# Cross-Bundling and (Anti) Competitive Behavior: Evidence from the Pharmaceutical Industry

Claudio Lucarelli *
Cornell University
U. de los Andes

Sean Nicholson†
Cornell University and NBER

Minjae Song ‡
University of Rochester

October 2009

**Abstract**

There is a substantial literature in economics on intra-firm product combinations such as bundling and tying. Little is known, however, about the economic implications of inter-firm product combinations. We propose and estimate a model to study pricing strategies and the welfare effects of this practice, focusing on the pharmaceutical industry. We find that firms increase their profits by participating in inter-firm product combinations. A less competitive equilibrium arises in this situation as the firms are able to partially internalize the externality their pricing decisions impose on their competitors. We also find that profit increases from the inter-firm product combinations could be as large as profit increases from mergers. Our results should help policy-makers evaluate the antitrust implications of mergers in the pharmaceutical industry.

*Department of Policy Analysis and Management, Cornell University, 105 MVR Hall, Ithaca NY 14853. E-mail: Claudio.Lucarelli@cornell.edu

†Department of Policy Analysis and Management, Cornell University, 123 MVR Hall, Ithaca NY 14853. E-mail: sn243@cornell.edu

‡Simon Graduate School of Business, University of Rochester, Rochester NY 14627. E-mail: minjae.song@simon.rochester.edu. We have benefited from discussions with Michael Waldman and comments by seminar participants at the Federal Trade Commission, the 2009 IIOC and the University of Rochester. All errors are ours.

# 1 Introduction

There is a substantial economic literature addressing product combinations, such as bundling or tying, that examines why a firm would want to bundle two or more of its products into one package. Bundling may allow a firm to engage in price discrimination (Adams and Yellen, 1976; McAfee et al., 1989), to leverage monopoly power in one market by foredosing sales and discouraging entry in another market (Whinston, 1990; Chen, 1997; Carlton and Waldman, 2002; Nalebuff, 2004), or alter a pricing game among oligopolists even when entry is not deterred or no firms exit (Carlton, Gans, and Waldman, 2007). A common feature of this literature is that bundled products are produced by the same firm.

There are many situations where consumers combine products produced by competing firms in order to exploit the complementarity that they provide. Industries in which the firms sell compatible systems and consumers can "mix and match" components are a clear example of this kind of behavior, which firms could avoid by making their products incompatible. Matutes and Regibeau (1988) provide a long list of industries where mix and match occurs [1] and a theory to explain why firms would allow their products to be compatible in the absence of network externalities. Other cases of inter-firm product combinations are those in which consumers combine substitutes. For example, fly from one city to another combining competing airlines. Empirically, economists know little about the pricing and welfare impact of these situations where the combined product (e.g., a gin and tonic) is an important source of profit for the two firms relative to the profit generated by the two stand-alone products. The lack of information is due primarily to the difficulty of separately identifying the market shares and attributes of the combined, or cocktail, product relative to the stand-alone products, or the quantity of each component product used in the cocktail because consumers combine products in different ways.

In this paper, we analyze the pricing and welfare effects of inter-firm product combinations in the pharmaceutical market because these combinations are common in this industry and we can surmount the empirical challenges described above. Two or more drugs are often combined by manufacturers in a single pill or combined by a physician in order to improve the efficacy of

[1] Some of them are photography, computers, home stereo, etc.

treating a disease. For example, most HIV/AIDS patients receive a cocktail regimen, such as efavirenz, lamivudine, and zidovudine, better known as AZT. Three of the six new cholesterol-reducing drugs entering phase 3 clinical trials in 2007 were combinations of drugs that had already been approved to treat the disease as stand-alone products (Blume-Kohut and Sood, 2009).

Combined pharmaceutical products are well defined, standardized, and have observable market share. Pharmaceutical cocktails are approved by the FDA if they demonstrate superior efficacy and/or fewer side effects relative to existing drugs. Data from clinical trials provide information on the attributes (e.g., median months of survival for patients who receive a regimen during a phase 3 randomized controlled trial) of the stand- alone drugs and the combined cocktail regimens. Organizations such as the National Comprehensive Cancer Network recommend the amount of each drug that oncologists should use in a regimen, based on the "recipe" used in clinical trial or in actual practice.

Our setting is similar to a situation where firms can engage in mixed bundling (both the stand-alone and the combined regimens are available to consumers), but it differs from the traditional mixed bundling situation because the bundle contains another firm's product and the firms control only the price of their component (e.g., per milligram of active ingredient), therefore, the bundle is only priced as the sum of the components' prices. Strategies such as offering the bundle at a discounted price as in Adams and Yellen (1976), are not available. The single pricing constraint, which also exists in non-pharmaceutical applications where consumers combine stand-alone products to produce combined products, is an important difference from intra-firm product combinations.

A pharmaceutical firm entering a market usually instigates the creation of a cocktail rather than the incumbent that is already selling a stand-alone drug. The entering firm can purchase existing products (without the approval of the incumbent), combine them with its experimental drug, and test the combination in clinical trials. Because clinical trials are expensive, the entering firm should only test the inter-firm product combination if it expects positive profits. The impact of the cocktail on the incumbent and on consumers is unclear. Similar to Matutes an Regibeau (1988), the cocktail regimen may soften price competition as the price decreases will also benefit

the rival firm through the combination, but departing from their analysis, the combined drug is a substitute for the existing stand-alone regimen and steals market share from it.[2] Depending on which effect is larger, it can render the market more collusive or more competitive.[3] With respect to the impact on consumers, the inter-firm product combination generates new varieties in the market, which allows consumers to find a product closer to their ideal increasing consumer surplus, however, depending on how collusive the market becomes, consumers may experience a net loss in consumer surplus.

For an empirical analysis we focus on the market for colorectal cancer chemotherapy drugs. In 2008, thirty-one percent of U.S. colon cancer patients receiving chemotherapy treatment were administered cocktail regimens where at least one component drug was still patent-protected. We estimate a demand system at the regimen level using the unique regimen level market share data, and then combine this system with a Nash-Bertrand equilibrium assumption to generate equilibrium prices and quantities. In the model we allow each firm's drug price to affect all regimens through the estimated demand system.

We use the model to perform counterfactuals to better understand the economic consequence of inter-firm product combinations. In the first counterfactual we remove cocktail regimens one at a time and compute new equilibrium prices. We find that in general inter-firm product combinations increase profits for all participating firms and are detrimental to consumers, compared to an equilibrium with no product combinations. This occurs because firms set higher drug prices when their drugs are used in cocktail regimens, and highlights that the effect of internalizing externalities dominates the business stealing effect in this particular application.

In the second counterfactual we study how close is the equilibrium with inter-firm product combinations to the one where the participating firms fully integrate through mergers. We consider

[2]Matutes and Regibeau (1988) are concerned with industries where firms can sell systems and/or components (e.g. in the home stereo industry, the firm can sell a system containing tape deck, receiver and speakers, or each of these components separately. However, a component is not a substitute for the whole system, in other words, the speakers cannot substitute for the complete audio system.

[3]We abstract away from modeling a firm's decision on whether and how to combine its product with others' and take existing combinations as given.

two merger scenarios. In the first scenario we remove one cocktail regimen and allow the two participating firms to merge instead. We find that firms can earn greater profits from product combinations than from mergers without product combinations. In the second merger scenario we allow a pair of firms to merge while maintaining their cocktail regimen. The profit that firms make in this scenario is the maximum profit they can make pairwise, and we compare this profit with the current profit firms make with the cocktail regimen. We find that a merger increases the participating firms' profits as expected but only marginally.

In the third counterfactual we allow a firm to set two separate drug prices, one for its stand-alone regimen and the other for cocktail regimens. This is equivalent to a case where a firm has two separate drugs, one used by itself and the other in a cocktail regimen. Setting two prices introduces a strategic incentive that we observe in some sectors of the pharmaceutical market, such as for HIV/AIDS treatment. Although we do not observe situations where one firm has two colorectal cancer drugs, we use this exercise as an out-of-sample validation test for our model. In the early 2000s the company Abbott launched Kaletra, a drug for treating HIV/AIDS. At the time Abbott was already selling Norvir, which was used in a cocktail regimen to help boost the performance of a drug manufactured by one of its competitors. Shortly after the launch of Kaletra, Abbott decided to increase the price of Norvir five-fold while pricing Kaletra more competitively, presumably to drive customers from the cocktail regimen to its new stand-alone regimen.[4] We find similar pricing behaviors in our counterfactual. In addition, we confirm that if firms are able to set two distinct prices, they earn higher profits. However, this pricing scheme may or may not hurt its competitors.

The paper is organized as follows: Section 2 presents an overview of colorectal cancer, and the data are described in Section 3. We present the model in Section 4 and simple numerical examples in section 5, such as where two firms have one stand-alone regimen each and have the third regimen by combining their drugs. Section 6 presents the results from our estimation and the counterfactual exercises and section 7 concludes.

[4]Choi (2009) develops a theoretical model that finds similar pricing behavior as the result of mergers. The merged firm lowers the price of the bundle and increases the price of the product their competitors will use in a combination to make those bundles less attractive to consumers.

## 2 Overview of Colorectal Cancer

Colorectal cancer is the fourth most common cancer based on the number of new patients, after breast, prostate, and lung cancers. About one in 20 people born today are expected to be diagnosed with colorectal cancer over their lifetime. The disease is treatable especially if it is detected before it has metastasized, or spread, to other areas of the body. Between 1996 and 2003, colorectal cancer patients had a 64 percent chance of surviving for five years. According to the National Comprehensive Cancer Network (NCCN), the probability a patient will survive for five years ranges from 93 percent for those diagnosed with Stage I cancer to eight percent for those diagnosed with Stage IV (or metastatic) cancer.[5]

Six of the 12 major regimens for which we have complete data are cocktail regimens, composed of two or more drugs produced by different firms. One cocktail regimen is a combination of irinotecan, produced by Pfizer, and capecitabine, produced by Roche. Another is a combination of oxaliplatin, produced by Sanofi, with capecitabine. Bevacizumab, a drug produced by Genentech, is combined with oxaliplatin in one regimen, with irinotecan in second, and with oxaliplaitin and capecitabine in third. Cetuximab, which is produced by ImClone, is combined with irinotecan.

Four of the remaining six regimens are stand-alone regimens and they are just the same individual drugs used in the cocktail regimens. One of the remaining two regimens is 5FU/LV which is a generic regimen and the other is Pfizer's Irinotecan combined with 5FU/LV. We take the generic regimen's price as given and assume that its price does not react to firms' strategic pricing. So we treat the latter regimen as Pfizer's second stand-alone regimen whose price is always the same as that of its other stand-alone regimen plus the generic regimen's price. The table in the appendix provides a complete dosage description of the twelve regimens we have data on.

Since each drug is sold separately to physicians who combine them into cocktail regimens in their offices, the only variable that a firm controls is the price of its own drug. However, this has an impact on the demand and profits for all the cocktail regimens the firm's drug is used in. We explicitly account for this impact in our supply side (pricing) model in section 4.

[5]Cancers are classified into four stages, with higher numbers indicating that the cancer has spread to the lymph nodes (Stage III) or beyond its initial location (Stage IV).

Most oncology drugs are infused into a patient intravenously in a physician's office or an outpatient hospital clinic by a nurse under a physician's supervision. Unlike drugs that are distributed through pharmacies, physicians (and some hospitals on behalf of their physicians) purchase oncology drugs from wholesalers or distributors (who have previously purchased the drugs from the manufacturers), store the drugs, and administer them as needed to their patients. Physicians then bill the patient's insurance company for an administration fee and the cost of the drug. In our model we assume physicians are imperfect agents for their patients, and the details of the imperfect agency will be explained in section 4.

# 3 Data

We use a number of different data sources to collect four types of information: drug prices, regimen market shares, the amount/dose of each drug typically used in a regimen, and regimen attributes from clinical trials (e.g., the median number of months patients survived when taking the regimen in a phase 3 clinical trial). IMS Health collects information on the sales in dollars and the quantity of drugs purchased by 10 different types of customers (e.g., hospitals, physician offices, retail pharmacies) from wholesalers in each quarter from 1993 through the third quarter of 2005. Prices and quantities are reported separately by National Drug Classification (NDC) code, which are unique for each firm-product-strength/dosage-package size. We calculate the average price paid per milligram of active ingredient of a drug by averaging across the different NDC codes for that drug. IMS Health reports the invoice price a customer actually pays to a wholesaler, not the average wholesale price (AWP) that is set by a manufacturer and often differs substantially from the true transaction price.

The price we calculate does not include any discounts or rebates a customer may receive from a manufacturer after purchasing the product from the wholesaler. Based on interviews with oncologists, we do not believe that manufacturers offered substantial rebates during this period. Although we have information on 10 different types of customers, we focus on the prices paid by the two largest customers - hospitals and physician offices - because most colon cancer chemotherapy

drugs are infused in a physician's office or hospital clinic.[6]

We then compute the price of each regimen for a representative patient who has a surface area of 1.7 meters squared (Jacobson et al., 2006), weighs 80 kilograms, and is treated for 12 weeks. Regimen prices are derived by multiplying the average price per milligram of active ingredient in a quarter by the recommended dosage of each drug in the regimen over a 12-week period.[7] The NCCN reports the typical amount of active ingredient used by physicians for the major regimens.[8] Dosage information is reported in the appendix. For example, the standard dosage schedule for oxaliplatin+5-FU/LV, the regimen with the second largest market share in 2005, is 85 milligrams (mg) of oxaliplatin per meter squared of a patient's surface area infused by IV on the first day of treatment, followed by a 1,000 mg infusion of 5-FU per meter squared of surface area on the first and second treatment days, and a 200 mg infusion of leucovorin (LV) per meter squared on the first and second treatment days. This process is repeated every two weeks.

The IMS Health data contain information on market share by drug, but not market share for combinations of drugs (regimens). We rely, therefore, on two different sources for regimen-specific market shares, where market share is defined as the proportion of colorectal cancer chemotherapy patients treated with a particular regimen. IntrinsiQ collects monthly data from its oncology clients on the types of chemotherapy drugs administered to patients. Based on these data, we derive monthly market shares for each regimen between January 2002 and September 2005.

Since IntrinsiQ's data only go back to 2002, we rely on the Surveillance Epidemiology and End Results (SEER) data set for market shares for the 1993 to 2001 period. SEER tracks the health and treatment of cancer patients over the age of 64 in states and cities covering 26 percent of the United States population.[9] Based on Medicare claims data available in SEER, we calculate

[6]Based on data from IMS Health, 59% of colorectal cancer drugs in the third quarter of 2005 were purchased by physician offices/clinics and 28% by hospitals. The remainder was purchased by retail and mail order pharmacies, health maintenance organizations, and long-term care facilities.

[7]The regimens are priced using price data for the contemporaneous quarter only.

[8]We supplement this where necessary with dosage information from drug package inserts, conference abstracts, and journal articles.

[9]SEER contains data on the incidence rate of cancer among the non-elderly, but only has medical claims available for Medicare patients.

each colorectal cancer regimen's market share in each quarter.[10]

In order to homologate market shares between the pre- and post-2002 periods, we take advantage of the fact that the two data sets overlap for the four quarters of 2002. We apply a regimen-specific factor to adjust the pre-2002 market shares based on the ratio of total (from IntrinsiQ) to Medicare-only (from SEER) market shares for the four quarters of 2002. Our underlying assumption in this adjustment is the proportion of total patients represented by Medicare does not vary over time for any regimen.

In our analysis, we include as inside goods all regimens that contain drugs that were approved by the FDA for colorectal cancer and had a market share greater than one percent at the end of the sample period. The outside option includes off-label drugs, regimens with less than one percent market share at the end of the sample period, and regimens with missing attribute data.[11]

Market shares for the 12 regimens in our sample and the outside option are plotted in Figure 1. Between 1993 and 1996, about 95 percent of colorectal cancer patients were treated with 5-FU/leucovorin, a generic regimen, with the remainder treated with off-label drugs or regimens with very small market share. Irinotecan (brand name Camptosar) was approved by the FDA for treating colorectal cancer in 1996, and over the next several years the market share of irinotecan and irinotecan combined with 5-FU/LV grew at the expense of 5-FU/LV.[12] Capecitabine (Xeloda), a tablet that produces the same chemical response as 5-FU/LV, was approved for treatment of colorectal cancer in April 2001 and was administered as a stand-alone therapy or combined with irinotecan. Besides capecitabine, all other drugs for treating colorectal cancer in our sample are delivered intravenously (IV) under the supervision of a physician or nurse.

Oxaliplatin (Eloxatin) was introduced in August 2002, followed by cetuximab (Erbitux) and bevacizumab (Avastin) in February 2004. By the third quarter of 2005, two of the regimens created by these three new drugs (oxaliplatin + 5-FU/LV and bevacizumab + oxaliplatin + 5-

[10] According to IntrinsiQ's data, approximately 48 percent of all colorectal cancer patients treated with chemotherapy were 65 years or older in October 2003.

[11] Off-label use occurs when a physician treats a colorectal cancer patient with a drug that has not been approved by the FDA for colorectal cancer.

[12] Because it takes Medicare a while to code new drugs into their proper NDC code, for several quarters a new drug will appear in the outside option.

FU/LV) surpassed the market share of 5-FU/LV, whose share had fallen to about 14 percent.

We obtain most of the attribute information from the FDA-approved package inserts. These inserts describe the phase 3 clinical trials and include the number and types of patients enrolled in the trials, the health outcomes for patients in the treatment and control groups, and the side effects experienced by those patients. Often there are multiple observations for a regimen, either because a manufacturer conducted separate trials of the same regimen, or because a regimen may have been used on the treatment group in one clinical trial and the control group in a subsequent trial. In these cases we calculate the mean attributes across the separate observations. Where necessary, we supplement the package insert information with abstracts presented at oncology conferences and journal articles.

The attribute information is summarized in Table 1, averaged across regimens in each quarter and then averaged for each year. We record three measures of a regimen's efficacy: the median number of months patients survive after initiating therapy (*Survival Months*); the percentage of patients who experience a complete or partial reduction in the size of their tumor (*Response Rate*); and the mean number of months (across patients in the trial) before the cancer advanced to a more serious state (*Time to Progression.*)

The side effect variables indicate the percentage of patients in phase 3 trials who experienced either a grade 3 or a grade 4 side effect for five separate conditions: abdominal pain, diarrhea, nausea, vomiting, and neutropenia. Although many more side effects are recorded for most regimens, these five were consistently recorded across the 12 regimens in the sample. Side effects are classified on a 1 to 4 scale, with grade 4 being the most severe. Higher values for the side effect attributes should be associated with worse health outcomes although regimens that are relatively toxic are likely to be both more effective and have more severe side effects.

Table 1 demonstrates that there was a large price increase in 1998. The average regimen price for a 24 week treatment cycle increases from about \$100 to over \$11,000. This jump is due to the introduction of Pfizer's irinotecan. Since then the average price continued to rise with significant jumps in 2002 when Sanofi's oxaliplatin was introduced and in 2004 when bevacizumab and cetuximab were launched. New regimens tend to be more efficacious than the existing regimens,

with side effect profiles that are sometimes more and sometimes less severe than earlier regimens (Lucarelli and Nicholson, 2009).

# 4 Model

## 4.1 Supply

We assume that firms play a static Nash-Bertrand game with differentiated products. A distinctive feature of our model is that additional product differentiation is achieved when the FDA approves a combination of drugs in a new regimen. Therefore, the equilibrium conditions are different from a situation where products are consumed separately or where firms produce multiple products.

A static Nash-Bertrand game may not fully describe pharmaceutical firms' behavior because these firms do more than set a profit-maximizing price. The most important non-price action is where pharmaceutical representatives market products to physicians (i.e., detailing). We do not observe detailing activity and do not attempt to include it in the model. We also do not explicitly model decisions by some pharmaceutical firms to provide a rebate to certain physicians if their purchased volume exceeds a certain threshold for the quarter or year. We are not aware of any study that documents the size of oncology rebates or how physicians react to such rebates, presumably because firms do not disclose rebates. Although these two features are not considered in the supply side model, we introduce a shock in the demand model to capture physicians' reaction to them.

Let $p_f$ be the price firm $f$ charges for its drug/product. Consistent with our data, we assume that each firm produces only one drug, and therefore, $p_f$ is the only endogenous variable in the firm's optimization problem. We denote $mc_f$ as the marginal cost for firm $f$, and $q_f(p)$ the quantity produced by firm $f$. Profits for firm $f$ are

$$\pi_f = (p_f - mc_f)q_f(p),$$

where $q_f(p)$ is obtained from the aggregation of quantities across the regimens in which the firm participates. Formally, if firm $f$ participates in $R_f$ regimens, and $r = 1, \ldots, R_f$, then $q_f(p)$ can be

written as

$$q_f(p) = \left( \sum_{r=1}^{R_f} s_r(p) q_{rf} \right) M,$$

where $s_r(p)$ is the share of patients treated with regimen $r$, $q_{rf}$ is the dosage of the drug produced by firm $f$ used in regimen $r$, and $M$ is the market size. $p_k^R$, the price of regimen $k$, is determined by $p_f$ and $q_{rf}$. For example, if regimen 1 is firm 1's stand-alone regimen, $p_1^R = q_{11}p_1$; if regimen 3 is a cocktail regimen, comprised of drugs from firm 1 and firm 2, $p_3^R = q_{31}p_1 + q_{32}p_2$.

The equilibrium conditions can then be written as

$$\frac{\partial \pi_f}{\partial p_f} = \sum_{r=1}^{R_f} s_r(p) q_{rf} + (p_f - mc_f) \sum_{k=1}^{R_f} \sum_{r=1}^{R_f} \frac{\partial s_r(p)}{\partial p_k^R} \frac{\partial p_k^R}{\partial p_f} q_{rf} = 0 \tag{1}$$

Equation (1) shows that a firm will take into account the effect of its drug price on the overall price of each regimen ($\partial p_k^R / \partial p_f$), and how changes in regimen prices impact the market shares of all regimens in which a drug participates ($\partial s_r(p) / \partial p_k^R$). The former effect is determined by the quantity of a drug used in a recommended regimen "recipe;" the latter effect is determined by the regimen's price elasticity of demand and is estimated using regimen-level data. We can recover the marginal costs for each drug by re-writing equation (1) for these costs.

Equation (1) highlights that an analytical analysis is not straightforward. Consider the simplest case where firm 1 and firm 2 each sell a stand-alone regimen and there is one cocktail regimen that combines the two firms' drugs. If all three regimens are substitutes for one another, the profit-maximizing first order condition for firm 1 becomes

$$\frac{\partial \pi_1}{\partial p_1} = (s_1(p)q_{11} + s_3(p)q_{31}) + (p_1 - mc_1) \left( \frac{\partial s_1}{\partial p_1^R} \frac{\partial p_1^R}{\partial p_1} q_{11} + \frac{\partial s_1}{\partial p_3^R} \frac{\partial p_3^R}{\partial p_1} q_{11} + \frac{\partial s_3}{\partial p_3^R} \frac{\partial p_3^R}{\partial p_1} q_{31} + \frac{\partial s_3}{\partial p_1^R} \frac{\partial p_1^R}{\partial p_1} q_{31} \right) = 0 \tag{2}$$

Note that while $\partial p_k^R / \partial p_f$ is fixed by the recommended recipe, $\partial s_r / \partial p_k^R$ is a function of price unless one assumes a constant elasticity demand. We rely, therefore, on numerical and empirical analyses to study the economic implications of cocktail regimens.

### 4.2 Demand

We obtain our demand system by aggregating over a discrete choice model of physician behavior. Following the Lancasterian tradition, products are assumed to be bundles of attributes, and preferences are represented as the utility derived from those attributes. As mentioned in section 2, we assume physicians are imperfect agents for their patients. A physician's objective is to extend a patient's life expectancy by administering patients to the most effective regimen. Because a physician also cares about a patient's financial status, price enters her utility function. However, physicians' decisions are also affected by elements other than regimen attributes, such as the profit earned by acquiring and administering a regimen. The rebate from pharmaceutical firms is a good example. To capture this aspect we include an idiosyncratic error term additively in the utility function.

The indirect utility of physician $i$ over regimens $j \in \{0, \ldots, J_t\}$ at time (market) $t$ is characterized as

$$u_{ijt} = -\alpha p_{jt} + \beta x_j + \xi_t + \Delta\xi_{jt} + \varepsilon_{ijt} \tag{3}$$

where $p_{jt}$ is the price of regimen $j$ at time $t$, $x_j$ are observable regimen attributes, $\xi_t$ is the mean of unobserved attributes for each period, and $\Delta\xi_{jt}$ is a time-specific deviation from this mean. $\varepsilon_{ijt}$ is an idiosyncratic shock to preferences and is assumed to have a Type I Extreme Value distribution as in McFadden (1981) and Berry (1994).

In this model all the individual-specific heterogeneity is contained in the idiosyncratic shock to preferences and, therefore, it suffers from the well-known independence of irrelevant alternatives criticism.[13] Berry and Pakes (2007) propose an alternative demand model that removes the idiosyncratic shock from the indirect utility function and assigns a random coefficient to at least one product attribute. In our pharmaceutical context, this pure characteristics model implies that physicians are perfect agents for their patients and are not affected by detailing or rebates. The

[13] Although we could alleviate this problem by allowing for random coefficients on price and product attributes following Berry, Levinsohn, and Pakes (BLP) (1995), we are unlikely to identify the random coefficients with our existing data set. Usually one needs consumer distribution from multiple markets, as in Nevo (2000), or micro choice data as in Petrin (2002). We, on the other hand, observe the same market over time and lack micro choice data on physicians' decisions.

pure characteristics model has a "local" substitution pattern, while the model with the idiosyncratic shock has a global pattern.[14] However, based on numerical simulations similar to those in Section 5, we conclude that the vertical model (the one-random-coefficient-pure characteristics demand model) does not correctly characterize the market with cocktail regimens. We find that firms charge lower price and earn lower profit with a cocktail regimen.

We estimate $\xi_t$ using quarterly indicator variables. $\Delta\xi_{jt}$ which represents demand shocks or regimen attributes that physicians observe but we do not, is likely to be correlated with price. That is, price is endogenous as in most demand models. All terms other than $\varepsilon_{ijt}$ represent patient utility (e.g., patient co-payments, observed and unobserved attributes of the treatment) and $\varepsilon_{ijt}$ captures any unobserved elements that affect a physician's choice independent of patients' utility. The outside option ($j = 0$) includes of-label colon cancer treatments, regimens with small market shares, or regimens without a complete set of attributes. The utility of the outside options is set to zero.

Market shares for each regimen $j$ are defined as

$$s_{jt} = \frac{\exp(-\alpha p_{jt} + \beta x_j + \xi_t + \Delta\xi_{jt})}{1 + \sum_{k=1}^{J_t} \exp(-\alpha p_{kt} + \beta x_k + \xi_t + \Delta\xi_{kt})}$$

This leads to the following demand equation

$$\ln s_{jt} - \ln s_{0t} = -\alpha p_{jt} + \beta x_j + \xi_t + \Delta\xi_{jt}. \tag{4}$$

Berry (1994) provides details of this derivation.

# 5 Numerical Analysis

Before we apply the models to data, we examine the inter-firm product combinations numerically in the simplest setting. In the benchmark case, firm 1 and firm 2 sell one stand-alone regimen each without having the inter-firm product combination (i.e., no cocktail regimen.) The firms compete a la Bertrand and consumer demand is based on the utility function in equation (3) . Assuming a

[14] See Berry and Pakes (2007) and Song (2007) for more discussions on the differences between these two models.

price coefficient of -1 and a certain product quality, which we denote $\delta_j$ for $j = 1$ and 2, the firms set price to maximize static profits.[15] In the empirical analysis we use actual market share data and observed regimen attributes to estimate product quality and fix its value, but in the numerical analysis we change quality to study how quality differentiation affects prices, profit, and consumer surplus.

We introduce a cocktail regimen by allowing the two firms to combine their drugs, given $\delta_1$ and $\delta_2$. We assume that this third regimen's product quality, say $\delta_3$, is the maximum of $\delta_1$ and $\delta_2$.[16] The cocktail regimen can be produced using different combinations of the two drugs. Recall from Section 4 that $q_{rf}$ is the dosage of a drug produced by firm $f$ used in regimen $r$. For simplicity we set $q_{11} = q_{22} = 1$ such that $p_1^R = p_1$ and $p_2^R = p_2$. For the cocktail regimen we let $r_{31}$ and $r_{32}$ be proportions of drugs 1 and 2 used in regimen 3 such that $r_{31} + r_{32} = 1$, $0 < r_{13} < 1$, and $0 < r_{23} < 1$. The price of regimen 3 will be determined by

$$p_3^R = r_{31}p_1 + r_{32}p_2.$$

We also allow $r_{31}$ to vary in order to study its impact. The profit-maximizing first order condition is identical to equation (2) with $q_{11} = q_{22} = 1$ and $q_{31} = r_{31}$. The marginal cost is assumed to be one-tenth of the stand-alone regimen's quality, *i.e.*, $mc_j = \delta_j/10$ for $j = 1, 2$.

In our first numerical analysis we fix $r_{31} = 0.5$ and $\delta_1 = 1$, and allow $\delta_2$ to change from 1 to 3 so that the quality difference between regimens changes from 0 to 2. For each value of $\delta_2$ a new equilibrium is computed. This simple exercise allows us to understand how firms' incentives change as the difference in regimen quality increases. Figure 2 compares firms' profit between cases with the cocktail regimen versus the benchmark case (no cocktails). The x-axis is the quality difference between firm 2's stand-alone regimen and firm 1's stand-alone regimen, *i.e.*, $\delta_2 - \delta_1$, and the y-axis measures profit. Figure 2shows that the presence of the cocktail regimen increases profit for both firms relative to not having a cocktail. Higher profit occurs as firms decide to charge higher prices with the presence of a cocktail regimen. This is similar to a case where a firm that

[15] Product quality is a linear function of observed and unobserved product attributes in equation (4), i.e. $\delta_j = \beta x_j + \xi_t + \Delta\xi_{jt}$.

[16] The FDA is not likely to approve a cocktail that is inferior to both already-approved stand-alone regimens.

produces multiple substitute products earns higher profit by being able to charge higher prices. An interesting difference is that the cocktail regimen serves a multiproduct function for both firms at the same time.

Figure 2 also shows that the low-quality firm's profit increases faster as the quality difference becomes larger. This occurs because the low-quality firm "free-rides" on the relatively high quality provided by the cocktail regimen. In the benchmark case the low-quality firm decreases its price while the high-quality firm increases it as the quality difference grows. With the cocktails present, however, the low-quality firm increases its price as the quality difference becomes larger, and it does so such that the market share for its stand-alone regime becomes negligible. But it still earns considerable profits from the cocktail regimen. The high-quality firm also increases its price, but not as dramatically as the low quality firm, so that it sells both its stand-alone regimen and the cocktail regimen together.

Consumers experience offsetting effects. They benefit from having one more product available in the market but are hurt by the resulting higher prices. In our case the latter (negative) effect is larger than the former (positive), so consumers are worse off with the cocktail regimen, and further worse off as the quality difference increases. Compared to the benchmark case, consumer surplus is about 0.4 percent lower when $\delta_2 - \delta_1 = 0$ and about 8.0 percent lower when $\delta_2 - \delta_1 = 2$.

We next ask whether the two firms can earn larger profits with a cocktail regimen or by merging without participating in a cocktail regimen. Figure 3 , which compares firms' profits between the cocktail regimen case and the merger case demonstrates that both firms earn larger profits with a cocktail regimen versus a merger. Firm 1's profit is about 20 percent higher when $\delta_2 - \delta_1 = 0$, and the profit difference grows as the quality gap increases. Firm 2's profit is also about 20 percent higher when $\delta_2 - \delta_1 = 0$ but the profit difference falls as the quality gap increases. This result is driven by firms charging higher prices with the cocktail regimen than in the merger case. Firm 2 charges a higher price as soon as $\delta_2 - \delta_1$ becomes larger than 0.05 and firm 1 charges a higher price when $\delta_2 - \delta_1$ becomes larger than 0.5. Despite higher prices, consumer surplus is 29 to 36 percent higher with the cocktail regimen due to the benefit of having another product available.

Interestingly, when we let the two firms merge while allowing them to keep the cocktail

regimen, the merger provides small incremental benefits. The combined profit is less than one percent higher. This implies that firms almost fully internalize externalities with the cocktail regimen. Thus, firms may not have a strong incentive to merge once they participate in a cocktail regimen, particularly if there are transactions costs associated with merging. Consumers are clearly worse off with the merger.

In the next numerical analysis we allow one of the two firms to set two separate prices: one for the stand-alone regimen and another for their drug in the cocktail regimen. This situation is equivalent to a case where a firm has two separate drugs, one used in a stand-alone regimen and the other used in a cocktail regimen. We first let firm 1, the low-quality firm, to set two separate prices while varying $\delta_2$ from 1 to 3. Figure 4 compares the two prices that firm 1 sets with its single price in the first numerical analysis. This figure demonstrates that the firm sets a much lower price for the stand-alone regimen (Price1_Single) than for the cocktail regimen (Price1_Cocktail). Over the entire range of the quality difference the former price is about a 50 percent lower than the latter.

Compared to the single price (Price1_Single) the firm sets about a 14 percent lower price for the stand-alone regimen price and a 66 percent higher price for the cocktail regimen when $\delta_2 - \delta_1 = 0$. As the quality difference increases the single price increases much faster than the other two prices. Recall that with the single pricing firm 1 sacrifices its stand-alone regimen's market share as the quality gap increases and earns profit mostly from the cocktail regimen. Now with more flexible pricing, firm 1's stand-alone regimen's market share is larger than that of the cocktail regimen, although it still free-rides the cocktail regimen's high quality by curbing the price increase for the cocktail regimen. (It is only 27 percent higher when $\delta_2 - \delta_1 = 2$ as compared to 66 percent higher when $\delta_2 - \delta_1 = 0$.)

Not surprisingly, firm 1 is better off with the more flexible pricing, while firm 2 is worse off. Firm 2 now charges about 89-90 percent of what it used to charge. Firm 1's profit is about 6 percent higher than in the single pricing case and it does not change much as the quality gap changes. Firm 2's profit is about 12 percent lower when $\delta_2 - \delta_1 = 0$ and 9 percent lower when $\delta_2 - \delta_1 = 2$. However, its profit is still higher than in the absence of the cocktail regimen (the benchmark case.)

We next let firm 2, the high quality firm, set two separate prices. Firm 2 also sets a much lower price for the stand-alone regime than for the cocktail regimen. However, both prices increase as the quality difference increases. This price increase seems to prevent firm 1 from free-riding on the cocktail regimen's high quality. Similarly as in the previous case, firm 2 is better off with the more flexible pricing while firm 1 is worse off.

We also fix $\delta_1 = 1$ and $\delta_2 = 1$, and let $r_{31}$ change from 0.5 to 0.9. This exercise helps us understand how the incentives to participate in making the cocktail regimen change when for chemical and/or biological reasons, one firm's drug constitutes a higher percentage of the cocktail recipe. We find, not surprisingly, that the profit for firm 1 increases as its mixture ratio increases, and the reverse is true for firm 2 as its mixture ratio decreases. Compared to the benchmark case, firm 1's profit is always higher and firm 2's profit is higher up to $r_{31} = 0.8$ and then becomes lower as $r_{31}$ becomes higher. We repeat this exercise by varying $r_{32}$ from 0.5 to 0.9 while fixing $\delta_1$ and $\delta_2$ and obtain qualitatively same results.

# 6 Empirical Analysis

We estimate equation (4) using regimen-level market share, price, and attribute data. Our identifying assumption is that regimen attributes other than price are not correlated with the contemporaneous demand shock. The price endogeneity problem requires using instruments to consistently estimate the demand equation. We consider two sets of instruments. The first set consists of counts and sums of attributes of other regimens in the market as in Berry, Levinsohn, and Pakes (1995) and Bresnahan, Stern, and Trajtenberg (1997). A crowded product space will shift price markups, all else equal. The price changes should not be correlated with the regimen's unobserved quality or demand shocks as long as product attributes are exogenous, as the literature usually assumes. Still one concern about these instruments is that they do not vary much over time due to infrequent product entry and exit. That is, the instruments may be weakly correlated with price.

The second set of instruments are constructed with the lagged prices of other regimens. In particular, instrument for the price of regimen $j$ in period $t$ with the average price in period $t-1$ of all regimens other than regimen $j$ and the average price in period $t-1$ of regimens produced by firms

whose drugs are not used in regimen $j$. We assume that these instruments are uncorrelated with the current period demand shock, but are correlated with the current period price. The latter part is obvious as all regimen prices are correlated in the same period through oligopolistic interactions and the price of a given product is usually autocorrelated. The former assumption requires that a demand shock for regimen $j$ in period $t$ is uncorrelated with a demand shock for regimen $k$ in period $t-1$, and is likely to hold true. However, this condition could be violated in the presence of a time persistent market level demand shock.

We use the generalized method of moments with $(\mathbf{Z}'\mathbf{Z})^{-1}$ as the weighting matrix, where $\mathbf{Z}$ includes the instrumental variables, all the observed regimen attributes other than price and the time indicators.[17] The estimates are presented in table 2. The first column shows the results of the OLS logit model. The second column, labeled IV Logit I, corresponds to the estimation with the product attribute instruments, and the third column, labeled IV Logit II, corresponds to the lagged price instruments. In all specifications we use the log of price.

The price coefficients across the columns show that there is a positive correlation between price and the demand shock, and the instrumental variables mitigate this problem. However, the attribute instruments do not seem to correct the price endogeneity as much as the lagged price instruments. We suspect this is mainly because the regimen attributes do not change over time. The price coefficient changes from -0.733 without instruments to -0.841 with the attribute instruments. The lagged price instruments, on the other hand, change the price coefficient from -0.733 to -2.176.[18]

The efficacy attribute coefficients such as the response rate and survival months show the expected positive signs and are statistically significant in OLS logit and IV logit I. The response rate coefficient becomes much larger in IV logit II, but the sign of the survival month variable becomes negative, although it is not statistically significant. Time to progression has an unexpected and statistically significant negative sign in all three specifications.

Among the side effect variables, only two of them are statistically significant and only one

[17] Our sample size is not large enough to use the optimal weighting matrix.

[18] The F-statistic from the first stage F-test for the lagged price instruments is 12.0, which confirms that our instruments are not weak.

of these two is negative as expected. This may be due to the fact that cancer patients often take drugs that ameliorate the impact of certain side effects, such as pain, nausea, and diarrhea. If a physician prescribes anti-pain and antiemetic drugs in conjunction with the anti-cancer drugs, she may downgrade the importance of these side effects when choosing a regimen. Another possible explanation is that the toxic drugs are more likely to cause side effects but have other favorable unmeasured attributes.

Given the demand estimates, we can recover the marginal cost of each drug from equation (1) , and given the marginal cost and demand estimates we can compute hypothetical equilibrium prices under various counterfactual scenarios. We focus on the last six quarters of the sample period, i.e., from the second quarter of 2004 to the third quarter of 2005. That is a period in which all 12 major regimens are present in the market. All results are averaged over these six quarters.

### 6.1 Counterfactual I

In the first counterfactual exercise we remove one cocktail regimen from the market at a time, find the new Nash equilibrium prices for all branded drugs, estimate profits for all major firms, and compute consumer surplus. This exercise is similar to the welfare counterfactual in Petrin (2002) . Because there are six cocktail regimens, we evaluate six hypothetical cases. The results are reported in Table 3. The baseline in the first row, which is what is actually observed in the market, is normalized to 100. Therefore, the table reports estimated percentage changes in prices, profits, and consumer surplus when one particular cocktail regimen is removed compared to the observed situation. The numbers in bold typeface are percentage changes for firms that participate in the removed regimen (which we refer to as "participating firms" hereafter.) The rows are ordered from the oldest to the most recent cocktail that entered the market, and the columns are ordered from the earliest firm at the left to the most recent at the right.

The first panel of the table reports the estimated price of each firm's drug, relative to the baseline situation (100.0), when the particular regimen in a row is absent. For example, the final row corresponds to a scenario where the cocktail regimen by Sanofi and Genentech, which had the highest market share of all regimens in 2005, is removed. Without this regimen, Sanofi and

Genentech are predicted to decrease their drug prices by 44.0 percent and 10.4 percent, respectively. There are several notable features of the first panel. In five out of six cases, prices of the participating firms' drugs fall as a regimen is removed. In all six cases, the price of the incumbent firm's drug in the cocktail is predicted to fall by more than the price of the entering firm, which indicates that incumbents may be setting prices to try to protect the market share of their stand-alone regimens. With a few notable exceptions, prices of drugs not used in the removed regimen generally go down as well.

The exceptions in the first panel, such as the predicted price increases in the second row, could be an outcome of having much more complicated structure of the inter-firm product combination. In the numerical analysis when the cocktail regimen is removed, each firm has one stand-alone regimen. In the market, on the other hand, all drugs other than ImClone's are used in three cocktail regimens. When one cocktail regimen is removed, therefore, participating firms will still consider their other cocktail regimens when setting prices.

The second panel of Table 3 reports estimated profit changes due to the removal of a particular regimen. No participating firm is better off without a regimen. Profit losses are sometimes substantial, especially when the market share of a cocktail is large relative to the market share of a firm's stand-alone regimen. Imclon'e profit (second to last row), for example, is predicted to fall by over 80 percent if its regimen, which has a market share three times larger than the market share of its stand-alone regimen, is removed. Non-participating firms are generally worse off too, although there are some exceptions like Roche in the Sanofi-Genentech case and ImClone in the Pfizer-Genentech case.

The final column of Table 3 reports changes in consumer surplus. The effect of removing a regimen on consumer surplus is not clear a priori. On the one hand, consumers are worse off with one fewer available product choice. In fact, the logit demand model allows variety to provide the maximum benefit. On the other hand, the lower prices that result from removing a regimen help consumers. Table 3 demonstrates that on net consumers would be better off without the cocktail regimens except in the Pfizer-Roche case, where the prices of all drugs increase. In general, the gains from the price decrease tend to outweigh the losses from having less variety.

The evidence on prices, profits and consumer welfare in Table 3 indicate that these particular inter-firm product combinations create a less competitive market that harms consumers. When firms set prices in the presence of cocktail regimens they consider the demand for the cocktail regimen as well as the demand for their stand-alone regimens. In doing so, they internalize part of the externalities they impose on their competitors, which results in a less competitive outcome.[19]

### 6.2 Counterfactual II

Table 4 reports the joint profit of the merging firms and consumer surplus when different pairs of firms merge, where the two firms' joint profit under the current situation of offering the cocktail regimen is normalized to 100. For comparison, the joint profit from the first counterfactual exercise is reported in the second column, which is labeled *Removed*. Recall that the profit loss can be as large as 49 percent when the Sanofi-Genentech regimen is removed.

In the next column labeled *Removed+Merger* we report the joint profit when the two firms merge without the cocktail regimen. This joint profit should be larger than the joint profit in the *Removed* column because firms have more market power after merging. However, this profit is not necessarily larger than the current profit with the cocktail regimen. In fact, in four of five cases the joint profit of the merger is smaller than the joint profit with the cocktail regimen; firms gain more from cocktail regimens than from mergers.[20] The difference is quite substantial in the last three cases where mergers are estimated to increase joint profit by less than 10 percent whereas cocktail regimens increase profit by at least 30 percent.

In the column labeled *Merger* in Table 4 we report the joint profit when two firms merge and maintain their cocktail regimen. This joint profit provides the maximum profit that two firms can earn pairwise because the merger allows them to fully internalize the externalities and the number of products offered is unchanged. Interestingly, this maximum joint profit is not much higher than the current joint profit. The largest increase (8.7 percent) occurs when Pfizer and Roche merge. Compared to the profit change from adding the cocktail regimen (column 1 - column

[19]This is similar to the outcome of a multiproduct monopoly which produces multiple substitutes, and sets its price maximizing total profits instead of having multiple subsidiaries (see Tirole (1998) p.70)

[20]There are five instead of six cases in this counterfactual exercise because we do not model a three-firm merger.

2), a merger increases the joint profit only marginally. This result confirms our finding in section 5 that cocktail regimens allow firms to almost fully internalize externalities.

As expected, consumer surplus decreases when firms merge without the cocktail (going from *Removed* to *Removed+Merger*) and increases when firms add the cocktail regimen while being merged (going from *Removed+Merger* to *Merger.*), as displayed toward the right of Table 4. In the former case consumer surplus falls as the market becomes less competitive; in the latter case consumer surplus rises as another product is added to the choice set.

Consumer surplus actually increases in two of the five cases where two firms offering a cocktail regimen are allowed to merge (going from *Current* to *Merger.*) Although the market becomes less competitive and the number of products is unchanged, drug prices sometimes fall. In the Pfizer-ImClone merger case, ImClone's drug price decreases by almost 30 percent. This reduces the profit of ImClone's drug but increases the profit of Pfizer's drug by more. In the Sanofi-Genentech merger case, Genentech's drug price decreases by 40 percent but the joint profit increases due to higher profits on Sanofi's drug. Consumers benefit from these price decreases, although the market becomes less competitive.

### 6.3 Counterfactual III

In our third counterfactual exercise, we allow one of the participating firms in a cocktail to set two separate prices for the same drug: one for its stand-alone regimen and one for its drug in the cocktail. This is the same exercise as the two-price setting case in section 5. Table 5 reports price, profit, and consumer surplus in these scenarios, where the baseline levels are indexed to 100. The column labeled *Solo* reports the optimal drug prices for the stand-alone regimen and the numbers in bold typeface are prices for the drug used in the cocktail regimen. In the second row, for example, Pfizer reduces the price of irinotecan by about eight percent for the stand-alone regimen while increasing the price of irinotecan by 40 percent for use in three cocktail regimens in which it participates.

Table 5 shows that the drug price for cocktail regimens can go up dramatically with additional price flexibility. Roche increases its drug price for cocktail regimens by a factor of 9 (in

the fourth row) and Sanofi does so by more than three times (in the fifth row). Drug prices for the stand-alone regimens usually decrease substantially, ranging from an eight to 18 percent. The exception is Sanofi, which increases its price by 14 percent. The other firms' reaction to the new price scheme is mixed . Roche decreases its price in all cases while the other firms increase their prices.

The second panel of the table shows that firms earn higher profits by setting two prices in all cases, which is consistent with the numerical example. However, the other firms are not necessarily worse off. Genentech is the only firm that becomes worse off in all cases. Roche and Sanofi are better off in all cases, and Pfizer and ImClone's profit changes depend on who sets two prices. This is not consistent with the numerical example where a firm's setting two prices makes the other firm worse off. The much more complicated structure of the inter-firm product combination may explain these mixed results.

We report consumer surplus in the last panel of Table 5. Since the regimen qualities do not change in this counterfactual, the only variable affecting consumer surplus is price. Consumer surplus is lower in all cases simply because consumers pay higher prices for the same quality regimens.

These counterfactual results suggest that Abott's pricing strategy with Norvir and Kaletra is not necessarily detrimental to its competitors. It depends on how firms are interconnected by other cocktail regimens. However, consumers will be hurt by Abott's pricing strategy if it drives its competitors to increase their prices significantly.

# 7 Conclusions

This paper is the first attempt to understand the economic decisions that firms need to make when their products are consumed with their competitors' products. The firm controls only the price of its own product, and therefore, it needs to take into account the effect of its pricing strategy on all the bundles its product is used.

We apply our framework to the pharmaceutical industry, in particular to colorectal cancer drugs. We estimate the regimen level demand using the unique data from IntrinsiQ and perform

counterfactual exercises using the estimated demand parameters and marginal cost. First of all, we find that inter-firm combinations are profit enhancing for all firms that participate in the combination, as the effect of internalizing externalities dominates the business stealing effect. However, consumers are worse off with the combined products, despite more variety, because they pay higher prices.

We also find that firms can earn higher profit with product combinations than with mergers. Even if firms that already have product combinations merge, the joint profit increases only marginally. Surprisingly, consumers are necessarily worse off as the merged firm may lower prices to fully internalize the externalities. These results suggest that the anticompetitive merger effects would be smaller when the products of merging firms are already consumed together in the market, and should help the government authority evaluate expected outcomes of the recent merger waves in the pharmaceutical market.

In addition, we find that if any of the firms has two drugs, one for the stand-alone regimen and another for the cocktail regimen, it sets a much higher price for the cocktail regimen, while setting a lower price for the stand-alone regimen, compared to the single price setting. This more flexible pricing brings in higher profits, but the other firms are not necessarily worse off as they may respond by increasing their prices. However, consumers are hurt by this price increase.

## References


[1] Adams, W, and J. Yellen (1976), "Commodity Bundling and the Burden of Monopoly," *Quarterly Journal of Economics*, 90, 475-498.

[2] Berry, S. (1994), "Estimating Discrete Choice Models of Product Differentiation," *RAND Journal of Economics*, 25, 242-262.

[3] Berry, S., J. Levinsohn, and A. Pakes (1995), "Automobile Prices in Market Equilibrium," *Econometrica*, 63, 841-890.

[4] Berry, S. and A. Pakes (2007), "The Pure Characteristics Demand Model," *International Economic Review,* 48, 1193-1225.

[5] Blume-Kohout, M. and Sood, N. (2008), "The Impact of Medicare Part D on Pharmaceutical R&D," *NBER Working Paper No.13857*

[6] Bresnahan, T., S. Stern, and M. Trajtenberg (1997). "Market segmentation and the sources of rents from innovation: personal computers in the late 1980s," *RAND Journal of Economics*, 28, 17–44.

[7] Carlton, D. and M. Waldman (2002), "The Strategic Use of Tying to Preserve and Create Market Power in Evolving Industries," *Rand Journal of Economics*, 33, 194–220.

[8] Carlton, D, J. Gans, and M. Waldman (2007), "Why Tie a Product Consumers Do Not Use?," NBER Working Paper 13339.

[9] Chen, Y. (1997), "Equilibrium Product Bundling," *Journal of Business*, 70, 85–103.

[10] Choi, J.P. (2008), "Mergers With Bundling in Complementary Markets," *Journal of Industrial Economics*, 56, 553-577.

[11] Jacobson, M., J. O'Malley, C. Earle, P. Gaccione, J. Pakes and J. Newhouse (2006), "Does Reimbursement Influence Chemotherapy Treatment for Cancer Patients?," *Health Affairs*, 25, 437-443.

[12] Lucarelli, C. and S. Nicholson (2009), "A Quality-Adjusted Price Index for Colorectal Cancer Drugs," *NBER Working Paper No. 15174*

[13] Matutes, C. and P. Regibeau (1988), "Mix and Match: Product Compatibility without Network Externalities," *RAND Journal of Economics*, 88, 221-234.

[14] McAfee, R., J. McMillan, and M. Whinston (1989), "Multiproduct Monopoly, Commodity Bundling, and Correlation of Values," *Quarterly Journal of Economics*, 104, 371–383.

[15] McFadden, D. (1981), "Econometric Models of Probabilistic Choice," *Structural Analysis of Discrete Data with Econometric Applications*, Manski. C and McFadden. D ed., The MIT Press.

[16] Nalebuff, B. (2004), "Bundling As an Entry Barrier," *Quarterly Journal of Economics*, 119, 159–187.

[17] Nevo, A. (2000), "Mergers with Differentiated Products: The Case of the Ready-to-Eat Cereal Industry," *RAND Journal of Economics,* 31, 395-421.

[18] Petrin, A. (2002), "Quantifying the Benefits of New Products: The Case of the Minivan," *Journal of Political Economy*, 110, 705-729.

[19] Song, M (2007), "Measuring Consumer Welfare in the CPU Market: An Application of the Pure Characteristics Demand Model," *RAND Journal of Economics,* 38, 429-446.

[20] Tirole, J. (1998), *The Theory of Industrial Organization*, MIT Press: Cambridge, MA.

[21] Town, R. (2001), "The Effects of HMO Mergers," *Journal of Health Economics*, 20, 733-753.

[22] Whinston, M. (1990), "Tying, Foreclosure, and Exclusion," *American Economic Review*, 80, 837–859.

Table 1: Regimen Attributes: The Sample Average

| | | Efficacy | | | Grade 3 or Grade 4 Side Effects (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Time | Regimen Price (24 week treatment) | Survival Months | Response Rate | Time to Progression | Abdominal Pain | Diarrhea | Nausea | Vomiting | Neutro-penia |
| 1993 | 120.93 | 12.48 | 20.80 | 4.73 | 5.50 | 10.40 | 4.80 | 4.40 | 33.70 |
| 1994 | 119.42 | 12.48 | 20.80 | 4.73 | 5.50 | 10.40 | 4.80 | 4.40 | 33.70 |
| 1995 | 115.95 | 12.48 | 20.80 | 4.73 | 5.50 | 10.40 | 4.80 | 4.40 | 33.70 |
| 1996 | 125.91 | 12.48 | 20.80 | 4.73 | 5.50 | 10.40 | 4.80 | 4.40 | 33.70 |
| 1997 | 94.38 | 12.48 | 20.80 | 4.73 | 5.50 | 10.40 | 4.80 | 4.40 | 33.70 |
| 1998 | 11,272.91 | 12.53 | 23.73 | 5.21 | 8.93 | 21.80 | 11.23 | 8.13 | 33.07 |
| 1999 | 12,122.11 | 12.53 | 23.73 | 5.21 | 8.93 | 21.80 | 11.23 | 8.13 | 33.07 |
| 2000 | 12,871.24 | 12.53 | 23.73 | 5.21 | 8.93 | 21.80 | 11.23 | 8.13 | 33.07 |
| 2001 | 12,955.49 | 12.78 | 23.83 | 5.14 | 8.85 | 20.72 | 10.00 | 7.49 | 28.13 |
| 2002 | 17,087.39 | 14.03 | 27.76 | 5.81 | 7.99 | 20.56 | 9.93 | 7.53 | 27.33 |
| 2003 | 20,181.95 | 14.81 | 30.02 | 6.28 | 7.66 | 20.24 | 9.94 | 7.67 | 26.31 |
| 2004 | 37,434.78 | 14.71 | 30.90 | 6.66 | 7.88 | 20.49 | 7.87 | 6.83 | 19.97 |
| 2005 | 37,169.33 | 14.71 | 30.90 | 6.66 | 7.88 | 20.49 | 7.87 | 6.83 | 19.97 |

See the text for variable explanations.

Table 2: Demand Estimation Results

| Variable | OLS Logit | IV Logit I | IV Logit II |
|---|---|---|---|
| $\log(price)$ | -0.733** | -0.841** | -2.176** |
| | (0.098) | (0.117) | (0.448) |
| Survival (months) | 0.179** | 0.155** | -0.138 |
| | (0.052) | (0.058) | (0.120) |
| Response Rate (%) | 0.285** | 0.341** | 1.030** |
| | (0.058) | (0.069) | (0.232) |
| Time to Progression (months) | -1.265** | -1.398** | -3.051** |
| | (0.215) | (0.224) | (0.599) |
| Diarrhea | 0.011 | 0.015 | 0.057 |
| | (0.018) | (0.014) | (0.034) |
| Nausea | 0.081 | 0.088 | 0.167 |
| | (0.065) | (0.067) | (0.098) |
| Abdom_pain | 0.186** | 0.236** | 0.851** |
| | (0.061) | (0.071) | (0.208) |
| Vomiting | -0.111 | -0.107 | -0.053 |
| | (0.097) | (0.096) | (0.143) |
| Neutropenia | -0.058** | -0.066** | -0.161** |
| | (0.010) | (0.011) | (0.032) |

Table 3: Counterfactual Simulation I

| | Price Changes (per mg) | | | | | Profit Changes | | | | | CS |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Pfizer | Roche | Sanofi | Imclone | Genentech | Pfizer | Roche | Sanofi | Imclone | Genentech | |
| Current | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| No Pf + Ro | **101.9** | **113.0** | 100.3 | 100.3 | 100.1 | **94.4** | **95.8** | 100.2 | 100.1 | 99.7 | 99.6 |
| No Ro + Sa | 92.4 | **70.1** | **89.1** | 97.8 | 93.4 | 91.8 | **80.3** | **87.1** | 89.8 | 96.3 | 107.6 |
| No Pf + Ge | **47.8** | 187.1 | 97.4 | 89.3 | **78.3** | **76.0** | 88.6 | 90.2 | 106.6 | **67.4** | 113.1 |
| No Ro + Sa + Ge | 97.7 | **88.9** | **96.4** | 99.3 | **96.0** | 97.2 | **94.9** | **97.7** | 95.9 | **96.7** | 102.8 |
| No Pf + Im | **59.7** | 234.9 | 92.0 | **71.6** | 95.5 | **85.5** | 94.5 | 90.1 | **19.8** | 102.2 | 107.5 |
| No Sa + Ge | 86.9 | 230.2 | **56.0** | 96.2 | **89.6** | 80.9 | 106.7 | **80.5** | 79.4 | **18.6** | 118.1 |

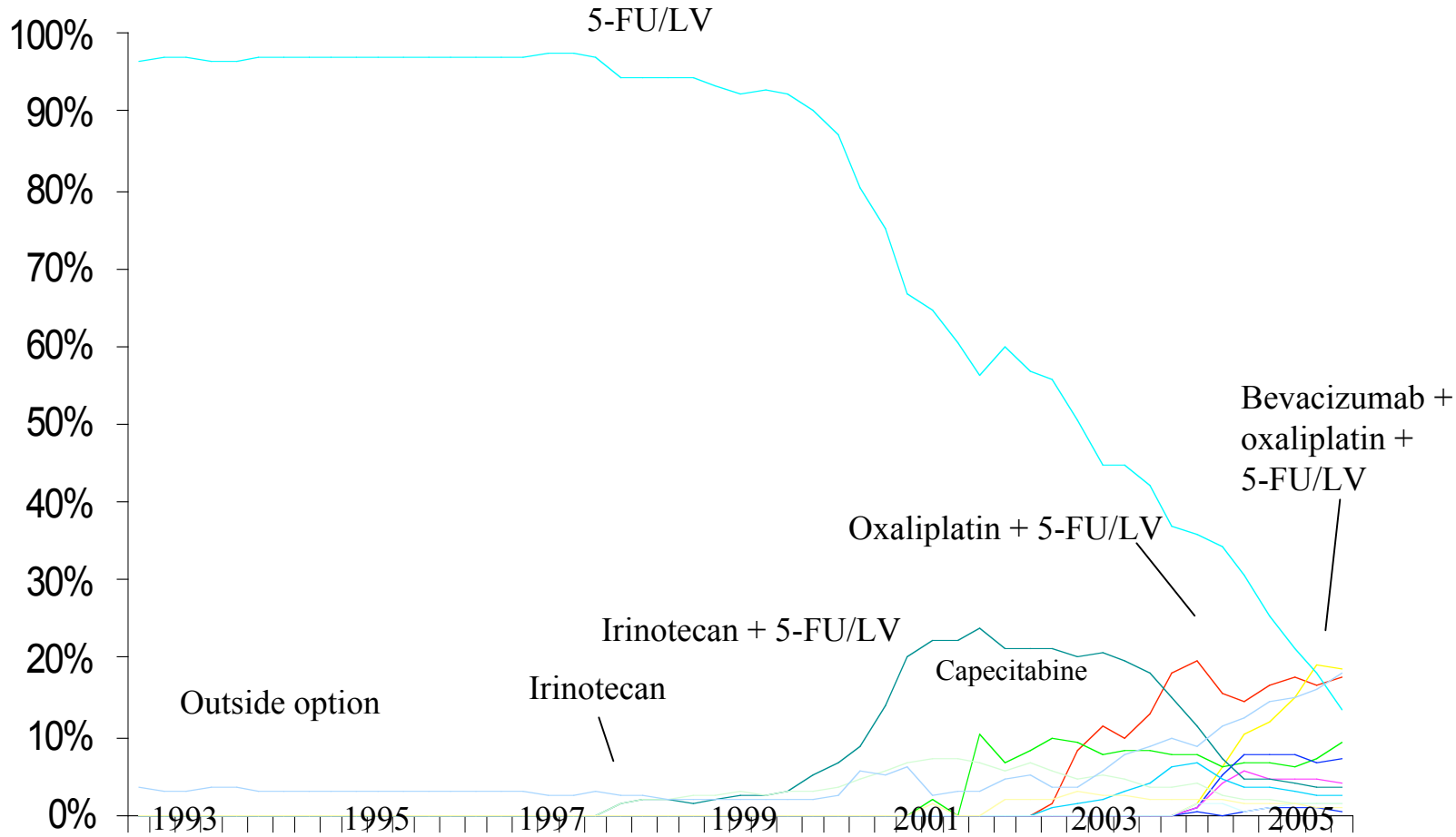
Table 4: Counterfactual Simulation II: Merger

| | Two Firms' Joint Profit Changes | | | | Consumer Surplus Changes | | | |
|---|---|---|---|---|---|---|---|---|
| | Current | Removed | Removed+Merger | Merger | Current | Removed | Removed+Merger | Merger |
| Pfizer + Roche | 100 | 94.6 | 105.5 | 108.7 | 100 | 99.6 | 85.7 | 87.3 |
| Roche + Sanofi | 100 | 86.7 | 99.0 | 105.5 | 100 | 107.6 | 88.0 | 90.7 |
| Pfizer + Genentech | 100 | 70.1 | 78.4 | 100.0 | 100 | 113.1 | 89.1 | 98.3 |
| Pfizer + Imclone | 100 | 63.2 | 64.6 | 102.2 | 100 | 107.5 | 102.9 | 105.0 |
| Sanofi + Genentech | 100 | 51.0 | 53.4 | 103.5 | 100 | 118.1 | 102.6 | 110.7 |

Table 5: Counterfactual Simulation III

| | Price Changes (per mg) | | | | | | Profit Changes | | | | | CS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Solo | Pfizer | Roche | Sanofi | Imclone | Genentech | Pfizer | Roche | Sanofi | Imclone | Genentech | |
| Current | | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| Pfizer 1 | 92.4 | **139.2** | 91.2 | 171.1 | 112.7 | 152.7 | **120.1** | 116.4 | 101.3 | 116.6 | 87.5 | 83.0 |
| Pfizer 2 | 85.0 | **225.2** | 90.4 | 176.1 | 123.7 | 157.8 | **120.5** | 125.3 | 108.4 | 96.2 | 85.1 | 78.0 |
| Roche | 87.4 | 211.0 | **935.3** | 186.7 | 122.7 | 162.5 | 113.3 | **179.6** | 100.4 | 105.8 | 86.1 | 75.2 |
| Sanofi | 113.7 | 197.3 | 82.3 | **371.3** | 120.4 | 218.7 | 96.5 | 114.0 | **107.2** | 98.8 | 47.3 | 80.9 |
| Imclone | 82.1 | 187.8 | 91.3 | 176.4 | **140.8** | 158.4 | 107.9 | 126.4 | 108.8 | **113.9** | 88.6 | 77.7 |

Figure 1: Regimen Market Shares, 1993-2005




Source: IntrinsiQ and SEER.
Market share is measured as the percentage of colon cancer patients who are treated with drugs that are treated with a specific regimen.

Figure 2: Profit Comprison between the Cocktail Regimen and the Benchmark Cases

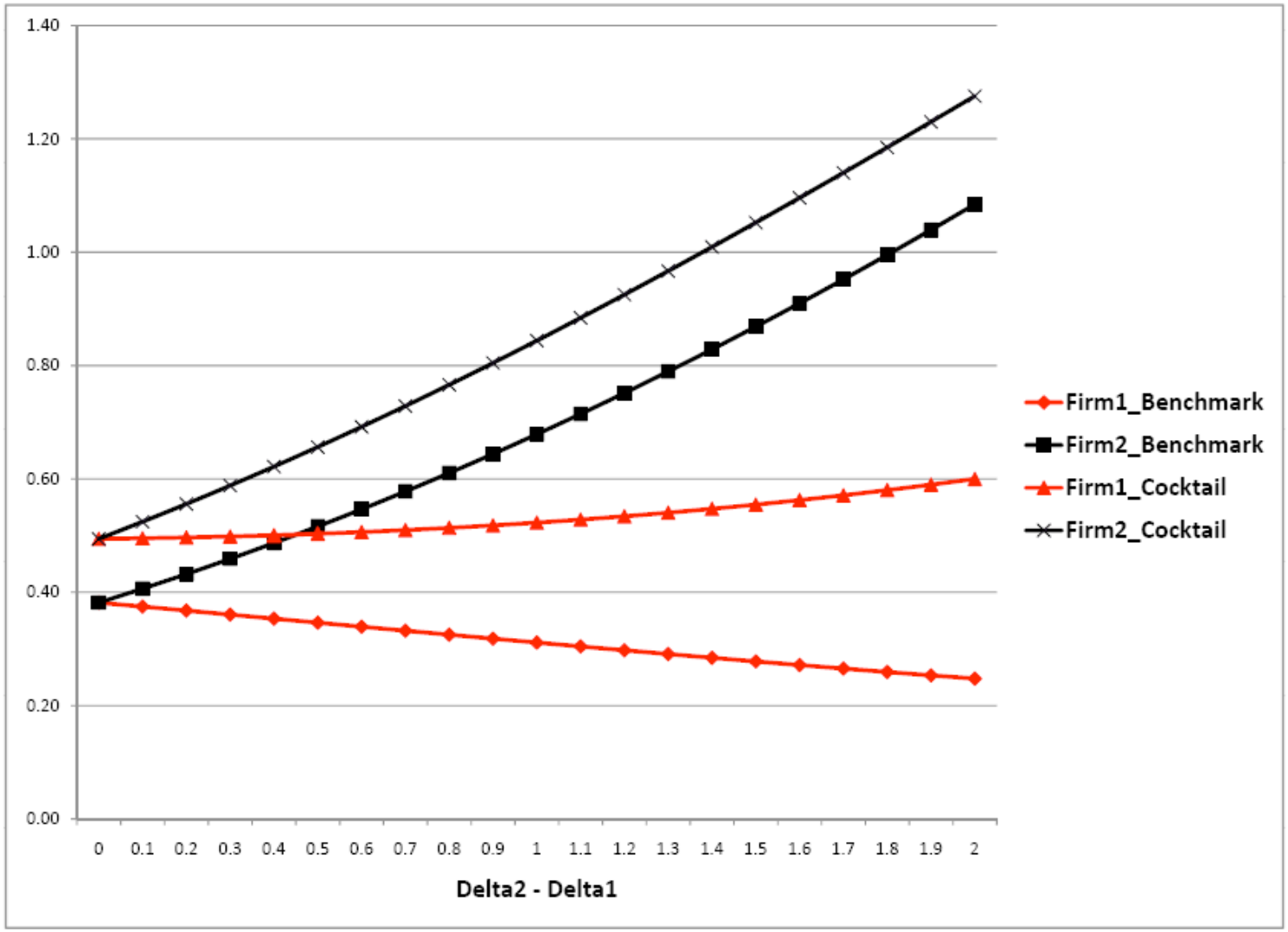


Figure 3: Profit Comparison Between the Cocktail Regimen and the Merger Cases

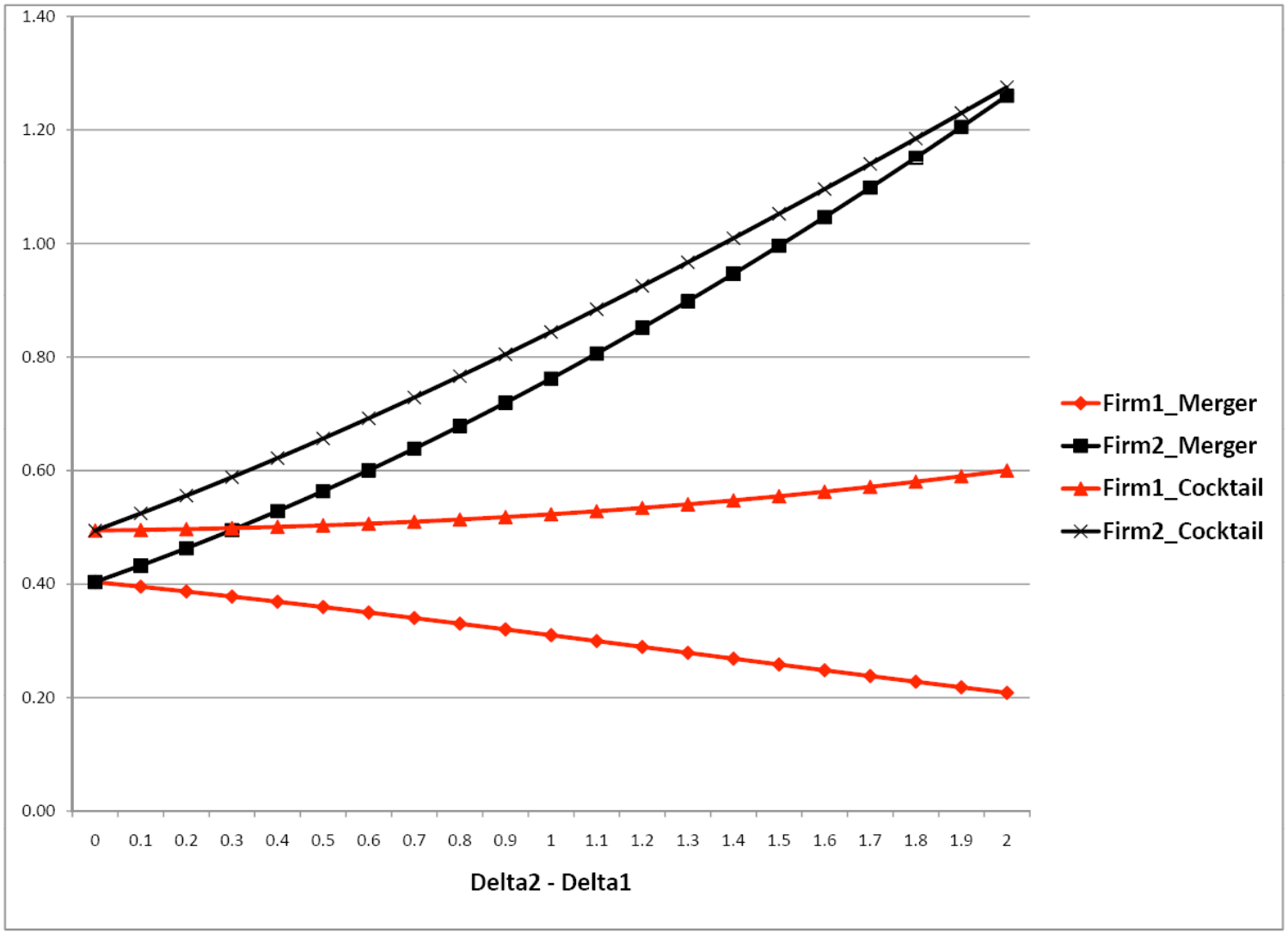
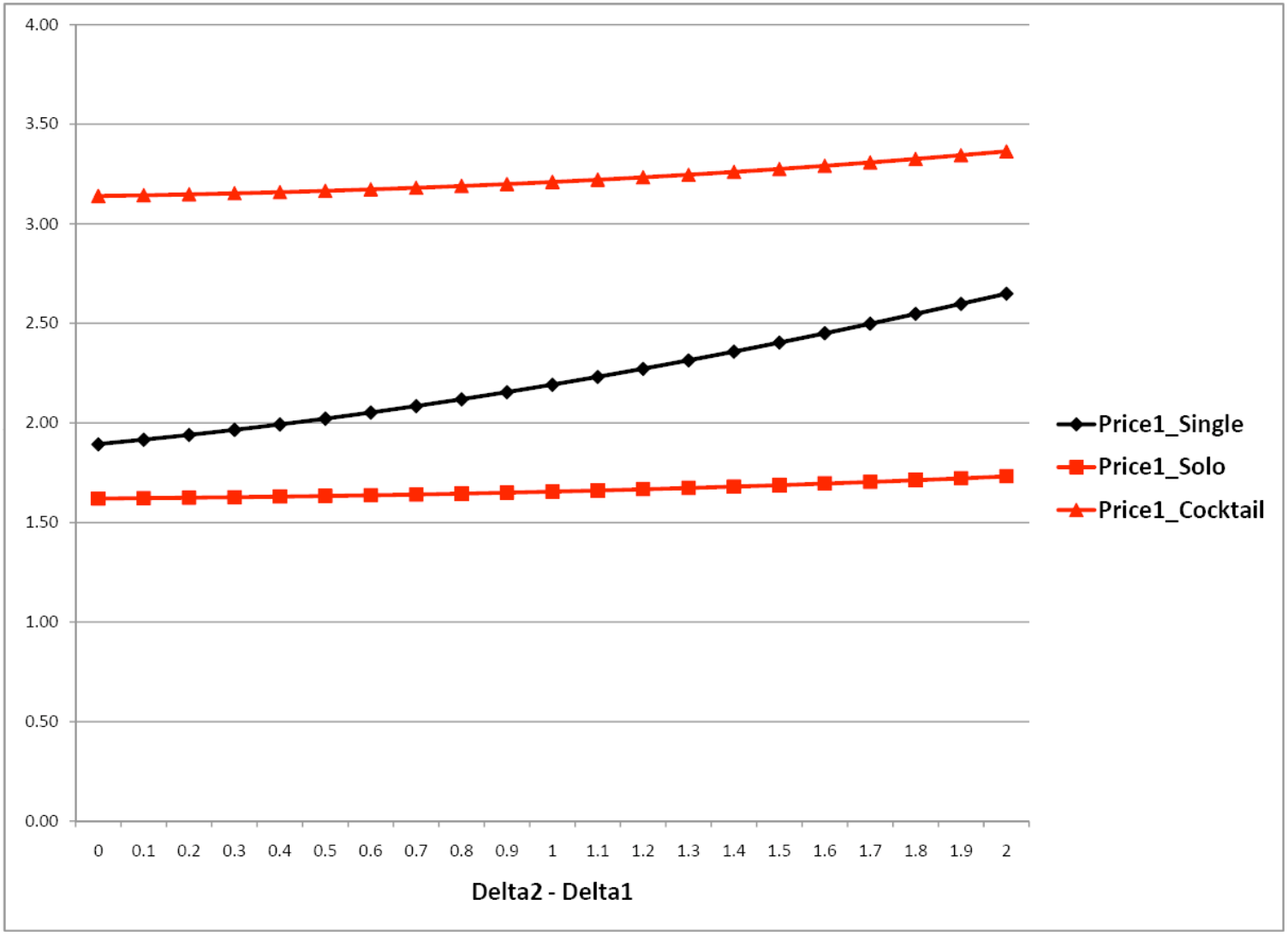


Figure 4: Price Comparison: The Low Quality Firm Setting Two Prices



**Appendix: Composition and Dosages of the Chemotherapy Regimen**

| Regimen | 1st Drug | 2nd Drug | 3rd Drug | 4th Drug |
|---|---|---|---|---|
| 5-FU + Leucovorin[20] | 425 mg of 5-FU/$m^2$/day for days 1-5, every 4 weeks | 20 mg of Leucovorin/$m^2$/day for days 1-5, every 4 weeks | | |
| Irinotecan | 125 mg of irinotecan per week/$m^2$ for 4 weeks, every 6 weeks | | | |
| Irinotecan + 5-FU/LV[21] | 180 mg of irinotecan/$m^2$ on day 1, every 2 weeks | 1,000 mg of 5-FU/$m^2$ on day 1 and 2, every 2 weeks | 200 mg of Leucovorin/$m^2$ on day 1 and day 2, every 2 weeks | |
| Capecitabine | 2,500 mg of capecitabine per $m^2$/day for days 1-14, every 3 weeks | | | |
| Capecitabine + irinotecan | 70 mg of irinotecan/$m^2$/week, every 6 weeks | 2,000 mg of capecitabine per $m^2$/day for days 1-14, every 3 weeks | | |
| Oxaliplatin + 5-FU/LV[22] | 85 mg of oxaliplatin per $m^2$ on day 1, every 2 weeks | 1,000 mg of 5-FU/$m^2$ on day 1 and day 2, every 2 weeks | 200 mg of Leucovorin/$m^2$ on day 1 and day 2, every 2 weeks | |
| Oxaliplatin + capecitabine | 130 mg of oxaliplatin per $m^2$ on day 1, every 3 weeks | 1,700 mg of capecitabine per $m^2$/day for days 1-14, every 3 weeks | | |
| Cetuximab | 400 mg of cetuximab per $m^2$ on day 1; then 250 mg/$m^2$ once a week, every 6 weeks | | | |

[20] Mayo treatment method.
[21] FOLFIRI treatment method.
[22] FOLFOX treatment method.

| | | | | |
|---|---|---|---|---|
| Cetuximab + irinotecan | 400 mg of cetuximab per $m^2$ on day 1; then 250 mg/$m^2$ once a week, every 6 weeks | 125 mg of irinotecan per week/$m^2$ for 4 weeks, every 6 weeks | | |
| Bevacizumab + oxaliplatin + 5-FU/LV | 5 mg of bevacizumab per kg, every 2 weeks | 85 mg of oxaliplatin per $m^2$ on day 1, every 2 weeks | 1,000 mg of 5-FU/$m^2$ on day 1 and day 2, every 2 weeks | 200 mg of Leucovorin/$m^2$ on day 1 and day 2, every 2 weeks |
| Bevacizumab + irinotecan + 5-FU/LV | 5 mg of bevacizumab per kg, every 2 weeks | 180 mg of irinotecan/$m^2$ on day 1, every 2 weeks | 1,000 mg of 5-FU/$m^2$ on day 1 and 2, every 2 weeks | 200 mg of Leucovorin/$m^2$ on day 1 and day 2, every 2 weeks |
| Bevacizumab + oxaliplatin + capecitabine[23] | 7.5 mg of bevacizumab per kg, every 3 weeks | 130 mg of irinotecan/$m^2$ on day 1, every 3 weeks | 1,700 mg of capecitabine per $m^2$/day for days 1-14, every 3 weeks | |

**Notes**: each regimen is assumed to last for 24 weeks. The four-week 5-FU + Leucovorin regimen, for example, is assumed to be repeated six times during a patient's treatment cycle. mg = milligram of active ingredient; $m^2$ = meter squared of a patient's surface area; kg = kilogram of a patient's weight. We price the regimens for a patient who has a surface area of 1.7 $m^2$ and weighs 80 kilograms.

Source: National Comprehensive Cancer Network, Colon Cancer, Version 2.2006; package inserts.

[23] CAPOX treatment method.