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Impact of Smoking on Health System Costs among Cancer Patients

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ABSTRACT

Objective

Smoking is the main modifiable cancer risk factor. The objective of this study was to examine the impact of smoking on health system costs among newly diagnosed adult cancer patients. Specifically, costs of cancer patients who were current smokers were compared with those of non-smokers from a publicly funded health system perspective.

Methods

This population-based cohort study of cancer patients used administrative databases to identify smokers and non-smokers (1 April 2014 - 31 March 2016) with ≥1-year follow-up. Researchers estimated the costs for health services such as hospitalizations, emergency room visits, drugs, home care services, and physician services (from time of diagnosis onwards). The difference in cost (i.e., incremental cost) between cancer patients who were smokers and those who were non-smokers was estimated using a generalized linear model (with log link and gamma distribution), and adjusted for age, sex, neighborhood income, rurality, cancer site, cancer stage, geographical region, and comorbidities,

Results

This study identified 3,606 smokers and 14,911 non-smokers. Smokers were significantly younger (61 vs 65 years), more likely to be male (53%), lived in poorer neighborhoods, had more advanced cancer stage, and were more likely to die within one year of diagnosis, compared to non-smokers. The regression model revealed that on average, smokers had significantly higher monthly healthcare costs ($5,091) than non-smokers ($4,847), $p<0.05$.

Conclusions

Smoking status has a significant impact on healthcare costs among cancer patients. On average, smokers incurred higher healthcare costs than non-smokers. These findings provide a further rationale for efforts to introduce evidence-based smoking cessation programs as a standard of care for cancer patients as they have the potential to not only improve patients' outcomes but also to reduce the economic burden of smoking on the healthcare system.

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Strengths and Limitations of this study

- Findings from this study support the integration of smoking cessation programs into cancer care treatment plans
- This study adds to the literature by providing up-to-date and precise health care cost estimates of smoking using existing administrative person-level costing approaches
- A limitation of this study is that it excludes a subset of relevant variables that may have had an influence on health outcomes and cost due to the nature of the study design (e.g., type of tumour, amount of duration of smoking)
- This study focused on the cost incurred to the public healthcare payer; and therefore, indirect costs were not considered and could be explored in future research
- The findings from this study should motivate policy makers to design, implement, and fund smoking cessation programs, which have the potential not only to improve patients' treatment outcomes but also to reduce the economic burden of smoking on the healthcare system

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INTRODUCTION

Cancer care is a substantial component of health care expenditures of developed countries.(1-3) In Canada, the economic burden of cancer was estimated to be $7.5 billion in 2012.(4) It is well recognized that smoking is the main modifiable risk factor for cancer (5) and it is estimated that it contributes to approximately 30% of all cancer deaths.(6, 7) Smoking can also harm directly or indirectly almost every organ of the body and is responsible for a number of other chronic diseases that contribute to higher health care costs.(5, 8-11) Quitting smoking after a diagnosis of cancer has been associated with improved general health, better quality of life, reduced toxicity, greater response to treatment (such as radiation therapy), and decreased risk of disease recurrence and second primary cancers.(12-14) Nevertheless, cancer patients are just as likely to smoke as the general public (with the smoking rate being approximately 20%);(15) furthermore, smoking cessation programs are rare in oncology settings.(12, 13, 16)

Although the impact of smoking on healthcare costs has been examined in the general population, there is very little information on the impact of smoking on the cost of cancer care in patients who are smokers compared to those who are not. We hypothesized that smoking would be associated with higher overall health system costs as a result of the need to manage more frequent and severe toxicities of treatment, more frequent disease recurrence, as well as more non-cancer related morbidities.

We compared the health system costs of cancer patients who were current smokers with those of non-smokers between 2014 and 2016, from the perspective of a public healthcare payer, using administrative databases in Ontario, Canada. Understanding the cost burden of smokers with cancer may help drive policy change by providing an economic argument for investing in cessation resources and programs for cancer patients who smoke.

MATERIALS AND METHODS

This study was a secondary data analysis using existing administrative databases at Cancer Care Ontario (CCO) and the Institute for Clinical Evaluative Sciences (ICES), both located in Toronto, Ontario, Canada. Research ethics approval was obtained from St. Michael's Hospital, Toronto, Ontario, Canada.

Study population and setting

The study population consisted of newly diagnosed adult cancer patients, aged ≥18 years, who received ambulatory care from one of the 14 Regional Cancer Centres (RCCs) in Ontario between 1 April 2014 and 31 March 2015. The Ontario Cancer Registry (OCR) was used to identify our study population. We excluded patients with: 1) an invalid health card (i.e., who were not eligible for public health care insurance); 2) an invalid death date (i.e., where death date was on or before the date of diagnosis); 3) missing data on smoking status; 4) a cancer stage of zero; 5) missing data on neighborhood-level income, geographical location, or rurality of residence; 6) lost health care coverage during the follow-up time; or 7) had multiple cancers. Each patient was followed until death or the end of the observation period (31 March 2016), whichever came first.

Study population sub-groups (smokers and non-smokers)

The study population of cancer patients was divided into those who were identified as smokers and non-smokers. Cancer patients who were either currently smoking at the time of diagnosis or who had smoked in the previous 6 months of their first ambulatory care visit were identified as *smokers*, whereas all others were identified as *non-smokers*. Information on *smoking status* was obtained from the *CCO Smoking Cessation Dataset* (CCOSCD), which is part of the Activity Level Reporting (ALR) database housed at CCO. The CCOSCD collects information on the self-reported smoking status of newly diagnosed ambulatory cancer patients, whether the current smoker has been advised to quit, and whether the patient has been referred for smoking cessation counselling and/or pharmacotherapy.(17) Each RCC submits the data on these metrics on a monthly basis to CCO as part of CCO's Smoking Cessation Program. S1 Appendix describes the data elements in the dataset and their definitions.

Data sources and variables

A number of databases were used to obtain healthcare utilization data: the ALR database, the New Drug Funding Program (NDFP) database, the Ontario Drug Benefit (ODB) claims database, the Discharge Abstract Database (DAD) obtained from the Canadian Institute for Health Information (CIHI), the National Ambulatory Care Reporting System (NACRS) obtained from CIHI, the Ontario Health Insurance Program (OHIP) claims database, the Home Care Database (HCD), the Continuing Care Reporting System (CCRS), and the National Rehabilitation Reporting System (NRS). Table 1 provides a brief description of each database.

Table 1. Administrative databases used in the analysis

Database	Description
OCR	The Ontario Cancer Registry is the largest population-based cancer registry in Canada. The OCR contains over 300 fields, including primary site of cancer, county of residence at diagnosis and health insurance number.
ALR	The Ontario Activity Level Reporting provides a set of data elements from selected Ontario Cancer Centers that cannot be obtained from other providers. This information is used to support management decision making process.
NDFP	The New Drug Funding Program data are used for reimbursement decisions and to support cancer system planning for systemic therapy. To be eligible for reimbursement through the NDFP, hospitals must submit eligibility/enrolment data and treatment data in compliance with monthly billing deadlines. For treatment reimbursement, each patient must be enrolled in the NDFP by providing eligibility/enrolment data that include patient-specific demographic information and answers to a series of medical questions.
ODB	The Ontario Drug Benefit Formulary lists prescription drugs that are covered for patients over 65 years, and selected other groups (e.g., those that require income supports).
CIHI DAD	Hospitalization and comorbidity data are in the Discharge Abstract Database from the Canadian Institute for Health Information.
CIHI NACRS	Emergency room visits and same day surgery data were obtained from the National Ambulatory Care Reporting System.

OHIP	Ontario Health Insurance Program reports outpatient physician visits based on fee-for-service claims.
HCD	Home Care Database captures all home care services in Ontario.
CCRS	The Continuing Care Reporting System reports utilization of continuing care.
NRS	National Rehabilitation Reporting System captures rehabilitation utilization.

Healthcare costs

The outcome of interest for the study was total and disaggregated healthcare costs from the perspective of the Ontario Ministry of Health and Long-Term Care (MOHLTC). Healthcare costs included costs associated with hospitalizations, same-day surgeries, emergency room (ER) visits, outpatient prescription drugs, rehabilitation, complex continuing care, home care services, physician services, and laboratory and diagnostic tests. Cost estimates were derived using an existing costing algorithm at ICES. For example, hospitalizations and ER visit costs were estimated by multiplying a resource intensity weight (measure of utilization) with an average cost per hospital stay or ER visit (unit cost).(18) Physician visit costs were obtained from the Ontario Schedule of Benefits for Physician Services.(19) Additional details on the methods to estimate cost can be found elsewhere.(4, 18, 20) Costs were adjusted to 2016 Canadian dollars (CAD) using the health component of the Consumer Price Index in health care category (1 CAD = approximately 0.78 US dollars).(21)

Other variables

Due to potential differences between smokers and non-smokers, we controlled for patient characteristics by adjusting for a number of variables such as age at diagnosis, sex, cancer site, cancer stage (where available), geographical location of residence (i.e., rurality and Local Health Integration Network (LHIN)), neighborhood income quintile, and comorbidity (measured by the Adjusted Clinical Groups® or ACG®), all of which were obtained from the previously mentioned databases. In Ontario, publicly funded health care services are administered on a regional basis by the LHINs, which serve as the regional health authority. Each of the 14 LHINs is responsible for a distinct geographical location.(22) The ACG® system is a patient case-mix adjustment system used to measure health status by grouping diagnoses into clinical groups. The goal of this system is to assign each patient a single value, which represents the patient's comorbidity (through his/her expected or actual use of health services), where a higher number refers to more comorbidities (0-4, 5-6, 7-9, and 10+).(23) For this study, we reported on cancer site according to the following sites or groupings: bladder; bronchus and lung; breast; colorectal; corpus uteri; head and neck; prostate; melanoma; and other. The extent of cancer was reported in one of 3 groups: stage 1-2; stage 3-4; and unknown stage.

Analysis

The raw costs for non-smokers and smokers were reported descriptively. To adjust for different follow up times, as some patients (particularly smokers) have a greater chance of dying than non-smokers, we estimated person-month costs.(24)

The output of the economic analysis was the incremental cost (reported in 2016 CAD) between cancer patients who smoked and those who did not. We analyzed our dependent

variable (monthly healthcare costs) using regression models to estimate the difference in expected health care cost between the two groups using recycled predictive methods,(24-26) as described in the following equation:

$$Cost_i = \beta_0 + \beta_1(smoking\ status)_i + \beta_2(age)_i + \beta_3(sex)_i + \beta_4(income\ quintile)_i + \beta_5(rurality)_i + \beta_6(cancer\ stage)_i + \beta_7(cancer\ type)_i + \beta_8(LHIN)_i + \varepsilon_i$$

where $cost_i$ represents a monthly cost of patient *I,* β_x refers to a coefficient estimate of each variable, *X*, such as smoking status, age, and sex and ε represents the error term. The smoking status variable was the primary independent variable, and the regression model was adjusted for potential confounding variables, such as age, sex, income, rurality, cancer stage, cancer site, geographical region (LHIN), and comorbidity. To accommodate for the skewness of cost data, a generalized linear model with log link and gamma family was used to estimate the incremental cost between smokers and non-smokers.(24, 27) We also conducted a Modified Park test to ensure that our selected model was the best fit.(24, 28)

Patient and public involvement

There was no involvement of patients during the study period but there are knowledge translation activities with various knowledge users.

RESULTS

There were 3,606 smokers and 14,911 non-smokers in our study cohort (see Table 2). Cancer patients who smoked were significantly younger (61 vs 65 years), more likely to be male (53% vs 45%), live in lower income neighborhoods (16% of non-smokers compared to 25% of smokers were in the lowest income quintile), and more likely to live in rural areas (18% vs 15%) compared to cancer patients who were non-smokers. Cancer stage data was available for approximately 70% of patients. Of those with available cancer stage data, smokers were more likely to have advanced cancer stages than non-smokers. Almost 40% of smokers were in stage 3-4 compared to approximately 27% of non-smokers. Roughly 25% of smokers died within 1 year of diagnosis compared to 15% of non-smokers who died over the same follow-up period. Approximately 30% of smokers were in the lowest comorbidity level (0-4) compared to 24% of non-smokers. Only 19% of smokers were in the highest comorbidity level (10+) compared to 23% of non-smokers. Lung cancer was the most common type of cancer among smokers followed by breast cancer. For non-smokers, the most common cancer type was breast cancer followed by prostate cancer and lung cancer (Table 2).

Table 2. Demographic characteristics of study population between smokers and non-smokers

Variable*	Non-smokers	Smokers
N	14,911	3,606
Mean age in years (SD)	65.1 (13.6)	60.6 (12.1)

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Male	6,681 (44.8%)	1,907 (52.9%)
Age groups in years, N (%)		
18-44	1,116 (7.5%)	310 (8.6%)
45-54	1,973 (13.2%)	661 (18.3%)
55-64	3,443 (23.1%)	1,217 (33.7%)
65-74	4,525 (30.3%)	1,035 (28.7%)
75+	3,854 (25.8%)	383 (10.6%)
Income quintile, N (%)		
1 (lowest)	2,387 (16.0%)	887 (24.5%)
2	2,597 (17.4%)	818 (22.7%)
3	3,065 (20.6%)	691 (19.2%)
4	3,351 (22.5%)	649 (18.0%)
5 (highest)	3,511 (23.5%)	561 (15.6%)
Living in rural areas, N (%)	2,267 (15.2%)	662 (18.4%)
Death within 1 year, N (%)	2,211 (14.8%)	850 (23.6%)
Mean time from diagnosis to death (SD)	255.2 days (163.3)	236.8 days (159.6)
Comorbidity (ACG), N (%)		
0-4	3,589 (24.1%)	1,092 (30.3%)
5-6	3,295 (22.1%)	838 (23.2%)
7-9	4,533 (30.4%)	985 (27.3%)
10+	3,494 (23.4%)	691 (19.2%)
Cancer stage, N (%)		
1-2	6,378 (42.8%)	1,289 (35.7%)
3-4	3,958 (26.5%)	1,392 (38.6%)
Unknown	4,575 (30.7%)	925 (25.7%)
Main cancer types, N (%)		
Lung	1,673 (11.2%)	1,017 (28.2%)
Breast	3,088 (20.7%)	497 (13.8%)
Head and neck	614 (4.1%)	292 (8.1%)
Prostate	1,694 (11.4%)	290 (8.0%)
Colorectal	1,460 (9.8%)	268 (7.4%)
Melanoma	563 (3.8%)	81 (2.2%)
Corpus uteri	701 (4.7%)	64 (1.8%)
Bladder	196 (1.3%)	43 (1.2%)
Other	4,922 (33.0%)	1,054 (29.3%)

Legend: ACG= Adjusted Clinical Groups®; N = sample size; SD = standard deviation.
Note: * the two groups were significantly different across all variables ($p < 0.05$).

Figure 1 reports the unadjusted monthly healthcare costs between the study groups. Generally, smokers incurred higher healthcare costs than non-smokers for hospitalizations, physician services, ER visits, home care services, and complex continuing care. Focusing on specific types of healthcare costs, smokers had approximately 30% higher hospitalization costs, 43% higher ER visit costs, 23% higher physician visit costs, and 30% higher home care costs

than non-smokers. Overall, total monthly health care costs were higher among smokers ($5,649 ± $7,169) than non-smokers ($4,704 ± $6,737).

*****Figure 1. Unadjusted monthly healthcare costs between cancer patients who were smokers and non-smokers (2016 CAD)*****

From the adjusted regression model (controlling for age, sex, income, rurality, stage, disease site, geographical region, and comorbidity), on average, smokers had significantly higher monthly healthcare costs ($5,091) than non-smokers ($4,847). Smokers incurred $244 (± 113) more in healthcare cost per month, or $2,928 more per year than non-smokers, p=0.0047.

DISCUSSION

Understanding the impact of smoking on the healthcare costs of cancer patients may strengthen the rationale for policy makers to further invest in smoking cessation programs. It is generally understood that smoking can lead to worse clinical outcomes, but there is a paucity of literature on the impact of smoking on healthcare costs among cancer patients. The findings from this analysis are aligned with the limited available literature. Specifically, we found that cancer patients who were smokers were younger and more commonly males compared to cancer patients who were not smokers, which is in line with the literature.(10, 29) Additionally, smokers had, on average, almost 20% higher total monthly healthcare costs than non-smokers. When focusing mainly on hospitalizations, the incremental cost due to smoking was approximately 30% higher than non-smokers, in contrast to an increase of up to 50% in incremental hospitalization costs among smokers reported in the literature.(9, 30) Our findings suggest that cancer patients who are smokers are responsible for a greater economic burden than non-smokers.

Evidence on the importance of smoking cessation for cancer patients has strengthened in recent years. Several cancer care institutions in the United States have emerged as leaders in this field by supporting smoking cessation programs.(31) Ontario is the first jurisdiction in North America to implement a systematic smoking cessation program in all of its RCCs. Under the leadership of CCO, the provincial agency responsible for improving the quality of cancer services in Ontario, a smoking cessation program provides support for new ambulatory cancer patients by screening patients for tobacco use, advising on the benefits of quitting, and offering referrals to smoking cessation resources. Understanding the impact of smoking on the healthcare costs incurred by cancer patients may further strengthen the rationale for the program and encourage policy makers (e.g., public healthcare payer) to invest in smoking cessation programs. The findings from this study may also be beneficial to other cancer agencies, and not-for-profit organizations (e.g., American Cancer Society, Worldwide Cancer Research, and Canadian Partnership Against Cancer) engaged in developing smoking cessation policies and implementing smoking cessation programs. In addition, this study may help to inform the general public about the burden of smoking among cancer patients, including motivating hospital and health system administrators about the incremental economic impact of failing to help cancer

patients quit smoking. The findings from this study support the integration of smoking cessation programs into cancer care treatment plans and will hopefully stimulate further research into the optimal implementation of smoking cessation programs in order to improve cancer care outcomes and reduce morbidity, mortality, and cost.

This study has strengths and limitations, which should be highlighted. The medical literature has called for more up-to-date and precise health care cost estimates of smoking.(9, 32) Existing Canadian literature has used cost estimates for smokers from the 1990s and/or employed high-level costing approaches, instead of using patient-level cost estimates. These prior estimates might not accurately reflect the true healthcare cost difference between smokers and non-smokers.(9, 32-34) This study represents a first step to systematically collect these data and to link them to data on system-level resources.

In terms of limitations, data on smoking status were limited to one assessment at the first ambulatory visit and, therefore, it is possible that patients may have changed their smoking status subsequently. Our analysis followed the intent-to-treat principle and was applied to both study groups (i.e., smokers at the time of diagnosis or who had quit in the last six months remained smokers throughout the analysis and vice versa). If some "smokers" quit smoking, their medical outcomes or tolerance to treatment may have been better than that of persistent smokers (presumably with less resource utilization and less cost). Consequently, this analysis may have provided a lower bound of the incremental cost. Individuals who had quit prior to 6 months would likely still have more health complications and resource utilization than life-long non-smokers. Classification of these patients as non-smokers may again lead to the possibility of an underestimation of the difference in cost between smokers and non-smokers.

Our analysis was also limited by the available follow-up data. As the follow-up period was relatively short, it is possible that the significant differences might be observed with a longer period of follow-up. It is also possible that, given the nature of the study design, relevant variables were not collected. For example, cancer stage data were available for the most common types of cancer (i.e., lung, breast, colorectal, and prostate cancer), but not for other tumour types, such as head and neck cancer. In addition, there were no data available on the amount or duration of smoking, which would likely have an influence on health outcomes and cost. Smoking has been shown to increase both direct and indirect costs.(9, 33, 34) However, because our study used administrative data, indirect costs were not explored – this could be an area for future research. Finally, there would be a cost to implement a smoking cessation program, which was not included in this analysis, and may cancel out some of the economic benefits of getting smokers to stop smoking.

In conclusion, cancer patient smoking status has a significant impact on health system costs. On average, smokers incurred higher healthcare costs than non-smokers. These findings provide an additional reason for the introduction of evidence-based smoking cessation programs for cancer patients. The findings from this study should motivate policy makers to design, implement, and fund smoking cessation programs, which have the potential not only to improve patients' treatment outcomes but also to reduce the economic burden of smoking on the healthcare system.

Abbreviations

ACG®	Adjusted Clinical Groups®
ARCC	Canadian Centre for Applied Research in Cancer Control
CAD	Canadian dollars
CCO	Cancer Care Ontario
CCOSCD	CCO Smoking Cessation Dataset
ER	emergency room
ICES	Institute for Clinical Evaluative Sciences
LHIN	Local Health Integration Network
MOHLTC	Ontario Ministry of Health and Long-Term Care
RCCs	Regional Cancer Centres

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Contributors

All authors made important contributions to this work.
WI, CdO, NM, WE, AP, RT, KKWC contributed to this study's conception and design.
WI, NM, AP, RT were responsible for data collection and assembly.
All authors (WI, CdO, NM, WE, AP, RT, KKWC) were involved in data analysis and interpretation.
WI, CdO, NM, WE drafted the paper, and all authors critically reviewed and suggested amendments prior to submission.
The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Competing interests:

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethics approval:

Research ethics approval was obtained from St. Michael's Hospital, Toronto, Ontario, Canada.

Data sharing statement:

This study made use of de-identified data from the Institute for Clinical Evaluative Sciences and Cancer Care Ontario who have the right and control over the data used.

Figure Legends

Figure 1. Unadjusted monthly healthcare costs between cancer patients who were smokers and non-smokers (2016 CAD)

Supporting Information

S1 Appendix: Data elements and their definition of Cancer Care Ontario's Smoking Cessation Dataset (PDF)

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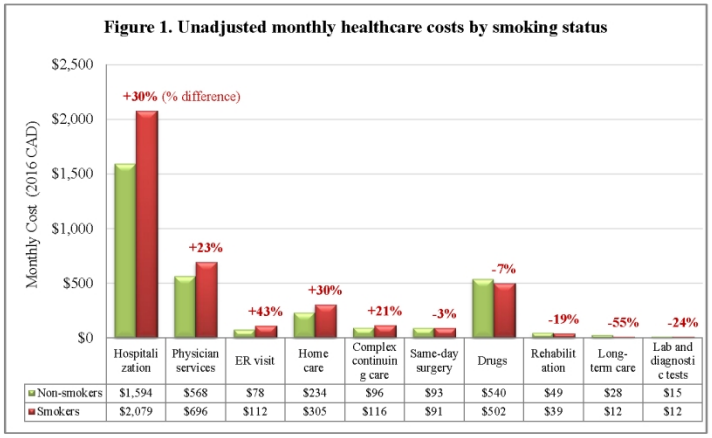
Figure 1. Unadjusted monthly healthcare costs between cancer patients who were smokers and non-smokers (2016 CAD)



Legend: CAD = Canadian dollars.

Unadjusted monthly healthcare costs between cancer patients who were smokers and non-smokers (2016 CAD)

215x279mm (200 x 200 DPI)

S1 Appendix: Data elements and their definition of Cancer Care Ontario's Smoking Cessation Dataset

Data Element	Definition
Patient Chart Number	Patient identifier code that is unique within the healthcare facility.
Submitting Hospital Number	The MOHLTC healthcare facility that submits activity to CCO.
Registration Date	Date this patient was first registered at this RCC and/or hospital for this disease.
Disease Sequence Number	The numeric sequence assigned to a primary cancer for a patient at a specific healthcare facility.
Visit Hospital Number	MOHLTC Master Number and name for the reporting healthcare facility where the cancer activity occurred (known by CIHI as Institution Numbers).
Visit Program Code	Primary cancer programs for clinic, planning and treatment activity. Includes; Radiation (RAD), Systemic (SYS), Surgical (SUR), Research (RE), Palliative (PA), Preventative Oncology (PO), or Psychosocial Oncology (PSO).
SMK_Q1	Patient self-reported as being a current smoker or indicated they had smoked within the past 6 months.
SMK_Q1 Date	The date the patient was asked SMK_Q1 (smoking status question).
SMK_Q2	Patient was advised of the benefits of smoking cessation.
SMK_Q3	Patient was recommended a referral to a smoking cessation program.
SMK_Q3 Date	The date when the patient was asked SMK_Q3 (assessed for quitting question).
SMK_Q4	Type of referral selected by patient. Referral is the act of directing or sending a patient to cessation service(s) for further action or support in making a quit attempt and becoming smoke free. The service should be arranged through the RCC (e.g., to a quit coach or to Canadian Cancer Society's Smokers Helpline fax referral program) to help the patient quit smoking. A referral is not simply the act of providing written information. Internal cessation referrals include services provided by the RCC (e.g. quit coaches), and external referrals are referred to outside the RCC.

Legend: MOHLTC = Ministry of Health and Long-Term Care; CCO = Cancer Care Ontario; RCC = Regional Cancer Centre; CIHI = Canadian Institute for Health Inf

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Impact of Smoking on Health System Costs among Cancer Patients in a retrospective cohort study in Ontario, Canada

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Impact of smoking on health system costs among cancer patients

ABSTRACT

Objective

Smoking is the main modifiable cancer risk factor. The objective of this study was to examine the impact of smoking on health system costs among newly diagnosed adult cancer patients. Specifically, costs of cancer patients who were current smokers were compared with those of non-smokers from a publicly funded health system perspective.

Methods

This population-based cohort study of cancer patients used administrative databases to identify smokers and non-smokers (1 April 2014 - 31 March 2016) and their health care costs in the 12-24 months following a cancer diagnosis. The health services included were hospitalizations, emergency room visits, drugs, home care services, and physician services (from time of diagnosis onwards). The difference in cost (i.e. incremental cost) between cancer patients who were smokers and those who were non-smokers was estimated using a generalized linear model (with log link and gamma distribution), and adjusted for age, sex, neighborhood income, rurality, cancer site, cancer stage, geographical region, and comorbidities.

Results

This study identified 3,606 smokers and 14,911 non-smokers. Smokers were significantly younger (61 vs 65 years), more likely to be male (53%), lived in poorer neighborhoods, had more advanced cancer stage, and were more likely to die within one year of diagnosis, compared to non-smokers. The regression model revealed that on average, smokers had significantly higher monthly healthcare costs ($5,091) than non-smokers ($4,847), $p<0.05$.

Conclusions

Smoking status has a significant impact on healthcare costs among cancer patients. On average, smokers incurred higher healthcare costs than non-smokers. These findings provide a further rationale for efforts to introduce evidence-based smoking cessation programs as a standard of care for cancer patients as they have the potential to not only improve patients' outcomes but also to reduce the economic burden of smoking on the healthcare system.

Keywords:

Smoking; Healthcare costs; Health system costs; Cancer; Economic burden

Impact of smoking on health system costs among cancer patients

Strengths and Limitations of this study

- Findings from this study represent one piece of evidence in support of the integration of smoking cessation programs into cancer care treatment plans as a standard of practice
- This study adds to the literature by providing up-to-date and precise health care cost estimates of smoking using existing administrative person-level costing approaches
- A limitation of this study is that it excludes a subset of relevant variables that may have had an influence on health outcomes and cost due to the nature of the study design (e.g., type of tumour, amount and duration of smoking)
- This study focused on the cost incurred to the public healthcare payer and, therefore, indirect costs were not considered but could be explored in future research
- The findings from this study should motivate policy makers to design, implement, and fund smoking cessation programs, which have the potential not only to improve patients' treatment outcomes but also to reduce the economic burden of smoking on the healthcare system

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INTRODUCTION

Cancer care is a substantial component of health care expenditures of developed countries.(1-3) In Canada, the economic burden of cancer was estimated to be $7.5 billion in 2012.(4) It is well recognized that smoking is the main modifiable risk factor for cancer (5) and it is estimated that it contributes to approximately 30% of all cancer deaths.(6, 7) Smoking can also harm directly or indirectly almost every organ of the body and is responsible for a number of other chronic diseases that contribute to higher health care costs.(5, 8-11) Quitting smoking after a diagnosis of cancer has been associated with improved general health, better quality of life, reduced toxicity, greater response to treatment (such as radiation therapy), and decreased risk of disease recurrence and second primary cancers.(12-18) Nevertheless, cancer patients are just as likely to smoke as the general public with the smoking rate being approximately 20%.(19) Furthermore, smoking cessation programs are rare in oncology settings.(12, 13, 20)

Although the impact of smoking on healthcare costs has been examined in the general population, there is very little information on the impact of smoking on the cost of cancer care in patients who are smokers compared to those who are not.

The study objective was to compare the health system costs of cancer patients who were current smokers with those of non-smokers between 2014 and 2016, from the perspective of a public healthcare payer, using administrative databases in Ontario, Canada. We hypothesized that smoking would be associated with higher overall health system costs as a result of the need to manage more frequent and severe toxicities of treatment, more frequent disease recurrence, as well as more non-cancer related morbidities. Understanding the cost burden of smokers with cancer may help drive policy change by providing an economic argument for investing in cessation resources and programs for cancer patients who smoke.

MATERIALS AND METHODS

This study was a secondary data analysis using existing administrative databases at Cancer Care Ontario (CCO) and the Institute for Clinical Evaluative Sciences (ICES), both located in Toronto, Ontario, Canada. Research ethics approval was obtained from St. Michael's Hospital, Toronto, Ontario, Canada.

Study population and setting

The study population consisted of newly diagnosed adult cancer patients, aged ≥18 years, who received ambulatory care from one of the 14 Regional Cancer Centres (RCCs) in Ontario, Canada, between 1 April 2014 and 31 March 2015. The Ontario Cancer Registry (OCR) was used to identify our study population. We excluded patients with: 1) an invalid health card (i.e., who were not eligible for public health care insurance); 2) an invalid death date (i.e., where death date was on or before the date of diagnosis); 3) missing data on smoking status; 4) a cancer stage of zero; 5) missing data on neighborhood-level income, geographical location, or rurality of residence; 6) lost health care coverage during the follow-up time; or 7) had multiple cancers. Each patient was followed until death or the end of the observation period (31 March 2016),

whichever came first. S1 Appendix provides a flow diagram of the number of patients excluded from the analysis.

Study population sub-groups (smokers and non-smokers)

The study population of cancer patients was divided into those who were identified as smokers and non-smokers. Cancer patients who were either currently smoking at the time of diagnosis or who had smoked in the previous 6 months of their first ambulatory care visit were identified as *smokers*, whereas all others were identified as *non-smokers*. Information on *smoking status* was obtained from the *CCO Smoking Cessation Dataset* (CCOSCD), which is part of the Activity Level Reporting (ALR) database housed at CCO. The CCOSCD collects information on the self-reported smoking status of newly diagnosed ambulatory cancer patients, whether the current smoker has been advised to quit, and whether the patient has been referred for smoking cessation counselling and/or pharmacotherapy.(21) Each RCC submits the data on these metrics on a monthly basis to CCO as part of CCO's Smoking Cessation Program. S2 Appendix describes the data elements in the dataset and their definitions.

Data sources and variables

A number of databases were used to obtain healthcare utilization data: the ALR database, the New Drug Funding Program (NDFP) database, the Ontario Drug Benefit (ODB) claims database, the Discharge Abstract Database (DAD) obtained from the Canadian Institute for Health Information (CIHI), the National Ambulatory Care Reporting System (NACRS) obtained from CIHI, the Ontario Health Insurance Program (OHIP) claims database, the Home Care Database (HCD), the Continuing Care Reporting System (CCRS), and the National Rehabilitation Reporting System (NRS). Table 1 provides a brief description of each database.

Table 1. Administrative databases used in the analysis

Database	Description
OCR	The Ontario Cancer Registry is the largest population-based cancer registry in Canada. The OCR contains over 300 fields, including primary site of cancer, county of residence at diagnosis and health insurance number.
ALR	The Ontario Activity Level Reporting provides a set of data elements from selected Ontario Cancer Centers that cannot be obtained from other providers. This information is used to support management decision making process.
NDFP	The New Drug Funding Program data are used for reimbursement decisions and to support cancer system planning for systemic therapy. To be eligible for reimbursement through the NDFP, hospitals must submit eligibility/enrolment data and treatment data in compliance with monthly billing deadlines. For treatment reimbursement, each patient must be enrolled in the NDFP by providing eligibility/enrolment data that include patient-specific demographic information and answers to a series of medical questions.
ODB	The Ontario Drug Benefit Formulary lists prescription drugs that are covered for patients over 65 years, and selected other groups (e.g., those that require income supports).
CIHI DAD	Hospitalization and comorbidity data are in the Discharge Abstract Database from

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	the Canadian Institute for Health Information.
CIHI NACRS	Emergency room visits and same day surgery data were obtained from the National Ambulatory Care Reporting System.
OHIP	Ontario Health Insurance Program reports outpatient physician visits based on fee-for-service claims.
HCD	Home Care Database captures all home care services in Ontario.
CCRS	The Continuing Care Reporting System reports utilization of continuing care.
NRS	National Rehabilitation Reporting System captures rehabilitation utilization.

Healthcare costs

The outcome of interest for the study was total and disaggregated healthcare costs from the perspective of the Ontario Ministry of Health and Long-Term Care (MOHLTC) from the time of diagnosis. From this perspective and given that patients in the study setting receive publicly funded health care insurance, cancer patients did not have to pay for health services. Healthcare costs included costs associated with hospitalizations, same-day surgeries, emergency room (ER) visits, outpatient prescription drugs, rehabilitation, complex continuing care, home care services, physician services, and laboratory and diagnostic tests. Cost estimates were derived using an existing costing algorithm at ICES. For example, hospitalizations and ER visit costs were estimated by multiplying a resource intensity weight (measure of utilization) with an average cost per hospital stay or ER visit (unit cost).(22) Physician visit costs were obtained from the Ontario Schedule of Benefits for Physician Services.(23) Additional details on the methods to estimate cost can be found elsewhere.(4, 22, 24) Costs were adjusted to 2016 Canadian dollars (CAD) using the health component of the Consumer Price Index in health care category (1 CAD = approximately 0.78 US dollars).(25)

Other variables

Due to potential differences between smokers and non-smokers, we controlled for patient characteristics by adjusting for a number of variables such as age at diagnosis, sex, cancer site, cancer stage (where available), geographical location of residence (i.e., rurality and Local Health Integration Network (LHIN)), neighborhood income quintile, and comorbidity (measured by the Adjusted Clinical Groups® or ACG®), all of which were obtained from the previously mentioned databases. In Ontario, publicly funded health care services are administered on a regional basis by the LHINs, which serve as the regional health authority. Each of the 14 LHINs is responsible for a distinct geographical location.(26) The ACG® system is a patient case-mix adjustment system used to measure health status by grouping diagnoses into clinical groups. The goal of this system is to assign each patient a single value, which represents the patient's comorbidity through his/her expected or actual use of health services, where a higher number refers to a greater number of comorbidities (0-4, 5-6, 7-9, and 10+).(27) In this study, this value was assigned at the time of the cancer diagnosis. Cancer sites or groupings were reported on as follows: bladder; bronchus and lung; breast; colorectal; corpus uteri; head and neck; prostate; melanoma; and "other". Other included anus and anal canal, brain, esophagus, hematopoietic, liver, ovary, pancreas, renal, stomach, testis, and thyroid. The extent of cancer was reported in one of 3 groups: stage 1-2; stage 3-4; and unknown stage. Cancer stage data in Ontario were available predominantly for the main types of cancer (e.g., lung, breast, prostate and colorectal); therefore, we have created a separate category for unknown cancer stage.

Analysis

The raw costs for non-smokers and smokers were reported descriptively. To adjust for different follow up times, as some patients (particularly smokers) have a greater chance of dying than non-smokers, we estimated person-month costs.(28)

The output of the economic analysis was the incremental cost (reported in 2016 CAD) between cancer patients who smoked and those who did not. We analyzed our dependent variable (monthly healthcare costs) using regression models to estimate the difference in expected health care cost between the two groups using recycled predictive methods,(28-30) as described in the following equation:

$$Cost_i = \beta_0 + \beta_1(smoking\ status)_i + \beta_2(age)_i + \beta_3(sex)_i + \beta_4(income\ quintile)_i + \beta_5(rurality)_i + \beta_6(cancer\ stage)_i + \beta_7(cancer\ type)_i + \beta_8(LHIN)_i + \varepsilon_i$$

where $cost_i$ represents a monthly cost of patient *I,* β_x refers to a coefficient estimate of each variable, *X*, such as smoking status, age, and sex and ε represents the error term. The smoking status variable was the primary independent variable, and the regression model was adjusted for potential confounding variables, such as age, sex, income, rurality, cancer stage, cancer site, geographical region (LHIN), and comorbidity. To accommodate for the skewness of cost data, a generalized linear model with log link and gamma family was used to estimate the incremental cost between smokers and non-smokers.(28, 31) We also conducted a Modified Park test to ensure that our selected model was the best fit.(28, 32) Collinearity was also explored using Variance Inflation Factor, and we found no evidence of collinearity. S3 Appendix reports a completed STROBE statement, a checklist of items that should be included in reports of cohort studies.

Patient and public involvement

There was no involvement of patients during the study period but there are knowledge translation activities with various knowledge users.

RESULTS

There were 3,606 smokers and 14,911 non-smokers in our study cohort (see Table 2). Cancer patients who smoked were significantly younger (61 vs 65 years), more likely to be male (53% vs 45%), live in lower income neighborhoods (25% of smokers compared to 16% of non-smokers were in the lowest income quintile), and more likely to live in rural areas (18% vs 15%) compared to cancer patients who were non-smokers. Cancer stage data was available for approximately 70% of patients over the study period. Of those with available cancer stage data, smokers were more likely to have advanced cancer stages than non-smokers. Almost 40% of smokers were in stage 3-4 compared to approximately 27% of non-smokers. Roughly 25% of smokers died within 1 year of diagnosis compared to 15% of non-smokers who died over the

same follow-up period. Approximately 30% of smokers were in the lowest comorbidity level (0-4) compared to 24% of non-smokers. Only 19% of smokers were in the highest comorbidity level (10+) compared to 23% of non-smokers. Among the main cancer types, lung cancer was the most common type of cancer among smokers followed by breast cancer. For non-smokers, the most common cancer type was breast cancer followed by prostate cancer and lung cancer (Table 2).

Table 2. Demographic characteristics of study population between smokers and non-smokers

Variable*	Non-smokers	Smokers
N	14,911	3,606
Mean age in years (SD)	65.1 (13.6)	60.6 (12.1)
Male	6,681 (44.8%)	1,907 (52.9%)
Age groups in years, N (%)		
18-44	1,116 (7.5%)	310 (8.6%)
45-54	1,973 (13.2%)	661 (18.3%)
55-64	3,443 (23.1%)	1,217 (33.7%)
65-74	4,525 (30.3%)	1,035 (28.7%)
75+	3,854 (25.8%)	383 (10.6%)
Income quintile, N (%)		
1 (lowest)	2,387 (16.0%)	887 (24.5%)
2	2,597 (17.4%)	818 (22.7%)
3	3,065 (20.6%)	691 (19.2%)
4	3,351 (22.5%)	649 (18.0%)
5 (highest)	3,511 (23.5%)	561 (15.6%)
Living in rural areas, N (%)	2,267 (15.2%)	662 (18.4%)
Death within 1 year, N (%)	2,211 (14.8%)	850 (23.6%)
Mean time from diagnosis to death (SD)	255.2 days (163.3)	236.8 days (159.6)
Comorbidity (ACG), N (%)		
0-4	3,589 (24.1%)	1,092 (30.3%)
5-6	3,295 (22.1%)	838 (23.2%)
7-9	4,533 (30.4%)	985 (27.3%)
10+	3,494 (23.4%)	691 (19.2%)
Cancer stage, N (%)		
1-2	6,378 (42.8%)	1,289 (35.7%)
3-4	3,958 (26.5%)	1,392 (38.6%)
Unknown	4,575 (30.7%)	925 (25.7%)
Main cancer types, N (%)		
Lung	1,673 (11.2%)	1,017 (28.2%)
Breast	3,088 (20.7%)	497 (13.8%)
Head and neck	614 (4.1%)	292 (8.1%)
Prostate	1,694 (11.4%)	290 (8.0%)
Colorectal	1,460 (9.8%)	268 (7.4%)
Melanoma	563 (3.8%)	81 (2.2%)

Corpus uteri	701 (4.7%)	64 (1.8%)
Bladder	196 (1.3%)	43 (1.2%)
Other	4,922 (33.0%)	1,054 (29.3%)

Legend: ACG= Adjusted Clinical Groups®; N = sample size; SD = standard deviation.
Note: * the two groups were significantly different across all variables ($p < 0.05$).

S4 Appendix reports the unadjusted monthly healthcare costs between the study groups. Generally, smokers incurred higher healthcare costs than non-smokers for hospitalizations, physician services, ER visits, home care services, and complex continuing care. Focusing on specific types of healthcare costs, smokers had approximately 30% higher hospitalization costs, 43% higher ER visit costs, 23% higher physician visit costs, and 30% higher home care costs than non-smokers. Overall, total monthly health care costs were higher among smokers ($5,649 ± $7,169) than non-smokers ($4,704 ± $6,737).

From the adjusted regression model (controlling for age, sex, income, rurality, stage, disease site, geographical region, and comorbidity), on average, smokers had significantly higher monthly healthcare costs ($5,091) than non-smokers ($4,847). Smokers incurred $244 (± 113; interquartile range $145 to $328) more in healthcare cost per month, or $2,928 more per year than non-smokers, p=0.0047.

DISCUSSION

Understanding the impact of smoking on the healthcare costs of cancer patients may strengthen the rationale for decision makers to further invest in smoking cessation programs. It is generally understood that smoking can lead to worse clinical outcomes, but there is a paucity of literature on the impact of smoking on healthcare costs among cancer patients. The findings from this analysis are aligned with the limited available literature. Specifically, we found that cancer patients who were smokers were younger and more commonly males compared to cancer patients who were not smokers, which is in line with the literature.(10, 33) Additionally, smokers had, on average, almost 20% higher total monthly healthcare costs than non-smokers. When focusing mainly on hospitalizations, the incremental cost due to smoking was approximately 30% higher than non-smokers, in contrast to an increase of up to 50% in incremental hospitalization costs among smokers reported in the literature.(9, 34) Our findings suggest that cancer patients who are smokers are responsible for a greater economic burden than non-smokers.

Evidence on the importance of smoking cessation for cancer patients has strengthened in recent years. Several cancer care institutions in the United States have emerged as leaders in this field by incorporating smoking cessation programs into practice.(35) Ontario is the first jurisdiction in North America to implement a systematic smoking cessation program in all of its RCCs. Under the leadership of CCO, the provincial agency responsible for improving the quality of cancer services in Ontario, a smoking cessation program provides support for new ambulatory cancer patients by screening patients for tobacco use, advising on the benefits of quitting, and offering referrals to smoking cessation resources. Understanding the impact of smoking on the healthcare costs incurred by cancer patients may further strengthen the rationale for the program

and encourage policy makers (e.g., public healthcare payer) to invest in smoking cessation programs. The findings from this study may also be beneficial to other cancer agencies, and not-for-profit organizations (e.g., American Cancer Society, Worldwide Cancer Research, and Canadian Partnership Against Cancer) engaged in developing smoking cessation policies and implementing smoking cessation programs. In addition, this study may help to inform the general public about the burden of smoking among cancer patients and motivate hospital and health system administrators about the incremental economic impact of failing to help cancer patients quit smoking. The findings from this study represent a further piece of evidence in support of the integration of smoking cessation programs into cancer care treatment plans (in settings similar to the study setting) and will hopefully stimulate further research into the optimal implementation of smoking cessation programs in order to improve cancer care outcomes and reduce morbidity, mortality, and cost.

This study has strengths and limitations, which should be highlighted. The medical literature has called for more up-to-date and precise health care cost estimates of smoking.(9, 36) Existing Canadian literature has used cost estimates for smokers from the 1990s and/or employed high-level costing approaches, instead of using patient-level cost estimates. These prior estimates might not accurately reflect the true healthcare cost difference between smokers and non-smokers.(9, 36-38) This study represents a first step in systematically collecting these data and linking them to data on system-level resources. Furthermore, using existing data from administration databases, we were able to conduct the analysis with adjustment of potential confounders to increase the validity of the findings.

In terms of limitations, data on smoking status were limited to one assessment during the initial consultation period (28 days) for new ambulatory cancer patients. Therefore, it is possible that patients may have changed their smoking status after their cancer diagnosis but data on change in smoking status were not captured. Our analysis followed the intent-to-treat principle and was applied to both study groups (i.e., smokers at the time of diagnosis or who had quit in the last six months remained smokers throughout the analysis and vice versa). If some "smokers" quit smoking, their medical outcomes or tolerance to treatment may have been better than that of persistent smokers (presumably with less resource utilization and less cost). Consequently, this analysis may have provided a lower bound of the incremental cost. Individuals who had quit prior to 6 months would likely still have more health complications and resource utilization than life-long non-smokers. Classification of these patients as non-smokers may again lead to the possibility of an underestimation of the difference in cost between smokers and non-smokers. The data available on smoking status limited our ability to analyze former smokers and recent quitters as separate groups.

Our analysis was also limited by the available follow-up data. As the follow-up period was relatively short, it is possible that significant differences might be observed with a longer period of follow-up. It is also possible that, given the nature of the study design, relevant variables were not collected. For example, cancer stage data were available for the main types of cancer (i.e., lung, breast, colorectal, and prostate cancer), but not for some other tumour types, such as head and neck cancer. In addition to the main tumour types, our study included other less common tumour types (e.g., brain, liver) but their smaller numbers did not allow us to examine them separately. This could be a future area of research. Patients with multiple cancers were excluded from the study to distinguish the impact of smoking on a single tumour type. In addition, there were no data available on the amount or duration of smoking, which would likely have an influence on health outcomes and cost. Smoking has been shown to increase both direct

and indirect costs.(9, 37, 38) However, because our study used administrative data, indirect costs were not explored. Finally, the cost to implement a smoking cessation program was not included in this analysis, and may cancel out some of the economic benefits of helping smokers to stop smoking.

In conclusion, cancer patient smoking status has a significant impact on health system costs. On average, smokers incurred higher healthcare costs than non-smokers. These findings provide an additional reason for the introduction of evidence-based smoking cessation programs for cancer patients. The findings from this study should motivate policy makers to fund, design, and implement smoking cessation programs, which have the potential not only to improve patients' treatment outcomes but also to reduce the economic burden of smoking on the healthcare system.

Abbreviations

ACG®	Adjusted Clinical Groups®
ARCC	Canadian Centre for Applied Research in Cancer Control
CAD	Canadian dollars
CCO	Cancer Care Ontario
CCOSCD	CCO Smoking Cessation Dataset
ER	emergency room
ICES	Institute for Clinical Evaluative Sciences
LHIN	Local Health Integration Network
MOHLTC	Ontario Ministry of Health and Long-Term Care
RCCs	Regional Cancer Centres

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Impact of smoking on health system costs among cancer patients

Contributors

All authors made important contributions to this work.
WI, CdO, NM, WE, AP, RT, KKWC contributed to this study's conception and design.
WI, NM, AP, RT were responsible for data collection and assembly.
All authors (WI, CdO, NM, WE, AP, RT, KKWC) were involved in data analysis and interpretation.
WI, CdO, NM, WE drafted the paper, and all authors critically reviewed and suggested amendments prior to submission.
The corresponding author attests that all listed authors meet authorship criteria and that others not meeting the criteria have been omitted.

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Competing interests:

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethics approval:

Research ethics approval was obtained from St. Michael's Hospital, Toronto, Ontario, Canada.

Data sharing statement:

This study made use of de-identified data from the Institute for Clinical Evaluative Sciences and Cancer Care Ontario who have the right and control over the data used.

Supporting Information

S1 Appendix: Flow diagram on the number of excluded patients

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S2Appendix: Data elements and their definition of Cancer Care Ontario's Smoking Cessation Dataset (PDF)

S3 Appendix: Completed STROBE statement, a checklist of items that should be included in reports of cohort studies

S4 Appendix: Unadjusted monthly healthcare costs between cancer patients who were smokers and non-smokers (2016 CAD)

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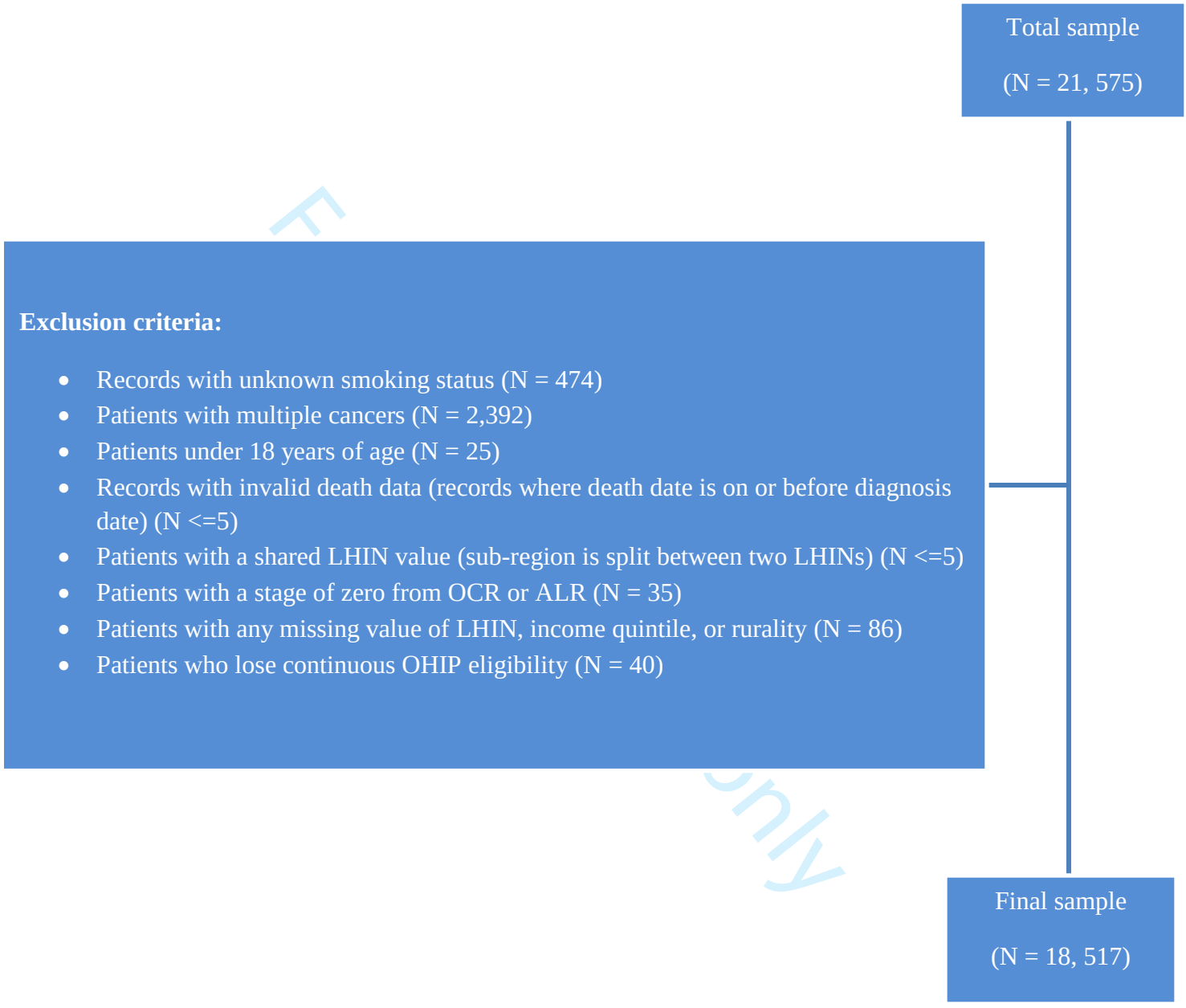
S1 Appendix: Flow diagram on the number of excluded patients



S2 Appendix: Data elements and their definition of Cancer Care Ontario's Smoking Cessation Dataset

Data Element	Definition
Patient Chart Number	Patient identifier code that is unique within the healthcare facility.
Submitting Hospital Number	The MOHLTC healthcare facility that submits activity to CCO.
Registration Date	Date this patient was first registered at this RCC and/or hospital for this disease.
Disease Sequence Number	The numeric sequence assigned to a primary cancer for a patient at a specific healthcare facility.
Visit Hospital Number	MOHLTC Master Number and name for the reporting healthcare facility where the cancer activity occurred (known by CIHI as Institution Numbers).
Visit Program Code	Primary cancer programs for clinic, planning and treatment activity. Includes; Radiation (RAD), Systemic (SYS), Surgical (SUR), Research (RE), Palliative (PA), Preventative Oncology (PO), or Psychosocial Oncology (PSO).
SMK_Q1	Patient self-reported as being a current smoker or indicated they had smoked within the past 6 months.
SMK_Q1 Date	The date the patient was asked SMK_Q1 (smoking status question).
SMK_Q2	Patient was advised of the benefits of smoking cessation.
SMK_Q3	Patient was recommended a referral to a smoking cessation program.
SMK_Q3 Date	The date when the patient was asked SMK_Q3 (assessed for quitting question).
SMK_Q4	Type of referral selected by patient. Referral is the act of directing or sending a patient to cessation service(s) for further action or support in making a quit attempt and becoming smoke free. The service should be arranged through the RCC (e.g., to a quit coach or to Canadian Cancer Society's Smokers Helpline fax referral program) to help the patient quit smoking. A referral is not simply the act of providing written information. Internal cessation referrals include services provided by the RCC (e.g. quit coaches), and external referrals are referred to outside the RCC.

Legend: MOHLTC = Ministry of Health and Long-Term Care; CCO = Cancer Care Ontario; RCC = Regional Cancer Centre; CIHI = Canadian Institute for Health Information

S3 Appendix: Completed STROBE statement, a checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page number
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4, 5, 6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4, 5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5, 6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one	5, 6

		group	
Bias	9	Describe any efforts to address potential sources of bias	6, 7, 9, 10
Study size	10	Explain how the study size was arrived at	4, 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5, 6, 7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	4
		(*d*) If applicable, explain how loss to follow-up was addressed	4
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed	5 (S1 Appendix), 7, 8, 9
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	5 (S1 Appendix)
Descriptive data	14*	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	7, 8, 9
		(b) Indicate number of participants with missing data for each variable of interest	5 (S1 Appendix)

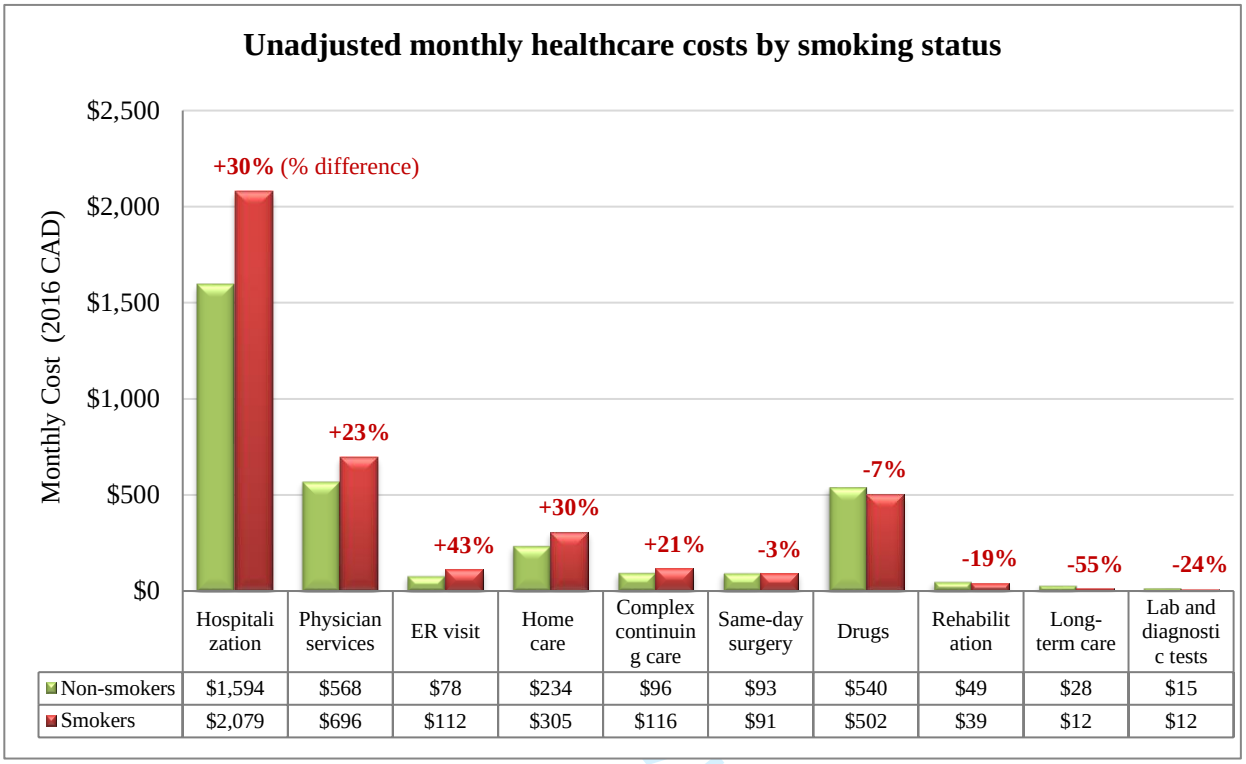
		(c) Summarize follow-up time (e.g., average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	7, 8, 9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarize key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10, 11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9, 10, 11
Generalizability	21	Discuss the generalizability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable,	12, 13

		for the original study on which the present article is based	

*Give information separately for exposed and unexposed groups.
N/A = Not applicable

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

S4 Appendix: Unadjusted monthly healthcare costs between cancer patients who were smokers and non-smokers (2016 CAD)



	Hospitalization	Physician services	ER visit	Home care	Complex continuing care	Same-day surgery	Drugs	Rehabilitation	Long-term care	Lab and diagnostic tests
Non-smokers	$1,594	$568	$78	$234	$96	$93	$540	$49	$28	$15
Smokers	$2,079	$696	$112	$305	$116	$91	$502	$39	$12	$12

Legend: CAD = Canadian dollars.

BMJ Open

Impact of Smoking on Health System Costs among Cancer Patients in a retrospective cohort study in Ontario, Canada

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Primary Subject Heading:	Health economics
Secondary Subject Heading:	Smoking and tobacco
Keywords:	Smoking, Healthcare costs, Health system costs, Cancer, Economic burden

Impact of Smoking on Health System Costs among Cancer Patients in a retrospective cohort study in Ontario, Canada

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Impact of smoking on health system costs among cancer patients

ABSTRACT

Objective

Smoking is the main modifiable cancer risk factor. The objective of this study was to examine the impact of smoking on health system costs among newly diagnosed adult cancer patients. Specifically, costs of cancer patients who were current smokers were compared with those of non-smokers from a publicly funded health system perspective.

Methods

This population-based cohort study of cancer patients used administrative databases to identify smokers and non-smokers (1 April 2014 - 31 March 2016) and their health care costs in the 12-24 months following a cancer diagnosis. The health services included were hospitalizations, emergency room visits, drugs, home care services, and physician services (from time of diagnosis onwards). The difference in cost (i.e. incremental cost) between cancer patients who were smokers and those who were non-smokers was estimated using a generalized linear model (with log link and gamma distribution), and adjusted for age, sex, neighborhood income, rurality, cancer site, cancer stage, geographical region, and comorbidities.

Results

This study identified 3,606 smokers and 14,911 non-smokers. Smokers were significantly younger (61 vs 65 years), more likely to be male (53%), lived in poorer neighborhoods, had more advanced cancer stage, and were more likely to die within one year of diagnosis, compared to non-smokers. The regression model revealed that on average, smokers had significantly higher monthly healthcare costs ($5,091) than non-smokers ($4,847), $p<0.05$.

Conclusions

Smoking status has a significant impact on healthcare costs among cancer patients. On average, smokers incurred higher healthcare costs than non-smokers. These findings provide a further rationale for efforts to introduce evidence-based smoking cessation programs as a standard of care for cancer patients as they have the potential to not only improve patients' outcomes but also to reduce the economic burden of smoking on the healthcare system.

Keywords:

Smoking; Healthcare costs; Health system costs; Cancer; Economic burden

Impact of smoking on health system costs among cancer patients

Strengths and Limitations of this study

- Findings from this study represent one piece of evidence in support of the integration of smoking cessation programs into cancer care treatment plans as a standard of practice
- This study adds to the literature by providing up-to-date and precise health care cost estimates of smoking using existing administrative person-level costing approaches
- A limitation of this study is that it excludes a subset of relevant variables that may have had an influence on health outcomes and cost due to the nature of the study design (e.g., type of tumour, amount and duration of smoking)
- This study focused on the cost incurred to the public healthcare payer and, therefore, indirect costs were not considered but could be explored in future research
- The findings from this study should motivate policy makers to design, implement, and fund smoking cessation programs, which have the potential not only to improve patients' treatment outcomes but also to reduce the economic burden of smoking on the healthcare system

Impact of smoking on health system costs among cancer patients

INTRODUCTION

Cancer care is a substantial component of health care expenditures of developed countries.(1-3) In Canada, the economic burden of cancer was estimated to be $7.5 billion in 2012.(4) It is well recognized that smoking is the main modifiable risk factor for cancer (5) and it is estimated that it contributes to approximately 30% of all cancer deaths.(6, 7) Smoking can also harm directly or indirectly almost every organ of the body and is responsible for a number of other chronic diseases that contribute to higher health care costs.(5, 8-11) Quitting smoking after a diagnosis of cancer has been associated with improved general health, better quality of life, reduced toxicity, greater response to treatment (such as radiation therapy), and decreased risk of disease recurrence and second primary cancers.(12-18) Nevertheless, cancer patients are just as likely to smoke as the general public with the smoking rate being approximately 20%.(19) Furthermore, smoking cessation programs are rare in oncology settings.(12, 13, 20)

Although the impact of smoking on healthcare costs has been examined in the general population, there is very little information on the impact of smoking on the cost of cancer care in patients who are smokers compared to those who are not.

The study objective was to compare the health system costs of cancer patients who were current smokers with those of non-smokers between 2014 and 2016, from the perspective of a public healthcare payer, using administrative databases in Ontario, Canada. We hypothesized that smoking would be associated with higher overall health system costs as a result of the need to manage more frequent and severe toxicities of treatment, more frequent disease recurrence, as well as more non-cancer related morbidities. Understanding the cost burden of smokers with cancer may help drive policy change by providing an economic argument for investing in cessation resources and programs for cancer patients who smoke.

MATERIALS AND METHODS

This study was a secondary data analysis using existing administrative databases at Cancer Care Ontario (CCO) and the Institute for Clinical Evaluative Sciences (ICES), both located in Toronto, Ontario, Canada. Research ethics approval was obtained from St. Michael's Hospital, Toronto, Ontario, Canada.

Study population and setting

The study population consisted of newly diagnosed adult cancer patients, aged ≥18 years, who received ambulatory care from one of the 14 Regional Cancer Centres (RCCs) in Ontario, Canada, between 1 April 2014 and 31 March 2015. The Ontario Cancer Registry (OCR) was used to identify our study population. We excluded patients with: 1) an invalid health card (i.e., who were not eligible for public health care insurance); 2) an invalid death date (i.e., where death date was on or before the date of diagnosis); 3) missing data on smoking status; 4) a cancer stage of zero; 5) missing data on neighborhood-level income, geographical location, or rurality of residence; 6) lost health care coverage during the follow-up time; or 7) had multiple cancers. Each patient was followed until death or the end of the observation period (31 March 2016),

whichever came first. S1 Appendix provides a flow diagram of the number of patients excluded from the analysis.

Study population sub-groups (smokers and non-smokers)

The study population of cancer patients was divided into those who were identified as smokers and non-smokers. Cancer patients who were either currently smoking at the time of diagnosis or who had smoked in the previous 6 months of their first ambulatory care visit were identified as *smokers*, whereas all others were identified as *non-smokers*. Information on *smoking status* was obtained from the *CCO Smoking Cessation Dataset* (CCOSCD), which is part of the Activity Level Reporting (ALR) database housed at CCO. The CCOSCD collects information on the self-reported smoking status of newly diagnosed ambulatory cancer patients, whether the current smoker has been advised to quit, and whether the patient has been referred for smoking cessation counselling and/or pharmacotherapy.(21) Each RCC submits the data on these metrics on a monthly basis to CCO as part of CCO's Smoking Cessation Program. S2 Appendix describes the data elements in the dataset and their definitions.

Data sources and variables

A number of databases were used to obtain healthcare utilization data: the ALR database, the New Drug Funding Program (NDFP) database, the Ontario Drug Benefit (ODB) claims database, the Discharge Abstract Database (DAD) obtained from the Canadian Institute for Health Information (CIHI), the National Ambulatory Care Reporting System (NACRS) obtained from CIHI, the Ontario Health Insurance Program (OHIP) claims database, the Home Care Database (HCD), the Continuing Care Reporting System (CCRS), and the National Rehabilitation Reporting System (NRS). Table 1 provides a brief description of each database.

Table 1. Administrative databases used in the analysis

Database	Description
OCR	The Ontario Cancer Registry is the largest population-based cancer registry in Canada. The OCR contains over 300 fields, including primary site of cancer, county of residence at diagnosis and health insurance number.
ALR	The Ontario Activity Level Reporting provides a set of data elements from selected Ontario Cancer Centers that cannot be obtained from other providers. This information is used to support management decision making process.
NDFP	The New Drug Funding Program data are used for reimbursement decisions and to support cancer system planning for systemic therapy. To be eligible for reimbursement through the NDFP, hospitals must submit eligibility/enrolment data and treatment data in compliance with monthly billing deadlines. For treatment reimbursement, each patient must be enrolled in the NDFP by providing eligibility/enrolment data that include patient-specific demographic information and answers to a series of medical questions.
ODB	The Ontario Drug Benefit Formulary lists prescription drugs that are covered for patients over 65 years, and selected other groups (e.g., those that require income supports).
CIHI DAD	Hospitalization and comorbidity data are in the Discharge Abstract Database from

	the Canadian Institute for Health Information.
CIHI NACRS	Emergency room visits and same day surgery data were obtained from the National Ambulatory Care Reporting System.
OHIP	Ontario Health Insurance Program reports outpatient physician visits based on fee-for-service claims.
HCD	Home Care Database captures all home care services in Ontario.
CCRS	The Continuing Care Reporting System reports utilization of continuing care.
NRS	National Rehabilitation Reporting System captures rehabilitation utilization.

Healthcare costs

The outcome of interest for the study was total and disaggregated healthcare costs from the perspective of the Ontario Ministry of Health and Long-Term Care (MOHLTC) from the time of diagnosis. Patients in Ontario receive publicly funded health care, which covers costs for health services (e.g., hospitalization) including the costs of most drugs for patients over the age of 65 years or who are on social assistance. Healthcare costs included costs associated with hospitalizations, same-day surgeries, emergency room (ER) visits, outpatient prescription drugs, rehabilitation, complex continuing care, home care services, physician services, and laboratory and diagnostic tests. Cost estimates were derived using an existing costing algorithm at ICES. For example, hospitalizations and ER visit costs were estimated by multiplying a resource intensity weight (measure of utilization) with an average cost per hospital stay or ER visit (unit cost).(22) Physician visit costs were obtained from the Ontario Schedule of Benefits for Physician Services.(23) Additional details on the methods to estimate cost can be found elsewhere.(4, 22, 24) Costs were adjusted to 2016 Canadian dollars (CAD) using the health component of the Consumer Price Index in health care category (1 CAD = approximately 0.78 US dollars).(25)

Other variables

Due to potential differences between smokers and non-smokers, we controlled for patient characteristics by adjusting for a number of variables such as age at diagnosis, sex, cancer site, cancer stage (where available), geographical location of residence (i.e., rurality and Local Health Integration Network (LHIN)), neighborhood income quintile, and comorbidity (measured by the Adjusted Clinical Groups® or ACG®), all of which were obtained from the previously mentioned databases. In Ontario, publicly funded health care services are administered on a regional basis by the LHINs, which serve as the regional health authority. Each of the 14 LHINs is responsible for a distinct geographical location.(26) The ACG® system is a patient case-mix adjustment system used to measure health status by grouping diagnoses into clinical groups. The goal of this system is to assign each patient a single value, which represents the patient's comorbidity through his/her expected or actual use of health services, where a higher number refers to a greater number of comorbidities (0-4, 5-6, 7-9, and 10+).(27) In this study, this value was assigned at the time of the cancer diagnosis. Cancer sites or groupings were reported on as follows: bladder; bronchus and lung; breast; colorectal; corpus uteri; head and neck; prostate; melanoma; and "other". Other included cancers of the anus and anal canal, brain, esophagus, hematopoietic, liver, ovary, pancreas, renal, stomach, testis, and thyroid. The four most common types of cancer were lung, breast, colorectal, and prostate cancer. The extent of cancer was reported in one of 3 groups: stage 1-2; stage 3-4; and unknown stage. Cancer stage data in Ontario were available predominantly for

the four most common types of cancer (e.g., lung, breast, prostate, and colorectal); therefore, it was necessary to create a separate category for unknown cancer stage.

Analysis

The raw costs for non-smokers and smokers were reported descriptively. To adjust for different follow up times, as some patients (particularly smokers) have a greater chance of dying than non-smokers, we estimated person-month costs.(28)

The output of the economic analysis was the incremental cost (reported in 2016 CAD) between cancer patients who smoked and those who did not. We analyzed our dependent variable (monthly healthcare costs) using regression models to estimate the difference in expected health care cost between the two groups using recycled predictive methods,(28-30) as described in the following equation:

$$Cost_i = \beta_0 + \beta_1(smoking\ status)_i + \beta_2(age)_i + \beta_3(sex)_i + \beta_4(income\ quintile)_i + \beta_5(rurality)_i + \beta_6(cancer\ stage)_i + \beta_7(cancer\ type)_i + \beta_8(LHIN)_i + \varepsilon_i$$

where $cost_i$ represents a monthly cost of patient *I,* β_x refers to a coefficient estimate of each variable, *X*, such as smoking status, age, and sex and ε represents the error term. The smoking status variable was the primary independent variable, and the regression model was adjusted for potential confounding variables, such as age, sex, income, rurality, cancer stage, cancer site, geographical region (LHIN), and comorbidity. To accommodate for the skewness of cost data, a generalized linear model with log link and gamma family was used to estimate the incremental cost between smokers and non-smokers.(28, 31) We also conducted a Modified Park test to ensure that our selected model was the best fit.(28, 32) Collinearity was also explored using Variance Inflation Factor, and we found no evidence of collinearity. S3 Appendix reports a completed STROBE statement, a checklist of items that should be included in reports of cohort studies.

Patient and public involvement

There was no involvement of patients during the study period but there are knowledge translation activities with various knowledge users.

RESULTS

There were 3,606 smokers and 14,911 non-smokers in our study cohort (see Table 2). Cancer patients who smoked were significantly younger (61 vs 65 years), more likely to be male (53% vs 45%), live in lower income neighborhoods (25% of smokers compared to 16% of non-smokers were in the lowest income quintile), and more likely to live in rural areas (18% vs 15%) compared to cancer patients who were non-smokers. Cancer stage data was available for approximately 70% of patients over the study period. Of those with available cancer stage data, smokers were more likely to have advanced cancer stages than non-smokers. Almost 40% of

smokers were in stage 3-4 compared to approximately 27% of non-smokers. Roughly 25% of smokers died within 1 year of diagnosis compared to 15% of non-smokers who died over the same follow-up period. Approximately 30% of smokers were in the lowest comorbidity level (0-4) compared to 24% of non-smokers. Only 19% of smokers were in the highest comorbidity level (10+) compared to 23% of non-smokers. Among all cancer types studied, lung cancer was the most common type of cancer among smokers followed by breast cancer. For non-smokers, the most common cancer type was breast cancer followed by prostate cancer and lung cancer (Table 2); all three were identified as common types of cancer.

Table 2. Demographic characteristics of study population between smokers and non-smokers

Variable*	**Non-smokers**	**Smokers**
N	14,911	3,606
Mean age in years (SD)	65.1 (13.6)	60.6 (12.1)
Male	6,681 (44.8%)	1,907 (52.9%)
Age groups in years, N (%)		
18-44	1,116 (7.5%)	310 (8.6%)
45-54	1,973 (13.2%)	661 (18.3%)
55-64	3,443 (23.1%)	1,217 (33.7%)
65-74	4,525 (30.3%)	1,035 (28.7%)
75+	3,854 (25.8%)	383 (10.6%)
Income quintile, N (%)		
1 (lowest)	2,387 (16.0%)	887 (24.5%)
2	2,597 (17.4%)	818 (22.7%)
3	3,065 (20.6%)	691 (19.2%)
4	3,351 (22.5%)	649 (18.0%)
5 (highest)	3,511 (23.5%)	561 (15.6%)
Living in rural areas, N (%)	2,267 (15.2%)	662 (18.4%)
Death within 1 year, N (%)	2,211 (14.8%)	850 (23.6%)
Mean time from diagnosis to death (SD)	255.2 days (163.3)	236.8 days (159.6)
Comorbidity (ACG), N (%)		
0-4	3,589 (24.1%)	1,092 (30.3%)
5-6	3,295 (22.1%)	838 (23.2%)
7-9	4,533 (30.4%)	985 (27.3%)
10+	3,494 (23.4%)	691 (19.2%)
Cancer stage, N (%)		
1-2	6,378 (42.8%)	1,289 (35.7%)
3-4	3,958 (26.5%)	1,392 (38.6%)
Unknown	4,575 (30.7%)	925 (25.7%)
Cancer types, N (%)		
Lung	1,673 (11.2%)	1,017 (28.2%)
Breast	3,088 (20.7%)	497 (13.8%)
Head and neck	614 (4.1%)	292 (8.1%)
Prostate	1,694 (11.4%)	290 (8.0%)

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Colorectal	1,460 (9.8%)	268 (7.4%)
Melanoma	563 (3.8%)	81 (2.2%)
Corpus uteri	701 (4.7%)	64 (1.8%)
Bladder	196 (1.3%)	43 (1.2%)
Other	4,922 (33.0%)	1,054 (29.3%)

Legend: ACG= Adjusted Clinical Groups®; N = sample size; SD = standard deviation.
Note: * the two groups were significantly different across all variables ($p < 0.05$).

S4 Appendix reports the unadjusted monthly healthcare costs between the study groups. Generally, smokers incurred higher healthcare costs than non-smokers for hospitalizations, physician services, ER visits, home care services, and complex continuing care. Focusing on specific types of healthcare costs, smokers had approximately 30% higher hospitalization costs, 43% higher ER visit costs, 23% higher physician visit costs, and 30% higher home care costs than non-smokers. Overall, total monthly health care costs were higher among smokers ($5,649 ± $7,169) than non-smokers ($4,704 ± $6,737).

From the adjusted regression model (controlling for age, sex, income, rurality, stage, disease site, geographical region, and comorbidity), on average, smokers had significantly higher monthly healthcare costs ($5,091) than non-smokers ($4,847). Smokers incurred $244 (± 113; 95% confidence interval of $242, $245 and interquartile range $145, $328) more in healthcare cost per month, or $2,928 more per year than non-smokers, p=0.0047.

DISCUSSION

Understanding the impact of smoking on the healthcare costs of cancer patients may strengthen the rationale for decision makers to further invest in smoking cessation programs. It is generally understood that smoking can lead to worse clinical outcomes, but there is a paucity of literature on the impact of smoking on healthcare costs among cancer patients. The findings from this analysis are aligned with the limited available literature. Specifically, we found that cancer patients who were smokers were younger and more commonly males compared to cancer patients who were not smokers, which is in line with the literature.(10, 33) Additionally, smokers had, on average, almost 20% higher total monthly healthcare costs than non-smokers. When focusing mainly on hospitalizations, the incremental cost due to smoking was approximately 30% higher than non-smokers, in contrast to an increase of up to 50% in incremental hospitalization costs among smokers reported in the literature.(9, 34) Our findings suggest that cancer patients who are smokers are responsible for a greater economic burden than non-smokers.

Evidence on the importance of smoking cessation for cancer patients has strengthened in recent years. Several cancer care institutions in the United States have emerged as leaders in this field by incorporating smoking cessation programs into practice.(35) Ontario is the first jurisdiction in North America to implement a systematic smoking cessation program in all of its RCCs. Under the leadership of CCO, the provincial agency responsible for improving the quality of cancer services in Ontario, a smoking cessation program provides support for new ambulatory cancer patients by screening patients for tobacco use, advising on the benefits of quitting, and

offering referrals to smoking cessation resources. Understanding the impact of smoking on the healthcare costs incurred by cancer patients may further strengthen the rationale for the program and encourage policy makers (e.g., public healthcare payer) to invest in smoking cessation programs. The findings from this study may also be beneficial to other cancer agencies, and not-for-profit organizations (e.g., American Cancer Society, Worldwide Cancer Research, and Canadian Partnership Against Cancer) engaged in developing smoking cessation policies and implementing smoking cessation programs. In addition, this study may help to inform the general public about the burden of smoking among cancer patients and motivate hospital and health system administrators about the incremental economic impact of failing to help cancer patients quit smoking. The findings from this study represent a further piece of evidence in support of the integration of smoking cessation programs into cancer care treatment plans (in settings similar to the study setting) and will hopefully stimulate further research into the optimal implementation of smoking cessation programs in order to improve cancer care outcomes and reduce morbidity, mortality, and cost.

This study has strengths and limitations, which should be highlighted. The medical literature has called for more up-to-date and precise health care cost estimates of smoking.(9, 36) Existing Canadian literature has used cost estimates for smokers from the 1990s and/or employed high-level costing approaches, instead of using patient-level cost estimates. These prior estimates might not accurately reflect the true healthcare cost difference between smokers and non-smokers.(9, 36-38) This study represents a first step in systematically collecting these data and linking them to data on system-level resources. Furthermore, using existing data from administration databases, we were able to conduct the analysis with adjustment of potential confounders to increase the validity of the findings.

In terms of limitations, data on smoking status were limited to one assessment during the initial consultation period (28 days) for new ambulatory cancer patients. Therefore, it is possible that patients may have changed their smoking status after their cancer diagnosis but data on change in smoking status were not captured. Our analysis followed the intent-to-treat principle and was applied to both study groups (i.e., smokers at the time of diagnosis or who had quit in the last six months remained smokers throughout the analysis and vice versa). If some "smokers" quit smoking, their medical outcomes or tolerance to treatment may have been better than that of persistent smokers (presumably with less resource utilization and less cost). Consequently, this analysis may have provided a lower bound of the incremental cost. Individuals who had quit prior to 6 months would likely still have more health complications and resource utilization than life-long non-smokers. Classification of these patients as non-smokers may again lead to the possibility of an underestimation of the difference in cost between smokers and non-smokers. The data available on smoking status limited our ability to analyze former smokers and recent quitters as separate groups.

Our analysis was also limited by the available follow-up data. As the follow-up period was relatively short, it is possible that significant differences might be observed with a longer period of follow-up. It is also possible that, given the nature of the study design, relevant variables were not collected. For example, cancer stage data were available for the common types of cancer (i.e., lung, breast, colorectal, and prostate cancer), but not for some other tumour types, such as head and neck cancer. In addition to the common cancer types, our study included other tumour types (e.g., brain, liver) but their smaller numbers did not allow us to examine them separately. This could be a future area of research. Patients with multiple cancers were excluded from the study to distinguish the impact of smoking on a single tumour type. In addition, there

were no data available on the amount or duration of smoking, which would likely have an influence on health outcomes and cost. Smoking has been shown to increase both direct and indirect costs.(9, 37, 38) However, because our study used administrative data, indirect costs were not explored. Future clinical trials could consider prospectively documenting the specific clinical and financial benefits of smoking cessation as part of clinical care to evaluate the smoking cessation programs. Finally, the cost to implement a smoking cessation program was not included in this analysis, and may cancel out some of the economic benefits of helping smokers to stop smoking.

In conclusion, cancer patient smoking status has a significant impact on health system costs. On average, smokers incurred higher healthcare costs than non-smokers. These findings provide an additional reason for the introduction of evidence-based smoking cessation programs for cancer patients. The findings from this study should motivate policy makers to fund, design, and implement smoking cessation programs, which have the potential not only to improve patients' treatment outcomes but also to reduce the economic burden of smoking on the healthcare system.

Abbreviations

ACG®	Adjusted Clinical Groups®
ARCC	Canadian Centre for Applied Research in Cancer Control
CAD	Canadian dollars
CCO	Cancer Care Ontario
CCOSCD	CCO Smoking Cessation Dataset
ER	emergency room
ICES	Institute for Clinical Evaluative Sciences
LHIN	Local Health Integration Network
MOHLTC	Ontario Ministry of Health and Long-Term Care
RCCs	Regional Cancer Centres

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Contributors

All authors made important contributions to this work.
WI, CdO, NM, WE, AP, RT, KKWC contributed to this study's conception and design.
WI, NM, AP, RT were responsible for data collection and assembly.
All authors (WI, CdO, NM, WE, AP, RT, KKWC) were involved in data analysis and interpretation.
WI, CdO, NM, WE drafted the paper, and all authors critically reviewed and suggested amendments prior to submission.
The corresponding author attests that all listed authors meet authorship criteria and that others not meeting the criteria have been omitted.

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Competing interests:

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethics approval:

Research ethics approval was obtained from St. Michael's Hospital, Toronto, Ontario, Canada.

Data sharing statement:

This study made use of de-identified data from the Institute for Clinical Evaluative Sciences and Cancer Care Ontario who have the right and control over the data used.

Supporting Information

S1 Appendix: Flow diagram on the number of excluded patients

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S2 Appendix: Data elements and their definition of Cancer Care Ontario's Smoking Cessation Dataset

S3 Appendix: Completed STROBE statement, a checklist of items that should be included in reports of cohort studies

S4 Appendix: Unadjusted monthly healthcare costs between cancer patients who were smokers and non-smokers (2016 CAD)

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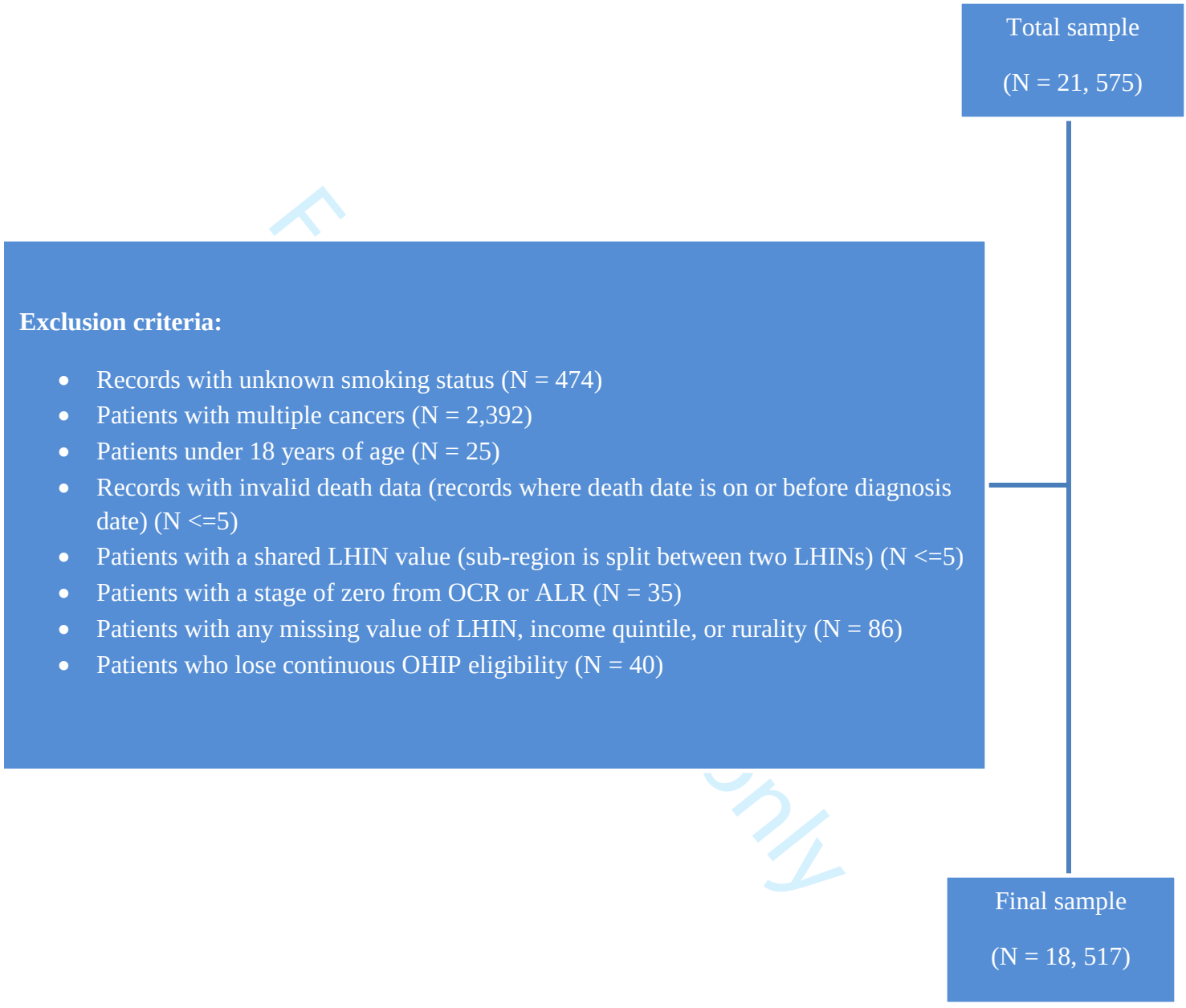
S1 Appendix: Flow diagram on the number of excluded patients



S2 Appendix: Data elements and their definition of Cancer Care Ontario's Smoking Cessation Dataset

Data Element	Definition
Patient Chart Number	Patient identifier code that is unique within the healthcare facility.
Submitting Hospital Number	The MOHLTC healthcare facility that submits activity to CCO.
Registration Date	Date this patient was first registered at this RCC and/or hospital for this disease.
Disease Sequence Number	The numeric sequence assigned to a primary cancer for a patient at a specific healthcare facility.
Visit Hospital Number	MOHLTC Master Number and name for the reporting healthcare facility where the cancer activity occurred (known by CIHI as Institution Numbers).
Visit Program Code	Primary cancer programs for clinic, planning and treatment activity. Includes; Radiation (RAD), Systemic (SYS), Surgical (SUR), Research (RE), Palliative (PA), Preventative Oncology (PO), or Psychosocial Oncology (PSO).
SMK_Q1	Patient self-reported as being a current smoker or indicated they had smoked within the past 6 months.
SMK_Q1 Date	The date the patient was asked SMK_Q1 (smoking status question).
SMK_Q2	Patient was advised of the benefits of smoking cessation.
SMK_Q3	Patient was recommended a referral to a smoking cessation program.
SMK_Q3 Date	The date when the patient was asked SMK_Q3 (assessed for quitting question).
SMK_Q4	Type of referral selected by patient. Referral is the act of directing or sending a patient to cessation service(s) for further action or support in making a quit attempt and becoming smoke free. The service should be arranged through the RCC (e.g., to a quit coach or to Canadian Cancer Society's Smokers Helpline fax referral program) to help the patient quit smoking. A referral is not simply the act of providing written information. Internal cessation referrals include services provided by the RCC (e.g. quit coaches), and external referrals are referred to outside the RCC.

Legend: MOHLTC = Ministry of Health and Long-Term Care; CCO = Cancer Care Ontario; RCC = Regional Cancer Centre; CIHI = Canadian Institute for Health Information

S3 Appendix: Completed STROBE statement, a checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page number
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4, 5, 6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4, 5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5, 6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one	5, 6

		group	
Bias	9	Describe any efforts to address potential sources of bias	6, 7, 9, 10
Study size	10	Explain how the study size was arrived at	4, 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5, 6, 7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	4
		(*d*) If applicable, explain how loss to follow-up was addressed	4
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed	5 (S1 Appendix), 7, 8, 9
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	5 (S1 Appendix)
Descriptive data	14*	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	7, 8, 9
		(b) Indicate number of participants with missing data for each variable of interest	5 (S1 Appendix)

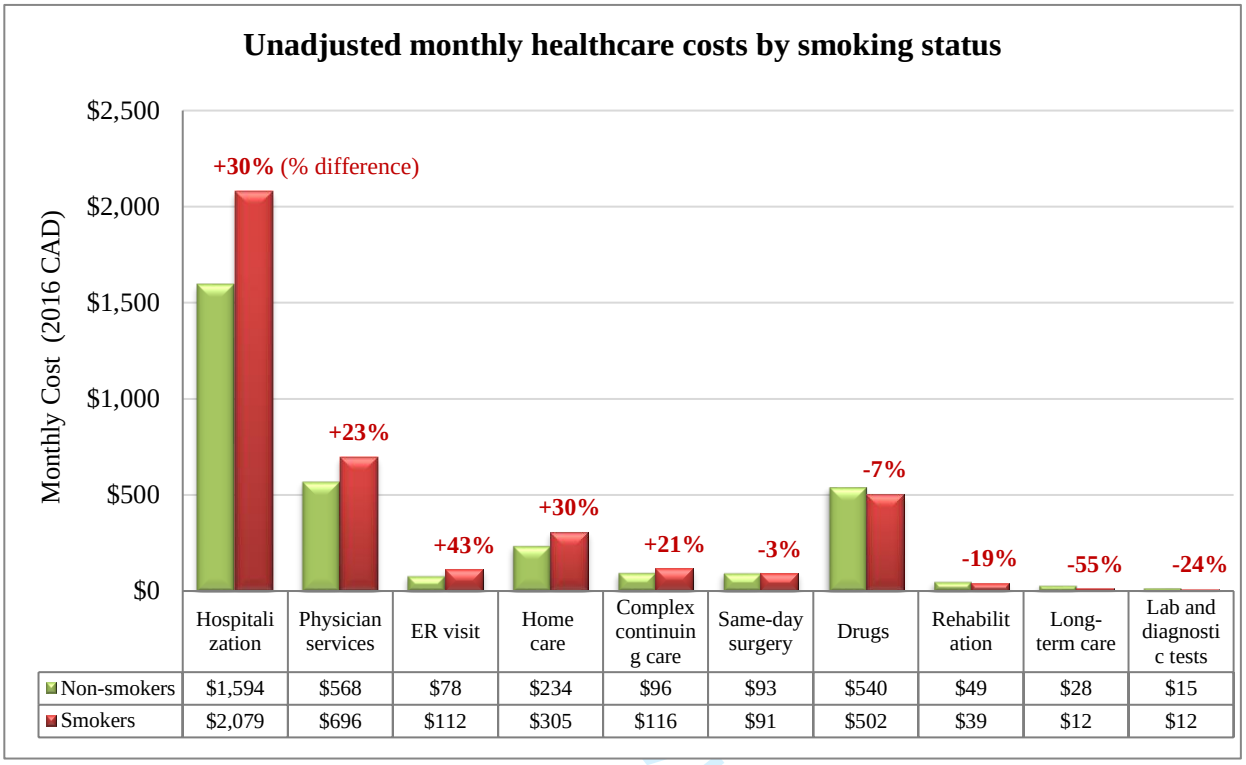
		(c) Summarize follow-up time (e.g., average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	7, 8, 9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarize key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10, 11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9, 10, 11
Generalizability	21	Discuss the generalizability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable,	12, 13

		for the original study on which the present article is based	

*Give information separately for exposed and unexposed groups.
N/A = Not applicable

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

S4 Appendix: Unadjusted monthly healthcare costs between cancer patients who were smokers and non-smokers (2016 CAD)



	Hospitalization	Physician services	ER visit	Home care	Complex continuing care	Same-day surgery	Drugs	Rehabilitation	Long-term care	Lab and diagnostic tests
Non-smokers	$1,594	$568	$78	$234	$96	$93	$540	$49	$28	$15
Smokers	$2,079	$696	$112	$305	$116	$91	$502	$39	$12	$12

Legend: CAD = Canadian dollars.

S3 Appendix: Completed STROBE statement, a checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page number
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4, 5, 6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4, 5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5, 6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one	5, 6

		group	
Bias	9	Describe any efforts to address potential sources of bias	6, 7, 9, 10
Study size	10	Explain how the study size was arrived at	4, 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5, 6, 7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	4
		(*d*) If applicable, explain how loss to follow-up was addressed	4
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5 (S1 Appendix), 7, 8, 9
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	5 (S1 Appendix)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7, 8, 9
		(b) Indicate number of participants with missing data for each variable of interest	5 (S1 Appendix)

		(c) Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	7, 8, 9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10, 11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9, 10, 11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable,	12, 13

		for the original study on which the present article is based	

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