http://pubsonline.informs.org/journal/msom

MANUFACTURING & SERVICE OPERATIONS MANAGEMENT
Articles in Advance, pp. 1–15
ISSN 1523-4614 (print), ISSN 1526-5498 (online)

Centers for Disease Control and Prevention as a Strategic Agent in the Pediatric Vaccine Market: An Analytical Approach

Kayla Cummings,[a] Banafsheh Behzad,[b] Susan Martonosi[c]

[a] Operations Research Center, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139; [b] College of Business, California State University, Long Beach, Long Beach, California 90840; [c] Department of Mathematics, Harvey Mudd College, Claremont, California 91711

Contact: kaylac@mit.edu, https://orcid.org/0000-0001-6289-4095 (KC); banafsheh.behzad@csulb.edu, https://orcid.org/0000-0002-0962-2565 (BB); martonosi@g.hmc.edu, https://orcid.org/0000-0002-9497-4943 (SM)

Received: November 9, 2018
Revised: September 24, 2019; January 28, 2020
Accepted: April 8, 2020
Published Online in Articles in Advance: October 8, 2020

https://doi.org/10.1287/msom.2020.0902

Abstract. ***Problem definition***: Pediatric vaccine markets in the United States are vulnerable to the development of monopolies due to few manufacturers and high research and development costs. This work addresses how the government can ensure the cost-effective procurement of pediatric vaccines by all U.S. children from private manufacturers. The Centers for Disease Control and Prevention's (CDC) significant patronage of pediatric vaccines affords them leverage in negotiating public-sector prices that prevent the formation of monopolies, but existing vaccine pricing literature excludes the CDC as a rational player. ***Academic/practical relevance***: We combine optimization and game theoretic techniques to address cost-effective immunization of all U.S. children. ***Methodology***: Our optimization model from the CDC's perspective minimizes negotiated government costs while ensuring adequate national vaccination levels, linking dynamics in public and private sectors, and incorporating competitive manufacturer behavior. The optimization model embeds an extant game theoretic price model to capture competitive interactions among manufacturers in the private sector, where they compete independently of the CDC. The model is validated in an extended case study of the Infanrix–Daptacel vaccine duopoly. ***Results***: The study indicates that dissimilar products advantageously segment markets with asymmetric manufacturers. Furthermore, markets are at lower risk when high-capacity manufacturers have moderate target profits, especially in cases of high demand and asymmetry. We demonstrate that our model can help restabilize a market that experiences a vaccine shortage and that the CDC might mitigate the same shortage using strategies that depend on which manufacturer is limited. We also underline scenarios in which the CDC may be able to prevent monopolies through financial incentives to manufacturers. The results support a paradigm shift from annual contracts to ongoing negotiations, which would enable the CDC to exercise control over high-risk markets. ***Managerial implications***: Our study demonstrates an analytical approach for managerial government officials to influence pediatric vaccine prices via the procurement of public-sector goods.

Funding: K. Cummings was supported by a National Science Foundation Graduate Research Fellowship [Grant 1122374].
Supplemental Material: The online appendix is available at https://doi.org/10.1287/msom.2020.0902.

Keywords: healthcare • optimization • game theory • public policy • pediatric vaccine pricing • contracts • vaccine shortages

1. Introduction

State and local governments in the United States purchase approximately 57% of all pediatric vaccines at prices negotiated on their behalf by the Centers for Disease Control and Prevention (CDC) (Orenstein et al. 2005). The Vaccines for Children (VFC) program administers these vaccines at no cost to eligible children (Coleman et al. 2005).

Four pharmaceutical companies manufacture all vaccines required by the U.S. Recommended Childhood Immunization Schedule (RCIS) (Robbins et al. 2010). Of these four firms, only three produce *competitive* vaccines, which are produced by two or more manufacturers that contain at least one similar antigen satisfying the same RCIS requirement (Robbins et al. 2010). Thus, the pediatric vaccine market is an *oligopoly*, a market dominated by a few sellers (Tirole 1988). A *monovalent* vaccine immunizes against exactly one strain of a given pathogen (Behzad et al. 2015), whereas *polyvalent* vaccines contain two or more antigens (U.S. Centers for Disease Control and Prevention 2017). A polyvalent vaccine is also a *combination* vaccine if a proper subset of its antigens can be found in another nonidentical vaccine on the market (Lauera et al. 2017). For ease of exposition, we refer to a polyvalent vaccine as *monovalent* if it is

not a combination vaccine. We restrict our focus in this paper to competitive monovalent vaccines. For example, the "monovalent" DTaP vaccine contains antigens against diphtheria, tetanus, and acellular pertussis, for which individual pediatric vaccines are not available (U.S. Centers for Disease Control and Prevention 2018a). Meanwhile, the combination DTaP-IPV vaccine immunizes against the three diseases covered by the DTaP vaccine as well as polio (U.S. Centers for Disease Control and Prevention 2018a). Competitive combination vaccines might not immunize against exactly the same set of pathogens. Combination vaccine markets therefore lie outside the scope of this work.

Competitive monovalent vaccine markets are commonly dominated by two manufacturers. For example, in the case of the DTaP monovalent vaccine market, the only two competing manufacturers are GlaxoSmithKline (Infanrix), and Sanofi Pasteur (Daptacel). Thus, we focus on *duopoly* markets, which are at highest risk of becoming monopolies. Manufacturers that have monopolized a vaccine market have more power to drastically increase prices. Note that we interchangeably reference a manufacturer using its company name and the vaccine that it produces.

Vaccine pricing is a challenge with no simple solution (Jacobson 2012). A few quantitative studies have analyzed pediatric vaccine pricing in the United States, focusing primarily on manufacturers' competitive interactions. Robbins and Jacobson (2015) review the analytical papers that discuss appropriate vaccine pricing and cost-effective vaccine selection. Among these papers, several use game-theoretic methods to analyze pediatric vaccine prices in the United States (Robbins et al. 2014, Behzad et al. 2015, Behzad and Jacobson 2016). Robbins et al. (2014) analyzed the U.S. pediatric vaccine market with a Bertrand oligopoly pricing model. A *Bertrand game* describes a static competition in which the strategic variable is the product's price (rather than the quantity, as in a *Cournot game*) (Cournot 1838, Bertrand 1883). This model determines oligopolistic interactions between manufacturers with unlimited capacities in a homogeneous, multiple-product market. An *Edgeworth* competition assumes capacitated manufacturers (Edgeworth 1925), and a *Chamberlin* competition assumes differentiated products (Chamberlin 1933). Behzad et al. (2015) and Behzad and Jacobson (2016) presented an extended Bertrand-Edgeworth-Chamberlin game to compute equilibrium prices for monovalent vaccines.

There are a few mathematical programming models that consider consumer needs in the pediatric vaccine market (Lunday and Robbins 2016, Robbins and Lunday 2016). Lunday and Robbins (2016) constructed a multiobjective mixed-integer nonlinear program to minimize injections and immunization costs for a given cohort of children and prescribed set of formularies, while ensuring maximum profits for the vaccine manufacturers. Robbins and Lunday (2016) also formulated a bilevel mathematical program, in which the manufacturer selects profit-maximizing vaccine prices in the upper level, while the customer decides which vaccines to purchase so that they satisfy the RCIS at the lowest possible cost in the lower level.

Because the government purchases the majority of pediatric vaccines and has also expanded the market by immunizing children who would not have otherwise been vaccinated (Coleman et al. 2005), the CDC has significant sway in the price negotiation process. Thus, the CDC has the opportunity to offer price points to manufacturers that mitigate the high risk for monopolies. The exclusion of the CDC as a player from extant pediatric vaccine pricing literature motivates the development of a model from their perspective. Following an approach outlined by Sinclair (2017) and Cummings (2018), this paper fills that gap by developing an optimization model to minimize the CDC's negotiated costs while incorporating competitive oligopoly behavior among manufacturers and ensuring adequate vaccination levels. This work also links dynamics in both public and private sectors.

We develop an optimization model of a monovalent vaccine duopoly from the CDC's point of view and validate the model in a case study of the Infanrix–Daptacel duopoly. We predict 2018 prices, public-sector costs, and demand fulfillment. After comparing our predictions with true 2018 prices, we confirm that our model is viable. We also perform sensitivity analysis to characterize a stable market, which is a market at low risk of becoming a monopoly. We find that high-capacity manufacturers with moderate target profits are at lowest risk of leaving the market. The study also indicates that a market with asymmetric manufacturers is advantageously segmented by highly dissimilar products but becomes high-risk when the larger manufacturer has a higher target profit. Because a vaccine market can occasionally experience shortages, we model how the CDC can restabilize the market when a manufacturer is unable to produce its contracted quantity. In doing so, we quantify the benefits of using optimization during the price negotiation process. Interestingly, our simulation indicates that the strategy the CDC should use to stabilize a market not only depends on the magnitude of the shortage but also on which manufacturer has limited capacity. These findings inform our recommendations that the CDC consider (1) continual negotiation with manufacturers rather than annual contracts

and (2) financial incentives in cases of high demand and manufacturer asymmetry. Both of these business standards would offer the CDC more control over markets at risk.

Section 2 describes the optimization model in which the CDC seeks to minimize its total expenditures in the public sector, while modeling private-sector vaccine market dynamics as a duopoly game. Section 3 studies the output of this model both generally and in the specific case of the Infanrix–Daptacel duopoly. Section 4 presents limitations and possible directions for future work, and Section 5 summarizes model results and provides recommendations.

2. CDC Price-Negotiation Model

A representative model of a monovalent pediatric vaccine duopoly should encode the CDC's goals of ensuring that all U.S. children are vaccinated and that vaccine manufacturers meet target profits so that they do not leave the market, all at minimum governmental cost. These goals are constrained by manufacturers' production capacities, linear supply and demand, and competitive private-sector pricing dynamics. In the public sector, the CDC negotiates vaccine prices with vaccine manufacturers for the purchases made by state and local government public health agencies. Manufacturers compete independently of the CDC in the private sector, but private-sector outcomes still impact public-sector operations due to coupled production capacity constraints and global target profits. The mechanism driving the model that we formulate in this section requires the CDC to consider whether the prices and quantities set in the public sector allow manufacturers to meet total demand and earn target profits. If these objectives can be met, then the CDC offers a price that minimizes government costs. This mechanism represents a realistic decision-making process for the CDC.

2.1. Public-Sector Optimization Model

We present our optimization model. Table 1 summarizes parameters and variables, and Equations (1)–(9) provide the full formulation of the model.

Each manufacturer $i \in M$ operates in both the public (CDC-negotiated) and private sectors, where q_i^s and p_i^s represent the quantities produced and prices charged by manufacturer i in sector $s \in S = \{\text{pub}, \text{priv}\}$. Because our optimization model is from the CDC's perspective, we treat the public-sector quantities and prices, q_i^{pub} and p_i^{pub}, as variables, and the private-sector quantities and prices, q_i^{priv} and p_i^{priv}, as parameters that will be determined from a pricing game in Section 2.2. The parameter γ encodes the degree of product similarity and ranges from 0 (completely differentiated) to 1 (perfectly identical). Some texts refer to γ as the product differentiation (i.e., Chamberlin 1933, Behzad et al. 2015, and Behzad and Jacobson 2016).

The CDC tries to minimize total public-sector costs. However, observed public-sector vaccine prices tend not to vary disparately between manufacturers. (For example, see Table 3 for the case of the DTaP vaccine.) Therefore, among alternative optima that minimize total public-sector costs, we require the model to return a solution for which the public-sector prices for the two manufacturers are as similar as possible. The weighted objective function given in (1) balances these two goals. The variable z denotes the absolute difference between the two prices (as enforced by constraint (2)), and the weighting parameter $0 < \mu < 1$, when appropriately tuned, prioritizes among cost-minimizing solutions those having a smaller absolute price difference.

The total U.S. demand for the vaccine is given by D, of which we assume that 57% must be satisfied in the public sector (Orenstein et al. 2005). All eligible U.S. children should receive the exact required dosage of

Table 1. Components of the Optimization Model, Equations (1)–(9)

Name	Type	Meaning
M	Set	Manufacturers
S	Set	Sectors {pub, priv}
p_i^{pub}	Variable	Public-sector vaccine price, $i \in M$
q_i^{pub}	Variable	Public-sector vaccine quantity, $i \in M$
z	Variable	Manufacturers' absolute public-sector price difference
γ	Parameter	Product similarity
p_i^{priv}	Parameter	Private-sector vaccine price, $i \in M$
q_i^{priv}	Parameter	Private-sector vaccine quantity, $i \in M$
ρ_i	Parameter	Inflation bound on public-sector price, $i \in M$
D	Parameter	Total U.S. demand
a^s, b, c	Parameters	Demand curve coefficients, $s \in S$
K_i	Parameter	Total production capacity, $i \in M$
P_i	Parameter	Minimum profit threshold, $i \in M$
U	Parameter	Private-sector capacity lower bound for surplus
μ	Parameter	Objective function weight

any particular vaccine—no more and no less—and the total quantity of vaccines that are sold should exactly meet demand. However, we use $0.57D$ as a lower bound on public-sector demand, as given in constraint (3), due both to a desire to avoid shortages and to our demand-estimation method described in the online supplement:

$$\text{minimize} \quad \mu\left(\sum_{i\in M} q_i^{\text{pub}} \cdot p_i^{\text{pub}}\right) + (1-\mu)z \tag{1}$$

$$\text{subject to} \quad z \geq p_i^{\text{pub}} - p_j^{\text{pub}} \qquad i,j \in M,\ i \neq j, \tag{2}$$

$$\sum_{i\in M} q_i^{\text{pub}} \geq 0.57D, \tag{3}$$

$$q_i^{\text{pub}} + bp_i^{\text{pub}} - cp_j^{\text{pub}} = a^{\text{pub}} \qquad i,j \in M,\ i \neq j, \tag{4}$$

$$\sum_{s\in S} q_i^s \cdot p_i^s \geq P_i \qquad i \in M, \tag{5}$$

$$\sum_{s\in S} q_i^s \leq K_i \qquad i \in M, \tag{6}$$

$$K_i - q_i^{\text{pub}} \geq U \qquad i \in M, \tag{7}$$

$$p_i^{\text{pub}} \leq \rho_i \qquad i \in M, \tag{8}$$

$$q_i^{\text{pub}},\ p_i^{\text{pub}},\ z \geq 0 \qquad i \in M. \tag{9}$$

Similar to Behzad et al. (2015) and Behzad and Jacobson (2016), we assume that each sector operates under a linear direct demand curve:

$$q_i^s = a^s - bp_i^s + cp_j^s \qquad i,j \in M, i \neq j, s \in S, \tag{10}$$

and we constrain this relationship explicitly for the public sector in constraint (4). The linear demand curve in the private sector is handled exogenously via model parameters, as described in Section 2.2.

To this point, the objective function and constraints have relied only on variables and parameters defined for the public sector. However, for a given manufacturer, the public and private sectors are coupled in two ways. First, both sectors determine a manufacturer's overall profitability in producing a given vaccine, determining whether that manufacturer remains in the market. Because we assume the CDC wishes to ensure that both manufacturers remain in the market to prevent a monopoly, constraint (5) ensures that each manufacturer i achieves at least a minimum profit threshold P_i. Second, each manufacturer has a production capacity, K_i for $i \in M$, which must be shared between the public and private sectors, as given by constraint (6). To ensure that certain pricing dynamics hold in the private sector, constraint (7) requires each manufacturer's remaining production capacity to exceed a threshold U after determining q_i^{pub}. In other words, the CDC's promised purchases must guarantee sufficient residual capacities that manufacturers can allocate to the private sector, in which they compete independently of the CDC. This model thus reflects the iterative nature of public-sector negotiations, in which annual public-sector price updates are naturally informed by the private-sector market. Lastly, constraint (8) enforces the legislative requirement that vaccine prices cannot exceed the previous year's price plus an inflation adjustment (U.S. Centers for Disease Control and Prevention 2016).

The next section describes the pricing game, developed by Behzad et al. (2015) and Behzad and Jacobson (2016), that determines the private-sector parameters q_i^{priv}, p_i^{priv}, and U.

2.2. Private-Sector Pricing Game

Our model directly embeds the results of an asymmetric, capacity-constrained, linear-demand, differentiated duopoly game developed by Behzad and Jacobson (2016). This work is an extension of the symmetric version developed by Behzad et al. (2015). Although they applied their model using parameter values drawn from the public-sector market, their model structure remains appropriate for determining our model's private-sector prices and quantities. This section summarizes these results applied to the private sector.

Behzad et al. (2015) and Behzad and Jacobson (2016) model the pediatric vaccine market using a *Bertrand-Edgeworth-Chamberlin* competition. The Bertrand framework is well suited to model the pediatric vaccine market because prices are set annually and are decided before purchases are made throughout the year (Robbins et al. 2014). The Edgeworth assumption of capacitated manufacturers is realistic in the vaccine market due to factors such as high research costs. Competing vaccines may be differentiated by factors including but not limited to side effects, associated histories of adverse events, administration method, and branding, which justifies the Chamberlin assumption of nonhomogeneous products (Behzad et al. 2015).

We assume a linear demand model, yielding the direct-demand equation given in Equation (10) and the following inverse-demand equation:

$$10^5 \cdot p_i = \alpha^s - q_i - \gamma q_j \qquad i,j \in M,\ i \neq j,\ \alpha^s > 0,\ s \in S. \tag{11}$$

Quantities are on the order of 10^6, whereas prices are on the order of 10^1. Prices are scaled by 10^5 in the demand curves so that quantities and prices have the same level of influence. By solving system (11)

for quantities, Behzad et al. (2015) derived the following values for a^s, b, and c:

$$a^s = \frac{\alpha^s}{1+\gamma}, \tag{12}$$

$$b = \frac{10^5}{(1+\gamma)(1-\gamma)}, \tag{13}$$

$$c = \gamma \cdot b. \tag{14}$$

They also assume that the manufacturers have asymmetric production capacities, K_i for $i \in M$. Behzad et al. (2015) and Behzad and Jacobson (2016) showed that there exist three Nash equilibria that fully characterize the optimal behavior of the two firms, under the assumption that each manufacturer has knowledge of its competitor's production capacity. Each equilibrium is a pricing strategy that a manufacturer employs when its capacity falls within one of three ranges.

We restrict our model's focus to the surplus scenario, in which each manufacturer's private-sector production capacity is sufficiently large for maximizing its private-sector profits independently of its capacity. The surplus scenario corresponds to the case that $K_i \geq U$, $i \in M$. Behzad et al. (2015) derive U to be

$$U = \frac{a^{\text{priv}}(1+\gamma)}{\gamma} \cdot \left(1 - \frac{2(1-\gamma)^{1/2}}{(1+\gamma)^{1/2}(2-\gamma)}\right). \tag{15}$$

Behzad et al. (2015) and Behzad and Jacobson (2016) denote U by $k(\gamma)$. We interpret U as the lowest private-sector production capacity that allows a manufacturer to produce the profit-maximizing quantity. This model choice positions our analysis toward characterizing the market when it is at lowest risk of becoming a monopoly. Moreover, although one year-long shortage of Daptacel occurred in 2012 (U.S. Food and Drug Administration 2018), both vaccines are typically in sufficient supply.

The price that maximizes profit is called the *Bertrand-Chamberlin* (BC) pure-strategy equilibrium. Equation (16) provides the BC equilibrium, which we adapt to the private sector:

$$p_i^{\text{priv}} = \frac{a^{\text{priv}}}{2b-c} \qquad i \in M. \tag{16}$$

Because manufacturers will always use the BC strategy in the optimization model, private-sector prices and quantities depend only on product similarity. Therefore, p_i^{priv} and q_i^{priv} are parameters for $i \in M$. We compute the private-sector quantities in Equation (17) by substituting each manufacturer's private-sector price into the linear demand curve:

$$q_i^{\text{priv}} = bp_i^{\text{priv}} \qquad i \in M. \tag{17}$$

We assume that the total quantity sold in the private sector meets or exceeds the private-sector demand, which is assumed to be 43% of total demand (Orenstein et al. 2005).

The following equations summarize all parameter definitions and assumptions.

3. Case Study of DTaP

We use the DTaP duopoly as a case study to examine how the recommended CDC price and quantity negotiations are influenced by model parameters. In Section 3.1, we summarize parameter estimates for the DTaP market. In Section 3.2, we first validate model outputs. We then perform a sensitivity analysis and characterize a market at low risk of becoming a monopoly. Finally, Section 3.3 simulates a vaccine shortage and weighs the benefits of different mitigation strategies that the CDC can employ:

$$\mu, \gamma \in [0,1]$$
$$a^s \geq 0 \qquad s \in S$$
$$b = \frac{10^5}{(1+\gamma)(1-\gamma)}$$
$$c = \gamma \cdot b$$
$$p_i^{\text{priv}} = \frac{a^{\text{priv}}}{2b-c} \qquad i \in M$$
$$q_i^{\text{priv}} = b \cdot p_i^{\text{priv}} \qquad i \in M$$
$$\sum_{i \in M} q_i^{\text{priv}} \geq 0.43D$$
$$U = \frac{a^{\text{priv}}(1+\gamma)}{\gamma} \cdot \left(1 - \frac{2(1-\gamma)^{0.5}}{(1+\gamma)^{0.5}(2-\gamma)}\right).$$

3.1. Parameter Estimation

In this subsection, we summarize our parameter estimates for the DTaP market case study. Table 2 shows the complete list of estimated values.

We provide estimates for the total demand (D), demand curve coefficients (a^s, b, c), manufacturer parameters (product similarity (γ), target profit (P_i), production capacity (K_i), and public-sector price upper bound (ρ_i)), and the objective function weight (μ).

Table 2. Parameter Estimates for 2018 DTaP Case Study

Model component	Base value	Sensitivity analysis
D	4.034M	[4.00M, 7.832M]
μ	10^{-4}	N/A
γ	0.25	[0, 0.5]
$K_{\text{Inf}}, K_{\text{Dap}}$	4.034M	[2.837M, 4.034M]
$P_{\text{Inf}}, P_{\text{Dap}}$	\$39.8M, \$45.1M	[\$26.5M, \$53.0M]
$\rho_{\text{Inf}}, \rho_{\text{Dap}}$	\$18.62, \$18.02	N/A

Note. M, million.

Extensive explanation of our estimation methods for these parameters are in the online appendix.

The demand intercepts as a function of $\gamma \in (0,1)$ are given by Equations (18) and (19), and they are graphed in Figure 1. Table 3 shows that private-sector prices are typically higher, driving the intercept a^{priv} to be higher than a^{pub} for all $\gamma \in (0,1)$, as seen in Figure 1. The intercepts vary inversely with product similarity because demand for a product is lower when the competitor's product is very similar:

$$a^{\text{priv}} = \left(1.030 + \frac{2.389}{1+\gamma}\right) \times 10^6, \tag{18}$$

$$a^{\text{pub}} = \left(1.365 + \frac{1.553}{1+\gamma}\right) \times 10^6, \tag{19}$$

$$p_i^{\text{priv}} = (34.190 + 10.300\gamma) \cdot \left(\frac{1-\gamma}{2-\gamma}\right) \qquad i \in M, \tag{20}$$

$$q_i^{\text{priv}} = \frac{3.419 + 1.030\gamma}{(1+\gamma)(2-\gamma)} \times 10^6 \qquad i \in M, \tag{21}$$

$$U = \left(\frac{3.419 + 1.030\gamma}{\gamma}\right) \cdot \left(1 - \frac{2(1-\gamma)^{1/2}}{(1+\gamma)^{1/2}(2-\gamma)}\right) \times 10^6. \tag{22}$$

Equations (20), (21), and (22), graphed in Figure 2, are our estimates of the private-sector prices p_i^{priv}, quantities q_i^{priv}, and the private-sector capacity threshold needed to assume a Bertrand-Chamberlin equilibrium U. Manufacturers must charge lower prices if their competitor's vaccine is more similar; however, charging lower prices enables them to sell more vaccines due to the inverse relationship of price and quantity.

Figure 1. Each Sector's Demand Curve Intercept vs. Product Similarity (γ)

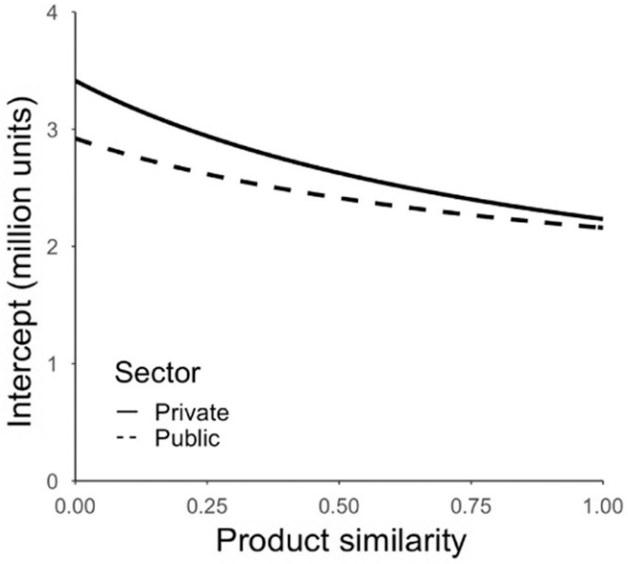


Table 3. Yearly Public- and Private-Sector Prices per Dose (U.S. Centers for Disease Control and Prevention 2018a)

	Public sector		Private sector	
Year	Infanrix	Daptacel	Infanrix[a]	Daptacel
2010	$13.75	$13.75	$21.20	$23.75
2011	$14.51	$13.25	$21.20	$24.40
2012	$15.35	$15.00	$21.20	$25.29
2013	$15.76[b]	$15.38	$21.20	$25.98
2014	$15.76[c]	$15.38	$21.20	$25.98
2015	$16.15	$16.04	$21.20	$27.17
2016	$16.85	$16.73	$22.40	$28.41
2017	$17.73	$17.16	$22.40	$29.20

Note. Contracts are finalized in March.
[a]Averaged price of syringe and vial forms.
[b]Adjusted in April from original contract price of $16.01.
[c]Adjusted in May from original contract price of $16.17.

3.2. Empirical Analysis

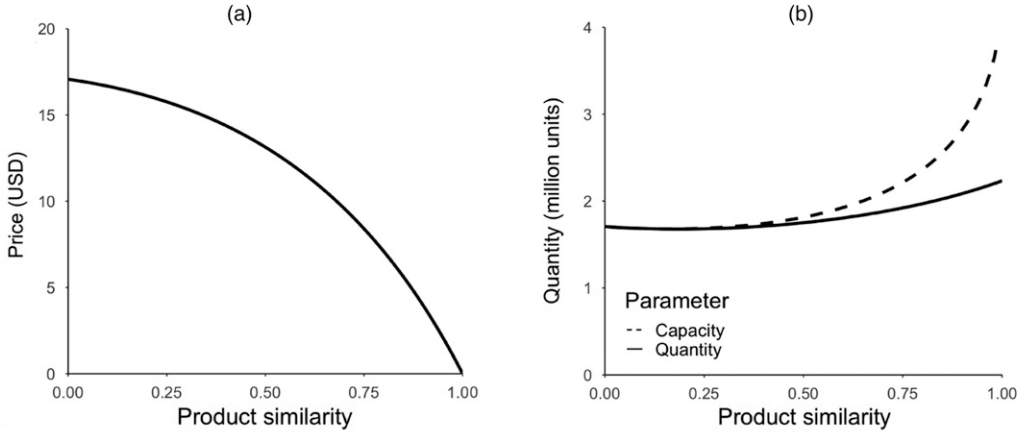
We compare true 2018 contract and private-sector prices to our model's predictions. We then perform broader sensitivity analysis to characterize a stable market in the special case of the DTaP duopoly. Finally, we leverage insights from our market validation and sensitivity analysis to make policy recommendations, whose value we attempt to quantify.

3.2.1. Pricing Validation. To validate our model, we compare predicted 2018 prices and quantities to their realized values. We refrain from using our parameter estimates to produce one definitive prediction to emphasize that our model is intended for analytic insights rather than direct decision support. Instead, we retrieve an approximate distribution of public-sector prices as follows.

We construct a joint distribution over the parameters by first assuming that all parameters within a sample are independent and then by fixing μ and ρ at their base values in Table 2. We assume that the remaining parameters each have triangular marginal distributions, whose modes and ranges are defined by the base values and sensitivity analysis ranges in Table 2. This distribution shape ensures that the most common draws are close to the base case and that all draws are within the feasible ranges that we have estimated. We solve the optimization model using 10,000 samples, 65% of which yielded feasible parameter combinations for the optimization model, and plot the results in Figure 3.

True 2018 contract prices for Infanrix and Daptacel were, respectively, $18.19 and $17.61, with private-sector prices of $24.05 and $30.00 (U.S. Centers for Disease Control and Prevention 2018b). Our model predicts $15.76 as both manufacturers' private-sector prices; we defer to Behzad and Jacobson (2016) for

Figure 2. Private-Sector Parameters vs. Product Similarity (γ)



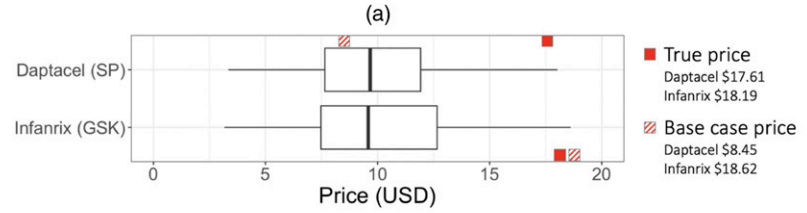
Private sector prices p_i^{priv} vs. γ. Maximum private sector price is \$17.10.

Private sector quantities q_i^{priv} and minimum private sector capacities U vs. γ.

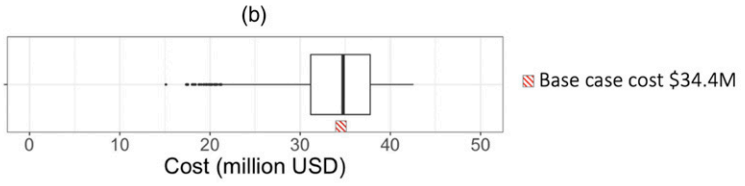
further discussion of this estimate. Figure 3(a) displays our model's public-sector price predictions. For the base case, we predict \$18.62 for Infanrix and \$8.45 for Daptacel. The majority of both manufacturers' price ranges are close in the order of magnitude to true public-sector prices.

Our predicted prices are lower than true prices, which is a similar outcome as in Behzad et al. (2015) and Behzad and Jacobson (2016). One contributing factor is that we have characterized the CDC as a multiobjective agency, with only one of its objectives being public-sector cost minimization. Furthermore, our

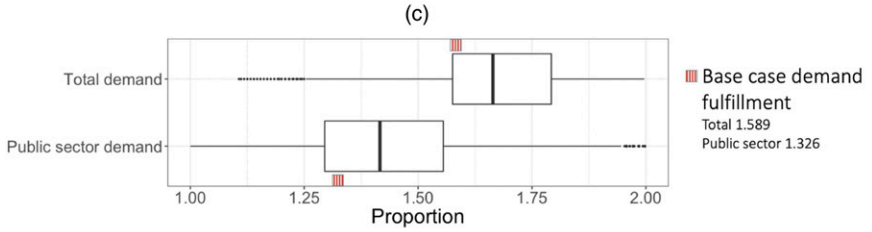
Figure 3. (Color online) Predicted Public-Sector Prices, Government Spending, and Demand Fulfillment for Market Validation Test Suite



Public sector prices. Median price of \$9.59 for Infanrix and \$9.67 for Daptacel.



Total CDC spending.



Proportion of demand fulfilled in total and in the public sector.

Note. 65% of test cases were feasible.

model assumes no *tacit collusion*, a cooperative strategy in which firms seek higher profits than Bertrand behavior permits by setting higher prices until an opposing firm undercuts (Robbins et al. 2014). We refer the reader to the work of Robbins et al. (2014) for a pricing model that assumes tacit collusion. In conclusion, we verify the validity of the model's outputs as we make conclusions about the market.

Panels (b) and (c) of Figure 3 depict distributions of CDC spending and demand fulfillment predictions. Our estimates of CDC spending are on the same order of magnitude that one would expect, given the size of the annual vaccine cohort and the typical order of magnitude of public-sector prices. Furthermore, the range of projected demand fulfillment is reasonable: it is always sufficient (as required by the model), and it never exceeds double the demand. It is appropriate that demand fulfillment is always slightly higher than necessary in our results, given that our demand-estimation method yields a lower bound on true demand. We also note that the distribution demonstrates that the CDC can benefit from purchasing in excess of demand, both to lower costs and to ensure market viability.[1]

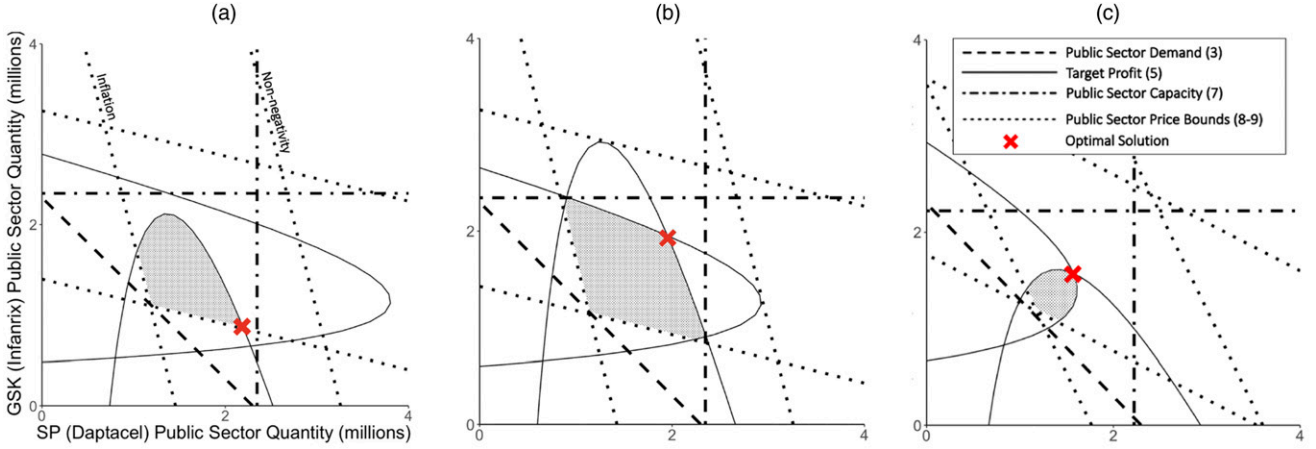
3.2.2. Market-Stability Analysis. We first explore a duopoly's risk of becoming a monopoly by developing geometric intuition of our optimization model. By replacing p_i^{pub} everywhere in the model with the inverse demand curve in Equation (11), we can visualize the feasible region in terms of q_i^{pub}. It can be shown algebraically from Equations (21) and (22) that $U \geq q_i^{\text{priv}}$ for $\gamma \in (0,1)$. We therefore omit public capacity constraint (6) and depict only public capacity constraint (7) in visualizations of the feasible region.

Figure 4(a) depicts the feasible region of the base case scenario from Section 3.2.1. Panels (b) and (c) of Figure 4 show two symmetric scenarios that differ only in their product similarity values. For less similar products (lower γ), we see that the feasible region widens to encompass more scenarios in which one manufacturer can *dominate* or produce significantly more vaccines than the other. Although not reflected in the plot, the large quantity difference triggers a large public-sector price difference via the linear demand curve. This strong consumer preference is not viable when vaccines are very similar. Figure 4 serves as a visual aid as we vary parameter values in the ensuing sensitivity analysis.

A market is *stable*, or at lowest risk of becoming a monopoly, if manufacturers are able to comfortably break even and meet demand without having to produce vaccines at capacity. To characterize an unstable market, we endeavor to identify scenarios in which the CDC spends more than the manufacturers require to stay in business, the CDC purchases more vaccines than the market demands, or manufacturers produce at capacity.

Infeasibility of the model sufficiently indicates a transition into a shortage scenario or the development of a monopoly, but it is not the only way to evaluate instability. We present a metric to approximately

Figure 4. (Color online) Feasible Regions of Selected DTaP Market Scenarios, Depicting All Optimal and Stable Solutions



Base case from Table 2.

Symmetric scenario based on net manufacturer values in base case from Table 2. Product similarity $\gamma = 0.25$.

Symmetric scenario identical to 7b, except with higher product similarity ($\gamma = 0.5$).

evaluate the stability of a feasible market instance. When the model is feasible, the CDC will always spend at least C^* in Equation (23), where C^* is the sum of the manufacturers' residual target profits and is the minimum amount that the CDC can hope to spend while satisfying all constraints:

$$C^* = \sum_{i \in M} \left(P_i - p_i^{\text{priv}} q_i^{\text{priv}} \right). \tag{23}$$

We interpret the result of our model's objective function to be the minimum amount that the CDC spends to achieve their goals. The optimization model therefore approximates the minimum public-sector cost of a market that fulfills every CDC goal, given the input market parameters. If this minimum cost exceeds C^*, then there must be a strain on the market. We therefore define $R \in [0, 1]$ in Equation (24) as our metric to evaluate the stability of a feasible scenario:

$$R = C^* \left(\sum_{i \in M} q_i^{\text{pub}} \cdot p_i^{\text{pub}} \right)^{-1}. \tag{24}$$

Stability increases with R. Note that $R = 1$ when it is feasible for both manufacturers to earn their exact target profits, which occurs when demand is low enough and capacities are high enough for an intersection of the manufacturers' target profit thresholds to be feasible.

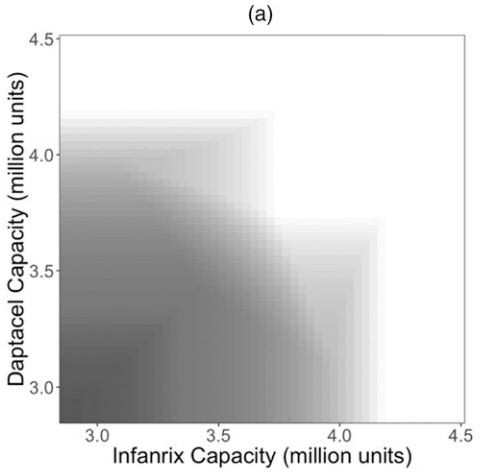
We demonstrate the utility of our stability metric by computing R for the three scenarios in Figure 4. In Figure 4(a), we compute $R = 0.929$ and observe that R is high because the optimal solution is geometrically very close to an intersection of the target profit constraints, where $R = 1$. The high value of R intuitively makes sense because neither manufacturer is supplying as much as they can produce, and demand is comfortably met, but $R < 1$ because of the artificial strain that the inflation-bound policy imposes on the market. In Figure 4, (b) and (c), we compute $R = 1$, which is geometrically due to at least one intersection of the target profit constraints being feasible and intuitively due to an absence of a strain on the market.

We list market traits that contribute to stability according to our sensitivity analysis.

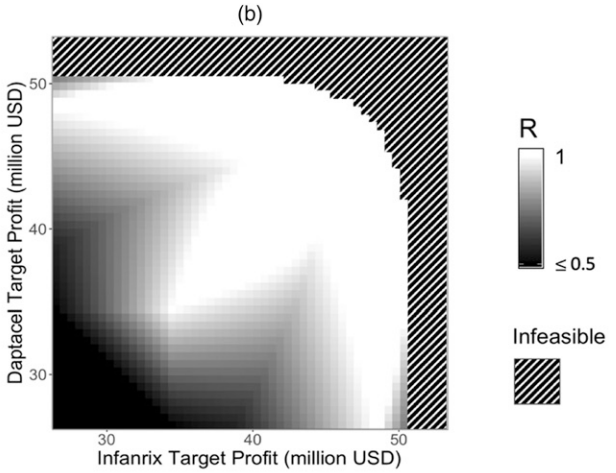
High Capacities. The market is more likely to be stable when manufacturers have high production capacities. Figure 5(a) provides a heat map of the stability metric, R, as it depends on the manufacturers' production capacities. The small values of R when one manufacturer's capacity is relatively low indicate that each manufacturer produces at full capacity unless its capacity is moderately high. When products are dissimilar, it is still possible to see market stability when one manufacturer has lower capacity if its competitor has very high capacity. This domination is not possible when products are very similar, which one can visualize by comparing the stable solutions in Figure 4, (b) and (c).

Moderate Target Profits. Figure 5(b) provides a heat map of the stability metric, R, as it depends on target profits. When the target profits are small, R is close to

Figure 5. Sensitivity of Market Stability to Manufacturer Parameters, with Demand $D = 4.034M$ and Product Similarity $\gamma = 0.25$



Market stability R vs. $(K_{\text{Inf}}, K_{\text{Dap}})$ with target profits $P_i = \$42.45M$.



Market stability R vs. $(P_{\text{Inf}}, P_{\text{Dap}})$ with capacities $K_i = 4.034M$.

zero because the quantities purchased by the CDC allow the target profits to be easily exceeded. Conversely, the outer border of infeasibility indicates that very large target profits destabilize the market. As the target profits decrease to more moderate levels, Figure 4(b) shows that the feasible region will expand and the optimal solution will move further away until it hits the upper capacity, causing R to increase as well.

Low Demand. High demand raises the minimum cost of an asymmetric public market and catalyzes a deficit of vaccines. Figure 6 depicts two series of line plots that show how R varies with demand and manufacturer asymmetry. Both plots show that $R = 1$ for lower values of demand and capacity difference. In Figure 6(a), we observe that the market destabilizes as both demand and the asymmetry in capacity increase, as indicated by decreasing values of R followed by infeasibility. In particular, we observe that asymmetric capacities can be stable as long as demand is low. However, increasing demand strains the manufacturer with the smaller capacity, leading to instability.

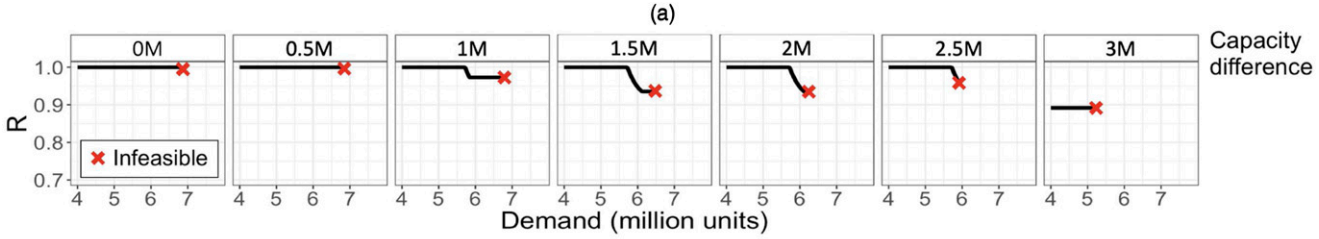
Figure 6(b) shows that R decreases with higher target profit imbalance, confirming that the manufacturer with the higher target profit cannot recover its debt unless the CDC negotiates a price at which it is unable to meet public-sector demand. Therefore, higher demand causes infeasibility for lower target profit differences. We observe that increasing demand amplifies this effect.

High-Capacity Manufacturer with Low Target Profit. Figure 6 hints that high demand increases market risk in an asymmetric market. To make this observation explicit, Figure 7 shows heat maps depicting how stability varies with both types of manufacturer asymmetry, for two different demand levels. These plots show that lower R values and infeasibility occur with scenarios in which the manufacturer with the higher capacity has the higher target profit (appearing in the upper-right region of Figure 7(a)). By contrast, when a high-capacity manufacturer has lower target profits, it is more financially capable of producing enough vaccines to cover the portion of demand that its competitor cannot fulfill. By comparing Figure 7, (a) and (b), we observe that higher demand corresponds with lower stability overall and a smaller set of feasible asymmetries. That is, even slightly higher demand exacerbates the negative impact of manufacturer asymmetry on market stability.

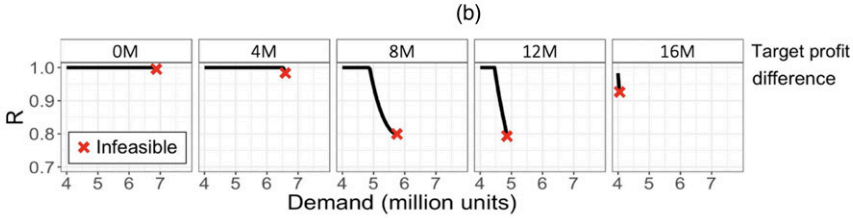
3.3. Deficiency Scenario Analysis

In 2012, Sanofi-Pasteur experienced a year-long shortage of Daptacel, and shortages of other vaccines also occur with some regularity. For instance, at the time of this writing, Merck is experiencing a shortage of its Hepatitis B monovalent vaccine (U.S. Centers for Disease Control and Prevention 2019). Generally, when a shortage occurs, the CDC takes no action to renegotiate the contract; negotiated prices pre- and postshortage are very similar to each other (U.S. Centers

Figure 6. (Color online) Sensitivity of Market Stability to Demand and Asymmetry, with $\gamma = 0.25$



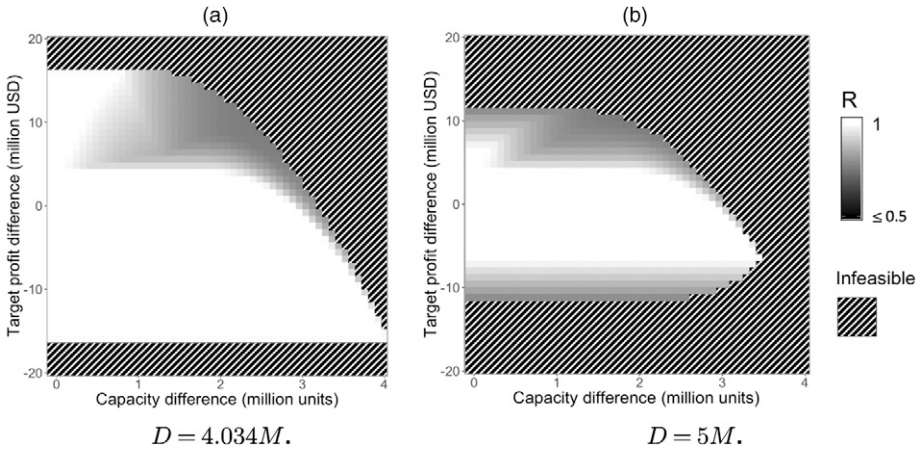
Market stability R vs. demand D and capacity difference $K_i - K_j$. Target profits $P_{\text{Inf}} = P_{\text{Dap}} = \$42.45M$ and net capacity $2 \cdot 4.034M$. Higher capacity differences were infeasible.



Market stability R vs. demand D and target profit difference $P_i - P_j$. Capacities $K_{\text{Inf}} = K_{\text{Dap}} = 4.034M$. Higher target profit differences were infeasible.

Note. M, million.

Figure 7. Sensitivity of Market Stability to Target Profit Asymmetry, Capacity Asymmetry, and Demand, with $\gamma = 0.25$, Net Profit \$84.9*M*, and Net Capacity 8.038*M*



Note. M, million.

for Disease Control and Prevention 2012). In the event of a shortage, the CDC will have two concerns: (1) ensuring that the public-sector demand is met so that all children can be vaccinated on schedule and (2) ensuring the stability of the duopoly. We evaluate strategies that the CDC might use to address a vaccine shortage in support of these two objectives.

In a true shortage, there is insufficient supply of the vaccine to meet total demand, and our private-sector equilibria would no longer be valid. As such a case is outside the scope of the model, we examine instead a *deficiency* scenario. We define a *deficiency* to occur when the production capacity of one manufacturer $i \in M$ decreases below the threshold necessary to produce both the public-sector contracted quantity and the private-sector equilibrium quantity, but for which the optimization model shown in Equations (1)–(9) is still feasible. That is, total demand in the private and public sectors can still be met overall, but doing so will require adjusting the quantities purchased from each manufacturer. We refer to the manufacturer experiencing the deficiency as the *limited manufacturer* and the manufacturer not experiencing the deficiency as the *nonlimited manufacturer*. Thus, letting K_{lim} (resp., $K_{\text{non-lim}}$) and q^s_{lim} (resp., $q^s_{\text{non-lim}}$) be the original capacity and optimal quantities in each sector s for the base scenario for the limited (resp., nonlimited) manufacturer, and letting $K^{\text{def}}_{\text{lim}}$ be the updated capacity of the limited manufacturer in the event of the deficiency, we consider cases where $K^{\text{def}}_{\text{lim}} < q^{\text{priv}}_{\text{lim}} + q^{\text{pub}}_{\text{lim}}$.

We simulate a year-long deficiency scenario and compare two strategies:

1. *Naive.* In this strategy, we assume that the CDC will use the original model's contracted prices (which assumed full capacity) and will adjust the contracted quantity of the nonlimited manufacturer to absorb the unmet contracted quantity of the limited manufacturer. That is, the CDC will purchase the remaining public-sector capacity, $K^{\text{def}}_{\text{lim}} - q^{\text{priv}}_{\text{lim}}$, from the limited manufacturer at the predeficiency contract prices. From the nonlimited manufacturer, the CDC will purchase the original contracted quantity of vaccines plus any deficient vaccines needed to fulfill the total original contracted quantity of the limited manufacturer. This is given by $q^{\text{pub}}_{\text{non-lim}} + q^{\text{pub}}_{\text{lim}} - (K^{\text{def}}_{\text{lim}} - q^{\text{priv}}_{\text{lim}})$.

2. *Updated contract.* In this strategy, we assume that the CDC will use the optimization model, Equations (1)–(9) to renegotiate prices and quantities for both manufacturers using the modified capacity for the limited manufacturer.

In both strategies, we assume that the CDC cannot influence manufacturers' decisions in the private sector and that total demand can be met throughout the deficiency without resorting to other polyvalent markets. Our results reveal the extent to which the CDC's deficiency-mitigation strategies can stay contained within the specific market experiencing the deficiency.

Using the DTaP market in the 2018 contract year as a case study, we consider first a deficiency of Daptacel and then a deficiency of Infanrix. We use base parameter values as in Table 2 for all parameters except the limited manufacturer's capacity. We test a range of deficient quantities and find the largest deficiency that the market can feasibly accommodate.

For the case of the Daptacel deficiency, the largest feasible deficiency is 1.158 million doses, which occurs when Sanofi-Pasteur's total capacity for Daptacel drops to 2.725 million doses. Table 4 compares CDC costs and Daptacel profit as a percentage of target profit for the no-deficiency base scenario and for the deficiency scenario using each of the two mitigation strategies. We see that total CDC costs are 13% higher under the naive strategy than under the updated contract

Table 4. Public-Sector Quantities and Prices Resulting from a Deficiency in Daptacel Supply as Compared with the No-Deficiency Scenario Analyzed in Section 3.2, Comparing the Naive Mitigation Strategy to the Optimization-Based Updated Contract-Mitigation Strategy

	Daptacel			Infanrix public sector		Daptacel public sector			
Deficiency scenario	Capacity (K_{Dap})	Deficiency	Strategy	Price	Quantity	Price	Quantity	CDC cost	Target profit (Daptacel)
No deficiency	4.034M	0	—	\$18.62	0.847M	\$8.45	2.202M	\$34,374M	100.0%
Deficiency	2.725M	1.158M	Naive	\$18.62	2.004M	\$8.45	1.044M	\$46.136M	78.3%
			Updated contract	\$12.91	1.709M	\$17.94	1.038M	\$40.676M	100.0%

Note. M, million.

strategy. Moreover, Daptacel can achieve only 78.3% of its target profits under the naive strategy, suggesting that the market could be at risk for becoming a monopoly. Under the updated contract strategy, prices for both Infanrix and Daptacel adjust so that both manufacturers' target profits are met at 100%.

Figure 8 illustrates the relative performance of our model in updating the contract prices and quantities versus using the naive strategy as a function of the size of the production deficiency. The plot on the left displays total CDC costs as a function of number of deficient doses under both the naive and updated contract-mitigation strategies. We see that the updated contract strategy consistently costs less than the naive strategy, except for very small deficiencies. The plot on the right shows the percentage of target profit attained by Daptacel as a function of the deficiency in Daptacel. We see that using the updated contract strategy allows the deficient manufacturer to maintain 100% of its target profit; under the naive strategy, Daptacel's profit erodes as the deficiency grows. (Under both strategies, Infanrix target profits remain at or above 100%.)

When we instead model the Infanrix deficiency, however, we find that the market cannot support any positive deficiency in Infanrix production. To understand why this is the case, we refer to Figure 9, showing the feasible regions for the base case (Figure 9(a)), the case of the lowest Daptacel capacity without deficiency (Figure 9(b)), and the case of the lowest Infanrix capacity without deficiency (Figure 9(c)). Observe that the feasible region remains the same as the base case in Figure 9(b) but is reduced to a single point in Figure 9(c). As deficiency grows, the public-sector capacity constraints move inward. If the capacity to produce Infanrix drops below $q_{\text{Inf}}^{\text{pub}} + U$, then the model is immediately infeasible. If the model were to become infeasible, then the CDC would need to fulfill deficient demand with vaccines from polyvalent markets, which is beyond the scope of this paper.

The different outcomes for Daptacel and Infanrix demonstrate the utility of an optimization-based approach to addressing a deficiency. Even within the same market, deficiencies from different manufacturers may require different repricing strategies to stabilize the market. Moreover, by neglecting to reprice public-sector vaccines during a deficiency, the CDC passes over an opportunity to ensure that the deficient manufacturer stays profitable enough to remain in the market, while also reducing total costs. The repricing strategy is less expensive and helps mitigate against the formation of a monopoly, in which the CDC would lose much of its negotiation power.

Figure 8. CDC Costs and Percentage of Daptacel Target Profits Attained Under the Naive and Updated Contract-Mitigation Strategies, as a Function of Daptacel Deficiency Amount

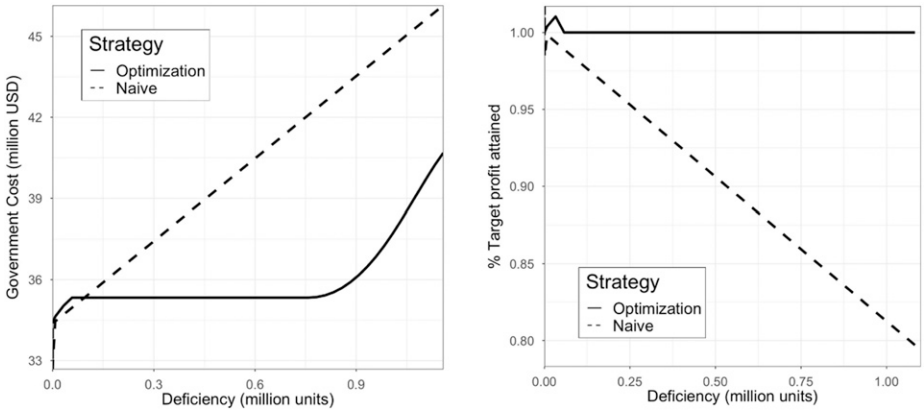
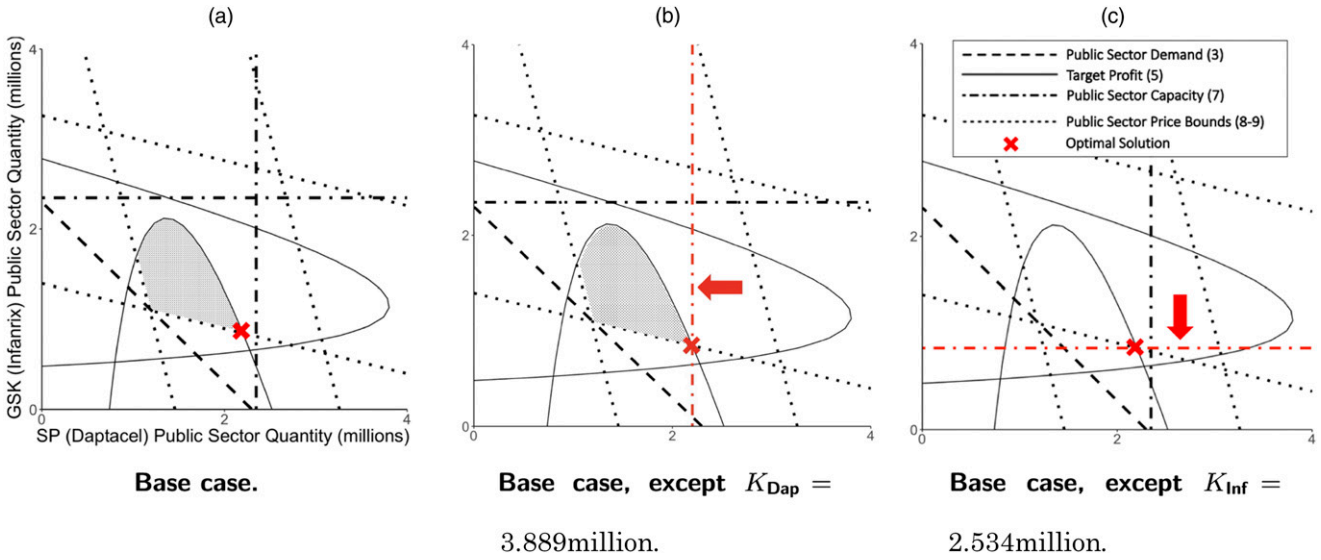


Figure 9. (Color online) Comparison of Feasible Regions for Scenarios Corresponding to the Lowest Capacities Yielding No Deficiency, with the Base Case Scenario from Table 2



Note. Arrows indicate the altered production capacity constraints in each deficiency scenario.

4. Limitations and Future Work

One limitation of our work is that we isolate one market for a single antigen. A reasonable assumption is that the CDC accounts for how one market's contract will impact the performance of other vaccine markets that are linked by the same antigens or manufacturers. Thus, U.S. pediatric vaccine market performance is a function of demand structures that overlap across different vaccines and their brands, which is a more intricate mechanism than our model portrays. Future work could investigate competition between manufacturers producing monovalent and combination vaccines covering a self-contained and exhaustive set of antigens. Such research would yield insight into how CDC contracts are impacted by more intricate demand structures. This approach can also broaden the portfolio of deficiency mitigation strategies available to the CDC.

Additionally, the U.S. pediatric vaccine market is a major actor within the global vaccine market, which exhibits dynamics that our model simplifies on a broader scale. In particular, PAHO and GAVI both negotiate vaccine prices on behalf of many countries (via UNICEF). A next step is to model PAHO in the South American vaccine market and GAVI and UNICEF in the market for developing countries as strategic agents in their respective markets, similarly to how we have characterized the CDC in the U.S. market.

Despite these limitations, our work develops intuition for analysis of larger, more complex markets. Our model also provides the foundation for a model that can be wrapped in a user-friendly software tool for decision makers.

5. Summary and Recommendations

When a monopoly develops, pediatric vaccine prices can be driven arbitrarily high. The CDC's significant patronage of pediatric vaccines affords them considerable influence in the price-negotiation process, which uniquely positions the CDC toward the prevention of monopolies. Our pricing model of a monovalent pediatric vaccine duopoly encodes the CDC's goals of ensuring that all U.S. children are vaccinated and that vaccine manufacturers do not leave the market, all at minimum cost to the government. This study contributes to existing work by directly incorporating the CDC as a decision-making and rational agent and by modeling dynamics in both public and private sectors.

We validated our model through an extended case study of the Infanrix–Daptacel duopoly. First, we predicted prices and public-sector costs for the 2018 contract year and confirmed that our model is viable. We then defined a stable market to be one in which the CDC can achieve all goals with minimal strain on manufacturer resources. We next performed sensitivity analysis on government costs to characterize a stable market.

Some of the findings are quite intuitive and serve as validation that the model realistically captures market behavior: (1) low demand puts less strain on manufacturers' resources; (2) manufacturers are at lowest risk of leaving the market when they have high capacities and moderate target profits; and (3) highly differentiated products advantageously segment the market. Additionally, our model shows that a high-demand market with asymmetric manufacturers is at highest risk when the manufacturer with higher capacity also has a high target profit.

We also illustrated how our model can assist the CDC in renegotiating contract prices and quantities in the event of one manufacturer falling short of its contracted amount.

This work extends to other monovalent pediatric vaccine duopolies in the United States and other international markets having both a private and a public sector. In the United States, Hepatitis B and Hib are the only two other monovalent pediatric vaccines, of which the Hepatitis B market is a duopoly while the Hib market is a triopoly. This analysis can be replicated in—and generalized to—the Hepatitis B market, but we omit this analysis for clarity of exposition. It is possible to price Hib vaccines in the style that we have outlined, because the private-sector surplus pricing strategy remains the same for a triopoly (Behzad and Jacobson 2016). However, the same notion of stability does not naturally extend to a triopoly, because of the relatively lower risk of monopoly development. The remaining combination vaccines in the U.S. market are better characterized using other methods, which yields an interesting avenue for future work.

We offer the following recommendations from our results.

1. *Financial incentives*. When the CDC enters negotiation in a high-demand market with manufacturers who have highly asymmetric capacities or target profits, financial incentives may be necessary to fulfill market demand. Even though there is no subsidy for vaccines in the United States, the CDC can agree to pay more per dose to vaccine manufacturers to maintain a high national immunization level. Coleman et al. (2005) and the Institute of Medicine (U.S.) Committee on the Evaluation of Vaccine Purchase Financing in the United States (2003) justify the need for financial incentives for the vaccine manufacturers. The need for financial incentives is greatest when the high-capacity manufacturer has a high target profit. A bonus to the manufacturer with larger capacity may help them fill the demand gap left by their competitor without going into debt. However, perhaps this bonus should go to the low-capacity manufacturer to provide incentive to stay in the market. This infusion of extra money into a duopoly market can be interpreted as the price that the CDC pays to prevent a monopoly, whose costs can become much harder to manage in the long term.

2. *Product differentiation*. We observe that the market is more likely to flourish when consumers have more differentiated products to choose from. Although factors like side effects are relatively immutable, manufacturers can control packaging, administration method, and branding, preventing the public from viewing one vaccine as an "off-brand" of the other. If a manufacturer is considering encroaching upon a market for a monopolized antigen, then the CDC might encourage the manufacturer to distinguish its vaccine in as many ways as possible from its competitor's vaccine.

3. *Ongoing negotiations*. When a shortage occurs in the middle of a contract season, manufacturers currently must continue to sell public-sector vaccines at contract price. Our stability analysis shows that asymmetric and low production capacities destabilize the market, and our deficiency scenario analysis demonstrates that the CDC can restabilize the market and reduce costs through revised contracts. An interesting insight is that, for a fixed deficiency, the strategy for revising the contract can depend on which manufacturer experiences the shortage. Thus, a paradigm shift from annual price contracts to ongoing negotiations may allow the CDC to exercise more control over the market in shortage situations.

These results demonstrate that merging the public and private sectors into a single optimization framework more realistically captures the characteristics of a vaccine duopoly and provides valuable insights for the CDC to use in its negotiations.

Acknowledgments

The authors thank the two anonymous reviewers for their thorough comments, which greatly improved the quality of the manuscript. A preliminary version of this work was published as the first author's undergraduate senior thesis (Cummings 2018).

Endnote

[1] The national pediatric vaccine stockpile system is in charge of supplying the vaccines purchased from the vaccine manufacturers. This system has the objective of providing a sufficient supply of all recommended vaccines to meet the demand in case of any shortage (Lane et al. 2006). Manufacturers are in charge of managing the vaccine inventory, from where the oldest doses are shipped to public buyers, and these orders are restocked with newer doses. As part of the financial incentives in place, the holding cost for this inventory system is not reflected as a cost for the manufacturers. Any vaccine surpluses are usually sold internationally to the Pan American Health Organization (PAHO) and the Global Alliance for Vaccines and Immunization (GAVI), via the United Nations Children's Fund (UNICEF) (Proaño 2019).

References

Behzad B, Jacobson S (2016) Asymmetric Bertrand-Edgeworth-Chamberlin competition with linear demand: A pediatric vaccine pricing model. *Service Sci.* 8(1):71–84.

Behzad B, Jacobson S, Robbins M (2015) A symmetric capacity-constrained differentiated oligopoly model for the United States pediatric vaccine market with linear demand. *IIE Trans.* 47(11): 1252–1266.

Bertrand J (1883) Review of "Théorie mathématique de la richesse sociale" by Leon Walras and "Recherches sur les principes mathématiques de la théorie des richesses" by Augustin Cournot. *J. des Savants* 67:499–508.

Chamberlin E (1933) *The Theory of Monopolistic Competition* (Harvard University Press, Cambridge, MA).

Coleman M, Sangrujee N, Zhou F, Chu S (2005) Factors affecting U.S. manufacturers' decisions to produce vaccines. *Health Affairs* 24(3): 635–642.

Cournot A (1838) *Recherches sur les principes mathématiques de la théorie des richesses* (L. Hachette, Paris).

Cummings K (2018) Operations research to incorporate government influence in vaccine pricing models. Unpublished senior thesis, Pomona College, Claremont, CA.

Edgeworth F (1925) The pure theory of monopoly. *Papers Relating to Political Econom.* 1:111–142.

Institute of Medicine (U.S.) Committee on the Evaluation of Vaccine Purchase Financing in the United States (2003) Financing vaccines in the 21st Century: Assuring access and availability. Report, Institute of Medicine, Washington, DC.

Jacobson SH (2012) Vaccine pricing: How can we get it right? *Expert Rev. Vaccines* 11(10):1163–1165.

Lane KS, Chu SY, Santoli JM (2006) The United States pediatric vaccine stockpile program. *Clinical Infectious Diseases* 42(Supplement 3): S125–S129.

Lauera K, Borrowa R, Blanchard T (2017) Multivalent and multipathogen viral vector vaccines. *Clinical Vaccine Immunology* 24(1):1–15.

Lunday B, Robbins MJ (2016) Informing pediatric vaccine procurement policy via the pediatric formulary design, pricing, and production problem. *IIE Trans.* 48(12):1112–1126.

Orenstein W, Douglas G, Rodewald L, Hinman A (2005) Immunizations in the United States: Success, structure, and stress. *Health Affairs* 24(3):599–610.

Proaño R (2019) Private communication, January 8, 2019.

Robbins MJ, Jacobson SH (2015) Analytics for vaccine economics and pricing: Insights and observations. *Expert Rev. Vaccines* 14(4):605–616.

Robbins MJ, Lunday BJ (2016) A bilevel formulation of the pediatric vaccine pricing problem. *Eur. J. Oper. Res.* 248(2):634–645.

Robbins M, Jacobson S, Sewell E (2010) Pricing strategies for combination pediatric vaccines and their impact on revenue: Pediarix or Pentacel? *Health Care Management Sci.* 13(1):54–64.

Robbins M, Jacobson S, Shanbhag U, Behzad B (2014) The weighted set covering game: A vaccine pricing model for pediatric immunization. *INFORMS J. Comput.* 26(1):183–198.

Sinclair D (2017) Incorporating the Centers for Disease Control and Prevention into vaccine pricing models. Unpublished senior thesis, Harvey Mudd College, Claremont, CA.

Tirole J (1988) *The Theory of Industrial Organization* (MIT Press, Cambridge, MA).

U.S. Centers for Disease Control and Prevention (2012) Archived CDC vaccine price list as of November 1, 2012. Retrieved September 19, 2019, https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/2012/2012-11-01.html.

U.S. Centers for Disease Control and Prevention (2016) VFC program distribution of pediatric vaccines. Retrieved April 3, 2019, https://www.cdc.gov/vaccines/programs/vfc/about/distribution.html.

U.S. Centers for Disease Control and Prevention (2017) Combination vaccines. Retrieved June 9, 2018, https://www.cdc.gov/vaccines/hcp/conversations/downloads/fs-combo-vac.pdf.

U.S. Centers for Disease Control and Prevention (2018a) VFC CDC vaccine price list archives. Retrieved March 3, 2018, https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/archive.html.

U.S. Centers for Disease Control and Prevention (2018b) Archived CDC vaccine price list as of December 3, 2018. Retrieved August 29, 2019, https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/2018/2018-12-03.html.

U.S. Centers for Disease Control and Prevention (2019) Current vaccine shortages and delays. Retrieved January 28, 2020, https://www.cdc.gov/vaccines/hcp/clinical-resources/shortages.html.

U.S. Food and Drug Administration (2018) CBER-regulated products: Resolved shortages. Retrieved June 22, 2018, https://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/Shortages/ucm351943.htm.