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A Game-Theoretic Model of International Influenza Vaccination Coordination

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Influenza vaccination decisions in one country can influence the size of an outbreak in other countries due to interdependent risks from infectious disease transmission. This paper examines the inefficiency in the allocation of influenza vaccines that is due to interdependent risk of infection across borders and proposes a contractual mechanism to reduce such inefficiencies. The proposed contract is based on an epidemic model that accounts for intranational transmission and that from a source country where the dominant strain emerges. The contract reduces the overall financial burden of infection globally and improves the total number infected by seasonal influenza outbreaks. This is consistent with recent recommendations to improve pandemic preparedness. Numerical experiments demonstrate that the benefits of the contract can prevent millions of influenza cases and save tens of millions of dollars, and that the benefits are even greater when cross-border transmission is higher, even if cross-border transmission parameters have moderate estimation errors.

Key words: healthcare management; game theory; incentives and contracting; public policy
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Influenza is an acute respiratory illness that spreads rapidly in seasonal outbreaks and that results in 300,000 to 500,000 deaths globally each year (World Health Organization 2008). The World Health Organization (WHO) also reports that the yearly costs of healthcare, lost days of work and schooling, and social disruption range between $1 million and $6 million per 100,000 inhabitants in industrialized countries (World Health Organization 2005). The World Bank (Burns et al. 2008) forecasts that economic losses from a global pandemic can range between $2 trillion and $3 trillion.

Vaccination is a key tool for controlling influenza. Vaccination programs involve several operational challenges. The challenge that is the focus of this paper is the coordination of incentives of different purchasers of influenza vaccines. Such incentives lead to a suboptimal allocation of vaccines for annual influenza relative to the objective of minimizing the global financial burden of influenza.

There are several reasons for such misaligned incentives, including interdependent risks due to transnational disease transmission as well as different economic sensitivities to influenza outbreaks in different countries that result in different objectives and hence in different decisions made by the governments of those countries. For instance, the bulk of vaccines may be allocated to wealthier developed countries, such as the United States and Western European countries, because of high economic costs of infection. That said, influenza outbreaks typically start in Southeast Asia, and transmission there can influence transmission globally. Such countries may be less able to afford vaccines in large quantities to counter seasonal or pandemic influenza.

In 2007, Indonesia stopped its voluntary sharing of the strains for human cases of the avian influenza to the WHO, arguing that Indonesia did not receive the benefit of the vaccines produced from their samples and that it was challenging to buy large vaccine quantities without external support (Gelling 2007). Garrett and Fidler (2007) report that Indonesia asked itself, "What's in it for us? We share virus samples, and pharmaceutical companies make vaccines from them that primarily benefit rich countries. Without better access

to vaccine, why should we share virus samples?" Some developed countries agree. Perry (2007) quotes Australia's former Health Minister Tony Abbott: "I think it is important that we work out fair international arrangements for ensuring that we don't get a situation where some countries get the disease and some countries get the vaccine."

To address these types of concerns, initiatives have been set forth to ensure that regions that are the source of infection receive guaranteed vaccine quantities. Garrett and Fidler (2007) propose that updated supplies of about 500 million doses of vaccine together with antiviral medicines, protective masks, and supplies be stockpiled in Hong Kong every year. The World Health Organization and UNICEF (2007) outline potential roles for the Global Alliance for Vaccines and Immunization (GAVI) to prepare for pandemic influenza, including the increased use of seasonal influenza vaccines to create market-driven production by the vaccine industry. Options include financial support for cold supply chains and working with industry and academics to assess the potential impact of increasing supply and provision to developing countries.

This paper uses a game-theoretic approach to construct contractual mechanisms that can increase vaccine supplies for seasonal influenza to developing countries. The key idea is that the source country is subsidized to increase its vaccination effort by other countries that also benefit from that vaccination effort due to interdependent risks of infection transmission. As such, our analysis addresses the following questions.

- How different are vaccine purchase decisions when pursuing global health objectives versus pursuing local country-focused policies?
- Can a coordinating contract for vaccination programs reduce any such differences, reduce the total number infected, and reduce the overall financial burden of a seasonal influenza outbreak?
- Does the benefit of such a coordinating contract differ greatly if the risk assessment for infection used by individual countries focuses primarily on intranational transmission and less so on global outcomes?
- How robust are the recommendations of the coordinating contract?
- What is the net benefit of such a contract relative to the benefit of other interventions?
- Does prioritizing the source country in case of a vaccine shortage reduce the need for such a contract?

To address these questions, we identify why a comprehensive model of infection transmission is mathematically challenging to address analytically and use it to motivate a simplified epidemic model that accounts for a number of key risks and that is tractable enough to allow for contracts to be designed. Numerical experiments respond to the above questions and demonstrate potentially significant benefits to global health that accrue with the use of contracts that are derived with the simplified epidemic model.

1. Background on Influenza, Its Vaccine, and the Related Supply Chain

This section provides the background on influenza, vaccination, and supply chain coordination that is needed for the rest of this paper. 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., Janeway et al. 2001).

Vaccines can reduce the risk of infection to exposed individuals that are susceptible to infection (vaccine effect on susceptibility) and can reduce the probability of transmission from a vaccinated individual that is infected with influenza (vaccine effect on infectiousness) (Longini et al. 1978, 2000). In a single homogeneous population, vaccines reduce the basic reproduction number, R_0, the mean number of new infections from a single infected person in an otherwise susceptible population (Diekmann and Heesterbeek 2000). Colloquially, if R_0 can be reduced below 1, then the dynamics of a large outbreak can be averted. The term R_0 depends on the contact rate, probability of transmission per contact, and duration of infectiousness, and can be estimated indirectly with those terms. Vaccination may alter the probability of transmission and duration of infectiousness. Let $\bar{f}$ be the so-called critical vaccination fraction, the minimum fraction of the population to vaccinate to reduce the reproduction number to 1 when a single infected person is introduced to an otherwise susceptible population. Section 2 describes how this can be generalized to multiple populations.

Vaccination is a principal means of preventing influenza. Although vaccination policies may vary from country to country, particular attention is typically paid to those aged 65 or more, healthcare workers, and those with certain risk factors (World Health Organization 2005). Vaccination is known to be effective and cost effective, and can be complemented with antiviral therapy and other interventions (Longini et al. 2000; Khazeni et al. 2009; Wu et al. 2009, 2010). Germann et al. (2006) argue that even if an influenza vaccine is poorly matched to the circulating strains, it can still slow or even contain the spread of influenza, especially if used in the context of slowing

an outbreak and to allow for additional interventions to be deployed (for the case of an influenza pandemic, options envisaged include reactive and rapid production of better-targeted influenza vaccines).

There are several key operational challenges in the influenza vaccine supply chain.

A challenge at the start of the chain is antigenic drift, which requires that influenza vaccines be reformulated each year. A number of authors have explored the choice of strains for the vaccine (Wu et al. 2005), the timing of the selection process (Kornish and Keeney 2008), dynamic selection policies (Cho 2010), and the interaction of production capacity with strain selection and its timing (Özaltın et al. 2011).

Another challenge occurs toward the end of the supply chain, after vaccines are produced, and involves the allocation of treatments to various subpopulations. Traditional cost–benefit analysis assumes linear costs and benefits, but optimizing costs and benefits for infectious disease interventions involves nonlinear dynamics that require optimization tools (Brandeau et al. 2003, Weycker et al. 2005, Sun et al. 2009, Wang et al. 2009). Proano et al. (2010) discuss related pricing and social utility issues for pediatric vaccines.

The focus of this paper is in a third category of challenges: misaligned incentives of decision makers that interact with each other and the design of contracts that can align their incentives. Chick et al. (2008) show that conventional contracts do not achieve coordination in the influenza vaccine supply chain because of yield uncertainty even between a single buyer and single supplier and design wholesale unit/cost-sharing contracts that can coordinate incentives and flexibly share profits. Deo and Corbett (2009) describe how yield uncertainty can help to explain the high concentration in influenza vaccine industry.

We extend the work of Chick et al. (2008) by considering the contract design problem with multiple governments and the possibility of disease transmission across national boundaries, rather than focusing on a single purchaser. Our epidemic model combines features of the work of Sun et al. (2009) (whose epidemic model has features similar to the next generation method of Diekmann and Heesterbeek (2000) used below to describe the initial stages of influenza transmission) and of Wang et al. (2009) (who modeled resource allocation based on the duration of the outbreak using a susceptible infected recovered (SIR) model with vaccination). We then apply that model to a new situation: to optimize purchasing volumes (rather than allocation of existing resources) in advance of seasonal influenza (rather than in response to a pandemic). In this model, the cost functions of interest are nonlinear and neither convex nor concave. The resulting game between the countries is neither submodular nor supermodular, which makes the analysis complex.

2. Epidemic Model for International Influenza Vaccination Coordination

This section summarizes the epidemic model that underpins the public health and vaccination program costs that will drive the international influenza vaccination coordination contracts in §3.

In terms of timeline, we assume that at the time the three strains are selected for the annual influenza vaccine, a source country (labeled country 0) is also identified as the location where the outbreak is anticipated to initiate. Each of $M+1$ countries then identifies its infection control plans (including vaccination, antivirals, social distancing, and any other relevant interventions that may depend dynamically on the progression of the outbreak) based on those strains. This determines an epidemic model of infection outcomes as a function of vaccine availability. Based on that epidemic model, which is assumed to be shared knowledge, a coordinating contract is designed. Next, the government of each country $i \in \{0, 1, \ldots, M\}$ selects a fraction f_i of its population of N_i individuals for which it orders vaccines. Let $\mathbf{f} = (f_0, f_1, \ldots, f_M)$. The vaccine manufacturer then produces vaccines to meet those orders, and then ships them in advance of the annual influenza season (northern and southern hemispheres are handled separately). Countries then vaccinate their populations in advance of (and during if appropriate) the outbreak.

To quantify vaccine effects, let $1-\theta$ be the vaccine effect on susceptibility (the probability of becoming infected is multiplied by θ with vaccination), and let $1-\phi$ be the vaccine effect on infectiousness (the probability that an infected individual will transmit is multiplied by ϕ with vaccination). Thus, the overall vaccine effect on transmission is $\psi = 1-\theta\phi$ (Longini et al. 1998). If R_0 is the mean number of transmissions from a single unvaccinated infected person to a population of unvaccinated susceptibles, then $(1-\psi)R_0$ is the mean number of such transmissions if all are vaccinated. Vaccines are presumed to be at least partially effective at reducing susceptibility (in susceptible persons) and/or infectivity (in infectious persons) so that $\psi > 0$.

To simplify presentation, we first assume that the manufacturer can supply all vaccines that are ordered. Section 6 relaxes this assumption by examining the challenge of yield uncertainty in vaccine production. That uncertainty may result in a shortfall of vaccines and poses the challenge of how to allocate vaccines if not all countries can receive their full order.

2.1. General Infection Transmission and Vaccination Model

There are many potential models of the transmission of influenza in population, ranging from a simple compartmental model (Diekmann and Heesterbeek 2000) to much more elaborate models with more

complex social interaction, vaccine prioritization to subgroups, plans that incorporate state-dependent deployment of antiviral therapy and social distancing, potential compliance issues of individuals to vaccination, and other interventions (Longini et al. 2000; Wang et al. 2009; Germann et al. 2006; Khazeni et al. 2009; Wu et al. 2009, 2010). We assume that the intervention policy is specified for each country, and denote the total number infected by the end of the outbreak in country i by $\tilde{T}_i(\mathbf{f})$ for each i. For stochastic epidemic models, $\tilde{T}_i(\mathbf{f})$ is assumed to represent the expected number infected.

The contracting results below will be valid for any set of fixed influenza transmission control policies that result in the $\tilde{T}_i(\mathbf{f})$ satisfying a few key properties (more vaccines do not increase the number infected, continuity in f_i, concavity in f_i smaller than a threshold, and convexity in f_i larger than that threshold when the f_j values for all $j \neq i$ are fixed, as specified below in Assumption 3). We presume that $\partial \tilde{T}_i(\mathbf{f})/\partial f_j$ exists and is bounded for each i and j.

Although the analysis below allows for general forms of the $\tilde{T}_i(\mathbf{f})$ that can model a variety of vaccination priorities within each country i, we use the specific SIR model with vaccination for influenza from Longini et al. (1978) to simplify exposition. With that model, R_{ij} is the number of secondary infections in country i from one randomly selected infectious individual in country j for every $i, j \in \{0, 1, \ldots, M\}$, assuming that all individuals are unvaccinated. The basic reproduction number's threshold of 1 to determine the stability of disease dynamics generalizes to multiple subpopulations by examining whether the dominant eigenvalue, R_0, of the matrix of $\mathbf{R} = [R_{ij}]$ values exceeds 1 or not (Diekmann and Heesterbeek 2000). That analysis requires that $\mathbf{R}$ be undecomposable, and we make the same assumption here.

Suppose that $S_i(0)$ is the fraction of susceptible individuals and that $I_i(0)$ is the fraction of infected and infectious individuals at the start of the epidemic in country i. The so-called attack rate $\tilde{p}_i$ for country i (the fraction infected by the end of the annual outbreak) satisfies (Longini et al. 1978)

$$\tilde{p}_i = S_i(0)\big(1 + I_i(0)/S_i(0) - e^{-\sum_{j=0}^{M} R_{ji}\tilde{p}_j}\big). \tag{1}$$

When vaccination is included, the fraction infected that are vaccinated and unvaccinated must be tracked separately to obtain $\tilde{p}_i$. Vaccine (θ, ϕ), vaccination $(\mathbf{f})$, and transmission (R_{ij}) parameters all influence the $\tilde{T}_i(\cdot) = N_i\tilde{p}_i$. In this paper, we refer to this model as the *complete model*.

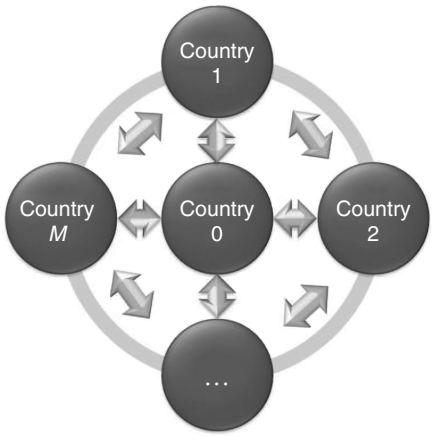
We also consider what we will call a *star model* of transmission, which directly accounts for transmission within a given country's borders, indirectly accounts for transmission to its population from the source country, and ignores other transmission to and from other countries. Figure 1 depicts both the complete model, where transmission can occur between any two countries, and the star model, which models only transmission within a given country except for the influence of the source country.

For the star model, let $T_i(f_i, f_0)$ be the number of individuals infected by the end of the influenza season in country i, given that the epidemic model only is concerned with the vaccination fractions in countries 0 and i. For $i \neq 0$, suppose that the initially infected in country 0 infect $I_i(0)$ individuals in country i, and then infection circulates in country i. If the vaccination fraction f_i is 0, then $I_i(0)$ may depend on f_0, and, when we focus on country i's transmission alone, (1) justifies the attack rate p_i approximation

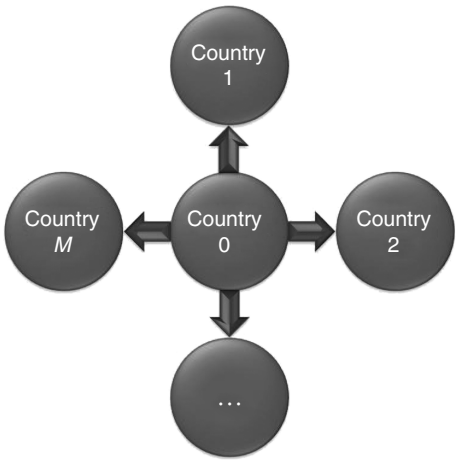
$$p_i = S_i(0)(1 + I_i(0)/S_i(0) - e^{-R_{ii}p_i}). \tag{2}$$

Figure 1 Network of Infection Transmission Between Countries

(a) Complete model with all connections



(b) Star model when $R_{ij}R_{jk} \approx 0$ for all $i, k \neq j$



One can further show that the critical vaccination fraction, $\bar{f}_i$, which limits the spread of infection in country i in the star model is (Diekmann and Heesterbeek 2000)

$$\bar{f}_i = (1/\psi)(1 - 1/R_{ii}). \tag{3}$$

Section 2.2 justifies when the star model makes sense both as an approximation to the complete model and for deriving insights for a contract designed to coordinate vaccine purchase decisions across countries.

2.2. The Next Generation Method to Justify the Star Model

An analysis of the complete model in (1) with nonzero vaccination levels involves manipulating implicit solutions to multivariate transcendental equations. We therefore seek a good approximate model to simplify the analysis. The star model is one such simplified model, and its use will be justified in this section.

Here, we use the star model to describe economic outcomes and to derive a supply contract below, by assuming the infection occurs in two phases. In the first phase, we use the next generation method (Diekmann and Heesterbeek 2000) to model the first few generations (g_0 of them) of transmission. This accounts for intercountry transmission. An individual is said to be infected in generation $g+1$ if he or she was infected by somebody that was infected in generation g. Thus, the time between generations is typically somewhat less than the mean duration of infection. For influenza, there are many generations in an outbreak. In the second phase, we account for nonlinear infection dynamics within each country from the g_0th generation to end of an outbreak using a compartmental model.

The next generation method approximates the spread of the disease at the start of an epidemic by linearizing the nonlinear epidemic dynamics. We now use that method to account for the dynamics of both unvaccinated and vaccinated individuals in each of the $M+1$ countries at the start of the influenza season. Let $y_{0i}(g)$ and $y_{1i}(g)$ be the expected number of secondary infections in population i, unvaccinated and vaccinated, respectively, at generation g. We summarize these values with the $2(M+1)$-vector

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

Following Diekmann and Heesterbeek (2000, p. 100), $\mathbf{y}(g+1) = \mathbf{N}\mathbf{y}(g)$ is the linearization of the infection transmission dynamics during the early stages of an outbreak in a large population, or equivalently,

$$\mathbf{y}(g+1) = \mathbf{N}^g \mathbf{y}(0), \tag{4}$$

where $\mathbf{N}_{2(M+1)\times 2(M+1)}$ is the next generation matrix for the vaccine allocation $\mathbf{f}$,

$$\mathbf{N} = \begin{bmatrix} R_{00}(1-f_0) & R_{00}\phi(1-f_0) & \ldots & R_{0M}(1-f_0) & R_{0M}\phi(1-f_0) \\ R_{00}\theta f_0 & R_{00}\theta\phi f_0 & \ldots & R_{0M}\theta f_0 & R_{0M}\theta\phi f_0 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ R_{M0}(1-f_M) & R_{M0}\phi(1-f_M) & \ldots & R_{MM}(1-f_M) & R_{MM}\phi(1-f_M) \\ R_{M0}\theta f_M & R_{M0}\theta\phi f_M & \ldots & R_{MM}\theta f_M & R_{MM}\theta\phi f_M \end{bmatrix}. \tag{5}$$

Each component of $\mathbf{N}^g$ is a nonlinear function of potentially all of the f_is. That nonlinearity would complicate the analysis significantly. If we adopt two assumptions, it can be shown that the complex network of interactions between countries in Figure 1(a) can be approximated by the simpler star model in Figure 1(b). Assumption 1 indicates that the outbreak originates in one country.

Assumption 1. *The epidemic starts only in country* 0, *so that* $\mathbf{y}(0) = [y_{00}(0), y_{10}(0), 0, 0, \ldots, 0, 0]^T$ *with at least one of* $y_{00}(0)$ *and* $y_{10}(0)$ *greater than* 0.

Lemma 1. *Given Assumption* 1, *for any generation* g, *the number of infected individuals,* $y_{0i}(g) + y_{1i}(g)$, *in population* i ($i \in \{0, 1, \ldots, M\}$) *can be written as*

$$y_{0i}(g) + y_{1i}(g) = R_{i0}\mathcal{F}_i^{(g)}(f_i, f_0) + \mathcal{G}_i^{(g)}(\mathbf{f}), \tag{6}$$

where $\mathcal{F}_i^{(g)}(f_i, f_0)$ *is a function of* f_i *and* f_0 *but not of any other* f_j, *and* $\mathcal{G}_i^{(g)}(\mathbf{f})$ *is a sum of terms involving potentially all vaccination fractions and where any summand that involves* f_j, *for any* $j \notin \{0, i\}$, *has a coefficient* $R_{ab}R_{bc}$ *for some* $a \neq b \neq c$, *where* $a, b, c \in \{0, 1, \ldots, M\}$.

Proofs of all claims in the main text are provided in the appendix.

Lemma 1 suggests that the following additional assumption is sufficient to justify approximating the complete model with the star model. Assumption 2 states that the number of people infected after two generations with both transmission crossing borders is small (e.g., the number of people in the United States that were directly infected by those in France that were directly infected by a single person in China is small). Its criterion is somewhat weaker than is sometimes assumed in related work. For example, Brandeau et al. (2003) assumed independent subpopulations in their analysis, and Sun et al. (2009) assumed that $R_{ij} \approx 0$, when $i \neq j$ (for example, $R_{ij}^2 = 0.0004$ is more easily approximated by zero than is $R_{ij} = 0.02$). Thus, the results of Sun et al. (2009) may be applicable in more settings than they originally claimed.

Assumption 2. *For every* $i \neq j$ *and* $k \neq j$, *we have* $R_{ij}R_{jk} \approx 0$, *so that we approximate the number infected,* $y_{0i}(g) + y_{1i}(g)$, *in the* g*th generation of the outbreak in country* i *by* $R_{i0}\mathcal{F}_i^{(g)}(f_i, f_0)$.

Lemma 2. *Given Assumptions* 1 *and* 2, *the term* $R_{i0}\mathcal{F}_i^{(g)}(f_i, f_0)$ *in* (6) *for the number infected during generation* g *in population* i *is a convex and decreasing function with respect to* f_i, f_0 $(i = 1, 2, \ldots, M)$.

The next generation method is best as an approximation only at the start of the epidemic because the underlying system is nonlinear, and this method makes a linearity assumption when the population is largely susceptible. As a result, the convexity properties in Lemma 2 are not valid for the overall number of infected individuals throughout the epidemic season.

In general, one wants to pick the number of generations in the first phase of the star model, g_0, to be small when the linear approximation to infection dynamics is best, yet large enough so that the infection takes off in all other countries (e.g., if infection occurs from country 0 to 2 only via the intermediary of country 1, then one needs $g_0 \geq 2$ to obtain infection in country 2).

2.3. Second Phase of Infection Transmission with the Star Model

Section 2.2 showed that when the transmission matrix $\mathbf{R}$ is undecomposable and when the terms $R_{ij}R_{jk}$ are small for all $i, k \neq j$, the star epidemic model is reasonable to use. It also modeled disease transmission during a first phase of the outbreak using the next generation method. This section explores the total number infected for the star model when the nonlinear dynamics of infection within each country continues during a second phase of disease transmission that accounts for the rest of an outbreak.

Transmission within country $i \in \{0, 1, \ldots, M\}$ in the second phase of transmission is modeled using a standard SIR model with vaccination. This can be accounted for by (2) if we assign initial conditions for the fraction of susceptibles $S_i(0)$, infected and infectious $I_i(0)$, and removed $R_i(0)$ in country i. If a fraction f_i of country i is vaccinated, then $R_i(0) = f_i\psi$. The initial number infected in country i is taken to be the number of infected in the initial ramp-up except for those who receive effective vaccination coverage, $I_i(0) = (1 - f_i\psi)\chi_i$, where $\chi_i = (R_{i0}\mathcal{F}_i^{(g_0)}(f_i, f_0))/N_i$ is the fraction infected during the first phase of disease transmission. All others are susceptible; $S_i(0) = 1 - I_i(0) - R_i(0)$. The total number that become infected during the influenza season is $T(f_i, f_0) = N_i p_i$, where the attack rate p_i from (2) implies that

$$p_i = 1 - \psi f_i - (1 - \chi_i)(1 - \psi f_i)e^{-R_{ii}p_i}, \tag{7}$$

assuming no further transmission from country 0 after the first phase of the epidemic.

Assumption 3 identifies properties of a star model approximation to an epidemic model that are useful below. For an epidemic model other than the SIR model, its star model approximation $T_i(\cdot) = N_i p_i$ counts the number infected assuming only transmission from country 0 and intranational transmission, so that $T_i(\cdot) = N_i p_i$ depends on $\mathbf{f}$ only through f_0 and f_i. Theorem 1 indicates that the set of accepted models that satisfy these properties is nonempty by showing that the SIR model above satisfies them.

Assumption 3. *If* $T_i(\cdot) = N_i p_i$, (a) p_i *is strictly decreasing in* f_i *for* $i \in \{0, 1, \ldots, M\}$; (b) p_i *is strictly decreasing in* f_0 *for* $i \in \{0, 1, \ldots, M\}$; (c) *there exists a* $\bar{\bar{f}}_i$ *such that* p_i *is a submodular function of* (f_i, f_0) *for* $f_i \leq \bar{\bar{f}}_i$ (*that is*, $\partial^2 p_i/\partial f_0 \partial f_i \leq 0$) *and a supermodular function for* $f_i \geq \bar{\bar{f}}_i$ *for* $i \in \{1, 2, \ldots, M\}$ (*that is*, $\partial^2 p_i/\partial f_0 \partial f_i \geq 0$); (d) p_i *is first strictly concave then strictly convex in* f_i *for* $i \in \{0, 1, \ldots, M\}$; *and* (e) *all first and second derivatives are continuous*.

We denote the vector of vaccine fractions in Assumption 3(c) by $\bar{\bar{\mathbf{f}}} = (\bar{\bar{f}}_0, \bar{\bar{f}}_1, \ldots, \bar{\bar{f}}_M)$. We note that the condition $\partial^2 p_i/\partial f_0 \partial f_i \leq 0$ for $f_i \leq \bar{\bar{f}}_i$ is associated with strategic substitutes and that the condition $\partial^2 p_i/\partial f_0 \partial f_i \geq 0$ for $f_i \geq \bar{\bar{f}}_i$ is associated with strategic complements (e.g., see Netessine and Zhang 2005).

Theorem 1. *The attack rates* p_i *of the SIR model with vaccination in* (7), *for each* i, *satisfy Assumption* 3 *with* $\bar{\bar{f}}_i$ *in Assumption* 3(c) *chosen to be* $\bar{f}_i$ *from* (3).

Theorem 1 suggests an interesting new interpretation for the critical vaccination fraction $\bar{f}_i$. From the perspective of country $i > 0$, the choice of f_i is measure of vaccination effort and the value of f_0 is a surrogate measure of effort to reduce exposure. Thus, $\bar{f}$ for the SIR model with vaccination is a threshold that determines whether vaccination effort and exposure reduction are strategic substitutes or strategic complements.

3. Vaccine Procurement Decisions and System-Optimal Allocations

This section formalizes a model for vaccine procurement decisions when each country orders vaccines to (selfishly) minimize the total of its vaccination program costs and its economic burden of infection. The problem has neither pure substitutability nor pure complementarity. Nonetheless, if Assumption 3 holds, then we can provide structural results for equilibria and coordinating contracts that can help a central planner who seeks a systemwide optimum that is more consistent with global health goals.

3.1. Decisions of Individual Countries: The Game Problem

Let v_i be the cost of procuring and administering vaccines per person, and let b_i be the average direct and indirect cost of an influenza infection in country $i \in \{0, 1, \ldots, M\}$ (e.g., see Weycker et al. 2005).

Country i's expected total vaccination and social costs with the complete model of infection is

$$b_i \tilde{T}_i(\mathbf{f}) + v_i f_i N_i. \tag{8}$$

The complete model's costs in (8) for country i are therefore formally dependent on the epidemic control decisions of each of the other countries via $\tilde{T}_i(\mathbf{f})$. But regulatory bodies may prefer to set vaccination policy for infectious disease control based only on actions and dynamics that are within their direct control. Such a phenomenon has been observed in other infectious disease control contexts, such as with water treatment policy for microbes in drinking water (Chick et al. 2003).

Therefore, we use the star model to examine the vaccination ordering decisions with respect to an infectious disease transmission model that primarily accounts for decisions within its own borders. We therefore define the *game problem* to be a one-shot game between the different governments that use the $T_i(\cdot) = N_i p_i$ model of health outcomes. Each government minimizes its perceived total cost, GF_i, of an outbreak including vaccination program costs and social costs.

Game problem:

$$\left\{ \begin{array}{l} \min\limits_{0 \le f_0 \le 1} GF_0 \triangleq b_0 T_0(f_0) + v_0 f_0 N_0, \\ \min\limits_{0 \le f_i \le 1 \,|\, f_0} GF_i \triangleq b_i T_i(f_i, f_0) + v_i f_i N_i, \\ \qquad\qquad \text{for } i = 1, 2, \ldots, M \end{array} \right\}. \tag{9}$$

Weycker et al. (2005) gave an example of an assessment of social costs.

We now characterize the set of equilibria for this game. To do so, we assume that the expected benefits of the first vaccination exceed its cost (as in Chick et al. 2008) as follows.

Assumption 4. (a) $dGF_0/df_0|_{f_0=0} < 0$ *and* (b) $dGF_i/df_i|_{f_i=0} < 0$ *for each* i *and* f_0.

For the SIR model with vaccination, this assumption implies $b_i\psi - v_i > 0$ for $i \in \{0, 1, \ldots, M\}$.

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

Lemma 3. *Given Assumptions* 3 *and* 4, *there exists a unique best response function and there exists a unique Nash equilibrium* $\mathbf{f}^G = (f_0^G, f_1^G, \ldots, f_M^G)$ *of the game problem in* (9) *that satisfies*

$$f_0^G = \sup\left\{ f \in [0,1]\colon b_0 \frac{\partial}{\partial f_0} T_0(f_0)\Big|_{f_0=f} + v_0 N_0 < 0 \right\}, \tag{10}$$

$$f_i^G = \sup\left\{ f \in [0,1]\colon b_i \frac{\partial}{\partial f_i} T_i(f_i, f_0^G)\Big|_{f_i=f} + v_i N_i < 0 \right\}, \quad \text{for } i = 1, 2, \ldots, M. \tag{11}$$

In (10), note that if $b_0 \partial T_0(f_0)/\partial f_0|_{f_0=1} + v_0 N_0 < 0$, then the benefits of vaccination in the source country is so much higher than its vaccination program costs that its government should aim to vaccinate its entire population ($f_0^G = 1$). Otherwise, its optimal vaccination fraction f_0^G is less than 1 and is the unique solution of $b_0 \partial T_0(f_0)/\partial f_0|_{f_0=f_0^G} + v_0 N_0 = 0$. A similar interpretation holds for the other f_is.

In general, the uniqueness of the best response functions does not necessarily guarantee a unique Nash equilibrium. Cachon and Netessine (2004) provide several methods, mostly based on second-order derivatives of the objective function, to establish that there is a unique Nash equilibrium for such a game. For the game problem in (9), the proof of Lemma 3 shows the uniqueness of Nash equilibrium because (10) provides a unique solution to f_0^G, independent of the other f_i ($i = 1, 2, \ldots, M$). The best response decisions of all the other countries depend solely on f_0^G. This justifies a unique Nash equilibrium based on the unique best responses in (10) and (11).

3.2. Coordinated Decisions: The System Problem

A central planner with a global health perspective is interested in minimizing the overall financial and health costs of the system as a whole. That cost, as defined by the summing the perceived costs of each government, determines the following *system problem* to identify vaccination fractions to optimize global health outcomes.

System problem:

$$\min_{0 \le \mathbf{f} \le 1} SF(\mathbf{f}) \triangleq b_0 T_0(f_0) + v_0 f_0 N_0 + \sum_{i=1}^{M} b_i T_i(f_i, f_0) + v_i f_i N_i. \tag{12}$$

This formulation is consistent with adding each governments perceived costs with the star model. Section 7 discusses health outcomes and coordination decisions with the complete model.

Lemma 4. *Given Assumptions* 3 *and* 4, *a global optimum for the system problem in* (12) *is* $\mathbf{f}^S = (f_0^S, f_1^S, \ldots, f_M^S)$, *where*

$$f_0^S = \sup\left\{ f \in [0,1]\colon b_0 \frac{\partial}{\partial f_0} T_0(f_0)\Big|_f + \sum_{i=1}^{M} b_i \frac{\partial}{\partial f_0} T_i(f_i^S, f_0)\Big|_f + v_0 N_0 < 0 \right\},$$

$$f_i^S = \sup\left\{ f \in [0,1]\colon b_i \frac{\partial}{\partial f_i} T_i(f_i, f_0^S)\Big|_f + v_i N_i < 0 \right\}, \quad \text{for } i = 1, 2, \ldots, M. \tag{13}$$

Unlike Lemma 3, Lemma 4 does not guarantee a unique optimal solution. Joint convexity of the objective function is a sufficient condition for uniqueness of the solution; however, that is clearly not the case for the system problem because its objective is not convex with respect to the individual variables.

Cachon and Netessine (2004) gave criteria to establish the uniqueness of a Nash equilibrium, and such methods might be adapted to show uniqueness for a system optimum, such as the one in (13). One of those criteria, the diagonal dominance criterion in their equation 2.2, indicates that a unique Nash equilibrium exists if there is a contraction mapping on the entire space, and that occurs if the absolute value of any given diagonal element in the Hessian matrix exceeds the sum of absolute values of the other elements in the same row. Assumption 3, (c) and (d), describes the structure of the Hessian. Although a global characterization may be elusive for general $T_i(\cdot)$ without additional assumptions, we found that, in numerical experiments of §4 with realistic parameter values for influenza, there was a unique global optimum. The intuition for why such a result holds may be explained with two points. First, for countries $i = 1, 2, \ldots, M$, the effect of a change in vaccination within its borders typically has a much bigger effect on infection transmission in country i than the effect of a similar change of vaccination in country 0. Second, a change in vaccination in country 0 is likely to have a greater effect on transmission within country 0 than the combined effect on transmission within the other countries, because the latter effect is indirect. These observations were consistent with numerical experiments reported below.

Theorem 2 indicates that a central planner would increase vaccine coverage in the source country, relative to the solution that arises from the decisions of individual countries. It also decreases vaccine coverage for the other countries if the game-optimal solution exceeds the supermodularity threshold (i.e., if $f_i^G \geq \bar{\bar{f}}_i$). The reason is that the risk of infection in other countries is influenced by the outcomes in the source country.

Theorem 2. *Let* $\mathbf{f}^G$ *be the unique solution of the game problem in* (10)–(11)*, and let* $\mathbf{f}^S$ *be a solution of the system problem as in* (13)*. If Assumptions* 3 *and* 4 *hold, then* (a) $f_0^G \leq f_0^S$. (b) *If* $f_i^G \geq \bar{\bar{f}}_i$*, then* $f_i^G \geq f_i^S$*; otherwise* $f_i^G \leq f_i^S$ *for* $i = 1, 2, \ldots, M$.

Theorem 3 shows that the "if" statement in Theorem 2(b) is always true for the SIR model in (7).

Theorem 3. *If the epidemic model is the SIR model with vaccination in* (7) *and Assumption* 4 *holds, then* $f_i^G \geq \bar{\bar{f}}_i$ *for* $i \in \{0, 1, \ldots, M\}$*, so that* (a) $f_0^G \leq f_0^S$*, and* (b) $f_i^G \geq f_i^S$ *for* $i = 1, 2, \ldots, M$.

Thus, the system-optimal solution results in fewer infections in the source country. Although the system-optimal solution may result in somewhat less vaccination in the other countries, decreased transmission from the source country to the other countries tends to decrease infection in countries $i = 1, 2, \ldots, M$. This occurred in numerical experiments below with the SIR model.

In a revenue-maximizing context, Netessine and Zhang (2005) show that competition with complements leads to inventory understocking by retailers compared with the setting in which complements are centrally managed, and that the opposite is true for substitutable products. The epidemic context behind Theorem 3 differs in two important ways from the setup of Netessine and Zhang (2005). First, our problem has a cost minimizing context, so their results for strategic complements would be more applicable for strategic substitutes in our context. Second, the role of the source country differs than that of the other countries, whereas such a difference is not found for the retailers in Netessine and Zhang (2005). That said, Theorem 3 indicates that $f_i^G \geq \bar{\bar{f}}_i = \bar{f}_i$ for $i = 1, 2, \ldots, M$ for the SIR model with vaccination. By Assumption 3(c), the number infected in country i is supermodular (a complement in our cost minimization context). We might therefore anticipate, based on Netessine and Zhang (2005), that country i would overstock in selfish play relative to a system optimum. That is precisely what Theorem 3(b) states. The result holds whenever $f_i^G \geq \bar{\bar{f}}_i$ for $i = 1, 2, \ldots, M$ even though the game problem is neither fully supermodular nor fully submodular.

3.3. A Coordinating Contract for System Optimality

Given the differences in the solutions of the game and system problems, we now describe a contract that can resolve the misaligned incentives between different governments and a central planner. The idea of Theorem 4 is to partly subsidize the source country's vaccine purchase and administration costs to encourage it to procure more. Nonsource countries pay for that subsidy, and in return receive benefits that accrue from increased vaccination efforts by the source country. In addition, one would hope that governments could flexibly split the total cost savings that accrues from shifting to the system-optimal solution. The following cost-sharing contract achieves this goal.

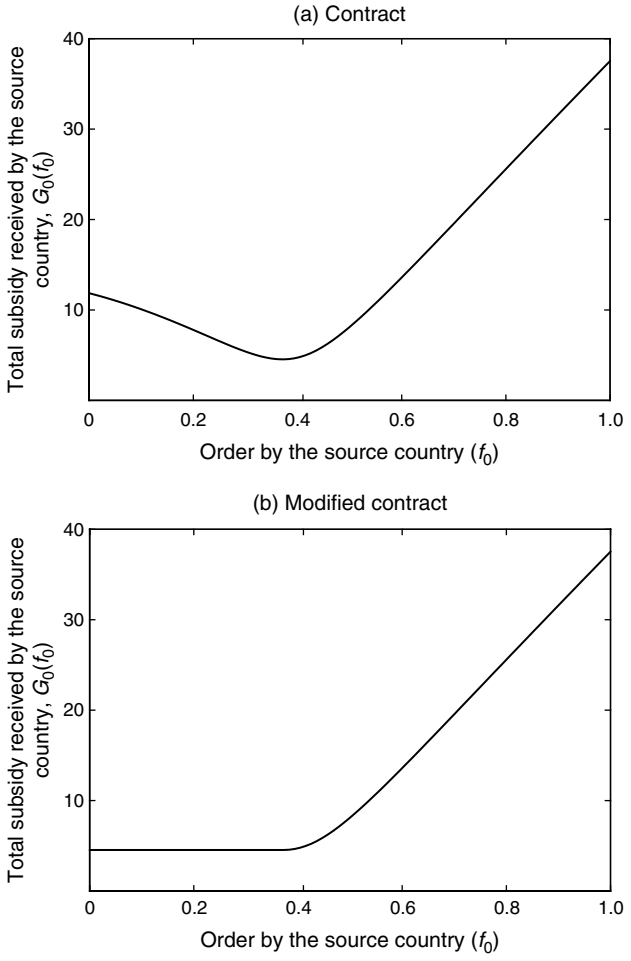
Theorem 4 (Coordinating Contract). *Let* $\alpha_i \in (0, 1)$ *be such that* $\sum_{i=1}^{M} \alpha_i < 1$*. If country* 0 *chooses a vaccination fraction* f_0*, then country* i *pays a subsidy to country* 0 *of* $G_i(f_0)$ *for* $i = 1, 2, \ldots, M$*, where*

$$G_i(f_0) = (\alpha_i - 1)GF_i(f_i^S, f_0) + \alpha_i \sum_{\substack{j=0 \\ j \neq i}}^{M} GF_j(f_j^S, f_0). \quad (14)$$

This contract is coordinating for the system problem in (12), *meaning that* (a) *it pushes country i to order the system-optimal* f_i^S *for* $i = 0, 1, \ldots, M$; (b) *the total cost to country* $i = 0, 1, \ldots, M$ *equals* $\alpha_i SF(\mathbf{f}^S)$, *where* $\alpha_0 = 1 - \sum_{i=1}^{M} \alpha_i$, *so the contract can flexibly share financial benefits by changing the* α_i*s; and* (c) *if* $\alpha_i = GF_i(f_i^G, f_0^G)/SF(\mathbf{f}^G)$ *for* $i = 1, 2, \ldots, M$, *then the total cost of each country is improved relative to the solution from the game problem* (*participation constraints are satisfied*).

The contract allocates the systemwide costs to the individual countries. The total subsidy received by the source country is $G_0(f_0) = \sum_{i=1}^{M} G_i(f_0) = (1 - \alpha_0) \cdot GF_0(f_0) - \alpha_0 \sum_{i=1}^{M} GF_i(f_i^S, f_0)$. This quantity is plotted in Figure 2(a). That figure demonstrates the subsidy per dose for the source country, assuming a cost per dose of 40. The total subsidy to the source country consists of two regions, one decreasing in f_0 and another increasing in f_0. Using Assumption 3(b) and the property that f_0^G lies in the convex region of GF_0, it follows that $dG_0(0)/df_0 \geq 0$ for all $f_0 \geq f_0^G$. Thus, one can simplify the coordinating contract so that payments are nondecreasing in the source country's order quantity by lowering all subsidies for f below f_0^G to that of the subsidy at f_0^G. Such a modification is depicted in Figure 2(b) and is formalized in the following corollary.

Figure 2 **Subsidy to the Source Country as a Function of f_0**



Corollary 1 (Modified Contract). *Let* $G_i(f_0)$ *be the payment of country i to the source country under the coordinating contract from Theorem* 4. *Then a modified contract with the following payments from country i* ($i = 1, 2, \ldots, M$) *to the source country is also coordinating*:

$$\hat{G}_i(f_0) = \begin{cases} GF_i(f_0^G) & \text{if } f_0 < f_0^G, \\ GF_i(f_0) & \text{if } f_0 \geq f_0^G. \end{cases}$$

The coordinating contract and modified contract result in equivalent behavior. One way to implement the contract is to have each country $i = 1, 2, \ldots, M$ pay its portion of the subsidy to the manufacturer, and the manufacturer would adjust its shipment and bill to country 0 accordingly.

4. Assessment of Proposed Contract with Numerical Experiments

This section presents numerical experiments that respond to the motivating questions in the introduction and that explore the differences in outcomes for the infection models and the coordinating contract proposed above. We use realistic values of parameters for seasonal influenza as described below.

As argued in §3.1, a country may prefer to set its influenza vaccination policy based on transmission within their borders and from the source country rather than on a model that accounts for transmission across all borders. This drives the use of the coordinating contract based on the star model.

That said, overall health outcomes are determined by that more complex set of interactions, and we would like to explore how effective such a coordinating contract can be to reach global health objectives. We therefore assess the outcomes of these experiments in terms of the number infected with the complete model in (1) and by the expected systemwide costs with the complete model, denoted

$$\widetilde{SF}(\mathbf{f}) \triangleq \sum_{i=0}^{M} b_i \tilde{T}_i(\mathbf{f}) + v_i f_i N_i. \tag{15}$$

We denote the minimizer of this complete model's cost by $\tilde{\mathbf{f}}^S = (\tilde{f}_0^S, \tilde{f}_1^S, \ldots, \tilde{f}_M^S) \triangleq \arg\min \widetilde{SF}(\mathbf{f})$.

In summary, §4.1 compares the differences between selfish play, as in the game problem of (9) and the coordinating contract from Theorem 4. When outcomes are evaluated based on the complete model, this contract can eliminate a significant portion (between 65% and 95% in experiments) of the total inefficiency in the system, which is defined as the difference between the costs of the game problem

of (10) and (11) and the minimizer of the complete model's costs in (15).

The coordinating contract requires that many parameters be estimated. Section 4.2 examines how parameter estimation errors may or may not negate the benefits gained by the contract. We find that even when the values of R_{ij}s are misestimated, the contract can still be effective in driving down systemwide costs. Overestimating the R_{ij} appears to be more favorable than underestimating it. A slight overestimation of R_{ij} can even lower the systemwide costs compared to using the true value of this parameter. This is because the coordinating contract is not necessarily a coordinating mechanism for the complete model's costs, and the complete model's costs are further lowered by a slight overestimation of the R_{ij}.

Finally, there are mechanisms other than contracts that can improve health outcomes due to disease transmission, such as travel restrictions. Section 4.3 examines how much transmission contact rates must be reduced by a such a public health intervention to have a health and cost benefit equal to that of the coordinating contract. We find that a 5% to 34% decrease in cross-border transmission rates is required to achieve a similar level of cost reductions that one can achieve with the proposed contract, depending on the degree of cross-border transmission.

In these experiments, we aggregate "countries" into three regions. The source country (indexed by $i = 0$) in our example represents Southeast Asia, $i = 1$ represents the Western European, and $i = 2$ represents the United States. We chose Southeast Asia as our source country because historically it has been the initiating region for many of influenza strains. Longini et al. (2004) argue that $R_0 \in [1.6, 2.4]$ is a reasonable range for the basic reproduction number. As the population tends to change behavior during a epidemic, an SIR model with a fixed reproduction number tends to overestimate the total number of infected individuals. Thus, we chose values at the lower end of that range ($R_{00} = R_{11} = R_{22} = 1.6$) to offset this effect and generate attack rates that are more realistic. We used populations of $N_0 = 6 \times 10^8$, $N_1 = 3.6 \times 10^8$, and $N_2 = 3 \times 10^8$ individuals, which correspond to the recent projected population sizes of the Southeast Asian region, Western Europe, and the United States, respectively. We set $y_{00}(0) = 0.01N_0$ and $y_{10}(0) = 0$ to satisfy Assumption 1.

To quantify cross-transmission parameters R_{ij} for $i \neq j$, we use population information for each region together with air travel rates. International trips to the United States numbered approximately 59.7 M (million) in 2010 (U.S. Office of Travel and Tourism Industries 2011). Assuming that infected and infectious people from country i are equally likely as susceptible people from country i to be in country j, we get $R_{ij} \approx R_{ii} \times 58$ M/300 M/365 ≈ 0.00087 where 300 M is the approximate population of the United States. Because most of these trips are through a small number of cities (e.g., New York, Los Angeles) with much smaller populations, this number may be higher than 0.00087. We use $R_{ij} = 0.03$ for all $i \neq j$ as a base case and do a sensitivity analysis. We vary $R_{ij} \in [0.00087, 0.05]$ for every $i \neq j$ to evaluate the effect of the R_{ij} over a range of situations. We use $g_0 = 4$ generations for the first phase of transmission in the star model unless specified otherwise.

Weycker et al. (2005) estimated $1 - \theta = 0.5$ and $1 - \phi = 0.8$ for vaccine effects on susceptibility and infectiousness, respectively. They also estimated total costs (direct and indirect) of each infected individual with $b = \$460$ on average over the different subpopulations in the United States. In our experiments, we fixed the social costs of the disease in the United States and Western Europe, $b_1 = b_2 = \$460$, and varied b_0 in the range of $[\$v_0, \$250]$ to account for the lower value of infection costs in the source country due to the economical factors. Chick et al. (2008) used [\$40, \$80] as a range for the total vaccination program costs in the United States. We set $v_i = \$60$ as an estimate for the total vaccination program costs for $i = 1, 2$ and set $v_0 = \$40$ to account for lower costs in the source country.

4.1. Does the Coordinating Contract Improve Outcomes?

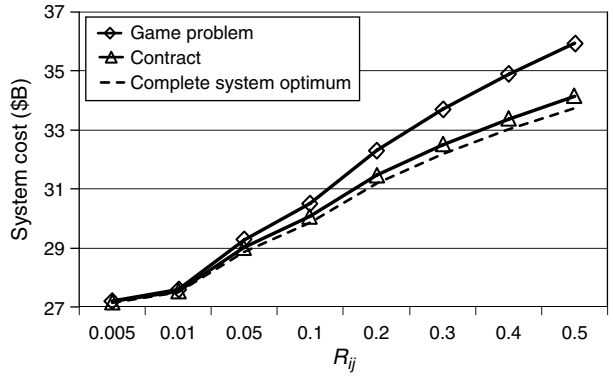
The first set of experiments compares the benefits that are gained by using the coordinating contract of Theorem 4 that is based on cost estimates that are self-reported by each country; that is, we examine the differences between the outcomes from the game problem and system problem.

As a base case we set $b_0 = \$50$ and $b_1 = b_2 = \$460$. The optimal order quantities for the game problem are $\mathbf{f}^G = (0.383; 0.477; 0.487)$. The optimal order quantities for system problem 2, which are achieved with the coordinating contract, are $\mathbf{f}^S = (0.441; 0.467; 0.477)$. The complete model's system optimum is $\tilde{\mathbf{f}}^S = (0.486; 0.437; 0.440)$. Thus, the contract, which is based on the star model, does shift the selected vaccination fraction toward the complete model's system optimum.

Even though the star model does not fully represent the complete infection transmission system, experiments indicate that the complete model's system cost in this case is reduced. The complete model's system cost savings is significant: \$1.09 B (billion). The percentage improvement in financial terms is therefore \$1.09 B/$\sum GF_i \approx 3.4\%$. This financial benefit eliminates 72% of the total inefficiencies (\$1.513 B) relative to outcomes without the coordinating contract.

Figure 3 illustrates the plots of selfish play, coordinating contract, and the complete model's system

Figure 3 **Comparison of Complete Model's System Costs for the Game Problem, the Coordinating Contract of Theorem 4, and the Complete Model's System Optimum**



optimum. The elimination of inefficiency occurs for each value of R_{ij} tested. The total number infected also decreases significantly with the coordinating contract, leading to 21.2 M infections averted in country 0, 1.2 M averted in country 1, and 1.0 M averted in country 2, for a total of 23.4 M infections averted, assuming $R_{ij} = 0.03$. For $R_{ij} = 0.00087$ (the lower bound for R_{ij} from the estimate with data for international travel to the United States), we obtain a cost savings of \$40 M and 4.6 M infections averted globally (see Table 1). The infections averted are primarily due to a significant increase in vaccination in the source country.

A sensitivity analysis assessed the value of the proposed contract based on changes in parameter values. Some of the results of these experiments are also shown in Table 1 (for $\mathbf{b} = \$[50; 460; 460]$, $\mathbf{v} = \$[40; 60; 60]$). The first column has the value of R_{ij} for all $i \neq j$, which is varied from 0.00087 to 0.05. The next three columns show the vaccine coverage vector for all the countries before the contract ($\mathbf{f}^G$) and after the contract ($\mathbf{f}^S$), and complete model's optimum ($\tilde{\mathbf{f}}^S$), respectively. The last two columns show the contract benefits in terms of reductions in the complete model's cost and total number of infections averted. Both health and financial benefits of the contract are increasing in the rate of international transmission (as measured by the R_{ij}). Moreover, we note that infections were reduced in every country. The total infections averted were not made at the expense of nonsource countries (data not shown) because the reduction in coverage for the source country was more than compensated for by the reduction in exposure from the source country.

Table 2 **Coordinating Contract Benefits as a Function of Source Country's Social Costs of Infection**

b_0 (\$)	Cost savings (\$B)	Infected (M) reductions
50	1.96	31.9
100	1.09	17.0
150	0.87	13.8
200	0.74	6.2

Table 2 shows the total cost savings and number of infections averted with the contract as a function of the social cost per infection in the source country. If the source country is a developing or emerging country, which is often the case, the value of b_0 would be smaller. The benefits of the coordinating contract of Theorem 4 are larger in absolute terms for smaller b_0, and therefore it is particularly favorable if the source country is developing or emerging.

Based on these and other scenarios not reported here, we observe that the coordinating contract

- reduces systemwide costs as estimated by both the star model and the complete model and reduces the total number infected,
- performs better when the expected benefit of the first vaccination less its cost in the source country ($b_0\psi - v_0$) is smaller, and
- performs better when the expected benefit of the first vaccination less its cost in other countries ($b_j\psi - v_j$ for $j > 0$) is larger, as social costs of the disease are the dominating costs in our model (data not shown).

In experiments that explored situations where the R_{ii} values were not equal across countries, to reflect differences in urbanization and family structure and size, we observed (data not shown) that (a) the percentage cost savings was greater for smaller values of the R_{ii}, (b) the gain in infections averted was greatest when the source country had the largest R_{ii}, and (c) the cost savings were more sensitive to changes in the R_{ii} than were the infections averted.

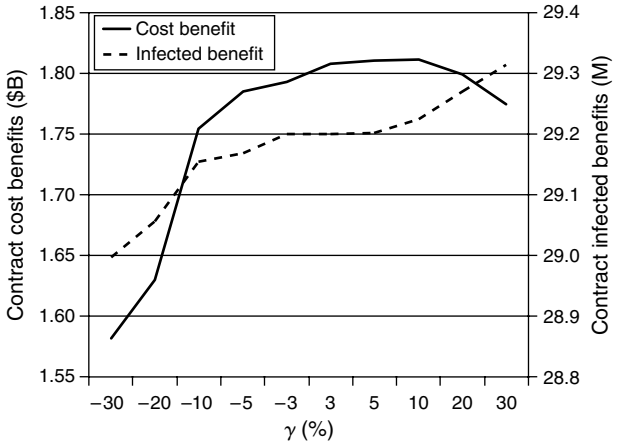
4.2. Does the Contract Still Help If Infection Parameters Are Misestimated?

Section 4.1 argues that the proposed contract can bring significant benefits. The contract requires that

Table 1 **Output with the Coordinating Contract of §3.3**

R_{ij}	$\mathbf{f}^G$	$\mathbf{f}^S$	$\tilde{\mathbf{f}}^S$	Cost benefit	Infections averted
0.05	[0.38; 0.51; 0.52]	[0.46; 0.49; 0.50]	[0.51; 0.46; 0.46]	1.738 B (5.1%)	30.0 M (50.8%)
0.03	[0.38; 0.48; 0.49]	[0.44; 0.47; 0.48]	[0.49; 0.44; 0.44]	1.090 B (3.4%)	23.4 M (42.2%)
0.01	[0.38; 0.43; 0.44]	[0.42; 0.43; 0.43]	[0.45; 0.41; 0.41]	403 M (1.4%)	14.2 M (27.6%)
0.005	[0.38; 0.41; 0.42]	[0.41; 0.41; 0.42]	[0.43; 0.40; 0.40]	212 M (0.8%)	10.4 M (20.7%)
0.00087	[0.38; 0.38; 0.39]	[0.39; 0.38; 0.39]	[0.40; 0.38; 0.38]	40 M (0.2%)	4.6 M (9.5%)

Figure 4 **Contract Benefits When All R_{ij} with $i \neq j$ Are Misestimated by γ%**



many parameters be known or estimated. But accurate estimates might not be readily available. This section investigates the sensitivity of the outcomes of the coordinating contract with respect to changes in the contract designer's estimated values of the epidemic model parameters relative to their true values.

Although country i need only know R_{ii} and R_{i0}, the contract designer may need to estimate all the R_{ij} values to compute the optimal payments. As estimating R_{ii} can be done more accurately, we study the case where the contract designers misestimate R_{ij} by γ% for all $i \neq j$ (the infection rates across the boundaries are stronger or weaker than anticipated). The values of other parameters are the same as in §4.1.

The benefits of the contract are plotted in Figure 4 as a function of the relative error, γ. Overestimating the parameters results in a more conservative vaccine coverage decision, and therefore a smaller number infected. In most of cases, overestimating the parameters is also preferred from a system cost point of view. In these and other experiments not reported, we observed that the benefit of the contract increases up to threshold γ (typically $5 \approx 10\%$) and then decreases for even larger γ. Thus, there may be an advantage to slightly overestimating the degree of cross-border transmission with the contract.

4.3. How Much Travel Restriction Gives as Much Benefit as the Coordinating Contract?

The implementation of a contract similar to those proposed in this paper would require coordination and could be costly to administer. An interesting question is whether other public health interventions achieve more benefits or fewer benefits, relative to those of the contract presented here. A full answer to this question would involve assessing a wide variety of costs and benefits of numerous programs. As the implementation costs of such programs may vary widely, we focus on a simpler question. We examine the percentage reduction in the intercountry transmission parameters R_{ij} (for $i \neq j$) that is required to achieve benefits that are similar to the cost and health benefits that are associated with the coordinating contract. Such reductions might be contemplated through public awareness and/or travel restrictions, for example.

Table 3 **Decrease in the R_{ij} Needed to Match Benefit of Coordinating Contract**

R_{ij}	Decrease in all R_{ij} (%)	Decrease in R_{i0} (%)
0.05	31	34
0.03	26	30
0.01	18	21
0.005	12	14
0.00087	5	6

Table 3 summarizes the results for the case of $\mathbf{b} = \$[50; 460; 460]$ and $\mathbf{v} = \$[40; 60; 60]$. The second column indicates the percentage reductions in R_{ij} (for $i \neq j$) that are needed to achieve the same cost savings as the contract. The third column shows similar numbers when travel bans are only imposed on the source country. In our test set the percentage reductions varied anywhere from 5% to 34%. Because the percentage reduction required for the R_{i0} alone is only marginally higher than the percentage reduction for all R_{ij}, we confirm that cross-border transmission from the source country is particularly important to reduce. These data also suggest that the coordinating contract can have a benefit that is similar to a nontrivial intervention to reduce transmission parameters.

5. The Game and System Problems with the Complete Epidemic Model

The coordinating contract is based on optimizing the total cost $SF(\mathbf{f})$ in (12) with the star model of infection, as opposed to optimizing the total cost $\widetilde{SF}(\mathbf{f})$ in (15) with the complete model of infection transmission, to obtain analytically tractable results. Although the proposed contract performs favorably in numerical experiments even when evaluated by the total cost with the complete epidemic model, the proposed contract cannot minimize the complete model's costs because the star model approximation is not exact. This section explores whether a contract can shift decisions to a system optimum of the complete model even if decision makers use the star model.

The natural generalization of the game problem to account for the complete model of transmission is

$$\min_{0 \le f_i \le 1 \,|\, f_{-i}} \widetilde{GF}_i \quad \text{for } i = 0, 1, \ldots, M, \tag{16}$$

where $\widetilde{GF}_i \triangleq b_i \tilde{T}_i(\mathbf{f}) + v_i f_i N_i$, and f_{-i} denotes the vaccination fractions of all the countries except for country i. We call the system in (16) the *complete game problem* and denote its solution by $\tilde{\mathbf{f}}^G$. This game's

solution involves multidimensional and implicit transcendental equations. Thus, we do not guarantee a unique Nash equilibrium for this game, and we explore numerical rather than analytical results to compare its equilibria with the complete model's optimum. We refer to $\min_{0\le\mathbf{f}\le 1}\widetilde{SF}(\mathbf{f})$ based on (15) as the *complete system problem* and recall that its solution is $\tilde{\mathbf{f}}^S$ (which was unique in numerical experiments).

Numerical results for the optimal solution of the complete game problem in (16) have the same qualitative behavior that we observed for the game problem with the star model: (1) the source country orders fewer vaccines than is system optimal ($\tilde{f}_0^G < \tilde{f}_0^S$), and (2) other countries order more vaccines than is system optimal ($\tilde{f}_i^G > \tilde{f}_i^S$). If the model parameters set to be consistent with the base case experiment of §4.1, the optimal solution to the complete system game leads to vaccination fractions that are very slightly higher (up to 1%) for nonsource countries compared to the fractions for the star model reported in Table 1, and a vaccination fraction for the source country that may be up to 1% higher or lower than for the star model. The total system cost with the complete model is only slightly lower with $\tilde{\mathbf{f}}^G$ compared to the optimal solution $\mathbf{f}^G$ of the star model game.

Can a simple contractual incentive (that avoids implicit multidimensional transcendental solutions to epidemic models) with financial transfers on top of the costs in (16) push decisions to the complete model's system optimum? Consider a modification of the subsidies of Theorem 4 that tries to push vaccine order fractions to the complete system problem's solution, $\tilde{\mathbf{f}}^S$, rather than to $\mathbf{f}^S$, with

$$\tilde{G}_i(f_0) = (\alpha_i - 1)GF_i(\tilde{f}_i^S, f_0) + \alpha_i \sum_{\substack{j=0\\ j\neq i}}^{M} GF_j(\tilde{f}_j^S, f_0). \quad (17)$$

We denote the optimal decisions of countries that each optimize $\widetilde{GF}_i + \tilde{G}_i(f_0)$ by $\tilde{\mathbf{f}}^C$.

Numerical experiments showed that the subsidy in (17) largely achieved this goal. The results in Table 4 give the complete game problem's solution as well as the solution with the subsidies in (17) in place. The results are comparable with the data in Table 1, which were based on the star model. The optimal vaccination fractions with the complete model are 1% lower to 1% higher for country 0 and 0%–1% lower for nonsource countries except when international transmission is quite high (when $R_{ij} = 0.05$). The total financial burden with $\tilde{\mathbf{f}}^C$ differs by less than 1% from the total financial burden with $\tilde{\mathbf{f}}^S$. Thus, the subsidy in (17) eliminates almost all inefficiency even though the subsidy is designed with a simplified model rather than the complete model (for tractability). In Figure 3 the cost curve with $\tilde{\mathbf{f}}^C$ would be about 1/10 of the way up from the "complete system optimum" curve to the "contract" curve.

Table 4 **Vaccination Fractions for the Complete Game Problem and with Subsidy from (17) (see Table 1)**

R_{ij}	$\tilde{\mathbf{f}}^G$	$\tilde{\mathbf{f}}^C$
0.05	[0.39; 0.49; 0.49]	[0.54; 0.45; 0.45]
0.03	[0.39; 0.46; 0.46]	[0.48; 0.43; 0.43]
0.01	[0.38; 0.42; 0.42]	[0.43; 0.41; 0.41]
0.005	[0.38; 0.41; 0.41]	[0.42; 0.40; 0.40]
0.00087	[0.37; 0.37; 0.38]	[0.40; 0.38; 0.38]

The star model still has value, however, in that (i) it is simpler to implement, (ii) requires countries to assess their own infectious disease outcomes based on only intranational transmission and that from the source country, rather than from all countries, and (iii) the contract with the star model eliminates a sizable fraction of the inefficiency (from 65% to 95% in numerical experiments). We therefore return to the star model in the next section, which examples potential vaccine production shortfalls.

6. Effect of Production Shortage on Coordination

Manufacturers might not be able to fulfill all orders of vaccines because the strain can influence the production yield (U.S. Government Accountability Office 2001). If there is a shortfall, an allocation mechanism is required to assign treatments to various countries and infection outcomes can suffer. The benefits of the coordinating contract from increasing vaccination rates in the source country might seem to suggest that prioritizing vaccines for the source country is a good idea. This section explores whether that is indeed the case as well as the effect of yield uncertainty in vaccine production on health and financial outcomes.

Section 6.1 presents a model of yield uncertainty, defines vaccine allocation policies, extends the game-theoretic formulations above to account for yield uncertainty, and identifies conditions to justify the validity of some of the theoretical results above. Section 6.2 summarizes experiments with numerical solutions to the vaccine allocation problem in the presence of yield uncertainty.

6.1. Formalization with Yield Uncertainty

As did Chick et al. (2008), we presume a proportional yield model, where $U \in [0, 1]$ is a random variable that models the manufacturer's yield uncertainty. The total demand for vaccines is $\sum_{i=0}^{M} f_i N_i$ so the total number of vaccines distributed is $P = U\sum_{i=0}^{M} f_i N_i$. We envisage a nonzero probability of fulfilling all demand ($U = 1$). A value of $U > 1$ is precluded (a government is willing to purchase only up to the amount ordered). If $U < 1$, then not all countries can receive their full order, and vaccines must be rationed.

We define an allocation $\mathbf{U}' = (U_0', U_1', \ldots, U_M')$ to be a random vector that depends on U so that (a) the number of vaccines allocated to country i is $U_i' f_i N_i$, and (b) all vaccines are allocated, $P = \sum_{i=0}^{M} U_i' f_i N_i$.

One allocation of particular interest is the *proportional allocation*, which allocates vaccines to country i in proportion to its demand $f_i N_i$ for each i, so that $U_i' = U$. Another allocation of interest is a so-called *priority allocation*, which allocates vaccines first to the source country, and then proportionally to other countries only after the source country's demand has been satisfied. To describe the priority allocation more formally, we let $\xi = \sum_{j=1}^{M} f_j N_j$ be the total demand of the nonsource countries. The priority allocation is defined by $U_0' = \min\{P/(f_0 N_0), 1\}$ and $U_i' = \max\{0, (P - f_0 N_0)/\xi\}$ for $i = 1, 2, \ldots, M$.

We modify the game problem in (9) to account for yield uncertainty with

Game problem ($\mathbf{U}'$):

$$\left\{ \begin{array}{l} \min\limits_{0 \le f_0 \le 1} GF_0(\mathbf{f}; \mathbf{U}') \triangleq \mathrm{E}[b_0 T_0(U_0' f_0) + v_0 U_0' f_0 N_0], \\ \min\limits_{0 \le f_i \le 1 \mid f_0} GF_i(\mathbf{f}; \mathbf{U}') \triangleq \mathrm{E}[b_i T_i(U_i' f_i, U_0' f_0) + v_i U_i' f_i N_i], \\ \qquad\qquad\qquad\qquad\qquad\qquad \text{for } i = 1, 2, \ldots, M \end{array} \right\}. \tag{18}$$

We modify the system problem in (12) with the star model to account for yield uncertainty with

System problem ($\mathbf{U}'$):

$$\min_{0 \le \mathbf{f} \le 1} SF(\mathbf{f}; \mathbf{U}') \triangleq \mathrm{E}\left[b_0 T_0(U_0' f_0) + v_0 U_0' f_0 N_0 + \sum_{i=1}^{M} b_i T_i(U_i' f_i, U_0' f_0) + v_i U_i' f_i N_i \right]. \tag{19}$$

The game-optimal and system-optimal solutions to the above games are denoted by $\mathbf{f}^G_{\mathbf{U}'}$ and $\mathbf{f}^S_{\mathbf{U}'}$, respectively.

The complete model's costs with yield uncertainty are modeled by $\widetilde{SF}(\mathbf{f}; \mathbf{U}') \triangleq \mathrm{E}[\sum_{i=0}^{M} b_i \tilde{T}_i(\mathbf{U}' \circ \mathbf{f}) + v_i U_i' f_i N_i]$, where $\circ$ is the Hadamard (entrywise) product. In each of these extensions, the optimal vector of vaccination fractions depends on the allocation, and the corresponding models from earlier sections are recovered if the yield is $U = 1$ deterministically.

We note that for general allocations, the games and any associated coordinating contracts may have very different characteristics than those for the proportional allocation. For the proportional allocation, the source country's decision does not depend on the vaccination levels of nonsource countries. For alternative allocations, the amount of vaccine available for the source country may depend on the amount ordered by other countries. The solution of the game problem for general $\mathbf{U}'$ therefore involves a system of nonlinear equations. The solution to the games for $\mathbf{U}'$ was done numerically.

6.2. Numerical Analysis with Vaccine Shortfalls

We computed the optimal vaccine fractions, the expected complete model's cost $\widetilde{SF}(\mathbf{f}; \mathbf{U}')$ (of vaccines, vaccination and cost of infections), and expected total number infected for both the proportional and priority allocations, and for both the game solution and system-optimal solution (of the star model).

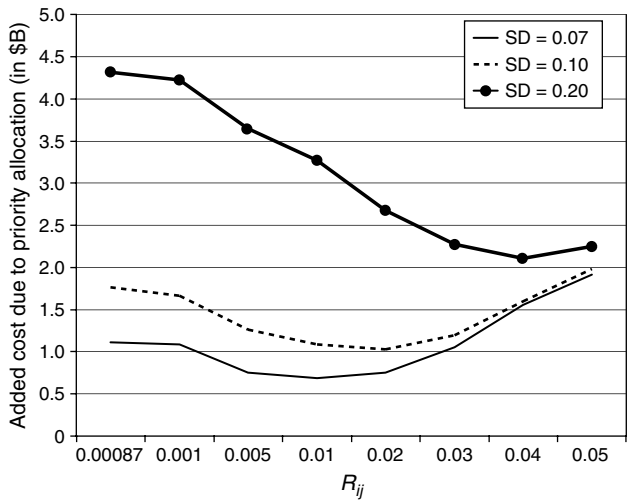
Different variances for the yield were obtained by setting $U = \min\{Z, 1\}$, where Z is uniform on the interval $[1 - a, 1 + a]$ for some $a \in [0, 1]$. Yield uncertainty was indexed by $\sigma_Z \triangleq \sqrt{\mathrm{Var}[Z]}$. We tested $\sigma_Z \in \{0.07, 0.1, 0.2\}$ for all $R_{ij} \in \{0.00087, 0.001, 0.005, 0.01, 0.02, 0.03, 0.04, 0.05\}$. Other parameters were as in the base case of §4. (Results are based on 10^4 samples of Z, reported $\widetilde{SF}(\mathbf{f}; \mathbf{U}')$ accurate to 3–4 significant digits, and reported $\mathbf{f}$ found by sample path optimization with common random numbers for sampled values of yield.)

Table 5 gives a representative subset of the outcomes. Greater yield uncertainty increased vaccine orders with either the proportional allocations or with

Table 5 **Expected Complete Model's Cost $\widetilde{SF}(\cdot)$ (in \$B) and Total Infected (in M) with Yield Uncertainty**

σ_Z	R_{ij}	$\mathbf{f}^G$	$\widetilde{SF}(\mathbf{f}^G)$	E[infect]	$\mathbf{f}^S$	$\widetilde{SF}(\mathbf{f}^S)$	E[infect]	$\mathrm{E}[U\mathbf{f}^S]$
					With proportional allocation			
0.07	0.05	[0.39, 0.53, 0.54]	36.33	33.77	[0.47, 0.51, 0.53]	34.58	17.11	[0.45, 0.49, 0.51]
	0.03	[0.39, 0.50, 0.51]	34.06	31.11	[0.46, 0.49, 0.50]	32.98	18.38	[0.44, 0.47, 0.48]
0.10	0.05	[0.40, 0.55, 0.56]	36.65	33.19	[0.48, 0.53, 0.55]	35.05	16.90	[0.45, 0.50, 0.52]
	0.03	[0.40, 0.51, 0.53]	34.41	30.80	[0.46, 0.50, 0.53]	33.41	15.62	[0.42, 0.47, 0.50]
σ_Z	R_{ij}	$\mathbf{f}^G_{\mathbf{U}'}$	$\widetilde{SF}(\mathbf{f}^G_{\mathbf{U}'}; \mathbf{U}')$	E[infect]	$\mathbf{f}^S_{\mathbf{U}'}$	$\widetilde{SF}(\mathbf{f}^S_{\mathbf{U}'}; \mathbf{U}')$	E[infect]	$\mathrm{E}[\mathbf{U}' \circ \mathbf{f}^S_{\mathbf{U}'}]$
					With priority allocation			
0.07	0.05	[0.38, 0.49, 0.49]	38.24	42.62	[0.47, 0.47, 0.45]	38.02	25.18	[0.47, 0.45, 0.44]
	0.03	[0.38, 0.48, 0.48]	35.12	36.08	[0.45, 0.46, 0.46]	34.62	21.85	[0.45, 0.45, 0.44]
0.10	0.05	[0.38, 0.52, 0.52]	38.63	42.10	[0.46, 0.50, 0.50]	37.77	23.45	[0.46, 0.46, 0.46]
	0.03	[0.38, 0.51, 0.51]	35.61	35.47	[0.42, 0.50, 0.52]	34.93	26.35	[0.42, 0.46, 0.46]

Figure 5 **Added Total Cost Due To Priority Allocation Over Proportional Allocation (SD = σ_Z)**



the game. For example, suppose that $\sigma_Z = 0.1$ (corresponding to $Z \sim \text{unif}[0.82, 1.18]$) and that $R_{ij} = 0.05$. With the proportional allocation, the vaccine orders satisfied $f_0^G = 0.40$, $f_1^G = 0.55$, and $f_2^G = 0.56$. These exceed the vaccine order fractions of [0.38, 0.51, 0.52] for the analogous case when yield was deterministic (see Table 1). Although the system-optimal number of vaccines ordered by the source country may be smaller with the priority allocation ($f^S_{U',0} \le f^S_0$), the far right column of Table 5 shows that the expected number of doses delivered is actually greater for the source country with the priority allocation than without ($\mathrm{E}[U'_0 f^S_{U',0}] \ge \mathrm{E}[U f^S_0]$).

In summary, numerical results from these experiments also suggested that

- the proportional allocation resulted in a lower expected total cost than did the priority allocation;
- the proportional allocation with the coordinating contract resulted in the fewest total infected;
- the proportional allocation resulted in fewer total infections except when yield variability was high ($\sigma_Z = 0.2$) or when international transmission was very low ($R_{ij} \le 0.001$);
- for a given allocation, the use of the contract decreased expected total costs compared to no contract;
- the surplus total cost of the priority allocation over the proportional allocation decreases then increases in R_{ij}, and the R_{ij} that minimizes the difference is larger if yield variability is larger (Figure 5); and
- the benefit of the proportional allocation was higher for larger yield variability.

7. Discussion and Model Limitations

Infectious disease transmission is one area where risks and risk mitigation actions are interdependent. Actors that focus exclusively on their own risks and that do not account for the full level of interdependencies can lead to suboptimal decisions. The proposed coordinating contract in Theorem 4 improves financial outcomes and infection events globally, assuming that *systemwide* is interpreted to mean the sum of individual countries' models of their burden of influenza. It does so flexibly and can satisfy the participation constraints of countries that can gain from influenza vaccination ("can gain" for the SIR model means $b_i\psi > v_i$).

Numerical results indicate that the coordinating contract also eliminates much of the inefficiency associated with ignoring much, but not all, of the interdependent risk (as expressed by use of the star model rather than the complete model). Use of the star model would imply that a country need not set its own vaccination policy as a function of transmission rates between two other countries. The use of the star model therefore appears to be a reasonable approximation to the complete epidemic model for purposes of designing a contract for improving global health outcomes for annual influenza.

The financial transfers in the proposed contract are compatible in spirit with the recommendation of the WHO to GAVI to find novel methods of insuring higher levels of seasonal influenza vaccine production to prepare for an eventual pandemic, using techniques that may include supply chain and financial support for developing countries (World Health Organization and UNICEF 2007).

There are several limitations of the above model, some of which we can already address as follows.

The model in this paper does not explicitly consider the incentives of manufacturers. The problem with one manufacturer's incentives and one buyer has been handled elsewhere (Chick et al. 2008). That said, we observed that a manufacturer sells more vaccines with the coordinating contract than without in numerical experiments above, so the manufacturer also appears to be a winner with this contract.

The framework allows for a relatively broad class of epidemic models, which may include policies for priority vaccination in targeted subpopulations, use of antivirals and social interventions, etc., as long as Assumption 3 is satisfied. The analysis assumes that all parameters are known to all parties. Numerical results with the SIR model suggest that if parameters are unknown, pessimistic estimates are likely to lead to better financial and health outcomes than optimistic ones.

Unequal social costs of the disease in different countries raises several issues. One, such inequality gives an incentive to the manufacturer to charge different vaccine prices to the governments, which may ultimately lead to diverting vaccines from one

country to another in the case of a production shortage. Two, different social costs influence system-optimum vaccine allocations from a central planner's point of view. Social costs reflect the average cost of an infected person, which may differ from one country to another because of different costs of prescription drugs and hospitalization, and indirect costs of the disease. This can, to some extent, justify the different economic sensitivity of the central planner to disease in different countries. Three, a multiattribute approach might be desired to examine the number of deaths or hospitalizations. These features can be modeled indirectly with our model by assessing the number infected and applying the relevant morbidity and mortality rates (to minimize the number of deaths or hospitalizations), or by setting the same social cost of disease to all countries (to assess the value of life equally across the different countries). Section 4 addresses some of these concerns by illustrating the effect of contract on the total number of infected individuals in each population. For example, the benefits of the contract increase as b_0 decreases, which is desirable if the source country is a developing country.

We assumed that the source country was known at the time that vaccine orders are placed. Although it is true that the identity of the source country is sometimes known in advance (e.g., through surveillance tracking up to the time of vaccine strain selection), it is possible to get this choice wrong. The H1N1 strain from Mexico, at a time when H5N1 was being watched in Southeast Asia, is one case in point. One way to handle this uncertainty would be to structure the contract in a way so that transfers of subsidies occur to country 0 after the identity of country 0 is revealed. Another way is to have the contract be conditional: the subsidies would be activated if the dominant strain of influenza that circulated indeed matched one of the strains that was originally selected for the vaccine, with subsidy directed to the country that had the highest initial prevalence of that strain, assuming that country shared its surveillance data. This type of funding would be consistent with encouraging and rewarding the sharing of strain information from surveillance.

Finally, we do not prognosticate as to whether governments could agree to a contract such as has been structured here. That question has political ramifications. This paper quantifies, however, that there is a nontrivial financial and health benefit if such an agreement can be found.

8. Conclusion

Our model indicates that a lack of coordination for global health goals results in a shortfall of influenza vaccines in regions that may need them most and an excess of vaccines in other regions. A variation of the cost-sharing contract is shown to be one option that can align incentives of different governments to achieve a globally optimum allocation of vaccines. Numerical experiments suggest the following:

- for realistic parameter values for influenza, our model predicts that millions of influenza cases can be averted annually by using the proposed contract, resulting in a global savings of tens of millions of dollars;
- in each numerical example we ran, there was a reduction in the number infected people in every country with the coordinating contract in place compared to the scenario without that contract;
- the health benefits and cost savings are greater if there is greater international travel;
- the benefits are also increased if the expected net benefit per dose is smaller in the source country, which is particularly interesting if the source country for the infection is a developing country;
- the benefits of the proposed contract can still be significant even if cross-boundary transmission parameters are estimated imperfectly, especially if the estimates are biased higher than their true values;
- the contract has benefits comparable to those from a 5%–35% reduction in international transmission as made possible by travel restrictions, for example;
- the coordinating contract with the proportional allocation outperforms a solution that is based on prioritizing the source country if yield uncertainty leads to a supply shortage.

This paper also contributes to the analysis of games that are neither submodular nor supermodular, but that satisfy the properties that are described in Assumption 3.

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Appendix. Mathematical Proofs

Proof of Lemma 1. By (4) and Assumption 1, it is enough to focus on the first two columns of the $2(M+1) \times 2(M+1)$

matrix $\mathbf{N}^g$. To show the desired result, we show that the matrix $\mathbf{N}^g$ has the following form:

$$\mathbf{N}^g = \begin{bmatrix} R_{00}\mathcal{F}_{00}^{(g)}(\mathbf{f}) & R_{00}\phi\mathcal{F}_{00}^{(g)}(\mathbf{f}) & \dots & R_{0M}\mathcal{F}_{0M}^{(g)}(\mathbf{f}) & R_{0M}\phi\mathcal{F}_{0M}^{(g)}(\mathbf{f}) \\ R_{00}\mathcal{H}_{00}^{(g)}(\mathbf{f}) & R_{00}\phi\mathcal{H}_{00}^{(g)}(\mathbf{f}) & \dots & R_{0M}\mathcal{H}_{0M}^{(g)}(\mathbf{f}) & R_{0M}\phi\mathcal{H}_{0M}^{(g)}(\mathbf{f}) \\ R_{M0}\mathcal{F}_{M0}^{(g)}(\mathbf{f}) & R_{M0}\phi\mathcal{F}_{M0}^{(g)}(\mathbf{f}) & \dots & R_{MM}\mathcal{F}_{MM}^{(g)}(\mathbf{f}) & R_{MM}\phi\mathcal{F}_{MM}^{(g)}(\mathbf{f}) \\ R_{M0}\mathcal{H}_{M0}^{(g)}(\mathbf{f}) & R_{M0}\phi\mathcal{H}_{M0}^{(g)}(\mathbf{f}) & \dots & R_{MM}\mathcal{H}_{MM}^{(g)}(\mathbf{f}) & R_{MM}\phi\mathcal{H}_{MM}^{(g)}(\mathbf{f}) \end{bmatrix}, \tag{20}$$

where $\mathcal{F}_{ij}^{(1)}(\mathbf{f}) = 1 - f_j$, and $\mathcal{H}_{ij}^{(1)}(\mathbf{f}) = \theta f_j$ for all $i, j \in \{0, 1, \dots, M\}$, and where $\mathcal{F}_{ij}^{(g)}(\mathbf{f})$ and $\mathcal{H}_{ij}^{(g)}(\mathbf{f})$ are defined for $g = 2, 3, \dots$ by

$$\begin{aligned} R_{ij}\mathcal{F}_{ij}^{(g)}(\mathbf{f}) &= (1-\psi f_j)\sum_{k=0}^{M} R_{ik}R_{kj}\mathcal{F}_{ik}^{(g-1)}(\mathbf{f}) \\ &\qquad \text{for all } i, j \in \{0, 1, \dots, M\}, \\ R_{ij}\mathcal{H}_{ij}^{(g)}(\mathbf{f}) &= (1-\psi f_j)\sum_{k=0}^{M} R_{ik}R_{kj}\mathcal{H}_{ik}^{(g-1)}(\mathbf{f}) \\ &\qquad \text{for all } i, j \in \{0, 1, \dots, M\}. \end{aligned} \tag{21}$$

The proof is by induction.

Induction base. For $g = 1$ we have the matrix in (5) which is clearly in the desired form. Furthermore, we note that every summand in terms $\mathcal{F}_{ij}^{(g)}$ and $\mathcal{H}_{ij}^{(g)}$ that involves f_k for any $k \notin \{i, j\}$ has a coefficient of the form $R_{ab}R_{bc}$ for some $a \neq b \neq c$ (this is trivial, because there are no such terms when $g = 1$).

Induction step. Suppose that $\mathbf{N}^g$ is of the form in (20). Recall that the $(2j+1, 2l+1)$th element of $\mathbf{N}$ is $R_{jl}(1 - f_l)$, and the $(2j+2, 2l+1)$th element of $\mathbf{N}$ is $R_{jl}\theta f_l$. Then the $(2k+1, 2l+1)$th element of $\mathbf{N}^{g+1}$ is

$$\begin{aligned} &(\mathbf{N}^{g+1})_{(2k+1,\,2l+1)} \\ &\quad = \sum_{\ell=1}^{2(M+1)} (\mathbf{N}^g)_{(2k+1,\,\ell)} \cdot (\mathbf{N})_{(\ell,\,2l+1)} \\ &\quad = \sum_{j=0}^{M} R_{kj}\mathcal{F}_{kj}^{(g)}(\mathbf{f}) \times R_{jl}(1-f_l) + R_{kj}\phi\mathcal{F}_{kj}^{(g)}(\mathbf{f}) \times R_{jl}\theta f_l \\ &\quad = \sum_{j=0}^{M} R_{kj}R_{jl}(1-(1-\theta\phi)f_l)\mathcal{F}_{kj}^{(g)}(\mathbf{f}) = R_{kl}\mathcal{F}_{kl}^{(g+1)}(\mathbf{f}), \end{aligned}$$

where the last equality is based on (21) and the definition of ψ.

Likewise, the $(2k+1, 2l+2)$th $(k, l \in \{0, 1, \dots, M\})$ element of matrix R^{g+1} is $R_{kl}\phi\mathcal{F}_{kl}^{(g+1)}(\mathbf{f})$. We can show similar relations to show that $(\mathbf{N}^{g+1})_{(2k+2,\,2l+1)} = R_{kl}\mathcal{H}_{kl}^{(g+1)}(\mathbf{f})$ and $(\mathbf{N}^{g+1})_{(2k+2,\,2l+2)} = R_{kl}\phi\mathcal{H}_{kl}^{(g+1)}(\mathbf{f})$, as required to conclude the induction argument for the form of $\mathbf{N}^g$.

Returning to (21) again gives

$$\begin{aligned} R_{ij}\mathcal{F}_{ij}^{(g)}(\mathbf{f}) &= (1-\psi f_j)R_{ij}\big(R_{ii}\mathcal{F}_{ii}^{(g-1)}(\mathbf{f}) + R_{jj}\mathcal{F}_{jj}^{(g-1)}(\mathbf{f})\big) \\ &\quad + (1-\psi f_j)\sum_{k:\,k\neq i,\,j} R_{ik}R_{kj}\mathcal{F}_{ik}^{(g-1)}(\mathbf{f}). \end{aligned} \tag{22}$$

Therefore, all of the summands in $\mathcal{F}_{ij}^{(g)}$ that involve f_k for any $k \notin \{i, j\}$ have a coefficient of the form $R_{ab}R_{bc}$ for some $a \neq b \neq c$. By mathematical induction, then, all of the summands $\mathcal{F}_{ij}^{(g)}$ that depend on f_k for any $k \notin \{i, j\}$ have a coefficient of the form $R_{ab}R_{bc}$ for any $a \neq b \neq c$.

The number infected, $y_{0i}(g) + y_{1i}(g)$, in country i at generation g is determined by $\mathbf{y}(0) = \mathbf{N}^g\mathbf{y}(0)$. Recall $\mathbf{y}(0) = [y_{00}(0), y_{10}(0), 0, 0, \dots, 0, 0]^T$. Thus,

$$\begin{aligned} y_{0i}(g) + y_{1i}(g) &= R_{i0}\mathcal{F}_{i0}^{(g)}(\mathbf{f})y_{00}(0) + R_{i0}\phi\mathcal{F}_{i0}^{(g)}(\mathbf{f})y_{10}(0) \\ &\quad + R_{i0}\mathcal{H}_{i0}^{(g)}(\mathbf{f})y_{00}(0) + R_{i0}\phi\mathcal{H}_{i0}^{(g)}(\mathbf{f})y_{10}(0) \\ &= R_{i0}(y_{00}(0) + \phi y_{10}(0))(\mathcal{F}_{i0}^{(g)}(\mathbf{f}) + \mathcal{H}_{i0}^{(g)}(\mathbf{f})). \end{aligned}$$

Applying the induction result about coefficients of the form $R_{ab}R_{bc}$ with $j = 0$ implies that

$$\begin{aligned} &y_{0i}(g) + y_{1i}(g) \\ &= R_{i0}(y_{00}(0) + \phi y_{10}(0))(\mathcal{F}_{i0}^{(g)}(\mathbf{f}) + \mathcal{H}_{i0}^{(g)}(\mathbf{f})) \\ &= (y_{00}(0) + \phi y_{10}(0))(1-\psi f_0)R_{i0} \\ &\quad \cdot \big(R_{ii}(\mathcal{F}_{ii}^{(g-1)}(\mathbf{f}) + \mathcal{H}_{ii}^{(g-1)}(\mathbf{f})) + R_{00}(\mathcal{F}_{00}^{(g-1)}(\mathbf{f}) + \mathcal{H}_{00}^{(g-1)}(\mathbf{f}))\big) \\ &\quad + (y_{00}(0) + \phi y_{10}(0))(1-\psi f_0)\sum_{k:\,k\neq i,\,0} R_{ik}R_{k0}(\mathcal{F}_{ik}^{(g-1)}(\mathbf{f}) + \mathcal{H}_{ik}^{(g-1)}(\mathbf{f})) \\ &= (y_{00}(0) + \phi y_{10}(0))(1-\psi f_0)R_{i0} \\ &\quad \cdot \big(R_{ii}(\mathcal{F}_{ii}^{(g-1)}(\mathbf{f}) + \mathcal{H}_{ii}^{(g-1)}(\mathbf{f})) + R_{00}(\mathcal{F}_{00}^{(g-1)}(\mathbf{f}) + \mathcal{H}_{00}^{(g-1)}(\mathbf{f}))\big) \\ &\quad + \mathcal{G}_i^{(g)}(\mathbf{f}), \end{aligned}$$

where $\mathcal{G}_i^{(g)}(\mathbf{f})$ is a function whose summands all have coefficients of the form $R_{ij}R_{jk}$ for some $i \neq j \neq k$, and where $\mathcal{F}_{ii}^{(g-1)}(\mathbf{f})$, $\mathcal{H}_{ii}^{(g-1)}(\mathbf{f})$ depend on $\mathbf{f}$ only through f_0 and f_i. Let

$$\begin{aligned} \mathcal{F}_i^{(g)}(f_i, f_0) &= (y_{00}(0) + \phi y_{10}(0))(1-\psi f_0) \\ &\quad \cdot \big(R_{ii}(\mathcal{F}_{ii}^{(g-1)}(\mathbf{f}) + \mathcal{H}_{ii}^{(g-1)}(\mathbf{f})) \\ &\quad + R_{00}(\mathcal{F}_{00}^{(g-1)}(\mathbf{f}) + \mathcal{H}_{00}^{(g-1)}(\mathbf{f}))\big) \end{aligned} \tag{23}$$

to obtain the desired result. For the special case of $\mathbf{y}(0) = N_0\omega(1 - f_0, \theta f_0, 0, 0, \dots, 0, 0)^T$, which assumes that ω percent of country 0 is infected at time zero (modulo the susceptibility effect of the vaccine), the number infected is

$$\begin{aligned} \mathcal{F}_i^{(g)}(f_i, f_0) &= N_0\omega(1-\psi f_0)^2\big(R_{ii}(\mathcal{F}_{ii}^{(g-1)}(\mathbf{f}) + \mathcal{H}_{ii}^{(g-1)}(\mathbf{f})) \\ &\quad + R_{00}(\mathcal{F}_{00}^{(g-1)}(\mathbf{f}) + \mathcal{H}_{00}^{(g-1)}(\mathbf{f}))\big). \quad \square \end{aligned}$$

Proof of Lemma 2. To prove this lemma, we show that the summand $\mathcal{F}_{ij}^{(g)}(\mathbf{f}) + \mathcal{H}_{ij}^{(g)}(\mathbf{f})$ from the preceding proof is a nonincreasing, convex function of f_i and f_j. The proof is by induction on g. The base case is straightforward $\mathcal{F}_{ij}^{(1)}(\mathbf{f}) + \mathcal{H}_{ij}^{(1)}(\mathbf{f}) = 1 - (1-\theta)f_j$ is a nonincreasing convex function. The induction step is carried out by adding the two lines in (21) and noting that nonincreasing and convexity properties are maintained under summation. Thus, using (23), $\mathcal{F}_i^{(g)}$ is a nonincreasing convex function of f_i and a nonincreasing function of f_0 (due to nonincreasing properties of $(1-\psi f_0)$ and $\mathcal{F}_{00}^{(g-1)}(\mathbf{f}) + \mathcal{H}_{00}^{(g-1)}(\mathbf{f})$). To show that $\mathcal{F}_i^{(g)}$ is convex in f_0, we take its second derivative with respect to f_0. Using (23),

$$\begin{aligned} \frac{\partial^2\mathcal{F}_i^{(g)}}{\partial f_0^2} &= R_{00}(y_{00}(0) + \phi y_{10}(0))\bigg[(1-\psi f_0)\frac{\partial^2(\mathcal{F}_{00}^{(g)}(f_0) + \mathcal{H}_{00}^{(g)}(f_0))}{\partial f_0^2} \\ &\quad - \psi\frac{\partial(\mathcal{F}_{00}^{(g)}(f_0) + \mathcal{H}_{00}^{(g)}(f_0))}{\partial f_0}\bigg], \end{aligned}$$

which is a nonnegative term by the nonincreasing and convexity properties of $\mathcal{I}_{00}^{(g)}(f_0)+\mathcal{H}_{00}^{(g)}(f_0)$. □

Proof of Theorem 1. To show the first part of the claim, we take p_i in (7) to the right-hand side and take the derivative with respect to f_i. Using the chain rule we have

$$\begin{aligned}&-\frac{\partial p_i}{\partial f_i}+R_{ii}(1-\chi)(1-\psi f_i)e^{-R_{ii}p_i}\frac{\partial p_i}{\partial f_i}-\psi+(1-\chi)\psi e^{-R_{ii}p_i}=0\\ &\Rightarrow\quad \frac{\partial p_i}{\partial f_i}=-\frac{\psi-(1-\chi)\psi e^{-R_{ii}p_i}}{1-R_{ii}(1-\chi)(1-\psi f_i)e^{-R_{ii}p_i}}.\end{aligned}\tag{24}$$

The numerator is clearly positive because $(1-\chi)e^{-R_{ii}p_i}<1$ for all $p_i\geq 0$ and $0<\chi<1$. So it is enough to show that the denominator is positive. To show this, consider the term in the denominator, and replace $1-\psi f_i$ from (7):

$$\begin{aligned}&1-R_{ii}(1-\chi)(1-\psi f_i)e^{-R_{ii}p_i}\\ &\quad=1-R_{ii}(1-\chi)\left(\frac{p_i}{1-(1-\chi)e^{-R_{ii}p_i}}\right)e^{-R_{ii}p_i}\\ &\quad=\frac{1}{1-(1-\chi)e^{-R_{ii}p_i}}(1-(1-\chi)e^{-R_{ii}p_i}-R_{ii}p_i(1-\chi)e^{-R_{ii}p_i})\\ &\quad=\frac{1}{1-(1-\chi)e^{-R_{ii}p_i}}(1-(1-\chi)(1+R_{ii}p_i)e^{-R_{ii}p_i})>0.\end{aligned}$$

The reason for the last inequality is that $(1+x)e^x$ obtains its maximum value at zero. The result for country 0 follows similarly if we assume that χ_0 does not depend on f_0 (the other χ_i may depend on f_0).

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

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

We showed before that the denominator is positive. The numerator is negative based on Lemma 2, so the initial number infected in country i is a decreasing function of f_0.

To show the third part, we take the derivative of p_i with respect to both variables which leads to

$$\begin{aligned}&-\frac{\partial^2 p_i}{\partial f_0\partial f_i}-R_{ii}^2(1-\chi)(1-\psi f_i)e^{-R_{ii}p_i}\frac{\partial p_i}{\partial f_0}\frac{\partial p_i}{\partial f_i}\\ &\qquad+R_{ii}(1-\chi)(1-\psi f_i)e^{-R_{ii}p_i}\frac{\partial^2 p_i}{\partial f_0\partial f_i}\\ &\qquad-R_{ii}(1-\chi)\psi e^{-R_{ii}p_i}\frac{\partial p_i}{\partial f_0}-\frac{\partial\chi}{\partial f_0}\psi e^{-R_{ii}p_i}\\ &\qquad-R_{ii}\frac{\partial\chi}{\partial f_0}(1-\psi f_i)e^{-R_{ii}p_i}\frac{\partial p_i}{\partial f_i}=0.\end{aligned}$$

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

$$-\left[R_{ii}(1-\chi)\frac{\partial p_i}{\partial f_0}+\frac{\partial\chi}{\partial f_0}\right]\left[\psi+R_{ii}(1-\psi f_i)\frac{\partial p_i}{\partial f_i}\right].$$

Note that $\partial p_i/\partial f_i\leq 0$ and $\partial\chi/\partial f_0\leq 0$. Thus, the left term is negative, and $\mathrm{SIGN}[\partial^2 p_i/(\partial f_0\partial f_i)]=\mathrm{SIGN}[\psi+R_{ii}(1-\psi f_i)\cdot(\partial p_i/\partial f_i)]$. To find the sign of this last term, we use the expression from the first part for $\partial p_i/\partial f_i$:

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

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

To show the fourth part, we use a different approach in computing the second derivative. In (7) we rearrange the terms so that f_i is a function of p_i,

$$f_i=\frac{1}{\psi}\left[1-\frac{p_i}{1-(1-\chi)e^{-R_{ii}p_i}}\right].$$

Because p_i is a decreasing function of f_i, $\partial^2 p_i/\partial f_i^2$ and $\partial^2 f_i/\partial p_i^2$ have the same signs. We now investigate the sign of $\partial^2 f_i/\partial p_i^2$:

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

The sign of the above expression is the same as the sign of the following term:

$$-R_{ii}p_i+2-(R_{ii}p_i+2)(1-\chi)e^{-R_{ii}p_i}.\tag{25}$$

We show that the typical sign of the above equation is first negative then positive, which corresponds to a first concave then convex function. To show this we simply show that the above term is an increasing function of f_i or equivalently a decreasing function of p_i, because p_i and f_i have inverse relations (from first part of claim). By taking the derivative of the above term with respect to p_i, we get

$$-R_{ii}+R_{ii}(1-\chi)(1+R_{ii}p_i)e^{-R_{ii}p_i}\leq 0,$$

where the inequality is due to decreasing property of function $(1+x)e^{-x}$. Thus, (25) is increasing in f_i (decreasing in p_i), and the sign of $\partial^2 f_i/\partial p_i^2$ is negative and then positive. This implies the attack rate is strictly concave and then strictly convex (the second derivative is not 0 at more than 1 point). Either of these sections can be empty (e.g., this function is always concave when $R_{ii}(1-\psi)>2$, with a large basic reproduction number and a weak vaccine effect).

The continuity of the derivatives of $T_i()$ with respect to f_j follows from inspection. □

Proof of Lemma 3. We prove the result for $i>0$. The derivative of country i's objective function, $b_i(\partial/\partial f_i)T_i(f_i,f_0)+v_iN_i$, is negative when evaluated at $f_i=0$ by Assumption 4. We now consider two cases.

Case 1. $b_i(\partial/\partial f_i)T_i(f_i,f_0)|_{f_i=1}+v_iN_i<0$. In this case, $b_i(\partial/\partial f_i)T_i(f_i,f_0)|_{f_i=f}+v_iN_i<0$ for all $0\leq f\leq 1$, as the

objective function is first concave and then convex, and its derivative is negative for $f=0$ and $f=1$. Therefore, $f_i^G=1$.

Case 2. $b_i\partial/(\partial f_i)T_i(f_i,f_0)|_{f_i=1}+v_iN_i\geq 0$. In this case, because the derivative exists, is continuous, is negative at $f_i=0$, and is positive at $f_i=1$, there exists at least one point where the derivative of the objective function (with respect to f_i) is zero.

These two cases provide the necessary conditions in (11) for a Nash equilibrium. The proof for $i=0$ to obtain (10) is the same as above except that $T_0(\cdot)$ depends on only f_0 and no other f_i.

To show that there is a unique Nash equilibrium, we first show that there exists a unique f_0^G that satisfies (10). To prove this, recall the strict monotonicity of p_0 in f_0 from Assumption 3(b) and the fact that it is first strictly concave and then strictly convex in f_0. The term on the left-hand side of the inequality in (10) therefore first decreases (in the concave part) and then increases monotonically (in the convex part). Thus, the optimal order quantity for the source country, f_0^G, has to lie in the convex region, which is also bounded. This shows its uniqueness. The same argument applies to show the uniqueness of f_i^G, given the uniqueness of f_0^G. □

Proof of Lemma 4. The proof follows from the KKT conditions for the problem in (12), namely,

$$0=b_0\frac{\partial}{\partial f_0}T_0(f_0)+\left(\sum_{i=1}^{M}b_i\frac{\partial}{\partial f_0}T_i(f_i,f_0)\right)+v_0N_0-\gamma_0+\eta_0,$$

$$0=b_i\frac{\partial}{\partial f_i}T_i(f_i,f_0)+v_iN_i-\gamma_i+\eta_i,\quad \text{for } i=1,2,\ldots,M,$$

where the γ_is and η_is are the KKT multipliers for the conditions $f_i\geq 0$, and $f_i\leq 1$, respectively.

By Assumptions 3 and 4, we have

$$b_0\frac{\partial}{\partial f_0}T_0(f_0)\bigg|_{f_0=0}+\left(\sum_{i=1}^{M}b_i\frac{\partial}{\partial f_0}T_i(f_i,f_0)\bigg|_{f_0=0}\right)+v_0N_0<b_0N_0\frac{\partial}{\partial f_0}p_0(f_0)\bigg|_{f_0=0}+v_0N_0<0$$

and $b_i\partial T_i(f_i,f_0)/\partial f_i|_{f_i=0}+v_iN_i<0$ for $i=1,2,\ldots,M$.

Thus, $\gamma_i=0$ for $i=0,1,\ldots,M$, as γ_i and η_i can not be both zero at the same time. Furthermore, the derivative of the objective function with respect to f_0 is less than $b_0(\partial/\partial f_0)T_0(f_0)+v_0N_0$. Therefore, if less than 1, the optimal f_0 happens to be in the convex region because $b_0(\partial/\partial f_0)T_0(0)+v_0N_0<0$. □

Proof of Theorem 2. To prove part (a), we consider two cases.

Case 1. Suppose $f_0^G=1$. Then $b_0(\partial/\partial f_0)T_0(f_0)|_{f_0=1}+v_0N_0\leq 0$, and the left-hand side of the first Equation in (13) is negative for any f_i^S, and thus $f_0^S=1$ as well. So in this case $f_0^G=f_0^S=1$.

Case 2. Suppose $f_0^G<1$. If $f_0^S=1$, then part (a) is true. We now suppose that $f_0^S<1$. Because $f_0^G<1$, Lemma 3 implies that $b_0(\partial/\partial f_0)T_i(f_0)|_{f_0=f_0^G}+v_0N_0=0$. We note that $(\partial/\partial f_0)T_i(f_i,f_0)\leq 0$ for $i=1,2,\ldots,M$ by properties of the attack rates in Assumption 3(b). Because $f_0^G<1$, a comparison of f_0^G from Lemma 3 (with equality holding in place of the inequality at the supremum) and f_0^S from Lemma 4 gives

$$\frac{\partial}{\partial f_0}T_0(f_0)\bigg|_{f_0^S}\geq\frac{\partial}{\partial f_0}T_0(f_0)\bigg|_{f_0^G}\quad\Longrightarrow\quad f_0^S\geq f_0^G.$$

The above inequality is true because f_0^S and f_0^G are both in the convex region of $T_0(\cdot)$ (see proofs of Lemmas 3 and 4).

We now turn to part (b). Let $i\in\{1,2,\ldots,M\}$. We consider two cases.

Case 1. If $f_i^G=1$, then $f_i^G\geq\bar{\bar{f}}_i$, and clearly $f_i^S\leq f_i^G=1$.

Case 2. If $f_i^G<1$, then $b_i(\partial/\partial f_i)T_i(f_i,f_0)|_{f_i=f_i^G}+v_iN_i=0$. Suppose that $f_i^G\geq\bar{\bar{f}}_i$. If, in addition, $f_i^S<\bar{\bar{f}}_i$, the claim is true. We now handle the case of $f_i^S\geq\bar{\bar{f}}_i$. Thus, both f_i^S and f_i^G lie in the supermodular section of the attack rate function due to Assumption 3(c). Proceeding by contradiction, suppose for the moment that $f_i^S>f_i^G$. Because $f_0^S>f_0^G$ was just shown, we have

$$\frac{\partial T_i(f_i,f_0^S)}{\partial f_i}\bigg|_{f_i^S}>\frac{\partial T_i(f_i,f_0^G)}{\partial f_i}\bigg|_{f_i^S}\tag{26}$$

$$>\frac{\partial T_i(f_i,f_0^G)}{\partial f_i}\bigg|_{f_i^G}.\tag{27}$$

The inequality in (26) is due to the supermodularity of the attack rate function at f_i^S, and (27) follows because both f_i^G and $f_i^S(>f_i^G)$ lie in the convex region of $T_i(f_i,f_0^G)$. Notice that, given (13), the left term in (26) is less than $-v_iN_i$. Given (11), the term in (27) equals $-v_iN_i$ (because $f_i^G<1$), a contradiction. Thus, $f_i^S<f_i^G$.

Now suppose that $f_i^G\leq\bar{\bar{f}}_i$. If, in addition, $f_i^S\geq\bar{\bar{f}}_i$, the claim is true. We now handle the case of $f_i^S<\bar{\bar{f}}_i$. Thus, both f_i^S and f_i^G lie in the submodular section of the attack rate function due to Assumption 3(c). Proceeding by contradiction, suppose for the moment that $f_i^S<f_i^G$. Because $f_0^S>f_0^G$, we have

$$\frac{\partial T_i(f_i,f_0^G)}{\partial f_i}\bigg|_{f_i^G}>\frac{\partial T_i(f_i,f_0^S)}{\partial f_i}\bigg|_{f_i^G}\tag{28}$$

$$>\frac{\partial T_i(f_i,f_0^S)}{\partial f_i}\bigg|_{f_i^S}.\tag{29}$$

The inequality in (28) is due to the supermodularity of the attack rate function at f_i^S, and (29) follows because both f_i^S and $f_i^G(>f_i^S)$ lie in the convex region of $T_i(f_i,f_0^S)$. Notice that, given (11), the term in (29) equals $-v_iN_i$, because $f_i^G<1$. Given (13), the left term in (28) also equals $-v_iN_i$ (because $f_i^S<\bar{\bar{f}}_i\leq 1$), a contradiction. Thus, $f_i^S\geq f_i^G$. □

Proof of Theorem 3. Given the setup of the theorem, $\bar{f}_i=\bar{\bar{f}}_i$ was shown by Theorem 1. We show that under Assumption 4, for any vaccination level $f_i<\bar{\bar{f}}_i$, the terms on the left-hand sides of the inequalities in (10) and (11) are negative, which will implies that the solution of the equilibrium state has to be at least the critical vaccination fraction. For this purpose we fix i and replace the left-hand side of (11) for this country with the derivative from (24),

$$b_i\frac{\partial}{\partial f_i}T_i(f_i,f_0^G)+v_iN_i=b_iN_i\frac{\partial}{\partial f_i}p_i(f_i,f_0^G)+v_iN_i$$

$$= N_i\left(-b_i\psi\frac{1-(1-\chi)e^{-R_{ii}p_i}}{1-R_{ii}(1-\chi)(1-\psi f_i)e^{-R_{ii}p_i}}+v_i\right)$$
$$< N_i(-b_i\psi+v_i)<0.$$

The first inequality in the third line uses $f_i<\bar{f}_i$ which is equivalent to $R_0(1-\psi f_i)>1$; thus, we get a larger term by replacing the term $R_0(1-\psi f_i)$ with 1 in the denominator. The last inequality uses Assumption 4. □

Proof of Theorem 4. Note that the total subsidy received by the source country is

$$G_0(f_0)=\sum_{i=1}^{M}G_i(f_0)=(1-\alpha_0)GF_0(f_0)-\alpha_0\sum_{i=1}^{M}GF_i(f_i^S,f_0).$$

Therefore, the total cost of the source country with the proposed contract, GFC_0, would be

$$\begin{aligned}GFC_0(f_0) &= GF_0(f_0)-G_0(f_0)\\ &= GF_0(f_0)-(1-\alpha_0)GF_0(f_0)+\alpha_0\sum_{i=1}^{M}GF_i(f_i^S,f_0)\\ &= \alpha_0\left[GF_0(f_0)+\sum_{i=1}^{M}GF_i(f_i^S,f_0)\right].\end{aligned}$$

Similarly, the total cost of country i, with the proposed contract, GFC_i, would be

$$\begin{aligned}&GFC_i(f_i,f_0)\\ &= GF_i(f_i,f_0)+G_i(f_0)\\ &= GF_i(f_i,f_0)+(\alpha_i-1)GF_i(f_i^S,f_0)+\alpha_i\sum_{j=0;\,j\neq i}^{M}GF_j(f_j^S,f_0)\\ &= GF_i(f_i,f_0)-GF_i(f_i^S,f_0)+\alpha_i\left[GF_0(f_0)+\sum_{i=1}^{M}GF_i(f_i^S,f_0)\right],\\ &\qquad i=1,2,\ldots,M.\end{aligned}$$

Taking the derivatives of GFC_i $(i=0,1,\ldots,M)$ with respect to f_i, and using (13), the optimal vaccine allocation would be $(f_0^S,f_1^S,\ldots,f_M^S)$. Therefore, the optimal total cost for each country i would be

$$\begin{aligned}GFC_i(f_i^S,f_0^S) &= \alpha_i\left[GF_0(f_0^S)+\sum_{i=1}^{M}GF_i(f_i^S,f_0^S)\right]\\ &= \alpha_i SF(\mathbf{f}^S),\quad (i=0,1,\ldots,M).\end{aligned}$$

Letting $\alpha_i=GF_i(f_i^G,f_0^G)/SF(\mathbf{f}^G)$, we have $GFC_i(f_i^S,f_0^S)=\alpha_i SF(\mathbf{f}^S)=(GF_i(f_i^G,f_0^G)/SF(\mathbf{f}^G))SF(\mathbf{f}^S)<GF_i(f_i^G,f_0^G)$. □

Proof of Corollary 1. The proof follows directly from the discussion above the statement of the corollary. □

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