# Using a Simulation Model to Assess the Impact of a Lung Cancer Screening Regimen on Wait Times and Cancer Stage Distribution

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# Using a Simulation Model to Assess the Impact of Lung Cancer Screening Regimen on Wait Times and Cancer Stage Distribution

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|---|---|
| CCO | Cancer Care Ontario |
| CT | Computed Tomography |
| CXR | Chest X-Ray |
| I-ELCAP | The International Early Lung Cancer Action Project |
| LDAP | Lung Diagnostic Assessment Program |
| LDCT | Low Dose Computed Tomography |
| LHIN | Local Health Integrated Network |
| Lung RADS | Lung imaging reporting and data system |
| NSCLC | Non-Small Cell Lung Cancer |
| NSLT | The National Lung Cancer Screening |
| SCLC | Small-Cell Lung Cancer |
| TOH | The Ottawa Hospital |

## Abstract

Lung cancer is the number one cause of cancer related deaths in Ontario and throughout Canada. The 5-year survival rate for those diagnosed with lung cancer in 2020 was approximately 22.2%. Poor screening techniques is the main cause of low survival rates and late detection. Recent advancements in screening for lung cancer have led researchers to look at the benefits of using low-dose CT (LDCT) scanning to screen patients at high risk for lung cancer in order to detect the cancer in its earlier stages. There is strong evidence that using this new method of testing in lung cancer screening can reduce lung cancer related mortality by increasing the chance that the disease is detected in an earlier stage and in turn improving the patient's chance at life saving treatment. Lung cancer screening requires LDCT resources and, based on the current recommendations, there is a concern that the new demand for imaging may exceed existing capacity of the imaging centers. This research evaluates impact of the Lung Cancer Screening Pilot for People at High Risk on the imaging resources and aims to answer the question: What would be the system performance for different imaging policies assuming a fixed imaging capacity? Administrative data from the Ottawa Hospital (TOH) as well as data from other research projects were used in order to develop and populate a simulation model. The policies that were assessed include: using biannual screening for patients who receive a negative baseline scan, using annual screening for patients with a negative baseline scan with all suspicious patients returning for a follow-up scan in six months, using annual screening for patients with a negative baseline scan with all suspicious patients returning for a follow-up scan in three months, using biannual screening for patients with a negative baseline scan with all suspicious patients returning for a follow-up scan in six months and using biannual screening for patients with a negative baseline scan with all suspicious patients returning for a follow-up scan in three months. These policies were assessed by looking at wait times for patients to be screened. Possible shift between lung cancer stages was also considered. The impact of this study is to look at system performances for different screening policies that could be used assuming a fixed imaging capacity. It represents a first step for further research should the data that is needed become available.

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## 1. Introduction

There is currently a need for a lung cancer screening program to be launched across Canada and specifically in the province of Ontario. Lung cancer is the number one cause of cancer related deaths in Ontario and throughout Canada. [34, 39, 40] Approximately 95% of the lung cancers being diagnosed can be classified into small-cell lung cancer (SCLC) or non-small cell lung cancer (NSCLC) which is a necessary distinction to make for prognosis, management, as well as screening efficacy. [26] SCLC is more centrally located, arises more commonly in the larger airways and is a very aggressive tumor which is characterized by its rapid doubling time as well as early metastasis. These characteristics make this type of lung cancer harder to detect during the earlier stages. [26] NSCLC, on the other hand, is more often found in the peripheral lung tissue which makes it easier to find during screening. [26] According to Cancer Care Ontario, 7124 people died of lung cancer in 2020. [3] This number of lung cancer related deaths is extremely high because cancer is usually detected at a very advanced stage, leaving the patient with a poor survival rate. [39] The 5-year survival rate for those diagnosed with lung cancer in 2020 was 22.2%. [4] However, it can vary from 50% for patients diagnosed with localized disease being stage I or II to 2% for patients diagnosed with distant disease being stage IV. [19] The cure rate for early-stage NSCLC after a resection of the tumour and 5-year survival rates are over 70%, which makes screening very important for potential early detection and decreased mortality rates from NSCLC. [6] Late detection of lung cancer due to poor screening techniques is the major cause of low survival rate.

Recent advancements in screening for lung cancer has led researchers to look at the benefits of using low-dose CT (LDCT) scanning to screen patients at high risk for lung cancer in order to detect the cancer in its earlier stages. [39] Strong evidence suggests that using this new method of testing in lung cancer screening can reduce lung cancer related mortality as it increases the chance that the cancer is detected in an earlier stage, thus improving the patient's chance at life saving treatment. [34, 35] The current recommendations for screening in the province of Ontario and across Canada are to use the two current screening techniques available, sputum cytology and chest x-rays (CXR), neither of which allow doctors to detect the cancer in the early stages as the patients must present symptoms before the tests are ordered. [28] Therefore, these techniques have proven to not improve lung cancer related mortality or a patient's 5-year survival rate. [24, 35] Other techniques such as advances in treatment methods including surgery, chemotherapy and radiotherapy have made little difference in the survival rate due to the fact that lung cancer is an aggressive and heterogenous disease. [31] The National Lung Cancer Screening Trial (NSLT) published their results. These results have started to change guidelines on lung cancer screening across North America, as they found that screening patients at high risk for lung cancer with LDCT showed a 20% reduction in lung cancer mortality when compared to screening using CXR. [34] Furthermore, according to Lung Cancer Canada, if a comprehensive LDCT screening program for Canadians at risk were to be implemented across the country, this program could be expected to save more than 1200 lives per year based on NSLT results. [41] Since the publication of these results by the NSLT, the Canadian Task Force on Preventative Health Care has changed their guidelines to recommend the use of LDCT screening for patients who are deemed at high risk for lung cancer and the province of Ontario has started the Lung Cancer Screening Pilot for People at High Risk in order to determine the best way to implement LDCT screening for high risk patients in Ontario. [34, 42] This is the first step in the implementation of a complete lung cancer screening program in the province and across Canada.

Lung cancer screening requires LDCT resources and based on the current recommendations there is a concern that the demand on imaging facilities may be too much if a screening program is widely implemented and becomes very successful. Using the NSLT guidelines for lung cancer screening as well as Statistics Canada's data for provincial age distribution and smoking rates and a microsimulation model done through the OncoSim model, approximately 1.4 million Canadians in 2018 would have been eligible for high-risk lung cancer screening. This raises the question of how the country currently can handle that many new patients. [9] The average wait time for a CT scan in Ontario currently is approximately 70 days, meaning the province is already over capacity with the patients it currently has. [43] Furthermore, the average wait time for a CT scan in the area that was formerly under the Champlain Local Health Integration Network (LHIN) jurisdiction is on average 65 days for patients who were deemed to have an elective need for a CT scan and who should be scanned within 28 days of the referral being sent, meaning that they are also already over capacity with the patients they currently have. [44] Further research and resource rationalization is needed in order to plan and implement an effective screening program in the province.

### 1.1 Research Question

This research initially aimed to answer the question: What are the impacts of a provincial lung cancer screening program on CT imaging resources? The subsequent question was what policies can mitigate these impacts? However, the research question for this project changed because of availability of data and we had to assume that the capacity of the system was fixed due to a lack of data from the pilot. Thus, the revised research question that this projects answers is: **What would be the system performance for different imaging policies assuming a fixed imaging capacity?**

### 1.2 Method

This research used discrete event simulation in order to simulate system performance for potential screening policies for a lung cancer screening program.

### 1.3 Objectives

The accomplishment of the following research objectives is needed in order to answer the research question:

1. Develop a discrete event simulation model that would support decision-making in selecting screening policies.
    1.1 Model different policies and their impacts on system performance considering the following metrics: wait times and cancer stage shifting in patients who are diagnosed with cancer after being screened measured as the proportions of patients in each cancer stage category.

## 2. Cost of Screening

Screening will have very significant clinical impacts on lung cancer diagnosis as it will shift diagnoses toward earlier stages which would make curative treatments possible. [29] Approximately 57.1% of all screened detected lung cancers are diagnosed in localized stage compared to 16.1% in the people who were not screened or missed their screening appointment.

[12] The shift from distant to localized stage cancers is what accounts for most of the difference in the stage distribution between the screened population and the non-screened population. [12] The proportion of regional stage cancers is quite similar in both populations with a percentage of 21.2% in the screened population and 23.7% in the non-screened population. [12] The cost of continuing care for stage III and stage IV lung cancer is higher than the cost of care for early-stage lung cancer on a monthly basis, even when the cost of chemotherapy is excluded in this calculation. [6] This is as a result of the high costs of care associated with managing advanced stage lung cancer, which includes the use of acute inpatient, intensive care as well as emergency department resources in the patient's last months of life. [6] When looking at the cost of screening, Goulart, et al. said that for a screening rate of 75% their model estimated approximately 2 billion dollars in national expenditures related to LDCT scanning and the procedures that follow a positive screening test in the United States. [12] LDCT scans account for 59% of these expenditures while follow-up CT scans account for 11%. [12] 60% of the lung cancer cases that are diagnosed in patients who missed screening are distant stage lung cancers. [12] The expected treatment cost for lung cancer without any screening is said to be 2.8 billion dollars which also accounts for overdiagnoses. [11]. Marshall et al. have determined that in a very high-risk population of patients who are between the ages of 60-74 years old, annual screening for lung cancer over a period of five years in Canada appears to be cost-effective at a cost of $18,968 per life year saved. [19]

In summary, the cost-effectiveness of lung cancer screening programs is still being debated. However, there is evidence that indicates that the cost of care for patients with advanced stage lung cancer is higher than the cost of care for patients with early-stage lung cancer and that this could potentially make screening for lung cancer cost-effective, leading to a stage shift in cancer diagnoses. [6, 12, 29]

## 3. The Lung Cancer Screening Pilot for People at High Risk

### 3.1 Program Description

The Lung Cancer Screening Pilot for People at High Risk was initiated in June 2017 at specific sites in Ontario which included the Renfrew Victoria, The Ottawa Hospital (TOH), Health Science North in Sudbury, Lakeridge Health in Oshawa and the Cornwall Community Hospital. [44] The Cornwall Community Hospital, TOH and the Renfrew Victoria were chosen by Cancer Care

Ontario in order to ensure diversity based on geography as well as hospital type being academic or community-based hospitals. [35] In the former Champlain LHIN, the pilot started off with two hospitals being the Renfrew Victoria as well as TOH. [2] These hospitals were chosen due to their geography, as one is rural and one is urban. [35] Out of the three campuses of TOH hospitals the only one currently doing lung cancer screening for the pilot is the Riverside campus as two other TOH's CT department are kept for traumas, emergencies or impatient care. [2] Each screening center has navigators, which are nurses, who give patients who are eligible for screening based on the eligibility criteria, information about the next steps and about the screening process. The navigators go to the Riverside campus and the Renfrew Victoria Hospital in order to meet patients that are coming in for their baseline scan. [2] When the pilot added the Cornwall Community Hospital to the list of hospitals which are conducting lung cancer screening, it made this site unique as it did not have the navigators meet with patients at this site. [2] If patients choose to get the screening done in Cornwall, they will be given all the necessary information over the phone. [2] This pilot recommends the use of LDCT scanning to screen people who are at high risk to develop lung cancer. [32] However, this screening needs to be done through an organized screening program such as the pilot. Ad hoc or opportunistic screening is not advised due to the potential harms of screening. [32] This recommendation for LDCT screening is based on the results of the evidence that was produced by the NSLT study. [44]

### 3.2 Eligibility Criteria

Currently, the recommendations for lung cancer screening are based on the NSLT study which selected their eligible participants based solely on clinical parameters. [35] A number of investigations have suggested that determining who is eligible for screening by using an individual's risk based on age, more detailed smoking history as well as other risk factors such as family history of lung cancer or ethnicity could lead to a more effective screening program. [19] Adding a refined risk-based assessment to the current method of selection could improve the effectiveness of screening in two ways; however, only one will be mentioned, the risk assessment model. [35] This model could identify the people who are at highest risk for developing lung cancer and thus would identify those who would most benefit from screening. [35] The Lung Cancer Screening Pilot for People at High Risk has incorporated this risk assessment step into their eligibility criteria making it a two-step process. [39] Patients who are 55-74 years of age who have smoked cigarettes daily for at least 20 years, not necessarily consecutively, may be referred or may self-refer to The Lung Cancer Screening Pilot for People at High Risk at which point they would undergo a risk assessment. If the patient has 2% chance or higher of being diagnosed with lung cancer in the next six years, they will be eligible to be included in the pilot. If it is below 2% they will not be eligible. [39] Other characteristics that could make a patient ineligible for the pilot include having previously been diagnosed with lung cancer, being under surveillance for lung nodules, experiencing hemoptysis in the past year or having experienced an unexplained weight loss of more than five kilograms in the past year. [39] The Lung Cancer Screening Pilot for People at High Risk used the eligibility criterion from the NSLT study but also added the risk assessment in order diminish the false positive results. [39]

### 3.3 Patient Flow through the Screening Process

Following the risk assessment step, if the patient is eligible for screening, they will undergo a LDCT scan. [23] Once the patient's LDCT scan is performed a radiologist will determine if the result is positive, suspicious or negative based on the Lung Rads scoring system. [23] Lung-Rads are a quality assurance tool used to standardize CT reporting for lung cancer screening in order to avoid confusion and facilitate outcome monitoring. [20] The patient will then receive a Lung-Rads result between 0 and 4X with 0 meaning, the scan was either unsuccessful or there is no scan to compare with – 1 being the best result a patient can receive, meaning that there is no suspected lung cancer, and 4X being the worst result, meaning that lung cancer in this patient is suspected. [20] For The Lung Cancer Screening Pilot for People at High Risk Lung Rads scores 4A, 4B and 4X are all considered positive screening results that are suspicious for malignancy. [23] If a patient has a Lung Rad score of 1 or 2 they must return in one year for another LDCT. [20, 23] If a patient has a Lung Rad score of 3 they will be asked to return for a follow-up LDCT in six months. [20, 23] Finally, if a patient has a Lung Rad score of 4A the patient will need a follow-up LDCT in three months and if a patient has a Lung Rad score of 4B or 4X they will be referred to the Lung Diagnostic Assessment Program (LDAP) in order to determine if they have lung cancer and obtain the necessary treatment. [20, 23] Throughout the screening process the pilot provides navigation to patients. [39] This includes navigation throughout the seven steps of the screening process used by the pilot which include, (1) the risk assessment to determine the eligibility of the patient, (2) informed decision-making process of the patient about participating in lung cancer screening, (3) smoking cessation support that is given to all current smokers in the pilot, (4) the LDCT scan which is run in accordance with radiology quality assurance, (5) communication of the scan results to the referring provider and the family physician of the patient if these two providers are different, (6) facilitation of the recall and follow-up of patients that need this service that is similar to the Ontario Breast Screening Program and a (7) seamless transition to the Lung Diagnostic Assessment Program (LDAP) for the assessment and/or the surveillance of scans that resulted in a suspicious finding. [39]

### 3.4 Statistics from the Pilot

As of June 2018, the pilot has recruited approximately 2,613 patients. [21] Furthermore, the pilot has booked 1,710 risk assessments of the 2,613 patients who are eligible based on age and smoking history. [21] Of those 1,710 people, 1,642 patients went ahead with the risk assessment and 994 of those patients were eligible for screening. [21] As of June 2018, the pilot has conducted approximately 816 LDCT scans. [21] There are currently no conclusions from the pilot program as it is ongoing and therefore the final results of the pilot are not yet available.

In summary, The Lung Cancer Screening Pilot for People at High Risk is a pilot in the province of Ontario which is being run in order to determine the best way to implement a lung cancer screening program in that province. [44] The recommendations for lung cancer screening that are being used in The Lung Cancer Screening Pilot for People at High Risk comes from the results of the NLST. However, the pilot has also revised the eligibility criterion used in the NSLT by adding a second step to the eligibility process, which is adding a risk assessment model and ensuring that the patients who are eligible for screening have a 2% chance or higher of developing lung cancer in the next six years. [19, 35, 44] This is an attempt to reduce the false-positive rates in the pilot. [19, 35, 44]

## 4. Literature review

This section provides an overview of lung cancer and screening methods. New innovative technologies for screening lung cancer have come to light in the past decade which include LDCT scanning for people at high-risk, however this type of screening comes with advantages and disadvantages to the people who are being screened as well as the health care system. (4.1)

Furthermore, simulation modelling will be explained (4.2) and how it has been used in cancer research and screening initiatives (4.3) and which policies were available in the literature to mitigate the impact of a lung cancer screening program on imaging resources. (4.4)

### 4.1 Lung Cancer and Screening

Screening is known as the periodic examination of a certain population in order to detect an early stage asymptomatic disease. [14] The goal of lung cancer screening is to detect lung cancer cases at an earlier stage in order to be able to more effectively intervene with potentially curative treatment for the patient, all while helping to reduce lung cancer related mortality without harming the patient or with limited harm to the patient. [1, 14, 29] Dating back to 1968, the strategy being employed to reduce lung cancer related deaths was the use of chest radiography with or without sputum cytology, serum biomarker testing, and fiber optic examination of the bronchial passage as methods of screening. [7, 26] Screening criteria for patients at high risk include being between 55 to 74 years old, currently smoking 30 pack-years, or former smokers who quit within the past 15 years; however, these criteria do change from study to study. [7, 17, 22] It is undetermined if screening patients that are at a lower risk for lung cancer will bring about the same changes in lung cancer related mortality and if patients that do not meet the criteria described above are in fact low risk. [31] Currently, the recommendation is to not screen patients who are not deemed high risk using the eligibility criteria mentioned above as the high-risk threshold, as it is unknown if this will bring about false positive findings, overdiagnosis, and unnecessary invasive testing. [31]

Some randomized control trials found that the use of chest x-ray and sputum cytology, serum biomarker testing, and fiber optic examination of the bronchial passage had detected some early-stage lung cancers. [7, 26] However, these early-stage cancer detections brought on by this screening technique was not accompanied by a reduction in lung cancer mortality, which meant that the screening technique was not beneficial. [7, 26] Advancements in multidetector CT machines has allowed for the acquisition of volumetric images of the lung by having the patient hold their breath one time and limiting their exposure to radiation. [14] Due to the high contrast between aerated lung and soft tissue, CT use, which provides a low radiation dose, preserves the detection of lung lesions despite high image noise and, therefore, allows screening with LDCT to become the focus of investigation for lung cancer screening. [14]

Many observational studies first started to find that low-dose computed tomography (LDCT) scans may be more effective in screening for the early detection of lung cancer then earlier modalities. [8, 26] In response to these studies, The International Early Lung Cancer Action Project (I-ELCAP) found that LDCT screening identified a higher portion of stage I cancers than chest radiographs. [8] A few years later, the National Cancer Institute started the National Lung Screening Trial (NSLT). Participants in the trial were randomized to three annual screenings either with chest x-ray or LDCT. [31] The primary end point of the study was lung cancer mortality.[31] The results determined that screening for lung cancer with LDCT in high-risk patients yields a 20% reduction in lung cancer mortality in comparison with screening with chest x-ray. [15] Furthermore, with the introduction of LDCT, single-arm studies showed a stage-shift in the cancers that were being diagnosed because 48-85% of screen-detected cancers were detected at stage I compared to 30-35% of clinically detected lung cancers. [1] The NSLT study, however, did not look at the difference between screening with LDCT and usual care. [16] One study, the Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays Trial (DANTE) trial, did look at the difference between screening with LDCT and usual care and determined that there was not a reduction in cancer related mortality. [16] However, this study was seen as a poor-quality study as it was skewed towards a bias for mortality outcomes and, therefore, the results of the study have not been used to determine recommendations. [16]

### 4.1.1 Advantages of Screening

The advantages of screening people at high-risk for lung cancer with LDCT includes diminishing the absolute risk of lung cancer death from 1.66% to 1.33% or three fewer deaths per 1000 people. [31] Screening also has significant clinical impacts on lung cancer diagnosis as it allows to shift diagnoses toward earlier stages which would make curative treatments possible. [29] Approximately 57.1% of all screened detected lung cancers are diagnosed in localized stage compared to 16.1% in the people who were not screened or missed their screening appointment. [12]

### 4.1.2 Disadvantages of Screening

The disadvantages of screening with LDCT are the chance of receiving a false-positive result and associated overdiagnosis. [1, 25, 26, 32] With regards to the false-positive results, there will be one or multiple benign or malignant tumours that will be found in about half of the individuals who decide to proceed with lung cancer screening. [1] However, only a few of these tumours will be cancerous once the patient has undergone an invasive diagnostic follow-up process. [1] False-positive screening results are a major issue because of the potential for unnecessary diagnostic follow-up for the patient, whether that be invasive or non-invasive. [1] In the NSLT over the three rounds of screening, 24.2% of the test results for the screening were positive and 39.1% of all patients that were screened in the trial received at least one positive test result. [1, 25] This study also mentioned that 95% of the positive results received through screening did not result in a diagnoses of cancer, meaning they were false-positive results. [1, 25] Most people in the NSLT who received a positive result underwent further imaging, according to the Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement, "… The first round of screening in the NSLT showed an average of one follow-up scan per positive screening test result." [25]

The second disadvantage to screening is overdiagnosis. Overdiagnosis is when detected lung cancer would have never been clinically diagnosed. [1] This means that the pathologist is diagnosing a lung cancer due to the screening process; however, this cancer would not progress to cause symptoms or result in fatality during a patient's normal anticipated life-span. [13] There are many consequences that come with overdiagnoses including unnecessary diagnostic work-up for the patient, unnecessary cancer treatments for the patient which includes all the negative physical as well as psychological consequences and unnecessary health-care costs both for the patient and the health-care system. [1] When overdiagnosis was examined in the NSLT it was found that 1.38 cases of overdiagnosis would be found in the 320 participants that needed to be screened in order to prevent one lung cancer death. [31]

In summary, the benefits of screening for lung cancer with LDCT have become increasingly evident over the past years. Screening with LDCT has shown a 20% reduction in lung cancer mortality in comparison with chest x-ray and has also shown a significant stage-shift in the cancers that were being diagnosed. [1, 15] Furthermore, annual lung cancer screening with LDCT has been proven advantageous in many ways but most importantly it has been proven to substantially diminish the number of lung cancer-related deaths as well as decrease overall mortality. [27, 37] However, while there are many benefits to lung cancer screening there, are also many potential risks. One must look at all the risks associated with screening and weigh the pros and cons in order to move towards the implementation of a national screening program. There are, however, ways to improve the risks associated with lung cancer screening which will be discussed in the following section.

## 4.2 Simulation Modelling

A simulation model is a computer model that aims to replicate some real-life situations. [38] Simulation modelling explicitly incorporates uncertainty in one or more of the input variables. [38] This being said, the simulation model is used to simulate the behaviour of a system that evolves over time based on probability distributions. When a simulation model is run, random input variables take on values generated from the probability distributions and the model keeps track of any resulting output variables of interest. [38] In other words, the probability distributions that are inputted will be used to randomly generate events that happen in the system. [38] This helps to observe how the outputs of the model vary as a function of the varying inputs. [38] In a screening domain, simulation model uses population data, specific disease related information such as the incidence or the natural history of the disease as well as screening characteristics in order to simulate what screening program should be implemented and how it should be implemented. [10, 18, 37] These models have been used in order to determine the cost-effectiveness, the potential benefits of screening and the potential outcomes that could happen while implementing different screening policies. [10, 18, 33] They are used to evaluate the full range of potential choices that could lead decision-makers to the implementation of a program or a change in the requirements for the screening program. [10] These models should be built with an understanding of the logic that governs each activity in the system. [38] The results of a simulation model can include, among others throughputs or delays. [10, 38] These models have been used in many different domains including cancer screening. [10] In a lung cancer screening program, the system is evolving as the number of people returning for screening and entering the screening program is always changing based on new information. This new information will make changes to the eligibility criteria and the screening process for patients at high risk to develop lung cancer. For example, simulation modelling can help determine how changing the eligibility criteria for a lung cancer screening program can affect the number of people in need of screening and how this in turn will influence the demand for CT imaging resources in a certain healthcare institution. It can also allow researchers to change other aspects of the program such as when patients will be returning for screening following a negative baseline scan to determine how this will impact demand on CT imaging resources, wait times for patients to receive their scans and stage shifting for diagnosed cancers or lung cancer related mortality. The models that were used in this project are waiting line models and include three basic components: the probability distribution of arrivals (inter arrival times) or how people arrive to the system, the probability distribution of a service time or how people are being served, the organization of line and servers or how the system is organized. For the simulation models used in this study, the stochastic inputs are the arrival of patients to the screening venue and the service time for each scan. Finally, the outputs for this model include the number of screened patients, the wait time for screening, and the stage shifting for patients that are diagnosed with cancer after receiving their scan.

### 4.3 Cancer Screening and Simulation Modeling

Simulation modeling has been used in order to help assess cancer screening programs for colorectal cancer, bowel cancer as well as breast cancer screening. [5, 30, 33, 37]

In bowel cancer screening, the model was used to help with the expansion of the National Bowel Cancer Screening Program. The model simulates a large population of individuals from birth to death. [5] The first simulation model was run without screening the individuals for bowel cancer and the second was run with the screening. [5] This model ran 5 different implementation scenarios. [5] The first one was the current scenario which modelled the existing screening program which included the addition of 70-year-olds to the screening eligibility. [5] The second scenario also called the slow scenario was based on a proposed implementation plan and it included the addition of one age cohort every two years starting with 70-year-olds in 2015. [5] In this scenario, the full implementation was achieved by 2035. [5] The other three scenarios were accelerations of the slow scenario. [5] The implementation was considered complete when all individuals aged 50-74 where invited for screening on a biennial basis. [5] The results of this simulation showed that the faster implementations also required more colonoscopy resources. [5] To prevent (an) additional 25,702 deaths between the current and slow scenario there needed to be an additional 1,943,395 colonoscopies performed. [5] The required number of colonoscopies over time where related to the speed of implementation, the faster the implementation the greater the increase in colonoscopy requirements. [5]

For lung cancer screening, one of the current models available to predict the outcomes of screening is the OncoSim model. This simulation platform has different cancer specific models including lung cancer. [10] It can be used in order to plausibly project lung cancer screening outcomes, resource use as well as cost for the scenarios that are being simulated. [10] This model captures the heterogeneity of a certain population's health and demographic history over time. [10] It also gives the user the capability to control the input parameters which may include risk factors such as current smoking status and smoking history, screening characteristics, test sensitivity and specificities, participant eligibility and follow-up protocols. [10] Furthermore, the outputs of the model can also be controlled by the user and these include incidence of the cancer, mortality, resource utilization which include follow-up procedures, treatments and scans, direct health care costs, etc. [10] Finally, this model includes several different jurisdictions which allows the user to customize their settings for their specific jurisdiction. [10] This allowed the model to be used in order to support decisions at the national as well as the jurisdictional level. [10] It has been used by the Canadian Task Force on Preventive Health Care in order to support their 2016 guidelines on colorectal and lung cancer screening. [10] It is also currently being used by various provincial health ministries in order to develop a case for introducing lung cancer screening and to explore potential ways to reduce wait times in colorectal cancer screening. [10] While OncoSim is used to simulate progression of a disease, this research aims to evaluate different policies from a perspective of wait times and cancer progression. This entails that the premise of this project is different from the objective of OncoSim. Secondly, OncoSim does not consider the wait times present for cancer screening which would mean that different metrics would need to be used to evaluate the policies. Finally, OncoSim does not allow for the addition of new model parameters associated with the screening policies to be evaluated in this research. Thus, this research cannot be done with a help of the OncoSim platform.

In summary, simulation modelling is one of the possible methods for evaluating cancer screening. While simulation modeling is being used in order to assess scenarios related to screening as well as to determine the cost-effectiveness, general effectiveness and resource allocation in cancer screening, it is more commonly being used to assess other cancer screening programs. [5, 10, 18, 33, 36, 37] Lung cancer screening is still new and there are few publications about the use of simulation modeling in lung cancer screening.

### 4.4 Cancer Screening Policies

The literature offers potential screening policies that can be implemented. The first policy involves changing the definition of a positive scan to a finding of a solid or part solid nodule that is of 6mm in diameter instead of 4mm in diameter. [8] This increases the positive predictive value from 6.9% to 17.3% and decreases the amount of false-positive results that occur without increasing the number of false-negatives. [8] This decrease in false-positive results would mean a decrease in follow-up CT scans. [6] Using this larger nodule size as a positive test result did not affect the number of cancers that were diagnosed in a study by McGee et al. [8] An increase in the nodule size threshold also did not affect the stage distributions of the lung cancers that were diagnosed, as a greater proportion of stage IV cancers were diagnosed in participants who had the smallest nodules being nodules with a diameter of 4-7mm. [11]

Another policy described in the literature is to offer biannual screening to patients who receive a normal baseline scan instead of offering these patients annual screening. [27] This policy is based on the fact that patients with a normal baseline scan have a lower lung cancer incidence rate (0.34% vs 1.02%) and a lower mortality rate compared with the other screening participants who received a positive or indeterminate baseline scan. [27] Due to these decreased rates, annual screening for this group may not be necessary and changing the screening regimen in this group could minimize the harms from false-positive results as well as the number of follow-up scans needed to be done. [27] The NELSON study looked at these patients with a negative baseline scan as well and determined that the risk for these patients of being diagnosed with a screen-detected lung cancer 5.5 years post screening strongly depended on the result of their first scan. [27] If the baseline scan was negative, the patients had a 0.6% incidence of lung cancer at the final screening round compared to 1.6% incidence in patients whose baseline scan was indeterminate or positive.

The current policy being used in The Lung Cancer Screening Pilot for People at High Risk is to scan people using LDCT who have a 2% or higher chance of developing lung cancer in the next six years based on the risk assessment model. [39] Once the scan is complete, if the patients receive a negative result, they are asked to return for a follow-up scan in one year. Changing the timeline for these follow-up scans could have a big impact on the number of people returning for lung cancer screening, lung cancer staging and wait times.

In summary, the literature identifies two possible variations in the policies: changing the definition of a positive scan and/or changing the frequency of scans for those who need to return later for another scan. In this research we consider the policy offering biannual screening to patients who had a negative baseline scan.  The other policy variation presented in this section was not assessed as it is too difficult to find data regarding nodule size at a granularity level required for model development.

# 5. Methods

## 5.1 Introduction

This project evaluates the use of different screening policies on system performance. The population involved in this study includes any person that is eligible for lung cancer screening through The Lung Cancer Screening Pilot for People at High Risk as this will likely be the eligibility criteria for a fully developed program.

A discrete event simulation (DES) model that supports decision making with regards to different screening policies was developed in collaboration with TOH experts using data obtained from Cancer Care Ontario, the literature, and the screening program. DES model simulates the behavior of a stochastic system. A lung cancer screening program is a stochastic system as the arrivals of patients eligible for screening, screening results, and patients returning for subsequent screens are non-deterministic and follow some probability distributions. With the help of DES model, it is possible to assess the impact of a screening policies parameters such as, the frequency of returns on system performance using metrics such as wait times or shifting between cancer severity stages. Validation of the model parameters was limited and has been done with experts in the field such as the Chief of Cancer Transformation and Strategy at TOH, Manager of the Integrated Cancer Screening and Prevention for the Champlain Regional Cancer Program and other experts involved in the Screening Pilot at Cancer Care Ontario and TOH

The simulation models were run in order to determine how different imaging policies will impact system performance if we assume a fixed imaging capacity.

### 5.2 Study Design

The simulation models that were used in this research were developed by TOH experts. The models were developed using two different system configurations:

- each imaging site is independent with independent intakes for its services.
- imaging resources are pooled and there is a single intake for the three sites.

Due to these different configurations, there was a need for two separate simulation models. The first model represented a single imaging centre with a single queue. The second model assumed one queue for the three centers.

### 5.3 Data

Weekly data for a period of two years came from The Lung Cancer Screening Pilot for People at High Risk and was supplemented with data from the literature. Patients waiting for lung cancer screening in the Pilot typically do not wait longer than a week therefore, in order to determine the wait time for patients, weekly data was needed. However, the Lung Cancer Screening Pilot for People at High Risk was able to provide very limited data and it led to the model having gaps of information that had to be filled from other sources. The breakdown of the data and its source can be found in Table 1.

**Table 1. Simulation model parameters.**

| Parameter | Source of Data | Probability |
|---|---|---|
| Negative baseline scan | Pilot | 85% |
| Positive baseline scan | Pilot | 2% |

| | | |
|---|---|---|
| Suspicious baseline scan | Pilot | 13% |
| Person with a negative baseline scan stays in the system | Pilot | 91% |
| Patient who receives a suspicious baseline scan who needs a biopsy | Literature | 38% |
| Patient who receives a positive biopsy after a suspicious scan | Literature | 75% |
| Patient who receives a positive biopsy after a positive scan | Literature | 85% |
| Scan result is suspicious, and patient must return for a follow up scan in 3 months | Pilot | 32.5% |
| Scan result is suspicious, and patient must return for a follow up scan in 6 months | Pilot | 67.5% |
| Patient with a positive biopsy has stage 1 cancer. | Literature | 63% |
| Patient with a positive biopsy has stage 2 cancer. | Literature | 7% |
| Patient with a positive biopsy has stage 3 cancer. | Literature | 15% |
| Patient with a positive biopsy has stage 4 cancer. | Literature | 15% |

### 5.4 Unmet Data Requirements

In order for this project to show an impact on cancer staging, wait times, and resource utilization based on different policies, more comprehensive data would be needed. Table 2 presents a summary about unmet data requirements.

**Table 2. Unmet Data Requirements**

| **Data Needed** |
|---|
| True arrival rate per site for the pilot |
| Percentage of patients with suspicious baseline scan who need a biopsy |
| Percentage of patients with a positive biopsy after a suspicious scan |
| Percentage of patients with a positive biopsy after a positive scan |
| Cancer staging for patients with a positive baseline scan and a positive biopsy. |
| Cancer staging for patients with a suspicious baseline scan and a positive biopsy. |
| Average length of time (weeks) required for shift in lung cancer severity staging |
| True service rate per site of the pilot |
| Changes in the imaging capacity for the system. (For example, overtime, dedicated slots for lung cancer screening, etc.) |

### 5.5 Simulation Models Used in the Study

The two models were developed by Konstantin Volodin with researcher's help. The model which is used to represent a single centre is an M/M/1 model where the first M represents the arrivals modelled according to a Poisson distribution, whereas the second M represents service time modelled as an exponential distribution. This model roughly represents the current situation for lung cancer screening, which is that each center has their own independent arrivals. The second model considers one queue for the three centres, it is an M/M/3 model, meaning that there is a single queue served by three independent servers (centers). This model considers the situation where there is a single intake line, and each patient can be assigned to any of the three centers. The main difference between these two models is the way in which screening queues are set up. The first one assumes that arrivals are dedicated to a specific center (M/M/1) whereas the second one assumes a single intake to all three centers (M/M/3). The way of organizing the queue using the M/M/3 model should be more efficient. To simplify, in this project, one M/M/1 model was run as the results from this model are assumed to be representative for each center. In each model cancer stages were grouped, and we assumed an increase of 50% for probability of the diagnosis of stage 3/ 4 cancers occurring every six months that the patient waited to be screened. The outputs of each model includes the number of patients that were screened, how long these patients waited to be screened and the stage shifting for patients that were diagnosed with lung cancer after their screening as a function of wait time. Analysis of the models outputs constitute the basis for assessing different screening policies.

### 5.5.1 Evaluation Setting of the Model

The model was developed using a simulation library in Python. The length of the models warm up period was three years and then the model simulated three years of the system behaviour for a total length of a simulation run of six years. The warm up period for this project was quite long and this was done to allow the reutterance to settle.

### 5.5.2 Assumptions

The following simplifying assumptions were followed in the model development:

1. One year is composed of twelve 30-day months, resulting in 360 days.
2. The model was run 30 times for each policy starting from an empty system.
3. False-positive results of the tests were not considered.
4. Each center has one day dedicated for lung cancer screening with the scan capacity of 32 patients per day for the M/M/1 model and 96 patients per day for the M/M/3 model.
5. The arrival rates were 10 new patients per day and 30 new patients per day for the M/M/1 and the M/M/3 models respectively. However, considering the models that were used model a system with one dedicated day for screening per week, these arrival rates will in fact represent weekly demands and capacities for screening. True arrival rates (new patients + returning patients for the scans) were very close to the scanning capacities.
6. There is a single cancer type. This implies no differentiation between types of cancers that have different mortality and aggressiveness of growth.
7. All three sites have the same characteristics
8. Arrival rate has no trend/seasonality. This assumption was used so a Poisson distribution could be used to model the arrival rates.

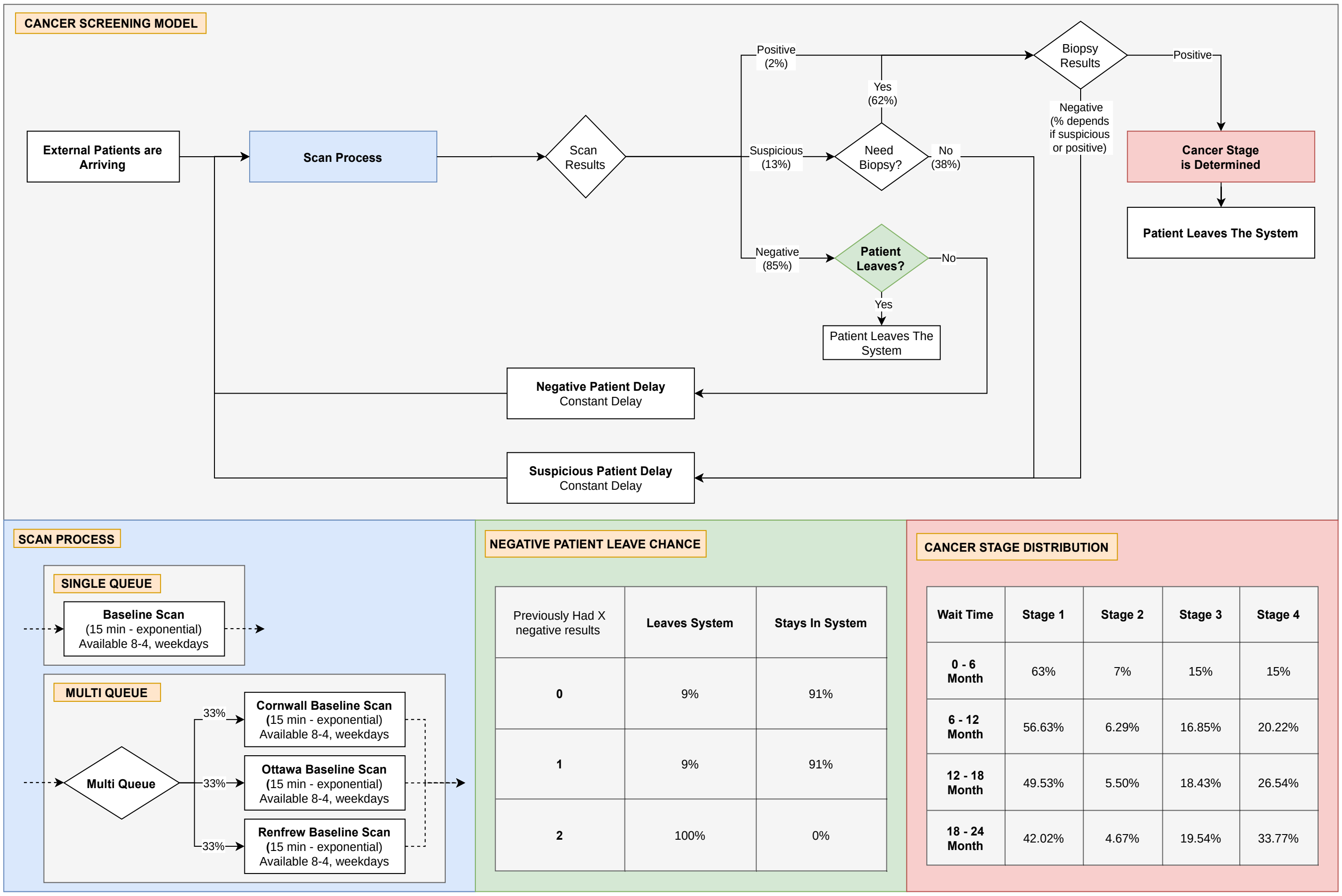
9. Service time follows an exponential distribution.
10. If a patient receives two negative scan results, then they leave the system. This assumption is based on studies that determined that most patients who receive a negative scan will only return for one follow-up scan in a year before leaving the system. In the case of this study each patient will receive two follow-up scans following a negative baseline scan.
11. Each center has fixed imaging capacity.
12. The queueing discipline is “first-come, first-served” for both patients arriving and patients who return for follow-up scans. There is no priority given to the patients who are returning to the system.
13. There is a 0.09 probability that a patient who received a negative scan result returns to the general population and does not receive their follow-up scan. This probability is the same as the probability of a patient choosing not to continue with screening after their risk assessment
14. The probability of a positive biopsy is different between suspicious and positive scan results.
    a) The overall probability that a patient receives a positive biopsy following a suspicious or positive baseline scan is 0.75. Furthermore, we assume that patients who receive a positive baseline scan have a probability of 0.85 of receiving a positive biopsy whereas, patients who receive a suspicious baseline scan have a probability of 0.75 of receiving a positive biopsy.
15. There are four cancer stages when a patient is being diagnosed with lung cancer. However, for this project the four stages were combined into two groups being, stage 1 and 2 together and stage 3 and 4 together. Therefore, only one stage transition was considered, being the transition from stage 1/ 2 to stage 3/ 4.
16. The probabilities of a patient being diagnosed with either stage 1 or 2 lung cancers or stage 3 or 4 lung cancers were taken from the data received from the pilot program.
17. The probability of cancer progressing to a later stage increases with the time spent waiting for a scan. This is being used to imitate the doubling time for cancer and determine how having patients wait longer to be screened can negatively impact the staging of the cancer that is diagnosed.
    a) The probabilities in a table below are used for illustrative purposes:

| | Stage 1 | Stage 2 | Stage 3 | Stage 4 |
|---|---|---|---|---|
| **0-6 Month** | 0.63 | 0.07 | 0.15 | 0.15 |
| **6-12 Month** | 0.5663 | 0.0629 | 0.1685 | 0.2022 |
| **12-18 Month** | 0.4953 | 0.0550 | 0.1843 | 0.2654 |

In order to calculate the combined probabilities for the different stages, individual probabilities after each 6-month were calculated as presented in Table 3. This assumption was made based on a conversation with the head of the pilot program.

**Table 3. Description of the change from 6-12 months**

| | Stage 1 | Stage 2 | Stage 3 | Stage 4 |
|---|---|---|---|---|
| **Initial value** | 0.63 | 0.07 | 0.15 | 0.15 |
| **Multiplier** | 1 | 1 | 1.25 | 1.5 |
| **Multiplication Results** | 0.63 | 0.07 | 0.1875 | 0.225 |
| **Sum of the Multiplication Results** | 1.1125 | | | |
| **Results of Division of each multiplication results by the sum (to normalize the values to 1)** | 0.5663 | 0.0629 | 0.1685 | 0.2022 |



| Previously Had X negative results | Leaves System | Stays In System |
|---|---|---|
| 0 | 9% | 91% |
| 1 | 9% | 91% |
| 2 | 100% | 0% |

| Wait Time | Stage 1 | Stage 2 | Stage 3 | Stage 4 |
|---|---|---|---|---|
| 0 - 6 Month | 63% | 7% | 15% | 15% |
| 6 - 12 Month | 56.63% | 6.29% | 16.85% | 20.22% |
| 12 - 18 Month | 49.53% | 5.50% | 18.43% | 26.54% |
| 18 - 24 Month | 42.02% | 4.67% | 19.54% | 33.77% |

**Figure 1. Graphical illustration of the models.**

On Figure 1 the top part illustrates the screening process and the flow of patients through this process. The section labeled "Scan process" represents the organization of the system as either a single line, single server system (M/M/1) or a single line, multiple server system (M/M/3). The section labeled "Negative patient leave chance" represents the assumption that patients with negative scan results have a 9% chance of leaving the system following their baseline scan and first follow-up and will all have a 100% chance of leaving the system following their second follow-up scan. Finally, the section labeled "Cancer stage distribution" links wait times to cancer staging for patients with a positive biopsy. Specifically, if the patient waits less then 6 months for screening there is no shifting in their cancer staging.

### 5.6 Policies to be assessed

The purpose of assessing different policies is to determine how the performance of the system changes in light of a fixed imaging capacity. The metrics used to assess the policies are:

- wait times
- number of the patients that moved from lower to higher cancer stage measured as the proportions of patients in each cancer stage category.

By looking at these metrics, the best policy option could be determined as the one with the least wait time and least shifting between cancer stages. These metrics were used because the relationship between wait times and cancer staging is not linear and, therefore, wait times up to a certain time will not significantly impact cancer staging.

**Policy 1: Biannual Screening**

This policy offers biannual screening to patients who received a negative baseline screen. [27] These patients will return for screening in 24 months instead of 12 months, which lowers the demand for CT resources. This policy also lowers the required number of follow-up scans (see [24]). Furthermore, offering biannual screening to patients who have received a negative baseline scan does not affect the patient's chances of being diagnosed with advance stage cancers later on (see [22]).

**Policy 2: Annual screening with all suspicious patients returning for a follow-up scan in 6 months.**

This policy assumes that patients who received a negative baseline scan return for a follow-up scan in 12 months. Patients who received a suspicious baseline scan return for a follow-up scan in 6 months. When compared to the baseline, this policy will bring a decrease in the frequency of returns for follow-up scans for patients who had a suspicious scan result.

**Policy 3: Annual screening with all suspicious patients returning for a follow-up scan in 3 months.**

This policy assumes that patients who received a negative baseline scan result return for a follow-up scan in 12 months. Patients who received a suspicious baseline scan return for a follow-up scan in 3 months. When compared to the baseline, this policy will bring an increase in the frequency of returns for follow-up scans for patients who had a suspicious scan result.

**Policy 4: Biannual screening with all suspicious patients returning for a follow-up scan in 6 months.**

This policy assumes that patients who received a negative baseline scan result return for a follow-up scan in 24 months. Patients who received a suspicious baseline scan will also return for a follow-up scan in 6 months. When compared to the baseline, this policy will bring a decrease in the frequency of returns for follow-up scans.

**Policy 5: Biannual screening with all suspicious patients returning for a follow-up scan in 3 months.**

This policy assumes that patients who received a negative baseline scan return for a follow-up scan in 24 months. Patients who received a suspicious baseline scan will return for a follow-up scan in 3 months. When compared to the baseline, this policy will bring a decrease in the frequency of returns for follow-up scans.

## 6. Results

Multiple simulations were conducted, assuming mean arrival rate of 10 patients per day for the M/M/1 model and 30 patients per day for the M/M/3 model.

### 6.1 Model Validation

A proper validation for this project could not be conducted because none of the simulation models truly reflect the current situation due to lack of available data. Thus, the models being used are significantly simplified.

### 6.2 Policy Option Results

The baseline policy is the current policy being used in The Lung Cancer Screening Pilot for People at High Risk and it has the following characteristics:

- Patients with a risk score of 2% or higher of developing lung cancer in the next six years are scanned using LDCT.

- Patients who receive a negative scan return for a follow-up scan in 12 months
- Patients who receive a suspicious scan return for a follow-up scan in 3 or 6 months.
- It is assumed that the two thirds of the patients return in 6 months and one third return for a follow-up scan in 3 months.
- Patients who receive a positive scan are referred to the LDAP and removed from the system.

**Table 4. Baseline policy:** Simulation results for the M/M/1 and M/M/3 models

| Model Type | | M/M/1 | M/M/3 |
|---|---|---|---|
| Arrival Rate | | 10 | 30 |
| | | Mean and SD | |
| Results | Percentage of patients in Stage 1/2 | 70.2 ± 36.9 | 70.1 ± 63.7 |
| | Percentage of patients in Stage 3/4 | 29.8 ± 24.9 | 29.9 ± 45.2 |
| | Number of days a patient waits to be screened | 80.5 ± 6.78 | 78.3 ± 3.00 |

When evaluating system performance for the baseline policy, where the system uses one intake per center, or one intake for three centers, there is very little impact on the wait time for screening as well as the percentage of advanced stage lung cancers that are being diagnosed post screening.

**Policy 1: Biannual screening.**

- Patients who receive a negative baseline scan return for a follow-up scan in 24 months.
- Patients with a positive scan are referred to the LDAP for further diagnostics
- Patients who receive a suspicious baseline scan return for a follow-up scan in 3 months or 6 months.
- It is assumed that the two thirds of the patients return in 6 months and one third return for a follow-up scan in 3 months.

**Table 5. Policy 1: Biannual Screening.** Simulation results for the M/M/1 and M/M/3 models.

| Model Type | M/M/1 | M/M/3 |
|---|---|---|

| Arrival Rate | | 10 | 30 |
|---|---|---|---|
| | | Mean and SD | |
| Results | Percentage of patients in Stage 1/2 | 71.6 ± 51.3 | 70.2 ± 75.1 |
| | Percentage of patients in Stage 3/4 | 28.4 ± 1.35 | 29.8 ± 51.3 |
| | Number of days a patient waits to be screened | 29.0 ± 2.79 | 28.4 ± 1.35 |

Considering that for baseline and Policy 1 wait times are well below 6 months, there is no difference in the percentage of the patients in cancer stages. However, decreasing the frequency of follow-up scans has a significant impact on the wait time for screening for both system configurations when compared to the baseline policy

**Policy 2: Annual screening with all suspicious patients returning for a follow-up scan in 6 months.**

- Patients with a negative baseline scan return for a follow-up in 12 months
- All patients with a suspicious baseline scan return for a follow-up in 6 months.
- Patients with a positive scan are referred to the LDAP program.

**Table 6. Policy 2: Annual screening with all suspicious patients returning for a follow-up scan in 6 months.** Simulation results for the M/M/1 and M/M/3 models

| Model Type | | M/M/1 | M/M/3 |
|---|---|---|---|
| Arrival Rate | | 10 | 30 |
| | | Mean and SD | |
| Results | Percentage of patients in Stage 1/2 | 69.9 ± 25.1 | 69.9 ± 63.9 |
| | Percentage of patients in Stage 3/4 | 30.1 ± 23.3 | 30.1 ± 57.3 |
| | Number of days a patient waits to be screened | 79.6 ± 6.39 | 77.9 ± 3.31 |

Policy 2 decreases the frequency of follow-up scans for patients with suspicious nodules. The baseline policy has patients who receive a suspicious scan returning for follow-up in two groups. In this policy two thirds of patients will return for a follow-up in 6 months whereas one third of patients will return in 3 months. Policy 2 however, allows all patients who receive a suspicious baseline scan to return for a follow-up scan in 6 months instead of separating these patients into two groups. This allows for a decrease in the frequency of follow-up scans for the portion that would otherwise have to return in 3 months. This change to the return of suspicious patients has a small impact on wait times for screening for both configurations when compared to the baseline policy.

**Policy 3: Annual screening with all suspicious patients returning for a follow-up scan in 3 months.**

- Patients with negative baseline scan return for a follow-up in 12 months
- All patients with a suspicious baseline scan return for follow-up in 3 months.
- Patients with a positive baseline scan are referred to the LDAP.

**Table 7. Policy 3: Annual screening with all suspicious patients returning for a follow-up scan in 3 months.** Simulation results for the M/M/1 and M/M/3 models

| Model Type | | M/M/1 | M/M/3 |
|---|---|---|---|
| Arrival Rate | | 10 | 30 |
| | | Mean and SD | |
| Results | Percentage of patients in Stage ½ | 70.0 ± 36.9 | 69.9 ± 60.6 |
| | Percentage of patients in Stage ¾ | 30.0 ± 21.8 | 30.1 ± 47.2 |
| | Number of days a patient waits to be screened | 81.7 ± 6.11 | 79.8 ± 3.55 |

Policy 3 increases the frequency of follow-up scans for patients with suspicious nodules. The baseline policy has patients who receive a suspicious scan returning for follow-up in two groups. In this policy two thirds of patients will return for a follow-up in 6 months whereas one third of patients will return in 3 months. Policy 3 allows all patients who receive a suspicious baseline scan to return for a follow-up scan in 3 months instead of separating these patients into two groups.

This allows for an increase in the frequency of follow-up scans for the portion that would otherwise have to return in 6 months. This change to the return of suspicious patients has a small impact on wait times for screening for both configurations when compared to the baseline policy.

**Policy 4: Biannual screening with all suspicious patients returning for a follow-up scan in 6 months.**

- Patients with a negative baseline scan return for a follow-up in 24 months
- All patients with a suspicious baseline scan return for a follow-up in 6 months.
- Patients with a positive baseline scan are referred to the LDAP.

**Table 8. Policy 4: Biannual screening with all suspicious patients returning for a follow-up scan in 6 months.** Simulation results for the M/M/1 and M/M/3 models

| Model Type | | M/M/1 | M/M/3 |
|---|---|---|---|
| Arrival Rate | | 10 | 30 |
| | | Mean and SD | |
| Results | Percentage of patients in Stage 1/2 | 69.9 ± 32.0 | 70.0 ± 66.6 |
| | Percentage of patients in Stage 3/4 | 30.1 ± 25.8 | 30.0 ± 35.1 |
| | Number of days a patient waits to be screened | 28.0 ± 2.75 | 27.2 ± 1.68 |

Policy 4 decreases the frequency of follow-up scans which has a significant impact on the wait time for screening for both system configurations when compared to the baseline policy. The results from this policy are similar to those obtained between Policy 1 and the baseline because biannual screening for patients with negative baseline scans has a bigger impact on wait times. There is a greater portion of the people who are being scanned that are going to receive negative baseline scans, therefore meaning a larger portion will have to return for follow-up scans in 24 months instead of 12 months. This decreases the number of required follow-ups. Furthermore, this policy also decreases the frequency of follow-up scans for patients who receive a suspicious baseline scan result which in turn explains the slightly lower wait times than those with Policy 1.

**Policy 5: Biannual screening with all suspicious patients returning for a follow-up scan in 3 months.**

- Patients with a negative baseline scan return for a follow-up in 24 months
- All patients with a suspicious baseline scan return for a follow-up in 3 months.
- Patients with a positive baseline scan are referred to the LDAP.

**Table 9. Policy 5: Biannual screening with all suspicious patients returning for a follow-up scan in 3 months.** Simulation results for the M/M/1 and M/M/3 model.

| Model Type | | M/M/1 | M/M/3 |
|---|---|---|---|
| Arrival Rate | | 10 | 30 |
| | | Mean and SD | |
| Results | Percentage of patients in Stage 1/2 | 69.9 ± 35.5 | 70.1 ± 54.8 |
| | Percentage of patients in Stage 3/4 | 30.1 ± 26.9 | 29.9 ± 45.8 |
| | Number of days a patient waits to be screened | 31.1 ± 2.75 | 29.9 ± 1.32 |

Policy 5 decreases the overall frequency of follow-up scans which has a significant impact on the wait time for screening for both system configurations when compared to the baseline policy. The results from this policy are similar to those obtained between Policy 1 and the baseline because biannual screening for patients with negative baseline scans has a greater impact on wait times as there is a larger portion of the people who are being scanned that are going to receive negative baseline scans. Therefore, there is a bigger portion who will have to return for follow-up scan in 24 months instead of 12 months. Furthermore, this policy increases the frequency of follow-up scans for patients who receive a suspicious baseline scan result which in turn explains the slightly higher wait times than Policy 1.

## 7. Discussion

The purpose of this research was to evaluate the different screening policies while assuming a fixed imaging capacity. The results of this research form a first step for further research on the implementation of a lung cancer screening program. This further research could be used to help determine which policy presented could potentially be beneficial to the implementation of a lung cancer screening program. This study used the baseline policy (currently being used by The Lung Cancer Screening Pilot for People at High Risk) as a benchmark to compare with the other policies. However, it is important to note that we assumed that one full day a week is devoted to the lung cancer screening program while in reality that is not the case.

### M/M/1 Model

When using an M/M/1 model with the different policies being evaluated, there is practically no difference in the proportions of patients in the two cancer staging groups for the different policies. This is as a result of wait times never going beyond 6 months – a time assumed to impact the shift between the stages. This will also be the case for the policies using the M/M/3 model. Wait times, however, are impacted by the different policies. Policies 1, 4 and 5 brought a decrease in wait times because they extend the period of time between screening for patients that have negative baseline scans, which we know to be a higher percentage of people. Having patients who receive a negative baseline scan return in 24 months instead of 12 months will result in fewer patients returning for scans in a short period of time and therefore, wait times for screening will be diminished. Policy 4 has a lower wait time than Policy 1 and 5 because it also decreases the frequency of follow-ups for patients with suspicious scan results. This in turn diminishes wait times a little more than the other two policies. Policies 2 and 3, like the baseline policy, offer annual screening for patients who received a negative baseline scan. Most patients who are screened will receive a negative baseline scan and therefore, similar to the baseline policy, more patients will be returning for a follow-up scan sooner which will increase wait times for screening. This explains why wait times for screening with Policies 2 and 3 are similar to those with the baseline policy. Policy 3 has wait times that are a little longer than the baseline and Policy 2 because it also increases the frequency of follow-ups for patients with suspicious baseline scans.

**M/M/3 Model**

When using an M/M/3 model with the different policies being evaluated wait times are impacted. Policies 1, 4 and 5 brought a decrease in wait times because they extend the period of time between screening for patients that have negative baseline scans, which represents a higher percentage of people. Having patients who receive a negative baseline scan return in 24 months instead of 12 months will mean fewer patients will be returning for scans in a short period of time and therefore, wait times for screening will be diminished. Policies 2 and 3, like the baseline, policy offer annual screening for patients who received a negative baseline scan. Most patients will receive a negative baseline scan and therefore with these policies, as with the baseline policy, more patients will be returning for a follow-up scan sooner, which in turn will increase wait times for screening. This explains why wait times for screening with policies 2 and 3 are similar to those with the baseline policy. As with the M/M/1 model, Policy 4 offers the shortest wait times while Policy 3 offers the longest and this is because Policy 4 also decreases the frequency of follow-ups for patients with suspicious scan results whereas Policy 3 increases that frequency.

**Organization of the Queues.**

The organization of the queues is an important factor in determining which policy is the best policy to implement. However, regardless of the queue organization there is very little difference between the results of each policy. There is a number of plausible explanations for this situation, including the fact that the simulation model might not reach a steady state.

## 7.1 Limitations

There are multiple limitations to this study. First, data available from the pilot program was scarce and this has had an impact on how comprehensive the simulation models might be. Scarcity of data was partially addressed by using data from the literature. Given the lack of data, the models do not simulate the screening regimen in sufficient detail and therefore, the results are different than what is to be expected. Furthermore, due to the lack of data, the models are simplistic. Secondly, the experimental setup has certain shortcomings. The warm-up period that was used is not long enough for steady state to be reached. It would have been beneficial to increase the simulation length in order to see how this would impact wait times and therefore, if there would be a difference in stage shifting. For further research, having better and more comprehensive data about screening and imaging centers capacities seem to be key factors for building models that better simulate the system.

### 7.2 Shortcomings of Research

There are several shortcomings for this research. One of these shortcomings is that the same characteristics were assumed for the three separate centers. A better way to do the analysis would have been to have each imaging center have their own distinct characteristics for screening. The second shortcoming is that one M/M/1 model was used instead of running three distinct M/M/1 models mimicking operations of three centers. Therefore, the results that are compared are different, as each different center would have different patients and that was not taken into account. Another shortcoming is related to how stage shifting was modelled. Specifically, progressing of cancer between the stages (stage shifting) was modelled in a simplistic manner. It did not take into account progression between the individual stages, shifting depending on a type of cancer, and often nonlinear progression between stages 3 and 4. Finally, it was assumed that cancer screening is conducted during one dedicated day in a week instead of being spread over the week and "competing" for the imaging resources with other screening requests.

## 8. Conclusion

### 8.1 Significance of Research

In order to run a comprehensive analysis two aspects need to be considered. The first aspect is resource implications, and the second would be screening policy implications given resource limitations. This project was not able to evaluate resource implications due to a lack of data however, the second aspect was considered. Evaluating screening policy implications given resource limitations is the first step for further research on the implementation of a lung cancer screening program. This research did not produce conclusive results with regards to policy selection however, it indicated possible paths for future research on how resource implications would affect screening policies and how these policies would affect stage distribution as well as wait times should more complete and comprehensive data be available.

### 8.2 Concluding Comments

In conclusion, through this research I have learned more about cancer screening as well as simulation modeling. More importantly, I have learned that determining policies that can change how a program will be run is extremely difficult and requires enough data from the current program in order to be succesful. Not having access to all of the necessary data makes it difficult to simulate the program and therefore, makes it difficult to determine how different policies would affect these programs should they be implemented. Based on the results obtained in this research, policies that impact the way patients return to the queue for follow-up screening after a baseline scan do not have significant impacts on the number of advanced stage lung cancers that are diagnosed post screening. This is because it does not impact wait times enough and therefore, there is no stage shifting towards more advanced cancers.

## Appendix 1

Input Parameters for the Simulation Model

**General Parameters.**

| Replications | Warm up duration (days) | Total Duration (days) | Initial Waitlist Size | Arrival Rate per Day | Service Time (minutes) | Scan Capacity TOH (machine) | Scan Capacity Renfrew (machine) | Scan Capacity Cornwall (machine) |
|---|---|---|---|---|---|---|---|---|
| 30 | 1080 | 2160 | 0 | 10 | 15 | 1 | 1 | 1 |

**Distributions.** Distributions that were used to populate the simulation model.

| Results | 1 | Negative | Suspicious | Positive | Probability a person with a negative result stay in the system | Suspicious Result Needs Biopsy probability | Scan Result | Probability Biopsy is positive (patient has cancer) | Number of negative results to leave the system |
|---|---|---|---|---|---|---|---|---|---|
| Negative | 1 | 85.00% | 13.00% | 2.00% | 91% | 38% | Suspicious | 75.00% | 2 |
| Suspicious | | | | | | | Positive | 85.00% | |
| Positive | | | | | | | | | |

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