Abstract
Lung cancer is the most common cause of cancer death worldwide. Yet, screening for lung cancer remains controversial. We compared the risks and benefits of lung cancer with low-dose helical CT (LDCT) relative to chest x-ray (CXR). Concerns have been raised about recommending LDCT as a routine screening tool because of the potential harms and benefits.

Background
According to the Canadian Cancer Statistics, almost half of all Canadians will develop cancer over their lifetime, and a quarter of all Canadians are expected to die of cancer. The leading cause of death from cancer is related to cardiovascular disease. Lung cancer alone accounts for over 13% of all newly diagnosed cancers, and is the leading cause of cancer death, accounting for over 35%. There is a main risk factor for developing lung cancer, and is associated with over 85% of the cases of this disease in Canada. Almost 98% of the estimated new cases of lung cancer in 2015 are expected to be identified in adults aged 50 years and older. Prevention efforts, such as screening programs, could reduce incidence rates, and result in earlier diagnosis and treatments, thereby improving survival rates.

We have much debate over safe and effective screening tests to identify lung cancer during its preclinical phase, when it is presumed to be more curative to treat. Early clinical trials showed that screening with CXR (CXR) did not reduce lung cancer mortality. Recently, there have been signs of emerging techniques that used low doses of radiation, with effective radiation doses approximately 25% that of the chest radiography (CXR) technique. Using helical CT (LDCT) in combination with conventional chest radiography. Newly published mortality results from The National Lung Screening Trial (NLST) showed that screening with LDCT compared to conventional chest radiography reduced lung cancer mortality. The US Preventive Services Task Force’s (USPSTF) endorses annual screening using LDCT for older adults who are current or former smokers. The Canadian Task Force on Preventive Health Care (CTFCPH) is currently reviewing the guidelines.

Despite numerous studies, screening for lung cancer remains controversial. Limiting screening to high-risk persons represents the most effective approach to screening. Extending eligibility criteria to include those at lesser risk will result in overdiagnosis and eventually reduce harm. The implications of both potential benefits and harms are becoming important issues to address, especially in the assessment of new technologies such as LDCT.

Objectives
LDCT is a promising new screening technology. Concerns have been raised about recommending LDCT as a routine screening tool because of the potential harms, including cumulative radiation risks. We compared the risks and benefits of lung cancer screening with low-dose helical CT (LDCT) relative to chest x-ray (CXR).

Methods
We developed a decision analytic Markov model to evaluate a potential lung cancer screening program with LDCT among high and low-risk patients in Canada. The model was used to follow the design of the National Lung Screening Trial (NLST) and the Prostate, Lung, Colorectal and Ovarian trial (PLCO) trial. Three screening rounds were defined for ages 55-74, current smokers with a 30 pack-year smoking history; former smokers with a 30 pack-year smoking history that have quit within the preceding 15 years, and never smokers at age 50. We included clinical staging, population data, and no evidence of other cancer within the preceding 5 years. Estimates of key parameters in our model were taken from the NLST, PLCO, the Canadian Cancer Registry, Statistics Canada, the National Cancer Institute’s Cancer Intervention and Surveillance Modeling Network Consortium, the National Research Council, clinical effects of lung cancer radiation insults, and the Surveillance Epidemiology, and End Results program (SEER). We estimated the lung cancer outcomes for current, former, and never smokers over a six-year follow-up period using a decision analytic modeling approach (Figure 3). The model included sensitivity and specificity of LDCT and CXR for lung cancer detection, as well as the effective radiation doses (Figure 1), screening interval and frequency, and patient characteristics such as age at screening, smoking status, history of COPD, and family history.

Results
The result of the model included: estimated incidence of lung cancer, number of lung cancer cases detected, number of false positive tests, number of lung cancer deaths, and the estimated number of radiation-induced solid cancer incidences and deaths.

The results are presented for a 62-year old current smoker. It is estimated that 1,104 per 100,000 population cases of lung cancer will be detected with one round of LDCT screening, as compared to 683 per 100,000 population, with CXR screening (Figure 2). For LDCT and CXR, false positive results account for 96% and 93% of all positive results.

For current smokers, screening with LDCT over a six year follow-up period will detect 3,900 per 100,000 population cases of lung cancer, with 1,831 per 100,000 leading to death. For current smokers, screening with CXR, the comparable numbers are 3,058 and 1,476, respectively (Figure 3, Figure 6 & Figure 7). Thus, for current smokers, screening with LDCT results in 443 per 100,000 fewer deaths than with the CXR. For former smokers, screening with LDCT will detect an additional 600 lung cancer cases per 100,000 population compared to CXR screening, and will result in 330 per 100,000 fewer deaths (Figure 4, Figure 6 & Figure 7). For never smokers, screening with LDCT will detect 1,305 lung cancer cases per 100,000, with 55 per 100,000 leading to death. For CXR screening, only 94 cancer are detected per 100,000 never smokers, with 69 per 100,000 leading to cancer death (2:3). The radiation-induced cancer risk is negligible for LDCT over a six year period compared to CXR screening. LDCT will result in 645 per 100,000 population cases of radiation-induced cancer, and 3 per 100,000 cases of radiation-induced mortality. For CXR the rates of radiation-induced cancer are close to zero (Figure 3B). Overall, the estimated six-year risk of lung cancer is 4,156 per 100,000 current smokers, 3,405 per 100,000 former smokers, and 128 per 100,000 never smokers (Figure 6).

Conclusions
Lung cancer is the most common cause of cancer death not only in Canada but in the world. Despite numerous studies screening for lung cancer remains controversial. Using simulation modeling techniques, the long term outcomes, including the tradeoffs between potential benefits and harms of lung cancer screening, can be quantified. Concerns have been raised about recommending LDCT as a routine screening tool for lung cancer. Key questions are, who should be targeted for screening using LDCT technology, what is a patient’s risk of death, and the potential utility of using LDCT relative to other clinical options, given the large number of false positive results? Our model addresses a number of public policy questions regarding who should be targeted for screening and what the trade-offs are in terms of potential harms and benefits.