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Incorporating the Centers for Disease Control and Prevention into Vaccine Pricing Models

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Abstract

The American vaccine pricing market has many actors, making it a complex system to model. Because of this, previous papers have chosen to model only vaccine manufacturers while leaving out the government. However, the government is also an important actor in the market, since it buys over half of vaccines produced. In this work, we aim to introduce the government into vaccine pricing models to better recommend pricing strategies to the Centers for Disease Control and Prevention.

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Chapter 1

Introduction

1.1   The Vaccine Market

Vaccines play a key role in preventative health care. For children born in the United States in 1994-2013, vaccinations are estimated to prevent 732 thousand deaths, 21 million hospitalizations and 322 million illnesses (Whitney et al. (2014)). The government has a large role in providing vaccines to the public: 57% of vaccines by volume are purchased by federal, state and local public agencies at federal contract prices, while the remaining vaccines are distributed across private markets (Orenstein et al. (2005)).

The government negotiates vaccine prices with manufacturers through several federal organizations. Every year, the Advisory Committee on Immunization Practices (ACIP) looks at all of the vaccines approved by the Food and Drug Administration (FDA) and suggests changes to the Recommended Childhood Immunization Schedule (RCIS) (Behzad et al. (2014)). The RCIS dictates which vaccines doctors administer to children and at what times, and thus largely determines the vaccine demand for that year (Robbins et al. (2013)). The Centers for Disease Control and Prevention (CDC) negotiates federal contract prices for vaccines listed on the RCIS (Robbins et al. (2013)). State and local governments then purchase vaccines at the federal government contract prices (Robbins et al. (2013)).

The number of manufacturers involved in the vaccine market is dwindling, likely due to large vaccine research costs and low profit margins. As of 2014, there are only five vaccine manufacturers left in the American vaccine market (Robbins and Jacobson (2015)). Of these, only three manufacturers (Merck, GlaxoSmithKline, and Sanofi Pasteur) make competing vaccines,

meaning vaccines that satisfy the same immunization requirements (Behzad et al. (2014)).

Keeping a large number of vaccine manufacturers in the market is in the government's best interest. Vaccine manufacturers do research to improve vaccine quality and disease coverage, and the government has more negotiating power in vaccine markets that are not monopolies. In order to encourage manufacturers to stay in the market, the government must keep prices high enough to maintain manufacturer profitability. However, the government doesn't want vaccine costs to get too high, since then not only will the government spend more money on health care, but high prices may also discourage people from getting vaccines. Thus, the government must balance its desire for manufacturer profitability (high prices) with affordability and coverage (low prices). This begs the question - what vaccine prices are best, from the perspective of the government?

1.2 Existing Models

As the government's ability to process and store data grows, so does the government's ability to use mathematical models to guide public policy. Techniques in operations research and game theory meant to better understand optima and equilibria can be applied to real-world problems to suggest ideal prices, schedules and other policy components(Stokey (1991)).

Previous research has looked at the American vaccine pricing market from a variety of perspectives. At first, researchers focused on optimizing the vaccine schedules themselves, to help the Centers for Disease Control and Prevention create schedules that minimize costs while incorporating newly released vaccines. For example, a pilot integer programming model by Jacobson et al. minimized overall vaccination cost while following the 1997 Childhood Immunization Schedule, taking into account the order in which vaccines must be administered and limiting the number of vaccines that could be administered in a single clinic visit (Jacobson et al. (1999)).

Jacobson then moved on to work with Robbins et al. to look at vaccine pricing itself (Robbins et al. (2013)). Using a static Bertrand oligopoly to model a set of vaccine manufacturers, the group analyzed the prices of two competing vaccines, Pediarix® and Pentacel®. Their model suggested that the two vaccines should be priced more similarly, and indeed the price gap between the two vaccines shrank in the years following the analysis. To describe demand, they used a weighted set covering optimization where

the weights were the prices each manufacturer set within the Bertrand competition. They then looked at the results of both a static and repeated game using Nash equilibria (Robbins et al. (2013)).

Although Bertrand oligopoly models are useful, they make three assumptions: Bertrand assumes that all manufacturers can fill all of market demand (no capacity constraints), that all manufacturer products are completely interchangeable (zero product differentiation), and that manufacturers compete only once (static competition) (Tirole (1988)). Other models have since been created that relax some of those assumptions. *Bertrand-Edgeworth competition* examines duopolies with capacity constraints. In Bertrand-Edgeworth competition, the existence of equilibria is guaranteed only in mixed strategies (Vives (2001)).

Relaxing the first two constraints of the Bertrand framework, *Bertrand-Edgeworth-Chamberlin competition* looks at capacity constrained symmetric manufacturers who sell differentiated products. Behzad et al. used this framework to analyze the vaccine market (Behzad et al. (2015)). The team first proved the existence of equilibria in Bertrand-Edgeworth-Chamberlin competition oligopolies using linear demand and a quadratic utility function, then applied those equilibria to three instances of competition in the vaccine market (Behzad et al. (2015)). This model was expanded upon in a later paper that looked at the same setup but with asymmetric manufacturer capacities (Behzad and Jacobson (2016)).

Although these models tackle many of the original assumptions made about manufacturers, none include the government as an actor along with the manufacturers. In the following chapters, we examine possible models that consider not only the actions of the vaccine manufacturers but also the government. The CDC sets the prices in the public sector market, and by creating models that focus on the CDC's choices, we can help suggest to the CDC what prices will allow them to best maintain a long-term supply of low-cost vaccines.

Chapter 2

A Preliminary Model of the Public Sector

2.1 Setup

In order to understand the vaccine pricing market overall, we can look at the market in progressively more complex steps. As a first step, consider a model of only the public sector, two competing manufacturers, and one vaccine. Assume that the products made by the two manufacturers are identical and that each manufacturer has an infinite capacity to make vaccines. We choose to ignore the private sector while introducing this initial supply and demand model, but will add in the private sector and additional math to accommodate for it in later chapters.

We can define p_1 and p_2 to be the vaccine prices set by the first and second manufacturers respectively. Let the marginal cost of a vaccine be defined as the production cost incurred by a manufacturer for producing an additional vaccine, given they have already produced a certain number of vaccines (Samuelson (1976)). Let MC_1 be the marginal cost for the first manufacturer and MC_2 be the marginal cost for the second manufacturer. We then get constraints

$$p_1 \geq MC_1$$
$$p_2 \geq MC_2$$

which force any vaccine produced by either manufacturer to generate a profit. This is useful in keeping manufacturers in the market, since the profit margins on vaccines are currently low. Along similar lines, if we let q_1 and

q_2 be the quantity produced by each of the two manufacturers, we can force both manufacturers to remain in the market with the constraints

$$q_1 \geq DT_1$$
$$q_2 \geq DT_2$$

for some constant minimum percent thresholds of market share T_1 and T_2 and annual demand for the vaccine D. Now that we have both manufacturers in the market and making a profit, we also want to satisfy demand. Looking at the quantity sold by both manufacturers,

$$q_1 + q_2 \geq D$$

which allows manufacturers to collectively exceed or meet demand as appropriate. Finally, we relate quantity and price using a linear demand curve (Lau and Lau (2003)). To do so, let

$$q_1 = a_1 - b_1 p_1 \tag{2.1}$$

$$q_1 = a_2 - b_2 p_2 \tag{2.2}$$

for non-negative constants a_1, b_1, a_2 and b_2. Here the a_i represent the component of the demand that's independent of the price and the b_i represent the component of demand that depends on the price. This allows us to solve for quantity in terms of price for each of the two manufacturers, and leaves us with a linear program of two variables, p_1 and p_2. Since we are using constraints to ensure that manufacturers remain in the market, we can then minimize government costs. This leads us to the objective function $\min p_1 q_1 + p_2 q_2$, or equivalently with the substitutions from above, $\min p_1(a_1 - b_1 p_1) + p_2(a_2 - b_2 p_2)$. Putting this all together gives the program

$$
\begin{aligned}
\min \; & p_1(a_1 - b_1 p_1) + p_2(a_2 - b_2 p_2) \\
& p_1 \geq MC_1 \\
& p_2 \geq MC_2 \\
& a_1 - b_1 p_1 \geq T_1 D \\
& a_2 - b_2 p_2 \geq T_2 D \\
& (a_1 - b_1 p_1) + (a_2 - b_2 p_2) \geq D \\
& p_1, p_2 \geq 0
\end{aligned}
\tag{2.3}
$$

Table 2.1   Public Sector Model Variables and Parameters

Name	Type	Meaning
p_i	Variable (float)	Price set by manufacturer i
q_i	Variable (float)	Quantity sold by manufacturer i
MC_i	Parameter	Vaccine marginal cost for manufacturer i
T_i	Parameter	Minimum threshold percent market share for manufacturer i
a_i	Parameter	Constant in linear demand curve $q_i = a_i - b_i p_i$
b_i	Parameter	Constant in linear demand curve $q_i = a_i - b_i p_i$
D	Parameter	Total vaccine demand

Figure 2.1   Public Sector 2D Model Feasible Region
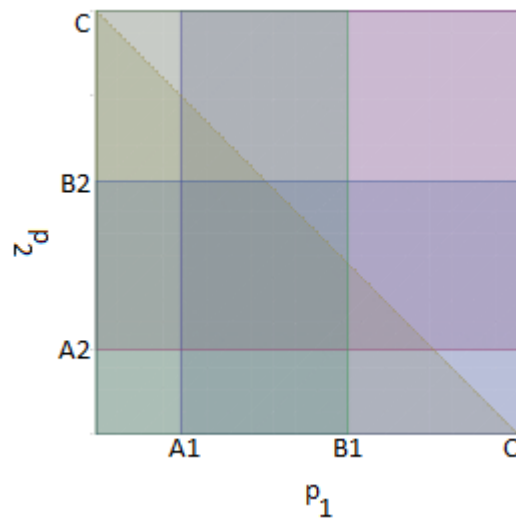
This figure shows the feasible region of the public sector model defined in equation 2.3 as a function of p_1 and p_2. $A1$ indicates the line $p_1 \geq MC_1$, $A2$ indicates the line $p_2 \geq MC_2$, $B1$ indicates the line $p_1 \leq \frac{a_1 - T_1 D}{b_1}$, $B2$ indicates the line $p_2 \leq \frac{a_2 - T_2 D}{b_2}$ and C indicates the line $(a_1 - b_1 p_1) + (a_2 - b_2 p_2) \geq D$.

2.2   Analysis

The feasible region of this first model is drawn in figure 2.1. The region is the intersection of the rectangle with vertices (MC_1, MC_2), $(\frac{a_1-T_1D}{b_1}, MC_2)$, $(\frac{a_1-T_1D}{b_1}, \frac{a_2-T_2D}{b_2})$ and $(MC_1, \frac{a_2-T_2D}{b_2})$ and the inequality

$$(a_1 - b_1p_1) + (a_2 - b_2p_2) \geq D. \tag{2.4}$$

Therefore, for the problem to be feasible we need

$$MC_1 \leq \frac{a_1 - T_1D}{b_1}$$
$$MC_2 \leq \frac{a_2 - T_2D}{b_2}$$

meaning that the marginal cost of each vaccine must be lower than the maximum manufacturer price (manufacturers will set their prices highest when they sell the smallest quantity, T_iD). Looking at the intersection of equation 2.4 and the other inequalities that dictate the feasible region, we also get that the problem is only feasible if at the bare minimum prices $p_1 = MC_1$ and $p_2 = MC_2$ that equation 2.4 still holds. Plugging in the marginal costs as p_1 and p_2,

$$(a_1 - b_1MC_1) + (a_2 - b_2MC_2) \geq D \tag{2.5}$$

is required in order for the problem to be feasible. We note that if

$$T_1 + T_2 \geq 1 \tag{2.6}$$

then not only does equation 2.5 always hold, but also and that the inequality 2.4 will not constrain the feasible region. We note that equation 2.6 implies that T_1 and T_2 constrain manufacturers to collectively control at minimum 100% of market share, which is a feasible although not necessary way to set T_1 and T_2. For example, saying that both manufacturers need to cover 50% of the market would satisfy equation 2.6 while saying that each manufacturer would need to cover only 20% of the market would not.

If equation 2.6 is satisfied, the feasible region will be a rectangle R. Let $O(p_1, p_2) = p_1(a_1 - b_1p_1) + p_2(a_2 - b_2p_2)$ represent the value of the objective function at a given set of prices (p_1, p_2). The optimal solution to equation 2.3 will occur on the boundary of the feasible region, the rectangle R seen in figure 2.1. Checking the first and second derivatives of the objective function

along the edges of R shows that no local minima exist along the edges, only local maxima. Therefore, the minimum value of the objective function will be on one of the four corners of R.

Similarly to in figure 2.1, let $A1 = MC_1$, $B1 = MC_2$, $A1 = \frac{a_1 - T_1 D}{b_1}$ and $B2 = \frac{a_2 - T_2 D}{b_2}$. The objective function at each of the four corners is

$$O(A1, A2) = MC_1(a_1 - b_1 MC_1) + MC_2(a_2 - b_2 MC_2)$$

$$O(A1, B2) = MC_1(a_1 - b_1 MC_1) + T_2 D \frac{a_2 - T_2 D}{b_2}$$

$$O(B1, A2) = T_1 D \frac{a_1 - T_1 D}{b_1} + MC_2(a_2 - b_2 MC_2)$$

$$O(B1, B2) = T_1 D \frac{a_1 - T_1 D}{b_1} + T_2 D \frac{a_2 - T_2 D}{b_2}$$

To better understand what these objective function values mean, we first note that $A1$ indicates setting the price for manufacturer 1 at its marginal cost MC_1 and will have manufacturer one produce its maximum allowable amount a_1 according to its linear demand curve, equation 2.1. $B1$ indicates setting the price for manufacturer 1 at $\frac{a_1 - T_1 D}{b_1}$, the highest cost the manufacturer can demand while still selling the minimum amount of vaccines $T_1 D$ to the market as according to its demand curve, equation 2.2. The quantity sold q_1 in situation $B1$ is the minimum amount $T_1 D$. The interpretation of $A2$ and $B2$ are comparable to $A1$ and $B1$ respectively but deal with manufacturer 2.

We can interpret these objective function values using a few examples. If $MC_1 = MC_2 = 0$, then $O(A1, A2) = 0$ will be the minimum value of the objective function. In this case, both manufacturers will set their price to zero, and their quantities to a_1 and a_2, the maximum possible quantities they can sell.

If the marginal cost of one vaccine is much higher than the other, then we'll likely end up in the $(A1, B2)$ case or the $(A2, B1)$ case. If both marginal costs are high, then likely both manufacturers will try to minimize the amount that they sell but sell at higher prices (as long as together they still fulfill demand).

2.3   What to Glean from a Simple Model

Although this model oversimplifies our problem, the small number of variables allows us to visualize what's going on. Here, we already see

some of the problems that arise in later more complex models - infeasibility when parameters are set too high or too low and optimal solutions that are sometimes symmetric across manufacturers and sometimes asymmetric, even when all inputs for the two manufacturers are identical. Although the objective function of this model is quadratic, the geometry of the solution often still allows us to check the corner points for solutions rather than having to check on the edges of the feasible region. This model allows us to get a visual grasp of the situation, before moving on to more complex problems. Even in the next chapter, adding in the private sector and a few more variables will make this convenient visualization no longer possible.

Chapter 3

Incorporating the Private Sector

3.1 Setup

Although looking at a model that focuses exclusively on the public sector can be useful to better understand the workings of this problem, such a model doesn't paint the whole picture. In reality, only 57% of vaccines are sold to the public sector, while the other 43% are sold to the private sector (Orenstein et al. (2005)). Therefore, a more complete model will look at not only at the prices and quantities sold in the public sector but also the prices and quantities sold in the private sector.

Let M be a set of manufacturers. Let p_{ui} and q_{ui} represent the public sector prices and quantities of a given vaccine for manufacturer i. Similarly, let p_{ri} and q_{ri} represent the private sector prices and quantities of that same vaccine for manufacturer i. Like before, we want all vaccines to be sold at a profit for the manufacturer, so if a manufacturer has marginal cost MC_i to create a vaccine,

$$
\begin{aligned}
p_{ui} &\geq MC_i \ \forall i \in M \\
p_{ri} &\geq MC_i \ \forall i \in M.
\end{aligned}
\tag{3.1}
$$

To require that quantities sold to the public sector should equal public demand, we get that

$$
\sum_{i \in M} q_{ui} = 0.57D.
\tag{3.2}
$$

for overall demand D. Similarly in the private sector,

$$
\sum_{i \in M} q_{ri} = 0.43D.
\tag{3.3}
$$

We choose to force supply to exactly meet demand rather than allow supply to exceed demand since unlike in our previous example where overflow production might enter the private sector, here we have accounted for the entire vaccine market in our model. Since children are often required to be vaccinated and have no incentive to receive the same vaccine more than once, we assume that any vaccines produced that exceed the total demand will not be purchased and therefore will neither contribute to the government's costs nor the manufacturer's profits.

Next, we want to ensure that all manufacturers stay in the market. To do so, we can constrain the problem by mandating that every manufacturer i sells at least $T_i D$ vaccines, whether those vaccines be sold in the public or private sectors. This gives a constraint

$$q_{ui} + q_{ri} \geq T_i D \ \forall i \in M. \tag{3.4}$$

Next, we can make use of our assumed linear supply and demand relationship in both sectors. This gives

$$q_{ui} = a_{ui} - b_{ui} p_{ui} \ \forall i \in M \tag{3.5}$$

for the public sector and

$$q_{ri} = a_{ri} - b_{ri} p_{ri} \ \forall i \in M \tag{3.6}$$

for the private sector.

Data from many years of vaccine prices in the public and private sectors indicate that the prices of a given vaccine in each sector can be described through a roughly linear relationship. For a given vaccine, we can constrain the prices using the equation

$$(\delta_i p_{ui} + \beta_i) - \kappa_i \leq p_{ri} \leq (\delta_i p_{ui} + \beta_i) + \kappa_i \ \forall i \in M \tag{3.7}$$

for constants δ_i and β_i from a linear fit and κ_i representing the error of that linear fit.

After thinking through the constraints, we must also choose an objective function. Since the private sector costs are somewhat tied to public sector costs and our main focus is still the government's pricing choices, we can keep our previous objective function that minimizes government costs. This means our objective function will be

$$\min \sum_{i \in M} q_{ui} p_{ui} \tag{3.8}$$

Putting all of these equations together, we get the mathematical program

$$\min \sum_{i \in M} q_{ui} p_{ui}$$
$$p_{ui} \geq MC_i \ \forall i \in M$$
$$p_{ri} \geq MC_i \ \forall i \in M$$
$$\sum_{i \in M} q_{ui} = 0.57D$$
$$\sum_{i \in M} q_{ri} = 0.43D$$
$$q_{ui} + q_{ri} \geq T_i D \ \forall i \in M$$
$$q_{ui} = a_{ui} - b_{ui} p_{ui} \ \forall i \in M$$
$$q_{ri} = a_{ri} - b_{ri} p_{ri} \ \forall i \in M$$
$$\delta_i p_{ui} + \beta_i - \kappa_i \leq p_{ri} \ \forall i \in M$$
$$p_{ri} \leq \delta_i p_{ui} + \beta_i + \kappa_i \forall i \in M$$
$$p_{ui}, p_{ri}, q_{ui}, q_{ri} \geq 0 \ \forall i \in M$$

(3.9)

3.2   Applying this Model to Pediarix® and Pentacel®

We can now see how this model behaves by applying it to a real situation in the American vaccine market. To do so, we look at Pediarix® and Pentacel®, two competing combination vaccines (Robbins et al. (2013)). Pediarix® is manufactured by Merck, and Pentacel® is manufactured by Sanofi Pasteur, two competing drug manufacturers. Both vaccines protect against diphtheria, tetanus, pertussis, haemophilus influenzae type b, hepatitis B and polio (Robbins et al. (2013)). These are the only two vaccines on the market that protect against this combination of diseases, so we can model this as an instance of our model with one vaccine and two competing manufacturers.

First, we have to determine the values of all constants in the model as applies to Pediarix® and Pentacel®. Let Merck be manufacturer 1 and Sanofi Pasteur be manufacturer 2. In order to determine the relationship between public and private sector costs for the two vaccines (to find the δ_i and β_i from equation 3.7), we can use data posted by the CDC. The Pediarix® and Pentacel® public and private sector prices from the past ten years can be seen in table 3.1.

We fit a linear regression model on these prices and find for Pediarix®

Table 3.1   Pediarix® and Pentacel® Vaccine Prices

	Pediarix®		Pentacel®	
Contract End Date	CDC	Private Sector	CDC	Private Sector
3/31/2017	$54.90	$72.73	$56.91	$87.48
3/31/2016	$53.86	$70.72	$54.38	$87.48
3/31/2015	$53.86	$70.72	$52.43	$80.43
3/31/2014	$52.58	$70.72	$56.02	$80.43
3/31/2013	$52.10	$70.72	$54.50	$80.43
3/31/2012	$51.15	$70.72	$52.55	$80.43
3/31/2011	$49.75	$70.72	$50.70	$77.48
3/31/2010	$48.75	$70.72	$51.49	$75.33
3/31/2009	$48.75	$70.72	$50.10	$72.91

Cost per dose for Pentacel® and Pediarix® in the private and public sectors from 2009-2016 (Vaccines for Children Program (2017)).

that

$$p_{r1} = 0.15p_{u1} + 63.13 \qquad (3.10)$$

and for Pentacel® that

$$p_{r2} = 1.64p_{u2} - 7.99 \qquad (3.11)$$

and thus $\delta_1 = 0.15$, $\beta_1 = 63.13$, $\delta_2 = 1.64$ and $\beta_2 = -7.99$.

   To find the demand D, we use a similar calculation to Behzad et al. (2015). According to the National Vital Statistics Report, about 4 million births occurred in 2011 (Martin et al. (2013)). The number of children younger than five immigrating to the US is small compared to the number of children born in the US, so we will assume that 4 million shots is a reasonable estimate of the vaccine demand D (Behzad et al. (2015)).

   Next, we consider what minimum presence threshold values T_1 and T_2 will ensure that both manufacturers are making enough profits to stay in the market. Here, there are two approaches to consider. The first is to look at markets in general and ascertain what fraction of market share a company needs on average in order to survive. Economics literature has shown that inequality in market share affects market power in a wide range of market types (Barla (2000)). After determining what minimum fraction of the market share T is necessary in a duopoly, we'd get the two constraint

$$q_{ui} + q_{ri} \geq TD \ \forall i \in \{1, 2\}. \qquad (3.12)$$

To find the marginal costs MC_1 and MC_2 of Pentacel® and Pediarix®, we can consult (Robbins et al. (2013)) and (Douglas et al. (2008)). For vaccines where these data are not available, a possible proxy for marginal cost is the price the manufacturers sell their vaccines to UNICEF and other foreign aid organizations (LeMoyne (2016)). Assuming that vaccine manufacturers do not have an incentive to sell their products at a loss, the prices they negotiate with UNICEF can be considered an upper bound on marginal costs.

Lastly, we can gather data for the demand curve a few different ways. To create a linear demand curve, we can use the strategy outlined by (Behzad et al. (2015)). This method uses product differentiation to define demand, with the number of adverse events per vaccine dose determining differentiation. A second nonlinear approach would be to use a logistic function to represent each manufacturer's fraction of the market share as a function of the price of their vaccine. To determine the functional relationship between market share and price, we can consult NHS data on each company's market share in tandem with the CDC's yearly price records.

3.3   What to Glean from a Slightly More Complex Model

Without coding up this model and analyzing the results, it's hard to tell whether or not its assumptions are within the scope of reason. However, this model does raise some good questions - how do we approximate constants that are not easily findable, and how do we allow for public-private sector interactions in our model?

We won't always know what the correct value for constants like MC_i, T_i, δ_i and β_i. Some we can approximate, like using UNICEF prices as a proxy for marginal cost. Some, we may be forced to parameterize, and simply observe what happens to prices as a parameter value changes over a reasonable range.

Also, how to mathematically relate the public and private sectors is by no means clear. We relate the two in some of our constraints, such as requiring that manufacturers make a certain number of vaccines across the two sectors combined. We also try directly relating the prices in both sectors, since in general the two appear to be linearly correlated. These ideas might come in handy in future work, and could possibly even be combined with the model concepts in chapter 4.

Chapter 4

An Equilibrium Model

4.1 Equilibrium Strategies

In sections 2 and 3, the models considered do not incorporate manufacturer self-interest. Left to their own devices, we would expect manufacturers to set their prices in a way that maximizes their profits. Since our models focus on the CDC's choice of prices in the public sector, we won't assume that manufacturers can simply maximize their public sector profits and disregard the CDC's negotiating power. However, in the private sector, there are no large negotiating powers preventing manufacturers from reaching their maximum profit potentials. To model these maximum profits, we look to game theory.

Game theory studies how players behave when they are placed in situations (games) in which participants' decisions affect not only their own outcomes but the outcomes of other players. Players often make choices based off of an optimal strategy, in which the choices they make will maximize their output. In some games, the optimal strategy is a *pure strategy*, in which the player will make the same choice every time. In other situations, the optimal strategy may be a *mixed strategy*, in which the player will make different choices dependent on some random variable. An equilibrium is said to be reached between the players in a game if no player can change their strategy to improve their outcome (Trick (1998)).

Games in which one player's gain is another one's loss are said to be *zero-sum games*, meaning player interests are directly opposed (Trick (1998)). In 1950, John Nash proved the existence of equilibrium points in all two player zero-sum games (Nash et al. (1950)). In our case, we

look at Bertrand-Edgeworth-Chamberlin equilibrium points, a subset of the equilibrium points Nash analyzed. More background on Bertrand-Edgeworth-Chamberlin equilibria can be found in section 1.2.

4.1.1   Vaccine Manufacturers as Players in a Game

Here, we have a two player game involving the two vaccine manufacturers, in which each manufacturer can choose its selling price in the private market. If a manufacturer sets its price too high, it will lose customers to the other manufacturer. On the flip-side, if a manufacturer sets its price too low, it won't make as much profit as it wants on the vaccines it does sell. By phrasing this situation as a game, we can calculate the ideal pricing strategy for each manufacturer that will maximize their profits.

We can describe each manufacturer in terms of two qualities: manufacturing capacity and product differentiation. Manufacturing capacity k_i of manufacturer i is the number of vaccines that manufacturer can produce in a given year, and is determined by the number of factories and amount of raw materials a manufacturer has. Product differentiation γ describes the degree of difference between two competing manufacturer products, with γ ranging from 0 (indicating complete product independence) to 1 (indicating perfect substitutes) (Behzad and Jacobson (2016)).

4.1.2   Three Strategies

Manufacturers described with k_i and γ as in section 4.1.1 above will act optimally according to one of three equilibrium strategies: a competitive strategy, a mixed strategy, or a Bertrand-Chamberlin strategy. Which type of strategy a manufacturer will use depends on their manufacturing capacity k_i (Behzad and Jacobson (2016)).

For example, a pure strategy Bertrand-Chamberlin equilibrium will occur when capacity is high and there is no risk of scarcity. More specifically, the Bertrand-Chamberlin equilibrium occurs when $k_i \geq k(\gamma)$, in which $k(\gamma)$ is defined as

$$k(\gamma) = \frac{\alpha}{\gamma}\left[1 - \frac{2(1 + (n-2)\gamma)^{1/2}(1-\gamma)^{1/2}}{(1 + (n-1)\gamma)^{1/2}(2 + 2(n-2)\gamma - (n-1)\gamma)}\right] \quad (4.1)$$

where α is a constant further discussed in section 4.7.1 and n is the number of manufacturers. Here we only consider the case where $n = 2$,

which allows equation 4.1 to simplify to

$$k(\gamma) = \frac{\alpha}{\gamma} \left[1 - \frac{2(1 - \gamma)^{1/2}}{(1 + \gamma)^{1/2}(2 - \gamma)} \right].$$ (4.2)

On the other hand, if capacity is low and there is a scarcity of vaccines, then manufacturers will optimally find themselves acting with a competitive strategy. Specifically, this occurs when $k_i \leq q^C$, where q^C is defined as

$$q_i^C = \frac{\alpha - \gamma \sum\limits_{j \neq i} k_j}{2}.$$ (4.3)

The final strategy, a mixed strategy, occurs when $q^C < k_i < k(\gamma)$. In this case, there is neither a clear scarcity nor a clear abundance of vaccines.

4.2 Assuming a Linear Demand Curve

In order to use the equilibria described in section 4.1, there are several assumptions we must make. One of these assumptions is that the demand for vaccines behaves linearly with price, as is done in Vives (1999). We can use the same linear demand function used in Behzad et al. (2015) and Behzad and Jacobson (2016), in which demand D_i of vaccines sold by manufacturer i is negatively correlated with the price of its vaccine p_i and positively correlated with the price of its competitors vaccines p_j. Specially, we define

$$D_i(p_i) = a - b p_i + c \sum_{j=1, j \neq i}^{n} p_j$$ (4.4)

where

$$a = \frac{\alpha}{1 - (n - 1)\gamma}$$ (4.5)

$$b = \frac{(1 + (n - 2)\gamma)}{(1 + (n - 1)\gamma)(1 - \gamma)}$$ (4.6)

and

$$c = \frac{\gamma}{(1 + (n - 1)\gamma)(1 - \gamma)}.$$ (4.7)

Our analysis will deal with the case when $n = 2$, in which equations 4.5, 4.6 and 4.7 simplify to

$$a = \frac{\alpha}{1 - \gamma}$$ (4.8)

$$b = \frac{1}{(1 + \gamma)(1 - \gamma)} \tag{4.9}$$

and

$$c = \frac{\gamma}{(1 + \gamma)(1 - \gamma)}. \tag{4.10}$$

4.3 Designing a Bertrand-Chamberlin Equilibrium Model

In chapter 3, we consider a model formulation that incorporates both the public and private sectors, but fails to mimic manufacturer tendency to maximize private sector profits. Here we employ game theory to add in private sector optimization.

To make the game-theoretic formulations simpler, we will assume here that the marginal cost of each vaccine is zero. Since most of the cost of vaccines is research and development, this assumption is reasonable. This is different than in chapter 3, where each vaccine has a specified marginal cost.

Like in equation 3.8, our objective function will still be to minimize public sector costs. The variables are still the public and private sector vaccine prices and quantities p_{ui}, p_{ri}, q_{ui} and q_{ri}, with the addition of k_{ri}, a measure of private sector capacity. In this model, every manufacturer will start out with an initial overall annual vaccine capacity K_i, which is the number of vaccines the manufacturer can make that year as determined by its maximum current factory and supply output. That capacity will be used up to some extent by public sector vaccine purchases, after which k_{ri} will keep track of remaining capacity for private sector sales.

To better understand the model constraints, we can view them in a certain order. First, allow the CDC to choose a certain set of public sector prices p_{ui}. Then the quantities q_{ui} sold in the public sector will follow as per the demand function defined in equation 4.4, giving

$$q_{ui} = a_{ui} - b_{ui}p_{ui} + c_{ui} \sum_{j=1, j\neq i}^{n} p_{uj} \tag{4.11}$$

where constants a_{ui}, b_{ui} and c_{ui} are defined according to equations 4.8, 4.9 and 4.10 respectively.

Once the quantities sold in the public sector are known, we can calculate the capacity k_{ri} each manufacturer has left to sell in the private sector. Since vaccines are sold only on the public or the private market, we can subtract the public quantity sold directly from the total capacity K_i to find k_{ri}, giving

$$k_{ri} = K_i - q_{ui}. \tag{4.12}$$

Next, we calculate the prices manufacturers will set in the private sector, assuming that they want to maximize their profits. In this chapter we will first consider the case where private sector manufacturer capacities are high (where there is no vaccine scarcity). Specifically, we require that

$$k_{ri} \geq k(\gamma) \tag{4.13}$$

where $k(\gamma)$ is defined in equation 4.1, so that manufacturers will behave according to the Bertrand-Chamberlin equilibrium. As proved by Behzad and Jacobson (2016), manufacturers whose capacity falls within the Bertrand-Chamberlin equilibrium range will price their vaccines according to

$$p_{ri} = \frac{a_{ri}}{2b_{ri} - (n-1)c_{ri}} \tag{4.14}$$

where constants a_{ri}, b_{ri} and c_{ri} come from the private sector demand curve, described below in equation 4.15.

As in the public sector, we assume that demand follows linearly with price. Therefore, we get a quantity sold of

$$q_{ri} = a_{ri} - b_{ri}p_{ri} + c_{ri} \sum_{j=1, j\neq i}^{n} p_{rj} \tag{4.15}$$

where a_{ri}, b_{ri} and c_{ri} are again defined according to equations 4.8, 4.9 and 4.10.

These price and quantity calculations will produce values in the public and private sectors, but might overly minimize manufacturer profits or not make enough vaccines to meet full market demand. To account for this, we add a few additional constraints into the model. First off, to ensure that the entire demand D is met across the public and private sectors, we require

$$\sum_{i \in M} \left(q_{ri} + q_{ui} \right) \geq D. \tag{4.16}$$

Equation 4.16 is an inequality rather than an equality as to not over-constrain the system. Empirical testing shows that results often don't exceed demand by much. Some excess of vaccine production is desirable, since then some doses can be lost or go unused as normally will occur with a small percentage of vaccines produced each year.

We also require that vaccine manufacturers make enough profits as to want to continue participating in the vaccine market. There are two main ways we can do this: dictate that each manufacturer must be responsible for some minimum percentage of the market, or dictate that each manufacturer must make some minimum profit each year. Here we opt for the second option, since it is easier to quantify. Thus, we require

$$q_{ui}p_{ui} + q_{ri}p_{ri} \geq P_i \tag{4.17}$$

where P_i is the minimum profit a manufacturer needs to make annually to maintain profitability. For a discussion on how to calculate P_i, consult section 4.7.2.

Putting together equations 4.11 through 4.17, we get a complete mathematical program of

$$\min \sum_{i \in M} q_{ui}p_{ui}$$

$$q_{ui} = a_{ui} - b_{ui}p_{ui} + c_{ui} \sum_{j=1, j \neq i}^{n} p_{uj} \forall i \in M$$

$$k_{ri} = K_i - q_{ui} \forall i \in M$$

$$k_{ri} \geq k(\gamma) \in M$$

$$p_{ri} = \frac{a_{ri}}{2b_{ri} - (n-1)c_{ri}} \tag{4.18}$$

$$q_{ri} = a_{ri} - b_{ri}p_{ri} + c_{ri} \sum_{j=1, j \neq i}^{n} p_{rj} \forall i \in M$$

$$\sum_{i \in M} \left(q_{ri} + q_{ui} \right) \geq D$$

$$q_{ui}p_{ui} + q_{ri}p_{ri} \geq P_i \ \forall i \in M$$

$$p_{ui}, p_{ri}, q_{ui}, q_{ri}, k_{ri} \geq 0 \ \forall i \in M$$

which describes the public and private markets when both manufacturers have large capacities and don't get close to scarcity conditions. This isn't always the case, and there are two other equilibrium points to add to our model to account for this. However, equation 4.18 is the most complex continuous program we will consider - when more equilibria are added, integer variables get thrown into the mix. Therefore, this system is solvable more simply than the system we will build in the following sections. We will

call this model the Bertrand-Chamberlin model, and we computationally analyze some of its proposed prices in chapter 5.

4.4   Considering Other Equilibria

The Bertrand-Chamberlin equilibrium is not the only possible equilibrium state. At low capacity, vaccines are scarce and manufacturers will price their vaccines differently. This competitive equilibrium is determined by a threshold q^C, defined in equation 4.3.

If $k \leq q^C$, then we hit a competitive equilibrium given by $P(k)$, where

$$P_i(k_i, \sum k_j) = \alpha - k_i - \gamma \sum k_j. \tag{4.19}$$

If $q^C < k < k(\gamma)$, then we hit a mixed strategy equilibrium. The distribution function of the mixed strategy is described in Behzad and Jacobson (2016). Rather than deal with a probability distribution, in this model we will assume that manufacturers will choose the maximum possible value of their mixed strategy distribution. Since the range of possible strategies suggested by the distribution function is small, this assumption won't hugely impact model results. The maximum price $\overline{p}$ in the mixed strategy case is defined in Behzad and Jacobson (2016) as

$$\overline{p} = \arg\max_p \{ p(\alpha - p - \gamma \sum_{i=2}^{n} k_i) \} \tag{4.20}$$

where k_{r1} is fixed as the largest capacity of all the k_{ri}. We can find $\overline{p}$ by taking the derivative of the right hand side and setting it equal to zero, getting

$$\overline{p} = \frac{\alpha - \gamma \sum_{i=2}^{n} k_{ri}}{2}. \tag{4.21}$$

Since the second derivative of the right hand side of equation 4.20 is $-2 < 0$, we indeed know that this is a maximum and not a minimum price. Combining these three equilibrium strategies, we get the set of equations

$$\text{If } k_{ri} \geq k(\gamma) \text{ then} \qquad p_{ri} = \frac{a_{ri}}{2b_{ri} - (n-1)c_{ri}}$$

$$\text{If } k_{ri} \leq q^C \text{ then} \qquad p_{ri} = \alpha - k_i - \gamma \sum k_j \qquad (4.22)$$

$$\text{If } q^C < k_{ri} < k(\gamma) \text{ then} \qquad p_{ri} = \frac{\alpha - \gamma \sum\limits_{i=2}^{n} k_i}{2}.$$

4.5 Defining Indicator Variables

In order to incorporate the three possible equilibria outlined in section 4.4 into our mathematical program simultaneously, we can use binary indicator variables. These indicators z_{ic}, z_{im} and z_{ib} will indicate if manufacturer i falls into a competitive, mixed or Bertrand-Chamberlin equilibrium respectively. We denote

$$z_{ie} = \begin{cases} 1 \text{ if manufacturer } i \text{ is using equilibrium } e \\ 0 \text{ otherwise.} \end{cases} \qquad (4.23)$$

To guarantee that exactly one equilibrium strategy is in use at any one time, we can use the equation

$$z_{ic} + z_{im} + z_{ib} = 1 \; \forall i \in M. \qquad (4.24)$$

Since we don't know which of the two k_{ri} will be larger (but the mixed equilibrium strategy requires $k_{r1} > k_{r2}$), we need an additional binary indicator z_k for which

$$z_k = \begin{cases} 1 \text{ if } k_{r1} > k_{r2} \\ 0 \text{ otherwise.} \end{cases} \qquad (4.25)$$

To guarantee that this indicator will indeed be equal to one if and only if $k_{r1} > k_{r2}$, we can use the equations

$$k_{r1} - k_{r2} \leq N z_k \qquad (4.26)$$

and

$$k_{r2} - k_{r1} \leq N(1 - z_k). \qquad (4.27)$$

If $k_{r1} > k_{r2}$, then the left hand side of equation 4.26 is positive, forcing $z_k = 1$. Similarly, equation 4.27 forces $z_k = 0$ if $k_{r2} > k_{r1}$.

Finally, since the definition of q^C (see equation 4.3) allows q^C to be negative for large private sector capacities, we need a binary indicator variable to maintain the nonnegativity of our q^C variable so that we can formulate our program in AMPL. Call this binary indicator z_{iq}, and let

$$z_{iq} = \begin{cases} 1 \text{ if } q_i^C < 0 \text{ according to equation 4.3} \\ 0 \text{ otherwise.} \end{cases} \tag{4.28}$$

We then want to prevent q_i^C from being negative by setting it to zero if $z_{iq} = 1$. To do so, we need the equation

$$q_i^C = \frac{\alpha - \gamma \sum\limits_{j \neq i} k_j}{2} (1 - z_{iq}). \tag{4.29}$$

In order to ensure that z_{iq} acts as specified, we need two more equations. To enforce that if equation 4.3 produces a positive number then $z_{iq} = 0$, we can require that

$$\frac{\alpha - \gamma \sum\limits_{j \neq i} k_j}{2} \leq N(1 - z_{iq}). \tag{4.30}$$

Similarly, to enforce that if equation 4.3 produces a negative number then $z_{iq} = 1$, we can require that

$$-\frac{\alpha - \gamma \sum\limits_{j \neq i} k_j}{2} \leq N z_{iq}. \tag{4.31}$$

4.6   Designing a Three-Equilibrium Model

Now that we have our three different equilibrium states and indicator variables to go along with them, we can consider a new model. We will call this final model the three-equilibrium model.

To create this model, we can use our indicator variables and a large number N to remove the if statements from equation 4.22. As an example, consider the mixed equilibrium case. If manufacturer i selects the mixed strategy, then $z_{im} = 1$, but otherwise $z_{im} = 0$. To use this, we can split the original price equation found in equation 4.22 into two inequalities.

$$p_{ri} \le \frac{\alpha - \gamma \sum\limits_{i=2}^{n} k_{ri}}{2} + N(1 - z_{im}) \tag{4.32}$$

$$p_{ri} \ge \frac{\alpha - \gamma \sum\limits_{i=2}^{n} k_{ri}}{2} - N(1 - z_{im}) \tag{4.33}$$

If $z_{im} = 0$, then neither of these equations then constrain p_{ri} at all, as desired.

If instead $z_{im} = 1$, then equations 4.32 and 4.33 together guarantee that

$$p_{ri} = \frac{\alpha - \gamma \sum\limits_{i=2}^{n} k_{ri}}{2} \tag{4.34}$$

as needed for the mixed equilibrium condition. For the competitive and Bertrand-Chamberlin equilibria, this manipulation of one equality into two inequalities is all that is necessary to get the program into a workable form. However, the mixed equilibrium requires an additional step. Since the equation in 4.22 defines k_{r1} to be the largest of the k_{ri}, we need to split the p_{ri} calculation into two parts: one that's true if k_{r1} is the largest (fulfilled when $z_k = 1$) and one that's true if k_{r2} is the largest (fulfilled when $1 - z_k = 1$). Adding on to equations 4.32 and 4.33, we get the final equations

$$p_{ri} \le \frac{\alpha_{ri} - \gamma k_{r2}}{2} z_k + \frac{\alpha_{ri} - \gamma k_{r1}}{2}(1 - z_k) + N(1 - z_{im}) \tag{4.35}$$

$$p_{ri} \ge \frac{\alpha_{ri} - \gamma k_{r2}}{2} z_k + \frac{\alpha_{ri} - \gamma k_{r1}}{2}(1 - z_k) - N(1 - z_{im}) \tag{4.36}$$

Performing similar operations on the competitive and Bertrand-Chamberlin equilibria, we get the following set of binary indicator equations:

$$k_{ri} \geq k(\gamma) - N(1 - z_{ib})$$

$$p_{ri} \leq \frac{a_{ri}}{2b_{ri} - (n - 1)c_{ri}} + N(1 - z_{ib})$$

$$p_{ri} \geq \frac{a_{ri}}{2b_{ri} - (n - 1)c_{ri}} - N(1 - z_{ib})$$

$$k_{ri} \leq q_{ri}^C + N(1 - z_{ic})$$

$$p_{ri} \leq \alpha_{ri} - k_{ri} - \gamma \sum k_{rj} + N(1 - z_{ic})$$

$$p_{ri} \geq \alpha_{ri} - k_{ri} - \gamma \sum k_{rj} - N(1 - z_{ic})$$

$$k_{ri} > q_{ri}^C - N(1 - z_{im})$$

$$k_{ri} < k(\gamma) + N(1 - z_{im})$$

$$p_{ri} \leq \frac{\alpha_{ri} - \gamma k_{r2}}{2} z_k + \frac{\alpha_{ri} - \gamma k_{r1}}{2}(1 - z_k) + N(1 - z_{im})$$

$$p_{ri} \geq \frac{\alpha_{ri} - \gamma k_{r2}}{2} z_k + \frac{\alpha_{ri} - \gamma k_{r1}}{2}(1 - z_k) - N(1 - z_{im})$$

(4.37)

$$k_{r1} - k_{r2} \leq N z_k$$

$$k_{r2} - k_{r1} \leq N(z_k - 1)$$

$$z_{ic} + z_{im} + z_{ib} = 1$$

$$q_i^C = \frac{\alpha - \gamma \sum_{j \neq i} k_j}{2}(1 - z_{iq})$$

$$\frac{\alpha - \gamma \sum_{j \neq i} k_j}{2} \leq N(1 - z_{iq})$$

$$-\frac{\alpha - \gamma \sum_{j \neq i} k_j}{2} \leq N z_{iq}.$$

We can add these on to the existing framework from the Bertrand-Chamberlin model to get our final three-equilibrium model. Table 4.1 keeps track of all of the variables and parameters used in the three-equilibrium model, including the binary indicators.

Table 4.1   Three-Equilibrium Model Variables and Parameters

Name	Type	Meaning
q_{ui}	Variable (float)	Public vaccine quantity sold
q_{ri}	Variable (float)	Private vaccine quantity sold
p_{ui}	Variable (float)	Public vaccine price
p_{ri}	Variable (float)	Private vaccine price
k_{ri}	Variable (float)	Private manufacturing capacity
q_i^C	Variable (float)	Competitive equilibrium threshold
z_{ci}	Variable (binary)	Competitive equilibrium indicator
z_{mi}	Variable (binary)	Mixed equilibrium indicator
z_{bi}	Variable (binary)	Bertrand equilibrium indicator
z_k	Variable (binary)	Private capacity size indicator
a_{ui}	Parameter	Public demand curve constant
b_{ui}	Parameter	Public demand curve constant
c_{ui}	Parameter	Public demand curve constant
a_{ri}	Parameter	Private demand curve constant
b_{ri}	Parameter	Private demand curve constant
c_{ri}	Parameter	Private demand curve constant
K_i	Parameter	Maximum production capacity
P_i	Parameter	Minimum necessary profit
$k(\gamma)_i$	Parameter	Bertrand equilibrium threshold
γ	Parameter	Product differentiation
D	Parameter	Total vaccine demand
n	Parameter	Number of manufacturers
N	Parameter	Constraint relaxation large number

4.7   Calculating Input Parameters

To apply this model to real-world situations, we need to find realistic values
for the parameters. Some of these parameters are more easily calculated
than others. In this paper, we only consider the case of two manufacturers,
so $n = 2$ in all cases. In the following section, we discuss how to calculate
the rest of these parameters.

4.7.1   Demand Curve Parameters

In order to find public parameters a_{ui}, b_{ui}, c_{ui} and private parameters a_{ri}, b_{ri},
c_{ri}, we can use the process outlined in Behzad and Jacobson (2016). Refer

back to equation 4.4. If all the prices p_i are set to zero, then we would assume that each manufacturer would sell an equal number of vaccines, half of the total market demand D. Thus for a given manufacturer i,

$$a_{ui} = \frac{D_u}{2} \text{ and } a_{ri} = \frac{D_r}{2}. \tag{4.38}$$

where D_u is the total demand from the public sector perspective and D_r is the total demand from the private sector perspective. Since the public sector bargains as a collective, we allow $D_u = 0.57D$. The private sector, on the other hand, does not bargain as a collective. Therefore, we set $D_r = D$. Since the private sector competes in a higher demand market, we would expect it to have higher prices on average than the public sector prices.

Although a is dependent on demand, b and c only depend on γ. Both the public and private sector b and c can be found using equations 4.9 and 4.10 respectively.

4.7.2   Minimum Necessary Profit

In equation 4.17, P_i represents the minimum total profit manufacturer i needs across the public and private sectors to willingly continue to participate in the vaccine market. Vaccine research and development costs far outweigh their production costs (Behzad and Jacobson (2016)), so we'll focus only on R&D costs here and assume production costs to be roughly zero.

In order to calculate how much profit each vaccine should produce, we can look at each vaccine manufacturer's R&D costs C_i and the total number of types of vaccines they sell to the American government v_i. In order to maintain a manufacturer's current R&D costs using only vaccine profits, each vaccine must make on average

$$P_i = \frac{C_i}{v_i} \tag{4.39}$$

since then total across all v_i vaccines, manufacturer i would make at least C_i profits. Defining P_i as above lets us assume that manufacturers will continue to participate in the vaccine market in following years and continue to research and develop new vaccines, as desired.

The 2016 R&D spending C_i for each manufacturer can be found on their website or approximated as shown in section 4.7.3 (GlaxoSmithKline (2017), Sanofi (2017)). The number of types of vaccines the American government purchases from each vaccine manufacturer v_i can be found on the CDC

Table 4.2   Vaccine Manufacturer R&D Per Vaccine

Manufacturer Name	Number of Vaccines in Production	Vaccine R&D (Million USD*)	Million USD R&D Spending/Vaccine
GlaxoSmithKline	13	645	49.6
Merck	11	1047**	95.2
Sanofi Pasteur	17	599	35.2

* All euro to USD conversions done on 3/21/17
** Approximated according to a process outlined in section 4.7.3
Data from 2016 financial reports and the CDC webpage (GlaxoSmithKline
(2017), Merck (2017), Sanofi (2017), CDC (2017)).

webpage (CDC (2017)). The results of these searches can be found in table 4.2.

4.7.3   Research and Development Cost Estimation

Although GlaxoSmithKline and Sanofi Pasteur have their 2016 research and development costs available on their websites, Merck's 2016 R&D spending is not easily available (GlaxoSmithKline (2017), Sanofi (2017)). However, we can use Merck's overall R&D costs combined with the ratio of their vaccine sales compared to their overall sales to make an approximation of their vaccine R&D. Specifically, we can approximate vaccine R&D spending using

$$\text{Vaccine R\&D Spending} \approx \left(\frac{\text{Vaccine Sales}}{\text{Overall Sales}}\right)(\text{Total R\&D Spending}). \quad (4.40)$$

This is the approximation used to get the Merck vaccine R&D value in table 4.2. To check the validity of such an approximation, we use the same formula to approximate the vaccine R&D spending of GlaxoSmithKline and Sanofi Pasteur, and compare the approximated values found to the actual values. The results are in table 4.3. At best, we find an error of only 0.5%, and at worst, 26.4%. Thus, we can use this estimation method with some confidence.

4.7.4   Product Differentiation

The product differentiation γ is a parameter that describes the amount of difference between two competing products, with γ ranging from 0 to 1.

Table 4.3   Vaccine Manufacturer R&D Estimation

Manufacturer	GlaxoSmithKline	Sanofi Pasteur
Total R&D Spending	3600	5172
Vaccine Sales	46000	4577
Total Sales	27900	33821
Predicted R&D/Vaccine	594	700
Actual R&D/Vaccine	597	554
Percent Error	0.50	26.4

Data from 2016 financial reports (GlaxoSmithKline (2017), Sanofi (2017)).
All monetary values are in millions of euros.

Table 4.4   Public Sector Vaccine Demand

Vaccine	Public Sector Demand (millions)
DTap (Infanrix®, Daptacel®)	2.3
HepB (Engerix B®, Recombivax HB®)	5.2
DTap-IPV-HIB (Pentacel®)	4.5
DTap-HepB-IPV (Pediarix®)	1.5

Calculations from Behzad et al. (2015), explained in section 4.7.6.
Data from 2012 National Immunization Survey.

In this scheme, $\gamma = 0$ represents two products being independent while $\gamma = 1$ represents two products being perfect substitutes (Behzad et al. (2015)). Behzad et al. approximates the degree of product differentiation between vaccine pairs by looking at the number of medical adverse effects that happen per dose for each vaccine. For more details on these calculations and and a list of calculated results for a wide variety of vaccines, consult Behzad et al. (2015) and Behzad and Jacobson (2016).

4.7.5   Bertrand-Chamberlin Threshold

Once a_{ri} has been calculated as per section 4.7.1 and γ has been calculated as per section 4.7.4, then $k(\gamma)$ can be calculated using equation 4.2. Although equation 4.1 refers to α_{ri}, we can substitute α_{ri} for a_{ri} using equation 4.8.

4.7.6   Total Demand

Here we again use a strategy outline in Behzad et al. (2015). In order to approximate the total demand for a specific vaccine type in a given year, we can look at the National Immunization Survey (NIS), which collects data on vaccine usage across the country (National Immunization Survey (2015)). The NIS reports what percentage of people take each vaccine, and how many doses each recipient received. This information can be used to calculate an expected number of doses per person, which we can multiply by the expected number of vaccine-age children in the upcoming year to find an expected vaccine demand. Using this method, the expected number of doses used in 2012 is reported in table 4.4.

In order to approximate the number of vaccine-age children in the upcoming year, we can look at the year's birth cohort size. Although not all children in a given birth cohort will be vaccinated, a high enough percentage will to make this estimation reasonable (Behzad et al. (2015)). Birth cohort data (the number of babies born in the US in a given year) can be found from the CDC (National Center for Health Statistics (2017)).

4.7.7   Total Capacity

Since manufacturers do not tend to publish their total capacity, for the three-equilibrium model we choose to use a wide variety of possible K_i values and note their effects rather than try to approximate a correct value for K_i. This allows us to examine the effects of both scarcity and abundance conditions on optimal pricing strategies.

For the Bertrand-Chamberlin model, we can use a value of K_i that is large enough to meet the Bertrand Chamberlin constraint (equation 4.13) regardless of how many vaccines get sold in the public sector. Any value of $K_i > D$ should be adequate for such a case, and increasing the value of K_i beyond that should not change the results.

Chapter 5

Results

5.1 Applying the Bertrand-Chamberlin Model to Infanrix® and Daptacel®

In this chapter, we look at how parameter variations affect the output of the Bertrand-Chamberlin model from equation 4.18. We focus on the Infanrix® Daptacel® duopoly. Both vaccines contain DTap, which immunizes children against tetanus, pertussis (whooping cough) and diphtheria (Tartof et al. (2013)). GlaxoSmithKline makes Infanrix® and Sanofi Pasteur makes Daptacel®. For the current prices of each, see table 5.1.

Looking at table 5.1 shows us that the actual private sector prices are higher than the actual public sector prices, and that the public sector prices of the two vaccines are almost identical while the private sector ones are not. These are qualitative traits to look for when comparing our model to actual vaccine prices. Also, since we have the demand for DTap vaccines as a whole rather than each specific brand, the input parameters for each of these vaccines are identical in this analysis. This means that although we are interested in if the optimum CDC prices are different for each manufacturer, which manufacturer receives the lower price is not of interest (the manufacturers are essentially interchangeable, from the perspective of the model).

There are a few more computational details to work out before the three-equilibrium model can provide feasible results, so we won't discuss results of that model here.

Table 5.1 Infanrix® and Daptacel® Vaccine Prices

Vaccine	Infanrix®	Daptacel®
Public Sector Price	$16.15	$16.04
Private Sector Price	$20.96	$28.41

Data from the Vaccines for Children Program (2017).
Prices from a contract that spans 3/31/15-3/31/2016.

5.2   Varying the Minimum Required Profit

In section 4.7.2, we approximate a minimum required profit for each vaccine manufacturer. Although our resulting P_i values (found in table 4.2) seem reasonable at first glance, they are too large for our model to handle. Since we are using a linear demand curve, there is a limit to how much each manufacturer can make - as they raise their prices, they will sell fewer vaccines. If the P_i values are set higher than this limit, the problem becomes infeasible.

Thus, our first investigation is: what is the maximum P_i value such that our model will produce prices that satisfy all of our constraints? Looking at the DTap vaccine case, we run a series of variations on our model with a range of P_i values and with other parameters taken from Behzad and Jacobson (2016). The results can be seen in figure 5.1. For simplicity, we let $P_1 = P_2$, assuming that both manufacturers require the same minimum profits. The model is feasible for any $P_i \leq \$15.2$ million, which is a little under half of our estimate for the minimum profit required for Sanofi Pasteur ($35.2 million) and a third of our estimate for GlaxoSmithKline ($49.6 million).

Since the private sector price is determined by the Bertrand-Chamberlin equilibrium, it remains a constant $10.76 throughout. More interestingly, the public sector prices shift as we increase P_i. For low P_i, the government can afford to buy vaccines at next to no cost from one manufacturer, since both manufacturers can make enough profits from the private sector alone. As P_i increases, the government is forced to buy vaccines at higher costs - a small number from the higher priced Daptacel® and a larger number from the lower priced Infanrix®. The two public prices converge to $1.94 then collectively rise to $3.33 just before P_i reaches infeasibility.

Excitingly, these values of $3.33 for the public sector and $10.76 for the private sector qualitatively mimic reality, with the public sector price being smaller than the private sector price. The $7.43 gap between the two prices is

Figure 5.1   Effects of Minimum Profit Required on Price and Quantity Sold
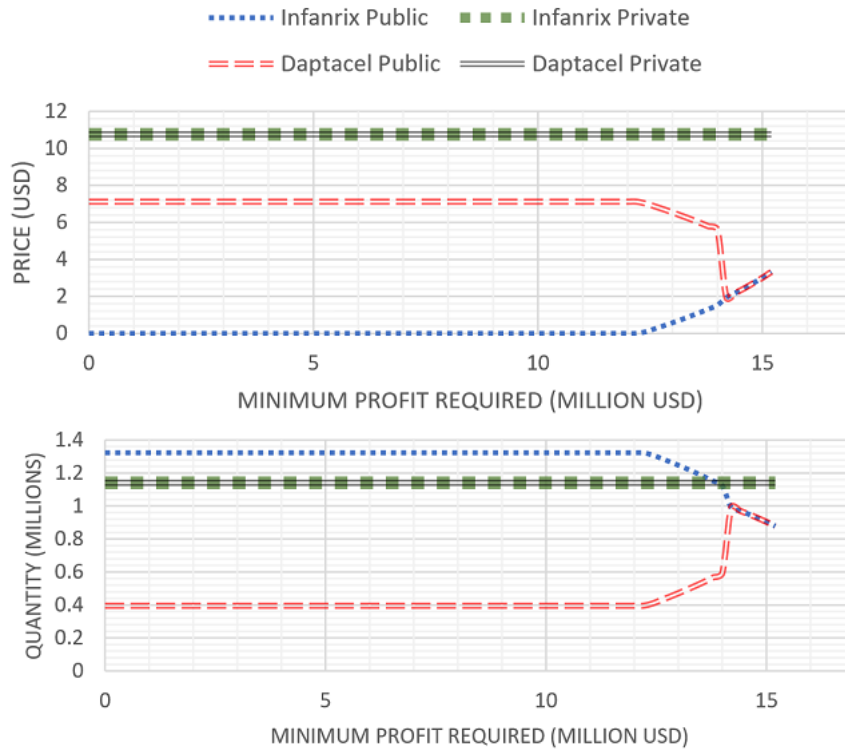
This figure shows the prices p_{ui} and p_{ri} (above) and the quantities sold q_{ui} and q_{ri} (below) for Infanrix® and Daptacel® for P_i ranging from 0 to 15.2×10^6 (the problem is infeasible for larger P_i). Here, $\gamma = 0.23$ and $D = 4 \times 10^6$ (meaning public demand is 2.3×10^6), like in Behzad and Jacobson (2016). $K_i = 4 \times 10^6$ for both manufacturers.

in between the $4.81 gap between the actual Infanrix® prices and the $12.37 gap between the actual Daptacel® prices.

## 5.3   Varying the Degree of Product Differentiation

Product differentiation, discussed further in section 4.7.4, is also a difficult quantity to estimate. In figure 5.1, we produced feasible results using $\gamma = 0.23$, but would all gamma values produce feasible solutions? Figure 5.2 looks at a range of γ values from 0 to 1, using the P_i threshold of $15.2 million determined in section 5.2. Here, we find feasible solutions for $\gamma = 0$ and γ ranging from 0.22-0.83.

There are several other features of figure 5.2 that are worthy of notice. For one, the public price is below the private sector price, except for $\gamma \geq 0.80$. This shows that except for large γ, overall qualitative behavior is not sensitive to changes in γ. We can also see in the bottom half of figure 5.2 that more vaccines are being sold in the private sector than the public sector, regardless of γ value.

Our goal is to have around 57% of the vaccines be sold in the public sector. Since more vaccines are being sold to the private sector, our model isn't maintaining the desired public-private quantity ratios. To mitigate this problem, we might want to constrain the amount sold in each sector, rather than just constraining the overall number sold between both sectors.

Along similar lines, we can also see that the number of vaccines sold overall does not stay constant. For lower values of γ, around 4 million vaccines are sold overall (approximately the total demand) while for the highest feasible γ values around 4.7 million vaccines are sold. While 4.7 million vaccines is still within reason, the fluctuation in total production is something worth keeping an eye on. At what point should we consider constraining the number of vaccines made exceeding overall demand?

Figure 5.2   Effects of Product Differentiation on Price and Quantity Sold
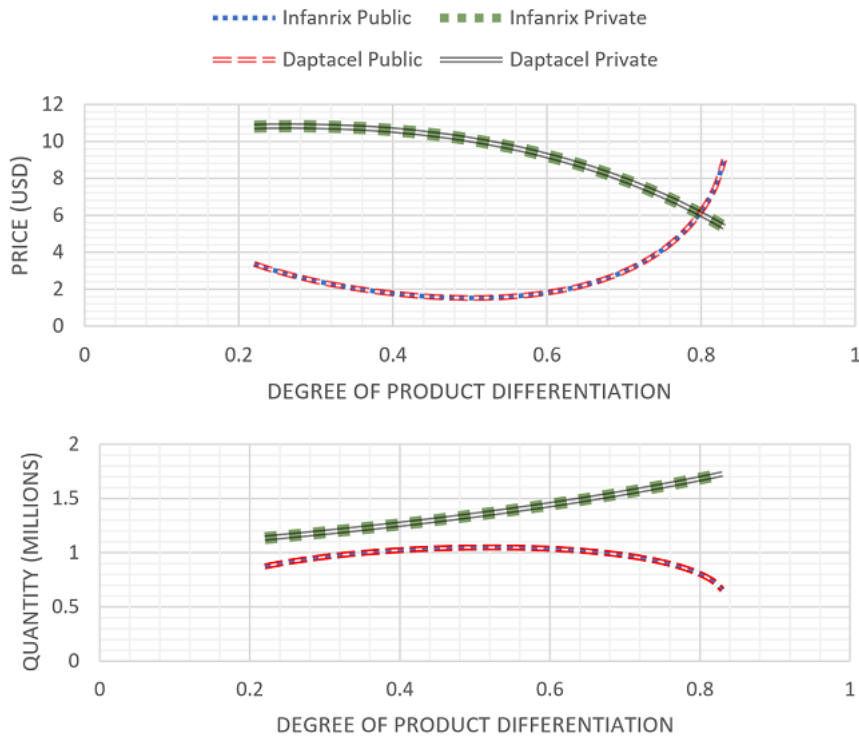
This figure shows the prices p_{ui} and p_{ri} (above) and the quantities sold q_{ui} and q_{ri} (below) for Infanrix® and Daptacel® for γ ranging from 0.22 to 0.83 (the problem is infeasible elsewhere). We use $D = 4 \times 10^6$ from Behzad and Jacobson (2016). $P_i = 15.2 \times 10^6$ and $K_i = 4 \times 10^6$ for both manufacturers.

Chapter 6

Model Concerns

6.1 Model and Input Issues

Although we do our best to model the vaccine pricing market with this approach, we can't capture everything. The following are a set of drawbacks and problems this model faces.

6.1.1 Data and Parameter Estimation

This model requires many pieces of data for input. Some, such as the demand D for a vaccine, can be approximated in a logical manner using a years' National Immunization Survey and the number of children born in the United States that year. Others, like the minimum profit P_i a manufacturer requires in order to continue to sell and research vaccines, are less clearly calculated. Even after choosing an approximation method to find P_i, it's hard to do error analysis on the calculation, since manufacturers don't publish their minimum desired profit margins.

Output accuracy is also difficult to gauge, since for many of these vaccines, we don't have many years of data to compare to. The CDC only publishes NIS results from 1995 onward (National Immunization Survey (2015)). On top of that, many vaccines in duopoly markets have only been recently developed. Pediarix® was approved in 2002 and Pentacel® in 2008, so the only relevant annual price negotiations in that duopoly have happened since 2008. This means that any model parameters that depend on annual data (such as the linear regression models in section 3.2) will be heavily affected by outliers and short-term trends.

There are also some smaller data discrepancies that are more easily fixed.

In this paper, we use 2016 data to approximate P_i, the most recent numbers available. However, these numbers don't match up with our calculations for D, which are based off of 2012 data. The NIS data takes a while to process, so the most current data available is the 2015 dataset (National Immunization Survey (2015)). Ideally, one would use the most recent NIS data available. Whether or not it is better to use NIS and vaccine R&D data that are in the same year or the most recent versions of each available is up for debate.

6.1.2 Modeling the Demand Curve

Demand is a tricky quantity to model, since there are many ways to describe the price-demand relationship. We choose to use a linear relationship between price and quantity sold, since it allows us to access the game theory results shown in Behzad and Jacobson (2016). However, a linear fit is not necessarily the best way of describing this relationship. Demand for vaccines is very inelastic, since most will choose to get vaccinated regardless of price fluctuations within a certain range. Also, consumers rarely pay the full price of their vaccines due to health insurance coverage, also implying that price fluctuations may not result in a large change in quantity sold. A more complex relationship, such as a logistic curve, may be more appropriate in this scenario. However, the nonlinearities introduced into the system due to the use of a logistic curve both add theoretical complexity and computational complexity.

After choosing a demand curve, another issue to consider is the amount of deviation one should allow from that curve. Our demand curve, as seen in equation 4.4, is an equality condition. That means that we do not allow any leeway - choosing a price exactly determines the quantity sold. This may not be the ideal way to set up a model. Future models might look at the demand curve as a suggested relationship between price and quantity, with some room to adjust as needed. Having more leeway both allows for a better understanding of the market forces in play in a given solution (were the prices higher or lower than expected, according to the demand curve?) and gives a higher likelihood of finding a feasible solution.

Similarly to how much we constrain the demand curve, we also should consider how much we constrain equation 4.16, the part of the model where we ensure that we meet overall demand. There are two choices to consider here: do we dictate that the number of vaccines sold exactly equals demand, or that it equals or exceeds demand? Also, should we look at the private and public sectors individually, or as a whole?

For the first question, there are positives and negatives to either choice. Exactly constraining the model ensures that you won't create a large excess of vaccines which a market would not have need for. Some number of vaccines are needed in addition to demand, since some small percentage of vaccines will be handled incorrectly as to render them unusable or distributed unevenly such that there are extra vaccines in some locations. The exact percentage extra needed is unclear, but one could approximate and then demand that number exactly using an equality.

If you choose not to exactly constrain the model and instead allow production to meet or exceed demand, you no longer get the exact control over how many vaccines are made. However, the system does gain flexibility. Since we are dealing with a highly constrained system, that added flexibility can be key to finding feasible solutions. Also, since the objective function (equation 3.8) is to minimize public sector costs, the tendency of the system is to not exceed vaccine demand by much. Due to the increased flexibility of the system, we choose this option rather than using an equality. However, this requires checking periodically to see how many vaccines are being over-produced, and deciding if the number over-produced is reasonable. If over-production becomes an issue, one could add another constraint to the system limiting the number of vaccines produced to some factor of total demand.

Looking at the second question, there are two different approaches: checking to see if demand is met in each sector individually (as seen in equations 3.2 and 3.3) and checking to see if demand is met overall (as seen in equation 4.16). The first method allows specific control over the ratio of vaccines sold in the public sector vs. the private sector, whereas the second method provides more flexibility. While we originally chose the first method for greater flexibility, the second may be the better choice, since the results in chapter 5 show that the public-private sector quantity ratio is not necessarily maintained without additional constraints.

6.1.3   Manufacturer Incentives

In this model, we've chosen to assume that manufacturers want to optimize their profits in the private sector. In the public sector, we only look to minimize government costs, with the thought that government negotiating power overrides manufacturers' incentives to make profits. However, this might not be the case - in an ideal world, we'd want to consider manufacturer incentives in both the public and private sectors, since they have roles in

both.

6.1.4   Marginal Cost

In chapter 4, we assume that vaccines can be produced at no marginal cost. Although it is true that the main cost of vaccine production is the years of R&D spending (Behzad et al. (2015)), vaccines do have a nonzero marginal cost. This cost is difficult to find directly, since manufacturers do not tend to post such information publicly. However, we can approximate marginal costs by using the prices manufacturers offer to UNICEF and other foreign aid organizations, as discussed in section 3.2. The game theory used in both equilibrium models in chapter 4 relies on vaccines having zero marginal cost, so for now this assumption remains. After more theory work, this assumption could potentially be relaxed.

6.2   Coding and Output Issues

To test out model, we coded it up in AMPL. The Bertrand-Chamberlin model can be solved with the MINOS solver, a solver that can handle linear constraints and a nonlinear objective function well (AMPL Optimization Inc. (2013)).

6.2.1   Coding up the Three-Equilibrium Model

The three-equilibrium model requires a solver that can handle integer variables, quadratic constraints, and a quadratic objective function. MINOS doesn't solve integer problems and thus another solver must be found.

   CPLEX or Gurobi might be good choices to solve the three-equilibrium model. However, maintaining $q_i^C \geq 0$ (equation 4.29) currently requires a quadratic equality constraint, which neither solver can handle. In order to properly code up the three-equilibrium model, either that constraint will need to be re-written or a different solver needs to be found.

6.2.2   Quantitatively Analyzing Price Output

Prices suggested by equilibrium calculations in Behzad et al. (2015) and Behzad and Jacobson (2016) are almost always far lower than actual vaccine prices. The same is true in this paper - our prices suggested in chapter 5 never go above \$10.83, while the actual prices are between \$16.04 and \$28.41.

Capturing these prices exactly is difficult, since there are many aspects of the health care system (subsidies, insurance companies, etc.) that we don't even begin to attempt to put in the model. For now, this may mean that we have to rely more on qualitative results than quantitative ones - which prices are higher and by how much?

6.2.3 Feasibility

As is shown with the P_i and γ calculations in chapter 5, this model doesn't always produce a solution at all. Sometimes, the parameters are set such that the model is over-constrained, and no solution exists. This is problematic because it limits the situations with which we can use our model. For example, we cannot use our original predicted values for P_i, since those fail to produce feasible solutions. The three-equilibrium model may be more flexible and have a larger solution set, but without a working coded version and appropriate solver that is difficult to determine.

Chapter 7

Conclusions and Future Work

7.1 Conclusions

Previous work by Behzad et al. (2015) and Behzad and Jacobson (2016) have modeled the public sector of the vaccine pricing market alone, without looking at the government as an actor. Here, we use that work and mathematical programming to incorporate the CDC into vaccine pricing models and expand those models to span both the public and private sectors. We suggest two main model model approaches: the Bertrand-Chamberlin model, which deals with systems that have an abundance of vaccines, and the three-equilibrium model, which can analyze systems with either a scarcity or abundance of vaccines.

Results from the Bertrand-Chamberlin model show predicted prices that are lower than actual prices, but are qualitatively similar, with the public sector prices being several dollars less than the private sector prices. These qualitative differences are somewhat resilient to changes in the degree of product differentiation γ for smaller values of γ. For $\gamma \geq 0.80$, public sector prices become larger than private sector ones.

Although our estimates for P_i, the minimum profit required for each manufacturer to maintain interest in the market, are too large and make the system infeasible, we can find the maximum feasible P_i computationally. For Infanrix® and Daptacel®, the model maintained feasibility for $P_i \leq$ \$15.2 × 10^6. This allows us to rethink our original P_i estimates, and perhaps come up with a new estimation method that better reflects the feasible minimum profits we see within the model.

This model helps us understand the impact of government pricing on

the market as a whole, and helps to optimize not only for government prices but also to keep vaccine manufacturers in the market. In a market where the number of manufacturers is on the decline and health care costs are rising, both of these priorities are key. Although mathematical models can't perfectly suggest ideal vaccine prices, they can bring in an additional perspective and help policymakers make informed choices. For salient issues like health care, the time spent on extra doses of mathematical understanding are a price worth paying.

7.2   Future Work

This work has many possible extensions. Most pressingly, the three-equilibrium model has yet to be analyzed computationally. Solving the coding issues described in section 6.2.1 and choosing an appropriate solver is a key next step in this modeling process.

Once computable, the three-equilibrium model opens up another line of inquiry: what happens to prices as manufacturer capacity K_i changes? Knowing how the CDC should price differently in times of scarcity vs abundance, or if one manufacturer has a much smaller production capacity than another, could be informative for policy making.

One could also do a more thorough investigation of the minimum required profit P_i. What is the maximum P_i value for different γ, K_i and D values? Further thought into why our system limits the maximum profit a manufacturer can make and how to increase that limit through different modeling choices would also be of use, since then we may be able to incorporate our original estimates for P_i into our model.

As seen from the Bertrand-Chamberlin model results, our current modeling approach doesn't always maintain the private-public sector quantity ratios we would hope for. Demand constraints like equation 4.16 might be better supplemented with sector-specific constraints (see equation 3.2), which would change model dynamics. Whether additional constraints should be equalities or inequalities and whether they should constrain both the public and private sectors or just one sector warrants additional thought.

As discussed in section 6.1.2, the linear demand curve may not be the best price-quantity relationship to employ in our situation. As a possible future line of research, other demand curves could be examined. This would involve theoretical work to recalculate equilibrium values, as well as computational work to then compare demand curve results.

Lastly, future research could try these models on a wider variety of cases. We looked at the Infanrix® Daptacel® duopoly, but there are many others. One key case to look at is the Pentacel® Pediarix® duopoly, where the government keeps track of the demand for both vaccines separately. Many of the analytical methods described in this research extend to more than two competing vaccines, so cases with three competing vaccines could also be investigated.

Bibliography

AMPL Optimization Inc. 2013. MINOS. http://ampl.com/products/solvers/solvers-we-sell/minos/. (Accessed on 05/24/2017).

Barla, Philippe. 2000. Firm size inequality and market power. *International Journal of Industrial Organization* 18(5):693–722.

Behzad, Banafsheh, and Sheldon H Jacobson. 2016. Asymmetric Bertrand-Edgeworth-Chamberlin competition with linear demand: A pediatric vaccine pricing model. *Service Science* 8(1):71–84.

Behzad, Banafsheh, Sheldon H Jacobson, Janet A Jokela, and Edward C Sewell. 2014. The relationship between pediatric combination vaccines and market effects. *American journal of public health* 104(6):998–1004.

Behzad, Banafsheh, Sheldon H Jacobson, and Matthew J Robbins. 2015. A symmetric capacity-constrained differentiated oligopoly model for the United States pediatric vaccine market with linear demand. *IIE Transactions* 47(11):1252–1266.

CDC. 2017. U.S. Vaccine Names. https://www.cdc.gov/vaccines/terms/usvaccines.html. (Accessed on 05/22/2017).

Douglas, R Gordon, Jerald Sadoff, and Vijay Samant. 2008. The vaccine industry. *Vaccines 5th ed New York, NY: Saunders* 37.

GlaxoSmithKline. 2017. GSK Annual Report 2016. https://annualreport.gsk.com/assets/downloads/1_GSK.AR.FULL.V3.pdf. (Accessed on 05/22/2017).

Jacobson, Sheldon H, Edward C Sewell, Robert Deuson, and Bruce G Weniger. 1999. An integer programming model for vaccine procurement and delivery for childhood immunization: a pilot study. *Health Care Management Science* 2(1):1–9.

Lau, Amy Hing Ling, and Hon-Shiang Lau. 2003. Effects of a demand-curve's shape on the optimal solutions of a multi-echelon inventory/pricing model. *European Journal of Operational Research* 147(3):530–548.

LeMoyne, Roger. 2016. Vaccine price data. https://www.unicef.org/supply/index_57476.html. (Accessed on 12/01/2016).

Martin, Joyce A, Brady E Hamilton, Stephanie J Ventura, Michelle JK Osterman, TJ Mathews, et al. 2013. Births: final data for 2011. *National Vital Statistics Report* 62(1):1–90.

Merck. 2017. Merck Announces Fourth-Quarter and Full-Year 2016 Financial Results. http://www.mrknewsroom.com/news-release/corporate-news/merck-announces-fourth-quarter-and-full-year-2016-financial-results.

Nash, John F, et al. 1950. Equilibrium points in n-person games. *Proceedings of the national academy of sciences* 36(1):48–49.

National Center for Health Statistics. 2017. Births and Natality. https://www.cdc.gov/nchs/fastats/births.htm. (Accessed on 05/23/2017).

National Immunization Survey. 2015. Datasets and Related Documentation for the National Immunization Survey, 2010 to 2014. https://www.cdc.gov/nchs/nis/data_files.htm. (Accessed on 05/23/2017).

Orenstein, Walter A, R Gordon Douglas, Lance E Rodewald, and Alan R Hinman. 2005. Immunizations in the United States: success, structure, and stress. *Health Affairs* 24(3):599–610.

Robbins, Matthew J, and Sheldon H Jacobson. 2015. Analytics for vaccine economics and pricing: insights and observations. *Expert review of vaccines* 14(4):605–616.

Robbins, Matthew J, Sheldon H Jacobson, Uday V Shanbhag, and Banafsheh Behzad. 2013. The weighted set covering game: a vaccine pricing model for pediatric immunization. *INFORMS Journal on Computing* 26(1):183–198.

Samuelson, Paul. 1976. *Economics*. McGraw-Hill, 10th ed.

Sanofi. 2017. Sanofi - Q4 and Full Year 2016 Results. http://en.sanofi.com/investors/events/Results/2017-02-08_Results_FY_2016.aspx. (Accessed on 05/22/2017).

Stokey, Nancy L. 1991. Credible public policy. *Journal of Economic dynamics and control* 15(4):627–656.

Tartof, Sara Y, Melissa Lewis, Cynthia Kenyon, Karen White, Andrew Osborn, Juventila Liko, Elizabeth Zell, Stacey Martin, Nancy E Messonnier, Thomas A Clark, et al. 2013. Waning Immunity to Pertussis Following 5 Doses of DTaP. *Pediatrics* 131(4):e1047–e1052.

Tirole, Jean. 1988. *The theory of industrial organization*. MIT press.

Trick, Michael. 1998. Quantitative methods course notes. http://mat.gsia.cmu.edu/classes/QUANT/NOTES/chap10.pdf. (Accessed on 05/22/2017).

Vaccines for Children Program. 2017. Current CDC Vaccine Price List. https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/. (Accessed on 05/24/2017).

Vives, X. 1999. Oligopoly pricing: Old ideas and new toolsmit press. *Cambridge, MA* .

Vives, Xavier. 2001. *Oligopoly pricing: old ideas and new tools*. MIT press.

Whitney, Cynthia, Fangjun Zhou, James Singleton, and Anne Schuchat. 2014. Benefits from immunization during the vaccines for children program era – United States, 1994-2013. *Morbidity and Mortality Weekly Report* 63(16):352–355.