The Application of Game Theory in Analyzing Public Health Issues

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Sharif University of Technology
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Research Summary

Issues in Public Health
- Adults
- Children

Empirical Analysis
- Behzad et al. (2013)
- Behzad et al. (2014)

Integer Programming
- Behzad et al. (2012)
- Behzad et al. (2014)

Game Theory
- Behzad et al. (2013)
- Behzad et al. (2015)
- Behzad et al. (2016)

Social Network Analysis
- Social Media vs. Traditional

Winter Seminar Series Sharif University of Technology

Figures:
- http://www.mcavoy.com/a_ts_obesity.html
- http://www.freewebs.com/mercurybabies
What is Game Theory?

- The branch of mathematics concerned with
  - the analysis of strategies for dealing with competitive situations
  - where the outcome of a participant’s choice of action depends critically on the actions of other participants.
- What economists call game theory psychologists call the theory of social situations.
Immunization

- Immunization against infectious diseases: single factor that has had the greatest impact on world health (Plotkin and Orenstein, 2004)
- Much work remains to be done.
  - In 1998, over 20% of worldwide deaths were attributable to infectious diseases.
  - Measles accounted for 8% of these deaths.
  - Emergence of new infectious diseases creates new challenges.
Centers for Disease Control and Prevention (CDC)

- Primary public health organization in the United States
- Responsible for management of the Recommended Childhood Immunization Schedule (RCIS) *(Source: CDC)*

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Birth</th>
<th>1 mo</th>
<th>2 mos</th>
<th>4 mos</th>
<th>6 mos</th>
<th>9 mos</th>
<th>12 mos</th>
<th>15 mos</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis B</strong> <em>(HepB)</em></td>
<td>1st dose</td>
<td>←2nd ‚dose→</td>
<td></td>
<td></td>
<td></td>
<td>←3rd ‚dose→</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Rotavirus</strong> <em>(RV)</em></td>
<td>1st dose</td>
<td>2nd dose</td>
<td>3rd dose</td>
<td></td>
<td></td>
<td>←4th ‚dose→</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV1 (2-dose series); RV5 (3-dose series)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diphtheria, tetanus, &amp; acellular pertussis</strong> <em>(DTaP; &lt;7 yrs)</em></td>
<td>1st dose</td>
<td>2nd dose</td>
<td>3rd dose</td>
<td></td>
<td></td>
<td>←4th ‚dose→</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Haemophilus influenzae type b</strong> <em>(Hib)</em></td>
<td>1st dose</td>
<td>2nd dose</td>
<td>See footnote 2</td>
<td></td>
<td></td>
<td>←3rd or 4th ‚dose, See footnote 4</td>
<td>←4th ‚dose→</td>
<td></td>
</tr>
<tr>
<td><strong>Pneumococcal conjugate</strong> <em>(PCV13)</em></td>
<td>1st dose</td>
<td>2nd dose</td>
<td>3rd dose</td>
<td></td>
<td></td>
<td>←4th ‚dose→</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Inactivated poliovirus</strong> <em>(IPV; &lt;18 yrs)</em></td>
<td>1st dose</td>
<td>2nd dose</td>
<td></td>
<td>←3rd ‚dose→</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The Problem

- Infanrix®(DTaP)
- ENGERIX®(HepB)
- Hiberix®(Hib)
- Pediarix®(DTaP-HepB-IPV)
- RECOMBIVAX HB®(HepB)
- PedvaxHIB®(Hib)
- Tripedia®(DTaP)
- ActHIB®(Hib)
- Pentacel®(DTaP-IPV-Hib)
Public Sector

Series of negotiations between the CDC and the vaccine manufacturers:

- State and local public health departments
- Public sector: 57% of the total pediatric purchases by volume in the United States (Vaccines for Children (VFC) Program)
- Limited profits and high research and development costs for manufacturers
- Six vaccine manufacturers in 2010 vs. 35 in 1970
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The Role of CDC

- Negotiate the vaccine prices with vaccine manufacturers
- Provide financial incentives for vaccine manufacturers to stay in the market
Motivation

A small number of pharmaceutical companies:
  • Manufacturing vaccines which are competing with each other
  • Seeking higher profits

CDC:
  • Seeks awareness on vaccine prices when preparing for series of negotiations

Question

Can game theory be used to better understand pediatric vaccine pricing in the United States?
Objectives

• Determine the equilibrium price of each vaccine in the public sector.
• Gain awareness about vaccine equilibrium prices in future years.
Nash Equilibrium

A stable state of a system involving the interaction of different players, in which no player can gain by a unilateral change of strategy if the strategies of the others remain unchanged.
Pure and Mixed Strategy Nash Equilibrium

- Pure strategy Nash equilibrium: provides a complete definition of how a player will play a game.
Pure and Mixed Strategy Nash Equilibrium

• Pure strategy Nash equilibrium: provides a complete definition of how a player will play a game.
• Mixed strategy Nash equilibrium: is an assignment of a probability to each pure strategy.
Bertrand Framework

- A pricing game
- Nash equilibrium occurs when each firm selects a price level which maximizes their profits, given the price level chosen by the other firms.

Main Assumptions:
- Each firm can entirely meet the market demand.
- Firms are not capacity-constrained.
- Firms' products are interchangeable.
- No product differentiation.
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  - No product differentiation

Is there a better model?
Bertrand-Edgeworth and Bertrand-Edgeworth-Chamberlin Competitions

**Bertrand-Edgeworth Competition:**
- Capacity-constrained firms compete on price.
- The first assumption of the Bertrand framework is relaxed.

**Bertrand-Edgeworth-Chamberlin Competition:**
- Capacity-constrained firms compete on price over the sale of differentiated products.
- The first and second assumptions of the Bertrand framework are relaxed.
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- Capacity-constrained firms compete on price over the sale of differentiated products.
  - The first and second assumptions of the Bertrand framework are relaxed.
Main Focus

Bertrand-Edgeworth-Chamberlin competition in which the price competition among asymmetric capacity-constrained sellers is studied.

- Asymmetric capacity-constrained sellers: sellers with unequal production capacity
- Nash equilibrium is the solution concept applied to study the formulated game.
Inverse and Direct Demands

\[ P_i(q) = \alpha - q_i - \gamma \sum_{j \neq i} q_j, \quad i = 1, 2, \ldots, n, \]

\[ P_i^{-1}(q) = a - bp_i + c \sum_{j \neq i} p_j = D_i(p), \quad i = 1, 2, \ldots, n \]

where \( a = \alpha / (1 + (n - 1)\gamma) \),
\( b = (1 + (n - 2)\gamma) / (1 + (n - 1)\gamma)(1 - \gamma) \),
\( c = \gamma / (1 + (n - 1)\gamma)(1 - \gamma) \).
Game Formulation

Inverse and Direct Demands

\[ P_i(q) = \alpha - q_i - \gamma \sum_{j \neq i} q_j, \quad i = 1, 2, \ldots, n, \]

\[ P_i^{-1}(q) = a - bp_i + c \sum_{j \neq i} p_j \equiv D_i(p), \quad i = 1, 2, \ldots, n \]

where

\[ a = \frac{\alpha}{1 + (n - 1)\gamma}, \]

\[ b = \frac{(1 + (n - 2)\gamma)}{(1 + (n - 1)\gamma)(1 - \gamma)}, \]

\[ c = \frac{\gamma}{(1 + (n - 1)\gamma)(1 - \gamma)}. \]

\[ \gamma \]

The degree of product differentiation, ranging from zero for independent products to one for perfect substitutes.

Manufacturer \( i \) is capacity-constrained with production capacity \( k_i \), \( i = 1, 2, \ldots, n \), where \( k_1 \geq k_2 \geq \cdots \geq k_n \), with the total production capacity of all manufacturers given by \( K \equiv k_1 + k_2 + \cdots + k_n \).
### Main Results

<table>
<thead>
<tr>
<th>Result 1</th>
<th>The pure strategy equilibrium exists if the production capacity of a manufacturer is at their extreme.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result 2</td>
<td>For the capacity regions where no pure strategy equilibrium exists, there exists a mixed strategy equilibrium (characterized).</td>
</tr>
</tbody>
</table>
United States Pediatric Vaccine Market

• Pharmaceutical companies
  • Merck (MRK)
  • GlaxoSmithKline (GSK)
  • Sanofi Pasteur (SP)
• Focus of the study: Competitive vaccines:
  • DTaP
  • HepB
  • Hib
  • Pediarix and Pentacel
Analysis of Equilibria

Equilibrium Prices

Equilibrium prices are sought for the vaccines in the United States pediatric vaccine market based on the 2012 federal contract.

Four games:

- DTaP monovalent vaccines
- HepB monovalent vaccines
- Hib monovalent vaccines
- Pediarix and Pentacel combination vaccines
Demand of a Vaccine

2012 National Immunization Survey (NIS)

Vaccine coverage rates

Expected value of the number of vaccine doses given to each child

Birth cohort of 2012 (4M)

Volume of the total pediatric purchases in public sector (0.57)

Total demand of a vaccine in public sector
Demand Provided by the Public Sector

Table: Demand provided by the public sector

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Demand (public sector)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTaP monovalents</td>
<td>2.3M</td>
</tr>
<tr>
<td>HepB monovalents</td>
<td>5.1M</td>
</tr>
<tr>
<td>Hib monovalents</td>
<td>3.3M</td>
</tr>
<tr>
<td>DTaP-IPV-HIB (Pediarix)</td>
<td>4.5M</td>
</tr>
<tr>
<td>DTaP-HepB-IPV (Pentacel)</td>
<td>1.5M</td>
</tr>
</tbody>
</table>
Degree of Product Differentiation

2012 Vaccine Adverse Event Reporting System (VAERS)

Number of adverse events reported

2012 National Immunization Survey (NIS)

Number of vaccine doses administered

Reporting rate = Number of adverse events reported / Number of vaccine doses administered

Relative Reporting rate (among two or more vaccines) = Smallest vaccine reporting rate / Sum of the reporting rates for all the vaccines
<table>
<thead>
<tr>
<th>Vaccine Manufacturer</th>
<th>Total number of adverse events</th>
<th>Percentage of total vaccine doses administered</th>
<th>( \gamma )</th>
<th>Adjusted ( \gamma )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>( \Gamma_{DTaP} )</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DTaP (Infanrix)</td>
<td>310</td>
<td>(Infanrix, Daptacel)</td>
<td>0.06</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(90%,10%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(80%,20%)</td>
<td>0.13</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(70%,30%)</td>
<td>0.23</td>
<td>-</td>
</tr>
<tr>
<td>DTaP (Daptacel)</td>
<td>573</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>( \Gamma_{HepB} )</strong></td>
<td></td>
<td>(Engerix B, Recombivax HB)</td>
<td>0.76</td>
<td>-</td>
</tr>
<tr>
<td>HepB (Engerix B)</td>
<td>488</td>
<td>(Engerix B, Recombivax HB)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(50%,50%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HepB (Recombivax HB)</td>
<td>635</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>( \Gamma_{Hib} )</strong></td>
<td></td>
<td>(ActHIB, PedvaxHIB)</td>
<td>0.60</td>
<td></td>
</tr>
<tr>
<td>Hib (ActHIB)</td>
<td>419</td>
<td>(ActHIB, PedvaxHIB)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hib (PedvaxHIB)</td>
<td>298</td>
<td>(ActHIB, PedvaxHIB)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(70%,30%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>( \Gamma_{Ped-Pent} )</strong></td>
<td></td>
<td>(Piarix, Pentacel)</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>DTaP-HepB-IPV (Pediarix)</td>
<td>400</td>
<td>(Piarix, Pentacel)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DTaP-IPV/HIB (Pentacel)</td>
<td>744</td>
<td>(74%,26%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: The vaccine manufacturers are generally able to meet the entire market demand, and the broad game theoretic model of this study can capture any capacity constraint, which may cause the shortage of pediatric vaccines (see Section 4.3).
Capacity

- The exact value of the production capacity of vaccine manufacturers is unknown (confidential and proprietary)
Capacity

• The exact value of the production capacity of vaccine manufacturers is unknown (confidential and proprietary).

Assumption

Total production capacity of the vaccines in one instance of Gamma is 10% higher than the total market demand for those vaccines (Jacobson et al., 2006).

• The percentages for the number of vaccine doses administered multiplied by 1.1 of the total market demand then give the production capacity of each vaccine manufacturer.
The Analysis

Data
- Vaccine demand data
- Vaccine adverse events data
- Production capacity data
- Manufacturers data

Game Model
Using the main results

Output
Vaccine equilibrium prices
### Equilibrium prices

#### Table 4: Vaccine Equilibrium prices ($K = 1.1D(p)$)

<table>
<thead>
<tr>
<th>Degree of product differentiation</th>
<th>Infanrix</th>
<th>Daptacel</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\gamma$</td>
<td>Capacity</td>
<td>Equilibrium price</td>
</tr>
<tr>
<td>0.06</td>
<td>0.90D(p)</td>
<td>$5.90$</td>
</tr>
<tr>
<td>0.13</td>
<td>0.80D(p)</td>
<td>$6.04$</td>
</tr>
<tr>
<td>0.23</td>
<td>0.70D(p)</td>
<td>$6.15$</td>
</tr>
</tbody>
</table>

#### Table 4: Vaccine Equilibrium prices ($K = 1.1D(p)$)

<table>
<thead>
<tr>
<th>Degree of product differentiation</th>
<th>Engerix B</th>
<th>Recombivax HB</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\gamma$</td>
<td>Capacity</td>
<td>Equilibrium price</td>
</tr>
<tr>
<td>0.76</td>
<td>0.50D(p)</td>
<td>$8.72$</td>
</tr>
</tbody>
</table>
## Equilibrium prices

### Table 4: Vaccine Equilibrium prices ($K=1.1D(p)$)

<table>
<thead>
<tr>
<th>Degree of product differentiation</th>
<th>ActHIB</th>
<th>PedvaxHIB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Capacity</td>
<td>Equilibrium price</td>
</tr>
<tr>
<td>Adjusted $\gamma$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.50</td>
<td>0.70D(p)</td>
<td>$8.21$</td>
</tr>
<tr>
<td>0.40</td>
<td>0.70D(p)</td>
<td>$8.62$</td>
</tr>
<tr>
<td>0.30</td>
<td>0.70D(p)</td>
<td>$8.79$</td>
</tr>
<tr>
<td>0.20</td>
<td>0.70D(p)</td>
<td>$8.76$</td>
</tr>
<tr>
<td>0.10</td>
<td>0.70D(p)</td>
<td>$8.56$</td>
</tr>
</tbody>
</table>

### Table 22: Vaccine Equilibrium prices ($\Gamma_{Ped-Pent}$)

<table>
<thead>
<tr>
<th>Degree of product differentiation</th>
<th>Pediarix</th>
<th>Pentacel</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Capacity</td>
<td>Equilibrium price</td>
</tr>
<tr>
<td>Adjusted $\gamma$</td>
<td>0.74D(p)</td>
<td>$46.61$</td>
</tr>
</tbody>
</table>
## 2012 Vaccine Prices

**Table:** Competitive vaccines analyzed using the model (2012)

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Trademark name</th>
<th>Vaccine manufacturer</th>
<th>2012 public sector price</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTaP</td>
<td>Infanrix®</td>
<td>GlaxoSmithKline</td>
<td>$15.35</td>
</tr>
<tr>
<td>DTaP</td>
<td>Daptacel®</td>
<td>Sanofi Pasteur</td>
<td>$15.00</td>
</tr>
<tr>
<td>HepB</td>
<td>Engerix B®</td>
<td>GlaxoSmithKline</td>
<td>$10.73</td>
</tr>
<tr>
<td>HepB</td>
<td>Recombivax HB®</td>
<td>Merck</td>
<td>$10.75</td>
</tr>
<tr>
<td>Hib</td>
<td>ActHIB®</td>
<td>Sanofi Pasteur</td>
<td>$9.20</td>
</tr>
<tr>
<td>Hib</td>
<td>PedvaxHIB®</td>
<td>Merck</td>
<td>$11.97</td>
</tr>
<tr>
<td>DTaP-IPV-HIB</td>
<td>Pentacel®</td>
<td>Sanofi Pasteur</td>
<td>$54.50</td>
</tr>
<tr>
<td>DTaP-Hep B-IPV</td>
<td>Pediarix®</td>
<td>GlaxoSmithKline</td>
<td>$52.10</td>
</tr>
</tbody>
</table>
The equilibrium prices are lower than the 2012 federal contract prices.

Why?

- Vaccine prices: affected by several factors
- The two main roles of the CDC: negotiating lower prices for the vaccines and maintaining public health goals
- The prices of the licensed vaccines are required to be negotiated to account for the research and development costs of the vaccines that are not licensed.
Conclusions

• Competition between asymmetric manufacturers with limited production capacities and linear demand, producing differentiated products.

• Pure strategy equilibrium exists if the production capacity of a manufacturers is at their extreme.

• In a duopoly setting, the distribution functions of the mixed strategy equilibrium for both manufacturers are provided.
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• This analysis could provide awareness to CDC about the vaccine equilibrium prices for future years.
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Thank You
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