

Optimal Treatment Allocation under Single-Payer  
Health Care with Pricing Competition

by

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## ABSTRACT

### OPTIMAL TREATMENT ALLOCATION UNDER SINGLE-PAYER HEALTH CARE WITH PRICING COMPETITION

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In this thesis we use dynamic programming and game theory background to build an optimal allocation model for a known treatment among population groups, given a single-payer health care provider. We model and analyze whether or not the presence of competition may help reduce the cost of vaccines and increase coverage to include more age groups under the same budgetary restrictions. We then show that there are best coverages to be achieved under various budget distributions of two distinct types: one from single-payer to population groups of distinct age, and another from single-payer to producers of treatment. Lastly, we incorporate and discuss a “copay” option for treatment payment such that consumers may be asked to pay up to 10% of the cost of the treatment directly to producers, showing potential increase to the available number of doses to be distributed at the expense of decreased consumer demand as a result of a copayment request.

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## Statement of Originality

This thesis is the first piece of work to blend a dynamic programming distribution with producer Nash pricing for single-payer constraints. We provide an iterative optimal allocation model, a generalized Nash pricing model for producers and a model with a “copay” option for pricing and distribution. We also include samples of code in the appendix for optimal allocation with dynamic programming for three groups, and for the Nash pricing game used in our analyses.

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## CHAPTER 1

### Introduction

#### 1.1. Overview & Motivation

Coverage for the shingles (herpes zoster) virus was recently announced in the Ontario Budget for 2016 for Ontario residents between the ages of 65 to 70 [29]. This will help eligible Ontarians save about \$170 per treatment, which will have a significant impact on their daily lives. The shingles disease creates painful skin rashes and blistering that typically occurs on specific spots of the body, and is caused by the reactivation of the chickenpox (varicella zoster) virus [27]. Although this announcement is well-received by the Ontario public, we note that most people who suffer from the virus start experiencing symptoms as early as age 50 [5]. With a 1-in-3 chance of developing the disease, many Canadians are struggling in their daily lives to cope with the severity of the illness.

The Ontario government will be investing \$68 million within a three year span in order to combat the reported 42,000 people that are affected by the disease in Ontario each year [27]. The decision to focus on such a limited age range is due to the efficacy of the current treatment

on the market for the 65-70 year old age group compared to other age groups, and is based on recommendations by Canada's National Advisory Committee on Immunization and Ontario's Provincial Infectious Diseases Advisory Committee on Immunization. It has been reported that approximately 850,000 seniors between the ages of 65-70 will be eligible to receive the publicly funded shingles vaccine [27]. Vaccination programs represent a valuable investment in health with positive economic return, and treatment coverage offered by the government of Ontario will always offer an improvement on the quality adjusted life years (QALYs) of elderly residents [38]. These improvements translate into positive economic outcomes as residents no longer need to seek out inefficient alternatives for pain relief for the shingles disease [38]. As such there is value in supporting effective vaccination agendas for the purpose of improving QALYs for Ontario residents while also taking advantage of economic solutions.

The Zostavax vaccine developed by Merck & Co. is currently the only treatment option for shingles on the market [22]. Having had no competition, there has been no drive to lower the cost of sale. We intend on exploring whether or not introducing a competitor to the Zostavax treatment can lead to competitive pricing, allowing for reduced purchasing costs for Public Health. By conducting a sensitivity

analysis, our aim is to test whether or not the current funding allocated to shingles coverage can assist more Ontarians susceptible to the disease.

In order to explore these improved coverage possibilities, we will be using a dynamic programming and game theoretic approach. Dynamic programming allows us to solve for optimal solution sets from a desired end stage and work backwards towards a solution. This means we can start programming from an initial coverage (age groups 65-70) and then expand coverage given improved constraints - such as improved budget, pricing and treatment efficacy rates - for other age groups that are not currently covered for the treatment. Dynamic programming also allows us to define integer parameters, which are necessary in order to assure we can cover individuals entirely and distribute a defined number of treatments to a specific population group. Finally, dynamic programming can also be used to test scenarios both from the perspective of Public Health and of the manufacturer to find optimal costs from both perspectives. We may then - through game theory - define optimal parameters for a sensitivity analysis that can maximize producer profit while simultaneously maximizing overall coverage given the current budget.

There have been previous publications that have dealt with optimization techniques in relation to vaccinations. Initial studies conducted over 20 years ago began work on an operations research problem focused on optimizing immunization schedules in order to reduce the overall costs on Public Health for administering multiple vaccinations to an individual [7]. Since then, more publications have been made in the field of optimization research exploring potential avenues of improving immunization scheduling and distribution, as listed in the following references [26, 30, 42]. A recent publication ties closely to the study we conduct, using dynamic programming to focus on reduced procurement costs for a single-payer government entity looking to adopt a manufacturer's treatment given uncertainty in product price, efficacy and safety [6].

What makes this thesis unique is that we seek to focus on improved vaccine coverage by taking into account both Public Health's budgetary restrictions while simultaneously accounting for each manufacturer's maximal profit. This allows us to focus on two unique perspectives for production costs, and we do so by blending dynamic programming and game theory in a novel way. We would like to analyze whether or not competition is possible to reduce the cost of vaccines, increasing coverage given the same budgetary restrictions while still maintaining a profit to producers. We would also further like to elaborate on the

generalizability of our model to diseases with multiple age groups and multiple treatment options such as influenza.

## 1.2. Literature Review

**1.2.1. Health Policy in Canada.** One of the main purposes of Public Health throughout Canada is to prevent the development and spread of disease. Typically this is conducted through immunization, acting as a good preventative measure with frequent success. Infectious diseases that were once major causes for mortality in Canada are now easily preventable through vaccination, but as long as new diseases continue to develop and mutate, vaccine-preventable diseases will continue to always be a Public Health concern [15, 32, 37].

Public Health is a combination of programs and policies that attempt to sustain healthy lifestyles by preventing illness, injury and premature death. It specifically focuses on the daily necessities we take for granted such as food safety, clean oxygen and daily interactions between humans and the environment [24, 25]. The definition of “public health” focuses on distinct realms that caters towards both individual and societal health, as well as the institutions, organizations and research that aim to develop, fund and expand knowledge on improving overall health [24]. In order to fulfill these goals, Public Health focuses



in fields that can improve individual lifestyles, specifically focusing on hygiene, nutrition, living standards and medical advancements [37].

The introduction of vaccines in our society have also helped improve the health of Canadians. As noted by the Chief Public Health Officer (CPHO) in 2013, the incidence of various infectious diseases began to drop at a significant rate once education and training on vaccine policies were introduced in Canada [15, 32]. However despite these improvements, as vaccine-preventable diseases become more successfully immunized, the CPHO notes that Canadians may be more complacent and question the impact of introducing new vaccination programs [10, 23, 32, 35]. This may lead to the potential resurgence of new diseases, where Canadians who become hesitant to new vaccinations due to potential negative side effects put themselves at risk of developing diseases that may have been easily treatable.

Typically any sort of hesitancy towards immunization can be due to a number of factors such as personal beliefs, values, opinions, lifestyle choices and possible health risks [4, 21, 23]. In Canada especially, where we pride ourselves on multiculturalism and the interconnection of various cultures, it is even more difficult to find a unified approach to educating on the value of vaccination. It is easy to focus on the possible negative outcomes of any treatment option despite its overall benefit when fixating on “how safe” a given vaccine is, the severity of

the disease one is attempting to remedy, and fears of “vaccine overloading” - especially in children [4, 10, 21, 23]. Education on treatment options and the impact of immunization is a lifelong process, and it is important to explore the reasons why Canadians accept and refuse vaccines in order to develop effective immunization strategies [32]. For the most part, immunization is considered a success in Canada, where the continued success of immunization depends primarily on the efforts of all governments, researchers, healthcare professionals and the public [37].

**1.2.2. Vaccination Programs.** Vaccines work by creating an immune response to one or more specified diseases by stimulating the body’s immune system. The body’s immune system creates antibodies that target these diseases in one of two ways: by either getting an infection or by getting vaccinated prior to infection [35, 36]. Public Health dictates that getting vaccinated is the safer way of developing antibodies as it prevents an individual from having to suffer through the risks of developing illness, disability or possibly even death (depending on the severity of the disease itself). After getting a vaccine, the human body sets up a defence system designed to combat that specific disease, and will often remember how to fight a bacterium or virus for the rest of a person’s life [35, 36]. There are instances however that may require routine booster shots in order for the immune system to adapt to

new strains and mutations, ranging from annual shots (e.g. influenza) to one every decade (e.g. diphtheria and tetanus) [35, 36].

Immunization has overall yielded positive results, proven to be both a cost-effective solution to disease prevention that ultimately improves quality of life [11, 45]. Vaccination programs compare favourably with other Public Health interventions that makes including inexpensive vaccines for common diseases a simplistic process [11, 32]. As for newer and relatively more expensive vaccines, the decision to include these vaccines in publicly funded immunization programs largely depends on demand for the product and a willingness for taxpayers to seek out these types of health benefits [32].

Due to the steady decline of vaccine-preventable diseases, there has been a shift in focus from the number of cases of disease reported to the perceived safety of vaccination [21]. Mass media plays a big role in sharing myths related to specific vaccines that instill public fear despite credible, scientific evidence proving otherwise [32]. One major example of this is the idea that vaccinations for various infant diseases is the cause of increased cases of autism in growing children [37]. Vaccine efficacy and safety are considered the highest importance for Public Health, and any myths that play against this agenda can threaten the current successful implementation immunization programs have had across Canada [32].

Recent literature in the field of cost-benefit analysis for vaccination programs has shown discrepancies between treatment providers and the consumer market. Whereas governments have a tendency to focus on financial benefices to routine vaccination investments, individuals decide whether or not to adopt a treatment based on their perception of risk [13]. From the perspective of the provider, the perceptions of the individual consumer are viewed in terms of monetary value, and imply solutions must be treated as “all-or-none” policies [11, 13]. The strategies conducted by manufacturers to sell their product are often misconstrued to highlight product value rather than efficacy, leaving Public Health to aim for maximized overall coverage based on boasted results [13].

Although it is publicly known that no vaccine is 100% effective or safe and may cause varying adverse levels of pain or discomfort, vaccines are designed to be safer than the diseases they aim to prevent [32, 34]. It takes approximately 10 years to compile the necessary data on specific treatment options needed for approval in Canada, and many surveillance systems such as IMPACT and CAEFISS exist to monitor continued safety of vaccines [31, 32, 34].

Review committees such as the National Advisory Committee on Immunization (NACI) exist to provide ongoing expert advice about vaccines approved for use in Canada, taking into account factors that

put individuals at risk due to their occupation, travel, underlying illnesses and ages. The NACI often deliberate on which new vaccines to recommend and the type of coverage these vaccines should focus primarily on (i.e. an entire population or just high risk population groups). The NACI also takes into account how varying vaccines may interact in combination with each other, dosing schedules and how to effectively distribute vaccinations throughout Canada. It is important that new vaccinations be thoroughly evaluated before becoming publicly available, in order to identify programs that deliver the greatest coverage while minimizing cost [19, 32]. An ideal vaccine would protect against a disease after a single dose with no adverse side effects, and would be effective in immunizing all individuals ranging from infants to the elderly. In order to attain the most benefit from vaccination programs, it is fundamental that we continually evaluate the safety of all available vaccines and the efficiency in their implementation [3, 32].

Although the NACI provides recommendations for vaccines throughout Canada, the responsibility lies on provincial and territorial governments by following reviews and recommendations provided by their own scientific advisory committees and/or immunization leads. These provincial and territorial legislations determine which immunization programs are most important to provide to Canadians for no direct cost

to public consumers. Although immunization programs are mostly consistent throughout jurisdictions, the ability to provide complete coverage across Canada given that some vaccines may be publicly funded in some jurisdictions but not others becomes more of a challenge. Provincial and territorial immunization schedules have continued to diverge more in recent years due to the increased number of vaccines being included into the Canadian market [33].

## CHAPTER 2

# Mathematical Background

### 2.1. Dynamic Programming

Below we give a few necessary definitions and theoretical results which we use throughout the thesis. We start first with the definition of an optimization problem in  $\mathbb{R}^n$  as follows. We assume the reader is familiar with the basic definitions of closed sets, convex sets and convex functions in  $\mathbb{R}^n$ .

DEFINITION 1. *Let  $K \subset \mathbb{R}^n$  be a closed and convex subset of the  $n$ -dimensional Euclidean space and  $f : \mathbb{R}^n \rightarrow \mathbb{R}$  a differentiable and convex (or concave) function. We denote by  $\underline{x} \in K$  the decision variable vector. In general, an optimization problem is defined by*

$$(1) \quad \max \mid \min f(\underline{x})$$

$$s.t. \underline{x} \in K.$$

*The set  $K$  is called the constraint set,  $\underline{x} \in K$  a feasible vector. A solution of problem (1) is given by a feasible vector  $\underline{x}^* \in K$  which maximizes (or minimizes) the objective function  $f$ .*

There are many possible solution methods to finding points  $\underline{x}^*$  (simplex algorithm for linear problems, branch-and-bound, interior point methods for nonlinear problems [41, 44]).

Whenever the decision variables are restricted to  $\mathbb{Z}^n$ , rather than  $\mathbb{R}^n$ , then the optimization problem (1) is said to be an integer optimization problem. When only some coordinates of  $\underline{x}$  need to be integers, the problem is called a mixed integer optimization problem. In our case we will later be solving an integer optimization problem, and as such we need to solve it in a framework that allows variables to be defined as integers. One such approach is a dynamic programming method, given that the dimensionality of our problems is small (for a variety of dynamic programming methods see [44].)

We next define what a dynamic programming framework for an integer optimization problem looks like, pertaining to this work. Assume the following integer optimization problem (a general resource allocation problem): suppose we have  $w$  units of resource available and  $T$  activities to which we could allocate the resource. If some activity  $t \in \{1, \dots, T\}$  is implemented at level  $x_t \in \mathbb{Z}_+$ , with  $0 \leq x_t \leq w$ , then  $g_t(x_t)$  units of the resource are used by activity  $t$  (thus retaining  $w - g_t(x_t)$  units for the rest of the stages) and a benefit  $r_t(x_t)$  is obtained.



DEFINITION 2. *We can formulate the problem as*

$$(2) \quad \max \sum_{t=1}^T r_t(x_t)$$

$$s. t. \quad \sum_{t=1}^T g_t(x_t) \leq w, \text{ where } x_t \in \mathbb{Z}.$$

To solve the optimization problem (2) by dynamic programming we define  $w \in \mathbb{Z}_+$  to be the maximum level of resources and we let  $0 \leq d \leq w$  and  $d \in \mathbb{Z}_+$  be a level of resource allocation such that for each  $d$ ,  $f_t(d)$  is the maximum benefit that can be obtained from stages  $\{t, t+1, \dots, T\}$ .

DEFINITION 3. *We then reformulate problem (2) as:*

$$(3) \quad f_{T+1} = 0, \forall d$$

$$\text{for each } 0 \leq d \leq w, f_t(d) := \max_{0 \leq x_t \leq d} \{r_t(x_t) + f_{t+1}(d - g_t(x_t))\},$$

where  $0 \leq x_t \leq d$  and  $0 \leq g_t(x_t) \leq d$ . Let  $x_t(d)$  be any value of  $x_t$  attaining  $f_t(d)$ . We then use (3) to determine an optimal allocation of resources to activities  $\{1, 2, \dots, T\}$ .

## 2.2. Game Theory

A game is a mathematical framework to describe decision-making by individuals engaged in either cooperative or non-cooperative competitive situations. Non-cooperative game theory is nowadays widely

used in applied areas such as economics, engineering, operations research, evolutionary biology and social sciences (psychology and cognitive sciences), see [2, 14, 16] and many references therein. The question of existence and computation of Nash strategies for a given game can be tackled with various methods, such as the reaction curves method, optimization techniques, variational inequalities, computational methods (such as genetic algorithms, evolutionary computation), or a replicator dynamics equilibrium, etc. [2, 8, 9, 18].

In general, a multiplayer game involves a finite number of players, denoted here by  $N > 0$ . A generic player  $i \in \{1, \dots, N\}$  is thought to have a strategy set  $S_i \subset \mathbb{R}^{n_i}$ , whose strategies are vectors  $\underline{x}_i \in S_i$ . In general we assume that each player has a payoff function dependent on all other players' strategy vectors, and a payoff function  $f_i : K \rightarrow \mathbb{R}$ , where  $K := S_1 \times \dots \times S_N$ . Then a Nash equilibrium vector of strategies of a multiplayer game is defined as follows:

DEFINITION 4. *Assume each player is rational and wants to maximize their payoff. Then a Nash equilibrium is a vector  $\underline{x}^* = (\underline{x}_1^*, \dots, \underline{x}_N^*) \in K := S_1 \times \dots \times S_N$  which satisfies the inequalities:*

$$\forall i, f_i(\underline{x}_i^*, \underline{x}_{-i}^*) \geq f_i(\underline{x}_i, \underline{x}_{-i}^*), \forall \underline{x}_i \in S_i$$

where  $\underline{x}_{-i} := (x_1, \dots, x_{i-1}, x_{i+1}, \dots, x_N)$ .<sup>1</sup>

There are many results asserting existence of Nash equilibria for the above type of game (see for instance [2, 8, 16] and references therein), one such approach being that of equivalently reformulating the Nash game of Definition 4 into a variational problem. Once a game is known to have solutions, computational methods are employed to find the solution set.

Using the reaction curves type approach (see [2]), we look to solve the nonlinear system of equations  $\nabla_{x_i} f_i(x) = 0, \forall i \in \{1, \dots, N\}$ , considering all  $x_j \neq x_i$  to be constant. A solution of this system, if it exists, will be denoted by  $x^* = (x_1^*, \dots, x_N^*) \in K$ , and is a Nash equilibrium strategy vector. However we solve this system in a novel way: we regard its solution set as the set of critical points of a projected dynamical system (see [1, 20]) given by

$$(4) \quad \frac{dx}{d\tau} = P_{TK}(x(\tau))(F(x(\tau))), \quad x(0) \in K,$$

where  $F(x) := (\nabla_{x_1} f_1, \dots, \nabla_{x_N} f_N)$ , where  $P_K : \mathbb{R}^n \rightarrow K$  so that  $P_K(v) \in K$  is the closest element in  $K$  to  $v$ , i.e.,  $P_K(v) = \min_{x \in K} \|x - v\|$ . This extra operation on the righthand side of equation (4) allows

---

<sup>1</sup> $\underline{x}_{-i}$  is a generic notation convention for the vector of all strategy vectors  $\underline{x}$  without it's  $i$ -th vector

us to be sure that all solutions of equation (4) remain in the set  $K$  for all times  $t > 0$ .

The advantages of this approach are three-fold: we can assert existence of solutions to the game (given known results of existence of solutions to (4)); we can assert uniqueness of Nash equilibria; we can use computational methods developed for projected systems to analyze and compute Nash equilibria for the game.

It is known that the system (4) is well-defined if  $F$  is Lipschitz continuous on  $K$ , where  $K$  is a closed and convex set. Under these assumptions solutions to this system exist and are unique through each initial point  $x(0) \in K$ . A projection type algorithm can be used to compute its trajectories and its stationary points such as the ones in [1, 20]. To answer the uniqueness question, we first check known conditions (monotonicity) of the mapping  $-F$  (as in [1, 20]); if monotonicity conditions hold, then the Nash equilibrium is unique. Otherwise, we numerically explore the set of initial conditions of system (4) and study how many (and what values of) Nash equilibrium strategies we uncover. The latter method is not useful in uncovering unstable Nash equilibria.

## CHAPTER 3

# Optimal Allocation Scheme under Budget

## Distributions

### 3.1. Model Description & Assumptions

We consider a number of population subgroups generally divided by age, denoted by  $G_i$  where  $i \in \{1, \dots, n\}$ . We consider that there is a total budget in a single payer health system, denoted by  $B$  and that there exist several treatments on the market, which we denote by  $m$  (where a generic product is indexed by  $j \in \{1, \dots, m\}$ ). We assume that a proportion  $\gamma_i$  of the total budget  $B$  is allocated to each group  $i$ , thus  $\sum_{i=1}^n \gamma_i = 1$ . Furthermore, we define  $B_i := \gamma_i B$  the part of the budget allocated to each group  $i$ . The prices of the treatments are denoted by  $p_1, \dots, p_m$  and their efficacy by  $e_1, \dots, e_m$ . In Chapter 4, we later discuss distributions  $k_j$ ,  $j \in \{1, \dots, m\}$  in which we distribute budget per treatment type such that  $B_j := k_j B$ .

Our variables are vectors of the number of doses allocated to a population group, from a particular type of treatment:

$$x_i := (x_i^1, \dots, x_i^m), \quad i \in \{1, \dots, n\}.$$

In order to explore the impact of budget use and producer pricing competition on overall population coverage, we seek to create a model that can maximize vaccine coverage when several companies are producing similar prophylactic treatments, at different prices and efficacies. To do so, we outline the following assumptions:

ASSUMPTION 1. *All manufacturers have their own unique product, with distinct efficacy and pricing;*

As more treatments are introduced into the market, there is the possibility of manufacturers using ideas, concepts and formulas from currently existing treatments, playing a role in treatment development and competition. For the purpose of simplicity, we omit such possibilities from occurring in our simulations. From assumption 1 we claim that each treatment producer  $j$  announces an efficacy for their treatment  $e_j$  and defines their own treatment prices  $p_j$  that are independent from other treatments.

ASSUMPTION 2. *Everyone in our defined age groups are afflicted by an illness to be possibly prevented by treatments  $\{1, \dots, m\}$ ;*

ASSUMPTION 3. *Everyone offered a treatment will adopt it (the case of deterministic demand);*

Assumptions 2 and 3 allow us to define values without concern for variability dependent on consumer interest. We make assumptions that define full demand and full distribution. Later on, we explore a scenario where demand plays a bigger role in distribution.

We compute the overall treatment cover in  $G_i$ ,  $i \in \{1, \dots, n\}$  as:  
 $f_i(x_i) = \sum_{j=1}^m x_i^j e_j$ . Since all treatments will be used by the consumer,  
the total sum of our distributed resources will equal 1, i.e.  $\sum_{i=1}^n \gamma_n = 1$ .  
Thus, the coverage in the population will be  $f := \sum_{i=1}^n f_i$ .

ASSUMPTION 4. *Single-payer health system determines the adoption value of each company's product;*

ASSUMPTION 5. *Single-payer health system will not exceed its budget allocation;*

We consider our single-payer to be the primary decision maker when it comes to our defined budget. Producers have no say in negotiating prices and must rely on their own strategies to maximize their share of the distribution.

In order to account for these assumptions, we begin by working with the following parameters as defined in Table 3.1:

| Notation                 | Description                                   |
|--------------------------|-----------------------------------------------|
| $i$                      | Number of groups, $i \in \{1, \dots, n\}$     |
| $j$                      | Number of treatments, $j \in \{1, \dots, m\}$ |
| $G_i$                    | Group size                                    |
| $B$                      | Total budget                                  |
| $B_i$                    | Budget per group                              |
| $\gamma_i$               | Distribution percentage                       |
| $p_j$                    | Price of each treatment                       |
| $e_j$                    | Efficacy of each treatment                    |
| $\alpha$                 | Population scaling factor                     |
| $u_{ij} = B_i/p_j$       | Number of vaccine doses available             |
| $w_{ij} = u_{ij}/\alpha$ | Scaled number of vaccine doses available      |

TABLE 3.1. Table of parameters.

### 3.2. Case Study: The Shingles (Herpes Zoster) Virus

Due to the nature of the Shingles virus, it is known that one third of the population is susceptible to the virus once reaching the age of 50 or over. By focusing on Ontario residents over 50, we may use data from Statistics Canada to define age groups by simply multiplying those values by  $1/3$  and further scale these values by 35% in order to account for the proportionality of the population size of Ontario compared to the entire population of Canada.

Recently the Ontario government announced in its 2016 budget full coverage for the Shingles vaccine for Ontario residents within the ages



of 65-70. Although this is a great starting point, this leaves many Ontario residents to pay out of pocket for an expensive treatment option. Notably those who may develop the illness at a much younger age will need to wait up to 15 years in order to seek out government aid.

A new vaccine developed by the GSK company currently named Shingrix is in development, aimed to combat the shingles virus. Testing for the Shingrix vaccine has recently entered its third phase study and yielded results showing 90% efficacy in elder adults when maintained over several years [17]. Due to the significantly higher efficacy rate, we predict the price of the Shingrix treatment to exceed the price of the treatment currently in the market. This vaccine will prove to be a viable competitor to the Zostavax treatment once commercially available due to its vastly higher efficacy rate, and we use this competition as a basis for our study.

Our model allows us to analyze the impact this secondary treatment option may have in further expanding this coverage. We may consider any number of population subgroups - defining one such age group as the guaranteed 65-70 age group - while using the same budgetary restrictions in order to seek out how many more groups can be covered should new treatment options be introduced into the market.

A recent official publication by the government of Ontario has given out exact values for the budget parameters to be used in our study. The Ontario government plans to spend \$68 million dollars over the span of three years to treat the 42,000 reported cases of shingles each year[27]. We thus assume a budget of approximately \$25 million per year focused solely on shingles treatment expenditure.

Expanding on the assumptions listed in the previous section, we must also note the following:

*ASSUMPTION 6. Age groups 65-70 will be covered as outlined in the 2016 Ontario Budget.*

Through experimentation with groups, budgets and both static and dynamic distributions, we will explore via sensitivity analysis which age groups would benefit the most from a competition-based model in addition to the promised 65-70 age group. We will also explore the impact an increased budget will have on overall coverage.

For the purpose of our sensitivity analysis below, we seek to focus our study on age groups between the ages of 50-70 in order to explore coverage options for those who may develop the Shingles virus at an age younger than already covered by the Ontario government. By doing so, we may also focus on working class Canadians and explore alternative options - such as a copay option discussed later in section 4.3 - should

full coverage not be possible. We choose to focus towards younger age groups as we feel they are more at risk of decreased QALYs when compared to older age groups.

| Group ages         | Population size |
|--------------------|-----------------|
| $G_1$ : ages 50-54 | 322,350         |
| $G_2$ : ages 55-64 | 564,200         |
| $G_3$ : ages 65-70 | 222,950         |

TABLE 3.2. Population sizes for our groups between the ages of 50-70 in Ontario susceptible to the shingles virus.

We estimate group sizes based on Statistics Canada population data and scaled as listed in the beginning of this subsection. We differentiate these groups as ‘working’, ‘non-working’ and ‘covered’ Canadians in need of the treatment respectively. For later sections where we explore two-group coverage, we define  $G_1$  for ages 50-64, and  $G_2$  for ages 65-70 using the same values, defining these groups as currently ‘uncovered’ and ‘covered’ for treatment respectively.

To compute an optimal allocation scheme of treatment in all the groups we implement a dynamic programming approach in Matlab, with the following steps, for two products  $j \in \{1, 2\}$  and up to  $i \in \{1, 2, 3\}$  groups as in Table 3.2.

**Step 1.** We give the exogenous values of efficacies  $(e_1, e_2)$ , prices  $(p_1, p_2)$ , budget  $B$  and scaled group sizes (in units of 1000 people);

**Step 2.** We introduce parameters  $\gamma_i \in [0, 1]$ , which allow for generic distribution of the budget in  $B_i = \gamma_i B$ ,  $i \in \{1, 2, 3\}$ . We thus compute the total number of doses to be distributed (scaled in units of 1000) per group, per type of vaccine as

$$u_{ij} = \frac{B_i}{p_j}, i \in \{1, 2, 3\}, j \in \{1, 2\}.$$

**Step 3.** We set the stages of the problems to be the number of groups:  $\{1, \dots, 3 = \#of\ groups\}$ .

**Step 4.** We allocate according to a scheme in (3) starting from the 65-70 year old group.

**Step 5.** We continue the allocation process until all doses of both products purchased are distributed. This is allowed by our assumption that the treatment is adopted to anyone who receives it.

**Step 6.** We compute the coverage levels in the overall population for each distribution and parameter values.

All of the above are now formulated into the following allocation problem: let the stages be  $t \in \{1, 2, 3\}$  with  $T = 3$ . Let the total

resources be  $w_t^j = \min\{G_t/1000, u_{tj}\}$  for all  $t \in \{1, 2, 3\}$  and  $j \in \{1, 2\}$ , and let the vector of allocations in stage  $t$  be in general  $x_t = (x_t^1, x_t^2) \in [0, w_t^1] \times [0, w_t^2]$ . Let  $g_t(x_t^j) := x_t^j$  for all  $j$ . Finally, we let the payoff from vaccine allocation in stage  $t$  be  $r_t(x_t^1, x_t^2) = e_1 x_t^1 + e_2 x_t^2$ . Now we maximize the vaccine coverage in the population by solving:

$$f_{T+1} = 0, \forall d$$

$$(5) \quad \text{for each } 0 \leq d \leq w, f_t(d) := \max_{0 \leq x_t \leq d} \{r_t(x_t) + f_{t+1}(d - x_t)\},$$

$$\text{with } 0 \leq x_t \leq d.$$

### 3.3. Sensitivity Analysis

In this section we consider two main sensitivity analyses cases for a 2-group and 3-group model as follows, presenting the results of our simulations on the figures below:

1. A static case where  $B$  is a fixed value, but we vary the budget distribution of  $\gamma_1 B, \gamma_2 B$ , where  $\gamma_1 + \gamma_2 = 1$  such that  $\gamma_1 \in [0, 1]$  in order to seek out optimal distributions  $(\gamma_1^*, \gamma_2^*)$ ;
2. A dynamic case where we vary the budget  $B$  - up to 20 times the current amount - given a budget distribution of  $\gamma = (\gamma_1^*, \gamma_2^*)$  for each possible  $B$ .

**3.3.1. Two Group Coverage.** For our first set of simulations, we explore the impact budget distribution between our two groups has on overall coverage. By doing so we are able to explore whether or not budget should be distributed based on population size or based on necessity for the treatment. In these sets of simulations, we scale budget distribution in increments of 10%, where increasing the budget allocated to one group will decreased the budget allocated to the other accordingly. In the following simulations we consider two age groups  $G_1 := 50 - 64$  and  $G_2 := 65 - 70$  using values defined in Table 3.2. Default values for the total budget  $B_{initial} = 2.5 \times 10^7$  and  $B_{10} = 2.5 \times 10^8$ , price  $(p_1, p_2) = (240, 170)$ , and efficacy  $(e_1, e_2) = (0.9, 0.64)$  were used. Figures 3.1-3.2 yield our results.

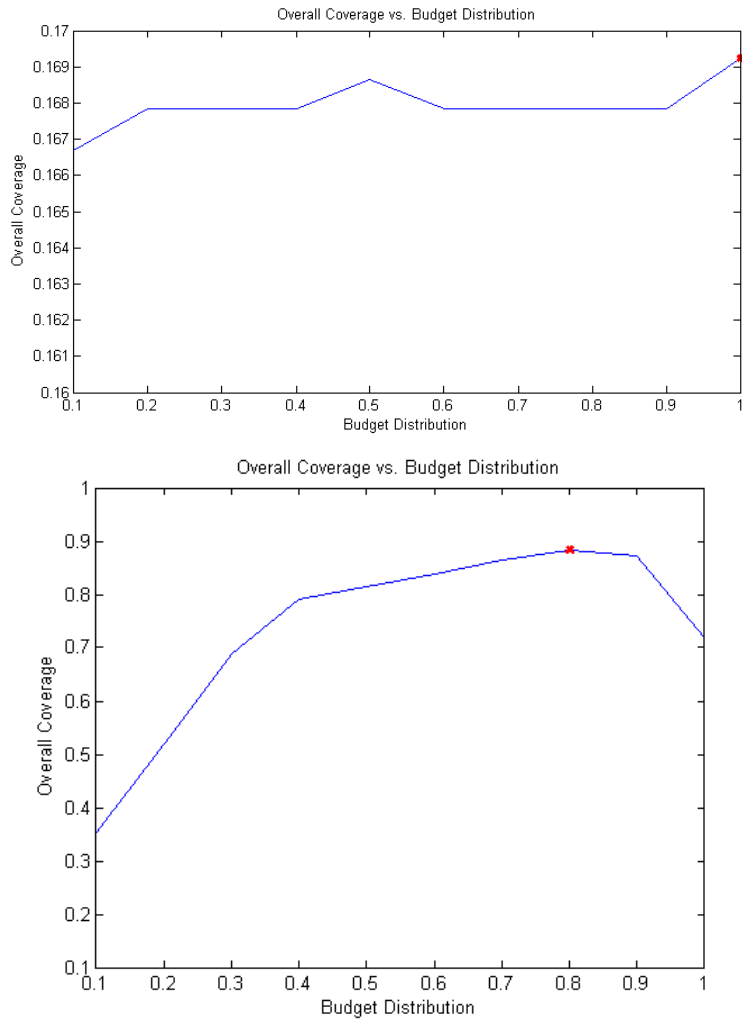


FIGURE 3.1. Overall coverage vs. budget distribution for two groups. The figures denote treatment coverage given the current budget (above) and given 10 times the budget (below).

Figure 3.1 displays a visualization of how overall coverage is impacted when varying distribution from one group to the other. Values for the budget distribution in our x-axis relate to how much of the budget is allocated to the uncovered 50-64 age group. Given the current

budget, we see very insignificant shifts in coverage as we lack proper funding to cover all age groups. However given a sufficient budget as outlined in the below figure, our data shows that as we shift budget distribution more in favour of the uncovered group, we see a vast improvement of up to 90%, at approximately  $\gamma = (0.8, 0.2)$ . These values align with the sizes of our defined age groups in the two-group case, where the uncovered group is approximately five times the size of our covered group. Results indicate that distribution of our resources proportional to group size yields optimal results for a sufficiently large budget.



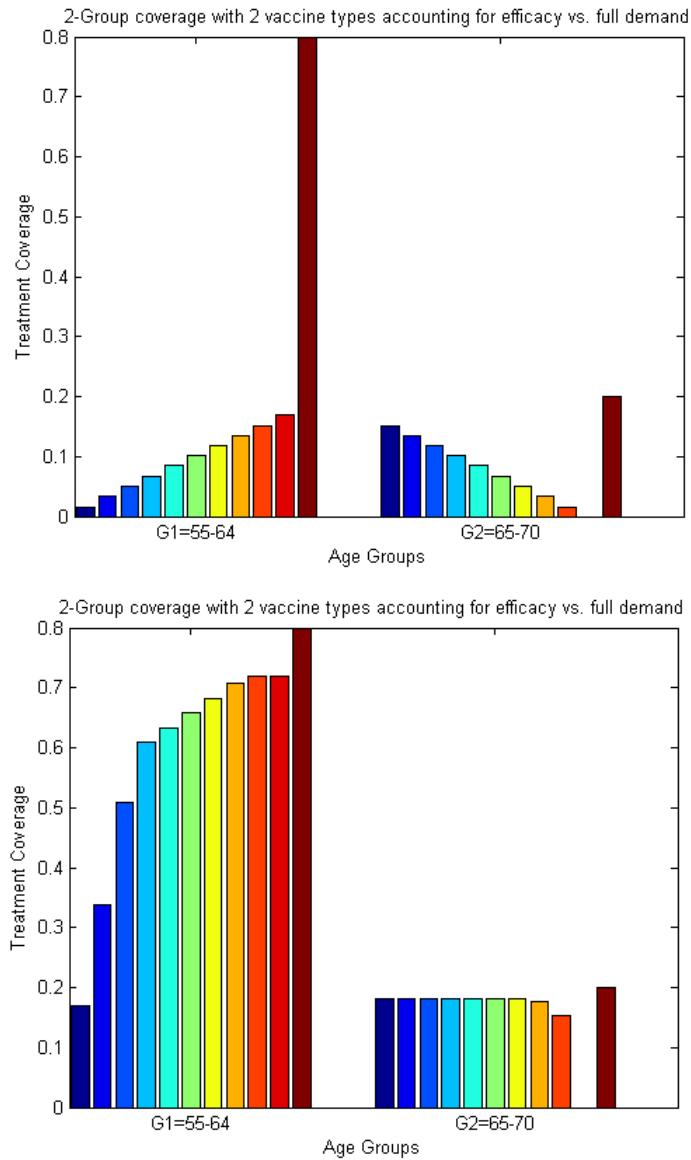


FIGURE 3.2. 2-Group coverage with 2 vaccine types. The figures denote treatment coverage given the current budget (above) and given 10 times the budget (below). The final bar for each plot denotes ideal distributions that do not account for vaccine efficacy.

Figure 3.2 shows the results as budget distribution varies between the two groups while accounting for efficacy in comparison to the desired full coverage denoted in the final bar plot of each set. The plots visualize trends as we move budget distribution in favour of our uncovered 50-64 age group. We observe that for sufficiently large budget, the uncovered group tends towards full demand but never reaches it, due to efficacy rates playing a role in coverage values (where the most effective treatment on the market will yield up to 90% coverage, meaning results maximize at 90% of the full demand).

**3.3.2. Three Group Coverage.** We continue exploring the impact budget distribution between the two treatment options has on overall coverage for a larger number of groups. In these sets of simulations, we continue to scale budget distribution in increments of 10%, however scale the distribution for the third group dependent on how much has already been distributed to the first two groups. In the following simulations we consider three age groups  $G_1 := 50 - 54$ ,  $G_2 := 55 - 64$  and  $G_3 := 65 - 70$  using values defined in Table 3.2. Default values for the total budget  $B_{initial} = 2.5 \times 10^7$  and  $B_{10} = 2.5 \times 10^8$ , price  $(p_1, p_2) = (240, 170)$ , and efficacy  $(e_1, e_2) = (0.9, 0.64)$  were used. Figures 3.3-3.8 yield our results.

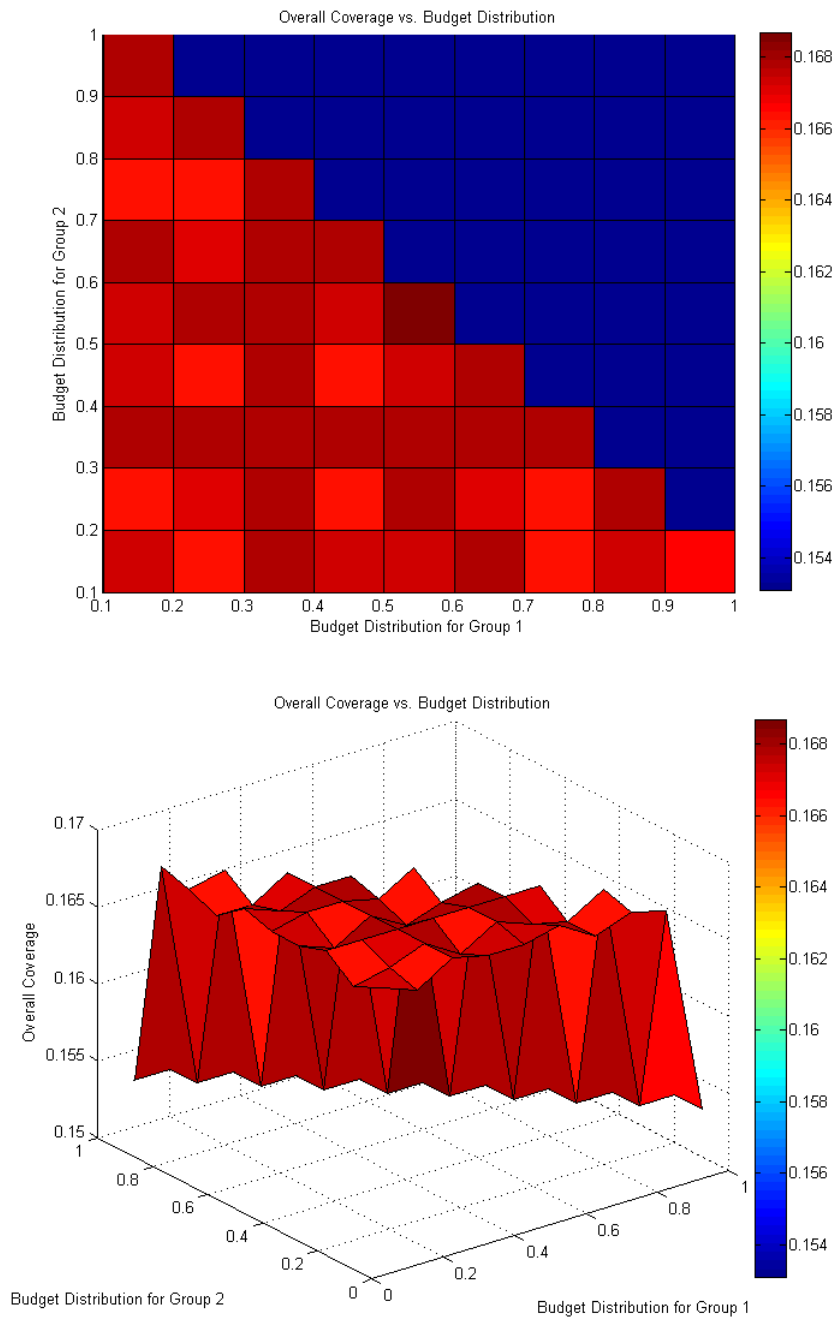


FIGURE 3.3. A 2-D (above) and 3-D (below) visualization for overall coverage dependent on budget distribution to groups  $G_1$  and  $G_2$  for the currently announced budget.

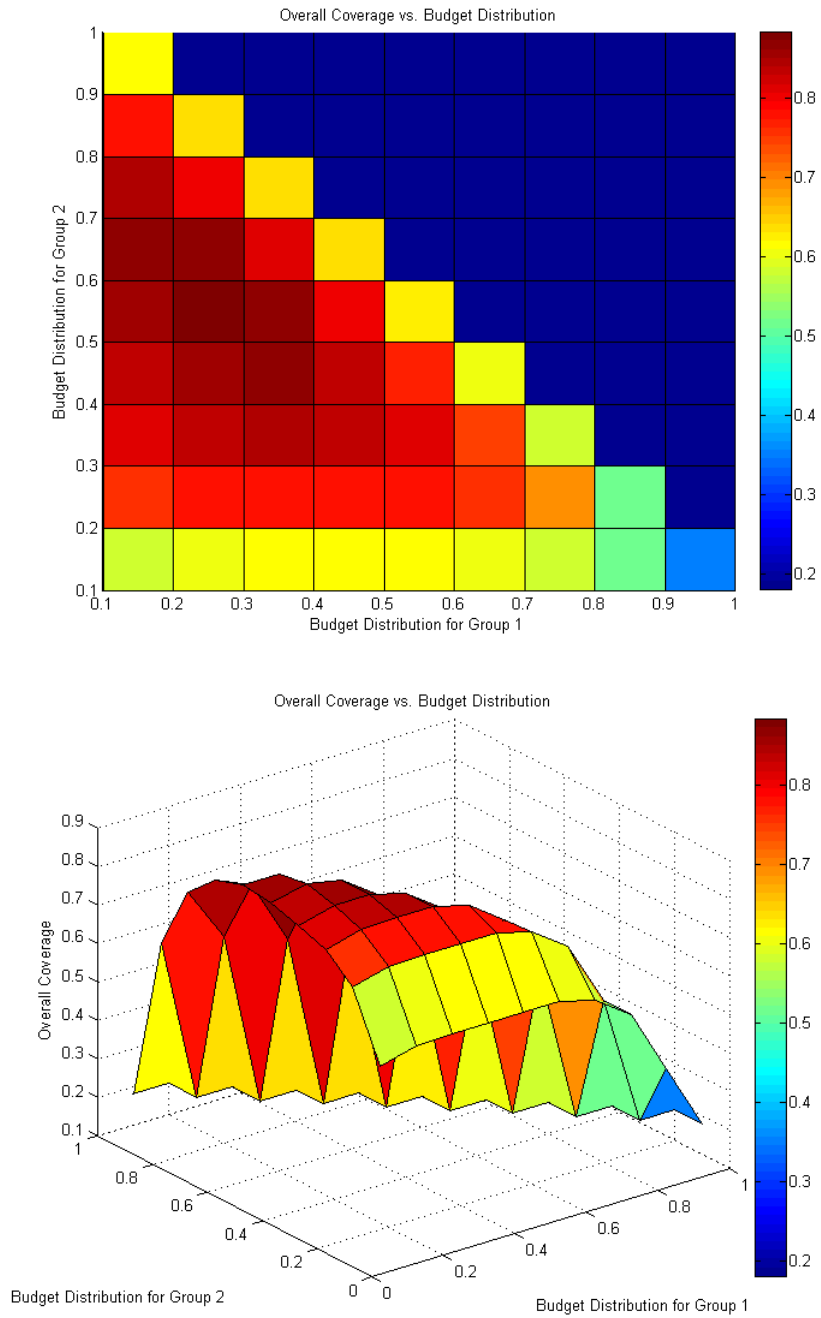


FIGURE 3.4. A 2-D (above) and 3-D (below) visualization for overall coverage dependent on budget distribution to groups  $G_1$  and  $G_2$  for ten times the currently announced budget distribution.

Figures 3.3 and 3.4 display the overall coverage for budget distribution among three groups. Given the currently announced budget, we see in Figure 3.3 that coverage options are limited due to an insufficient number of resources to allocate to our total population. However when we expand the budget as show in Figure 3.4, we find that optimal coverage occurs at approximately  $\gamma = (0.3, 0.5, 0.2)$ . As in the previous section, we find that this implies optimal distribution occurs when distributing proportional to population size, based on group sizes denoted in Table 3.2. It should be noted that for low budget distributions in group 1, we achieve high overall coverage, and for low budget distributions for group 2 we see significantly reduced overall coverage, demonstrating more value in funding Canadians in group 2 that are nearing the ages denoted in group 3. We will explore later the overall impact an increased budget has on coverage options. It should also be noted that the upper right triangular section of the plot denotes situations where we exceed 100% budget distribution and as such should be dismissed.

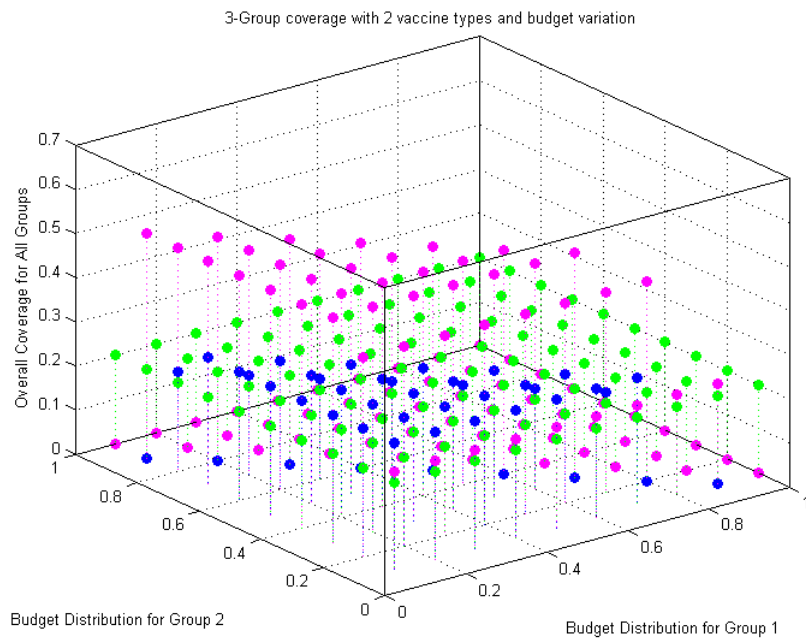
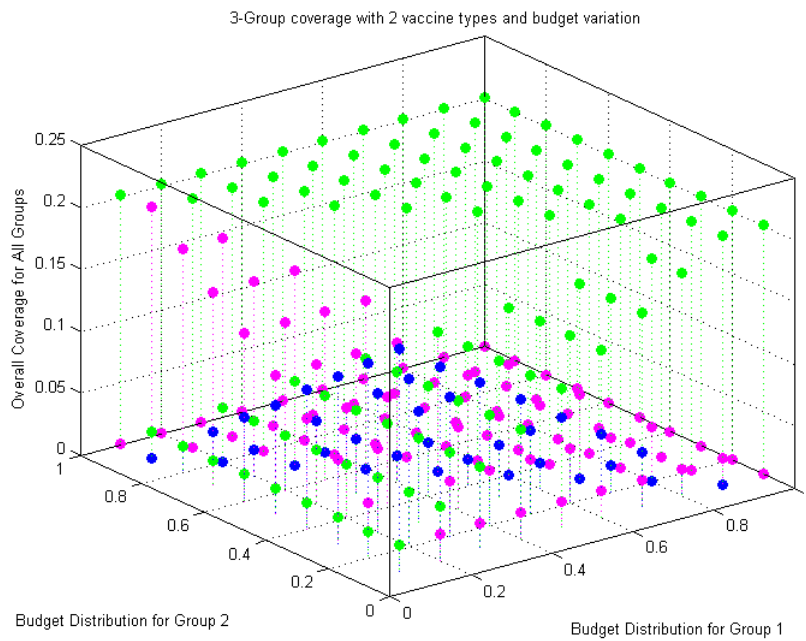


FIGURE 3.5. 3-Group coverage with 2-vaccine types and budget variation. Blue plots denote group 3, Magenta denotes group 2 and green plots denote group 1. The figures denote overall coverage given the current budget (above) and given 10 times the budget (below).

Figure 3.5 denotes a stem plot visualization of coverage for our three groups. Blue depicts age group 65-70 ( $G_1$ ), magenta depicts age group 55-64 ( $G_2$ ) and green depicts age group 50-54 ( $G_3$ ). Each age group is depicted separately in Figures 3.6 - 3.8 below, where we observe that optimal treatment is achieved when distribution favours each respective group. We recall that all plots such that  $\sum_{i=1}^n \gamma_i > 1$  will result in error, however observe that for Figure 3.8 this is not the case. This result is due to the way we distribute our resources via our simulations (code sample located in Appendix) - when conducting our second distribution round, we no longer account for budget distributions as we simply allocate whatever treatments are leftover to whichever groups have yet to be covered. Since we design our resource allocation to begin distribution from  $G_3$  and end at group  $G_1$ , we distribute leftover treatments to  $G_1$ , where results indicate that the current and expanded budget will always leave enough spare treatments after the initial distribution round to allow for full coverage of  $G_1$ .

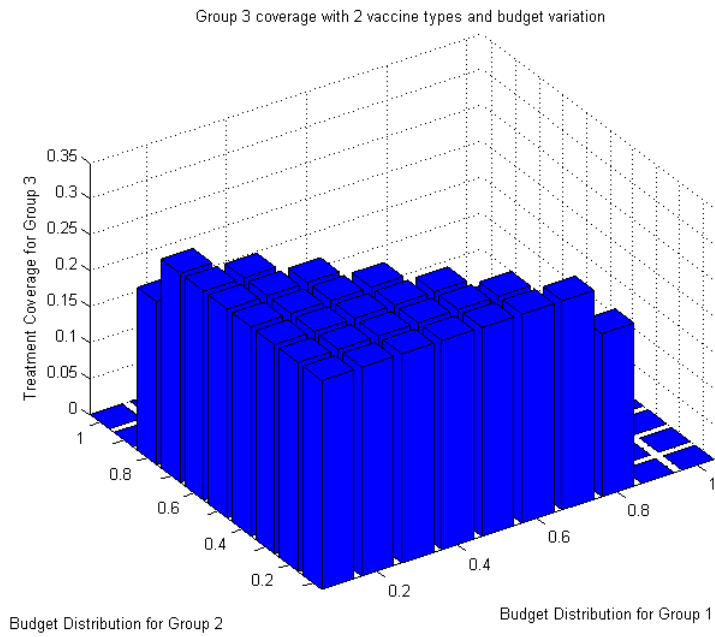
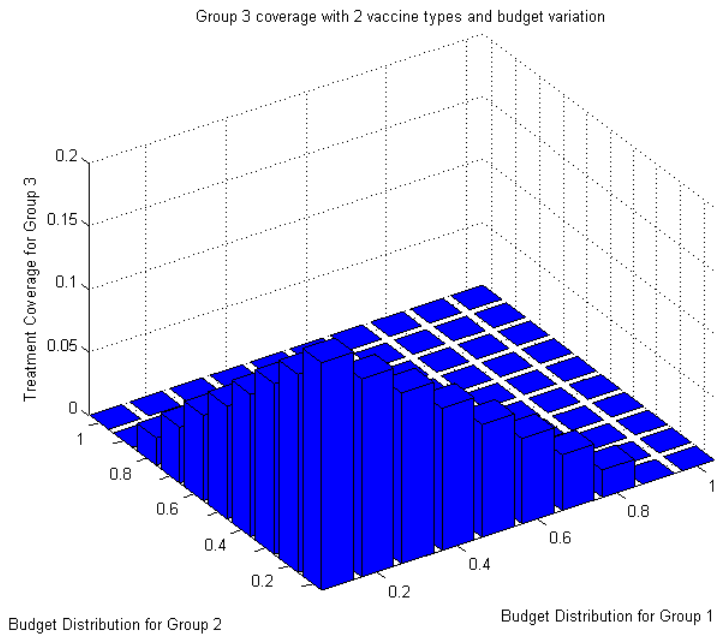


FIGURE 3.6. Group 3 coverage with 2 vaccine types and budget variation. The figures denote treatment coverage given the current budget (above) and given 10 times the budget (below).



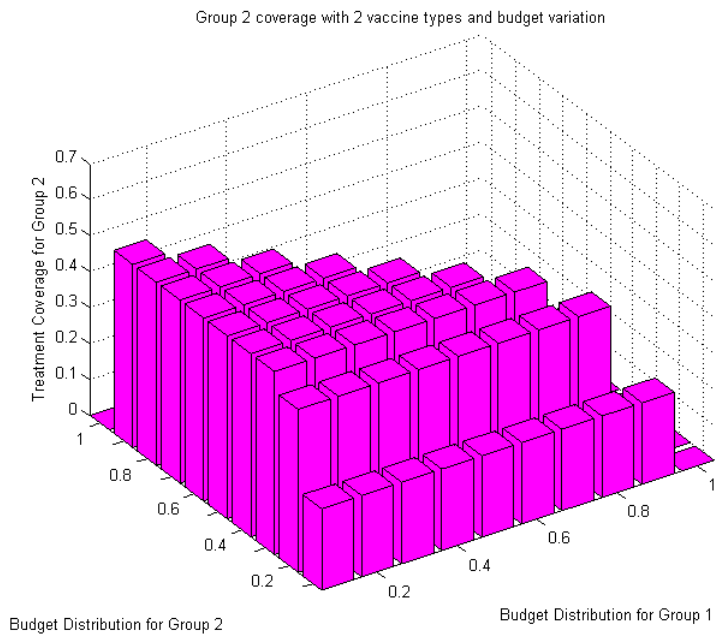
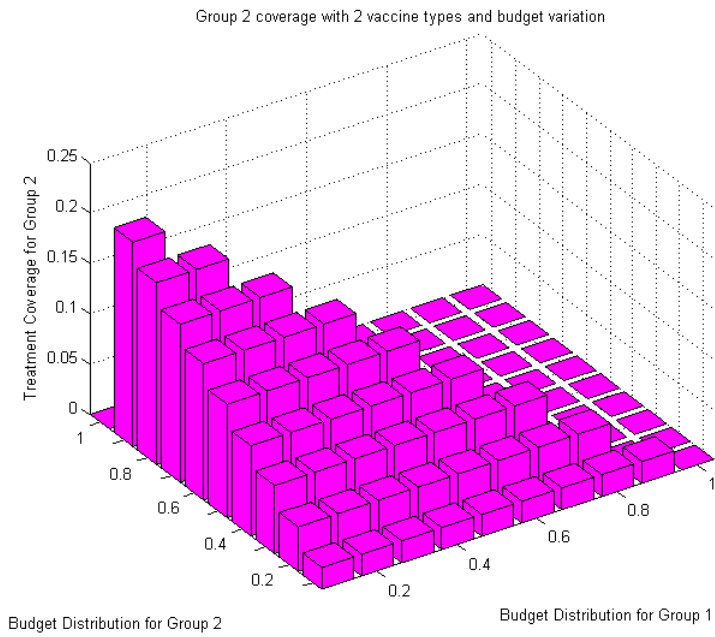


FIGURE 3.7. Group 2 coverage with 2 vaccine types and budget variation. The figures denote treatment coverage given the current budget (above) and given 10 times the budget (below).

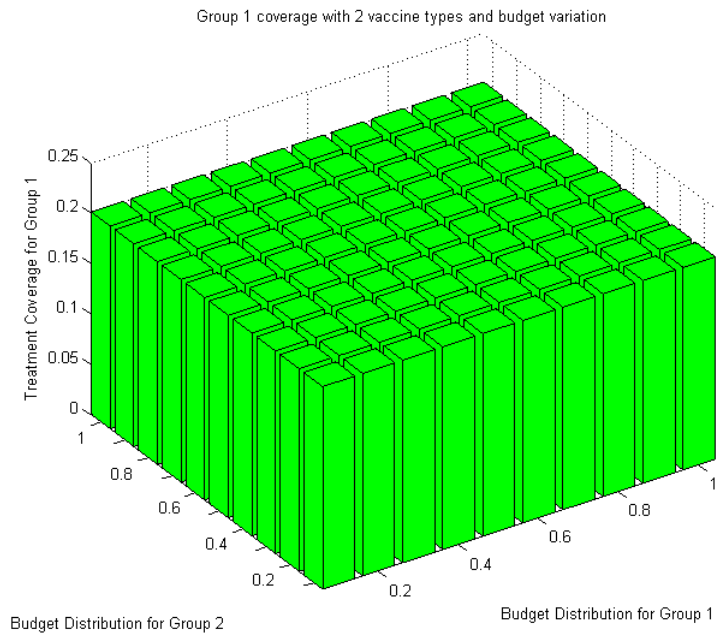
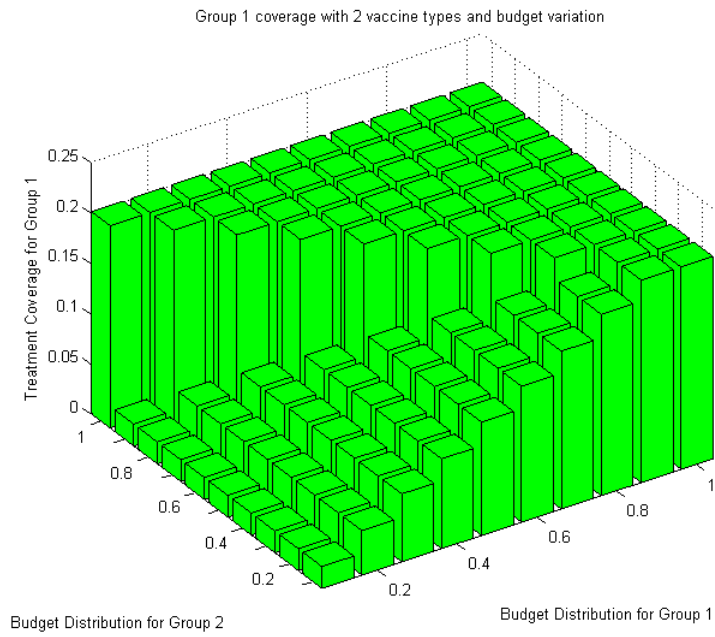


FIGURE 3.8. Group 1 coverage with 2 vaccine types and budget variation. The figures denote treatment coverage given the current budget (above) and given 10 times the budget (below).

### 3.4. Dynamic Budget Distribution

In this section we look at the possibility of increasing the total budget for acquiring vaccines in Ontario from the currently published amount of \$25 million to approximately 20 times its size, in search for an optimal treatment coverage vs. size of budget [27]. In the next two sections we explore the case of two groups (the 65-70, i.e., covered group and 50-64, i.e., uncovered group), and then the case of three groups as given in Table 3.2.

**3.4.1. Two Group Coverage.** We seek to explore the impact increasing our budget in fixed increments has on overall coverage. Based on recent publications, we use  $B_{initial} = 2.5 \times 10^7$  as our initial total budget, multiplying this budget up to a factor of 20 to reach a maximum budget of  $5.0 \times 10^8$ . For our fixed distribution, we choose  $\gamma = (0.8, 0.2)$ . The observations we make stem from the following questions: As we inflate our total budget, can we pinpoint which budget value will yield optimal results given our inputted parameters? Do we achieve a linear relationship between total budget and coverage, or will our results start to converge at a specific limit point? In the following simulations we consider two age groups  $G_1 := 50 - 64$  and  $G_2 := 65 - 70$ . Default values for the total budget  $B = 2.5 \times 10^7$ ,

price  $(p_1, p_2) = (240, 170)$ , and efficacy  $(e_1, e_2) = (0.9, 0.64)$  were used.

Figures 3.9 and 3.10 yield our results.

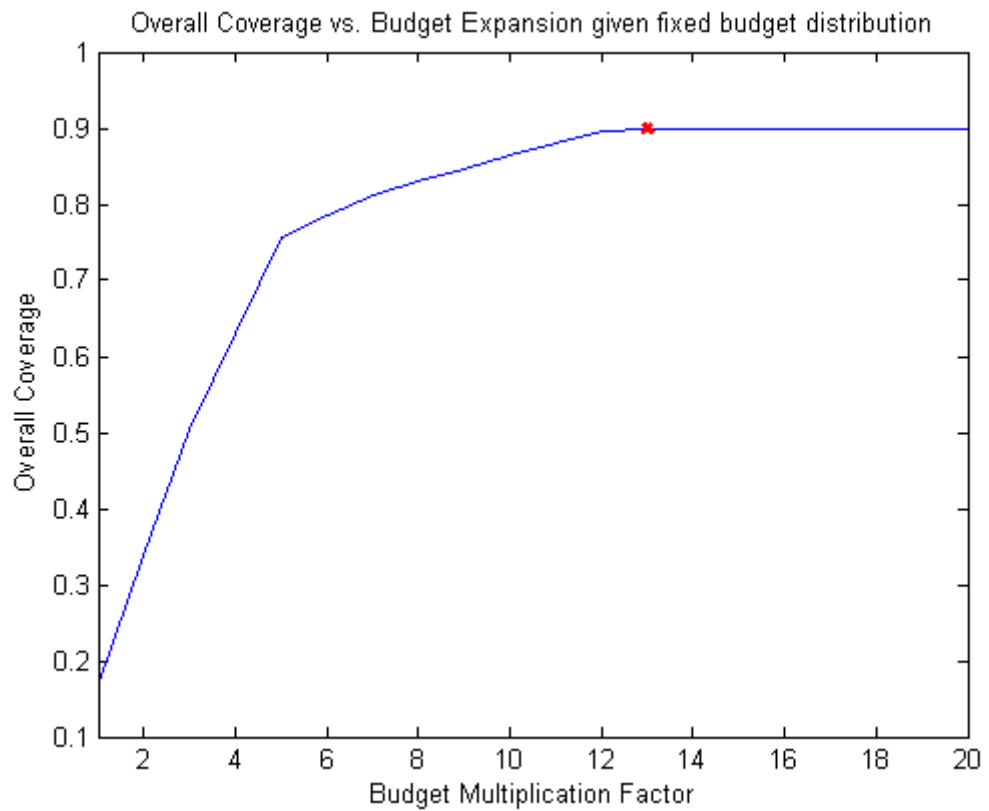


FIGURE 3.9. Overall coverage vs. budget expansion given fixed budget distribution for two groups.

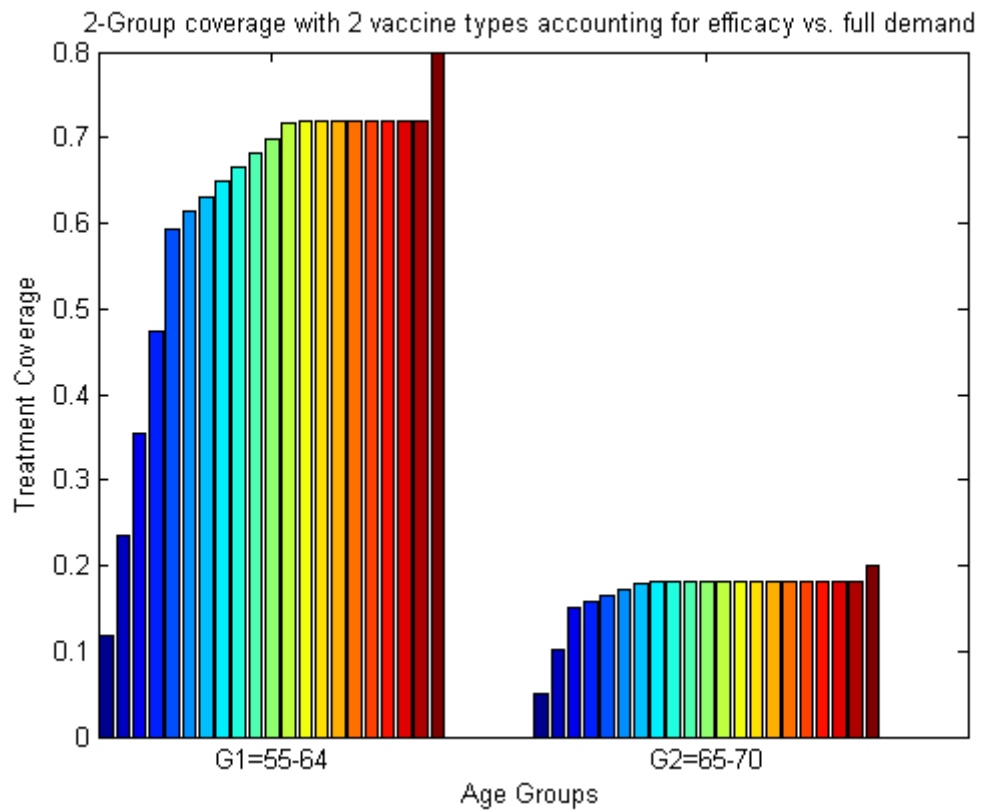


FIGURE 3.10. 2-Group coverage with 2 vaccine types with budget expansion. The final bar for each plot denotes ideal distributions that do not account for vaccine efficacy.

Figure 3.9 offers a visualization of how increasing the budget from our initial budget of \$25 million to \$500 million affects total coverage of our two population groups. We note that we achieve optimal overall coverage at approximately a budget multiplication factor (BMF) of 13, implying Public Health would need to expand their budget significantly if they wished to fully protect Ontarians from the disease. Although

this is an unrealistic request, we do see that overall coverage increases dramatically for larger scale increases. Simply multiplying the current budget by 2 yields approximately double the coverage, and multiplying the budget by 5 raises overall coverage from 15% to 70%. Given that we seek to cover a larger population size, this budgetary increase does show positive results for overall coverage. Figure 3.10 denotes total coverage for each group individually. We see that coverage eventually peaks close to full coverage, but is slightly off due to the efficacy of treatments used.

**3.4.2. Three Group Coverage.** We seek to explore the impact increasing our budget in fixed increments has on overall coverage. For our fixed distribution, we chose  $\gamma = (0.3, 0.5, 0.2)$ . The observations we make stem from the following questions: As we inflate our total budget, can we pinpoint which budget value will yield optimal results given our inputted parameters? Do we achieve a linear relationship between total budget and coverage, or will our results start to converge at a specific limit point? In the following simulations we consider three age groups  $G_1 := 50 - 54$ ,  $G_2 := 55 - 64$  and  $G_3 := 65 - 70$ . Default values for the total budget  $B = 0.25 \times 10^7$ , price  $(p_1, p_2) = (240, 170)$ , and efficacy  $(e_1, e_2) = (0.9, 0.64)$  were used. Figures 3.11 and 3.12 yield our results.

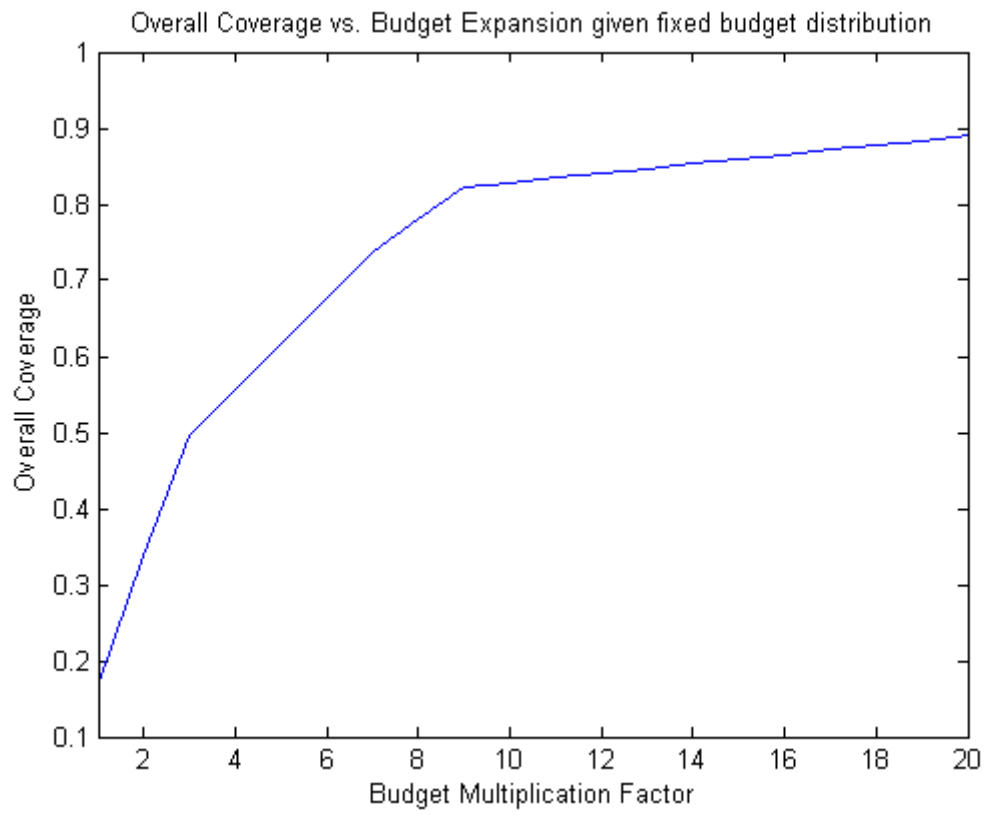


FIGURE 3.11. Overall coverage vs. budget expansion given fixed budget distribution for three groups.

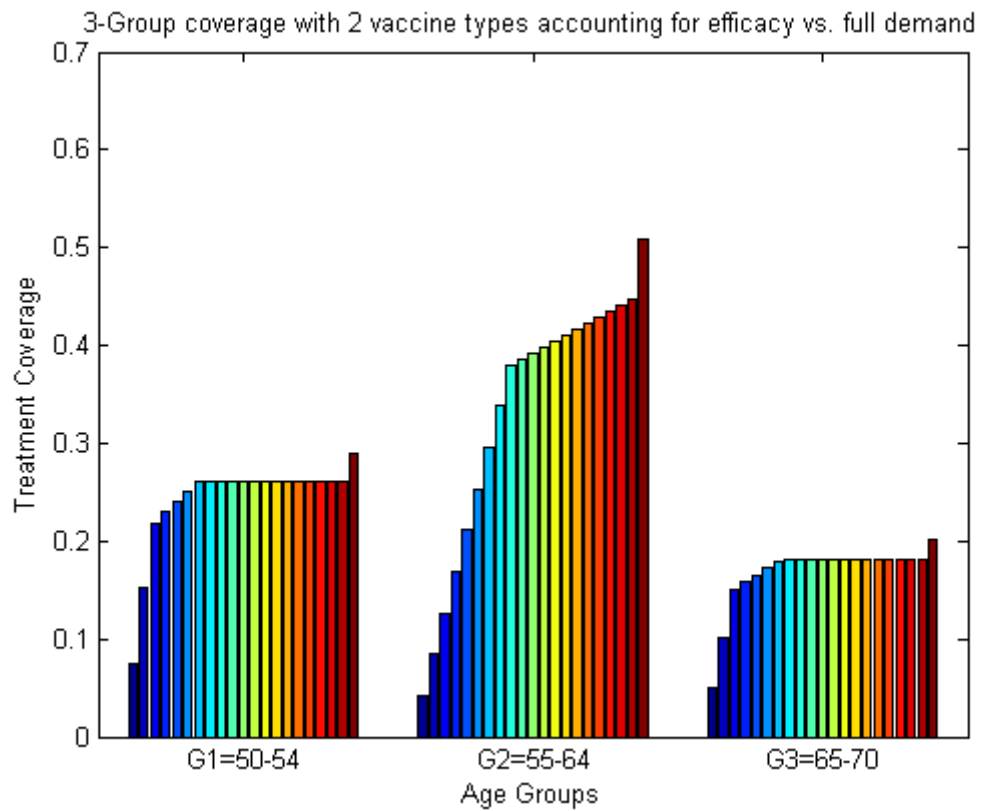


FIGURE 3.12. 3-Group coverage with 2 vaccine types with budget expansion. The final bar for each plot denotes ideal distributions that do not account for vaccine efficacy.

Figure 3.11 shows a visualization of how increasing the budget from our initial budget of \$25 million to \$500 million affects total coverage of our three population groups. We note that it takes longer to achieve optimal coverage than our 2-group plot demonstrated in Figure 3.9. Although we would require a significantly larger budget to achieve optimal



overall coverage, we do see again a significant increase as from multiplying the budget by smaller amounts. Doubling the budget would again increase overall coverage by 200% while we can increase overall coverage from approximately 15% to 60% when multiplying the budget by 5. Figure 3.12 denotes total coverage for each group individually. We see that coverage eventually peaks close to full coverage, but is slightly off due to the efficacy of treatments used.

## CHAPTER 4

### **Pricing Game under Common Budget Constraints**

In order to effectively conduct our study we can set up a generalized Nash game between our two producers, where each producer plays a non-cooperative game in an attempt to strategically maximize their profits.

There are multiple parameters in our system that play a role in consumer price responsiveness, dependent on consumer demands and availability. First, the cost of the vaccine plays a role in how much Public Health is willing to invest in each vaccine. Thus in order to maximize profits, producers must seek out an optimal price ( $p_j^*, j \in \{1, 2\}$ ) for their vaccine that allows them a favourable distribution of the total budget. Furthermore, the efficacy of the vaccine ( $e_j, j \in \{1, 2\}$ ) will play a role in consumer interest and willingness to take the vaccine. If the vaccine is unable to help a significant number of Canadians with their illness, then investing in the treatment option may prove to be a financial loss. Finally, we must also take into account any concerns or hesitance consumers may have with the available treatment options. Due to the susceptibility of elder Canadians to multiple illnesses, if a vaccine is not considered efficient enough it may be seen as a waste. As

discussed in section 1.2.2, we must also consider any hesitations consumers may have with criticisms associated with treatment options on the market (especially if the treatment option is new). These concerns will all be accounted for when we later introduce our copay fraction  $\delta$ .

#### 4.1. Static Model

Let us consider  $n$  to be the number of age groups denoted by  $i \in \{1, \dots, n\}$ , and  $m$  to be the number of treatment options denoted by  $j \in \{1, \dots, m\}$ . Furthermore we denote  $q_j$  as the number of treatment doses produced for each age group, where  $j \in \{1, 2\}$  denotes our treatments. We consider the following expressions for the number of doses produced - assuming only one producer per treatment option - as follows:

$$q_1 = a_1 - b_{11}p_1 - b_{12}p_2$$

$$q_2 = a_2 - b_{21}p_1 - b_{22}p_2$$

which can be written in the matrix form

$$(6) \quad \underline{q} = \underline{a} - B\underline{p}, \text{ where}$$

$$(7) \quad \underline{q} = (q_1, q_2)^T, \underline{a} = (a_1, a_2)^T, \underline{p} = (p_1, p_2)^T \text{ and } B = \begin{pmatrix} b_{11} & b_{12} \\ b_{21} & b_{22} \end{pmatrix}$$

In essence, equations (6) represent the demand for quantities  $q_j$  in response to prices at both producers. The scalars  $a_j$  represent the demanded quantity in an ideal situation (as when for instance the treatment would be completely free), whereas the coefficients  $b_{ij}$  represent consumers' sensitivity to treatment price given knowledge of alternative treatment  $j$ . In our case, we will always be left with a diagonally dominant matrix  $B$  as consumers will favour a treatment more when unaware of alternative treatment options in the market, i.e.  $b_{ii} \geq b_{ij}$ ,  $\forall i \neq j$ . Moreover, diagonal dominance of matrix  $B$  ensures uniqueness of Nash equilibria of the producers game below (as stated earlier in chapter 2).

In order to maximize their profit, we must first define a producer's revenue expression based on the production of doses above:  $R_1 = p_1(\underline{q})q_1$  and  $R_2 = p_2(\underline{q})q_2$ , where prices  $p_i = p_i(\underline{q}), i \in \{1, 2\}$  are functions dependent on available treatments created by each producer, and expressions are given by solving (6) as in:  $\underline{p} := B^{-1}(\underline{a} - \underline{q})$ , assuming  $B^{-1}$  exists. As a result, we can define the profit functions as follows:

$$(8) \quad \pi_j(\underline{q}) = R_j(\underline{q}) - c_j(\underline{q}) + \tau_j(\underline{q}), \text{ for all producers } j \in \{1, 2\}$$

where  $c_j(\underline{q})$  is the cost function of  $j$  and  $\tau_j(\underline{q})$  accounts for possible policy incentives that may impact total profit, for all  $j \in \{1, 2\}$ .

REMARK 1. *It should be noted that  $\tau_j(\underline{q}) \geq 0$  and can be thought of as a possible copay option paid directly by the consumer, in case Public Health decides to only partially cover the treatment costs. In this case, the expression of this term will simply be:  $\tau_j(\underline{q}) = \delta_i p_j(\underline{q}) \left( q_j \frac{G_i}{G_1 + G_2 + G_3} \right)$ , where  $\delta_i$  is the fraction of the price  $p_j$  that a consumer in age group  $i$  may have to pay directly when adopting the treatment. In this case, the Public Health Budget is covering  $(1 - \delta_i)p_j$  of treatment  $j$  in group  $i$ .*

Therefore producers share a common goal of maximizing profits given the following conditions  $\forall j \in \{1, 2\}$ :

$$(9) \quad \max \pi_j(\underline{q})$$

$$\text{s.t.} \quad \begin{cases} 0 \leq q_j \leq cap_j \\ p_j(\underline{q})q_j = k_j B \end{cases}$$

for some budget split  $k_1 B, k_2 B \in [0, B]$  and  $k_1 + k_2 = 1$ , and for some upper limit imposed to treatment production of  $j$  such that 100% of the budget allocated for treatments are used ( $cap_j$  is maximal production capacity of producer  $j$ , independent of the local Canadian market).

We observe that our model can be generalized for  $n > 2$  age groups

and  $m > 2$  producers, which can be used for other case studies in treatments for more complex illnesses.

In general, the game (9) is a generalized Nash game, as the constraints involving the pricing functions  $p_j$  are dependent on both variables,  $q_1$  and  $q_2$ , which then makes each player's strategy set dependent on the choices of all players. In fact, this formulation is a generalized Nash game without shared constraints, meaning the constraints involving the pricing functions have different functional expressions for each player. The state of the art for solving such games is meager at best, with only one attempt at addressing this problem.

For our purpose here however, we can propose a way to simplify the game in (9). Assume that the matrix  $B$  in (6) can be taken as  $B = \begin{pmatrix} b_{11} & 0 \\ 0 & b_{22} \end{pmatrix}$ , in which case then the inverse will be  $B^{-1} = \begin{pmatrix} \frac{1}{b_{11}} & 0 \\ 0 & \frac{1}{b_{22}} \end{pmatrix}$  and so the pricing functions will be

$$p_1 = \frac{a_1 - q_1}{b_{11}} \text{ and } p_2 = \frac{a_2 - q_2}{b_{22}}.$$

With these expressions, the game (9) becomes a standard Nash game between producers, which can be solved readily as described in

chapter 2. Specifically, we solve the game (9) by solving for the zeros of the system:

$$(10) \quad \frac{d(q_1(t), q_2(t))}{dt} = P_{T_K(q_1(t), q_2(t))} \left( \frac{\partial \pi_1}{\partial q_1}, \frac{\partial \pi_2}{\partial q_2} \right),$$

where

$$K := \{(q_1, q_2) \in \mathbb{R}^2 \mid 0 \leq q_1 \leq cap_1, 0 \leq q_2 \leq cap_2, \frac{a_1 - q_1}{b_{11}} q_1 = k_1 B, \\ \frac{a_2 - q_2}{b_{22}} q_2 = k_2 B\}.$$

Another way of transforming the game would be to consider that quantities  $q_j$  depend nonlinearly on their respective prices  $p_j$  in the form

$$p_j := \frac{p_0^j q_j}{\sqrt{q_j^2 + const_j}}, \text{ for } q_j \geq 0,$$

where  $p_0$  is a maximal price that local market may support, and where  $const_j > 0$  is how fast (smaller values) or slow (higher values) the price functions tend towards their horizontal asymptote  $p_0^j$ . In this case, the game is solved by the same equation (10), however the constraint set  $K$  will be given by

$$K := \{(q_1, q_2) \in \mathbb{R}^2 \mid 0 \leq q_1 \leq cap_1, 0 \leq q_2 \leq cap_2, \frac{p_0^1 q_1}{\sqrt{q_1^2 + const_1}} q_1 = k_1 B, \\ \frac{p_0^2 q_2}{\sqrt{q_2^2 + const_2}} q_2 = k_2 B\}.$$

In the sections below we study the following questions:

1. For each of the games above, we compute their Nash point values  $(q_1^*, q_2^*)$  and their price function values  $(p_1^*(q_1^*, q_2^*), p_2^*(q_1^*, q_2^*))$ , as functions of the estimated fraction of budget  $k_1, k_2 = 1 - k_1$  a producer might get from the Public Health budget  $B$ . In both the linear and nonlinear cases of the game we can theoretically check that the Nash equilibrium strategies are unique.
2. We study here whether a copay option for groups  $G_1$  and  $G_2$  will impact the Nash prices of the products and the quantities produced.
3. In the last section, we show how the results of the competitors' games affect the optimal allocation distribution from Public Health to consumers. We especially show how the copay presence in the allocation schemes act, in that we assume that the demand at consumers will be inversely proportional with the size of the copay fraction  $\delta_i, i \in \{1, \dots, 3\}$ .

For the simulations conducted below, we use the following parameter estimations given in Table (4.1).



| Parameters                           | Values           |
|--------------------------------------|------------------|
| $[a_1, a_2]$                         | [1108,1108]      |
| $[p_0^1, p_0^2]$                     | [240,170]        |
| $[const_1, const_2]$                 | [500,400]        |
| $[b_{11}, b_{22}]$                   | [-30, -20]       |
| $\{c_{11}, c_{12}, c_{21}, c_{22}\}$ | {1, 0.5, 0.5, 1} |
| $k_1$                                | vary in [0,1]    |

TABLE 4.1. Default values for our parameters.

## 4.2. Nash Prices under Variable Budget Allocation between Producers

In the previous chapter we showed how we think of the available budget  $B = \sum_{i=1}^3 \gamma_i B$  being divided among population groups for a given vector of price values. The vector we chose was  $[p_1 = 240, p_2 = 170]$ , where \$170 is the current price of the only vaccine available. Another one has been announced, with higher efficiency and thus, we expect, with a higher entry price. We saw that from Figure 3.4, the best overall coverage can be achieved for  $\gamma_1 = 0.3, \gamma_2 = 0.5, \gamma_3 = 0.2$ .

For the pricing game simulations below, there is another budget allocation to consider (from Public Health to producers) which we denoted by  $[k_1 B, k_2 B]$  with  $k_1 + k_2 = 1$ . The latter is the one that we observe as a sensitivity parameter in the Nash pricing game, as it directly affects the market size of each producer. The former will be

used in section 4.3 below, where we blend the pricing results from the games, finding the ideal allocation that optimizes overall coverage in our defined groups.

We first present the results of our linear pricing game - with all parameters discussed above - in the plots below. We present values of the optimal prices, profits and quantities in Figure 4.1 whenever we vary the budget distribution  $k_1 \in [0, 1]$ . We note that the presence of a copay for  $\delta_1 = 0.1$  as described above does not affect the optimal pricing and quantities produced, but just slightly affects profits. We then present our results of the nonlinear pricing game - with all parameters as discussed - in the plots below. We present values of the optimal prices, profits and quantities in Figure 4.2 whenever we vary the budget distribution  $k_1 \in [0, 1]$ .

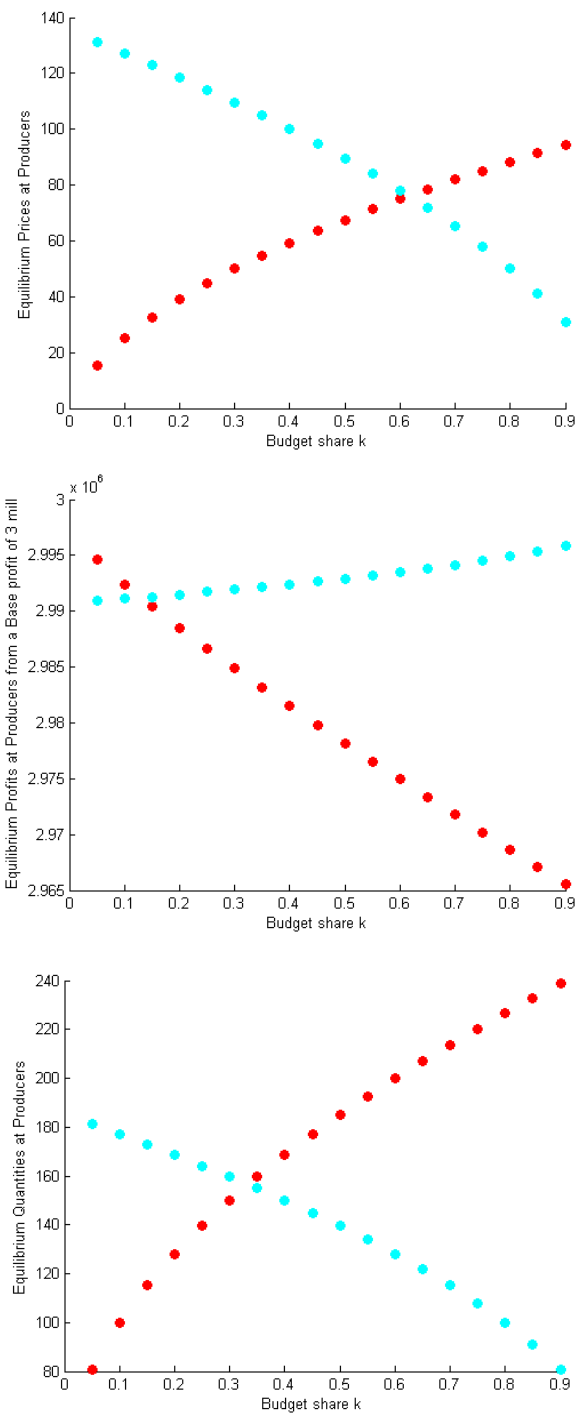


FIGURE 4.1. Linear prices, profits and quantities with no copy. Plots in red denote the more expensive treatment option while plots in cyan denote the current treatment.

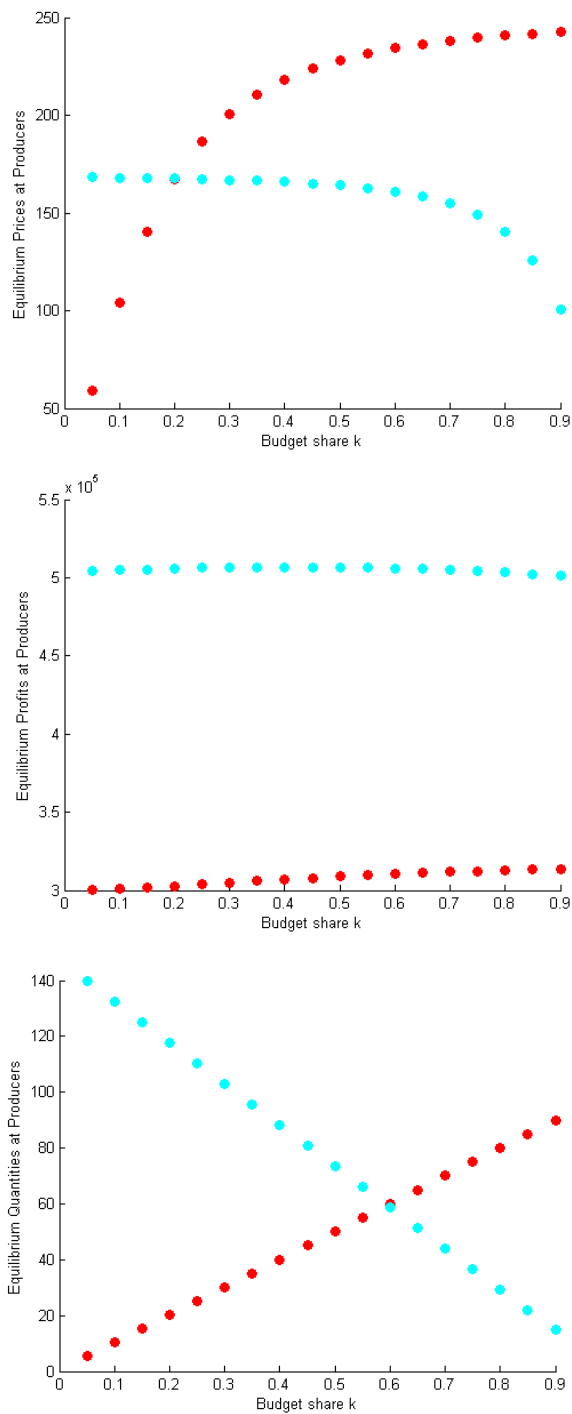


FIGURE 4.2. Nonlinear prices, profits and quantities with no copay. Plots in red denote the more expensive treatment option while plots in cyan denote the current treatment.

We see that in the linear pricing scheme the two producers produce and price as opposites to each other (when one peaks, the other lowers production almost to nil and vice-versa). In the nonlinear game, we see that as one producer logarithmically increases their price as their budget share increases, the other producer steadily drops their price until they receive very little budget share, at which point they drastically reduce their price. In the nonlinear pricing model it appears the optimal budget share occurs just prior to the severe drop in producer two's pricing.

Below are the results of what the optimal vaccine allocation would be in each of the three age groups, given the Nash prices and quantities from both the linear game (Figure 4.3) and nonlinear game (Figure 4.4). First we see that in the linear Nash pricing and production case for the current budget, the optimal allocation seems to produce a coverage of 22%, where the nonlinear Nash pricing and production yields a coverage of only 10%. Clearly, these optimal values are strongly dependent on the Nash models adopted, as well as on the  $\gamma_i$  parameter values considered. The conclusion that we can draw, given our assumptions, is that the linear pricing game gives better overall coverage in the population, however to perceive more accurate results a higher budget would be required. Once budget is expanded 10 times its current size, we achieve heightened coverage results.

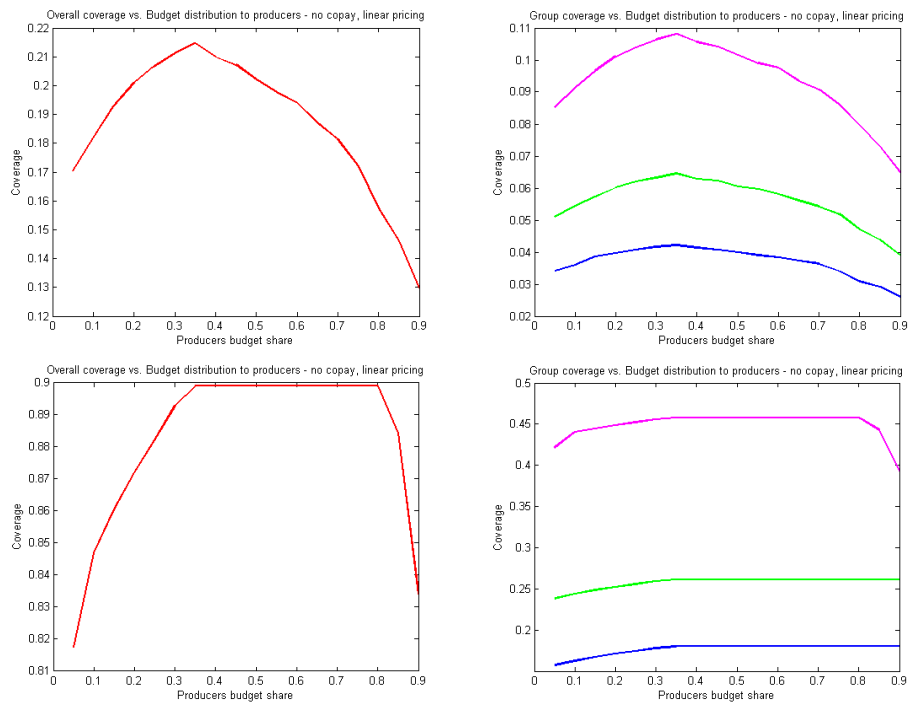


FIGURE 4.3. Linear optimal allocation for all groups (left panel) and linear optimal allocation per group (right panel). The figures denote treatment coverage given the current budget (above) and given 10 times the budget (below).

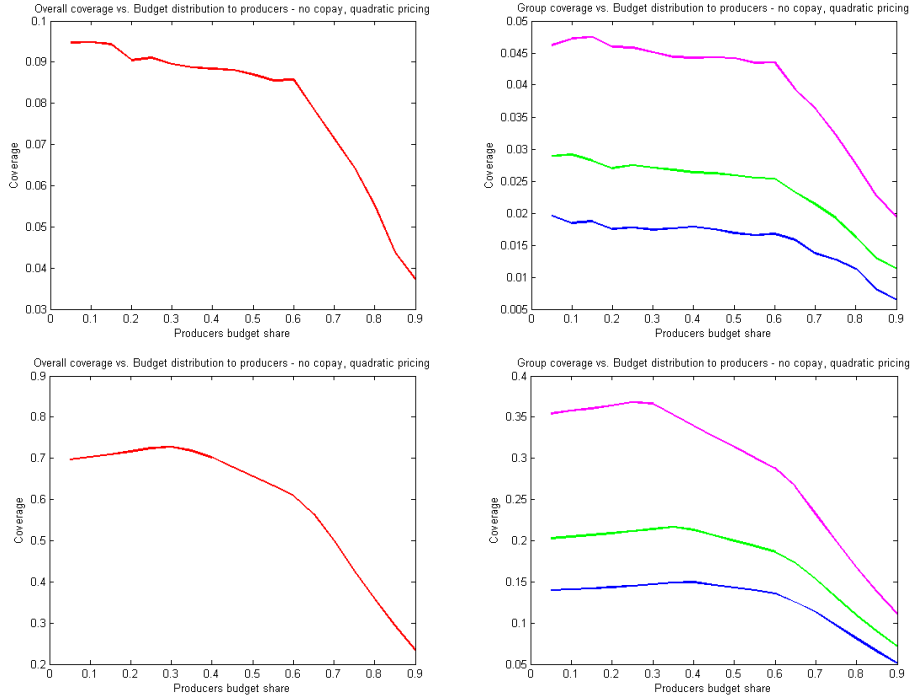


FIGURE 4.4. Nonlinear optimal allocation and optimal allocation per group with no copay. The figures denote treatment coverage given the current budget (above) and given 10 times the budget (below).

### 4.3. Treatment Allocation under Nash Pricing and Copay Option

In this last section we study the copay presence in the allocation schemes prior, where we assume that the demands at consumers will be inverse proportional with the size of the copay fraction  $\delta_i$ ,  $i \in \{1, \dots, 3\}$ . Specifically, we are interested in testing a copay option for  $G_1$  and  $G_2$ , which are on average of full and reduced employment age respectively.

That is to say we consider  $\delta_1 = \delta_2 = \delta = 0.1 > 0$ , while  $\delta_3 = 0$ , as the other groups are either covered or retirees. So for the purpose of this simulation, individuals of each group 1 or 2 will be asked to support 10% of the price of the treatment out of pocket.

If we assume everyone still wants the treatment regardless of the out of pocket expense, the overall coverage can be as high as 24% with the current budget, as Public Health is able to acquire more doses for the same budget. However this is unrealistic, and we must consider the demand of each group being affected (inverse proportionally) by the presence of the copay  $\delta_i \approx \frac{2}{\delta(p_1^* + p_2^*)}$ ,  $i \in \{1, 2\}$ , even though the number of doses for group 1 and group 2 will be higher:  $\frac{k_1 B}{(1-\delta)p_1^*}$  for product 1, and  $\frac{k_2 B}{(1-\delta)p_2^*}$  for product 2 - we assume the same value of copay regardless of producer.



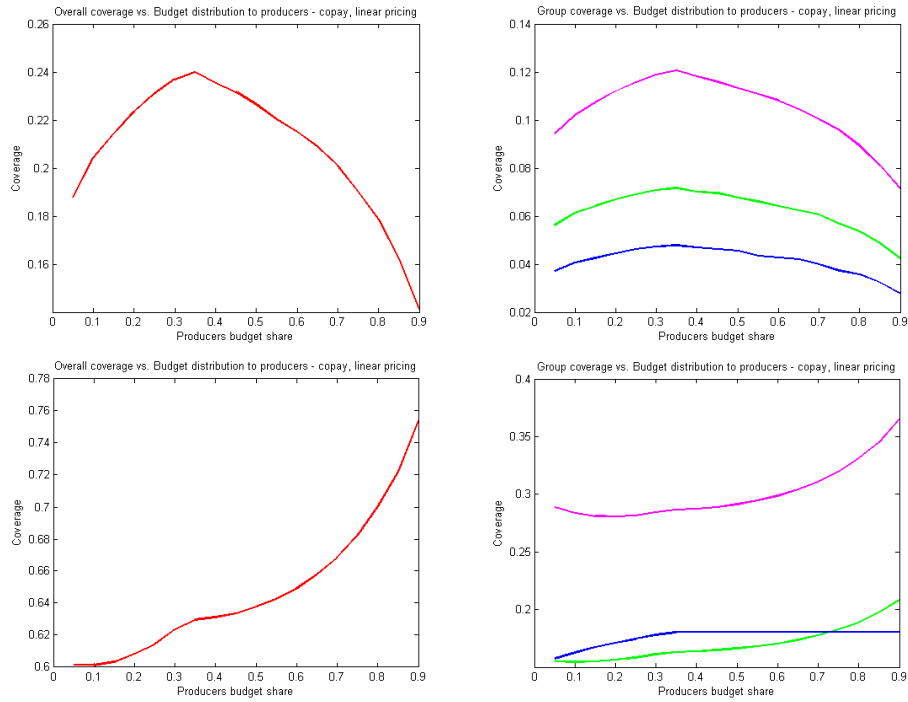


FIGURE 4.5. Linear optimal allocation for all groups (left panel) and optimal allocation per group (right panel) with copay. The figures denote treatment coverage given the current budget (above) and given 10 times the budget (below).

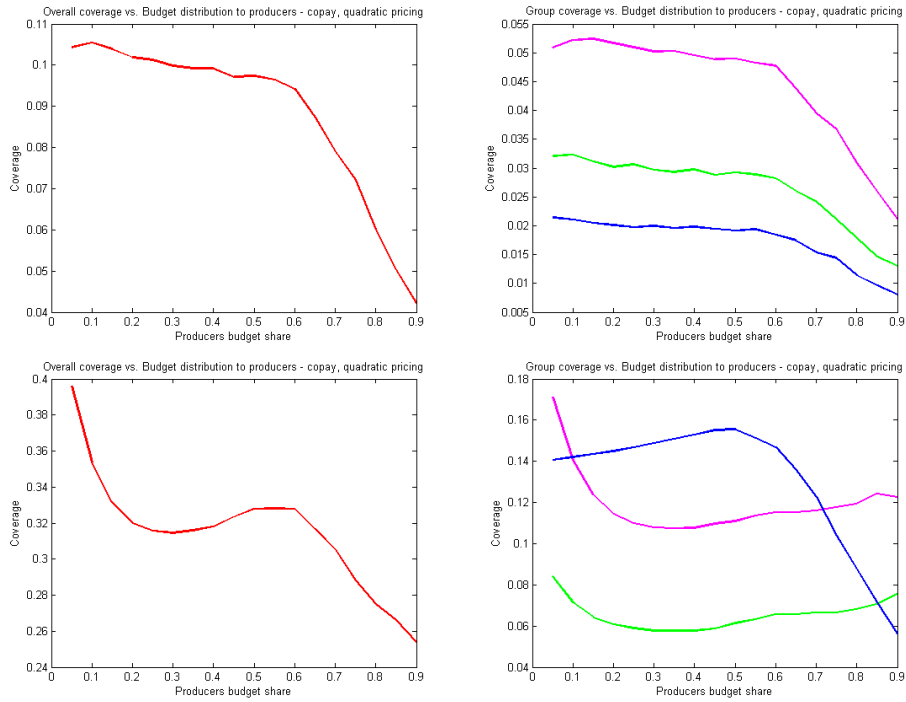


FIGURE 4.6. Nonlinear optimal allocation and optimal allocation per group with copay. The figures denote treatment coverage given the current budget (above) and given 10 times the budget (below).

We note that for the current budget, linear and nonlinear trends in Figures 4.5 and 4.6 are nearly identical, likely due to insufficient funding to allocate all resources effectively among our defined age groups. However for expanded budget, from Figure 4.5 we see that coverage peaks when distribution tends towards the more expensive treatment option while Figure 4.6 favours the cheaper treatment option. We also

observe from Figure 4.6 that a “dip” occurs when the budget is distributed evenly, which can be attributed to the proportionality between the increased number of treatments that can be distributed due to the introduction of copay vs. decreased consumer demand when asked to pay for treatment. We see that for both the linear and nonlinear cases, group 3 ( $G_3$ ) trends are altered noticeably from its group 1 ( $G_1$ ) and group 2 ( $G_2$ ) counterparts. We recall that as  $G_3$  relates to age group 65-70, as this group is already covered by Public Health it does not account for copay. As such we can visualize the impact copay has on distribution trends, yielding varied results.

## CHAPTER 5

### **Conclusion & Future Work**

By our optimal allocation scheme for the current market budget, we find overall that the current budget would not effectively sustain population groups surpassing the promised 65-70 age group. In fact, we see that the current budget does not sufficiently sustain coverage for the 65-70 age group as announced either, although this may be due to assumptions made by the Ontario government relating to consumer demand. Possible assumptions included by the government that are not immediately obvious may take into account consumer reaction to the severity of the disease, consumer perception of vaccines and alternative avenues of pain relief adopted by consumers in today's current market. Despite lacking full coverage from the given budget, we do see vast improvements when budget is expanded. When the budget is doubled we see that coverage is nearly doubled as well, and when the budget is expanded 6 times we see a spike from 20% overall coverage to nearly 75-80% overall coverage. The obvious response to this would be a necessity to increase the budget allocated to shingles treatments beyond what is currently promised in order to further expand overall coverage, which

we expect will be done once positive feedback is received during the announced three-year promise.

We observe that trends do not shift significantly when expanding the number of groups from two to three aside from a slight decrease in coverage for the three group study. For a largely expanded budget we note that optimal coverage tends to occur when budget is distributed proportional to group size, as evidenced in Figure 3.1. This makes sense in a single-year case study, as we primarily want to make sure all members of the population have equal access to treatment. We do note however that this may not be the case when focusing on a multi-year model, and should be considered a potential avenue for future study in order to determine whether or not focusing resources on distinct age groups per year could yield better long-term coverage results. In general we do see an improved overall coverage when a secondary treatment option is introduced into the market under the assumption that efficacy and pricing are scaled accordingly (i.e. the price of the second treatment option is realistic for its announced efficacy rate).

By our Nash pricing scheme for the current market budget we note trends in prices, profits and quantities of treatments for the linear and nonlinear game. For the linear game denoted in Figure 4.1, we observe opposing trends in price - as the more expensive producer raises the price of their treatment given higher budget distribution, the other

drops their price accordingly. However we see that the second producer in this scenario does see a slight increase in profits in this scenario while the other decreases - likely due to production costs of the treatment being too high to take on alone when more of the budget is being allocated to them. For the nonlinear game denoted in Figure 4.2 we see that optimal budget share occurs when the more expensive treatment option receives approximately 60% of the budget distribution, where after that point the cheaper treatment option decreases at a large rate afterwards. It should be noted however that regardless of budget distribution, profits appear to stay consistent.

Due to the nature of the pricing game being a generalized Nash game, we are able to find up to an infinite number of Nash points. This allows us to always find a “better” or “more relevant” Nash game for our outlined game. Mathematically, this game is at the cutting-edge with respect to the possible types of games that can be used in socioeconomic modeling, where novelty lies in its unique ability to solve for multiple Nash points at once. For our model we chose a simplified game where generalized assumptions do not apply and yield unique computed Nash point values. There is value in expanding this work for more complex cases.

Higher coverage for our defined age groups is certainly possible by introducing competition into the market, but there are still many avenues to explore in future work. One of the more immediate extensions to our research would be a focus on Canada-wide coverage for the same age groups using a larger budget. Would we still achieve the same coverage as we do Ontario-wide if our budgets and group sizes were increased proportionally? Would we achieve better results by focusing on national coverage, or is it better to leave coverage on a provincial scale where each province dictates how much budget to use? How would these results change as we focus on larger numbers of groups and treatment options?

So far our research has focused on what would happen in the market based on a single distribution of the vaccine, but how would our results change if we enacted a multi-year model? This would allow us to account for how effective treatments were the year prior and to focus on the impact reducing or increasing the budget on a yearly basis may have on overall coverage. Would the Canadian government be required to spend more or less in subsequent years if the first year proves to be successful? What about the impact of producers either improving from or replicating competition - how would the shift in budget distribution impact our results?

The questions we seek to ask from our results primarily focus on demand for the treatment. Even if full coverage for the shingles vaccine were possible given our defined age groups, would the majority of elderly Canadians take it? If so, then how wide can we expand coverage while still making it a viable use of taxpayer money? If not, is there value in covering these age groups? There is economic benefit in studying consumer demand in this situation simply due to views of the efficacy of vaccination programs by the general public.

The main benefit of the research conducted in this thesis is the adaptability of our work for larger group sizes and larger treatment options, allowing us to further optimize coverage for more common illnesses such as the flu. The introduction of a copay option may also prove beneficial for large-scale diseases if treatment is popular enough; if consumers are willing to invest in treatments that may significantly improve their QALY, they may be willing to spend more than the explored 10% copay discussed in this thesis without a significant decrease in demand. This could vastly improve the number of treatments covered by Public Health, yielding tremendous economic benefit.



## Appendix

### Code Sample for Optimal Allocation with Dynamic Programming (Three Group Case)

```
function distribute3G
% define variables:

G(1)=322*10^3;
G(2)=564*10^3;
G(3)=223*10^3;

BB=2.5*10^7;
p=[240,170]
e=[0.9;0.64]
alpha = 1000;

for k1=1:10
    k1
    for k2=1:10
        k2

B(3)=max(0.1*k1*BB,0);
if (k1+k2 <= 10)
    B(2)=max(0.1*k2*BB,0);
else
    B(3)=BB;
    B(2)=0;
end
B(1)=max((1-(0.1*k1)-(0.1*k2))*BB,0);

for i=1:3
    for j=1:2
        u(i,j)=floor(B(i)/p(j));
    end
end
end
```

```

for i=1:3
    for j=1:2
        w_total(i,j)=floor(u(i,j)/alpha);
    end
end

%—— Distribution Round #1

for i=1:3;
    T=4-i;

% define the vector of resources by size of group:
w=[min(G(T)/alpha , w_total(T,1)) , min(G(T)/alpha ,
    w_total(T,2))];

clear xt1 xt2

% define counters for our available resources:
xt1=0:1:w(1);
xt2=0:1:w(2);

xt=[xt1 , xt2];

clear rev

% generate revenue at each counter value:
for s=1:(w(1)+1)
    for t=1:((w(2)+2)-s)
        rev(s,t)=e(1)*xt1(s) + e(2)*xt2(t);
    end
end

% locate maximum revenue from those generated:
[M,I] = max(rev(:));
f(i)=M;
[I_row , I_col] = ind2sub(size(rev),I);
max_vacc1(T,1)=I_row-1;
max_vacc2(T,1)=I_col-1;

% resetting our resources:
w_total(T,:)=max(w_total(T,:) - [max_vacc1(T,1) ,
    max_vacc2(T,1)] , zeros(1,2));

end

```

```

% percentage of people vaccinated in each group:
for i=1:3
    perc_effr1(k1,k2,i)= (dot(mv(i,:),e)
    *alpha)/sum(G);

g(i)=G(i)/sum(G); % Full demand in each group
end

sum(g);

%—— Distribution Round #2 (emptying w_total)

for i=1:3
    GG(i)= G(i)-sum(mv(i,:)*alpha);
end

clear mv max_vacc1 max_vacc2

for i=1:3;
    T=4-i;

% define the vector of resources by size of group:
w=[min(GG(T)/alpha , w_total(T,1)) , min(GG(T)/alpha ,
    w_total(T,2))];

clear xt1 xt2

% define counters for our available resources:
xt1=0:1:w(1);
xt2=0:1:w(2);

xt=[xt1 , xt2];

clear rev

% generate revenue at each counter value:
for s=1:(w(1)+1)
    for t=1:((w(2)+2)-s)
        rev(s,t)=e(1)*xt1(s) + e(2)*xt2(t);
    end
end
end

```

```

% locate maximum revenue from those generated:
[M,I] = max(rev (:));
f(i)=M;
[I_row , I_col] = ind2sub(size(rev),I);
max_vacc1(T,1)=I_row-1;
max_vacc2(T,1)=I_col-1;

% resetting our resources:
w_total(T,:)=max(w_total(T,:)-[max_vacc1(T,1) ,
max_vacc2(T,1)] , zeros(1,2));

end

% percentage of people vaccinated in each group:
for i=1:3
    perc_effr2(k1,k2,i)= (dot(mv(i,:),e)
    *alpha)/sum(G);
end

% final Computation:
for i=1:3
    perc_eff(k1,k2,i)=perc_effr1(k1,k2,i)
    +perc_effr2(k1,k2,i);
end

    end

end

end

```

### Code Sample for Nash Pricing Game

```

function scriptoli(T)
global s
global b c a det k Budget delta1

Budget=25*10^3;
a=[50;50];
b=[2,0;0,1];
c=[1,0.5;0.5,1];
det=b(1,1)*b(2,2)-b(2,1)*b(1,2);

% To run the code for copay=0, set delta1=0;
delta1=0.1;

xin (: , 1) = [ 100; 200 ];
u = [ 0 ; 0 ];
    v = [1108 ; 1108];
        xb = [ u,v ];

for k = 0.05:0.05:0.9
kk=floor(20*k)

for i = 1:T
    [z] = vfield( xin( : , i));
    s = xin( : , i) + (0.005*z);
        [x] = solnp (xb);
        xin( : , i+1 ) = [x];
        if norm(xin(:,i+1)-xin(:,i),2)
<= 10^(-4)
            i
            break
        end
    end

end

xfinal( : , kk ) = xin( : , end);

%—Prices for linear case

price_xfinal1(kk)=b(2,2)*( xfinal(1,kk)-a(1))/det)
    -b(1,2)*( xfinal(2,kk)-a(2))/det);

price_xfinal2(kk)=-b(2,1)*( xfinal(1,kk)-a(1))/det)
    +b(1,1)*( xfinal(2,kk)-a(2))/det);

```

```

%——Profits for linear case:

profit1(kk)=(price_xfinal1(kk))*xfinal(1,kk)
             -c(1,1)*xfinal(1,kk)^2-c(1,2)*xfinal(2,kk)
             +3*10^6+delta1*(price_exfinal1(kk)
             *xfinal(1,kk)-price_xfinal2(kk)
             *xfinal(2,kk))*4/5;

profit2(kk)=(price_xfinal2(kk))*xfinal(2,kk)
             -c(2,1)*xfinal(1,kk)-c(2,2)*xfinal(2,kk)^2
             +3*10^6+delta1*(-(price_exfinal1(kk)
             *xfinal(1,kk)+(price_xfinal2(kk)
             *xfinal(2,kk))*4/5;

end

end

```

This code requires the following programs to run: cost.m, solnp.m, subnp.m, vfield.m.

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