

SIMULATION METHODS AND SOFTWARE ENGINEERING PRINCIPLES FOR THE ANALYSIS OF COST-EFFECTIVE DISEASE PREVENTION

by

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Abstract

Simulation methods and software engineering principles for the analysis of cost-effective disease prevention, Arman Hamzehlou Kahrizi, Master of Science in Management (MScM), Ryerson University, 2020.

The Canadian healthcare system is among the most well-recognized healthcare systems in the world; however, it has been facing many challenges in several recent years.

In this paper, we plan to understand how Software Engineering and Software Reuse can help the Canadian Healthcare system become more efficient and effective in treating chronic illnesses and for this thesis primarily Type-2 Diabetes (T2D).

The investigators in this research, attempt to understand the current state of healthcare in Canada and then, with the help of Software Engineering and Software Reusability concepts, propose a simulation software package.

In the end, we used the developed software to simulate a randomized controlled trial (RCT) for testing the cost-effectiveness of two prevention programs of gym incentives and diabetes prevention program versus a control group not enrolled in any prevention program.

Acknowledgment

I want to express my gratitude toward my supervisor Dr. Aziz Guergachi, who made this research possible through his continuous guidance and advice. During our weekly meetings, there was always something to learn and explore. When I started working with Dr. Guergachi, I thought I knew a lot, and it took me almost a year to realize that I do not know enough in this field. He has always notified me of possible conference opportunities and workshops which could advance my knowledge and put me in a higher position.

I am thankful to Dr. Guergachi for opening my eyes to realize the challenges I should prepare for if I want to pursue a Ph.D., and I believe this thesis has been a significant step in the right direction to prepare for the academic world.

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List of Terms

Term	Short Explanation	Field
Quality-Adjusted Life-Years	A year of life adjusted for its quality. One year in perfect health is equal to one QALY unit whereas the value of a year in ill health discounts the QALY unit (William C. Shiell, 2018).	Healthcare
Quality-Adjusted Life Expectancy	Measures of the burden of disease. In other words, it measures the quantity and quality of years of life lived (NCCID, 2015).	Healthcare
Life Expectancy	The number of years a person would be expected to live, starting from birth (Statistics Canada, 2009).	Healthcare
Life-Years	The additional years of life lived as a result of an intervention (European Patients' Academy, 2015).	Healthcare
Class	A class is a set of objects sharing a common structure and a common behaviour manifested by the set of methods within that class (Selvarani, Gopalakrishnan Nair, Ramachandran, & Prasad, 2009).	Computer Science

List of Abbreviations

Abbreviation	Full Written Form	Context
ANN	Artificial Neural Network	Computer Science
AUSDRISK	Australian Type 2 Diabetes Risk	Healthcare
CBO	Coupling between Object Classes	Computer Science
CEA	Cost-Effectiveness Analysis	Economics
DIT	Depth of Inheritance Tree	Computer Science
GTA	Greater Toronto Area	Geography
IDE	Integrated Development Environment	Computer Science
LCOM	Lack of Cohesion of Methods	Computer Science
LE	Life Expectancy	Healthcare
LY	Life-Years	Healthcare
MVC	Model-View-Controller	Computer Science
MVVM	Model-View-ViewModel	Computer Science
NOC	Number of Children	Computer Science
OO	Object-Oriented	Computer Science
QALE	Quality-Adjusted Life Expectancy	Healthcare
QALY	Quality-Adjusted Life-Years	Healthcare
RFC	Responses for a Class	Computer Science
RCT	Randomized Controlled Trials	Medical Science
SE	Software Engineering	Computer Science
SPA	Single-Page Application	Computer Science
T2D	Type 2 Diabetes	Healthcare
WMC	Weighted Methods per Class	Computer Science

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Introduction

Trends in Canadian Healthcare System:

In recent years, the provincial governments within Canada have increased their healthcare expenditure, and currently, they are reaching their expenditure limits, and this inclination has been observable since the past five years (Friday, 2018).

The population of Canada is expected to increase over the next 25 years to range from 40.1 million to 47.7 million by the year 2036 (Statistics Canada, 2011).

The percentage of senior Canadians has been increasing since 1960, growing from 8% during the 1960's to 14% in 2009. According to all population projection scenarios, seniors Canadians are expected to account for 23% to 25% of the Canadian population by the year 2036, and 24% to 28% by the year 2061 (Statistics Canada, 2011).

While Canadians aged 65 and older form only 16% of Canada's population, they require approximately 46% of all public-sector health care budgets. Although seniors are a diverse group (Canadian Institute for Health Information, 2018).

In a report by the Canadian Institute for Health Information (2018), individual expenditure for senior Canadians increases with age. The average individual spending annually was CAD 6,607 for the age group of 65 to 69, CAD 8,495 for the age group of 70 to 74, CAD 11,570 for the age group of 75 to 79, and CAD 21,407 for the age group of 80 years old and older.

In 2016, approximately 63,459 Canadians sought non-emergency medical treatment outside Canada, of which 9,454 of them have been for general surgeries. This upsurge is considered an

immense jump from the year 2014 with only 52,513 Canadians having sought non-emergency medical treatments from abroad. There has been a 20.84% increase in just two years (Esmail, 2017)

Chronic Illnesses

Annually, 67% of all deaths are a result of one of the four primary chronic diseases: cancer, diabetes, cardiovascular and chronic respiratory diseases. Comparing with the given figure, more Canadian adults of working age between 34 to 64 years old are living with chronic conditions. Four out of five Canadians are at risk of chronic illness, while three out of five Canadians of twenty years of age or older already have a chronic disease (Public Health Agency of Canada, 2013).

The direct cost of chronic diseases forms 58% of the annual healthcare costs in Canada (Chronic Disease Prevention Alliance of Canada, 2017).

Type 2 Diabetes (T2D)

Amongst the four primary chronic diseases, since the year 2004 until 2008, a total of 120,050 Type-2 Diabetes (T2D) related deaths were documented in Canada. This number accounts for 10.6% of all documented deaths in Canada during that period. Remarkably, T2D was more than twice as likely to be an influential factor rather than being the primary cause of the deaths (Park & Peters, 2014).

Software Engineering and Software Reuse in Healthcare Systems

In healthcare settings, traditional software engineering, in most scenarios, has primarily focused on machinery rather than people, as it models the communication between people and machinery as a function of the machine. This concept is practical only if the software engineer has a profound understanding of the system functions. However, in healthcare software engineering where software and process structures are more complex, building a software system that acts as the central entity to control the system will potentially fail. Healthcare systems and software applications are successful only if they seamlessly support medical experts and integrate patients in all of the processes (Solanas, Weber, Bener, van der Linden, & Capilla, 2017).

In recent years, many communities and venues in the healthcare system have appeared as a result of software engineering (SE). The popularity of this topic has been negatively affected by dangerous failures of software-intensive networks which were designed and developed to address the challenges in the healthcare field (Weber-Jahnke, Price, & Williams, 2013).

The concept of software reuse can help make information technology products more efficient for clients and cheaper to develop. Software reuse is not limited to only the code aspects; it can be the reuse of existing documents, coding styles, components, models, patterns and knowledge (Macedo, Baranauskas, & Bulcão-Neto, 2018).

As discussed earlier, the Canadian population is progressively becoming older, and costs associated with healthcare will rise.

Literature review

This review will inspect the current knowledge of T2D, the prevention and treatment strategies for this disease and the economics and cost-effectiveness of the prevention programs. In this section review, we will also explore the literature of Software Engineering and Software Reuse. We will then use the reviewed research to identify an area in which Software Engineering and Software Reuse can help improve the state of healthcare in Canada in dealing with Type 2 Diabetes.

Type 2 Diabetes (T2D)

T2D is a chronic metabolic illness which leads to higher than average blood glucose (sugar) and is the most common type of diabetes. In type 2 diabetic individuals, the body is not able to consume the insulin properly (insulin resistance), and so to compensate for the absence of sugar due to body's inability to use it, the body starts to release more sugar into the bloodstream to respond to the shortage of sugar it is sensing. If untreated T2D can become a fully developed disease (Ministry of Health and Long-Term Care - Government of Ontario, 2012).

There is increasing evidence that the number of T2D incidences has significantly grown in recent years. This increase is affected by several factors such as obesity, sedentary lifestyle, and the fact that the population of Canada is getting older (Ministry of Health and Long-Term Care - Government of Ontario, 2012).

Diabetes can lead to countless severe health conditions and cause severe damage to body cells and organs. Diabetes may cause eye damage resulting in blindness. Type 2 Diabetes can also cause Kidney damage resulting in kidneys not being able to eliminate the waste, additional salt, and water from the body, and in such circumstances, the patient will require dialysis as it can be life-threatening health complication. Diabetes can also impair the heart tissues and muscles, which

leads to strokes and heart attack. There are many occurrences in which diabetes has led to infection and nerve damage beyond the point of recovery, and, in that case, amputation surgery is necessary for the patient to survive (Ministry of Health and Long-Term Care - Government of Ontario, 2012).

With the growing number of diabetes incidents, the cost of treatment also increases, and in several countries and regions around the world, it has become a priority to design a model which will help healthcare systems and clinics to better diagnose those individuals at risk of developing T2D. Most arguments against the prevention are that these prevention practices are not cost-effective.

Prior Prevention Studies:

A study was conducted in the Australian healthcare setting to compare the diabetes prevention outcomes and costs of screening strategies for type 2 diabetes prevention programs which included an oral glucose tolerance test. The study used the Australian type 2 diabetes risk assessment (AUSDRISK) tool and consisted of 4,864 participants from the “Australian Diabetes, Obesity, and Lifestyle” study 40 years old or older. The researchers determined that a blood test assessment is a vital step for registering participants in a diabetes prevention program. There will be unqualified patients who still proceed to diabetes (C. M. Y. Lee et al., 2018).

The study above proposes a cost-effective step to recognize individuals at risk of T2D. Though, it fails to address those cases that individuals were not eligible for the prevention program and continued to develop diabetes. From the social-value viewpoint, we need to implement a more competent system or algorithm that could reduce the possibilities of such oversights.

A study by Hoogendoorn, Rutten, Hart, de Wolf, & Vos (2019) for two Dutch primary healthcare centers measured the result of a supervised walking program in highly motivated individuals with type 2 diabetes or at risk of developing it. The study concluded that once a week, a rigorous and

supervised walking program, has beneficial results for the body, blood pressure, as well as the well-being of the individuals.

Anderson (2012) argues that lifestyle interventions in the United States for individuals of 65 years old and older are very cost-effective and inexpensive for a healthcare insurance payer. He similarly recommends that it is possible that nutrition therapy can be even more cost-effective, and that it brings monetary benefits to insurance companies by implementing such practices in healthcare settings. This practice is useful, and as we discussed earlier in the introduction of this proposal, medical expenditures increase with age for senior individuals 65 years old or older. The study expects that lifestyle interventions become increasingly cost-effective with the increment of age.

Another study revealed that intensive lifestyle modification for patients with impaired glucose tolerance is cost-saving and very cost-effective both short-run and long-run through a one-on-one counselling and consulting setting. The study finally argues that if clinicians can reduce the costs for lifestyle modification, then the intervention can be more cost-effective and can result in health improvement and efficiency of usage in healthcare resources (R. Li, Zhang, Barker, Chowdhury, & Zhang, 2010).

It is not possible to decrease the costs of lifestyle interventions across all programs since it highly varies on the type of intervention and by which healthcare setting it is being practiced. In such situations, clinicians and specialists will have to prescribe what is essential to get the best result for the intervention and not incur any additional costs.

Neumann et al. (2017) investigated the Type 2 Diabetes in a Swedish healthcare setting, and authors concluded that the prevention or the delaying of the inception of type 2 diabetes is cost-effective, and a small investment in lifestyle intervention can be very cost-effective. In this study

they used a Markov Model¹ with one treatment group receiving a lifestyle intervention and a control group receiving no lifestyle modification. A Monte Carlo simulation was later used to validate the result of the Markov model for different age groups and genders.

Among various types of interventions, Drug interventions are also a popular strategy. For example, “Atorvastatin” is a medication which is often prescribed to help lower cholesterol levels and avoid cardiovascular diseases (WebMD, 2019).

An investigation for Chinese healthcare settings argues that because diabetic individuals are likely to develop cardiovascular diseases, it is vital to lessen the risks of cardiovascular diseases in those individuals. The study determined that assumed a cost-effectiveness minimum of CAD 27,351 per QALY² gained, Statin³ treatment with Atorvastatin⁴ is 80% likely to be cost-effective for newly diagnosed individuals (T. Li, Wan, Ma, & Wu, 2018).

Herman (2015) investigated Type 2 Diabetes prevention cost-effectiveness through a simulated lifetime as well as a 10-year trial economic analysis. The author determined that lifestyle and metformin (a medicine to manage type 2 diabetes) interventions were cost-effective compared to no intervention at all. The study concluded that prevention programs for diabetes in high-risk individuals would bring substantial health benefits, have good value for money, and promote social value and well-being.

¹ Markov model is a stochastic model that uses probabilities specified by researchers to predict the next state of a set of data only by studying one last state of those data (Kaelbling, Littman, & Cassandra, 1998).

² Quality adjusted life year (QALY) is a year of life that is adjusted for its quality. This means that one year in perfect health is considered equal to 1.0 QALY while the value of a year in ill health is discounted (William C. Shiel, 2018).

³ A medication to help lower cholesterol levels in the blood (WebMD, 2019).

⁴ A medication to help lower cholesterol levels in the blood (WebMD, 2019).

During a study by Palmer & Tucker (2012) in Australia for high-risk patients treated with metformin or intensive lifestyle intervention, it was determined that from a 3rd-party payer standpoint, the metformin and lifestyle intervention approaches for T2D individuals is good value for money, and may lead to long-term cost-saving for the intensive lifestyle interventions.

Sussman, Kent, Nelson, & Hayward (2015) carried out a clinical investigation to determine whether there were individuals in the Diabetes Prevention Program (a clinical trial in the United States) who were likely benefit from drug or a lifestyle intervention program compared to the rest of the participants. The study determined that even though the Diabetes Prevention Program proposed that both lifestyle and drug intervention can prevent progression of diabetes, individuals who are likely to develop T2D at a younger age, benefited more from the lifestyle intervention and the prevention for these individuals is more valuable.

In a study by Herman (2017), the author concluded that lifestyle interventions for Type 2 Diabetes are useful for nearly all groups of diabetic individuals, and that it is associated with enhanced quality of life as it has fewer side-effects compared to medication approach, and that it is a cost-effective practice. The study additionally confirms that metformin⁵ is similarly beneficial, safe and cost-effective, particularly in younger and more overweight individuals who are pre-diabetic as well as women with past gestational diabetes.

This study is highlighting mainly on interventions aiming at individuals with the highest risk of diabetes, whereas individuals with lower risk cannot enroll in the intervention program. The drawback of such a tactic is that it will leave many individuals with the potential of disease progression out of the prevention program.

⁵ A medicine to manage type 2 diabetes

Up until now, the literature points to the exclusion of a cluster of patients to make a prevention program economical, while some studies proposed a rudimentary clinical follow-up with diabetic individuals with the assumption of patient adherence to the given tasks and practices. Finally, only a few papers and reports point to existing knowledge for the Canadian healthcare setting.

An Inspirational Model

Briggs, Claxton, & Sculpher (2006) performed a cost-effectiveness analysis of type 2 diabetes in which they accounted for a set of controlled and fixed variables such as probability ratios and costs of the symptom or symptomatic disease annually as well as independent variables such as the natural risk of death based on age.

Use of Markov Model

Briggs, Claxton, & Sculpher (2006) used those variables to develop a Markov Model and Monte Carlo Simulation that helped them examine the cost-effectiveness of a prevention program with a length of 45 (cycles) years, enrolling 1,000 diabetic individuals over the age of 55 in the United Kingdom.

Variables of the Study

Table 1 is a preview of all the variables used in the development of their model. These variables all have ranged from Min to Max, so the Monte Carlo simulation can use those ranges to generate a stochastic value and perform the simulation based on that.

Name	Mean	Min	Max	Variable description
cAsymp	500	250	750	Cost of one cycle in the asymptomatic disease state
cDeath	1000	500	1500	The cost associated with the transition to the dead state
cDrug	1000	800	1200	Cost of the drug for one cycle
tpDcm	0.15	0.10	0.20	Probability of dying from the disease in a single cycle
cProg	3000	2000	4000	Cost of one cycle in the progressive disease state
effect	50%	40%	60%	Effectiveness of drug in terms of reducing disease progression
tpProg	0.010	0.005	0.015	Coefficient of increase for probability of entering the progressive disease state
uAsymp	0.95	0.90	1.00	Quality of life weight for one cycle in the asymptomatic disease state

uProg	0.75	0.6	0.9	Quality of life weight for one cycle in the progressive disease state
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Table 1: Independent Variables Used in Markov Model to Examine the cost-effectiveness of Diabetes Prevention Program (Briggs et al., 2006)

Table 2 demonstrates a list of controlled variables Briggs et al. (2006) used in the development of their Markov Model.

cycle	Value	Length in years of one cycle
ini_age	55	The initial age at which patients are deemed to start the model
cDR	6%	The discount rate ⁶ for costs
oDR	6%	The discount rate for outcomes
nD35	0.0017	Natural death risk for over 35's
nD45	0.0044	Natural death risk for over 45's
nD55	0.0138	Natural death risk for over 55's
nD65	0.0379	Natural death risk for over 65's
nD75	0.0912	Natural death risk for over 75's
nD85	0.1958	Natural death risk for over 85's

Table 2: Controlled Variables Used in Markov Model to Examine the cost-effectiveness of Diabetes Prevention Program (Briggs et al., 2006)

⁶ Discount Rate: In economic evaluations we need to adjust the value of costs and benefits for the time at which they occur, this technique is also known as discounting. Effects of discounting on final outcomes may be substantial (Attema, Brouwer, & Claxton, 2018).

In Table 3, we have listed a list of all response variables Briggs et al. (2006) have used in their study.

Name	Description	Formula
Cycle	The current cycle/year	N/A
nDeath	Natural risk of death for individuals at their current age	This variable is computed manually using multiple conditional statements.
Asymp	The number of individuals being in the asymptomatic stage of the disease	$Asymp_{Previous} - Death - Prog$
Prog	The number of individuals being in the progressive state of the disease	$Prog_{Previous} \times (1 - tpDcm - nDeath_{Previous}) + Asymp_{Previous} \times tpProg \times Cycle$
Death	The total number of deaths as of the current cycle	$Previous_{Death} + Prog_{Previous} \times tpDcm + (Asymp_{Previous} + Prog_{Previous}) \times Cycle_{Previous}$
LE	Total number of years all individuals in the program are expected to live	$Asymp + Prog$
QALE	Total units of quality of life for the additional life-years gained due to intervention	$Asymp \times uAsymp + Prog \times uProg$
LY	Total Additional number of life-years individuals live as a result of the intervention	$\frac{Asymp + Prog}{(1 + oDR)^{Cycle}}$
QALY	Total units of disease burden, including both the quality and the quantity of life, lived across all individuals	$\frac{Asymp \times uAsymp \times Prog \times uProg}{(1 + oDR)^{Cycle}}$
StateCost	Cost of staying in the current state of the disease for all individuals	$\frac{Asymp \times cAsymp + Prog \times cProg}{(1 + cDR)^{Cycle}}$
TransCost	Cost of transitioning to another state of the disease for all individuals.	$\frac{PreviousProg \times tpDcm \times cDeath}{(1 + cDR)^{Cycle}}$
TotalCost	The total cost of staying in the current state of the disease plus the cost of transitioning to another state of the disease	$StateCost + TransCost$

Table 3 Response Variables Used in Markov Model to Examine the cost-effectiveness of Diabetes Prevention Program (Briggs et al., 2006)

Briggs et al. (2006) have confirmed the robustness of the model output through a Monte Carlo Simulation. Monte Carlo Simulation uses the Max and Min values of each independent variable to generate a stochastic value, which then can be processed by a Markov Model in each cycle of simulation.

In this thesis, we plan to use the logic defined in the above paper and model to create a simulation package to use in the software we have specially developed which allows to dynamically run and analyze as many scenarios as possible.

There are certain variables which remain the same for our paper, while several other variables must be updated to match the Canadian settings. Among the variables which stay the same are the discount rates and natural death risk base on the age group of individuals.

Variables such as the cost of the drug or being in an asymptomatic/progressive state of the diabetes type 2 disease for one year and costs associated with death of a diabetic type 2 individual need to be updated and adjusted to Canadian prices and healthcare settings.

Cost of Diabetes in Canada

A.1.1.1 Drug Cost

According to a report by Canadian Agency for Drugs and Technologies in Health (2018), the price of a drug called Metformin, that individuals in an asymptomatic state need to take in order to manage their diabetes type 2 symptoms is CAD 0.29 per day for a 2,000mg dosage which is the average required dose for a diabetic individual. Please note that in this report, the average weight of individuals was 87 kilograms.

The above information allows us to compute the annual expenses associated with metformin each year for individuals not in a progressive state of the disease. The annual cost of the medication is as follow:

$$\text{CAD } 0.29 \times (\text{number of days a year})365 = \text{CAD } 105.85 \text{ per year}$$

A.1.1.2 Cost of the Disease in Asymptomatic State

Type 2 Diabetes can be either in an asymptomatic state or progressive state. According to Bilandzic & Rosella (2017), we expect the costs of being in an asymptomatic state on average to be CAD 1,240 per year.

A.1.1.3 Cost of the Disease in Acute/Progressive State

Nevertheless, the costs associated with being in a progressive state of diabetes is much higher. According to an official report released by the Canadian Institute for Health Information (2007) on the average cost of acute/progressive diabetes type 2 for a Canadian is CAD 3,661 annually. After inflation adjusting this amount, it becomes a whopping CAD 4,478.19, which is more than three times more expensive compared to an asymptomatic stage of the disease.

A.1.1.4 Cost of Death

A recent study by Tanuseputro et al. (2015) argues that for each individual the average cost of the health care in the last year of life is CAD 53,661 and this number jumps to reach a CAD 14,000 in the final month of their life.

A.1.1.5 The Inflation Adjusted Costs

Using the online inflation rate calculator by the Bank of Canada (2019), we can adjust all the above values for the annual inflation rate.

Description	Original Cost	Year Obtained	Inflation Rate Acquired from the Bank of Canada (2019-08-27)	Inflation Adjusted Cost
Cost of Metformin Drug for one year	CAD 105.85	2018	%2.01	CAD 107.98
Cost of being in the Progressive State of T2D for one year	CAD 3,661	2007	%22.32	CAD 4,478.19
Cost of being in the Asymptomatic State of T2D ⁷ for one year	CAD 1,240	2017	%5.06	CAD 1,302.76
Average Costs 1 Year Before Death	CAD 53,661	2015	%7.62	CAD 57,749.86

Table 4 Inflation Adjusted Costs associated with Type 2 Diabetes annually for a Canadian

Software Reuse

Software reuse is any use of previously developed software's life cycle such as product line requirements, functions, architecture, design patterns and codes to develop new software. Software developers should plan for reuse from the conception and initiation phases of software development (RADU, 2018).

Software reuse is a systematic practice of developing software from a set of building blocks so that similarities in requirements and architecture between software applications can be exploited to accomplish considerable benefits in productivity, quality and business performance (Morisio, Ezran, & Tully, 2002).

⁷ Type 2 diabetes

Software reuse must not be confused with Software Reusability. Reusing any existing or accessibly available software components to save time, computation, financial and human resources are called software reusability (Padhy, Singh, & Satapathy, 2018).

To avoid system abandonment or code rot⁸, Software developers and engineers need to develop software systems with extensibility and reusability in mind. We define extensibility as the ability of a software system to be extended with new functionality at minimal or no effects on its internal structure. Extensibility ultimately promotes reusability as they have many features in common with each other (Johansson, Löfgren, & Olsson, 2009).

Advantages

Software reuse promotes dependability and effective use of specialist and creates standard compliance. In software reuse, we can implement more technology and tools on the same product domain (Huzumi, Mao, Kasi, & Zhe, 2008).

Software Reuse allows the development of software frameworks as an abstraction of functionalities to build and deploy applications. Software frameworks are reusable designs of all or part of a software system. We describe Software framework as a set of codes, libraries, tools, APIs, and primarily abstract classes and the way these classes communicate with one another. Consequently, the key objective of a software framework is to allow the production of new software more efficiently through reuse (Macedo et al., 2018).

⁸ Code Rot happens when software system ultimately becomes abandoned as the system is too hard to maintain and extend (Johansson et al., 2009).

Disadvantages

Padhy et al. (2018) argue that Software ageing not only affects software reusability but also is a symptom of extreme reuse in the software environment, and it happens when there is excess reusability. There is a threshold value, which is one of the measurements of the reusability estimation level and exceeding that value will cause the software system to crash or fail. There are two types of software ageing:

A.1.1.6 Lack of Movement

Lack of movement happens when product's owners fail to modify it to meet the changing needs (Padhy et al., 2018).

A.1.1.7 Ignorant Surgery

In this type of software ageing, some changes are made to the system, introducing software faults, also known as software ageing. These faults could be component, OS (operating system) or application failure. In many cases, software ageing occurs as a result of excessive reuse, which is also known as a software fault. Failure will result in flawed services such as stopping, system crashes or incorrect results (Padhy et al., 2018).

Software Reuse Measurements

Some techniques can help categorize the reusability factor and help the choice of parameters and metrics related to software reusability. These techniques are evolutionary computing based ANNs for software reusability prediction, support vector machines, neural networks, genetic algorithms, fuzzy logic (Padhy et al., 2018).

Types of Software Reuse

Depending on the type of components we are reusing, the type of reuse is different as well. We can categorize components into a Black box, White box and Glass box components (Mijač & Stapic, 2015).

A.1.1.8 Black box Components and Black box Reuse

In Black box reuse, the components are reused without any changes typically because the component is a Black box component (RADU, 2018).

The external user of a Black box component can only see the interface of the component, while the implementation details of the component and its interfaces remain hidden (Mijač & Stapic, 2015).

A.1.1.9 White box Components and White box Reuse

In White box reuse, the components must be modified based on the new requirements. The components to be reused could be libraries, software specifications, software design, interfaces, prototypes, planning, documentation, frameworks, test cases or templates. Some components are also interrelated. For instance, the reuse of source components indirectly involves the reuse of analysis and design stages (RADU, 2018).

White-box components allow an external user to view the internal assembly of the component, with the difference that the white box component allows users to modify the source code (Mijač & Stapic, 2015).

A.1.1.10 Glass-box Components and Glass-Box Reuse

Very similar to Whitebox reuse, in Glass-box reuse, software developers reuse Glass-Box components which cannot be modified; however, the user can see the internal structure of the component to develop software applications (Mijač & Stapic, 2015).

Knowledge Gap

The prevention programs can have multiple combinations of strategies and practices to achieve the desired objective by identifying and connecting with individuals at risk of T2D. This task will require human resources such as doctors, nurses, and facilitators, and there is a threshold which we must consider if we plan to keep the prevention more cost-effective compared to the treatment plan.

The implementation of a T2D prevention program in a real-world scenario is linked to high costs and could prevent only a few cases of diabetes, Therefore, in a cost-effectiveness analysis, we must also consider costs such as staff training, intervention participation and adherence (Icks et al., 2007).

A clinical trial was performed in the United States to understand the threshold at which lifestyle interventions for people aged 65 years and older become cost-effective (Anderson, 2012). It concluded that in a perfect case, for a 3-year prevention program to be cost-effective 212,225 cases of diabetes would need to be prevented and for a 10-year program to be cost-effective, up to 452,303 cases would need to be prevented. The study determined that the program is likely to have saved costs and increased health among women in two areas, but in the other three study groups, the changes in costs and QALYs (quality-adjusted life-years) were more unfavorable compared to the control group.

Schwarz et al. (2008) argued that the development of effective screening and core intervention plans for the prevention of the T2D would significantly improve the ability of healthcare experts to swiftly respond to the drastic increase of T2D and its burden to the healthcare system.

For a healthcare prevention plan to become cost-effective, there must be a behavioural change strategy, and the absence of an intensive provisioned individualized delivery will only resemble the control group interventions used by the Randomized controlled trials, and it cannot be valid (Baker, Simpson, Lloyd, Bauman, & Singh, 2011).

Passey et al. (2012) suggested that prevention of diabetes with metformin or lifestyle interventions will significantly benefit the labour force and increases incomes for individuals as these individuals will remain healthy for longer and can continue with their daily tasks.

The first challenge is that most of the papers in the field of healthcare and diabetes have not targeted Canada for their study, which by itself is a knowledge gap that we can address. The number of studies conducted in Canadian health system settings is not significant.

Currently and based on the literature reviewed in the earlier part of this thesis, the translation of the outcomes from international studies into real-world within Canadian settings can be very challenging.

Research Question

Throughout this investigation, we have documented a knowledge gap. We realize that it is naïve to claim that we can fill this knowledge gap on our own through this paper. Nevertheless, we recognize the opportunity to help contribute to filling this gap using information technology, software engineering and software reusability.

Currently, the challenge for preventing chronic diseases and for our investigation, T2D, is that there are few studies in this field for Canadian settings. Other international studies also confirm that prevention cannot be entirely cost-effective compared to treatment. This concern brings us to the following research question:

How can Information Technology help in healthcare to develop cost-effective prevention strategies for Type-2 Diabetes?

As the primary objective of this investigation, we attempt to examine if we can engineer a reusable software model which can facilitate the researchers in the future studies in the field of health economics or not.

Nevertheless, even if we can design such a model, it still is vital to make sure that future developers and engineers can extend and reuse parts of it, and as a result we need to make sure that our software is reusable, And for this purpose we will use the software reusability metrics we introduced in the methodologies section.

After the tests of reusability, we will use the software engineered to execute an RCT and compare the cost-effectiveness of two prevention programs of “Gym Incentives” and “Drug Group” with the control group not enrolled in any prevention program within the Canadian settings.

Software Proposal

To this day, there have been various reports and papers in different countries and regions for healthcare programs' effectiveness. In each case, when the researchers and scientists attempt to study a specific aspect of healthcare. They must perform a set of tasks, which are always the same. For instance, the use of a Markov Model and Monte Carlo simulation is widespread in healthcare and medical field for managerial decision making.

Variables and their associated values in each study are different but the way a concept and model work, for instance, Markov Model, remains the same. In the field of healthcare, every study that relies on a Markov Model or Monte Carlo simulation, or any other mathematical methods, some steps are entirely repetitive, among them the development of methods and algorithms required to perform the calculations.

In this thesis, we propose the development of an open-source software package for the Canadian healthcare system, specialized in hosting different mathematical models and algorithms that can facilitate the way scientists conduct their studies. This Simulation Software can be hosted online and accessed online by all researchers worldwide.

As we discussed in the earlier part of this research, Software Reusability is an essential part of today's software engineering era, and for this reason, we will develop the proposed software with software reusability in mind to allow for future extension of the software package.

Methodologies

There are several models and theories which help establish the grounds of this paper. This project will profoundly focus on mathematical calculations to forecast a future we need to be aware of far ahead of the time. Majority of the models and theories that we must benefit from are those of artificial intelligence area. Some of these models are as following:

Software Reusability Metrics

In the preview chapter, we proposed an open-source simulation software application. According to the types of software component we discussed earlier in literature review, any software component that can be internally investigated and modified by the developer is a White Box component, and as a result, we must evaluate our simulation software with the White Box reusability metrics.

C.K Metrics:

Chidamber & Kemerer (1994) conducted a study and proposed software reusability metrics that are still in use and most elements of it remain accessible to this day. The authors proposed a software reusability metrics call C.K metrics and over the years there have been many reviews and adjustments over how the metrics work, and it has incorporated into many code metrics software suites such as NDepend v.2019 (ZEN PROGRAM LTD, 2019).

The following metrics are part of the proposed model:

A.1.1.11 Weighted Methods per Class (WMC)

In a more recent study, H.M & Nandakumar (2016) define WMC as the sum of complexity in a class. In whole, it signifies the complexity of the software classes and this measure can be used to identify the development and maintenance effort needed for the classes across the application.

Selvarani et al. (2009) define a good WMC value to be between 0 to 20 thresholds, a moderate to high WMC to be between 20 to 100, and any WMC above 100 requires investigation as it signifies a high-class complexity. WMC is a class⁹ level metric, and its value shows the classes and the relative number of methods. Classes with large numbers of methods are possibly more application-specific, and less likely to be reusable.

A.1.1.12 Responses for a Class (RFC)

H.M & Nandakumar (2016) explain that RFC represents the number of growing and called methods within a set as a response to a message sent to an object performing a specific task.

The RFC is the set of internal and external methods which we can invoke in response to a message sent to an object of the class or a response to a message sent by a method in that class. RFC and complexity are directly related, and as the RFC increases, so will the ability to test, debug and maintain a class. For calculate on of RFC, inherited methods count, while overridden methods do not (Selvarani et al., 2009).

⁹ A class is a set of objects sharing a common structure and a common behaviour manifested by the set of methods within that class (Selvarani et al., 2009).

A.1.1.13 Depth of Inheritance Tree (DIT)

DIT is a frequently used metric in evaluating maintainability and reusability by estimating the extent of depth in the hierarchy of the classes (H.M & Nandakumar, 2016).

This metric primarily evaluates efficiency and reuse but also relates to understandability and testability. The deeper the hierarchy of the class, the greater the number of methods it is likely to inherit become. The more methods a class inherits, the more complex it becomes, and it is difficult to predict its behaviour. Deeper hierarchies increase design complexity as well as the potential for reuse of inherited methods (Selvarani et al., 2009).

According to CachéQuality (2019), a DIT value of zero signifies a root class without any reuse or inheritance while a value of 2 or 3 signifies a higher degree of reuse.

A.1.1.14 Number of Children (NOC)

NOC measures the number of classes associated with a specific class through inheritance relationship. A class with many children suggests a bad class with bad design (H.M & Nandakumar, 2016).

The more children a class has, the amount of reuse and the likelihood of improper parent abstraction increases, and it may be a sign of subclassing misuse (Selvarani et al., 2009).

A.1.1.15 Coupling between Object Classes (CBO)

CBO is the number of all other sets of classes for which a class couples with, and it is helpful in determining the complexity of the system during testing and reusability phases (H.M & Nandakumar, 2016).

Selvarani et al. (2009) define CBO as the strength of association established by a connection from one entity to another. The higher the value of this metric, the more sensitive the entities become to changes in other parts of the design; maintenance is, therefore, more difficult. For reusability, this metric should remain low.

A.1.1.16 Lack of Cohesion of Methods (LCOM)

Cohesion is the degree to which methods within a class are related to one another and work together to provide a well-bounded behaviour. An Effective object-oriented design maximizes cohesion as it promotes encapsulation. We can subdivide classes with low cohesion into subclasses with increased cohesion or increase the degree of similarity between their objects and properties. The more cohesive a design is, the more complex and reusable it can become (Selvarani et al., 2009).

Markov Model

Markov Model is a stochastic technique developed for randomly changing the system. This model is also known as a memoryless method that does not account for the previous states of the system and uses only the current state and one previous state to forecast the future states. It compares at least two different models, also known as groups in the same cycle length. The groups can be treatment and control groups (Kaelbling, Littman, & Cassandra, 1998).

In this paper we will use Markov Model as a base for the development of our software package as this will enable us to see the value and costs associated with each approach as see which approach is more reasonable and why.

Monte Carlo Simulation

There are situations where we cannot rely on approximate values, and we need precise values to make a managerial decision. Monte Carlo simulation will enable us to get all the possible exact results and outcomes of a specific model (Walter & Barkema, 2015).

These simulations and techniques are often used in artificial intelligence to predict accurate outcomes when there are multiple unknown variables through repeated random sampling.

We will use this model to confirm our results further to calculate the expected costs of treatment and number of T2D cases that we will have to prevent the prevention program to be more cost-effective.

Cost-effectiveness analysis Theory (CEA)

In a healthcare setting, the cost-effectiveness analysis will compare the expenses and output of two or more programs or initiatives that perform the same task (Bang & Zhao, 2014).

We can use this theory to answer questions such as “Which method is the most cost-effective?” or “What is the most cost-effective approach?”. We often express CEA as a ratio. The denominator is going to be units of a measure we gain as a result of the investment, and we are willing to compare that gain of units across two or more scenarios. The numerator in healthcare scenarios remains to be the costs associated with each program or investment (Bleichrodt & Quiggin, 1999).

The following formula demonstrates the calculation of the CEA:

$$\frac{\textit{Cost of the intervention}}{\textit{Quality – Adjusted Life Years}}$$

Rational Choice Theory

Rational choice theory is the outline to produce models of social and economic behaviour. This theory assumes that social behaviour is an accumulation of individuals' choices who have options to choose and make decisions based on those options (Allingham, 2002).

This model will allow us to understand why some people even though informed of their health conditions, are not participating in the prevention programs. This model will allow health care centers to address those barriers and issues to make that specific program more efficient. It is essential to mention that for a prevention program to be effective, attendance and participation of all sides is a crucial element to give us an accurate output.

Development Tools and Design Patterns

Microsoft SQL Server Express

Microsoft SQL Server Express is a relational database management system that is free to download, distribute and use. We will use this software package to design a database for our software package to store the information of the study models and their parameters.

Microsoft Visual Studio 2019 Community Edition

A software development environment developed and released by Microsoft Corporation. We will use this IDE to develop the proposed simulation software using the ASP.NET Core MVC and C# programming language (Microsoft Corporation, 2019b).

A.1.1.17 ASP.NET Core MVC

The ASP.NET Core MVC is an open-source framework optimized for use with ASP.NET Core. ASP.NET Core MVC provides a patterns-based way to build responsive web applications that promote the separation of concerns (Microsoft Corporation, 2019a).

NDepend 2019 Extension for Visual Studio 2019

NDepend is code metrics tools which we will use to calculate the C.K metrics of the software developed as part of this thesis (ZEN PROGRAM LTD, 2019).

NodeJs

An open-source, cross-platform and JavaScript run-time environment which promotes reusability and scalability of web applications and is highly adaptable to MVC and MVVM design patterns (Node.js Foundation, 2019).

React

React is a JavaScript library developed by Facebook and is used in developing web user interfaces. It is primarily used to develop single-page applications (SPA) as it promotes a highly interactive interface (Facebook Inc., 2019).

Redux

Redux is a state management JavaScript library which we will incorporate into our application and works seamlessly with React library to improve the state management of our application (Dan Abramov, 2015).

MVC Design Pattern

The Model-View-Controller (MVC) is an architectural pattern that separates an application into three groups of components: Models, Views, and Controllers. MVC pattern promotes the concept of separation of concerns (Microsoft Corporation, 2019a).

First Software Milestone

The first developed software milestone consists of several sections that help better define the aspects of a study and begin examining the effectiveness of it throughout the given cycles or years.

Home page

Home page, as the name implies, will be the first section the user will view upon accessing the application.

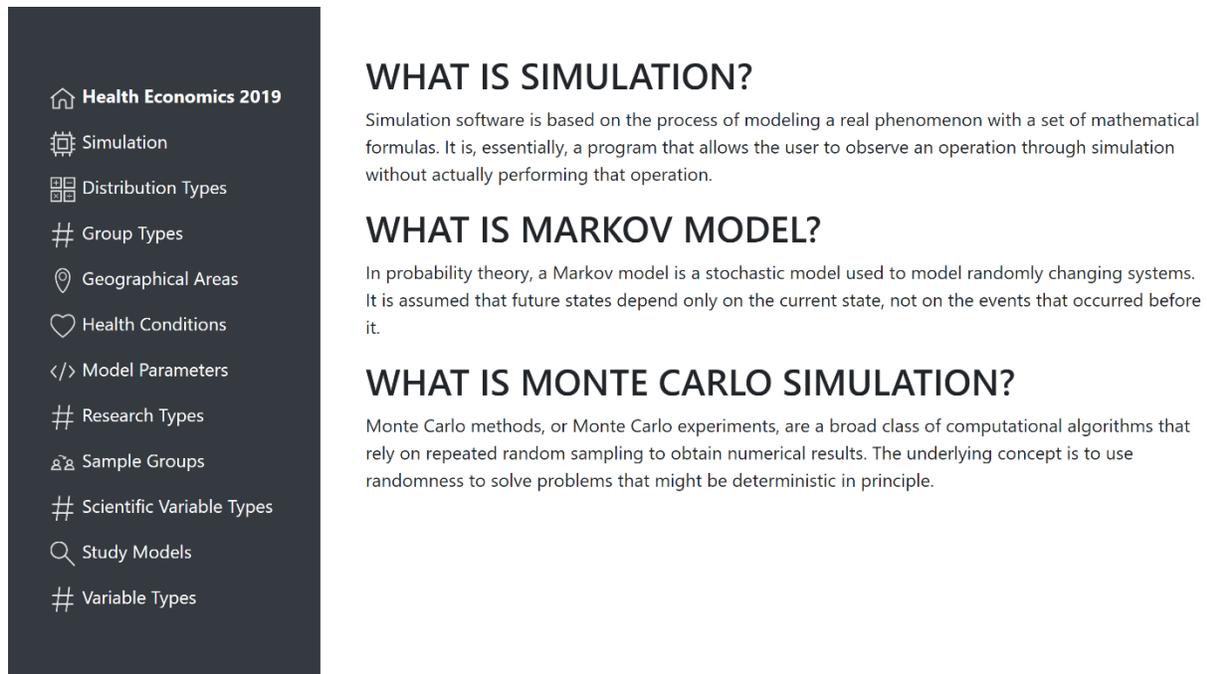
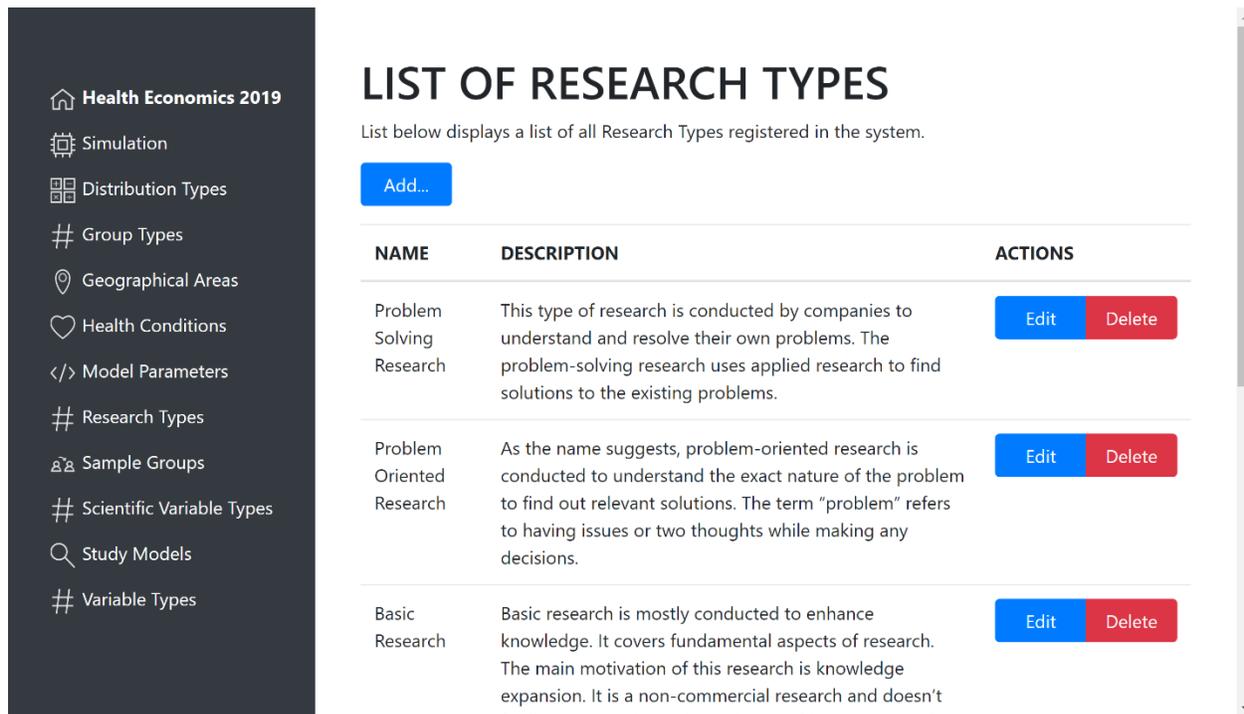


Figure 1 Simulation Software - Home Section

Research Types

We define Research Types to give a bit of clarity to the project, and as of now, they do not affect the calculations. This section allows the researchers to categorize their study models for better understanding.



The screenshot displays the 'LIST OF RESEARCH TYPES' section. On the left is a dark sidebar with navigation icons and labels: Home (Health Economics 2019), Simulation, Distribution Types, Group Types, Geographical Areas, Health Conditions, Model Parameters, Research Types, Sample Groups, Scientific Variable Types, Study Models, and Variable Types. The main content area has the title 'LIST OF RESEARCH TYPES' and a sub-header 'List below displays a list of all Research Types registered in the system.' Below this is an 'Add...' button. A table lists three research types, each with 'Edit' and 'Delete' buttons.

NAME	DESCRIPTION	ACTIONS
Problem Solving Research	This type of research is conducted by companies to understand and resolve their own problems. The problem-solving research uses applied research to find solutions to the existing problems.	Edit Delete
Problem Oriented Research	As the name suggests, problem-oriented research is conducted to understand the exact nature of the problem to find out relevant solutions. The term "problem" refers to having issues or two thoughts while making any decisions.	Edit Delete
Basic Research	Basic research is mostly conducted to enhance knowledge. It covers fundamental aspects of research. The main motivation of this research is knowledge expansion. It is a non-commercial research and doesn't	Edit Delete

Figure 2 Simulation Software - Research Types Section

Study Models

In Study Models section, we will get to introduce the nature of the study we are planning to conduct, by defining its sample group and number of cycles and its parameters.

Health Economics 2019

Simulation

Distribution Types

Group Types

Geographical Areas

Health Conditions

Model Parameters

Research Types

Sample Groups

Scientific Variable Types

Study Models

Variable Types

LIST OF STUDY MODELS

List below displays a list of all Study Models registered in the system.

[Add...](#)

NAME	RESEARCHABSTRACT	CYCLES	ACTIONS
Diabetes Intervention Study in GTA	Objective In a randomized 5-yr multi-intervention trial, we tested the efficacy of intensified health education (IHE) in improving metabolic control and reducing the level of coronary risk factors and incidence of ischemic heart disease (IHD).	45	<div style="display: flex; gap: 5px;"> <div style="background-color: #007bff; color: white; padding: 2px 10px; border-radius: 3px;">Edit</div> <div style="background-color: #dc3545; color: white; padding: 2px 10px; border-radius: 3px;">Delete</div> </div>

Figure 3 Simulation Software - Study Models Section

Group Types

For the nature of this application, we need to define the types of sample groups. Sample groups can be either control or treatment.

LIST OF GROUP TYPES

List below displays a list of all Group Types registered in the system.

[Add...](#)

NAME	DESCRIPTION	ACTIONS
Control Group	A control group is used as a baseline measure. The control group is identical to all other items or subjects that you are examining with the exception that it does not receive the treatment or the experimental manipulation that the treatment group receives. For example, when examining test tubes for catalytic reactions of enzymes when added to a specific substrate, the control test tube would be identical to all other test tubes with the exception of lacking the enzyme.	Edit Delete
Treatment Group	The treatment group is the item or subject that is manipulated. In our example, all other test tubes containing enzyme would be part of the treatment group.	Edit Delete

Figure 4 Simulation Software - Group Types Section

Sample Groups

In this section, we define the actual sample groups, along with their descript. Please note that because the population of samples must be the same, samples within a study model will have the same number for population size inherited from their parent study model.

LIST OF SAMPLE GROUPS

List below displays a list of all Sample Groups registered in the system.

[Add...](#)

NAME	ACTIONS
Gym Group	Edit Delete
Control Group	Edit Delete
Drug Group	Edit Delete

Figure 5 Simulation Software - Sample Groups Section

Geographical Locations

The geographical area is implemented as part of the plans for this research when we introduce more variables into the studies we conduct. As of now, this section only helps the completeness of the study model and does not affect the calculations.

LIST OF GEOGRAPHICAL AREAS

List below displays a list of all Geographical Areas registered in the system.

[Add...](#)

PROVINCE	NAME	COUNTRY	ACTIONS
Ontario	Belleville	Canada	Edit Delete
Ontario	Markham	Canada	Edit Delete
Ontario	Brampton	Canada	Edit Delete
Ontario	Mississauga	Canada	Edit Delete
Ontario	Ottawa (national capital)	Canada	Edit Delete
Ontario	Toronto (provincial capital)	Canada	Edit Delete

Figure 6 Simulation Software - Geographical Locations Section

Health Conditions

This section will help the researcher define the health condition they plan to study. If they need to edit or remove a specific health condition, it is effortlessly accessible through the command buttons defined within the page. In Figure 7, we demonstrate a preview of the discussed section.

Health Economics 2019

- Simulation
- Distribution Types
- Group Types
- Geographical Areas
- Health Conditions
- Model Parameters
- Research Types
- Sample Groups
- Scientific Variable Types
- Study Models
- Variable Types

LIST OF HEALTH CONDITIONS

List below displays a list of all Health Conditions registered in the system.

[Add...](#)

NAME	DESCRIPTION	ACTIONS
Arthritis	Arthritis is inflammation or degeneration of one or more joints. A joint is the area where 2 bones meet. There are more than 100 different types of arthritis.	Edit Delete
Asthma	Asthma is a disease that causes the airways of the lungs to swell and narrow. It leads to wheezing, shortness of breath, chest tightness, and coughing.	Edit Delete
Chronic obstructive pulmonary disease (COPD)	Chronic obstructive pulmonary disease (COPD) is a common lung disease. Having COPD makes it hard to breathe.	Edit Delete
Cancer	Cancer is the uncontrolled growth of abnormal cells in the	Edit Delete

Figure 7 Simulation Software - Health Conditions Section

Distribution Types

The section “Distribution types” allows the researchers to define the list of probability distributions which they are going to use during the research. For the scope of this study, we have limited these definitions to Inverse Normal Distribution and Inverse Beta Distribution used in the calculation of our Markov Model. Figure 8 displays a preview of this section:

Health Economics 2019

- Simulation
- Distribution Types
- Group Types
- Geographical Areas
- Health Conditions
- Model Parameters
- Research Types
- Sample Groups
- Scientific Variable Types
- Study Models
- Variable Types

LIST OF DISTRIBUTION TYPES

List below displays a list of all Distribution Types registered in the system.

Add...

NAME	DESCRIPTION	ACTIONS
None	None.	Edit Delete
Normal inverse cumulative distribution	The inverse distribution function for continuous variables $F_x^{-1}(\alpha)$ is the inverse of the cumulative distribution function (CDF). In other words, it's simply the distribution function $F_x(x)$ inverted. The CDF shows the probability a random variable X is found at a value equal to or less than a certain x .	Edit Delete
Normal cumulative	In probability theory, the normal (or Gaussian or Gauss or Laplace-Gauss) distribution is a very common continuous	Edit Delete

Figure 8 Simulation Software - Distribution Types Section

Model Parameters

The Model Parameters section in the primary hub to define all the model parameters, overall sample groups. Using this panel, we can define the type of parameter, describe how it works or define a formula for it.

🏠 Health Economics 2019

🔧 Simulation

📊 Distribution Types

Group Types

📍 Geographical Areas

❤️ Health Conditions

</> Model Parameters

Research Types

👤 Sample Groups

Scientific Variable Types

🔍 Study Models

Variable Types

LIST OF MODEL PARAMETERS

List below displays a list of all Model Parameters registered in the system.

Add...

NAME	DESCRIPTION	ACTIONS
Prog	Progressive disease or progressive illness is a disease or physical ailment whose course in most cases is the worsening, growth, or spread of the disease. This may happen until death, serious debility, or organ failure occurs. Some progressive diseases can be halted and reversed by treatment.	Edit Delete
DEATH_RISK	Natural death risk for under 35's (from standard life-tables)	Edit Delete
Population	The sample size.	Edit Delete
Prog	Progressive disease or progressive illness is a disease or physical ailment whose course in most cases is the worsenina. arrowth. or spread of the disease. This mav	Edit Delete

Figure 9 Simulation Software - Model Parameters Section

Variable Types

This section allows you to define the variable types. A variable type helps the simulation software to use the proper mathematical methods such as distribution types when computing the models.

🏠 Health Economics 2019

🔧 Simulation

📊 Distribution Types

Group Types

📍 Geographical Areas

❤️ Health Conditions

</> Model Parameters

Research Types

🗂️ Sample Groups

Scientific Variable Types

🔍 Study Models

Variable Types

LIST OF VARIABLE TYPES

List below displays a list of all Variable Types registered in the system.

Add...

NAME	ACTIONS
Range	<div style="display: inline-block; background-color: #3498db; color: white; padding: 2px 10px; margin-right: 5px;">Edit</div> <div style="display: inline-block; background-color: #e74c3c; color: white; padding: 2px 10px;">Delete</div>
Decimal	<div style="display: inline-block; background-color: #3498db; color: white; padding: 2px 10px; margin-right: 5px;">Edit</div> <div style="display: inline-block; background-color: #e74c3c; color: white; padding: 2px 10px;">Delete</div>
Percentage	<div style="display: inline-block; background-color: #3498db; color: white; padding: 2px 10px; margin-right: 5px;">Edit</div> <div style="display: inline-block; background-color: #e74c3c; color: white; padding: 2px 10px;">Delete</div>
Currency	<div style="display: inline-block; background-color: #3498db; color: white; padding: 2px 10px; margin-right: 5px;">Edit</div> <div style="display: inline-block; background-color: #e74c3c; color: white; padding: 2px 10px;">Delete</div>
Integer	<div style="display: inline-block; background-color: #3498db; color: white; padding: 2px 10px; margin-right: 5px;">Edit</div> <div style="display: inline-block; background-color: #e74c3c; color: white; padding: 2px 10px;">Delete</div>
String	<div style="display: inline-block; background-color: #3498db; color: white; padding: 2px 10px; margin-right: 5px;">Edit</div> <div style="display: inline-block; background-color: #e74c3c; color: white; padding: 2px 10px;">Delete</div>

Figure 10 Simulation Software - Variable Types Section

Scientific Variable Types

Define the correct scientific variable types is vital as the simulation software categorizes the parameters based on this factor. Scientific variable types can be dependent, independent, controlled or extraneous.

🏠 Health Economics 2019

🔧 Simulation

📊 Distribution Types

Group Types

📍 Geographical Areas

❤️ Health Conditions

</> Model Parameters

Research Types

👤 Sample Groups

Scientific Variable Types

🔍 Study Models

Variable Types

LIST OF SCIENTIFIC VARIABLE TYPES

List below displays a list of all Scientific Variable Types registered in the system.

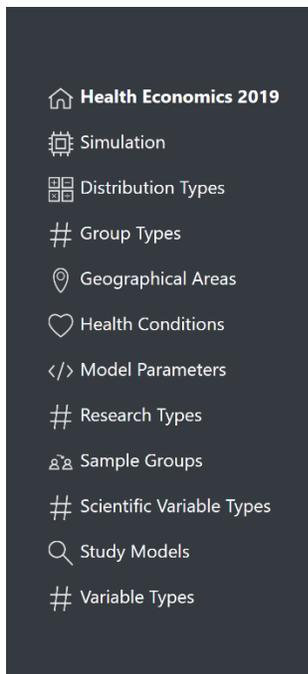
Add...

NAME	DESCRIPTION	ACTIONS
Dynamic	this variable accepts formula and overrides the value of another variable.	Edit Delete
None	Functions such as ranges will be defined in this category.	Edit Delete
Extraneous	Extraneous variables are "extra" variables that may influence the outcome of an experiment but aren't taken into account during measurement. Ideally, these variables won't impact the final conclusion drawn by the experiment, but they may introduce error into scientific results. If you are aware of any extraneous variables, you should enter them in your lab notebook. Examples of extraneous variables include accidents, factors you either can't control or can't measure or factors you consider unimportant. Every experiment has extraneous	Edit Delete

Figure 11 Simulation Software - Scientific Variables Section

Simulation

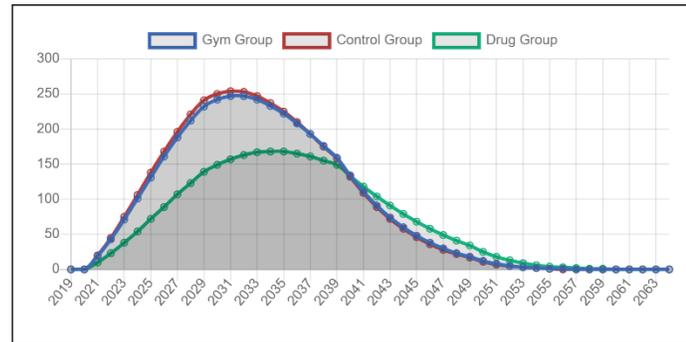
The most important part of this software is the simulation page. It allows the researcher to compare the results of their intervention through a responsive plot using the variable of their choice. We can also download the comma-separated values file (CSV) of the graph through the available options on this section.



A MARKOV MODEL OF ALL GROUPS DEFINED FOR THE STUDY

The chart below displays the outcome for variable 'Prog'.

Prog : Progressive disease or progressive illness is a disease or physical ailment whose course in most cases is the worsening, growth, or spread of the disease. This may happen until death, serious debility, or organ failure occurs. Some progressive diseases can be halted and reversed by treatment.



THE DASHBOARD BELOW ALLOWS YOU TO MODIFY THE OUTCOMES

Figure 12 Simulation Software - Simulation Section

Simulation Dashboard

Dashboard section is an extension to the simulation page. It allows the researchers to dynamically update the controlled variables of the study, change the variable being compared across the sample groups and update the results instantly.

THE DASHBOARD BELOW ALLOWS YOU TO MODIFY THE OUTCOMES.

Population of the groups	<input type="text" value="1000"/>
Cost / Asymp. State	<input type="text" value="500"/>
Gym Membership (\$)	<input type="text" value="30"/>
Initial age of the group participants	<input type="text" value="55"/>
Drug Costs	<input type="text" value="1000"/>
Cost / Terminal stage	<input type="text" value="1000"/>
Effectiveness of the drug	<input type="text" value="0.5"/>
Exercise Outcomes	<input type="text" value="0.05"/>
List of variables to compare	<input type="text" value="Disease Progression"/>

Figure 13 Simulation Software - Simulation Dashboard Section

Software Reusability Test Results

In this chapter, we will use C.K metrics and the NDepend 2019 Extension for Visual Studio 2019 to evaluate the reusability of the proposed and developed software. Please note we have attached all the scripts which were used to produce the results in the appendices section.

WMC Metric Result

Figure 14 illustrates a list of classes with $20 < WMC \leq 100$.

7 types	wmc
7 types matched	
<ul style="list-style-type: none"> ▲ HealthEconomics (7 types) <ul style="list-style-type: none"> ▲ {} HealthEconomics.DataModels (1 type) <ul style="list-style-type: none"> ModelParameter 49 ▲ {} HealthEconomics.Controllers (1 type) <ul style="list-style-type: none"> ModelsController 43 ▲ {} HealthEconomics.SimulationPackages.MarkovModel (1 type) <ul style="list-style-type: none"> MarkovModel 42 ▲ {} HealthEconomics.DatabaseAccessLayers (1 type) <ul style="list-style-type: none"> DatabaseAccessLayer 40 ▲ {} HealthEconomics.SimulationPackages.MonteCarloSimulation (1 type) <ul style="list-style-type: none"> MonteCarloSimulation 30 ▲ {} HealthEconomics.Helpers (2 types) <ul style="list-style-type: none"> PropertyExtensions 23 TypeExtensions 22 	

Figure 14 Classes with “ $20 < WMC \leq 100$ ”

Figure 15 demonstrates a list of classes with $20 \leq WMC \leq 100$.

30 types		wmc
30 types matched		
▲ ■■ HealthEconomics (30 types)		
▲ {} HealthEconomics.DataModels (10 types)		
🔗 StudyModel		20
🔗 SampleGroup		16
🔗 GeographicalArea		8
🔗 HealthCondition		8
🔗 DistributionType		6
🔗 ExperimentGroupType		6
🔗 ResearchType		6
🔗 ScientificVariableType		6
🔗 MainContext		4
🔗 VariableType		4
▲ {} HealthEconomics.Helpers (8 types)		
🔗 MathExtensions		19
🔗 StringExtensions		16
🔗 MarkovModelExtensions		14
🔗 DatabaseExtensions		12
🔗 NCalcExtensions		12
🔗 PresetDataGenerator		11
🔗 JsonExtensions		8
🔗 ModelExtensions		8
▲ {} HealthEconomics.SimulationPackages.MonteCarloSimulation (2 types)		
🔗 SimulationResultsHolder		10
🔗 SimulationResult		3
▲ {} HealthEconomics.SimulationPackages.MarkovModel (2 types)		
🔗 MarkovModelResult		6
🔗 MarkovModelGroupsResults		3
▲ {} HealthEconomics.Pages (1 type)		
🔗 ErrorModel		5
▲ {} HealthEconomics.DataModels.GenericDefinitions (5 types)		
🔗 BaseModel		5
🔗 JsonKeyValue		3
🔗 FieldInfo		1
🔗 ModelInfo		1
🔗 ModelSpecs		1
▲ {} HealthEconomics (1 type)		
🔗 Program		2
▲ {} HealthEconomics.Controllers (1 type)		
🔗 ModelParameterBinder		1

Figure 15 Classes with “1 <= WMC <= 20”

There were no classes within the solution which had a WMC value greater than 100. The overall WMC values displays a low to moderate class complexity which provides a good opportunity for reuse and maintenance.

RFC Metric Result

Figure 16 demonstrates a list of classes with their associated RFC values, direct and indirect method calls. To keep the figure size standard and readable, we have removed the classes with no methods and RFC value of 0. Even though most of the classes have a low RFC value, classes such as “DatabaseAccessLayer” or “MonteCarloSimulation” require a moderate level of understanding of the code for the software developer to test and debug the program.

47 types	methodsUsedDirectly	methodsUsedIndirect	rfc
47 types matched			
HealthEconomics (47 types)			
DatabaseAccessLayer	12 methods	97 methods	97
ModelsController	40 methods	95 methods	95
Program	2 methods	95 methods	95
PresetDataGenerator	64 methods	82 methods	82
MonteCarloSimulation	9 methods	51 methods	51
MarkovModelExtensions	9 methods	46 methods	46
MarkovModel	18 methods	30 methods	30
DatabaseExtensions	6 methods	20 methods	20
ModelExtensions	7 methods	14 methods	14
ModelSpecs	1 method	10 methods	10
ModelParameterBinder	2 methods	8 methods	8
NCalcExtensions	5 methods	5 methods	5
MathExtensions	4 methods	4 methods	4
ResearchType	1 method	3 methods	3
ExperimentGroupType	1 method	3 methods	3
GeographicalArea	1 method	3 methods	3
HealthCondition	1 method	3 methods	3
StudyModel	1 method	3 methods	3
VariableType	1 method	3 methods	3
ModelParameter	1 method	3 methods	3
ScientificVariableType	1 method	3 methods	3
MarkovModelGroupsResults	3 methods	3 methods	3
SampleGroup	1 method	3 methods	3
MainContext	1 method	3 methods	3
DistributionType	1 method	3 methods	3
TypeExtensions	2 methods	2 methods	2
BaseModel	1 method	2 methods	2
JsonExtensions	1 method	1 method	1
SimulationResultsHolder	1 method	1 method	1

Figure 16 RFC Value for classes across the solution

DIT Metric Result

Figure 17 displays only a list of classes which inherited from a base class. We removed the root classes from the list generated to keep the list short. According to the earlier discussion, the value of DIT being 2, signifies a reasonable and higher degree of reuse. Please note that values higher than three does not automatically signify better reuse, and on the contrary can cause overly complicated code structure (Selvarani et al., 2009).

10 types	baseClasses	Depth of inheritance
10 types matched		
<ul style="list-style-type: none"> ▲ ■■ HealthEconomics (10 types) <ul style="list-style-type: none"> 🔗 DistributionType 🔗 ExperimentGroupType 🔗 GeographicalArea 🔗 HealthCondition 🔗 ModelParameter 🔗 ResearchType 🔗 SampleGroup 🔗 ScientificVariableType 🔗 StudyModel 🔗 VariableType 		
	1 type	2

Figure 17 DIT Value for classes across the solution

NOC Metric Result

Figure 18 displays the result of the NOC metric test across the software solution returning only one class with ten children/inherited classes. In this case, the solution is easily maintainable and changeable.

17 types	childClasses
17 types matched	
<ul style="list-style-type: none"> ▲ ■■ HealthEconomics (1 type) <ul style="list-style-type: none"> ■ ■ ■ BaseModel 10 types ▶ ■■ System.Runtime (8 types) ▶ ■■ mscorlib (2 types) ▶ ■■ System.Collections (1 type) ▶ ■■ Microsoft.AspNetCore.Mvc.Core (1 type) ▶ ■■ Microsoft.AspNetCore.Mvc.RazorPages (1 type) ▶ ■■ Microsoft.EntityFrameworkCore (1 type) ▶ ■■ System.Linq.Expressions (1 type) ▶ ■■ Microsoft.AspNetCore.Mvc.ViewFeatures (1 type) 	

Figure 18 NOC Value for the HealthEconomics Solution

CBO Metric Result

Figure 19 demonstrates the value CBO metric for each of the classes across the solution with most of the classes having a very low CBO compared to the classes “ModelsController” and “PresetDataGenerator.”

“PresetDataGenerator” is responsible for generating dummy data for testing, and we can remove it from the project without affecting the functionality of the software. Please note that we removed the classes with CBO value of zero from the list.

Class “ModelsController” is the main entrance to the web application for client users accessing the website. It can be divided into different MVC controllers once the cohesion becomes low within that class. Overall the project displays a good CBO value, meaning that there is low coupling across the classes which promotes maintainability and reusability.

48 types	CBO
48 types matched	
<ul style="list-style-type: none"> ▲ ■■ HealthEconomics (48 types) <ul style="list-style-type: none"> ModelsController 23 types PresetDataGenerator 13 types ModelExtensions 10 types MonteCarloSimulation 10 types MarkovModelExtensions 9 types DatabaseExtensions 8 types ModelParameter 7 types DatabaseAccessLayer 6 types MarkovModel 6 types StudyModel 6 types SampleGroup 5 types DistributionType 3 types ExperimentGroupType 3 types GeographicalArea 3 types HealthCondition 3 types ResearchType 3 types ScientificVariableType 3 types VariableType 3 types BaseModel 3 types Program 2 types MathExtensions 2 types NCalcExtensions 2 types TypeExtensions 2 types MarkovModelGroupsResults 2 types MainContext 2 types ModelSpecs 2 types JsonExtensions 1 type PropertyExtensions 1 type ModelParameterBinder 1 type MonteCarloSimulationResults 1 type SimulationResult 1 type SimulationResultsHolder 1 type FieldInfo 1 type 	

Figure 19 CBO Value for classes across the solution

LCOM Metric Result

Figure 20 Demonstrates a graph of Lack of Cohesion of Methods (LCOM) generated by NDepend 2019 Extension for Visual Studio 2019. Majority of classes display a low value for “Lack of Cohesion of Methods,” which is a desirable result for reusable software. We did not find any

classes or types having a high LCOM value. The low LCOM value fundamentally means that the classes across the solution have high cohesion of methods and that their methods are relevant to each other and work together.

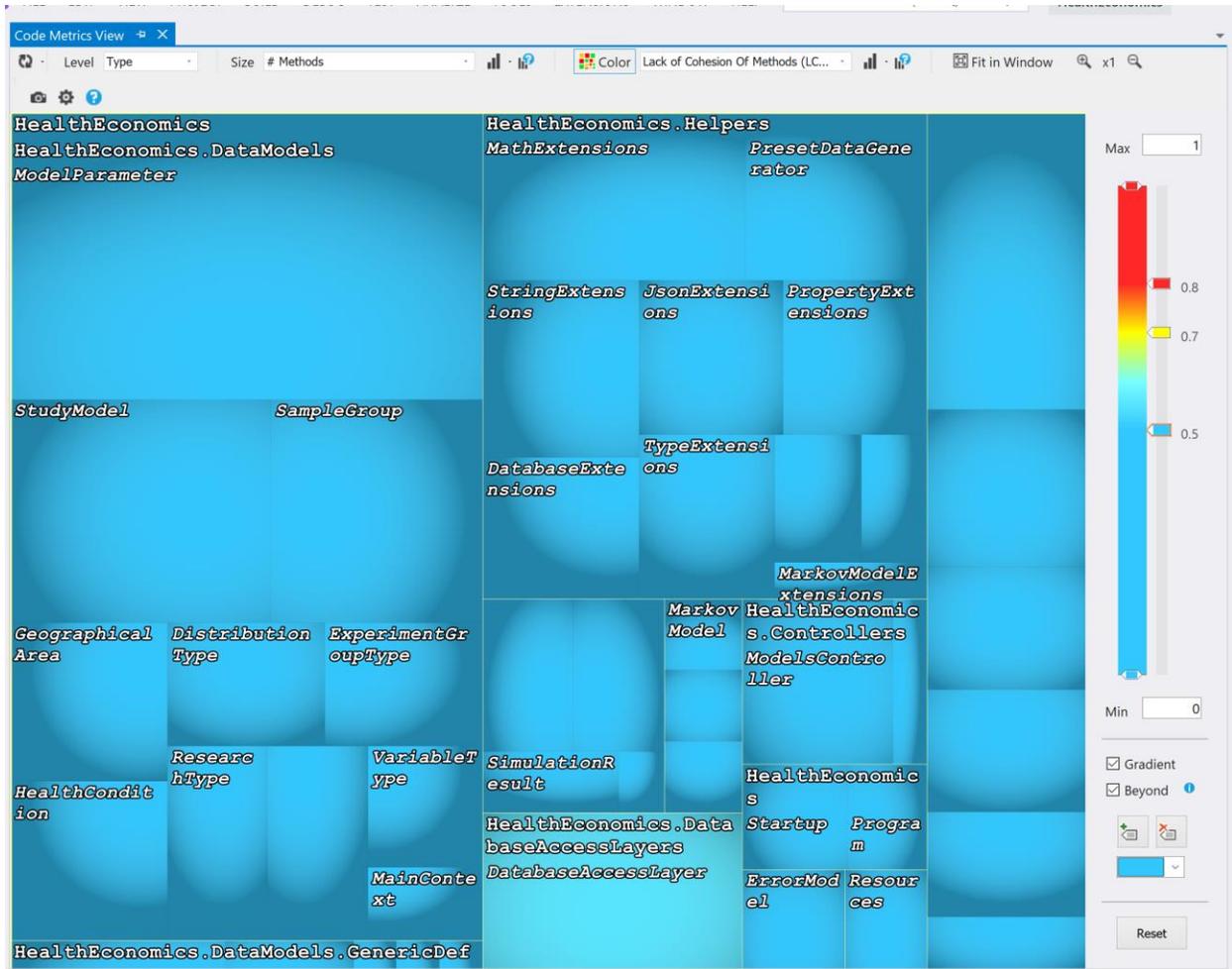


Figure 20 LCOM graph for the HealthEconomics Solution generated by NDepend 2019 (ZEN PROGRAM LTD, 2019)

Discussion of Metrics Results

Table 5 demonstrates the overall result of the six different metrics tests. We can conclude that according to the results of this test, the first milestone of the proposed software is reusable, maintainable, adaptable and testable.

Metric	Result	Comments
CBO	Low coupling	Maintainable Reusable
DIT	Moderate Inheritance, Promotes	Reusable Understandable
LCOM	Low Lack of Cohesion	Reusable
NOC	Low Number of Children	Maintainable Adaptable Reusable
RFC	Moderate level of classes' complexity and communication with each other	Average Level of Understanding Required To Test And Debug
WMC	Moderate Complexity	Reusable

Table 5 Results of the Reusability Metrics Test

First Simulation

As we stated in the research question, we plan to put our simulation software to the test and perform an RCT to see if we can achieve cost-effectiveness of prevention for T2D in Canadian Healthcare settings during a 10-Year time horizon from the year 2019 until the year 2029.

We will attempt to compare the cost-effectiveness of two separate interventions with a control group across the Greater Toronto Area (GTA) and investigate which approach brings more social value aside from monetary benefits. The following will be our intervention groups:

Gym Group

We provide this group with a gym membership at Humber River Hospital that costs CAD 65.00 for six months of membership before taxes. Using this strategy, we aim at promoting exercise and physical activity across the group population. According to the Canadian Diabetes Association (2019), 150 minutes of moderate to vigorous aerobic exercise weekly can be as effective as medication. Please note that we only used the price and numbers from the above to simulate the study outcomes, and we did not conduct a gym incentive program in the real-world setting.

Medication Group

Medication group is a group of patients receiving the medication (Metformin) as a form of intervention.

Choice of Variables

The variables in the simulation software are very similar to those of the Markov Model designed by Briggs et al. (2006). However, we have adjusted all the prices to Canadian Dollars. Table 4,

which we introduced in the literature review, reveals the annually inflation-adjusted costs associated with Type 2 Diabetes for each patient in Canada.

Based on the latest report by Statistics Canada (2019), the prevalence of diabetes across the Canadian population is 7.1% of the entire community, which is equal to 435,898 of GTA population. Nevertheless, for the scope of this study, we have to start with prevention strategy, which is realistic and testable, and as such, we have decided to conduct this analysis with a 5,000-sample size per each group.

According to a study by Marinho et al. (2018), authors revealed that the adherence to physical activity and exercise is only 22.5% while the adherence to medication is a whopping 93.5%. We will include the adherence values and expect to observe differences in the outcome of the Gym and Medication Group.

List of Variables Used in the model

Name	Description	Source	Range	Mean
Acute/Progressive Disease Cost	Annual Cost of disease in the progressive state for each patient	Canadian Institute for Health Information (2007)	CAD 4,478.19	CAD 4,478.19
Age of Participants	The age at which the participants enter the program	Government of Canada (2017)	40	40
Asymptomatic Disease Cost	Annual Cost of disease in the asymptomatic state for each patient	Bilandzic & Rosella (2017)	CAD 1,302.76	CAD 1,302.76
Cost of Drug	Annual Cost of Metformin	Canadian Agency for Drugs and Technologies in Health (2018)	CAD 107.98	CAD 107.98

Cost of Gym Membership Annually	CAD 65.00 for six months of membership before taxes.	Humber River Hospital (2019)	CAD 146.9	CAD 146.9
Diabetic Percentage	Percentage of type 2 diabetic individuals in Canada.	Statistics Canada, (2019)	7.1%	7.1%
Exercise Adherence	Adherence of individuals to exercise and physical activity required for controlling their condition	Marinho et al. (2018)	22.5%	22.5%
Medication Adherence	Adherence of individuals to medication required for controlling their condition	Marinho et al. (2018)	93.5%	93.5%
Effectiveness of Medication	Likelihood of Medication controlling the symptom of the disease.	Briggs et al. (2006)	40%-60% × Medication Adherence	50% × Medication Adherence
Effectiveness of Gym	Likelihood of Gym controlling the symptom of the disease.	Canadian Diabetes Association (2019)	40%-60% × Exercise Adherence	50% × Exercise Adherence
GTA Population	Population of Greater Toronto Area	World Population Review (2019)	6,139,404	6,139,404
Sample Size	Diabetic Percentage X GTA Population	N/A	435,898	435,898
Terminal Cost	The cost associated with the death of a patient	Tanuseputro et al. (2015)	CAD 57,749.86	CAD 57,749.86

Table 6 Variables and Values used for simulation

Results

In this section, we first demonstrate the results of the first simulation using the variables and values defined in the previous section and finally, we proceed to discuss the results of these simulations.

Markov Model Results

A.1.1.18 A Preview of The Dashboard Variables

The following figure demonstrates an interactive panel that allows us to enter the variables and update the simulation dynamically.

Age of Participants	40
Annual Cost of Asymptomatic Disease / Patient	1302.76
Annual Cost of Gym Incentive / Patient	146.9
Annual Cost of Medication / Patient	107.98
Annual Cost of Progressive Disease / Patient	4478.19
Cost of Death / Patient	57749.86
Drug Effectiveness as Ratio	0.4675
Gym Effectiveness as Ratio	0.1125
Population of the groups	5000

Figure 21 Overview of The Dashboard Values of The First Simulation

A.1.1.19 Number of Individuals in an Asymptomatic State of Disease Across All Groups

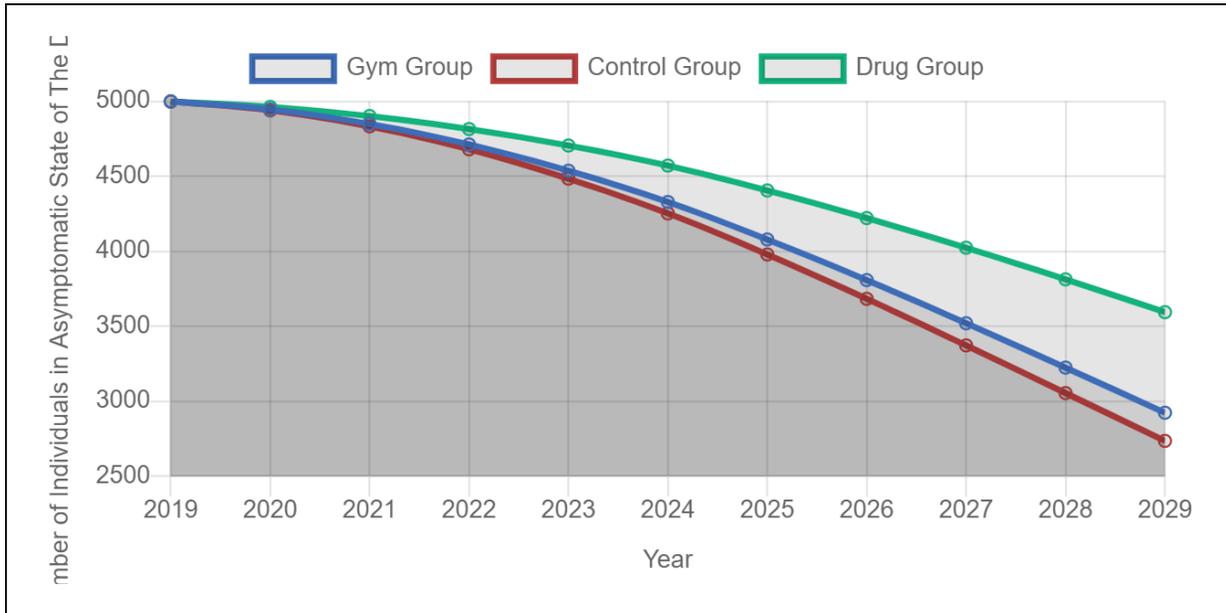


Figure 22 Plot of The Total Number of Individuals in an Asymptomatic Stage of the Disease

A.1.1.20 Number of Individuals in a Progressive State of Disease Across All Groups

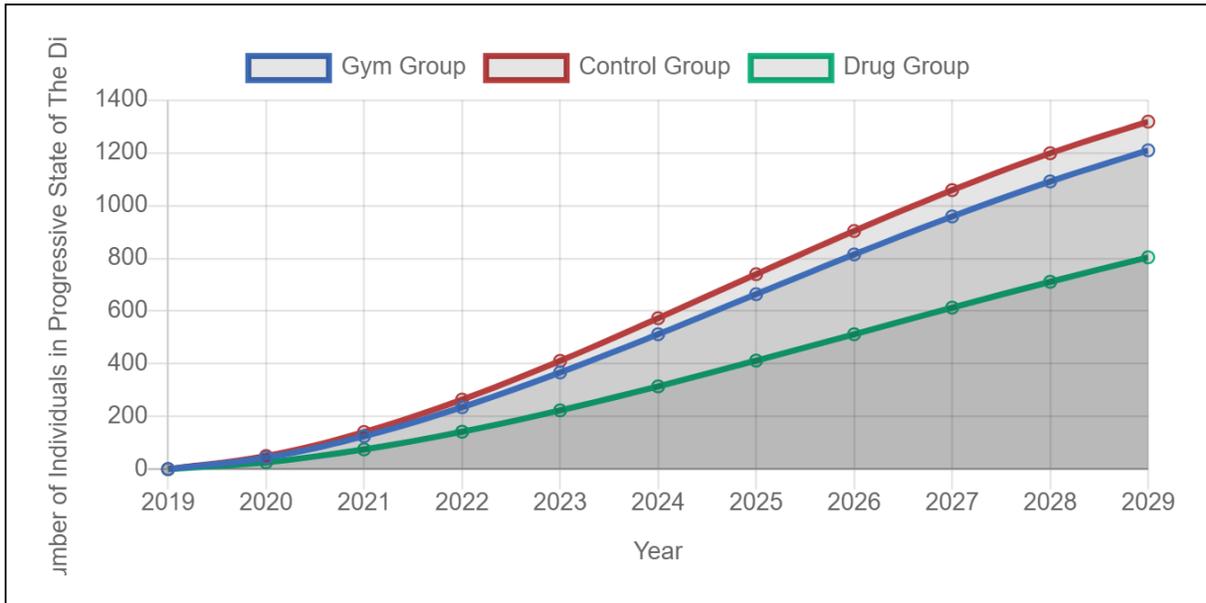


Figure 23 Plot of The Total Number of Individuals in a Progressive State of the Disease

A.1.1.21 Quality-Adjusted Life-Years Across All Groups

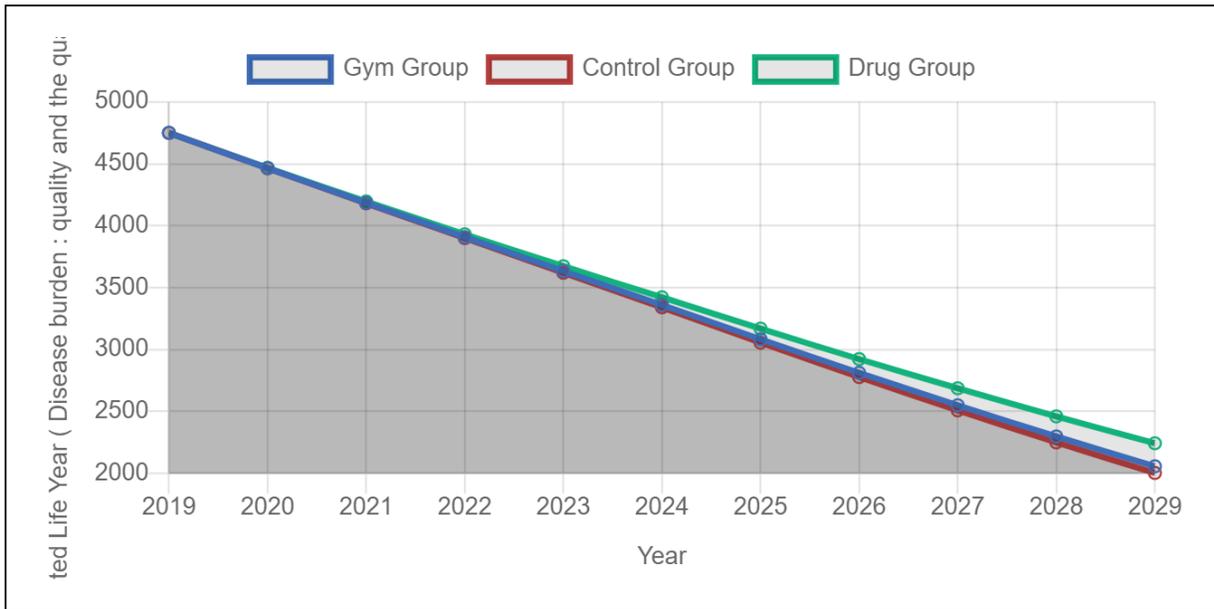


Figure 24 Plot of Total Quality-Adjusted Life-Years Across for the Three Participating Groups

A.1.1.22 Total Annual Cost of Remaining in the Current State of the Disease Across the Groups

StateCost : Cost of remaining in the current state of disease.

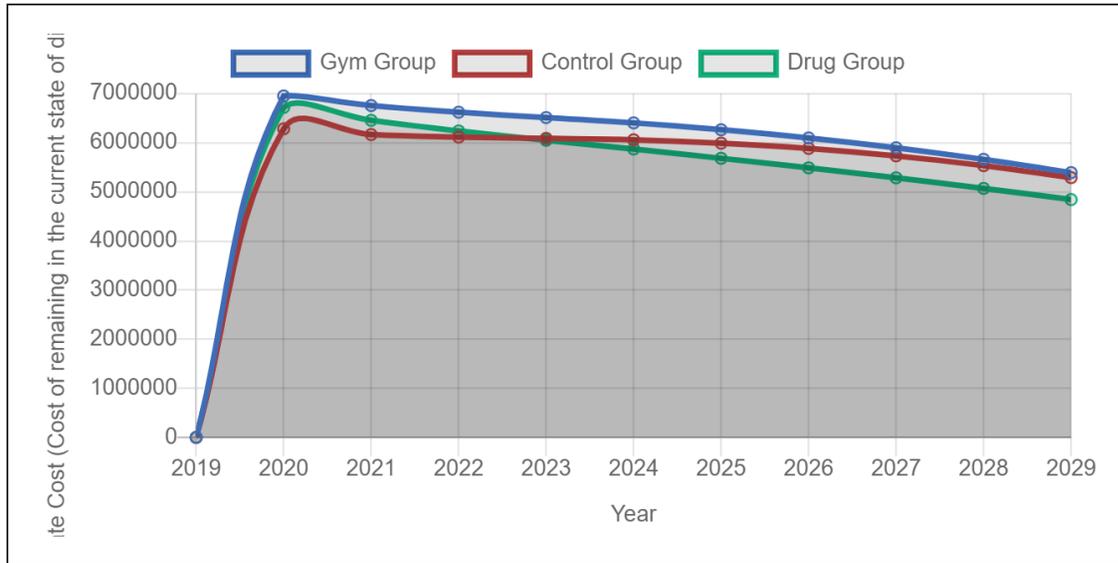


Figure 25 Plot of Average Annual Cost of Remaining in the Current State of The Disease for the Three Participating Groups

A.1.1.23 Total Costs Across All Groups

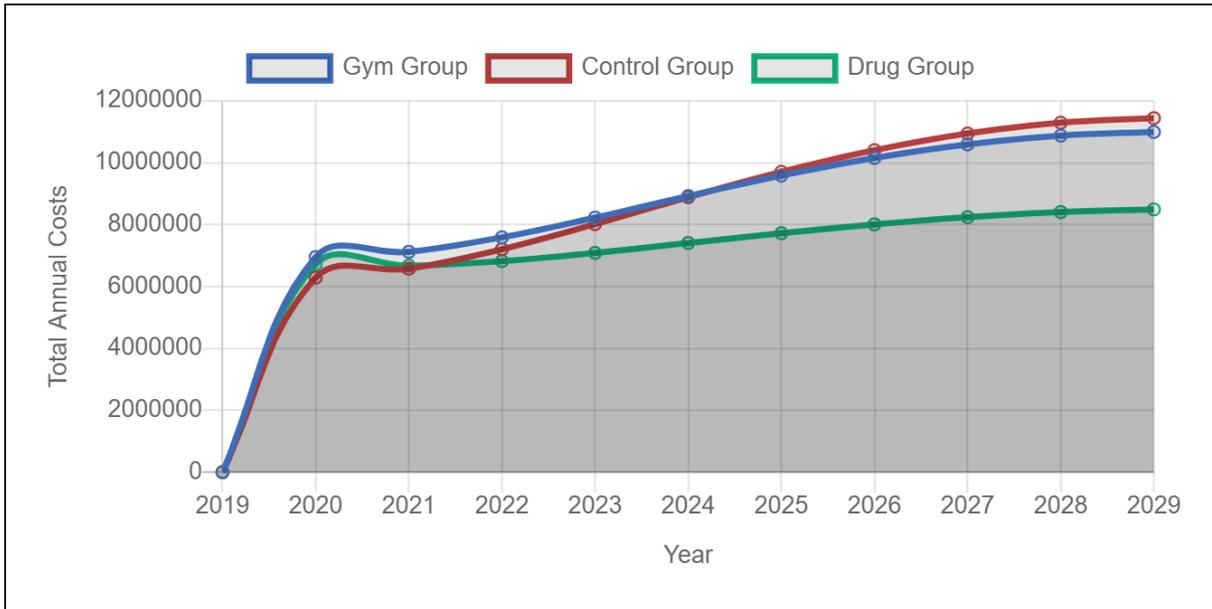


Figure 26 Plot of the Annual Total Costs of the Three Participating Groups

A.1.1.24 Total Deaths Across All Groups

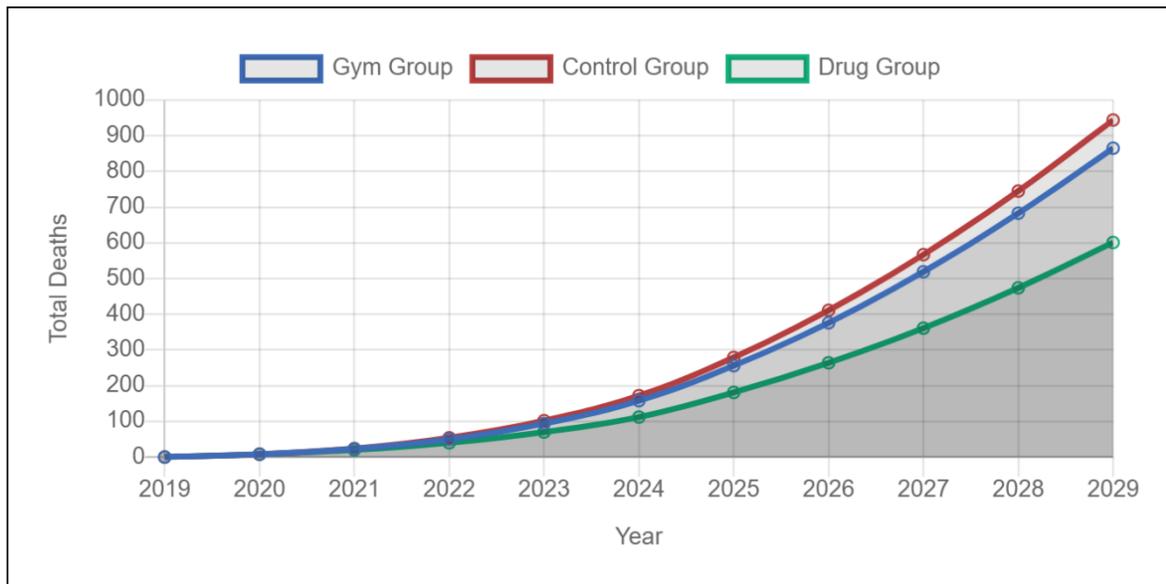


Figure 27 Plot of The Accumulated Deaths per Group Over the Years

Monte Carlo Simulation

In the second stage of this simulation, we performed a 1,000 simulation through Monte Carlo Simulation model to check for the robustness of the Markov Model's results. Table 7 demonstrates the results of this simulation on both a group and individual basis.

Group Name	LE	LYs	QALE	QALYs	StateCost	TotalCost	TransitionCost
Gym Group	51,781.94	39,776.66	49,211.29	37,906.08	\$62,071,605.16	\$92,509,907.15	\$30,438,301.99
Gym Group Per Patient	10.36	7.96	9.84	7.58	\$12,414.32	\$18,501.98	\$6,087.66
Control Group	51,513.61	39,608.73	48,860.46	37,682.63	\$57,909,566.48	\$91,643,041.93	\$33,733,475.46
Control Group Per Patient	10.3	7.92	9.77	7.54	\$11,581.91	\$18,328.61	\$6,746.70
Drug Group	52,845.92	40,440.87	50,619.90	38,800.17	\$57,330,616.29	\$75,391,490.98	\$18,060,874.69
Drug Group Per Patient	10.57	8.09	10.12	7.76	\$11,466.12	\$15,078.30	\$3,612.17

Table 7 Results of the 1,000 simulations through Monte Carlo Simulation

Discussion of The Simulation Results

According to the first result of the simulation demonstrated in Figure 22, the medication (drug) group has the most number of individuals in an asymptomatic state of the disease compared to the rest of the sample groups. This trend essentially means that in this group, we have more percentage of people feeling well. In the Gym group, even though not as good as medication group. However, the group is still better performing in achieving healthier individuals compared to our control group.

In the plot, displayed in Figure 23, we observe a pattern in which the individuals in the control group are falling sick and entering a progressive state of the T2D in more numbers compared to the Gym and Medication Group. Medication group, on the other hand, due to a higher compliance rate, can outperform the rest of the group and have a lower percentage of the individuals within a progressive state of the disease.

Figure 24 demonstrates the overall increased quality-adjusted life-years per group. Referring to Table 8 in the appendices section, the medication group is displaying a slightly higher quality-adjusted life-years. This result means that the individuals within the medication group are having more top quality of life compared to the gym and control group. The reason behind the gym group not having as much significance as the medication is the lack of adherence of its participants.

In Figure 25, the control group's annual total costs are cheaper on the State-Cost basis, and it is because we are not integrating any interventions in this group. However, based on Figure 26 which demonstrates the total annual costs associated with each group, three years into the prevention program, and the overall total costs of the control group start to rise and surpass the other two groups. This rise is primarily because individuals in the control group seem to have a more unstable

disease state which is shifting more often, causing the increased jump in their annual Transition Costs (For instance, Hospitalization) and Total Costs. Individuals in the Gym group and Drug group have a more stable life, and their disease is under better control, promoting a better quality of life.

Figure 27 and Table 8 demonstrate a frightening difference in accumulated deaths between the three groups. At the end of the year 2029, 945 from 5,000 participants of the control group are expected to lose their lives due to the disease. This loss means that 945 individuals will not make it to their 50th birthday due to T2D. In the medication group, we have far fewer deaths as this number is only 602. This number of deaths means that total deaths in the medication group are only 63% to that of the control group, and this brings up an important point about social value. By the end of the year 2029, in the medication group, we would have saved almost 243 individuals' lives.

As stated by the results of the Monte Carlo Simulation demonstrated in Table 7, the average total cost of a patient living in GTA in control group is CAD 18,328.60 annually while the medication group will only face CAD 15,078.29 each year on average. However, the Gym group is the most expensive of our three groups based on Total Annual Costs for each individual, as each individual in this group will face an annual expense of \$18,501.98. Gym group has a slightly higher cost compared to the control group.

Nevertheless, According to Table 7, both Gym and Medication groups promote the QALY, QALE, LYs and LE while the control group suffers due to disease burden against their quality-adjusted life expectancy.

In conclusion, any of the Medication or Gym group are good moral and social options, while medication intervention is the most valuable route in both monetary and social value. This intervention promotes quality of life, lowers death rates, increases the life expectancy and reduces the annual costs.

Discussion

The primary purpose of this investigation was to design a software model that can enhance and facilitate future research in the field of healthcare and primarily chronic illnesses. During this investigation, we asked the following question:

- **How Information Technology can help in healthcare to develop cost-effective prevention strategies for Type-2 Diabetes?**

To answer the question above, we initially conducted a literature review in the field of healthcare in Canada, and later we proposed the development of a software model which can help facilitate the study of health economics. We performed a reusability test using C.K reusability metrics on the developed simulation software design and architecture, and the results suggested that the proposed and developed software is maintainable, reusable and extendable.

Finally, we used the simulation software to simulate an RCT across three diabetic sample groups in the Greater Toronto Area and investigated the results in a separate section.

The results of the simulation suggested that prevention using medication, due to mainly its high adherence rates compared to prescription exercise is more successful and beneficial in terms of being cost effective and promoting quality of life compared to the gym and control groups.

Conclusion

The primary purpose of this thesis was to understand the nature of chronic diseases and primarily Type 2 Diabetes and the current practices and prevention strategies available to reduce the burden of this disease.

After understanding what type of challenges scientists in Canada are facing when testing the nature of Type 2 Diabetes in Canadian settings, we proposed a simulation software and developed the first software milestone.

We later ran our first simulation to test the software and discussed our first results generated by the software running a Markov Model along with a Monte Carlo Simulation. As results suggested the cost-effectiveness of the prevention strategies, we hope that in future investigators use this software to compare different healthcare strategies and promote a healthier society through an efficient and cost-saving approach which benefits both the patients and the healthcare organizations.

In the following sections will discuss the contributions, limitations and recommendations for future research.

Recommendation

We recommend future researchers to consider the environmental factors which can affect the outcome of the models. These elements could be the income level of the families, type of commute to work, the industry the individuals work in, and the highest level of education.

As this system passes the reusability test, we can recommend this work to be the groundwork for future developments and researches and introduce more variables which they believe can affect

the outcomes of the studies, into the models. Extending the software package by adding further simulation methods and algorithms into it can certainly help improve the accuracy of the simulations.

Contributions

The main contribution of this research is the preparation of the tool that can be reused by many scientists around the world to test their hypothesis without having to code a model over and over.

The second contribution is that if implemented nationally, this simulation software can be used to accelerate and increase the number of studies conducted in Canadian healthcare settings.

The patterns used in this software application allow for reusability, maintainability and scalability and as a result, this can provide the groundwork for future software developers and scientists to improve and scale the software and introduce more simulation models to it without having to redesign an entire application.

Limitations

The application of the software proposed and developed as part of this thesis needs further testing by scientists and doctors, primarily in the field of chronic illnesses. The scope and area of this thesis only allowed us to academically prepare this paper, which has the potential of translating into a real-world tool.

Hosting the web application on a hosting environment suitable for testing could facilitate the process of development as we could invite experts to test the system and hear their feedback about how it could be further improved.

Appendices

A.1 Ndepend Query Codes

A.1.1 NDepend 2019 Query Scripts

A.1.1.1 WMC

```
let wmcFor = new Func<IType, int>(t =>
    t.MethodsAndConstructors
        .Select(m => (int) m.CyclomaticComplexity.GetValueOrDefault())
        .Sum())
from t in JustMyCode.Types
let wmc = wmcFor(t)
where wmc >= 20 & wmc <= 100
orderby wmc descending
select new { t, wmc }
```

A.1.1.2 RFC

```
from t in Application.Types
where !t.IsInterface && !t.IsEnumeration
let methodsUsedDirectly =
    t.TypesUsed
        .Where(tUsed => !tUsed.IsThirdParty)
        .ChildMethods()
        .Where(m => m.IsUsedBy(t))

let methodsUsedIndirectly = methodsUsedDirectly
    .FillIterative(
        methods => methods.SelectMany(
            m => m.MethodsCalled
                .Where(mCalled => !mCalled.IsThirdParty))
    )
    .DefinitionDomain.ToArray()

let rfcLoC = methodsUsedIndirectly.Sum(m=>m.NbLinesOfCode)

select new { t,
    methodsUsedDirectly,
    methodsUsedIndirectly,
    rfc = methodsUsedIndirectly.Length,
    rfcLoC }
rftLoC }
```

A.1.1.3 DIT

```
from t in JustMyCode.Types
where t.IsClass
let baseClasses = t.BaseClasses.ExceptThirdParty()
where baseClasses.Count() >= 1
select new { t, baseClasses, t.DepthOfInheritance
}
```

A.1.1.4 NOC

```
from t in Application.Types
where t.IsClass
let childClasses = t.DerivedTypes
where childClasses.Count() > -1
orderby childClasses.Count() descending
select new { t, childClasses }
```

A.1.1.5 CBO

```
from t in Application.Types
let CBO = t.TypesUsed.ExceptThirdParty()
orderby CBO .Count() descending
select new { t, CBO }
```

A.1.1.6 LCOM

This section has no additional script, as the NDepend v2019 extension for Visual Studio 2019 has generated this view.

A.2 Markov Model Results for All Groups

Gym Group													
AsymptomaticCases	CurrentAge	Cycle	DeathCases	LE	LYs	ProgressiveCases	QALE	QALYs	RiskOfNaturalDeath	StateCost	TotalCost	TransitionCost	Ye
5,000.00	40	0	0	5,000.00	5,000.00	0	4,750.00	4,750.00	0.17%	\$0.00	\$0.00	\$0.00	20.
4,947.13	41	1	8.5	4,991.50	4,708.96	44.38	4,733.05	4,465.14	0.17%	\$6,953,178.22	\$6,953,178.22	\$0.00	20.
4,850.90	42	2	23.64	4,976.36	4,428.94	125.45	4,702.45	4,185.16	0.17%	\$6,758,607.15	\$7,121,246.31	\$362,639.16	20.
4,713.50	43	3	50.92	4,949.08	4,155.34	235.58	4,654.51	3,908.02	0.17%	\$6,622,866.87	\$7,590,069.97	\$967,203.10	20.
4,538.16	44	4	94.67	4,905.33	3,885.48	367.17	4,566.63	3,633.04	0.17%	\$6,513,424.11	\$8,226,830.67	\$1,713,406.56	20.
4,329.06	45	5	158.08	4,841.92	3,618.16	512.85	4,497.25	3,360.61	0.44%	\$6,405,734.37	\$8,925,073.69	\$2,519,339.33	20.
4,079.49	46	6	256.32	4,743.68	3,344.11	664.19	4,373.66	3,083.26	0.44%	\$6,265,863.42	\$9,585,607.75	\$3,319,744.32	20.
3,808.10	47	7	376.82	4,623.18	3,074.68	815.08	4,229.01	2,812.53	0.44%	\$6,098,925.89	\$10,154,938.89	\$4,056,013.01	20.
3,520.97	48	8	519.42	4,480.58	2,811.17	959.61	4,064.63	2,550.20	0.44%	\$5,898,622.73	\$10,594,319.93	\$4,695,697.20	20.
3,224.24	49	9	683.08	4,316.92	2,555.18	1,092.68	3,882.54	2,298.07	0.44%	\$5,662,861.19	\$10,878,263.25	\$5,215,402.06	20.
2,923.91	50	10	865.97	4,134.03	2,308.42	1,210.12	3,685.30	2,057.85	0.44%	\$5,392,878.14	\$10,995,384.04	\$5,602,505.90	20.
Control Group													
AsymptomaticCases	CurrentAge	Cycle	DeathCases	LE	LYs	ProgressiveCases	QALE	QALYs	RiskOfNaturalDeath	StateCost	TotalCost	TransitionCost	Ye
5,000.00	40	0	0	5,000.00	5,000.00	0	4,750.00	4,750.00	0.17%	\$0.00	\$0.00	\$0.00	20.
4,941.50	41	1	8.5	4,991.50	4,708.96	50	4,731.93	4,464.08	0.17%	\$6,284,432.11	\$6,284,432.11	\$0.00	20.
4,834.27	42	2	24.49	4,975.51	4,428.19	141.25	4,698.49	4,181.64	0.17%	\$6,168,044.51	\$6,576,652.01	\$408,607.50	20.
4,681.02	43	3	54.13	4,945.87	4,152.65	264.85	4,645.61	3,900.54	0.17%	\$6,116,023.08	\$7,204,962.07	\$1,088,938.99	20.
4,485.82	44	4	102.27	4,897.73	3,879.46	411.91	4,570.47	3,620.24	0.17%	\$6,090,062.64	\$8,016,338.01	\$1,926,275.38	20.
4,253.91	45	5	172.38	4,827.62	3,607.48	573.71	4,471.50	3,341.36	0.44%	\$6,061,027.94	\$8,887,346.03	\$2,826,318.09	20.
3,979.96	46	6	279.68	4,720.32	3,327.64	740.37	4,336.23	3,056.87	0.44%	\$5,992,469.75	\$9,706,185.47	\$3,713,715.73	20.
3,683.85	47	7	411.5	4,588.50	3,051.61	904.65	4,178.14	2,778.70	0.44%	\$5,886,001.55	\$10,407,207.37	\$4,521,205.82	20.
3,372.93	48	8	567.39	4,432.61	2,781.08	1,059.68	3,999.04	2,509.05	0.44%	\$5,734,280.57	\$10,946,017.32	\$5,211,736.75	20.
3,054.53	49	9	745.84	4,254.16	2,518.03	1,199.63	3,801.52	2,250.12	0.44%	\$5,535,129.77	\$11,294,439.91	\$5,759,310.14	20.
2,735.63	50	10	944.51	4,055.49	2,264.57	1,319.86	3,588.75	2,003.94	0.44%	\$5,290,486.90	\$11,441,359.80	\$6,150,872.90	20.
Drug Group													
AsymptomaticCases	CurrentAge	Cycle	DeathCases	LE	LYs	ProgressiveCases	QALE	QALYs	RiskOfNaturalDeath	StateCost	TotalCost	TransitionCost	Ye
5,000.00	40	0	0	5,000.00	5,000.00	0	4,750.00	4,750.00	0.17%	\$0.00	\$0.00	\$0.00	20.
4,964.88	41	1	8.5	4,991.50	4,708.96	26.63	4,736.60	4,468.49	0.17%	\$6,720,169.40	\$6,720,169.40	\$0.00	20.
4,903.56	42	2	20.98	4,979.02	4,431.31	75.46	4,714.98	4,196.31	0.17%	\$6,457,439.74	\$6,675,023.33	\$217,583.49	20.
4,816.89	43	3	40.76	4,959.24	4,163.87	142.35	4,682.81	3,931.77	0.17%	\$6,240,757.13	\$6,822,536.39	\$581,779.26	20.
4,706.10	44	4	70.55	4,929.45	3,904.59	223.35	4,638.31	3,673.98	0.17%	\$6,051,045.57	\$7,086,373.82	\$1,035,328.25	20.
4,572.80	45	5	112.43	4,887.57	3,652.28	314.77	4,580.24	3,422.62	0.44%	\$5,873,925.01	\$7,406,468.08	\$1,532,543.07	20.
4,406.58	46	6	181.15	4,818.85	3,397.10	412.27	4,485.45	3,169.12	0.44%	\$5,683,932.20	\$7,721,480.28	\$2,037,548.08	20.
4,222.93	47	7	264.19	4,735.81	3,149.58	512.87	4,396.44	2,923.88	0.44%	\$5,489,514.71	\$8,007,135.39	\$2,517,620.68	20.
4,024.46	48	8	361.96	4,638.04	2,909.66	613.58	4,283.42	2,687.47	0.44%	\$5,286,072.37	\$8,240,750.01	\$2,994,677.65	20.
3,813.88	49	9	474.41	4,525.59	2,678.69	711.72	4,156.97	2,460.50	0.44%	\$5,071,143.73	\$8,405,926.57	\$3,334,782.85	20.
3,594.01	50	10	601.08	4,398.92	2,456.34	804.92	4,017.99	2,243.63	0.44%	\$4,843,950.75	\$8,493,141.08	\$3,649,190.34	20.

Table 8 Results of the Markov Model

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