# Systems Modeling of Lung Cancer Screening Programs to Improve Quality

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## Abstract

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The main aim of this thesis is to study the factors that affect the quality of lung cancer screening with special focus on community based lung cancer screening programs. The variation in false positives and other outcomes found across screening centers and across different healthcare elements within a screening center motivates the need to study this problem. Conceptual modeling and simulation modeling are the systems modeling tools employed to study this problem. This conceptual modeling portion of the thesis, deduces some qualitative insights on the importance of the role of lung cancer screening program coordinators and database management systems used in screening programs. The simulation modeling portion of the thesis utilizes a Monte Carlo simulation extended from the conceptual model. The scope of the model was restricted to the factors of importance identified by an advisory board from participating institutions. Analysis of the model develops quantitative insights on the impact of these

identified factors and processes on the overall quality outcomes of the screening program as indicated by the false positive rate, early detection rate, radiation induced harms and quit rates in the smoking cessation program. In addition to the typical factors such as nodule detection sensitivity and nodule length variation, the simulation model observes the effect of recall bias in smoking history and shared decision making visits on the quality outcomes of lung cancer screening. It is concluded that, following a nodule management system like LUNGRADS can help achieve the best balance of the quality outcomes, establishing peer evaluation committees that reduce the variation in nodule length could significantly improve quality and that there should be increased focus on helping candidates quit smoking earlier on in the screening process. Though recall bias in smoking history affects false positive rate in a statistically significant way, the effect on the process is quantitatively small when compared to other factors like nodule detection sensitivity and nodule length variation.

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# GLOSSARY

1. **LDCT** – Low Dose Computed Tomography
2. **NLST** – National Lung Cancer Screening Trial
3. **USPSTF** – United States Preventive Services Task Force
4. **CDC** – Centers for Disease Control and Prevention
5. **PCP** – Primary Care Provider
6. **Pack years –** number of packs of cigarettes smoked per day multiplied by the number of years smoked. It is a numerical indicator of smoking history.
7. **False Positives** – A positive screening result from LDCT that is not due to lung cancer
8. **Early Detection** – Cancer diagnosed in an early stage enabling higher likelihood of cure for the patient
9. **Overdiagnosis** – A diagnosis of lung cancer that would have never caused symptoms or death during a patient's lifetime
10. **Quit Rate** – Percentage of initial smokers who have quit smoking during the period they underwent lung cancer screening
11. **Recall bias in smoking history** – Errors caused by differences in recollections of participants regarding their smoking history
12. **Nodule detection sensitivity** – Percentage of candidates with actual nodules that are correctly identified as having nodules in the LDCT scan
13. **Nodule detection specificity** – Percentage of candidates without a nodule that are correctly identified as not having a nodule in the LDCT scan
14. **Nodule length variation** – The difference between the actual nodule length and the length measured by the radiologist from the LDCT scan

15. **SDM** – Shared Decision Making. The collaborative process used by PCP's to accurately assess a candidate's risk for lung cancer
16. **SADT** – Structured Analysis and Design Technique. The method used to develop the conceptual model.
17. **Nodule management** – The management decision on the course of action to be taken after a positive LDCT scan result.
18. **Threshold based** – a nodule management algorithm wherein a positive scan is defined on the basis of nodule length above a certain threshold length
19. **LUNGRADS** – A nodule management algorithm designed by the American college of Radiology (ACR) wherein a positive scan is defined on the basis of nodule growth rate.
20. **Smoking cessation** – it is the process of discontinuing the smoking of tobacco
21. **PET** – Positron Emission Tomography scan, is first among the diagnostic procedures after LDCT scanning in lung cancer screening
22. **Biopsy** – an examination of lung tissue to determine the extent of tumor.
23. **Bronchoscopy** – Examining the tissue growth through a scope that passes through the airway
24. **LCS Coordinators** – Lung Cancer Screening program coordinators
25. **DBMS application** – An application that is programmed with services like email, calendars and reporting integrated with the database of patients in a healthcare organization

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# DEDICATION

To my dear husband, Krishnan, for his support and trust in my dreams.

To my dear father, Nandakumar, for teaching me to aspire for great dreams and ambitions.

To my dear mother, Usha, for showing me what dedication to work and family means.

# Chapter 1. INTRODUCTION

Lung cancer is the leading cause of cancer related deaths in the United States. As of 2015, it was estimated that 14% of the population will be diagnosed with lung cancer and 28% of cancer-related deaths in the population in US would be due to lung cancer. In the world, the incidence rate and mortality rate of lung cancer in developed countries in 44.7 and 36.8 per 100,000 respectively in the year 2012. [1]

The cancer statistics projection elaborates in detail, the difference in incidence rates observed across genders, age, geographical region, education and ethnicity [2]. For instance, in case of lung cancer, the incidence rates in the ages 60-79 is more than twice the incidence rates in the age range 40-59. There are similar variations in incidence rates of lung cancer found across the other factors. These differences in the prevalence of lung cancer across various population level factors indicate that the preparation required to screen a particular geographical area or a section of the population for lung cancer can be very unique.

## 1.1 CURRENT PRESCRIBED LUNG CANCER SCREENING PRACTICES

Lung cancer is categorized into different types based on the morphological appearance of the cancerous cells observed under a light microscope. All lung cancer cases are categorized into two types: non-small cell carcinoma (85% of cancer cases) and small cell carcinoma (14% of cancer cases). Surgical resection is the primary treatment for stage I and II non-small cell carcinoma. By contrast, localized-stage small cell lung cancer is treated with concurrent chemo-radiotherapy [3]. Early detection of cancer is key in the ability of a screening candidate to survive and cope with side effects from surgical treatment. This is why screening in high risk population is the recommended course of action for better population health.

The available methods of screening are chest radiograph, sputum cytology and computed tomography. Research studies have conducted several randomized controlled trials to establish the best screening method. The National Lung Cancer Screening Trial (NLST) was a large-scale trial of over 50000 candidates who participated in randomized control trials comparing the effectiveness of low dose computed tomography (LDCT) versus chest radiographs (CXR) in lung cancer detection and treatment [4]. This trial was able to establish with statistical significance that LDCT is better for early detection and treatment of cancer. Subsequently, governing guideline organizations for treatment of cancer have all recommended the use of LDCT for lung cancer screening.

The LDCT scanner is a rotating emitter of X-Rays that collects image points from different parts of the chest at different angles and reconstructs them into an image of the chest. There are several factors associated with radiation and quality of LDCT images [5]. It is estimated that with continued annual screening in a US birth cohort of age 55-80, for every 100,000 adults screened, there would be 24 radiation induced lung cancer deaths [6]. Thus additional imaging must be avoided in patients as far as possible. There is also the factor associated with image quality. Lower radiation dose adds additional noise to the diagnostic image, leading to increased false nodule detection or interpretation. This leads to additional invasive diagnostic procedures performed on the patient such as surgical/non-surgical biopsy and bronchoscopy, causing complications in an already susceptible patient.

Each aspect of lung cancer screening has a governing association that prescribes relevant guidelines for selecting patients for the screening process. Prescribed guidelines represent factors that indicate risk for cancer. These guidelines generally include an age requirement and smoking history requirement. Table 1-1 is a list of these guideline institutions.

Table 1-1 Prescribed Guidelines for Lung Cancer Screening

| Organization | Groups Eligible for Screening | Year |
|---|---|---|
| American Academy of Family Practice | Evidence is insufficient to recommend for or against screening | 2013 |
| American Association for Thoracic Surgery | 1. Age 55 to 79 years with ≥ 30 pack year smoking history.<br>2. Long-term lung cancer survivors who have completed 4 years of surveillance without recurrence and who can tolerate lung cancer treatment following screening to detect second primary lung cancer until the age of 79.<br>3. Age 50 to 79 years with a 20 pack year smoking history and additional comorbidity that produces a cumulative risk of developing lung cancer ≥ 5% in 5 years. | 2012 |
| American Cancer Society | Age 55 to 74 years with ≥ 30 pack year smoking history, who either currently smoke or have quit within the past 15 years, and who are in relatively good health | 2015 |
| American College of Chest Physicians | Age 55 to 74 years with ≥ 30 pack year smoking history, who either currently smoke or have quit within the past 15 years. | 2013 |
| American College of Chest Physicians and American Society of Clinical Oncology | Age 55 to 74 years with ≥ 30 pack year smoking history, who either currently smoke or have quit within the past 15 years. | 2012 |
| American Lung Association | Age 55 to 74 years with ≥ 30 pack year smoking history and no history of lung cancer. | 2012 |
| Centers for Medicare and Medicaid services | Age 55 to 77 years with ≥ 30 pack year smoking history and smoking cessation < 15 years. | 2015 |
| National Comprehensive Cancer Network | 1. Age 55 to74 years with ≥ 30 pack year smoking history and smoking cessation < 15 years.<br>2. Age ≥ 50 years and ≥ 20 pack year smoking history and 1 additional risk factor (other than secondhand smoke exposure). | 2015 |
| US Preventive Services Task Forces | Age 55 to 80 years with ≥ 30 pack year smoking history and smoking cessation < 15 years. | 2013 |

The US Preventive Services Task Forces (USPSTF) guidelines elucidate that annual screening for lung cancer with low dose computed tomography must be conducted in adults aged 55-80 and having a 30 pack year history of smoking, who are either current smokers or quit within the past 15 years [6]. The guidelines explicitly state that the screening must be discontinued after 15 years of quitting smoking or there are other comorbid conditions that prevent a candidate from having curative lung surgery. There is a clear age and smoking bracket in these criteria. However, the National Comprehensive Cancer Network (NCCN) issued guidelines for lung cancer screening recommend that screening can be performed in adults aged 50 or higher who have evidence of a risk factor other than smoking (family history, radon or asbestos exposure) [7]. This leaves room for qualitative interpretation and could lead to a higher of number of patients not satisfying eligibility criteria to be screened with LDCT.

Through NLST results and subsequent research studies, there were several economic cost and procedural implications made available to the lung cancer screening community. A key learning point was that for a program performed at that scale, a large number of patients must be screened to provide a life-saving benefit for a small number of patients. For instance, in NLST, 320 patients had to be screened for every life saved [4]. Another important learning point among these, was the variation found in false positives across the several screening centers that participated in the NLST. It was observed that the variation in false positive rates across different screening centers or across different radiologists in the same screening center was very high [8]. This has led to increased focus on quality standardization in lung cancer screening similar to the Mammography Quality Standards Act that came into place after the observation of variation in false positive rates in breast cancer screening [9]. There have been several other cohort trials and

randomized control trials that studied the effectiveness of LDCT and recorded similar results on the variation in false positives [10].

## 1.2 Quality Gaps and Improvement

Assuring quality in a lung cancer screening process involves ensuring standards in several aspects of the process. The American Association for Chest Physicians and American Thoracic Society Policy Statement discusses 9 essential components of a high-quality screening program [11].

1. Who is offered lung cancer screening
2. How often, and for how long to screen
3. How the CT Scan is performed
4. Lung nodule identification
5. Structured Reporting
6. Lung Nodule management algorithms
7. Smoking cessation
8. Patient and provider education
9. Data collection

Typical outcomes of interest in lung cancer screening activities are the number of people screened, the false positives in screening, false positives in diagnosis, the number of CT scans and invasive procedures undergone by each candidate, the number of early detections, the number of documented cancer cases and the utilization of smoking cessation resources [12]. Gaps in quality primarily occur due to inherent population difference factors, organizational management factors and the LDCT scanning process. The following sections are about these factors.

## 1.3 PRIMARY AND SECONDARY RISK FACTORS AND THEIR PREVALENCE

As the screening criteria suggest, certain sections of the population are more susceptible to lung cancer than others. The incidence and death rates of lung cancer within United States vary by race, ethnicity and geography [13]. Among men, the incidence and death rates are highest among blacks as compared to other racial and ethnic groups. But among women these rates are more similar across groups. Geographically lung cancer is more prevalent in the South and least prevalent in the West [2]. These differences are associated with multiple socio economic causes that led to their tobacco use and/or other secondary exposures that led to lung cancer. These add to the availability of healthcare across different sections of the society and result in higher mortality rates and lower screening rates in selected communities.

There are several factors that are responsible for causing lung cancer. The primary factor is cigarette smoking. In the years 2005-2009, 84% of the annual male deaths from lung cancer and 76% of annual female deaths in lung cancer were attributed to cigarette smoking [14]. The most effective preventive measures are to never start smoking or to stop cigarette smoking as soon as possible. The risk for developing lung cancer is 20 times greater for smokers than for non-smokers. Second hand smoke is the primary cause for lung cancers in children [14]. It increases background risk for non-smokers by 20 – 30%. There are several other substances that increase the risk of lung cancer such as radon exposure and asbestos exposure [5]. Thus it is evident that screening the right segment of the population that are at high risk for lung cancer is an extremely important determinant for quality in a lung cancer screening process.

There has been considerable debate as to whether a rule-based age and smoking criteria is sufficient to screen patients for lung cancer. Lung cancer risk assessment models are a recent addition to the screening process literature [15]. Depending on accuracy, these risk estimation

models may be used in the future in the screening process. However, currently, the prescribed guidelines for screening and for nodule management are rule-based criteria as discussed earlier. These criteria may also contribute to increase in misclassification, false positives and more importantly, missed early detection of cancer in a susceptible candidate not satisfying the screening criteria.

## 1.4 LDCT PROCESS, IMAGE INTERPRETATION VARIABILITY, RADIATION INDUCED HARMS

The entire process of scanning, imaging and interpretation are very key to the screening process and can cause substantial variability in the process. The LDCT scanning process is the process of acquiring scans by applying the right tube current on the equipment and positioning the candidate appropriately on the table to get raw data from the CT machine [5]. This raw data is further processed using image reconstruction algorithms to obtain different 2D sections on the chest. Depending on the clarity of the image obtained and noise level, the radiologist may present variations in both detection and measurement. A peer review committee helps reach a consensus in cases with anomalies in the LDCT scanning process [16]. Consistent quality of LDCT images is critical to identifying abnormalities and tracking changes in suspicious findings over time, while avoiding excessive exposure to radiation. The scanning and image interpretation processes directly affect the false positive rate. Higher false positive rate indicates that more candidates undergo additional diagnostic testing and are subject to invasive procedures that may create further complications when they are not at risk for lung cancer [10].

## 1.5 HEALTHCARE PROCESS VARIATION: PARTICIPATION, FOLLOW UP, PRIMARY CARE

Though the LDCT scanning process is the heart of the lung cancer screening process, initiation and follow up of screening involve many organizational processes which create opportunities for candidates to be lost in the system. Typical processes include the shared decision making (SDM) process with a primary care physician, followed by an order for screening which has to be followed up diligently by the care provider. There are also resources to be provided for smoking cessation to ensure population health. The utilization of these resources and the capability of the screening program to keep track of the utilization by the candidate plays an important role in ensuring quality in the screening process.

In the context of lung cancer screening with LDCT, even if the primary care provider only refers candidates to a structured program that offers lung cancer screening and follow-up management, the involvement of the primary care physician plays an important role in the risk perception of the candidate. Several examples of potential activities for the primary care provider include identification of patients eligible for lung cancer screening with LDCT, informed and shared decision-making discussions with patients before referral, promotion of smoking cessation, management of comorbid conditions that are not addressed by specialists, and eliminating barriers to timely care. Each of these steps represent aspects of quality in a lung cancer screening program.

## 1.6 GUIDELINE INSTITUTIONS AND PRESCRIPTION VARIANCE

Though most guidelines are the same across several institutions that prescribe guidelines for lung cancer screening, there could be some variance in the screening population selected, depending on the guideline used. Primarily this difference comes from some institutions that

prescribe screening in people with lower pack year history and age if there is evidence that there are secondary risk factors that increase the cumulative risk for developing lung cancer in the next 5 years to at least 5% [3]. These risk factors include secondary exposure factors such as radon exposure, asbestos exposure and family history of lung cancer. Depending on the nature of evidence that is accepted in the screening centers, there is considerable probability that a low risk candidate may be screened for lung cancer resulting in higher false positives. However, including secondary risk factors for screening are also likely to increase the early detection rates. In addition to the variance induced by including secondary risk factors, there are also age related screening differences across the institutions in that some institutions recommend 55-80 whereas others recommend 55-74 years old as the appropriate age for screening. The cause for concern here is that the Center for Medicare and Medicaid Services (CMS) will reimburse preventive screening costs only for the candidates who are in the age range of 55-74 [17]. This may result in older candidates not willing to participate in the screening process in lieu of expenses.

## 1.7 COMMUNITY BASED SCREENING PROGRAMS

Research for quality improvement in lung cancer screening centers is focused on analysis of studies like the NLST which are characteristically different from a standalone lung cancer screening center. 25 out of the 32 participating centers in NLST were large academic medical centers with competent staff unlike community screening centers which have limited staff especially surgeons [18]. These smaller screening centers are more likely to have lesser adherence rates and more variability in false positive rates from the scanning process [10]. They are also more constrained in terms of resources and need to effectively use their smaller number of resources to screen a specific portion of the population. But the benefit from these centers could be their strategic placement in demographically more susceptible population areas.

## 1.8 USING INDUSTRIAL ENGINEERING TOOLS

The objective of this research study is to use industrial and systems engineering tools to identify and improve factors that affect quality in community based lung cancer screening centers. Quality assurance in lung cancer screening has been discussed in literature from an organizational framework perspective and from a cost effectiveness perspective ( [19], [11]). Using tools from Industrial and Systems engineering for studying this problem helps to quantify the gaps in quality and their health consequences.

Quality Assurance in the lung cancer screening process presents itself as a system problem. Focus is required on aspects such as prioritization of activities, utilization of resources, identifying areas with gaps in quality (of process and care) and assessing their impact on the overall process. Systems Modeling consists of effective tools for the analysis of problems that are complex, hierarchical and multidisciplinary in nature. Functional modeling will help understand the lung cancer screening process to the level of detail required and the use of systems modeling and simulation will help quantify the impact of the various factors that affect quality in a screening program.

Developing a functional block diagram will help understand the various activities and interrelationships in the lung cancer screening process. The subsequent chapters discuss the development of a conceptual model and using the conceptual model for qualitative insights as well as developing a simulation model that can be used to explore the quantitative impact of several factors in the lung cancer screening process. This research study focuses on how to recognize important quality outcomes in lung cancer screening programs and the factors that affect these outcomes.

# Chapter 2. CONCEPTUAL MODEL DEVELOPMENT

Lung cancer is the leading cause of cancer related deaths in the United States. Through randomized trials, NLST (National Lung Cancer Screening Trial) established that Low Dose Computed Tomography (LDCT) scanning is a viable method for early detection and treatment of lung cancer. While LDCT promises to be a relatively non-invasive screening procedure for early detection of lung cancer, the variability in false positives across the screening centers (or across different radiologists in the same screening center) may be very high. There are also other institutional and population factors that lead to variation in several quality outcomes in a screening center. The objective of this chapter is to study the variation in these quality outcomes by developing a hierarchical conceptual model of a community-based lung cancer screening center. The conceptual model was built using the Structured Analysis and Design Technique (SADT). The hierarchical levels of the lung cancer screening process were informed by literature, prescribed standards and community-level implementations. The conceptual modeling process gives insights on the required resources to operate a community-based lung cancer screening center such as database management system service requirements and lung cancer screening (LCS) program coordinator responsibilities.

## 2.1 INTRODUCTION

Quality assurance is defined as all activities that contribute to defining, designing, assessing, monitoring and improving the quality of healthcare [20]. The problem of particular interest here is quality assurance in lung cancer screening. Systems modeling was chosen as the analysis tool for this problem. In this paper the focus is on systems thinking and soft operations research that aid in conceptualization of the system. The body of literature on systems thinking

and soft operations research refers to soft methodologies as operating without rigorous quantitative foundation [21]. However, these methodologies are more capable of enabling stakeholders to view their real problem in a systems perspective thus bringing them closer to the solution than they were earlier.

Conceptual modeling is one of the soft approaches to systems modeling and is the first step towards assessment of a system [20]. Conceptual modeling is defined as the process of abstracting a model from a real or proposed system [22]. Cancer screening centers are often an extension program in existing healthcare organizations. A typical screening center involves some cancer diagnosing aspects as well as healthcare organizational aspects. For developing a conceptual model of a lung cancer screening center, existing literature on healthcare conceptual modeling as well as cancer screening conceptual models can be studied. In general, conceptual models are developed in the context of a simulation analysis. However, in this chapter, the development of the conceptual model and its analysis will be discussed in terms of their qualitative contribution to understanding the lung cancer screening process.

The objective of the research study is to develop a conceptual model of a hypothetical lung cancer screening center consisting of all the activities relevant to ensuring quality in the screening process. This activity helps to develop a better understanding of all the processes that contribute towards the quality outcomes of a screening center and helps identify areas where gaps in quality may occur. Insights into various activities and components of lung cancer screening that are used to develop the conceptual model are derived from literature.

## 2.2 Literature Review

Since the objective of this research study is to gain a better understanding of the screening process, the best approach is to develop a model that can decompose a complex, ambiguous

problem with multiple hierarchies and stakeholders and help reach a consensus. Such a model need not be restricted by typical simulation model data availability or assumptions. It is however limited by the modeler's understanding of the system that is modeled. The next few sections focus on reviewing information available in literature to understand the real life situation in detail.

### 2.2.1 *Conceptual modeling in healthcare*

Conceptual modeling in healthcare has been used primarily in two applications. The first application is, as a conceptual framework in communicating complexities in a typical healthcare process or organizational aspect [23]. It is also used as a model description methodology before using a systems dynamics tool such as discrete event simulation to model a particular aspect of a healthcare system [24].

### 2.2.2 *Conceptual modeling in cancer screening*

In cancer screening, conceptual models have been used primarily to define and communicate a conceptual framework [23] and to provide theoretical details to a mathematical model of disease progression [25]. There is very little research on developing a consolidated conceptual model that represents disease progression as well as organizational aspects of screening centers. A screening center and its quality is an amalgamation of the organizational aspects as well as the disease progression aspects. Both these factors play an important role in determining screening center quality. In order to gain insight into some of the typical organizational activities conducted in lung cancer screening in particular, a literature review of some lung cancer screening program demonstrations was undertaken.

### 2.2.3 *Lung cancer screening studies*

There are several prescribed recommendations for lung cancer screening center operations that give considerable insight into the screening process. For example, the document by the Center for Medicare and Medicaid Services on the requirements candidates in order to receive reimbursement for preventive care for lung cancer [17]. This document establishes the need for the screening centers to provide several services to the candidate if they are to be eligible for reimbursement. Though there are some healthcare organizations that do not have the need to adhere to the requirements of CMS such as the Veterans Heath Administration, most of the commercially operating healthcare organizations need to follow this statement in order to draw more candidates for their screening programs and subsequently to their cancer treatment facilities. Some of the requirements included in the recommendation statement is the age criteria for screening (55-74), ACR accredited LDCT scanner and staff, a signed shared-decision-making document and a certified tobacco addiction specialist to offer cessation advice to every candidate. This helps solidify some essential components and activities in a lung cancer screening program. The International Early Lung Cancer Action Program (IELCAP) is a demonstration project that proposed organizational flow for lung cancer screening [26]. Though some aspects such as the shared decision making was not enforced, the course of action for a positive result in the LDCT scan was very clear. Some of the more recent results from the IELCAP study demonstrate the differences in the disease progression trends experienced in the baseline year versus the follow up years [27].

The Lung Cancer Screening Demonstration Project by the Veterans Health Administration (VHA) is the most recent demonstration project that implemented an organized lung cancer screening program following USPSTF guidelines for screening [16]. The VHA established a

document for implementing a program which include several aspects such as peer review for radiologists on anomalies in scanning with LDCT, shared decision making visits and the role of the LCS coordinator for the program. However, since the VHA is a large organization providing service to veterans all over the United States, they did not have to do an outreach to bring candidates for their screening program. They only had to search their database for candidates satisfying the age criteria and ask them to fill out their smoking information. VHA is a good representation of the effect of population segment differences in prevalence of lung cancer. The actual prevalence of nodules and lung cancer is higher than their estimates leading to higher workload than anticipated [16].

### 2.2.4 *Conceptual modeling framework*

Research on conceptual modeling discusses in considerable detail thought processes and methods for building models [28]. Over the years the procedure for conceptual modeling has progressed from its description as being art rather than science to a specified set of steps that describe the process of developing a conceptual model to encompassing software requirements engineering methodologies to specify a system using a conceptual model. Lakhoua and Khanchel (2011), discuss three methodologies for systems modeling particularly in healthcare: structured analysis and design technique (SADT), objective oriented project planning (OOPP) and graph with results and actions interrelated (GRAI).

SADT is an activity oriented modeling approach. The representation of activities or functions in an SADT model is static in nature in that they do not show logical and time dependence between activities. However, SADT offers a simple methodology that can decompose any complex hierarchical system to the level desired. Since available literature on lung cancer screening was the best data that was available for the study and a certain amount of generalizability

was required for the conceptual model, SADT was chosen as the tool for the conceptual modeling framework.

### 2.2.5 *Structured Analysis and Design Technique*

Similar to the other conceptual modeling frameworks, SADT was developed in military planning and computer aided manufacturing [29]. This research follows the convention described in the research paper by Ahmed et al., (2014) for specifying the activities of lung cancer screening centers. Figure 2-1 represents the basic structure of an activity block in a conceptual model. The definitions consist of the following:

**Activity:** An activity is any function or process that transforms inputs into outputs. It is described as a verb phrase that signifies the activity that happens at this part of the model. For example, a process can be lung cancer screening but the activity must be named ‘screening for lung cancer’.

**Input:** The data/information required by an activity to start the transformation process. In this conceptual model, entities flow in and out of the activity boxes as inputs and outputs. Candidates, data and images are some examples of entities that flow through the model.

**Output:** The products that result from the activity. In the conceptual model the outputs are candidates, images, scans and other entities that are transformed to a different state from their inputs.

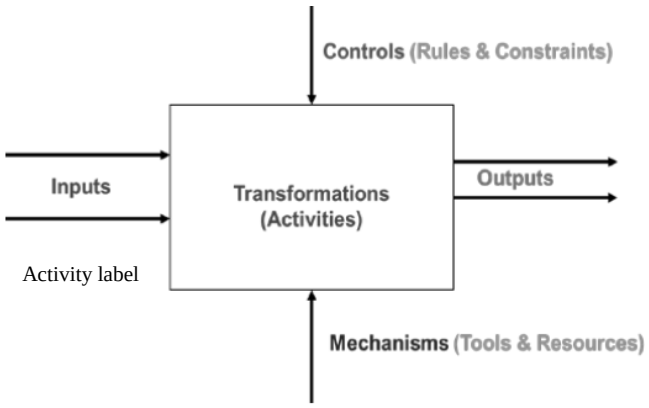


Figure 2-1 Structured Analysis and Design Technique Example Block Diagram

**Control:** Any constraint that affects the behavior of activity in some way including availability of time, guidelines, limitations on ability to organize/send out CTs for double-reading, etc.

**Mechanism:** Persons, resources, or any means that are required to run the activity.

**Hierarchical level:** A hierarchical level is associated with a sequence of events that explain a process at a particular degree of detail.

**Activity label:** An activity label is number that indicates the chronological sequence of the event and the hierarchical level to which it belongs.

SADT uses a "top-down" approach for the hierarchical modeling of functions. The process starts with specifying the highest simplified level of detail in the top-level diagram which is then decomposed into further details at each step until the required level of detail has been reached. SADT is useful for this research because it provides structure to the problem by defining the system components (entities, resources and controls) at high and low levels. This helps to identify individual interactions among these components along with any resource or constraint requirement. The low-level models may be created by modelers at different places and then integrated into a complete system description. The SADT approach has also serves as the basis for

future simulation models of the broader impact of quality assurance on overall costs and cost-effectiveness of lung cancer screening programs.

## 2.3 FUNDAMENTAL ELEMENTS OF A LUNG CANCER SCREENING PROGRAM

This section elucidates the important elements that contribute to the design and development of the conceptual model for lung cancer screening. These elements were identified from the 9 essential components of a quality screening program as prescribed by Mazzone, et al. (2015). The choice on how to model these elements were inferences from the VHA demonstration project [16] , other small-scale lung cancer screening implementations [30] and the decisions made in those implementations.

### 2.3.1 *Outreach for candidates*

Depending on the type of healthcare organization with which the screening program is affiliated, different methods of outreach may be employed to reach out to candidates to participate in the screening program. Typically, a screening center associated with a large welfare network such as the VHA has a database of candidates with contact details to whom they can reach out directly to participate in the screening process [16]. Other screening programs that are a part of new or small private initiative have to undertake marketing initiatives to reach out to prospective candidates in a geographical area of interest [30]. In addition to these outreach methods, a considerable portion of screening requests are placed directly by Primary Care Providers from affiliated Primary Care Networks based on any incidental lung problems that occurred in these candidates [31].

### 2.3.2 *Screening criteria*

Organizational policy on lung cancer screening establishes what guideline the screening center will follow for selecting candidates for the low dose computed tomography (LDCT) scan. The USPSTF guideline allows screening centers to accept candidates aged 55-80 who are current smokers with a smoking history of 30 pack years or more and candidates with the same smoking history who quit within the last 15 years [6]. For the conceptual model, it has been assumed that the screening center follows the USPSTF guidelines and allows a portion of their candidate intake to come from primary care providers. This portion of candidates do not satisfy the screening criteria.

### 2.3.3 *Shared Decision Making*

An essential component of quality in screening centers is the choice of tools and method to be used for patient education on the risks and benefits of undergoing lung cancer screening. Two frameworks that enable patient education are informed decision making and shared decision making [5]. Informed decision making is two-way communication between the primary care provider and the candidate, where the primary purpose of the communication is to ensure that the candidate receives the information that is relevant to the healthcare decision to be made and recording the final decision of the candidate. Shared decision making (SDM) is a collaborative process that allows candidates and their providers to make high-quality decisions that align with the candidate's preferences [17]. SDM meetings typically involve more reading and awareness from the candidate in order to ensure that the right decision is made. This conceptual model assumes the use of the shared decision making process. The assessment of higher risk or harm is made at the end of the process. In the model after the SDM meeting, there are two ways by which

a candidate can exit the process. The candidate can choose to discontinue from the screening program due to discomfort with the primary care provider or unavailability of the provider. The candidate can choose to continue but the assessment after the SDM meeting by the provider and care giver may conclude that the candidate is low risk and the same will be communicated to the candidate.

### 2.3.4 *Smoking Cessation*

The lung cancer risk for non-smokers is 20 times lower than that of smokers [14]. The smokers who wish to quit have to be provided with medical interventions and behavioral counselling to assist them in their efforts. In the conceptual model, the candidates' smoking preference is gathered at different points of time in the screening process and for those who are willing to quit, resources for cessation are supplied and their utilization status is gathered.

### 2.3.5 *Lost candidates*

Candidates are lost from the screening process at different points due to organizational glitches, unavailability and their decision to discontinue [32]. In the conceptual model, these points of exit are consolidated in the coordinating care sub-process where in a candidate exits the screening process due to a reason that is not associated with the screening center's risk assessment such as availability, discomfort with the provider or lack of insurance coverage.

### 2.3.6 *Outcomes*

There are several outcomes of a lung cancer screening process: number of candidates screened, number of CT scans recorded, number of candidates undergoing diagnostic procedures and number of intake candidates who were low risk. Out of these outcomes, those of that are

chosen as an indicator of quality in this study are false positives, early detections, documented cancers and quit rates for smokers in the screening process.

## 2.4 MODEL OVERVIEW

The conceptual model is developed from the perspective of the care provider who offers the lung cancer screening service to the population. By developing the model from this perspective, it is possible to model the quality gaps that occur due to organizational processes and the LDCT scanning process. The 5 sub-processes of lung cancer screening are shown in Figure 2-2. Deriving knowledge from demonstration projects such as IELCAP, VHA, cohort studies and randomized trials mentioned by Bach, et al. (2012) and McKee, et al. (2013), the process of screening for lung cancer can be divided into 5 sub-processes:

### 2.4.1 *Connect with participant*

The objective of this activity is to reach out to candidates for screening and choose the means for accomplishing this activity. Different types of screening centers may choose to reach out to candidates within their healthcare network, in their geographical vicinity or just through Primary Care Provider orders ( [16], [30], [31]). The model displays methods to intake candidates through all three means and the corresponding resources required to accomplish these outreach tasks.

### 2.4.2 *Complete Prescreening*

The objective of this activity is to assess the smoking history and screening preparedness of the candidates and appropriately classify them as eligible, low risk or ineligible candidates. Prescreening activity is dependent on primary care providers to accomplish this task [30].

Therefore, the first step in this activity is to associate or assign a candidate with a primary care provider. Then, using the provider as a resource, the smoking history assessment and screening preparedness assessment are carried out.

### 2.4.3 *Perform LDCT Scan*

The objective of this activity is to scan a selected candidate or a follow up or annual candidate with LDCT and to assess the scanned image. This step is the heart of the screening process and consists of the Low Dose CT scanning process, after which, the scanned image is read by a radiologist to detect the presence of a nodule and determine its length. Then the image based on the nodule features is classified into a type based on the nodule management system [33]. Based on the sensitivity and specificity of each of these processes, the candidate maybe falsely classified as a suspected candidate or a prospective cancer patient may be missed.

### 2.4.4 *Perform additional tests*

The objective of this activity is to further diagnose an abnormal LDCT scan result and to determine the next medical action to be taken on a candidate. This step includes several follow up diagnostic procedures in case of a suspicious nodule characteristic. Some of the medical procedures covered here are the PET scan, biopsy and bronchoscopy [27]. Some candidates exit this step as an annual candidate and return back to get scanned with LDCT next year.

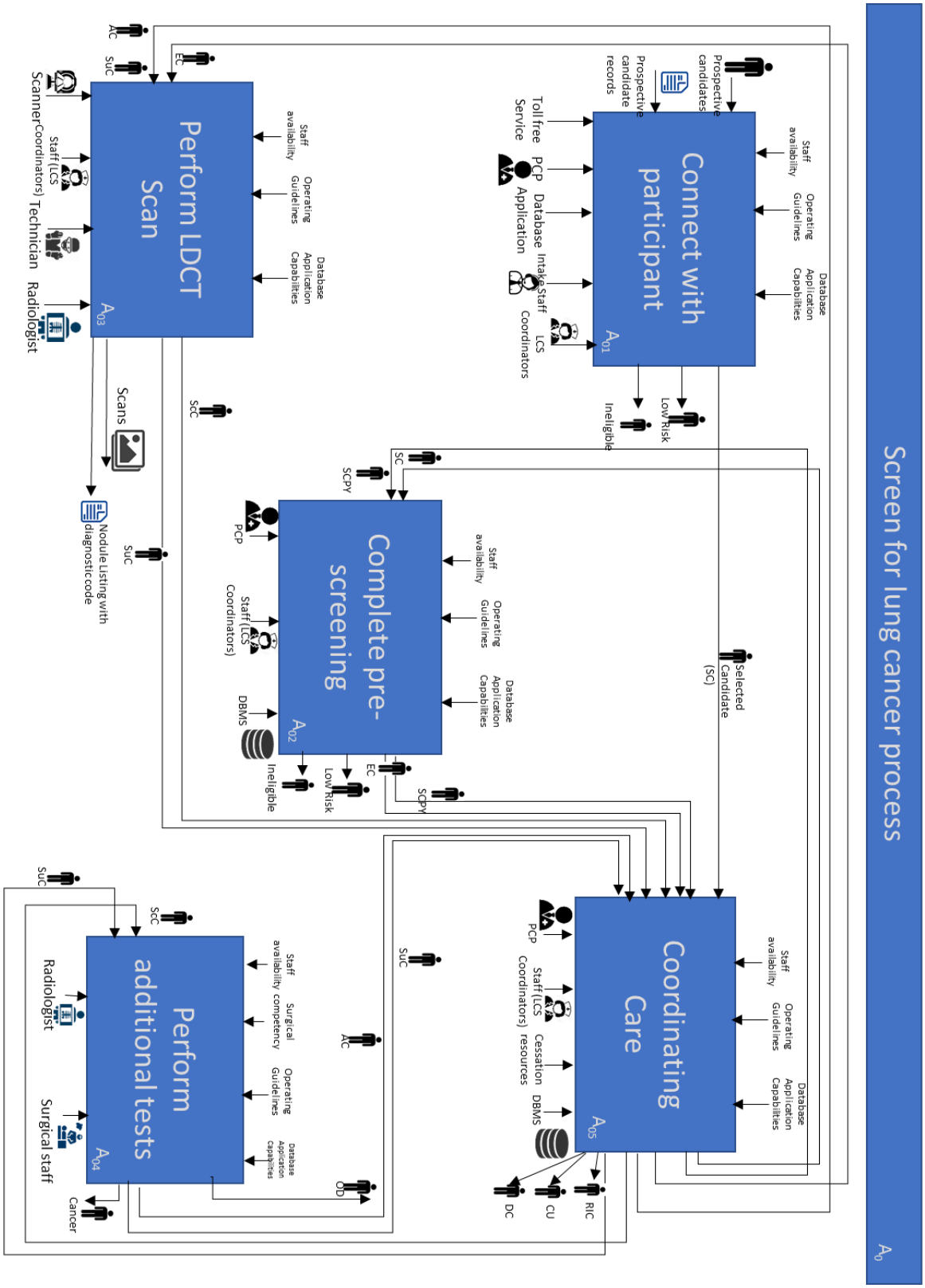


Figure 2-2 Overview of the lung cancer screening sub-processes in SADT

### 2.4.5 *Coordinating care*

The objective of this activity is to ensure the smooth transition of candidates from one activity to another. This activity also serves to track the candidates' meetings with their providers and their smoking cessation status. There are organizational coordination activities that happen at the end of every step such as sending out appointment reminders, filling out forms, shared decision making and tracking smoking cessation status. These activities are grouped under the coordinating care block. At the end of every other sub-process all candidates are routed to this sub-process where each step presents a chance for the candidate to be lost to organizational hiccups and procedures.

## 2.5 INFERENCES

The developed SADT conceptual model of a lung cancer screening process can be used to infer important insights on achieving quality by identifying the potential barriers in the process. The barriers to quality are generally processes that may lend to defects in the system and resources or constraints that can restrict the performance of the system. This section elaborates some of these barriers and their effect on the quality of lung cancer screening.

### 2.5.1 *Perceived pack year history*

The sensitivity of nodule detection and the procedure for managing nodules have been a point of in depth research in several papers (Pinsky et al., (2013) and Pinsky, et al., (2015)). The nodule detection sensitivity value is related to a type of misclassification where candidates who do may not have nodules may undergo further diagnostic procedures. Along similar lines, when smoking history is wrongly assessed, the intake of low risk candidates into the screening process is also a form of misclassification.

The information on smoking history is gathered by calculating the number of pack years for an individual. Pack years are calculated by multiplying the number of years smoked multiplied the packs of cigarette smoked in a day. Since this number is calculated retrospectively it is dependent upon the recall capabilities of the individual. Bernaards et al., (2001) found that 'bias' in perception is proportional to the actual smoking history, that is, the higher the smoking history, the higher the recall bias. Recall bias is a systemic error caused by differences in the accuracy of the recollections recalled by study participants regarding events or experiences from the past. There are very few studies performing the assessment of this recall bias in smoking history since these are expensive and time consuming [34]. However, the smoking history assessment is a very pivotal point in the screening process. Understating the pack year history may cause a viable cancer case to be missed. For example, a candidate is considered a low-risk candidate due to his perception of lower pack years smoked. If this person has cancer, a false-negative is created and affects the early detection rate.

At the other end of the spectrum overstating the smoking value may cause a low risk individual to undergo several invasive procedures. For example, a low risk candidate may undergo an LDCT scan, depending on the sensitivity of the LDCT process an abnormality may be detected. This results in unnecessary radiation exposure, invasive procedures. This creates a false positive in the process. Figure 2-3 represents a state transition diagram of how two misclassified candidates can go through different states causing reduced quality of life.

### 2.5.2 *LCS coordinator*

The role of a program coordinator is a required resource for many activities in the lung cancer screening process. Table 2-1 lists the activities in the entire model which require an LCS coordinator as a resource followed by the required skills to accomplish that task.

As evidenced by Table 2-1, it can be seen that the LCS coordinator is a very important position, one on whom several organizational procedures rest. 11 out of 13 activities in lung cancer screening model require a program coordinator for implementation. The extent of smoking cessation enforcement depends on the level of resources and time available to the program coordinator. The number of candidates who are lost to follow up can be reduced by the coordinator. The extent of follow up possible by the coordinator is determined by their availability. Based on empirical estimations of the number of candidates that will be accepted into the screening program, an estimation of the number and extent of the time for which the program coordinators must be hired can be estimated.

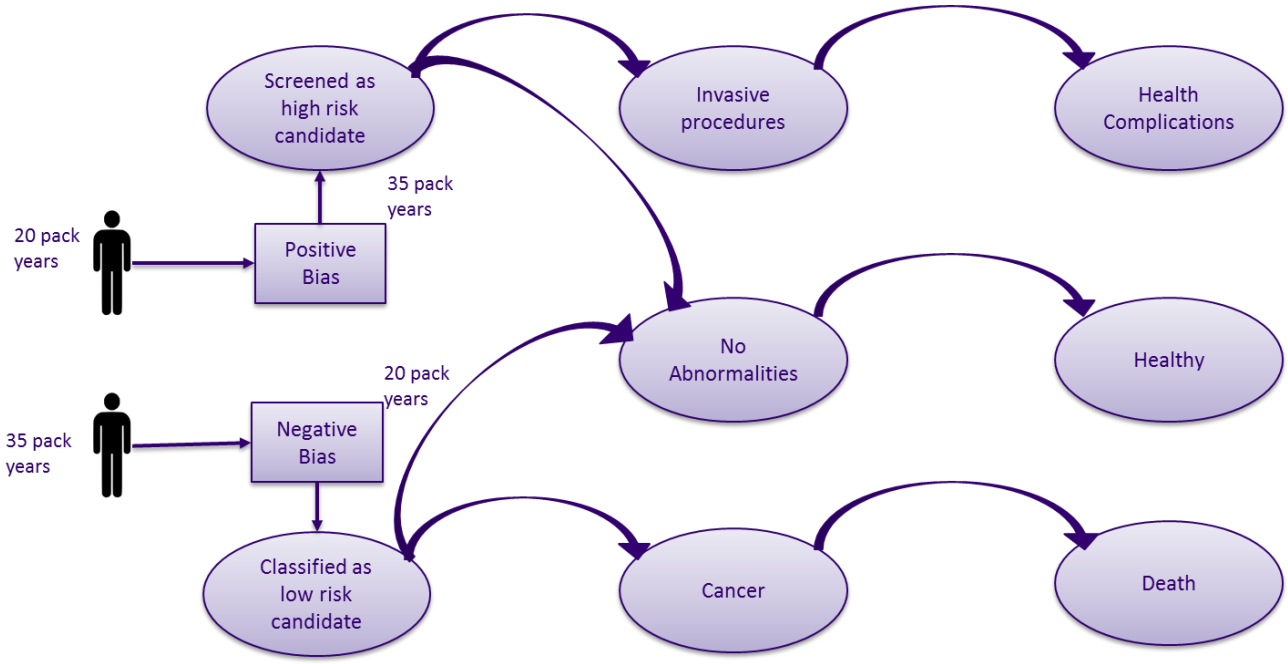


Figure 2-3 State transition diagram for candidates with recall bias.

Table 2-1. Lung cancer screening coordinator responsibilities and skills

| **Activity** | **LCS Actions** | **Coordinator Skill** |
|---|---|---|
| Search Internal Candidates | Retrieve records from the database | Database application knowledge |
| Process External Contact | Planning and implementing the marketing intervention, add new records | Database application knowledge, |
| Get Orders from PCP | Receive orders from PCP network | Communication skills, Database application |
| Assess Initial eligibility | Search database so that initial USPSTF screening criteria are met | Knowledge of the screening exclusion criteria |
| Associate PCP | Contact candidates and PCPs, enter any associations in the database | Communication skills, Database application |
| Assess Smoking History | Follow up on candidates to get their smoking history | Follow up and assessment skills |
| Assess LCS Preparedness | Follow up on candidates and primary care providers to get LCS assessment | Follow up and assessment skills |
| Classify patient from Image | Get candidate scans and interpretations from radiologists and use nodule management system to classify the nodules, issue result letter to candidate | Knowledge of LUNGRADS, DBMS, written communication skills |
| Determine Nodule Severity | Get the nodule details for the candidate and make appointment for the next step in the diagnostic process | Organization and scheduling capabilities, Oncological knowledge about lung cancer nodules and their severity |
| Determine Nodule Growth | Retrieve records on nodule length from the database, compare with current nodule length, calculate the growth rate and determine the next step in the diagnostic process | Know about probability of malignancy based on nodule growth rate, organizing and scheduling capabilities |
| Perform Diagnostic Function | Follow up with surgical staff and issue result letters to candidates | Follow up skills and written communication skills |
| Document Cancer | Issue result letters to candidates and refer candidates to treatment centers | Follow up skills and written communication skills |

| Activity | LCS Actions | Coordinator Skill |
|---|---|---|
| Track Reminder Status | Follow up with candidates to complete their reminders | Persuasion skills |
| Schedule Appointment | Follow up with candidates to schedule their appointment | Persuasion skills |
| Initiate and ensure shared decision making | Follow up with PCP, and complete SDM if PCP was unavailable | Lung Cancer Risk Assessment, Ability to hold a SDM session |
| Initiate and ensure smoking cessation | Track smoking status and ensure cessation resources are available | Tobacco addiction counselling, Knowledge on smoking cessation counselling |

### 2.5.3 *Database management system service*

A database management system service provides a good foundation on which several screening tasks can be accomplished seamlessly. An enterprise database management system must meet some special needs with respect to lung cancer screening. Database Management System requirements can be assessed from the conceptual model. Similar to analyzing program coordinator role, all the activities that are constrained by the quality of the database management system are listed in Table 2-2. Table 2-2 also lists the aspect of database management systems that are required to accomplish that task.

Specifics on the type of database management systems to keep can be made by a trade-off analysis made on the time required to accomplish a task by using that particular system as opposed to the cost for that service.

Table 2-2. Database management system characteristics

| Activity | DBMS Service Feature |
|---|---|
| Search Internal Candidates | Retrieve existing medical records and parse for age |
| Process External Contact | Create new records for every external candidate |
| Get Orders from PCP | Merge incoming records by parsing into the data |
| Assess Initial eligibility | Simple querying capabilities on the data in the records |

| **Activity** | **DBMS Service Feature** |
|---|---|
| Associate PCP | Management of multiple databases, querying across databases |
| Assess Smoking History | Enter new fields into candidate records |
| Assess LCS Preparedness | Enter new fields into candidate records (SDM visit, document candidate decision) |
| Classify patient from Image | Integrate Nodule management system into the database, storing image files and other files (result letters) along with each record |
| Determine Nodule Severity | Retrieve and query fields from records |
| Determine Nodule Growth | Calculation and mathematical capabilities |
| Perform Diagnostic Function | Enter new fields into candidate records |
| Document Cancer | Enter new fields into candidate records |
| Track Reminder Status | Integration with email services (optional to integrate with automated telephone service) to send reminders automatically to candidates |
| Schedule Appointment | Integration with calendar services and merge calendars from multiple databases |
| Initiate and ensure smoking cessation | Enter new fields and edit existing records with new status |

## 2.6 CONCLUSION

This chapter focused on identifying some aspects of lung cancer screening that are critical to ensuring quality. The conceptual model developed in this paper using Structured Analysis and Design Technique (SADT), is used to gain these structural insights. The key insights from the modeling process were that the perception bias of smoking history represents a pivotal point in the screening process from where candidates who do not satisfy screening criteria enter the process and undergo several invasive procedures. It is similar in nature to nodule detection sensitivity but occurs earlier in the screening process. This model can be used to analyze the job requirements for an LCS coordinator which involves conducting shared decision making meetings and tobacco

addiction counselling in addition to other follow up duties. A DBMS system used in lung cancer screening programs consists ways to add, edit and integrate electronic medical records, along with the capabilities to send automated calendar reminders for the next appointment and store result letters and scanned images along with the medical records. This conceptual model can also be used to develop a simulation model which can then be used to quantify the impact of these factors in quality outcomes.

# Chapter 3. SYSTEM DESCRIPTION

The objective of this chapter is to provide a detailed description of the lung cancer screening process conceptual model developed in the previous chapter. Engaging in the process of model description helps smoothing the transition from the conceptual model to developing a simulation model. It also serves as documentation in detail for the developed conceptual model. This documentation activity is accomplished by describing every activity followed by the block diagram of the activity represented in the SADT format. In the first and second levels of hierarchy, the focus is on expanding the organizational aspects that help us gain qualitative insights into the conceptual model and the lung cancer screening system. In the next two levels of hierarchy the focus is on the mathematical aspects, in terms of the prevalence assumptions and the transition probabilities. This facilitates a quicker transition from the conceptual model to the simulation model. The next few paragraphs expand each block of the hierarchical conceptual model.

## 3.1 SCREEN FOR LUNG CANCER ($A_0$)

This is the highest block of the SADT conceptual model, the represents the overall screening process as a black box, with all its inputs, outputs, resources and controls included. The activity is represented in Figure 3-1.

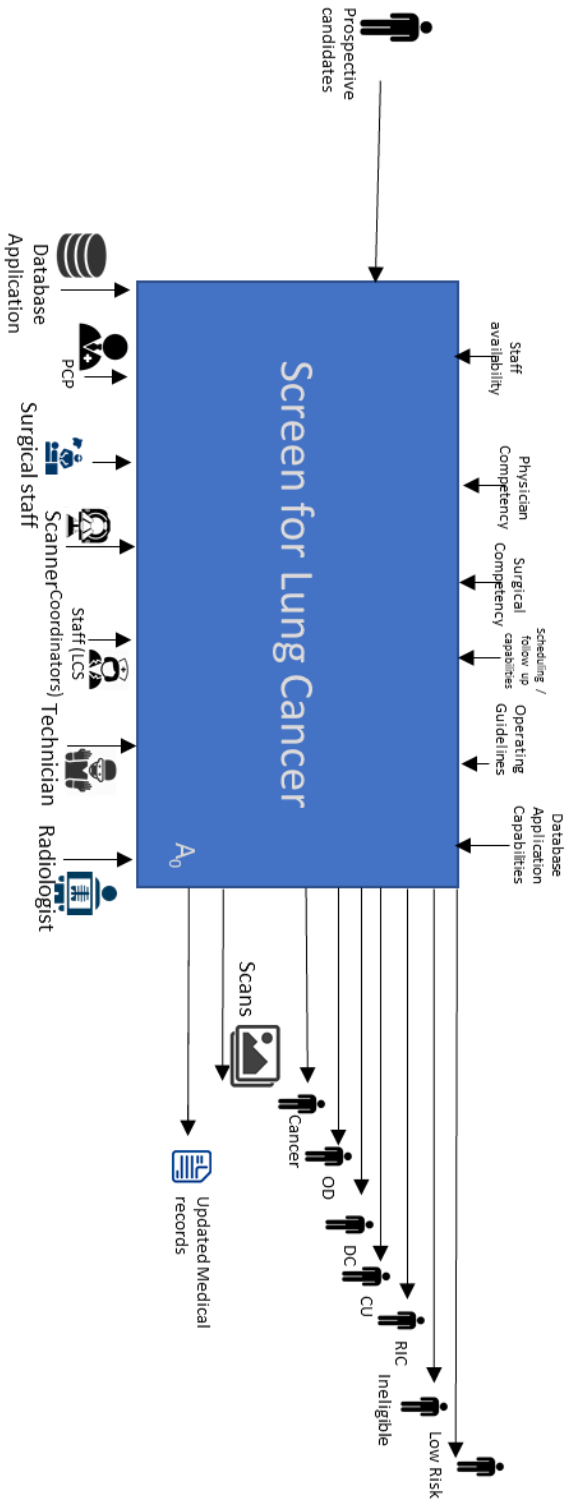


Figure 3-1. The highest hierarchical representation of a lung cancer screening process

Each of the output arrows represent candidates who exit the screening process at different points of time due to different reasons such as low risk candidates, ineligible candidates, reminder incomplete (RIC), candidate unavailable (CU), discontinued candidate (DC), over diagnosed candidate (OD) and cancer candidate. The main process can be divided into 5 sub-processes as shown in Figure 3-2.

### 3.1.1 *Connect with participant ($A_{01}$)*

As explained earlier, different types of screening centers may choose to reach out to candidates within their healthcare network, in their geographical vicinity or just through Primary Care Provider orders. The conceptual model displays methods to intake candidates through all three means and the corresponding resources required to accomplish these outreach tasks.

Internal candidates are part of a healthcare network that a screening center belongs to. These candidates are already filtered by age. This step involves just issuing the internal candidates with a birthday reminder letter for screening.

External candidates contact the screening program as a result of one of their marketing interventions such as advertisements and banners. They may belong to slightly lower age ranges than the internal candidates. A screening center requires more resources for the intake of these candidates such as a dedicated staff that receives their calls and medical information.

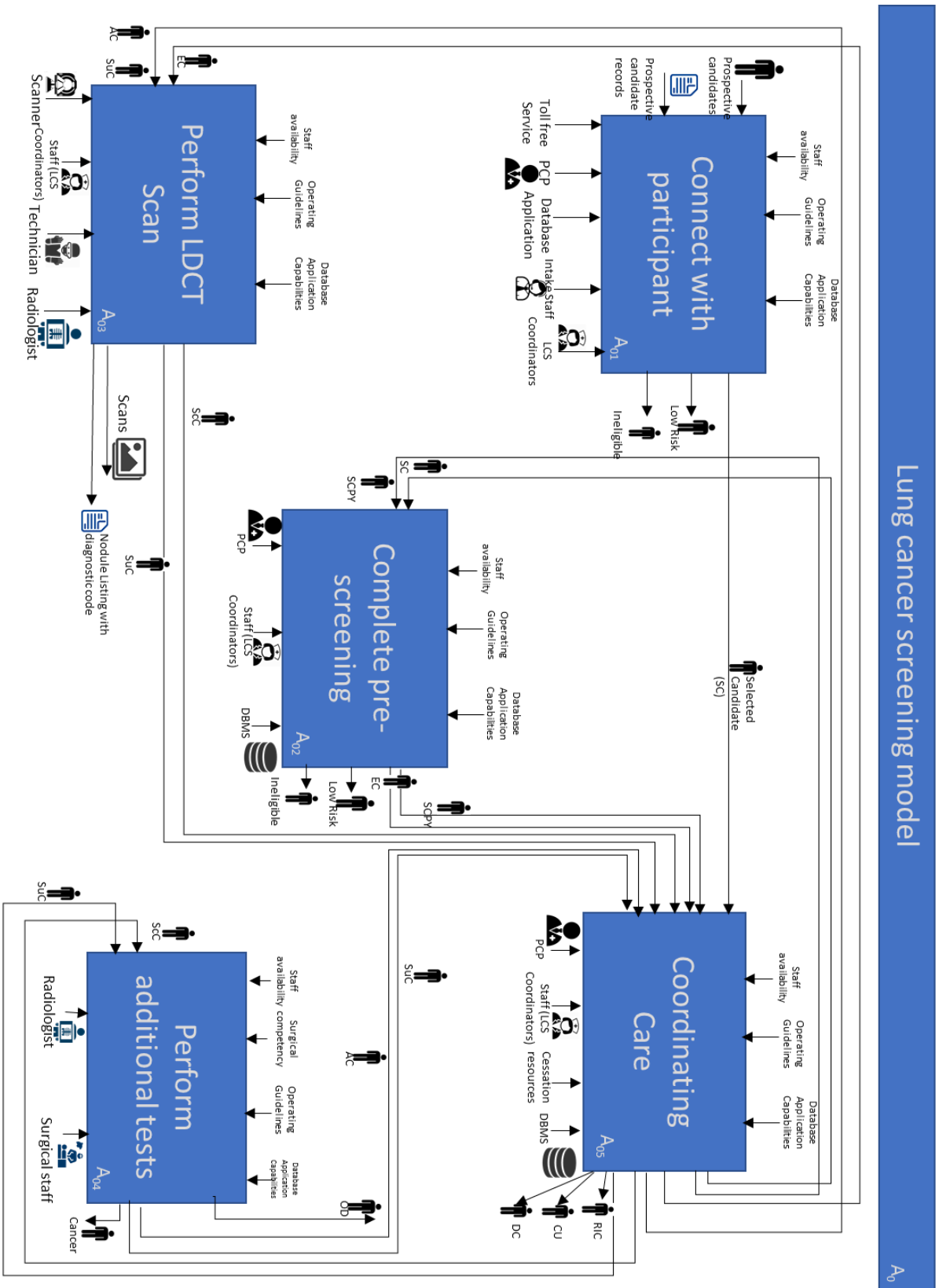


Figure 3-2 SADT expansion describing the 5 sub-processes in lung cancer screening

Primary Care Provider orders in a screening center represent candidates for whom a solitary pulmonary nodule was discovered incidentally when they were admitted for another medical condition. They may or may not satisfy the USPSTF screening criteria. However, for the purposes of the study, it is assumed that all these candidates do not satisfy the screening criteria in terms of age or smoking history. The portion of intake from this source indicates the extent of willingness of a healthcare organization to provide screening facilities for candidates who do not satisfy screening criteria.

### 3.1.2 *Complete Prescreening ($A_{02}$)*

Prescreening is the part of the screening process where the candidate's smoking history and screening eligibility is assessed. Depending on the values for each candidate, they are classified as low risk, ineligible and selected candidates. In this activity, a candidate is associated with a primary care provider either through their previous history of providers or by putting them in contact with the providers in an associated primary care network. Following that, the completed tobacco pack year reminder is received from the candidate. Here the care provider selects the candidates who satisfy the smoking history criteria as prescribed by the USPSTF. After the completion of this activity, the candidates are sent to the coordinating care to finish their shared decision making meeting and their smoking cessation sessions. They return to this activity block to complete their LCS assessment information and leave the activity block after completing the prescreening processes.

It is assumed that the recall bias in smoking history happens in the assessment of smoking history step. If the candidate completes the Shared Decision Making meeting at the end of this step the bias is reduced by half. Depending on the perceived value of the smoking history candidates are classified as low risk, if their pack year value is less than 30. A small portion of the candidates

are assumed to be ineligible for screening, considering that a small portion of the population is less capable of coping with surgery.

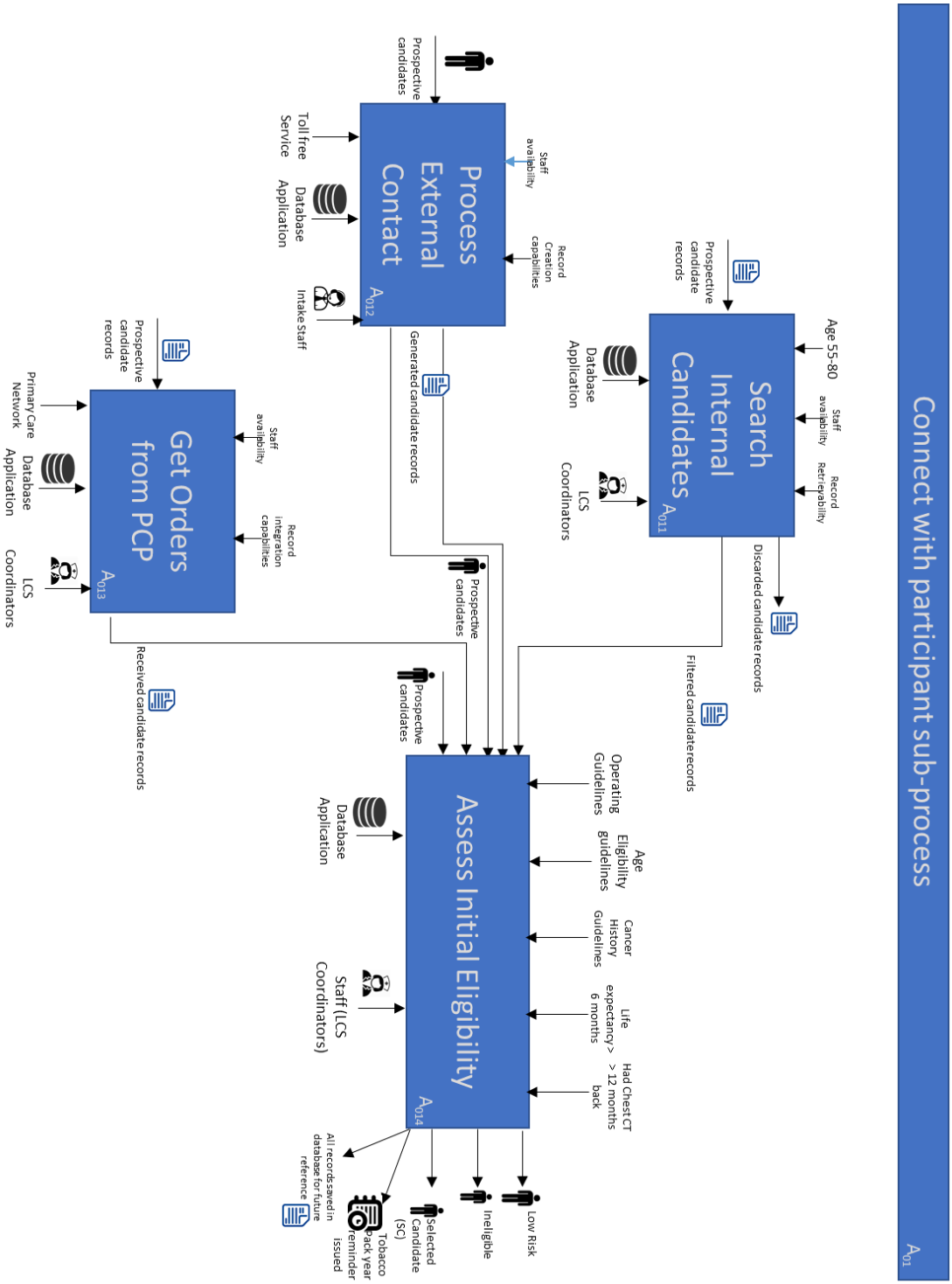

Figure 3-3 Activities within Each of the output arrows represent candidates who exit the screening process at different points of time due to different reasons such as low risk candidates, ineligible candidates, reminder incomplete (RIC), candidate unavailable (CU), discontinued candidate (DC), over diagnosed candidate (OD) and cancer candidate. The main process can be divided into 5 sub-processes as shown in Figure 3-2.

Connect with participant ($A_{01}$) sub-process

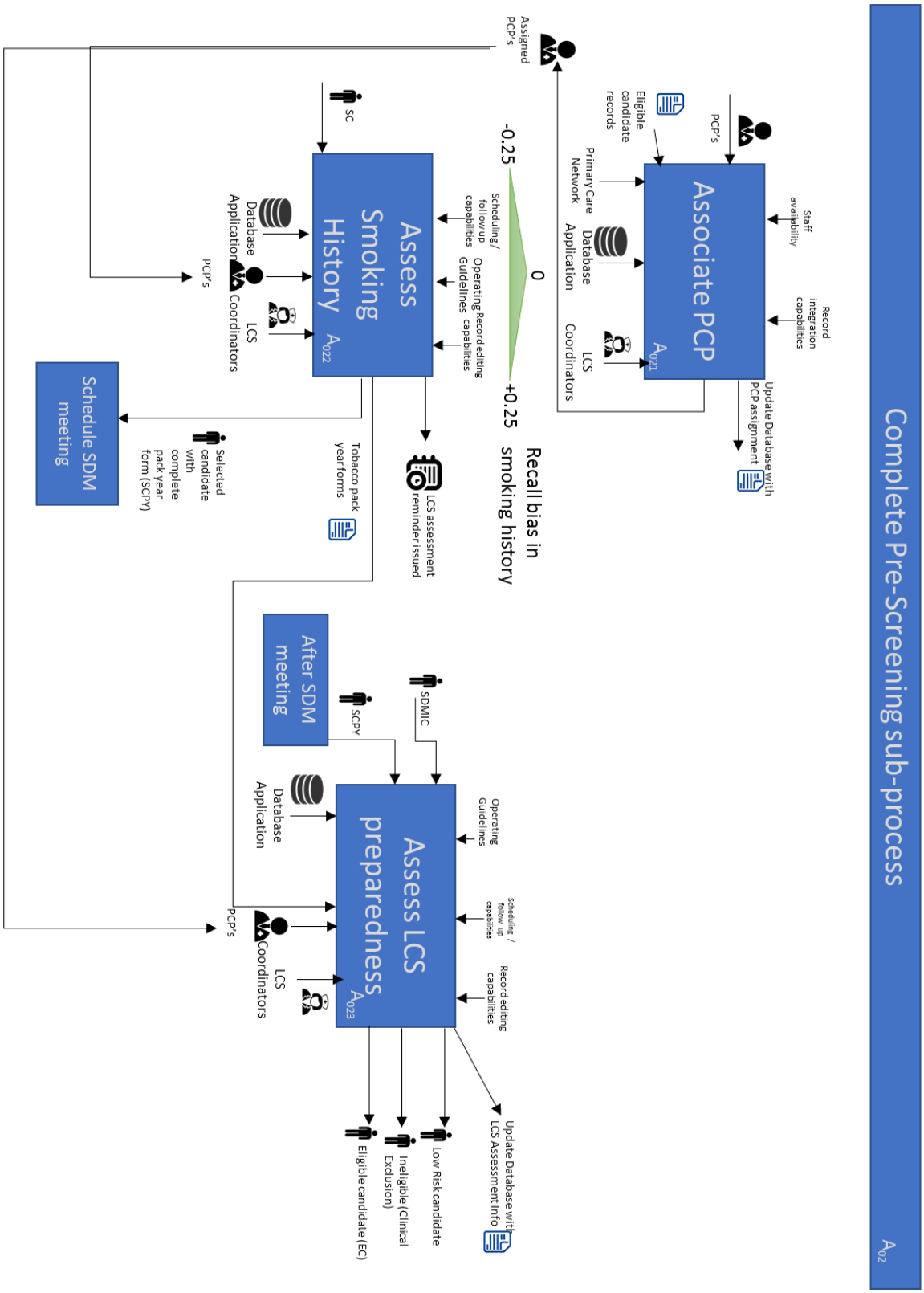


Figure 3-4 Activities within Complete Prescreening ($A_{02}$) sub-process

### 3.1.3 *Perform LDCT Scan ($A_{03}$)*

This step is arguably the heart of the screening process. It consists of Low Dose CT scanning process, where the selected candidate undergoes the scanning process and the scanned image is read by a radiologist to detect the presence of a nodule and its length. Then the image based on the nodule features is classified into a type based on the nodule management system. Based on the sensitivity and specificity of each of these processes, the candidate maybe falsely classified as a suspected candidate or a prospective cancer patient may be missed. Each of the three sub-processes are expanded hierarchically and their block diagrams are shown in Figure 3-6, Figure 3-7, and Figure 3-8.

Figure 3-5 shows the primary steps involved in performing the LDCT scanning process. Figure 3-6 expands the step of acquiring the LDCT scan. The primary rationale in this step is that the position of the candidate determines the noisiness in the image and the radiation exposure of a candidate. These two factors further determine quality outcomes of radiation induced harms and nodule sensitivity. However, in this model the nodule sensitivity is an assumption and not an inference from this process. Figure 3-7 elaborates the interpretation of an LDCT scan by radiologists. Presence of solitary pulmonary nodules by prevalence data and assumptions for sensitivity are made. Nodule detection sensitivity is analyzed as an input factor to assess its quantitative effect on the quality outcomes. Peer agreement happens on abnormal cases where the radiologist is unable to determine the length from the image. Since there is not enough data on the prevalence of such abnormalities, this step is ignored in the simulation study. Figure 3-8 elaborates the nodule management method. LUNGRADS is the method used here. LUNGRADS prescribes the course of further diagnosis for nodules of different lengths. Misclassification and

mismanagement of nodules may happen due to variability in length perception of nodules and by using a management system other than LUNGRADS.

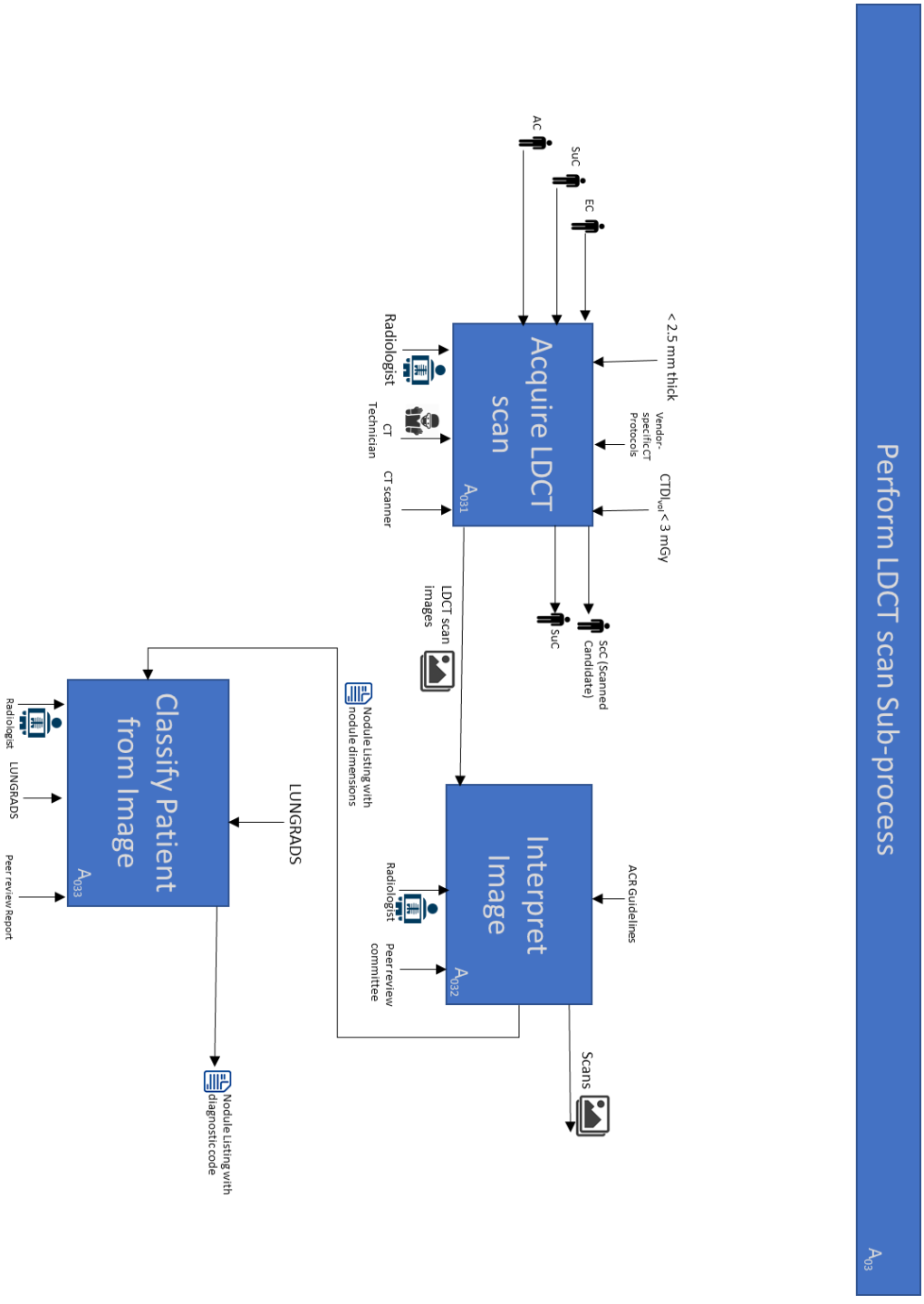


Figure 3-5 Activities within Perform LDCT Scan ($A_{03}$) sub-process.

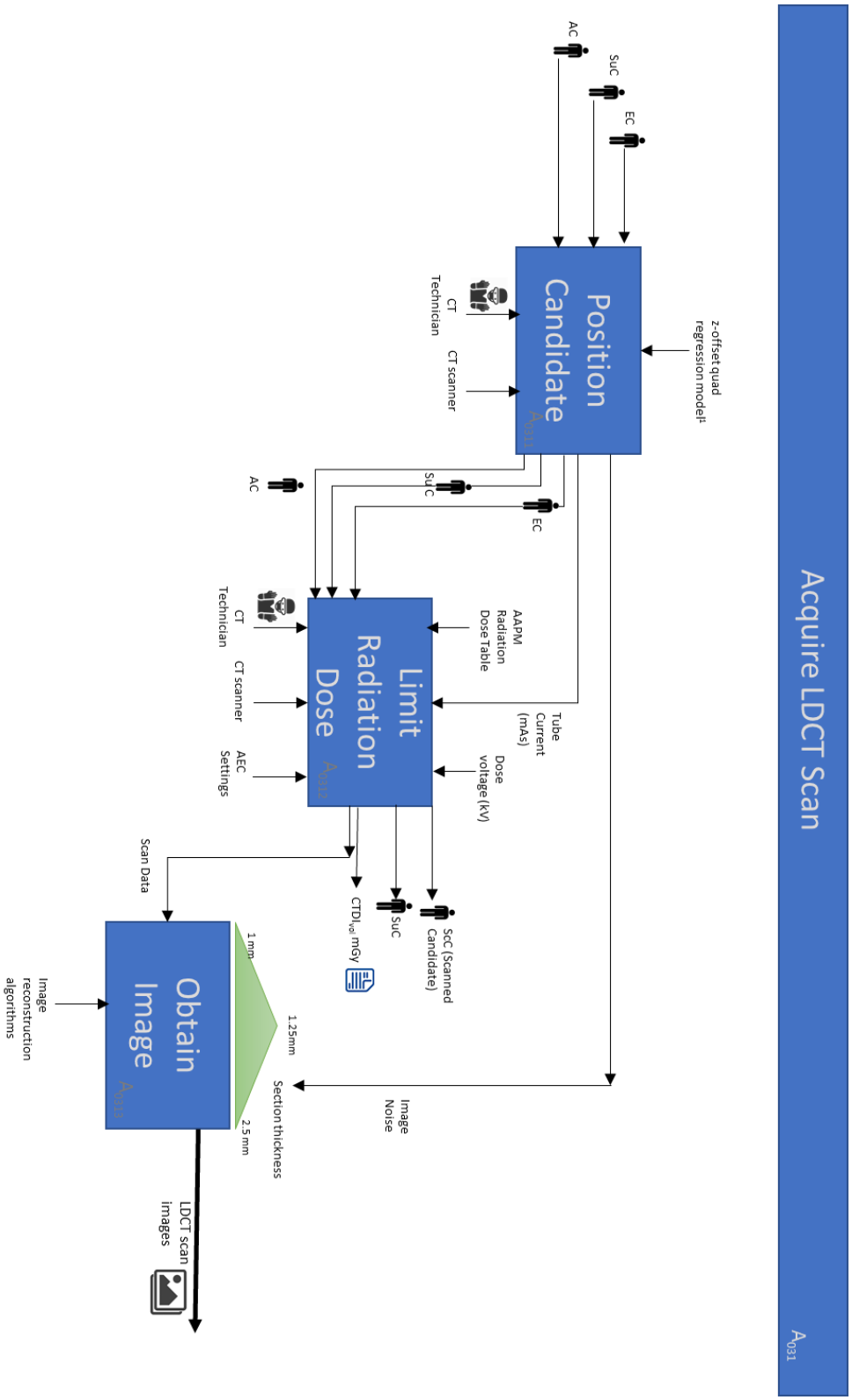


Figure 3-6 Hierarchical expansion of the Acquire LDCT scan activity.

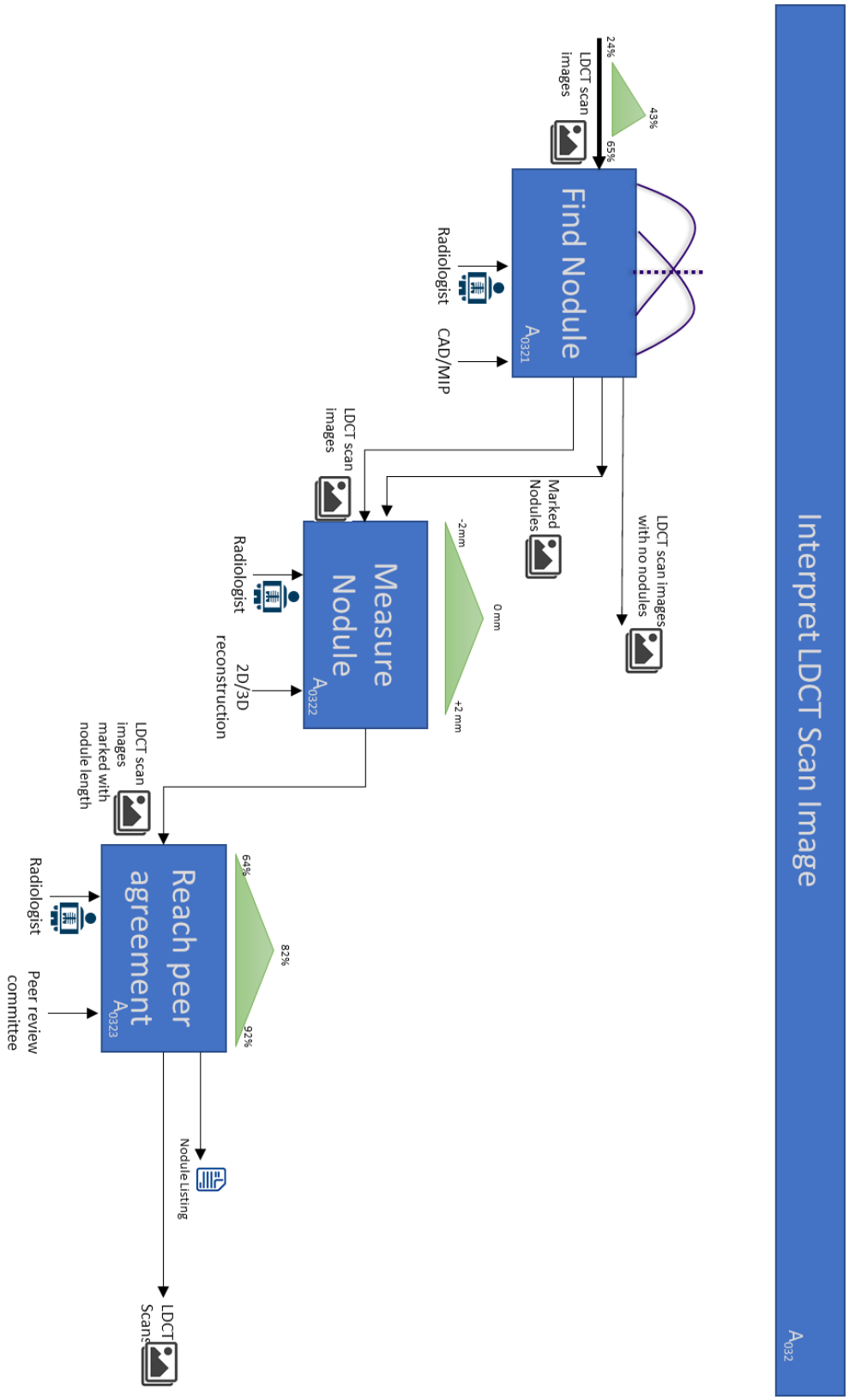


Figure 3-7 Hierarchical expansion of the Interpret LDCT Scan Image Activity.

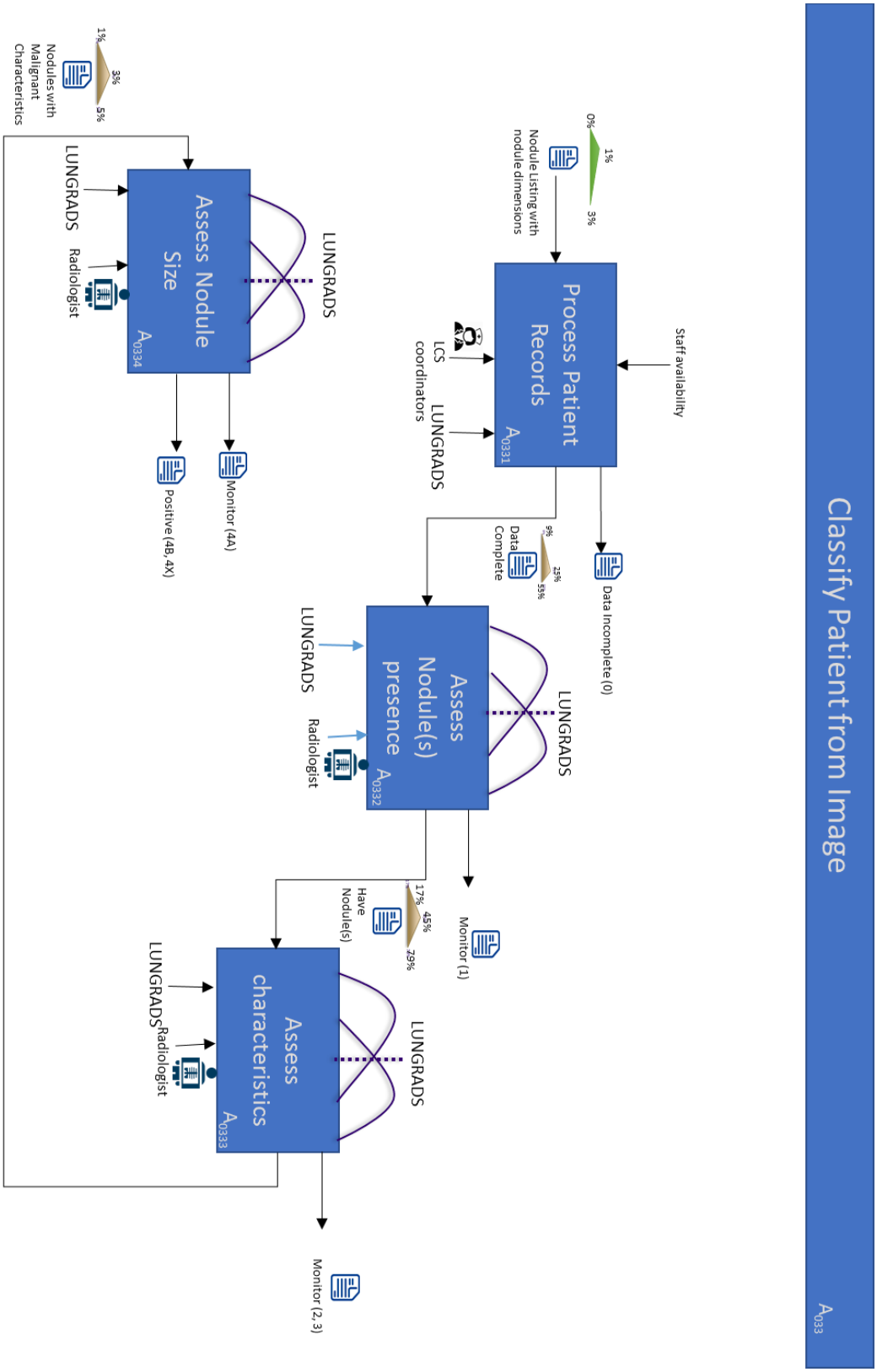


Figure 3-8 Hierarchical expansion of the Classify Patient from Image Activity.

### 3.1.4 *Perform additional tests ($A_{04}$)*

This step includes several follow up diagnostic procedures and management decisions in case of a suspicious nodule characteristic. Some candidates exit this step as an annual candidate and return back to get scanned with LDCT next year. The broad set of steps involved in this process are to determine the course of action by the assigned nodule management category, to determine the nodule growth rate from last year for an annual candidate, to determine the appropriate diagnostic course of action, document cancer candidates and determine the overdiagnosed candidates with the help of a pulmonologist.

Some of the diagnosis procedures covered within the Perform Diagnostic Function activity are the PET scan, biopsy and bronchoscopy. Black, et al. (2014) covers a comprehensive set of diagnostic activities and their cost. For the sake of simplicity, the flow of diagnostic activities is determined from the IELCAP document [27]. The document mentions the PET scan, biopsy and bronchoscopy as the procedures use to diagnose the nodules in addition to LDCT scans. The simulation model uses transition probabilities from the work by Bach, et al. (2012).

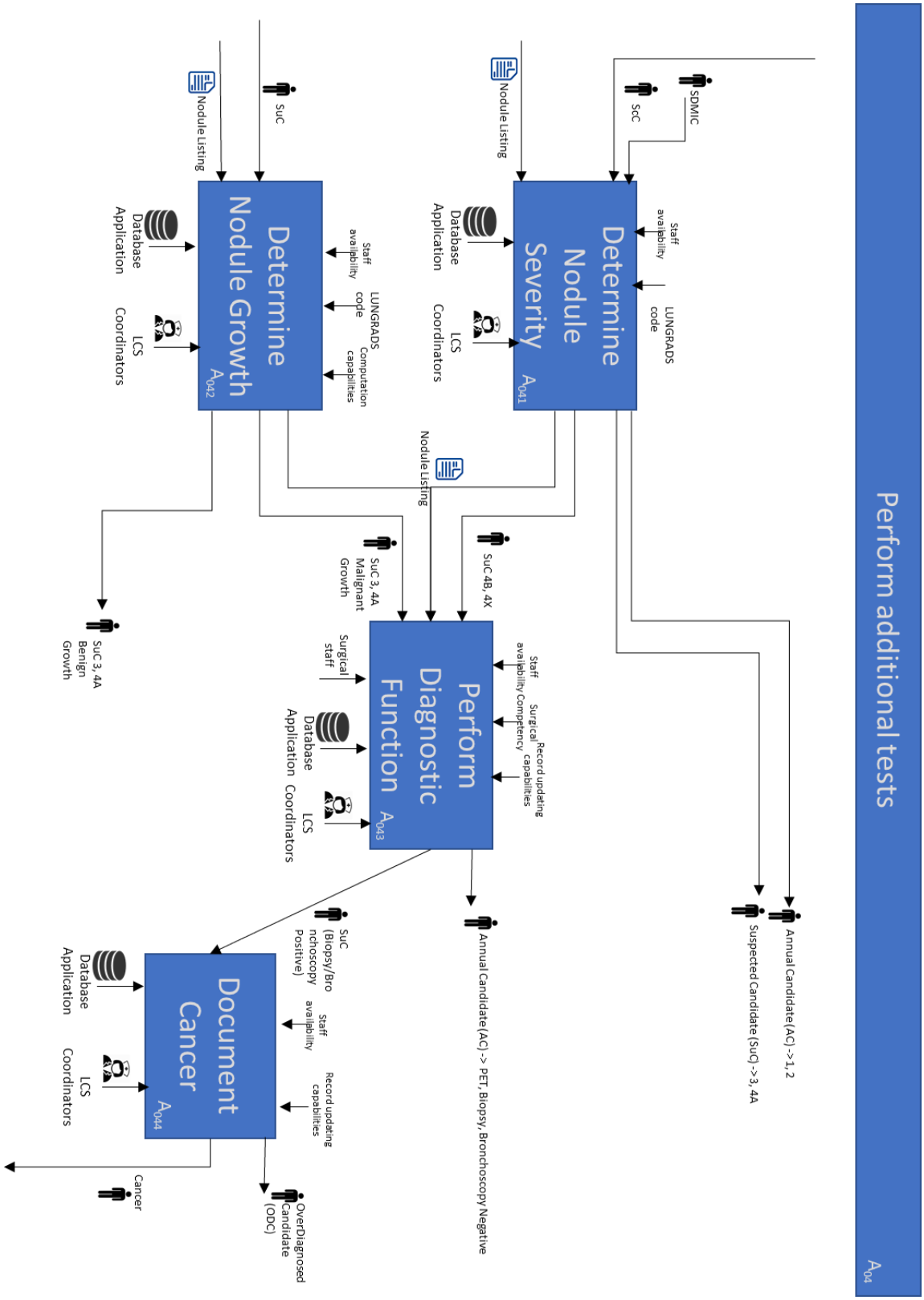


Figure 3-9 Activities within Perform additional tests sub-process

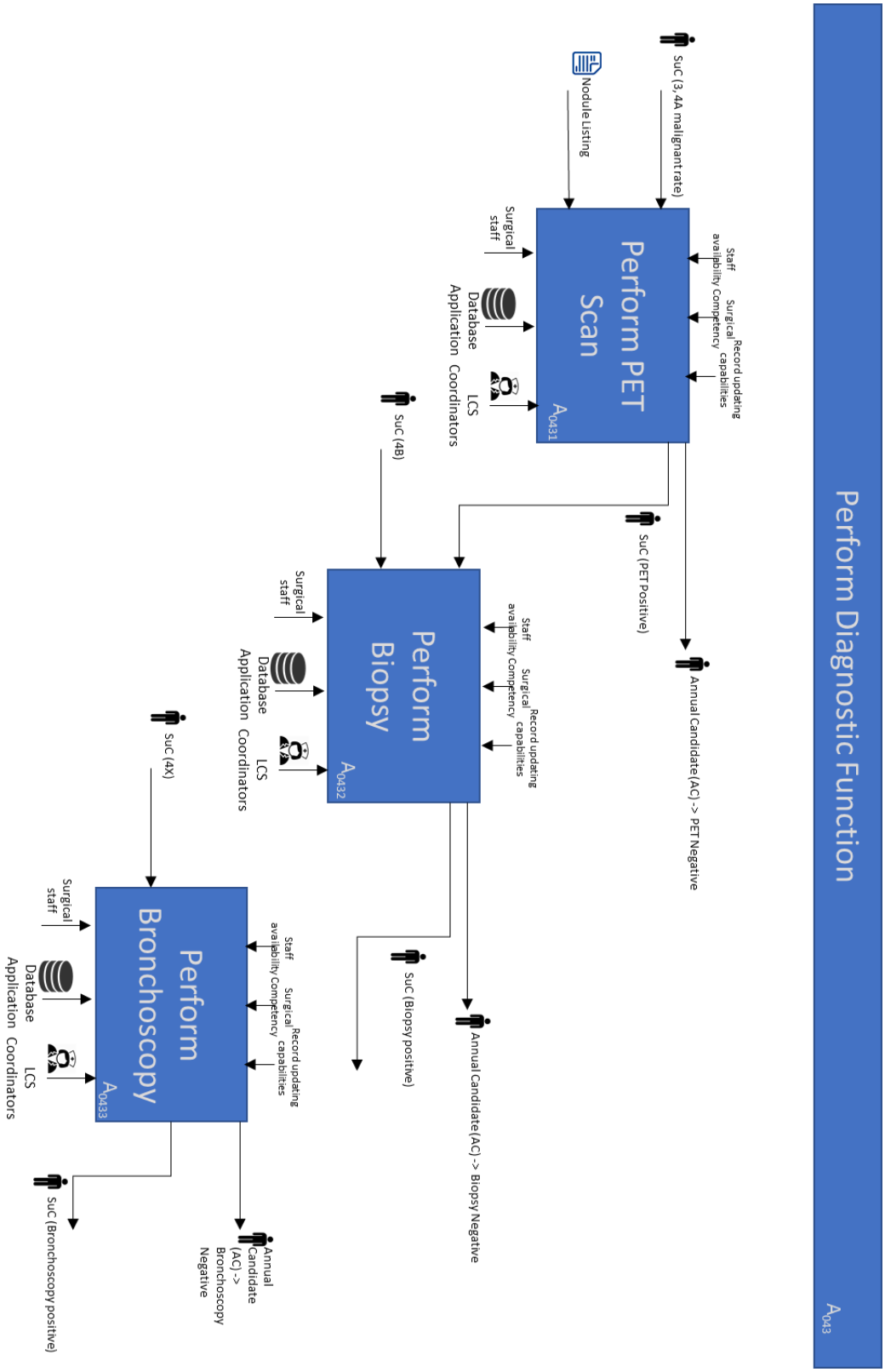


Figure 3-10 Hierarchical expansion of the Perform Diagnostic Function activity

### 3.1.5 *Coordinating care ($A_{05}$)*

There are certain organizational coordination activities that happen at the end of every step such as sending out appointment reminders, forms to fill out, shared decision making and tracking smoking cessation status. These activities are grouped under the coordinating care block. At the end of every other sub-process all candidates are routed to this sub-process where each step presents a chance for the candidate to be lost to organizational hiccups and procedures. Ensure shared decision making and smoking cessation steps have been expanded further in the next hierarchical level in Figure 3-12 and Figure 3-13 respectively. Reminders are a portion of the application for lung cancer screening that need to be filled such as pack years. Appointments are for meetings with either LCS coordinators or Primary Care Physicians. In addition to this, activities that happen often in the lung cancer screening process are SDM meetings and tracking smoking cessation. These are also included in the sub-process for modeling simplicity. Each one of the three activities of tracking reminders, scheduling appointments and holding shared decision making meetings, there are chances that a candidate may leave the system and be “lost to follow up” activities. Smoking cessation activities are accomplished by the LCS coordinator in three steps shown in Figure 3-13. The first step is to get the smoking preference of the candidate. If the preference has changed to a willingness to quit, then cessation resources are issued. In the next visit of the candidate to coordinating care, the status of resource utilization is gathered.

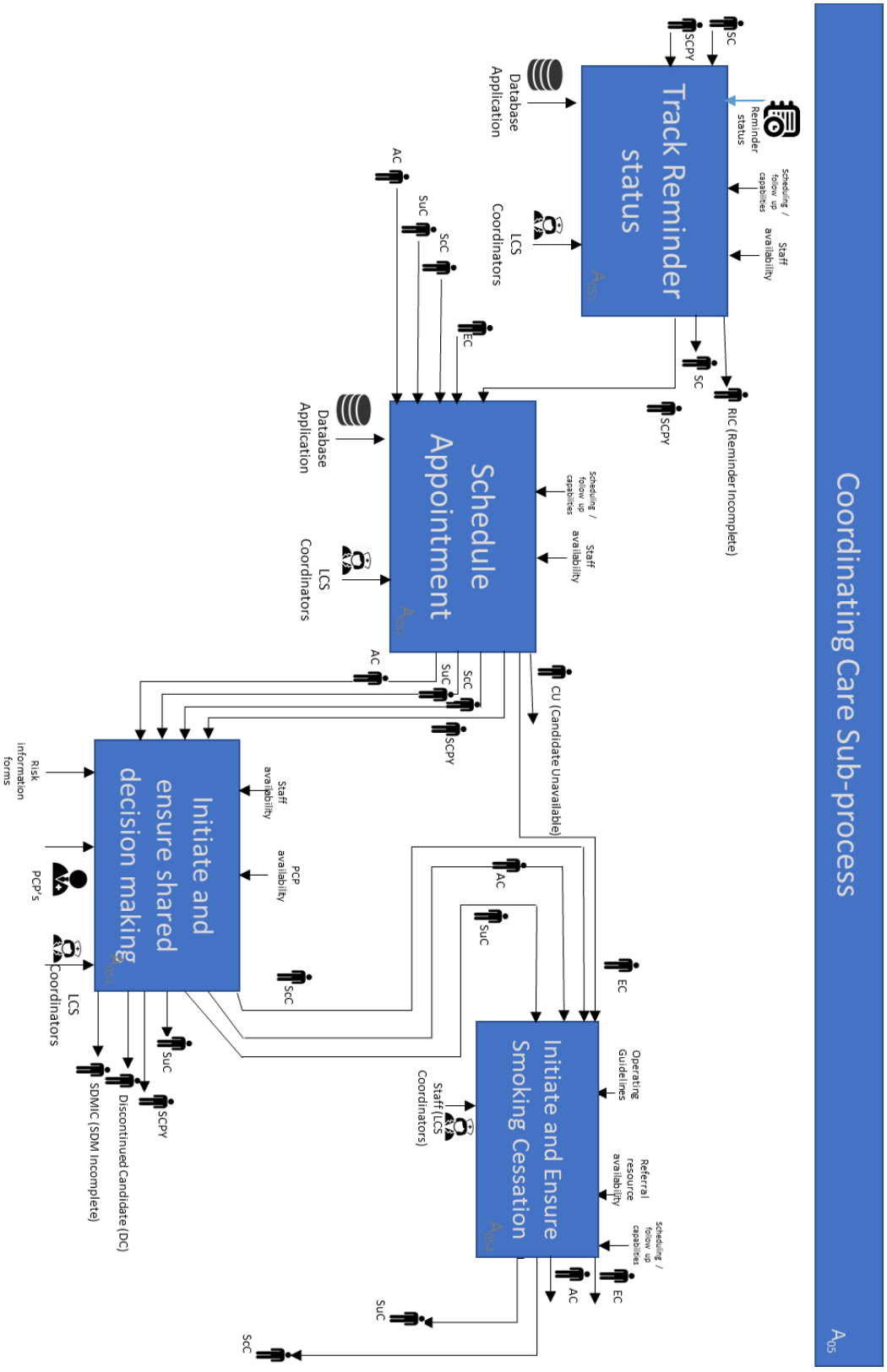


Figure 3-11 Activities within coordinating care sub-process

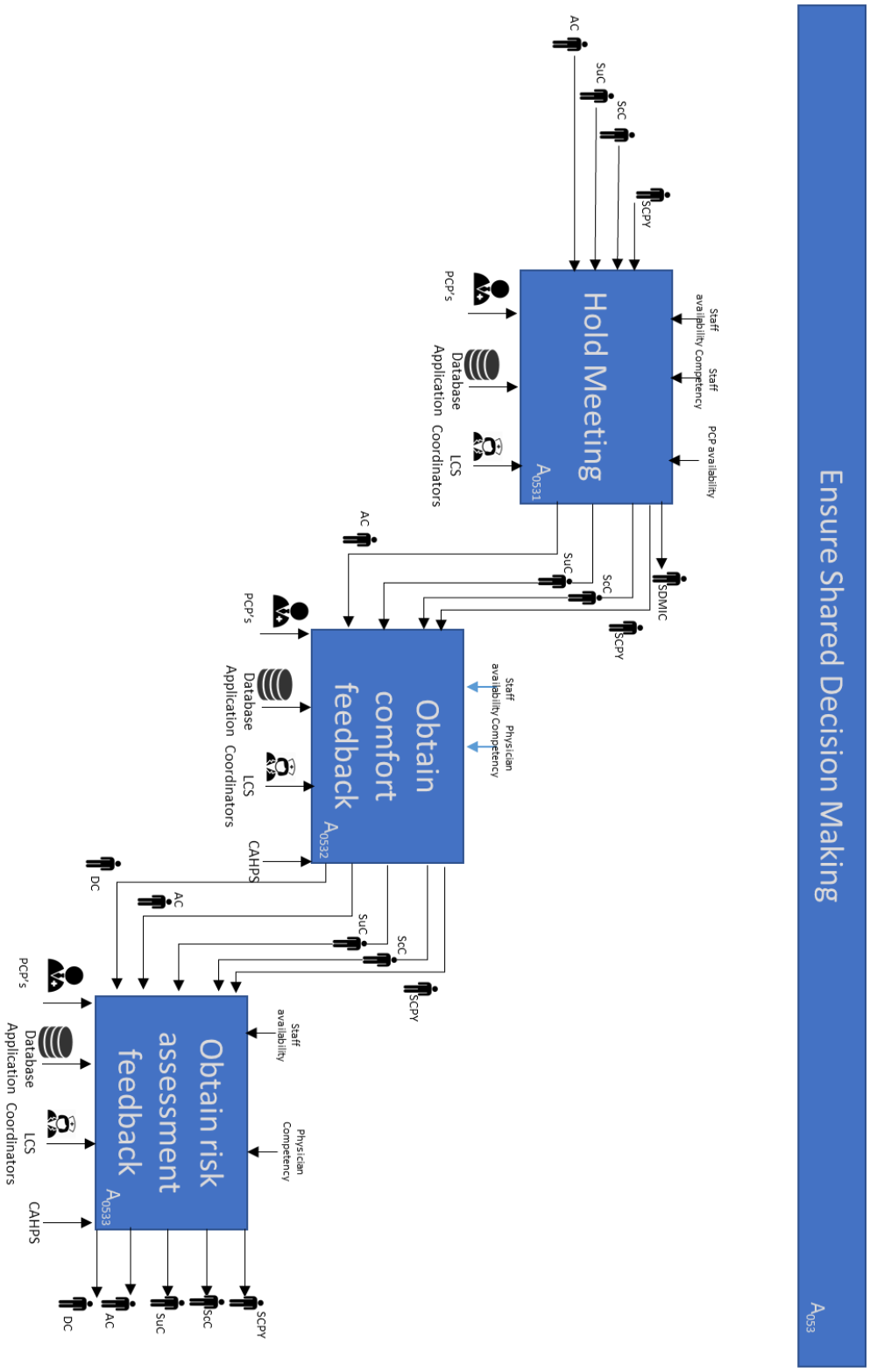


Figure 3-12 Hierarchical expansion of ensure shared decision making activity

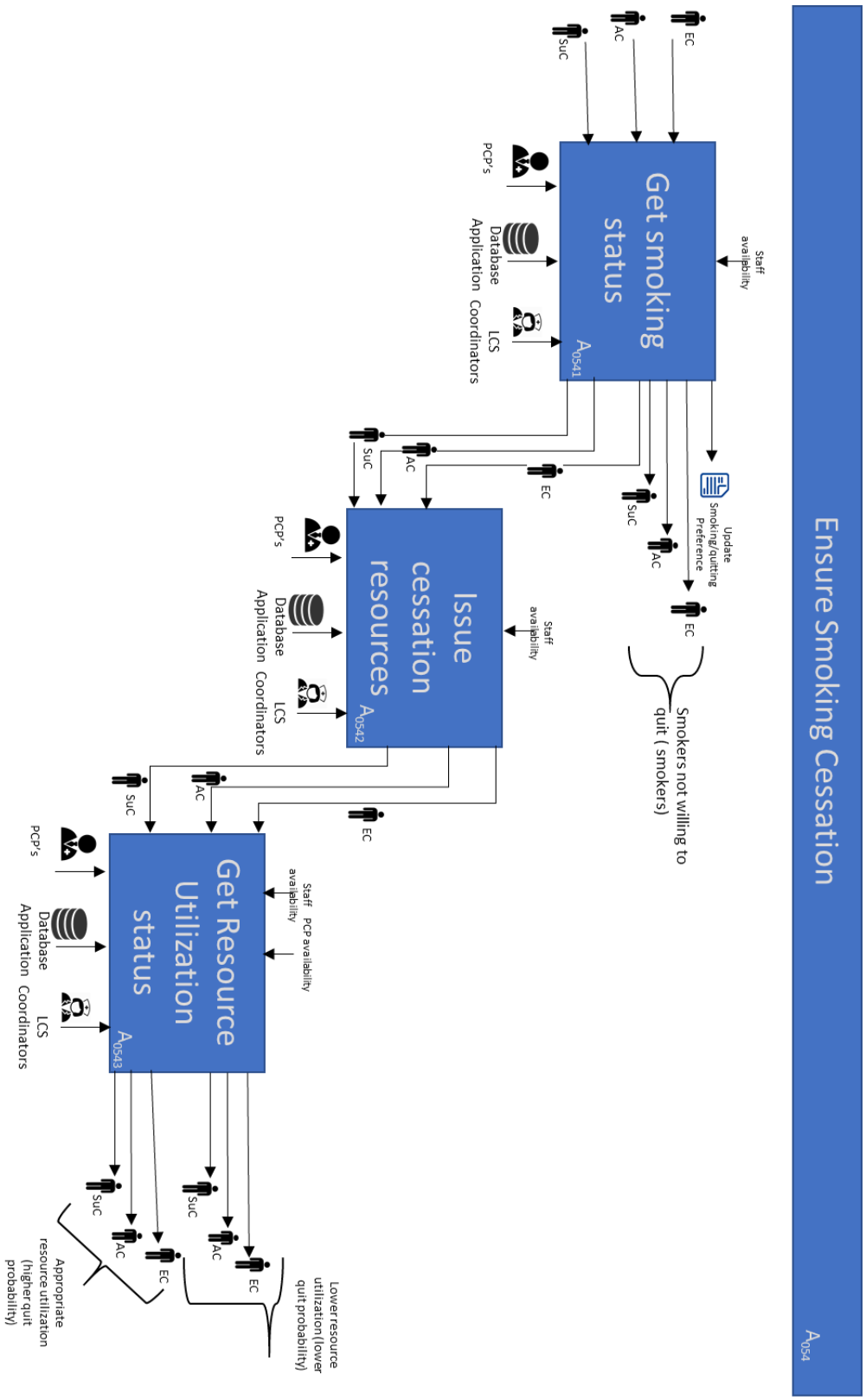


Figure 3-13 Hierarchical expansion of ensure smoking cessation activity

## 3.2 MODELING TOOLS

In the next chapter, these factors are chosen to be studied using a Monte Carlo simulation model of a hypothetical lung cancer screening center. The aspects of the model are the candidate states and sub-models that determine several organizational factors. Since there are no time frame and queues taken into consideration, a Monte Carlo Simulation model was determined to be sufficient instead of a discrete event simulation model. The tool used for this purpose was a discrete event simulation software (SIMIO). SIMIO offers intuitive graphical platform to model simulation scenarios as well as run any number of experiments with different scenarios. The software also plots graphs and confidence intervals for every experiment scenario. Section 6.2 gives more information on adapting SIMIO to Monte Carlo simulation.

# Chapter 4. SIMULATION MODEL DEVELOPMENT

The objective of this section is to develop a Monte Carlo simulation model that can compare the effect of various factors on the quality outcomes of a lung cancer screening process. The factors to be modeled in the simulation were chosen by advisory board members using the methodology followed in Measuring What Matters project in hospice and palliative care [35]. The simulation model was extended from the SADT conceptual model by annotating the conceptual model with the relevant input from the top ranked factors from those voted on by the advisory board members. The model was then verified and validated against the National Lung Cancer Screening Trial (NLST). The effect of recall bias, shared decision making meeting completion rate, nodule detection sensitivity and specificity, nodule length variation and nodule management system on the quality outcomes were modeled as what-if scenarios.

## 4.1 INTRODUCTION

Monte Carlo simulation is a widely used technique in systems modeling and dynamics. The key advantage of simulation is that it can model a system that evolves probabilistically over time. A lung cancer screening center is such a stochastically evolving system, given the differences in lung cancer prevalence in different sections of the population as well as the complexity of procedures involved in the screening process. The use of simulation enables what-if scenario analysis of a range of input factors on a selected list of responses. The challenge of quality assurance in lung cancer screening is number of variables and interactions that exist, and these may be studied via simulation. In order to select the factors in this paper, an advisory board, comprised of practitioners from existing screening programs, prioritized a number of screening characteristics and outcomes. The objective of this paper is to utilize a Monte Carlo simulation

model of a hypothetical lung cancer screening program to identify the factors that influence lung cancer screening quality through key outcomes of the process.

## 4.2 LITERATURE REVIEW

### 4.2.1 *Outcomes of interest*

Some studies model outcomes in lung cancer screening based on the models for disease progression [25]. There are 5 such competing models, and they all focus on similar outcomes such as the number of deaths due to cancer, the number of false positives, number of early detections and the number of candidates who quit smoking. The USPSTF Task Force Guideline statement for lung cancer screening was determined based on running the CISNET models [36]. These outcomes listed in Table 4-1 will be the point of interest in this study.

Table 4-1 Lung Cancer screening quality outcomes

| Outcomes of interest | USPSTF outcomes as estimated by CISNET |
|---|---|
| Percentage screened out of intake | 19.30% |
| CT scans per person | 2.86 |
| False positives percentage of total screened | 33.65% |
| Early detection percentage out of cancer cases | 50.50% |
| Cancers diagnosed | 3.72% |
| Screening per lung cancer death averted | 550 |
| Overdiagnosis out of total screened | 3.70% |
| Radiation induced lung cancer deaths % | 0.80% |

### 4.2.2 *Types of input factors*

The types of input factors are logically classified into two types: population and organizational characteristics.

*Population characteristics*

The intake population can be a very important factor in determining the quality of lung cancer screening process. Depending on the gender, geographical location and ethnicity, the prevalence of cancer, smoking and other lung disorders varies [37]. There are some sections of the population that are more genetically and culturally prone to lung cancer than others, and these can be modeled as either as a sub-model or a probability distribution into the simulation model.

The Brock University Cancer risk calculators offer a logistic regression model that covers six factors like family history, age, education, smoking history and other lung disorders which can determine the probability of risk for lung cancer in a particular individual [38]. If data is available about the average demographics of a particular section of the population of interest, the risk for developing lung cancer can be derived from the values. Though the accuracy of these models that estimate cancer prevalence is very high, there is no parallel model that estimates the pulmonary nodule prevalence for various population factors. Since the pulmonary nodule prevalence plays a very important role in determining false positives in the screening process, it was decided to use probability distributions instead of sub-models. There are several randomized controlled trials and cohort studies that furnish details of their nodule prevalence and cancer prevalence information. Some examples are the DLCST [39] and NELSON studies [40] .

*Organizational characteristics*.

In the context of the model, many of these factors follow a simple probability distribution or even a sub-model within the lung cancer screening model. Some organizational factors of interest are: fraction of the total candidate intake obtained internally, externally or through direct Primary Care Provider orders; candidate availability for the screening process; procedural

completion rate for the LCS coordinator; shared decision making meeting completion rate; utilization of a nodule management system; nodule detection sensitivity and length variability.

### 4.2.3 *Data available in literature*

The development of a simulation model is dependent on finding data sources for the population-level as well as organization-level factors, and this work compiles data from many sources. For example, these sources provided values for a typical percentage of candidates lost to follow up, typical percentage of candidates who respond to external outreach programs, etc. [41] NLST and the clinical study in Spain [31] provided the population prevalence values for lung cancer, smoking cessation, invasive procedures, nodule prevalence, nodule length distribution other details required for specific population generation. National Lung Cancer Screening Trial that was conducted for over 26,000 candidates with LDCT. In addition, there were 6 such large scale randomized controlled trials conducted and summarized in the literary work by Bach, et al. (2012). There are summary data from these trials can be used to gather data about population prevalence for various input factors. The exact values used in the model will be covered in later sections.

### 4.2.4 *Studies related to cost effectiveness*

Quantification of quality assurance in lung cancer screening is an interesting focus area. By trying to quantify the effect of various factors on the outcomes of screening it is possible to allocate financial and other resources to the problems that have the highest effect on the screening process. There are studies that focus on assessing the cost effectiveness of screening by assigning numbers to different outcomes of the screening process. Several of these values are intangible. For example, the question of whether it is worth changing the process to getting an additional early

detection or for having a lower rate of false positives. One of these improvements have a higher impact on population health. In order to quantify these numbers, these cost effectiveness studies use a number called Quality of Adjusted Life Years (QALY). The study on cost effectiveness in the NLST is one such paper which assesses the cost effectiveness of lung cancer screening keeping in mind the results from NLST [19]. Such studies are useful to try to unify the results with several responses and choose one scenario over another.

#### 4.2.5 *Disease progression models*

CISNET focusses on modeling disease progressions for different aspects of lung cancer screening (reference). One of the CISNET models assesses the impact of different smoking cessation policies [42]. These studies model lung cancer stages as states in a Markov chain or a Bayes model and then utilizes NLST data to validate these models. As such even a complex lung cancer screening problem can be modeled in terms of state transition as a Monte Carlo simulation model.

#### 4.2.6 *Facilitative factor selection*

Stakeholder involvement in problem solving in the subject of many research works. A conceptual modeling framework has been developed that involves an intensive two-day workshop that can be used to gain stakeholder input to develop a conceptual model [24]. Literature search reveals research work that involved stakeholder input to identify problems of interest in the Hospice and Palliative care domain by involving medical professional belonging to several disciplines under that umbrella, and following a systematic methodology to assess their input and selecting factors of importance to be addressed [35]. In this portion of the thesis, the need for

stakeholder involvement is in reducing the scope of the problem considerably. Therefore, stakeholder input has been used here to select the factors that will be varied in the simulation model and analyzed for their effect on the quality outcomes.

## 4.3 MODEL BUILDING METHODOLOGY

### 4.3.1 *MWM methodology*

The Measuring What Matters project in hospice and palliative care, outlined a methodology to gather stakeholder input on problems to be addressed in a healthcare domain [35]. Drawing inspiration from that method, 5 participating institutions in Centers for Disease Control research grant were involved in gathering input.

Table 4-2 Participating institutions and members for the advisory board meeting

| Program | Board members | Designations |
|---|---|---|
| VHA Lung Cancer Screening Demonstration Project | David Au, MD MS; Julie Takasugi, MD; | Clinical Pulmonologist; Chest Radiologist |
| Swedish Tobacco Related Diseases and Lung Cancer Screening Program | Joelle Thirsk Fathi, DNP, RN, ARNP; Jed Gorden, MD, FCCP; Deborah Klein MD | Program director of tobacco related diseases; Director of Interventional Pulmonology; Primary Care Provider |
| Group Health Cooperative | Diana Buist, PhD | Senior Investigator and Epidemiologist |
| UW Physicians Lung Cancer Screening Program | Laura Feemster, MD MS | Pulmonologist |
| Seattle Cancer Care Alliance Lung Cancer Screening Program | Farhood Farjah MD MPH | Thoracic surgeon and Health services investigator |

Each of these participants were asked to vote on over 150 selected factors of interest in lung cancer screening on 4 different aspects: importance, feasibility, scientific soundness and clinical logic. From the list of over 150 factors, 10 factors of the highest score were chosen. Table

4-3 describes the factors and what kind of model element the factor is. A 'User Input' is either a value or a parameter of a probability distribution. A 'Model Assumption' is usually a valued that is drawn from the literature such as the NLST value for % of individuals who underwent an invasive procedure.

Table 4-3 Advisory board input

| Metric Number | Category | Description | Model Element |
|---|---|---|---|
| 1 | Population | % of individuals who were screened but don't meet eligibility criteria | Model Characteristic/User Input |
| 2 | Population | % of screened individuals who have a documented SDM visit | User Input |
| 3 | Safety | % of individuals who receive recommended follow-up of positive findings (Lung-RADS 3, 4a, 4b, 4x) | Model Assumption/User Input |
| 4 | Safety | % of individuals who have an invasive pulmonary procedure for negative/low risk (LungRADS 1,2,3) | Model Assumption/User Input |
| 5 | Interpretation | % of screened individuals where standardized reporting was used? (have LungRADS score) | Model Assumption/User Input |
| 6 | Patient Experience | % of screened individuals with positive results who receive person-to-person counseling | Model Characteristic / Assumption |
| 7 | Patient Experience | % of screened individuals (normal findings) returning for repeat annual screening (adherence) | Model Assumption |
| 8 | Smoking cessation | ACR: % screened individuals who are current smokers who were offered smoking cessation advice (Yes/No) | Model Assumption/User Input |
| 9 | Smoking cessation | % current smokers sent home with medication/treatment for smoking cessation | Model Outcome |
| 10 | Technical | % of screened individuals who receive higher than necessary radiation dose (e.g. >3 mSv or by gender >1.8 females/>2.2 males, or by BMI-adjustment) | Model Outcome |

### 4.3.2 *Extension of the SADT model*

The conceptual model for the lung cancer screening process was developed in the earlier sections of the thesis. Extending the developed conceptual model with the mathematical assumptions, facilitates the transition from the conceptual model to the simulation model. So wherever required the SADT model was extended to another hierarchical level, until a sub-model was available for that activity. The capability of hierarchical expansion has been demonstrated in detail in Chapter 3. For example, the overall lung cancer screening process, Screen for Lung Cancer (A0), shown in Figure 3-1, can be hierarchically expanded into the 5 sub-processes, shown in Figure 3-2), one of which is the Perform LDCT Scan (A03) sub-process. This sub-process is expanded hierarchically into 3 activities as shown in Figure 3-5, each of which can be further expanded. For instance, the acquire LDCT scan activity is expanded further in Figure 3-6. The hierarchical relationship has been described concisely in Figure 4-1.

In addition to the hierarchical expansion, the conceptual model is marked with the elements selected by the advisory board meeting, indicating where in the model these elements are reflected as seen in Figure 4-2.

### 4.3.3 *Candidate States*

A Monte Carlo simulation model is driven by the different states that a candidate is in as that person goes through the lung cancer screening process. In this model, a candidate going through a screening process is in one of the14 states described in Table 4-4.

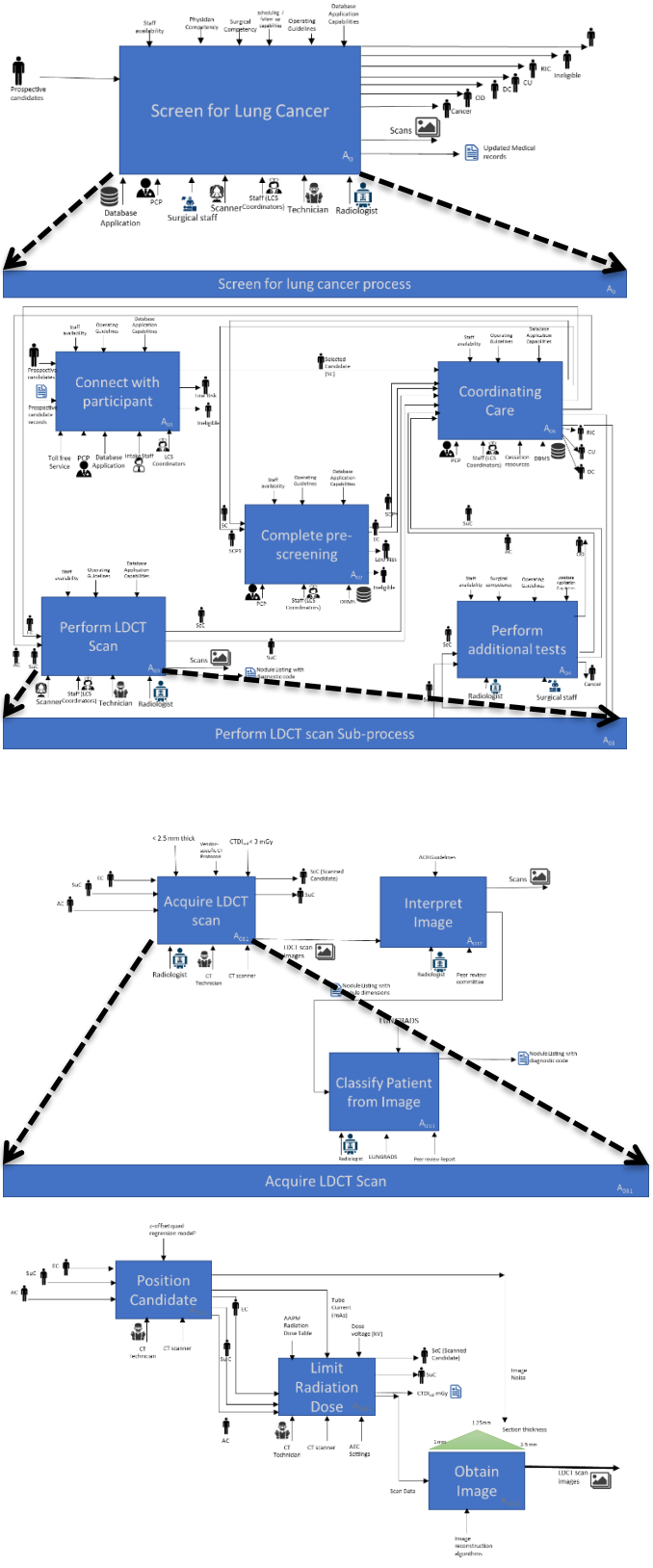


Figure 4-1 Hierarchical expansion scope of the SADT conceptual model

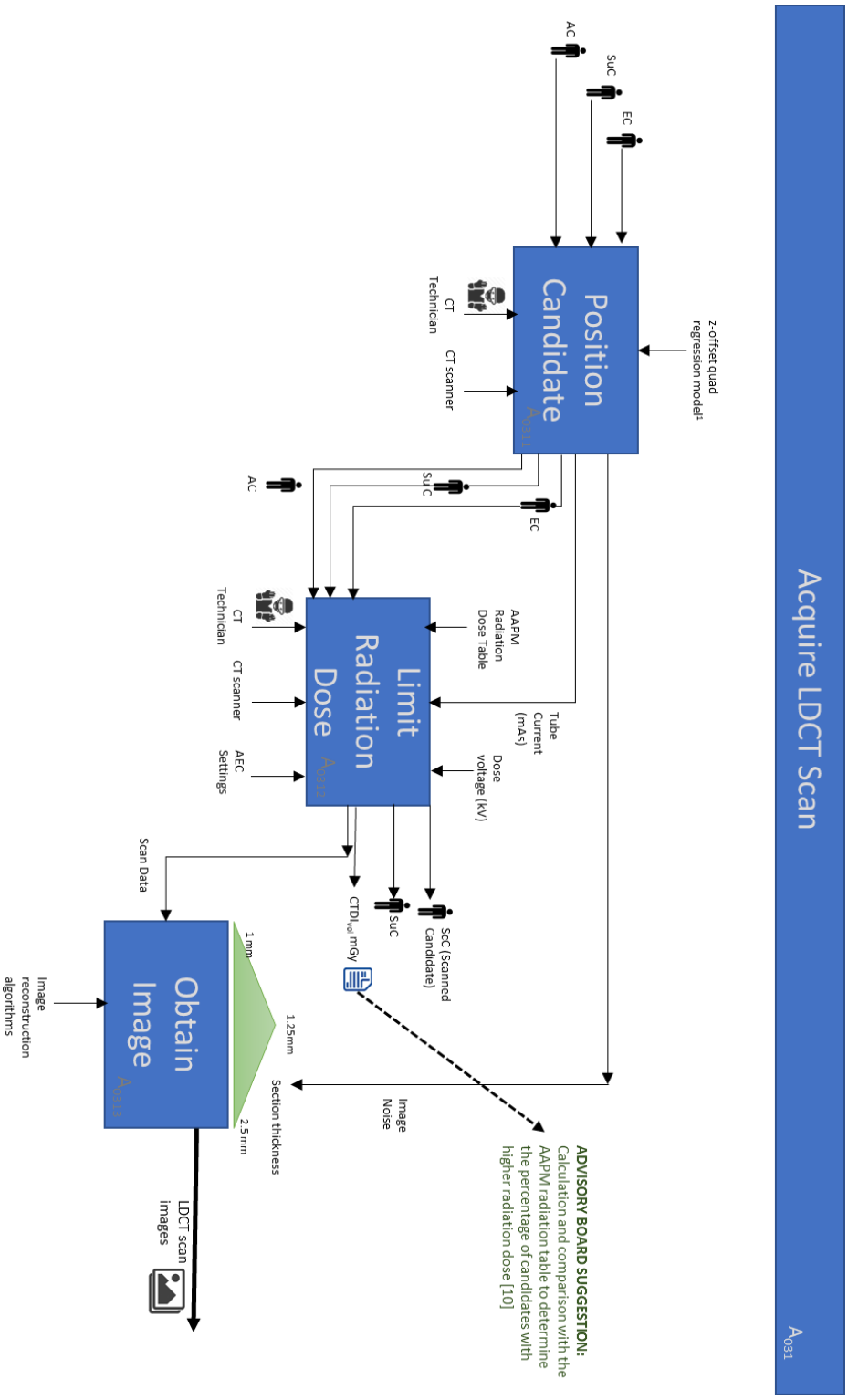


Figure 4-2 SADT Activity diagram annotated with the advisory board meeting suggestion

Table 4-4 State transitions that candidates undergo in the screening process

| Candidate States | Abbreviation in SADT | Description |
|---|---|---|
| Intake candidate | Candidate | Initial state of candidates when they contact/get contacted by the screening center |
| Ineligible candidate | Ineligible | Candidates who are determined to be ineligible for screening due to a condition that excludes them from surgery |
| Low risk candidate | Low Risk | Candidates who are determined to be low risk as per the USPSTF screening criteria |
| Eligible candidate | EC | Candidates who are determined to be eligible for LDCT scanning |
| Selected candidate | SC | Candidates who are selected from the intake candidates and are furnished with the tobacco pack year form |
| Scanned candidate | ScC | Candidates who just completed the LDCT scan |
| Suspected candidate | SuC | Candidates who are diagnosed with a positive result from the LDCT scan and are recommended for additional diagnostic procedures |
| Annual candidate | AC | Candidates who are tracked annually following their LDCT result |
| Incomplete candidate | RIC | Candidates for whom completed reminders (Tobacco or LCS assessment) have not been received yet |
| Unavailable candidate | CU | Candidates who are unavailable to schedule appointments |
| Discontinued candidate | DC | Candidates who choose to discontinue the screening process because they are uncomfortable or perceive too much harm from the screening process |
| Cancer candidate | Cancer | Candidates who are diagnosed and documented with cancer |
| Overdiagnosed candidate | ODC | Candidates with a form of harmless tumor that does not lead to cancer |
| Selected candidate with complete pack year history | SCPY | Candidates who are selected from the intake candidates and have completed the tobacco pack year form |
| BaselineCandidate | BC | Candidates who complete their first LDCT scan in the screening process |

## 4.4 MODEL ASSUMPTIONS

### 4.4.1 *Candidate intake and screening criteria*

Starting from the intake of candidates to the documentation of cancer and smoking cessation status, there are several assumptions made in the model development process that are a direct inference from the conceptual modeling process and others that have been made based on survey of existing demonstration projects in lung cancer screening. The total number of candidates for intake can be acquired as an input from the user, as can the fraction of intake from external means and Primary Care Provider orders. The reminder of the intake candidates come from the internal database of a screening center. Here the assumption is that candidates coming through internal intake already satisfy age criteria as per USPSTF guidelines. Candidates coming through external means represent a more general population in several age ranges. In the literature on participation in breast cancer screening programs [43], it is found that typically 40% of the candidates coming through these means do not satisfy screening requirements such as age, cancer history and surgical exclusions. Candidates recommended by the Primary Care Provider is a proxy for the fraction of candidates who are accepted into the program even though they do not satisfy screening criteria. Though this may not be the case in real screening centers where orders by Primary Care Physicians may actually include candidates who satisfy screening criteria, for the purposes of the simulation model, those candidates are covered in the internal and external means. What this means is that if the fraction of PCP intake candidates is higher, the screening center accepts a lot of candidates who do not satisfy the USPSTF screening guidelines. Testing with a higher fraction for candidate intake though PCP recommendation would enable users to study the effects of screening candidates who do not satisfy the guidelines.

The intake fractions represent a direct way of identifying the candidates who do not satisfy screening requirements. However, several screening programs inadvertently select candidates who do not satisfy the screening criteria. Smoking history recall bias is expected to be one of the reasons for this. Since pack year history number for smoking is retrospectively calculated, Bernaards, et al. 2001, studies the possibility of bias in recall and establishes that the bias is directly proportional to number of years smoked. The simulation model attempts to quantify the effect of this bias in the final cancer screening outcomes. For the purposes of simulation, it is assumed that the bias in perception is a fraction of the actual smoking history. This fraction can be changed by the user, thus enabling the model to quantify the effect of recall bias on the screening outcomes.

### 4.4.2 *Nodule Detection and management*

Another major point of false positive generation that has been extensively studied in literature is the nodule detection and nodule length variation between and within radiologists [8] . This variation in detection is caused by the possibility of noise in the LDCT images that causes air bubbles and other lung tissues to look like nodules causing false detection. Since the measurement of length is a one-dimensional approximation of a three-dimensional nodule, there is possibility of variation in perception of nodule length. This variation is typically of the order of 2 mm.

Bach, et al., (2012), summarized different randomized controlled trials for LDCT and each study chose a different threshold nodule length. Threshold nodule length is the nodule length in millimeters beyond which the screening program management decides to treat the nodule as abnormal and suggests further invasive scans and procedures to diagnose the nodule. The American College of Radiology (ACR) published LUNGRADS, a nodule management system modeled on BIRADS system developed for breast cancer [33]. It is a rule based management system rather than just a threshold number that divides nodules into abnormal and normal. It is

expected that this method of nodule management will find a good balance between reducing false positives and having a high early detection rate. Pinsky, et al., (2015) retrospectively compares the use of LUNGRADS on a set of NLST cases and compares it with a set of different threshold nodule lengths and establishes that the use of a nodule management system makes a difference to the screening process. In this paper, both the threshold and the LUNGRADS nodule management system have been modeled. After nodule detection, McWilliams, et al., (2013), predict the probability of malignancy given nodule and patient variables.

### 4.4.3 *Follow up processes*

The Centers for Disease Control and Prevention (CDC) recommends that more than 85% of all candidates in the screening program must receive the recommended follow up within 90 days of their result [44]. It is widely understood that timely follow up on every single candidate is dependent upon the availability of the lung cancer screening program coordinators. Zapka et al. (2014), report a particular portion of candidates who are lost to follow up activities in breast cancer screening [45]. In this simulation model, these activities are grouped under scheduling of appointments and completion of reminders at different points of time in a program. The simulation model assumes a rate of completion for these processes.

### 4.4.4 *Shared Decision Making*

Shared decision making is an essential component of the screening process. It is enabled by a PCP or another medical professional to inform the candidate about all the risks and benefits of participating in cancer screening and to inform them of the benefits of smoking cessation. It is estimated that with informed decisions candidates perceive their risks better and leave the screening program when they perceive higher risks and attend screening programs when they

perceive higher benefits [46]. With that effect in mind, this simulation model makes an elementary assumption that a candidate completing a shared decision making meeting perceives their smoking history with lesser recall bias. This assumption was made because as far as this simulation model was concerned, smoking history is the only measure of risk of developing lung cancer. Therefore, this particular risk is more accurately perceived by the candidate as a results of the shared decision making visit. It is also assumed, there are candidates who discontinue the screening process due to one of the following reasons: discomfort with the healthcare services provided in the screening program or perception of more harms than benefits in the screening process.

### 4.4.5 *Smoking cessation*

One of the stakeholder insights on smoking cessation was that their interventions were most effective when there was an abnormal finding on the LDCT scan, in that they were able to convince a candidate to take up efforts towards quitting cigarette smoking. This is an indicator that the likelihood of candidate quitting smoking is different at different points of time in the process. A study of smoking patterns in NLST [38], evaluates these probability values for the NLST trial. The same assumptions are made for quit probabilities of the candidate at different points of time in the process for the simulation model.

## 4.5 MODEL LIMITATIONS

The simulation model is limited in scope by a number of factors. The number of intake candidates is the first of these factors. For the VHA demonstration project, [16] which involved 8 screening centers across the United States, the number of candidates screened was over 7000. For NLST, [18] the number of candidates screened on the CT arm was over 26000. Since the objective of this simulation study is to examine the factors that affect quality in a community based screening

center, the intake number of candidates need to reflect that situation. However, since there is a need to validate the simulation model with NLST data, the limit on the number of candidates in the simulation model was increased to 50000.

There are models in literature that represent the transition of nodules from one lung cancer stage to another (Schultz, Boer, & de Koning, (2012); McMahon, et al., (2012); Holford, Ebisu, McKay, Oh, & Zheng, (2012)). However, since there has not been a consensus on the applicability of these models, it was decided that the NLST prevalence values would be used as state transition probabilities for different nodule lengths. This study uses data primarily from NLST and the VA demonstration project to model the prevalence and transition probabilities for nodules, their length, type and histology.

The only precursor for the estimate on the recall bias is the research work by Bernaards et al., (2001). There is not much research on the subject available in literature since it involves a lot of time investment to estimate the recall bias. This simulation study models recall bias as a simple variance from the actual smoking history based on the results from the above literature.

This simulation study models the effect of shared decision making on the lung cancer screening quality as the reduction in the recall bias of smoking history for candidates. Studies which observe the effect of decision aids on candidates who undergo screening and show improved decision quality such as 79% more accurate risk perceptions and 14% improvement in knowledge [46]. The study on whether smoking history recall bias is really affected by shared decision making visits is outside the scope of this modeling exercise as is modeling other indicators of lung cancer risk apart from cigarette smoking.

Presence of incidental lung diseases and conditions such as emphysema and chronic obstructive pulmonary disorder is quite common in lung cancer screening. In several cases, the

candidate cannot undergo further screening due to these conditions. In this work, the effect of incidental conditions on the screening process has not been modeled.

## 4.6 BASELINE CONDITIONS AND VALUE RANGE FOR SCENARIOS

The primary purpose of the baseline scenario is to verify and validate the model. The data that is used for validation is the NLST dataset. It was decided that an outreach to 26000 candidates would be conducted. Since NLST, represents an academic study, it can be assumed that all the candidates were internally contacted and satisfied the USPSTF screening criteria. The age distribution for candidates is modeled from the NLST data [18]. It is assumed that there was no recall bias in the baseline scenario. The nodule detection sensitivity used for the model is the average sensitivity and specificity found in NLST. It is important to note that, sensitivity and specificity change with the length of the nodule [47]. The baseline model also uses the 2 mm variation in nodule length and the threshold nodule length management system of 4 mm like the NLST. Cancer overdiagnosis occurs when a cancer that is diagnosed is found to not cause any of the symptoms or death. For this simulation model in the baseline scenario, the transition probability for overdiagnosis is 18% [10].

For scenarios other than the baseline, to model a general screening center, a candidate outreach value of 20000 is assumed. For modeling candidates who represent a more general population than NLST some of whom may not satisfy the USPSTF guidelines, the data from Health and Retirement Survey (HRS), 2012 [48], gives considerable information on the age and smoking prevalence among general population and the candidates who satisfy the USPSTF guidelines. Therefore, for the simulation model, age and smoking prevalence assumptions internal candidates and external candidates from the HRS study. In addition to this, from the clinical study in Spain [31], it is possible to gather the prevalence for incidental pulmonary nodules. The age and

smoking prevalence for intake candidates through PCP orders can be inferred this study. The main input factors varied for the what-if scenario analysis are the recall bias, the SDM meeting completion rate, the nodule detection sensitivity and specificity, nodule length variation and the nodule management system.

## 4.7 RESULTS

### 4.7.1 *Verification and validation*

Model verification ensures that the implementation of the model has been made correctly. In other words, the model has to be programmed without any errors and has to perform as intended. For a Monte Carlo simulation model, a simple entity balance can be performed to verify the model. With respect to the baseline conditions of the simulation model, it can be inferred that there are no candidates who are classified as low risk or ineligible because all of them satisfy the USPSTF screening criteria. In addition to this, all other completion rates have been set to 100% for validation. As a result, all candidates who enter will be screened and diagnosed. Table 4-5, shows the number of candidates entering and exiting the simulation model through different means, verifying that the model is behaving as per the input parameters for the baseline scenario.

Table 4-5 Model verification table

| Input Parameter | Value | Corresponding output | Value expected | Actual Value |
|---|---|---|---|---|
| External Intake Fraction<br>PCP Intake Fraction | 0<br>0 | External Source - Candidates Entered | 0 | 0 |
| | | PCP Source - Candidates Entered | 0 | 0 |
| | | Internal Source - Candidates Entered | 26000 | 26000 |
| Record Completion Rate<br>Lost to scheduling<br>SDM completion rate<br>PCP comfort | 1<br>0<br>1<br>1 | Low Risk Candidates | 0 | 0 |
| | | Ineligible Candidates | 0 | 0 |
| | | Reminder Incomplete | 0 | 0 |
| | | Candidates Unavailable | 0 | 0 |
| | | Discontinued Candidates | 0 | 0 |
| | | Overdiagnosed candidates | Adds to 26000 | 94 |
| | | Cancer Candidates | | 480 |
| | | Rescreened Population | | 25426 |

The objective of model validation is to check the accuracy of the model's representation of the real system. In this case, the model has to be validated against the baseline data conditions reflecting the NLST criteria. The model has been run for 30 replications to get a confidence interval on the outcomes. In Table 4-6, the quality outcomes of the model are compared against the values observed in NLST for validation.

Table 4-6 Model validation table

| Quality Outcomes | Simulation Results | Confidence Intervals (95%) | NLST Numbers |
|---|---|---|---|
| False Positives | 24.85% | 24.5 - 25.5 | 25.30% |
| Early Detection Rate | 1.62% | 1.5 - 1.7 | 1.19% |
| Documented Cancers | 4.10% | 3.9 - 4.2 | 3.95% |
| Quit Rate | 23.72% | 23.3 – 24.2 | 23.50% |
| Radiation Induced deaths | 0.56% | 0.55 - 0.57 | 0.80% |

### 4.7.2 *Recall bias in smoking history and SDM completion*

Recall bias is assumed to be a fraction of the actual pack year history of the candidate. The perceived smoking history is calculated as follows:

*Perceived Pack Years = Actual Pack Years * (1 + Triangular (-recall bias, 0, recall bias))*

It is assumed that in case of a completed SDM meeting, the recall bias fraction is reduced to half of its original value and perceived smoking history is calculated as follows:

*Perceived Pack Years = Actual Pack Years * (1 + 0.5 * Triangular (-recall bias, 0, recall bias))*

In the simulation model, the effect of SDM completion and recall bias were studied separately. The recall bias fraction was varied from 0 to 0.5 (with values 0, 0.1, 0.2, 0.3, 0.4 and 0.5). The effect of this value on the quality outcomes were studied. The results are published in Table 4-7. Similar study was done with SDM completion rate varied from 0.5 to 1.0 (with values 0.5, 0.6, 0.7, 0.8 0.9 and 1.0). The results are published in Table 4-8. It can be observed from these tables that the false positives increase only slightly as the bias fraction increases. Even the slight significant increase is not observed when the SDM completion rate is varied. This can be explained by the fact that the recall bias affects only a small number of candidates who have a smoking pack year value close to 30. This variance is again only slightly lowered by the completion of the SDM meeting. Recall bias in smoking history was the chosen indicator of cancer risk perception in this study. There are several other factors that contribute to risk and variance in perception [49]. With the use of risk-based screening rather than age and smoking criteria, followed by the inclusion of these criteria and their education in the SDM meetings, it is possible to further examine the scope of SDM meetings and the extent of their effect on the cancer screening processes more accurately.

Table 4-7 The effect of recall bias on quality outcomes

| Recall Bias | False Positives | | Early detection | | Quit Rate | |
|---|---|---|---|---|---|---|
| | Average | Half Width | Average | Half Width | Average | Half Width |
| 0 | 24.64 | 0.065 | 1.02 | 0.015 | 14.2 | 0.322 |
| 0.1 | 24.75 | 0.077 | 1.05 | 0.009 | 14.8 | 0.237 |
| 0.2 | 24.89 | 0.098 | 1.06 | 0.008 | 15.3 | 0.397 |
| 0.3 | 25.06 | 0.08 | 1.09 | 0.005 | 15.9 | 0.224 |
| 0.4 | 25.3 | 0.12 | 1.15 | 0.004 | 16.2 | 0.126 |

| Recall Bias | Radiation Induced Deaths | | Documented Cancers | |
|---|---|---|---|---|
| | Average | Half width | Average | Half width |
| 0 | 0.83 | 0.0127 | 5.32 | 0.522 |
| 0.1 | 1.06 | 0.0255 | 5.15 | 0.458 |
| 0.2 | 1.27 | 0.0376 | 4.96 | 0.228 |
| 0.3 | 1.56 | 0.0265 | 4.57 | 0.055 |
| 0.4 | 1.79 | 0.0211 | 4.13 | 0.114 |

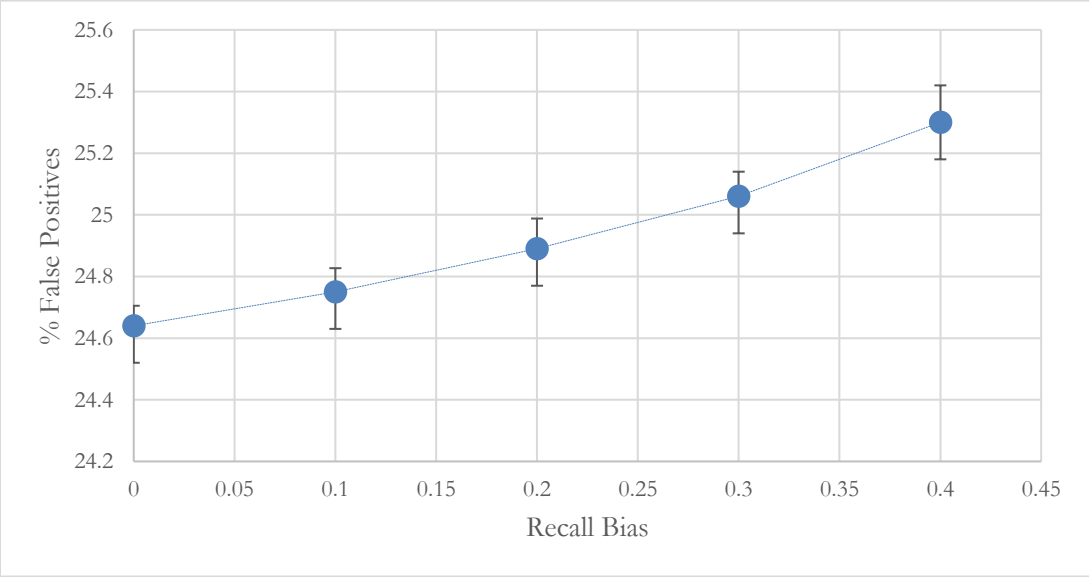


Figure 4-3 The effect of recall bias on the false positive rate

Table 4-8 The effect of completing SDM meetings on quality outcomes

| SDM Completion rate | False Positives | | Early detection | | Quit Rate | |
|---|---|---|---|---|---|---|
| | Avg | Half Width | Avg | Half Width | Avg | Half Width |
| 1 | 25.3 | 0.0555 | 1.02 | 0.015 | 14.2 | 0.322 |
| 0.9 | 25.43 | 0.0443 | 1.05 | 0.009 | 14.8 | 0.237 |
| 0.8 | 25.48 | 0.0663 | 1.06 | 0.008 | 15.3 | 0.397 |
| 0.7 | 25.52 | 0.068 | 1.09 | 0.005 | 15.9 | 0.224 |
| 0.6 | 25.58 | 0.0768 | 1.15 | 0.004 | 16.2 | 0.126 |
| 0.5 | 25.8 | 0.0554 | 1.18 | 0.0035 | 16.38 | 0.096 |

| SDM Completion rate | Radiation Induced Deaths | | Documented Cancers | |
|---|---|---|---|---|
| | Avg | Half width | Avg | Half width |
| 1 | 0.83 | 0.0127 | 5.42 | 0.522 |
| 0.9 | 1.06 | 0.0255 | 5.32 | 0.458 |
| 0.8 | 1.27 | 0.0376 | 5.15 | 0.228 |
| 0.7 | 1.56 | 0.0265 | 4.96 | 0.055 |
| 0.6 | 1.79 | 0.0211 | 4.57 | 0.114 |
| 0.5 | 1.86 | 0.0345 | 4.13 | 0.079 |

### 4.7.3 *Nodule length variation and Nodule Sensitivity*

Nodule sensitivity and specificity are an indirect measure of the number of false nodules detected and the number of true nodules missed respectively. There are several studies that try to quantify the typical values of nodule sensitivity. Gierada, et al. (2014) found that the value of sensitivity and specificity change with the length of the nodule or lesion on the CT scan. However, in this simulation study, a constant value for sensitivity and specificity were used and the values of this constant were varied in the experiments to examine their effect of the quality outcomes. Simplifying these values to a single fraction enabled a what-if scenario analysis with multiple values. In the simulation model, the value of sensitivity and specificity are both varied

from 0.7 to 1.0 and their effect on the quality outcomes is observed. Since the effect on the other quality outcomes were not statistically significant, only the false positive rates were tabulated in Table 4-9.

Table 4-9 The effect of nodule detection quality on false positive rate

| Nodule Detection | | False Positives | |
|---|---|---|---|
| Sensitivity | Specificity | Avg | Half Width |
| 0.7 | 0.7 | 26.56% | 0.70% |
| 0.7 | 0.8 | 23.46% | 0.92% |
| 0.7 | 0.9 | 19.98% | 0.61% |
| 0.7 | 1 | 16.79% | 0.34% |
| 0.8 | 0.7 | 29.51% | 0.50% |
| 0.8 | 0.8 | 25.83% | 1.06% |
| 0.8 | 0.9 | 22.53% | 1.39% |
| 0.8 | 1 | 19.12% | 0.61% |
| 0.9 | 0.7 | 31.97% | 1.07% |
| 0.9 | 0.8 | 28.61% | 0.77% |
| 0.9 | 0.9 | 25.04% | 0.54% |
| 0.9 | 1 | 21.93% | 1.05% |
| 1 | 0.7 | 34.86% | 0.65% |
| 1 | 0.8 | 30.95% | 0.40% |
| 1 | 0.9 | 27.51% | 0.44% |
| 1 | 1 | 24.39% | 0.44% |

In order to understand the relationship further, a two factor ANOVA table represented by Table 4-10 was computed. It can be seen from the table that both sensitivity and specificity significantly contribute to the variance in false positive rates. In addition to this, the interaction between these factors also significantly contributes to the outcome.

Table 4-10 ANOVA table for false positive rate as the response with 2 factors

| Source of Variation | SS | DF | MS | F | P-value | F crit |
|---|---|---|---|---|---|---|
| Sensitivity | 0.0230695 | 3 | 0.0076898 | 2539.314 | 1.722E-13 | 3.8625484 |
| Specificity | 0.0133431 | 3 | 0.0044477 | 1468.7 | 2.015E-12 | 3.8625484 |
| Interaction | 2.725E-05 | 9 | 3.028E-06 | | | |

Nodule length variation is another factor considered for analysis. The value for this variation was varied from 0 to 2 mm (with values 0, 0.5, 1, 1.5, 2mm) and its effect on the quality outcomes were studied. Table 4-11 displays the results of this analysis.

Table 4-11 Effect of nodule length variance (in mm) on quality outcomes

| Nodule Length Variance | False Positives | | Early detection | | Quit Rate | |
|---|---|---|---|---|---|---|
| | Average | Half Width | Average | Half Width | Average | Half Width |
| 0 | 2.42% | 0.38% | 1.08% | 0.31% | 7.32% | 0.10% |
| 0.5 | 25.89% | 0.81% | 1.09% | 0.32% | 15.30% | 0.40% |
| 1 | 26.07% | 0.86% | 1.09% | 0.32% | 15.90% | 0.22% |
| 1.5 | 26.32% | 0.94% | 1.09% | 0.34% | 16.20% | 0.13% |
| 2 | 26.32% | 0.94% | 1.09% | 0.32% | 16.40% | 0.16% |

| Nodule Length Variance | Radiation Induced Deaths | | Documented Cancers | |
|---|---|---|---|---|
| | Average | Half width | Average | Half width |
| 0 | 1.768 | 0.045 | 3.40% | 0.32% |
| 0.5 | 1.736 | 0.027 | 3.40% | 0.31% |
| 1 | 1.736 | 0.027 | 3.40% | 0.31% |
| 1.5 | 1.738 | 0.013 | 3.39% | 0.31% |
| 2 | 1.744 | 0.023 | 3.38% | 0.39% |

It can be seen from the results the nodule sensitivity and specificity have a higher quantitative impact than the recall bias or SDM meetings. However, it is important to observe the effect of nodule length variation on the quality outcomes. Its effect on false positive rate is non-linear in nature and increases suddenly from 2.5% to 25% when the variation is increased from 0

to 0.5 mm (Figure 4-4). It can be inferred from this pattern that the misclassification caused by variation in nodule length contributes more significantly to the false positives than the nodule sensitivity and specificity. Therefore, establishing a peer evaluation system that reduces this variation can contribute significantly to increased quality in lung cancer screening centers.

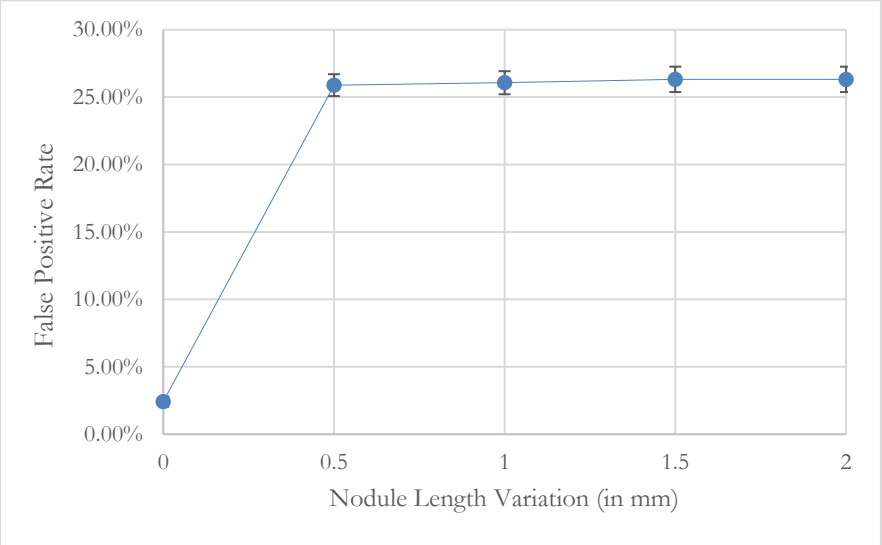


Figure 4-4 The effect of nodule length variation on false positive rate

### 4.7.4 *Smoking Cessation*

In all the above experiments, it is observed that quit rates for smokers is directly proportional to the false positive rates (trend shown in Figure 4-5). The model for smoking cessation assumes that quit rates are higher when the candidate receives abnormal results from their LDCT scan. This was the inference from analyzing data for smokers in the NLST. This is the reason why quit rates are higher when there are more candidates going through invasive procedures. However, the objective of a screening program is to reduce the false positives while simultaneously increasing the quit rates for smokers. In order to achieve this, more interventions or smokers should be placed early on in the screening program rather later.

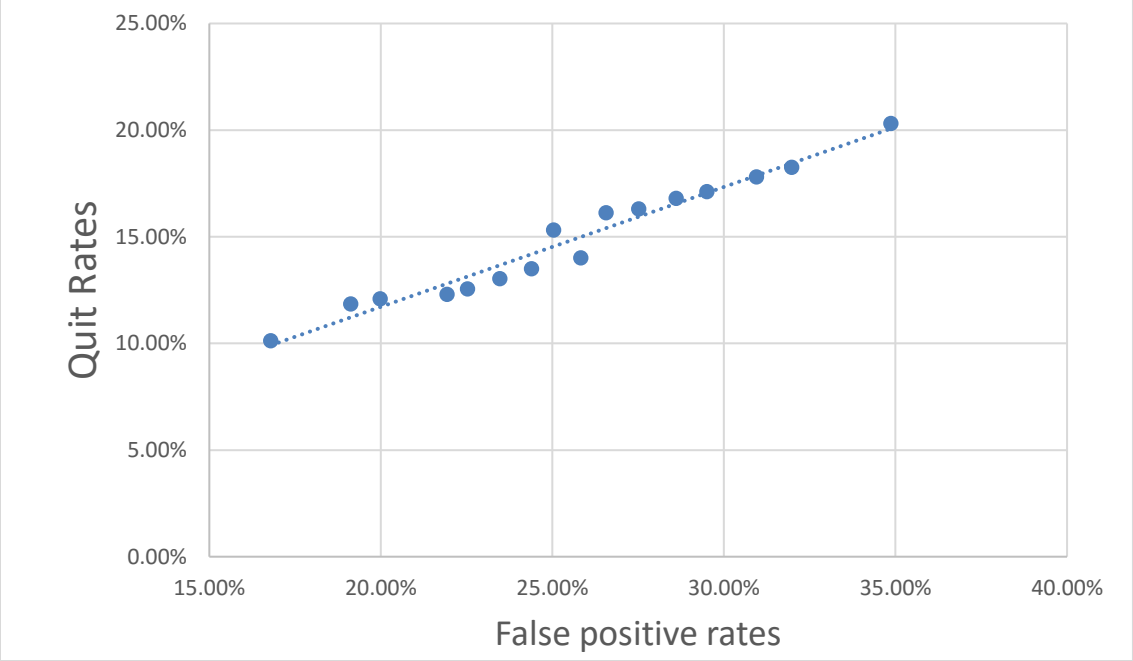


Figure 4-5 Relationship between false positive rate and quit rate for smokers

### 4.7.5 *Nodule management system*

The randomized controlled trials discussed by Bach, et al., (2012), use a threshold value for nodule length beyond which nodules are considered abnormal and diagnosed further for malignancy. ACR instituted a nodule management system modeled on similar grounds as BIRADS used for breast cancer screening, called LUNGRADS. It is a rule based nodule management system. In the simulation study the LUNGRADS system is compared with threshoild-based management with different threshold values. Table 4-12 displays the simulation results for the experiment.

Table 4-12 Comparison of LUNGRADS and Threshold management of nodules

| Nodule Management | False Positives | | Early detection | | Quit Rate | |
|---|---|---|---|---|---|---|
| | Avg | Half Width | Avg | Half Width | Avg | Half Width |
| LUNGRADS | 25.30% | 1.30% | 3.50% | 0.33% | 16.30% | 0.02 |
| Threshold - 4 | 28.50% | 1.10% | 9.05% | 0.65% | 12.10% | 0.0127 |
| Threshold - 5 | 27.61% | 1.02% | 4.62% | 0.39% | 12.52% | 0.0255 |
| Threshold - 6 | 26.34% | 0.93% | 3.64% | 0.35% | 12.83% | 0.0376 |
| Threshold - 7 | 24.64% | 0.52% | 2.79% | 0.28% | 13.21% | 0.0265 |
| Threshold - 8 | 22.07% | 0.91% | 2.13% | 0.12% | 13.51% | 0.0211 |
| Threshold - 9 | 11.61% | 0.57% | 1.80% | 0.06% | 13.75% | 0.016 |

| Nodule Management | Radiation Induced Deaths | | Documented Cancers | |
|---|---|---|---|---|
| | Avg | Half width | Avg | Half width |
| LUNGRADS | 0.8 | 0.015 | 4.10% | 0.50% |
| Threshold - 4 | 1.43 | 0.026 | 9.86% | 0.93% |
| Threshold - 5 | 1.81 | 0.080 | 5.97% | 0.54% |
| Threshold - 6 | 1.83 | 0.015 | 4.72% | 0.66% |
| Threshold - 7 | 1.81 | 0.038 | 3.60% | 0.17% |
| Threshold - 8 | 1.80 | 0.024 | 2.75% | 0.11% |
| Threshold - 9 | 1.75 | 0.018 | 2.10% | 0.09% |

It can be observed that using LUNGRADS achieves the best balance of all the quality measures. The quit rates are high when compared to threshold based management and radiation induced harms are very low. This is an indicator that fewer candidates undergo repeated screening with LDCT when LUNGRADS is used to manage nodules.

## 4.8 CONCLUSION

This section compared the effects of various input factors on the final quality outcomes of a typical lung cancer screening center. The input factors to be used were chosen by stakeholders from different aspects of different lung cancer screening programs in the Seattle area. Measuring What Matters methodology was used to get their assessments for the various input factors and the highest rated factors were used in the simulation model. The Monte Carlo simulation model was extended from the conceptual model developed in the previous section. The main data used for validation of the model was from the National Lung Cancer Screening Trial (NLST). In the comparison from the simulation experiments, it was observed that following a nodule management system like LUNGRADS can help achieve the best balance of the quality outcomes. In this study, using LUNGRADS as the nodule management system seemed to increase the quit rates and decrease the radiation induced harms. Nodule Length variation contributes the highest to the false positive generation. Working towards decreasing that variability by establishing peer evaluation committees could significantly improve quality. Since smokers are more likely to quit when there is an abnormal finding in their LDCT scan, it is not possible to increase quit rates for smokers while decreasing false positives. Thus there should be increased focus on helping candidates quit smoking earlier on in the screening process. Though recall bias in smoking history affects false positive rate in a statistically significant way, the effect is quantitatively small when compared to other factors like nodule detection sensitivity and nodule length variation.

Recall bias is only one way to quantify the difference in risk perceptions across different sections of the population. In future research studies, a better factor can be modeled for cancer risk perception than smoking history recall bias. The effect of complete SDM meetings can be appropriately studied then. In this study, since the effect of recall bias is low, the effect of

incomplete SDM meetings on the quality outcomes is not statistically significant. From the conceptual study, Lung Cancer Screening coordinator availability can be gathered as one of the important factors in quality. However, the quantitative effect of lower number of coordinators or their lower time availability can be evaluated only in a discrete event simulation model. This can be a part of a future study that focusses on the design of a lung cancer screening program.

Evaluating the best case scenario with multiple quality output responses of interest involves an evaluation by the stakeholder on the Quality Adjusted Life Years of one factor versus another. For example, if Scenario 1 increases both false positive rate and early detection rate, how does 1% increase in false positive rate compare with a 0.2% decrease in early detections that would be experienced by choosing another Scenario as the operating condition. Estimating QALY's for each quality outcome will facilitate this comparison. With the cost data for QALY's in lung cancer screening available in the work by Black, et al., (2014), it will be possible to estimate even the cost trade-offs for one experimental scenario in comparison with another. This kind of analysis can be used in cost effectiveness analysis for one quality intervention versus another.

# Chapter 5. CONCLUSION

## 5.1 CONCEPTUAL MODEL APPLICATIONS

The conceptual modeling activity focused on identifying factors that are critical to ensuring a high quality screening program. The conceptual model developed in this paper using Structured Analysis and Design Technique (SADT), is used to gain these structural insights. The key insights from the modeling process were that the bias in smoking history perception on part of the candidate represents a pivotal point in the screening process from where candidates who do not satisfy screening criteria enter the process and undergo several invasive procedures. It is similar in nature to nodule detection sensitivity but occurs earlier in the screening process. What it represents is an error in risk perception on part of the candidate and its effect on the process.

A lung cancer screening program coordinator (LCS coordinator) is a very critical resource required to implement several processes. The contribution of the LCS coordinator is intangible in some places. For instance, the number of candidates lost to follow up depends on the extent of availability of coordinator to assist the candidate with navigation through the screening center [50]. The conceptual model can be used to analyze the job requirements for an LCS coordinator which involves conducting shared decision making meetings and tobacco addiction counselling in addition to other follow up duties. A review of these job requirements helps the management recruit a coordinator with the right qualifications. It also helps the management design a training regimen that helps newly recruited program coordinators to be updated with the required knowledge to perform in their jobs.

A typical medical practice management software is a set of services such as email, calendar appointments, billing and reporting integrated with a database management system that contains

the electronic medical records of all patients in the system. The conceptual model reveals the need for such a software system service in several activities in lung cancer screening. It is possible to infer the required feature for practice management software when every activity is hierarchically decomposed. Some of the features of the DBMS services inferred from the model are: ability to add, edit and integrate electronic medical records, along with the capabilities to send automated calendar reminders for the next appointment and store result letters and scanned images along with the medical records. The review of these features helps the management in selecting the right medical practice management software product when establishing a lung cancer screening program. Choosing a practice management software with pragmatic communication facilities helps in timely and efficient follow up of candidates, ensuring that fewer candidates are lost to the follow up process.

## 5.2 Simulation Model Applications

The simulation model is used to compared the quantitative effect of various input factors on the final quality outcomes of a typical lung cancer screening center. The input factors to be used were chosen by stakeholders from different aspects of different lung cancer screening programs in the Seattle area. Measuring What Matters methodology was used to get their assessments for the various input factors and the highest rated factors were used in the simulation model. The Monte Carlo simulation model was extended from the conceptual model developed in the previous section. The main data used for validation of the model was from the National Lung Cancer Screening Trial (NLST). In the comparison from the simulation experiments, it was observed that following a nodule management system like LUNGRADS can help achieve the best balance of the quality outcomes. In this study, using LUNGRADS as the nodule management system seemed to

increase the quit rates and decrease the radiation induced harms. Nodule Length variation contributes the highest to the false positive generation. Working towards decreasing that variability by establishing peer evaluation committees could significantly improve quality. Since smokers are more likely to quit when there is an abnormal finding in their LDCT scan, it is not possible to increase quit rates for smokers while decreasing false positives. Thus there should be increased focus on helping candidates quit smoking earlier on in the screening process. Though recall bias in smoking history affects false positive rate in a statistically significant way, the effect is quantitatively small when compared to other factors like nodule detection sensitivity and nodule length variation.

## 5.3 FUTURE RESEARCH WORK

Recall bias is only one way to quantify the difference in risk perceptions across different sections of the population. In future research studies, a better factor can be modeled for cancer risk perception than smoking history recall bias. The effect of complete SDM meetings can be appropriately studied then. In this study, since the effect of recall bias is low, the effect of incomplete SDM meetings on the quality outcomes is not statistically significant. From the conceptual study, Lung Cancer Screening coordinator availability can be gathered as one of the important factors in quality. However, the quantitative effect of lower number of coordinators or their lower time availability can be evaluated only in a discrete event simulation model. This can be a part of a future study that focusses on the design of a lung cancer screening program.

Evaluating the best case scenario with multiple quality output responses of interest involves an evaluation by the stakeholder on the Quality Adjusted Life Years of one factor versus another. For example, if Scenario 1 increases both false positive rate and early detection rate, how does 1% increase in false positive rate compare with a 0.2% decrease in early detections that would be

experienced by choosing another Scenario as the operating condition. Estimating QALY's for each quality outcome will facilitate this comparison. With the cost data for QALY's in lung cancer screening available in the work by Black, et al., (2014), it will be possible to estimate even the cost trade-offs for one experimental scenario in comparison with another. This kind of analysis can be used in cost effectiveness analysis for one quality intervention versus another.

# Chapter 6. APPENDIX

## 6.1 SIMULATION MODEL ASSUMPTIONS

This section elaborates some of the implicit modeling assumptions made while developing the Monte Carlo simulation model of a lung cancer screening program. It is widely stated in Section 4.4 that data from NLST has been used to model the probabilities for pulmonary nodule presence and length. This is because there is no existing model or study that predicts the presence of a pulmonary nodule in a candidate. The numerical values for these probabilities have been explicitly stated in this section.

### 6.1.1 *Cancer candidate: nodule length and prevalence*

The simulation model uses the cancer risk prediction model Tammemägi, Church et al., (2014) to assign whether candidate will develop cancer over the course of the screening process. Then nodule prevalence and nodule length distribution for candidates who have cancer is calculated from the NLST data on the above measures. This has been tabulated in Table 6-1.

Table 6-1 Nodule prevalence and length distribution for cancer candidates

| Nodule Size | Total | Cancer diagnosed | Cancer nodule probability | Cancer nodule cumulative probability |
|---|---|---|---|---|
| 0 | 14673 | 14 | | |
| 1 mm - 3mm | 4445 | 4 | 0.02 | 0.02 |
| 4mm | 990 | 4 | 0.02 | 0.03 |
| 5mm | 1475 | 3 | 0.01 | 0.04 |
| 6mm | 1204 | 10 | 0.04 | 0.08 |
| 7mm | 843 | 9 | 0.03 | 0.11 |
| 8mm | 568 | 7 | 0.03 | 0.14 |
| 9mm | 371 | 5 | 0.02 | 0.16 |
| 10-14mm | 906 | 58 | 0.22 | 0.38 |
| 15-19mm | 322 | 56 | 0.21 | 0.59 |
| 20-29mm | 218 | 58 | 0.22 | 0.81 |
| >= 30mm | 124 | 50 | 0.19 | 1.00 |

### 6.1.2 *Non-cancer candidate: nodule length and prevalence*

For candidates who do not have cancer, the data on nodule prevalence and length distributions is gathered from the NLST data and is used in the simulation model for candidates who do not have cancer as per the risk prediction model by Tammemägi, Church et al., (2014). The values of cumulative probability used in the simulation model are tabulated in Table 6-2.

Table 6-2 Nodule prevalence and length distribution for non-cancer candidates

| Nodule Size | Total | Non cancer candidates | Non cancer nodule length distribution | Non cancer nodule length cumulative probability |
|---|---|---|---|---|
| 0 | 14673 | 14659 | 0.57 | 0.57 |
| 1 mm - 3mm | 4445 | 4441 | 0.40 | 0.40 |
| 4mm | 990 | 986 | 0.09 | 0.48 |
| 5mm | 1475 | 1472 | 0.13 | 0.62 |
| 6mm | 1204 | 1194 | 0.11 | 0.72 |
| 7mm | 843 | 834 | 0.07 | 0.80 |
| 8mm | 568 | 561 | 0.05 | 0.85 |
| 9mm | 371 | 366 | 0.03 | 0.88 |
| 10-14mm | 906 | 848 | 0.08 | 0.96 |
| 15-19mm | 322 | 266 | 0.02 | 0.98 |
| 20-29mm | 218 | 160 | 0.01 | 0.99 |
| >= 30mm | 124 | 74 | 0.01 | 1.00 |

## 6.2 ADAPTING SIMIO

This section elaborates on the use of the discrete event simulation software, SIMIO, for the development of a Monte Carlo simulation model. This software was chosen in order to use an object oriented interface that enabled easier development of a state transition model. However, the use of a discrete event software for a Monte Carlo simulation requires that some of the queuing features be disabled. The general model structure in SIMIO and the measures taken to observe only the Monte Carlo simulation effects in the simulation model have been described in this section.

### 6.2.1 *Candidate generation and processing*

SIMIO uses the library object called “Source” to generate entities. The model consists of three sources represented three means of intake for candidates: internal,

external and PCP orders. Each of the 5 sub-processes of lung cancer screening are represented by the library object “Server” and the components of these sub-processes are modeled as a task sequence.

### 6.2.2 *DES to MC simulation*

The straight forward method to use a discrete event simulation tool for Monte Carlo simulation is to remove all queues and to increase the capacity of the objects to infinity so that entities don’t wait to be processed. In SIMIO this is accomplished by connecting the standard objects using a “Connector” as opposed to a “Time Path” that introduces time delays between processing and increasing all Server capacities to infinity. However, in terms of entity generation, generating more than 20000 entities at the same time creates an error in the software. In order to prevent this, there is an interarrival time between entities in the model. All other queues have been removed from the model. The drawback of this method is that the run time for the model is higher due to the number of events generated from the interarrival time. In addition to this, computational resources of the software are spent in automatic generation of statistics such as the time in system, utilization which have to be ignored. The advantage of using SIMIO is that the process of simulation experimentation is simplified due to the design of the software. Additionally, lesser time was spent in the design of the simulation model due to the object oriented interface of the software. In the future this model can easily be extended to a discrete event simulation model by simply enabling queues and adding finite capacities to the servers.

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