Supply Chain Coordination and Influenza Vaccination

by

Hamed Mamani

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Abstract

Annual influenza outbreaks incur great expenses in both human and monetary terms, and billions of dollars are being allocated for influenza pandemic preparedness in an attempt to avert even greater potential losses. Vaccination is a primary weapon for fighting influenza outbreaks. The influenza vaccine supply chain has characteristics that resemble the Newsvendor problem, but possesses several characteristics that distinguish it from many other supply chains. Differences include a nonlinear value of sales (caused by the nonlinear health benefits of vaccination that are due to infection dynamics) and vaccine production yield issues. In this thesis we present two models in the interface of operations and supply chain management and public health policy.

In the first model, we focus on a supply chain with a government and a manufacturer. We show that production risks, taken currently by the vaccine manufacturer, lead to an insufficient supply of vaccine. Several supply contracts that coordinate buyer (governmental public health service) and supplier (vaccine manufacturer) incentives in many other industrial supply chains can not fully coordinate the influenza vaccine supply chain. We design a variant of the cost sharing contract and show that it provides incentives to both parties so that the supply chain achieves global optimization and hence improves the supply of vaccines.

In the second mode, we consider the influenza vaccine supply chain with multiple countries. Each government purchases and administers vaccines in order to achieve an efficient cost-benefit tradeoff. Typically different countries have different economics sensitivities to public outcomes of infection and vaccination. It turns out that the initiating country, while having a significant role in the spread of the disease, does not receive enough vaccine stockpiles. Our model indicates that lack of coordination results in vaccine shortfalls in the most needed countries and vaccine excess in the regions where are not as effective, if the governments in the model act rationally. We show the role of contracts to modify monetary flows that purchase vaccination programs, and therefore modify infectious disease flows.

Thesis Supervisor: David Simchi-Levi
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I dedicate this dissertation to my parents for having dedicated their lives to their children.

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Chapter 1

Introduction

1.1 Influenza: Overview, Control and Operational Challenges

Influenza is an acute respiratory illness that spreads rapidly in seasonal epidemics. Annually influenza outbreaks result in 250,000 to 500,000 deaths around the globe. The World Health Organization (WHO, 2005) reports that the costs of health care, lost days of work and education, and social disruption are between $1 million and $6 million per 100,000 inhabitants yearly in industrialized countries. A moderate, new influenza pandemic could increase those losses by an order of magnitude. The World Bank (Brahmbhatt, 2005) reports that the present value of the economic losses associated a global pandemic can be up to $200 billion for the US and $550 billion dollars for all high income counties (in 2004 dollars). This estimate excludes the outcomes for developing countries where health systems are much less developed and mortality could be much higher.

This thesis provides background about influenza and vaccination, a key tool for controlling influenza outbreaks, then highlights some operational challenges for delivering those vaccines. Specifically we look at two different challenges which happen throughout this value chain.

One challenge is the design of contracts to coordinate the incentives of actors in a supply chain that crosses the boundary between the public sector (health care service systems) and

private sector (vaccine manufacturers).

> Some experts suggest the U.S. government should promise to purchase a fixed amount of flu vaccine—despite the cost and the likelihood that some of the money would end up being wasted. Canada, for instance, has contracts with vaccine makers to cover most of its population. ... That takes much of the risk out of the company's business, but still lets it manufacture additional doses for the private market... (Wysocki and Lueck, 2006)

> I recently met with leaders of the vaccine industry. They assured me that they will work with the federal government to expand the vaccine industry, so that our country is better prepared for any pandemic. ... I'm requesting a total of $7.1 billion in emergency funding from the United States Congress... (Bush, 2005)

We then present a model of a government's decision of purchase quantities of vaccines, which balances the public health benefits of vaccination and the cost of procuring and administering those vaccines, and a manufacturer's choice of production volume. We characterize the optimal decisions of each in both selfish and system-oriented play, then assess whether several contracts can align their incentives. Due to special features of the influenza value chain, wholesale price and pay back contracts are shown to be unable to fully coordinate decisions. We conclude by demonstrating a variation of a cost sharing contract that can coordinate incentives, improve public health cost-benefit outcomes, increase manufacturer revenues, and increase vaccine production volumes. The Appendices in an Online Companion provide mathematical proofs for the analytical results that are given below.

Another challenge is the design of contracts to coordinate the incentives of multiple governments in the influenza vaccine value chain. One of the main reasons for such misaligned incentives is that different countries have different economic sensitivities to influenza infection which result in different objectives and hence in different decisions made by their governments. For instance, most of the vaccine stockpiles are allocated to wealthier and developed countries, such as the US or western European countries, due to high economic costs of infection. On the other hand, the influenza epidemic typically starts from regions

in Southeast Asia which have a significant impact on the spread of the disease. However, countries in this region are typically developing nations which are less able to afford vaccine stockpiles to prevent an outbreak. We show that such an allocation of vaccines to different countries is suboptimal from a central planner point of view. We then propose international agreements that can achieve optimal vaccine allocation to different countries and hence can greatly reduce the spread of the disease or even contain the epidemic right at the onset of first infections.

Although the current influenza vaccine allocation might seem to benefit the richer countries, it can create international concerns such as the global spread of the disease. Since 2007, Indonesia stopped its voluntary sharing of the strains for human cases of the Avian Flu to the World Health Organization (WHO), since they would not receive the benefit of the vaccines produced from their samples and they couldn't afford to buy the vaccines on their budget. They said:

> What's in it for us? We share virus samples, and pharmaceutical companies make vaccines from them that primarily benefit rich countries. Without better access to vaccine, why should we share virus samples? (Garrett and Fidler, 2007)

Some more developed countries also agree on this perspective. Australia's Health Minister Tony Abbott said:

> Obviously it is easier for countries like Australia and Britain and America to purchase vaccines than it is for poorer countries, such as Indonesia. I think it is important that we work out fair international arrangements for ensuring that we don't have a situation where some countries get the disease and others get the vaccines. (Asian Economic News, 2007)

To address this concern, some countries have set forth initiatives to ensure that regions that are the source of infection receive guaranteed vaccine stockpiles. Garrett and Fidler (2007) offer a novel proposal to overcome the virus sharing impasse. They propose that updated supplies of about 500 million doses of vaccine together with antiviral medicines, protective masks, etc. be stockpiled in Hong Kong every year. They have selected Hong

Kong since it has shown 'absolute transparency regarding disease emergences going back several decades'. Also Hong Kong is a dynamic center of virus research and it sits in the middle of the region that has been the source of the bulk of all flu strains known to have emerged over the last three decades.

We present a model of multiple governments' decisions of purchasing quantities of vaccines, whose optimal solution balances the public health benefits of vaccination and the cost of procuring and administering those vaccines. We characterize the optimal decisions of each of the countries with a game theory model in both selfish and system-oriented play. In the selfish model, countries store vaccine stockpiles considering only their own benefit. In the system-oriented setting, we assume a central planner, such as the WHO, allocates vaccine stockpiles to the countries minimizing the overall financial and health-related costs of the disease. It turns out that, not surprisingly, there are discrepancies between order quantities under those two settings. The central planner requires more vaccines for the initiating countries, which have significant impact on the spread of the disease, and less for others. Such a vaccine allocation increases the probability of containing the epidemic right at the onset. We then assess whether there is a contract that can align incentives of all the governments in order to ensure enough volume of vaccines at the right locations and respond affirmatively in certain conditions.

1.1.1 Influenza and Influenza Transmission

Influenza is characterized by fever, chills, cough, sore throat, headache, muscle aches and loss of appetite. It is most often a mild viral infection transmitted by respiratory secretions through sneezing or coughing. Complications of influenza include pneumonia due to secondary bacterial infection, which is more common in children and the elderly (e.g., see `http://www.cdc.gov/flu` or Janeway et al. 2001). Martone (2000) puts pneumonia and influenza together as the sixth most common cause of death in the US.

The various strains of influenza experience slight mutations in their genome through time (antigenic drift). This allows for annual outbreaks, as previously acquired adaptive immunity may not cover emerging strains. Every few decades, a highly virulent strain may

emerge that causes a global pandemic with high mortality. This may be caused by a larger genomic mutation (antigenic shift), if the novel reassorted viral strain has a high case fatality coupled with high human-to-human transmissibility.

The three pandemics that occurred in the twentieth century came from strains of avian flu. The "Spanish flu" (H1N1) of 1918 killed 20–40 million people worldwide (WHO, 2005), far more than died in World War I. Milder pandemics occurred in 1957 (H2N2) and 1968 (H3N2). The first killed around 70,000 Americans; the second around 35,000. The H5N1 virus is the most likely potential culprit for a future pandemic (`http://www.who.int/csr/disease/influenza/`).

1.1.2 Vaccination as a Control Tool

Vaccines can reduce the risk of infection to exposed individuals that are susceptible to infection (vaccine effect on susceptibility), and can reduce the probability of transmission from a vaccinated individual that is infected with influenza (vaccine effect on infection) (Longini et al., 1978, 2000; Smith et al., 1984). In a single homogenous population, vaccines act on the basic reproduction number, R_0, the mean number of new infections from a single infected in an otherwise susceptible population (Dietz, 1993). Colloquially, if R_0 can be reduced below 1, then the dynamics of a large outbreak can be averted. Let f' be the so-called critical vaccination fraction, the minimum fraction of the population to vaccinate to reduce the reproduction number to 1 when a single infected is introduced to an otherwise susceptible population. Appendix A of the Online Companion provides precise definitions for these terms. In a model with multiple populations similar concepts govern. We define R_{ij} to be the expected number of secondary infections in unvaccinated people in population i resulting from a single randomly selected unvaccinated infectious person in population j. The potential for an outbreak is determined by the dominant eigenvalue of the matrix of R_{ij} values (Hill and Longini, 2003).

Vaccination is seen as a principal means of preventing influenza. Although vaccination policies may vary from country to country, particular attention is typically paid to those aged 65 or more, health care workers, and those with certain risk factors (WHO, 2005).

Vaccination can be complemented with antiviral therapy.

Germann et al. (2006) argue that even if flu vaccine is poorly matched to the circulating strains, it can still drastically slow the spread of the disease or even contain a global pandemic. Not only effective, vaccination is also cost effective. Nichol et al. (1994) found that immunization in the elderly saved $117/person in medical costs. Weycker et al. (2005) argue for the systematic vaccination of children, not only the elderly, as a means to obtain a significant population-wide benefit for vaccination.

1.1.3 Operational Challenges in the Influenza Vaccine Supply Chain

Gerdil (2003) overviews the highly challenging and time-constrained vaccine production and delivery process. We focus on the predominant method, inactivated virus vaccine production. For the northern hemisphere, the WHO analyzes global surveillance data and in February announces the selection of three virus strains for the fall vaccination program. Samples of the strains are provided to manufacturers. High-volume production of vaccine for each of the three strains then proceeds separately. Production takes place in eleven day old embryonated eggs, so the number of eggs needed must be anticipated well in advance of the production cycle. Blending and clinical trials begin in May-June. Filling and packaging occur in July and August. Governmental certification may be required at various steps for different countries. Shipping occurs in September for vaccination in October-November. Immunity is conferred two weeks after vaccination. The southern hemisphere uses a separate 6-month cycle. Within two 6-month production cycles, almost 250 million doses are delivered to over 100 countries per year. Saluzzo and Lacroix-Gerdil (2006) provide additional information, particularly with respect to avian flu preparedness. Figure 1-1 provides a graphic summary. There are several key operational challenges that are presented by the influenza vaccine value chain.

A challenge at the start of the value chain is antigenic drift, which requires that influenza vaccines be reformulated each year. Influenza vaccines are one-time Newsvendor products, as opposed to all other vaccines, which closely resemble (perishable) EOQ-type products. Not only are production volumes hard to predict, but the selection of the target strains is a

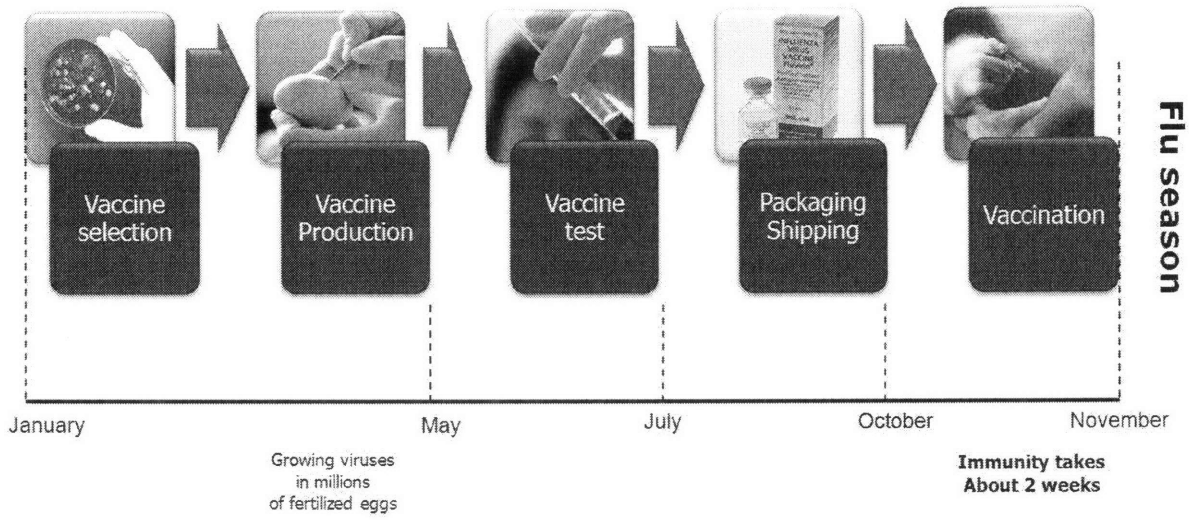


Figure 1-1: Influenza vaccine time line.

challenge. Wu et al. (2005) develop an optimization model of antigenic changes. Their results suggest that the current selection policy is reasonably effective. They also identify heuristic policies that may improve the selection process. Kornish and Keeney (2006) consider the strain selection's timing issue by considering the uncertainty in the vaccine production. They look at the dynamic strain selection problem with alternatives that commit to one of the several flu strains now and an alternative to defer the decision in order to gather more information. They describe the optimal strategies for such a commit-or-defer decision.

Another challenge occurs toward the end of the value chain, after vaccines are produced. That involves the allocation of vaccines to various subpopulations, and the logistics of transhipment to insure appropriate delivery. Brandeau et al. (2003) argue that the traditional cost-effectiveness analysis is not an effective tool when considering epidemic control problems due to highly nonlinear cost functions. They combine epidemic modeling with optimization methods to determine the optimal allocation of a limited resource for epidemic control. They show that either of the objectives of minimizing total number of newly infected individuals or maximizing quality-adjusted life years (QALY), are neither convex nor concave in general. Under some conditions of the epidemic model parameters where these functions become either convex or concave, they characterize the optimal decisions. For all other cases, some general properties of the optimal policies are derived. Hill and Longini (2003) describe a

mathematical model to optimally allocate vaccines to several subpopulations with potentially heterogeneously mixing individuals. Weycker et al. (2005) use a different, stochastic simulation model to illustrate the benefits of vaccinating certain subpopulations (children). Those articles do not discuss the logistics of delivery. Yadav and Williams (2005) propose an information clearinghouse for vaccine supply and demand to provide a market overview and to help to eliminate the gaming of orders and price gouging. They also propose the use of demand forecasting tools, and regional vaccine redistribution pools to shift supplies from areas with surpluses to areas experiencing shortages. Alternative production technologies, such as attenuated live-virus vaccines, may be one way to improve reactivity and reduce the dependence upon forecasts.

This thesis is concerned with two challenges in the middle of the value chain: (1) the design of contracts that align manufacturer choices for production volume and the need for profitability, and governmental choices that balance the costs and public health benefits of vaccination programs, and (2) the design of contracts that align different governmental choices that balance the costs and public health benefits with different priorities. Special characteristics of the influenza vaccine supply chain that differentiate it from many other supply chains include a nonlinear value of a sale (the value of averting an infection by vaccination depends upon nonlinear infection dynamics), and a dependence of production yields on the virus strains that are selected for the vaccine. In a different stream of work, Sun et al. (2007) look at a model to allocate a fixed volume of drugs to multiple countries, which is similar to the second point above. They consider the resulting game between countries and compare it to the optimal solution of a central planner. Our model differs from Sun et al. (2007) work in several ways. First and foremost, we focus on contractual agreements between governments to achieve the global optimum solution. There is also a fundamental difference in the epidemic models. Sun et al. (2007) use a multivariate Reed-Frost model to represent the infection dynamics by looking at the first two stages of the disease development. This two-period approach, under some conditions, allows for a supermodular game with some convexity-like properties of the objective functions. In this thesis, however, we use the standard SIR compartmental model (Longini et al., 1978) combined with the next generation matrix method (Hill and Longini, 2003) to model the spread of the epidemic. This way we

are able to model the entire epidemic season and compute the final outcome of the disease. With such an infection model, the cost functions turn out to be neither convex nor concave. The game between countries are also neither submodular nor supermodular.

Current production technology for inactivated virus vaccines, market forces, and business practices also combine to limit the ability to stockpile vaccines, limit production capacity, and slow the ability to respond to outbreaks. Governmental and industry partnerships may help to improve responsiveness (U.S. GAO, 2001; Pien, 2004; Bush, 2005; Wysocki and Lueck, 2006; Asian Economic News, 2007; Garrett and Fidler, 2007). The ideal way to structure those partnerships is an open question. This thesis addresses one dimension of that multi-faceted question.

1.1.4 Relation to Operations Management Literature and an Overview

This work relates to the operations management literature in three ways. First, this thesis considers the random production yield of influenza vaccine production, a Newsvendor setting. Silver (1976) considers random production yields in an EOQ setting, and shows that the optimal lot size is a slight modification of usual EOQ. Yano and Lee (1995) review approaches to lot sizing in the presence of five different types of yield randomness. We assume perfect correlation, which is what they call stochastically proportional yield, and which has been studied by Shih (1980) and Henig and Gerchak (1990).

Second, this thesis relates to the supply contract literature (Lariviere, 1999; Cachon, 2003). One stream in that literature focuses on optimizing the terms of a contract so as to improve supply chain coordination. Examples of these contracts include buy-back contracts (Pasternack, 1985), revenue sharing contracts (Cachon and Lariviere, 2005) and option contracts (Barnes-Schuster et al., 2002). The objective is to characterize contracts that allow each party to optimize its own profit but lead to a globally optimized supply chain.

The first model that we propose in this thesis is similar to the Newsvendor situation with an exchange of demand uncertainty by production uncertainty. Since the buy-back contract coordinates the supply chain for the Newsvendor (Pasternack, 1985), one could expect that the corresponding contract with uncertain yield (i.e., a payback contract) should be able

to achieve the same. We will show that this is not the case for our model. On the other hand, we show that a cost sharing contract that accounts for a manufacturer's effort can coordinate such a supply chain. That is, while contracts like payback, which only depend on the production *output*, do not align the manufacturer's incentive, contracts that take into account the production *effort* are able to do so by shifting enough risk due to uncertain production yields from the supplier to the buyer.

The pricing strategy proposed below to coordinate incentives in our general setting is nonlinear. This is, of course, not the first work to use nonlinear pricing as a coordination mechanism. For example, Bernstein and Federgruen (2005) show that in a single supplier, multiple retailer environment, coordination is possible when retailers face additive (or multiplicative) price-dependent demand. They show that a linear price-discount sharing (PDS) scheme along with a buy-back scheme may be used to coordinate the supply chain for multiple non-competing retailers. In the case of competing retailers, there exists a Nash Equilibrium for the retailers where coordination may again be achieved via a *nonlinear* PDS scheme coupled with a buy-back scheme. Our model differs from Bernstein and Federgruen (2005) in that we consider yield variability and risk for the manufacturer, rather than random demand for a buyer, and the nonlinearity in our contract is directly induced by the nonlinearity in the value of a sale due to epidemic dynamics.

The cost functions in the second model of this thesis are nonlinear in general. In fact those cost functions are neither convex nor concave. They also are not sub- or super-modular functions with respect to their parameters which make the analysis a bit more involved. We show that a cost sharing contract that accounts for the contribution of each country in the global cost function can still coordinate such a system.

The third way in which our work relates to the operations management literature is via the intersection of operations management modeling and disease modeling. In addition to articles that are cited below, Kaplan et al. (2002) assesses operational decisions for vaccination policy, with capacity constraints, to respond to smallpox bioterrorism attacks. Su and Zenios (2004) examine the role of queueing and patient choice in kidney allocation. Güneş et al. (2004) examine service capacity and quality in the context of breast cancer screening. Zaric et al. (2008) merge an inventory model with an anthrax outbreak model to

assess inventory management decisions for bio-terror preparedness. See also Brandeau et al. (2004) and references therein. To the best of our knowledge, the current thesis appears to be the first to link supply contract design with epidemic modeling in order to provide a system-wide cost benefit analysis.

Chapter 2 and Chapter 3 focus on a model with one manufacturer and one government. Section 2.1 presents a model to assess contractual mechanisms that align manufacturer risks and incentives with governmental health care policy objectives for influenza vaccination. Section 2.2 and Chapter 3 analyze the first model. Chapter 4, then considers a model with multiple governments.

Chapter 2

A Government/Manufacturer Supply Chain - Case of Piecewise Linear Attack Rate

In this chapter and next we analyze a supply chain consisting of one manufacturer and one government. We first develop the general model for this supply chain in Section 2.1 and consider two different cases, (1) when the initial exposure to infection is extremely small, and (2) when the initial exposure to infection is somewhat large. The first case leads to a piecewise linear form for the total number of infected individuals as a function of the vaccination level in the population. The second model, however, leads to a strictly convex number of infected population as a function of the vaccination level. Section 2.2 analyze the first model and Chapter 3 considers the second model.

2.1 Joint Epidemic and Supply Chain Model

This section links two distinct streams of literature. The epidemic literature provides epidemic models and cost benefit analysis for interventions such as vaccination (Murray, 1993; Hill and Longini, 2003), but does not address logistical and manufacturing concerns. The supply chain literature addresses logistical and manufacturing concerns in general, but does

not address the special characteristics of the influenza vaccine supply chain that are highlighted above.

We use simplified epidemic and supply chain models to focus on contractual issues between a single government and a single manufacturer. The single government is intended to represent centralized aggregate planning decisions for vaccination policy. The government initially selects a fraction f of a population of N individuals to vaccinate. Given the demand by the government, the manufacturer then decides how much to produce. Production volume decisions are indexed by the number of eggs, n_E, a critical factor in influenza vaccine production. Production costs are c per egg. The actual amount produced, $n_E U$, is a random variable that is indexed by a yield, U. The U.S. GAO (2001) reports that the strain can strongly influence the production yield. In this model, we assume that the yield U has a continuous probability density function $g_U(u)$ with mean μ and variance σ^2, independent of n_E. This assumption means that the yield is affected by the specific strain of the virus, and may vary from year to year, more so than from one statistically independent batch to the next within a given production campaign. We discuss the potential of a small probability of losing all production, due to quality problems for example, at the end of Section 2.2.1.

The manufacturer then sells whatever vaccine is produced, up to the amount initially requested by the government (a maximum of Nfd doses, where N is the population size, and d is the number of doses per individual). Unmet demand is lost, and excess vaccines are initially assumed not generate any revenues (due to drift and shift of strains). Later, Section 2.2.2 allows excess vaccines to be purchased at a lower price, along the lines of the analysis of the 'usual' Newsvendor model when secondary markets are present.

When acting separately, the government seeks to minimize the variable cost of procuring, p_r, and administering, p_a, each dose, plus the total social cost due to infection, $bT(f)$, where $T(f)$ is the total expected number of infected individuals by the end of the influenza season, and b is the average direct and indirect cost of an influenza infection (Weycker et al., 2005, provide estimates of such costs). Define $\bar{f}$ to be the maximum fraction of the population for which the net benefit of administering more vaccine is positive, and define $\bar{\bar{f}}$ similarly with

respect to both vaccine procurement and administration costs,

$$\bar{f} = \sup\{f : bT'(f) + p_a Nd < 0, \text{ for } f \text{ such that } T'(f) \text{ exists}\} \tag{2.1}$$

$$\bar{\bar{f}} = \sup\{f : bT'(f) + (p_a + p_r)Nd < 0, \text{ for } f \text{ such that } T'(f) \text{ exists}\}. \tag{2.2}$$

The epidemic model determines the number of individuals, $T(f)$, that are infected by the end of the influenza season. While vaccine effects and health outcomes may vary by subpopulation, and vaccination programs can take advantage of that fact (Weycker et al., 2005), we simplify the model in order to focus on contract issues for production volume, rather than including details about optimal allocation of a given volume. We use a deterministic compartmental model of N homogeneous and randomly mixing individuals that start out Susceptible to infection, but may also be infected and Infectious, or Removed upon recovery from infection, a standard SIR compartmental model that is a reasonable model for the natural history of infection of influenza (Murray, 1993). The fraction of susceptible, infectious and removed individuals ($S(t)$, $I(t)$, and $R(t)$, respectively) in the population varies as a function of time t according to a deterministic differential equation (see Appendix A of the Online Companion).

We assume that a fraction f of the population is vaccinated, and that a fraction ψ of those vaccinated are immune to infection (so $R(t) = f\psi$ for $t \leq 0$). At the start of the influenza season, at time $t = 0$, a fraction χ of the remaining susceptible population that becomes infected due to exposure from exogenous sources, so that $S(0) = (1 - f\psi)(1 - \chi)$ and $I(0) = (1 - f\psi)\chi$. The total number that become infected during the influenza season is $T(f) = Np$, where the so-called attack rate p (see the Online Companion or Longini et al. 1978) satisfies

$$p = S(0)(1 + \frac{I(0)}{S(0)} - e^{-R_0 p}). \tag{2.3}$$

The critical vaccination fraction is $f' = (R_0 - 1)/(R_0\psi)$ when $R_0 > 1$ (Hill and Longini, 2003).

Rather than deriving results via such an implicit solution from the epidemic model, we derive results for a nonincreasing $T(f) \geq 0$ with specific general characteristics. When the

values of all of the epidemic and vaccine parameters are known, Appendix B describes why it is reasonable to consider two functional forms: a piecewise linear $T(f)$ when χ is close to 0, or a strictly convex $T(f)$ when χ is sufficiently large. This removes the details of an implicit solution for an epidemic model from the supply chain analysis. Section 2.2 handles the piecewise linear case. Chapter 3 handles the convex case.

2.1.1 Generic $T(f)$ and Parameter Uncertainty

In practice, the basic reproduction number R_0, the initial fraction of susceptibles that become infected due to exogenous exposure χ, and the vaccine efficacy ψ are unknown at the time that the order quantities are chosen. It may be hard to precisely predict these parameters, due to the evolutive nature of the strains. Even for annual influenza strains, such as H3N2, a new "cluster" of drift variants tends to appear every 3-5 years (Plotkin et al., 2002; Smith et al., 2004).

The above generic approach to modeling the number infected, $T(f)$, is important because it also allows for an analysis when the values of epidemic and vaccine parameters are unknown. A probability distribution can be used to describe these types of uncertainty about the epidemic and vaccine parameters parameters, based upon past experience with strains that are similar to those that are selected for the current year's formulation. A Bayesian would do this with a prior distribution. Let $T(f; R_0, \chi, \psi)$ make the parameter values for (2.3) explicit. When parameters are uncertain, then $T(f) = \mathrm{E}[T(f; R_0, \chi, \psi)]$ describes the number of infected individuals, in expectation, based upon information that is available at the time a vaccination fraction is selected. This is compatible with the expected-value models in the remainder of the thesis that assume risk-neutral decision makers, but requires an assumption that there is no stochastic recourse to change the vaccine order quantity between the time the order is originally placed and the time that the influenza season begins, due to additional data about the strain. This last assumption is presently reasonable. More advanced influenza surveillance systems and modified production seasons may make the assumption less reasonable in the future, at which case an explicit stochastic recourse model may become more appropriate.

Table 2.1: Summary of Notation for the Manufacturer-Government Supply Chain.

Supply Chain	
n_E	Number of eggs input into vaccine production by the manufacturer
U	Random variable for the yield per egg, with pdf of $g_U(u)$, mean μ, and variance σ^2
d	Doses of vaccine needed per person
c	Unit cost of production for manufacturer, per egg input
p_r	Revenue to the manufacturer from government, per dose of vaccine
p_a	Cost per dose for government to administer vaccine
b	Average total social cost per infected individual
Z	Number of doses sold from manufacturer to government
W	Number of doses administered by government to susceptible population
Infection Transmission	
N	Total number of people in the population
R_0	Basic reproduction number, or expected number of secondary infections caused by one infected in an otherwise susceptible, unvaccinated population
f	fraction of the population to vaccinate announced by government to manufacturer
$T(f)$	Total expected number infected during the infection season, a function of the fraction vaccinated
χ	The fraction of susceptibles that are initially infected due to exogenous exposure
$I(0)$	The initial fraction of infected people introduced to the population
$S(0)$	The initial fraction of susceptible people in the population
ψ	Vaccine effects on transmission, including susceptibility and infectiousness effects
ν	Linear approximation to number of direct and indirect infections averted by a vaccination
A	bTotal number of infected individuals if nobody is vaccinated
f'	The critical vaccination fraction (fraction of population to vaccinate to halt outbreak)
$\bar{f}$	The maximum fraction for which (free) vaccine can be cost-effectively administered
$\bar{\bar{f}}$	The maximum fraction for which vaccine can be cost-effectively procured and administered
k	Relates vaccination fractions and vaccine production inputs, $k = fNd/n_E$

For example, when χ is close to 0, $T(f; R_0, \chi, \psi)$ will be shown to approximate a (convex) piecewise linear function. An expectation of convex functions is convex, so $T(f) = \mathrm{E}[T(f; R_0, \chi, \psi)]$ is convex, for an uncertain R_0, ψ and a small χ. When the parameters have a continuous distribution, this may result in a strictly convex attack rate. If the distribution implies a convex, but not strictly convex, attack rate, the sensitivity analysis in Appendix B suggests that our proposed coordinating contract may still be effective if there are small errors that are introduced by approximating the convex attack rate with a strictly convex attack rate. Results for a strictly convex $T(f)$, then, may also be useful when parameters are uncertain.

For some values of and distributions for R_0, χ, ψ, we will show (in Section 3.3 and Appendix B) that the value of $T(f; R_0, \chi, \psi)$ and $T(f)$ may initially be concave decreasing, then convex decreasing. Section 3.3 demonstrates how to coordinate contracts when $T(f)$ is an initially concave then convex, decreasing function.

Before deriving the results described above, we first complete the statement of the supply chain optimization problems.

2.1.2 Game setting

The epidemic and supply chain models above define a sequential game. The government announces a fraction f of the population for which it will purchase vaccines. The manufacturer then decides on a production quantity, indexed by n_E, in order to maximize expected profits (minimize expected costs), subject to potential yield losses and market capacity constraints. The **manufacturer problem** is:

$$\begin{array}{lll} \min\limits_{n_E} & MF = \mathrm{E}\left[cn_E - p_r Z\right] & \text{(net manufacturer costs)} \\ \text{s.t.} & Z = \min\{n_E U, fNd\} & \text{(doses sold} \leq \text{yield and demand)} \\ & n_E \geq 0 & \text{(nonnegative production volume).} \end{array} \tag{2.4}$$

So that the optimal production level is not zero, $n_E^* > 0$, we assume:

Assumption 1 *The expected revenue exceeds the cost per egg, $p_r\mu > c$, so vaccines can be profitable.*

Given that assumption, we characterize the optimal production quantity. The optimal production level is characterized by an equation that resembles the optimality newsvendor equation, except that a conditional expectation replaces a conditional probability.

Proposition 1 *For any random egg yield, U, with pdf $g_U(u)$, and given the government's vaccine order quantity fNd, the optimal production level n_E^* for the manufacturer is determined by*

$$\int_0^{\frac{fNd}{n_E^*}} u g_U(u)du = \frac{c}{p_r}. \tag{2.5}$$

Proof: The expected cost function for the manufacturer is

$$\begin{aligned} MF(n_E) &= cn_E - p_r \mathrm{E}\big[\min\{n_E U, fNd\}\big] \\ &= cn_E - p_r n_E \mathrm{E}\big[\min\{U, \frac{fNd}{n_E}\}\big] \\ &= cn_E - p_r n_E \Big(\int_0^{\frac{fNd}{n_E}} u g_U(u)du + \int_{\frac{fNd}{n_E}}^{\infty} \frac{fNd}{n_E} g_U(u)du\Big) \\ &= cn_E - p_r n_E \int_0^{\frac{fNd}{n_E}} u g_U(u)du - p_r fNd \int_{\frac{fNd}{n_E}}^{\infty} g_U(u)du \end{aligned}$$

So to get the minimum of MF we need to see the behavior of its derivative:

$$\begin{aligned} \frac{\partial MF}{\partial n_E} &= c - p_r \int_0^{\frac{fNd}{n_E}} u g_U(u)du - p_r n_E \Big[(\frac{fNd}{n_E}) g_U(\frac{fNd}{n_E})(-\frac{fNd}{n_E^2})\Big] \\ &\quad - p_r fNd \Big[- g_U(\frac{fNd}{n_E})(-\frac{fNd}{n_E^2})\Big] \\ &= c - p_r \int_0^{\frac{fNd}{n_E}} u g_U(u)du \end{aligned}$$

Note that $\frac{\partial^2 MF}{\partial n_E^2} = p_r[(\frac{(fNd)^2}{n_E^3}) g_U(\frac{fNd}{n_E})] \geq 0$ so the first order optimality condition is sufficient. Hence the optimum production quantity n_E^* is solution of the following equation: $\int_0^{\frac{fNd}{n_E^*}} u g_U(u)du = \frac{c}{p_r}$. $\square$

A useful corollary follows directly.

Corollary 1 *If c, p_r, $g_U(u)$, N and d are held constant, then the relationship between the fraction of people to be vaccinated, f, and optimum production level, n_E^*, is linear. That is, there is a fixed constant, k^G, such that $k^G n_E^* = fNd$.*

The **government problem** is to select a fraction f that indexes demand, knowing that the manufacturer will behave optimally, as in (2.5), and may deliver less, in expectation, than what is ordered due to yield losses. The government may order some excess (even $f > \bar{f}$), in order to account for potential yield losses. In this base model, we assume that the government purchases up to the amount it announced, but will administer only those doses that have a nonnegative cost-health benefit.

$$
\begin{array}{lll}
\min\limits_{f} & GF = \mathrm{E}\left[\, bT(\frac{W}{Nd}) + p_a W + p_r Z \,\right] & \text{(net government costs)} \\
\text{s.t.} & Z = \min\{n_E U, fNd\} & \text{(doses bought} \leq \text{yield and demand)} \\
& W = \min\{n_E U, fNd, \bar{f}Nd\} & \text{(doses given} \leq \text{doses bought, cost effective level)} \\
& \displaystyle\int_0^{\frac{fNd}{n_E}} u g_U(u)du = \frac{c}{p_r} & \text{(manufacturer acts optimally)} \\
& 0 \leq f \leq 1 & \text{(fraction of population)} \\
& n_E \geq 0 & \text{(nonnegative production volume)}
\end{array}
\tag{2.6}
$$

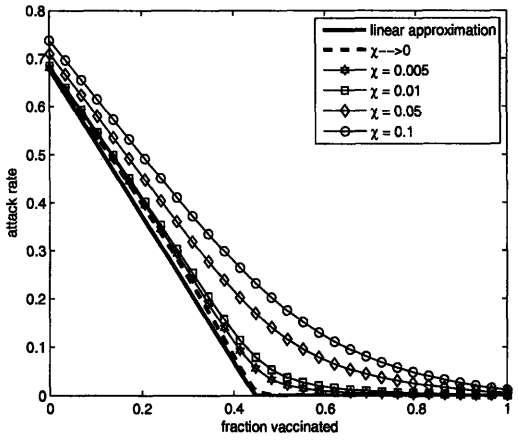
Such a two-actor game has a Nash equilibrium (Nash, 1951), which we will identify below.

2.1.3 System setting

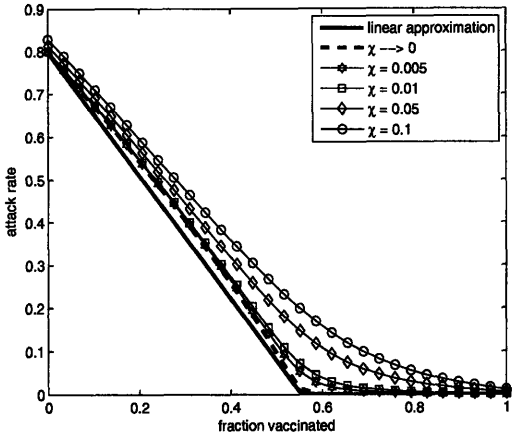
The system setting assesses whether the manufacturer and government can collaborate via procurement contracts to reduce the sum of their expected financial and health costs, to a level that is below the sum of those costs if each player acts individually as in Section 2.1.2. System costs do not include monetary transfers from government to manufacturer. Formally, the **system problem** is

$$
\begin{array}{lll}
\min\limits_{f,n_E} & SF = \mathrm{E}\left[bT(\frac{W}{Nd}) + p_a W + cn_E\right] & \text{(total system costs)} \\
\text{s.t.} & W = \min\{n_E U, fNd, \bar{f}Nd\} & \text{(doses given} \leq \text{yield, demand, cost effective level)} \\
& 0 \leq f \leq 1 & \text{(fraction of population)} \\
& n_E \geq 0 & \text{(nonnegative production volume).}
\end{array}
\tag{2.7}
$$

This formulation does not explicitly link f and n_E together, since we seek system-optimal behavior rather than local profit-maximizing behavior.



(a) $R_0 = 1.67$



(b) $R_0 = 2.0$

Figure 2-1: The fraction of the population infected during the outbreak (or attack rate, p) as a function of the fraction vaccinated (f), for different values of the fraction of susceptibles that are initially infected (χ) and the basic reproduction number (R_0).

2.2 Piecewise Linear Number of Infected

Figure 2-1 plots the attack rate, p, which is directly proportional to the total number infected, $T(f)$, as a function of the initial fraction of susceptibles that become infected due to exogenous exposure, χ, and reasonable values of R_0 for influenza transmission (Gani et al., 2005; Rvachev and Longini, 1985; Longini, 1986). If there are few that are initially infected due to exogenous exposure (small χ, or small $I(0)/S(0)$) and the parameters are accurately known, then Appendix B in the justifies the following piecewise linear approximation for $T(f)$,

$$T(f) = \begin{cases} A - N\nu f, & 0 \leq f \leq f' \\ 0, & f' \leq f \leq 1, \end{cases} \tag{2.8}$$

where ν is interpreted here as the marginal number of infections averted per additional vaccination, and A is the number of infected individuals if nobody is vaccinated.

We seek structural results to compare the values of the game equilibrium and system optimum. With this approximation for $T(f)$, the maximum cost-effective number of individuals to vaccinate equals the critical vaccination fraction, $\bar{f} = f'$. The government's objective

function from Problem (2.6) is

$$GF = \mathrm{E}\left[b\max\{A - \nu\frac{W}{d}, 0\} + p_a W + p_r Z\right]. \tag{2.9}$$

The manufacturer problem is the same.

The system's objective function from Problem (2.7) is

$$SF = \mathrm{E}\Big[b\max\{A - \nu\frac{W}{d}, 0\} + p_a W + cn_E\Big]. \tag{2.10}$$

2.2.1 Optimal solutions for game and system settings

This section describes the equilibria of the game setting and the optimal system solution for the manufacturer and government. It assumes that the parameters of the model in Section 2.1 are given. A series of assumptions and results are developed to show that the optimal system solution requires a higher vaccine production level than in the game setting. Section 2.2.2 uses those results to design contracts that create a new game, to get the individual actors to behave in a system optimal way.

The following two assumptions will be useful in the this chapter and next. If Assumption 2 were not valid, then even free vaccines would not be cost effective. Assumption 3 is a somewhat more restrictive.

Assumption 2 *The expected health benefit of vaccination exceeds the administration cost,* $\nu b - p_a d > 0$.

Assumption 3 *The expected health benefit of vaccination exceeds the cost of administering and procuring the doses,* $\nu b - (p_a + p_r)d > 0$.

Proposition 2 *Let* f^S, n_E^S *be optimal for the system setting with objective function in (2.10). If Assumptions 1 and 3 hold, then (1) all values of* f^S *that are between* f' *and* 1 *are optimal; and (2)* n_E^S *satisfies*

$$\int_0^{\frac{f'Nd}{n_E^S}} u g_U(u)du = \frac{c}{\frac{\nu b}{d} - p_a}. \tag{2.11}$$

Proof: To show these results, we analyze SF in two different regions, $f \leq f'$ and $f \geq f'$. Let $SF_1(f, n_E)$ denotes the value of SF when $f \leq f'$, and likewise $SF_2(f, n_E)$ is the value of SF where $f \geq f'$. Note that if $f \leq f'$ then $W = Z = \min\{n_E U, fNd\}$, and the value of SF_1 is

$$\begin{aligned} SF_1(f, n_E) =& b \int_0^{\frac{fNd}{n_E}} (A - \nu \frac{n_E u}{d}) g_U(u) du + b(A - N\nu f) \int_{\frac{fNd}{n_E}}^{\infty} g_U(u) du \\ &+ p_a n_E \int_0^{\frac{fNd}{n_E}} u g_U(u) du + p_a (fNd) \int_{\frac{fNd}{n_E}}^{\infty} g_U(u) du + c n_E \qquad (f \leq f'). \end{aligned} \tag{2.12}$$

For $f > f'$, given that $A - N\nu f = A - N\nu f' = 0$, the value of SF is

$$\begin{aligned} SF_2(f, n_E) =& b \int_0^{\frac{f'Nd}{n_E}} (A - \nu \frac{n_E u}{d}) g_U(u) du + p_a n_E \int_0^{\frac{f'Nd}{n_E}} u g_U(u) du \\ &+ p_a (f'Nd) \int_{\frac{f'Nd}{n_E}}^{\infty} g_U(u) du + c n_E \qquad (f \geq f'). \end{aligned} \tag{2.13}$$

The limits of integration in the right hand side of (2.13) use f', not f. In order to get the overall optimal values for f^S, n_E^S, we solve the following two subproblems.

$$\begin{array}{lll} SF1 = & \min & SF_1 \\ & \text{s.t.} & 0 \leq f \leq f' \\ & & n_E \geq 0 \end{array} \qquad \begin{array}{lll} SF2 = & \min & SF_2 \\ & \text{s.t.} & f' \leq f \leq 1 \\ & & n_E \geq 0 \end{array}$$

Optimality conditions for subproblem $SF1$**:** The KKT conditions, if $f \leq f'$, are,

$$-N\nu b \int_{\frac{fNd}{n_E}}^{\infty} g_U(u) du + p_a N d \int_{\frac{fNd}{n_E}}^{\infty} g_U(u) du + \xi - \theta_0 = 0$$

$$-\frac{\nu b}{d} \int_0^{\frac{fNd}{n_E}} u g_U(u) du + p_a \int_0^{\frac{fNd}{n_E}} u g_U(u) du + c - \varphi = 0$$

$$\xi(f - f') = \theta_0 f = \varphi n_E = 0 \quad ; \quad \xi, \theta_0, \varphi \geq 0,$$

where the first equation is obtained by taking the derivative with respect to f and the second equation is obtained by taking the derivative with respect to the n_E. Moreover ξ, θ_0, φ are KKT multipliers of constraints $f \leq f'$, $f \geq 0$, $n_E \geq 0$, respectively. Recall that Assumption 3 implies that Assumption 2 is valid. Note that if Assumption 2 were not valid, then the second equation of KKT conditions would require $\varphi > 0$, and the third equation would imply that $n_E^* = 0$.

We are interested in the case where $n_E > 0, f > 0$ which is a conclusion of Assumption 2. This implies that $\theta_0 = \varphi = 0$, and the KKT conditions simplify:

$$\Big[-N\nu b + p_a N d \Big] \int_{\frac{fNd}{n_E}}^{\infty} g_U(u)du + \xi = 0$$

$$\Big[-\frac{\nu b}{d} + p_a \Big] \int_0^{\frac{fNd}{n_E}} u g_U(u)du + c = 0$$

$$\xi(f - f') = 0 \quad ; \quad \xi \geq 0$$

In the first equation above, Assumption 2 suggests that $\xi > 0$. If $\xi > 0$, the last of the KKT conditions would give rise to $f^* = f'$. So SF_1 will always get its minimum at the extreme f'. The optimal n_E in this case can be obtained from the second equation of the KKT conditions and using the fact that $f^* = f'$, and

$$\int_0^{\frac{f'Nd}{n_E^*}} u g_U(u)du = \frac{c}{\frac{\nu b}{d} - p_a}. \tag{2.14}$$

The left hand side of this equation can take any value from 0 to $\mu = \mathrm{E}[U]$ by varying n_E^*. Assumption 1 together with Assumption 3 implies that the right hand side is strictly between 0 and μ. These assumptions therefore guarantee a solution to (2.14).

Optimality conditions for the problem $SF2$: If $f \geq f'$, then SF_2 does not depend on f (the vaccination fraction declared by the government does not change the value of objective function). It follows that all values $f' \leq f \leq 1$ are optimum and so the first part of the claim is proved.

Now SF_2 is a function of n_E only and the derivative of GF with respect to n_E is

$$\frac{\partial SF_2}{\partial n_E} = (-\frac{\nu b}{d} + p_a) \int_0^{\frac{f'Nd}{n_E}} u g_U(u) du + c.$$

Note that $\frac{\partial^2 SF_2}{\partial n_E^2} = (\frac{\nu b}{d} - p_a)(\frac{f'Nd}{n_E^2})(\frac{f'Nd}{n_E}) g_U(\frac{f'Nd}{n_E})$, which is nonnegative by Assumption 2, hence $SF_2(n_E)$ is a convex function on n_E and the first order optimality condition is sufficient. By getting the root of the derivative of SF_2 above, we can see that the optimum n_E for SF_2 is the same as the solution of (2.14). So the optimum value for n_E^S satisfies the same equation in both cases. □

Observe that if Assumption 3 does not hold, then vaccines at market costs are not cost effective. To see this, set $\tilde{f} = \min\{f, f'\}$. Then for all $0 \leq f \leq 1$,

$$\begin{aligned} GF(f, n_E) \geq \; & b \int_0^{\frac{\tilde{f}Nd}{n_E}} (A - \nu \frac{n_E u}{d}) g_U(u) du + b(A - N\nu\tilde{f}) \int_{\frac{\tilde{f}Nd}{n_E}}^{\infty} g_U(u) du \\ & + (p_a + p_r) n_E \int_0^{\frac{\tilde{f}Nd}{n_E}} u g_U(u) du + (p_a + p_r)(\tilde{f}Nd) \int_{\frac{\tilde{f}Nd}{n_E}}^{\infty} g_U(u) du \\ = \; & bA + n_E \frac{1}{d} \big((p_a + p_r)d - \nu b \big) \int_0^{\frac{\tilde{f}Nd}{n_E}} u g_U(u) du \\ & + \tilde{f} N \big((p_a + p_r)d - \nu b \big) \int_{\frac{\tilde{f}Nd}{n_E}}^{\infty} g_U(u) du. \end{aligned}$$

If $\nu b - (p_a + p_r)d < 0$, then $GF(f, n_E) > bM$ for all $f, n_E > 0$, and $f^G = n_E^G = 0$ would be optimal.

Given Assumption 3 and Proposition 2, we can compare the values of (2.5) and (2.11) to obtain Corollary 2.

Corollary 2 *Let f^S, n_E^S be optimal values of the system problem and define $k^S = \frac{f'Nd}{n_E^S}$. Let f^G, n_E^G denote optimal values of the game setting and define $k^G = \frac{f^G Nd}{n_E^G}$. If Assumption 3 holds, then $k^S < k^G$.*

The concept $k = \frac{fNd}{n_E}$ that relates vaccination fractions to vaccine production volumes is useful below.

Proposition 2 characterized the optimal vaccination fraction and production level for the system setting. We now assess optimal behavior in the game setting. (2.5) indicates that it suffices to characterize the optimal vaccination fraction, which then determines the optimal production level in the game setting. Notice that the optimal vaccination fraction depends upon problem data in the game setting, unlike the system setting.

Proposition 3 *Let f^G, n_E^G be optimal solutions for the game setting, and set $k^G = \frac{f^G N d}{n_E^G}$. If Assumption 3 holds, then $f^G \geq f'$. Furthermore, $f^G = f'$ if and only if*

$$(-\frac{\nu b}{d} + p_a + p_r) \int_0^{k^G} u g_U(u)du + p_r k^G \int_{k^G}^{\infty} g_U(u)du \geq 0. \tag{2.15}$$

Proof: We break this into two subproblems, as with $SF1$ and $SF2$ above. Define GF_1 to be the objective function for subproblem $GF1$, which handles the case where $f \leq f'$. Then

$$\begin{aligned}
GF_1(f, n_E) = \; & b \int_0^{k^G} (A - \nu \frac{n_E u}{d}) g_U(u)du + b(A - N\nu f) \int_{k^G}^{\infty} g_U(u)du \\
& + (p_a + p_r) \left[n_E \int_0^{k^G} u g_U(u)du + (fNd) \int_{k^G}^{\infty} g_U(u)du \right] \\
= \; & bM - \frac{\nu b}{d} n_E \int_0^{k^G} u g_U(u)du - N\nu b f \int_{k^G}^{\infty} g_U(u)du \\
& + (p_a + p_r) \left[n_E \int_0^{k^G} u g_U(u)du + fNd \int_{k^G}^{\infty} g_U(u)du \right] \quad (\int_0^{\infty} g_U(u)du = 1) \\
= \; & bM - \frac{\nu b}{d} n_E \int_0^{k^G} u g_U(u)du - \nu b \frac{n_E k^G}{d} \int_{k^G}^{\infty} g_U(u)du \\
& + (p_a + p_r) \left[n_E \int_0^{k^G} u g_U(u)du + n_E k^G \int_{k^G}^{\infty} g_U(u)du \right] \quad (fNd = n_E k^G) \\
= \; & bM + n_E (-\frac{\nu b}{d} + p_a + p_r) \left[\int_0^{k^G} u g_U(u)du + k^G \int_{k^G}^{\infty} g_U(u)du \right].
\end{aligned}$$

By Assumption 3, the coefficient of n_E in the last equality is negative, so the optimum value for n_E in GF_1 lies on the upper boundary, where $f = f'$. This proves the first part of the claim.

For the second part, similarly define GF_2 to be the government objective function for the case $f \geq f'$. Use the fact that $T(f) = 0$ for all $f \geq f'$, and the optimal manufacturing

constraint, $f = \frac{n_E k^G}{Nd}$, to obtain

$$
\begin{aligned}
GF_2(f, n_E) =& b \int_0^{\frac{f'Nd}{n_E}} (A - \nu \frac{n_E u}{d}) g_U(u) du + p_a n_E \int_0^{\frac{f'Nd}{n_E}} u g_U(u) du + p_r n_E \int_0^{k^G} u g_U(u) du \\
&+ p_a (f'Nd) \int_{\frac{f'Nd}{n_E}}^{\infty} g_U(u) du + p_r (fNd) \int_{k^G}^{\infty} g_U(u) du \\
=& b \int_0^{\frac{f'Nd}{n_E}} (A - \nu \frac{n_E u}{d}) g_U(u) du + p_a n_E \int_0^{\frac{f'Nd}{n_E}} u g_U(u) du \\
&+ p_a (f'Nd) \int_{\frac{f'Nd}{n_E}}^{\infty} g_U(u) du + p_r n_E \left[\int_0^{k^G} u g_U(u) du + k^G \int_{k^G}^{\infty} g_U(u) du \right] \\
\frac{\partial GF_2}{\partial n_E} =& (-\frac{\nu b}{d} + p_a) \int_0^{\frac{f'Nd}{n_E}} u g_U(u) du + p_r \int_0^{k^G} u g_U(u) du + p_r k^G \int_{k^G}^{\infty} g_U(u) du \\
\frac{\partial^2 GF_2}{\partial n_E^2} =& (\frac{\nu b}{d} - p_a) \frac{f'Nd}{n_E^2} g_U(\frac{f'Nd}{n_E})
\end{aligned}
$$

for $f \geq f'$. Note that $\frac{f'Nd}{n_E} \leq k^G$. By Assumption 2, $\frac{\partial^2 GF_2}{\partial n_E^2} \geq 0$, so GF_2 is a convex function of n_E. To find the minimum it suffices to look at the sign of its first derivative. If Condition (2.15) holds, then Assumption 2 implies that $\frac{\partial GF_2}{\partial n_E} \geq 0$ on $f \geq f'$, so that the minimum of GF_2 for $f \in [f', 1]$ is obtained at f'. The optimum for both GF_1 and GF_2 lead to the claimed optimum, namely $f^G = f'$.

If Condition (2.15) does not hold (i.e. $(-\frac{\nu b}{d} + p_a + p_r) \int_0^{k^G} u g_U(u) du + p_r k^G \int_{k^G}^{\infty} g_U(u) du < 0$); then because of the convexity of function GF_2 on n_E (non-decreasing derivative), there are two cases:

Case 1: $\exists \tilde{n}_E$; $\frac{\partial GF_2}{\partial \tilde{n}_E^G} = 0$. In this case clearly the optimum values for the f, n_E are the following: $n_E^G = \tilde{n}_E$, $f^G = k^G n_E^G / Nd$.

Case 2: If $n_E(1)$ denotes the maximum n_E corresponding to $f = 1$ (i.e. $n_E(1) = \frac{1Nd}{k^G}$) and still $\frac{\partial GF_2}{\partial n_E^G} < 0$ then $f^G = 1$, $n_E^G = n_E(1)$.

Combined, the two cases complete the proof. □

Although it may seem, at first glance, that the condition in (2.15) depends on f^G through k^G, this is not true. Given the problem data, the value of k^G is determined by (2.5), independently of the values of f^G and n_E^G. The condition in this claim is therefore verifiable by having the initial data of the problem.

Intuitively, the inequality in Condition (2.15) shows that if b is sufficiently higher than the other costs, then the game pushes the government to order a higher amount of vaccine than the amount specified by the critical vaccination fraction, f'. It is possible to have both equality and strict inequality, based upon numerical examples (not shown).

Theorem 1 uses our results on the optimal production level in the system setting, Proposition 2, and the game setting, Proposition 3, to prove the main result of this section: optimal production volumes are higher in the system setting than in the game setting. The intuition behind Theorem 1 is that the manufacturer bears all the risk of uncertain production yields in the game setting and hence is not willing to produce enough.

Theorem 1 *Given Assumption 3 and the setup above,* $n_E^S > n_E^G$.

Proof: Proposition 2 shows that $f^G \geq f'$. We consider the two cases $f^G = f'$ and $f^G > f'$ separately, and prove that both cases lead to the relation $n_E^S > n_E^G$.

Case 1: $f^G = f'$. Using the inequality in Corollary 2 (i.e. $k^S < k^G$) and using the definitions of k^G, k^S it immediately follows that $n_E^S > n_E^G$, as desired.

Case 2: $f^G > f'$. (Proof by contradiction.) Assume to the contrary that $n_E^S \leq n_E^G$. First of all we obtain the sign of $\left[\frac{\partial GF_2}{\partial n_E}\right]_{n_E^G}$. As in the proof of Proposition 3, there are two cases for n_E^G. If the condition in case 1 of Proposition 3 holds, then $\left[\frac{\partial GF_2}{\partial n_E}\right]_{n_E^G} = 0$. If case 2 holds, then $\left[\frac{\partial GF_2}{\partial n_E}\right]_{n_E^G} \leq 0$. In either case, the following relation is true:

$$\left[\frac{\partial GF_2}{\partial n_E}\right]_{n_E^G} \leq 0 \tag{2.16}$$

On the other hand,

$$\begin{aligned}
\left[\frac{\partial GF_2}{\partial n_E}\right]_{n_E^G} =& (-\frac{\nu b}{d} + p_a)\int_0^{\frac{f'Nd}{n_E^G}} u g_U(u)du + p_r\int_0^{k^G} u g_U(u)du + p_r k^G \int_{k^G}^{\infty} g_U(u)du \\
\geq& (-\frac{\nu b}{d} + p_a)\int_0^{\frac{f'Nd}{n_E^S}} u g_U(u)du + p_r\int_0^{k^G} u g_U(u)du + p_r k^G \int_{k^G}^{\infty} g_U(u)du \\
=& (-\frac{\nu b}{d} + p_a)(\frac{c}{\frac{\nu b}{d} - p_a}) + c + p_r k^G \int_{k^G}^{\infty} g_U(u)du \\
=& p_r k^G \int_{k^G}^{\infty} g_U(u)du > 0
\end{aligned}$$

The inequality in the second line comes from the assumption $n_E^S \leq n_E^G$, and with Assumption 2. The third line is valid by (2.5) and Proposition 2. But the last inequality contradicts (2.16), so $n_E^G \geq n_E^S$ is false. $\square$

Before closing this section, we examine the potential that the entire vaccine production is lost with some probability $\zeta \geq 0$. Such a significant loss of production was experienced by a manufacturer in 2004 after contamination concerns were raised (FDA, 2005). In particular, suppose that the cumulative distribution function for the vaccine yield is $G_U(u) = \zeta + (1 - \zeta) \int_0^u g_U(s)ds$ for some density $g_U(u)$ that represents the conditional density of the yield, given that catastrophic production loss does not occur. The following proposition notes that the optimal production quantities for both the game and system problems decrease as the probability of catastrophic production loss increases, as might be expected given the revenue implications of such an event.

Proposition 4 *Suppose that the production yield is a mixed distribution with* $G_U(u) = Pr(U \leq u) = \zeta + (1 - \zeta) \int_0^u g_U(s)ds$ *for some density* $g_U(u)$. *Then both* n_E^G *and* n_E^S *decrease as* ζ *increases.*

Proof: We first show the claim for n_E^S. Suppose that the yield is changed from having a density function $g_U(u)$ to the more general CDF $G_U(u)$, which is essentially a shift from $\zeta = 0$ to $\zeta > 0$. The effect of that change on the system's objective function is equivalent to multiplying the function SF in Problem (2.7) by $(1 - \zeta)$ and adding $\zeta bT(0)$. A shift in SF by the constant $\zeta bT(0)$ does not change the optimal decisions. We can therefore find the optimal system decisions by using the ideas of the proof of Proposition 2, except that all integrals in (2.12) and (2.13) are multiplied by $(1 - \zeta)$.

Using the same logic as in the proof of Proposition 2, we can show that f^S can be any number in the period $[f', 1]$. To determine the production quantity, the straightforward generalization of (2.11) for $G_U(u)$ with $\zeta \in (0, 1)$ indicates that the optimal n_E satisfies

$$\int_0^{\frac{f'Nd}{n_E^S}} u g_U(u)du = \frac{1}{1-\zeta}\left(\frac{c}{\frac{\nu b}{d} - p_a}\right).$$

The right hand side of this last equation increases with ζ. Because $ug_U(u) \geq 0$, this implies that the integrand in the left hand side does not decrease with ζ. With other parameters fixed, an increase in ζ therefore decreases (or, does not increase) n_E^S.

To show that n_E^G also decreases in ζ, we first show that k^G increases with ζ. Notice that the manufacturer problem is the same as in Proposition 1 except that all integrals are multiplied by $(1-\zeta)$, so that

$$\int_0^{k^G} ug_U(u)du = \frac{1}{1-\zeta}\left(\frac{c}{p_r}\right),$$

as claimed. Now we show that n_E^G decreases in ζ. As in system problem, we can show that the government's objective function, GF, is multiplied by $(1-\zeta)$ and increased by $\zeta bT(0)$. All of the optimality conditions in the proof of Proposition 3 are still valid then, except that integral terms in the definition of GF_1 and GF_2 would be multiplied by $(1-\zeta)$. Again we come to the two cases discussed at the end of Proposition 3.

Case 1: In this case since all terms of GF are multiplied by $(1-\zeta)$, we can simply divide both sides by the same term and get:

$$\frac{\partial GF_2}{\partial n_E} = (-\frac{\nu b}{d} + p_a)\int_0^{\frac{f'Nd}{n_E}} ug_U(u)du + p_r\int_0^{k^G} ug_U(u)du + p_r k^G\int_{k^G}^{\infty} g_U(u)du = 0$$

Observe that the term $p_r\int_0^{k^G} ug_U(u)du + p_r k^G\int_{k^G}^{\infty} g_U(u)du$ is an increasing function of k^G. As we discussed before k^G is also an increasing function of ζ, which implies that the term $(-\frac{\nu b}{d} + p_a)\int_0^{\frac{f'Nd}{n_E}} ug_U(u)du$ should be decreasing in ζ. Thus n_E^G is decreasing with ζ and the claim is proved in this case.

Case 2: In this case we know that $n_E^G = \frac{1Nd}{k^G}$. Since k^G is increasing in ζ, the result easily follows. $\square$

It is also easy to show that for a given governmental order fraction f, a higher probability ζ of no production yield results in a lower optimal manufacturer production volume.

We now assume $\zeta = 0$ for the balance of the thesis to simplify the analysis.

2.2.2 Coordinating Contracts

The objective of this section is to design contracts that will align governmental and manufacturer incentives. There are a variety of contracts in use, include wholesale pricing (CDC, 2005). Recent support by the U.S. Dept. of Health and Human Services (2004) to a major manufacturer for the development of a stable egg supply resembles a payment that is proportional to effort, a characteristic that is shared with the cost sharing contract below. We show that wholesale or pay back contracts can not coordinate this supply chain. We then demonstrate a cost sharing contract that is able to do so.

Wholesale price contracts

In wholesale price contract, the supplier and government negotiate a price p_r. Unfortunately, the system optimum can not be fully achieved just by adjusting the value of p_r.

Proposition 5 *There does not exist a wholesale price contract which satisfies the condition in Assumption 3 and coordinates the supply chain.*

Proof: The proof of Theorem 1 shows that there does not exist a wholesale contract which coordinate this supply chain. That proof proceeded in two cases. The first case requires $n_E^S > n_E^G$. For full coordination, we require $n_E^S = n_E^G$ for some p_r. In case 2, $n_E^S = n_E^G$ for some p_r implies that $\frac{\partial GF}{\partial n_E}\big|_{n_E^G} > 0$, which would not be true for the optimizer of GF. □

Pay back contracts

In a pay back contract, the government agrees to buy any excess production, beyond the desired volume, for a discounted price p_c (with $0 < p_c < p_r$) from the manufacturer. This shifts some risk of excess production from the manufacturer to the government, and would typically increase production. Since the buy-back contract coordinates the supply chain for the Newsvendor (Pasternack, 1985), one could expect that the corresponding contract with uncertain yield (i.e., a payback contract) should be able to achieve the same.

We show that the pay back contract does not provide sufficient incentive to coordinate the influenza supply chain, unlike typical supply chains, for any reasonable value of p_c. Full coordination will be shown to be prevented by the combination of yield uncertainty and a

maximal purchase quantity (a government is unwilling to buy vaccine beyond the amount ordered). Assumption 4 defines a reasonable p_c as one that precludes the manufacturer from producing an infinite volume for an infinite profit.

Assumption 4 *The average revenue per egg at the discounted price is less than its cost,* $p_c\mu < c$.

The pay back contract increases the manufacturer's profit by adding the revenue associated with $n_E U - \min\{n_E U, fNd\}$ doses of excess production. This changes the manufacturer problem from Problem (2.4) to

$$\begin{aligned} \min_{n_E} \quad & MF = \mathrm{E}\Big[cn_E - p_r Z - p_c(n_E U - Z)\Big] \\ \text{s.t.} \quad & Z = \min\{n_E U, fNd\} \\ & n_E \geq 0. \end{aligned}$$

By adapting the argument of Proposition 1, the optimal production level n_E^* can be shown to satisfy

$$\int_0^{\frac{fNd}{n_E^*}} u g_U(u)du = \frac{c - p_c\mu}{p_r - p_c}. \tag{2.17}$$

The effect of this contract on the government problem in Problem (2.6) is to change the objective to

$$GF = \mathrm{E}\left[b\max\{A - \nu\frac{W}{d}, 0\} + p_a W + p_r Z + p_c(n_E U - Z)\right],$$

and to change the "manufacturer acts optimally" constraint, which determines the optimal production input quantity n_E as a function of f, from (2.5) to (2.17).

Denote the optimal values of this pay back contract problem by f^N, n_E^N. Set $k^N = \frac{f^N Nd}{n_E^N}$.

Proposition 6 *If Assumptions 1, 2 and 4 hold, then there does not exist a pay back contract which could coordinate this supply chain. In fact, under any pay back contract, the resulting production level is less than the optimal system production level,* $n_E^N < n_E^S$.

Proof: Note that $\int_0^{k^N} u g_U(u)du = \frac{c - p_c\mu}{p_r - p_c}$. By rewriting the GF in terms of values of f, n_E

and by replacing $f = \frac{k^N n_E}{Nd}$ we have:

$$GF(n_E) = b\int_0^{\frac{f'Nd}{n_E}} (A - \nu\frac{n_E u}{d})g_U(u)du + p_a n_E \int_0^{\frac{f'Nd}{n_E}} ug_U(u)du + p_a(f'Nd)\int_{\frac{f'Nd}{n_E}}^{\infty} g_U(u)du$$
$$+(p_r - p_c)n_E\int_0^{k^N} ug_U(u)du + (p_r - p_c)(k^N n_E)\int_{k^N}^{\infty} g_U(u)du + p_c\mu n_E$$

By Assumption 2, $\frac{\partial^2 GF_2}{\partial n_E^2} = (\frac{\nu b}{d} - p_a)\frac{f'Nd}{n_E^2}g_U(\frac{f'Nd}{n_E}) \geq 0$, so GF is a convex function on n_E. The optimal value of GF can therefore be found by setting its derivative to zero:

$$\begin{aligned}\frac{\partial GF}{\partial n_E} =& (-\frac{\nu b}{d} + p_a)\int_0^{\frac{f'Nd}{n_E}} ug_U(u)du + p_c\mu \\ &+ (p_r - p_c)\Big[\int_0^{k^N} ug_U(u)du + k^N\int_{k^N}^{\infty} g_U(u)du\Big] \\ =& (-\frac{\nu b}{d} + p_a)\int_0^{\frac{f'Nd}{n_E}} ug_U(u)du + c + (p_r - p_c)k^N\int_{k^N}^{\infty} g_U(u)du\end{aligned}$$

The last inequality comes from (2.17). The last term indicates implicitly that $n_E^N < n_E^S$. To see this, plug n_E^S into the last terms, use Proposition 2 and using the fact that $p_r > p_c$, to obtain $\frac{\partial GF}{\partial n_E}\Big|_{n_E^S} = (p_r - p_c)k^N\int_{k^N}^{\infty} g_U(u)du > 0$. That implies that $n_E^N < n_E^S$. □

Proposition 6 suggests that compensating the manufacturer for having excess inventory is not enough to achieve global optimization. Indeed, a pay back contract does not compensate the manufacturer when the production volume (n_E) is high while the yield ($n_E U$) is low. The cost sharing agreement described below is designed to address this issue.

Cost sharing contracts

In a cost sharing contract, the government pays proportional to the production volume n_E at a rate of p_e per each egg. Such an agreement decreases the manufacturer's risk of excess production, and provides an incentive to increase production. Here, we describe a contract that increases production to the system optimum, f', n_E^S.

With the cost sharing contract, the manufacturer problem is:

$$\min_{n_E} MF = \mathrm{E}\big[(c - p_e)n_E - p_r Z\big]$$

$$\text{s.t. } Z = \min\{n_E U, fNd\}$$
$$n_E \geq 0.$$

The optimality condition for n_E given f follows immediately, as for the original problem,

$$\int_0^{\frac{fNd}{n_E^*}} u g_U(u)du = \frac{c - p_e}{p_r}. \tag{2.18}$$

Cost sharing increases the government's costs, changing its objective function to

$$GF = \mathrm{E}\left[b\max\{A - \nu\frac{W}{d}, 0\} + p_a W + p_r Z + p_e n_E\right]. \tag{2.19}$$

The cost sharing contract therefore results in the following optimization problem for the government.

$$\min_f GF = \mathrm{E}\left[b\max\{A - \nu\frac{W}{d}, 0\} + p_a W + p_r Z + p_e n_E\right]$$
$$\text{s.t. } Z = \min\{n_E U, fNd\}$$
$$W = \min\{n_E U, fNd, f'Nd\}$$
$$\int_0^{\frac{fNd}{n_E}} u g_U(u)du = \frac{c - p_e}{p_r}$$
$$0 \leq f \leq 1$$
$$n_E \geq 0.$$

Denote the optimal solutions of this problem by f^e, n_E^e, and set $k^e = \frac{f^e Nd}{n_E^e}$.

For any given p_r, choose $p_e > 0$ so that $\frac{c-p_e}{p_r} = \frac{c}{\frac{\nu b}{d} - p_a}$. Such a p_e exists since $p_r < \frac{\nu b}{d} - p_a$. If p_e is chosen this way, then $k^e = k^S$. Further, if p_r satisfies Assumption 3, such a p_e not only moves k^e to k^S, but it aligns the vaccination fractions and production volumes, as in Theorem 2. Intuitively, this occurs because $\frac{c-p_e}{p_r}$ is the manufacturer's effective cost per egg divided by its benefit per vaccine, and it equals $\frac{c}{\frac{\nu b}{d} - p_a}$, the system's effective total cost per egg divided by the system's total benefit per vaccine.

Theorem 2 *If Assumption 3 holds and p_e is chosen so that $\frac{c-p_e}{p_r} = \frac{c}{\frac{\nu b}{d} - p_a}$, then the optimal*

values (f^e, n_E^e) for Problem (2.19) equal (f', n_E^S), so this cost sharing contract will coordinate the supply chain.

Proof: First we show that $f^e \geq f'$ by showing that optimum value for GF_1 for $f \in [0, f']$ is always obtained at f'. By replacing $f = \frac{k^e n_E}{Nd}$ we get GF_1 to be only a function of n_E:

$$\begin{aligned} GF_1(n_E) = \; & b\int_0^{k^e}(A - \nu\frac{n_E u}{d})g_U(u)du + b(A - N\nu\frac{n_E k^e}{Nd})\int_{k^e}^{\infty} g_U(u)du \\ & +(p_a + p_r)n_E\int_0^{k^e} ug_U(u)du + (p_a + p_r)(k^e n_E)\int_{k^e}^{\infty} g_U(u)du + p_e n_E \end{aligned}$$

Now by taking the derivative of GF_1 with respect to n_E we obtain that:

$$\begin{aligned} \frac{\partial GF_1}{\partial n_E} =& -\frac{\nu b}{d}\int_0^{k^e} ug_U(u)du - \frac{\nu b}{d}k^e\int_{k^e}^{\infty} g_U(u)du \\ & + (p_a + p_r)\int_0^{k^e} ug_U(u)du + (p_a + p_r)k^e\int_{k^e}^{\infty} g_U(u)du + p_e \\ =& (-\frac{\nu b}{d} + p_a)\int_0^{k^S} ug_U(u)du + p_r\int_0^{k^e} ug_U(u)du \qquad (2.20) \\ & + (-\frac{\nu b}{d} + p_a + p_r)k^e\int_{k^e}^{\infty} g_U(u)du + p_e \\ =& -c + (c - p_e) + (-\frac{\nu b}{d} + p_a + p_r)k^e\int_{k^e}^{\infty} g_U(u)du + p_e \qquad (2.21) \\ =& (-\frac{\nu b}{d} + p_a + p_r)k^e\int_{k^e}^{\infty} g_U(u)du, \qquad (2.22) \end{aligned}$$

in which (2.20) is obtained because $k^e = k^S$, and (2.21) is obtained using Proposition 2 and (2.18). On the other hand (2.22) is negative by Assumption 3, so that GF_1 is decreasing for all eligible n_E. Hence f' and the corresponding n_E (i.e. $n_E = \frac{f'Nd}{k^e} = \frac{f'Nd}{k^S}$) are optimal in this case. So $f^e \geq f'$. Because $k^e = k^S$, it immediately follows that $n_E^e \geq n_E^S$.

Now we show that the optimum of GF_2, for $f \in [f', 1]$, also occurs at f', completing the proof. Note that $f \geq f'$ and $k^e = k^S$ imply that $n_E \geq n_E^S$. Consider GF_2.

$$\begin{aligned} GF_2(n_E) = b\int_0^{\frac{f'Nd}{n_E}}(A - \nu\frac{n_E u}{d})g_U(u)du + p_a n_E\int_0^{\frac{f'Nd}{n_E}} ug_U(u)du + p_a f'Nd\int_{\frac{f'Nd}{n_E}}^{\infty} g_U(u)du \\ +p_r n_E\int_0^{k^e} ug_U(u)du + p_r(k^e n_E)\int_{k^e}^{\infty} g_U(u)du + p_e n_E \end{aligned}$$

The derivative is nonnegative,

$$\begin{aligned}
\frac{\partial GF_2}{\partial n_E} =& (-\frac{\nu b}{d} + p_a) \int_0^{\frac{f'Nd}{n_E}} u g_U(u) du + p_r \int_0^{k^e} u g_U(u) du + p_r k^e \int_{k^e}^{\infty} g_U(u) du + p_e \\
=& (-\frac{\nu b}{d} + p_a) \int_0^{\frac{f'Nd}{n_E}} u g_U(u) du + c + p_r k^e \int_{k^e}^{\infty} g_U(u) du \qquad (2.23) \\
\geq& (-\frac{\nu b}{d} + p_a) \int_0^{\frac{f'Nd}{n_E^S}} u g_U(u) du + c + p_r k^e \int_{k^e}^{\infty} g_U(u) du \qquad (2.24) \\
=& p_r k^e \int_{k^e}^{\infty} g_U(u) du \geq 0 \qquad (2.25)
\end{aligned}$$

(2.23) comes from (2.18). As before, (2.24) comes from Assumption 2 and the fact that $n_E \geq n_E^S$. Finally, (2.25) is true by Proposition 2. The last inequality shows that the optimum value for GF_2 occurs at f' hence $f^e = f'$ and because of the fact that $k^e = k^S$, we obtain $n_E^e = n_E^S$. □

The cost sharing contract can coordinate incentives, unlike the pay back contract, because the manufacturer's risk of both excess and insufficient yield can be handled by the contract's balance between paying for outputs (via p_r) and for effort (via p_e).

Chapter 3

A Government/Manufacturer Supply Chain - Case of Strictly Convex Attack Rate

Based on the supply chain model developed in Section 2.1, this chapter initially presumes that $T(f)$ is strictly convex. While $T(f)$ may not be convex for all choices of the parameters of the infection model, it is strictly convex for sufficiently large χ (a large initial exposure from exogenous sources) and values of R_0 that are representative of influenza (see Appendix B).

We first explore the game equilibrium and the optimal system solution. We then show that a variation of the cost sharing contract can coordinate the supply chain. Finally, we demonstrate that this proposed cost sharing contract can be modified to coordinate a broader class of attack rates, such as when $T(f)$ is first concave decreasing and after a point becomes convex decreasing. Such curves are observed for some realistic values of the parameters. Convex curves, and curves that are first concave then convex, are also realistic when $T(f)$ results from averaging over uncertain parameters (as described prior to Section 2.1.2).

3.1 Optimal solutions for game and system settings

The solution to the manufacturer problem in Problem (2.4) with convex $T(f)$ remains the same as above, as the manufacturer's objective function does not depend upon $T(f)$. The analysis of the government problem in Problem (2.6) and the system problem in Problem (2.7) is somewhat more complicated when $T(f)$ is strictly convex, but the general ideas are similar to those in the linear model.

For the system setting, the following analog of Proposition 2 holds.

Proposition 7 *If $T(f)$ is strictly convex, $\bar{f}$ is the solution of (2.1), and the optimum values of the system problem in Problem (2.7) are denoted by f^S, n_E^S, then (a) f^S can be picked to be any value between $\bar{f}$ and 1; and (b) n_E^S is the solution of the following equation:* $\int_0^{\frac{\bar{f}Nd}{n_E^S}} \left[\frac{b}{Nd}T'(\frac{n_E^S u}{Nd}) + p_a\right] u g_U(u)du + c = 0.$

Proof: The proof resembles the proof of Proposition 2, except for the change in role of f' to $\bar{f}$, and the definitions of $SF1, SF_1$ and $SF2, SF_2$. We first show that the optimum value of SF_1 always occurs at the border, i.e. $f^* = \bar{f}$, by examining the KKT condition for SF_1:

$$bT'(f)\int_{\frac{fNd}{n_E}}^{\infty} g_U(u)du + p_a Nd\int_{\frac{fNd}{n_E}}^{\infty} g_U(u)du + \xi = 0$$
$$-\frac{b}{Nd}\int_0^{\frac{fNd}{n_E}} T'(\frac{n_E u}{Nd}) u g_U(u)du + p_a\int_0^{\frac{fNd}{n_E}} u g_U(u)du + c = 0$$
$$\xi(f-\bar{f}) = 0 \quad ; \quad \xi \geq 0$$

If $f < \bar{f}$, then by the convexity of $T(f)$ and the definition in (2.1), we conclude that $bT'(f) + p_a Nd < 0$. So the first equation forces $\xi > 0$, then by the third equation we obtain $f^* = \bar{f}$. So the optimum value for SF_1 occurs at the border which is $\bar{f}$. Since SF does not change as f varies in $[\bar{f}, 1]$, we have shown the first part of the claim. The optimum value for n_E^* in this case can be obtained using the second equation of the KKT conditions and the fact that $f^* = \bar{f}$. Namely, the optimum n_E solves the following equation: $\int_0^{\frac{\bar{f}Nd}{n_E^*}} \left[\frac{b}{Nd}T'(\frac{n_E^* u}{Nd}) + p_a\right] u g_U(u)du + c = 0$, as claimed.

It is now enough to show that in the second case where $f \geq \bar{f}$, the same relation holds for the optimum production level. To show this, note that first of all, SF_2 is a function of

n_E only, hence to get the optimum it suffices to find the root of its derivative:

$$\frac{\partial SF_2}{\partial n_E} = \int_0^{\frac{\bar{f}Nd}{n_E}} \Big[\frac{b}{Nd}T'(\frac{n_E u}{Nd}) + p_a\Big] u g_U(u)du + c$$

By setting this equation to zero we will end up by the same type of relation for n_E^* which we obtained before from SF_1, hence always $\int_0^{\frac{\bar{f}Nd}{n_E^S}} \Big[\frac{b}{Nd}T'(\frac{n_E^S u}{Nd}) + p_a\Big] u g_U(u)du + c = 0$. □

The following analog of Proposition 3 for convex $T(f)$ characterizes the set of the game equilibria.

Proposition 8 *Let f^G, n_E^G denote the game solution, let $k^G = \frac{f^G Nd}{n_E^G}$ and set $\bar{n}_E = \frac{\bar{f}Nd}{k^G}$. If $T(f)$ is strictly convex, then (a) $\int_0^{k^G} u g_U(u)du = \frac{c}{p_r}$; and (b) $f^G \leq \bar{f}$ if and only if*

$$\int_0^{k^G} \Big[\frac{b}{Nd}T'(\frac{\bar{n}_E u}{Nd}) + p_a\Big] u g_U(u)du + c + p_r k^G \int_{k^G}^{\infty} g_U(u)du \geq 0. \tag{3.1}$$

Proof: The first part of this claim is just the optimality condition for the manufacturer. As above, this does not depend on the shape of $T(f)$ so this relation remains the same. The fraction k^G is therefore determined by the values of c, p_r and the egg yield variability, and are assumed to be known.

To prove the second part, if $\int_0^{k^G} \Big[\frac{b}{Nd}T'(\frac{\bar{n}_E u}{Nd}) + p_a\Big] u g_U(u)du + c + p_r k^G \int_{k^G}^{\infty} g_U(u)du < 0$, then by replacing $f = \frac{n_E k^G}{Nd}$, we can rewrite GF_1 just as a function of n_E as follows:

$$\begin{aligned} GF_1(n_E) = \; & b\int_0^{k^G} T(\frac{n_E u}{Nd}) g_U(u)du + bT(\frac{n_E k^G}{Nd}) \int_{k^G}^{\infty} g_U(u)du \\ & + (p_a + p_r) n_E \int_0^{k^G} u g_U(u)du + (p_a + p_r)(n_E k^G) \int_{k^G}^{\infty} g_U(u)du \end{aligned}$$

$GF_1(n_E)$ is a convex function of n_E so the first derivative shows the behavior of this function completely:

$$\begin{aligned} \frac{\partial GF_1}{\partial n_E} = & \int_0^{k^G} \Big[\frac{b}{Nd}T'(\frac{n_E u}{Nd}) + p_a\Big] u g_U(u)du + p_r \int_0^{k^G} u g_U(u)du \\ & + \frac{k^G}{Nd}\Big[bT'(\frac{n_E k^G}{Nd}) + p_a Nd\Big] \int_{k^G}^{\infty} g_U(u)du + p_r k^G \int_{k^G}^{\infty} g_U(u)du \end{aligned}$$

$$= \int_0^{k^G} \Big[\frac{b}{Nd} T'(\frac{n_E u}{Nd}) + p_a\Big] u g_U(u)du + c + p_r k^G \int_{k^G}^{\infty} g_U(u)du$$
$$+ \frac{k^G}{Nd}\Big[bT'(\frac{n_E k^G}{Nd}) + p_a Nd\Big] \int_{k^G}^{\infty} g_U(u)du \qquad (3.2)$$

However, note that the function GF_1 is a convex function so clearly for every $f \leq \bar{f}$ or equivalently $n_E \leq \bar{n}_E$ we have: $\frac{\partial GF_1}{\partial n_E} \leq \Big[\frac{\partial GF_1}{\partial n_E}\Big]_{n_E=\bar{n}_E}$. On the other hand if we plug $\bar{n}_E$ into (3.2) we have:

$$\Big[\frac{\partial GF_1}{\partial n_E}\Big]_{n_E=\bar{n}_E} = \int_0^{k^G} \Big[\frac{b}{Nd} T'(\frac{\bar{n}_E u}{Nd}) + p_a\Big] u g_U(u)du + c + p_r k^G \int_{k^G}^{\infty} g_U(u)du$$
$$+ \frac{k^G}{Nd}\Big[bT'(\frac{\bar{n}_E k^G}{Nd}) + p_a Nd\Big] \int_{k^G}^{\infty} g_U(u)du$$
$$= \int_0^{k^G} \Big[\frac{b}{Nd} T'(\frac{\bar{n}_E u}{Nd}) + p_a\Big] u g_U(u)du + c + p_r k^G \int_{k^G}^{\infty} g_U(u)du$$

in which the last equality comes from the fact that $\bar{n}_E = \frac{\bar{f}Nd}{k^G}$, and recalling (2.1). Note that the last expression is less than zero by assumption, so the optimum of GF_1 occurs at its border, $f^* = \bar{f}$. Because the inequality is strict, optimum of GF_2 also is greater than $\bar{f}$, so $f^G > \bar{f}$.

To show the reverse direction, we first show that the function

$$H(n_E) = \int_0^{\frac{\bar{f}Nd}{n_E}} \Big[\frac{b}{Nd} T'(\frac{n_E u}{Nd}) + p_a\Big] u g_U(u)du$$

is a nondecreasing function on n_E.

$$\frac{\partial H}{\partial n_E} = \int_0^{\frac{\bar{f}Nd}{n_E}} \Big[\frac{b}{(Nd)^2} T''(\frac{n_E u}{Nd})\Big] u^2 g_U(u)du + \Big[\frac{b}{Nd} T'(\bar{f}) + p_a\Big] \frac{\bar{f}Nd}{n_E} g_U(\frac{\bar{f}Nd}{n_E}) \times (-\frac{\bar{f}Nd}{n_E^2})$$
$$= \int_0^{\frac{\bar{f}Nd}{n_E}} \Big[\frac{b}{(Nd)^2} T''(\frac{n_E u}{Nd})\Big] u^2 g_U(u)du \geq 0$$

The second equation follows from the definition of $\bar{f}$, and the last inequality is due to the convexity of $T(f)$ in f. Hence we have $H(n_E) \geq H(\bar{n}_E)$ for all $n_E \geq \bar{n}_E$. By replacing

$H(n_E)$ with its definition,

$$\int_0^{\frac{\bar{f}Nd}{n_E}} \Big[\frac{b}{Nd}T'(\frac{n_E u}{Nd}) + p_a\Big] u g_U(u)du \geq \int_0^{\frac{\bar{f}Nd}{\bar{n}_E}} \Big[\frac{b}{Nd}T'(\frac{\bar{n}_E u}{Nd}) + p_a\Big] u g_U(u)du \quad ;\forall n_E \geq \bar{n}_E \tag{3.3}$$

If we assume $\int_0^{k^G} \Big[\frac{b}{Nd}T'(\frac{\bar{n}_E u}{Nd}) + p_a\Big] u g_U(u)du + c + p_r k^G \int_{k^G}^{\infty} g_U(u)du \geq 0$ we will show that $f^G \leq \bar{f}$, which is the reverse direction of part 2 of the claim.

Because this is the game setting, f can be replaced by $\frac{n_E k^G}{Nd}$, and

$$\begin{aligned}
GF_2(n_E) =& b\int_0^{\frac{\bar{f}Nd}{n_E}} T(\frac{n_E u}{Nd}) g_U(u)du + bT(\frac{n_E k^G}{Nd}) \int_{\frac{\bar{f}Nd}{n_E}}^{\infty} g_U(u)du + p_r n_E \int_0^{k^G} u g_U(u)du \\
&+ p_r(n_E k^G) \int_{k^G}^{\infty} g_U(u)du + p_a n_E \int_0^{\frac{\bar{f}Nd}{n_E}} u g_U(u)du + p_a(\bar{f}Nd) \int_{\frac{\bar{f}Nd}{n_E}}^{\infty} g_U(u)du \\
\frac{\partial GF_2}{\partial n_E} =& \int_0^{\frac{\bar{f}Nd}{n_E}} \Big[\frac{b}{Nd}T'(\frac{n_E u}{Nd}) + p_a\Big] u g_U(u)du + p_r \int_0^{k^G} u g_U(u)du + p_r k^G \int_{k^G}^{\infty} g_U(u)du \\
=& \int_0^{\frac{\bar{f}Nd}{n_E}} \Big[\frac{b}{Nd}T'(\frac{n_E u}{Nd}) + p_a\Big] u g_U(u)du + c + p_r k^G \int_{k^G}^{\infty} g_U(u)du \qquad (3.4) \\
\geq& \int_0^{\frac{\bar{f}Nd}{\bar{n}_E}} \Big[\frac{b}{Nd}T'(\frac{\bar{n}_E u}{Nd}) + p_a\Big] u g_U(u)du + c + p_r k^G \int_{k^G}^{\infty} g_U(u)du \geq 0
\end{aligned}$$

The second equality for $\frac{\partial GF_2}{\partial n_E}$ comes from (2.5). If $f \geq \bar{f}$ then $n_E \geq \bar{n}_E$, so the inequality in the third line is justified by (3.3). Finally the last inequality comes by assumption, and implies that for every $f \geq \bar{f}$ the function GF_2 is nondecreasing under the stated assumptions, so the optimum f^* for GF_2 can be obtained at $f^* = \bar{f}$. Hence $f^G \leq \bar{f}$, completing the proof. □

The inequality in Condition (3.1) shows that if b is not sufficiently higher than the other costs, such that the marginal health benefit obtained by vaccination do not cover the vaccine costs, then the game pushes the government to order less vaccine than is required to vaccinate a fraction $\bar{f}$ of the population.

Theorem 3, the main result of this section, shows that, as in the linear case, the system optimal production level exceeds that of the game equilibrium.

Theorem 3 *Let n_E^S and n_E^G denote the production level under the system optimum and game*

equilibrium, respectively. For all nonincreasing strictly convex $T(f)$, we have $n_E^S > n_E^G$.

The proof of **Theorem 3** requires the following three lemmas.

Lemma 1 *If $n_E^G \geq n_E^S$, then $f^G \leq \bar{f}$.*

Proof: To proof this lemma we show that the function GF_2 obtains its minimum at its border ($\bar{f}$). We use the function $H(n_E)$ that was defined in the proof of Proposition 8, which was shown to be nondecreasing, and $n_E^G \geq n_E^S$ to conclude that

$$\int_0^{\frac{\bar{f}Nd}{n_E^G}} \Big[\frac{b}{Nd}T'(\frac{n_E^G u}{Nd}) + p_a\Big] u g_U(u)du \geq \int_0^{\frac{\bar{f}Nd}{n_E^S}} \Big[\frac{b}{Nd}T'(\frac{n_E^S u}{Nd}) + p_a\Big] u g_U(u)du.$$

By plugging n_E^G into the derivative function of GF_2 in (3.4), and using the above relation,

$$\begin{aligned}
\Big[\frac{\partial GF_2}{\partial n_E}\Big]_{n_E=n_E^G} &= \int_0^{\frac{\bar{f}Nd}{n_E^G}} \Big[\frac{b}{Nd}T'(\frac{n_E^G u}{Nd}) + p_a\Big] u g_U(u)du + c + p_r k^G \int_{k^G}^{\infty} g_U(u)du \\
&\geq \int_0^{\frac{\bar{f}Nd}{n_E^S}} \Big[\frac{b}{Nd}T'(\frac{n_E^S u}{Nd}) + p_a\Big] u g_U(u)du + c + p_r k^G \int_{k^G}^{\infty} g_U(u)du \\
&= p_r k^G \int_{k^G}^{\infty} g_U(u)du > 0
\end{aligned}$$

The equality in the third line comes from (7). The last inequality shows that the derivative of the function GF_2 at the optimum point n_E^G is strictly positive, which is not possible unless n_E^G is at its lower extreme, $n_E^G = \bar{n}_E$, where $\bar{n}_E$ introduced earlier. □

Lemma 2 *Let $\bar{\bar{f}}$ be the solution of $bT'(\bar{\bar{f}}) + (p_a + p_r)Nd = 0$. Then $f^G > \bar{\bar{f}}$.*

Proof: By the definitions of $\bar{f}$ and $\bar{\bar{f}}$, and strict convexity of $T(f)$, we have $\bar{\bar{f}} < \bar{f}$. Let $\bar{\bar{n}}_E = \frac{\bar{\bar{f}}Nd}{k^G}$. Because $\bar{\bar{f}} < \bar{f}$, we examine the government subproblem $GF1$ with objective function GF_1 to analyze the pair $(\bar{\bar{f}}, \bar{\bar{n}}_E)$.

$$\begin{aligned}
\Big[\frac{\partial GF_1}{\partial n_E}\Big]_{n_E=\bar{\bar{n}}_E} &= \int_0^{k^G} \Big[\frac{b}{Nd}T'(\frac{\bar{\bar{n}}_E u}{Nd}) + p_a + p_r\Big] u g_U(u)du \\
&\quad + \frac{k^G}{Nd}\Big[bT'(\frac{\bar{\bar{n}}_E k^G}{Nd}) + p_a Nd + p_r Nd\Big] \int_{k^G}^{\infty} g_U(u)dus
\end{aligned}$$

$$= \int_0^{k^G} \Big[\frac{b}{Nd} T'(\frac{\bar{\bar{n}}_E u}{Nd}) + p_a + p_r\Big] u g_U(u) du < 0$$

The second equality is true because the second term in the derivative is zero, by the definition of $\bar{\bar{f}}, \bar{\bar{n}}_E$. The last inequality comes from the strict convexity of $T(f)$, so $T'(f) < T'(\bar{\bar{f}})$; for all $f < \bar{\bar{f}}$. The derivative of GF_1 is negative at $\bar{\bar{f}}$. By the convexity of $T(f)$, it follows that the optimum of GF_1 is attained for a point bigger than $\bar{\bar{f}}$ (since $\bar{\bar{f}} < \bar{f}$), and so $f^G > \bar{\bar{f}}$. □

Lemma 3 *Let* $k^S = \frac{\bar{f} Nd}{n_E^S}$. *Then for all* $k > 0$,

$$\int_0^{k^S} \Big[\frac{b}{Nd} T'(\frac{n_E^S u}{Nd}) + p_a\Big] u g_U(u) du \leq \int_0^{k} \Big[\frac{b}{Nd} T'(\frac{n_E^S u}{Nd}) + p_a\Big] u g_U(u) du.$$

Proof: To prove the lemma, we show that $I(k) = \int_0^{k} \Big[\frac{b}{Nd} T'(\frac{n_E^S u}{Nd}) + p_a\Big] u g_U(u) du$ attains its minimum at $k^* = k^S$. The derivative of $I(k)$ is $\frac{\partial I}{\partial k} = \Big[\frac{b}{Nd} T'(\frac{n_E^S k}{Nd}) + p_a\Big] k g_U(k)$. Note that for $k < k^S$, we have $\frac{k n_E^S}{Nd} < \frac{k^S n_E^S}{Nd} = \bar{f}$, and so by the definition of $\bar{f}$, the derivative of $I(k)$ is negative. So $I(k)$ is decreasing for $k < k^S$. If $k > k^S$, then $\frac{k n_E^S}{Nd} > \bar{f}$ so $\frac{\partial I}{\partial k} > 0$, and $I(k)$ is increasing. Therefore $I(k)$ attains its minimum at k^S. □

Theorem 3. *Proof:* Equipped with the three lemmas, we turn to a proof of Theorem 3 by contradiction. Let us assume that $n_E^G \geq n_E^S$. First of all by Lemma 1, we have $f^G \leq \bar{f}$. We consider two cases:

Case 1: $f^G < \bar{f}, n_E^G \geq n_E^S$. In this case, the optimum solution (f^G, n_E^G) would occur in the middle of the region for GF_1, so that $\Big[\frac{\partial GF_1}{\partial n_E}\Big]_{n_E = n_E^G} = 0$. By plugging n_E^G into (3.2), we have

$$\begin{aligned} 0 &= \int_0^{k^G} \Big[\frac{b}{Nd} T'(\frac{n_E^G u}{Nd}) + p_a\Big] u g_U(u) du + c \\ &\quad + \frac{k^G}{Nd}\Big[b T'(\frac{n_E^G k^G}{Nd}) + p_a Nd + p_r Nd\Big] \int_{k^G}^{\infty} g_U(u) du \\ &= \int_0^{k^G} \Big[\frac{b}{Nd} T'(\frac{n_E^G u}{Nd}) + p_a\Big] u g_U(u) du + c \end{aligned}$$

$$+\frac{k^G}{Nd}\Big[bT'(f^G)+p_aNd+p_rNd\Big]\int_{k^G}^{\infty}g_U(u)du \quad ;\text{(because of } n_E^Gk^G=f^GNd)$$

$$>\int_0^{k^G}\Big[\frac{b}{Nd}T'(\frac{n_E^Gu}{Nd})+p_a\Big]ug_U(u)du+c \quad ;\text{(Lemma 2 and convexity of } T(f)) \qquad (3.5)$$

On the other hand note that the function $J(n_E)=\int_0^k\big[\frac{b}{Nd}T'(\frac{n_Eu}{Nd})+p_a\big]ug_U(u)du$ is an increasing function of n_E. This is because $\frac{\partial J}{\partial n_E}=\int_0^k\big[\frac{b}{(Nd)^2}T''(\frac{n_Eu}{Nd})\big]u^2g_U(u)du\geq 0$, as $T(f)$ is a convex function. So $n_E^G\geq n_E^S$, means that $J(n_E^G)\geq J(n_E^S)$. By the definition of $J(n_E)$, and for $k=k^G$,

$$\int_0^{k^G}\big[\frac{b}{Nd}T'(\frac{n_E^Gu}{Nd})+p_a\big]ug_U(u)du\geq\int_0^{k^G}\big[\frac{b}{Nd}T'(\frac{n_E^Su}{Nd})+p_a\big]ug_U(u)du \qquad (3.6)$$

If $\int_0^{k^G}\big[\frac{b}{Nd}T'(\frac{n_E^Su}{Nd})+p_a\big]ug_U(u)du\geq\int_0^{k^S}\big[\frac{b}{Nd}T'(\frac{n_E^Su}{Nd})+p_a\big]ug_U(u)du$, then (3.6) implies

$$\int_0^{k^G}\big[\frac{b}{Nd}T'(\frac{n_E^Gu}{Nd})+p_a\big]ug_U(u)du+c\geq\int_0^{k^S}\big[\frac{b}{Nd}T'(\frac{n_E^Su}{Nd})+p_a\big]ug_U(u)du+c$$

$$=0; \qquad \text{(by Proposition 7)},$$

which contradicts (3.5). So we should have:

$$\int_0^{k^G}\big[\frac{b}{Nd}T'(\frac{n_E^Su}{Nd})+p_a\big]ug_U(u)du<\int_0^{k^S}\big[\frac{b}{Nd}T'(\frac{n_E^Su}{Nd})+p_a\big]ug_U(u)du,$$

but this inequality also contradicts Lemma 3. So case 1 results in a contradiction.

Case 2: $f^G=\bar{f},n_E^G\geq n_E^S$. In this case, the production level would be $n_E^G=\bar{n}_E=\frac{\bar{f}Nd}{k^G}$. As $(\bar{f},\bar{n}_E)$ is the optimum pair for GF_1, we should have: $\big[\frac{\partial GF_1}{\partial n_E}\big]_{\bar{n}_E}\leq 0$ or equivalently:

$$0\geq\int_0^{k^G}\Big[\frac{b}{Nd}T'(\frac{\bar{n}_Eu}{Nd})+p_a\Big]ug_U(u)du+c+p_rk^G\int_{k^G}^{\infty}g_U(u)du$$

$$+\frac{k^G}{Nd}\Big[bT'(\frac{\bar{n}_Ek^G}{Nd})+p_aNd\Big]\int_{k^G}^{\infty}g_U(u)du$$

$$=\int_0^{k^G}\Big[\frac{b}{Nd}T'(\frac{\bar{n}_Eu}{Nd})+p_a\Big]ug_U(u)du+c+p_rk^G\int_{k^G}^{\infty}g_U(u)du$$

$$> \int_0^{k^G} \Big[\frac{b}{Nd} T'(\frac{\bar{n}_E u}{Nd}) + p_a\Big] u g_U(u) du + c$$

On the other hand, the last expression can be written as:

$$\int_0^{\frac{\bar{f}Nd}{\bar{n}_E}} \Big[\frac{b}{Nd} T'(\frac{\bar{n}_E u}{Nd}) + p_a\Big] u g_U(u) du + c < 0 \tag{3.7}$$

Note however that $\bar{n}_E = n_E^G \geq n_E^S$. By the monotonicity of the function $H(n_E)$ from Proposition 8,

$$\int_0^{\frac{\bar{f}Nd}{\bar{n}_E}} \Big[\frac{b}{Nd} T'(\frac{\bar{n}_E u}{Nd}) + p_a\Big] u g_U(u) du + c \geq \int_0^{\frac{\bar{f}Nd}{n_E^S}} \Big[\frac{b}{Nd} T'(\frac{n_E^S u}{Nd}) + p_a\Big] u g_U(u) du + c = 0,$$

which contradicts (3.7). Since both cases lead to a contradiction, the claim is proven. □

Hence, there is an opportunity for an effective contract to align incentives and to improve vaccination coverage.

3.2 Coordinating Contracts

This section constructs a contract which can coordinate this supply chain. Unfortunately, the cost sharing contract of Section 2.2.2, defined by the pair p_r, p_e, does not coordinate the supply chain. Observe that in the piecewise linear case, the government orders enough, i.e., $f^G \geq f'$, even without a coordinating contract. This may not be true for the convex case, where without the contract, f^G maybe smaller than $\bar{f} \leq f^S$, as shown by Proposition 7 and Proposition 8.

Thus, a coordinating contract should provide an incentive for the government to vaccinate a higher fraction of the population, and provide a manufacturer with an incentive to produce enough. Section 3.2.1 shows that this goal can be achieved using a whole-unit discount for the vaccine purchased by the government. In return, the government will pay the manufacturer a portion of the production cost. The relation between the whole-unit discount and the cost sharing portion is such that the more people the government plans to vaccinate, the greater the discount they get and the higher its participation in the production cost.

3.2.1 Whole-unit discount/cost sharing contract

Consider a contract where the vaccine price depends on the fraction of the population the government plans to vaccinate, that is, the government pays the manufacturer $p_r(f)$ per dose. The cost sharing component of the contract is such that the government pays proportional to the production level, n_E. The per unit price paid by the government, $p_e(f)$ depends on f.

This section first constructs a specific class of pricing policies. It then shows how the original game is modified by the pricing policy, and that the given pricing policies indeed align incentives.

The following two assumptions constrain the set of pricing policies of interest.

Assumption 5 *The price $p_r(f) \geq 0$ has the following characteristics:*

1. *There is a whole-unit discount, i.e., $p_r'(f) \leq 0$.*
2. *The total vaccine cost $(p_r(f)fNd)$ is nondecreasing in f,*
   (a) *$(p_r(f)fNd)' = p_r'(f)fNd + p_r(f)Nd \geq 0$ for all $0 \leq f \leq \bar{f}$.*
   (b) *$p_r'(\bar{f})\bar{f}Nd + p_r(\bar{f})Nd = 0$.*
3. *The total cost to the government, excluding the cost sharing component, is convex in f,*
   (a) *$bT''(f) + p_r''(f)fNd + 2p_r'(f)Nd \geq 0$ for all $0 \leq f \leq \bar{f}$.*
4. *There are no further volume discounts beyond a certain threshold, $p_r(f) = p_r(\bar{f})$ for all $\bar{f} \leq f \leq 1$.*

If the derivative $p_r'(f)$ does not exist at $f = \bar{f}$, then use the left derivative in Assumption 5.

The first two characteristics in Assumption 5 allow for many pricing policies. The third characteristic restricts pricing policies to ones for which the total cost of vaccine procurement and social costs are convex[1]. Below we introduce a set of such policies that satisfies all of these properties.

[1] In reality, the total cost is likely to be convex as required. There is a heterogeneous population in reality, and priority for vaccination may be given to "easy" cases first, such as children, the elderly and health care workers, which give greater marginal benefits for prevention and stopping transmission.

Assumption 6 *Given $p_r(f)$, let $p_e(f) \geq 0$ satisfy $\dfrac{c - p_e(f)}{p_r(f)} = \displaystyle\int_0^{k^S} u g_U(u) du$ for all $f \in [0,1]$.*

In Assumption 6, $k^S = \frac{\bar{f}Nd}{n_E^S}$ is the same as before, where $\bar{f}, n_E^S$ are the solutions for the system setting.

Before proceeding, we show first that the set of the conditions in Assumptions 5 and 6 results in a feasible set. We give an example that satisfies the conditions in Assumption 5, then modify it to obtain functions that satisfy all of the conditions in both assumptions. Consider the following pricing strategy,

$$p_r(f) = \begin{cases} \kappa \dfrac{b}{fNd} \left[-T(f) + T'(\bar{f}) f + T(0) \right], & 0 \leq f \leq \bar{f} \\ p_r(\bar{f}), & \bar{f} < f \leq 1. \end{cases} \tag{3.8}$$

The following result shows that pricing strategies exist that satisfy these assumptions. A range of choices of κ for (3.8) is feasible for both assumptions.

Claim 1 *If $0 < \kappa < 1$, then the pricing strategy introduced in (3.8) gives a nonnegative price for any f and satisfies all the conditions in Assumption 5.*

Proof: First we show that $p_r(f) \geq 0$. Note that the function $-T(f) + T'(\bar{f}) f + T(0)$ is an increasing function of f on $[0, \bar{f}]$, as its derivative $-T'(f) + T'(\bar{f})$ exceeds 0 for all $f < \bar{f}$ because $T(f)$ is strictly convex. Further, its value is zero at $f = 0$, so $-T(f) + T'(\bar{f}) f + T(0)$ is a nonnegative function over $[0, \bar{f}]$. Therefore $p_r(f) \geq 0$ for $f \in [0, \bar{f}]$. For $f \in (\bar{f} < f]$, it is clear that $p_r(f) = p_r(\bar{f}) \geq 0$.

We show that this $p_r(f)$ satisfies all the conditions in assumption in the reverse order. Multiplying $p_r(f)$ by fNd and taking the second derivative implies $\left(p_r(f) fNd\right)'' = -\kappa b T''(f)$. So $bT''(f) + \left(p_r(f) fNd\right)'' = (1 - \kappa) bT''(f)$. But $bT''(f) + \left(p_r(f) fNd\right)''$ is the left hand side of the third condition in Assumption 5. By the strict convexity of $T(f)$,

$$bT''(f) + p_r''(f) fNd + 2p_r'(f) Nd = \frac{b}{2} T''(f) \geq 0; \quad \forall\, 0 \leq f \leq \bar{f}$$

For all $\bar{f} < f \leq 1$ we have $bT''(f) + p_r''(f) fNd + 2p_r'(f) = bT''(f) \geq 0$.

To prove validity of the second part of assumption, by taking the derivative of $\big(p_r(f)fNd\big)$ we have: $\big(p_r(f)fNd\big)' = \kappa b\big[-T'(f)+T'(\bar{f})\big]$ which is nonnegative for $0 \le f \le \bar{f}$ (by convexity of $T(f)$) and is zero for $f = \bar{f}$. For $\bar{f} < f \le 1$; $\big(p_r(f)fNd\big)' = p_r(\bar{f})Nd \ge 0$.

Finally to show the first part we take the derivative of $p_r(f)$ for $0 \le f \le \bar{f}$:

$$\frac{\partial p_r}{\partial f} = -\kappa b\Big[\frac{T'(f)f - T(f) + T(0)}{f^2}\Big]$$

The numerator in the bracket is positive due to convexity of $T(f)$ indicating the desired result for $0 \le f \le \bar{f}$. Finally, for $\bar{f} < f \le 1$ we have $p_r'(f) = 0$. $\square$

Claim 2 *If* $0 < \kappa < \min\{1, \frac{c}{[T'(\bar{f})-T'(0)]\mu}\}$, *then the pricing strategy in (3.8) satisfies Assumptions 5 & 6.*

Proof: Claim 1 states that (3.8) satisfies Assumption 5 for the range of κ in question.

We now show that for some κ, (3.8) satisfies Assumption 6. If we set $p_e(f) = c - p_r(f)\int_0^{k^S} ug_U(u)du$, then it suffices to show that $p_e(f) \ge 0$ for all f. Since $p_r(f)$ is nonincreasing in f, we only need to show that $p_r(0)\int_0^{k^S} ug_U(u)du \le c$. For any $p_r(f)$ that satisfies (3.8),

$$\begin{aligned} p_r(0) = \lim_{f\to 0} p_r(f) &= \lim_{f\to 0} \kappa \frac{b}{fNd}\big[-T(f) + T'(\bar{f})f + T(0)\big] \\ &= \kappa\frac{b}{Nd}\big[T'(\bar{f}) - \lim_{f\to 0}\big(\frac{T(f)-T(0)}{f}\big)\big] \\ &= \kappa\frac{b}{Nd}\big[T'(\bar{f}) - T'(0)\big] \end{aligned}$$

Observe that $\int_0^{k^S} ug_U(u)du \le \mu$. We therefore satisfy Assumption 6 if $\kappa\frac{b}{Nd}\big[T'(\bar{f})-T'(0)\big]\mu \le c$. $\square$

All the ingredients are in place to build a coordinating contract. The key idea is to keep the relationship between the optimal production level and order quantity linear. Assumption 6 accomplishes this. To see this, observe that this contract changes the manufacturer objective, for a given f, to:

$$MF(n_E) = (c - p_e(f))n_E - p_r(f)n_E\int_0^{\frac{fNd}{n_E}} ug_U(u)du - p_r(f)fNd\int_{\frac{fNd}{n_E}}^{\infty} g_U(u)du.$$

By taking derivatives, we have:

$$\frac{\partial MF(n_E)}{\partial n_E} = (c - p_e(f)) - p_r(f) \int_0^{\frac{fNd}{n_E}} u g_U(u) du$$
$$\frac{\partial^2 MF(n_E)}{\partial n_E^2} = p_r(f) \frac{fNd}{n_E^2} (\frac{fNd}{n_E}) g_U(\frac{fNd}{n_E}) \geq 0.$$

Therefore, this MF is convex in n_E, and the optimal n_E satisfies $\int_0^{\frac{fNd}{n_E^*}} u g_U(u) du = \frac{c - p_e(f)}{p_r(f)}$. Together with Assumption 6, this implies that $\int_0^{\frac{fNd}{n_E^*}} u g_U(u) du = \int_0^{k^S} u g_U(u) du$. So for any given f, the optimal production level for the manufacturer is linear in f, with

$$n_E^* = \frac{fNd}{k^S}. \tag{3.9}$$

Therefore this contract changes the government objective to

$$\min_f \quad GF = E\big[\, bT(\tfrac{W}{Nd}) + p_a W + p_r(f) Z + p_e(f) n_E \,\big], \tag{3.10}$$

and changes the manufacturing constraint to $\frac{fNd}{n_E} = k^S$. This restatement of the game setting for the whole-unit discount/cost sharing contract permits the statement of the main result of this section.

Theorem 4 *For any $p_e(f), p_r(f)$ that satisfy Assumptions 5 and 6, the optimal values of Problem (3.10), denoted by (f^c, n_E^c), are equal to $(\bar{f}, n_E^S)$. That is, this cost sharing contract coordinates the supply chain.*

Proof: In order to analyze Problem (3.10), we again split it into two separate subproblems.

Case 1 *($0 \leq f \leq \bar{f}$):* In this case the optimization problem would be

$$\begin{aligned}\min_f \quad GF_1 = \Big[\, & b \int_0^{\frac{fNd}{n_E}} T(\frac{n_E u}{Nd}) g_U(u) du + bT(f) \int_{\frac{fNd}{n_E}}^{\infty} g_U(u) du + p_a n_E \int_0^{\frac{fNd}{n_E}} u g_U(u) du \\ & + p_a fNd \int_{\frac{fNd}{n_E}}^{\infty} g_U(u) du + \underbrace{p_e(f) n_E + p_r(f) n_E \int_0^{\frac{fNd}{n_E}} u g_U(u) du}_{= c n_E \text{(by Assumption 6)}} \\ & + p_r(f)(fNd) \int_{\frac{fNd}{n_E}}^{\infty} g_U(u) du \,\Big],\end{aligned}$$

subject to the constraints $fNd = k^S n_E$; $0 \le f \le \bar{f}$; and $n_E \ge 0$. Substituting the constraint $n_E = \frac{fNd}{k^S}$ into the objective function gives

$$\begin{aligned}\min_f GF_1 = \; & \Big[b\int_0^{k^S} T(\frac{f}{k^S}u)g_U(u)du + bT(f)\int_{k^S}^{\infty} g_U(u)du + p_a\frac{fNd}{k^S}\int_0^{k^S} ug_U(u)du \\ & + p_a fNd\int_{k^S}^{\infty} g_U(u)du + c\frac{fNd}{k^S} + p_r(f)fNd\int_{k^S}^{\infty} g_U(u)du \Big] \\ \text{s.t.} \quad & 0 \le f \le \bar{f}.\end{aligned}$$

We show that in this case the optimum value is at $\bar{f}$. For this purpose, it is enough to analyze the first derivative of GF_1:

$$\begin{aligned}\frac{\partial GF_1}{\partial f} =& \Big[\frac{b}{k^S}\int_0^{k^S} T'(\frac{f}{k^S}u)ug_U(u)du + bT'(f)\int_{k^S}^{\infty} g_U(u)du + p_a\frac{Nd}{k^S}\int_0^{k^S} ug_U(u)du \\ & + p_a Nd\int_{k^S}^{\infty} g_U(u)du + c\frac{Nd}{k^S} + p_r(f)Nd\int_{k^S}^{\infty} g_U(u)du + p_r'(f)fNd\int_{k^S}^{\infty} g_U(u)du \Big] \\ =& \frac{Nd}{k^S}\Big(\int_0^{k^S} [\frac{b}{Nd}T'(\frac{f}{k^S}u) + p_a]ug_U(u)du + c\Big) \\ & + \big[bT'(f) + p_a Nd + p_r(f)Nd + p_r'(f)fNd \big]\int_{k^S}^{\infty} g_U(u)du.\end{aligned} \tag{3.11}$$

We show that each of the two components in (3.11) is negative, making the derivative of GF_1 negative for all $0 \le f \le \bar{f}$. To see this, first note that the function $J(f) = \int_0^{k^S}[\frac{b}{Nd}T'(\frac{f}{k^S}u) + p_a]ug_U(u)du$ is an increasing function of f, as $J'(f) = \int_0^{k^S}[\frac{b}{Ndk^S}T''(\frac{f}{k^S}u)]u^2 g_U(u) \ge 0$. Hence $J(f) \le J(\bar{f})$, $\forall f \le \bar{f}$. However, using $\bar{f}Nd = n_E^S k^S$, we get $J(\bar{f}) = \int_0^{k^S}[\frac{b}{Nd}T'(\frac{n_E^S u}{Nd}) + p_a]ug_U(u) = -c$ (by Proposition 7). As a result $J(f) + c \le 0$, so

$$\int_0^{k^S} [\frac{b}{Nd}T'(\frac{f}{k^S}u) + p_a]ug_U(u)du + c \le 0, \qquad \forall\, 0 \le f \le \bar{f}.$$

This shows that the first term in parenthesis in (3.11) is negative. To show that the second term of the derivative of GF_1 is also negative, we consider the term $bT'(f)+p_aNd+p_r(f)Nd+p_r'(f)fNd$. The derivative of this expression is $bT''(f) + p_r''(f)fNd + 2p_r'(f)Nd$, which is positive using the third part of Assumption 5. This means that $bT'(f) + p_aNd + p_r(f)Nd + p_r'(f)fNd \le bT'(\bar{f}) + p_aNd + p_r(\bar{f})Nd + p_r'(\bar{f})\bar{f}Nd$ for all $0 \le f \le \bar{f}$. Note that $bT'(\bar{f}) +$

$p_a Nd = 0$ by the definition of $\bar{f}$, and that $p_r(\bar{f})Nd + p_r'(\bar{f})fNd = 0$ by the second part of Assumption 5. This suggests

$$bT'(f) + p_a Nd + p_r(f)Nd + p_r'(f)fNd \leq 0, \qquad \forall\, 0 \leq f \leq \bar{f},$$

which shows that the second term of the derivative of GF_1 is also negative. By the strict convexity of $T(f)$, equality occurs only at $\bar{f}$. Hence (3.11) implies that $GF_1(f) \leq 0$ for all $0 \leq f \leq \bar{f}$, meaning that the minimum of GF_1 is attained at $\bar{f}$. The corresponding production value to $\bar{f}$ is n_E^S (using 3.9). So in this case, the only candidate for optimality is the system optimal solution.

Case 2 *($\bar{f} \leq f \leq 1$):* In this case, using the definition of $p_r(f)$, $p_r(f) = p_r(\bar{f})$, and hence $p_e(f) = p_e(\bar{f})$ for all $f \geq \bar{f}$. As a result, the government objective becomes:

$$\begin{aligned} GF_2 = \Big[\, & b\int_0^{\frac{\bar{f}Nd}{n_E}} T(\frac{n_E u}{Nd}) g_U(u)du + bT(\bar{f})\int_{\frac{\bar{f}Nd}{n_E}}^{\infty} g_U(u)du + p_a n_E \int_0^{\frac{\bar{f}Nd}{n_E}} u g_U(u)du \\ & + p_a \bar{f} Nd \int_{\frac{\bar{f}Nd}{n_E}}^{\infty} g_U(u)du + \underbrace{p_e(\bar{f})n_E + p_r(\bar{f})n_E \int_0^{\frac{fNd}{n_E}} u g_U(u)du}_{= cn_E \text{(by Assumption 5)}} \\ & + p_r(\bar{f}) fNd \int_{\frac{fNd}{n_E}}^{\infty} g_U(u)du \,\Big], \end{aligned}$$

subject to the constraints $fNd = k^S n_E$; $\bar{f} \leq f \leq 1$; and $n_E \geq 0$. Substituting the constraint $fNd = k^S n_E$ to remove f from the objective gives:

$$\begin{aligned} GF_2 = \Big[\, & b\int_0^{\frac{\bar{f}Nd}{n_E}} T(\frac{n_E u}{Nd}) g_U(u)du + bT(\bar{f})\int_{\frac{\bar{f}Nd}{n_E}}^{\infty} g_U(u)du + p_a n_E \int_0^{\frac{\bar{f}Nd}{n_E}} u g_U(u)du \\ & + p_a \bar{f} Nd \int_{\frac{\bar{f}Nd}{n_E}}^{\infty} g_U(u)du + cn_E + p_r(\bar{f})n_E k^S \int_{k^S}^{\infty} g_U(u)du \,\Big] \end{aligned}$$

with the constraint $\bar{f} \leq f$ replaced by the constraint $n_E \geq n_E^S$.

We now show that the derivative of the objective function in this case is positive, and

hence GF_2 is minimized when that constraint is tight, $n_E = n_E^S$. Consider:

$$\frac{\partial GF_2}{\partial n_E} = \int_0^{\frac{\bar{f}Nd}{n_E}} [\frac{b}{Nd} T'(\frac{n_E u}{Nd}) + p_a] u g_U(u) du + c + p_r(\bar{f}) k^S \int_{k^S}^{\infty} g_U(u) du. \tag{3.12}$$

The first term above is exactly the function $H(n_E)$ introduced in the proof of Proposition 8. By using its nondecreasing property, we get $H(n_E) \geq H(n_E^S)$ for all $n_E \geq n_E^S$. Recall that Proposition 7 suggests $H(n_E^S) = \int_0^{\frac{\bar{f}Nd}{n_E^S}} [\frac{b}{Nd} T'(\frac{n_E^S u}{Nd}) + p_a] u g_U(u) du = -c$. This implies that

$$\int_0^{\frac{\bar{f}Nd}{n_E}} [\frac{b}{Nd} T'(\frac{n_E u}{Nd}) + p_a] u g_U(u) du + c \geq 0; \qquad \forall\, n_E \geq n_E^S.$$

By using this result with (3.12), we obtain the desired result,

$$\begin{aligned} \frac{\partial GF_2}{\partial n_E} &= \int_0^{\frac{\bar{f}Nd}{n_E}} [\frac{b}{Nd} T'(\frac{n_E u}{Nd}) + p_a] u g_U(u) du + c + p_r(\bar{f}) k^S \int_{k^S}^{\infty} g_U(u) du \\ &\geq p_r(\bar{f}) k^S \int_{k^S}^{\infty} g_U(u) du \geq 0. \end{aligned}$$

In both case 1 and case 2, the optimum values for the game setting are $\bar{f}, n_E^S$. □

3.3 Numerical Results

This section uses the idea behind Theorem 4, together with estimates of parameters from the influenza literature, in order to develop a contract that can coordinate the supply chain empirically, even though the actual $T(f)$ may slightly deviate from strict convexity.

Longini et al. (2004) estimate $R_0 = 1.68$ and Weycker et al. (2005) argue that $\psi = 0.90$ is a reasonable value for vaccine effects, so we chose ψ to vary between $[0.85, 0.95]$ and R_0 between $[1.5, 2]$. Weycker et al. (2005) estimate the direct costs (not indirect) of each infected individual with $b = \$95$ on average over the different groups. In our experiments, b takes values between 70 and 120. The vaccine price is set to $p_r = \$12$ (CDC, 2005). For vaccine administration costs, we tested each of $p_a = \$20$, approximately the value in Pisano (2006) for Medicare reimbursement; $p_a = \$40$, the value that Weniger et al. (1998) estimated for pediatric vaccines, based on the cost of a doctor visit; and $p_a = \$60$, which accounts for

inflation and provides a sensitivity analysis. We used $d = 1$ dose of vaccine, the usual value, per adult vaccinated. We are not aware of published estimates of the variance of vaccine production yields, although it is clear that variable vaccine yields are significant enough to cause noticeable fluctuations in the quantity of vaccine delivered (U.S. GAO, 2001). We assumed that U has a gamma distribution with mean $\mu = 1$ (Palese, 2006) and tested different values for the variance, $\sigma^2 = 0.025, 0.05, 0.06, 0.1, 0.2$. We assumed a population of $N = 3 \times 10^8$ individuals and a production cost of $c = \$6$ (not necessarily the actual value).

We implemented the whole-unit discount/cost sharing contract in Section 3.2.1 for cases of $T(f)$ that are based upon the above parameters and using $\chi = 0.01$. For example, Figure 3-1 depicts the contract prices, government costs, and manufacturer profit when $b = \$95$, $p_a = \$60$, $\sigma^2 = 0.2$ and $\kappa = 0.128$. While $T(f)$ in this case is not precisely convex, a strict application of the prices implied by (3.8) and Assumption 6 leads to a whole-unit discount price, $p_r(f)$ and cost sharing price $p_e(f)$ that coordinates incentives. Figure 3-1(a) shows that the wholesale price obtained by (3.8) is not monotone in this case.

We can show that a modification of the wholesale price in which the increasing part of the price is replaced by a constant value equal to the maximum wholesale price, as in Figure 3-1(b), is still coordinating. The intuition for why such a change can coordinate incentives is as follows. The convex payment, under the contract $p_r(f)$, for the government offsets the convexity of the cost function and pushes the government to order enough vaccines (f^S). In the case of concave-convex attack rates, one need not push the government to order higher amounts while f is in the concave region, assuming that the first dose is cost effective, $bT_0'(0) + p_a N d < 0$, and that the social optimal f is in the convex region. With those two assumptions, the government order as much as possible in the concave region even without the contract incentive. Thus there is no need for a non-linear payment in the concave region. As f is raised into the convex region, the contract regains its nominal shape and gives an incentive for government to order more. This variation for our proposed contract can therefore potentially coordinate incentives even for a larger class of attack rates in which $T(f)$ is first concave and after a point becomes convex, assuming $bT'(0) + p_a N d < 0$. Appendix B notes that $T(f)$ is convex, or first concave then convex, for almost all of parameters that are valid for influenza transmission and vaccination (or when there is parameter uncertainty),

and that in each case the associated contract is coordinating.

In this example, the manufacturer's effort is increased from 195M eggs to 233M eggs ($\sim$ 19.5% increase), and its profit increases from $\$8.82 \times 10^8$ to $\$9.56 \times 10^8$ (by \$74M, or 8.4%). The government's order changes from 0.73 to 0.48, and its vaccine and social costs increase from $\$1.001 \times 10^{10}$ to $\$1.060 \times 10^{10}$ ($\sim$ 5.9% increase) and $\$3.103 \times 10^9$ to $\$2.510 \times 10^9$ ($\sim$ 19.1% decrease), respectively. The total governmental outlay decreases from $\$1.312 \times 10^{10}$ to $\$1.311 \times 10^{10}$ (by \$10M, or $\sim$ 0.1%).

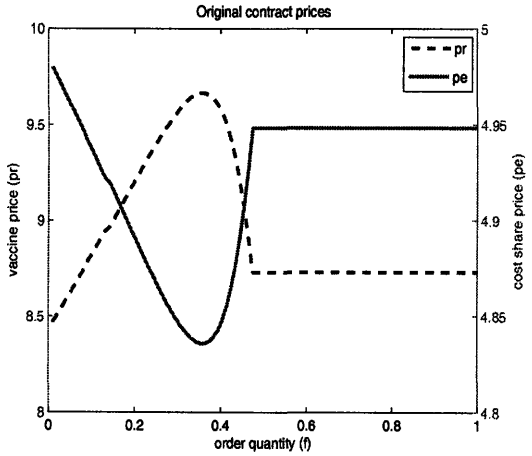
Table 3.1 provides a sensitivity analysis with respect to the model's parameters. The particular choice of κ in the fourth column of Table 3.1 insures that both government and manufacturer are better off under the contract. The following three columns show the increase in the manufacturer cost and decrease in the government social (cost of the infected population) and vaccine costs (procurement, administration, and cost sharing costs), respectively, when the contract is implemented. Notice that the government vaccine cost denotes all the vaccine procurement, administration and cost sharing costs (i.e. terms related to p_r, p_a, p_e) and the government social costs represents only the social costs of the disease (i.e. the term related to b). Although the government is better off after the contract in each row of the table, this benefit is primarily through a reduction in social costs due to increased vaccination expenditures. In our tests, we observed:

- There are always choices for κ so that with the contract, (a) the manufacturer's profit increases, (b) the government's social cost decreases, (c) the government's vaccination cost increases.

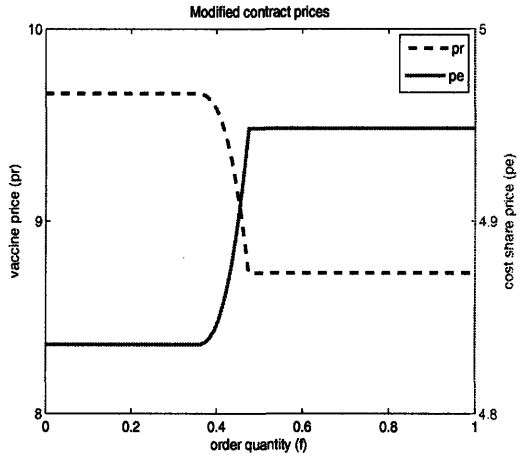
- Higher variability in yield leads to greater manufacturer profit and higher government vaccine costs, but also to lower government social costs (more yield volatility pushes the government to order more vaccine, and the manufacturer to produce more, resulting in greater coverage on average).

- For a given set of parameters, a larger κ increases the manufacturer's profit and governmental vaccine costs, but the governmental social costs do not fluctuate as much.

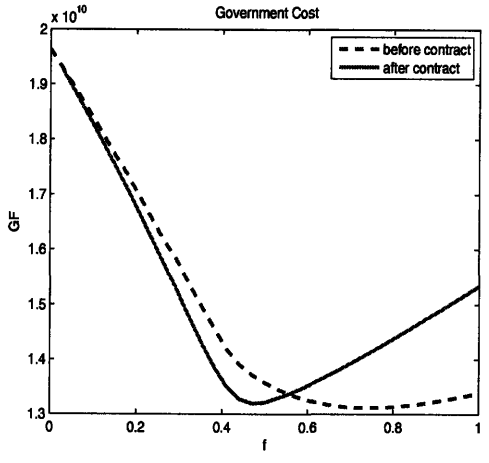
The parameter κ can be set by the government in order to provide incentives to manufacturers



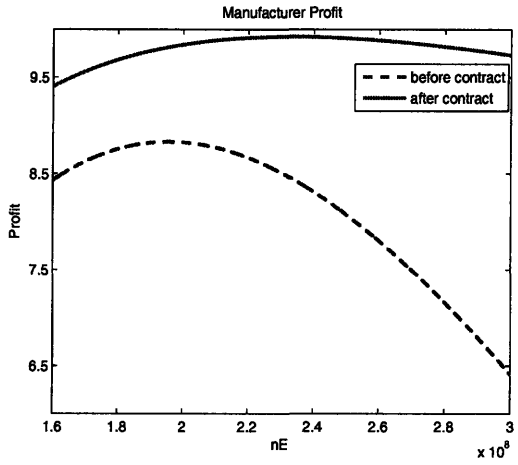
(a) Contract prices before modification (left vertical axis has $p_r(f)$, right vertical axis gives $p_e(f)$).



(b) Cost per dose, $p_r(f)$ (scale on left vertical axis), and per unit production effort, $p_e(f)$ (scale on right vertical axis).



(c) Governmental vaccine procurement, vaccine administration, and health costs, $GF(f)$.



(d) Manufacturer profit, $-MF(n_E)$.

Figure 3-1: Cost sharing/whole-unit discount contract.

Table 3.1: Sensitivity analysis for contract outcomes, with $R_0 = 1.68$ and $\psi = 0.9$.

b	p_a	σ^2	κ	manufacturer profit increase	gov. vaccine cost increase	gov. social cost decrease	before contract		after contract	
							f	n_E	f	n_E
95	20	0.2	0.092	7.90%	7.67%	23.69%	0.88	234 M	0.56	2.75 M
95	60	0.2	0.128	8.4%	5.9%	19.1%	0.73	195 M	0.48	233 M
120	20	0.2	0.073	6.97%	7.13%	23.02%	0.95	253 M	0.58	296 M
70	40	0.2	0.159	9.39%	7.68%	22.41%	0.69	183 M	0.49	221 M
95	20	0.1	0.109	27.84%	9.99%	36.61%	0.72	205 M	0.50	235 M
120	60	0.06	0.082	3.90%	3.21%	11.62%	0.51	148 M	0.42	163 M
95	40	0.06	0.099	4.77%	4.11%	14.23%	0.51	147 M	0.44	163 M

to produce, while keeping social costs at a desired level.

Sections 3.3.1 and 3.3.2 provide additional sensitivity analysis that evaluates the effect of inaccurately estimating $T(f)$ on the decision parameters and the economic result of taking an under-informed decision. In particular, for the numerical experiments reported there, the benefit of a coordinating contract, relative to the game setting, tends to be more significant than the potential penalty of some level of error in estimating $T(f)$. The benefit is still gained, but the benefit is less significant, when the linear approximation is used and χ is not close to 0, or when χ is estimated much too high. If the value of χ is uncertain, it is therefore better to estimate χ on the low side than on the high side, and to use the concave-then-convex contract that is illustrated here, as opposed to using the linear approximation. The coordinating contract did very well in an example where there was uncertainty in R_0.

We performed two sets of sensitivity analysis experiments. The results are directly comparable with those from the this section.

The first set addresses a sensitivity analysis with respect to the parameters of the model. The second set addresses a sensitivity analysis with respect to uncertainty about the parameters and/or the functional form of the epidemic model. We discuss each in turn.

3.3.1 Sensitivity Analysis for Model Parameters

Table 3.1 provides a sensitivity analysis with respect to the model's parameters, as those parameters are changed from their values in Section 3.3. The particular choice of κ in the fourth column of Table 3.1 insures that both government and manufacturer are better off

under the contract. The following three columns show the increase in the manufacturer cost and decrease in the government social (cost of the infected population) and vaccine costs (procurement, administration, and cost sharing costs), respectively, when the contract is implemented. Notice that the government vaccine cost denotes all the vaccine procurement, administration and cost sharing costs (i.e. terms related to p_r, p_a, p_e) and the government social costs represents only the social costs of the disease (i.e. the term related to b). Although the government is better off after the contract in each row of the table, this benefit is primarily through a reduction in social costs due to increased vaccination expenditures.

In our tests, we observed:

- There are always choices for κ so that with the contract, (a) the manufacturer's profit increases, (b) the government's social cost decreases, (c) the government's vaccination cost increases.

- Higher variability in yield leads to greater manufacturer profit and higher government vaccine costs, but also to lower government social costs (more yield volatility pushes the government to order more vaccine, and the manufacturer to produce more, resulting in greater coverage on average).

- For a given set of parameters, a larger κ increases the manufacturer's profit and governmental vaccine costs, but the governmental social costs do not fluctuate as much.

The parameter κ can be set by the government in order to provide incentives to manufacturers to produce, while keeping social costs at a desired level.

3.3.2 Sensitivity Analysis for Model Uncertainty

We performed a set of numerical experiments in order to test the sensitivity of the coordinating contract to changes in the attack rate function that are due to uncertainty about epidemic parameters, or to uncertainty about the functional form of the attack rate. They allow for an assessment of the penalty for assuming a piecewise linear attack rate (which has a simpler coordinating contract) when the actual attack rate is nonlinear (and the co-

ordinating contract is more complex). They also assess potential penalties for incorrectly estimating epidemic parameters.

In summary, the benefit of a coordinating contract, relative to the game setting, tends to be more significant than the potential penalty of some level of error in estimating $T(f)$.

The experimental settings are:

- Base linear case: the manufacturer and government both believe that the attack rate is a piecewise linear function, and the believed attack rate is the same as the actual attack rate.

- The first experiment illustrates the differences between the decision variables and the cost functions when the attack rate is assumed to be a piecewise linear function by the manufacturer and the government, but the true attack rate is not precisely piecewise linear ($\chi \to 0$).

- The second experiment illustrates the differences between the decision variables and the cost functions when the attack rate is assumed to be a piecewise linear function by the manufacturer and the government, but the true attack rate is associated with a higher initial exposure to infection ($\chi = 0.01$).

- Base nonlinear case: the manufacturer and government both believe that the attack rate is a concave-then-convex function, with $\chi = 0.01$, and the believed attack rate is the same as the actual attack rate.

- The third experiment illustrates the differences between the decision variables and the cost functions when the attack rate is assumed to be a concave-then-convex function with $\chi = 0.01$ by the manufacturer and the government, but the actual attack rate has $\chi = 0.02$.

- The fourth experiment illustrates the differences between the decision variables and the cost functions when the attack rate is assumed to be a concave-then-convex function with $\chi = 0.01$ by the manufacturer and the government, but the actual attack rate has $\chi \to 0$.

- The fifth experiment illustrates the differences between the decision variables and the cost functions when the attack rate is assumed to be a concave-then-convex function with $\chi = 0.01$ and $R_0 = 1.68$ by the manufacturer and the government, but the actual R_0 actual attack rate is random with continuous uniform distribution on $[1.58, 1.78]$ (to evaluate the effectiveness when a point estimate is used in the presence of unpredictable disease transmission parameters).

In order to provide results that are comparable with Section 3.3 we chose $R_0 = 1.68, \psi = 0.9$, $b = 95, p_a = 60, p_r = 12, c = 6, d = 1, N = 3 \times 10^8, U \sim gamma[5, 1/5]$, unless otherwise specified. Each experiment leads to a row in Tables 3.2-3.3.

Table 3.2 indicates that decisions may differ from their optimal values, if the epidemic model is incorrectly specified, and by how much. The first column corresponds to f^G if the government knew the true value of χ. Similarly the second column is f^G under the "believed" value of χ, i.e. in reality this value will be ordered. Finally the third column is the gap between the first and second column. The next nine columns are the analogous values for n_E^G, f^S, and n_E^S respectively.

Table 3.3 compares the governmental costs and manufacturer profits for those same experiments, when the true model is not known precisely. The first column is the actual government cost under the game setting if he knew the parameter correctly. Likewise the second column is the government cost if he orders based on his belief. Hence the difference between these two columns gives us the governmental loss in total cost. The next four columns are analogous numbers for the system wide cost and manufacturer's profit.

One key observation from these experiments is that the economic benefit that is associated with the coordinating contract exceeds the penalty that is associated with a somewhat incorrect estimate of the epidemic model. Consider the values for experiment 1 in Table 3.3. The total cost to the system when the government and the manufacturer optimize individually equals the government total costs minus the manufacturer profits (which can be considered a transfer from the government to the manufacturer), or \$11.51B – \$992.5M = \$10.52B. The benefit of the contract for the total system costs is therefore \$10.52B – \$10.44B, or \$80 M. The penalty for not having the correct model for $T(f)$ is \$10.46B – \$10.44B $\approx$ \$20 M. In

Table 3.2: Gap in the decision variables when parameter estimates are incorrect

Experiment #	actual f^G	believed f^G	gap in f^G	actual n_E^G	believed n_E^G	gap in n_E^G	actual f^S	believed f^S	gap in f^S	actual n_E^S	believed n_E^S	gap in n_E^S
Base lin.	0.757	0.757	0%	200.4 M	200.4 M	0%	0.449	0.449	0%	235.2 M	235.2 M	0%
1	0.831	0.757	8.9%	219.9 M	200.4 M	8.9%	0.456	0.449	1.5%	257.5 M	235.2 M	8.6%
2	0.739	0.757	2.4%	195.6 M	200.4 M	2.4%	0.484	0.449	7.2%	233.6 M	235.2 M	0.68%
Base nonlin.	0.739	0.739	0%	195.6 M	195.6 M	0%	0.484	0.484	0%	233.6 M	233.6 M	0%
3	0.706	0.739	4.7%	186.8 M	195.6 M	4.7%	0.498	0.484	2.8%	234.6 M	233.6 M	0.42%
4	0.831	0.739	11%	219.9 M	195.6 M	11%	0.456	0.484	6%	257.5 M	233.6 M	9.2%
5	0.796	0.739	7.1%	210.7 M	195.6 M	7.1%	0.485	0.484	0.2%	245.3 M	233.6 M	4.7%

Table 3.3: Gap in the cost functions when parameter estimates are incorrect

Experiment #	gov cost w/ true parameters	gov cost w/ believed parameters	sys cost w/ true parameters	sys cost w/ believed parameters	man profit w/ true parameters	man profit w/ believed parameters
Base lin.	10.92 B	10.92 B	9.948 B	9.948 B	904.6 M	904.6 M
1	11.51 B	11.55 B	10.44 B	10.46 B	992.5 M	904.6 M
2	13.12 B	13.12 B	12.15 B	12.21 B	882.9 M	904.6 M
Base nonlin.	13.12 B	13.12 B	12.15 B	12.15 B	882.9 M	882.9 M
3	13.84 B	13.85 B	12.91 B	12.93 B	842.9 M	882.9 M
4	11.51 B	11.57 B	10.44 B	10.47 B	992.5 M	882.9 M
5	13.27 B	13.30 B	12.25 B	12.26 B	950.9 M	882.9 M

this and each of the other cases, the benefit of coordinating the contract is more significant than having a precise estimate of the epidemic curve. The effect is particularly noticable in experiment 5, where the principal uncertainty is in the value of R_0, and the benefit of the contract is about \$70 M, and the penalty for not knowing the exactly correct R_0 is less than \$1 million.

While the benefit of the coordinating contract in experiments 2 and 4 still outweighs the penalty for not having a precise estimate of $T(f)$, the margin is less significant in those experiments. The worst case is in experiment 2, where the benefit of the contract is only \$87 million, and the penalty for not estimating $T(f)$ accurately is \$60 M. Both of those experiments are examples where χ is either overestimated significantly, or a piecewise linear approximation is used with an incorrect estimate of χ. The suggestion is therefore to not overestimate χ, and to avoid the linear approximation in applications where it is not truly a good approximation.

Another important observation from these experiments is that the percentage error for the decision variables is smaller in the system setting, than for the game setting (except for experiment 2, which is a scenario that is to be avoided in practice on economic grounds as described above). For example, in experiment 5, the percent difference between the true

and believed optimal fraction of the population to vaccinate is 7.1%. With the coordinating contract, the difference between the true and believed optimal fraction to vaccinate is 0.2%. A similar comparison holds for the number of eggs to use for manufacturing. The coordinating contract, therefore, tended to narrow the gap between the true optimal and believed optimal values in these experiments, as measured by percentage error. The only exception to that observation is when the value of χ is believed to be rather larger than its true value. This reinforces the importance of not overestimating χ. The sensitivity for the unknown R_0 in this case is encouraging for the use of the proposed contract.

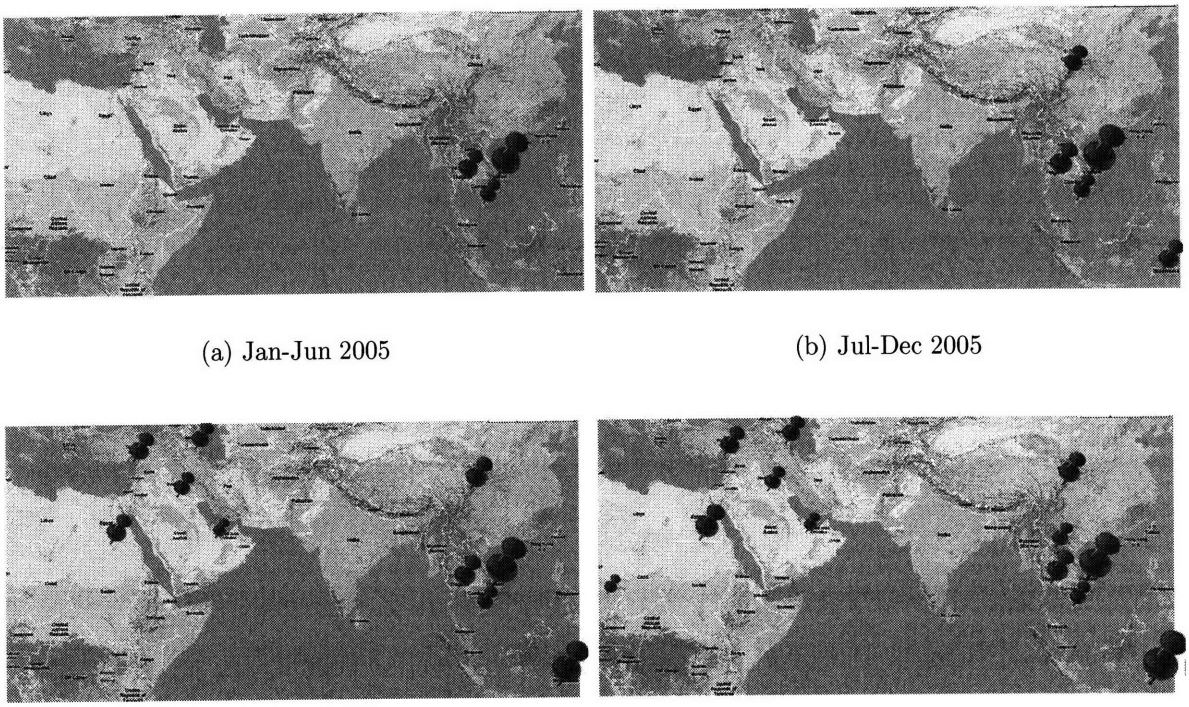
Chapter 4

Supply Chain with Multiple Countries

In this chapter we consider the global influenza vaccine supply chain and model the interaction between different countries. The model with multiple governments can not be simply replaced by several copies of the single government case from the previous two chapters due to the disease transmission effect across the different countries. Figure 4-1 shows the countries which have shown a number of human cases of Avian Flu. The size of each pin is proportional to the size of the epidemic in that country. It is clear that as time passes, the epidemic transmits to the neighborhoods of the originating countries. In other words, epidemic outcomes in each country is affected by the actions taken by other governments as well. The epidemic model in this chapter is different than the previous model since various countries can potentially have different characteristics for the disease and its transmission. As a result we use an epidemic model with heterogenous population in this chapter, as opposed to a homogeneous population from previous chapters. Notice that in this setting we do not model the manufacturer explicitly in the supply chain so that we can focus on logistical issues across different governments.

4.1 Joint Epidemic and Supply Chain model

We assume that there are $M + 1$ countries in our model. One country will be denoted as the index country in which the epidemic initiates (country 0). Following the notation



(a) Jan-Jun 2005

(b) Jul-Dec 2005

(c) Jul-Dec 2006

(d) Jan-Jul 2007

Figure 4-1: Spread of human cases of Avian Flu to different countries

from previous chapters, each government $i \in \{0, 1, \cdots, M\}$ initially selects a fraction f_i of a population of N_i individuals to vaccinate. Given the demand by the governments, the manufacturer then decides how much to produce. However, due to production uncertainty, the manufacturer might be able to fulfill the whole or part of initial orders by governments as discussed in previous chapters. In this chapter, however, we model the production uncertainty differently. Suppose that the final vaccine dose that government i receives is $\alpha f_i N_i d$ in which $0 \leq \alpha \leq 1$ is a random variable that models the yield uncertainty. We use a different notion for production uncertainty since there is no manufacturer in this setting, however we can relate the two notations (U and α). Suppose that there is only one government in the model, then we have $\alpha = \min\{\frac{n_E U}{fNd}, 1\}$. Notice that such an allocation of vaccines to governments means that in the case of insufficient production of vaccine, the manufacturer allocates the total supply of vaccine proportional to the initial orders of governments. Such an allocation might not necessarily be an optimal assignment of the scarce vaccine to dif-

ferent governments. However, in this chapter we do not examine manufacturer incentives to work with one country over another. Moreover the manufacturer is not a part of our optimization model, so public benefits of various vaccine allocations to countries is not modeled as a primary concern for the manufacturer.

When acting separately, like the single government case, each government i seeks to minimize its cost of procuring and administering vaccines (v_i per dose), plus the total social cost due to infection, $b_i T_i(f_0, f_1, \cdots, f_M)$, where $T_i(\cdot)$ is the total expected number of infected individuals by the end of the influenza season (a generalization of $T(f)$ from Section 2.1) and b_i is the average direct and indirect cost of an influenza infection. Like before, we simplify the model *in each country* to a homogeneous model in order to focus on contract issues for vaccine sharing across different countries, rather than including details about optimal allocation of a given volume in a specific country. Notice, however, that the overall epidemic model in this chapter is a heterogenous model.

The epidemic model drives the analysis for supply chain behavior through the functions $T_i(f_0, \cdots, f_M)$, which model the expected number of infected individuals in country i by the end of the influenza season, as a function of vaccinated population fractions. Longini et al. (1978) gives a characterization of these functions in a heterogenous population as a system of deterministic differential equations. Let θ be the vaccine effect on susceptibility, i.e., probability of becoming infected decreases by $1-\theta$, given the exposure. Denote the vaccine effect on infectiousness by ϕ, i.e., probability of transmitting the disease decreases by $1-\phi$, given an exposure. Moreover let f_i be the fraction of population i that gets vaccinated, and *generalized basic reproduction number*, R_{ij}, be the number of secondary infections in country i from one randomly selected infectious individual in country j for every $i, j \in \{0, 1, \cdots, M\}$. Finally let $S_i(0)$ be the fraction of susceptible population and $I_i(0)$ be the fraction of infected and infectious population at the start of the epidemic. The attack rate, p_i, for country i, or fraction of the infected population throughout the epidemic season in country i, is then (Longini et al., 1978)

$$p_i = S_i(0)\left(1 + \frac{I_i(0)}{S_i(0)} - e^{\left\{-\sum_{j=0}^{M} R_{ji} p_j\right\}}\right) \tag{4.1}$$

Such a characterization, though general, is mathematically intractable from the supply chain analysis point of view. As a result we use a two-folded epidemic model in order to mimic the dynamics of the spread of the disease both within and across different countries while simplifying the mathematics. Section 4.4.1 shows that such an approximation has a small error, typically in the order of 3% on average, for computing the final attack rates of influenza in each population. At the start of the epidemic, we use the *next generation matrix* method (e.g., Hill and Longini, 2003). This approach enables us to model the interaction across the different countries. After a few generations of evolving the disease and once the epidemic is going in each country, the disease outcomes are somewhat insensitive to the exposure from the other regions. Hence the purpose of the second stage of our epidemic model is to use the feedback from the first stage, and model the dynamic of the spread of the disease within each individual country. For each country i, we use a deterministic compartmental model of N_i homogeneous and randomly mixing individuals that start out Susceptible to infection, but may also be infected and Infectious, or Removed upon recovery from infection, a standard SIR compartmental model that is a reasonable model for the natural history of infection of influenza. Table 4.1 summarizes the notation used throughout this chapter.

The next two sections explain these models and some of their properties with further details.

4.1.1 Epidemic Model - Start of the Epidemic

The next generation matrix method approximates the spread of the disease at the start of an epidemic. Based on the notation above, we can model the beginning of the epidemic process as the following system of equations in which $y_{0i}(g)$ and $y_{1i}(g)$ are the expected number of secondary infections in population i, unvaccinated and vaccinated, respectively, at generation g (Hill and Longini, 2003):

$$y_{0i}(g+1) = \sum_{j=0}^{M} \left[R_{ij}(1-f_j)y_{0j}(g) + R_{ij}\phi f_j y_{1j}(g)\right]$$
$$y_{1i}(g+1) = \sum_{j=0}^{M} \left[R_{ij}\theta(1-f_j)y_{0j}(g) + R_{ij}\phi\theta f_j y_{1j}(g)\right]$$

Table 4.1: Summary of Notation for Multiple Governments Supply Chain.

Infection Transmission

$M+1$	Total number of countries
N_i	Total number of people in country i, $i = 0, 1, \cdots, M$
R_{ij}	The number of secondary infections in country i from one randomly selected infectious individual in country j
f_i	fraction of the population in country i to vaccinate announced by its government to the manufacturer
θ	Vaccine effect on susceptibility
ϕ	Vaccine effect on infectiousness
χ_i	The initial fraction of susceptibles in country i that are infected due to exogenous exposure to infection (from the index country)
$I_i(0)$	The fraction of infected and infectious population in country i at the start of the second phase of the epidemic
$S_i(0)$	The fraction of susceptible population in country i at the start of the second phase of the epidemic
f_i'	The critical vaccination fraction in country i (fraction of population to vaccinate to halt outbreak), assuming that country i were considered alone
p_i	The true attack rate, or the fraction of infected population throughout the epidemic season, in country i
$\tilde{p}_i$	The true attack rate approximation based on the two-tier epidemic model presented in this chapter
$T_i(\cdot)$	Total expected number of infected during the infection season in country i based on the two-tier epidemic model, i.e. $T_i(\cdot) = N_i\tilde{p}_i$ (a function of the fraction vaccinated in potentially all countries)

Supply Chain

α	Random variable for the yield per egg.
v_i	Vaccination program costs for government i, including vaccine purchasing and administration costs. i.e., using notation used in Chapter 2 and Chapter 3, $v = p_r + p_a$ for each country
b_i	Average total social cost per infected individual in country i
$\tilde{f}_i$	Maximum fraction of the population in country i that can be vaccinated based on the budget constraint.

So if we define the $2(M+1)$-vector of vaccinated and unvaccinated infected population as

$$\mathbf{y}(g) = \left[y_{00}(g), y_{10}(g), \cdots, y_{0M}(g), y_{1M}(g)\right]^T$$

then the above system of equations can be written as:

$$\mathbf{y}(g+1) = \mathbf{R}\mathbf{y}(g)$$

or equivalently

$$\mathbf{y}(g+1) = \mathbf{R}^g\mathbf{y}(0) \tag{4.2}$$

where $\mathbf{R}_{2(M+1)\times 2(M+1)}$, is the next generation matrix for vaccine allocation $(f_0, \cdots, f_M)$:

$$\mathbf{R} = \begin{bmatrix} R_{00}(1-f_0) & R_{00}\phi f_0 & \cdots & R_{0M}(1-f_M) & R_{0M}\phi f_M \\ R_{00}\theta(1-f_0) & R_{00}\theta\phi f_0 & \cdots & R_{0M}\theta(1-f_M) & R_{0M}\theta\phi f_M \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ R_{M0}(1-f_0) & R_{M0}\phi f_0 & \cdots & R_{MM}(1-f_M) & R_{MM}\phi f_M \\ R_{M0}\theta(1-f_0) & R_{M0}\theta\phi f_0 & \cdots & R_{MM}\theta(1-f_M) & R_{MM}\theta\phi f_M \end{bmatrix} \tag{4.3}$$

Notice that each component of $\mathbf{R}^g$ is a nonlinear function of potentially all of the f_i's. This nonlinearity complicates the analysis significantly. Given the following two assumptions it can be shown that the complex network of interactions between countries (see Figure 4-2-a) can be approximated by a much simpler network in which only relations from the index country (country 0) to others (countries $1, \cdots, M$) are important (see Figure 4-2-b).

Assumption 7 *The epidemic starts only at one of the countries, denoted by country 0.*

Assumption 8 *For every $i \neq j$, and $k \neq j$, we have $R_{ij}R_{jk} \approx 0$.*

The second assumption simply indicates that the value for R_{ij} can not be big. Notice that a stronger version of this assumption is usually made in the literature (Brandeau et al., 2003; Sun et al., 2007) in which $R_{ij} \approx 0$. Our assumption relaxes the previous ones by allowing $R_{ij} > 0$, however restricts its second order effect. Intuitively, this assumption states that

the probability of one person in China infecting a person in France *and* the same person in France infecting an individual in the US is very small. This assumption is therefore is less restrictive than in Brandeau et al. (2003); Sun et al. (2007). To illustrate this point, we show later in Section 4.4 that $[0.01, 0.05]$ is a reasonable range for R_{ij}'s when $i \neq j$. As a result, while $R_{ij} = 0.02$ might not be approximated by zero, $R_{ij}^2 = 0.0004$ is more easily approximated by zero. The following two lemmas explain the significant role of the index country in the spread of the disease under Assumption 7 and Assumption 8.

Lemma 4 *Given assumption 7, for any generation g, the number of infected individuals, $\mathbf{y}_{2i+1}(g) + \mathbf{y}_{2i+2}(g)$, in population i $(i = 1, \cdots, M)$ can be written as*

$$\mathbf{y}_{2i+1}(g) + \mathbf{y}_{2i+2}(g) = R_{i0}\, \mathcal{J}_g(f_i, f_0) + \Delta \times \mathcal{G}_g(f_0, \cdots, f_M) \tag{4.4}$$

where $\mathcal{J}_g(\cdot)$ is a function of only f_i and f_0 parameters, $\mathcal{G}_g$ is some general function of potentially all vaccination fractions, and $\Delta = \max_{i \neq j \neq k} \{R_{ij} R_{jk}\}$. Moreover,

$$\lim_{\Delta \to 0} \left| \mathcal{G}_g(f_0, \cdots, f_M) \right| < \Big(\sum_i \pi_i^g \Big) \frac{1 - \big(2R_{0i}(R_{ii} + R_{00})\big)^g}{1 - 2R_{0i}(R_{ii} + R_{00})} \tag{4.5}$$

where π_i^g is the expected number of infected individuals in population i after g generations in the absence of any vaccination.

Proof: Notice that using Assumption 7, $\mathbf{y}(0) = [1, 0, 0, 0, \cdots, 0, 0]^T$. Hence by (4.2), it is enough to show that all entries in the first column of the matrix $\mathbf{R}^g$ depend on f_0 and the corresponding f_i or formally matrix $\mathbf{R}^g$ gets the following form:

$$\mathbf{R_{2M+1 \times 2M+1}}^g = \tag{4.6}$$

$$\begin{bmatrix}
R_{00}\,\mathcal{J}_g(f_0) + \Delta \times \mathcal{G}_g(\cdot) & R_{00}\,\mathcal{J}_g(f_0) + \Delta \times \mathcal{G}_g(\cdot) & \cdots & R_{0M}\,\mathcal{J}_g(f_0, f_M) + \Delta \times \mathcal{G}_g(\cdot) & R_{0M}\,\mathcal{J}_g(f_0, f_M) + \Delta \times \mathcal{G}_g(\cdot) \\
R_{00}\,\mathcal{J}_g(f_0) + \Delta \times \mathcal{G}_g(\cdot) & R_{00}\,\mathcal{J}_g(f_0) + \Delta \times \mathcal{G}_g(\cdot) & \cdots & R_{0M}\,\mathcal{J}_g(f_0, f_M) + \Delta \times \mathcal{G}_g(\cdot) & R_{0M}\,\mathcal{J}_g(f_0, f_M) + \Delta \times \mathcal{G}_g(\cdot) \\
R_{10}\,\mathcal{J}_g(f_0, f_1) + \Delta \times \mathcal{G}_g(\cdot) & R_{10}\,\mathcal{J}_g(f_0, f_1) + \Delta \times \mathcal{G}_g(\cdot) & \cdots & R_{1M}\,\mathcal{J}_g(f_1, f_M) + \Delta \times \mathcal{G}_g(\cdot) & R_{1M}\,\mathcal{J}_g(f_1, f_M) + \Delta \times \mathcal{G}_g(\cdot) \\
R_{10}\,\mathcal{J}_g(f_0, f_1) + \Delta \times \mathcal{G}_g(\cdot) & R_{10}\,\mathcal{J}_g(f_0, f_1) + \Delta \times \mathcal{G}_g(\cdot) & \cdots & R_{1M}\,\mathcal{J}_g(f_1, f_M) + \Delta \times \mathcal{G}_g(\cdot) & R_{1M}\,\mathcal{J}_g(f_1, f_M) + \Delta \times \mathcal{G}_g(\cdot) \\
\vdots & \vdots & \ddots & \vdots & \vdots \\
R_{M0}\,\mathcal{J}_g(f_0, f_M) + \Delta \times \mathcal{G}_g(\cdot) & R_{M0}\,\mathcal{J}_g(f_0, f_M) + \Delta \times \mathcal{G}_g(\cdot) & \cdots & R_{MM}\,\mathcal{J}_g(f_M) + \Delta \times \mathcal{G}_g(\cdot) & R_{MM}\,\mathcal{J}_g(f_M) + \Delta \times \mathcal{G}_g(\cdot) \\
R_{M0}\,\mathcal{J}_g(f_0, f_M) + \Delta \times \mathcal{G}_g(\cdot) & R_{M0}\,\mathcal{J}_g(f_0, f_M) + \Delta \times \mathcal{G}_g(\cdot) & \cdots & R_{MM}\,\mathcal{J}_g(f_M) + \Delta \times \mathcal{G}_g(\cdot) & R_{MM}\,\mathcal{J}_g(f_M) + \Delta \times \mathcal{G}_g(\cdot)
\end{bmatrix}$$

In the above expression we use notation $\mathcal{J}_g(.)$ to show a general function of some parameters. So the first component of this matrix represents a product of R_{00} times some function of f_0. Likewise the bottom element in the first row shows R_{0M} times a function of f_0 and f_M. Notice that the notation above can be misleading. For instance, in the first row the two $\mathcal{J}_g(f_0)$'s in columns 1 and 2 are mathematically different. The reason we used this notation is that at the time being the nature of these functions does not make any difference and only their parameter dependencies are important. So to prove the statement of the lemma, we only need to prove that the above equation hold for $\mathbf{R}^g$. The proof is by induction:

Induction base: For $g = 1$ we have the matrix in (4.3) which is clearly in the desired form.

Induction step: Let's suppose that $\mathbf{R}^g$ is the form of (4.6), then $\mathbf{R}^{g+1} = \mathbf{R}^g\,\mathbf{R}$. Hence the $(2k+1, 2l+1)^{th}$ $(k, l = 0, \cdots, M)$ element of this matrix becomes:

$$
\begin{aligned}
&(2k+1, 2l+1)^{th} \text{ (element)} \\
&= \Big[R_{k0}\,\mathcal{J}_g(f_0, f_k),\ R_{k0}\,\mathcal{J}_g(f_0, f_k),\ R_{k1}\,\mathcal{J}_g(f_1, f_k),\ R_{k1}\,\mathcal{J}_g(f_1, f_k),\ \cdots,\ R_{kM}\,\mathcal{J}_g(f_k, f_M),\ R_{kM}\,\mathcal{J}_g(f_k, f_M)\Big]
\begin{bmatrix} R_{0l}(1-f_l) \\ R_{0l}\theta(1-f_l) \\ \vdots \\ R_{Ml}(1-f_l) \\ R_{Ml}\theta(1-f_l) \end{bmatrix} \\
&\quad + \Big[R_{k0}\,\Delta\times\mathcal{G}_g(\cdot),\ R_{k0}\,\Delta\times\mathcal{G}_g(\cdot),\ R_{k1}\,\Delta\times\mathcal{G}_g(\cdot),\ R_{k1}\,\Delta\times\mathcal{G}_g(\cdot),\ \cdots, R_{kM}\,\Delta\times\mathcal{G}_g(\cdot),\ R_{kM}\,\Delta\times\mathcal{G}_g(\cdot)\Big]
\begin{bmatrix} R_{0l}(1-f_l) \\ R_{0l}\theta(1-f_l) \\ \vdots \\ R_{Ml}(1-f_l) \\ R_{Ml}\theta(1-f_l) \end{bmatrix} \\
&= \sum_{j=0}^{M}\Big[R_{kj}\,\mathcal{J}_g(f_j, f_k)R_{jl}(1-f_l) + R_{kj}\,\mathcal{J}_g(f_j, f_k)R_{jl}\theta(1-f_l)\Big] + \Delta\sum_{j=0}^{M}\Big[R_{kj}\,\mathcal{G}_g(\cdot)\,R_{jl}(1-f_l) + R_{kj}\,\mathcal{G}_g(\cdot)\,R_{jl}\theta(1-f_l)\Big] \\
&= [R_{kk}\,\mathcal{J}_g(f_k)R_{kl}(1-f_l) + R_{kk}\,\mathcal{J}_g(f_k)R_{kl}\theta(1-f_l) + R_{kl}\,\mathcal{J}_g(f_l, f_k)R_{ll}(1-f_l) + R_{kl}\,\mathcal{J}_g(f_l, f_k)R_{ll}\theta(1-f_l)] \qquad (4.7) \\
&\quad + \sum_{j\neq k,l} R_{kj}R_{jl}\Big[\mathcal{J}_g(f_j, f_k)(1-f_l) + \mathcal{J}_g(f_j, f_k)\theta(1-f_l) + \Delta\mathcal{G}_g(\cdot)\,(1-f_l) + \Delta\mathcal{G}_g(\cdot)\,\theta(1-f_l)\Big] \qquad (4.8) \\
&\quad + \Delta(1-f_l)\Big[R_{kk}\mathcal{G}_g(\cdot)R_{kl} + \theta R_{kk}\mathcal{G}_g(\cdot)R_{kl} + R_{kl}\mathcal{G}_g(\cdot)R_{ll} + \theta R_{kl}\mathcal{G}_g(\cdot)R_{ll}\Big] \qquad (4.9) \\
&= R_{kl}\,[R_{kk}\,\mathcal{J}_g(f_k)(1-f_l) + R_{kk}\,\mathcal{J}_g(f_k)\theta(1-f_l) + \mathcal{J}_g(f_l, f_k)R_{ll}(1-f_l) + \mathcal{J}_g(f_l, f_k)R_{ll}\theta(1-f_l)] + \Delta\times\mathcal{G}_{g+1}(\cdot) \\
&= R_{kl}\,\mathcal{J}_{g+1}(f_k, f_l) + \Delta\mathcal{G}_{g+1}(\cdot)
\end{aligned}
$$

Likewise the $(2k+1, 2l+2)^{th}$ $(k, l = 0, \cdots, M)$ element of matrix R^{g+1} becomes:

$$
\begin{aligned}
&(2k+1, 2l+1)^{th} \text{ (element)} \\
&= \Big[R_{k0}\,\mathcal{J}_g(f_0, f_k),\ R_{k0}\,\mathcal{J}_g(f_0, f_k),\ R_{k1}\,\mathcal{J}_g(f_1, f_k),\ R_{k1}\,\mathcal{J}_g(f_1, f_k),\ \cdots,\ R_{kM}\,\mathcal{J}_g(f_k, f_M),\ R_{kM}\,\mathcal{J}_g(f_k, f_M)\Big]
\begin{bmatrix} R_{0l}\phi f_l \\ R_{0l}\theta\phi f_l \\ \vdots \\ R_{Ml}\phi f_l \\ R_{Ml}\theta\phi f_l \end{bmatrix}
\end{aligned}
$$

$$+\left[R_{k0}\,\Delta\times\mathcal{G}_g(\cdot),\ R_{k0}\,\Delta\times\mathcal{G}_g(\cdot),\ R_{k1}\,\Delta\times\mathcal{G}_g(\cdot),\ R_{k1}\,\Delta\times\mathcal{G}_g(\cdot),\ \cdots,R_{kM}\,\Delta\times\mathcal{G}_g(\cdot),\ R_{kM}\,\Delta\times\mathcal{G}_g(\cdot)\right]\begin{bmatrix}R_{0l}\phi f_l\\ R_{0l}\theta\phi f_l\\ \vdots\\ R_{Ml}\phi f_l\\ R_{Ml}\theta\phi f_l\end{bmatrix}$$

$$=\sum_{j=0}^{M}\left[R_{kj}\,\mathcal{J}_g(f_j,f_k)R_{jl}\phi f_l+R_{kj}\,\mathcal{J}_g(f_j,f_k)R_{jl}\theta\phi f_l\right]+\Delta\sum_{j=0}^{M}\left[R_{kj}\,\mathcal{G}_g(\cdot)\,R_{jl}\phi f_l+R_{kj}\,\mathcal{G}_g(\cdot)\,R_{jl}\theta\phi f_l\right]$$

$$=\left[R_{kk}\,\mathcal{J}_g(f_k)R_{kl}\phi f_l+R_{kk}\,\mathcal{J}_g(f_k)R_{kl}\theta\phi f_l+R_{kl}\,\mathcal{J}_g(f_l,f_k)R_{ll}\phi f_l+R_{kl}\,\mathcal{J}_g(f_l,f_k)R_{ll}\theta\phi f_l\right] \tag{4.10}$$

$$+\sum_{j\neq k,l}R_{kj}R_{jl}\left[\mathcal{J}_g(f_j,f_k)\phi f_l+\mathcal{J}_g(f_j,f_k)\theta\phi f_l+\Delta\mathcal{G}_g(\cdot)\,\phi f_l+\Delta\mathcal{G}_g(\cdot)\,\theta\phi f_l\right] \tag{4.11}$$

$$+\Delta\phi f_l\left[R_{kk}\mathcal{G}_g(\cdot)R_{kl}+\theta R_{kk}\mathcal{G}_g(\cdot)R_{kl}+R_{kl}\mathcal{G}_g(\cdot)R_{ll}+\theta R_{kl}\mathcal{G}_g(\cdot)R_{ll}\right] \tag{4.12}$$

$$=R_{kl}\left[R_{kk}\,\mathcal{J}_g(f_k)\phi f_l+R_{kk}\,\mathcal{J}_g(f_k)\theta\phi f_l+\mathcal{J}_g(f_l,f_k)R_{ll}\phi f_l+\mathcal{J}_g(f_l,f_k)R_{ll}\theta\phi f_l\right]+\Delta\times\mathcal{G}_{g+1}(\cdot)$$

$$=R_{kl}\,\mathcal{J}_{g+1}(f_k,f_l)+\Delta\mathcal{G}_{g+1}(\cdot)$$

Similarly we can show that similar relations hold for the $(2k+2,2l+1)^{th}$ element and $(2k+2,2l+2)^{th}$ element as desired. Using Assumption 7, $\mathbf{y}_{2i+1}(g)+\mathbf{y}_{2i+2}(g)=\mathbf{R}^g_{2i+1,1}+\mathbf{R}^g_{2i+2,1}$, so the first part of the lemma is proven. By bounding $\mathcal{G}_g(\cdot)$ terms, we use induction to show the second statement of this lemma for the $(2k+1,2l+1)^{th}$ component of matrix $\mathbf{R}^{g+1}$. Replacing $R_{kj}R_{jl}$ by Δ within (4.8), equations (4.7)-(4.9) lead to,

$$\begin{aligned}\mathcal{G}_{g+1}(\cdot)\leq\sum_{j\neq k,l}\Big[&\mathcal{J}_g(f_j,f_k)(1-f_l)+\mathcal{J}_g(f_j,f_k)\theta(1-f_l)\\&+\Delta\mathcal{G}_g(\cdot)\,(1-f_l)+\Delta\mathcal{G}_g(\cdot)\,\theta(1-f_l)\Big]\\&+(1-f_l)\Big[R_{kk}\mathcal{G}_g(\cdot)R_{kl}+\theta R_{kk}\mathcal{G}_g(\cdot)R_{kl}+R_{kl}\mathcal{G}_g(\cdot)R_{ll}+\theta R_{kl}\mathcal{G}_g(\cdot)R_{ll}\Big]\\<\sum_{j\neq k,l}\Big[&\pi^g_j(1-f_l)+\pi^g_j\theta(1-f_l)+\Delta\mathcal{G}_g(\cdot)\,(1-f_l)+\Delta\mathcal{G}_g(\cdot)\,\theta(1-f_l)\Big]\\&+(1-f_l)\Big[R_{kk}\mathcal{G}_g(\cdot)R_{kl}+\theta R_{kk}\mathcal{G}_g(\cdot)R_{kl}+R_{kl}\mathcal{G}_g(\cdot)R_{ll}+\theta R_{kl}\mathcal{G}_g(\cdot)R_{ll}\Big]\end{aligned}$$

$$\Longrightarrow$$

$$\begin{aligned}\lim_{\Delta\to0}\mathcal{G}_{g+1}(\cdot)<\sum_{j\neq k,l}&\Big[\pi^g_j(1-f_l)+\pi^g_j\theta(1-f_l)\Big]\\&+(1-f_l)R_{kl}\lim_{\Delta\to0}\Big[R_{kk}\mathcal{G}_g(\cdot)+\theta R_{kk}\mathcal{G}_g(\cdot)+\mathcal{G}_g(\cdot)R_{ll}+\theta\mathcal{G}_g(\cdot)R_{ll}\Big]\end{aligned}$$

in which the second inequality is obtained based on the fact that for any generation g, the attack rate in each population is maximum when no vaccine is administered. Likewise by

replacing $R_{kj}R_{jl}$ with Δ in (4.11) and using (4.10)-(4.12) we get

$$\lim_{\Delta\to 0}\mathcal{G}_{g+1}(\cdot) < \sum_{j\neq k,l}\Big[\pi_j^g\phi f_l + \pi_j^g\theta\phi f_l\Big] + \phi f_l R_{kl}\lim_{\Delta\to 0}\Big[R_{kk}\mathcal{G}_g(\cdot) + \theta R_{kk}\mathcal{G}_g(\cdot) + \mathcal{G}_g(\cdot)R_{ll} + \theta\mathcal{G}_g(\cdot)R_{ll}\Big].$$

In order to find the Δ coefficient in $\mathbf{y}_{2i+1}(g)+\mathbf{y}_{2i+2}(g)$, we just need to add these two terms when $k=i$ and $l=0$. Using inequalities $\theta,\ \phi\leq 1$ we get

$$\lim_{\Delta\to 0}\mathcal{G}_{g+1}(\cdot) < 2\Big(\sum_{j\neq 0,i}\pi_j^g\Big) + 2R_{i0}\lim_{\Delta\to 0}\Big[R_{ii}\mathcal{G}_g(\cdot) + \mathcal{G}_g(\cdot)R_{00}\Big].$$

As a result if $\mathcal{G}_g(\cdot) < 2\Big(\sum_j \pi_j^g\Big)\dfrac{1-\big(2R_{0i}(R_{ii}+R_{00})\big)^g}{1-2R_{0i}(R_{ii}+R_{00})}$, for the induction step, then clearly $\mathcal{G}_{g+1}(\cdot) < 2\Big(\sum_j \pi_j^{g+1}\Big)\dfrac{1-\big(2R_{0i}(R_{ii}+R_{00})\big)^{g+1}}{1-2R_{0i}(R_{ii}+R_{00})}$ which finishes the proof. □

Now notice that based on (4.5), the coefficient of Δ in (4.4) is a constant number when $\Delta\to 0$. Hence using (4.4) and Assumption 8, this lemma states that for each country $i=1,\cdots,M$, the expected infected population at country i would be a function of its own vaccination level and the vaccination level in the index country. Moreover the expected infected population at the index country is a function of its own vaccination level only. The following lemma illustrate some properties of this function.

Lemma 5 *Given assumption 7, for any generation g and population i, the function $\mathcal{J}_g(f_i,f_0)$ of Lemma 4, is a convex and decreasing function with respect to f_i, f_0.*

Proof: We can no longer work with the previous general forms for functions $\mathcal{J}(.)$ in 4.6. The only important elements in the matrix $\mathbf{R}^g$ are the first column elements. So:

$$\mathbf{R}^g = \begin{bmatrix}
R_{00}\,\mathcal{J}_{00}^g(f_0) & R_{00}\,\mathcal{J}(f_0) & R_{01}\,\mathcal{J}(f_0,f_1) & R_{01}\,\mathcal{J}(f_0,f_1) & \cdots & R_{0M}\,\mathcal{J}(f_0,f_M) & R_{0M}\,\mathcal{J}(f_0,f_M)\\
R_{00}\,\mathcal{J}_{10}^g(f_0) & R_{00}\,\mathcal{J}(f_0) & R_{01}\,\mathcal{J}(f_0,f_1) & R_{01}\,\mathcal{J}(f_0,f_1) & \cdots & R_{0M}\,\mathcal{J}(f_0,f_M) & R_{0M}\,\mathcal{J}(f_0,f_M)\\
R_{10}\,\mathcal{J}_{20}^g(f_0,f_1) & R_{10}\,\mathcal{J}(f_0,f_1) & R_{11}\,\mathcal{J}(f_1) & R_{11}\,\mathcal{J}(f_1) & \cdots & R_{1M}\,\mathcal{J}(f_1,f_M) & R_{1M}\,\mathcal{J}(f_1,f_M)\\
R_{10}\,\mathcal{J}_{30}^g(f_0,f_1) & R_{10}\,\mathcal{J}(f_0,f_1) & R_{11}\,\mathcal{J}(f_1) & R_{11}\,\mathcal{J}(f_1) & \cdots & R_{1M}\,\mathcal{J}(f_1,f_M) & R_{1M}\,\mathcal{J}(f_1,f_M)\\
\vdots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots\\
R_{M0}\,\mathcal{J}_{2M,0}^g(f_0,f_M) & R_{M0}\,\mathcal{J}(f_0,f_M) & R_{M1}\,\mathcal{J}(f_1,f_M) & R_{M1}\,\mathcal{J}(f_1,f_M) & \cdots & R_{MM}\,\mathcal{J}(f_M) & R_{MM}\,\mathcal{J}(f_M)\\
R_{M0}\,\mathcal{J}_{2M+1,0}^g(f_0,f_M) & R_{M0}\,\mathcal{J}(f_0,f_M) & R_{M1}\,\mathcal{J}(f_1,f_M) & R_{M1}\,\mathcal{J}(f_1,f_M) & \cdots & R_{MM}\,\mathcal{J}(f_M) & R_{MM}\,\mathcal{J}(f_M)
\end{bmatrix}$$

Here subscripts show the elements for which the function belongs and superscript g is used to show the generation number. Notice that functions in other columns are left in their general form since they will not be used in the analysis. This matrix can be further simplified in the following manner. A second look at matrix in (4.3) reveals that all the even rows are θ times their preceding row. Thus the g-generation matrix can be written as follows.

$$\mathbf{R}^g = \begin{bmatrix}
R_{00}\,\mathcal{J}^g_{00}(f_0) & R_{00}\,\mathcal{J}(f_0) & R_{01}\,\mathcal{J}(f_0,f_1) & R_{01}\,\mathcal{J}(f_0,f_1) & \cdots & R_{0M}\,\mathcal{J}(f_0,f_M) & R_{0M}\,\mathcal{J}(f_0,f_M) \\
R_{00}\theta\,\mathcal{J}^g_{00}(f_0) & R_{00}\,\mathcal{J}(f_0) & R_{01}\,\mathcal{J}(f_0,f_1) & R_{01}\,\mathcal{J}(f_0,f_1) & \cdots & R_{0M}\,\mathcal{J}(f_0,f_M) & R_{0M}\,\mathcal{J}(f_0,f_M) \\
R_{10}\,\mathcal{J}^g_{10}(f_0,f_1) & R_{10}\,\mathcal{J}(f_0,f_1) & R_{11}\,\mathcal{J}(f_1) & R_{11}\,\mathcal{J}(f_1) & \cdots & R_{1M}\,\mathcal{J}(f_1,f_M) & R_{1M}\,\mathcal{J}(f_1,f_M) \\
R_{10}\theta\,\mathcal{J}^g_{10}(f_0,f_1) & R_{10}\,\mathcal{J}(f_0,f_1) & R_{11}\,\mathcal{J}(f_1) & R_{11}\,\mathcal{J}(f_1) & \cdots & R_{1M}\,\mathcal{J}(f_1,f_M) & R_{1M}\,\mathcal{J}(f_1,f_M) \\
\vdots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\
R_{M0}\,\mathcal{J}^g_{M,0}(f_0,f_M) & R_{M0}\,\mathcal{J}(f_0,f_M) & R_{M1}\,\mathcal{J}(f_1,f_M) & R_{M1}\,\mathcal{J}(f_1,f_M) & \cdots & R_{MM}\,\mathcal{J}(f_M) & R_{MM}\,\mathcal{J}(f_M) \\
R_{M0}\theta\,\mathcal{J}^g_{M,0}(f_0,f_M) & R_{M0}\,\mathcal{J}(f_0,f_M) & R_{M1}\,\mathcal{J}(f_1,f_M) & R_{M1}\,\mathcal{J}(f_1,f_M) & \cdots & R_{MM}\,\mathcal{J}(f_M) & R_{MM}\,\mathcal{J}(f_M)
\end{bmatrix}$$

We know that $\mathbf{R}^{g+1} = \mathbf{R}\,\mathbf{R}^g$, hence similar to the previous section we can obtain the elements of the first column of $\mathbf{R}^{g+1}$ as follows. Like equation 4.7 we can obtain the $(2k+1,0)^{th}$ element of $\mathbf{R}^{g+1}$ to be

$$\begin{aligned}
\mathcal{J}^{g+1}_{0,0}(f_0) &= R_{00}\,\mathcal{J}^g_{00}(f_0)(1-f_0) + R_{00}f_0\theta\phi\,\mathcal{J}^g_{00}(f_0) \\
\mathcal{J}^{g+1}_{k,0}(f_0,f_k) &= R_{00}\,\mathcal{J}^g_{00}(f_0)(1-f_0) + R_{00}f_0\theta\phi\,\mathcal{J}^g_{00}(f_0) \\
&\qquad + R_{kk}(1-f_k)\,\mathcal{J}^g_{k0}(f_0,f_k) + R_{kk}\theta\phi f_k\,\mathcal{J}^g_{k0}(f_0,f_k)
\end{aligned}$$

Here we prove the claim by induction for country 0. Other cases can be shown with similar arguments. To show the decreasing property of $\mathcal{J}^{g+1}_{00}(f_0)$, we take the derivative of this function with respect f_0:

$$\frac{1}{R_{00}}\frac{\partial}{\partial f_0}\mathcal{J}^{g+1}_{00}(f_0) = [(-1+\theta\phi)\,\mathcal{J}^g_{00}(f_0)] + \left[(1-f_0+\theta\phi f_0)\,\frac{\partial}{\partial f_0}\mathcal{J}^g_{00}(f_0)\right]$$

The first term in the right hand side is negative due to the fact that $\theta\phi < 1$. The second term is also negative due based on the assumption that $\mathcal{J}^g_{00}(f_0)$ is decreasing. Thus $\mathcal{J}^{g+1}_{00}(f_0)$ is also decreasing. Now to show the convexity, the second derivative gives us:

$$\frac{1}{R_{00}}\frac{\partial^2}{\partial f_0^2}\mathcal{J}^{g+1}_{00}(f_0) = 2\left[(-1+\theta\phi)\,\frac{\partial}{\partial f_0}\mathcal{J}^g_{00}(f_0)\right] + \left[(1-f_0+\theta\phi f_0)\,\frac{\partial^2}{\partial f_0^2}\mathcal{J}^g_{00}(f_0)\right]$$

The first term is positive since $\theta\phi < 1$ and function $\mathcal{J}_{00}^{g}(f_0)$ is decreasing and second term is positive since $\mathcal{J}_{00}^{g}(f_0)$ is convex.

This completes the induction step for the proof and the induction base is clearly held true. □

Hence based on Lemmas 4 and 5 and Assumption 8, the expected number of infected population in each country i, $\mathbf{y}_{2i+1}(g) + \mathbf{y}_{2i+2}(g)$, is a decreasing convex function of each of its parameters.

The next generation matrix provides a good approximation to the total number of infected individuals only at the start of the epidemic. As a result the convexity properties in Lemma 5 are not valid for the overall number of infected individuals throughout the epidemic season. Notice that we use the total number of infected individuals obtained above (output of the first model presented in this section) as the initial infected population for the next section (input for the second model).

4.1.2 Epidemic Model - Middle of the Season

The previous section gives a suitable model of the infection dynamics at the start of the epidemic, however it might provide a rather poor approximation after the few initial steps of the disease transmission.

As a result, we formulate the rest of the epidemic by the same SIR model which used in Chapter 2, using the output of the previous model to model the initial infected population for each country. Such a model will allow us to look at independent countries, except for the way that the initial infected population in each country is influenced by the interaction between countries modeled in the first stage.

Like the homogenous model, we group the population in country i into three distinct subgroups at any given time t: the fraction of Susceptible, Infectious and Removed individuals ($S_i(t), I_i(t)$, and $R_i(t)$, respectively). These fractions in the population vary as a function of time t according to a deterministic differential equation. Like Chapter 2 we denote $\psi = 1 - \theta\phi$ to be the combined vaccine effect on susceptibility and infectiousness. We assume that a fraction f_i of population i is vaccinated so $R_i(t) = f_i\psi$ for $t \leq 0$. At

the start of the influenza season, at time $t = 0$, a fraction χ_i of the remaining susceptible population becomes infected due to exposure from exogenous sources, that is interacting with the index country and hence $\chi_i = \chi_i(f_0)$. As a result $S_i(0) = (1 - f_i\psi)(1 - \chi_i)$ and $I_i(0) = (1 - f_i\psi)\chi_i$. The total number that become infected during the influenza season is $T_i(f_i, f_0) = N_i\tilde{p}_i$, where the attack rate $\tilde{p}_i$ (Longini et al. 1978) satisfies

$$\tilde{p}_i = S_i(0)\big(1 + \frac{I_i(0)}{S_i(0)} - e^{-R_{ii}\tilde{p}_i}\big)$$

or alternatively

$$\tilde{p}_i = 1 - \psi f_i - (1 - \chi_i)(1 - \psi f_i)e^{-R_{ii}\tilde{p}_i}. \tag{4.13}$$

Notice that we use $\tilde{p}_i$ to distinguish the attack rate of this approximation from the true attack rate, from (4.1). Rather than deriving results via such an implicit solution from the epidemic model, we derive results for a nonincreasing $T_i(\cdot) \geq 0$ with specific general characteristics. This removes the details of an implicit solution for an epidemic model from the supply chain analysis.

We showed in the previous section that for every i, $\chi_i = \chi_i(f_0)$ is a decreasing convex function of its parameter (Lemma 5). Similar to the homogeneous population, it can be shown that the critical vaccination fraction can be obtained as

$$f_i' = \frac{R_{ii} - 1}{R_{ii}\psi}$$

The following proposition is the main result of this section:

Proposition 9 *Let $\tilde{p}_i$ be the attack rate of country i that satisfies (4.13), then for $i = 0, 1, \cdots, M$*

1. *$\tilde{p}_i$ is decreasing in f_i*
2. *$\tilde{p}_i$ is decreasing in f_0*
3. *$\tilde{p}_i$ is a submodular function of (f_i, f_0) for $f_i \leq f_i'$, and a supermodular function for $f_i \geq f_i'$, where f_i' is the critical vaccination level for country i if country i is considered alone.*

4. $\tilde{p}_i$ is first concave then convex in f_i

Proof: For the first part, in equation 4.13 we take $\tilde{p}_i$ to the righthand side and take the derivative with respect to f_i. Using chain rule we have:

$$\begin{aligned} & -\frac{\partial \tilde{p}_i}{\partial f_i} + R_{ii}(1-\chi)(1-\psi f_i)e^{-R_{ii}\tilde{p}_i}\frac{\partial \tilde{p}_i}{\partial f_i} - \psi + (1-\chi)\psi e^{-R_{ii}\tilde{p}_i} = 0 \\ \Rightarrow \quad & \frac{\partial \tilde{p}_i}{\partial f_i} = -\frac{\psi - (1-\chi)\psi e^{-R_{ii}\tilde{p}_i}}{1 - R_{ii}(1-\chi)(1-\psi f_i)e^{-R_{ii}\tilde{p}_i}} \end{aligned} \tag{4.14}$$

The numerator is clearly positive since $(1-\chi)e^{-R_{ii}\tilde{p}_i} < 1$ for all $\tilde{p}_i \geq 0$ and $0 < \chi < 1$. So it is enough to show that the denominator is positive. To show this consider the term in the denominator and replace $1 - \psi f_i$ from equation 4.13:

$$\begin{aligned} 1 - R_{ii}(1-\chi)(1-\psi f_i)e^{-R_{ii}\tilde{p}_i} &= 1 - R_{ii}(1-\chi)\left(\frac{\tilde{p}_i}{1-(1-\chi)e^{-R_{ii}\tilde{p}_i}}\right)e^{-R_{ii}\tilde{p}_i} \\ &= \frac{1}{1-(1-\chi)e^{-R_{ii}\tilde{p}_i}}\left(1-(1-\chi)e^{-R_{ii}\tilde{p}_i} - R_{ii}\tilde{p}_i(1-\chi)e^{-R_{ii}\tilde{p}_i}\right) \\ &= \frac{1}{1-(1-\chi)e^{-R_{ii}\tilde{p}_i}}\left(1-(1-\chi)(1+R_{ii}\tilde{p}_i)e^{-R_{ii}\tilde{p}_i}\right) \\ &\geq 0 \end{aligned}$$

the reason for the last inequality is that the function $(1+x)e^x$ obtains its maximum value at zero. Hence this part is shown ✓.

To show the second part of the claim, we follow the same approach as above except that now we should take the derivative with respect to f_0:

$$\begin{aligned} & -\frac{\partial \tilde{p}_i}{\partial f_0} + R_{ii}(1-\chi)(1-\psi f_i)e^{-R_{ii}\tilde{p}_i}\frac{\partial \tilde{p}_i}{\partial f_0} + \frac{\partial \chi}{\partial f_0}(1-\psi f_i)e^{-R_{ii}\tilde{p}_i} = 0 \\ \Rightarrow \quad & \frac{\partial \tilde{p}_i}{\partial f_0} = \frac{\frac{\partial \chi}{\partial f_0}(1-\psi f_i)e^{-R_{ii}\tilde{p}_i}}{1 - R_{ii}(1-\chi)(1-\psi f_i)e^{-R_{ii}\tilde{p}_i}} \end{aligned}$$

We have shown before that the denominator is positive. On the other hand numerator is negative based on Lemma 5. It indicates that the initial number of infected population in country i is a decreasing function of f_0. Thus the second part of the claim is also shown ✓.

To show the third statement, we take the derivative of $\tilde{p}_i$ with respect to both variables which leads to the following expression.

$$-\frac{\partial^2\tilde{p}_i}{\partial f_0\partial f_i} - R_{ii}^2(1-\chi)(1-\psi f_i)e^{-R_{ii}\tilde{p}_i}\frac{\partial\tilde{p}_i}{\partial f_0}\frac{\partial\tilde{p}_i}{\partial f_i} + R_{ii}(1-\chi)(1-\psi f_i)e^{-R_{ii}\tilde{p}_i}\frac{\partial^2\tilde{p}_i}{\partial f_0\partial f_i}$$
$$- R_{ii}(1-\chi)\psi e^{-R_{ii}\tilde{p}_i}\frac{\partial\tilde{p}_i}{\partial f_0} - \frac{\partial\chi}{\partial f_0}\psi e^{-R_{ii}\tilde{p}_i} - R_{ii}\frac{\partial\chi}{\partial f_0}(1-\psi f_i)e^{-R_{ii}\tilde{p}_i}\frac{\partial\tilde{p}_i}{\partial f_i} = 0$$

By rearranging the terms and using the fact that $1 - R_{ii}(1-\chi)(1-\psi f_i)e^{-R_{ii}\tilde{p}_i} \geq 0$, it turns out that the sign of $\frac{\partial^2\tilde{p}_i}{\partial f_0\partial f_i}$ is the same as the sign of

$$-\Big[R_{ii}(1-\chi)\frac{\partial\tilde{p}_i}{\partial f_0} + \frac{\partial\chi}{\partial f_0}\Big]\Big[\psi + R_{ii}(1-\psi f_i)\frac{\partial\tilde{p}_i}{\partial f_i}\Big]$$

On the other hand, both $\frac{\partial\tilde{p}_i}{\partial f_i} \leq 0$ and $\frac{\partial\chi}{\partial f_0} \leq 0$. Thus the left terms is negative and

$$\text{SIGN}\Big[\frac{\partial^2\tilde{p}_i}{\partial f_0\partial f_i}\Big] = \text{SIGN}\Big[\psi + R_{ii}(1-\psi f_i)\frac{\partial\tilde{p}_i}{\partial f_i}\Big]$$

In order to find the sign of the right hand side, we use the expression from the first part to replace $\frac{\partial\tilde{p}_i}{\partial f_i}$.

$$\begin{aligned}\psi + R_{ii}(1-\psi f_i)\frac{\partial\tilde{p}_i}{\partial f_i} &= \psi - R_{ii}(1-\psi f_i)\frac{\psi - (1-\chi)\psi e^{-R_{ii}\tilde{p}_i}}{1 - R_{ii}(1-\chi)(1-\psi f_i)e^{-R_{ii}\tilde{p}_i}} \\ &= \underbrace{\frac{\psi}{1 - R_{ii}(1-\chi)(1-\psi f_i)e^{-R_{ii}\tilde{p}_i}}}_{\geq 0}\Big[1 - R_{ii}(1-\psi f_i)\Big]\end{aligned}$$

So for $1 - R_{ii}(1-\psi f_i) \geq 0$, the sign of the right hand side term, and hence the sign of $\frac{\partial^2\tilde{p}_i}{\partial f_0\partial f_i}$, is positive. This is equivalent to $f_i \geq \bar{f}_i$ where $\bar{f}_i$ is the critical vaccination fraction ✓.

To show the final part, we use a different approach in computing the second derivative.

In 4.13 rearrange the terms so that the f_i is a function of $\tilde{p}_i$. i.e.,

$$f_i = \frac{1}{\psi}\Big[1 - \frac{\tilde{p}_i}{1-(1-\chi)e^{-R_{ii}\tilde{p}_i}}\Big]$$

Since $\tilde{p}_i$ is a decreasing function of f_i, then $\frac{\partial^2 \tilde{p}_i}{\partial f_i^2}$ and $\frac{\partial^2 f_i}{\partial \tilde{p}_i^2}$ have the same signs. So from this point on, we investigate the sign of $\frac{\partial^2 f_i}{\partial \tilde{p}_i^2}$.

$$\frac{\partial^2 f_i}{\partial \tilde{p}_i^2} = -\frac{1}{\psi}\left[\frac{R_{ii}(1-\chi)e^{-R_{ii}\tilde{p}_i}\big[R_{ii}\tilde{p}_i - 2 + (R_{ii}\tilde{p}_i+2)(1-\chi)e^{-R_{ii}\tilde{p}_i}\big]}{\big[1-(1-\chi)e^{-R_{ii}\tilde{p}_i}\big]^3}\right]$$

The sign of the statement above is the same as the sign of the following term

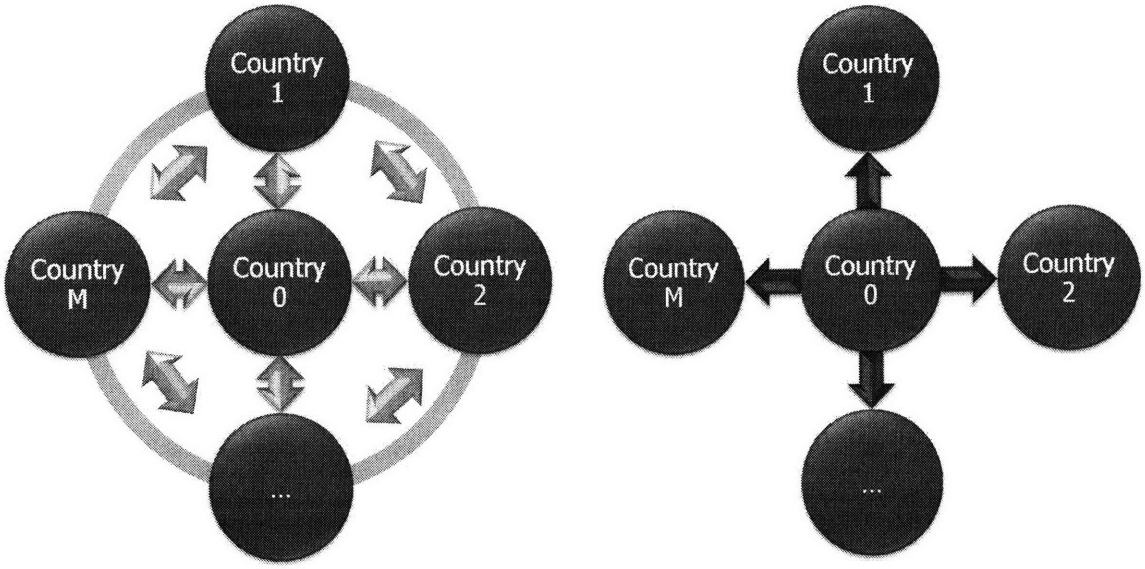
$$-R_{ii}\tilde{p}_i + 2 - (R_{ii}\tilde{p}_i + 2)(1-\chi)e^{-R_{ii}\tilde{p}_i} \tag{4.15}$$

We show that the typical sign of the above equation is first negative then positive which corresponds to first concave then convex function. To show this we simply show that the above term is an increasing function of f_i or equivalently a decreasing function of $\tilde{p}_i$, since $\tilde{p}_i$ and f_i have inverse relations (based on part 1). So by taking the derivative the above term with respect to $\tilde{p}_i$ we get

$$-R_{ii} + R_{ii}(1-\chi)(1+R_{ii}\tilde{p}_i)e^{-R_{ii}\tilde{p}_i} \leq 0$$

again the reason for this inequality is due to decreasing property of function $(1+x)e^{-x}$. So we have been able to show that (4.15) is increasing in f_i (decreasing in $\tilde{p}_i$). This means that the typical behavior is that it is negative then becomes positive, and thus attack rate is concave then convex. Notice that each of these sections can be empty, namely attack rate can be a concave or convex function for some parameters of the epidemic. For instance this function is always concave under the condition that $R_{ii}(1-\psi) > 2$, in other words the basic reproduction number is large and at the same time the vaccine is not potent enough. □

We will derive all of the results of the supply chain model based on these general characteristics of functions $\tilde{p}_i$. Next sections define the supply chain model with further detail.



(a) The general Network

(b) The network under Assumptions 7 and 8

Figure 4-2: Network of interaction between countries

4.1.3 The Game Problem

The epidemic and supply chain models above define a one-shot game between different governments. Each country i acts selfishly and selects a fraction f_i that indexes its demand, knowing that all other countries, in particular the index country, behave optimally. The cost function for each individual country consists of two major components: social costs of the disease, and vaccination program costs. As a result the cost function for each country i can be written as follows:

$$GF_0 = \mathrm{E}\big[b_0\, T_0(\alpha f_0) + v_0\, \alpha f_0 N_0 d\big]$$

$$GF_i = \mathrm{E}\big[b_i\, T_i(\alpha f_i, \alpha f_0) + v_i\, \alpha f_i N_i d\big] \quad ; \forall 1 \leq i \leq M$$

In this formulation, functions $T_i(\cdot)$ denote the total number of infected people in each population, i.e., $T_i(\cdot) = \tilde{p}_i N_i$ where $\tilde{p}_i$ is obtained from 4.13.

Such an $(M+1)-$player game has a Nash Equilibrium Nash (1951) which is the solution of the following system of equations:

$$\left\{ \begin{array}{l} \min\limits_{f_0 \geq 0} \left\{ \mathrm{E}\left[b_0\, T_0(\alpha f_0) + v_0\, \alpha f_0 N_0 d \right] \right\} \\ \\ \min\limits_{f_1 \geq 0 \,|\, f_0} \left\{ \mathrm{E}\left[b_1\, T_1(\alpha f_1, \alpha f_0) + v_1\, \alpha f_1 N_1 d \right] \right\} \\ \\ \vdots \\ \\ \min\limits_{f_M \geq 0 \,|\, f_0} \left\{ \mathrm{E}\left[b_M\, T_M(\alpha f_M, \alpha f_0) + v_M\, \alpha f_M N_M d \right] \right\} \end{array} \right\}$$

Our first task is in this section is to characterize the set of equilibria for this game. In order to proceed with the analysis of this section we need another assumption.

Assumption 9 *The expected health benefits of vaccination, exceeds the vaccination program costs for each country, i.e.*

$$b_i \psi - v_i d > 0; \qquad \forall i = 0, 1, \cdots, M$$

This is not a very limiting assumption based on the data in the epidemiology literature (CDC, 2005; Weycker et al., 2005; Chick et al., 2007).

Even though functions $T_i(\cdot)$ are not well-behaved, it turns out that the first order optimality conditions can characterize the equilibrium points of this game.

Lemma 6 *Given Assumption 9, the unique Nash Equilibrium $(f_0^G, f_1^G, \cdots, f_M^G)$ of the game resulting between countries is the solution of the following system of equations:*

$$\left\{ \begin{array}{l} b_0 \mathrm{E}\left[\dfrac{\partial}{\partial f_0} T_0(\alpha f_0)\Big|_{f_0^G} \right] + v_0 \mathrm{E}[\alpha] N_0 d = 0 \\ \\ b_i \mathrm{E}\left[\dfrac{\partial}{\partial f_i} T_i(\alpha f_i, \alpha f_0^G)\Big|_{f_i^G} \right] + v_i \mathrm{E}[\alpha] N_i d = 0 \qquad ; (\forall 1 \leq i \leq M) \end{array} \right. \tag{4.16}$$

Proof: We prove the result for government 0. The claim for other countries can be followed similarly. The derivative of the objective function for country 0 is $b_0 \mathrm{E}\left[\frac{\partial}{\partial f_0} T_0(\alpha f_0) \right] + v_0 \mathrm{E}[\alpha] N_0 d$. We will first show that the left side derivative is negative. For this purpose we

replace the derivative from (4.14)

$$
\begin{aligned}
b_0\mathrm{E}\Big[\frac{\partial}{\partial f_0}T_0(\alpha f_0)\Big|_{f_0=0}\Big] + v_0\mathrm{E}[\alpha]N_0 d &= b_0 N_0 \mathrm{E}\Big[\frac{\partial}{\partial f_i}\tilde{p}_0(\alpha f_0)\Big|_{f_0=0}\Big] + v_0\mathrm{E}[\alpha]N_0 d \\
&= N_0\mathrm{E}\Big[\alpha\Big(-b_0\psi\frac{1-(1-\chi)e^{-R_{ii}\tilde{p}_0}}{1-R_{ii}(1-\chi)e^{-R_{ii}\tilde{p}_0}} + v_0 d\Big)\Big] \\
&< N_0\mathrm{E}\Big[\alpha\big(-b_0\psi + v_0 d\big)\Big] \\
&< 0.
\end{aligned}
$$

The equality in the second line is just based on replacing the derivative of attach rate function from (4.14). The inequality in the third line is true since $R_{ii} > 1$. Finally the last inequality is based on Assumption 9. Hence while in the concave region, the sign of the derivative of GF_0 would be still negative. So the optimal vaccination fraction should lie in the convex region. The argument then follows since optimal f_0 lies in the convex region. □

Surprisingly, it turns out that there is a direct relationship between the Nash Equilibrium of the resulting game between countries which is obtained based on economic parameters in the model (e.g., vaccination costs and benefit), and the critical vaccination level which is obtained based on purely epidemic parameters (e.g., characteristics of strains, vaccine strength, etc.). The following lemma shows that under Assumption 9, governments always order quantities such that the disease is contained.

Lemma 7 *Let $(f_0^G, f_1^G, \cdots, f_M^G)$ be the solution of the game between countries. Moreover, let $(f_0', f_1', \cdots, f_M')$ be the critical vaccination levels. Then*

$$f_i^G \geq f_i' \qquad \textit{for all } i = 0, 1, \cdots, M$$

*Proof:*To prove the statement in this lemma we show that under Assumption 9, for any vaccination level $f_i < f_i'$, the terms on the left hand side of (4.16) are negative, implying that the solution of the equilibrium state has to be at least the critical vaccination level. For this purpose we fix i and replace the left hand side of (4.16) for this country with the

derivative from (4.14),

$$
\begin{aligned}
b_i \mathrm{E}\left[\frac{\partial}{\partial f_i} T_i(\alpha f_i, \alpha f_0^G)\right] + v_i \mathrm{E}[\alpha] N_i d &= b_i N_i \mathrm{E}\left[\frac{\partial}{\partial f_i} \tilde{p}_i(\alpha f_i, \alpha f_0^G)\right] + v_i \mathrm{E}[\alpha] N_i d \\
&= N_i \mathrm{E}\left[\alpha\Big(- b_i \psi \frac{1-(1-\chi)e^{-R_{ii}\tilde{p}_i}}{1-R_{ii}(1-\chi)(1-\psi f_i)e^{-R_{ii}\tilde{p}_i}} + v_i d\Big)\right] \\
&< N_i \mathrm{E}\Big[\alpha\big(- b_i \psi + v_i d\big)\Big] \\
&< 0
\end{aligned}
$$

The equality in the second line is just based on replacing the derivative of attach rate function from (4.14). The inequality in the third line is based on our assumption that $f_i < f_i'$ which is equivalent to $R_0(1-\psi f_i) > 1$, hence we get a larger term by replacing the term $R_0(1-\psi f_i)$ with 1 in the denominator. Finally the last inequality is based on Assumption 9. □

4.1.4 The System Problem

The System Problem, alternatively, assesses whether all governments can reduce their overall cost (financial and health-related costs) of the system as a whole by perfect coordination between them. In this case the cost incurred by the system is simply the sum over all government costs. i.e.,

$$
SF = \mathrm{E}\Big[b_0 T_0(\alpha f_0) + v_0 \alpha f_0 N_0 d + \sum_{i=1}^{M} \big(b_i T_i(\alpha f_i, \alpha f_0) + v_i \alpha f_i N_i d\big)\Big]
$$

As a result, the system optimum is the solution for the following system of equations.

Lemma 8 *Given Assumption 9, the global optimum* $(f_0^S, f_1^S, \cdots, f_M^S)$ *should satisfy*

$$
\begin{cases}
b_0 \mathrm{E}\left[\dfrac{\partial}{\partial f_0} T_0(\alpha f_0)\Big|_{f_0^S}\right] + \displaystyle\sum_{i=1}^{M} b_i \mathrm{E}\left[\frac{\partial}{\partial f_0} T_i(\alpha f_i^S, \alpha f_0)\Big|_{f_0^S}\right] + v_0 \mathrm{E}[\alpha] N_0 d = 0 \\
b_i \mathrm{E}\left[\dfrac{\partial}{\partial f_i} T_i(\alpha f_i, \alpha f_0^S)\Big|_{f_i^S}\right] + v_i \mathrm{E}[\alpha] N_i d = 0 \qquad \textit{for all } 1 \le i \le M
\end{cases}
\tag{4.17}
$$

Proof: The proof is simple by just writing the KKT conditions for the System Problem below:

$$\begin{aligned} \min SF \quad &= \mathrm{E}\left[b_0 T_0(\alpha f_0) + v_0 \alpha f_0 N_0 d + \sum_{i=1}^{M} (b_i T_i(\alpha f_i, \alpha f_0) + v_i \alpha f_i N_i d)\right] \\ \text{s.t.} \quad & f_i \geq 0; \quad \forall i = 0, 1, \cdots, M \end{aligned}$$

The KKT conditions give rise to

$$\begin{aligned} & b_0 \mathrm{E}\left[\frac{\partial}{\partial f_0} T_0(\alpha f_0)\right] + \sum_{i=1}^{M} b_i \mathrm{E}\left[\frac{\partial}{\partial f_0} T_i(\alpha f_i, \alpha f_0)\right] + v_0 \mathrm{E}[\alpha] N_0 d - \mathrm{E}[\alpha]\gamma_0 = 0 \\ & b_i \mathrm{E}\left[\frac{\partial}{\partial f_i} T_i(\alpha f_i, \alpha f_0)\right] + v_i \mathrm{E}[\alpha] N_i d - \mathrm{E}[\alpha]\gamma_i = 0 \qquad ; \forall 1 \leq i \leq M \end{aligned}$$

where γ_i's are the KKT multipliers for the conditions $f_i \geq 0$. Then using Assumption 9, and similar argument to in the proof of Lemma 6, i.e., negativity of the left hand sides for $f_i = 0$, we can prove the statement of this lemma. □

4.2 Results

In this section using the characterization of the Nash equilibrium of the game between governments and global system optimum and their relationship with epidemic parameters, Lemma 7, we show the suboptimality of the Game Problem. In other words, misaligned incentives of different governments lead to the diversion of vaccine stockpiles from the regions where they are needed the most (index countries), to countries where they are not as needed (all other countries in our model). The following proposition formalizes this argument.

Theorem 5 *Let* $(f_0^G, f_1^G, \cdots, f_M^G)$ *to be the solution of the Game Problem obtained in (4.16) and let* $(f_0^S, f_1^S, \cdots, f_M^S)$ *be the solution of the System Problem obtained in (4.17). Then*

1. $f_0^G \leq f_0^S$
2. $f_i^G \geq f_i^S, \quad$ *for* $i = 1, \cdots, M$.

Proof: We prove this theorem using Lemma 9. Since the set $\mathcal{L}$ (see Lemma 9) is empty, the statement of this theorem is clear based on the following lemma. □

Lemma 9 *Let* $(f_0^G, f_1^G, \cdots, f_M^G)$ *be the solution of the Game Problem obtained in (4.16) and* $(f_0^S, f_1^S, \cdots, f_M^S)$ *be the solution of the System Problem obtained in (4.17). Moreover let* $\mathcal{L} \subset \{1, \cdots, M\}$ *be the set of countries such that their optimal order quantity under the Game Problem is below their critical vaccination level, i.e.* $f_i^G < f_i'$ *for all* $i \in \mathcal{L}$. *Likewise let* $\mathcal{U} \subset \{1, \cdots, M\}$ *be the set of countries such that their optimal order quantity under the Game Problem is greater than their critical vaccination level, i.e.* $f_i^G \geq f_i'$ *for all* $i \in \mathcal{U}$. *Then we have:*

1. $f_0^G \leq f_0^S$
2. $f_i^G \leq f_i^S, \quad \forall i \in \mathcal{L}$
3. $f_i^G \geq f_i^S, \quad \forall i \in \mathcal{U}$

Proof: We show each part separately,

1. Notice that for all $i = 1, \cdots, M$ we have $\frac{\partial}{\partial f_0} T_i(\alpha f_i, \alpha f_0) \leq 0$ by the properties of the attack rate functions (Proposition 9, part 2). Thus by comparing f_0^S, f_0^G from Lemma 6 and Lemma 8 we can observe that:

$$\mathrm{E}\left[\frac{\partial}{\partial f_0} T_0(\alpha f_0)\Big|_{f_0^S}\right] \geq \mathrm{E}\left[\frac{\partial}{\partial f_0} T_0(\alpha f_0)\Big|_{f_0^G}\right] \Longrightarrow f_0^S \geq f_0^G \tag{4.18}$$

   Notice that the above inequality is correct since both f_0^S and f_0^g are in the convex region of $T_0(\cdot)$.

2. Since $i \in \mathcal{L}$, we know that $f_i^G < f_i'$. If $f_i^S \geq f_i'$, the the statement is clearly correct, so we need to consider the case where $f_i^S < f_i'$. Now since both order quantities are below the critical vaccination level (hence the attack rate function in this region is submodular based on Proposition 9, part 3) and using $f_0^S > f_0^G$ we have,

$$\frac{\partial T_i(\alpha f_i, \alpha f_0^S)}{\partial f_i} < \frac{\partial T_i(\alpha f_i, \alpha f_0^G)}{\partial f_i}$$

We prove the statement by contradiction. Suppose, on the contrary, that $f_i^S < f_i^G$ then from the above equation we have

$$\frac{\partial T_i(\alpha f_i, \alpha f_0^S)}{\partial f_i}\Big|_{f_i^S} < \frac{\partial T_i(\alpha f_i, \alpha f_0^G)}{\partial f_i}\Big|_{f_i^S} \tag{4.19}$$

$$< \frac{\partial T_i(\alpha f_i, \alpha f_0^G)}{\partial f_i}\Big|_{f_i^G} \tag{4.20}$$

where the second inequality is obtained based on the convexity of function $T_i(\cdot)$ at the region, and our assumption of $f_i^S < f_i^G$. Now notice that, according to (4.16) and (4.17), the left term in (4.19) and the last term in (4.20) are both equal to $-v_i \mathrm{E}[\alpha] N_i d$ which is a contradiction hence $f_i^S > f_i^G$.

3. The proof of this part is very similar to the proof in the previous section. Recall that $i \in \mathcal{U}$ indicates that $f_i^G \geq f_i'$. If $f_i^S < f_i'$, the statement is clear, otherwise both ordering quantities lie in the supermodular section of the attack rate function (based on Proposition 9). Since $f_0^S > f_0^G$, we have

$$\frac{\partial T_i(\alpha f_i, \alpha f_0^S)}{\partial f_i} > \frac{\partial T_i(\alpha f_i, \alpha f_0^G)}{\partial f_i}.$$

If, on the contrary, we have $f_i^S > f_i^G$ then from this last equation we have

$$\frac{\partial T_i(\alpha f_i, \alpha f_0^S)}{\partial f_i}\Big|_{f_i^S} > \frac{\partial T_i(\alpha f_i, \alpha f_0^G)}{\partial f_i}\Big|_{f_i^S} \tag{4.21}$$

$$> \frac{\partial T_i(\alpha f_i, \alpha f_0^G)}{\partial f_i}\Big|_{f_i^G} \tag{4.22}$$

The second inequality is obtained based on the convexity of function $T_i(\cdot)$ at the region. Now notice that, according to (4.16) and (4.17), the left term in (4.21) and the last term in (4.22) are both equal to $-v_i \mathrm{E}[\alpha] N_i d$ which is a contradiction hence $f_i^S < f_i^G$.

□

This result suggests that the system wants more vaccine stockpiles for the index country. This is fairly intuitive; since when acting selfishly, the index country does not take into account its system-wide effect on the spread of the disease which was the result of the analysis in section 4.1.1, and therefore orders less than the socially optimum level. On the

other hand the System Problem requires less vaccine stockpile for all other countries. The intuition behind this result is that enough vaccine is allocated to the origin so other countries would not need as much as their game setting level. In other words the System Problem's optimal solution leans toward a strategy that contains the epidemic at its source.

Now that there is such a suboptimal vaccine allocation under the Game Problem, the next question would be how to design mechanisms that can align governments' incentives and push their order quantities to system optimum level. We achieve this goal by providing financial incentives for the index country to order more vaccines. In particular, the index country gets partly reimbursed for each dose of vaccine it administers because the other countries share the vaccination program costs of the index country. The following cost sharing contract achieves this goal.

Theorem 6 *Suppose that for every vaccine dose that country 0 receives, each government i ($i = 1, \cdots, M$) pays:*

$$-\eta_i \sum_{j=1}^{M} \frac{1}{N_0} b_j N_j \mathrm{E}\left[\frac{\partial}{\partial f_0} T_j(\alpha f_j^S, f_0)\Big|_{\alpha f_0^S}\right]$$

where $\eta_i \geq 0$ and $\sum_i \eta_i = 1$, then the resulting contract is coordinating. i.e.,

- *It pushes all governments to purchase what is optimum for the system*
- *It is flexible. By changing η_i's, governments can allocate the system cost reduction in any possible way between themselves.*

Proof: Notice that under the contract, the new objective functions for each government would be:

$$\begin{aligned}
GF_0 =& \mathrm{E}\left[b_0 T_0(\alpha f_0) + \sum_{i=1}^{M} \eta_i \sum_{j=1}^{M} b_j N_j d\, \mathrm{E}\left[\frac{\partial}{\partial f_0} T_j(\alpha f_j^S, f_0)\Big|_{\alpha f_0^S}\right] \alpha f_0 + v_0 \alpha f_0 N_0 d\right] \\
=& \mathrm{E}\left[b_0 T_0(\alpha f_0) + \sum_{j=1}^{M} b_j N_j d\, \mathrm{E}\left[\frac{\partial}{\partial f_0} T_j(\alpha f_j^S, f_0)\Big|_{\alpha f_0^S}\right] \alpha f_0 \underbrace{\sum_{i=1}^{M} \eta_i}_{=1} + v_0 \alpha f_0 N_0 d\right] \\
=& \mathrm{E}\left[b_0 T_0(\alpha f_0) + \sum_{j=1}^{M} b_j N_j d\, \mathrm{E}\left[\frac{\partial}{\partial f_0} T_j(\alpha f_j^S, f_0)\Big|_{\alpha f_0^S}\right] \alpha f_0 + v_0 \alpha f_0 N_0 d\right]
\end{aligned}$$

$$GF_i = \mathrm{E}\left[b_i T_i(\alpha f_i, \alpha f_0) - \eta_i \sum_{j=1}^{M} b_j N_j d\, \mathrm{E}\left[\frac{\partial}{\partial f_0} T_j(\alpha f_j^S, f_0)\Big|_{\alpha f_0^S}\right] \alpha f_0 + v_i \alpha f_i N_i d\right]; \ (\forall i > 0)$$

Taking the derivatives of the objective function for different countries leads to

$$\begin{cases} \dfrac{\partial GF_0}{\partial f_0} = \mathrm{E}\left[b_0 \dfrac{\partial T_0(\alpha f_0)}{\partial f_0} + \alpha \sum_{j=1}^{M} b_j N_j d\, \mathrm{E}\left[\dfrac{\partial}{\partial f_0} T_j(\alpha f_j^S, f_0)\Big|_{\alpha f_0^S}\right] + v_0 \alpha N_0 d\right] \\ \dfrac{\partial GF_i}{\partial f_i} = \mathrm{E}\left[b_i \dfrac{\partial T_i(\alpha f_i, \alpha f_0)}{\partial f_i} + v_i \alpha N_i d\right] \qquad (\forall 1 \leq i \leq M) \end{cases} \tag{4.23}$$

First order optimality conditions require to find the root for each of these derivatives. We know that by Assumption 9 the derivative of the index country is negative at $f_0 = 0$, hence the optimum value of f_0 happens in the convex region and so by comparing the first line of (4.23) to the first line of (4.17) we get that the optimum $f_0 = f_0^S$. Comparing the second line of (4.23) to the second line of (4.17) and using $f_0 = f_0^S$, we get that $f_i = f_i^S$ for all i. □

4.3 Budget Constraints

So far in the supply chain model, we have ignored the role of the vaccination program budget constraints within the countries. In reality some countries might not be able to afford the vaccine volume which is optimum for their population. To take this issue into account we assume that each country i, sets asides a budget of B_i for its vaccination program costs. There are two ways to formalize this argument:

1. Each country i is willing to pay up to the budget B_i in the vaccination program costs. i.e. $v_i f_i N_i d \leq B_i$

2. Each country i, on average, is willing to pay up to the budget B_i in the vaccination program costs. i.e. $v_i f_i N_i d \mathrm{E}[\alpha] \leq B_i$

Since the analysis for both of these cases is similar, we focus on the first case. Notice that for simplicity the budget constraint $v_i f_i N_i d \leq B_i$ can be replaced by $f_i \leq \tilde{f}_i$ for each country

i in which $\tilde{f}_i = \frac{B_i}{v_i N_i d}$ is a constant value showing the maximum fraction of the population i that can be vaccinated under the budget B_i.

As a result the cost function for each country i with the budget constraint can be written as follows:

$$\begin{aligned} &\text{country 0:} \quad \min_{0 \le f_0 \le \tilde{f}_0} \mathrm{E}\big[b_0 T_0(\alpha f_0) + v_0 \alpha f_0 N_0 d\big] \\ &\text{country } i\text{:} \quad \min_{0 \le f_i \le \tilde{f}_i \,|\, f_0} \mathrm{E}\big[b_i T_i(\alpha f_i, \alpha f_0) + v_i \alpha f_i N_i d\big] \quad \text{for all } 1 \le i \le M \end{aligned} \tag{4.24}$$

The Game Problem then is simply the solution of the above system of optimization problems. The System Problem can also be written in the same fashion. Before doing so, we make the following assumption in order to simplify the System Problem.

Assumption 10 *There is enough budget in the system to purchase the system optimum level vaccine needed for all of the countries. i.e., if* $(f_0^S, \cdots, f_M^S)$ *is the solution of (4.17) then,*

$$\sum_{i=0}^{M} B_i \ge \sum_{i=0}^{M} v_i f_i^S N_i d$$

Based on this assumption the budget constraints are not binding for the System Problem and as a result the system problem is the same as in (4.17), the case without budget constraints.

With the additional budget constraints and using Theorem 6 we have the following result:

Corollary 3 *Let* $(f_0^G, f_1^G, \cdots, f_M^G)$ *be the solution of the budget constrained Game Problem obtained in (4.24) and let* $(f_0^S, f_1^S, \cdots, f_M^S)$ *be the solution of the System Problem obtained in (4.17). Let* $\bar{f}_i$ *be the maximum vaccination fraction based on the budget constraint for country* i*, then*

1. $f_0^G \le f_0^S$
2. $f_i^G \le f_i^S, \quad \forall i = 1, \cdots, M;\ \bar{f}_i \le f_i^S,$
3. $f_i^G > f_i^S, \quad \forall i = 1, \cdots, M;\ \bar{f}_i > f_i^S,$

This result generalizes Theorem 5, and suggests that the central planer allocates more vaccines, compared to the Game Problem, to the index country as well countries whose

budget constraints do not let them to vaccinate up to the critical vaccination levels in their populations. On the other hand, the system problem requires less vaccines for other countries that can vaccinate more than their critical vaccination levels. The cost sharing contract also is modified accordingly to take this budget constraint effect into account. Similar to Theorem 6, the contract should financially help the countries for which $f_i^S < f_i^G$.

Theorem 7 *Let* $\mathcal{B} = \left\{ i \mid \bar{f}_i < f_i^S \right\}$ *be the set of countries that receive less than their system optimum level vaccines. Suppose that government* $i \notin \mathcal{B}$ *pays* $\eta_i^k(v_k f_k^S N_k d - B_k)$ *to government* $k \in \mathcal{B}$ *independent of the vaccines purchased by government* k*. Moreover, suppose that for every vaccine dose purchased by the index country, each government* $i \notin \mathcal{B}$ *pays to the index country*

$$-\eta_i^0 \sum_{j=1}^{M} \frac{1}{N_0} b_j N_j \mathrm{E}\left[\frac{\partial}{\partial f_0} T_j(\alpha f_j^S, \alpha f_0)\Big|_{f_0^S} \right]$$

where for all $k \in \mathcal{B}$ *and* $i \notin \mathcal{B}$ *we have* $\eta_i^k \geq 0$, $\sum_i \eta_i^k = 1$, *and* $\sum_k \eta_i^k(v_k f_k^S N_k d - B_k) \leq B_i - v_i f_i^S N_i d$, *then the resulting contract is coordinating. i.e.,*

- *It pushes all governments to purchase what is optimum for the system*
- *It is flexible. By changing* η_i^k*'s, governments can allocate the system cost reduction in any possible way between themselves.*

Proof: Using Assumption 10 we notice that there exist η_i^k's that satisfy the set of conditions mentioned in the statement of this theorem. Payments $\eta_i^k(v_k f_k^S N_k d - B_k)$ to the budget-constrained countries and also the choice of η_i^k ensure that no budget constraints would be binding and the rest of the proof is similar to Theorem 6. □

4.4 Numerical Results

This section uses the idea behind Theorem 6, together with estimates of parameters from the influenza literature, in order to develop a contract that can coordinate the incentives of the purchasers in the supply chain.

In this example, in order to simplify the analysis we look at different populations at an aggregate level and focus only on three different regions as "countries" ($i = 0, 1, 2$). The index country in our example is the Southeast Asia region, country 1 is the Western European union, and country 2 is the United States. Longini et al. (2004) argue that $R_0 \in [1.6, 2.4]$ is a reasonable range for basic reproduction number within the US. As a result we choose the basic reproduction numbers to be $R_{00} = 2.4$, $R_{11} = 1.9$, $R_{22} = 2.1$. To quantify cross-transmission effects and obtain R_{ij}'s when $i \neq j$, we use population information for each region together with the air travel rates across the different countries (U.S. Department of Transportation, 2006). If we assume that infected and infectious people from country i are equally likely as susceptible people from country i, to be in country j, then we can get an estimate on R_{ij} given the number of international contacts per day per person. Such an analysis gives an estimate of $R_{ij} \in [0.01, 0.05]$ for every $i \neq j$. For the specific example in this section we use $R_{ij} = 0.03$ for all $i \neq j$.

Weycker et al. (2005) estimated $\theta = 0.50$ and $\phi = 0.20$ for vaccine effects of susceptibility and infection respectively. They also estimate the direct costs of each infected individual with $b = \$95$ on average over the different subpopulations in the US. If indirect costs of the disease are included, this number can jump up to $b = \$460$. In our experiments, b_2 takes values from this range for the US. Cost for other countries are adjusted since direct and indirect costs will be different. Chick et al. (2007) argue that $[\$30, \$70]$ is a reasonable range for the total vaccination program costs in the US. We used $d = 1$ dose of vaccine, the usual value, per adult vaccinated. We are not aware of published estimates of the variance of vaccine production yields, although it is clear that variable vaccine yields are significant enough to cause noticeable fluctuations in the quantity of vaccine delivered (U.S. GAO, 2001). We assumed that $\alpha = \min\{\omega, 1\}$ where ω has a uniform distribution in $[0.5, 1.5]$. We assumed populations of $N_0 = 6 \times 10^8$, $N_1 = 3.6 \times 10^8$, and $N_2 = 3 \times 10^8$ individuals which correspond to the recent projected population sizes of the Southeast Asia region, Western Europe and the United States, respectively. We further assumed that, at time 0, the only infected individuals are in the index country, with $I_0(0) = 0.01$.

We implemented the cost sharing scheme in Section 4.2 for cases of $T_i(\cdot)$ that are based upon the above parameters. Consider the case when $b_0 = \$30$, $b_1 = \$120$, and $b_2 = \$200$.

Notice that we chose b_0 to be significantly lower than the social costs for other countries to illustrate the lower economic sensitivity of the index country to infection. The vaccination program costs are also chosen to be $v_0 = \$20$, $v_1 = \$40$, and $v_2 = \$60$ per dose of vaccines administered. Finally we chose a zero budget for vaccination program in the index country. In Section 4.4.2 we examine the effect of increasing index country's budget on the system. For countries 1 and 2, the vaccination program budget is assumed to be non-binding. Optimal order quantities for the Game Problem are $f_0^G = 0$, $f_1^G = 0.69$, and $f_2^G = 0.78$. Optimal order quantities for the System Problem are $f_0^S = 0.70$, $f_1^S = 0.66$, and $f_2^S = 0.74$. The order quantity for the index country has grown significantly due to both the budget constraint and its global effect. This change for other countries is not as significant. Under the contract, the system-wide cost would be reduced by almost \$6.47 B. Notice that not only is the contract cost-effective, social effects of this change in the vaccination levels are also significant. After implementing this contract, the total number of infected people globally will be reduced by 456 million individuals, i.e., about 454 million in the index country, more than 1.1 million at country 1, and more than 884 thousand individuals at country 2.

In the next sections we perform a set of experiments to assess the validity of the two-tier epidemic model, the value of the coordinating contract as the values of the parameters change, and when the precise form of the epidemic model is unknown. In summary:

- Coordinating contracts are effective in deriving down system-wide costs as well as the total number of infected individuals.
- Higher interaction rates between countries, and/or higher social costs of the disease lead to greater cost savings throughout the global supply chain
- The benefit of a coordinating contract, relative to the game setting, tends to be more significant when the true value of an epidemic model parameter in unknown.

4.4.1 Sensitivity Analysis for Epidemic Model

This section provides some numerical experiments to examine the validity of the proposed two-tier epidemic model in this paper with respect to the true epidemic model for heteroge-

Table 4.2: Comparing p_i's with $\tilde{p}_i$'s

f_0	f_1	f_2	p_0	$\tilde{p}_0$	Gap 0	p_1	$\tilde{p}_1$	Gap 1	p_2	$\tilde{p}_2$	Gap 2
0.47	0.11	0.30	0.33	0.30	0.03	0.65	0.62	0.03	0.49	0.44	0.05
0.07	0.10	0.10	0.81	0.81	0.00	0.69	0.64	0.05	0.74	0.70	0.04
0.30	0.13	0.10	0.54	0.53	0.01	0.64	0.60	0.04	0.73	0.70	0.03
0.34	0.19	0.41	0.49	0.49	0.00	0.56	0.52	0.04	0.36	0.28	0.08
0.15	0.10	0.10	0.72	0.72	0.00	0.69	0.65	0.04	0.74	0.70	0.04

neous populations (Longini et al., 1978). We noticed, in general, that the attack rate $\tilde{p}_i$ from the approximation in (4.13) differs from the attack rate in the full model in (4.1), by about 3% on average. Table 4.2 summarizes the results for random selections of vaccination levels, when $\theta = 0.5, \phi = 0.2, R_{00} = 2.4, R_{11} = 1.9, R_{22} = 2.1$, and $I_0(0) = 0.01$. The first column represents (random) vaccination levels in each country. The next three columns show the attack rates in the true and two-tier epidemic models and the gap between them at the index country, respectively. The next six columns represent the similar values for other countries.

We have tested the sensitivity of the attack rates in the proposed model with respect to change in other parameters, such as θ, ϕ, the matrix $\mathbf{R}$, and the initial infected population at the index country, $I_0(0)$. In all of those experiments we observe similar error margins between the two epidemic models. As a result we can conclude that the approximation in (4.13) is a reasonable approximation for (4.1).

4.4.2 Sensitivity Analysis for Model Parameters

Table 4.3 provides a sensitivity analysis with respect to the model's parameters, as those parameters are changed from their values in Section 4.4. In this example we chose $\mathbf{b} = \$(30, 120, 200)$, $\mathbf{v} = \$(20, 40, 60)$, $R_{00} = 2.4$, $R_{11} = 1.9$, $R_{22} = 2.1$, $\theta = 0.8$, and $\phi = 0.5$. The first column shows different values for cross-transmission rates between countries. The following two columns show the decrease in the overall system cost and the decrease in the overall number of infected individuals, respectively, when the contract is implemented. Finally the last six columns show the order quantities under the Game and System Problems. Notice that as the interaction rate between countries increases, the benefit of the contract becomes more visible.

Table 4.3: Sensitivity analysis for contract outcomes.

R_{ij}	Cost Decrease	Global Decrease in Infected Individuals	f_0^G	f_1^G	f_2^G	f_0^S	f_1^S	f_2^S
0.05	$ 7.07 B	460 M	0	0.70	0.79	0.71	0.66	0.74
0.04	$ 6.78 B	458 M	0	0.70	0.78	0.71	0.66	0.74
0.03	$ 6.47 B	456 M	0	0.69	0.78	0.70	0.66	0.74
0.02	$ 6.12 B	455 M	0	0.68	0.76	0.70	0.66	0.74
0.01	$ 5.72 B	453 M	0	0.67	0.75	0.70	0.66	0.74

Table 4.4: Sensitivity analysis for budget constraints.

$\tilde{f}_0$	Cost Decrease	Global Decrease in Infected Individuals	f_0^G	f_1^G	f_2^G	f_0^S	f_1^S	f_2^S
0	$ 6.47 B	456 M	0	0.69	0.78	0.7	0.65	0.74
0.1	$ 5.63 B	397 M	0.1	0.68	0.76	0.7	0.65	0.74
0.2	$ 4.74 B	334 M	0.2	0.68	0.76	0.7	0.65	0.74
0.3	$ 3.80 B	270 M	0.3	0.67	0.75	0.7	0.65	0.74
0.4	$ 2.79 B	202 M	0.4	0.67	0.75	0.7	0.65	0.74
0.5	$ 1.70 B	130 M	0.5	0.65	0.75	0.7	0.65	0.74
0.6	$ 0.57 B	58 M	0.6	0.65	0.74	0.7	0.65	0.74
0.7	$ 6.31 M	5 M	0.69	0.65	0.74	0.7	0.65	0.74
0.8	$ 6.31 M	5 M	0.69	0.65	0.74	0.7	0.65	0.74

Table 4.4 summarizes the results for sensitivity analysis on the budget constraint value for the index country. By increasing its budget for vaccination, $\tilde{f}_0$, the contract effects become less significant. As $\tilde{f}_0$ goes above 0.69, the budget constraint becomes non-binding. Notice that even though the cost savings from the contract are not very attractive when budget constraint is relaxed, the social effects of the contract (i.e., total infected population) are still fairly significant.

4.4.3 Sensitivity Analysis for Model Uncertainty

We performed a set of numerical experiments in order to test the sensitivity of the coordinating contract to the changes in the attack rate function that are due to uncertainty about epidemic parameters, or to uncertainty about the functional form of the attack rate. They assess potential penalties for incorrectly estimating epidemic parameters.

In summary, the benefit of a coordinating contract, relative to uncoordinated selfish

activity, tends to be far more significant than the potential penalty of some level of error in estimating $T_i(\cdot)$, when some of the epidemic model parameters are unknown. The contract is also more efficient in deriving down the total number of infected population when the epidemic model parameters are unknown.

The experimental settings are:

- Base model: All the governments have incorrect information about an epidemic model parameter. They also choose not to proceed with the proposed contract.
- Model #1: All the governments have incorrect information about an epidemic model parameter. However, they choose accept the proposed contract (with incorrect information).
- Model #2: All the governments have the correct information about all epidemic model parameters, but they choose not to proceed with the proposed contract and act selfishly.

As a result the benefit of implementing the contract, with incorrect information, would be benefit of model #1 compared to the base model. Similarly the benefit of having the perfect forecast would be obtained by comparing model #2 and the base model.

In order to provide results that are comparable with Section 4.4, we chose $R_{00} = 2.4, R_{11} = 1.9, R_{22} = 2.1$, $\mathbf{b} = \$(30, 120, 200)$, $\mathbf{v} = \$(20, 40, 60)$, $d = 1, \mathbf{N} = 3 \times 10^8(2, 1.2, 1)$, and $\alpha = \min\{\omega, 1\}$ where $\omega \sim$ Uniform$[0.5, 1.5]$, unless otherwise specified. In each experiment we assume one of the parameters θ, ϕ, or $I_0(0)$ is estimated incorrectly. Notice that for each parameter we consider the following three possibilities: governments' belief over-estimates the true value, under-estimates the true value or the true value is a random variable which is estimated by its mean. In the first six experiments true values of the epidemic model parameters are as follows: $\theta = 0.5, \phi = 0.2$, and $I_0(0) = 0.01$. For the last two experiments, we assumed these parameters are random variable with the following distributions: the seventh row example is the case with true $\theta \sim$ Uniform$[0.4, 0.6]$, the eighth row is the case where true $\phi \sim$ Uniform$[0.15, 0.25]$, and finally the last row is when true $I_0(0) \sim$ Uniform$[0.005, 0.015]$.

Table 4.5 indicates that decisions may differ from their optimal values, if the epidemic

Table 4.5: Contract effects when parameter estimates are incorrect

believed (incorrect) θ	believed (incorrect) ϕ	believed (incorrect) $I_0(0)$	base model f_0^G	base model f_1^G	base model f_2^G	model #1 f_0^G	model #1 f_1^G	model #1 f_2^G	model #2 f_0^G	model #2 f_1^G	model #2 f_2^G	contract benefit versus forecast benefit (cost-wise)	contract benefit versus forecast benefit (attack rate)
0.4	0.2	0.01	0	0.67	0.77	0.69	0.64	0.73	0	0.69	0.78	$ 6.44 B	448 M
0.6	0.2	0.01	0	0.70	0.79	0.72	0.66	0.76	0	0.69	0.78	$ 6.45 B	463 M
0.5	0.15	0.01	0	0.67	0.76	0.69	0.65	0.73	0	0.69	0.78	$ 6.45 B	448 M
0.5	0.3	0.01	0	0.72	0.81	0.74	0.68	0.78	0	0.69	0.78	$ 6.37 B	473 M
0.5	0.5	0.005	0	0.77	0.87	0.80	0.74	0.84	0	0.69	0.78	$ 5.64 B	500 M
0.5	0.5	0.015	0	0.80	0.90	0.83	0.74	0.84	0	0.69	0.78	$ 5.50 B	504 M
0.5	0.20	0.01	0	0.69	0.78	0.70	0.66	0.75	0	0.69	0.77	$ 647 B	456 M
0.5	0.20	0.01	0	0.69	0.78	0.70	0.66	0.75	0	0.69	0.78	$ 647 B	456 M
0.5	0.20	0.01	0	0.69	0.78	0.70	0.66	0.74	0	0.69	0.78	$ 646 B	456 M

model is incorrectly specified, and by how much. The first three columns show the potentially incorrect estimates of the epidemic model parameters by the governments. Next three columns represent order quantities under the base model. Similarly the next six columns are orders under the model #1 and model #2. The one to the last column represent the cost benefit generated by the contract minus cost benefit generated by the true forecast, hence the positive quantity shows strength of the proposed contract and a negative quantity represents that forecast is more effective. Finally the last column show a similar quantity for the decrease in attack rates.

One key observation from these experiments is that the economic benefit that is associated with the coordinating contract by far exceeds the penalty that is associated with a somewhat incorrect estimate of the epidemic model. Similar behavior is noticeable for the final attack rate reductions: the benefit from using such a contract, even if parameter estimates are somewhat imperfect, outperforms the corresponding benefit of having a perfect forecast.

Chapter 5

Summary, Discussion, and Model Limitations

5.1 Discussion and Model Limitations

This thesis derived the equilibrium state of an interaction between different players in the influenza vaccine supply chain. In Chapter 2 and Chapter 3 we considered a model with one government and one manufacturer, with the realistic feature that a manufacturer bears the risk of uncertain production yields. The model shows that *a rational manufacturer will always underproduce influenza vaccines* in that setting, relative to the levels that provide an optimal system-wide cost-benefit tradeoff.

When the levels of exogenous introduction of influenza into a population are extremely small, and good estimates for the infection transmission parameters are available, the piecewise linear approximation for $T(f)$ in Section 2.2 is appropriate. A relatively simple cost sharing contract can coordinate the incentives of the actors to obtain a system optimal solution.

When the levels of exogenous introduction of influenza into a population are not extremely small, or when the function $T(f)$ is estimated by averaging over prior distributions for unknown parameter values, the analysis of Chapter 3 is more appropriate. The simple cost sharing contract must be modified to account for the nonlinear population-level health

benefits that are provided by influenza vaccination programs. It is therefore not surprising that the whole-unit discount/cost sharing contracts that can align incentives depend on the expected number of infections averted by a given magnitude of the vaccination program effort.

Additional insights can be found by relating this analysis to the standard Newsvendor model. For example, the standard Newsvendor model allows for secondary markets for products that are unsold during the initial selling season, and allows for the modeling of goodwill effects for sales. Those features might be modeled in the current framework using an approach like that for the pay back contract in Section 2.2.2. Further, the shapes of the reward functions show that there is some insensitivity to manufacturer and governmental costs, should there be some reasonable error in the number of eggs ordered, or in the shape of $T(f)$. For the Newsvendor, an error in specifying the demand variability can also cause some level of errors when the cost structure causes one to order a quantity that is far from the mean.

In Chapter 4 we changed our focus to a model with multiple countries, with the realistic feature that important countries, from the spread of the disease point of view, do not receive enough vaccines. The model showed that rational governments order vaccine quantities which are suboptimal, relative to the levels that provide a system-wide optimal allocation, unless contractual incentives are provided. When there are no budget constraints, and good estimates for the infection transmission parameters are available, the concave-convex approximation for $T_i(\cdot)$ in Section 4.1.2 is appropriate. A relatively simple cost sharing contract can coordinate the incentives of the actors to obtain a system optimal solution (Section 4.2). When considering the budget constraints, the analysis of Section 4.3 is more appropriate. The simple cost sharing contract must be modified to account for countries that can not receive enough vaccines due to budget restrictions. The contract is therefore modified to pay fixed dollar amounts to those countries with not enough vaccine-related budget.

There are several limitations of these models. Some of the limitations can be handled with existing methods. Other limitations could lead to interesting future work, but do not limit the value of insights above regarding contract design for governmental/industry

collaboration for influenza outbreak preparedness.

One, an epidemic model with homogeneous and homogeneously mixing populations ignores the potential to target specific critical subpopulations, such as children or the elderly. In the short run, the contractual designs here that determine production volumes could be accompanied in a second stage analysis with other work (e.g., Hill and Longini, 2003) that can optimally allocate vaccines to different subpopulations. The generality of the analysis for piecewise linear (Chapter 2), convex (Chapter 3), or concave-convex $T(\cdot)$ (Chapter 4) allows some flexibility in adapting the incentive alignment results above to more complex epidemic models that prioritize certain subgroups.

Two, the coupling of drift variants and residual immunity from previous vaccination or past infection can complicate the multi-year dynamics of influenza vaccination (Plotkin et al., 2002; Smith et al., 2004; Duschoff et al., 2004). In a given year, information about previous strains can in principle be used to update prior information about the parameters of the next outbreak. The current formulation does not examine any multiyear benefits from vaccination that may accrue from projecting vaccine strains for multiple years. This thesis presents a positive first step for approaching the first-order effects of the current year's outbreak.

Four, the model assumes that health consequences can be quantified by direct and indirect monetary costs, but a multi-attribute approach might be desired to more fully examine issues like the number of deaths or hospitalizations. These features can be modeled indirectly with our proposed model by assessing the number infected and applying the relevant morbidity and mortality rates.

Five, the analysis assumes that the government is risk neutral, but a government may wish to specify a higher level of vaccines in order to prepare for a worst case scenario. This issue is addressed, to some extend, by Lemma 7, in that it is shown that in the case of multiple countries, each government would vaccinated at least the critical vaccination level if there are no budget constraints. A more direct way to account for this issue would be to perform the optimization with the added constraint that the governments announced fraction to vaccinate exceed a threshold. Another would be to inflate the value b, which models the cost per infection, to reflect a penalty for having too many infections.

Six, the model assumes that the government can precisely specify the number of indi-

viduals to vaccinate. This is a potential drawback of the other epidemic models mentioned in this thesis, too. The inclusion of an individual's choice to become vaccinated would also require additional complexity (e.g., Bauch and Earn 2004 consider epidemic outcomes with individual vaccination choice, but not manufacturer and government decisions).

Seven, the analysis assumes that all parameters are known to all parties. The epidemic model parameters, yield distributions and even social costs of the disease are not likely to be public information. Nevertheless the equilibrium might still be modeled as an outcome of interactions between rational actors of the model. Section 4.4.3 shows even with an incorrect estimate of the model parameters, effects of implementing the contract is far more significant.

Appendix A

Epidemic Model

At a high level, the epidemic model drives the analysis for supply chain behavior through the function $T(f)$, which models the expected number of infected individuals in the population, as a function of the fraction of the population that is vaccinated. The details of the underlying epidemic model are decoupled from the analysis.

This section recalls one specific epidemic model in detail, the closed-population SIR model, and an analysis of that model which is not an advance to the literature *per se*, but that fixes ideas for the paper. It also provides some structural results for the SIR model with an initial vaccination (a nonzero $R(0)$) that are not readily accessible in standard texts. That model gives rise to the formula for the attack rate p in (2.3).

A standard formulation for the SIR epidemic model in a closed population of N individuals is:

$$\frac{dS}{dt} = -\lambda\beta SI/N \tag{A.1}$$

$$\frac{dI}{dt} = +\lambda\beta SI/N - I/\delta \tag{A.2}$$

$$\frac{dR}{dt} = +I/\delta, \tag{A.3}$$

where $\lambda > 0$ is the number of contacts per unit time, $\beta \in [0, 1]$ is the probability of infection per contact, $\delta > 0$ is the duration of infection, and I/N is the probability that a contact is infectious. Timely vaccination followed by the onset of (instantaneous) infections from

exogenous sources results in initial conditions $R(0) = Nf\psi$, $S(0) = N(1 - f\psi)(1 - \chi)$, $I(0) = N(1 - f\psi)\chi$.

If $S(0), I(0), R(0)$ are given initial conditions, then Murray (1993) defines an outbreak by $dI(0)/dt > 0$, which happens if and only if $\lambda\beta\delta S(0)/N > 1$ (in the notation here). Once the derivative is negative, it stays negative. Murray (1993) calls $\lambda\beta\delta S(0)/N$ the basic reproductive number. With the stated initial conditions, an outbreak occurs if and only if

$$\frac{\lambda\beta\delta - \frac{1}{1-\chi}}{\lambda\beta\delta\psi} > f. \tag{A.4}$$

In the main paper, an outbreak refers to the transmission of influenza during a single season, following its introduction at time $t = 0$, whether $dI(0)/dt > 0$ or not. This allows for a seasonal influenza outbreak to be stunted by a successful vaccination program. A large outbreak refers to an outbreak with $dI(0)/dt > 0$.

What we have defined as the basic reproduction number, $R_0 = \lambda\beta\delta$, corresponds to the common epidemiological interpretation of R_0 as the expected number of individuals that are infected by a single infectious individual in an otherwise susceptible population (Anderson and May, 1991). This definition of R_0 is also consistent with the definition of Murray (1993) in the limit as $S(0)/N \to 1$ (a single infected in a large population).

Our definition of the critical vaccination fraction,

$$f^0 = \frac{R_0 - 1}{R_0\psi},$$

corresponds to setting f to the left hand side of (A.4), and letting $\chi \to 0$. Operationally, this f^0 corresponds to the (limiting) fraction of the population that must be vaccinated in order to halt an outbreak for *any* nonzero level for the fraction of individuals that are infected from exogenous sources.

We now analyze that formulation from two perspectives. Diekmann and Heesterbeek (2000) suggest every individual experiences the same state-dependent hazard of infection. Therefore every susceptible that is not infected from exogenous sources has the same probability of getting infected, q. The attack rate p can therefore be expressed as $p = S(0)q + I(0)$.

Note that every individual imposes a hazard of infection $\lambda\beta/N$ on all susceptible individuals for an average duration of δ. By integrating the hazard function through time, the total force of infection that is faced by an individual that is initially susceptible is therefore

$$\frac{\lambda\beta}{N} \cdot \delta \cdot pN = R_0 p.$$

Therefore, the probability that a susceptible at time 0 continues to be uninfected at the end of the epidemic is $\exp(-R_0 p)$, which equals $1 - q$ by definition, and which in turn equals $1 - (p - I(0))/S(0)$. Therefore $p = S(0)(1 - \exp(-R_0 p)) + I(0)$, justifying (2.3) from the main body.

An alternative derivation of (2.3) follows. From (A.1) and (A.3),

$$\begin{aligned} \frac{dS}{dR} =& -\frac{\lambda\beta\frac{SI}{N}}{I/\delta} = -\lambda\beta\delta\frac{S}{N} = -\frac{R_0}{N}S \\ \Rightarrow S =& \left[S(0)\exp(\frac{R_0}{N}R(0))\right]\exp(-\frac{R_0}{N}R). \end{aligned} \tag{A.5}$$

The constant $S(0)\exp(\frac{R_0}{N}R(0))$ comes from solving for initial conditions. Using (A.3), the conservation of the total population size ($N = S + I + R$ is constant, from adding equations (A.1) through (A.3)), and (A.5), we get an equation for dR/dt that only involves R and constants:

$$\begin{aligned} \frac{dR}{dt} =& \frac{I}{\delta} = \frac{1}{\delta}(N - R - S) \\ =& \frac{1}{\delta}(N - R - S(0)\exp(-\frac{R_0}{N}(R - R(0)))) \end{aligned} \tag{A.6}$$

At the end of the epidemic, the number that are ultimately infected is $R(\infty)$ and the derivative in (A.6) converges to 0. Set (A.6) to 0 and multiply by δ to get:

$$R(\infty) = N - S(0)\exp(-\frac{R_0}{N}(R(\infty) - R(0))). \tag{A.7}$$

Rescaling to $N = 1$, to obtain fractions of the population, the above formula is:

$$R(\infty) = 1 - S(0)\exp(-R_0(R(\infty) - R(0))). \tag{A.8}$$

We now subtract out the fraction of those that were vaccinated, $R(0) = 1 - S(0) - I(0)$, to obtain the attack rate $p = R(\infty) - R(0)$, the fraction infected during the outbreak.

$$p = R(\infty) - R(0) = S(0) + I(0) - S(0)\exp(-R_0 p) \tag{A.9}$$

That justifies (2.3) from the main paper.

Appendix B

Justification Why Linear and Convex $T(f)$ are of Interest

Figures 2-1 and B-1 show the shape of $T(f)$ with respect to different values of the initial fraction of susceptibles that become infected due to exogenous exposure, χ, and the expected number of secondary transmissions caused by one infected in an otherwise susceptible population, R_0. The four graphs correspond to $R_0 = 1.67, 2.0, 2.5, 3.0$, which are the range for R_0 for the different flu pandemics (Gani et al., 2005). In each graph, $T(f)$ is drawn for $\chi = 0, 0.005, 0.01, 0.05, 0.1$. The graphs look like a piecewise linear function as χ moves towards smaller values (lowest curve). If χ is sufficiently large, then $T(f)$ looks strictly convex. The function $T(f)$ may also appear convex when averaging over unknown parameter values. Finally, the contract in Section 3.3 may still coordinate incentives if $T(f)$ is convex for all sufficiently large f, even if it is concave for small f. This section formalizes those statements.

Piecewise linear. If the initial fraction of the population that is infected is due to a very small exogenous exposure (small χ, so $I(0)$ is close to 0), then we can replace $I(0)/S(0)$ by zero in (2.3) and conclude:

$$\frac{p}{1 - e^{-R_0 p}} = S(0) = 1 - \psi f \tag{B.1}$$

Note that the function $\frac{p}{1-e^{-R_0 p}}$ looks like a linear function if R_0 is not very large, which is the case for influenza. So the relationship between f and p is almost linear.

By replacing $\frac{p}{1-e^{-R_0 p}}$ with its Taylor series expansion around zero we have

$$\frac{p}{1-e^{-R_0 p}} \approx \lim_{p_0 \to 0}\left[\frac{p_0}{1-e^{-R_0 p_0}}\right] + \lim_{p_0 \to 0}\left[\frac{1-(1+R_0 p_0)e^{-R_0 p_0}}{(1-e^{-R_0 p_0})^2}\right](p-0).$$

In order to find the limits we use the Taylor approximation $1 - R_0 p$ for $e^{-R_0 p}$ around zero. Substitute this approximation into the Taylor series expansion above to obtain

$$\begin{aligned}\frac{p}{1-e^{-R_0 p}} \approx & \lim_{p_0 \to 0}\left[\frac{p_0}{1-1-R_0 p_0}\right] + \lim_{p_0 \to 0}\left[\frac{1-(1+R_0 p_0)(1-R_0 p_0)}{(1-1-R_0 p_0)^2}\right](p-0) \\ = & \frac{1}{R_0} + p.\end{aligned}$$

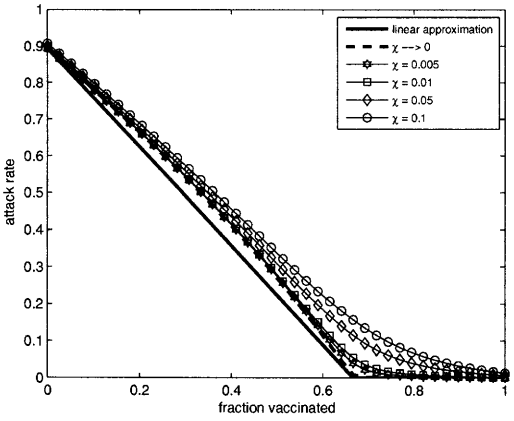
Hence by plugging this last equation instead of $\frac{p}{1-e^{-R_0 p}}$ into (B.1) we have the following linear relationship between attack rate and vaccination fraction:

$$p = (1 - \frac{1}{R_0}) - \psi f$$

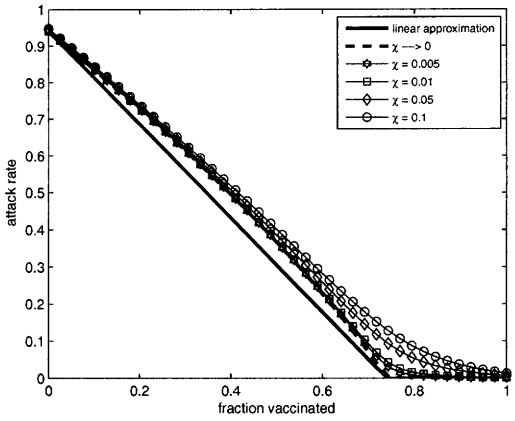
Note that the above line has a zero intercept at $f = \frac{R_0 - 1}{R_0 \psi}$, which is exactly the critical vaccination fraction in the case of homogeneous population (Hill and Longini, 2003). So clearly p remains zero for the case where f is greater than the critical vaccination fraction as the attack rate is a nonnegative parameter, and $T(f)$ is approximated by

$$T(f) = \begin{cases} N(1 - 1/R_0) - N\psi f, & 0 \leq f \leq f^0 \\ 0, & f^0 \leq f \leq 1 \end{cases}$$

While this equation has an epidemiologically attractive interpretation, it estimates the actual $T(0)$ poorly due to the Taylor series approximations. However, the f- and p-axis intercepts of the roughly linear plot when $I(0) \approx 0$ can be more accurately modeled by replacing $N(1 - 1/R_0)$ with $M = Np_0$, where p_0 solves (B.1) when $f = 0$; and by replacing the usual individual-level vaccine effect parameter, ψ, with a parameter ν that represents the number of infections averted in the population by one additional vaccination. (The parameters ψ and ν are not necessarily the same, due to nonlinear infection dynamics.)



(a) $R_0 = 2.5$



(b) $R_0 = 3.0$

Figure B-1: The fraction of the population infected during the outbreak (or attack rate, p) as a function of the fraction vaccinated (f), for different values of the fraction of susceptibles that are initially infected (χ) and the basic reproduction number (R_0).

Hence we define the adjusted piecewise linear approximation for total number infected to be

$$T(f) = \begin{cases} Np_0 - N\nu f, & 0 \leq f \leq f^0 \\ 0, & f^0 \leq f \leq 1, \end{cases}$$

where $\nu = p_0 \frac{R_0 \psi}{R_0 - 1}$ is chosen such that $T(f)$ hits the f axis at the critical vaccination fraction. Figure 2-1 and Figure B-1 show the linear approximation versus the actual values of χ. We have tested this approximation on a variety of parameters which are reasonable for the case of influenza. The cost gaps for the government and system between the actual $T(f)$ and the piecewise linear approximation for the game and the system problems is almost zero and the gap between the optimal decision variables is typically less than $2 \sim 3\%$ for the system and a bit higher for the game problem. Table 3.2 illustrates these outcomes together with additional sensitivity results.

Convex case. We now derive some of the properties of $T(f) = Np$ to argue that it is convex when χ, and therefore $I(0) = (1 - \psi f)\chi$, is sufficiently large. Recall (2.3) and that

$S(0) = (1 - \psi f)(1 - \chi)$ to obtain

$$p = (1 - \psi f) - (1 - \psi f)(1 - \chi)e^{-R_0 p} \tag{B.2}$$

Our goal is to show that p is a convex function of f. Notice that in (B.2) p is an implicit function of f and to find its second derivative we will use the following fact from from calculus that if $y = f(x)$ then

$$\frac{\partial^2 f^{-1}(y)}{\partial y^2} = -\frac{1}{\left(\frac{\partial f(x)}{\partial x}\right)^3}\frac{\partial^2 f(x)}{\partial x^2}$$

By rearranging terms in (B.2), we can solve for f in terms of p:

$$f = \frac{1}{\psi}\Big[1 - \frac{p}{1 - (1 - \chi)e^{-R_0 p}}\Big].$$

Hence by taking the derivative:

$$f'(p) = -\frac{1}{\psi}\Big[\frac{1 - (1 + R_0 p)(1 - \chi)e^{-R_0 p}}{(1 - (1 - \chi)e^{-R_0 p})^2}\Big]$$

First of all we show that $f'(p) \leq 0$. It is enough to show that the numerator in $f'(p)$ is positive. But we know that:

$$\begin{aligned} 1 - (1 + R_0 p)(1 - \chi)e^{-R_0 p} &\geq 1 - (1 + R_0 p)e^{-R_0 p} \\ &\geq 0 \end{aligned}$$

The last inequality is based on the fact that the function $(1 + x)e^x$ obtains its maximum at zero in the interval $[0, 1]$. Hence by basic calculus since $\frac{\partial f}{\partial p}$ is negative so is $\frac{\partial p}{\partial f}$. So far we have shown that p is a decreasing function of f, when $\chi > 0$.

The second piece of the puzzle is to find the relationship for $f''(p)$ or the sign of it. By

taking the second derivative of f we have:

$$f''(p) = -\frac{1}{\psi}\left[\frac{R_0(1-\chi)e^{-R_0p}\left[R_0p-2+(R_0p+2)(1-\chi)e^{-R_0p}\right]}{\left[1-(1-\chi)e^{-R_0p}\right]^3}\right]$$

Note that if the second derivative of $f(p)$ were nonnegative, then by the nonpositivity of $f'(p)$ and using the above lemma, we would have $\frac{\partial^2 p}{\partial f^2} \geq 0$, which is the desired result in this part.

We will show that $f''(p)$ is not always positive, but that $f''(p) \geq 0$ for values of χ far enough from zero and small enough values of p. To show this, we note that the denominator is positive, and we evaluate the sign of the $f''(p)$'s numerator. Since $R_0(1-\chi)e^{-R_0p}$ is always positive, we find the sign of $(R_0p-2)+(R_0p+2)(1-\chi)e^{-R_0p}$.

Note that if $R_0p \geq 2$, then $f(p)$ would be concave (since the numerator would be positive), and by the lemma, $T(f)$ would be concave, independent of the value of χ. The numerator may also be positive if p is big enough (so that f is small enough). On the other hand, many estimates of R_0 for influenza are less than 2, and for those estimates that are larger than 2, $R_0p < 2$ for even small to moderate values of f. We observe two things, numerically. (i) If $R_0 \leq 2$ and χ big enough, then the attack rate is convex for all f. (ii) Otherwise the attack rate is convex for big enough values of f (which lead to small enough p). The reason is that for sufficiently small p, terms in the numerator that contain p become negligible, so the numerator is negative, making f convex. The related statement for the attack rate is that for big enough values of f (small enough p), the attack rate is a convex function of f.

The numerical tests in Section 3.3 and Sections 3.3.1 and 3.3.2 show empirically that our proposed contract can still coordinate even when the attack rate is not completely convex. Specifically, the contract is still coordinating in these examples when the function $T(f)$ is first a concave but after some point convex function of f, it is optimal to vaccinate at least one person ($bT'(0)+p_aNd < 0$), and the system optimal f is in the region where $T(f)$ is convex.In fact, the examples in Section 3.3 of the main paper and the sensitivity analysis in Sections 3.3.1 and 3.3.2 below are based on this property, since $T(f)$ is not precisely convex for those sets of values of the parameters.

Uncertain outbreak parameters. Throughout the main paper, it is assumed that exact values of the reproduction number (R_0), the vaccine efficiency (ψ) and the fraction of susceptible individuals that are initially infected (χ) are known. This might not be the case for a real influenza season. Although in general R_0, ψ, χ are random variables, our analysis only depends on these parameters through the function $T(f)$. In this section we show that the shape of function $T(f)$ can still be convex, even with uncertainty about the values of epidemic parameters. In order to incorporate this randomness, the definition of

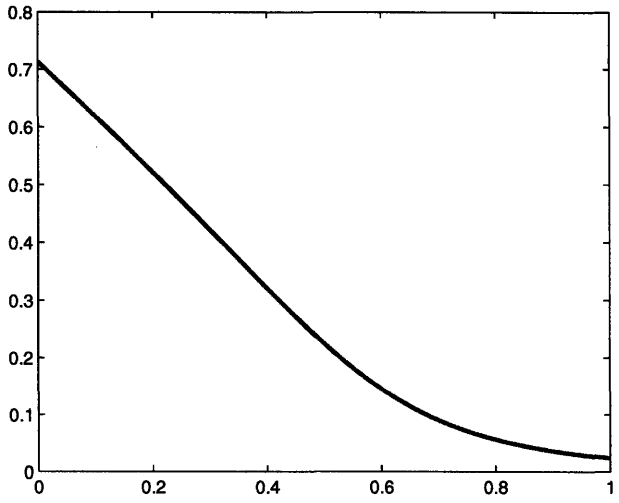


Figure B-2: Graph of $T(f)$ by averaging over random R_0, ψ, χ.

$T(f)$ should be the expected number of infected population, where expectation is taken over the uncertain R_0, ψ, χ. This way the definition of $\bar{f}$ requires that the marginal (expected) benefit balance with the (expected) marginal cost. For this purpose we take a mixture of $T_{R_0,\psi,\chi}(f)$ (the number infected, given the specified R_0, ψ, χ), in order to obtain $T(f) = E_{R_0,\psi,\chi}[T_{R_0,\psi,\chi}(f)]$. So it is not surprising that if each individual $T_{R_0,\psi,\chi}(f)$ is convex then $T(f)$ is convex as well, since integration preserves convexity. To illustrate this, Figure B-2 shows the graph $T(f)$ when $R_0 \sim$ uniform$[1.5, 2]$, $\psi \sim$ beta$(\alpha = 15, \beta = 5)$ (i.e. $\mu = 0.75$, $\sigma^2 = 0.0945$), and $\chi \sim$ beta$(\alpha = 0.96, \beta = 47.04)$ (i.e. $\mu = 0.02$, $\sigma^2 = 0.02^2$). For this purpose we sampled 99 observation of each random variable, corresponding to CDF values at $0.005, 0.015, 0.025, \cdots, 0.995$ then by taking the inverse integral obtained the cor-

responding values, and numerically averaged to find the resulting $T(f)$.

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