Original Investigation

Cost-effectiveness of Lung Cancer Screening in Canada

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IMPORTANCE The US National Lung Screening Trial supports screening for lung cancer among smokers using low-dose computed tomographic (LDCT) scans. The cost-effectiveness of screening in a publically funded health care system remains a concern.

OBJECTIVE To assess the cost-effectiveness of LDCT scan screening for lung cancer within the Canadian health care system.

DESIGN, SETTING, AND PARTICIPANTS The Cancer Risk Management Model (CRMM) simulated individual lives within the Canadian population from 2014 to 2034, incorporating cancer risk, disease management, outcome, and cost data. Smokers and former smokers eligible for lung cancer screening (30 pack-year smoking history, ages 55-74 years, for the reference scenario) were modeled, and performance parameters were calibrated to the National Lung Screening Trial (NLST). The reference screening scenario assumes annual scans to age 75 years, 60% participation by 10 years, 70% adherence to screening, and unchanged smoking rates. The CRMM outputs are aggregated, and costs (2008 Canadian dollars) and life-years are discounted 3% annually.

MAIN OUTCOMES AND MEASURES The incremental cost-effectiveness ratio.

RESULTS Compared with no screening, the reference scenario saved 51 000 quality-adjusted life-years (QALY) and had an incremental cost-effectiveness ratio of CaD $52 000/QALY. If smoking history is modeled for 20 or 40 pack-years, incremental cost-effectiveness ratios of CaD $62 000 and CaD $43 000/QALY, respectively, were generated. Changes in participation rates altered life years saved but not the incremental cost-effectiveness ratio, while the incremental cost-effectiveness ratio is sensitive to changes in adherence. An adjunct smoking cessation program improving the quit rate by 22.5% improves the incremental cost-effectiveness ratio to CaD $24 000/QALY.

CONCLUSIONS AND RELEVANCE Lung cancer screening with LDCT appears cost-effective in the publicly funded Canadian health care system. An adjunct smoking cessation program has the potential to improve outcomes.

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Lung cancer kills more Canadians than breast, colorectal, and prostate cancers combined and confers a substantial burden of suffering on patients and their families, as well as cost to the health care system.[1] The number of lung cancer cases is expected to continue to rise in keeping with population growth and aging.[1,2]

Non–small-cell lung cancer (NSCLC) is potentially curable in its early stages.[3] Unfortunately, fewer than 25% of patients are eligible for surgery at the time of diagnosis,[4] and the survival rate for nonsurgical patients is very poor.[3] Until recently, screening studies have identified more early cases of NSCLC without reduction in mortality.[5-10] However, the US National Lung Screening Trial (NLST) of low-dose computed tomographic (LDCT) screening found a 20% reduction in lung cancer–specific mortality at 6 years and an overall mortality reduction of 6.7%.[11]

These results have generated enthusiasm for population-based screening programs but also concern about their cost-effectiveness. Using the Canadian Partnership Against Cancer's (CPAC) Cancer Risk Management Model (CRMM),[12,13] we have estimated the impact of the introduction of LDCT screening in Canada in terms of net cost, life-years saved, and cost-effectiveness. The CRMM was developed for use by health policy decision makers to assess the impact of potential changes in the health care system, from prevention through end of life. This study represents the first publication involving the use of CRMM to address a policy question for lung cancer.

Methods

The CRMM (version 2.1.2) and the lung cancer screening module have been described in detail and are available online.[12-15] The CRMM was developed by CPAC in collaboration with Statistics Canada and is a comprehensive microsimulation model. It incorporates Canadian demographic and risk exposure data, standard disease-specific diagnostic and treatment practices, health care costs, health utilities (selected values in eTable 1 and eTable 2 in the Supplement), general mortality rates, expected personal income, and tax revenue. It performs simulations of individuals' lifespans, and aggregates millions of simulations to determine the net impact of policy changes in the health care system on health outcomes and costs.

The CRMM uses an annualized hazard of developing lung cancer each year of the simulated person's life based on radon exposure and smoking applied to a background lung cancer incidence rate. Persons developing lung cancer have survival based on published data.[3,16,17] As the NLST represents the largest published LDCT lung cancer screening experience, model screening parameters were estimated to fit the NLST incidence, staging and stage-specific survival data, as well as the proportion of screen and interval detected cancers (see eTable 3 in the Supplement). The overdiagnosis rate was set at 18% over 3 annual screens (10% on the first screen, and 4% on each subsequent screen).[18,19] The CRMM has undergone testing for internal validity, and model behavior has been compared with other work for plausibility with encouraging results.[14]

Costs are expressed in 2008 Canadian dollars, increasing annually by 1% to reflect real relative price changes in the health sector. All costs and health-adjusted life-years are discounted at a 3% real annual rate.[20,21] Incremental cost-effectiveness ratios (ICERs) and related total costs are based on lifetime costs of all persons recruited during 2014 to 2034. For the single-age cohorts, results are based on cohorts recruited in 2014.

The control group was an unscreened population representative of the Canadian population, and all costs and health-related quality-adjusted life measures are stated in relation to this control population. We analyzed the impact of screening first according to the published NLST schedule, with 1 baseline LDCT scan and then 2 annual screening LDCT scans. We then examined a reference Canadian population-based scenario that simulated annual screening to age 75 years for those in the 55 to 74 years having at least a 30 pack-year history of smoking and smoking within the last 15 years (ie, NLST eligibility criteria). It was assumed that there was linear uptake of the screening program among the eligible population ramping up to 60% at 10 years, the rescreening compliance was set at 70%, and the last scan at age 75 years. We also assessed a modified reference scenario, which included an NLST-like population in terms of age, sex, and smoking status (termed NLST age 55-74 years). In the reference scenario, there was no adjunct smoking cessation program and no change in the background quit rate. For the reference smoking cessation scenario included here, the cost of smoking cessation was set at CaD $440 per smoker, representing a single course of nicotine replacement or varenicline,[22] and the program was considered to add 22.5% to the background quit rate.

At a Glance

- This study assesses the cost-effectiveness of low-dose computed tomographic (LDCT) scan screening for lung cancer within the Canadian health care system using the Cancer Risk Management Model.
- Annual LDCT scans in the reference scenario had an incremental cost-effectiveness of CaD $52 000 per quality-adjusted life-year.
- Adding an adjunct smoking cessation program to screening could lower the incremental cost-effectiveness to CaD $24 000 per quality-adjusted life-year.
- All scenarios appeared to be cost-effective when screening did not worsen the background smoking cessation rate.
- Policy makers can use the model to determine the effects for their own jurisdiction, and estimate the budget impact and incremental resource needs necessary to mount a LDCT lung cancer screening program.

A series of 1-way sensitivity analyses was performed by varying key parameters.

Results

Without screening, the model generates an expected number of deaths from lung cancer in Canada of 20 600 in 2014, increasing to 24 700 by 2034, and estimates the cost of treating Canadians for lung cancer without screening over this period at CaD $28.1 billion.

The characteristics of the Canadian population eligible for screening in 2014 according to NLST criteria are shown in **Table 1**. The eligible Canadian population is older, composed of more males, and composed of more current smokers than the NLST. Approximately 1.4 million Canadians would be eligible for screening in 2014 in the reference screening scenario.

Three Annual Screening LDCT Scans

Assuming that 100% of individuals meeting the eligibility criteria of the NLST are recruited, and that 3 annual screens are undertaken with 95% compliance, the incremental system cost of such a screening program in Canada would be CaD $2.3 billion. A total of 87 000 life-years would be saved by this program, 32 000 quality-adjusted life-years (QALYs) would be saved, and the ICER, compared with no screening, is estimated to be CaD $74 000 (**Table 2**).

Continuous Annual Screening

The reference annual screening simulation estimates the incremental health care system cost would be CaD $2.7 billion. The total life-years saved would be 130 000, and QALYs saved, 51 000. The ICER, compared with no screening, is estimated at CaD $52 000/QALY (Table 2). If the participating population is matched to that of the NLST (the NLST age 55-74 scenario), the eligible population in the first year is smaller (555 000 vs 1 420 000), fewer life-years are saved, and the ICER is minimally increased (CaD $56 000/QALY).

Extending the upper limit of the screening age to 79 years increases the ICER to CaD $56 000/QALY. Restricting the age range

Table 1. Eligible Canadians by NLST Criteria vs NLST LDCT Distributions

Characteristic	% Eligible Canadian Population	% NLST LDCT
Age range, y		
55-59	32	43
60-64	30	31
65-69	23	18
70-74	15	9
Sex		
Female	35	41
Male	65	59
Smoker		
Current	59	48
Former	41	52

Abbreviation: NLST LDCT, National Lung Screening Trial low-dose computed tomographic scan.

to 55 to 64 years is more cost-effective (ICER, CaD $51 000/QALY) than a 65- to 74-year-old cohort (ICER, CaD $66 000/QALY).

If the minimum smoking history required for screening eligibility were reduced to 20 pack-years, the ICER would increase to CaD $62 000/QALY and the incremental net program cost over 20 years would be CaD $3.9 billion. Conversely, a 40 pack-year minimum decreases the ICER to CaD $43 000/QALY.

Changes in the screening participation rate minimally alter the cost-effectiveness of the program but do impact the number of QALYs saved. Compared with the reference screening scenario with a 60% participation rate, which increases QALYs by 51 000, a participation rate of 30% results in 26 000 QALYs saved, and 90%, 75 000 QALYs saved.

Unlike changes in the participation rate, changes in adherence to screening alter cost-effectiveness. A 20% drop in adherence (to 50%) decreases the incremental cost of the program to CaD $1.8 billion while maintaining most of the QALYs saved in the reference scenario (50 600 vs 51 300), and results in an ICER of CaD $40 000/QALY. Conversely, while saving more lives

Table 2. Life-years Saved and Incremental Cost-effectiveness Ratios for Annual Screening

Scenario	Incremental Cost, CaD $ (Billions)	Life-years Saved	QALY Saved	ICER, CaD $[a]
Three annual NLST	2.3	87 000	32 000	74 000
Reference age 55-74 y	2.7	130 000	51 000	52 000
NLST age group, y				
55-74	2.1	95 000	38 000	56 000
55-79	3.5	163 000	62 000	56 000
55-64	1.0	44 000	20 000	51 000
65-74	1.2	56 000	18 000	66 000
50-64	1.4	56 000	26 000	54 000
Smoking, pack-years				
20	3.9	160 000	63 000	62 000
40	1.8	102 000	41 000	43 000
Participation, %				
30	1.4	66 000	26 000	52 000
90	4.0	191 000	75 000	53 000
50	1.8	117 000	51 000	40 000
90	3.3	134 000	46 000	71 000
Smoking cessation program rate[b]				
0.5	2.9	177 000	85 000	34 000
1.0	2.8	224 000	117 000	24 000
1.5	2.7	271 000	150 000	18 000
3.0	2.6	411 000	248 000	10 000
Smoking cessation program cost				
0.5	2.7	224 000	117 000	23 000
1.5	2.9	224 000	117 000	25 000
3.0	3.3	224 000	117 000	28 000
Background cessation[c]				
0.5	2.8	36 000	−11 000	−263 000
1.5	2.7	139 000	58 000	46 000
3.0	2.6	172 000	81 000	32 000
Low-dose LDCT scan cost, %				
50	2.0	130 000	51 000	39 000
150	3.4	130 000	51 000	66 000

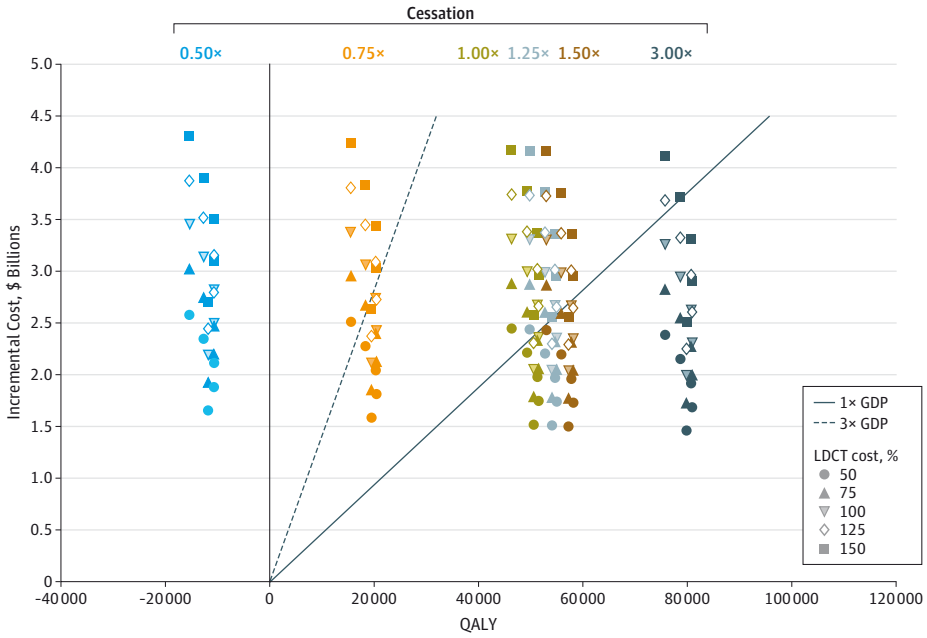
Abbreviations: ICER, incremental cost-effectiveness ratio; LDCT, low-dose computed tomography; NLST, National Lung Screening Trial; QALY, quality adjusted life-year.

[a] ICERs are compared with the no-screening scenario.

[b] Smoking cessation program at a rate of 1.0 increases background quit rates by 22.5%; 0.5, 11.25%; 1.5, 33.75%; 3.0, 67.5%.

[c] Background cessation rate of the eligible 55- to 74-year-old population is approximately 5%; 0.5, 2.5%; 1.5, 7.5%; 3.0, 15%.

Figure. Incremental Cost vs Change in QALY, Smoking Cessation Rates, and Rate of Adherence to Screening



The incremental cost is represented in 2008 Canadian dollars with a discount rate of 3%. The threshold of 1× GDP is CaD $47 000; 3× GDP, CaD $141 000. Changes in background smoking cessation rates are labeled and result in clear vertical bands. Rate of adherence to screening is not labeled but can be understood by observing a corresponding LDCT cost within a vertical smoking cessation band. The corresponding LDCT costs begin with a rate of adherence to screening of 0.5, and each ascending similar symbol within a vertical smoking cessation band represents a 0.1 increase (from 0.5 to 0.9). GDP indicates gross domestic product; LDCT, low-dose computed tomography; QALY, quality-adjusted life-years.

Table 3. Outcomes by Single-Age Cohorts

Cohort Age, y	Incremental Cost, $ (Billions)	Life-years Saved	QALY Saved	ICER, CaD $[a]
50	0.4	12 000	5000	73 000
60	0.4	15 000	4000	86 000
70	0.1	5000	1000	81 000

Abbreviations: ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

[a] ICERs are compared with the no-screening scenario.

(134 000 vs 130 000 for reference screening), a 20% increase in adherence results in an ICER of CaD $71 000/QALY.

If an adjunct smoking cessation program is not introduced with a screening program but the expected background smoking quit rate were to improve by 50%, the ICER improves from CaD $52 000 to CaD $46 000. Conversely, if the background quit rate declined by 50%, it would result in a net loss in QALYs and a negative ICER. An adjunct smoking cessation program results in an ICER of CaD $24 000/QALY. As expected, higher cessation rates result in lower ICERs, as do lower cessation program costs.

The impact of LDCT scan cost change was tested in the CRMM model. A 50% reduction in the cost of an LDCT screening decreases the incremental cost to CaD $2 billion, resulting in an ICER of Cad $39 000/QALY. A 50% increase in screening LDCT cost increases incremental costs to CaD $3.4 billion, resulting in an ICER of CaD $66 000/QALY.

The **Figure** shows the cost-effectiveness plane of the reference annual screening simulation with a 3-way analysis, including the uncertainty parameters of background smoking cessation (0.5, 0.75, 1.0, 1.25, 1.5, and 3.0 × background), LDCT cost (0.5, 0.75, 1.0, 1.25, and 1.5 × baseline cost), rate of adherence to screening (0.5, 0.6, 0.7, 0.8, 0.9) and thresholds of 1 and 3× gross domestic product (GDP) per capita (1× GDP, CaD $47 000; 3× GDP, CaD $141 000).[23,24] The model is sensitive to changes in the background smoking cessation rate, with each rate change resulting in a clear vertical band. Low-dose computed tomography cost changes do not alter QALYs gained. Rate of adherence to screening is not labeled in the Figure but can be understood by observing a specific LDCT cost within a vertical cessation band. Adherence affects cost more than QALYs. All values with 1× or higher background smoking cessation fall within the 3× GDP, as well as the CaD $100 000, thresholds (CaD $100 000 threshold not shown on Figure). In these simulations, 42% (63 of 150) of ICER values fall below the 1× GDP threshold, and 76% (114 of 150) fall below the 3× GDP threshold.

Single-Age Cohorts

To assess the impact of screening from an age-specific perspective, cohorts of 50-, 60-, and 70-year-olds recruited in 2014 were simulated with annual screening. It was assumed that there was 100% uptake and compliance (**Table 3**). The ICER was CaD $73 000/QALY for the cohort aged 50 years; CaD $86 000, 60 years; and CaD $81 000, 70 years. The lower relative cost of the 50-year-old group is driven by a greater number of QALYs gained, despite gaining fewer total life-years.

Discussion

Screening for lung cancer by LDCT reduces both overall and disease-specific mortality,[11] but cost-effectiveness is a concern. The CRMM is a powerful tool for modeling the risks of

developing cancer and assessing the cost-effectiveness of an LDCT screening program from the perspective of a publicly funded health care system.[12,13]

The CRMM estimate of the ICER for an annual LDCT screening program to age 74 years in Canada was CaD $52 000/QALY, a level generally considered cost-effective. By comparison, modeling a commercially insured US population aged 50 to 64 years, calibrated to NLST data, and framed from the payer perspective, Villanti et al[25] found an ICER of CaD $47 000 per QALY saved, a result very similar to our own. In addition, a cost-effectiveness analysis of the NLST showed CaD $81 000/QALY, similar to our value of CaD $74 000/QALY for that scenario, and providing some evidence of external validity.[26]

The consistency of our cost-effectiveness results with cost-effectiveness results from the United States supports the view that LDCT scans are cost-effective in both privately and publicly funded health care systems. While our results have been developed using detailed Canadian data, especially for smoking, lung cancer incidence, patterns of treatment, and treatment costs, other jurisdictions where these key parameters are similar are likely to find similar results. Although there are important differences between the Canadian and US health care systems, it is unlikely that the relative differences we have found between screening scenarios would differ in the 2 countries.

The yield of screening will vary with the population risk. Our study demonstrated improved cost-effectiveness in a population with a greater smoking history than that defined for NLST eligibility, which is consistent with other data.[21,27] More detailed models to assess at-risk populations have been created,[28,29] and these may further improve cost-effectiveness at the expense of increased complexity by excluding some lower-risk individuals from screening. Of note, ongoing European studies accepting individuals with a 20-pack-year smoking history have not yet shown a mortality reduction with LDCT screening.[7,30-32]

The age of the population targeted for screening affects cost-effectiveness. Two studies found a U-shaped distribution for cost-effectiveness, with cohorts centered around 60 years of age being the most cost-effective.[21,33] We found that screening a 55- to 64-year-old cohort was more cost-effective than screening a 65- to 74-year-old cohort. However, our single-age cohort analysis found that screening the 50-year-old group was most cost-effective, while screening the 60-year-old group was least cost-effective. These findings are a result of 2 factors: more QALYs are saved by screening a younger population, while fewer screening LDCTs are needed in the older population owing to fewer screening scans due to age and competing causes of mortality.

There is no clear evidence that a negative screening LDCT finding affects smoking cessation efforts,[34] but an analysis from the NLST suggests that abnormalities on screening scans are associated with higher quit rates.[35] The active incorporation of a smoking cessation program could improve the cost-effectiveness of screening. In our modeling, we found that such a program halved the ICER, a result also seen in other studies.[21,25] While smoking cessation did not decrease screening costs, it decreased mortality from smoking-related conditions, resulting in a substantial number of QALYs gained. These results underscore the need to incorporate smoking cessation into any lung cancer screening program.

Our data show that improvements in screening program participation rates add to the overall costs but also increase QALYs saved, with no change in cost-effectiveness. For our reference simulation, we assumed that uptake and compliance rates would be similar to breast cancer screening rates in Canada and better than the uptake of fecal occult blood testing for colon cancer.[36-39] However, the uptake and compliance rates for lung cancer screening may be less than mammography because of the addictive nature of smoking and the generally lower socioeconomic level of the smoking population.[40] We assumed that the time to maximum uptake was 10 years, though other values could be chosen.

There is uncertainty as to what the optimal duration of screening should be. Limited data suggest that early-stage lung cancer continues to be diagnosed throughout 5 to 10 years of screening.[32,41] Our simulations did not show large differences in cost-effectiveness with screening over periods of 10 to 25 years. The value of long-term screening can only be addressed through monitoring future population-based screening cohorts.

Our results must be interpreted in the light of several limitations. The CRMM is a complex model incorporating many data elements. The data have been gathered from a variety of Canadian sources. Resources used and costs will not be the same across all Canadian provinces. The patient cost perspective was not assessed, nor were costs related to the startup of the screening program incorporated into the model. While analyses of individual variables (eg, age range or amount smoked) are likely generalizable to other jurisdictions, the ICER dollar values are most relevant to the Canadian health care system. Also, while a probabilistic sensitivity analysis is the preferred standard in cost effectiveness analysis, the CRMM does not presently allow this, so limited deterministic sensitivity analyses were undertaken.

While there is an established model for the progression of polyps to colon cancer,[42] the progression of lung cancer is less understood. Therefore, this model does not simulate the underlying disease biology. While nonbiologic models have been criticized,[43] there is no published comparison of the 2 model types. Moreover, our model accounts for lead time and length biases through adjustments in the duration of the preclinical period during screening and by altering within-stage mortality.

Factors not assessed by this model could affect our estimates of cost-effectiveness. For example, changes in nodule management algorithms could affect cost.[44] While the current model does not incorporate the risk of repeated exposure to radiation from LDCTs, other data suggest the impact is very low.[21,34] In addition, the management of advanced NSCLC has continued to evolve since the CRMM lung cancer module was built. The CRMM does not incorporate oral tyrosine kinase inhibitors into first-line treatment,[45,46] nor does it incorporate maintenance therapy.[47] These newer treatment approaches are effective but costly.

The reduction in mortality observed in the NLST is compelling, and several organizations have now published guidelines supporting lung cancer screening.[34,48,49] We have evaluated whether screening is also cost-effective. While there is no universally accepted definition of cost-effectiveness, the World Health Organization defines ICERs costing less than 1× GDP per

capita as highly cost-effective, and ICERs between 1 and 3× GDP per capita as cost-effective.[23] By this definition, LDCT screening would only fail to be cost-effective if it actually promoted smoking, and there is no evidence to suggest this. However, it can be argued that the ICER of an intervention taken in isolation is an insufficient basis for policy. Opportunity cost within the health care system and beyond is a consideration.[50] Canada spent an estimated CaD $215 billion on health care in 2014, compared with an incremental undiscounted cost of CaD $90 to CaD $180 million annually for screening in our reference model.[51] Although this is less than a 0.1% increment, Canadian health care faces serious cost constraints.

Conclusions

In considering implementation of a screening program, decision makers will need to evaluate multiple factors that could affect both the QALYs saved and the cost and cost-effectiveness of the program. Our simulations using the CRMM provide inputs to this decision-making. Policymakers can use the CRMM to determine impacts for their own jurisdiction and, importantly, estimate the effect on budget and incremental resource needs necessary to mount an LDCT lung cancer screening program.

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Study concept and design: Goffin, Fitzgerald, Wolfson, Evans.
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