

Supply Chain Coordination and Influenza Vaccination

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Abstract

Billions of dollars are being allocated for influenza pandemic preparedness, and vaccination is a primary weapon for fighting influenza outbreaks. The influenza vaccine supply chain has characteristics that resemble the news vendor problem, but possesses several characteristics that distinguish it from typical supply chains. Differences include a nonlinear value of sales (caused by the nonlinear health benefits of vaccination due to infection dynamics) and vaccine production yield issues. We show that production risks, taken currently by the vaccine manufacturer, lead to insufficient supply of vaccine. Unfortunately, several supply contracts that coordinate buyer (governmental public health service) and supplier (vaccine manufacturer) incentives in 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 guarantees sufficient supply of vaccine.

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1 Influenza: Overview, Control and Operational Challenges

Influenza is an acute respiratory illness that spreads rapidly in seasonal epidemics. Globally, annual influenza outbreaks result in 250,000 to 500,000 deaths. The World Health Organization reports that costs in terms of health care, lost days of work and education, and social disruption have been estimated to vary 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 (WHO, 2005).

This paper provides background about influenza and vaccination, a key tool for controlling influenza outbreaks, then highlights some operational challenges for delivering those vaccines. 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...(WSJ, 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...(George W. 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 concerns for both public health outcomes and production economics.

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).

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 rates. This may be caused by a larger genomic mutation (antigenic shift).

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 H5N1 virus is the most likely potential culprit for a future pandemic (<http://www.who.int/csr/disease/influenza/>).

1.2 Vaccination as a Control Tool

Vaccines can reduce the risk of infection to exposed individuals that are susceptible to infection, and can reduce the probability of transmission from a vaccinated individual that is infected with influenza (Longini et al., 1978; Smith et al., 1984; Longini et al., 2000; Chick et al., 2001). Vaccines therefore 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). If R_0 can be reduced below 1, then the dynamics of a large outbreak can be averted. Let f^0 be the so-called critical vaccination fraction, the minimum fraction of the population to vaccinate to reduce the reproduction number to 1 (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 those those aged 65 or more, health care workers, and

those that may have certain risk factors (Bridges et al., 2002; WHO, 2005). Vaccination can be complemented with antiviral therapy.

Vaccination is cost effective. Nichol et al. (1994) found that immunization in the elderly saved \$117 per 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.

1.3 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. Figure 1 provides a graphic summary. Saluzzo and Lacroix-Gerdil (2006) provide additional information, particularly with respect to avian flu preparedness.

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 news-vendor 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 challenge. Wu et al. (2005) develop an optimization model

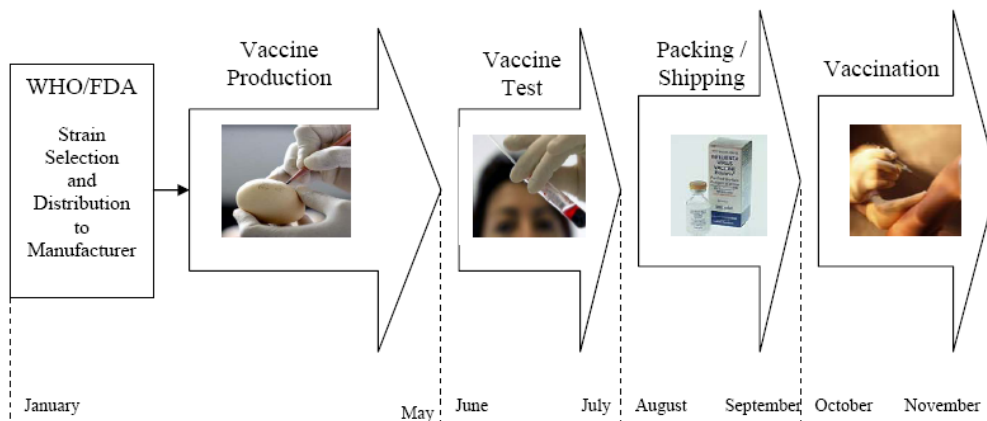


Figure 1: Influenza vaccine time line.

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.

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 transshipment to insure appropriate delivery. 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 clearing-house for vaccine supply and demand to provide a market overview and help to eliminate order gaming and price gouging, as well as demand forecasting tools, and regional vaccine redistribution pools to shift supplies from areas with surpluses to areas experiencing shortages.

This paper is concerned with a challenge in the middle of the value chain: 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. 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 selected for the vaccine.

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 (Pien, 2004; Bush, 2005; Wysocki and Lueck, 2006). The ideal way to structure those partnerships is an open question. This paper addresses one dimension of that multi-faceted question.

Section 2 presents a model to assess contractual mechanisms that align manufacturer risks and incentives with governmental health care policy objectives for influenza vaccination. Section 3 and Section 4 analyze the model. A variant of the cost sharing contract, which we show can align incentives for public health benefits and production costs, also increases production volumes. Increased production volumes for annual vaccination are consistent with the recommendations of the Pandemic Influenza Plan of the U.S. Dept. of Health and Human Services (2005). Section 5 discusses implications and limitations of the analysis.

2 Joint Epidemic and Supply Chain Model

The work here unites two previously separate streams of literature. The epidemic literature provides epidemic models and cost benefit analysis for interventions such as vaccination (Jacquez, 1996; Diekmann and Heesterbeek, 2000; 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 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 announces 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 . We assume that the yield U has a continuous probability density function $f_U(u)$ with mean μ and variance σ^2 . 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.

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 discarded (due to antigenic shift).

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 of the outbreak, $bT(f)$, where $T(f)$ is the total number of infected individuals by the end of the outbreak, and b is the average direct and indirect cost of influenza infection per outbreak (Weycker et al., 2005, provides 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,

$$\bar{f} = \sup\{f : bT'(f) + p_a N d < 0, \text{ for } f \text{ such that } T'(f) \text{ exists}\} \quad (1)$$

$$\bar{\bar{f}} = \sup\{f : bT'(f) + (p_a + p_r) N d < 0, \text{ for } f \text{ such that } T'(f) \text{ exists}\}. \quad (2)$$

The epidemic model determines the number of individuals, $T(f)$, that are infected by the end of the outbreak. 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 (Diekmann and Heesterbeek, 2000), of which a fraction S_0 of the population is initially Susceptible. A fraction I_0 is Infected and infectious (an initial seeding due to exposure from exogenous sources). After recovery, individuals are

Table 1: Summary of Notation.

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 $f_U(u)$, 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 (direct + indirect costs)
Z	Number of doses sold from manufacturer to government
W	Number of doses administered by government to susceptible population

Outbreak

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 number infected during the infection season, a function of the fraction vaccinated
I_0	The initial fraction of infected people introduced to the population
S_0	The initial fraction of susceptible people in the population
ϕ	Vaccine effects on transmission, including susceptibility and infectiousness effects
ψ	Linear approximation to number of direct and indirect infections averted by a vaccination
f^0	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, $k = \frac{fNd}{n_E}$

Removed and no longer infectious. This so-called SIR epidemic model is consistent with the natural history of infection of influenza. Table 1 summarizes the notation.

We assume that vaccination removes some fraction ϕ of individuals from the pool of susceptibles, where ϕ is interpreted as a combination of vaccine effects. If $S_0 = 1 - I_0 - \phi f$, then $T(f) = Np$, where the so-called attack rate p (Longini et al., 1978) satisfies

$$p = S_0 \left(1 + \frac{I_0}{S_0} - e^{-R_0 p} \right). \quad (3)$$

The critical vaccination fraction is $f^0 = (R_0 - 1)/(R_0 \phi)$ when $R_0 > 1$ (Hill and Longini, 2003).

Rather than deriving results via such an implicit characterization from the epidemic model, we derive results for a nonincreasing $T(f) \geq 0$ with specific general characteristics. Appendix B describes why it is reasonable to consider two functional forms: a piecewise linear $T(f)$, or a strictly convex $T(f)$. This removes

the details of an implicit solution for an epidemic model from the supply chain analysis. Section 3 handles the piecewise linear case. Section 4 handles the convex case. Any further characteristics of the epidemic model that are needed below are compatible with Longini et al. (1978), specialized to one subpopulation.

2.1 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:

$$\begin{aligned} \min_{n_E} \quad & MF = \mathbb{E}[cn_E - p_r Z] \quad (\text{net manufacturer costs}) \\ \text{s.t.} \quad & Z = \min\{n_E U, fNd\} \quad (\text{doses sold} \leq \text{yield and demand}) \\ & n_E \geq 0 \quad (\text{nonnegative production volume}) \end{aligned} \quad (4)$$

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.

Proposition 1 *For any random egg yield, U , with pdf $f_U(u)$, and given the order quantity $D = fNd$ by government, the optimal production level for the manufacturer is*

$$\int_0^{\frac{fNd}{n_E^*}} u f_U(u) du = \frac{c}{p_r}. \quad (5)$$

Claims that are not justified in the main text are proven in Appendix A.

A useful corollary follows directly.

Corollary 1 *If c , p_r , $f_U(u)$, 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 (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.

$$\begin{aligned}
\min_f \quad & GF = E \left[bT\left(\frac{W}{Nd}\right) + p_a W + p_r Z \right] \quad (\text{net government costs}) \\
\text{s.t.} \quad & Z = \min\{n_E U, fNd\} \quad (\text{doses bought} \leq \text{yield and demand}) \\
& W = \min\{n_E U, fNd, \bar{f}Nd\} \quad (\text{doses given} \leq \text{doses bought, cost effective level}) \\
& \int_0^{\frac{fNd}{n_E}} u f_U(u) du = \frac{c}{p_r} \quad (\text{manufacturer acts optimally}) \\
& 0 \leq f \leq 1 \quad (\text{fraction of population}) \\
& n_E \geq 0 \quad (\text{nonnegative production volume})
\end{aligned} \tag{6}$$

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

2.2 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. System costs do not include monetary transfers from government to manufacturer. Formally, the **system problem** is

$$\begin{aligned}
\min_{f, n_E} \quad & SF = E \left[bT\left(\frac{W}{Nd}\right) + p_a W + cn_E \right] \quad (\text{total system costs}) \\
\text{s.t.} \quad & W = \min\{n_E U, fNd, \bar{f}Nd\} \quad (\text{doses given} \leq \text{yield, demand, cost effective level}) \\
& 0 \leq f \leq 1 \quad (\text{fraction of population}) \\
& n_E \geq 0 \quad (\text{nonnegative production volume}).
\end{aligned} \tag{7}$$

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

3 Piecewise Linear Number of Infected

Figure 2 plots the attack rate, p , which is directly proportional to the total number infected, $T(f)$, as a function of the fraction of initially exposed individuals, I_0 and reasonable values of R_0 for influenza transmission (Gani et al., 2005). If there are few that are initially infected due to exogenous exposure (small I_0/S_0), then Appendix B justifies the following piecewise linear approximation for $T(f)$.

$$T(f) = \begin{cases} M - N\psi f, & 0 \leq f \leq f^0 \\ 0, & f^0 \leq f \leq 1, \end{cases} \quad (8)$$

where ψ is interpreted here as the marginal number of infections averted per additional vaccination.

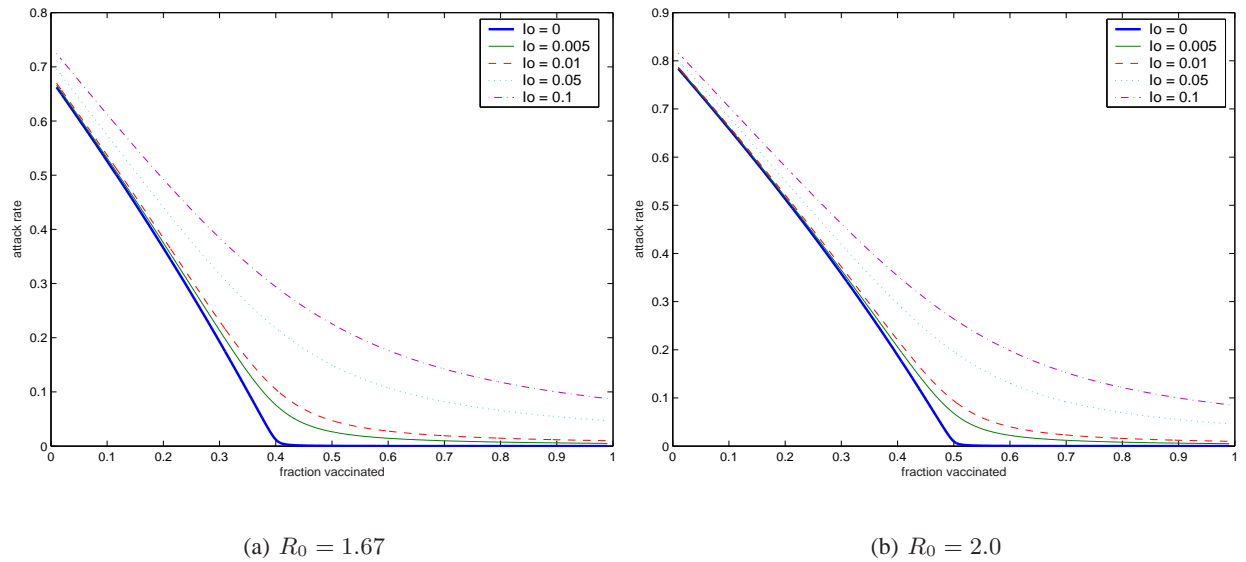


Figure 2: Attack rate versus f for different values of I_0 and R_0

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, $\bar{f} = f^0$. The government's objective function from Problem (6) is

$$GF = E \left[b \max\left\{M - \psi \frac{W}{d}, 0\right\} + p_a W + p_r Z \right]. \quad (9)$$

The manufacturer problem is the same.

The system's objective function from Problem (7) is

$$SF = E \left[b \max \left\{ M - \psi \frac{W}{d}, 0 \right\} + p_a W + c n_E \right]. \quad (10)$$

3.1 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 are given. A series of assumptions and results are developed to show that the optional system solution requires a higher vaccine production level than in the game setting. Section 3.2 uses those results to design contracts that create a new game, to get individual actors to behave in a system optimal way.

If the following assumption were not valid, then even free vaccines would not be cost effective.

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

Proposition 2 *Let f^S, n_E^S be optima for the system setting with objective function in (10). If Assumption 2 holds, then (1) f^S could be any value between f^0 and 1; and (2) n_E^S satisfies*

$$\int_0^{\frac{f^0 N d}{n_E^S}} u f_U(u) du = \frac{c}{\frac{\psi b}{d} - p_a}. \quad (11)$$

The next assumption implies that vaccination is cost effective from the government's point of view.

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

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

$$\begin{aligned} GF(f, n_E) &\geq b \int_0^{\frac{\tilde{f} N d}{n_E}} \left(M - \psi \frac{n_E u}{d} \right) f_U(u) du + b(M - N \psi \tilde{f}) \int_{\frac{\tilde{f} N d}{n_E}}^{\infty} f_U(u) du \\ &\quad + (p_a + p_r) n_E \int_0^{\frac{\tilde{f} N d}{n_E}} u f_U(u) du + (p_a + p_r) (\tilde{f} N d) \int_{\frac{\tilde{f} N d}{n_E}}^{\infty} f_U(u) du \\ &= bM + n_E \frac{1}{d} ((p_a + p_r) d - \psi b) \int_0^{\frac{\tilde{f} N d}{n_E}} u f_U(u) du + \tilde{f} N ((p_a + p_r) d - \psi b) \int_{\frac{\tilde{f} N d}{n_E}}^{\infty} f_U(u) du. \end{aligned}$$

If $\psi b - (p_a + p_r)d < 0$, 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 (5) and (11) to obtain Corollary 2.

Corollary 2 Let f^S, n_E^S be optimal values of the system problem and define $k^S = \frac{f^0 Nd}{n_E^S}$. 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 vaccine fraction and production level for the system setting. We now assess optimal behavior in the game setting. (5) indicates that it suffices to characterize the optimal vaccine fraction, which then determines the optimal production level in the game setting.

Proposition 3 Let f^G, n_E^G be optimal solutions for the game setting, and set $k^G = \frac{f^G Nd}{n_E^G}$. If Assumption 3 holds, then $f^G \geq f^0$. Furthermore, $f^G = f^0$ if and only if

$$\left(-\frac{\psi b}{d} + p_a + p_r\right) \int_0^{k^G} u f_U(u) du + p_r k^G \int_{k^G}^{\infty} f_U(u) du \geq 0. \quad (12)$$

Although it may seem, at first glance, that Condition (12) depends on f^G through k^G , this is not true. Given the problem data, the value of k^G is determined by (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 the second part of Proposition 3, Condition (12), 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 vaccine fraction, f^0 .

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.

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

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.

3.2 Coordinating Contracts

The objective of this section is to design contracts that will align governmental and manufacturer incentives. 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.

3.2.1 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 4 *There does not exist a wholesale price contract which satisfies the condition in Assumption 3 and coordinates the supply chain.*

3.2.2 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.

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 . 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 (4) to

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

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

$$\int_0^{\frac{fNd}{n_E^*}} u f_U(u) du = \frac{c - p_c \mu}{p_r - p_c}. \quad (13)$$

The effect of this contract on the government problem in Problem (6) is to change the objective to

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

and to change the “manufacturer acts optimally” constraint, which determines the optimal production input quantity n_E as a function of f , from (5) to (13).

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 5 *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, $n_E^N < n_E^S$.*

Proposition 5 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.

3.2.3 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^0, n_E^S .

With the cost sharing contract, the manufacturer problem is:

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

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

$$\int_0^{\frac{fNd}{n_E}} u f_U(u) du = \frac{c - p_e}{p_r}. \quad (14)$$

Cost sharing increases the governments costs, changing its objective function to:

$$GF = E \left[b \max\{M - \psi \frac{W}{d}, 0\} + p_a W + p_r Z + p_e n_E \right], \quad (15)$$

and resulting in the following optimization problem.

$$\begin{aligned} \min_f \quad & GF = E \left[b \max\{M - \psi \frac{W}{d}, 0\} + p_a W + p_r Z + p_e n_E \right] \\ \text{s.t.} \quad & Z = \min\{n_E U, fNd\} \\ & W = \min\{n_E U, fNd, f^0 Nd\} \\ & \int_0^{\frac{fNd}{n_E}} u f_U(u) du = \frac{c - p_e}{p_r} \\ & 0 \leq f \leq 1 \\ & n_E \geq 0 \end{aligned}$$

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 $\frac{c - p_e}{p_r} = \frac{c}{\frac{\psi b}{d} - p_a}$. Such a p_e exists since $p_r < \frac{\psi b}{d} - p_a$. 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.

Theorem 2 *If Assumption 3 holds and p_e is chosen so that $\frac{c - p_e}{p_r} = \frac{c}{\frac{\psi b}{d} - p_a}$, then the optimal values (f^e, n_E^e) for Problem (15) equal (f^0, n_E^S) , so this cost sharing contract will coordinate the supply chain.*

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).

4 Strictly Convex Number of Infected

This section 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 I_0 and values of R_0 that are representative of influenza (see Appendix B). This corresponds to a larger initial exposure to members of the population, such as may occur in an initial pandemic wave.

Below we 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.

4.1 Optimal solutions for game and system settings

The solution to the manufacturer problem in Problem (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 (6) and the system problem in Problem (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 6 *If $T(f)$ is strictly convex, \bar{f} is the solution of (1), and the optimum values of the system problem in Problem (7) are denoted by f^S, n_E^S , then (a) f^S could be any value between \bar{f} and 1; and (b) n_E^S is the solution of the following equation: $\int_0^{\frac{\bar{f}Nd}{n_E^S}} \left[\frac{b}{Nd} T' \left(\frac{n_E^S u}{Nd} \right) + p_a \right] u f_U(u) du + c = 0$.*

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

Proposition 7 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) $\int_0^{k^G} u f_U(u) du = \frac{c}{p_r}$; and (b) $f^G \leq \bar{f}$ if and only if

$$\int_0^{k^G} \left[\frac{b}{Nd} T' \left(\frac{\bar{n}_E u}{Nd} \right) + p_a \right] u f_U(u) du + c + p_r k^G \int_{k^G}^{\infty} f_U(u) du \geq 0. \quad (16)$$

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. The proof requires the following three lemmas.

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

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

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

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

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 $n_E^S > n_E^G$.

Thus, the theorem suggests that the production level set by the manufacturer, n_E , is below the amount required by the system. Hence, the need for effective contracts.

4.2 Coordinating Contracts

This section constructs a contract which can coordinate this supply chain. Unfortunately, the cost sharing contract of Section 3.2.3, 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., $f^G \geq f^0$, even without the contract. This is not the case for the convex case, where without the contract, f^G maybe smaller than $\bar{f} \leq f^S$, see Proposition 6 and Proposition 7.

Thus, the contract should provide incentive for the government to vaccinate a higher fraction of the population, and provide a manufacturer incentive to produce enough. Section 4.2.1 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.

4.2.1 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. The section concludes with a proof 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 ,*

$$(a) (p_r(f)fNd)' = p'_r(f)fNd + p_r(f)Nd \geq 0 \text{ for all } 0 \leq f \leq \bar{f}.$$

$$(b) p'_r(\bar{f})\bar{f}Nd + p_r(\bar{f})Nd = 0.$$

3. *The total cost to the government excluding the cost sharing component is convex in f ,*

$$(a) bT''(f) + p''_r(f)fNd + 2p'_r(f)Nd \geq 0 \text{ for all } 0 \leq f \leq \bar{f}.$$

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.

Assumption 6 Given $p_r(f)$, let $p_e(f) \geq 0$ satisfy $\frac{c - p_e(f)}{p_r(f)} = \int_0^{k^S} u f_U(u) du$ 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,

$$p_r(f) = \begin{cases} \kappa \frac{b}{fNd} [-T(f) + T'(\bar{f})f + T(0)], & 0 \leq f \leq \bar{f} \\ p_r(\bar{f}), & \bar{f} < f \leq 1. \end{cases} \quad (17)$$

Claim 1 If $0 < \kappa < 1$, then the pricing strategy introduced in (17) gives a nonnegative price for any f and satisfies all the conditions in Assumption 5.

Now we show that for some κ , (17) satisfies Assumption 6. It suffices to show that $p_e(f) \geq 0$ for all f , so the goal is to choose a pricing strategy such that $p_r(f) \int_0^{k^S} u f_U(u) du \leq c$. Since $p_r(f)$ is nonincreasing in f , it suffices to show that $p_r(0) \int_0^{k^S} u f_U(u) du \leq c$. For any $p_r(f)$ that satisfies (17),

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

Observe that $\int_0^{k^S} u f_U(u) du \leq \mu$. It suffices to have $\kappa \frac{b}{Nd} [T'(\bar{f}) - T'(0)] \mu \leq c$ in order to insure that Assumption 6 holds. This justifies Claim 2: pricing strategies exist that satisfy both assumptions.

Claim 2 If $0 < \kappa < \min\{1, \frac{c}{[T'(\bar{f}) - T'(0)]\mu}\}$, then the pricing strategy $p_r(f)$ in (17) satisfies Assumptions 5 and 6.

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:

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

By taking the derivatives, we have:

$$\begin{aligned} \frac{\partial MF(n_E)}{\partial n_E} &= (c - p_e(f)) - p_r(f) \int_0^{\frac{fNd}{n_E}} u f_U(u) du \\ \frac{\partial^2 MF(n_E)}{\partial n_E^2} &= p_r(f) \frac{fNd}{n_E^2} \left(\frac{fNd}{n_E} \right) f_U\left(\frac{fNd}{n_E} \right) \geq 0 \end{aligned}$$

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

$$n_E^* = \frac{fNd}{k^S}. \quad (18)$$

Therefore this contract changes the government objective to

$$\min_f GF = E \left[bT\left(\frac{W}{Nd}\right) + p_a W + p_r(f)Z + p_e(f)n_E \right], \quad (19)$$

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 (19), 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 (19), we again split it into two separate subproblems.

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

$$\begin{aligned} \min_f GF_1 = & \left[b \int_0^{\frac{fNd}{n_E}} T\left(\frac{n_E u}{Nd}\right) f_U(u) du + bT(f) \int_{\frac{fNd}{n_E}}^{\infty} f_U(u) du + p_a n_E \int_0^{\frac{fNd}{n_E}} u f_U(u) du \right. \\ & + p_a f Nd \int_{\frac{fNd}{n_E}}^{\infty} f_U(u) du + \underbrace{p_e(f) n_E + p_r(f) n_E \int_0^{\frac{fNd}{n_E}} u f_U(u) du}_{= cn_E \text{ (by Assumption 6)}} \\ & \left. + p_r(f) (fNd) \int_{\frac{fNd}{n_E}}^{\infty} f_U(u) du \right] \end{aligned}$$

subject to the constraints $fNd = k^S n_E$; $0 \leq f \leq \bar{f}$; and $n_E \geq 0$. Substituting the constraint $n_E = \frac{fNd}{k^S}$

into the objective function gives

$$\begin{aligned} \min_f GF_1 = & \left[b \int_0^{k^S} T\left(\frac{f}{k^S} u\right) f_U(u) du + bT(f) \int_{k^S}^{\infty} f_U(u) du + p_a \frac{fNd}{k^S} \int_0^{k^S} u f_U(u) du \right. \\ & \left. + p_a f Nd \int_{k^S}^{\infty} f_U(u) du + c \frac{fNd}{k^S} + p_r(f) fNd \int_{k^S}^{\infty} f_U(u) du \right] \\ \text{s.t. } & 0 \leq f \leq \bar{f} \end{aligned}$$

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 .

$$\begin{aligned} \frac{\partial GF_1}{\partial f} = & \left[\frac{b}{k^S} \int_0^{k^S} T'\left(\frac{f}{k^S} u\right) u f_U(u) du + bT'(f) \int_{k^S}^{\infty} f_U(u) du + p_a \frac{Nd}{k^S} \int_0^{k^S} u f_U(u) du \right. \\ & \left. + p_a Nd \int_{k^S}^{\infty} f_U(u) du + c \frac{Nd}{k^S} + p_r(f) Nd \int_{k^S}^{\infty} f_U(u) du + p_r'(f) fNd \int_{k^S}^{\infty} f_U(u) du \right] \\ = & \frac{Nd}{k^S} \left(\int_0^{k^S} \left[\frac{b}{Nd} T'\left(\frac{f}{k^S} u\right) + p_a \right] u f_U(u) du + c \right) \\ & + \left[bT'(f) + p_a Nd + p_r(f) Nd + p_r'(f) fNd \right] \int_{k^S}^{\infty} f_U(u) du \end{aligned} \quad (20)$$

We show that each of the two components in (20) is negative, making the derivative of GF_1 negative for all $0 \leq f \leq \bar{f}$. To see this, first note that the function $J(f) = \int_0^{k^S} \left[\frac{b}{Nd} T'\left(\frac{f}{k^S} u\right) + p_a \right] u f_U(u) du$ is an increasing function of f , as $J'(f) = \int_0^{k^S} \left[\frac{b}{Nd k^S} T''\left(\frac{f}{k^S} u\right) \right] u^2 f_U(u) \geq 0$. Hence $J(f) \leq J(\bar{f})$, $\forall f \leq \bar{f}$. However, using $\bar{f}Nd = n_E^S k^S$, we get $J(\bar{f}) = \int_0^{k^S} \left[\frac{b}{Nd} T'\left(\frac{n_E^S u}{Nd}\right) + p_a \right] u f_U(u) du = -c$ (by Proposition 6). As a result $J(f) + c \leq 0$, so

$$\int_0^{k^S} \left[\frac{b}{Nd} T'\left(\frac{f}{k^S} u\right) + p_a \right] u f_U(u) du + c \leq 0; \quad \forall 0 \leq f \leq \bar{f}$$

This shows that the first parenthesis in (20) 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 $bT'(f) + p_aNd + p_r(f)Nd + p'_r(f)fNd \leq bT'(\bar{f}) + p_aNd + p_r(\bar{f})Nd + p'_r(\bar{f})\bar{f}Nd$ for all $0 \leq f \leq \bar{f}$. Note that $bT'(\bar{f}) + p_aNd = 0$ by the definition of \bar{f} , and that $p_r(\bar{f})Nd + p'_r(\bar{f})\bar{f}Nd = 0$ by the second part of Assumption 5. This suggests

$$bT'(f) + p_aNd + p_r(f)Nd + p'_r(f)fNd \leq 0, \quad \forall 0 \leq f \leq \bar{f}$$

which shows 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 (20) 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 18). 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:

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

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:

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

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

We show the derivative of the objective function in this case is positive and hence GF_2 is minimized when that constraint is tight, i.e., $n_E = n_E^S$. Consider,

$$\frac{\partial GF_2}{\partial n_E} = \int_0^{\frac{\bar{f}Nd}{n_E}} \left[\frac{b}{Nd} T' \left(\frac{n_E u}{Nd} \right) + p_a \right] u f_U(u) du + c + p_r(\bar{f}) k^S \int_{k^S}^{\infty} f_U(u) du \quad (21)$$

The first term above is exactly the function $H(n_E)$ introduced in the proof of Proposition 7, and by using its nondecreasing property, we get $H(n_E) \geq H(n_E^S)$ for all $n_E \geq n_E^S$. However, Proposition 6 suggests $H(n_E^S) = \int_0^{\frac{\bar{f}Nd}{n_E^S}} \left[\frac{b}{Nd} T' \left(\frac{n_E^S u}{Nd} \right) + p_a \right] u f_U(u) du = -c$. This implies that

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

By using this result with (21), we obtain the desired result,

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

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

4.2.2 Coordinating Contract: Numerical Application

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 make a slight deviation from strict convexity.

Hill and Longini (2003) suggest $R_0 = 1.87$ and Weycker et al. (2005) argue that $\phi = 0.90$ is a reasonable value for vaccine effects. We use the data from Weycker et al. (2005) to estimate the direct costs (not indirect) of each infected individual, with to $b = \$95$ on average over the different groups. The vaccine price is set to $p_r = \$12$ (CDC, 2005). For vaccine administration costs, there are no explicit data, so we used $p_a = \$40$ as a base case, as did Weniger et al. (1998) for pediatric vaccines, being roughly the cost of doctor visit. We used $d = 1$ dose of vaccine, the usual value, per adult vaccinated. We are not aware of literature to define the variance of vaccine production yields, so we assumed that U has a gamma distribution with mean

$\mu = 1$ (Palese, 2006) and standard deviation $\sigma = 1/5 = 0.2$, so that $U \sim \text{Gamma}(25, 1/25)$. We assumed a population of $N = 10^7$ individuals and a production cost of $c = \$6$ (not necessarily the actual number).

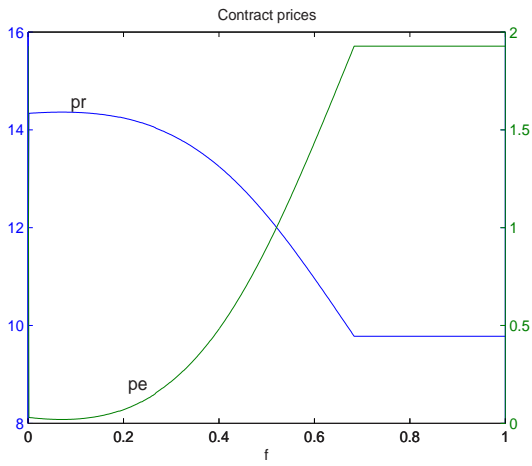
Figure 3 depicts the optimal contract, governmental costs and manufacturer profits, for the special case of $T(f)$ that is based upon the above parameters and a large initial epidemic wave (using $I_0 = 0.1$). While $T(f)$ in this case is not precisely convex (slight nonconvexity near $f = 0.08$), a strict application of the prices implied by (17) and Assumption 6 leads to a whole-unit discount price, $p_r(f)$ (scale on left-hand of y -axis of 3(a)), and cost sharing price $p_e(f)$ (scale on right-hand side of y -axis), that empirically coordinates incentives. The particular choice of $\kappa = 0.215$ for Figure 3 insures that the government overall vaccine procurement and health benefit costs are reduced by the contract from $\$528M$ to $\$527M$; that the government orders more (up from $f^G = 0.65$ to $\bar{f} = 0.68$); that the manufacturer is willing to produce more (n_E^* increases from $6.3M$ to $7M$); and that the manufacturer's profits increase (from $\$32.8M$ to $\$33.7M$).

For sensitivity analysis, we ran the contract under different administration costs [$p_a = \$20$, approximately the value in Pisano 2006 for Medicare reimbursement, and $p_a = \$60$]; and different values for health benefits [$b = \$275$, a value from Gessner 2000 converted into 2000 dollars, and $b = \$450$, the combined direct and indirect costs calculated using data from Weycker et al. 2005]. For values of $b \geq \$250$, we found $\bar{f} = 1$ due to the high benefit of vaccination compared with the cost of administration. In general, a smaller p_a or higher b will increase \bar{f} , and increasing p_a or decreasing b will decrease \bar{f} .

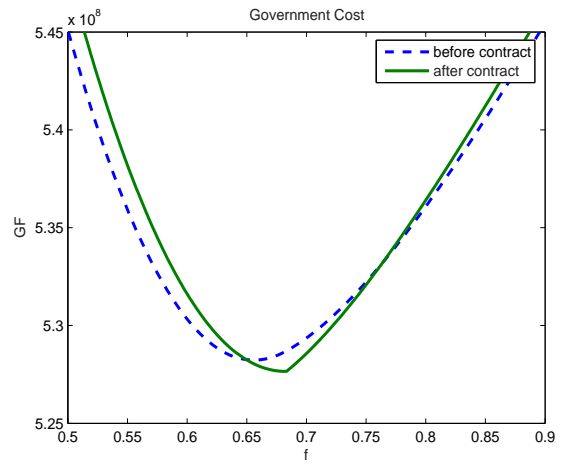
5 Discussion and Model Limitations

This work derived the equilibrium state of an interaction between a government and a manufacturer, with the realistic feature of a manufacturer that 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.

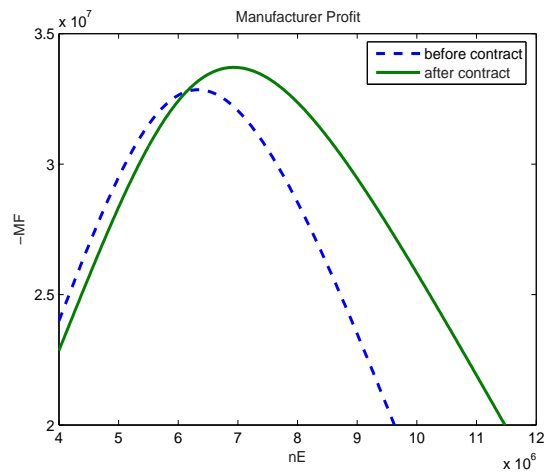
When the levels of exogenous introduction of influenza into a population are small, leading to the



(a) $p_r(f), p_e(f)$



(b) $GF(f)$



(c) $-MF(n_E)$

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

piecewise linear approximation for $T(f)$ in Section 3, 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 somewhat large, as in a large-wave pandemic situation, the analysis of Section 4 may be 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.

There are several limitations of this model. 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 or convex $T(f)$ allows some flexibility in adapting the incentive alignment results here to more complex epidemic models that account for the prioritization of certain subgroups.

Two, the analysis above assumes that the per person benefit b and the cost to administer p_a are constant. The results may generalize nicely to the case of variable marginal benefits of vaccination, $b(f)$, as long as $b(f)T(f)$ is convex. Terms like $bT'(f)$ in the definition of \bar{f} , for example, would be replaced with $(b(f)T(f))' = b'(f)T(f) + b(f)T'(f)$. Similarly, a convex increasing administration cost, $p_a(f)$, might be appropriate too. The net effect of these two changes is expected to decrease the optimal vaccination fraction.

Three, 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 the present work by assessing the number infected and applying the relevant morbidity and mortality rates.

Four, the model assumes that the government can precisely specify the number of individuals to vaccinate. This is potential drawback of the other epidemic models mentioned in this paper, too. The inclusion of individual's choice to become vaccinated would also require much additional complexity.

Five, the model currently examines a single manufacturer and a single government, and assumes that all parameters are known to all parties. The cost per dose and yield distributions are not likely to be public information, and there are several providers and many purchasers. Nevertheless the equilibrium still might still be modeled as an outcome of interactions between two rational actors of the model. Multiple buyers and suppliers would be an interesting extension. Contracts in the presence of multiple manufacturers and/or suppliers could be complicated, to avoid collusion on the part of a subset of the players.

6 Conclusion

This work developed the first integrated supply-chain/health economics model of two key players in the influenza vaccine supply chain: a government that purchase and administer vaccines in order to achieve an efficient cost-benefit tradeoff, and a manufacturer that optimizes production input levels to achieve cost-effective delivery of vaccines in the presence of yield uncertainty. The model indicates a lack of coordination for contracts that leave the manufacturer with the production yield risks. That lack of coordination results in vaccine production shortfalls.

We show that a global social optimum cannot be fully attained by changing the vaccine price alone, or by reducing the risk of production yields by having the government contractually pay a reduced rate for doses that are produced in excess of the original demand. A variation of the cost sharing contract is one option that can align incentives to achieve a social optimum.

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REFERENCES

- BRIDGES, C. B., K. FUKUDA., T. M. UYEKI., N. J. COX., AND J. A. SINGLETON. 2002. Prevention and control of influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recommendations and Reports* 51(RR03), 1–31.
- BUSH, G. W. 2005. President outlines pandemic influenza preparations and response. Accessed 22 January 2006 at <http://www.whitehouse.gov/news/releases/2005/11/20051101-1.html>.
- CDC 2005. Vaccine price list. Available from http://www.cdc.gov/nip/vfc/cdc_vac_price_list.htm.
- CHICK, S. E., D. C. BARTH-JONES., AND J. S. KOOPMAN. 2001. Bias reduction for risk ratio and vaccine effect estimators. *Statistics in Medicine* 20(11), 1609–1624.
- DIEKMANN, O. AND J. HEESTERBEEK. 2000. *Mathematical Epidemiology of Infectious Diseases*. Chichester: Wiley.
- DIETZ, K. 1993. The estimation of the basic reproduction number for infectious diseases. *Statistical Methods in Medical Research* 2, 23–41.
- GANI, R., H. HUGHES., D. FLEMING., T. GRIFFIN., J. MEDLOCK., AND S. LEACH. 2005. Potential impact of antiviral drug use during influenza pandemic. *Emerging Infectious Diseases* 11(9), 1355–1362.
- GERDIL, C. 2003. The annual production cycle for influenza vaccine. *Vaccine* 21, 1776–1779.

- GESSNER, B. D. 2000. The cost-effectiveness of a hypothetical respiratory syncytial virus vaccine in the elderly. *Vaccine 18*, 1485–1494.
- HILL, A. N. AND I. M. LONGINI. 2003. The critical fraction for heterogeneous epidemic models. *Mathematical Biosciences 181*, 85–106.
- JACQUEZ, J. A. 1996. *Compartmental Analysis in Biology and Medicine* (3rd ed.). Ann Arbor: BioMedware.
- JANEWAY, C. A., P. TRAVERS., M. WALPORT., AND M. SHLOMCHIK. 2001. *Immunobiology* (5th ed.). New York: Garland Publishing.
- LONGINI, I. M., E. ACKERMAN., AND L. R. ELVEBACK. 1978. An optimization model for influenza A epidemics. *Mathematical Biosciences 38*, 141–157.
- LONGINI, I. M., M. E. HALLORAN., A. NIZAM., M. WOLFF., P. M. MENDELMAN., P. E. FAST., AND R. B. BELSHE. 2000. Estimation of the efficacy of live, attenuated influenza vaccine from a two-year, multi-center vaccine trial: implications for influenza epidemic control. *Vaccine 18*, 1902–1909.
- NASH, J. F. 1951. Non-cooperative games. *Annals of Mathematics 54*, 286–295.
- NICHOL, K. L., K. L. MARGOLIS., J. WUORENMA., AND T. V. STERNBERG. 1994. The efficacy and cost effectiveness of vaccination against influenza among elderly persons living in the community. *The New England Journal of Medicine 331*(12), 778–784.
- PALESE, P. 2006. Making better influenza virus vaccines. *Emerging Infectious Diseases 12*(1), 61–65.
- PIEN, H. 2004. Statement presented to Committee on Aging, United States Senate, by President and CEO, Chiron Corporation. Accessed 22 January 2006 at http://aging.senate.gov/_files/hr133hp.pdf.
- PISANO, W. 2006. Keys to strengthening the supply of routinely recommended vaccines: View from industry. *Clinical Infectious Diseases 42*, S111–S117.

- SALUZZO, J.-F. AND C. LACROIX-GERDIL. 2006. *Grippe aviaire: Sommes-nous prêts?* Paris: Belin-Pour la Science.
- SMITH, P. G., L. C. RODRIGUES., AND P. E. FINE. 1984. Assessment of the protective efficacy of vaccines against common diseases using case-control and cohort studies. *International Journal of Epidemiology* 13(1), 87–93.
- U.S. DEPT. OF HEALTH AND HUMAN SERVICES 2005. HHS Pandemic influenza plan: Supplement 6–Vaccine distribution and use. Accessed 26 January 2006 at <http://www.dhhs.gov/pandemicflu/plan/>.
- WENIGER, B. G., R. T. CHEN., S. H. JACOBSON., E. C. SEWELL., R. DEMON., J. R. LIVENGOOD., AND W. A. ORENSTEIN. 1998. Addressing the challenges to immunization practice with an economic algorithm for vaccine selection. *Vaccine* 16(9), 1885–1897.
- WEYCKER, D., J. EDELSBERG., M. E. HALLORAN., I. M. LONGINI., A. NIZAM., V. CIURYLA., AND G. OSTER. 2005. Population-wide benefits of routine vaccination of children against influenza. *Vaccine* 23, 1284–1293.
- WHO 2005. Influenza vaccines. *Weekly Epidemiological Record* 80(33), 277–287, Accessed 21 Jan 2006 at <http://www.who.int/wer/2005/wer8033.pdf>.
- WU, J. T., L. M. WEIN., AND A. S. PERELSON. 2005. Optimization of influenza vaccine selection. *Operations Research* 53(3), 456–476.
- WYSOCKI, B. AND S. LUECK. 2006. Margin of safety: Just-in-time inventories make U.S. vulnerable in a pandemic. *Wall Street Journal*. 12 January 2006.
- YADAV, P. AND D. WILLIAMS. 2005. Value of creating a redistribution network for influenza vaccine in the U.S. Presentation at INFORMS 2006 Annual Conference, San Francisco.

A Appendix: Proofs of mathematical results

Proposition 1. *Proof:* The expected cost function for the manufacturer is

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

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

$$\begin{aligned}
 \frac{\partial MF}{\partial n_E} &= c - p_r \int_0^{\frac{fNd}{n_E}} u f_U(u) du - p_r n_E \left[\left(\frac{fNd}{n_E} \right) f_U\left(\frac{fNd}{n_E}\right) \left(-\frac{fNd}{n_E^2} \right) \right] - p_r fNd \left[-f_U\left(\frac{fNd}{n_E}\right) \left(-\frac{fNd}{n_E^2} \right) \right] \\
 &= c - p_r \int_0^{\frac{fNd}{n_E}} u f_U(u) du + p_r \frac{(fNd)^2}{n_E^2} f_U\left(\frac{fNd}{n_E}\right) - p_r \frac{(fNd)^2}{n_E^2} f_U\left(\frac{fNd}{n_E}\right) \\
 &= c - p_r \int_0^{\frac{fNd}{n_E}} u f_U(u) du
 \end{aligned}$$

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

$$\int_0^{\frac{fNd}{n_E^*}} u f_U(u) du = \frac{c}{p_r}$$

□

Corollary 1. *Proof:* Immediate upon inspection of the values of the parameters. □

Proposition 2. *Proof:* To show these results, we analyze SF in two different regions, $f \leq f^0$ and $f \geq f^0$.

Let $SF_1(f, n_E)$ denotes the value of SF when $f \leq f^0$, and likewise $SF_2(f, n_E)$ is the value of SF where $f \geq f^0$. Note that if $f \leq f^0$ then $W = Z = \min\{n_E U, fNd\}$, and the value of SF_1 is

$$\begin{aligned}
 SF_1(f, n_E) &= b \int_0^{\frac{fNd}{n_E}} \left(M - \psi \frac{n_E u}{d} \right) f_U(u) du + b(M - N\psi f) \int_{\frac{fNd}{n_E}}^{\infty} f_U(u) du \\
 &\quad + p_a n_E \int_0^{\frac{fNd}{n_E}} u f_U(u) du + p_a (fNd) \int_{\frac{fNd}{n_E}}^{\infty} f_U(u) du + cn_E \quad (f \leq f^0).
 \end{aligned} \tag{22}$$

For $f > f^0$, given that $M - N\psi f = M - N\psi f^0 = 0$, the value of SF is

$$SF_2(f, n_E) = b \int_0^{\frac{f^0 Nd}{n_E}} (M - \psi \frac{n_E u}{d}) f_U(u) du + p_a n_E \int_0^{\frac{f^0 Nd}{n_E}} u f_U(u) du + p_a (f^0 Nd) \int_{\frac{f^0 Nd}{n_E}}^{\infty} f_U(u) du + c n_E \quad (f \geq f^0). \quad (23)$$

The limits of integration in the right hand side of (23) use f^0 , not f . In order to get the overall optimal values for f^S, n_E^S , we solve the following two subproblems.

$$\begin{aligned} SF1 = \min \quad & SF_1 & SF2 = \min \quad & SF_2 \\ \text{s.t.} \quad & 0 \leq f \leq f^0 & \text{s.t.} \quad & f^0 \leq f \leq 1 \\ & n_E \geq 0 & & n_E \geq 0 \end{aligned}$$

Optimality conditions for subproblem $SF1$: The KKT conditions, if $f \leq f^0$, are,

$$-N\psi b \int_{\frac{fNd}{n_E}}^{\infty} f_U(u) du + p_a Nd \int_{\frac{fNd}{n_E}}^{\infty} f_U(u) du + \xi - \theta_0 = 0$$

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

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

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 $f \leq f^0, f \geq 0, n_E \geq 0$, respectively. 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:

$$[-N\psi b + p_a Nd] \int_{\frac{fNd}{n_E}}^{\infty} f_U(u) du + \xi = 0$$

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

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

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

$$\int_0^{\frac{f^0 Nd}{n_E^*}} u f_U(u) du = \frac{c}{\frac{\psi b}{d} - p_a}. \quad (24)$$

Optimality conditions for the problem SF_2 : If $f \geq f^0$, then SF_2 does not depend on f (the vaccine fraction declared by the government does not change the value of objective function). It follows that all values $f^0 \leq f \leq 1$ 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

$$\frac{\partial SF_2}{\partial n_E} = \left(-\frac{\psi b}{d} + p_a\right) \int_0^{\frac{f^0 Nd}{n_E}} u f_U(u) du + c.$$

Note that $\frac{\partial^2 SF_2}{\partial n_E^2} = \left(\frac{\psi b}{d} - p_a\right) \left(\frac{f^0 Nd}{n_E^2}\right) \left(\frac{f^0 Nd}{n_E}\right) f_U\left(\frac{f^0 Nd}{n_E}\right)$, 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 (24). So the optimum value for n_E^S satisfies the same equation in both cases. \square

Proposition 3. *Proof:* If we define GF_1, GF_1 like SF_1, SF_1 for the case where $f \leq f^0$, then GF_1 is:

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

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 $f = f^0$. This proves the first part of the claim.

For the second part, similarly define GF_2, GF_2 to represent the government objective functions for the cases $f \leq f^0$ and $f \geq f^0$, respectively. Using the fact that $T(f) = 0$ for all $f \geq f^0$, and the constraint In the second equation above, $f = \frac{n_E k^G}{Nd}$, to obtain

$$\begin{aligned}
 GF_2(f, n_E) &= b \int_0^{\frac{f^0 Nd}{n_E}} (M - \psi \frac{n_E u}{d}) f_U(u) du + p_a n_E \int_0^{\frac{f^0 Nd}{n_E}} u f_U(u) du + p_r n_E \int_0^{k^G} u f_U(u) du \\
 &\quad + p_a (f^0 Nd) \int_{\frac{f^0 Nd}{n_E}}^{\infty} f_U(u) du + p_r (f^0 Nd) \int_{k^G}^{\infty} f_U(u) du \\
 &= b \int_0^{\frac{f^0 Nd}{n_E}} (M - \psi \frac{n_E u}{d}) f_U(u) du + p_a n_E \int_0^{\frac{f^0 Nd}{n_E}} u f_U(u) du + p_a (f^0 Nd) \int_{\frac{f^0 Nd}{n_E}}^{\infty} f_U(u) du \\
 &\quad + p_r n_E [\int_0^{k^G} u f_U(u) du + k^G \int_{k^G}^{\infty} f_U(u) du] \\
 \frac{\partial GF_2}{\partial n_E} &= (-\frac{\psi b}{d} + p_a) \int_0^{\frac{f^0 Nd}{n_E}} u f_U(u) du + p_r \int_0^{k^G} u f_U(u) du + p_r k^G \int_{k^G}^{\infty} f_U(u) du \\
 \frac{\partial^2 GF_2}{\partial n_E^2} &= (\frac{\psi b}{d} - p_a) \frac{f^0 Nd}{n_E^2} f_U(\frac{f^0 Nd}{n_E})
 \end{aligned}$$

for $f \geq f^0$. Note that $\frac{f^0 Nd}{n_E} \leq k^G$. 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 (12) holds, then Assumption 2 implies that $\frac{\partial GF_2}{\partial n_E} \geq 0$ on $f \geq f^0$, so that the minimum of GF_2 for $f \in [f^0, 1]$ is obtained at f^0 . The optimum for both GF_1 and GF_2 lead to the claimed optimum, namely $f^G = f^0$.

If Condition (12) does not hold (i.e. $(-\frac{\psi b}{d} + p_a + p_r) \int_0^{k^G} u f_U(u) du + p_r k^G \int_{k^G}^{\infty} f_U(u) du < 0$); then because of the convexity of function GF_2 on n_E (non-decreasing derivative), there are two cases:

Case 1: $\exists \tilde{n}_E$; $\frac{\partial GF_2}{\partial \tilde{n}_E} = 0$. 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 $\frac{\partial GF_2}{\partial n_E} < 0$ then $f^G = 1, n_E^G = n_E(1)$.

Combined, the two cases complete the proof. \square

Theorem 1. *Proof:* Proposition 2 shows that $f^G \geq f^0$. We consider the two cases $f^G = f^0$ and $f^G > f^0$ separately, and prove that both cases lead to the relation $n_E^S > n_E^G$.

Case 1: $f^G = f^0$. 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: $f^G > f^0$. (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:

$$\left[\frac{\partial GF_2}{\partial n_E}\right]_{n_E^G} \leq 0 \quad (25)$$

On the other hand,

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

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 (5) and Proposition 2. But the last inequality contradicts (25), so $n_E^G \geq n_E^S$ is false. \square

Proposition 4. *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 $\left.\frac{\partial GF}{\partial n_E}\right|_{n_E^G} > 0$, which would not be true for the optimizer of GF . \square

Theorem 2. *Proof:* First we show that $f^e \geq f^0$ by showing that optimum value for GF_1 for $f \in [0, f^0]$ is always obtained at f^0 . By replacing $f = \frac{k^e n_E}{Nd}$ we get GF_1 to be only a function of n_E :

$$GF_1(n_E) = b \int_0^{k^e} (M - \psi \frac{n_E u}{d}) f_U(u) du + b(M - N\psi \frac{n_E k^e}{Nd}) \int_{k^e}^{\infty} f_U(u) du \\ + (p_a + p_r) n_E \int_0^{k^e} u f_U(u) du + (p_a + p_r) (k^e n_E) \int_{k^e}^{\infty} f_U(u) du + p_e n_E$$

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

$$\begin{aligned} \frac{\partial GF_1}{\partial n_E} &= -\frac{\psi b}{d} \int_0^{k^e} u f_U(u) du - \frac{\psi b}{d} k^e \int_{k^e}^{\infty} f_U(u) du \\ &\quad + (p_a + p_r) \int_0^{k^e} u f_U(u) du + (p_a + p_r) k^e \int_{k^e}^{\infty} f_U(u) du + p_e \\ &= (-\frac{\psi b}{d} + p_a) \int_0^{k^S} u f_U(u) du + p_r \int_0^{k^e} u f_U(u) du \end{aligned} \quad (26)$$

$$\begin{aligned} &\quad + (-\frac{\psi b}{d} + p_a + p_r) k^e \int_{k^e}^{\infty} f_U(u) du + p_e \\ &= -c + (c - p_e) + (-\frac{\psi b}{d} + p_a + p_r) k^e \int_{k^e}^{\infty} f_U(u) du + p_e \end{aligned} \quad (27)$$

$$= (-\frac{\psi b}{d} + p_a + p_r) k^e \int_{k^e}^{\infty} f_U(u) du, \quad (28)$$

in which (26) is obtained because $k^e = k^S$, and (27) is obtained using Proposition 2 and (14). On the other hand (28) is negative by Assumption 3, so that GF_1 is decreasing for all eligible n_E . Hence f^0 and the corresponding n_E (i.e. $n_E = \frac{f^0 Nd}{k^e} = \frac{f^0 Nd}{k^S}$) are optimal in this case. So $f^e \geq f^0$. 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 $f \in [f^0, 1]$, also occurs at f^0 , completing the proof. Note that $f \geq f^0$ and $k^e = k^S$ imply that $n_E \geq n_E^S$. Consider GF_2 .

$$GF_2(n_E) = b \int_0^{\frac{f^0 Nd}{n_E}} (M - \psi \frac{n_E u}{d}) f_U(u) du + p_a n_E \int_0^{\frac{f^0 Nd}{n_E}} u f_U(u) du + p_a f^0 Nd \int_{\frac{f^0 Nd}{n_E}}^{\infty} f_U(u) du \\ + p_r n_E \int_0^{k^e} u f_U(u) du + p_r (k^e n_E) \int_{k^e}^{\infty} f_U(u) du + p_e n_E$$

The derivative is nonnegative,

$$\begin{aligned} \frac{\partial GF_2}{\partial n_E} &= \left(-\frac{\psi b}{d} + p_a\right) \int_0^{\frac{f^0 Nd}{n_E}} u f_U(u) du + p_r \int_0^{k^e} u f_U(u) du + p_r k^e \int_{k^e}^{\infty} f_U(u) du + p_e \\ &= \left(-\frac{\psi b}{d} + p_a\right) \int_0^{\frac{f^0 Nd}{n_E}} u f_U(u) du + c + p_r k^e \int_{k^e}^{\infty} f_U(u) du \end{aligned} \quad (29)$$

$$\geq \left(-\frac{\psi b}{d} + p_a\right) \int_0^{\frac{f^0 Nd}{n_E^S}} u f_U(u) du + c + p_r k^e \int_{k^e}^{\infty} f_U(u) du \quad (30)$$

$$= p_r k^e \int_{k^e}^{\infty} f_U(u) du \geq 0 \quad (31)$$

(29) comes from (14). As before, (30) comes from Assumption 2 and the fact that $n_E \geq n_E^S$. Finally, (31) is true by Proposition 2. The last inequality shows that the optimum value for GF_2 occurs at f^0 hence $f^e = f^0$ and because of the fact that $k^e = k^S$, we obtain $n_E^e = n_E^S$. \square

Proposition 6. *Proof:* The proof resembles the proof of Proposition 2, except for the change in role of f^0 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 :

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

If $f < \bar{f}$, then by the convexity of $T(f)$ and the definition in (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:

$$\int_0^{\frac{\bar{f}Nd}{n_E^*}} \left[\frac{b}{Nd} T'\left(\frac{n_E^* u}{Nd}\right) + p_a \right] u f_U(u) du + c = 0, \text{ as claimed.}$$

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:

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

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 $\int_0^{\frac{\bar{f}Nd}{n_E^S}} \left[\frac{b}{Nd} T' \left(\frac{n_E^S u}{Nd} \right) + p_a \right] u f_U(u) du + c = 0$. \square

Proposition 5. *Proof:* Note that $\int_0^{k^N} u f_U(u) du = \frac{c - p_c \mu}{p_r - p_c}$. By rewriting the GF in terms of values of f , n_E and by replacing $f = \frac{k^N n_E}{Nd}$ we have:

$$\begin{aligned} GF(n_E) = & b \int_0^{\frac{f^0 Nd}{n_E}} \left(M - \psi \frac{n_E u}{d} \right) f_U(u) du + p_a n_E \int_0^{\frac{f^0 Nd}{n_E}} u f_U(u) du + p_a (f^0 Nd) \int_{\frac{f^0 Nd}{n_E}}^{\infty} f_U(u) du \\ & + (p_r - p_c) n_E \int_0^{k^N} u f_U(u) du + (p_r - p_c) (k^N n_E) \int_{k^N}^{\infty} f_U(u) du + p_c \mu n_E \end{aligned}$$

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

$$\begin{aligned} \frac{\partial GF}{\partial n_E} = & \left(-\frac{ab}{d} + p_a \right) \int_0^{\frac{f^0 Nd}{n_E}} u f_U(u) du + p_c \mu \\ & + (p_r - p_c) \left[\int_0^{k^N} u f_U(u) du + k^N \int_{k^N}^{\infty} f_U(u) du \right] \\ = & \left(-\frac{ab}{d} + p_a \right) \int_0^{\frac{f^0 Nd}{n_E}} u f_U(u) du + c + (p_r - p_c) k^N \int_{k^N}^{\infty} f_U(u) du \end{aligned}$$

The last inequality comes from (13). 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 $\left. \frac{\partial GF}{\partial n_E} \right|_{n_E^S} = (p_r - p_c) k^N \int_{k^N}^{\infty} f_U(u) du > 0$. That implies that $n_E^N < n_E^S$. \square

Proposition 7. *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, note that if $\int_0^{k^G} \left[\frac{b}{Nd} T'(\frac{\bar{n}_E u}{Nd}) + p_a \right] u f_U(u) du + c + p_r k^G \int_{k^G}^{\infty} f_U(u) du < 0$, then by replacing $f = \frac{n_E k^G}{Nd}$, we can rewrite GF_1 just as a function of n_E as follows:

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

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

$$\begin{aligned} \frac{\partial GF_1}{\partial n_E} &= \int_0^{k^G} \left[\frac{b}{Nd} T'(\frac{n_E u}{Nd}) + p_a \right] u f_U(u) du + p_r \int_0^{k^G} u f_U(u) du \\ &\quad + \frac{k^G}{Nd} \left[b T'(\frac{n_E k^G}{Nd}) + p_a Nd \right] \int_{k^G}^{\infty} f_U(u) du + p_r k^G \int_{k^G}^{\infty} f_U(u) du \\ &= \int_0^{k^G} \left[\frac{b}{Nd} T'(\frac{n_E u}{Nd}) + p_a \right] u f_U(u) du + c + p_r k^G \int_{k^G}^{\infty} f_U(u) du \\ &\quad + \frac{k^G}{Nd} \left[b T'(\frac{n_E k^G}{Nd}) + p_a Nd \right] \int_{k^G}^{\infty} f_U(u) du \end{aligned} \tag{32}$$

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: $\frac{\partial GF_1}{\partial n_E} \leq \left[\frac{\partial GF_1}{\partial n_E} \right]_{n_E = \bar{n}_E}$. On the other hand if we plug \bar{n}_E into (32) we have:

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

in which the last equality comes from the fact that $\bar{n}_E = \frac{\bar{f} Nd}{k^G}$, and recalling (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

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

is a nondecreasing function on n_E .

$$\begin{aligned} \frac{\partial H}{\partial n_E} &= \int_0^{\frac{\bar{f} Nd}{n_E}} \left[\frac{b}{(Nd)^2} T''(\frac{n_E u}{Nd}) \right] u^2 f_U(u) du + \left[\frac{b}{Nd} T'(\bar{f}) + p_a \right] \frac{\bar{f} Nd}{n_E} f_U\left(\frac{\bar{f} Nd}{n_E}\right) \times \left(-\frac{\bar{f} Nd}{n_E^2}\right) \\ &= \int_0^{\frac{\bar{f} Nd}{n_E}} \left[\frac{b}{(Nd)^2} T''(\frac{n_E u}{Nd}) \right] u^2 f_U(u) du \geq 0 \end{aligned}$$

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,

$$\int_0^{\frac{\bar{f}Nd}{n_E}} \left[\frac{b}{Nd} T' \left(\frac{n_E u}{Nd} \right) + p_a \right] u f_U(u) du \geq \int_0^{\frac{\bar{f}Nd}{\bar{n}_E}} \left[\frac{b}{Nd} T' \left(\frac{\bar{n}_E u}{Nd} \right) + p_a \right] u f_U(u) du \quad ; \forall n_E \geq \bar{n}_E \quad (33)$$

If we assume $\int_0^{k^G} \left[\frac{b}{Nd} T' \left(\frac{\bar{n}_E u}{Nd} \right) + p_a \right] u f_U(u) du + c + p_r k^G \int_{k^G}^{\infty} f_U(u) du \geq 0$ 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

$$\begin{aligned} GF_2(n_E) &= b \int_0^{\frac{\bar{f}Nd}{n_E}} T \left(\frac{n_E u}{Nd} \right) f_U(u) du + b T \left(\frac{n_E k^G}{Nd} \right) \int_{\frac{\bar{f}Nd}{n_E}}^{\infty} f_U(u) du + p_r n_E \int_0^{k^G} u f_U(u) du \quad (34) \\ &\quad + p_r (n_E k^G) \int_{k^G}^{\infty} f_U(u) du + p_a n_E \int_0^{\frac{\bar{f}Nd}{n_E}} u f_U(u) du + p_a (\bar{f}Nd) \int_{\frac{\bar{f}Nd}{n_E}}^{\infty} f_U(u) du \\ \frac{\partial GF_2}{\partial n_E} &= \int_0^{\frac{\bar{f}Nd}{n_E}} \left[\frac{b}{Nd} T' \left(\frac{n_E u}{Nd} \right) + p_a \right] u f_U(u) du + p_r \int_0^{k^G} u f_U(u) du + p_r k^G \int_{k^G}^{\infty} f_U(u) du \\ &= \int_0^{\frac{\bar{f}Nd}{n_E}} \left[\frac{b}{Nd} T' \left(\frac{n_E u}{Nd} \right) + p_a \right] u f_U(u) du + c + p_r k^G \int_{k^G}^{\infty} f_U(u) du \quad (35) \\ &\geq \int_0^{\frac{\bar{f}Nd}{\bar{n}_E}} \left[\frac{b}{Nd} T' \left(\frac{\bar{n}_E u}{Nd} \right) + p_a \right] u f_U(u) du + c + p_r k^G \int_{k^G}^{\infty} f_U(u) du \geq 0 \end{aligned}$$

The second equality for $\frac{\partial GF_2}{\partial n_E}$ comes from (5). If $f \geq \bar{f}$ then $n_E \geq \bar{n}_E$, so the inequality in the third line is justified by (33). 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. \square

Lemma 1. *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 7, which was shown to be nondecreasing, and $n_E^G \geq n_E^S$ to conclude that

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

By plugging n_E^G into the derivative function of GF_2 in (35), and using the above relation,

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

The equality in the third line comes from (6). 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. \square

Lemma 2. *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 GF_1 to analyze the pair $(\bar{\bar{f}}, \bar{\bar{n}}_E)$.

$$\begin{aligned} \left[\frac{\partial GF_1}{\partial n_E} \right]_{n_E=\bar{\bar{n}}_E} &= \int_0^{k^G} \left[\frac{b}{Nd} T' \left(\frac{\bar{\bar{n}}_E u}{Nd} \right) + p_a + p_r \right] u f_U(u) du \\ &\quad + \frac{k^G}{Nd} \left[b T' \left(\frac{\bar{\bar{n}}_E k^G}{Nd} \right) + p_a Nd + p_r Nd \right] \int_{k^G}^{\infty} f_U(u) du \\ &= \int_0^{k^G} \left[\frac{b}{Nd} T' \left(\frac{\bar{\bar{n}}_E u}{Nd} \right) + p_a + p_r \right] u f_U(u) du < 0 \end{aligned}$$

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 $f^G > \bar{\bar{f}}$. \square

Lemma 3. *Proof:* To prove the lemma, we show that $I(k) = \int_0^k \left[\frac{b}{Nd} T' \left(\frac{n_E^S u}{Nd} \right) + p_a \right] u f_U(u) du$ attains its minimum at $k^* = k^S$. The derivative of $I(k)$ is $\frac{\partial I}{\partial k} = \left[\frac{b}{Nd} T' \left(\frac{n_E^S k}{Nd} \right) + p_a \right] k f_U(k)$. Note that for $k < k^S$, we have $\frac{kn_E^S}{Nd} < \frac{k^S n_E^S}{Nd} = \bar{f}$, 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 $\frac{kn_E^S}{Nd} > \bar{f}$ so $\frac{\partial I}{\partial k} > 0$, and $I(k)$ is increasing. Therefore $I(k)$ attains its minimum at k^S . \square

Theorem 3. *Proof:* The proof is by contradiction, namely let's 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 $\left[\frac{\partial GF_1}{\partial n_E}\right]_{n_E=n_E^G} = 0$. By plugging n_E^G into (32), we have

$$\begin{aligned}
 0 &= \int_0^{k^G} \left[\frac{b}{Nd} T' \left(\frac{n_E^G u}{Nd} \right) + p_a \right] u f_U(u) du + c \\
 &\quad + \frac{k^G}{Nd} \left[b T' \left(\frac{n_E^G k^G}{Nd} \right) + p_a Nd + p_r Nd \right] \int_{k^G}^{\infty} f_U(u) du \\
 &= \int_0^{k^G} \left[\frac{b}{Nd} T' \left(\frac{n_E^G u}{Nd} \right) + p_a \right] u f_U(u) du + c \\
 &\quad + \frac{k^G}{Nd} \left[b T'(f^G) + p_a Nd + p_r Nd \right] \int_{k^G}^{\infty} f_U(u) du \quad ; \text{(because of } n_E^G k^G = f^G Nd \text{)} \\
 &> \int_0^{k^G} \left[\frac{b}{Nd} T' \left(\frac{n_E^G u}{Nd} \right) + p_a \right] u f_U(u) du + c \quad ; \text{(Lemma 2 and convexity of } T(f) \text{)} \quad (36)
 \end{aligned}$$

On the other hand note that the function $J(n_E) = \int_0^k \left[\frac{b}{Nd} T' \left(\frac{n_E u}{Nd} \right) + p_a \right] u f_U(u) du$ is an increasing function of n_E . This is because $\frac{\partial J}{\partial n_E} = \int_0^k \left[\frac{b}{(Nd)^2} T'' \left(\frac{n_E u}{Nd} \right) \right] u^2 f_U(u) du \geq 0$, 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 $k = k^G$,

$$\int_0^{k^G} \left[\frac{b}{Nd} T' \left(\frac{n_E^G u}{Nd} \right) + p_a \right] u f_U(u) du \geq \int_0^{k^G} \left[\frac{b}{Nd} T' \left(\frac{n_E^S u}{Nd} \right) + p_a \right] u f_U(u) du \quad (37)$$

If $\int_0^{k^G} \left[\frac{b}{Nd} T' \left(\frac{n_E^S u}{Nd} \right) + p_a \right] u f_U(u) du \geq \int_0^{k^S} \left[\frac{b}{Nd} T' \left(\frac{n_E^S u}{Nd} \right) + p_a \right] u f_U(u) du$, then (37) implies

$$\begin{aligned}
 \int_0^{k^G} \left[\frac{b}{Nd} T' \left(\frac{n_E^G u}{Nd} \right) + p_a \right] u f_U(u) du + c &\geq \int_0^{k^S} \left[\frac{b}{Nd} T' \left(\frac{n_E^S u}{Nd} \right) + p_a \right] u f_U(u) du + c \\
 &= 0 \quad ; \text{(by Proposition 6),}
 \end{aligned}$$

which contradicts (36). So we should have:

$$\int_0^{k^G} \left[\frac{b}{Nd} T' \left(\frac{n_E^S u}{Nd} \right) + p_a \right] u f_U(u) du < \int_0^{k^S} \left[\frac{b}{Nd} T' \left(\frac{n_E^S u}{Nd} \right) + p_a \right] u f_U(u) du$$

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: $[\frac{\partial GF_1}{\partial n_E}]_{\bar{n}_E} \leq 0$ or equivalently:

$$\begin{aligned} 0 &\geq \int_0^{k^G} \left[\frac{b}{Nd} T' \left(\frac{\bar{n}_E u}{Nd} \right) + p_a \right] u f_U(u) du + c + p_r k^G \int_{k^G}^{\infty} f_U(u) du \\ &\quad + \frac{k^G}{Nd} \left[b T' \left(\frac{\bar{n}_E k^G}{Nd} \right) + p_a Nd \right] \int_{k^G}^{\infty} f_U(u) du \\ &= \int_0^{k^G} \left[\frac{b}{Nd} T' \left(\frac{\bar{n}_E u}{Nd} \right) + p_a \right] u f_U(u) du + c + p_r k^G \int_{k^G}^{\infty} f_U(u) du \\ &> \int_0^{k^G} \left[\frac{b}{Nd} T' \left(\frac{\bar{n}_E u}{Nd} \right) + p_a \right] u f_U(u) du + c \end{aligned}$$

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

$$\int_0^{\frac{\bar{f}Nd}{\bar{n}_E}} \left[\frac{b}{Nd} T' \left(\frac{\bar{n}_E u}{Nd} \right) + p_a \right] u f_U(u) du + c < 0 \quad (38)$$

Note however that $\bar{n}_E = n_E^G \geq n_E^S$. By the monotonicity of the function $H(n_E)$ from Proposition 7,

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

which contradicts (38). Since both cases lead to a contradiction, the claim is proven. \square

Claim 1. *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 $f \in (\bar{f}, \infty)$, 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 $(p_r(f)fNd)'' = -\kappa b T''(f)$. So $bT''(f) + (p_r(f)fNd)'' = (1 - \kappa)bT''(f)$. But $bT''(f) + (p_r(f)fNd)''$ 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 $(p_r(f)fNd)$ we have: $(p_r(f)fNd)' = \kappa b[-T'(f) + T'(\bar{f})]$ which is nonnegative for $0 \leq f \leq \bar{f}$ (by convexity of $T(f)$) and is zero for $f = \bar{f}$. For $\bar{f} < f \leq 1$; $(p_r(f)fNd)' = p_r(\bar{f})Nd \geq 0$.

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

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

The numerator in the bracket is positive due to convexity of $T(f)$ indicating the desired result for $0 \leq f \leq \bar{f}$.

Finally, for $\bar{f} < f \leq 1$ we have $p_r'(f) = 0$. \square

B Appendix: Justification why linear and convex $T(f)$ are of interest

Figures 2 and 4 show the shape of $T(f)$ with respect to different values of I_0 and 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 $I_0 = 0, 0.005, 0.01, 0.05, 0.1$. The graphs look like a piecewise linear function as I_0 moves towards smaller values (thick blue curve). If I_0 is sufficiently large, then $T(f)$ looks strictly convex. This section formalizes those statements.

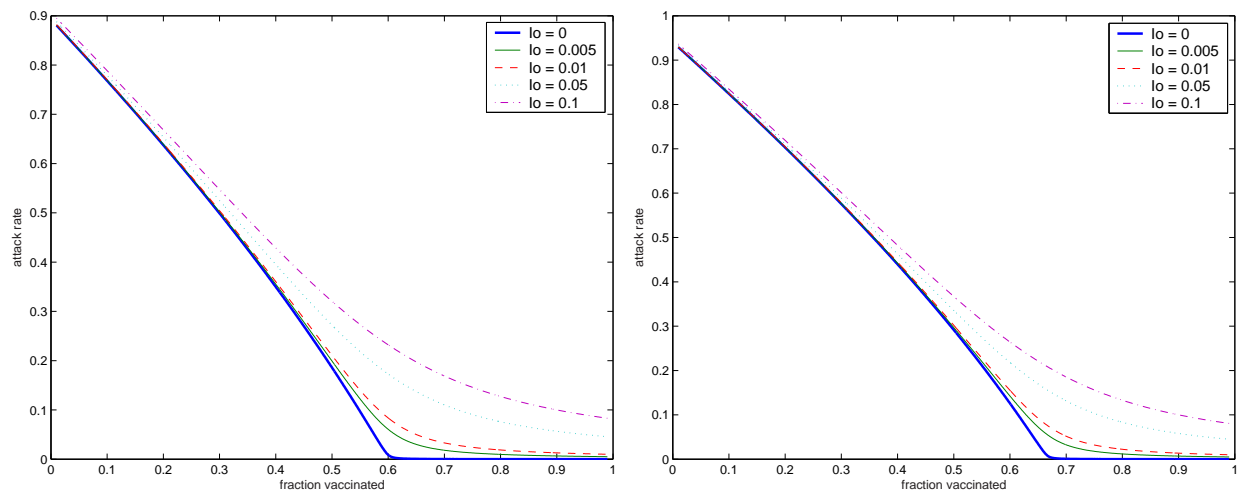
Piecewise linear. If the initial fraction of the population that is infected due to exogenous exposure (I_0 close to 0), then we can replace I_0/S_0 by zero in (3) and conclude:

$$\frac{p}{1 - e^{-R_0 p}} = S_0 = 1 - \phi f \tag{39}$$

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

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



(a) $R_0 = 2.5$

(b) $R_0 = 3.0$

Figure 4: Attack rate versus f for different values of I_0 and R_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

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

Hence by plugging this last equation instead of $\frac{p}{1 - e^{-R_0 p}}$ into (39) we have the following linear relationship between attack rate and vaccination fraction:

$$p = \left(1 - \frac{1}{R_0}\right) - \phi f$$

Note that the above line has a zero intercept at $f = \frac{R_0 - 1}{R_0 \phi}$, which is exactly the critical vaccine 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

$$T(f) = \begin{cases} N(1 - 1/R_0) - N\phi f, & 0 \leq f \leq f^0 \\ 0, & f^0 \leq f \leq 1 \end{cases} \quad (40)$$

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 (39) when $f = 0$; and by replacing the usual individual-level vaccine effect parameter, ϕ , with the marginal population-level benefit of infections averted, ψ , by additional vaccinations. (The two are not necessarily the same, due to nonlinear infection dynamics.)

Convex case. We now derive some of the properties of $T(f)$ to argue that it is convex when I_0 is sufficiently large. Recall (3) for the attack rate, and set $S_0 = 1 - I_0 - \phi f$ to obtain

$$\frac{p - I_0}{1 - e^{-R_0 p}} + I_0 = 1 - \phi f. \quad (41)$$

(41) gives rise to the relation $p \geq I_0$, as $1 - I_0 - \phi f = S_0 \geq 0$. This is expected. If the initial infected population is I_0 then the fraction that is ultimately infected should be at least I_0 .

Our goal is to show that p is a convex function of f . Notice that in (41) p is an implicit function of f and to find its second derivative we will use the following lemma from calculus.

Lemma 4 *If $y = f(x)$ then*

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

We rearrange (41) in terms of f to obtain

$$f = \frac{1}{\phi} \left[1 - I_0 - \frac{p - I_0}{1 - e^{-R_0 p}} \right].$$

Using the above lemma for $y = f$ and $x = p$ it turns out: $f(p) = \frac{1}{\phi} \left[1 - I_0 - \frac{p - I_0}{1 - e^{-R_0 p}} \right]$. So

$$f'(p) = -\frac{1}{\phi} \left[\frac{1 - e^{-R_0 p} - e^{-R_0 p}(p - I_0)}{(1 - e^{-R_0 p})^2} \right]$$

First of all we show that $f'(p) \leq 0$. To prove this notice that (41) suggests we can replace $p - I_0$ by $(1 - e^{-R_0 p})(1 - I_0 - \phi f)$ in the above relation. So by extending the numerator in $f'(p)$:

$$\begin{aligned}
 1 - e^{-R_0 p} - e^{-R_0 p}(p - I_0) &= 1 - e^{-R_0 p} - e^{-R_0 p}(1 - e^{-R_0 p})(1 - I_0 - \phi f) \\
 &\geq 1 - e^{-R_0 p} - e^{-R_0 p}(1 - e^{-R_0 p})(1 - I_0) \\
 &= (1 - e^{-R_0 p})(1 - (1 - I_0)e^{-R_0 p}) \\
 &\geq (1 - e^{-R_0 p})(1 - e^{-R_0 p}) \geq 0
 \end{aligned}$$

The last inequality together with the definition of $f'(p)$ suggests that $f'(p) \leq 0$.

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

$$f''(p) = -\frac{1}{\phi} \left[\frac{-(R_0 + 1)e^{-R_0 p}(1 - e^{-R_0 p})^2 + R_0(p - I_0)e^{-R_0 p}(1 - e^{R_0 p})(1 + e^{R_0 p})}{(1 - e^{-R_0 p})^4} \right]$$

Note that if the second derivative of $f(p)$ were nonnegative, then by the nonpositivity of $f'(p)$ and using the 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 I_0 far enough from zero. To show this, we evaluate the sign of the $f''(p)$'s numerator, $-(R_0 + 1)e^{-R_0 p}(1 - e^{-R_0 p})^2 + R_0(p - I_0)e^{-R_0 p}(1 - e^{R_0 p})(1 + e^{R_0 p}) = e^{-R_0 p}(1 - e^{R_0 p})[-(R_0 + 1)(1 - e^{R_0 p}) + R_0(p - I_0)(1 + e^{R_0 p})]$. So it is enough to find the sign of $-(R_0 + 1)(1 - e^{R_0 p}) + R_0(p - I_0)(1 + e^{R_0 p})$ which is hoped to be negative.

$$\begin{aligned}
 -(R_0 + 1)(1 - e^{R_0 p}) + R_0(p - I_0)(1 + e^{R_0 p}) &\leq -(R_0 + 1)(1 - e^{R_0 p}) + R_0(1 - I_0)(1 + e^{R_0 p}) \\
 &\leq -(R_0 + 1)(1 - e^{R_0 p}) + R_0(p - I_0)(1 + e^{-R_0 I_0})
 \end{aligned}$$

The first inequality is obtained because $p \leq 1$. The second inequality is obtained because the right hand side of the first inequality is a decreasing function of p and obtains its maximum at I_0 (as $p \geq I_0$).

The last statement in the above relation is a decreasing function of I_0 , and for $I_0 = 0$ it is positive, however it is negative for all $I_0 \geq 0.1$, for the range of R_0 that we are considering ($1.5 \leq R_0 \leq 3$). For

those values of I_0 , R_0 , this shows that $-(R_0 + 1)(1 - e^{R_0 p}) + R_0(p - I_0)(1 + e^{-R_0 p})$ is negative. Therefore $f''(p)$ is positive in this range, showing the desired convexity result for $I_0 \gg 0$.