

Expected Cost Savings From Low-Dose Computed Tomography Scan Screening for Lung Cancer in Alberta, Canada



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ABSTRACT

Introduction: The expensive modern therapeutic regimens for advanced lung cancer (LC) stages have been recently approved. We evaluated whether low-dose computed tomography (LDCT) LC screening of high-risk Albertans is cost saving.

Methods: We used a decision analytical modeling technique with a health system perspective and a time horizon of 3 years to compare benefits associated with reduced health service utilization (HSU) from earlier diagnosis to the costs of screening. Using patient-level data, HSU costs by stage of disease were estimated for patients with LC, including inpatient, outpatient, and physician services, and costs for prescription drugs and cancer treatments.

Results: Of 101,000 people aged 55 to 74 years eligible for screening, an estimated 88,476 scans would be performed in Alberta in 3 years. Given LDCT sensitivity and specificity of 90.5% and 93.1%, respectively, we estimated that a stage shift toward earlier diagnosis would be expected whereby 43% more patients would be identified at stage 1 or 2 as compared with without screening. The estimated cost of screening is \$35.6 million (M), whereas the stage shift associated with screening would avoid \$42M in HSU costs. The net cost avoidance associated with screening is therefore \$6.65M. The probability for the screening to be cost saving is estimated at 72%.

Conclusions: This study has revealed that LDCT LC screening is likely to be cost saving in Alberta. Adoption of

this program into the provincial health care system is worth considering provided constraints in the system related to surgical capacity and CT wait times could be addressed.

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Introduction

Cancer is the leading cause of death in high-income countries.¹ Of cancer-related deaths, lung cancer (LC) is the leading cause.² In Canada, LC is the second most often diagnosed cancer and the leading cause of cancer death for both men and women. It is estimated that 29,800 Canadians will be diagnosed with LC (13% of all new cancer cases) and 21,200 Canadians will die from LC (25% of all cancer deaths) in 2020.³ In the province of Alberta, corresponding numbers are 2608 diagnosed cases and 1596 deaths.⁴

Early diagnosis through screening could reduce mortality from several cancers, including LC. According to The National Lung Screening Trial,⁵ low-dose computed tomography (LDCT) scan screening reduced mortality from LC by 20% and from any cause by 6.7%. The efficacy of LDCT scan screening in reducing mortality from LC is supported by findings of other trials,⁶ including Multicentric Italian Lung Detection trial⁷ and the Dutch-Belgian Randomized Lung Cancer Screening trial.⁸

Accordingly, the Canadian Task Force on Preventive Health Care recommends screening for LC with three consecutive annual LDCT scans in high-risk adults aged 55 to 74 years who currently smoke or quit less than 15 years ago, with a smoking history of at least 30 pack-years.⁹ There are several studies reporting that LC with LDCT screening would be cost-effective in Canada. For example, the Alberta Thoracic Oncology Program Lung Cancer Screening Working Group estimated that the incremental cost-effectiveness ratio (ICER) for LC screening would be approximately \$47,000 per quality-adjusted life-year (QALY) gained.¹⁰ Goffin et al.¹¹ used Canadian data and estimated the ICER at \$52,000 per QALY gained. More recently, the British Columbia Ministry of Health performed a comprehensive cost estimate for the provincial screening program and estimated that LDCT screening for LC would have an ICER of \$1556 per QALY gained.¹²

Although there is currently no formal provincial LC screening program in Canada, several pilot programs are active or in the planning phase,¹³ including in the province of Alberta. As health care is under provincial jurisdiction, each province would need to design and adopt their own formal program. As health care budgets are limited, the question as to how formal LC screening programs will be funded is of interest to all jurisdictions. Screening would reduce mortality by a “stage shift” from late-stage incurable cancer (stages III and IV) to early stage curable disease (stages I and II),¹⁴ and presumably

treatment costs, as modern therapies are increasingly more expensive for later stages than for early stages. But to date, cost-effectiveness analyses have not considered the increased cost of contemporary targeted and chemioimmunotherapy regimens used for advanced stages. Modeling current therapeutic regimens and costs, we aim to explore the possibility and scenarios under which LDCT scan screening for LC could become cost saving to health systems.

Methods

Study Design and Outcomes

We used a decision analytical modeling technique with a health system perspective and a time horizon of 3 years to estimate the cost avoidance of the screening. We included health service utilization (HSU) costs and excluded patient’s health outcomes, such as mortality, utility score (health-related quality of life), and life years gained, which were previously studied.^{10–12}

Cost avoidance was calculated by comparing the costs between the following two arms: screening versus no screening (Fig. 1). The structure of model for treatment costs was identical between the two arms. Patients with LC were categorized into early stages I to II versus late stages III to IV. Nevertheless, the two arms were different from each other in terms of distribution (percentages) of the cancer stages, and therefore also by treatment costs. For example, in the current practice (no screening), most LCs was detected at a late-stage III to IV, and therefore, the treatment cost was expected to be higher than the screening scenario where most LCs were detected at an earlier stage I to II.

In this study, treatment costs were costs for HSU, including inpatient, outpatient, and physician services, and costs for prescription drugs and cancer treatment services (e.g., visits to cancer centers, radiotherapy, chemotherapy, and immunotherapy). To estimate the net benefit (cost avoidance), we added the screening cost, including the cost of three annual LDCT scans for the screening population and the cost of further investigations for those who had a false-positive result, to the screening arm treatment cost. To estimate the return on investment (ROI) ratio, we divided the difference in treatment costs between the two arms for the screening cost.

Study Population and Model Inputs

The eligibility criteria for LC screening were based on the recommendations of the Canadian Task Force on Preventive Health Care: Albertans aged 55 to 74 years with at least a 30 pack-year smoking history who currently smoke or quit less than 15 years ago.¹⁵ We conservatively applied an initial screening uptake

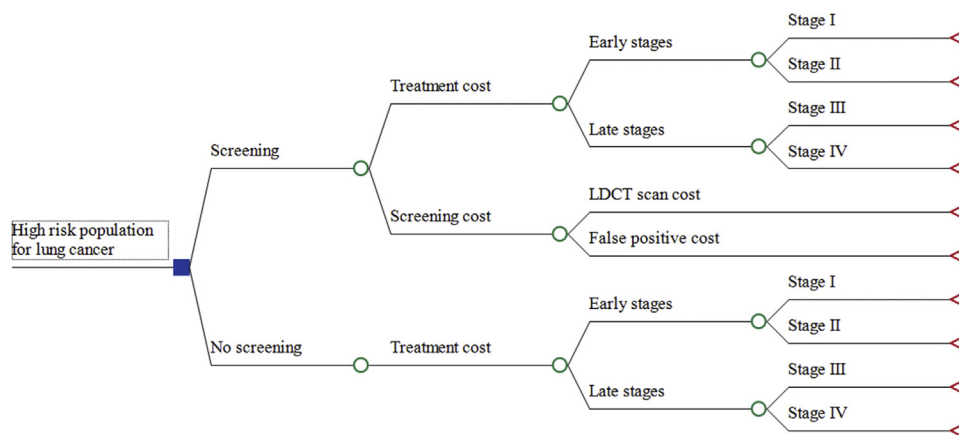


Figure 1. Model structure. LDCT, low-dose computed tomography.

rate of 40% and a re-screening adherence rate of 70% to the screening population,¹⁶ to estimate the number of people screened and the number of LDCT scans.

The distribution of LC stages at diagnosis for the current practice was calculated from the Alberta Cancer Registry database using the latest data (2017) where the information on cancer stages was available. The distribution of LC stages at diagnosis for the screening scenario was retrieved from the Pan-Canadian Early Detection of Lung Cancer study.¹⁴ From this study, we also obtained the incidence of LC among the screening population. Sensitivity and specificity of the screening were retrieved from the Alberta Lung Cancer Screening Study.¹⁷ As this was a secondary analysis of previously collected data by Alberta Health, the HREBA.CC indicated that obtaining additional informed consent was not required.

Data Sources for HSU

A cohort of patients aged 55 to 74 years diagnosed with LC by stage from 2004 to 2017 and their cancer treatment data were extracted from the Alberta Cancer Registry. We used their unique lifetime identifiers to link to the Alberta Health Administrative databases to identify their HSU.¹⁸ Specifically, inpatient services were retrieved from the discharge abstract database. Outpatient services were retrieved from the National Ambulatory Care Reporting System. Practitioner services were retrieved from the Alberta Health Care Insurance Plan claims database. Prescription drugs were retrieved from the Pharmaceutical Information Network database. Relapse rates after a surgery for stages I, II, or III were calculated from the Alberta Glans-Look lung cancer database (<http://glanslook.ca/>). We assumed that all relapse LCs were treated as stage IV.

Costing Methods

Inpatient and outpatient service cost estimates were based on the Canadian Institute for Health Information Case Mix Group+ methodology, which included both medical and nonmedical (e.g., support and administrative departments, such as information systems, house-keeping, and finance) costs.¹⁹ The cost for each Case Mix Group+ or Comprehensive Ambulatory Classification System group was retrieved from the Alberta Health Interactive Health Data Application.²⁰ The cost for physician services was defined as paid amounts available in claims that physicians made to the Alberta Health Care Insurance Plan. For alternative payment plan (e.g., salary) claims (~10%), where the paid amounts are not available, we used the system assessed amounts. Costs for prescription drugs were based on prices per unit listed in the Alberta Drug Benefit List.²¹

Cost per cancer center visit or appointment was assumed to be equal to that per general practitioner visit.²² Cost for radiotherapy was retrieved from the Cancer Care Alberta. Costs for new chemotherapies (e.g., newer than 2017) for patients with LC at different stages were estimated by a tree model (as the followings), as actual data were not yet available.

Tree Model to Estimate Treatment Costs for LC by Stage (Based on Experts' Opinions)

Standard of care treatment at stage IV is dependent on the presence of oncogene; patients at stage IV were separated into "Driver oncogene present" or "Driver oncogene absent" group (Supplementary Fig. 1). Of the "Driver oncogene present," patients were further grouped into *EGFR*-sensitizing mutation, *ALK* rearrangement, or *ROS-1* rearrangement. If having *EGFR*-sensitizing mutation, patients were treated with osimertinib for 20.7 months as the first-line therapy,

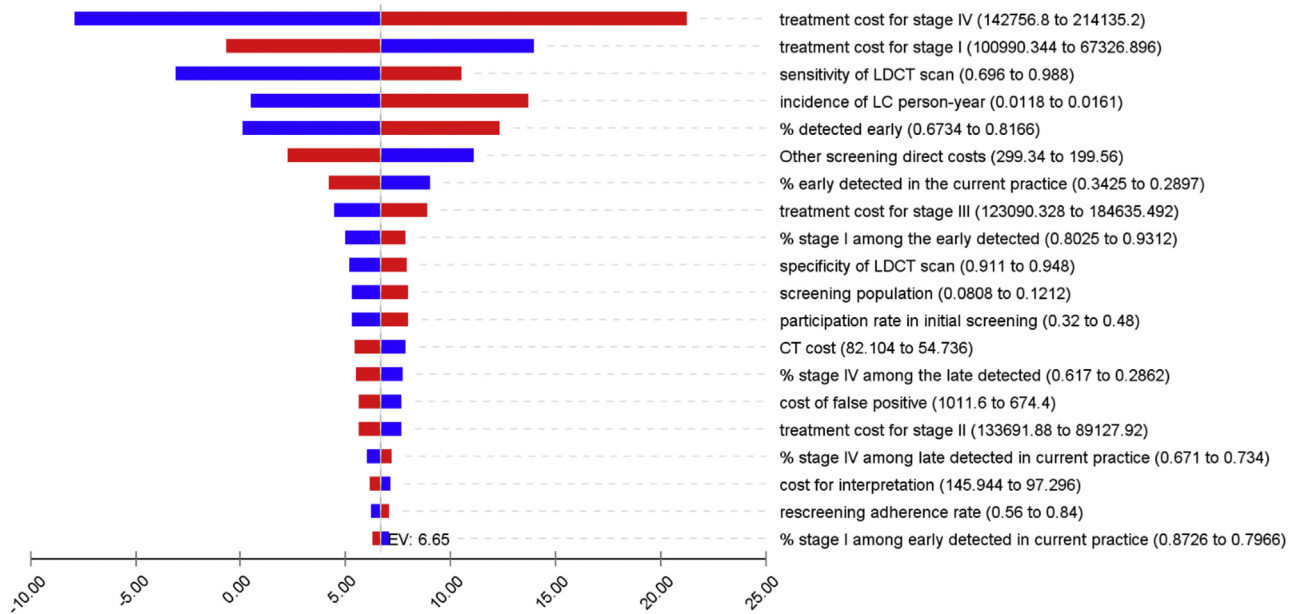


Figure 2. Variations of cost avoidance (\$ million) by input parameter. CT, computed tomography; EV, expected value; LC, lung cancer; LDCT, low-dose computed tomography.

platinum-pemetrexed for 10 cycles (each cycle is 3 wk) as the second-line therapy, and pembrolizumab, nivolumab, or atezolizumab for six cycles as the third-line therapy. For patients with *ALK* rearrangement, their first- and second-line therapies were alectinib for 28.1 months and platinum-pemetrexed for 10 cycles of 3 weeks, respectively. Patients with *ROS-1* rearrangement were treated with crizotinib for 22.4 months as the first-line and platinum-pemetrexed for 10 cycles as the second-line therapy. Of the “Driver oncogene absent,” patients were separated into two groups, including programmed death-ligand 1 (PD-L1) more than or equal to 50% group and PD-L1 1% to 49% or PD-L1 less than 1% group. If PD-L1 more than or equal to 50%, patients were treated with pembrolizumab for 7.9 months as the first-line, platinum double for 10 cycles as the second-line, and docetaxel for four cycles as the third-line therapy. If PD-L1 1% to 49% or PD-L1 less than 1%, patients were treated with pembrolizumab plus platinum double for 10 cycles as the first-line therapy and docetaxel for four cycles as the second-line therapy. To estimate costs of chemoimmunotherapy per patient, we multiplied the weight (proportion) with the cost of each therapy by duration (retrieved from the pan-Canadian Oncology Drug Review; [Supplementary Table 1](#)) and then summed it up.

Of patients with stage III LC, approximately 50% being ineligible for curative approach (due to

comorbidities, tumor volume, etc.) was treated as stage IV above. The other 50% fit for curative treatment were treated with surgery and radical chemoradiation of whom 70% then received durvalumab for 5 months. For stages I and II, if tumor was greater than 4 cm or node positive, patients were treated with platinum-pemetrexed for four cycles. Methods to add costs for relapse cancer to the treatment costs of stages I, II, and III were illustrated in [Supplementary Table 2](#).

Sensitivity Analysis

Both deterministic and probabilistic sensitivity analyses were performed for the uncertainty of parameters. For the deterministic analysis, we used a one-way sensitivity analysis—each variable was varied independently (one at a time) from the lower to the upper values of 95% confidence interval (CI) or the base-case value plus or minus 20% if 95% CI was not available. The results were presented by a tornado diagram, where the most sensitive variable is on the top and the least is at the bottom ([Fig. 2](#)). For the probabilistic sensitivity analysis, all variables were varied simultaneously, and we assumed a normal distribution for the number of people who are eligible for screening, a beta distribution for probabilities and a gamma distribution for costs. We ran the model 30 times (the minimal sample size for normal distribution) of 1000 trials to calculate mean and

Table 1. Model Inputs

Variables	Base-Case	Range		Source
		Lower	Higher	
Number of eligible people	101,000	80,800	121,200	16
Participation rate	0.4000	0.3200	0.4800	16
Adherence rate	0.7000	0.5600	0.8400	16
Incidence of LC	0.0138	0.0118	0.0161	14
Sensitivity	0.9050	0.6960	0.9880	17
Specificity	0.9310	0.9110	0.9480	17
Stage distribution at diagnosis				
Early stages				
No screening	0.3157	0.2897	0.3425	Calculated
Screening	0.7500	0.6734	0.8166	14
Of the early stages				
Stage I—no screening	0.8372	0.7966	0.8726	Calculated
Stage I—screening	0.8772	0.8025	0.9312	14
Of the late stages				
Stage IV—no screening	0.7032	0.6710	0.7340	Calculated
Stage IV—screening	0.4474	0.2862	0.6170	14
Costs, \$				
Treatment—stage I	84,158.62	67,326.89	100,990.34	Calculated
Treatment—stage II	111,409.90	89,127.92	133,691.88	Calculated
Treatment—stage III	153,862.91	123,090.33	184,635.50	Calculated
Treatment—stage IV	178,446.00	142,756.80	214,135.20	Calculated
False-positive	843.00	674.40	1011.60	Calculated
LDCT scan	68.42	54.74	82.10	AHS Finance
Interpretation	121.62	97.30	145.94	AHS Finance
Other screening direct costs	249.45	199.56	299.34	AHS Finance

AHS, Alberta Health Services; LC, lung cancer; LDCT, low-dose computed tomography.

95% CI of the probability for the screening to be cost saving (cost avoidance >0).

All costs and savings were converted to 2019 Canadian dollars using the Canadian Price Index by the Bank of Canada Inflation Calculator.²³ Stata SE 16 (www.stata.com/) and TreeAge Pro 2019 (www.treeage.com/) were used for data analyses.

This study was ethically approved (HREBA.CC-21-0251) by the Health Research Ethics Board of Alberta—Cancer Committee on August 3, 2021.

Results

The model inputs are found in Table 1. The total number of people who are eligible for the screening was estimated at 101,000.¹⁶ The participation and adherence rates were estimated at 40% and 70%, respectively. Yearly incidence rate of LC among the screening population was 1.38%.¹⁴ Sensitivity and specificity of the LDCT scan screening were 90.5% and 93.1%, respectively.¹⁷

Patients with LC, including date and stage of diagnosis, were identified using the Alberta Health Administrative databases 2017. We calculated the percentage of LC early stages at diagnosis at 31.57% for current

practice (no screening) option. Of this, stage I accounted for 83.72%. The percentage of LC late stages at diagnosis was 68.43% (=100%–31.37%). Of this, stage IV accounted for 70.32%. For the screening option, we would expect a stage shift. According to the PANCAN study,¹⁴ the screening detected 75% of LC at early stages, of which stage I accounted for 87.72%. Of the 25% (=100%–75%) LC diagnosed at later stages, stage IV accounted for 44.74%.

The treatment costs for a LC case in a period of 3 years were estimated at \$84,158 for stage I, \$111,410 for stage II, \$153,863 for stage III, and \$178,446 for stage IV (Table 1 and Supplementary Table 3, for more details). Of note, these treatment costs of LC were estimated in Alberta, which can be lower or high than other jurisdictions. For example, it is higher than the estimate in Spain,²⁴ but lower than that in the United States, especially the treatment cost for the latest stage.²⁵ The cost of further investigation for a false-positive result was estimated at \$843. According to Alberta Health Services (AHS) Finance, the cost per LDCT scan was \$68.42 with an interpretation fee of \$121.62. Other screening direct cost was estimated at \$249.45 per scan.

On the basis of the above-mentioned inputs, our model estimated 88,476 scans performed in 3 years

Table 2. Cost Avoidance Due to Screening

Base-Case Analysis	Stage I	Stage II	Stage III	Stage IV	Total
No-screening arm					
Number of LC cases detected	292	57	224	532	1105
Treatment costs, \$ (million) (1)	24.58	6.33	34.53	94.89	160.32
Screening arm					
Number of LC cases detected	727	102	152	124	1105
Treatment costs, \$ (million)	61.19	11.33	23.46	22.08	118.06
Screening costs, \$ (million)					35.61
Total costs for screening arm, \$ (million) (2)					153.67
Cost-avoidance, \$ = (1) - (2)					6.65
ROI = (\$160.32-\$118.06)/\$35.61					1.2
Sensitivity analysis					
Range of cost avoidance, \$ (million)					-7.91 to 21.22
Probability for cost avoidance > 0					71.9% (95% CI: 71.2%-72.5%)

CI, confidence interval; LC, lung cancer; ROI, return on investment.

(40,400 in year 1, 28,280 in year 2, and 19,796 in year 3), and 1105 LC cases were detected. At the same time, the screening produced 6021 false-positive cases [$88,476 \times (1 - 0.0138) \times (1 - 0.931)$]. Applying respective costs to these numbers, the screening cost for AHS was estimated at \$35.61 million.

If no screening, the number of LC cases by stage at diagnosis was 292 stage I, 57 stage II, 224 stage III, and 532 stage IV (Table 2). Multiplying these numbers with the respective treatment cost per case by stage (Table 1) and then summing them up, the total cost for the no-screening arm was estimated at \$160.32 million.

If screening, the corresponding numbers were 727 stage I, 102 stage II, 152 stage III, and 124 stage IV. Multiplying these numbers with the respective treatment cost per case by stage (Table 1) and then summing them up, the total treatment cost for the screening arm was estimated at \$118.06 million. Adding the screening cost (\$35.61 million) mentioned earlier, the total cost for screening arm was \$153.67 million. Comparing the total cost between the no screening and screening arms, the cost avoidance by the screening was estimated at \$6.65 million (Table 2).

The one-way sensitivity analysis revealed that the cost avoidance varied from -\$9.71 million to \$21.22 million. Top five of the most sensitive variables were the treatment cost for stage IV, the treatment cost for stage I, sensitivity of LDCT scan screening for LC, and the percentage of LC cases detected at early stages by screening (Fig. 2).

The probabilistic sensitivity analysis revealed that the probability for cost avoidance more than 0 was 72% (95% CI: 71%-73%) (Table 2). Regarding the distribution of cost avoidance, the probability to get a cost avoidance between \$0 and \$10 million was 34%, between \$10 and \$20 million was 22%, between \$20 and

\$30 million was 10%, and more than \$30 million was 6% (Fig. 3).

Discussion

Using a modeling technique together with an analysis of the Alberta Health Administrative databases, this study estimated an expected cost avoidance if the province adopted a screening program for LC with 3-year LDCT scan among the high-risk population. The results revealed that, by detecting more patients at earlier stages (I and II) in comparison with the current practice, the screening would save the health system approximately \$6.7 million in the 3-year period. In terms of ROI, the ROI ratio is 1.2, meaning that every \$1 being invested in the screening program would bring \$1.2 in return. There is a good chance for the screening to be cost saving as the probabilistic sensitivity analysis estimated this probability at 72% of 1000 trials.

Since 2011 when the National Lung Screening Trial revealing the efficacy of LDCT scan screening on reducing mortality of LC has been published,⁵ several studies on cost-effectiveness of LDCT scan screening for LC have been performed in Canada. They concluded that the screening is cost-effective with an ICER of \$1556 to \$46,594 per QALY.¹⁰⁻¹² Nevertheless, this is the first study (to our knowledge) which has revealed that the screening is cost saving owing to our incorporation of modern therapeutic regimens for advanced LC stages.

Although this information would help inform policy regarding adopting LDCT scan screening for LC program into Alberta and other jurisdiction health systems, there are several related issues that need to be considered. First, as the cost avoidance results from the stage shift, a health system may need to shift resource allocation from the more expensive treatment of stages III and IV (i.e., targeted and chemo-immuno-therapy) to the cheaper

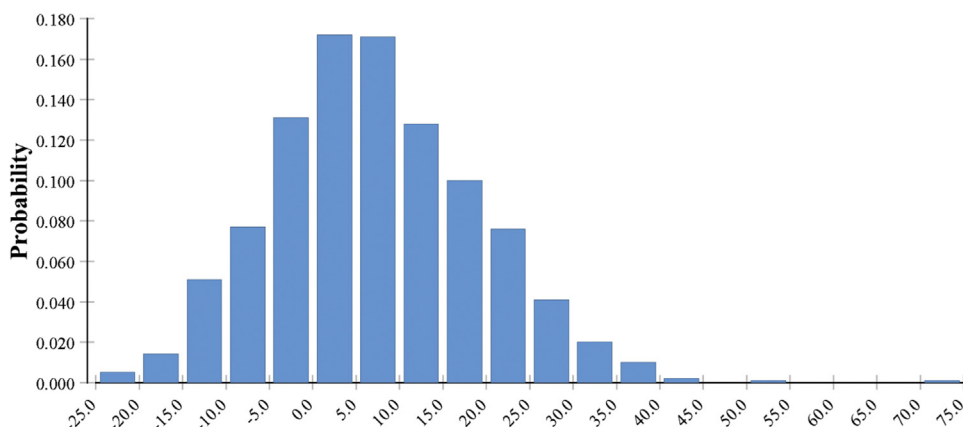


Figure 3. Probability of cost avoidance (\$ million).

treatment of stages I and II (i.e., surgery). In this study, there is a reduction in chemo-immuno-therapy use for 36 patients with stage III and 408 patients with stage IV. At the same time, we estimated that AHS would need to prepare for an addition of 444 (435 stage I + 45 stage II – 36 stage III) surgeries if the screening is adopted. This would increase the burden for AHS in terms of improving the wait time for cancer-related surgeries, which is already days-to-weeks longer than that of other provinces and the national average.²⁶ Therefore, an increase of surgical capacity, such as increasing operating room time and staffing, including surgeons, anesthesiologists, and nursing personnel, is desirable. Second, one of the most sensitive variables influencing the cost avoidance was the treatment cost of stage I (Fig. 2). Besides the cost of surgeries, relapse cancer (treated as stage IV) cost is considerable. Of note, the annual relapse rates in Alberta were as high as 15% after stage I and 36% after stage II surgeries (Supplementary Table 2). These rates of relapse may be due to an underestimation of the true cancer stage or dissemination of cancer cells during surgery, or both.²⁷ Interventions to reduce these relapse rates would be desirable although they could also add costs such as more accurate novel staging tests or novel adjuvant therapy approaches. Third, the wait time for diagnostic imaging, including CT scans and positron emission tomography scans, is currently problematic in Alberta. According to the Auditor General of Alberta,²⁸ the wait list for a CT examination tripled in 5 years to 60,181 patients as of March 2020. Albertans waited approximately 2.2 weeks longer than the national average for a CT examination, ranking Alberta first for longest wait times among the Canadian provinces in 2019.²⁹ Therefore, when considering the LDCT scan screening adoption, it is important to consider if the wait time of CT scan would become worse adding the screening and how to improve it. In contrast,

radiographic imaging in LC stages III and IV is extensive and expensive as such patients require frequent chest CTs and roentgenograms, brain magnetic resonance imaging scans, bone scans, and positron emission tomography scans. The stage shift by the screening would result in decreases in the necessity for such imaging. These resources can be shifted to the less expensive and more efficacious screening exams. Finally, in this study, we used an uptake rate of 40% which is higher than has been achieved in the United States,³⁰ but significantly lower than what has been achieved in other Canadian cancer screening programs. It remains to be proven whether population-wide (e.g., at the provincial level) LC screening programs in publicly funded health care environments will be able to achieve this or higher uptake rates. But to maximize the population impact of LC screening, more effective and innovative approaches will be needed to achieve higher uptake rates.

There are several limitations to be acknowledged. First, according to Statistics Canada,³¹ the rate of smoking is decreasing in Alberta. In 2015, there were 640,600 smokers accounting for 18.4% of people aged 12 years or older. In 2019, these number and percentage were 568,400 and 15.5%. In line with this trend, the age-standardized incidence of LC is also decreasing.⁴ Therefore, the cost avoidance could be overestimated as we did not factor the smoking decrease in estimating the eligible population for screening and used the same incidence rate of LC in 3 years of the study period. Nevertheless, although the eligible population decreases overtime, the decrease in incidence of LC among high-risk population is unlikely or small. Second, although a stage shift is found in the initial years of screening, the cost savings from preventing a more advanced case of cancer through early detection are delayed whereas the costs of the early stage treatment are not. As such, any cost savings would only be detected with a long-term

lens. Third, we did estimate stage I recurrence based on clinical data from a local registry and did not model differences that may be found within stage changes in distribution (e.g., more T1a and less T2a within stage I) which may be different in screened versus incidental LC cases. This may affect costs related to disease recurrence. Fourth, as data on utilization of new targeted and chemo-immuno-therapies were not available, we used a modeling technique to estimate their costs which could result in an over- or underestimate. Nevertheless, we believe that sensitivity analyses have minimized the above-mentioned biases. Similarly, treatment standards are likely to continue to change over time, including the use of more expensive adjuvant treatments in earlier stages of the disease which would require recalculation of our estimates. Finally, as cessation of screening at 3 years results in an increase of LC deaths,³² current immunotherapy regimens seem to prolong survival of advanced-stage LC,³³ implying continuing utilization beyond the time horizon of 3 years would come with substantial costs, and the restriction of LC screening entry criteria results in major disparities¹⁴; further study of comparative effectiveness that also includes more scenarios, such as longer time horizon and longer screening programs with different screening intervals and expanded eligible criteria (such as to include patients aged from 50 to 80 y with 20 pack-years), is desirable. In addition, further study should consider different LC risk levels of the screening population to provide policymakers with more information as it is suggested that costs and benefits are varied by risk level. For example, Cressman et al.³⁴ used a refined risk prediction tool for selection to compare the cost-effectiveness of screening low-risk and high-risk populations with no-screening option and found that cost-effectiveness and budget impact are improved by screening high-risk population.

In conclusion, there is a good chance for the LDCT scan screening for LC to be cost saving in a Canadian jurisdiction such as Alberta. Adoption of this program into the provincial health care system is worth considering provided constraints in the system related to surgical capacity and CT wait times could be addressed.

CRediT Authorship Contribution Statement

Nguyen Xuan Thanh, Douglas Stewart, Alain Tremblay, Huiming Yang: Conceptualization.

Truong-Minh Pham, Nguyen Xuan Thanh, Michelle L. Dean: Data curation.

Nguyen Xuan Thanh, Truong-Minh Pham: Formal analysis.

Nguyen Xuan Thanh, Arianna Waye, Randeep Sangha: Methodology.

Tracy Wasylak, Douglas Stewart: Project administration, Resources, Software, Supervision.

Nguyen Xuan Thanh, Arianna Waye: Writing - original draft.

Nguyen Xuan Thanh, Truong-Minh Pham, Arianna Waye, Alain Tremblay, Huiming Yang, Michelle L. Dean, Tracy Wasylak, Randeep Sangha, Douglas Stewart: Interpretation of data and results, Writing - review & editing, Final approval of the submission.

Supplementary Data

Note: To access the supplementary material accompanying this article, visit the online version of the *JTO Clinical and Research Reports* at www.jtocrr.org and at <https://doi.org/10.1016/j.jtocrr.2022.100350>.

References

1. Dagenais GR, Leong DP, Rangarajan S, et al. Variations in common diseases, hospital admissions, and deaths in middle-aged adults in 21 countries from five continents (PURE): a prospective cohort study. *Lancet*. 2020;395:785-794.
2. Barta JA, Powell CA, Wisnivesky JP. Global epidemiology of lung cancer. *Ann Glob Health*. 2019;85:1-16.
3. Canadian Cancer Society. Lung cancer statistics 2020. <https://www.cancer.ca/en/cancer-information/cancer-type/lung/statistics/?region=pe>. Accessed November 25, 2020.
4. Cancer Care Alberta, Alberta Health Services. Surveillance and Reporting: The 2021 Report on Cancer Statistics in Alberta. <https://public.tableau.com/app/profile/cancercontrol.ab/viz/The2021ReportonCancerStatisticsinAlberta/Highlights>. Accessed January 12, 2022.
5. National Lung Screening Trial Research Team, Aberle DR, Adams AM, et al. Reduced lung-cancer mortality with low dose computed tomographic screening. *N Engl J Med*. 2011;365:395-409.
6. Rota M, Pizzato M, La Vecchia C, Boffetta P. Efficacy of lung cancer screening appears to increase with prolonged intervention: results from the MILD trial and a meta-analysis. *Ann Oncol*. 2019;30:1040-1043.
7. Pastorino U, Silva M, Sestini S, et al. Prolonged lung cancer screening reduced 10-year mortality in the MILD trial: new confirmation of lung cancer screening efficacy. *Ann Oncol*. 2019;30:1162-1169.
8. De Koning H, Van De Aalst C, Ten Haaf K, Oudkerk M. PL02.05 Effects of volume ct lung cancer screening: mortality results of the nelson randomised-controlled population based trial. *J Thorac Oncol*. 2018;13(suppl):S185.
9. Canadian Task Force on Preventive Health Care. Lung cancer 2016. <https://canadiantaskforce.ca/guidelines/published-guidelines/lung-cancer/>. Accessed November 25, 2020.

10. Alberta Thoracic Oncology Program. Report of the Alberta Lung Cancer Screening Working Group 2012. <https://www.albertahealthservices.ca/assets/healthinfo/poph/hi-poph-surv-cancer-lung-2012.pdf>. Accessed November 25, 2020.
11. Goffin JR, Flanagan WM, Miller AB, et al. Cost-effectiveness of lung cancer screening in Canada. *JAMA Oncol*. 2015;1:807-813.
12. Government of British Columbia. "The Lifetime Prevention Schedule": Establishing Priorities among Effective Clinical Prevention Services in British Columbia. <https://www2.gov.bc.ca/gov/content/health/about-bc-s-health-care-system/health-priorities/lifetime-prevention>. 2016. Accessed November 25, 2020.
13. Lung Cancer Canada. Lung cancer screening in Canada 2020. <https://www.lungcancer.ca/Lung-Cancer/Screening.aspx>. Accessed November 25, 2020.
14. Tammemagi MC, Schmidt H, Martel S, et al. Participant selection for lung cancer screening by risk modelling (the Pan-Canadian Early Detection of Lung Cancer [PanCan] study): a single-arm, prospective study. *Lancet Oncol*. 2017;18:1523-1531.
15. Canadian Partnership Against Cancer. Lung cancer screening with low dose computed tomography: Guidance for Business Case Development. Version 1.0 - March 2020. <https://www.partnershipagainstcancer.ca/db-sage/sage20181504/>. Accessed April 21, 2021.
16. Canadian Partnership Against Cancer (CPAC). Lung Cancer (LC) Screening Business Case for Alberta. Toronto Health Economics and Technology Assessment Collaborative (theta) report 2020. https://view.officeapps.live.com/op/view.aspx?src=https%3A%2F%2Fwww.partnershipagainstcancer.ca%2Fwp-content%2Fuploads%2F2020%2F03%2FLung-Cancer-Screening_Business-Case_EN_FIN.AL.docx&wdOrigin=BROWSELINK. Accessed June 16, 2022.
17. Trembley A, Taghizadeh N, MacGregor JH, et al. Application of lung-screening reporting and data system versus pan-canadian early detection of lung cancer nodule risk calculation in the Alberta Lung Cancer Screening Study. *J Am Coll Radiol*. 2019;16:1425-1432.
18. Alberta Health. Overview of Administrative Health Datasets. Analytics and Performance Reporting Branch, April 28, 2017. <https://open.alberta.ca/dataset/657ed26d-eb2c-4432-b9cb-0ca2158f165d/resource/38f47433-b33d-4d1e-b959-df312e9d9855/download/research-health-datasets.pdf>. Accessed November 26, 2020.
19. CIHI. CMG+. <https://www.cihi.ca/en/cmgi>. Accessed November 26, 2020.
20. Alberta Health. Analytics and Performance Reporting Branch. Interactive Health Data Application: Dementia. http://www.ahw.gov.ab.ca/IHDA_Retrieval/selectCategory.do. Accessed November 26, 2020.
21. Alberta Health. Drug benefit list - publication. <https://www.ab.bluecross.ca/dbl/publications.php>. Accessed November 26, 2020.
22. Alberta Medical Association. Fee navigator. <https://www.albertadoctors.org/fee-navigator/hsc/03.03A>. Accessed November 26, 2020.
23. Bank of Canada. Inflation Calculator. www.bankofcanada.ca/rates/related/inflation-calculator. Accessed November 15, 2021.
24. Corral J, Espinàs JA, Cots F, et al. Estimation of lung cancer diagnosis and treatment costs based on a patient-level analysis in Catalonia (Spain). *BMC Health Serv Res*. 2015;15:70.
25. Mariotto AB, Enewold L, Zhao J, Zeruto CA, Yabroff KR. Medical care costs associated with cancer survivorship in the united states. *Cancer Epidemiol Biomarkers Prev*. 2020;29:1304-1312.
26. CIHI. Wait times for priority procedures in Canada, 2016. https://secure.cihi.ca/free_products/wait_time_report2016_en.pdf. Accessed December 1, 2021.
27. Uramoto H, Tanaka F. Recurrence after surgery in patients with NSCLC. *Transl Lung Cancer Res*. 2014;3:242-249.
28. Auditor General of Alberta. Alberta Health Services - use of publicly funded MRI and CT services. <https://www.oag.ab.ca/reports/oag-ahs-publicly-funded-ct-and-mri>. Accessed January 12, 2022.
29. Fraser Institute. Waiting your turn: wait times for health care in Canada, 2020 report. <https://www.fraserinstitute.org/studies/waiting-your-turn-wait-times-for-health-care-in-canada-2020>. Accessed November 19, 2021.
30. US Preventive Services Task Force, Krist AH, Davidson KW, et al. Screening for lung cancer: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2021;325:962-970.
31. Statistics Canada. Table 13-10-0096-10 Smokers, by age group. <https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310009610>. Accessed November 19, 2021.
32. National Lung Screening Trial Research Team. Lung cancer incidence and mortality with extended follow-up in the National Lung Screening Trial. *J Thorac Oncol*. 2019;14:1732-1742.
33. Gettinger S, Horn L, Jackman D, et al. Five-year follow-up of nivolumab in previously treated advanced non-small-cell lung cancer: Results from the CA209-003 Study. *J Clin Oncol*. 2018;36:1675-1684.
34. Cressman S, Peacock SJ, Tammemägi MC, et al. The cost-effectiveness of high-risk lung cancer screening and drivers of program efficiency. *J Thorac Oncol*. 2017;12:1210-1222.