoms.^{51, 52} Importantly, there is some evidence that treating depression while providing smoking cessation support may increase smoking abstinence.⁵³ Interestingly, a previous diagnosis of depression but not HADS-D score at enrollment was associated with smoking in our study, suggesting that a pre-existing mood disorder is more relevant to smoking outcomes than potentially transient depressive symptoms among newly diagnosed cancer patients. Pain has been shown to motivate smoking behavior,⁵⁴ and cancer patients who smoke report higher pain scores than those who do not.⁴⁸ Furthermore, those with higher pain scores smoke more, as confirmed in our study.⁵⁵ We also found that participants who experienced mucositis during treatment had poor long-term smoking outcomes, which may be related to the severe pain attributable to this common treatment-related toxicity that disproportionately affects head and neck cancer patients.⁵⁶ Although the relationship between chronic pain and smoking is complex,⁵⁷ the impact of successful pain management on long-term abstinence among cancer survivors should be explored.

E-cigarettes have recently emerged as a popular alternative to traditional cigarettes. The impact of e-cigarette use on smoking behaviors among cancer patients specifically is not well understood, but initial evidence suggests that e-cigarette use neither improves abstinence rates nor decreases smoking intensity.^{58, 59} Prior to enrollment, e-cigarette use was common amongst study participants and was motivated by a desire to quit or cut down on smoking. During the intervention, e-cigarette use did not increase abstinence, but was associated with lower smoking intensity; however, this was not significant after adjustment for other factors, and was not sustained in long-term follow-up. Another recent study of head and neck cancer patients describes similar findings.⁵⁹ Although intriguing, these initial results do not yet justify recommending e-cigarettes to aid smoking cessation, but rather highlight the need for further investigation of how these increasingly popular devices impact smoking behaviors among cancer patients.

Despite abundant evidence that smoking is associated with worse outcomes for cancer patients^{5-7, 46} and strong recommendations that cessation support be integrated into cancer treatment,^{15, 17} clinical support for smoking cessation is inconsistent. Many U.S. cancer treatment centers lack tobacco dependence treatment services and few oncologists report providing support beyond advising patients to quit.^{60, 61} Indeed, only one participant in our

study reported follow-up from a healthcare provider on a recommendation to quit smoking in the previous year. Reasons that tobacco dependence treatment is often overlooked are likely systemic, including deficits in funding, expertise and infrastructure,^{61, 62} but may also reflect an undercurrent of pessimism given the limited success thus far of smoking cessation interventions for cancer patients.²⁴ Our study suggests that it is indeed possible to help these patients quit through intensive combination therapy, at least during treatment. The time-intensive nature of our intervention also highlights the significant resource commitment that may be required to integrate efficacious smoking cessation support into cancer treatment.

Strengths of this study include the comprehensiveness and intensity of the intervention. The excellent follow-up provides a detailed picture of participant smoking behavior throughout cancer treatment. ExCO monitoring contributes an additional degree of objectivity to self-reported smoking status. The small and heterogeneous study population, however, limits broad generalizability and analysis of long-term disease-related outcomes.

Conclusions

This comprehensive and intensive smoking cessation intervention decreased smoking among patients with tobacco-related upper aerodigestive cancers undergoing radiation therapy. Its success may inform the design of tobacco addiction treatment programs for cancer patients. Further research is necessary to refine this intervention and ultimately to determine whether efficacious smoking cessation interventions during cancer treatment may prospectively improve survival.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Figure 2.

Figure 3.

Figure 4.

Table 1

Characteristics of participants randomized to Control compared with Intervention group.

Characteristic	Control No. of participants (%)	Intervention N. of participants (%)	Total No. of participants (%)
DEMOGRAPHIC CHARACTERISTICS			
Age [Median (IQR)]	55 (54–62)	55 (50–61)	55 (52–62)
Sex			
Male	7 (70)	11 (58)	18 (62)
Female	3 (30)	8 (42)	11 (38)
Race			
White	5 (50)	13 (68)	18 (62)
Black or other non-white	5 (50)	6 (32)	11 (38)
Marital status			
Married or living as married	3 (30)	8 (42)	11 (38)
Unmarried or separated	7 (70)	11 (58)	18 (62)
Education			
Did not finish high school	4 (40)	3 (16)	7 (24)
High school graduate or GED	5 (50)	6 (32)	11 (38)
Post-high school	1 (10)	10 (53)	11 (38)
Income			
<\$15,000	5 (50)	6 (32)	11 (38)
\$15,000–\$49,999	2 (20)	4 (21)	6 (21)
\$50,000–99,999	0 (9)	4 (21)	4 (14)
>\$100,000	2 (20)	5 (26)	7 (24)
SUBSTANCE USE AND MENTAL HEALTH			
Pack-years smoking [Median (IQR)]	50 (35–60)	45 (27–68)	48 (28–64)
Cigarettes smoked per day before diagnosis [Median (IQR)]	20 (20–30)	20 (20–30)	20 (20–30)
Cigarettes smoked per day at enrollment [Median (IQR)]	7.5 (3–15)	10 (3–15)	8 (3–15)
Baseline exhaled CO: [Median (IQR)]	11 (5–18)	9 (4–17)	10 (5–17)
Ever used electronic cigarettes			
No	2 (20)	8 (42)	10 (34)
Yes	8 (80)	11 (58)	19 (66)
Ever drank alcohol regularly			
No	3 (30)	7 (37)	10 (34)
Yes	7 (70)	12 (63)	19 (66)
Ever used injection drugs			
No	8 (80)	15 (79)	23 (79)
Yes	2 (20)	4 (21)	6 (21)
Mental health history			
Anxiety	2 (20)	1 (5)	3 (10)
Depression	2 (20)	4 (21)	6 (21)

Characteristic	Control No. of participants (%)	Intervention N. of participants (%)	Total No. of participants (%)
Bipolar disorder	1 (10)	1 (5)	2 (7)
HADS-D score			
<8 (not depressed)	8 (80)	12 (63)	20 (69)
8+ (depressed)	2 (20)	7 (37)	9 (31)
CANCER CHARACTERISTICS			
Cancer site [*]			
Head and Neck	5 (50)	10 (53)	15 (52)
Thoracic	5 (50)	9 (47)	14 (48)
Cancer stage [†]			
I-II	2 (20)	1 (6)	3 (12)
III	4 (40)	6 (38)	10 (38)
IV	4 (40)	9 (56)	13 (50)
Surgery			
No	8 (80)	16 (84)	22 (76)
Yes	2 (20)	3 (16)	7 (24)
Chemotherapy			
No	2 (20)	1 (5)	3 (10)
Yes	8 (80)	18 (95)	26 (90)
Vital status at 12 months [‡]			
Alive without disease	7 (70)	13 (68)	20 (69)
Alive with disease	1 (10)	1 (5)	2 (7)
Died of disease	2 (20)	5 (26)	7 (24)
TOTAL	10 (34)	19 (66)	29

^{*} Head and neck cancers were nasopharyngeal (N=2), oropharyngeal (N=8), hypopharyngeal (N=1), and laryngeal (N=4) squamous cell carcinoma. Thoracic cancers were non-small cell lung cancer (N=9), small cell lung cancer (N=3), and esophageal adenocarcinoma (N=2).

[†] 3 participants in Intervention group had limited stage small cell lung cancer and are not included in this stage categorization.

[‡] All participant deaths occurred after the primary study endpoint of 8 weeks after the baseline visit.

Abbreviations: IQR, interquartile range; GED, General Education Development; HADS-D, Hospital Depression and Anxiety Scale – Depression index; CO, carbon monoxide

Table 2

Characteristics associated with smoking cessation during the first 8 weeks of the study.

	Likelihood of smoking abstinence		Likelihood of smoking abstinence	
Characteristic	OR (95%CI) Unadjusted model [*]	p-value	aOR (95%) Adjusted model [†]	p-value
Study group				
Control	REF		REF	
Intervention	4.83 (1.31, 17.76)	0.02	14.70 (3.56, 60.76)	<0.001
Study visit				
Per 1 week	1.31 (1.13, 1.53)	<0.001	1.52 (1.29, 1.80)	<0.001
Sex				
Male	REF			
Female	0.42 (0.13, 1.38)	0.15		
Age				
<55 years	REF			
55 years	1.17 (0.34, 4.07)	0.81		
Race				
Black	REF			
White	1.95 (0.65, 5.85)	0.23		
Marital status				
Not married	REF		REF	
Married	4.78 (1.46, 15.63)	0.01	2.98 (0.89, 10.01)	0.08
Income				
<\$50,000	REF			
>\$50,000	1.98 (0.62, 6.28)	0.25		
Education				
High school or less	REF			
Post-high school	0.40 (0.11, 1.47)	0.17		
Cancer site				
Head and neck	REF			
Thoracic	1.74 (0.52, 5.87)	0.37		
HADS-D at baseline				
<8 (not depressed)	REF			
8+ (depressed)	1.02 (0.89, 1.17)	0.74		
History of depression				
No	REF		REF	
Yes	0.16 (0.03, 0.95)	0.04	0.16 (0.03, 0.97)	0.05
History of IDU				
No	REF		REF	

	Likelihood of smoking abstinence		Likelihood of smoking abstinence	
Characteristic	OR (95%CI) Unadjusted model [*]	p-value	aOR (95%) Adjusted model [†]	p-value
Yes	0.04 (0.005, 0.28)	0.001	0.04 (0.004, 0.29)	0.002
E-cigarette use (vaping) during previous week				
No	REF			
Yes	0.87 (0.29, 2.61)	0.80		
Pain score at weekly study visit [§]				
Per 1 point increase	1.03 (0.94, 1.13)	0.56		
Mucositis [‡]				
No	REF			
Yes	0.38 (0.11, 1.29)	0.12		

^{*} Unadjusted ORs for characteristics other than study group are adjusted for study group only.

[†] Adjusted analysis model includes study group and all risk factors with aOR displayed.

[§] E-cigarette use and pain score assessed weekly at corresponding study visit.

[‡] Patient reported to have Common Toxicity Criteria for Adverse Events 3.0 grade 2 or higher mucositis, including esophagitis, at any time during weeks 1–8.

Abbreviations: OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval; HADS-D, hospital anxiety and depression scale – Depression index; IDU, injection drug use

Bold font represents statistical significance (p<0.05)

Table 3

Characteristics associated with smoking intensity (number of total cigarettes smoked in the previous 7 days) during the first 8 weeks of the study.

	No. of cigarettes smoked previous 7 days		No. of cigarettes smoked previous 7 days	
Characteristic	IRR (95%CI) Unadjusted model*	p-value	aIRR (95%) Adjusted model†	p-value
Study group				
Control	REF		REF	
Intervention	0.41 (0.17, 0.98)	0.05	0.16 (0.06, 0.40)	<0.001
Study visit				
Per 1 week	0.87 (0.78, 0.99)	0.03	0.76 (0.64, 0.89)	0.001
Sex				
Male	REF			
Female	0.93 (0.37, 2.33)	0.87		
Age				
<55 years				
55 years	0.32 (0.16, 0.65)	0.002	0.58 (0.26, 1.30)	0.19
Race				
Black	REF			
White	1.64 (0.59, 4.56)	0.35		
Marital status				
Not married	REF		REF	
Married	0.43 (0.19, 1.00)	0.05	1.26 (0.52, 3.04)	0.60
Income				
<\$50,000	REF			
>\$50,000	0.74 (0.26, 2.06)	0.56		
Education				
High school or less	REF			
Post-high school	1.69 (0.58, 4.92)	0.29		
Cancer site				
Head and neck	REF			
Thoracic	1.06 (0.43, 2.61)	0.91		
HADS-D at baseline				
<8 (not depressed)	REF			
8+ (depressed)	1.06 (0.99, 1.15)	0.11		
History of depression				
No	REF		REF	
Yes	3.61 (1.70, 7.70)	0.001	6.60 (2.35, 18.55)	<0.001
History of IDU				

	No. of cigarettes smoked previous 7 days		No. of cigarettes smoked previous 7 days	
Characteristic	IRR (95%CI) Unadjusted model [*]	p-value	aIRR (95%) Adjusted model [†]	p-value
No	REF		REF	
Yes	3.86 (1.79, 8.30)	0.001	5.10 (2.02, 12.87)	0.001
E-cigarette use during previous week [§]				
No	REF		REF	
Yes	0.45 (0.26, 0.79)	0.005	1.46 (0.85, 2.52)	0.17
Pain score at weekly study visit [§]				
Per 1 point increase	0.97 (0.93, 1.01)	0.12		
Mucositis [‡]				
No	REF			
Yes	1.39 (0.48–3.98)	0.54		

^{*} Unadjusted IRRs for characteristics other than study group are adjusted for study group only.

[†] Adjusted analysis model includes study group and all risk factors with aIRR displayed.

[§] E-cigarette use and pain score assessed weekly at corresponding study visit.

[‡] Patient reported to have Common Toxicity Criteria for Adverse Events 3.0 grade 2 or higher mucositis, including esophagitis, at any time during weeks 1–8.

Abbreviations: IRR, incidence rate ratio; aIRR, adjusted incidence rate ratio; CI, confidence interval; HADS-D, hospital anxiety and depression scale – Depression index; IDU, injection drug use

Bold font represents statistical significance (p<0.05)