CURRENT ONCOLOGY
A Canadian Cancer Research Journal

ORIGINAL ARTICLE

The cost of failed first-line cancer treatment related to continued smoking in Canada

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ABSTRACT

Background Smoking by cancer patients and survivors causes adverse cancer treatment outcomes, but little information is available about how smoking can affect cancer treatment costs.

Methods We developed a model to estimate attributable cancer treatment failure because of continued smoking after a cancer diagnosis (AF_s). Canadian health system data were used to determine the additional treatment cost for AF_s for the most common cancers in Canada.

Results Of 206,000 patients diagnosed with cancer annually, an estimated 4789 experienced AF_s. The annual incremental cost associated with treating patients experiencing AF_s was estimated at between $198 million and $295 million (2017 Canadian dollars), reflecting an added incremental cost of $4,810–$7,162 per patient who continued to smoke. Analyses according to disease site demonstrated higher incremental costs where the smoking prevalence and the cost of individual second-line cancer treatment were highest. Of breast, prostate, colorectal, and lung cancers, lung cancer was associated with the highest incremental cost for treatment after AF_s.

Conclusions The costs associated with AF_s in Canada after a cancer diagnosis are considerable. Populations in which the smoking prevalence and treatment costs are high are expected to benefit the most from efforts aimed at increasing smoking cessation capacity for patients newly diagnosed with cancer.

Key Words Attributable cancer treatment failures, cost burden, smoking cessation

Curr Oncol. 2020 December:27(6)307–312 www.current-oncology.com

INTRODUCTION

Smoking by cancer patients and survivors decreases the effectiveness of cancer treatment[1,2], and smoking cessation after a cancer diagnosis can improve cancer treatment outcomes[3–9]. A recent report demonstrated substantial additional cancer treatment costs for patients who smoke after a cancer diagnosis[10], suggesting that smoking could add $3.4 billion annually to the cost of cancer treatment in the United States. The model estimating the added cost of treatment relies on identifying attributable failures associated with smoking (AF_s), which are defined as the excess number of cancer treatment failures caused by smoking. However, the overall estimates depend on baseline risks of cancer treatment failure in nonsmoking patients and on the prevalence of smoking, which can vary substantially by cancer disease site. No prior studies have estimated costs according to disease site or using defined health systems data.

Smoking cessation is critical for reducing the incidence of cancer, and cessation is advocated as a critical component of clinical care for cancer patients[9,11], but little information has been uncovered about which cancer disease sites and conditions provide the highest value from mitigating the incremental costs attributable to smoking. Given the high costs associated with continuing care and second-line therapies for patients with cancer[12,13], evaluating the effect of smoking on health outcomes within discrete cancer diagnoses could help to strengthen the economic justification for smoking cessation programs. The purpose of the present

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Supplemental material available at http://www.current-oncology.com

study was to use Canadian national metrics to estimate the cost of smoking by cancer disease site to create an economic framework for understanding where smoking might have the largest clinical impact on cancer care.

METHODS

Population and Model Overview

We developed a risk model to estimate failures of first-line cancer treatment attributable to smoking in an overall annual incident cancer cohort (Figure 1). The model was populated with Canadian inputs for all-cause cancer incidence, smoking prevalence, and first-line cancer treatment failure rates (Table I). First-line cancer treatment efficacy was modelled as a binary outcome (treatment failed, or patient cured) and continued smoking was modelled as an effect modifier for efficacy. The risk of first-line cancer treatment failure related to smoking (FR_s) was estimated as 1.6 based on the median risk for cancer-related mortality derived from Warren *et al.*[10] and the report *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General*[1].

The probability of FR_s for patients who smoked was evaluated using the method described by Warren *et al.*[10] and was derived using the failure rate for patients who were nonsmokers (FR_{ns}) and the odds ratio (OR) for treatment failure:

$$FR_s = (FR_{ns} * OR) / [1 - FR_{ns} + (OR * FR_{ns})].$$

The number of patients with cancer who continued smoking after diagnosis was estimated as $N * P_s$, where N is the annual incident population of patients with cancer in Canada (in 2017), and P_s is the smoking prevalence among patients with cancer. The number of patients with cancer

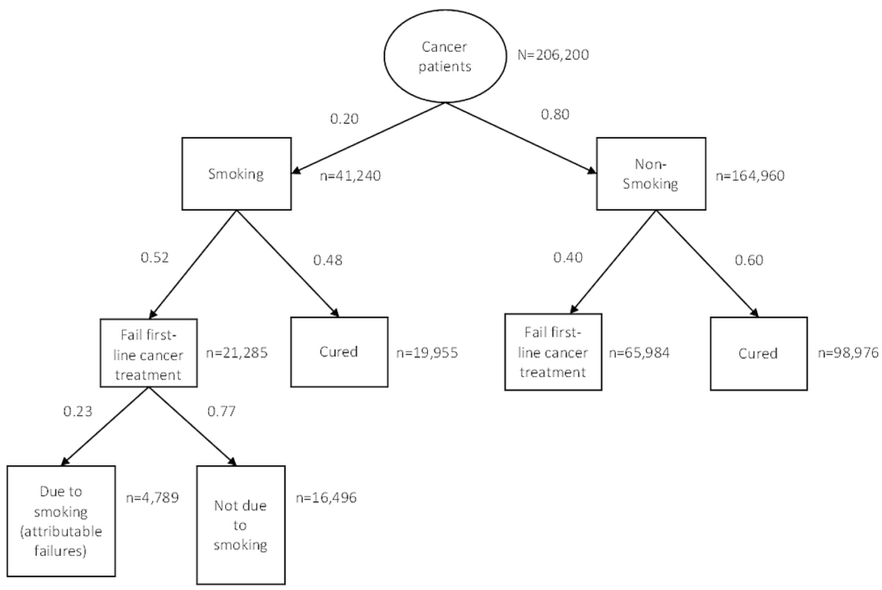

FIGURE 1 Cancer incidence, prevalence of smoking, and effects of first-line cancer treatment failure. See Table I for model inputs.

TABLE I Model inputs for cancer incidence, treatment failure, risk, and smoking prevalence

Parameter	Value	Source
Estimated annual incident patients with cancer, 2017 (all cancers)	206,200	Canadian Cancer Statistics Advisory Committee, 2018[14]
• Estimated annual incident patients with lung cancer, 2017	28,868	
• Estimated annual incident patients with breast cancer, 2017	26,600	
• Estimated annual incident patients with colorectal cancer, 2017	25,775	
• Estimated annual incident patients with prostate cancer, 2017	29,280	
Expected first-line treatment failure rate in patients who are nonsmokers	0.4	
Odds ratio of first-line cancer treatment failure in patients who are current smokers compared with those who are nonsmokers	1.6	United States, Department of Health and Human Services, 2014[1]
Smoking prevalence in patients with cancers in Canada	20%	Liu et al., 2016[15]
• Smoking prevalence in patients with breast cancer	18%	Berubé *et al.,* 2014[16]
• Smoking prevalence in patients with lung cancer	39%	Park et al., 2012[17]
• Smoking prevalence in patients with colorectal cancer	18%	Phipps et al., 2011[18], Martel et al., 2008[19]
• Smoking prevalence in patients with prostate cancer	16%	Rieken et al., 2015[20]

who smoked and for whom first-line treatment failed was estimated as $N * P_s * FR_s$. The AF_s is the difference between the number of patients with cancer who smoked and experienced first-line cancer treatment failure minus the failures expected if patients had not been smoking[10]:

$$AF_s = (N * P_s * FR_s) - (N * P_s * FR_{ns}) = N * P_s * (FR_s - FR_{ns}).$$

Costs

The economic burden associated with AF_s was estimated using the average costs for second-line treatment. The analysis was further disaggregated by cancer site, incorporating site-specific treatment costs and the incidence and smoking prevalence rates for the 4 most common cancers in Canada: lung, breast, colorectal, and prostate. The total cases of AF_s were estimated for the combination of smoking prevalences specific to each disease site. The total cost incurred as a result of AF_s was estimated by multiplying the total cases of first-line AF_s by the average annual second-line treatment cost. The average cost of second-line treatment was assumed to be at least as high as the average initial-phase treatment cost in Canada, as estimated by De Oliveira *et al.*[21] (Table II). A weighted average of the cost of initial-phase treatment for all cancer sites was estimated and adjusted to 2017 Canadian dollars using the Bank of Canada inflation calculator (see supplementary Appendix 1). A sensitivity analysis was conducted to evaluate the effect of varying the smoking prevalence and the annual total cost of second-line treatment, assuming that the initial-phase treatment cost was equal to the second-line treatment cost ($41,420) or assuming that the second-line treatment cost was the same as the terminal-phase cost ($61,670)[21] (see supplementary Appendix 2). A secondary analysis was conducted to evaluate the costs associated with cases of AF_s for prostate, lung, breast, and colorectal cancers individually, assuming initial- and terminal-phase costs as second-line treatment costs. An average initial-phase treatment failure rate of 0.4 was assumed for the various cancer sites.

RESULTS

Table I presents Canadian model inputs for incidence and prevalence of smoking and risk of AF_s. An estimated 206,200 patients will be diagnosed with cancer annually, with a 40% risk of cancer-related mortality[14]. For the purposes of the model presented here, the 40% risk of cancer-related mortality was used as the value for the overall estimate of first-line cancer treatment failure. Estimates for smoking prevalence ranged between 14% and 39% depending on the disease site[16–20] and 20% for patients with cancer overall[15].

Figure 1 summarizes the distribution of the annual incident cancer cases and cancer treatment failures in Canada according to smoking status. Of 206,200 incident cancer cases diagnosed annually, first-line cancer treatment failure is expected in 87,269 cases. Of 41,240 patients with cancer who are estimated to smoke at the time of diagnosis, 21,285 (52%) are predicted to experience failure of first-line cancer treatment, including 4789 first-line AF_s (23%). As Figure 2 shows, the AF_s per 10,000 patients increases linearly with smoking prevalence and increases as the risk for AF_s escalates. Because approximately 30% of patients with cancer who smoke misrepresent their tobacco use[22,23], those estimates are likely to be conservative.

We estimated the initial- and terminal-phase treatment costs for patients with cancer overall and for patients with cancer at specific disease sites (Table II). Table III shows the costs of treating AF_s across Canada by smoking prevalence. Under conditions of a 20% smoking prevalence, between CA$198 million and CA$295 million is spent treating patients who experience AF_s each year in Canada. Distributed across 41,240 patients who continue to smoke, the result is an estimated incremental cost per such patient of between CA$4,810 and CA$7,162. Results from Table III can be used to estimate cost savings if the smoking prevalence were to be reduced. For instance, reducing the prevalence of smoking from 20% to 5% would represent a cost savings of between CA$149 million and CA$221 million because of fewer cases of AF_s.

Table IV shows the cases of AF_s and the associated incremental costs for additional treatment in breast, prostate, colorectal, and lung cancer. Of those 4 cancer sites, lung cancer has the highest associated cost burden. Approximately 1300 cases of AF_s were estimated in the lung cancer group because of a high smoking prevalence (39%) and a high disease incidence (almost 29,000 annual cases). The estimated cases of AF_s for patients in the breast,

TABLE II Estimated cost of treating one first-line cancer treatment failure, by disease site, initial- or terminal-phase estimates[a]

Parameter	Second-line treatment cost equivalency	Value ($)
Average cost of treating patients for whom first-line treatment failed, all cancers	Initial phase	41,420
	Terminal phase	61,671
Average cost of treating patients for whom first-line treatment failed, lung cancer	Initial phase	23,957
	Terminal phase	58,570
Average cost of treating patients for whom first-line treatment failed, breast cancer	Initial phase	13,188
	Terminal phase	45,357
Average cost of treating patients for whom first-line treatment failed, colorectal cancer	Initial phase	27,972
	Terminal phase	54,589
Average cost of treating patients for whom first-line treatment failed, prostate cancer	Initial phase	7,951
	Terminal phase	44,222

[a] In 2017 Canadian dollars, based on estimates from De Olivera *et al.,* 2017[21].

prostate, and colorectal cancer groups were alike in number. However, the range of costs associated with initial- or terminal-phase treatment for disease at those sites (from Table I) highlights how such differences can play a dynamic role in the overall cost burden. For example, although the AF_S incidence was slightly higher for prostate cancer than for lung cancer, the higher smoking rate and the higher cost of treatment for patients with lung cancer (Table II) resulted in a considerably higher cost to treat the patients with AF_S in the lung cancer group. Using estimates for terminal-phase costs, cases of AF_S in lung cancer represent approximately 25% of the cost for treating AF_S in cancer overall, but just 14% of incident cancer cases.

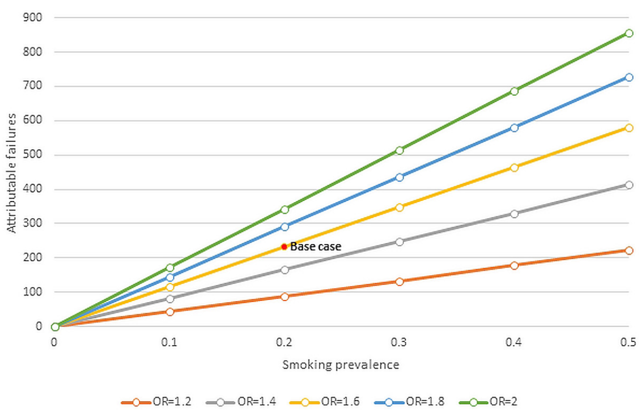

FIGURE 2 Attributable failures related to continued smoking per 10,000 total cancer patients. First-line cancer treatment failure rate in nonsmokers = 0.4, for 10,000 incident cases, all cancers. OR = odds ratio.

TABLE III Cost of treating attributable failures from smoking across Canada by cost of second-line treatment and smoking prevalence

Smoking prevalence	Second-line treatment cost, by phase ($)	
	Initial phase ($41,420/pt)	Terminal phase ($61,671/pt)
0.05	49,591,765	73,838,091
0.1	99,183,530	147,676,183
0.2	198,367,061	295,352,366
0.3	297,550,591	443,028,549
0.4	396,734,121	590,704,732
0.5	495,917,652	738,380,915

Pt = patient.

DISCUSSION

Costs associated with treating cases of AF_S are significant and vary with the prevalence of smoking and with disease-specific treatment costs. Reducing the smoking prevalence by 5 percentage points in cancer cases overall is estimated to save between CA$50 million and CA$74 million annually, related to the decreased need for additional cancer treatments. Because reductions in smoking are well known to lower other health care costs[1], those estimates of the cost savings are likely to be conservative. Disease sites such as lung cancer—for which the treatment cost and smoking prevalence are both higher—are most likely to yield the largest cost benefits. However, mitigation for disease sites with lower smoking prevalences, but highly curative treatment options (such as breast and prostate cancer) could potentially manifest in cost savings for non-cancer-related health conditions. Given the considerable economic burden of cancer treatment costs for the system and for patients, and increasing concerns about the sustainability of current levels of expenditure[24], there is an imperative to ensure that cancer treatments can achieve optimal outcomes for patients.

Our study reinforces the importance of implementing smoking cessation programs alongside cancer treatment across Canada as a key mechanism to improve treatment outcomes for patients and to reduce treatment costs in the system. In 2015, the Canadian Partnership Against Cancer formed the Pan-Canadian Tobacco Cessation and Cancer Care Network with the objective of implementing, by 2022, smoking cessation initiatives for patients with cancer attending all ambulatory cancer centres in all provinces and territories in Canada. To date, 6 provinces have reported implementing smoking cessation in their ambulatory cancer centres; the remaining 7 jurisdictions are in varying stages of implementation[25]. Key facilitators that encourage the integration of smoking cessation support include early engagement of leadership, clearly defined roles within project teams, engagement with patients and family, cessation support embedded into existing care pathways, leveraging of existing cessation support resources, use of electronic medical records, and use of key indicators to measure and track performance. Barriers to widespread implementation

TABLE IV Cost of treating attributable failures[a] from continued smoking (AF_S) in Canada, by disease site

Site	Annual incident cases (*n*)	Smoking prevalence in diagnosed pts (%)	AF_S	Estimated annual cost ($) of AF_S	
				Initial-phase costing	Terminal-phase costing
Lung cancer	28,868	39	1,307	31,322,364	76,576,821
Breast cancer	26,600	18	556	7,332,868	25,219,662
Colorectal cancer	25,775	18	539	15,070,772	29,441,496
Prostate cancer	29,280	16	544	4,325,672	24,058,593
All cancers	206,200	20	4,789	198,367,061	295,352,366

[a] Using an estimated 40% expected failure rate in patients who were nonsmokers, all disease sites.

and coverage of such programs include patient stigma, health care provider attitudes and knowledge, lack of perceived clinical skills to provide cessation support, lack of access to pharmacotherapy, competing priorities in oncology care, and cultural norms[26]. Sustained funding is key to the long-term success of programs after adoption, and the data herein assist in justifying support for cessation activities. Analyses of the cost of smoking cessation support in Canada, compared with cancer treatment costs, indicate strong financial justification[27,28].

Our study has several limitations. Although the median risk of treatment failure was derived from a U.S. Surgeon General's report[1], data about the actual overall risk of treatment failure by disease site and type of treatment are limited. Differences in mortality, recurrence, and toxicity for radiotherapy, surgery, and systemic therapy are possible, but treatment questions of that type remain untested. The average failure rate of 0.4 across a variety of cancer sites as assumed here might not accurately represent the true failure rates for each disease site. The baseline failure rate is a significant modulator of attributable failure, with higher consequential effects in disease sites with a higher expected cure rate[10]. However, the analyses presented here included both initial- and terminal-phase cancer treatment cost estimates to produce a conservative range for the total cost of AFs. Furthermore, given that the costs estimated by de Oliveira *et al.*[21] were based on clinical practice in 2009, the base-case cancer treatment costs are very likely conservative and underestimate the current cost of cancer treatment[10,24,29–31]. New approaches such as immunotherapy (estimated to cost US$130,000 per quality-adjusted life–year compared with conventional chemotherapy) are increasingly used in first or subsequent lines of cancer therapy[32–34]. In the era of advancing cancer costs, the estimates reported here are expected to be conservative, and measures to reduce AFs and its associated costs are expected to be increasingly cost-effective. However, the degree to which smoking cessation after a cancer diagnosis will prevent AFs, mitigate other smoking-related health conditions, and affect associated costs remains to be determined[35].

Our data demonstrate the costs associated with treating cases of AFs in patients with cancer, but the costs of implementing smoking cessation programs were not included. Earlier economic evaluations that have estimated the value of implementing smoking cessation programs in Canada as preventive measures for lung cancer screening[36,37] and as mitigation in cancer care[27] support cost-effectiveness. However, the methods and approaches that are best suited to achieve the optimal combination of reach and efficacy in cancer care on a national scale, while also ensuring equitable access to such services by the subpopulations that are most at risk of smoking-related treatment failures, remain unclear. Patient characteristics, access to care, and system resources vary across Canadian provinces, and it is expected that varied approaches to smoking cessation will be needed to standardize access to evidence-based smoking cessation support as a part of cancer treatment.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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