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Innovative Applications of O.R.

A bilevel formulation of the pediatric vaccine pricing problem

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ABSTRACT

We consider the characterization of optimal pricing strategies for a pediatric vaccine manufacturing firm operating in an oligopolistic market. The pediatric vaccine pricing problem (PVPP) is formulated as a bilevel mathematical program wherein the upper level models a firm that selects profit-maximizing vaccine prices while the lower level models a representative customer's vaccine purchasing decision to satisfy a given, recommended childhood immunization schedule (RCIS) at overall minimum cost. Complicating features of the bilevel program include the bilinear nature of the upper-level objective function and the binary nature of the lower-level decision variables. We develop and test variants of three heuristics to identify the pricing scheme that will maximize a manufacturer's profit: a Latin Hypercube Sampling (LHS) of the upper-level feasible region, an LHS enhanced by a Nelder–Meade search from each price point, and an LHS enhanced by a custom implementation of the Cyclic Coordinate Method from each price point. The practicality of the PVPP is demonstrated via application to the analysis of the 2014 United States pediatric vaccine private sector market. Testing results indicate that a robust sampling method combined with local search is the superlative solution method among those examined and, in the current market, that a manufacturer acting unilaterally has the potential to increase profit per child completing the RCIS by 35 percent (from 231.84 to 312.55 dollars) for GlaxoSmithKline, 47 percent (from 63.96 to 93.70 dollars) for Merck, and 866 percent (from 25.99 to 251.04 dollars) for Sanofi Pasteur over that obtained via current pricing mechanisms.

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1. Introduction

Routine administration of pediatric vaccines is one of the most effective means of preventing the spread of infectious diseases. In the United States, the Centers for Disease Control and Prevention (CDC) is the primary federal public health agency responsible for prescribing pediatric immunization policy. The CDC issues guidelines concerning the proper methods and scheduling for vaccinating a child. The Advisory Committee on Immunization Practice (ACIP), an advisory body to the CDC, provides specific guidance regarding policies to effectively reduce incidents of vaccine-preventable infectious diseases. Based on the ACIP's counsel, the CDC publishes the recommended childhood immunization schedule (RCIS), specifying appropriate periodicity and dosages for pediatric vaccines (Centers for Disease Control & Prevention, 2014a). The American Academy of Pediatrics, the American Academy of Family Physicians, and the American College of Obstetricians and Gynecologists provide input into the RCIS approval process as well. Public and private health care providers in the United States purchase and administer vaccines in accordance with the RCIS. This vaccine delivery system ensures proper coverage for a single child and provides public health protection for society at large.

The pediatric vaccine purchasing decision faced by health care providers grows increasingly complicated as an increasing number of diseases are added to the RCIS and new vaccines are developed by manufacturers for immunization against those diseases. Indeed, the RCIS has grown increasingly complex in the past 25 years, requiring children to receive numerous vaccine injections over the first two years of life. Meeting the current RCIS (see Fig. 1 from Centers for Disease Control and Prevention, 2014a) may require up to 29 separate injections and, during a single clinical visit, a child may be required to receive up to six separate injections (e.g., at the two- or six-month well-child visit). The vaccine industry has responded to this increased complexity by designing and producing *combination vaccines*. A combination vaccine contains antigens for immunization against more than one infectious disease. The CDC recognizes a number of compelling reasons for using combination vaccines to reduce the number injections required to satisfy the RCIS (Centers for Disease Control & Prevention, 1999). The reasons for using combination vaccines include simplifying the administration process, reducing the pain and discomfort experienced by children, and increasing

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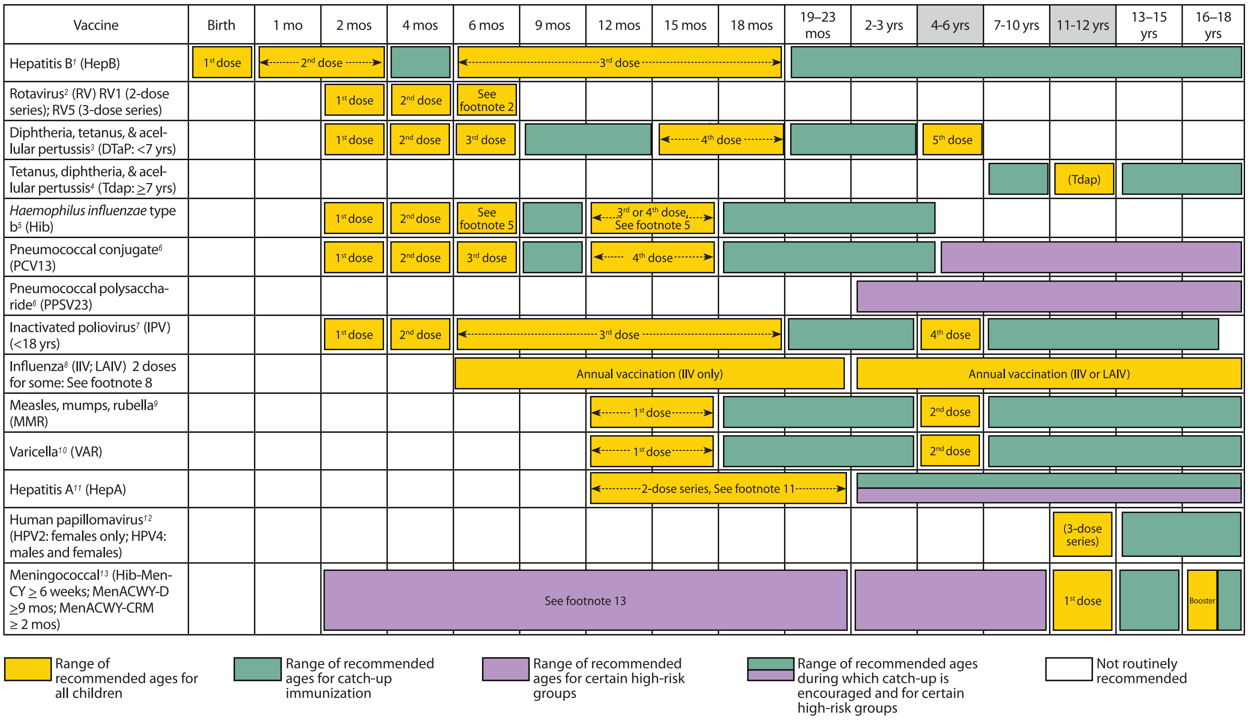

Fig. 1. United States 2014 recommended childhood immunization schedule (from Centers for Disease Control & Prevention, 2014a).

vaccination compliance rates (Kuppermann et al., 2000; LeBaron, Rodewald, & Humiston, 1999; Meyerhoff, Weniger, & Jacobs, 2001; Pellissier, Coplan, Jackson, & May, 2000). The advent of these new vaccines results in a large, combinatorial number of possible vaccine formularies.

The pediatric vaccine pricing decision faced by vaccine manufacturers grows increasingly complicated as well, as manufacturers must consider both the combinatorial nature of a health care provider's purchasing decision and the vaccine prices of the competing manufacturers. A relatively small number of pharmaceutical companies participate in the research, development, manufacture, and distribution of pediatric vaccines in the United States market. Participation in the vaccine industry is a difficult and costly enterprise. Over the past few decades, the manufacture of pediatric vaccines has become less profitable due to rising costs and limited demand, causing many pharmaceutical companies to exit the market (Douglas & Samant, 2012; Offit, 2005; Shrestha, Wallace, & Meltzer, 2010). As of 2014, just five pharmaceutical companies manufacture vaccines for young children (not including influenza virus vaccines), two of which manufacture only one pediatric vaccine (Centers for Disease Control & Prevention, 2014b; Food & Drug Administration, 2014). The contraction of the pediatric vaccine industry negatively impacts the provision of vaccines. A robust vaccine industry ensures that appropriate immunization coverage levels can be maintained and is very important to the nation's public health and well being. Many public health experts suggest that vaccine manufacturers should earn higher returns on their investments in order to sustain and expand the production of vaccines (Hinman, 2005; Jacobson, 2012; McGuire, 2003; Orenstein, Douglas, Rodewald, & Hinman, 2005; Poland & Marcuse, 2004).

Indeed, many public health policy studies examine the issue of pediatric vaccine pricing and purchasing in the United States vaccine market. Zhou et al. (2005) and Zhou et al. (2014) provide excellent context for the discussion by presenting an analysis concerning the economic benefit of vaccines to society. McGuire (2003) suggests an economic model to determine vaccine prices, arguing that, while vaccines have considerable value to society, vaccine manufacturers do not receive appropriate financial incentives for market participation. Hinman (2005) suggests pricing a vaccine in advance of its development based on its estimated value to society. Freed, Cowan, and Clark (2008) and Clark, Cowan, and Freed (2011) study generalities concerning private sector vaccine purchase costs using cross-sectional surveys. Adida, Dey, and Mamani (2013) investigate incentive mechanisms for both consumers and vaccine manufacturers to coordinate a vaccine market. Glazner, Beaty, Pearson, and Berman (2004) and Glazner, Beaty, and Berman (2009) conduct empirical analyses of actual variable costs of vaccine administration among private pediatric practices. The results obtained by Glazner et al. (2009) provide excellent information concerning the cost incurred by a health care provider to administer a single injection; we utilize their results in our numerical example, presented in a subsequent section of the paper.

Operations research efforts in the area of vaccine economics study the purchase of an optimal set of vaccines from a purchaser's (i.e., a health care provider's) perspective as well as the determination of optimal vaccine prices from a manufacturer's perspective. Weniger et al. (1998) and Jacobson, Sewell, Deuson, and Weniger (1999) introduce an integer program model to aid health care policy makers in determining a *vaccine formulary* (i.e., a set of vaccines) that minimizes the cost to fully immunize a child according to a given RCIS; such a set of vaccines is labeled a *minimum cost formulary*. Hall, Jacobson, and Sewell (2008) introduce the general vaccine formulary selection problem, providing fundamental insights into the structure of problems concerning minimum cost satisfaction of a RCIS. Sewell, Jacobson, and Weniger (2001) and Sewell and Jacobson (2003) adopt a reverse engineering scheme, using a bisection algorithm to compute a vaccine's *maximum inclusion price*; a maximum inclusion price is the maximum price at which a vaccine is selected by a customer to be part of the minimum cost formulary. Jacobson and Sewell (2003) and Jacobson, Sewell, and Karnani (2005) conduct similar studies. Robbins, Jacobson, and Sewell (2010) present a method to optimally price a single pediatric vaccine so as to maximize a vaccine manufacturer's expected revenue given an uncertain cost of injection parameter. Robbins and Jacobson (2011) formulate a mixed integer nonlinear program to examine the