

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

Luv Khandelwal¹, Housne Begum², Pria Nippak^{2*}

¹Master of Science in Management (Operations and Information Systems), 2021-2023 Brock University, St Catharines, Canada ²School of Health Services Management, Ryerson University, Toronto, Canada Email: *pnippak@ryerson.ca

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Abstract

Background and Purpose: Most cancer deaths in the world are due to lung cancer and diagnosis and treatment delays 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. Method: This was a secondary data analysis from published literature and openly available data sources. Cancer Statistics from existing literature were used as a proxy for the month-wise distribution of lung cancer cases in Canada. The incidence of lung cancer, using population statistics from Statistics Canada and incidence rates from the Canadian Cancer Statistics in 2020, was estimated. The population-based Excel model employed compounded cuts on the incidence to arrive at the outcomes. Plotdigitzer.com tool was used to digitize the survival versus time curves for each stage from secondary sources. 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 5004 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 9801 although the observed incidence was expected to be 6571 due to reduced screenings. Hence, it was within the missing 3231 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). Conclusions: This study using a mathematical model showed that in 2020, the COVID epidemic resulted in higher mortality and fewer lung cancer diagnoses in Canada. As a result of the delays in assessment, screening, and treatment that accompanied the pandemic lockdowns, there has been a rise in total life years

lost due to lung cancer, demonstrating the pandemic's huge impact on lung cancer patients.

Keywords

Impact, Delays, Pandemic, Survival, Lung Cancer Patients

1. Background

Lung cancer is the leading cause of mortality worldwide [1]. This trend is anticipated to continue in 2020, with lung cancer expected to kill more people than colorectal, pancreatic, and breast cancers together [2]. Lung cancer is often regarded as one of the costliest malignancies to treat [3]. The cost of lung cancer treatment in Canada's public healthcare system is expected to reach \$2 billion by 2020. This works out to almost \$70,000 per lung cancer case on average [3]. Furthermore, these figures do not take into consideration the immediate and indirect financial consequences for the individual and their family, which are very certain to be significant [4]. Since half of all lung cancers are diagnosed at stage 4, the survival rates are extremely low [2]. As expected, when delays are incorporated into this mix of low survival, they sharply reduce rates further in lung cancer patients [5]. Myrdal et al. [6] explained 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 of 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 [6] 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 [6]. Further, some studies have demonstrated that longer delays are not associated with a poorer prognosis of lung carcinoma [7].

A recent study analyzed the impact of delays caused by COVID-19 on various cancer patients in the US [8]. 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 percent increase in deaths in Italy for colorectal cancer patients [9]. However, there exists an inadequacy of studies analysing the impact of the COVID-19 pandemic on newly diagnosed lung cancer patients. The analysis was conducted for the months of March, April, May and June. Because they were the peak months of the epidemic, this choice was made [10]. A huge number of lung cancer patients may not have been discovered fully due to

different constraints on transportation and a rush of patients burdening healthcare systems. Because data is scarce during the epidemic, prospective extrapolation of current data sources remains the most viable approach for establishing the pandemic's influence on lung cancer detection and treatment, particularly the severe limits imposed. As a result, research into the effects of late identification of new lung cancer patients is critical. This study examined the impact of delays during the early months of the pandemic on the survival of newly diagnosed lung cancer patients in Canada in 2020.

2. Methods

This was a secondary data analysis from published literature and openly available data sources, which negated the necessity for research ethics approval. A systematic procedure [11] was followed for sourcing appropriate data for the secondary data analysis. Already existing data points were collected from the available literature that was utilized in addressing the research question. The modelling approach was not tested on a different dataset given the novel nature of the problem under investigation.

2.1. 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" [2] the incidence rates, mortality rates and stage-wise distribution for both the sexes were retrieved 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 [12] [13]. Alanen *et al.* [14] provided the Kaplan Meir curves from which impact of delay was assessed and delays were considered based on Bakouny *et al.* [12] for Massachusetts General Brigham hospital. Average life expectancy in Canada was drawn from the World Bank data [13].

2.2. Variables Included

The model began with the population numbers of Canada stratified by sex 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. Since the study was based on the detection of new patients it was deemed fit to use the general life expectancy.

2.3. Outcomes

There were two major outcomes in our model: the 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.* [14]. The authors defined a delay as, any diagnosis where the time to diagnosis for the whole clinical pathway was more than 130 days, which was also applied within the current study. The current investigation only focused on diagnosis delays and excluded treatment delays. The 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 [14]. 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 number of early deaths were calculated for each stage [1] [2] for three time periods: 10 months, 20 months, and 40 months. The survival percentages were considered for the month corresponding to the duration.

2.4. Statistical Analysis

The population-based Excel model employed compounded cuts on the incidence to arrive at the results. Plotdigitzer.com tool was used to digitize the survival versus time curves for each stage from Alanen *et al.* [14]. The model was a population-based model and applied multiple cuts at each stage. The total population of Canada stratified by sex and further by age groups of "<45", "45 - 54", "55 - 64", "65 - 74", "75 - 84" and "85+". Incidence rates for each subgroup were applied to obtain the incidences for the corresponding group. Using stage-wise incidence and month of diagnosis distribution the expected number of cases were calculated for 2020. Reduced incidence because of delays and subsequently the reduced survival was calculated. Reduced survival was calculated as the difference in the estimated incidence and estimated reduced incidence. Further, 10-month, 20-month and 40-month survival was calculated [15]. Based on the median age of each group and average life expectancy in Canada the life years lost were calculated.

3. Results

In 2020, Canada's overall population surpassed 38 million, with 19.1 million females and 18.9 million men [2]. A total of 438,871 patients were diagnosed with lung cancer and 72.1% (316,544) died from this type of cancer in Canada between 2000 and 2019 [2]. 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**). A total of 9801 cases were projected to arise in Canada during the months of March, April, May, and June. However, the observed incidence was expected to be only 6571 largely because of the 67% reductions in cancer screenings during that



Figure 1. Lung cancer in canada, January-December 2020 (expected cases).

period [16]. Subsequently, it was within the difference between the expected and observed cases, 3231 cases that delay would occur. These are the cases that should have been diagnosed during the COVID-19 pandemic but were not due to a variety of causes such as healthcare service access hurdles or other associated factors [7].

3.1. 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 was expected in Stage IV. A cumulative 9801 Canadians, 4770 females and 5031 males were expected to be diagnosed with lung cancer between March and June 2020.

However, it can be observed from **Table 2**, which populates the incidence stratified by age group and stage for the months March-June, the observed incidence accounted for the fewer diagnoses of patients during the lockdowns. Accounting for this reduction using the Cancer.gov data [12] 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 [14].

3.2. 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. The death rate increased across the time periods (**Table 3** and **Table 4**). **Table 3** shows the survival equations by the time of delay (>130 days) and no delay (\leq 130 days) for all stages (stages 1 to 4). **Table 4** shows the difference in deaths for no delay versus delay over different time periods of 10 months, 20 months and 40 months. 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).

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 5004 life years would have been lost due to 448 deaths in the long term (40 months) caused by 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 3055 life years lost. Finally, in the short horizon of 10 months, it would be 151 early deaths and 1691 life years lost.

Table 1. Monthly cases in 2020 by stages and sex.

Sex			Fen	nale			Ма	ale	
Month		March	April	May	June	March	April	May	June
Stage 1	<45	3	3	3	3	2	2	2	2
	45 - 54	15	15	15	15	9	9	9	9
	55 - 64	60	59	59	60	45	44	44	45
	65 - 74	108	106	106	108	86	84	84	86
	75 - 84	81	79	79	81	69	68	68	69
	85+	29	28	28	29	24	23	23	24
	<45	1	1	1	1	1	1	1	1
	45 - 54	5	5	5	5	4	4	4	4
Stage 2	55 - 64	20	20	20	20	20	19	19	20
	65 - 74	36	35	35	36	38	37	37	38
	75 - 84	27	26	26	27	31	30	30	31
	85+	10	9	9	10	10	10	10	10
	<45	2	2	2	2	2	2	2	2
	45 - 54	12	12	12	12	10	10	10	10
C t	55 - 64	48	47	47	48	50	49	49	50
Stage 3	65 - 74	86	84	84	86	95	93	93	95
	75 - 84	64	63	63	64	77	75	75	77
	85+	23	22	22	23	26	26	26	26
	<45	5	5	5	5	5	5	5	5
Stage 4	45 - 54	29	29	29	29	26	25	25	26
	55 - 64	118	115	115	118	129	126	126	129
	65 - 74	212	207	207	212	247	241	241	247
	75 - 84	159	155	155	159	200	195	195	200
	85+	56	55	55	56	68	67	67	68
Total		1207	1179	1179	1207	1273	1243	1243	1273
Total for both sexes		2480	2422	2422	2480				

Total Obse	rved Incidence	March	April	May	June
	<45	3	3	3	3
	45 - 54	16	16	16	16
C44 1	55 - 64	70	69	69	70
Stage 1	65 - 74	130	127	127	130
	75 - 84	101	98	98	101
	85+	35	34	34	35
	<45	1	1	1	1
	45 - 54	6	6	6	6
Stage 2	55 - 64	27	26	26	27
Stage 2	65 - 74	50	49	49	50
	75 - 84	39	38	38	39
	85+	13	13	13	13
	<45	3	3	3	3
	45 - 54	15	14	14	15
Stage 2	55 - 64	65	64	64	65
Stage 5	65 - 74	121	118	118	121
	75 - 84	94	92	92	94
	85+	33	32	32	33
	<45	7	7	7	7
	45 - 54	37	36	36	37
Stage 4	55 - 64	166	162	162	166
Jiage 4	65 - 74	308	301	301	308
	75 - 84	240	235	235	240
	85+	83	81	81	83

 Table 2. Total observed incidence.

 Table 3. Survival vs time equation (Kaplan Meir Curves).

Total Obse	erved Incidence	March	April	May	June
	<45	3	3	3	3
	45 - 54	16	16	16	16
Stage 1	55 - 64	70	69	69	70
Stage I	65 - 74	130	127	127	130
	75 - 84	101	98	98	101
	85+	35	34	34	35
	<45	1	1	1	1
Store 2	45 - 54	6	6	6	6
Stage 2	55 - 64	27	26	26	27
	65 - 74	50	49	49	50

Continued					
	75 - 84	39	38	38	39
	85+	13	13	13	13
	<45	3	3	3	3
	45 - 54	15	14	14	15
Stars 2	55 - 64	65	64	64	65
Stage 5	65 - 74	121	118	118	121
	75 - 84	94	92	92	94
	85+	33	32	32	33
	< 45	7	7	7	7
	45 - 54	37	36	36	37
Stage 1	55 - 64	166	162	162	166
Stage 4	65 - 74	308	301	301	308
	75 - 84	240	235	235	240
	85+	83	81	81	83

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 1	15%	15%	15%
Stage 2	15%	0%	23%
Stage 3	-3%	9%	19%
Stage 4	2%	7%	10%

Source: Association of diagnostic delays to survival in lung cancer: single-centre experience, Alanen 2019 [15].



Life years lost due to premature death

Figure 2. Life years lost due to premature death.

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 threshold amount is an estimate from the cost per DALYs averted calculated from 3 sources for Canada and each of its provinces. The same translates to \$91 million for an intermediate horizon of 20 months and \$50.7 million for 10 months.

4. 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]. The trend is however not uniform across the stages. This can be attributed to different impacts from diagnosis delays on patients of different stages.

During the pandemic, a meta-analysis found that the hazard ratios increased with a 12-week wait in several malignancies [7]. Because lung cancer is generally linked with a poor prognosis, with over half of those diagnosed dying within one year of diagnosis and a 5-year survival rate of less than 18% [20], reducing any delay in detection becomes even more crucial. These delays equate to days of life lost, and studies reveal that lung cancer has the highest burden of cancer death in terms of potential years of life lost [21].

Our findings show how the COVID-19 pandemic hampered healthcare delivery, causing delays in lung cancer patient detection, and they substantiate findings from several other research studies throughout the world [11] [22]. In the United Kingdom, the most years of life are lost owing to delays in diagnostic processes for colorectal cancer and lung cancer [23].

Based on these findings, in the future, if any such similar situation arises equal consideration should be given for patients of other critical diseases [8] [23]. 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 [23] 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 [24]. According to our results 5004 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 is essential. Integrating fast tracking approaches to diagnosis and treatment of lung cancer were already being explored in the pre-COVID-19 period in Nordic countries (except Finland) to improve patient outcomes [25] and continue to be a very pressing issue. Studies demonstrate that reduced delays result in better survival for lung cancer patients [26] and as such a fast-track approach to diagnosis and treatment should be recommended in the Canadian healthcare system, particularly given the compounded constraints presented with the pandemic associated delays.

There were a few influencing factors in this study that may have impacted the findings, like only new lung cancer patients in Canada in 2020 were estimated and the calculated incidence reflects a part of the total lung cancer population. Additionally, only delays in diagnosis were considered, while delays in treatment were not included, which may have impacted the findings [22]. The focus was primarily on delays caused by the pandemic. However, studies have shown that cancer patients of all types have undergone a similar or worse situation with their surgeries getting cancelled or delayed [22] [27] [28]. These could be 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 [27]. Like the situation in Canada, Corley et al. [28] also showed that during the COVID-19 pandemic there was a considerable decrease in lung cancer and other cancer screening rates in the USA. The majority of lung cancer patients in later stages are patients progressed from the previous stages and not newly diagnosed patients [2]. Hence, the study is only concerned with a section of lung cancer patients and not all the lung cancer patients. Our analysis proxies a monthly trend of cancer incidence and impact of COVID-19 restrictions on lung cancer patients' incidence in Canada from US-based sources [10] [12]. Since along with the similarities in the lung cancer incidence rates, 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 [29] [30].

This study has some limitations, including the use of US-based population data because their healthcare delivery model differs greatly from that of Canada, which could represent a potential hurdle to the above argument of using US data. Other studies both within and outside of Canada demonstrate that there is considerable variation in study findings. For example, Alanen *et al.* [14], a single centre retrospective study, showed the inverse relationship between delay and survival of lung cancer patients. Whereas a systematic review from Australia suggested that there was no association between delay to treatment and survival in lung cancer [31].

Future Scope

Different mathematical models have been used during COVID-19 pandemic period and served as useful tools for policymakers to help respond to societal pandemic need [32]. With the real time input of data, this model can also be used for any future similar health related predictions, especially for cancers of all types enabling the predictions of cases and outcomes. Predictive modelling is

becoming increasingly important to ensure that healthcare systems can be responsive and adaptive to changing population needs.

5. Conclusion

Different mathematical models have been used during COVID-19 pandemic period for societal needs. This study is also a mathematical model, developed to assess the impact of delays during the early months of the pandemic on the survival of newly diagnosed lung cancer patients in Canada in 2020 using population-based Statistics Canada data from published literature and openly available data sources. This model showed that in 2020, the COVID epidemic resulted in higher mortality and fewer lung cancer diagnoses in Canada. As a result of the delays in assessment, screening, and treatment that accompanied the pandemic lockdowns, there has been a rise in total life years lost due to lung cancer, demonstrating the pandemic's huge impact on lung cancer patients. This study also showed 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. This model may be used to make comparable future health-related predictions, particularly for cancers of all sorts, making it possible to anticipate cases and outcomes.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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