Bundling Among Rivals: A Case of Pharmaceutical Cocktails

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Abstract

We empirically analyze the welfare effects of inter-firm bundling in the pharmaceutical industry, also known as "cocktail" regimens. Firms often cannot price discriminate because each drug is produced by a different firm and a physician creates a bundle in her office from component drugs. We show that under this linear pricing a new cocktail regimen tends to make the market less competitive by increasing the prices of all regimens that use the same component drugs. We also show that a merger between the firms that have a cocktail regimen in common is less anticompetitive than the standard merger. This is because the cocktail regimen is a complement to the merging firms’ other regimens that use the same drugs.
1 Introduction

In the pharmaceutical market patients often take a combination of two or more drugs in order to improve the efficacy of treating a disease or to alleviate side effects. Most HIV/AIDS patients, for example, receive a "cocktail" regimen, such as efavirenz, lamivudine, and zidovudine. Three of the six new cholesterol-reducing drugs entering phase 3 clinical trials in 2007 were combinations of drugs that had already been approved as stand-alone products to treat the disease (Blume-Kohout and Sood, 2008). In 2008, thirty-one percent of U.S. colorectal cancer patients receiving chemotherapy treatment were administered cocktail regimens.

A pharmaceutical cocktail is an example of inter-firm bundling where a bundle consists of products produced by different and often competing firms. Armstrong (2012) lists several examples of inter-firm bundling including a city pass that allows tourists to visit all participating tourist attractions, a subscription for a bundle of academic journals owned by different publishers, alliances between airlines, and discounts for joint purchase of gasoline at gas stations and groceries at supermarkets. A pharmaceutical cocktail is also an example of mixed bundling where a bundle and stand-alone products are substitutes for one another. In the colorectal cancer treatment market in the early 2000s, for example, five patent-protected drugs were used in 12 major regimens. Four drugs were used as stand-alone regimens while eight cocktail regimens were created by combining the five drugs in various ways. Armstrong’s (2012) examples above also represent mixed bundling situations.

In this paper we analyze empirically the welfare effects of inter-firm bundling, focusing on pharmaceutical treatment of colorectal cancer patients. The existing literature on bundling does not provide much guidance in understanding the economic implications of inter-firm bundling, especially in a setting where a bundle and its components are substitutes for one another. The literature identifies two main motivations for firms to offer a bundle. One is to extract more consumer surplus when consumers have heterogeneous valuations for two individual products produced by the same multiproduct firm (Adams and Yellen, 1976; Long, 1984; McAfee, McMillan, and Winston, 1989, among many others). Bundles in these settings typically consist of entirely unrelated products such that the utility consumers receive from the bundle is the same as the sum of the utilities they receive from the individual products. The other motivation is to leverage monopoly power in the
primary market by foreclosing sales and discouraging entry in the secondary market (Whinston, 1990; Chen, 1997; Carlton and Waldman, 2002; Nalebuff, 2004; Carlton, Gans, and Waldman, 2007). This motivation usually involves a bundle of complements such as Microsoft’s Internet Explorer bundled with its operating system, although the argument still holds for a bundle of unrelated products.

More recently, Armstrong (2012) relaxes two key assumptions in the literature by allowing products in a bundle to be (1) produced by separate sellers and (2) substitutes. In his model products are substitutes in a sense that the purchase of one product decreases a consumer’s incremental utility of the second product. He shows that an integrated firm typically has a greater incentive to offer a bundle discount when products are substitutes (than when products are unrelated) and that separate sellers also wish to offer a joint-purchase discount when there is a constant disutility of consuming the two products together. Gans and King (2006) also analyze inter-firm bundling but only consider a bundle of unrelated products such as discounts for joint purchase of gasoline at gas stations and groceries at supermarkets. They show that such bundling can give these firms a strategic advantage against competitors who are not engaged in inter-firm bundling.

The pharmaceutical cocktail case is most closely related to Armstrong (2012) in the sense that a bundle consists of products of rival firms and these individual products are substitutes for each other and for the bundle. Unlike Armstrong, however, we do not restrict the utility of consuming the bundle to be smaller than the sum of the utilities of consuming the individual products separately. It is important to note that cocktail regimens must be approved by the Food and Drug Administration (FDA) by demonstrating superior efficacy, fewer side effects, or greater convenience relative to existing drugs, even if the cocktails combine already-approved drugs. This means that cocktails are as preferable as, or more preferable to, existing regimens for a subset of consumers, and thus, their utilities cannot be restricted in simplistic ways. At the same time, cocktails are imperfect substitutes for existing regimens in the sense that the demand for one regimen goes down as the price of another regimen goes down. For these reasons we use a discrete-choice framework to describe and estimate regimen demand.

We address the following welfare questions. First, do pharmaceutical firms benefit when their drugs are used in cocktail regimens? Firms entering the oncology market often test their experimental drug in combination with a drug that is already approved. The entering firm can
purchase the approved drug without the permission of the incumbent firm, and administer the two
drugs together in a clinical trial. Since this cocktail regimen is a new treatment option, firms whose
drugs are used in it now have an additional product. Whether firms benefit from cocktails will
depend on how cocktails impact drug prices and overall drug demand. However, since this new
product is a bundle "co-owned" by two competing firms, cocktails will not affect equilibrium prices
and profits in the same way as in the standard multiproduct oligopoly setting.

An anecdote in the HIV/AIDS treatment market shows an interesting strategic pricing
behavior stemming from inter-firm bundling. In the early 2000s Abbott launched Kaletra, a new
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 its competitor’s drug. Shortly after the launch
of Kaletra, Abbott increased Norvir’s price four-fold while pricing Kaletra more competitively,
presumably to drive customers from the cocktail regimen to its new stand-alone regimen. We show
later that Abbott’s behavior is consistent with a profit-maximizing firm’s pricing behavior in the
presence of inter-firm bundles, and that consumers are not necessarily hurt by this pricing strategy.

Second, do patients (as consumers) benefit from the presence of cocktail regimens? By
revealed preference the patients treated with a new cocktail regimen experience a positive net
benefit. However, the welfare effects for those treated with existing regimens depend on how the
new cocktail regimen affects existing drug prices. Again, because the cocktail regimen is a bundle
of drugs produced by competing firms, the standard oligopolistic pricing theory does not provide
complete guidance here.

Third, how would the market structure change if firms who share a bundle merged? This
is an important antitrust policy question for the pharmaceutical industry as well as the industries
mentioned above where firms are interconnected through bundles. However, little is known about
the merger effects in the presence of inter-firm bundling.

To answer these questions we estimate a structural model that allows us to estimate the
welfare effects of each regimen and to analyze hypothetical merger effects. We begin by estimating
a demand system at the regimen level using data on regimen prices, market shares, and attributes.
Regimens, which can be single drugs or cocktails of two or more drugs, are well defined and
standardized. The National Comprehensive Cancer Network (NCCN) recommends the amount of
each drug that oncologists should use in each regimen based on the dosages used in clinical trials
or in actual practice. Market share is defined as the proportion of chemotherapy patients treated with a particular regimen. Data from randomized clinical trials provide information on attributes such as regimen efficacy (e.g., the median number of months patients survived in the clinical trial) and side effects (e.g., the percent of patients in the clinical trial who experienced abdominal pain).

A regimen price is determined by the prices of drugs used and their dosages. It is important to note that for colorectal cancer regimens, pharmaceutical firms are constrained to charge the same price (per milligram of active ingredient) for their drugs whether they are used in stand-alone regimens or in cocktail regimens. This pricing constraint exists because oncologists purchase the component drugs from different manufacturers and then infuse them into a patient in an office or hospital clinic.\(^1\) This means that firms set single drug prices, i.e., a price per milligram, regardless of how their drugs are used.\(^2\) This linear pricing constraint also means that a cocktail regimen can be a complement to stand-alone regimens that use the same drugs. Suppose a cocktail regimen consists of two drugs that are produced by two different firms and these two drugs are also used in stand-alone regimens. If one of the firms lowers the price of its own drug, it increases demand not only for its stand-alone regimen but also for the cocktail regimen.\(^3\)

We use the demand estimates and profit maximization conditions to recover the marginal cost for each drug. Then we fix the marginal costs and demand parameters and compute new equilibrium prices arising from a series of counterfactual scenarios. We address the first two welfare questions by removing cocktail regimens one at a time and computing new equilibrium prices and market shares. We assume that drug-level marginal costs and patients’ preference regarding efficacy and side effects do not change when a regimen is removed, whereas regimen-level own- and cross-price elasticities do change. We find that profits of all firms involved in that cocktail decrease and consumer surplus increases when a cocktail is removed. This suggests that cocktail regimens increase profits for an entrant as well as the incumbent, but harm consumers. Profits increase because cocktail regimens are sufficiently differentiated such that they tend to increase both overall drug demand and prices. Consumers are hurt because the cost of higher prices outweighs the benefit

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\(^1\) Most HIV/AIDS patients, on the other hand, take a single pill that contains two or more separate drugs, which allows a single firm to set a bundle price.

\(^2\) This linear pricing case is more restrictive than cases where firms set different prices for component drugs used in a bundle, but our analysis can be easily extended to cases where firms set a bundle discount (or premium). See 6.3.

\(^3\) This complementarity can also arise with a bundle discount (premium) if the discount (premium) rate is fixed ex ante. See Gans and King (2006).
of having additional treatment options.

In the second counterfactual we address the third question posed above by comparing the observed market to markets with hypothetical mergers between firms that contribute a component drug to a cocktail. We consider two merger scenarios. In the first scenario we remove a cocktail regimen that two firms have in common and allow them to merge in order to compare profits from having a cocktail regimen with profits from a merger. We find that firms can earn higher profits from having a cocktail regimen than from merging. In the second merger scenario we allow a pair of firms to merge while maintaining their cocktail regimen. We find that this merger never increases profits substantially and prices even go down in some cases. Specifically, a firm’s profit never increases by more than 12 percent. This result arises because of the complementarity between the cocktail regimen and the stand-alone regimen, which suggests that mergers among firms that already have cocktail regimens in common may have relatively small incremental anticompetitive effects.4

In the third counterfactual we select one cocktail regimen at a time and allow its two firms to set two separate drug prices, one for the component drug when used in the cocktail regimen and the other for the drug when used in other regimens (stand-alone regimens or other cocktails). This is equivalent to a case in Armstrong (2012) where firms can unilaterally offer a discount or premium for an inter-firm bundle. We find that firms usually set the price of the cocktail component drug much higher, resulting in a bundle premium, when allowed this flexibility. We also confirm one of the main propositions in Armstrong (2012) that the relative price elasticity of a bundle to total demand determines whether firms offer a bundle discount or premium. This nonlinear pricing behavior is similar to what we observe in the Abbott case mentioned above and provides an "out-of-sample" validation for our static Nash pricing assumption.

In addition to the bundling literature, this paper is also related to the literature on the determinants of pharmaceutical prices. Saha et. al. (2006), Frank and Salkever (1997), and Grabowski and Vernon (1992) show how prices fall as generic firms enter following the expiration of a patent; Duggan and Scott Morton (2006) examine how Medicaid policy affects pharmaceutical prices in the non-Medicaid market; and Duggan and Scott Morton (2010), Lichtenbeg and Sun (2007), Ketcham and Simon (2008), Yin et. al. (2008), and Lakdawalla and Yin (2010) demonstrate

\[4\text{\ However, this result only holds under the linear pricing.}\]
that the expansion of prescription drug insurance to Medicare beneficiaries caused pharmaceutical prices to fall. Unlike the studies mentioned above, we use a demand model to analyze the welfare effects of firms' pricing decisions, focusing on a sector where all chemotherapy options are imperfect substitutes for one another. The structural model allows us to estimate the welfare effects of each regimen and also to analyze hypothetical merger effects.

In Section 2 we present an overview of colorectal cancer treatment and describe the data in Section 3. We present the model in Section 4, followed by results from the demand estimation in Section 5. We present the three counterfactual exercises in Section 6. We conclude in Section 7.

## 2 Overview of Colorectal Cancer

Colorectal cancer is the fourth most common cancer based on the number of newly-diagnosed patients, after breast, prostate, and lung cancers. About one in 20 people born today is expected to be diagnosed with colorectal cancer over their lifetime. The disease is treatable if it is detected before it metastasizes, or spreads, to other areas of the body. According to the National Cancer Institute, colorectal cancer patients had a 65 percent chance of surviving for five years and a 58 percent chance of surviving for 10 years between 1999 and 2006. The probability that a patient will survive for five years ranges from 90 percent for those diagnosed with Stage I cancer to 12 percent for those diagnosed with Stage IV (or metastatic) cancer.\(^5\)

The way a colorectal cancer patient is treated depends on the stage of the tumor at diagnosis. Most patients with a Stage I, II, or III tumor will have the tumor removed surgically, i.e., resected. The NCCN recommends that patients with Stage III disease receive six months of chemotherapy following the resection; they do not recommend chemotherapy for Stage I patients and they encourage Stage II patients to discuss the benefits and costs of chemotherapy with their oncologist before deciding. The majority of patients diagnosed with Stage IV disease have an unresectable tumor. Some of these patients receive chemotherapy to shrink the tumor such that it can be resected, and many receive chemotherapy without prior surgical treatment. Our demand model describes patients’ chemotherapy treatment choices once they have decided to receive chemotherapy; we assume patients have already decided whether or not to receive surgery prior to

\(^5\)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).
chemotherapy treatment.

Five pharmaceutical firms produced a patent-protected (or branded) colorectal cancer drug during our study period: Pfizer (which produced irinotecan), Roche (capecitabine), Sanofi (oxaliplatin), ImClone (cetuximab), and Genentech (bevacizumab). There were 12 major treatment regimens during our sample period, half of which were cocktail regimens composed of two or more branded drugs, five of which consisted of a single branded drug, and one that was a generic drug. In one cocktail regimen, Roche’s capecitabine is combined with Pfizer’s irinotecan. In another capecitabine is combined with Sanofi’s oxaliplatin. Genentech’s bevacizumab is combined separately with oxaliplatin and capecitabine; oxaliplatin; irinotecan to create three distinct cocktail regimens. Finally, ImClone’s cetuximab is combined with Pfizer’s irinotecan.

Three of the six non-cocktail regimens are individual drugs used in the cocktail regimens mentioned above, but in different dosages. The other non-cocktail regimens are fluourouracil combined with leucovorin (5-FU/LV), both of which are generic drugs, Pfizer’s irinotecan combined with 5-FU/LV, and Sanofi’s oxaliplatin combined with 5-FU/LV. We take the generic drug prices as given and assume they are priced at marginal cost, not the result of firms’ strategic pricing. We therefore treat the last two regimens above as being stand-alone regimens. Appendix I provides a complete description of the recommended dosage for the 12 regimens for which we have complete data.

The National Comprehensive Cancer Network (NCCN) divides colorectal cancer chemotherapy regimens into two groups. For early-stage patients who cannot tolerate intensive therapy, it recommends 5-FU/LV (the generic regimen), Roche’s stand-alone regimen, or the Pfizer-Roche cocktail regimen. The other regimens are recommended for those who can tolerate the possible side effects of intensive therapy. The NCCN also provides chemotherapy guidelines for patients whose cancer progresses in spite of the first chemotherapy treatment. For example, if the Roche-Sanofi cocktail regimen was selected for initial therapy, the NCCN recommends the Pfizer-ImClone cocktail for second-line chemotherapy treatment. In Section 4.2 we use these guidelines to define the

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6 Drugs have brand names in addition to the generic names that we provide in the text. The brand names of the five patent-protected drugs are as follows: Camptosar (irinotecan), Xeloda (capecitabine), Eloxatin (oxaliplatin), Avastin (bevacizumab), and Erbitux (cetuximab). ImClone has since been acquired by Bristol Myers; Genentech has since been acquired by Roche; and Pharmacia, which developed irinotecan, has since been acquired by Pfizer.

7 Some of the cocktail regimens also include generic drugs such as fluourouracil (5-FU) and leucovorin (LV), whose patents have expired and are now produced by many firms.
nests for a nested-logit demand model.

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. Patients usually pay a percentage of the price. Medicare patients, for example, pay 20 percent of the price if they have Part B coverage and no Medigap supplemental insurance.

Although physicians are eventually reimbursed by health insurers, they do take temporary ownership of oncology drugs. As such, physicians face the possible risk of not being reimbursed by health insurers and may incur substantial carrying costs. For example, a physician who pays $50,000 for the drugs in a patient’s regimen and experiences a three-month delay between when he acquires the drugs and when he is reimbursed by a health insurer would incur an inventory carrying cost of $1,333 at an interest rate of eight percent. Because we observe the full price that physicians pay for colorectal cancer drugs, we can estimate physicians’ demand for those drugs. In our model we assume physicians act as agents for their patients, in which case we indirectly observe patients’ willingness to pay for these drugs. We explain details of physician agency in Section 4.2.

Because each drug is sold separately to physicians who then combine them (when relevant) into a cocktail regimen, the only variable a firm controls is the price of its own drug. This price, in turn, affects the demand of all regimens in which the drug is used. We explicitly account for this impact in our supply-side (pricing) model in Section 4.1.

3 Data

We use several data sources to collect four types of information: drug prices, regimen market shares, the quantity/dose of each drug typically used in a regimen, and regimen attributes from clinical trials. IMS Health records transactions between wholesalers, who previously purchased the drugs from manufacturers, and the end customer, such as a physician practice. IMS Health reports 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) codes, 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 across the different NDC codes for a particular 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 or the wholesale acquisition cost (WAC).

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 and an analysis reported in Lucarelli, Nicholson, and Town (2010), 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.

We compute the price of each regimen for a representative patient who has a surface area of 1.7 meters squared, weighs 80 kilograms, and is treated for 12 weeks (Jacobson and Newhouse, 2006). 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. The NCCN reports the typical amount of active ingredient used by physicians for the major regimens. We supplement this where necessary with dosage information from drug package inserts, conference abstracts, and journal articles. Dosage information is reported in Appendix I. 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 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 LV per meter squared on the first and second treatment days. This process is repeated every two weeks.

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8 For the five patent-protected colorectal cancer drugs in our study, Lucarelli, Nicholson, and Town (2010) compared prices that include discounts and rebates to the IMS prices that we use in this paper. They found that prices from the two data sources were within two to four percent of one another, which is consistent with no or small rebates/discounts.

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

10 Our data show that the dosage of drugs in cocktail regimens are usually no larger than their dosages in stand-alone
The IMS Health data contain information on market share by drug, but not market share for combinations of drugs (i.e., 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, a company that sells information systems to help oncologists dose chemotherapy regimens, collects monthly data from its oncologist 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.\textsuperscript{11} Based on Medicare claims data available in SEER, we calculate each colorectal cancer regimen’s market share in each quarter.\textsuperscript{12}

In order to standardize 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. The underlying assumption in this adjustment is that the proportion of total patients represented by Medicare is time invariant for each regimen.

All regimens we include in the sample 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.\textsuperscript{13}

We plot market shares for the 12 regimens in the sample and the outside option in Figure 1.

\textsuperscript{11}SEER, which contains data on the cancer incidence rate among the non-elderly, only has medical claims available for Medicare patients.

\textsuperscript{12}According to IntrinsiQ’s data, approximately 48 percent of all colorectal cancer chemotherapy patients were 65 years or older in October 2003.

\textsuperscript{13}Off-label use occurs when a physician treats a colorectal cancer patient with a drug that has not been approved by the FDA explicitly for colorectal cancer.
a generic regimen, with the remainder treated with off-label drugs or regimens with small market share. In 1996 irinotecan was approved by the FDA for treating colorectal cancer, 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.\textsuperscript{14} Capecitabine, 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 (i.e., by IV) under the supervision of a physician or nurse.

Oxaliplatin was introduced in August 2002, followed by cetuximab and bevacizumab 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-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 that accompany each drug. These inserts describe the performance of the drug/regimen in phase 3 clinical trials, including 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 these patients. Because patients are randomized to the treatment or control regimens in phase 3 trials, the attributes are not subject to selection bias, such as the possibility that healthier patients might choose more toxic regimens. 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 for 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 conferences and journal articles.

We summarize the attribute information in Table 1, taking a weighted (by market share) average across regimens in each quarter, and then averaging across quarters for each year. The efficacy and side effect attributes are time invariant while price can change each quarter. We record three measures of a regimen’s efficacy: the median number of months patients survive after initi-

\textsuperscript{14}Because it takes Medicare a while to code new drugs into their proper NDC code, a new drug will appear in the outside option for several quarters.
ating therapy (*Survival Months*); the percentage of patients who experience a complete or partial reduction in the size of their tumor (*Response Rate*); and the median number of months (across patients in the trial) before the cancer advanced to a more serious state (*Time to Progression*).

We also record 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.

This table demonstrates that there was a large price increase in 1998. The average regimen price for a 12-week treatment cycle increased from about $50 to over $300. This jump is due to the introduction of Pfizer’s irinotecan. Since then the average price continued to rise with significant jumps in 2001 when Roche’s capecitabine was introduced, and in 2004 when bevacizumab and cetuximab were launched.\(^\text{15}\) 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, 2008).

### 4 Model

#### 4.1 Supply

We assume that firms play a static Bertrand-Nash game with differentiated products. Although the firms have considerable market power due to patent protection, they are in an oligopolistic competitive environment as physicians and patients have multiple treatment options. The price hike by Abbott in the HIV/AIDS drug market mentioned above provides evidence that price is a crucial strategic variable in the pharmaceutical market.\(^\text{16}\)

Nevertheless, Bertrand-Nash price setting may not fully describe pharmaceutical firms’ strategic behavior. Marketing to physicians (i.e., detailing) is the most important non-price action.

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\(^{15}\)The price jump in 2000 is due to a market share increase of irinotecan+5-FU/LV.

\(^{16}\)The prices of individual drugs do not show any common time trend consistent with dynamic pricing, such as a below-marginal-cost pricing or intertemporal price discrimination.
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 rebates to certain physician practices if their purchased volume exceeds a certain threshold. We are not aware of any study that examines how physicians react to rebates, presumably because firms do not disclose rebates. Moreover, as mentioned above, discounts/rebates in the colorectal chemotherapy market appear to be small. Although these features are not considered in the supply side model, we introduce a random shock in the demand model to capture physicians’ choices that are influenced by characteristics other than price and measured efficacy and side effects.

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 profit maximization 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 by aggregating quantities across the regimens in which the firm’s drug is used. Formally, if firm $f$’s drug is used in $R_f$ regimens, $q_f(p)$ can be written as

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

where $s_r(p^R(p))$ 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

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

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 is used \((\partial s_r(p)/\partial p^R_r)\). The former effect is determined by the quantity of a drug used in a regimen, which is fixed by a recommended "recipe", and the latter effect is determined by the regimen's price elasticity of demand, which we estimate using regimen-level data. Note that the recommended recipe is generally chosen years earlier when structuring the clinical trial. Using this profit-maximization condition, we can recover the marginal costs of each drug.

We may gain some insights from the profit-maximizing condition by considering a simple case where firm 1 and firm 2 each sell a stand-alone regimen (regimens 1 and 2 respectively) and one cocktail regimen (regimen 3) that combines these two firms’ drugs. Given that these three regimens are substitutes for one another, the first-order condition for firm 1 is simplified to

\[
\frac{\partial \pi_1}{\partial p_1} = (s_{11} + s_{33}) + (p_1 - mc_1) \left( \frac{\partial s_1}{\partial p^R_1} \frac{\partial p^R_1}{\partial p_1} q_{11} + \frac{\partial s_1}{\partial p^R_3} \frac{\partial p^R_3}{\partial p_1} q_{11} + \frac{\partial s_3}{\partial p^R_3} \frac{\partial p^R_3}{\partial p_1} q_{31} + \frac{\partial s_3}{\partial p^R_1} \frac{\partial p^R_1}{\partial p_1} q_{31} \right) = 0
\]

(2)

Now suppose the two firms’ stand-alone regimens use one unit of their own drugs and the cocktail regimen combines one unit of each drug. Then the stand-alone regimen prices are the same as the drug prices \((p^R = p)\) and the cocktail regimen price is the sum of the stand-alone regimen prices \((p_3 = p_1 + p_2)\), and equation (2) is further simplified to

\[
\frac{\partial \pi_1}{\partial p_1} = (s_{1}(p_1, p_2) + s_{3}(p_1, p_2)) + (p_1 - mc_1) \left( \frac{\partial s_1}{\partial p_1} + \frac{\partial s_3}{\partial p_1} \right) = 0
\]

(3)

Notice that equation (3) looks exactly the same as the profit-maximization condition for a firm selling two stand-alone regimens but being constrained to charge a single price. However, because regimen 3 is a cocktail regimen, \(\partial s_3/\partial p_2 < 0\), while \(\partial s_3/\partial p_2 > 0\) if regimen 3 were another stand-alone regimen. In other words, one of firm 1’s products is a complement to its rival’s product.\(^{17}\)

This simplification demonstrates that the cocktail regimen may benefit a firm by increasing the overall demand for its product (drug). This occurs when the cocktail regimen attracts "enough" new consumers without stealing "too many" existing consumers from its own stand-alone regimen. The ideal situation for a firm is when the cocktail regimen is distinct from, and not a close substitute to, its stand-alone regimen. This would also be the ideal situation when a firm introduces a new

\(^{17}\) If two firms have one cocktail regimen without any stand-alone regimens, prices are strategic substitutes under the linear pricing strategy.
stand-alone regimen. However, the benefit of having a new cocktail is likely to be different from the benefit of having a new stand-alone regimen because: (1) the new cocktail is a complement to a competing firm’s product and (2) a firm cannot set a different price for its drug when used in the stand-alone regimen and its drug when used in the cocktail regimen. Whether the net effect of the new cocktail is positive is, therefore, an empirical question.\footnote{An interesting question is how equilibrium outcomes would change if firms could set different prices for their component drugs used in the cocktail regimen. This is analyzed in 6.3.}

Consider next what would happen if these two firms merged. In the standard merger case, the merged firm raises prices because of the price effects on other products it now owns. In other words, because $p_k (\partial s_k / \partial p_j) > 0$ for products $j$ and $k$ that it owns, the merged firm sets higher prices than before. When the firms that share a cocktail regimen merge, the merged firm’s profit maximization condition becomes

$$\frac{\partial \pi^M}{\partial p_1} = (s_1 + s_3) + (p_1 - mc_1) \left( \frac{\partial s_1}{\partial p_1} + \frac{\partial s_3}{\partial p_1} \right) + (p_2 - mc_2) \left( \frac{\partial s_2}{\partial p_1} + \frac{\partial s_3}{\partial p_1} \right) = 0$$

for drug 1. This can be re-written as

$$\frac{p_1 - mc_1}{p_1} = \frac{1}{\varepsilon_{13,1}} + (p_2 - mc_2) \frac{\varepsilon_{23,1} (s_2 + s_3)}{\varepsilon_{13,1} p_1 (s_1 + s_3)}$$

(4)

where $\varepsilon_{13,1} = - (\partial (s_1 + s_3) / \partial p_1) (p_1 / (s_1 + s_3))$ and $\varepsilon_{23,1} = (\partial (s_2 + s_3) / \partial p_1) (p_1 / (s_2 + s_3))$. Whether prices go up after a merger depends on the sign of $\varepsilon_{23,1}$. In the standard oligopolistic market with substitutes, the cross-price elasticity term is positive so the post-merger price is higher. Notice that because $\partial s_2 / \partial p_1 > 0$ and $\partial s_3 / \partial p_1 < 0$, the sign of $\varepsilon_{23,1}$ can be positive or negative. Even when the term is positive, it will not be as large as in the merger case without cocktails.

### 4.2 Demand

We obtain our demand system by aggregating over a discrete choice model of physician behavior. Following the Lancasterian tradition, regimens are assumed to be a set of attributes, and preferences are represented as the utility derived from those attributes. We also allow physicians to observe regimen-specific attributes beyond those we observe in the clinical trials, i.e., physicians observe attributes that we do not. A physician may choose a highly effective regimen if a patient can tolerate...
side effects, or she may choose a less effective regimen with more bearable side effects. We also include price as an attribute. It is not obvious whether physicians pay attention to price because of health insurance. However, most Medicare patients pay about 20 percent of the treatment cost out of their pocket, most private insurance plans require patient cost sharing, and private plans often have a lifetime maximum coverage limit. Therefore, as long as physicians place some weight in their utility functions on their patients’ out-of-pocket costs, physicians will take price into consideration when recommending or selecting a regimen. Furthermore, as mentioned above, because physicians take ownership of the drugs, they incur carrying costs and face reimbursement risk.

Regimen attributes, no matter how many we control for, are not adequate to describe physicians’ choices fully. Factors such as patient health conditions, detailing activities, and rebates affect regimen choices as well. Because of data limitations, we summarize all these factors with an idiosyncratic shock. We assume a physician draws an i.i.d. shock from the Type I Extreme Value distribution every time she makes a choice. Thus, a physician choice is a probabilistic event with regimen attributes determining the probability.

We partition the whole set of regimen choices into multiple disjoint subsets according to recommendations by the NCCN and estimate a nested logit demand model. As mentioned in Section 2, the NCCN recommends 5-FU/LV (the generic regimen), Roche’s stand-alone regimen, and the Pfizer-Roche cocktail regimen for patients who cannot tolerate intensive therapy and other regimens for less frail patients. Following this recommendation, we categorize the former three regimens as non-intensive treatment regimens and the other nine as intensive treatment regimens, and form three subsets: a non-intensive treatment regimen group, an intensive treatment regimen group, and the outside option. This nested logit model allows physicians’ preferences to be correlated across regimens within groups and thus allows for more reasonable substitution patterns as compared to the simple logit model.

The indirect utility of physician $i$ for regimen $j$ in group $g$ in period (market) $t$ is

$$u_{ijt} = \delta_{jt} + \zeta_{ig} + (1 - \sigma) \varepsilon_{ij}$$

where $\delta_{jt} = -\alpha p_{jt} + x_j \beta + \xi_t + \Delta \xi_{jt}$ and $\varepsilon_{ijt}$ represents the idiosyncratic shock from Type I Extreme

\(^{19}\)We also form four subgroups by dividing the intensive treatment regimens into two groups but the estimation and simulation results do not change much as a result. See Section 5.1.
Value distribution. $\zeta_{ig}$ is physician $i$'s utility that is common to all regimens in group $g$. It is well known that if $\varepsilon_{ij}$ is an extreme value random variable, $\zeta_{ig} + (1 - \sigma) \varepsilon_{ij}$ is also an extreme value random variable and that $\sigma$ determines the degree of the within-group correlation of utility. $p_{jt}$ is the price of regimen $j$ at time $t$, $x_j$ a set of observable regimen attributes such as efficacy and side effects, $\xi_t$ the mean of unobserved attributes for each period, and $\Delta \xi_{jt}$ the regimen specific deviation from $\xi_t$ and represents demand shocks or regimen attributes that physicians observe but we do not. The outside option ($j = 0$) includes off-label colon cancer treatments, regimens with small market shares, or regimens without a complete set of attributes. The utility of the outside option is set to zero.

One concern with this model is that if physicians earn profits on chemotherapy drugs, profits are correlated with the observed price and/or the attributes, and profits influence physicians' prescribing decisions, then the $\alpha$ and $\beta$ coefficients may be biased. In a 2001 study, the federal government concluded that oncologists could earn profits on most chemotherapy drugs by acquiring them for less than the Medicare reimbursement amount (General Accounting Office, 2001). This occurred because Medicare reimbursed oncologists 95 percent of a drug's listed average wholesale price (AWP), whereas physicians could usually acquire drugs from wholesalers for less than the AWP. For example, physicians were acquiring irinotecan in 2001 for 23 percent less than AWP, on average, which allowed them to earn an approximate 18 percent profit (General Accounting Office, 2001). Most private health insurance companies reimburse physicians using a similar formula as used by Medicare, so these profits occurred for all patient types.\(^{20}\) Most of these profits were eliminated in 2005 when Medicare started reimbursing oncologists based on the actual average selling price (ASP) of a drug rather than the list price (MedPAC, 2006). In the first quarter of 2005, for example, oncologists were acquiring three branded colorectal cancer drugs (bevacizumab, irinotecan, and oxaliplatin) for two or three percent less than the new Medicare reimbursement amount, on average.

The profits that oncologists earned on chemotherapy drugs prior to 2004 did not have a pronounced effect on patient treatment. Jacobson and Newhouse (2006) exploit exogenous variation between oncologists in the generosity of Medicare reimbursement for chemotherapy drugs to

\(^{20}\)In the IntrinsiQ data set that we use in this paper, Medicare patients account for just over one-half of all colorectal cancer patients who receive chemotherapy.
estimate the influence of physician profits on treatment decisions. Although they find that oncologists who were reimbursed relatively generously did prescribe more expensive chemotherapy drugs, the magnitude of the effect is small: a one-standard deviation increase in reimbursement generosity is associated with an increase of about five percent in the cost of chemotherapy prescribed to colorectal cancer patients. Shea et al. (2008) find that the 2004 reduction in reimbursement had little impact on how long patients had to wait to initiate treatment or how far they had to travel to receive chemotherapy. Finally, Jacobson et. al. (2010) find that the new reimbursement method increased the likelihood that lung cancer patients received chemotherapy and shifted the mix slightly, away from drugs that formerly had high profit levels.

It is important to note that a cocktail regimen has different efficacy and side effects than the stand-alone regimens that use the same drugs. This allows us to directly estimate the utility of choosing the bundle instead of separating out the degree of complementarity. In our model physicians only care about how the regimen works so it is not important to them whether it is a stand-alone regimen or a cocktail. Our approach is different from that of other empirical studies on bundles, such as Gentzkow (2007), where the utility of the bundle is the sum of the utilities of the individual products plus a constant term.

As shown in Berry (1994), we can derive and estimate the following demand equation:

\[
\ln s_{jt} - \ln s_{0t} = -\alpha p_{jt} + \beta x_j + \sigma \ln s_{jt} + \xi_t + \Delta \xi_{jt}
\]  

(5)

where \( s_{jt} \) is a regimen’s within-group market share. \( \Delta \xi_{jt} \) is likely to be correlated with prices and within-group market shares. 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 shocks that affect a physician’s choice.

One might consider two alternative demand models. The random coefficient logit model of Berry, Levinsohn, and Pakes (1995), referred to hereafter as “BLP”, allows for more flexible substitution patterns by allowing random coefficients for price and product attributes. We do not use the BLP model for two reasons. First, we are unlikely to precisely estimate the random coefficients with our data set. Usually one needs the 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. Second, our nesting structure based on the NCCN recommendations may impose more realistic substitution patterns than BLP. The key factor in our nesting is whether patients can tolerate intensive treatments, which may not necessarily be correlated with observed consumer characteristics such as income, age, gender, etc. The NCCN recommendations allow us to capitalize on experts’ knowledge regarding the similarity between regimens that is difficult to obtain from typical product- and consumer-level data.

A second alternative demand model is the pure characteristics model of Berry and Pakes (2007), which has no idiosyncratic taste term in the utility function. Because of the absence of the idiosyncratic taste term, choices are perfectly explained by product attributes and random coefficients that describe consumers’ heterogeneous preferences for product attributes. In such a model we cannot allow for the aforementioned unobserved shocks that affect physicians’ regimen choices. Furthermore, in the one random coefficient pure characteristics model all consumers should agree on the quality ranking of products. It is unlikely, however, that oncologists have a consensus regarding which regimen is superior. Moreover, it is not obvious that pharmaceutical firms would want to invest substantially in researching and developing a new cocktail regimen even if there is a consensus among oncologists. In Appendix II we provide numerical examples where firms are worse off with cocktail regimens when regimen choice is described by the pure characteristics model.

5 Estimation Results

5.1 Demand Estimates

We estimate equation (5) using regimen-level market share, price, and attribute data. The price variable is likely to be correlated with unobserved attributes or the contemporaneous demand shock because firms observe these before setting prices. This price endogeneity problem requires using instruments to estimate the demand equation consistently. We construct two instruments using the lagged prices of other regimens. In particular, for the price of regimen $j$ in period $t$, one instrument is the average price in period $t - 1$ of all regimens other than regimen $j$. The other instrument is the average price in period $t - 1$ of regimens produced by firms whose drugs are not used in regimen

\footnote{Although the pure characteristics model becomes more flexible as additional random coefficients are added, adding more than two random coefficients creates a nontrivial computational challenge. See Song (2007) for details.}
Our identifying assumptions are that these instruments are uncorrelated with the current-period demand shock, but are correlated with the current period price of regimen \( j \). The latter correlation should occur due to oligopolistic interactions and the evidence that 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 if there exists a time-persistent market-level demand shock.\(^{22}\)

We use the generalized method of moments with \((Z'Z)^{-1}\) as the weighting matrix, where \( Z \) includes the instrumental variables, all the observed regimen attributes other than price, and the time indicator variables.\(^{23}\) We report the demand estimates in Table 2. The first column reports the results of the OLS logit model; the second column, labeled IV Logit, reports results using lagged prices as instruments; and the third column, labeled Nested Logit I, reports results of the nested logit with two regimen groups. The last column, labeled Nested Logit II, corresponds to the nested logit where regimens for patients who can tolerate intensive therapy are again divided into two groups (three regimen groups in total). In the two nested logit models we treat the within-group share variable as an endogenous variable in addition to the price variable. In all specifications we use the logarithm of price as a regressor, and standard errors are reported in parentheses.

Comparing the price coefficient from the first column with the other three reveals that there is a positive correlation between price and the demand shock and that the instrumental variables mitigate this problem. The price coefficient increases in absolute value from -0.690 without instruments (OLS Logit) to -2.150 in IV Logit, and to -1.557 and -1.794 in the two nested logit models. The price coefficient is significantly different from zero at the one-percent level in all models. The F-statistic from the first stage F-test for the joint significance of the instruments is over 10 in all three specifications. The coefficients for the within-group share variable are 0.403 and 0.421 for the Nested Logit I and Nested Logit II models respectively, and are statistically significant. This indicates that regimens are closer substitutes within a group than between groups.\(^{24}\) Allowing

\(^{22}\) We do not use other products’ attributes as instruments because they do not vary much over time due to infrequent product entry and exit. The first stage F-statistics on joint significance when using these instruments is less than five, and the estimation results are not substantially different from the OLS logit results that we present.

\(^{23}\) Our sample size is not large enough to use the optimal weighting matrix.

\(^{24}\) The first stage F-statistics reported for the nested logit models in Table 2 are for the within-group share variable.
for more nesting in the Nested Logit II model does not substantially affect the results.

The efficacy attribute coefficients are statistically significant in the IV logit and nested logit models, but only the response rate coefficient is positive. Because these three variables are correlated with one another, we use a linear combination of these three variables to evaluate preferences for efficacy. In the IV logit model, the average willingness to pay for obtaining the mean efficacy from a 12-week treatment (relative to the outside option) is about $70,000 in 2005. The average cost for that treatment in the same year is about $18,000. The average willingness to pay for the mean efficacy is slightly smaller (about $3,000) in the nested logit models.

Among the side effect variables, only the neutropenia coefficient is both statistically significant and negative as expected. Its estimate implies that the average willingness to pay to reduce a chance of having neutropenia by one percent is about $900. The other side effect variables are either positive or insignificant. This may occur because cancer patients often take drugs that ameliorate the impact of certain side effects, such as pain, nausea, and diarrhea, while neutropenia is fatal and harder to prevent with other drugs. If a physician prescribes anti-pain and antiemetic drugs in conjunction with the chemotherapy 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. Thus, it is important to include these side-effect variables because, if left in the unobserved attribute term, they are likely to be correlated with the efficacy variables.  

5.2 Reaction Function

In order to better understand how firms compete when they share a cocktail regimen, we numerically derive firms' reaction functions, using the demand estimates of the Nested Logit I model. We first recover the marginal cost of each drug using the demand estimates and equation (1) and, for a specific cocktail regimen, we fix the prices of drugs that are not used in this cocktail regimen at the observed prices. We then search for the profit-maximizing price of one of the drugs used in this cocktail regimen while varying the price of the other component drug of the cocktail. For the Roche-Sano\-\-Genentech cocktail regimen, we fix the price of one of the three firms while deriving

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25Estimation results do not change substantially with different specifications. In Table A-1 we report estimates of alternative versions of the OLS and IV logit models, including versions without side effect variables and versions with manufacturer fixed effects.
the reaction functions for the other two firms.

We find evidence for two types of interactions between the firms whose drugs are used in the same cocktail regimen (which we refer to as "participating firms" or "participants" hereafter). In the first type, the reaction functions of the participants are upward sloping as in the standard oligopolistic market: firm 1 increases the price of its drug in response to an increase in firm 2’s drug price. However, only two cases belong to this type: the Pfizer-Genentech cocktail case and Roche and Genentech in the Roche-Sanofo-Genentech cocktail case. In the second more common type of interaction, the reaction function of one of the participating firms is downward sloping while the other participant’s reaction function is upward sloping. Figure 2 depicts such an example where the solid lines are the reaction functions for Pfizer (downward sloping) and ImClone (upward sloping) in the Pfizer-ImClone cocktail case. In this figure Pfizer’s reaction function is downward sloping while ImClone’s reaction function is upward sloping.

The downward-sloping reaction function results from the complementarity between the cocktail regimen and stand-alone regimen. Consider an extreme case where the only regimen in the market is a cocktail regimen shared by two firms. One can show that price is a strategic substitute because the demand for firm 1’s drug is adversely affected by an increase in firm 2’s price. In Figure 2, however, only one firm’s reaction function is downward sloping, implying that the complementarity is stronger for Pfizer than ImClone. That is, when ImClone increases the price of its drug, demand for Pfizer’s drug falls when combined across its stand-alone regimen (an increase in demand) and the cocktail regimen (a decrease in demand). Pfizer responds to this situation by cutting its price. When Pfizer increases the price of its drug, on the other hand, demand for ImClone’s drug rises, and ImClone responds by increasing the price of its drug.

6 Counterfactual Exercises

Given the estimates for the demand parameters and the marginal cost of each regimen, we 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 because that is a period when all 12 major regimens are present in the market. We average the

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26 This figure uses the estimates of the fourth quarter of 2004.
results over these six quarters and use the estimates reported in the third column of Table 2 (Nested Logit I). Results using the estimates in the second column (IV Logit) are also presented in Tables A-2 and A-3.

6.1 Welfare Analysis

To analyze welfare we remove the cocktail regimens from the market one at a time and calculate the new Nash equilibrium prices for all branded drugs. We then use these equilibrium prices to compute variable profits and consumer surplus. Because there are six cocktail regimens, we evaluate six hypothetical cases. The results are reported in Table 3. The baseline, which is the equilibrium currently observed in the market, is normalized to 100 in the first row. The numbers in the other rows are levels relative to the baseline. Therefore, one can conveniently calculate percentage changes in prices, profits, and consumer surplus compared to the observed equilibrium. The numbers in bold typeface are changes for the firms participating in the removed cocktail regimen. 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 that sold a cocktail at the left to the most recent at the right.

The first panel of Table 3 reports the new equilibrium price of each firm’s drug, relative to the baseline (100.0), when the particular regimen in a row is absent. For example, the final row corresponds to a scenario where the Sanofi-Genentech cocktail regimen, 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 46.9 percent and 24.8 percent respectively.

There are at least two notable patterns in the first panel. First, in five out of six cases, the prices of participating firms’ drugs fall when a regimen is removed. Prices fall in these five cases as the reaction functions shift inward. However, in three cases (including the Roche-Sanofi, the Pfizer-ImClone, and the Sanofi-Genentech cases) the downward-sloping reaction function for at least one of the participating firms pivots around when the cocktail is removed and becomes upward sloping. This shows that these three cocktail regimens have strong enough complementarity effects such that their presence transforms price from being a strategic complement to a strategic substitute.

27 Since we solve a system of non-linear equations, there may be multiple sets of solutions. In most cases we do not encounter multiplicity with different starting points. In the few situations with multiplicity, we select the single equilibrium with the largest profits.

28 We use consumers, patients, and physicians interchangeably in our welfare analysis.
Figure 2 illustrates how the reaction functions change when the Pfizer-ImClone cocktail is removed. The dotted lines are the reaction functions without the cocktail regimen, and are upward sloping as expected with substitute products. Both reaction functions shift inward when the cocktail is removed, and Pfizer’s reaction function is no longer downward sloping. The figure also shows that both Pfizer and ImClone react to each other’s price changes more sensitively with the cocktail regimen. ImClone has one stand-alone regimen and the cocktail regimen with Pfizer. Without the cocktail regimen ImClone’s drug is not a close substitute for Pfizer’s drug.

In the Roche-Sanofi-Genentech cocktail case Roche’s price is a strategic substitute for Sanofi’s price and Sanofi’s price is a strategic substitute for Genentech’s price. When this cocktail regimen is removed, their reaction functions are still downward sloping although they shift inward. This is because they have other cocktail regimens with each other that have stronger complementarity effects. In the Pfizer-Genentech cocktail regimen case the participants’ reaction functions are upward sloping, and they just shift inward when this cocktail is removed.

The only instance where prices do not fall is Pfizer’s reaction to the removal of the Pfizer-Roche cocktail regimen: Pfizer increases its price by 8.7 percent while Roche decreases its price by 9.4 percent. Figure 3 shows that Pfizer’s reaction function shifts outward when the cocktail regimen is removed, which results in a higher price for Pfizer in the new equilibrium. This suggests that the Pfizer-Roche cocktail is a close substitute for Pfizer’s other regimens and not as much differentiated as the other cocktail regimens are. This is not surprising considering the fact that this is the first cocktail regimen introduced for colorectal cancer chemotherapy treatment.

The second notable pattern on the first panel of Table 3 is that Roche’s reaction to the removal of other firms’ cocktail regimens is consistently different than the other firms. While the other non-participating firms change their prices in the same direction as the cocktail participants, Roche changes its price in the opposite direction. For example, when the Pfizer-ImClone cocktail regimen is removed (second to last row), Roche’s drug price increases by 51.5 percent while the drug prices of Sanofi and Genentech goes down by 16.3 percent and 9.8 percent respectively. This suggests that the cocktail regimens that Roche shares with other firms have strong complementarity effects: as other firms raise their prices in response to the removal of a particular cocktail, Roche

\[29\] Table A-2 shows that Roche also increases its drug price in the IV logit model.
reduces its price because it shares a separate cocktail with these firms.\(^{30}\) Note that Roche has cocktail regimens with Pfizer, Sanofi, and Genentech, and its price is a strategic substitute for the prices of Pfizer and Sanofi. Roche’s price is still a strategic complement for ImClone’s price, but its complementarity with Pfizer’s drug dominates when the Pfizer-ImClone cocktail regimen is removed, resulting in a higher price for Roche.\(^{31}\)

The second panel of Table 3 reports predicted profits when a particular regimen is removed. None of the participating firms except Roche in the Pfizer-Roche cocktail case are better off when a regimen is removed, which indicates that cocktail regimens are likely to increase profits for all participants no matter who introduces them. Profit losses are sometimes substantial, especially when the cocktail’s market share is much larger than that of the participant’s other regimens. ImClone’s profit, for example, is predicted to fall by 83.3 percent when the ImClone-Pfizer cocktail regimen is removed. This regimen has a market share three times larger than that of ImClone’s stand-alone regimen. Genentech’s profit is predicted to fall by 84.9 percent when the Sanofi-Genentech cocktail regimen is removed. Out of the three cocktail regimens Genentech has, this regimen has the largest market share, about 60 percent larger than the Pfizer-Genentech regimen and more than 10 times larger than the Roche-Sanofi-Genentech regimen.

When the introduction of a cocktail regimen results in a higher price and higher drug demand, participating firms are definitely better off, and ImClone and Genentech in the examples above belong to this case. However, even when total drug sales fall, the firms can still earn higher profits if consumer demand is sufficiently inelastic. A general pattern is that the cocktail regimen decreases total demand for the "incumbent" drug, i.e., the firm that entered the market earlier, while it increases total demand for the "entrant" drug, i.e., the firm that introduced the cocktail.\(^{32}\) In the Sanofi-Genentech cocktail case, for example, the total sales for Genentech’s drug go up five times thanks to the cocktail regimen while Sanofi’s sales go down about 40 percent, where Sanofi is the incumbent and Genentech the entrant. Although both firms still increase prices, the former

\(^{30}\)This makes sense because the principal benefit of Roche’s drug, capecitabine, is its convenience (it is a pill that can be ingested in a patient’s home rather than a liquid that must be infused in a physician’s office). Adding capecitabine to a cocktail makes the regimen more convenient, whereas the distinguishing efficacy and side effects of the regimen derive from the other component drug(s).

\(^{31}\)As Pfizer’s reaction function shifts inward, it moves along the downward-sloping curve of Roche’s reaction function, resulting in a higher price for Roche.

\(^{32}\)In Appendix II we show that in a simple logit demand model with symmetric firms, prices always rise when total demand increases from the introduction of a cocktail regimen. However, this result does not necessarily hold in a more complicated inter-firm bundling structure.
firm is exploiting higher demand while the latter firm is responding to the entrant’s price increase. This asymmetric demand effect implies that cocktail regimens are usually closer substitutes for the incumbent’s "existing" regimens than the entrant’s stand-alone regimen.

Again, the Pfizer-Roche case provides an exception. Roche in this case is the only participant that is better off without the cocktail regimen, although its profit is higher by a mere 0.1 percentage point. All of the non-participants are better off without this cocktail regimen too, while they are usually worse off in the other cocktail cases. Roche’s price goes down without the cocktail but the total demand goes up sufficiently to increase its profit. The non-participants’ prices go up mainly because Pfizer’s reaction function shifts outward with respect to their prices as it does with respect to Roche’s price in Figure 3. Their total drug sales go down but this decrease is not large enough to decrease their profits.

We report consumer surplus in the last column of Table 3. The effect of removing a cocktail regimen on consumer surplus is not clear a priori. On the one hand, consumers are worse off with one fewer available regimen. Some consumers are hurt more than others depending on the nesting group from which the removed regimen belongs. On the other hand, consumers benefit if prices go down, and this is usually the case as shown above. In five of the six cases, consumers would be better off without the cocktail regimens. The results demonstrate that the consumer gain from the price decrease tends to outweigh the loss due to reduced variety. In all five of the cases where the net benefit is positive, the prices of most drugs decrease, and in the one case where consumers are worse off without the cocktail, the prices of all drugs except that of Roche increase.

The results presented in Table 3 indicate that this particular inter-firm bundling creates a less competitive market that benefits firms but harms consumers. This is especially disappointing especially because making a cocktail regimen is a cost-effective way of providing more treatment options for cancer patients. Recall that the twelve major regimens only use five patented drugs. Empirical studies such as Petrin (2002) show that new products usually increase consumer welfare, especially when they are of higher quality than existing products, by providing more and better choices for consumers. A firm that introduces a new product may increase its prices but the other firms lower their prices in response. However, most of the cocktail regimens in the colorectal cancer

\[33\] The only other case where a non-participant is better off is Genentech in the Roche-Sanofi case. In the IV logit model this happens more frequently but non-participants are usually worse off with that model as well.
treatment market hurt consumers by increasing the prices of all regimens that use the same drugs.

This negative welfare result is due not only to having an inter-firm bundle but also due to the linear pricing. In Section 6.3 we consider an alternative pricing structure where firms unilaterally set different prices for a cocktail regimen and show how it affects welfare. This pricing is feasible if they can sell cocktail regimens as separate products as in the HIV/AIDS treatment market.

6.2 Merger Analysis

In the next counterfactual exercise we consider two kinds of hypothetical mergers: (1) a merger after removing a cocktail regimen and (2) a merger with a cocktail regimen. Table 4 reports the joint profit of the merging firms and consumer surplus when different pairs of firms merge. The two firms' joint profit under the current situation (of offering the cocktail regimen) is normalized to 100 in the first column, which is labeled Current, and the joint predicted profit from the counterfactual exercise in Section 6.1 is reported for comparison in the second column, labeled Removed.

In the column labeled Removed+Merger we report the joint profit when the two firms merge without the cocktail regimen. Although the joint profit in this column exceeds that of the second because the two firms have more market power, this profit is not necessarily larger than the current profit with the cocktail regimen. In fact, in four of the five cases the joint profit of this type of merger is smaller than the joint profit with the cocktail regimen, which implies that firms are likely to gain more from cocktail regimens than from mergers.\textsuperscript{34} The difference can be quite substantial; the merger between Pfizer and ImClone (without the cocktail regimen) is estimated to increase joint profit by 5.1 percent whereas their cocktail regimen increases profit by 75.1 percent. The difference is even larger in the Sanofi-Genentech case.

In the column labeled Merger in Table 4 we report the joint profit when two firms merge while maintaining their cocktail regimen. Interestingly, this joint profit is not much higher than the current joint profit. The largest increase (11.8 percent) occurs when Pfizer and Roche merge. Mergers tend to increase the joint profit much less than the addition of a cocktail regimen (column 1 - column 2). Moreover, when Pfizer and ImClone merge, their joint profit is predicted to fall by 2.3 percent.

This result arises because the merged firm does not always increase the prices of the com-

\textsuperscript{34} We consider five instead of six cases because we exclude a three-firm merger case.
ponent drugs when it has a cocktail regimen. In the Pfizer-Roche, the Roche-Sanofi, and the Pfizer-Genentech mergers, the merged firm raises both drug prices as in the standard oligopoly market. In the Sanofi-Genentech merger, on the other hand, the merged firm reduces Genentech’s drug price while raising Sanofi’s drug price. More interestingly, in the Pfizer-ImClone merger the merged firm reduces both drug prices, resulting in lower joint profit.

This mixed pricing result is driven by a tension between complementarity and market power. A merged firm usually increases prices to exploit its market power, but this incentive is dampened when it has the cocktail regimen because a higher price decreases demand for the cocktail regimen. Equation (4) demonstrates this effect in a duopoly market where two firms that sell one stand-alone regimen each and share one cocktail regimen merge. As explained in Section 4.1, the direction of price change following the merger depends on the sign of $\varepsilon_{23,1} = (\partial (s_2 + s_3)/\partial p_1)(p_1/(s_2 + s_3))$, which can be positive or negative because $\partial s_2/\partial p_1 > 0$ and $\partial s_3/\partial p_1 < 0$. Even when this term is positive, the price increase will not be as large as without the cocktail regimen. If the merged firm reduces prices because of dominant complementarity effects, the other firms’ prices may go down as well and can hurt all firms, including the merged firm. This is what happens in the Pfizer-ImClone merger case.35

As expected, consumer surplus decreases when firms merge without the cocktail (going from Removed to Removed+Merger), which is a typical merger outcome in an oligopoly market; consumer surplus falls as the market becomes less competitive. When two firms offering a cocktail regimen are allowed to merge (going from Current to Merger), consumer surplus can change in either direction. Since the number of regimens does not change, the direction depends on how the firms change prices after a merger. In the first three cases of Table 4 consumer surplus falls because most of the firms, including both cocktail participants, raise their prices. In the last two cases consumer surplus increases as at least four firms lower their prices. The last two cases provide interesting examples where consumers are better off when firms merge.

It is also interesting to compare the outcome of the two types of mergers (going from Removed+Merger to Merger). This is the case where a firm that has multiple stand-alone regimens

35 There are other situations where a merger does not increase profit. It is well known that in a symmetric three-firm Cournot environment, a merger between any two firms is not profit enhancing. This is because the third firm responds to a merger by increasing its quantity. Another well-known case is a merger between two price-setting firms independently selling perfect complements. This merger is not necessarily profitable if there is a third firm selling a bundle of differentiated complements.
introduces a cocktail regimen using its own drugs, i.e., an intra-firm bundle. The third and the fourth columns of the table show that the joint profit goes up when the merged firm introduces a cocktail regimen using its own drugs, suggesting that an intra-firm bundle benefits firms. However, the profit increase is smaller than when two firms participate in a cocktail regimen (i.e., an inter-firm bundle). Although the merged firm sells more of its drugs by introducing a cocktail regimen, it is less likely to increase prices. In the first three cases all firms, including the merged firm, lower drug prices. In the Pfizer-ImClone case the merged firm increases the prices of both drugs by a small amount. In the Sanofi-Genentech case the merged firm increases Sanofi’s drug price but decreases Genentech’s drug price. Consumer surplus can rise or fall depending on how prices change. Consumers are definitely better off in the first three cases where all firms lower their prices. In the last two cases consumers are worse off because the higher prices outweigh the benefit of having a new regimen, although the welfare change is less than two percent. This comparison provides a sharp contrast to the inter-firm bundling case where consumers are usually worse off when a cocktail regimen is added.

6.3 Nonlinear Pricing

Until now we have maintained the linear pricing assumption in the counterfactual exercises. As explained above, firms in the colorectal cancer chemotherapy treatment market are constrained to use the linear pricing strategy because cocktail regimens are created by oncologists. Linear pricing is a key factor that makes cocktail regimens complements relative to the stand-alone regimens of the same drugs, and some of the results presented above are driven by this complementarity. In this section we relax this constraint by selecting one cocktail regimen at a time and allowing each participating firm to set a different price for that cocktail regimen. For the Pfizer-Roche cocktail regimen, for example, we allow Pfizer and Roche to set two prices: one for this cocktail regimen and a different price for their other regimens. This nonlinear pricing is feasible and observed in other segments of the pharmaceutical market. In the HIV/AIDS treatment market, for example, a single pill contains drugs from two or more firms.

Table 5 reports price changes and welfare effects under the nonlinear pricing. The columns under *Cocktail* report a pair of prices that the participating firms set for the cocktail regimen. The first price belongs to the first firm in bold typeface in a row and the second price belongs
to the second firm in bold typeface. For example, the results in the second row (*Pfizer*+*Roche*) indicates that Pfizer would offer a bundle discount (103.1 for the cocktail component versus 110.0 for the stand-alone product) whereas Roche would charge a huge bundle premium for their cocktail regimen component. The table also demonstrates that Pfizer’s two prices and Roche’s bundle price are higher, while Roche’s non-bundle price is lower than the linear prices.

The first panel of Table 5 shows that in three out of the five cases the firms charge a bundle premium on the cocktail regimen. In all three of these cases the participating firms’ non-bundle prices are lower than the linear prices while their bundle prices are higher. In the other two cases one firm offers a bundle discount while the other charges a bundle premium.

Armstrong (2012) shows that when a firm sells a stand-alone product and an inter-firm bundle at linear prices, whether it offers a bundle discount or premium depends on the price elasticity of the bundle relative to total demand elasticity for its product. In particular, he shows that a firm has an incentive to offer a bundle discount (premium) whenever the price elasticity of the bundle is higher (lower) than the total demand elasticity for its product. The intuition behind this result is that offering a lower price to more elastic consumers enhances profit.

The relative price elasticities explain most of the price changes in Table 5. In four out of the five cases the relative price elasticity with linear prices correctly predicts whether the firms offer a bundle discount or premium when pricing is more flexible. In the Roche-Sanoﬁ cocktail case, however, Sanoﬁ charges a bundle premium even though the bundle demand is more elastic than total demand. A closer look shows that as Roche increases the price for this cocktail regimen, the bundle demand becomes less elastic than total demand for Sanoﬁ’s drug and, thus, Sanoﬁ also charges a bundle premium in equilibrium.

The second panel of Table 5 shows how this nonlinear pricing affects firms and consumers. In all five cases at least one participating firm is worse off relative to linear pricing, and in two cases all participating firms are worse off. This result is interesting because it shows that firms can be worse off with more flexible pricing strategies. The firms that are worse off under flexible pricing have an incentive to set nonlinear prices if other firms must charge linear prices. However, these firms become worse off when other participating firms can also set nonlinear prices (and non-participating firms alter their prices as a result). Moreover, in the two cases where all participating

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36 See Proposition 3 in Armstrong (2012).
firms are worse off with flexible pricing, the firms are in a Prisoner’s Dilemma-type situation where they can be better off by agreeing to use linear pricing.

The last column of Table 5 demonstrates that in four cases consumers are better off when firms set nonlinear prices. While the price of one cocktail regimen is much higher, the prices of other regimens are usually lower, resulting in higher consumer surplus. Recall that with linear pricing the presence of a cocktail regimen is likely to increase profits but reduce consumer surplus. The results here suggest that consumers may benefit from cocktail regimens if the firms can set nonlinear prices.

These results also suggest that Abbott’s pricing strategy with Norvir and Kaletra is not necessarily detrimental to consumers. The situation is not exactly the same; Abbott introduced a stand-alone regimen, Kaletra, when its other drug, Norvir, was being used in an inter-firm cocktail regimen. Nevertheless, the price hike of Norvir after the launch of Kaletra is consistent with the profit-maximizing outcome shown in this section. It is possible that this price change benefits consumers if other firms also reduce their prices in response.

7 Conclusions

This paper empirically analyzes firms’ strategic behavior when their products are consumed in conjunction with their competitors’ products. We focus on the pharmaceutical industry, and on colorectal cancer chemotherapy drugs in particular. We estimate regimen-level demand using unique data from IntrinsiQ, and perform a series of counterfactual exercises using estimates of the demand parameters and marginal cost.

We show that inter-firm bundling in the pharmaceutical industry, known as pharmaceutical cocktails, is likely to render the market less competitive, benefitting firms and harming consumers. This result stems from (1) cocktail regimens being inter-firm bundles and (2) firms charging single prices no matter how their drugs are used, i.e., linear pricing. Under these two conditions a new cocktail regimen is likely to increase the prices of all regimens that use the same drug as the new cocktail regimen. Without either of these two conditions the cocktail regimen is more likely to make consumers better off. In particular, we show that if firms are able to set nonlinear prices, they would become worse off while consumers better off. This occurs because while firms tend to
charge a bundle premium for one cocktail regimen when giving pricing flexibility, the prices for the other regimens are lower. This nonlinear pricing, although unlikely to happen in the colorectal cancer market, is consistent with what we observe in other sectors of the pharmaceutical industry, such as Abbott’s pricing strategy with Norvir and Kaletra, and supports our static Nash pricing assumption.

We also find that a merger between firms that have a cocktail regimen in common does not have as strong an anticompetitive effect as standard mergers. The cocktail regimen that the merging firms have in common is a complement to their other regimens that use the same drug. Therefore, the merged firm increases drug prices much less substantially, or even decreases them, when the complementarity effect dominates. This result should help the government evaluate the expected outcomes of the recent merger wave in the pharmaceutical market.
References


Table 1: Regimen Attributes: The Sample Average

<table>
<thead>
<tr>
<th>Time</th>
<th>Regimen Price (12 week treatment)</th>
<th>Efficacy</th>
<th>Grade 3 or Grade 4 Side Effects (%)</th>
</tr>
</thead>
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<tr>
<td></td>
<td></td>
<td>Survival Months</td>
<td>Response Rate</td>
</tr>
<tr>
<td>1993</td>
<td>60</td>
<td>12.5</td>
<td>20.8</td>
</tr>
<tr>
<td>1994</td>
<td>60</td>
<td>12.5</td>
<td>20.8</td>
</tr>
<tr>
<td>1995</td>
<td>58</td>
<td>12.5</td>
<td>20.8</td>
</tr>
<tr>
<td>1996</td>
<td>63</td>
<td>12.5</td>
<td>20.8</td>
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<tr>
<td>1997</td>
<td>47</td>
<td>12.5</td>
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<tr>
<td>1998</td>
<td>344</td>
<td>12.5</td>
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<td>1999</td>
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<td>2002</td>
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<td>2003</td>
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<td>2004</td>
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<td>2005</td>
<td>17,590</td>
<td>16.8</td>
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See the text for variable explanations.
Table 2: Demand Estimation Results

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<tr>
<th>Variable</th>
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<th>IV Logit</th>
<th>Nested Logit I</th>
<th>Nested Logit II</th>
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<td>(\log(\text{price}))</td>
<td>-0.690*</td>
<td>-2.150*</td>
<td>-1.557*</td>
<td>-1.794*</td>
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<tr>
<td></td>
<td>(0.125)</td>
<td>(0.483)</td>
<td>(0.411)</td>
<td>(0.412)</td>
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<tr>
<td>Survival (months)</td>
<td>-0.087</td>
<td>-0.421*</td>
<td>-0.323*</td>
<td>-0.356*</td>
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<tr>
<td></td>
<td>(0.056)</td>
<td>(0.116)</td>
<td>(0.093)</td>
<td>(0.097)</td>
</tr>
<tr>
<td>Response Rate (%)</td>
<td>0.166*</td>
<td>0.913*</td>
<td>0.644*</td>
<td>0.784*</td>
</tr>
<tr>
<td></td>
<td>(0.072)</td>
<td>(0.254)</td>
<td>(0.214)</td>
<td>(0.215)</td>
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<tr>
<td>Time to Progression (months)</td>
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<td>-1.395*</td>
<td>-1.830*</td>
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<td>(0.244)</td>
<td>(0.644)</td>
<td>(0.538)</td>
<td>(0.545)</td>
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<td>Diarrhea</td>
<td>0.024</td>
<td>0.072*</td>
<td>0.051*</td>
<td>0.052</td>
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<tr>
<td></td>
<td>(0.023)</td>
<td>(0.034)</td>
<td>(0.026)</td>
<td>(0.030)</td>
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<td>(0.078)</td>
<td>(0.116)</td>
<td>(0.082)</td>
<td>(0.090)</td>
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<td>Abdom_pain</td>
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<td>0.561*</td>
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<td>(0.077)</td>
<td>(0.229)</td>
<td>(0.196)</td>
<td>(0.193)</td>
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<tr>
<td>Vomiting</td>
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<td>0.245</td>
<td>0.196</td>
<td>0.176</td>
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<td></td>
<td>(0.118)</td>
<td>(0.166)</td>
<td>(0.116)</td>
<td>(0.134)</td>
</tr>
<tr>
<td>Neutropenia</td>
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<td>-0.082*</td>
<td>-0.098*</td>
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<td>(0.011)</td>
<td>(0.034)</td>
<td>(0.027)</td>
<td>(0.028)</td>
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<tr>
<td>(\log(s_{j/g}))</td>
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<td>0.403*</td>
<td>0.421*</td>
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<td></td>
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<td>(0.154)</td>
<td>(0.166)</td>
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<td>R-square</td>
<td>0.836</td>
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<td>1st Stage F-statistics</td>
<td>11.983</td>
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Table 3: Welfare Effects

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<th>Prices Per mg (current situation = 100)</th>
<th>Profit (current situation = 100)</th>
<th>CS</th>
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<tr>
<td></td>
<td>Pfizer</td>
<td>Roche</td>
<td>Sanofi</td>
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<tr>
<td>Current</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
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<tr>
<td>No Pf + Ro</td>
<td>108.7</td>
<td>90.6</td>
<td>105.1</td>
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<tr>
<td>No Ro + Sa</td>
<td>98.0</td>
<td>80.2</td>
<td>93.2</td>
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<tr>
<td>No Pf + Ge</td>
<td>59.0</td>
<td>151.2</td>
<td>93.8</td>
</tr>
<tr>
<td>No Ro + Sa + Ge</td>
<td>99.4</td>
<td>94.4</td>
<td>98.2</td>
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<tr>
<td>No Pf + Im</td>
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<td>151.5</td>
<td>83.7</td>
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<tr>
<td>No Sa + Ge</td>
<td>77.4</td>
<td>161.3</td>
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Table 4: Merger Analysis

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<th>Two Firms’ Joint Profit</th>
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<tr>
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<td>Current</td>
<td>Removed</td>
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<tr>
<td>Pfizer + Roche</td>
<td>100</td>
<td>97.3</td>
<td>111.2</td>
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<tr>
<td>Roche + Sanofi</td>
<td>100</td>
<td>91.3</td>
<td>99.6</td>
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<tr>
<td>Pfizer + Genentech</td>
<td>100</td>
<td>70.7</td>
<td>93.6</td>
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<tr>
<td>Pfizer + ImClone</td>
<td>100</td>
<td>57.1</td>
<td>60.0</td>
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<td>Sanofi + Genentech</td>
<td>100</td>
<td>49.8</td>
<td>53.9</td>
</tr>
<tr>
<td></td>
<td>Prices Per mg (current situation = 100)</td>
<td>Profit (current situation = 100)</td>
<td>CS</td>
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<td>----------------</td>
<td>----------------------------------------</td>
<td>----------------------------------</td>
<td>----</td>
</tr>
<tr>
<td></td>
<td>Cocktail</td>
<td>Pfizer</td>
<td>Roche</td>
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<tr>
<td>Current</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Pfizer + Roche</td>
<td>(103.1, 405.4)</td>
<td>110.0</td>
<td>93.5</td>
</tr>
<tr>
<td>Roche + Sanofi</td>
<td>(441.0, 130.9)</td>
<td>100.1</td>
<td>82.2</td>
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<tr>
<td>Pfizer + Genen</td>
<td>(185.5, 172.1)</td>
<td>66.2</td>
<td>118.6</td>
</tr>
<tr>
<td>Pfizer + ImClone</td>
<td>(290.5, 143.9)</td>
<td>43.4</td>
<td>156.6</td>
</tr>
<tr>
<td>Sanofi + Genen</td>
<td>(210.0, 110.0)</td>
<td>95.7</td>
<td>156.2</td>
</tr>
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</table>
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: Reaction Functions of Pfizer and ImClone
Figure 3: Reaction Functions of Pfizer and Roche
## Appendix I: Composition and Dosages of the Chemotherapy Regimen

<table>
<thead>
<tr>
<th>Regimen</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; Drug</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt; Drug</th>
<th>3&lt;sup&gt;rd&lt;/sup&gt; Drug</th>
<th>4&lt;sup&gt;th&lt;/sup&gt; Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-FU + LV</td>
<td>425 mg of 5-FU/m&lt;sup&gt;2&lt;/sup&gt;/day for days 1-5, every 4 weeks</td>
<td>20 mg of LV/m&lt;sup&gt;2&lt;/sup&gt;/day for days 1-5, every 4 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irinotecan (Pfizer)</td>
<td>125 mg of irinotecan per week/m&lt;sup&gt;2&lt;/sup&gt; for 4 weeks, every 6 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irinotecan + 5-FU/LV</td>
<td>180 mg of irinotecan/m&lt;sup&gt;2&lt;/sup&gt; on day 1, every 2 weeks</td>
<td>1,000 mg of 5-FU/m&lt;sup&gt;2&lt;/sup&gt; on day 1 and 2, every 2 weeks</td>
<td>200 mg of LV/m&lt;sup&gt;2&lt;/sup&gt; on day 1 and 2, every 2 weeks</td>
<td></td>
</tr>
<tr>
<td>Capecitabine (Roche)</td>
<td>2,500 mg of capecitabine per m&lt;sup&gt;2&lt;/sup&gt;/day for days 1-14, every 3 weeks</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Capecitabine + Irinotecan</td>
<td>70 mg of irinotecan/m&lt;sup&gt;2&lt;/sup&gt;/week, every 6 weeks</td>
<td>2,000 mg of capecitabine per m&lt;sup&gt;2&lt;/sup&gt;/day for days 1-14, every 3 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxaliplatin + 5-FU/LV</td>
<td>85 mg of oxaliplatin per m&lt;sup&gt;2&lt;/sup&gt; on day 1, every 2 weeks</td>
<td>1,000 mg of 5-FU/m&lt;sup&gt;2&lt;/sup&gt; on day 1 and day 2, every 2 weeks</td>
<td>200 mg of LV/m&lt;sup&gt;2&lt;/sup&gt; on day 1 and day 2, every 2 weeks</td>
<td></td>
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<tr>
<td>Oxaliplatin + Capecitabine</td>
<td>130 mg of oxaliplatin per m&lt;sup&gt;2&lt;/sup&gt; on day 1, every 3 weeks</td>
<td>1,700 mg of capecitabine per m&lt;sup&gt;2&lt;/sup&gt;/day for days 1-14, every 3 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cetuximab (ImClone)</td>
<td>400 mg of cetuximab per m&lt;sup&gt;2&lt;/sup&gt; on day 1; then 250 mg/m&lt;sup&gt;2&lt;/sup&gt; once a week, every 6 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cetuximab + Irinotecan</td>
<td>400 mg of cetuximab per m&lt;sup&gt;2&lt;/sup&gt; on day 1; then 250 mg/m&lt;sup&gt;2&lt;/sup&gt; once a week, every 6 weeks</td>
<td>125 mg of irinotecan per week/m&lt;sup&gt;2&lt;/sup&gt; for 4 weeks, every 6 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bevacizumab + Oxaliplatin+ 5-FU/LV</td>
<td>5 mg of bevacizumab per kg, every 2 weeks</td>
<td>85 mg of oxaliplatin per m&lt;sup&gt;2&lt;/sup&gt; on day 1, every 2 weeks</td>
<td>1,000 mg of 5-FU/m&lt;sup&gt;2&lt;/sup&gt; on day 1 and day 2, every 2 weeks</td>
<td>200 mg of LV/m&lt;sup&gt;2&lt;/sup&gt; on day 1 and day 2, every 2 weeks</td>
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<tr>
<td>Bevacizumab + Irinotecan + 5-FU/LV</td>
<td>5 mg of bevacizumab per kg, every 2 weeks</td>
<td>180 mg of irinotecan per m&lt;sup&gt;2&lt;/sup&gt; on day 1, every 2 weeks</td>
<td>1,000 mg of 5-FU/m&lt;sup&gt;2&lt;/sup&gt; on day 1 and day 2, every 2 weeks</td>
<td>200 mg of LV/m&lt;sup&gt;2&lt;/sup&gt; on day 1 and day 2, every 2 weeks</td>
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<td>Bevacizumab + Irinotecan + Capecitabine</td>
<td>7.5 mg of bevacizumab per kg, every 3 weeks</td>
<td>130 mg of irinotecan per m&lt;sup&gt;2&lt;/sup&gt; on day 1, every 3 weeks</td>
<td>1,700 mg of capecitabine/m&lt;sup&gt;2&lt;/sup&gt;/day for days 1-14, every 3 weeks</td>
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</table>

Each regimen is assumed to last for 24 weeks. mg=miligram of active ingredient; m<sup>2</sup>=meter squared of a patient’s surface area; kg=kilogram of a patient’s weight.

Appendix II: Inter-firm Bundling and Demand Models

Firms benefit from a new cocktail regimen when it increases overall demand without making the market much more competitive. This is likely to happen in markets where consumers are substantially heterogeneous. In such markets a new product does not steal as many consumers from existing products as in markets where consumers are more homogeneous. This can be clearly seen in a simple logit model where the indirect utility of consumer i for product j is

\[ u_{ij} = \delta_j - \alpha p_j + \varepsilon_{ij} \]

where \( \delta_j \) is product j’s quality, \( p_j \) its price, and \( \varepsilon_{ij} \) represents the idiosyncratic shock from the Type I extreme value distribution.

Suppose two firms, firms A and B, sell one stand-alone product each. Without inter-firm bundling the equilibrium price is

\[ \tilde{p}_j = \frac{1}{\alpha (1 - \tilde{s}_j)} \]

for \( j = A, B \). Now suppose these firms have a bundle that consists of one unit of each stand-alone product such that \( p_C = p_A + p_B \). The profit maximization condition is

\[ \frac{\partial \pi_j}{\partial p_j} = (s_j + s_C) - \alpha p_j \left[ s_j + s_C - (s_j + s_C)^2 \right] = 0 \]

and the equilibrium price is

\[ p_j^* = \frac{1}{\alpha \left[ 1 - (s_j^* + s_C^*) \right]} \]

Compared with the no cocktail case, the firms charge higher prices and earn higher profits as long as \( (s_j^* + s_C^*) > \tilde{s}_j \). This shows that the firms in this market have an incentive to have an inter-firm bundle as long as it increases the overall demand.

However, the demand expansion is not a sufficient condition for a higher profit if consumers are less heterogeneous. Consider a one random coefficient pure characteristics model, i.e., the vertical model, where consumer heterogeneity is uniformly distributed on the unit interval. The utility of consumer i is

\[ u_{ij} = v_i \delta_j - p_j \]

where \( v_i \) is consumers’ quality valuation and \( j = A, B \). Suppose \( \delta_B > \delta_A \). In this model market shares are determined by the value of \( v_i \) such that consumers with \( v_i \in \left( \frac{p_A}{\delta_A}, \frac{p_A - p_B}{\delta_B - \delta_A} \right) \) choose firm A’s stand-alone product and those with \( v_i \in \left( \frac{p_B - p_A}{\delta_B - \delta_A}, 1 \right) \) choose firm B’s stand-alone product. Suppose that \( \delta_A = 1 \) and \( \delta_B = 2 \) and the cost of production is zero. Without an inter-firm bundle the equilibrium prices are \( (\tilde{p}_A, \tilde{p}_B) = (0.143, 0.571) \) and the market shares are \( (\tilde{s}_A, \tilde{s}_B) = (0.286, 0.571) \). The profits are 0.041 for firm A and 0.327 for firm B.

Suppose that the firms introduce a bundle that mixes a half unit of the two stand-alone products such that its price, \( p_C \), is 0.5 \( (p_A + p_B) \) and that its quality is \( \delta_C \). Note that \( \delta_C \) should be higher than 0.5 \( (\delta_B + \delta_A) \) for the bundle to have a positive market share. This is because consumers with \( v_i \in \left( \frac{p_C - p_A}{\delta_C - \delta_A}, \frac{p_B - p_C}{\delta_B - \delta_C} \right) \) choose the bundle but \( \frac{p_C - p_A}{\delta_C - \delta_A} > \frac{p_B - p_C}{\delta_B - \delta_C} \) if \( \delta_C \leq 0.5 (\delta_B + \delta_A) \). Numerical simulations show that as \( \delta_C \) increases from 1.5 to 1.8, firm A’s price goes down from 0.143 to 0.115 and firm B’s price goes down from 0.571 to 0.378. The market share for the bundle goes up from 0 to 0.492 but the market share for the stand-alone products of firms A and B goes down to 0.049 and 0.344 respectively. Nevertheless, both firms sell more units: a total demand for firm A’s product is
0.295, up from 0.286 while it is 0.590 for firm B’s product, up from 0.571.

Although both firms sell more units with the inter-firm bundle, their profits are lower because the prices go down “too much”. Firm A’s profit goes down from 0.041 to 0.034 and firm B’s profit goes down from 0.327 to 0.223. The firms now compete more fiercely as the bundle makes their products closer substitutes. This can be seen in their best response functions. Without the bundle the best response functions are

\[
P_A = \frac{1}{4} P_B \\
P_B = \frac{1}{2} + \frac{1}{2} P_A
\]

for firms A and B respectively. With the bundle they change to

\[
P_A = \frac{1}{2 + 2\Psi} P_B \\
P_B = \frac{\Psi}{2} + \frac{1}{2} P_A
\]

where \(\Psi = 4(2 - \delta_C)(\delta_C - 1)\) and \(0 < \Psi \leq 1\). This shows that when the bundle is introduced, firm A wants to increase its price while firm B wants to lower it. This is because the bundle is a higher quality new product for firm A while it is a lower quality new product for firm B. However, firm B’s best response function shifts further than that of firm A, and both firms set lower prices in the new equilibrium.

Consider another case where the firms introduce a bundle that mixes one unit of the two stand-alone products such that its price, \(p_C\), is \(p_A + p_B\). Note that \(\delta_C\) should be larger than \(\delta_B\) for the bundle to have a positive market share and be no larger than 2.5 for firm B’s stand-alone product to have a positive market share. Now consumers with \(v_i \in \left(\frac{p_C - p_B}{\delta_B - \delta_A}, \frac{p_C - p_B}{\delta_C - \delta_B}\right]\) choose the bundle, those with \(v_i \in \left(\frac{p_B - p_A}{\delta_B - \delta_A}, \frac{p_B - p_A}{\delta_C - \delta_B}\right]\) choose firm B’s stand-alone product, and those with \(v_i \in \left(\frac{p_A}{\delta_A}, \frac{p_B - p_A}{\delta_B - \delta_A}\right]\) choose firm A’s stand-alone product. The best response functions with this bundle are

\[
P_A = \frac{\delta_C - 2}{2(2\delta_C - 3)} (p_B + 1) \\
P_B = \frac{1}{2} + \frac{1}{2} P_A
\]

Notice that firm B’s best response function is the same as without the bundle. This is because the total share of consumers choosing firm B’s product, which is \(1 - \frac{p_B - p_A}{\delta_B - \delta_A}\), does not depend on the bundle’s quality.

Algebra shows that when this bundle is introduced, firm A deviates to decrease its price if \(2 < \delta_C \leq 16/7\) and increase its price if \(16/7 < \delta_C \leq 2.5\). Since firm B’s best response function does not change, new equilibrium prices depend on how firm A deviates: they are higher when firm A increases its price and lower when it decreases its price. In both types of equilibrium firm A sells more units than before with its total demand monotonically increasing from 0.752 to 0.800 as \(\delta_C\) increases from 2.01 to 2.50. However, the total demand for firm B’s product is lower when \(2 < \delta_C \leq 16/7\) and higher when \(16/7 < \delta_C \leq 2.5\). In other words, when the quality of the bundle is not sufficiently high (\(\delta_C < 16/7\)), both firms compete more fiercely and firm B, whose stand-
alone product is a closer substitute for the bundle, loses its consumers and becomes worse off than before. Firm A, whose stand-alone product is not a “direct” substitute for the bundle, makes a higher profit even with lower prices when $\delta C > 2.09$ but is also worse off when $2 < \delta C \leq 2.09$. When $16/7 < \delta C \leq 2.5$, however, both firms can exploit the bundle’s high quality such that they can charge higher prices and sell more of their products, which of course results in higher profits.

These two cases show that in the vertical model an inter-firm bundle makes firms compete more fiercely unless its quality is "high enough" and that all firms benefit from it only when its quality falls within a narrow range. This is different from the case of the logit model where firms are better off as long as the bundle increases total demand. This suggests that the pure characteristics model, at least the vertical model, is a less appropriate demand model for markets where inter-firm bundling is prevalent.
Table A-1: Demand Estimation with Various Specifications in the Logit Demand Model

<table>
<thead>
<tr>
<th>Variable</th>
<th>Specification 1</th>
<th>Specification 2</th>
<th>Specification 3</th>
<th>Specification 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OLS</td>
<td>IV</td>
<td>OLS</td>
<td>IV</td>
</tr>
<tr>
<td>log (price)</td>
<td>-0.473* (0.039)</td>
<td>-0.281* (0.060)</td>
<td>-0.493* (0.051)</td>
<td>-0.392* (0.060)</td>
</tr>
<tr>
<td></td>
<td>-0.690* (0.064)</td>
<td>-1.210* (0.302)</td>
<td>-1.290* (0.218)</td>
<td>-1.606* (0.437)</td>
</tr>
<tr>
<td>Response</td>
<td>0.025* (0.008)</td>
<td>0.043* (0.008)</td>
<td>0.043* (0.009)</td>
<td>0.074* (0.010)</td>
</tr>
<tr>
<td>Rate (%)</td>
<td>0.001 (0.006)</td>
<td>-0.011* (0.006)</td>
<td>-0.022* (0.008)</td>
<td>-0.045* (0.009)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td></td>
<td></td>
<td>-0.022* (0.006)</td>
<td>-0.045* (0.009)</td>
</tr>
<tr>
<td>Pfizer</td>
<td>-0.695* (0.266)</td>
<td>-0.027 (0.205)</td>
<td>-0.515 (0.276)</td>
<td>-0.515 (0.276)</td>
</tr>
<tr>
<td></td>
<td>2.730* (1.213)</td>
<td>2.439* (0.743)</td>
<td>4.293* (1.827)</td>
<td>4.293* (1.827)</td>
</tr>
<tr>
<td>Roche</td>
<td>-1.315* (0.174)</td>
<td>-0.063 (0.485)</td>
<td>-1.314* (0.161)</td>
<td>-1.892* (0.178)</td>
</tr>
<tr>
<td></td>
<td>-1.621* (0.219)</td>
<td></td>
<td>-1.577* (0.233)</td>
<td></td>
</tr>
<tr>
<td>ImClone</td>
<td>-0.988* (0.333)</td>
<td>2.029* (1.095)</td>
<td>-1.252* (0.304)</td>
<td>-1.252* (0.304)</td>
</tr>
<tr>
<td>Sanofi</td>
<td>-0.125 (0.298)</td>
<td>3.244* (1.236)</td>
<td>-0.948* (0.300)</td>
<td>-0.948* (0.300)</td>
</tr>
<tr>
<td></td>
<td>2.752 (1.463)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genentech</td>
<td>-0.332 (0.241)</td>
<td>0.553 (0.504)</td>
<td>-1.255* (0.246)</td>
<td>-1.439* (0.440)</td>
</tr>
<tr>
<td>R-square</td>
<td>0.819</td>
<td>0.862</td>
<td>0.875</td>
<td>0.899</td>
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<tr>
<td>1st Stage</td>
<td>80.204</td>
<td>8.231</td>
<td>14.828</td>
<td>5.782</td>
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<tr>
<td>F-statistics</td>
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<tr>
<td></td>
<td>Prices Per mg (current situation = 100)</td>
<td>Profit (current situation = 100)</td>
<td>CS</td>
<td></td>
</tr>
<tr>
<td>---------------------</td>
<td>----------------------------------------</td>
<td>----------------------------------</td>
<td>----</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pfizer</td>
<td>Roche</td>
<td>Sanofi</td>
<td>ImClone</td>
</tr>
<tr>
<td>Current</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>No Pf + Ro</td>
<td>101.9</td>
<td>111.9</td>
<td>100.3</td>
<td>100.3</td>
</tr>
<tr>
<td>No Ro + Sa</td>
<td>91.7</td>
<td>69.4</td>
<td>88.6</td>
<td>97.6</td>
</tr>
<tr>
<td>No Pf + Ge</td>
<td>45.9</td>
<td>190.0</td>
<td>95.8</td>
<td>88.4</td>
</tr>
<tr>
<td>No Ro + Sa + Ge</td>
<td>97.5</td>
<td>88.4</td>
<td>96.2</td>
<td>99.2</td>
</tr>
<tr>
<td>No Pf + Im</td>
<td>58.2</td>
<td>240.3</td>
<td>91.1</td>
<td>70.9</td>
</tr>
<tr>
<td>No Sa + Ge</td>
<td>84.9</td>
<td>231.1</td>
<td>54.7</td>
<td>95.6</td>
</tr>
</tbody>
</table>
Table A-3: Merger Analysis in the IV Logit Model

<table>
<thead>
<tr>
<th></th>
<th>Two Firms’ Joint Profit</th>
<th>Consumer Surplus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Current</td>
<td>Removed</td>
</tr>
<tr>
<td>Pfizer + Roche</td>
<td>100</td>
<td>94.6</td>
</tr>
<tr>
<td>Roche + Sanofi</td>
<td>100</td>
<td>86.5</td>
</tr>
<tr>
<td>Pfizer + Genentech</td>
<td>100</td>
<td>69.1</td>
</tr>
<tr>
<td>Pfizer + ImClone</td>
<td>100</td>
<td>63.0</td>
</tr>
<tr>
<td>Sanofi + Genentech</td>
<td>100</td>
<td>50.6</td>
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</tbody>
</table>