Analyzing the effects of contract and structural design in health care supply chains

A thesis presented by

Gerardo Pelayo Rubio

In partial fulfillment of the requirements for the degree of

Doctor of Philosophy in Logistics and Supply Chain Management

in the

MIT-Zaragoza International Logistics Program

at the

Zaragoza Logistics Center, a research institute associated with the University of Zaragoza

March 2014

[page left intentionally blank]

Abstract

Introduction

Balancing access to needed medicines against escalating costs is one of the most challenging tasks in health care system design and reform. From 2000 to 2008, the average growth in the per capita spending on pharmaceuticals for Organisation for Economic Co-operation and Development (OECD) countries was almost 60%. The trade-off is particularly present in the introduction of new drugs aimed at treating chronic conditions where list prices proposed by the pharmaceutical manufacturers tend to be high in order to recoup their investment, sometimes contrasting with a lack of robust evidence regarding the cost-effectiveness of the treatment at the time when price is negotiated; moreover, such cost-effectiveness may vary across a drug's different indications, i.e., for different patient groups. As a result, in traditional agreements a health-payer - e.g., National Health Systems, Health Maintenance Organizations, large insurance companies - may be forced either to restrict access or to risk paying high prices that are not ex-post justified due to the uncertainty about the real value of a drug's therapeutic innovation, the lack of solidity of the results presented by the manufacturer, or the replicability of those results in clinical practice. But as pressures to control health care spending keep increasing, health-payers have pushed pharmaceutical manufacturers to decrease prices, potentially decreasing the incentives to invest in innovative treatments, and often resulting in the (temporary or definitive) absence of an agreement between both players at the loss of patient welfare and manufacturer's profits. This has motivated manufacturers - particularly those in the cardiovascular or oncology sectors - to explore more sophisticated agreements where risks can be more efficiently shared.

Motivated by the above trend, we understand that a health-payer must decide not only whether to accept a new drug under (partial or full) reimbursement for the patient population it serves, but also determine the service level (what will be the volume purchased to satisfy patient demand), access level (which patient groups will be serviced by the health-payer), and reimbursement conditions to the manufacturers (contract parameters). Furthermore we acknowledge that a health-payer may have different priorities affected by the social and industry environment where it operates (e.g., maximizing resource efficiency versus maximizing social welfare), and constraints (e.g., expenditure cap per demand period for some drug/therapeutic indication, and minimum cost-effectiveness threshold). As for pharmaceutical manufacturers, we consider: that price-setting may occur exogenously (through external reference pricing) or endogenously (through direct negotiations with the health-payers); that they may internalize (partially or fully) the risk of holding inventory; and that they are able to segment the market through the creation of distinguishable products targeted at each patient group.

Research Questions

Within the above context where an innovative drug with multiple therapeutic indications looks to enter the market, the research aims at analytically responding to the questions below. Thus, it expects to contribute to a wider understanding of the system's behavior, eventually leading to structural and contract designs in health care supply chains which are better aligned with the players' objectives.

- In a vertically integrated system, how do access and service levels interact as a function of the system's priorities and constraints?
- In a manufacturer-health payer system, what changes as the selling price is exogenously (*vs.* endogenously) set, and the manufacturer is (*vs.* isn't) willing to share some of the risks associated with demand and health outcomes?
- How does the decision of segmenting vs. consolidating the design/distribution channel

for a drug with multiple therapeutic indications reflect on the service level and the incentives for innovation effort?

- What is the effect of all the above on: pharmaceutical manufacturer's profits, health payer's expenditures, and patient welfare?

Methodology and key assumptions

The approach followed in this thesis is to mathematically model the described situations based on the newsvendor model framework. This choice is driven by: i)the long lead times (approximately 4 months) for capacity building, sourcing, manufacturing, and delivery of drugs; ii)the industry's common practice to offer preferential pricing for large orders, thus supporting the partition of demand into long periods; iii)the industry's high utilization levels, limiting the ample supply assumption; and iv)the low probability of, and negative health implications associated with, delaying a patient's treatment. The supply chain considered is that of a single pharmaceutical manufacturer that offers to sell a drug to a health-payer who is in charge of making that drug available to the patient population. Patient heterogeneity is assumed so that at least two patient groups could potentially benefit by receiving the drug, where each group is expected to receive different health-benefits by consuming the same drug. We analyze the constrained optimization problem for the manufacturer, health-payer, or the integrated system (depending on the case), making use of game theory concepts to characterize the equilibrium solution under simultaneous and sequential decisions.

Theoretical Contribution

In his seminal paper, Arrow (1963)[1] sustains that the uncertainty both in the incidence of disease (i.e., the size of the demand) and in the efficacy of treatment (i.e., the revenue/health

[1]Arrow, K. 1963. Uncertainty and the welfare economics of medical care. *The American Economic Review* 53(5): 941-973.

benefit per unit of treatment) generates adaptations that limit the descriptive power of the traditional competitive model and the implications for economic efficiency. Taking this into account, the dissertation contributes mainly to three research streams. First, the health economics literature focuses on determining access level given the heterogeneity in patients' characteristics and the uncertainty in the treatment's efficacy (e.g., Barros, 2011[2]; Zaric, 2008[3]), or on the binary decision to include a drug in a health payer's list of reimbursable treatments given demand uncertainty (e.g., Zhang et al., 2011[4]). In contrast, the thesis simultaneously analyzes the problem of access level and demand uncertainty under the sector's particularities. Such situation is similar to the problem studied in operations management where selling price and stocking quantity are simultaneously determined in the presence of random, price-dependent demand. The thesis contributes to the latter line of research (e.g., Petruzzi et al., 1999[5]; Salinger et al., 2011[6]) by analyzing the interaction with different contract designs under a combination of objectives and constraints, and additionally contributes to the supply chain coordination works (e.g., Bernstein et al., 2005[7]; Cachon et al., 2005[8]) by allowing the "revenue" per unit "sold" to be a random variable, *i.e.,* the health benefits. Finally, we contribute to the inventory pooling literature (e.g., Eppen, 1979)[9] by incorporating patient heterogeneity in a first-come first-serve system with no possibility of reservations, providing contrasting results with popular belief regarding the benefits of aggregation.

[2]Barros, P. P. 2011. The simple economics of risk-sharing agreements between the NHS and the pharmaceutical industry. *Health Economics* 20: 461-470.

[3]Zaric, G. S. and B.J. O'Brien. 2005. Analysis of a pharmaceutical risk sharing agreement based on the purchaser's total budget. *Health Economics* 14: 793-803.

[4]Zhang, H., G.S. Zaric, and T. Huang. 2011. Optimal design of a pharmaceutical price-volume agreement under asymmetric information about expected market size. *Production and Operations Management* 20(3): 334-346.

[5]Petruzzi, N., M. Dada. 1999. Pricing and the newsvendor problem: a review with extensions. *Operations Research.* 47(2): 183-194.

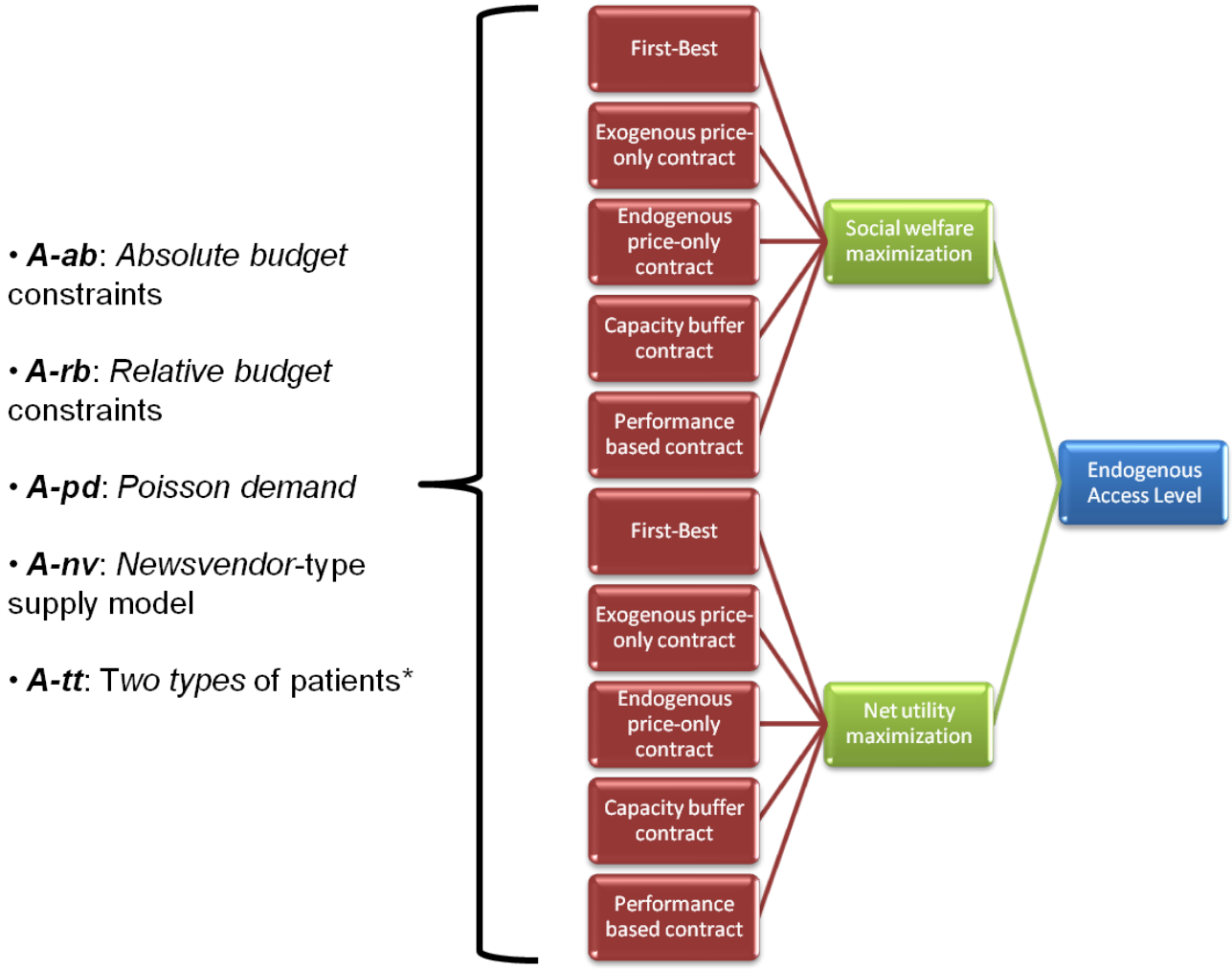
[6]Salinger, M. and M. Ampudia. 2011. Simple economics of the price-setting newsvendor problem. *Management Science.* 57(11): 1996-1998.

[7]Bernstein, F., A. Federgruen. 2005. Decentralized Supply Chains with Competing Retailers Under Demand Uncertainty. 2005. 51(1): 18-29.

[8]Cachon, G. and M. Lariviere. 2005. Supply Chain Coordination with Revenue-Sharing Contracts: Strengths and Limitations. *Management Science* 51(1): 30-44.

[9]Eppen, G. D. 1979. Effects of centralization on expected costs in a multi-location newsboy problem. *Management Science.* 25(5), 498-501.

Figure 1: Snapshot of Chapters 2 and 3



Structure of the Dissertation

Chapter 1 provides an extended introduction to the problem. Chapters 2 and 3 focus on the simultaneous access and service level decisions, while Chapter 4 takes the access level as exogenously given and analyzes the optimal structural design and effort decisions. Final comments are offered in Chapter 5. Table 1 and Table 2 provide a snapshot of the analysis, along with the key associated assumptions.

Chapter 2

We begin the analysis by modeling the introduction process of a new drug treatment that can be used by multiple patient categories who benefit differently from it. A profit-

maximizing pharmaceutical manufacturer offers to sell the new drug to a health-payer, who decides the access and service levels for the patient population he serves. An analytical comparison is done assuming that the health-payer either maximizes patient welfare, or maximizes the entire utility function (i.e., incorporating purchasing costs). Under both decision-making criteria two constraints are included: an absolute budget constraint to set a limit on health care spending, and a cost-effectiveness constraint to maintain a balance between costs and benefits. First, the analysis for the vertically integrated chain is presented both as an efficiency benchmark and as a simplified setting for understanding the dynamics between access and service level under the problem's particular characteristics. Second, the exogenous price contract is formulated, setting the grounds for the analysis of contracts where the manufacturer can endogenously determine at least some contract parameters.

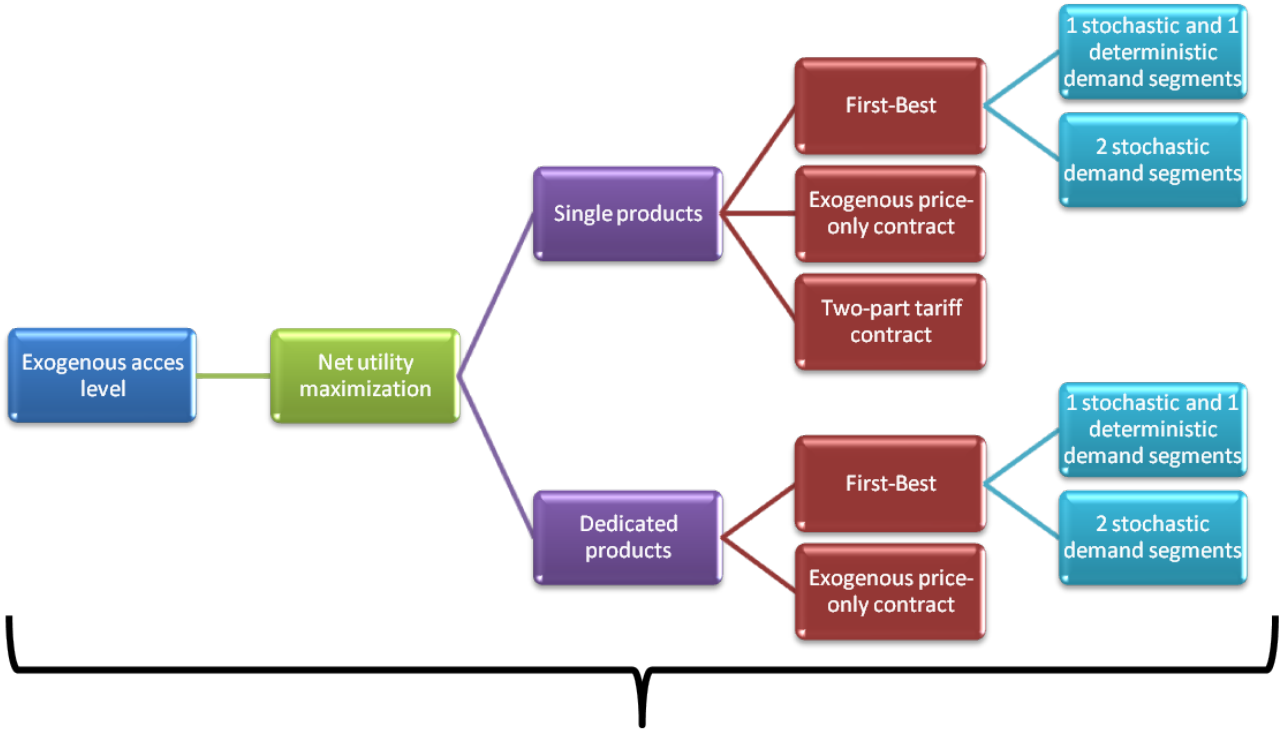
Chapter 3

In this chapter we keep the structure of the model presented earlier but focus on the decisions made by the pharmaceutical manufacturer, given that she can anticipate the health-payer's access and service level decisions. Specifically, we analyze three contracting mechanisms: endogenous price-only contracts; exogenous price contracts with capacity buffer; and performance-based contracts. Endogenous price-only contracts have been thoroughly studied, but not in a supply chain setting as the one we consider where the downstream player has such decision space (as mentioned above for Chapter 2). The last two contracts are novel proposals based on existing models, but adapted to the needs of the system. The virtues and drawbacks of each mechanism are detected, with an emphasis on the search for Pareto improvements.

Chapter 4

The last part of the dissertation departs from the analysis of the access level decision and captures a different consequence of patient heterogeneity by analytically comparing the performance of two supply chain designs. Under the first design, (up to) two patient categories are served by a single inventory stock on a first-come first-serve basis, while on the second design a dedicated inventory stock is used to serve each patient category. It is

Figure 2: Snapshot of Chapter 4



assumed that the realization of the second category is stochastically contingent on innovation efforts made by the pharmaceutical manufacturer, that such manufacturer chooses the supply chain design by having the option to commercialize two differentiated products (*e.g.,* through different presentations, different delivery formats, exclusive distribution channels), and that the health-payer is responsible for making the inventory decision. First, the optimal decision path for a vertically integrated chain is analyzed, and then the incentive misalignments derived from vertical separation are explained along with some theoretical and managerial extensions to the model.