

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/280584011>

Cost-effectiveness of Lung Cancer Screening in Canada

Article · July 2015

DOI: 10.1001/jamaoncol.2015.2472 · Source: PubMed

CITATIONS

27

READS

206

7 authors, including:



Anthony Miller

University of Toronto

642 PUBLICATIONS 37,327 CITATIONS

[SEE PROFILE](#)



Natalie Fitzgerald

Canadian Partnership Against Cancer Corporation

22 PUBLICATIONS 63 CITATIONS

[SEE PROFILE](#)



Michael Wolfson

University of Ottawa

132 PUBLICATIONS 4,135 CITATIONS

[SEE PROFILE](#)



William K Evans

Cancer Care Ontario

348 PUBLICATIONS 10,685 CITATIONS

[SEE PROFILE](#)

Some of the authors of this publication are also working on these related projects:



Cancer waiting times [View project](#)




The financing of long-term care (home care and residential) in Canada [View project](#)

Original Investigation

Cost-effectiveness of Lung Cancer Screening in Canada

John R. Goffin, MD, FRCPC; William M. Flanagan, BM; Anthony B. Miller, MD, FRCPC; Natalie R. Fitzgerald, MA; Saima Memon, MBBS, MPH; Michael C. Wolfson, PhD; William K. Evans, MD, FRCPC

 Supplemental content at jamaoncology.com

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 publicly 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.

JAMA Oncol. 2015;1(6):807-813. doi:10.1001/jamaoncol.2015.2472
Published online July 30, 2015.

Author Affiliations: Department of Oncology, McMaster University, Hamilton, Ontario, Canada (Goffin, Evans); Statistics Canada, Ottawa, Ontario, Canada (Flanagan); Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada (Miller); Canadian Partnership Against Cancer, Toronto, Ontario, Canada (Fitzgerald, Memon); Department of Epidemiology and Community Medicine, University of Ottawa, Ottawa, Ontario, Canada (Wolfson).

Corresponding Author: John R. Goffin, MD, FRCPC, Juravinski Cancer Centre, 699 Concession St, Hamilton, ON L8V 5C2, Canada (goffin@mcmaster.ca).

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

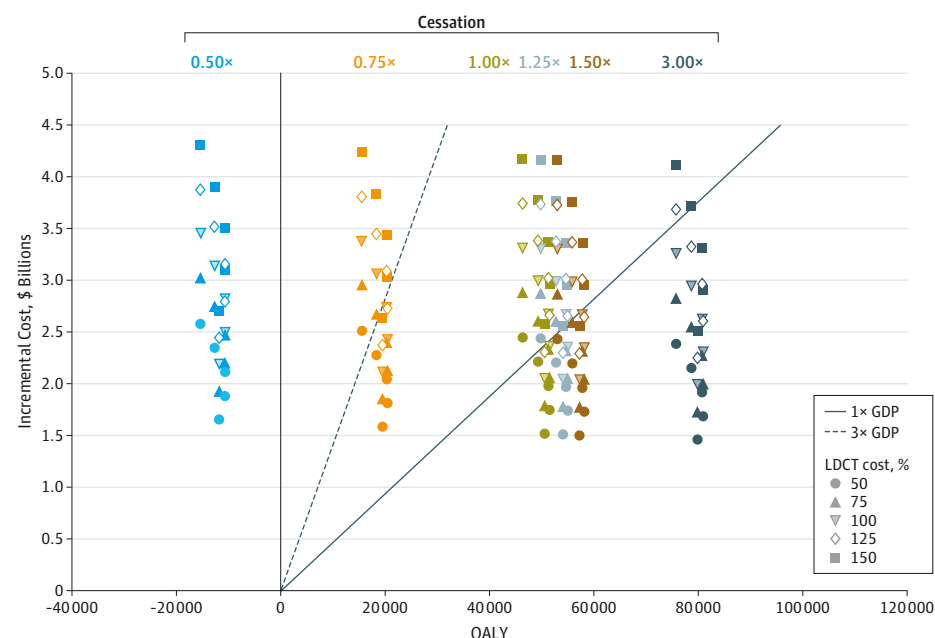
Abbreviations: ICER, incremental cost-effectiveness ratio; LDCT, low-dose computed tomography; NLST, National Lung Screening Trial; QALY, quality adjusted life-year.

^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 al²⁵ 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.

ARTICLE INFORMATION

Accepted for Publication: June 8, 2015.

Published Online: July 30, 2015.

doi:10.1001/jamaoncol.2015.2472.

Author Contributions: Dr Goffin had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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

Acquisition, analysis, or interpretation of data: Goffin, Flanagan, Miller, Fitzgerald, Memon, Evans. **Drafting of the manuscript:** Goffin, Miller, Fitzgerald, Evans.

Critical revision of the manuscript for important intellectual content: Goffin, Flanagan, Miller, Fitzgerald, Memon, Wolfson, Evans.

Statistical analysis: Goffin, Fitzgerald, Memon, Wolfson.

Obtained funding: Goffin.

Administrative, technical, or material support: Flanagan, Fitzgerald, Evans.

Study supervision: Evans.

Conflict of Interest Disclosures: Dr Goffin has received grant support from the Canadian Partnership Against Cancer and has served on an advisory board with Amgen. Mr Flanagan has received travel support from the Canadian Partnership Against Cancer. Dr Miller has received fees from the Canadian Partnership against Cancer. Ms Fitzgerald and Saima Memon are employees of the Canadian Partnership Against Cancer, which is funded by Health Canada. Dr Wolfson is employed by the University of Ottawa and has grants from the Canadian Foundation for Innovation, the Social Science and Humanities Research Council, and Genome Canada. Dr Evans has received a grant and fees from the Canadian Partnership Against Cancer, has had advisory board roles with Astellas, BMS and Lilly, has consulted for Roche, Boehringer-Ingelheim, and Becton Dickinson, and has received speaker fees from Celgene and Takeda Canada. No other conflicts are reported.

Funding/Support: This work was funded by the Canadian Partnership Against Cancer.

Role of the Funder/Sponsor: The Canadian Partnership Against Cancer was involved in design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, and approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: The authors thank the many contributors to the CRMM, a listing of whom may be found on the Cancerview.ca website.

REFERENCES

1. Canadian Cancer Society's Advisory Committee on Cancer Statistics. *Canadian Cancer Statistics 2013*. Toronto: Canadian Cancer Society; 2013.
2. Canadian Partnership Against Cancer. Lung cancer in Canada: a supplemental system performance report. May 2011. <http://www.cancerview.ca/idc/groups/public/documents/webcontent/cpac015706.pdf>. Accessed June 15, 2015.
3. Goldstraw P, Crowley J, Chansky K, et al; International Association for the Study of Lung Cancer International Staging Committee; Participating Institutions. The IASLC Lung Cancer Staging Project: proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM Classification of malignant tumours. *J Thorac Oncol*. 2007;2(8):706-714.
4. Laroche C, Wells F, Coulden R, et al. Improving surgical resection rate in lung cancer. *Thorax*. 1998; 53(6):445-449.
5. Oken MM, Hocking WG, Kvale PA, et al; PLCO Project Team. Screening by chest radiograph and lung cancer mortality: the Prostate, Lung, Colorectal, and Ovarian (PLCO) randomized trial. *JAMA*. 2011;306(17):1865-1873.
6. Henschke CI, Yankelevitz DF, Libby DM, Pasmantier MW, Smith JP, Miettinen OS; International Early Lung Cancer Action Program Investigators. Survival of patients with stage I lung cancer detected on CT screening. *N Engl J Med*. 2006;355(17):1763-1771.
7. Infante M, Cavuto S, Lutman FR, et al; DANTE Study Group. A randomized study of lung cancer screening with spiral computed tomography: three-year results from the DANTE trial. *Am J Respir Crit Care Med*. 2009;180(5):445-453.
8. Swensen SJ, Jett JR, Hartman TE, et al. CT screening for lung cancer: five-year prospective experience. *Radiology*. 2005;235(1):259-265.
9. Veronesi G, Bellomi M, Scanagatta P, et al. Difficulties encountered managing nodules detected during a computed tomography lung cancer screening program. *J Thorac Cardiovasc Surg*. 2008;136(3):611-617.
10. Wilson DO, Weissfeld JL, Fuhrman CR, et al. The Pittsburgh Lung Screening Study (PLUSS): outcomes within 3 years of a first computed tomography scan. *Am J Respir Crit Care Med*. 2008; 178(9):956-961.
11. Aberle DR, Adams AM, Berg CD, et al; National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med*. 2011;365(5):395-409.
12. Evans WK, Wolfson M, Flanagan WM, et al. The evaluation of cancer control interventions in lung cancer using the Canadian Cancer Risk Management Model. *Lung Cancer Manag*. 2012;1(1):25-33.
13. Evans WK, Wolfson MC, Flanagan WM, et al. Canadian Cancer Risk Management Model: evaluation of cancer control. *Int J Technol Assess Health Care*. 2013;29(2):131-139.
14. Flanagan WM, Evans WK, Fitzgerald NR, Goffin JR, Miller AB, Wolfson MC. Performance of the cancer risk management model lung cancer screening module. *Health Rep*. 2015;26(5):11-18.
15. The Canadian Partnership Against Cancer. Cancer Risk Management Model: an evidence-based tool to inform cancer control decision-making. 2011. <http://cancerview.ca/cancerriskmanagement> Accessed June 18, 2015.
16. Butts CA, Ding K, Seymour L, et al. Randomized phase III trial of vinorelbine plus cisplatin compared with observation in completely resected stage IB and II non-small-cell lung cancer: updated survival analysis of JBR-10. *J Clin Oncol*. 2010;28(1):29-34.
17. Douillard JY, Tribodet H, Aubert D, et al; LACE Collaborative Group. Adjuvant cisplatin and vinorelbine for completely resected non-small cell lung cancer: subgroup analysis of the Lung Adjuvant Cisplatin Evaluation. *J Thorac Oncol*. 2010; 5(2):220-228.
18. de Koning HJ, Meza R, Plevritsis SK, et al. *Benefits and Harms of Computed Tomography Lung Cancer Screening Programs for High-Risk Populations*. AHRQ Publication No. 13-05196-EF-2. Rockville, MD: Agency for Healthcare Research and Quality; 2013.
19. Patz EF Jr, Pinsky P, Gatsonis C, et al; NLST Overdiagnosis Manuscript Writing Team. Overdiagnosis in low-dose computed tomography screening for lung cancer. *JAMA Intern Med*. 2014; 174(2):269-274.
20. Grusenmeyer PA, Wong YN. Interpreting the economic literature in oncology. *J Clin Oncol*. 2007; 25(2):196-202.
21. McMahon PM, Kong CY, Bouzan C, et al. Cost-effectiveness of computed tomography

screening for lung cancer in the United States. *J Thorac Oncol*. 2011;6(11):1841-1848.

22. Tran K, Asakawa K, Cimon K, et al. *Pharmacologic-based Strategies for Smoking Cessation: Clinical and Cost-Effectiveness Analyses*. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2010.

23. World Health Organization. Cost-effectiveness thresholds; *Cost effectiveness and strategic planning (WHO-CHOICE)*. 2015. http://www.who.int/choice/costs/CER_thresholds/en/. Accessed May 14, 2014.

24. Statistics Canada. Gross domestic product per capita, Canada, provinces and territories, 2005/2006 to 2009/2010 (in current dollars). 2013; <http://www.statcan.gc.ca/pub/81-595-m/2011095/tbl/tbla.34-eng.htm>. Accessed May 21, 2015.

25. Villanti AC, Jiang Y, Abrams DB, Pyenson BS. A cost-utility analysis of lung cancer screening and the additional benefits of incorporating smoking cessation interventions. *PLoS One*. 2013;8(8):e71379.

26. Black WC, Gareen IF, Soneji SS, et al; National Lung Screening Trial Research Team. Cost-effectiveness of CT screening in the National Lung Screening Trial. *N Engl J Med*. 2014;371(19):1793-1802.

27. Kovalchik SA, Tammemägi M, Berg CD, et al. Targeting of low-dose CT screening according to the risk of lung-cancer death. *N Engl J Med*. 2013;369(3):245-254.

28. Maisonneuve P, Bagnardi V, Bellomi M, et al. Lung cancer risk prediction to select smokers for screening CT—a model based on the Italian COSMOS trial. *Cancer Prev Res (Phila)*. 2011;4(11):1778-1789.

29. Tammemägi MC, Katki HA, Hocking WG, et al. Selection criteria for lung-cancer screening. *N Engl J Med*. 2013;368(8):728-736.

30. Lopes Pegna A, Picozzi G, Falaschi F, et al; ITALUNG Study Research Group. Four-year results of low-dose CT screening and nodule management in the ITALUNG trial. *J Thorac Oncol*. 2013;8(7):866-875.

31. Pastorino U, Rossi M, Rosato V, et al. Annual or biennial CT screening versus observation in heavy smokers: 5-year results of the MILD trial. *Eur J Cancer Prev*. 2012;21(3):308-315.

32. Saghir Z, Dirksen A, Ashraf H, et al. CT screening for lung cancer brings forward early disease: the randomised Danish Lung Cancer Screening Trial: status after five annual screening rounds with low-dose CT. *Thorax*. 2012;67(4):296-301.

33. Mahadevia PJ, Fleisher LA, Frick KD, Eng J, Goodman SN, Powe NR. Lung cancer screening with helical computed tomography in older adult smokers: a decision and cost-effectiveness analysis. *JAMA*. 2003;289(3):313-322.

34. Bach PB, Mirkin JN, Oliver TK, et al. Benefits and harms of CT screening for lung cancer: a systematic review. *JAMA*. 2012;307(22):2418-2429.

35. Tammemägi MC, Berg CD, Riley TL, Cunningham CR, Taylor KL. Impact of lung cancer screening results on smoking cessation. *J Natl Cancer Inst*. 2014;106(6):dju084.

36. Canadian Partnership Against Cancer. Breast cancer control in Canada: a system performance special focus report. Toronto; 2012. http://www.cancerview.ca/idc/groups/public/documents/webcontent/breast_cancer_control_rep.pdf. Accessed June 15, 2015.

37. Public Health Agency of Canada. Organized breast cancer screening programs in Canada: report on program performance in 2003 and 2004. Ottawa. 2008. <http://www.phac-aspc.gc.ca/publicat/2008/obcsp-podcs-03-04/index-eng.php>. Accessed June 15, 2015.

38. Tatla RK, Paszat LF, Bondy SJ, Chen Z, Chiarelli AM, Mai V. Socioeconomic status & returning for a second screen in the Ontario breast screening program. *Breast*. 2003;12(4):237-246.

39. Cancer Care Ontario. ColonCancerCheck 2010 program report. Toronto, Canada. 2012. <https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileid=156747>. Accessed June 22, 2015.

40. Reid JL, Hammond D, Driezen P. Socio-economic status and smoking in Canada, 1999-2006: has there been any progress on disparities in tobacco use? *Can J Public Health*. 2010;101(1):73-78.

41. Veronesi G, Maisonneuve P, Rampinelli C, et al. Computed tomography screening for lung cancer: results of ten years of annual screening and validation of cosmos prediction model. *Lung Cancer*. 2013;82(3):426-430.

42. Markowitz SD, Bertagnolli MM. Molecular origins of cancer: Molecular basis of colorectal cancer. *N Engl J Med*. 2009;361(25):2449-2460.

43. Knudsen AB, McMahon PM, Gazelle GS. Use of modeling to evaluate the cost-effectiveness of cancer screening programs. *J Clin Oncol*. 2007;25(2):203-208.

44. Cressman S, Lam S, Tammemägi MC, et al; Pan-Canadian Early Detection of Lung Cancer Study Team. Resource utilization and costs during the initial years of lung cancer screening with computed tomography in Canada. *J Thorac Oncol*. 2014;9(10):1449-1458.

45. Goffin JR, Zbuk K. Epidermal growth factor receptor: pathway, therapies, and pipeline. *Clin Ther*. 2013;35(9):1282-1303.

46. Solomon BJ, Mok T, Kim DW, et al; PROFILE 1014 Investigators. First-line crizotinib versus chemotherapy in ALK-positive lung cancer. *N Engl J Med*. 2014;371(23):2167-2177.

47. Gentzler RD, Patel JD. Maintenance treatment after induction therapy in non-small cell lung cancer: latest evidence and clinical implications. *Ther Adv Med Oncol*. 2014;6(1):4-15.

48. Jaklitsch MT, Jacobson FL, Austin JH, et al. The American Association for Thoracic Surgery guidelines for lung cancer screening using low-dose computed tomography scans for lung cancer survivors and other high-risk groups. *J Thorac Cardiovasc Surg*. 2012;144(1):33-38.

49. Roberts H, Walker-Dilks C, Sivjee K, et al. *Screening high-risk populations for lung cancer*. Toronto: Cancer Care Ontario; 2013.

50. Birch S, Gafni A. The biggest bang for the buck or bigger bucks for the bang: the fallacy of the cost-effectiveness threshold. *J Health Serv Res Policy*. 2006;11(1):46-51.

51. Canadian Institute for Health Information. National Health Expenditure Trends. 2014. http://apps.cihi.ca/mstrapp/asp/Main.aspx?Server=apmstxtprd_i&project=Quick+Stats&uid=pce_pub_en&pwd=&evt=2048001&visualizationMode=0&documentID=9DOE83BC4BACDADE9D4938B338C6B6D5. Accessed April 4, 2015.