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Post-operative smoking status in lung and head and neck cancer patients: association with depressive symptomatology, pain, and fatigue

Erika Litvin Bloom[1,2], Jason A. Oliver[3,4], Steven K. Sutton[4,5,6], Thomas H. Brandon[3,4,6], Paul B. Jacobsen[3,4,6] and Vani Nath Simmons[3,4,6]

[1]*Department of Psychiatry and Human Behavior, Alpert Medical School of Brown University, Providence, RI, USA*
[2]*Butler Hospital, Providence, RI, USA*
[3]*Department of Health Outcomes and Behavior, H. Lee Moffitt Cancer Center, Tampa, FL, USA*
[4]*Department of Psychology, University of South Florida, Tampa, FL, USA*
[5]*Department of Biostatistics and Bioinformatics, H. Lee Moffitt Cancer Center, Tampa, FL, USA*
[6]*Department of Oncologic Sciences, University of South Florida, Tampa, FL, USA*

* *Correspondence to: Tobacco Research & Intervention Program, Moffitt Cancer Center, 4115 Fowler Avenue, Tampa, FL 33617, USA. E-mail: Vani.simmons@moffitt.org*

Abstract

***Objective*: An estimated 35–50% of lung and head and neck cancer patients are smoking at diagnosis; most try to quit; however, a substantial proportion resumes smoking. As cancer treatments improve, attention to the effects of continued smoking on quality of life in the survivorship period is increasing. The current study examines if smoking abstinence following surgical treatment is associated with better quality of life.**

***Methods*: Participants were 134 patients with head and neck or lung cancer who received surgical treatment. Smoking status and indices of quality of life (depressive symptoms, fatigue, and pain) were assessed at the time of surgery (baseline) and at 2, 4, 6, and 12 months post-surgery. Analyses were performed using a generalized estimating equations approach. A series of models examined the correlation between smoking status and post-surgery quality of life while adjusting for demographics, clinical variables, and baseline smoking status and quality of life.**

***Results*: Continuous post-surgery abstinence was associated with lower levels of depressive symptoms and fatigue; however, the relationship with fatigue became nonsignificant after adjusting for baseline fatigue and income. There was no significant relationship observed between smoking status and pain.**

***Conclusions*: Findings add to a growing literature showing that smoking cessation is not associated with detrimental effects on quality of life and may have beneficial effects, particularly with regard to depressive symptoms. Such information can be used to motivate smoking cessation and continued abstinence among cancer patients and increase provider comfort in recommending cessation.**

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Background

Cigarette smoking is a primary risk factor for cancer, with the strongest associations for lung and head and neck cancers [1]. An estimated 35–50% of lung and head and neck cancer patients are current smokers at the time of diagnosis [2,3]. Most will spontaneously quit after diagnosis [4,5], and smoking cessation interventions for these patients have produced high short-term cessation rates [2]. Less is known about relapse rates in this population, but estimates have ranged from 13% to 60% [5–11]. Relapse prevention among these patients is a priority, as continued smoking has a negative impact on morbidity and mortality [12,13], including risk for other smoking-related illnesses (e.g., coronary heart disease) and second primary tumors [14], and recurrence [13,14]. Smoking also has more immediate adverse effects on cancer treatment outcomes, including reduced treatment efficacy [e.g., 15] and higher rates of complications and side effects [16–19], as well as quality of life indices including physical and emotional functioning [e.g., 20–22].

As cancer treatments improve, attention to potential negative effects of continued smoking on quality of life in the survivorship period is increasing. In particular, quality of life indices that would likely be affected by both (a) cancer diagnosis and treatment and (b) continued smoking, such as pain and fatigue, have received the most attention. Current smokers have generally reported poorer quality of life than never smokers, with former smokers reporting an intermediate level [e.g., 23]. Regarding emotional functioning, continued smoking has been associated with greater depressive symptomatology [e.g., 24]. Limitations of these studies include small sample sizes and

assessments that occurred at a single point in time among patients at varying stages of treatment.

We recently conducted a prospective study of relapse trajectories and predictors among lung and head and neck cancer patients who underwent surgical treatment and either (a) had quit smoking after their diagnosis and within 6 months prior to surgery or (b) were smoking prior to surgery but made a quit attempt immediately following surgery, beginning during their hospital stay when smoking was not permitted [9]. Predictors of relapse in patients who had quit pre-surgery included higher perceived difficulty quitting and lower perceived risks of resuming smoking. For patients who were smoking pre-surgery, lower quitting self-efficacy, higher depression proneness, and greater fears about cancer recurrence were predictive of relapse.

The current analyses extend these findings from our prospective study and examine whether continuous smoking abstinence post-surgery is associated with differences in post-surgery quality of life with respect to both emotional (depressive symptoms) and physical (pain and fatigue) functioning indices. We address limitations of previous research on the relationship between smoking status and quality of life among cancer patients by including a larger sample of patients with two cancer types and using a prospective design with assessments at multiple time points post-surgery (2, 4, 6, and 12 months). We hypothesized that in the year following surgery, patients who were continuously abstinent would report lower levels of depressive symptoms, fatigue, and pain relative to patients who resumed smoking.

Methods

Participants

Please refer to previously published reports for details regarding recruitment, participants, and study procedures [9,25]. In brief, patients ($N = 134$) were recruited in person from the thoracic ($n = 65$) and head and neck ($n = 69$) clinics at Moffitt Cancer Center following a medical chart review for tobacco use history among all patients scheduled for surgery. We screened 353 patients in person, of whom 220 were eligible and 154 enrolled and completed the baseline assessment. Patients ($N = 134$) included in the current analyses were those who completed at least one of the four follow-up surveys (103 completed all four, 15 completed three, 11 completed two, and 5 completed one) and survived the 1-year follow-up period. Eligible patients had smoked at least 10 cigarettes per day for at least 1 year prior to diagnosis, received surgical cancer treatment, and were abstinent for at least 24 h; 64.2% smoked during the week prior to surgery. All Moffitt Cancer Center patients have access to a certified tobacco cessation specialist who is available to provide brief intervention based on the 5A's model (*ask* if patient smokes, *advise* smokers to quit, *assess* willingness to quit, *assist* in referring to treatment, and *arrange* follow-up) [see 25]. However, no intervention was provided as part of the study. This study was approved by the Institutional Review Board of the University of South Florida.

Procedure

After eligibility was confirmed, interested patients provided informed consent and then completed a baseline assessment (see the Measures section). Head and neck (HN) patients completed the baseline at a preoperative appointment that usually occurred within 1 week prior to surgery. Thoracic (TH) patients completed the baseline in their hospital room, generally within 2 to 3 days after surgery and when they had recovered sufficiently to consent and participate readily. Telephone follow-up assessments occurred at 2, 4, 6, and 12 months post-surgery. Patients were compensated $25 for each of the five assessments.

Measures

Demographics, clinical variables, and smoking history

At baseline, participants reported demographics (gender, age, race, ethnicity, marital status, education, and income), alcohol use history (frequency and history of treatment), and smoking history including years smoked, average and lifetime maximum number of cigarettes smoked per day, and nicotine dependence (*Fagerström Test for Nicotine Dependence*) [26], with items worded to reflect pre-quit cigarettes smoked per day and dependence for those who had already quit ('when you were a regular smoker'). Cancer stage and treatments received (chemotherapy and/or radiation) were abstracted from patients' medical records.

Smoking status

At baseline and all follow-up assessments, patients reported the number of cigarettes smoked during the previous 7 days. Self-reports were confirmed via exhaled carbon monoxide from a subsample who reported abstinence and were seen at a hospital visit [9]. For the current analyses, participants who reported 7-day abstinence at all four follow-ups were classified as abstinent; those who reported smoking at one or more follow-ups were classified as smoking.

Quality of life

Depressive symptomatology during the past week was assessed at baseline with the 20-item version of the Center for Epidemiologic Studies Depression Scale (CES-D) [27] and with a 10-item short version [28] at follow-ups to minimize participant burden. At both baseline and follow-up visits, *fatigue* was assessed with the 9-item

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Brief Fatigue Inventory (BFI) [29], and *pain*, including severity and interference with functioning, was assessed with the 15-item Brief Pain Inventory [30]. Preliminary analyses found that pain severity and interference were highly correlated across all follow-up visits ($rs > 0.81$). Therefore, we performed primary analyses on pain severity only (BPI-Severity).

Data analysis

Variable-level missing data, less than 9% of all data, were imputed using multiple imputation (MI). Twenty datasets were created using PROC MI in SAS/STAT software version 9.3 (SAS Institute; Cary, NC). A Markov Chain Monte Carlo method [e.g., 31] with adaptive rounding [32] for binary variables (e.g., smoking status) was employed. Fifty-eight variables across the five time points were entered in the MI: (a) smoking status at all time points; (b) quality of life variables at all time points; (c) cancer type, smoking history, and demographic variables that were used as control variables in the models evaluated. For 16 variables in the third cluster, the interaction with cancer type was also included in the MI.

Imputed datasets were analyzed using a generalized estimating equations framework to accommodate the repeated measurements at unequal time intervals (2, 4, 6, and 12 months). The identity link function was used for all quality of life variables. A first-order autoregressive structure was specified for the working correlation matrix. Robust estimation of standard errors was used. Alpha was set at 0.05 for all analyses. Preliminary analyses examined the bivariate relationships between baseline measures and quality of life during follow-up. Significant baseline measures and significant interactions with either cancer type or month were incorporated in primary analyses.

The goal of the primary analyses was to compare post-surgery quality of life of patients who were abstinent at all follow-ups versus patients who had smoked during at least one follow-up period. Each quality of life outcome variable (depressive symptoms, fatigue, and pain severity) was assessed using a three-step modeling procedure (A, B, and C), increasing the number of variables at each step in order to provide a complete context for the effect of smoking status on quality of life. In the first step, the basic model (model A) assessed smoking status as a predictor of quality of life with cancer type (HN versus TH) and follow-up month (2, 4, 6, and 12) in the model. The second step (model B) added the traditional control variables of gender, age, and cancer stage along with any significant two-way interactions with model A variables observed in preliminary analyses. The third step (model C) added significant predictors observed in preliminary analyses. All

Table 1. Demographic, smoking, and clinical characteristics

Demographic variables	All ($N = 134$)	Head and neck ($n = 69$)	Thoracic ($n = 65$)
Sex: Female* (%)	43.3	30.5	56.9
Age M (SD)**	58.6 (11.2)	55.3 (9.7)	62.0 (11.8)
Race			
White/Caucasian (%)	96.2	97.1	95.3
Black/African American (%)	2.3	2.9	1.6
Other (%)	1.5	0.0	3.1
Hispanic (%)	1.5	2.9	0.0
Marital status			
Married (%)	53.7	50.7	56.9
Single (%)	14.9	15.9	13.9
Divorced (%)	21.6	24.6	18.5
Widowed (%)	9.7	8.7	10.8
Education: less than 12th grade (%)	20.2	23.2	16.9
Household income: median category	$30K–$40K	$30K–$40K	$30K–$40K
Smoking and alcohol variables			
Years smoking: M (SD)**	39.3 (12.8)	35.1 (11.7)	43.7 (12.6)
CPD average: M (SD)	24.2 (11.7)	23.6 (12.7)	24.9 (10.5)
CPD maximum: M (SD)	34.9 (15.2)	36.0 (15.6)	33.7 (14.9)
Fagerström Dependence: M (SD)	5.8 (2.2)	5.7 (2.3)	5.9 (2.1)
Alcohol consumption: 2+ drinks/week (%)	43.6	44.1	43.1
Alcohol abuse or treatment (%)	24.6	26.1	23.1
Clinical variables			
Stage 1 or 2** (%)	55.2	44.9	66.2
Received chemotherapy treatment	40.3	40.6	40.0
Received radiation treatment**	41.8	63.8	18.5

CPD, cigarettes smoked per day; SD, standard deviation.
For comparisons of thoracic versus head and neck patients,
*Denotes $p \leq 0.01$.
**Denotes $p \leq 0.001$.

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possible two-way interactions with cancer type and month were also assessed at each step. Our presentation of multiple models—from basic to traditional to complex with inclusion of statistically driven predictors—allows for a thoughtful examination of under what circumstances a relationship is evident between smoking status and quality of life as well as the strength of this relationship in the context of other influences on quality of life. Moreover, this analytic strategy allows for examination of significant relationships between disease-related and sociodemographic variables on quality of life.

Results

Participant characteristics

Table 1 presents descriptive statistics by cancer type. Compared with TH patients, HN patients were less likely to be female and were significantly younger ($ps < 0.01$), had smoked for fewer years and were less likely to have Stage 1 or 2 cancer and more likely to have received radiation treatment ($ps < 0.001$).

Post-surgical smoking status

The number of abstinent participants varied slightly across the 20 imputed datasets with either 67 or 68 patients (50–51%) designated as abstinent. Smoking abstinence rates were significantly different by cancer type ($p < 0.001$). Among TH patients, 43 of 65 (66%) were abstinent, whereas among HN patients, 24 or 25 (35–36%) were abstinent. As noted earlier, cancer type was included in all primary analyses.

Quality of life measures

Overall means and standard errors (averaged across the 20 imputed datasets) for depressive symptoms, fatigue, and pain severity at 2, 4, 6, and 12 months post-surgery are presented in Figure 1. Preliminary analyses found that the baseline measure was a significant predictor for each quality of life measure ($ps < 0.001$). In addition, income and its interaction with cancer type and month were also significant predictors for each quality of life measure. Therefore, these two variables and the two interaction terms were included in model C for the primary analyses. No other measure presented in Table 1 was a significant predictor of post-surgery quality of life.

The following three sections present significant results for model A (smoking status, month, cancer type, and interactions), then model B (model A plus gender, age, cancer stage, and any significant two-way interactions with the model A variables), and then model C (model B plus baseline measure, income, and the interaction of income with month and cancer type). Detailed results for the models assessing each quality of life measure are shown in Table 2.

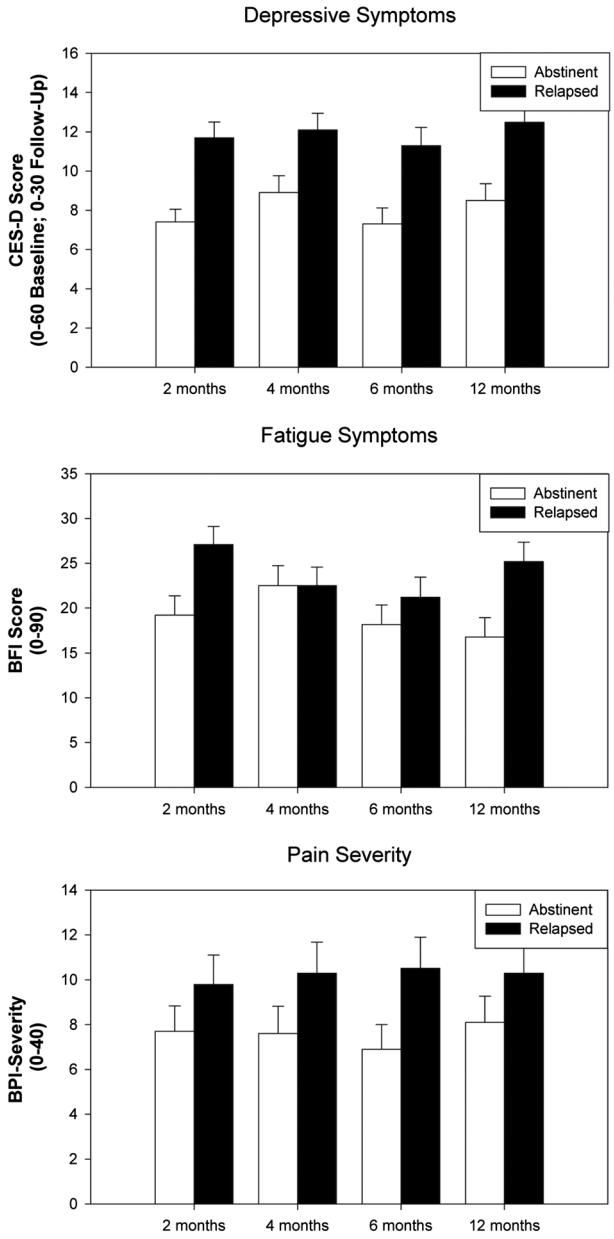

Figure 1. Means (standard errors) of quality of life outcomes as a function of smoking status. Means were averaged across the 20 imputed datasets. CES-D, Center for Epidemiologic Studies Depression Scale; BFI, Brief Fatigue Inventory; BPI, Brief Pain Inventory

Depressive symptoms

Model A showed that abstinent participants exhibited lower CES-D scores ($p < 0.001$) as well as an increase in scores over time ($p = 0.05$). Model B showed that abstinent participants exhibited lower CES-D scores ($p = 0.007$). Model B also showed that women exhibited higher CES-D scores ($p = 0.009$) and there

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Table 2. Post-surgical quality of life for abstinent versus smoking patients

	Model A			Model B			Model C		
	B	95% CI	*p*	B	95% CI	*p*	B	95% CI	*p*
CES-Depression									
Predictor									
Smoking status	**−3.64**	**−5.52, −1.75**	**0.000**	**−2.81**	**−4.72, −0.90**	**0.007**	**−1.93**	**−3.58, −0.28**	**0.028**
Smoking status*month	0.09	−0.17, 0.36	0.484	0.09	−0.17, 0.36	0.393	0.18	−0.08, 0.44	0.180
Smoking status*cancer type	-0.00	−3.81, 3.81	0.867	1.71	−2.20, 5.62	0.486	−0.80	−4.19, 2.60	0.653
Month	0.12	0.00, 0.24	0.050	0.12	0.00, 0.24	0.054	0.11	0.00, 0.22	0.061
Cancer type	−1.06	−2.95, 0.83	0.274	−1.33	−3.28, 0.62	0.184	−1.75	−3.50, −0.01	0.050
Month*cancer type	−0.26	−0.52, 0.00	0.059	−0.26	−0.51, 0.00	0.058	**−0.27**	**−0.53, −0.02**	**0.039**
Gender				**2.61**	**0.74, 4.48**	**0.009**	**1.74**	**0.14, 3.34**	**0.038**
Age				−0.48	−0.14, 0.04	0.340	0.00	−0.07, 0.07	0.762
Stage				0.65	−0.18, 1.47	0.132	0.39	−0.31, 1.08	0.285
Gender*cancer type				**4.29**	**0.54, 8.03**	**0.028**	2.42	−0.95, 5.79	0.160
Baseline							**0.23**	**0.16, 0.30**	**0.000**
Income							**−0.57**	**−0.98, −0.17**	**0.010**
Income*month							**−0.11**	**−0.17, −0.14**	**0.003**
Income*cancer type							**1.05**	**0.20, 1.91**	**0.019**
BFI-Fatigue									
Predictor									
Smoking status	**−5.72**	**−10.3, −1.13**	**0.018**	**−5.73**	**−10.4, −1.07**	**0.021**	−3.05	−7.32, 1.22	0.172
Smoking status*month	−0.31	−1.00, 0.39	0.389	−0.30	−0.99, 0.39	0.396	−0.17	−0.90, 0.55	0.651
Smoking status*cancer type	0.96	−8.19, 10.1	0.795	1.52	−7.62, 10.7	0.734	−3.01	−11.6, 5.56	0.498
Month	−0.09	−0.40, 0.22	0.572	−0.09	−0.41, 0.22	0.554	−0.11	−0.42, 0.20	0.482
Cancer type	−0.69	−5.25, 3.88	0.793	−0.30	−5.29, 4.69	0.840	−1.39	−6.09, 3.30	0.566
Month*cancer type	−0.23	−0.92, 0.46	0.521	−0.23	−0.92, 0.46	0.512	−0.27	−0.97, 0.42	0.444
Gender				2.35	−2.27, 6.98	0.321	0.77	−3.47, 5.01	0.726
Age				0.05	−0.16, 0.27	0.622	0.13	−0.05, 0.30	0.152
Stage				**2.23**	**0.26, 4.20**	**0.030**	1.58	−0.24, 3.39	0.089
Stage*cancer type				−2.25	−6.22, 1.73	0.279	−1.46	−5.11, 2.19	0.442
Baseline							**0.37**	**0.22, 0.52**	**0.001**
Income							**−1.22**	**−2.41, −0.03**	**0.050**
Income*month							−0.15	−0.34, 0.05	0.173
Income*cancer type							1.65	−0.65, 3.95	0.139
BPI-Severity									
Predictor									
Smoking status	−1.39	−4.21, 1.43	0.338	−0.71	−3.43, 2.02	0.617	1.40	−1.02, 3.82	0.260
Smoking status*month	0.08	−0.26, 0.42	0.643	0.08	−0.26, 0.41	0.648	0.20	−0.13, 0.54	0.242
Smoking status*cancer type	1.41	−4.21, 7.04	0.627	2.72	−2.46, 7.91	0.311	0.48	−3.67, 4.62	0.799
Month	0.05	−0.11, 0.22	0.510	0.05	−0.11, 0.22	0.514	0.05	−0.11, 0.21	0.537
Cancer type	**−3.57**	**−6.37, −0.76**	**0.016**	−2.84	−5.75, 0.08	0.064	**−4.30**	**−6.83, −1.77**	**0.002**
Month*cancer type	−0.03	−0.36, 0.31	0.836	−0.03	−0.37, 0.30	0.826	−0.08	−0.40, 0.24	0.651
Gender				2.44	−0.34, 5.21	0.090	1.75	−0.66, 4.16	0.162
Age				−0.11	−0.25, 0.02	0.118	−0.04	−0.13, 0.06	0.482
Stage				**1.34**	**0.21, 2.47**	**0.025**	0.48	−0.46, 1.41	0.320
Baseline							**0.37**	**0.25, 0.48**	**0.000**
Income							**−0.81**	**−1.43, −0.20**	**0.018**
Income*month							**−0.16**	**−0.24, −0.07**	**0.001**
Income*cancer type							**2.28**	**1.15, 3.41**	**0.000**

Smoking status is coded abstinent at all follow-ups [1] and not abstinent at all follow-ups [0].
Cancer type is coded as head and neck [0] and thoracic [1]. Gender is coded as male [0] and female [1].
Model A: The base model assesses abstinent versus not abstinent in the context of cancer type (H/N versus thoracic) and month (2, 4, 6, 12).
Model B: This model assesses abstinent versus not abstinent after adding three traditional control variables (age, gender, and stage) to the base model A.
Model C: This model assesses abstinent versus not abstinent after adding two variables found to be a predictor of the outcome measure in preliminary analyses—baseline quality of life measure and income—to model B.
Bold font denotes $p \leq 0.050$.
CES, Center for Epidemiological Studies; BFI, Brief Fatigue Inventory Scale; BPI, Brief Pain Inventory; CI, confidence interval.

was an interaction of gender with cancer type ($p = 0.028$) with the gender difference greater for TH patients. Model C found that abstinent participants exhibited lower CES-D scores ($p = 0.028$). As observed in the preliminary analyses, baseline CES-D, income, and the interactions of income with month and cancer type were significant predictors ($ps < 0.02$). Gender, cancer type, and the interaction of month and cancer type also predicted CES-D scores in this model ($ps < 0.05$).

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Fatigue

Model A showed that those abstinent exhibited lower BFI scores ($p = 0.018$). Model B also showed that abstinent participants exhibited lower BFI scores ($p = 0.021$). In addition, model B showed that later-stage patients exhibited higher BFI scores ($p = 0.030$). In contrast, model C did not show a significant effect for smoking status on BFI scores ($p = 0.172$) when baseline BFI ($p < 0.001$) and income ($p = 0.050$) were included. There were no other significant predictors in model C.

Pain severity

Model A showed that HN patients exhibited greater BPI-Severity scores ($p = 0.016$). Model B showed that those with later-stage cancer exhibited greater BPI-Severity scores ($p = 0.025$). Model C showed that cancer type, baseline BPI-Severity, income, and the interaction of income with month and cancer type were significant predictors ($ps < 0.02$). Smoking status was not a significant predictor in any of the three models ($ps > 0.25$).

Conclusions

In the current study, we examined relationships among smoking status and quality of life indicators in lung and head and neck cancer patients who underwent surgical treatment and had quit smoking within 6 months prior to surgery or made a quit attempt immediately after surgery. Results revealed that during the year after surgery, patients who maintained abstinence from smoking reported lower levels of depressive symptoms than patients who resumed smoking, even after adjusting for follow-up month, cancer type (lung versus head and neck) gender, cancer stage, income, and baseline (i.e., at the time of surgery) depressive symptoms.

Most smokers are motivated to quit smoking to improve their long-term physical health, regardless of whether they have been diagnosed with cancer [33,34]. At the same time, concerns about more immediate negative effects of smoking cessation on quality of life may represent a significant barrier to maintaining abstinence, for both the general population of smokers [35] and cancer patients [34]. The current study adds to a growing literature suggesting that smoking abstinence is associated with beneficial, rather than detrimental, effects on depressive symptomatology [36] and extends this important finding to cancer patients. This information may be used to alleviate concerns of both patients and oncology providers that smoking cessation would have a negative effect on mood [34], and to motivate quit attempts and sustained abstinence in these patients, for whom smoking cessation is especially urgent and medically warranted.

Our analyses also revealed that post-surgery smoking abstinence was associated with reduced fatigue after adjusting for follow-up month, cancer type, gender, and cancer stage; however, this relationship was no longer significant after additional adjustment for income and baseline fatigue. Additionally, post-surgery smoking abstinence was not significantly associated with pain severity. Although some previous studies have found that smoking among head and neck and lung cancer patients was associated with increased pain and fatigue, for example, [20,21,23], these studies compared current smokers with former (distant and recent grouped together) and never smokers, rather than with only recent former smokers who had quit since diagnosis as in the current study.

Models in the current analyses also revealed that higher income was associated with higher quality of life (lower depressive symptoms, fatigue, and pain) at follow-up. Furthermore, there were significant interactions between income and cancer type and between income and follow-up month for depressive symptoms and pain, such that the protective effect of higher income on these variables was more pronounced for HN patients relative to TH patients. The relationship between these variables and income also grew stronger over time, perhaps because quality of life at earlier time points was driven more by factors directly related to surgery (i.e., medical complications) and the protective effects of socioeconomic status did not truly emerge until later. Furthermore, higher income may provide more resources for connecting patients with support services including both social support and instrumental supports (e.g., help with daily living tasks) during the survivorship period. These outcomes are consistent with previous literature demonstrating a significant relationship between socioeconomic status and treatment outcomes in head and neck and lung cancer patients, including morbidity, mortality, and quality of life [37,38].

There are several limitations of the current study that must be acknowledged. First, the sample was predominantly Caucasian and limited to patients diagnosed with head and neck or lung cancer who evidenced baseline differences by cancer type. However, it is important to note that our analytic approach included cancer type and any significant interactions between cancer type and baseline variables to account for such differences. Future studies should extend this work to more diverse patients with other types of cancer and appropriately control for differences between cancer types, as was performed in the current study. Second, a more comprehensive battery that includes other quality of life indicators such as social, relationship, educational/work, and leisure functioning would also be beneficial. Third, because participants were not randomized to abstain or smoke, the temporal order of the relationship between abstinence and quality of life cannot be determined and causal inferences cannot be made.

Findings from the current study add to a growing body of research indicating that smoking cessation is associated with long-term benefits for quality of life; specifically, the

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current study found that patients who abstained from smoking for 1 year after surgical cancer treatment reported reduced depressive symptoms relative to patients who resumed smoking. Prior research reflects a discomfort among oncology providers in discussing smoking cessation that may be in part be due to a reluctance to take away something pleasurable from patients at a time of heightened distress [34]. Thus, our findings may be incorporated into interventions for this population to motivate sustained abstinence among patients as well as changing attitudes and behaviors of providers.

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Conflict of interest

There are no financial disclosures for any of the authors.

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