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Original Article

Smoking Is Related to Worse Cancer-related Symptom Burden

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Abstract

Background: Cigarette smoking is related to greater cancer incidence, worse cancer-related clinical outcomes, and worse patient quality of life. Few studies have evaluated the role of smoking in patients' experiences of cancer-related symptom burden. This study examined relationships between smoking and total symptom burden as well as the incidence of severe symptoms among adult cancer patients.

Patients and Methods: Patients at Moffitt Cancer Center completed self-report surveys as part of routine cancer care. Symptom burden was evaluated as the sum of individual symptom ratings (total symptom burden) and the number of symptoms rated severe (incidence of severe symptoms). Zero-inflated negative binomial modeling was used to evaluate the relationships between smoking status (ever vs never smoker) and symptom burden outcomes controlling for relevant sociodemographic and clinical covariates and accounting for the proportion of participants reporting no symptom burden.

Results: This study included 12 571 cancer patients. More than half reported a history of cigarette smoking (n = 6771, 55%). Relative to never smokers, participants with a smoking history had 15% worse expected total symptom burden (ratio = 1.15, 95% confidence interval [CI] 1.11-1.20, P < .001) and 13% more expected severe symptoms (ratio = 1.13, 95% CI 1.05-1.21, P = .001) above and beyond the effects of relevant sociodemographic and clinical characteristics.

Conclusion: Results provide support that smoking is associated with worse cancer symptom burden. More research is needed to evaluate how smoking history (ie, current vs former smoker) and smoking cessation influence cancer symptom burden.

Key words: cancer; cigarette smoking; patient-reported outcomes; symptom burden.

Implications for Practice

Any history of cigarette smoking was associated with worse total cancer symptom burden and greater incidence of severe symptoms in a large sample of adult cancer patients evaluated as part of routine cancer care. Results may be used to develop interventions to reduce cancer symptom burden and assist patients with quitting smoking.

Cigarette smoking is a strong predictor of cancer incidence,[1-4] with recent estimates indicating that smoking is linked to up to 40% of cancer diagnoses in the United States.[5] Smoking is also related to worse treatment outcomes (eg, more days hospitalized post-stem cell transplant),[6] worse post-treatment outcomes (eg, greater risk of surgical site infections),[7] and worse long-term outcomes (eg, mortality,[8-10] recurrence).[10-12] In addition to clinical outcomes, there is growing evidence that smoking is related to worse patient-reported outcomes (PROs), such as quality of life and symptom burden. PROs provide valuable information about patients' lived experiences and often have prognostic value for clinical outcomes above and beyond disease-related clinical indicators.[13,14] Although substantial work shows that smoking is associated with worse quality of life in cancer populations,[15-18] few studies have evaluated how smoking relates to patients' experiences of cancer-related symptom burden. This is a critical oversight, as cancer symptom burden has implications for treatment tolerability[19] and potentially treatment efficacy. Thus, assessing and managing cancer symptom burden is a critical component of high-quality cancer care that has important public health implications.

There are some exceptions in the literature. One recent study evaluated the effects of cigarette smoking on symptom

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burden among more than 700 cancer patients, of whom approximately 14% were current (n = 85) or past smokers (n = 17).[20] Current smokers (relative to non-smokers) reported a greater total symptom burden during cancer treatment and 6 months post-treatment. However, a more recent study of 300 patients with advanced cancers, of whom 49% were former smokers (n = 148) and 11% were current smokers (n = 33), observed no differences in total symptom burden between smokers and non-smokers.[21]

A limitation of these past studies is the small samples of current and/or past smokers included (ie, less than 300 individuals with a smoking history across both studies), which limits the generalizability of conclusions. More research is warranted to determine the association between smoking history and symptom burden, which may help future researchers develop interventions to reduce cancer symptom burden and assist patients with quitting smoking. The goal of this study was to examine the relationship between cigarette smoking history and patient-reported symptom burden among adult cancer patients. Symptom burden was considered in two ways: (1) similar to past research, total symptom burden was assessed as the sum of individual symptom ratings using a validated PRO measure, and (2) building on past research, the incidence of severe symptoms was assessed as the number of symptoms rated severe by each patient. It was hypothesized that patients with a history of smoking would report a worse symptom burden than patients without a history of smoking across both outcomes.

Methods

Participants and Procedures

The study was reviewed by the Advarra Institutional Review Board (IRB) and determined to be exempt from IRB oversight (Pro00039944). Participants were patients at Moffitt Cancer Center who completed PRO measures during routine clinical care from February 2017 to July 2020 as part of a larger effort to collect real-world PRO data from cancer patients outside the context of clinical trials. At the time of data analysis, data were available from patients seen in the Radiation Oncology and Supportive Care Medicine clinics. The Supportive Care Medicine clinic includes experts in integrative, palliative, and behavioral medicine who focus on improving patients' well-being. For this analysis, eligible patients were at least 18 years old, diagnosed with cancer, and completed PRO measures at least once. There were no exclusion criteria. For patients who completed PRO measures more than once, their first PRO responses were included in these analyses.

Measures

Demographic and Clinical Data

Participants' demographics and clinical data were abstracted from internal databases at Moffitt Cancer Center. Demographic data included age, gender, race, ethnicity, and marital status. Clinical data included age at the time of cancer diagnosis, primary cancer site, stage of disease, cancer status (ie, current active disease vs no active disease), and treatment history (ie, current, past, or never treated with surgery, chemotherapy, radiation therapy, endocrine therapy, and immunotherapy).

Cigarette Smoking History

Information about participants' cigarette smoking history was obtained from 2 data sources: electronic survey items that are routinely completed by new patients at Moffitt Cancer Center and documented in the electronic health record, and data from the Florida Cancer Data System (FCDS) that corresponds to a patient's most recent cancer diagnosis. Items related to cigarette smoking across the 2 data sources were merged to minimize missingness. Example patient-reported items included *current cigarette smoking status* (current, former, never smoker) and *lifetime smoking history* (positive history, negative history). Example FCDS items include *cigarette use* (current, former, never user). Combining data from these two sources resulted in a single variable with minimal missing data that indicated each participants' cigarette smoking history (any cigarette smoking history, never smoker).

Symptom Burden

Symptom burden was assessed with a modified version of the Edmonton Symptom Assessment System (ESAS-r-CSS).[22] The ESAS-r-CSS is comprised of 9 items included in the original ESAS that assess the incidence and severity of common symptoms experienced during cancer treatment (ie, anxiety, depression, drowsiness, lack of appetite, nausea, overall well-being, pain, shortness of breath, tiredness). The modified ESAS used institutionally also assessed the incidence and severity of 3 additional symptoms: constipation, difficulty sleeping, and spiritual well-being.[23,24] Symptoms were rated on an 11-point Likert-type scale from 0 (none) to 10 (worst possible). This study considered symptom burden in two ways. First, a total symptom burden score was calculated by summing all individual symptom ratings with higher scores indicating worse symptom burden (possible range 0-120). Second, a severe symptom score was calculated by summing the number of symptoms rated severe (ie, ≥7; possible range 0-12).

Statistical Analyses

Statistical analyses were performed using SAS 9.4 (Cary, NC). Descriptive statistics (ie, means, standard deviations, ranges, frequencies, and percentages) were used to characterize patients' demographic and clinical characteristics. Zero-inflated negative binomial (ZINB) models were used to evaluate predictors of total symptom burden and severe symptoms. ZINB analyses model zero-inflated count variables with overdispersion and a high incidence of zero scores. In this study, ZINB models included predictors of no symptom burden and predictors of any symptom burden. First, multivariable logistic regression models were estimated to identify relevant sociodemographic and clinical variables that predicted the zero-inflation component of the model (eg, reports of zero symptom burden, zero severe symptoms) using backward selection and a criterion of 0.05 for removal of a variable. Then, ZINB models were fit to model the expected outcome scores in the negative binomial component of the model (eg, quantifying the symptom burden and severe symptom scores) while accounting for the proportion of participants reporting a zero score (zero-inflation component). Variables selected from the multivariable logistic regression model were included as predictors in the zero-inflation component of the model and held fixed. All relevant sociodemographic and clinical variables were entered as

Table 1. Participants' demographic and clinical characteristics (N = 12 571).

Variables	Statistic
Cigarette smoking history; *n* (%)	
Any smoking history	6771 (55%)
Never smoker	5446 (45%)
Missing	354 (-)
Age at time of cancer diagnosis, years; M (SD), range	60.68 (12.79), 18-94
Gender; *n* (%)	
Female	5759 (46%)
Male	6810 (54%)
Missing	2 (-)
Race; *n* (%)	
Asian	209 (2%)
Black/African American	944 (8%)
Other	546 (4%)
White	10 764 (86%)
Missing	108 (-)
Ethnicity; *n* (%)	
Hispanic/Latino	1115 (9%)
Non-Hispanic/Latino	11 320 (91%)
Missing	136 (-)
Marital status; *n* (%)	
Married	7228 (58%)
Not married	3260 (26%)
Missing	2083 (17%)
Cancer status; *n* (%)	
Active disease	6614 (54%)
No active disease	5624 (46%)
Missing	233 (-)
Primary cancer site; *n* (%)	
Bone	64 (1%)
Breast	2089 (17%)
Endocrine	182 (2%)
Gastrointestinal	1205 (10%)
Gynecologic	633 (5%)
Genitourinary	415 (3%)
Head and neck	1136 (9%)
Hematologic	840 (7%)
Lung	2014 (16%)
Male genital	2212 (18%)
Neurologic	447 (4%)
Sarcoma	491 (4%)
Skin	784 (6%)
Missing	59 (-)
Stage of disease; *n* (%)	
0	234 (2%)
I	2612 (21%)
II	2809 (22%)
III	2246 (18%)
IV	2504 (20%)
Missing	2166 (17%)
Surgery; *n* (%)	
Current	3327 (27%)
Past	3827 (30%)
Never	5417 (43%)
Chemotherapy; *n* (%)	
Current	1119 (9%)
Past	4028 (32%)
Never	7424 (59%)
Radiation therapy; *n* (%)	
Current	1804 (14%)
Past	3494 (28%)
Never	7273 (58%)
Endocrine therapy; *n* (%)	
Current	568 (5%)
Past	1444 (12%)
Never	10 559 (84%)
Immunotherapy; *n* (%)	
Current	361 (3%)
Past	1040 (8%)
Never	11 170 (89%)

Percentages may not sum to 100 due to rounding.

predictors in the negative binomial component of the model and refined using backward selection with a criterion of 0.05. Any variable removed from the negative binomial component in the backward selection process resulted in the software also removing the variable from the zero-inflation component. To evaluate the relationship between smoking history and the symptom burden outcomes, smoking history was included as a predictor in the zero-inflation and negative binomial components of the ZINB models for each outcome. Finally, the Vuong test was used to test the appropriateness of the ZINB model compared with standard negative binomial regression.[25]

Results

Patient Characteristics

A total of 12 571 participants were included in these analyses. The demographic and clinical characteristics of the sample are shown in Table 1. Approximately half of the participants reported a history of smoking (55%) and were male (54%). Most participants were White (86%) and non-Hispanic (91%). The majority of participants with a known marital status were married (58%). Approximately half of the participants had active cancer (54%) and the average age at diagnosis was 60.68 years old (SD = 12.79, range 18-94). The three most common diagnoses were male genital cancer (eg, testicular, penile; 18%), breast cancer (17%), and lung cancer (16%).

Only 1% of participants (n = 137) were missing any symptom burden data. A total of 15% of participants (n = 1798) reported no symptom burden (ie, total score = 0), and the average total symptom burden score was 21.73 (SD = 21.82, median = 15, range 0-113). A total of 59% of participants (n = 7291) reported no severe symptoms, and the

Table 2. Zero-inflation and negative binomial components of the ZINB model predicting total symptom burden.

Predictors of zero-inflation component of ZINB model predicting total symptom burden	**Estimate**	**OR**	**95% CI**	***P*-value**
Any smoking history	−0.23	0.75	0.66-0.84	<.001
Age	0.05	1.05	0.99-1.10	.087
Female gender	−0.61	0.54	0.45-0.65	<.001
Active disease	−0.19	0.82	0.72-0.94	.004
Primary cancer site				<.001
Bone	−0.82	0.44	0.12-1.58	.209
Breast	0.31	1.36	0.99-1.87	.056
Endocrine	0.32	1.38	0.80-2.37	.245
Gastrointestinal	−0.42	0.66	0.47-0.92	.016
Gynecologic	−0.18	0.83	0.54-1.28	.403
Genitourinary	−0.32	0.73	0.47-1.12	.149
Head and neck	−0.03	0.97	0.71-1.33	.858
Hematologic	0.02	1.02	0.70-1.50	.910
Lung	−0.33	0.72	0.53-0.98	.034
Male genital	0.48	1.61	1.24-2.09	<.001
Neurologic	0.29	1.33	0.87-2.04	.186
Sarcoma	0.31	1.37	0.97-1.93	.077
Skin (reference group)	-	-	-	-
Stage of disease				<.001
I	−0.21	0.81	0.55-1.19	.280
II	−0.51	0.60	0.41-0.89	.012
III	−0.37	0.69	0.46-1.04	.073
IV	−0.82	0.44	0.29-0.68	<.001
Unknown	−0.66	0.52	0.34-0.79	.002
0 (reference group)	-	-	-	-
Chemotherapy				<.001
Current	−0.62	0.54	0.40-0.73	<.001
Past	−0.15	0.86	0.73-1.02	.081
Never (reference group)	-	-	-	-
Radiation therapy				.001
Current	0.30	1.35	1.12-1.62	.002
Past	0.21	1.23	1.06-1.43	.006
Never (reference group)	-	-	-	-
Endocrine therapy				.003
Current	−0.05	0.95	0.73-1.24	.709
Past	−0.37	0.69	0.55-0.86	.001
Never (reference group)	-	-	-	-

Predictors of negative binomial component of ZINB model predicting total symptom burden	**Estimate**	**Ratio**	**95% CI**	***P*-value**
Any smoking history	0.14	1.15	1.11-1.20	<.001
Age	−0.08	0.93	0.91-0.94	<.001
Female gender	0.13	1.13	1.08-1.18	<.001
Race				
Asian	−0.15	0.86	0.76-0.99	.031
Black/African American	0.17	1.18	1.11-1.26	<.001
Other	0.09	1.10	1.01-1.19	.033
White (reference group)	-	-	-	-
Marital status				<.001
Married	−0.13	0.88	0.84-0.91	<.001
Unknown	−0.05	0.95	0.90-1.01	.085

Table 2. Continued

Predictors of negative binomial component of ZINB model predicting total symptom burden	Estimate	Ratio	95% CI	*P*-value
Not married (reference group)	-	-	-	-
Active disease	0.20	1.22	1.17-1.27	<.001
Primary cancer site				<.001
Bone	0.26	1.29	1.02-1.64	.033
Breast	0.03	1.03	0.94-1.12	.560
Endocrine	0.11	1.11	0.95-1.30	.198
Gastrointestinal	0.18	1.19	1.09-1.31	.001
Gynecologic	0.24	1.27	1.14-1.41	<.001
Genitourinary	0.31	1.36	1.21-1.52	<.001
Head and neck	0.10	1.10	1.00-1.21	.040
Hematologic	0.14	1.15	1.03-1.27	.010
Lung	0.18	1.19	1.10-1.30	<.001
Male genital	–0.23	0.79	0.73-0.86	<.001
Neurologic	–0.09	0.91	0.81-1.03	.137
Sarcoma	0.17	1.19	1.06-1.33	.003
Skin (reference group)	-	-	-	-
Stage of disease				<.001
I	0.07	1.08	0.94-1.23	.307
II	0.12	1.12	0.98-1.29	.101
III	0.15	1.17	1.01-1.34	.033
IV	0.24	1.27	1.11-1.47	.001
Unknown	0.19	1.21	1.05-1.40	.010
0 (reference group)	-	-	-	-
Chemotherapy				<.001
Current	0.20	1.22	1.15-1.30	<.001
Past	0.08	1.08	1.04-1.13	.001
Never (reference group)	-	-	-	-
Radiation therapy				<.001
Current	–0.21	0.81	0.77-0.86	<.001
Past	–0.05	0.95	0.91-0.99	.023
Never (reference group)	-	-	-	-
Endocrine therapy				<.001
Current	0.04	1.04	0.95-1.14	.380
Past	0.15	1.16	1.09-1.23	<.001
Never (reference group)	-	-	-	-

Abbreviations: CI, confidence interval; OR, odds ratio.

average incidence of severe symptoms was 1.21 (SD = 1.05, median = 0, range 0-12).

Total Symptom Burden

Supplementary Table 1 shows the results of the multivariable logistic regression model to identify relevant sociodemographic and clinical variables associated with zero total symptom burden. Table 2 shows the results of the ZINB model predicting total symptom burden. In the zero-inflation component (ie, participants with zero symptom burden), participants with a smoking history had lower odds of reporting zero symptom burden relative to never smokers (OR = 0.75, 95% confidence interval [CI] 0.66-0.84, $P < .001$) above and beyond the effects of sociodemographic and clinical covariates. In the negative binomial component (ie, participants with any symptom burden), participants with a smoking history had 15% worse expected symptom burden than never smokers (ratio = 1.15, 95% CI 1.11-1.20, $P < .001$) above and beyond the effects of sociodemographic and clinical covariates. Worse symptom burden was also associated with female gender, Black and other race (relative to White), active disease, specific disease sites (ie, bone, gastrointestinal, gynecologic, genitourinary, head and neck, hematologic, lung, and sarcoma relative to skin cancer), stage III and IV disease (relative to stage 0), current and past treatment with chemotherapy, and past treatment with endocrine therapy. Less expected symptom burden was associated with younger age, Asian race (relative to White), being married, male genital cancer (relative to skin cancer), and current and past treatment with radiation therapy. The Vuong test showed that the ZINB model was preferable to a standard negative binomial regression model ($P < .001$).

Table 3. Zero-inflation and negative binomial components of the ZINB model predicting severe symptoms.

Predictors of zero-inflation component of ZINB model predicting severe symptoms	Estimate	OR	95% CI	*P*-value
Any smoking history	–0.41	0.66	0.58-0.76	<.001
Age	0.07	1.07	1.01-1.13	.016
Female gender	–0.39	0.68	0.57-0.81	<.001
Race				.287
Asian	0.45	1.56	0.95-2.59	.082
Black/African American	–0.12	0.89	0.71-1.12	.312
Other	–0.04	0.96	0.72-1.29	.800
White (reference group)	-	-	-	-
Active disease	–0.39	0.68	0.59-0.78	<.001
Primary cancer site				<.001
Bone	–1.19	0.31	0.08-1.23	.096
Breast	–0.11	0.90	0.65-1.24	.506
Endocrine	–0.17	0.85	0.46-1.54	.587
Gastrointestinal	–0.46	0.63	0.45-0.89	.008
Gynecologic	–0.64	0.53	0.35-0.80	.003
Genitourinary	-0.37	0.69	0.45-1.04	.078
Head and neck	0.09	1.09	0.79-1.52	.596
Hematologic	–0.27	0.76	0.53-1.10	.148
Lung	–0.47	0.62	0.45-0.86	.004
Male genital	0.34	1.40	1.02-1.93	.035
Neurologic	0.12	1.13	0.71-1.79	.608
Sarcoma	–0.30	0.74	0.49-1.12	.156
Skin (reference group)	-	-	-	-
Stage of disease				<.001
I	–0.46	0.63	0.40-1.00	.054
II	–0.60	0.55	0.34-0.87	.011
III	–0.69	0.50	0.31-0.80	.004
IV	–0.87	0.42	0.26-0.68	<.001
Unknown	–0.88	0.42	0.25-0.68	.001
0 (reference group)	-	-	-	-
Radiation therapy				.438
Current	–0.14	0.87	0.69-1.09	.222
Past	–0.01	0.99	0.85-1.16	.941
Never (reference group)	-	-	-	-

Predictors of negative binomial component of ZINB model predicting severe symptoms	Estimate	Ratio	95% CI	*P*-value
Any smoking history	0.12	1.13	1.05-1.21	.001
Age	–0.08	0.92	0.90-0.95	<.001
Female gender	0.17	1.19	1.10-1.29	<.001
Race				<.001
Asian	–0.14	0.87	0.64-1.17	.350
Black/African American	0.28	1.33	1.19-1.49	<.001
Other	0.20	1.22	1.05-1.42	.009
White (reference group)	-	-	-	-
Active disease	0.20	1.23	1.14-1.32	<.001
Primary cancer site				<.001
Bone	0.03	1.03	0.68-1.55	.896
Breast	0.12	1.13	0.95-1.35	.183
Endocrine	0.10	1.10	0.82-1.49	.532
Gastrointestinal	0.18	1.20	1.00-1.43	.046

Table 3. Continued

Predictors of negative binomial component of ZINB model predicting severe symptoms	Estimate	Ratio	95% CI	*P*-value
Gynecologic	0.23	1.26	1.03-1.53	.022
Genitourinary	0.31	1.36	1.10-1.69	.005
Head and neck	0.18	1.19	0.99-1.44	.069
Hematologic	0.16	1.17	0.97-1.42	.102
Lung	0.11	1.12	0.94-1.33	.197
Male genital	−0.31	0.73	0.60-0.89	.002
Neurologic	−0.16	0.85	0.67-1.09	.191
Sarcoma	0.07	1.07	0.86-1.33	.549
Skin (reference group)	-	-	-	-
Stage of disease				<.001
I	0.02	1.02	0.74-1.40	.917
II	0.12	1.12	0.82-1.55	.475
III	0.16	1.17	0.85-1.61	.346
IV	0.27	1.31	0.95-1.81	.101
Unknown	0.18	1.20	0.86-1.66	.281
0 (reference group)	-	-	-	-
Radiation therapy				<.001
Current	−0.33	0.72	0.65-0.80	<.001
Past	−0.07	0.93	0.86-1.01	.088
Never (reference group)	-	-	-	-

Abbreviations: CI, confidence interval; OR, odds ratio.

Severe Symptoms

Supplementary Table 2 shows the results of the multivariable logistic regression model to identify relevant sociodemographic and clinical variables associated with zero severe symptoms. Table 3 shows the results of the ZINB model predicting number of severe symptoms. In the zero-inflation component (ie, participants with zero severe symptoms), participants with a smoking history had lower odds of reporting zero severe symptoms relative to never smokers (OR = 0.66, 95% CI 0.58-0.76, $P < .001$) above and beyond the effects of sociodemographic and clinical covariates. In the negative binomial component (ie, participants with at least one severe symptom), participants with a history of smoking had 13% more expected severe symptoms than never smokers (ratio = 1.13, 95% CI 1.05-1.21, $P = .001$) above and beyond the effects of sociodemographic and clinical covariates. More severe symptoms were also associated with female gender, Black and other race (relative to White), active disease, and specific disease sites (ie, gastrointestinal, gynecologic, and genitourinary cancers relative to skin cancer). Fewer expected severe symptoms were associated with younger age, male genital cancer (relative to skin cancer), and current and past treatment with radiation therapy. The Vuong test showed that the ZINB model was preferable to a standard negative binomial regression model ($P < .001$).

Discussion

This study examined relationships between cigarette smoking (ever vs never), total symptom burden, and incidence of severe symptoms in a large sample of adult cancer patients evaluated as part of routine cancer care at Moffitt Cancer Center. Consistent with hypotheses, smoking was associated with worse total symptom burden and more severe symptoms, above and beyond the effects of sociodemographic and clinical factors. This contributes to a small but growing body of literature and provides additional support that smoking is broadly associated with worse cancer-related symptom burden.

Past research has led to inconsistent conclusions regarding a relationship between cigarette smoking and total cancer-related symptom burden, possibly due to differences in sample characteristics. For example, one study found an association between smoking and worse total symptom burden among cancer patients who were mostly naive to chemotherapy and/or radiation therapy and were receiving treatment with curative rather than palliative intent (although exact proportions were not reported).[20] By contrast, all participants in another study had advanced cancer, and patients were excluded if they were treated with curative intent.[21] The current study included participants with more variability in the stage of disease than observed in either of these past studies. It is possible that the strength of the association between smoking and total symptom burden differs across disease stages, and this possibility should be explored in future research. Moreover, past studies included relatively small samples of smokers (ie, less than 300 patients with a smoking history across both studies). The proportion of patients with a smoking history in this study was considerably larger ($n = 6771$), and thus improves the generalizability of findings relative to past research. To the best of our knowledge, this was the first study to evaluate the relationship between smoking and incidence of severe cancer-related symptoms, and findings complement a body of work that has evaluated smoking in relation to individual symptoms, such as shortness of breath[26,27] and pain.[21,28-30]

Smoking cessation can improve clinical cancer outcomes, even when initiated at the time of cancer diagnosis.[11,31]

Smoking cessation may also reduce cancer symptom burden, and future work should explore this possibility. Cessation treatments that are developed with the unique circumstances of cancer patients in mind should be evaluated, which would allow for the targeting of specific factors relevant to this population (eg, physical pain, maladaptive coping strategies, shame, guilt).[32-35] Additional recommendations include having low-barrier treatment options (eg, telemedicine), leveraging warm handoffs between clinical teams and smoking cessation programs, and using opt-out approaches.[35] However, researchers and clinicians must be sensitive to the role of stigma when discussing smoking cessation with cancer patients. History of smoking carries a distinct stigma among cancer patients and survivors, particularly those diagnosed with lung cancer, due to the perception of having contributed to their disease.[36-38] Smoking stigma among cancer patients, in turn, is associated with worse quality of life and depression.[38,39] Thus, messaging around smoking cessation and smoking relapse prevention programs for cancer populations must be tailored to this population's unique psychosocial needs and concerns relative to other populations.[40,41]

Limitations of this study include the unavailability of more specific information about cigarette smoking status (eg, current vs past smoker for participants with a history of smoking). PRO data were only collected from patients treated in the Radiation Oncology and Supportive Care Medicine clinics, and thus results may not generalize to all cancer patients seen in other clinic settings. Lastly, we are unable to determine the degree to which reported symptoms were attributable to cancer versus other issues (eg, recent quit attempts, nicotine withdrawal). However, this study included a large and heterogeneous sample of real-world cancer patients who completed PRO measures as part of routine clinical care. PRO data were integrated with electronic medical records data, which allowed for analysis of sociodemographic and clinical data in relation to PROs. Finally, this study used multiple indicators of symptom burden as well as advanced statistical modeling to account for the proportion of patients reporting zero symptom burden.

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Conflict of Interest

Naomi Brownstein: American Cancer Society (Personal fees and non-financial support), American Statistical Association Section on Statistical Consulting, American Statistical Association Section on Statistical Learning and Data Science (Personal fees); **Kedar Kirtane**: Seattle Genetics, Oncternal Therapeutics, Veru, Myovant Sciences, and Immunomedics (OI); **Brian D. Gonzalez**: SureMed Compliance, Elly Health, KemPharm (C/A); **Heather S.L. Jim**: Janssen Scientific Affairs, Merck (C/A), Kite (RF). The other authors indicated no financial relationships.

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Author Contributions

Conception/design: L.B.O., P.A.S.J., and H.S.L.J. Data analysis and interpretation: N.C.B. and J.W. Manuscript writing: All authors. Final approval of manuscript: All authors. Formal analysis: J.W. and N.C.B. Data curation: J.W. Supervision: H.S.L.J., P.A.S.J., and N.C.B. Visualization: J.W. and L.B.O.

Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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