

The Impact of Delays During the Pandemic Months on Survival of Lung Cancer Patients in Canada in 2020.

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Abstract

Objective

Most cancer deaths in the world are due to lung cancer and delays in diagnosis and treatment sharply reduce survival in lung cancer patients. This study examined the impact of delays during the early months of the pandemic on the survival of newly identified lung cancer patients in Canada in 2020.

Methods

The incidence of lung cancer, using population statistics from Statistics Canada and incidence rates from the Canadian Cancer Statistics in 2020, was estimated. Stage-wise incidences for each sex were calculated for each age group for each month of 2020. Using delay impact on each stage the final results were calculated.

Results

A total of 5,004 life years would have been lost due to 448 deaths in the long term (40 months) attributed to the delays caused during March, April, May and June in Canada. The estimated incidence for all stages of lung cancer for these months was 9,801 although the observed incidence was expected to be 6,571 due to reduced screenings. Hence, it was within the missing 3,231 cases that delays would occur. Over the short term (10 months) there are expected to be 151 early deaths and 273 deaths in the intermediate-term (20 months).

Conclusion

The COVID pandemic is estimated to result in increased mortality and fewer diagnosis' of lung cancer patients in Canada in 2020.

Background:

Most cancer deaths in the world are due to lung cancer (1, 2). This trend continues in 2020 as lung cancer is expected to cause more deaths than colorectal, pancreatic and breast cancers combined (2, 3). Treatment of lung cancer is generally considered one of the most expensive amongst cancers (4, 5). An expected estimate of \$2 billion was prospected to be spent in 2020 to treat lung cancer in Canada's public healthcare system. This amounts to an average of \$70,000 per lung cancer case (6). Moreover, these estimates do not account for the direct and indirect financial impact on the individual and their family, which are bound to be substantial (7). Since half of all lung cancers are diagnosed at stage 4, the survival rates are extremely low (3). As expected when delays are incorporated into this mix of low survival, they sharply reduce rates further in lung cancer patients (8). Myrdal et al. (9) demonstrated the impact of this

relation between delay and survival in patients receiving treatment for non-small-cell lung carcinoma (NSCLC). They noted delays from the first symptom and the first hospital visit to the initial treatment. They identified specific factors that contributed to poor survival, which were older age, advanced tumour stage, and non-surgical treatment delays including prolonged hospital delays and symptom to treatment delays. In a final multivariate model only increased symptom to treatment delay suggested an association with a better prognosis. There was an association between a short delay and a poor prognosis (9) which was most prominent in patients with advanced disease and this likely reflected the fact that patients with severe signs and symptoms received prompt treatment (9).

A recent study analyzed the impact of delays caused by Covid-19 on various cancer patients in the US (10). It reported surgical interventions as the main source of delays, which resulted in a reduction in survival. Similarly, another study gauged the impact of the delays from the pandemic in terms of a defined 3-month delay to more than a 12-month delay. The outcome of this type of delay was estimated to result in a 12 per cent increase in deaths in Italy (11). In a US study screening for breast cancer dropped by 89.2% and colorectal cancer screenings by 84.5% through May 2020 in Nebraska (2, 12). However, there exists an inadequacy over studies analysing the impact of the COVID-19 pandemic on newly diagnosed lung cancer patients in Canada. Due to various restrictions on movement and surge of patients burdening the healthcare systems, a large number of lung cancer patients may not have been identified entirely. Since available data is limited in the pandemic period, a prospective extrapolation of the existing data sources remains the most feasible option for determining the impact of the pandemic, more specifically the severe restrictions imposed, on lung cancer diagnosis and treatment. Hence, studying the impact of delayed detection of new lung cancer patients becomes imperative. This study examined the impact of delays during the early months of the pandemic on the survival of newly identified lung cancer patients in Canada in 2020.

Methods And Materials:

This was a secondary data analysis from published literature or openly available data sources, which negated the necessity for research ethics approval. A systematic procedure (13) was followed for secondary data analysis. It started with an investigation to learn what is already known and what remains to be learned about the topic including related and supporting literature and also incorporated previously collected data on this topic. Already existing data were collected from the available literature that was utilized in addressing the research question.

Data Sources:

A population-based study using the Statistics Canada data set of July 1st 2020 (1) was undertaken. The data set reported annual male and female populations from 2000 to 2020. From 'Canadian Cancer Statistics, a 2020 special report on lung cancer' (3) the incidence rates, mortality rates and stage-wise distribution for both the sexes were received for various age groups. United States Cancer Statistics (USCS) were used as a proxy for the month-wise distribution of lung cancer cases in Canada (14). Alanen

et al (15) provided the Kaplan Meir curves from which impact of delay was assessed and delays were considered based on Bakouny et al (16) for Massachusetts General Brigham hospital. Average life expectancy in Canada was drawn from the World Bank data (17).

Variables Included:

The model began with the population numbers of Canada segregated into sexes and further into age groups of less than 45, 45 to 54, 55 to 64, 65 to 74, 75 to 84 and 85 plus. Incidence and mortality rates per 100,000 were used for both the sexes to arrive at the yearly incidence and mortality. Subsequently, a stage-wise distribution for stages I-IV was applied to get the stage-wise incidence in each year. The month of diagnosis facilitated the splitting of the 2020 incidence into months while delay data allowed for the calculation of the percentage of patients that were actually diagnosed from the expected incidence. Finally, equations from no delay and delay cases were taken for each stage to calculate the number of early deaths. The difference of median age with average life expectancy was defined as the number of life-years lost.

Outcomes:

There were mainly two major outcomes in our model: number of early deaths and cumulative number of life years lost by a 130 day delay. The classification of early deaths was based on the usual survival curve in Alanen et al (15). They defined the delay as, if the time to diagnosis for the whole clinical pathway was more than 130 days, it is considered to be a delay. If the diagnosis falls under 130 days, it is considered as no delay. Alanen et al study was used as the source because it rendered recent data (2019) and clearly differentiated survival variation in different stages of lung cancer based on delay or no delay (15).

Statistical Analysis:

The population-based Excel model employed compounded cuts on the incidence to arrive at the results. Plotdigitizer.com tool was used to digitize the survival versus time curves for each stage from Alanen et al (15). The early deaths were calculated for three periods: a short period of 10 months, an intermediate period of 20 months and a long period of 40 months. Within these three periods, the survival varied across the stages. The survival percentages were considered for the month corresponding to the duration.

Results:

The total population of Canada exceeded a total of 38 million in 2020 with 19.1 million females and 18.9 million males (3). A total of 438,871 patients were diagnosed with lung cancer and 72.1% (316,544) died from it in Canada between 2000 and 2019 (3). Based on this, it was estimated that 29,239 new incident cases of lung cancer would have been identified in Canada with 14,231 of them in the female population and 15,008 in the male population in 2020 (Figure-1). Out of these, it was estimated that a total of 9,801 cases were expected to appear in March, April, May and June in Canada. However, the

observed incidence was expected to be only 6,571 largely because of the reductions in cancer screenings during that period. Subsequently, it was within the difference between the expected and observed cases, 3,231 cases, that delay would occur. These are the number of cases that should have appeared but because of the many factors contributing to healthcare service access barriers or related factors during the COVID-19 pandemic, these cases did not get diagnosed (10).

Incidences:

Table - 1 shows that across the age groups, the 65–74 year group had the highest number of expected incidences of lung cancer in Canada. Across stages, the highest number of expected incident cases were expected in Stage IV. A cumulative 9,801 Canadians, 4,770 females and 5,031 males were expected to be diagnosed with lung cancer between March and June 2020.

Table 1
Monthly cases in 2020 by Stages and Sex

Sex		Female				Male			
Month		March	April	May	June	March	April	May	June
Stage 1	< 45	3	3	3	3	2	2	2	2
Stage 1	45-54	15	15	15	15	9	9	9	9
Stage 1	55-64	60	59	59	60	45	44	44	45
Stage 1	65-74	108	106	106	108	86	84	84	86
Stage 1	75-84	81	79	79	81	69	68	68	69
Stage 1	85+	29	28	28	29	24	23	23	24
Stage 2	< 45	1	1	1	1	1	1	1	1
Stage 2	45-54	5	5	5	5	4	4	4	4
Stage 2	55-64	20	20	20	20	20	19	19	20
Stage 2	65-74	36	35	35	36	38	37	37	38
Stage 2	75-84	27	26	26	27	31	30	30	31
Stage 2	85+	10	9	9	10	10	10	10	10
Stage 3	< 45	2	2	2	2	2	2	2	2
Stage 3	45-54	12	12	12	12	10	10	10	10
Stage 3	55-64	48	47	47	48	50	49	49	50
Stage 3	65-74	86	84	84	86	95	93	93	95
Stage 3	75-84	64	63	63	64	77	75	75	77
Stage 3	85+	23	22	22	23	26	26	26	26
Stage 4	< 45	5	5	5	5	5	5	5	5
Stage 4	45-54	29	29	29	29	26	25	25	26
Stage 4	55-64	118	115	115	118	129	126	126	129
Stage 4	65-74	212	207	207	212	247	241	241	247
Stage 4	75-84	159	155	155	159	200	195	195	200
Stage 4	85+	56	55	55	56	68	67	67	68
Total		1207	1179	1179	1207	1273	1243	1243	1273

Table 2
Total observed incidence

Total Observed Incidence	March	April	May	June
Stage 1 < 45	3	3	3	3
Stage 1 45-54	16	16	16	16
Stage 1 55-64	70	69	69	70
Stage 1 65-74	130	127	127	130
Stage 1 75-84	101	98	98	101
Stage 1 85+	35	34	34	35
Stage 2 < 45	1	1	1	1
Stage 2 45-54	6	6	6	6
Stage 2 55-64	27	26	26	27
Stage 2 65-74	50	49	49	50
Stage 2 75-84	39	38	38	39
Stage 2 85+	13	13	13	13
Stage 3 < 45	3	3	3	3
Stage 3 45-54	15	14	14	15
Stage 3 55-64	65	64	64	65
Stage 3 65-74	121	118	118	121
Stage 3 75-84	94	92	92	94
Stage 3 85+	33	32	32	33
Stage 4 < 45	7	7	7	7
Stage 4 45-54	37	36	36	37
Stage 4 55-64	166	162	162	166
Stage 4 65-74	308	301	301	308
Stage 4 75-84	240	235	235	240
Stage 4 85+	83	81	81	83

However, the observed incidence (Table - 2) accounted for the fewer diagnoses of patients during the lockdowns. Accounting for this reduction using the Cancer.gov data (14) for Massachusetts General

Brigham, observed incidence numbers were extrapolated. A cumulative of 6571 patients, 3198 females and 3373 males were to be diagnosed with lung cancer out of the expected 9801 incident cases. This left 3231 patients undiagnosed for lung cancer within the lockdown months. About half of these undiagnosed patients (1634) were from the stage IV category alone, which is associated with the lowest survival rates (15).

Time Horizon Analysis:

Three different horizons ensured that the impacts, both short term and long term, from the lockdown on the newly diagnosed patients of lung cancer were gauged properly. There was a general increased death rate across the time periods (Table-3 and 4). Table - 3 shows the survival equations by the time of delay (> 130 days) and no delay (≤ 130 days) for all stages (stages 1 to 4). However, there were anomalies where delays led to a lower death percentage as compared to no delay. Results from one study (8) also reported such anomalies where a delay in treatment did not necessarily result in reduced survival. Though, over a longer period, the impact of such delays was starkly visible. Stage I patients had 15%, stage II had 23% higher, stage III had 19% higher and stage IV had a 10% higher death rate in the long term (Table-4).

Table 3
Survival vs Time Equation (Kaplan Meir Curves)

	Whole clinical pathway delay ≤ 130 days		Whole clinical pathway delay > 130 days	
	Equation	R ²	Equation	R ²
Stage 1	$y = 1$		$y : \{ 1, x < 2; 0.93426, 7 > x \geq 2; 0.85259, x > 7 \}$	
Stage 2	$y = 0.0008x^2 - 0.0409x + 0.9881$, $y = 0.482$ after 21 months	R ² = 0.9539	$y = 0.0004x^2 - 0.031x + 1.0715$	R ² = 0.9532
Stage 3	$y = 0.001x^2 - 0.0542x + 1.0284$	R ² = 0.9621	$y = 0.0006x^2 - 0.051x + 1.0594$	R ² = 0.97
Stage 4	$y = 0.0009x^2 - 0.0524x + 0.8157$	R ² = 0.9712	$y = 0.0017x^2 - 0.0766x + 0.9198$	R ² = 0.9856

Table 4

Difference in early deaths between time to diagnosis 130 days > and < 130 days (delay vs. no delay)

Overall	10 months period (short term)	20 months (intermediate term)	40 months (long term)
Stage I	15%	15%	15%
Stage II	15%	0%	23%
Stage III	-3%	9%	19%
Stage IV	2%	7%	10%

Source: Association of diagnostic delays to survival in lung cancer: single-centre experience, Alanen 2019 (15)

Life Years Lost And Burden Due To Premature Death:

Life years lost due to premature death was calculated using average life expectancies in Canada (17). Figure 2 shows that a cumulative 5,004 life years would have been lost due to 448 deaths in the long term (40 months) caused by the delays linked to the delays during March, April, May and June in Canada. For the intermediate horizon of 20 months, it would translate to 2723 early deaths and 3,055 life years lost. Finally, in the short horizon of 10 months, it would be 151 early deaths and 1,691 life years lost.

Using a cost per life-years lost threshold of \$30,000 (18), it can be calculated that this loss of life over a 40 month horizon translates to a burden of \$150 million. The same translates to \$91 million for an intermediate horizon of 20 months and \$50.7 million for 10 months.

Discussion:

Considering just 4 months of delay from March to June, there is a profound impact on additional deaths due to delays, especially in the long term, in Canada. The difference in estimated cases (cases based on the previous trend) and observed cases (expected cases to be seen in real), drive the increase in deaths and eventually the overall cumulative life years lost (19).

A meta-analysis has already established how the hazard ratios increased with a delay of 12 weeks during the pandemic in various cancers(10). Since lung cancer is often associated with a poor prognosis where over half of people diagnosed with lung cancer die within one year of diagnosis and the 5-year survival is less than 18% (20), it becomes even more critical to reduce any kind of delay in its diagnosis and treatment. These delays translate directly into days of life lost, and studies show that lung cancer is associated with the largest burden of cancer mortality measured in potential years of life lost (21).

Our results have presented how the COVID pandemic created healthcare provision limitations that resulted in delays in the diagnosis of lung cancer patients, confirming findings from many other similar

studies around the world (12, 22–25). Colorectal cancer and lung cancer are associated with the largest number of years of life lost due to delays in the diagnostic pathways in the UK (22).

Based on these findings, in the future, if any such similar situation arises equal consideration should be taken for patients of other critical diseases (10, 26, 27). Following stringent social distancing and lockdown measures, hospital systems have increasingly transitioned to telemedicine for non-pandemic health care services which have not been easy for oncology patients (26) and the impact of these approaches will continue to be examined.

Models of care aimed at creating solutions to minimize interruptions in diagnosis and treatment of cancer remain a top priority. It has been established that reducing time to treatment for cancer patients will improve survival, particularly for those with manageable disease at diagnosis (28). According to our results 5,004 life-years might be lost over the horizon of 40 months by delays in screening from March to June 2020, which will need to be addressed immediately. The need for expediency essential. Integrating fast tracking approaches to diagnosis and treatment of lung cancer were already being explored in the pre-COVID period in Nordic countries (except Finland) to improve patient outcomes (29). Studies demonstrate that reduced delays result in better survival for lung cancer patients (30) and a fast-track approach to diagnosis and treatment should be accommodated in the Canadian healthcare system as well, particularly given the current constraints presented with the pandemic.

Our study considered only new lung cancer patients in Canada in 2020 and since incidence only reflects a part of the total lung cancer population, the results from this analysis are unable to be extended to the total lung cancer population. Similarly, all cancer patients have undergone a similar or worse situation with their surgeries getting cancelled or delayed (22, 23, 31–34). These were driven by factors such as bed shortages, unavailability of intensive care unit (ICU) beds and or ventilators and the continued human health care resource shortages of hospital personnel due to sickness, quarantine, and the increased demands within the home (31). Similar to the situation in Canada, Corley et al (34) also showed that during the Covid-19 pandemic there was a considerable decrease in lung cancer and other cancer screening rates in the USA.

Our analysis proxies a monthly trend of cancer incidence and impact of COVID restrictions on lung cancer patients' incidence in Canada from US-based sources (14, 16). Since, the US shares higher similarities in terms of geography, life expectancy and death rate, with Canada, it was deemed fit to use US-based data as a proxy for Canada (35). However, their populations are significantly different as well as their healthcare service model, which can pose a potential barrier for the above justification of using US data. For, Alanen et al (15), a single centre retrospective study, showed the inverse relationship between delay and survival of lung cancer patients. Whereas a systematic review suggested that there was no association between delay to treatment and survival in lung cancer (36).

With the correct input of data, this model can be used for any future similar health related predictions, especially for cancers of all types enabling the predictions of cases and outcomes.

Conclusion

The COVID pandemic has resulted in increased mortality and fewer diagnoses of lung cancer patients in Canada in 2020. Subsequently, there has been an increase in the total life years lost due to lung cancer following the delays in assessment, screening and treatment that accompanied the pandemic lockdowns. The burden of life years lost over a horizon of 40 months due to delays in screening is estimated to be \$150 million, demonstrating the enormous impact that the pandemic has had on lung cancer patients.

Declarations

Author Contributions Statement:

PN drafted the study protocol, designed the study, analysed portions of the results, interpreted the results, and was a major contributor to the writing of the manuscript. LK prepared the model using secondary data sources and applied it toward the data collection, conducted the statistical analysis, data cleaning and quality check, interpreted the results and was a major contributor to the writing of the manuscript.

HB contributed to the literature review required for selection of an appropriate model, designed the study, conducted the data verification, analysed portions of the results, interpreted the results, and assisted with the manuscript writing. All authors read and approved the final manuscript.

Ethics approval and consent to participate:

Name of the ethics committee that approved the study: Ryerson University Research Ethics Board (REB). This study did not require REB approval because of usage of literature review and secondary data analysis.

Link to public listing of the ethical approval (if available): Not Available

Consent to publish: Not applicable

Availability of data and materials:

The datasets generated and/or analysed during the current study are available in the supplementary file: Model_Lung_Cancer_2021_07_31_Final

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Competing interest

There is no conflict of interest.

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Figures

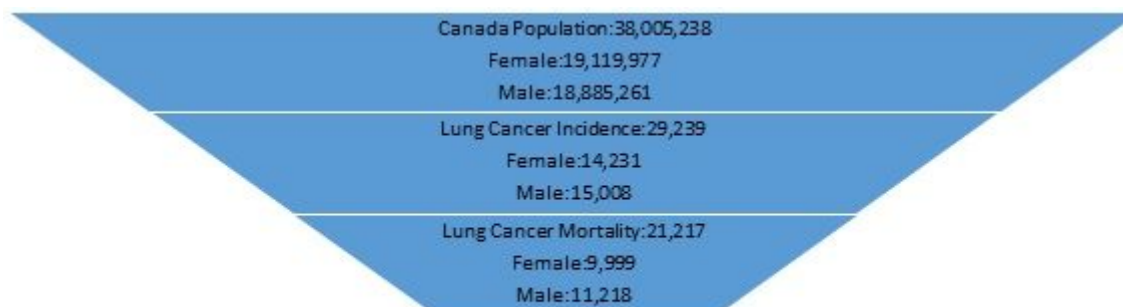


Figure 1

Lung Cancer in Canada, January-December 2020 (expected cases)

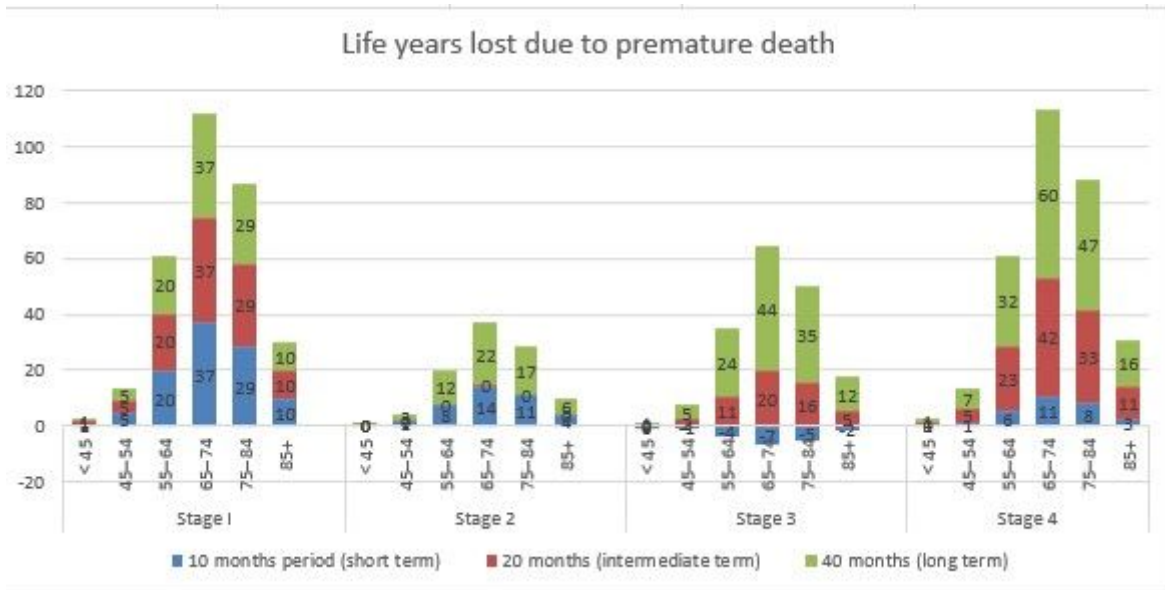


Figure 2

Life Years Lost Due To Premature Death

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [ModelLungCancer20210731Final.xlsx](#)