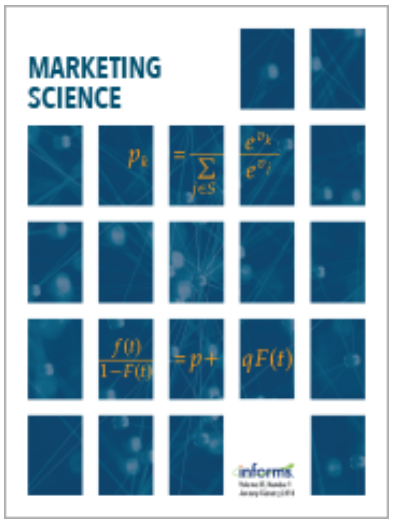

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Promotion Spillovers: Drug Detailing in Combination Therapy

Hongju Liu,[a] **Qiang Liu,**[b] **Pradeep K. Chintagunta**[c]

[a] University of Connecticut School of Business, Storrs, Connecticut 06269; [b] Krannert School of Management, Purdue University, West Lafayette, Indiana 47907; [c] Booth School of Business, University of Chicago, Chicago, Illinois 60637

Contact: hliu@business.uconn.edu (HL); liu6@purdue.edu (QL); pradeep.chintagunta@chicagobooth.edu (PKC)

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Abstract. This paper examines the spillover effects of promotions when products from different firms are consumed in a bundle. Using data from the HIV/AIDS category, a canonical example of combination therapy, we estimate a hierarchical Bayesian logit model across treatment regimens and show that detailing for one drug can increase demand for other drugs that are often combined with the focal drug. Such spillover effects could lead to free riding by the drugs benefitting from the spillover. We investigate the managerial and policy implications of detailing spillover effects via counterfactual policy simulations based on a dynamic oligopoly game of detailing. For managers, we show how firms can internalize the spillover effects and reduce the incentive for free riding. For policy makers, the implications of our findings relate to detailing restrictions that are often proposed on branded drugs. These restrictions aim to increase social welfare by encouraging the use of generic drugs. However, in combination therapies generic drugs may actually benefit from the detailing of complementary branded products. If detailing was curtailed, this could adversely affect generic drug prescriptions as well, which runs counter to policy makers' objectives of encouraging use of generic drugs.

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Keywords: pharmaceutical marketing • combination therapy • spillover • free riding • dynamic oligopoly game

1. Introduction

There has been a growing body of research investigating the spillover effects of firms' promotional efforts (e.g., Erdem and Sun 2002, Balachander and Ghose 2003, Sahni 2016, Shapiro 2015, Lewis and Nguyen 2015, Liu et al. 2015). Different mechanisms could cause the promotion of one product to increase demand for other products. When a firm owns multiple products across categories, advertising and sales promotions for one product might increase demand for the firm's other products with the same brand (Erdem and Sun 2002). In the case of brand extensions, advertising for one brand may help the related brands in the same firm (Balachander and Ghose 2003). Advertising for one product may also remind consumers of other products in the same category, thus having a positive effect on the demand for competing products through a category-expansion effect (Sahni 2016, Lewis and Nguyen 2015). Specific to the pharmaceutical market, the category-expansion effect on physicians' prescriptions has been found for direct-to-consumer advertising and professional meetings and events (Liu et al. 2015, Shapiro 2015). In addition, advertising can spill over across media (Naik et al. 2005, Wilbur 2008, Feit et al. 2013). In this paper, we examine another potential source of spillover effects of promotion, i.e., when products from different firms are consumed as a bundle. The empirical context on which we focus is combination therapy in the pharmaceutical industry.

Combination therapy refers to the simultaneous administration of two or more medications to treat a single disease. In practice it can be achieved by using separate drugs or a combination drug with multiple active ingredients. The advantages of combination therapy may include reduced drug resistance, better efficacy, and fewer side-effects. Because of medical research advances in the past few decades, combination therapies have become essential in an increasing number of key categories including HIV/AIDS, cancer, hypertension, asthma, hepatitis, rheumatoid arthritis, tuberculosis, leprosy, malaria, etc.

A drug category involving combination therapy typically includes medications from more than one pharmaceutical firm. Incentives behind firms' promotional efforts become more complicated in this environment. On one hand, firms have incentives to promote their own drugs, and hence combinations involving those drugs, to better compete against other combinations. On the other hand, their promotional efforts will not

only benefit their own drugs but also spill over to other drugs in the same combination, creating incentives for other drugs to free ride on the promotional efforts of the focal drug. So firms need to consider the trade-off between these incentives to determine their marketing spending.

This study aims to: (i) Identify the effects, especially the spillover effects, of drug detailing in the context of combination therapy; (ii) understand firms' optimal detailing strategies for drugs involved in combination therapies; and (iii) highlight the managerial and policy implications of spillover effects. Using physician panel data on prescriptions and detailing visits in the HIV/AIDS category, we uncover preliminary evidence for the spillover of drug detailing on physicians' prescription decisions. Next, we estimate a hierarchical Bayesian logit demand model of HIV treatment regimens to formally examine such spillover effects. Based on our demand estimates, we then solve the dynamic detailing game between competing drug makers to investigate their optimal detailing strategies.

The empirical estimation of the parameters of our demand model reveals significant spillover effects of drug detailing in this category. More specifically, our results indicate that a drug's detailing may not only increase its own prescriptions but may also increase prescriptions of the drugs that are often combined with the focal drug. To assess the market structure of the category, we identify the drugs that have strong clout in detailing spillovers to other drugs, and the drugs that are more susceptible to other drugs' detailing spillovers.[1] For example, we find that Epzicom, Reyataz, and Prezista have strong spillover clout, while Norvir and Sustiva exhibit strong spillover susceptibility.

We further decompose the net cross-drug detailing effect for each cross-drug pair into a *competition* effect and a *spillover* effect. Consider two drugs, A and B, which are prescribed together as parts of the same regimen but are also separately prescribed in other regimens. The competition effect measures how much drug B's detailing *hurts* the demand for drug A's regimens not including B because drug B's own regimens become more attractive. The spillover effect measures how much drug B's detailing helps regimens containing A and B, and hence *increases* demand for drug A.

To illustrate, consider two drugs, Truvada and Reyataz, which are part of the same cocktail but also belong to cocktails with other drugs. We find that eliminating the competition effect of Reyataz's detailing on Truvada would have increased demand for Truvada by 0.47%, but eliminating the spillover effect would have reduced demand for Truvada by 1.35%. Therefore, in this case, the spillover effect is bigger than the competition effect, i.e., the detailing for Reyataz benefits Truvada. On the other hand, detailing for Truvada has a strong competition effect and a strong spillover effect on demand for Reyataz, likely due to the asymmetry in market power between the two drugs; Truvada is a component of many popular cocktails while Reyataz faces intense competition. According to our results, eliminating the competition effect of Truvada's detailing would have increased demand for Reyataz by 5.22%, and eliminating the spillover effect would have reduced demand for Reyataz by 3.97%.

Next, we model firms as forward-looking decision makers, and solve the dynamic oligopoly detailing game between them to obtain their optimal detailing strategies. In particular, we analyze specific scenarios in which firms have incentives to free ride due to the spillover effects of other firms' detailing efforts. The spillover effects of detailing and the incentives for free riding create special considerations for firms and regulators.

For regulators, detailing restrictions on branded drugs are often proposed to increase social welfare by reducing wasteful expenditures and encouraging generic use. However, counterfactual simulations based on our model reveal unintended consequences of detailing restrictions. For example, generic drugs may benefit from the detailing of complementary branded drugs, and hence may be adversely affected if detailing of the branded drugs was curtailed. In such cases detailing restrictions could actually hurt generics although policy makers may be interested in promoting their use.

Because of the concern over free riding, firms may be interested in ways to internalize the spillover effects and reduce incentives for free riding. For example, Atripla is a fixed-dose combination drug that combines Truvada from Gilead Sciences and Sustiva from Bristol-Myers Squibb (BMS). We show that, if Gilead and BMS do not coordinate their detailing efforts, Gilead would engage in minimal detailing for Atripla and free ride on the strong detailing efforts by BMS. Gilead and BMS could eliminate the concern over free riding by setting up an independent joint venture to market Atripla, or by merging their assets in the HIV category into a new company. Our results indicate that, holding prices constant, a merger would be more profitable than an independent joint venture. Because of savings on detailing costs, a merger would raise profits by 2.5% despite a lower market share for the merged company.

Note that our framework has applications beyond combination therapies. For example, in case of comorbidities, drugs from different categories are used together to control the simultaneous presence of two chronic conditions. This may lead to spillover effects and our model can be applied to study the optimal detailing or advertising decisions of firms in such markets. Similarly, our model can be applied to situations where certain drugs are compatible and even positively

interacting, while others are incompatible. Such interaction effects between drugs may also induce spillover effects of detailing.

Although the pharmaceutical industry is large and important by itself, our framework and findings are not restricted to that industry. Whenever products from different companies can be consumed as a bundle, promotion for one product may have spillover effects on other products, potentially creating incentives to free ride. Such examples are abundant. For example, Nike and Apple jointly develop and market Nike+products; Citibank, American Airlines, and Visa issue a credit card together; Verizon sells Samsung Galaxy smartphones with the Android operating system from Google; Intel and Dell engage in cooperative advertising campaigns to promote Dell computers with Intel CPUs inside. Our framework can be readily adapted to study such promotion decisions of firms.

2. Literature

Our paper is related to several streams of literature. We provide a brief, non-comprehensive, review and focus on studies of pharmaceutical markets.[2] The first area is that of demand spillovers of marketing activities. A growing marketing literature has examined the cross-category impact of marketing activities in the context of frequently purchased packaged goods (see Russell et al. 1999 and Seetharaman et al. 2005 for comprehensive reviews of multicategory models). These multicategory models typically impose some structure on how the utilities of individual products affect the utility of a product bundle to reduce the number of parameters (e.g., Manchanda et al. 1999, Russell and Peterson 2000, Gentzkow 2007, Liu et al. 2010, Sriram et al. 2010, Kumar et al. 2011, Ma et al. 2012). Specific to multicategory behavior in pharmaceutical marketing, but using a different model structure compared to those above, Dong et al. (2011) develop a simultaneous-equation multivariate count data model that allows a firm's prescriptions in one category to be influenced by its detailing activities in other categories.

This broad stream of studies is also related to the extensive literature on bundling strategies, for which Stremersch and Tellis (2002) provide an informative synthesis. Illustrative of studies in this area is the work by Venkatesh and Mahajan (1997) who propose an analytical approach that helps marketers of products with branded components make optimal pricing and partner selection decisions. Although their focus is pricing rather than advertising, their model is applied to the context of ingredient branding involving a Compaq PC and an Intel CPU, which resembles our context of combination therapy.

A second area of the literature to which our paper pertains is the carryover effects of marketing activities across time periods. In particular, the literature on pharmaceutical products has documented the intertemporal effects of detailing (e.g., Gönül et al. 2001, Manchanda et al. 2004, Mizik and Jacobson 2004, Venkataraman and Stremersch 2007, Janakiraman et al. 2008, Narayanan and Manchanda 2009, Ching and Ishihara 2010, Chintagunta et al. 2012, Stremersch et al. 2013). In those studies, the structural mechanisms underlying such intertemporal effects include learning by physicians about the efficacy (e.g., Narayanan et al. 2005) and side effects (e.g., Chan et al. 2013) of a new medication, as well as the carryover effects of detailing (e.g., via goodwill accumulation) from one period to another even for drugs that have been on the market for a while. In particular, Narayanan et al. (2005) show that the learning effect dominates in the introductory phase of a product life cycle, while goodwill accumulation dominates later on. Ching and Ishihara (2012) focus on disentangling the learning and goodwill accumulation roles of detailing. Their identification strategy takes advantage of a special type of co-marketing agreement in which two companies promote the same chemical but with different brand names.

Several recent papers have moved beyond the demand side of the analysis to study pharmaceutical firms' optimal detailing strategies by solving the dynamic decision problem induced by the intertemporal effects of detailing described above. For example, Montoya et al. (2010) use a hidden Markov model to capture the long-term effects of marketing activities (detailing and sampling) for a new drug, and then solve the single-agent dynamic decision process to obtain the optimal promotion schedule for each physician. Based on a demand model of physicians' prescription decisions that are affected by the goodwill stocks generated by firms' detailing visits, Liu et al. (2016) propose a two-stage estimation approach to recover the detailing costs from equilibrium conditions based on dynamic detailing competition among firms. Given that detailing is akin to advertising, our paper is also related to the broader area of optimal allocation of marketing communication resources. In particular, Dubé et al. (2005) develop a model of dynamic advertising competition to study the optimal advertising scheduling over time. They find evidence for a threshold effect that is indicative of an *S*-shaped advertising response curve.

Because the pharmaceutical industry is heavily regulated, the effects of certain regulations have been analyzed in prior literature. For example, Stremersch and Lemmens (2009) study the role of regulatory regimes in explaining the international sales growth of new products by using a regression model with time-varying coefficients. They investigate regulatory constraints such as manufacturer price controls, restrictions of physician prescription budgets, and the prohibition of direct-to-consumer advertising. Using a learning model, Ching and Ishihara (2010) study the policy of

encouraging physicians to share their patients' experiences with a public health agency. Larkin et al. (2014) investigate the impact of restrictions on detailing by academic medical centers and find that restrictions reduce physicians' prescriptions for branded drugs, but increase prescriptions for generic drugs. Similarly, Liu et al. (2016) find that detailing restrictions enhance the prescriptions for non-drug treatment in the high cholesterol category and asymmetrically impact competing firms.

Our study combines elements of and further complements the above literatures. Because we focus on spillovers of marketing across drugs, our research is related to the demand literature on how physicians respond to detailing. At the same time, we need to account for the carryover effects of marketing activities on how detailing today influences prescription decisions in the future. Together, spillover and carryover effects have implications for the optimal spending policies of firms in these categories. This also represents the contribution of our research to these domains. Although previous studies have examined the effects of detailing restrictions, we show that, in the presence of combination therapies, such restrictions may have unintended consequences that need to be taken into account by regulators.

3. Data and Preliminary Analyses

The empirical context of this study is the HIV/AIDS category. To manage HIV infection, it is critical to control the growth and reproduction of HIV. Combinations of antiretroviral drugs create multiple obstacles to HIV replication and reduce the possibility of a superior mutation. Therefore, the current standard of care for patients infected with HIV involves a combination of three or more antiretroviral drugs taken every day for life; this is known as a Highly Active Antiretroviral Treatment (HAART) *regimen*. In principle physicians can prescribe any drug combination as long as it is effective. So the formulation of regimens is not controlled by pharmaceutical companies. A number of popular HAART regimens consist of three drugs, i.e., two nucleoside reverse transcriptase inhibitors (NRTI), plus a protease inhibitor (PI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or an integrase inhibitor (II). Such a three drug combination is commonly known as a triple cocktail.

For model estimation, we restrict attention to the top 11 drugs and 20 regimens formed by these drugs. The major antiretroviral drugs used for the treatment of infection by HIV are listed in Table 1. Atripla is a combination drug with two NRTI component drugs and one NNRTI component drug. Because the two NRTI components are from Gilead while the NNRTI component is from BMS, Atripla is jointly marketed by Gilead and BMS. The convenience of taking a single, once-daily pill makes this a very successful product in this category. Most HAART regimens require two NRTI drugs. Both Truvada from Gilead and Epzicom from GlaxoSmithKline (GSK) are combination drugs with two NRTI components. Thus they compete against each other, while Truvada or Epzicom can be combined with other NNRTI, PI or II drugs to form a treatment regimen. Among the PI drugs Norvir (Abbott) is special. Usually it is not used individually, but together with another PI drug to boost the effectiveness of the other PI drug. The popular combinations are Norvir + Lexiva, Norvir + Prezista, and Norvir + Reyataz. However, Abbott also markets Kaletra, a combination drug containing Norvir and another PI, Lopinavir.

In the HIV category a single firm often markets multiple drugs. In addition to the aforementioned example of Abbott marketing Norvir and Kaletra, Gilead markets Atripla and Truvada, and BMS markets Atripla, Sustiva, and Reyataz. Because all drugs are involved in combination therapies, there can be complementarities or substitution effects between the drugs marketed by the same firm. This results in a complicated resource allocation problem for firms to decide on their optimal detailing strategies.

The data set used for the empirical analysis in this study was collected by a marketing research firm from a panel of 131 physicians who specialize in HIV treatment.[3] Each physician reported the detailing visits they received and regimens they prescribed. We have access to data for the period from September 2008 to December 2009. During this period these physicians received 7,354 detailing visits in this category and prescribed 5,378 HAART regimens for new patient visits, corresponding to 9,974 antiretroviral drugs.[4] None of the drugs under consideration was close to patent expiration in our study period, so in this paper we are not concerned about the potential entry of generics.

The shares for the drug-level detailing activities are provided in Table 1. Notably Norvir had the fewest detailing visits. On the other hand, we observe physicians' prescription decisions at the regimen level, i.e., physicians always prescribe a treatment regimen for a particular patient visit. The descriptive statistics for the regimen-level prescription volumes are provided in Table 2. The top regimens are Atripla, Truvada + Norvir + Reyataz, Truvada + Norvir + Prezista, Truvada + Kaletra, and Isentress + Truvada.

Although we observe detailing visits at the individual drug level, physicians prescribe regimens that may consist of several individual drugs. It is clear in this context then that physicians' substitute between different regimens in their prescription decisions, as shown in Table 3.[5] This mismatch creates two interesting situations. First, we need to model physicians' choices

Table 1. Major Drugs in the HIV/AIDS Category and Their Detailing Shares of the Category

Drug name	Drug class	Year approved	Company	Detailing share (%)
Atripla (Truvada + Sustiva)	NRTI/NRTI/NNRTI	2006	Gilead and BMS	12.71
Epzicom	NRTI/NRTI	2004	GSK	10.08
Isentress	II	2007	Merck	10.40
Kaletra (Norvir + Lopinavir)	PI/PI	2000	Abbott	12.17
Lexiva	PI	2003	GSK	9.21
Norvir	PI	1996	Abbott	0.69
Prezista	PI	2006	Tibotec	13.58
Reyataz	PI	2003	BMS	11.52
Sustiva	NNRTI	1998	BMS	2.23
Truvada	NRTI/NRTI	2004	Gilead	8.85
Viramune	NNRTI	1996	Boehringer Ingelheim	8.56

between regimens while accounting for the effects of drug-level detailing activities. Second, a firm's detailing decisions must be based on the demand for different regimens, while one drug can be a component of multiple regimens. In Section 4, we present a formal econometric model that accounts for these features of the data.

As noted above, a particular drug in the HIV category can often be combined with other drugs to form different regimens from which physicians can choose. Consequently, marketing efforts for one drug can have a positive impact on physicians' choice probabilities of the regimens containing this drug, and hence can spill over to other drugs in these regimens. To look for preliminary evidence of the spillover of drug detailing, we examine the case of Norvir. Norvir is a PI drug commonly used to boost the effectiveness of other PI drugs such as Lexiva, Prezista, and Reyataz. Although other PI drugs can be used without Norvir, in many cases they are prescribed with Norvir. Therefore, detailing efforts for the other PI drugs may not only benefit these drugs themselves but may also increase the prescriptions of Norvir.

This conjecture is supported by observed detailing and prescription patterns in our data. For each physician in our sample, we calculate the total detailing visits for Lexiva, Prezista, and Reyataz as a percentage of the total detailing visits the physician received. After removing the physicians with fewer than 10 details or prescriptions, we take a median split of this percentage and compare the two groups of physicians in their drug prescriptions. For the group of physicians receiving fewer details for Lexiva, Prezista, and Reyataz, 24.8% of the prescribed regimens contain Norvir. For the other group, 29.4% of the prescribed regimens contain Norvir. The results provide crude evidence that Norvir benefited from the spillover of detailing for Lexiva, Prezista, and Reyataz. Note that we do not explicitly control for the detailing on Norvir due to its low level and hence small impact. In fact, the group of physicians with fewer details for Lexiva, Prezista, and Reyataz actually received more details for Norvir than the other group (accounting for 0.86% versus 0.22% of all details).

Table 2. Descriptive Statistics of Prescription Over Physician/Month Combination[a]

Regimen	Mean	S.D.
Atripla	0.800	1.203
Atripla + Isentress	0.022	0.173
Epzicom + Isentress	0.013	0.112
Epzicom + Kaletra	0.018	0.146
Epzicom + Norvir + Lexiva	0.024	0.177
Epzicom + Norvir + Prezista	0.015	0.128
Epzicom + Norvir + Reyataz	0.048	0.244
Epzicom + Reyataz	0.031	0.192
Epzicom + Sustiva	0.020	0.158
Epzicom + Viramune	0.023	0.177
Isentress + Truvada + Kaletra	0.014	0.128
Isentress + Norvir + Prezista	0.012	0.123
Isentress + Truvada + Norvir + Prezista	0.040	0.221
Isentress + Truvada	0.134	0.521
Truvada + Kaletra	0.129	0.436
Truvada + Norvir + Lexiva	0.048	0.271
Truvada + Norvir + Prezista	0.205	0.776
Truvada + Norvir + Reyataz	0.286	0.654
Truvada + Sustiva	0.039	0.374
Truvada + Viramune	0.073	0.327

[a]These are the means and standard deviations for the number of prescriptions for each regimen. For example, on average, each physician wrote 0.800 prescriptions for Atripla per month.

4. Model

To investigate the spillover effects and the optimal detailing strategies under combination therapy, we first set up a hierarchical Bayesian multinomial logit model to capture how the demand for various HAART regimens varies according to firms' detailing efforts. In our demand model, we assume that physicians directly choose from different regimens. To quantify salience effects in physician learning about drug quality, Camacho et al. (2011) used a similar approach to model physicians' prescriptions decisions in the context of

Table 3. Regimen Switching Between the First and Last Patient Visits to Each Physician

First\Last	Atripla	Isentress + Truvada	Truvada + Kaletra	Truvada + Norvir + Prezista	Truvada + Norvir + Reyataz	Other
Atripla	38	3	1	7	9	11
Isentress + Truvada	0	1	0	0	0	1
Truvada + Kaletra	6	3	0	0	2	1
Truvada + Norvir + Prezista	1	0	0	0	0	1
Truvada + Norvir + Reyataz	7	0	1	1	4	2
Other	7	5	1	5	4	9

combination therapy for the obstructive airways disease category. An alternative approach might be a two-step choice process, i.e., (i) selecting the combination of drug classes (NRTI/NNRTI/PI/II); and (ii) selecting the appropriate drugs in each class. We believe that our approach is more flexible and better reflects a physician's decision making process. For example, the treatment guidelines released by the U.S. Department of Health and Human Services (HHS) specifically recommend four regimens for people taking anti-HIV medications for the first time.

Pharmaceutical firms' detailing activities may affect physicians' prescription decisions through different mechanisms. Detailing visits may provide information about the drugs so that physicians can learn about their efficacies, or detailing may persuade physicians through goodwill accumulation. Narayanan et al. (2005) show that the informative effect is more prominent in the early stages of a product life cycle (the first 6 to 14 months after launch), whereas the persuasive effect dominates later on. During our study period, all drugs under consideration appear to be well established. Even the most recently introduced drug, Isentress, was on the market for a year, and the oldest Norvir was introduced in 1996. Therefore in this study we focus only on the persuasive role of detailing through goodwill accumulation.

4.1. Physicians' Prescription Decisions

We assume that physicians maximize the utilities of their patients based on their professional judgment. Specifically, when a patient k visits physician i at time t, the physician chooses an HIV treatment regimen j that provides the greatest utility for her patient. The latent utility function, U_{ijtk} is specified as

$$U_{ijtk} = \alpha_{ij} + \beta_i \log(1 + G_{ijt}) + \varepsilon_{ijtk};$$
$$\text{where } \theta_i = (\alpha_{i1}, \ldots, \alpha_{iJ}, \beta_i)' \sim \text{MVN}(\theta, \Sigma). \quad (1)$$

Here α_{ij} represents physician i's preference for regimen j; and β_i is that physician's responsiveness to the goodwill stock of regimen j's detailing. We assume the error term ε_{ijtk} follows a type-I extreme value distribution, and that the distribution of random coefficients follows a multivariate-normal distribution. The latter accounts for heterogeneity across physicians in their preferences for the various drugs and in the effects of detailing. The hierarchical Bayesian logit model specified here is flexible and helps to overcome the IIA restrictions (McFadden and Train 2000) across regimens in the aggregate.

In Equation (1), G_{ijt} is the goodwill stock generated from the detailing efforts for all drugs in regimen j. The goodwill stock evolves according to

$$G_{ijt} = \lambda G_{ij,t-1} + \sum_{b \in B_j} \gamma_{bj} D_{ibt} + \tau_{ijt}, \quad \tau_{ijt} \sim \text{N}(0, \sigma_\tau^2). \quad (2)$$

Here $\lambda \in (0,1)$ is the retention rate of the detailing stock carried over from the previous period. B_j is the set of component drugs in regimen j, and D_{ibt} represents the number of detailing visits to physician i on drug b in time period t. γ_{bj} measures the marginal contribution of drug b's detailing visits to regimen j's goodwill stocks. We assume that, in a detailing visit for drug b, the salesperson mentions all regimens that contain drug b, thus contributing to the goodwill stocks of these regimens. The drug-regimen specific marginal contribution captures the effectiveness of different drugs' detailing activities in generating regimen-level goodwill stocks. For example, if salespeople for Kaletra focus more on Truvada + Kaletra than on Epzicom + Kaletra, we would expect a larger γ_{bj} for the former regimen. The error term τ_{ijt} captures the randomness in the goodwill stock evolution. Equation (2) indicates that the goodwill stock of a regimen is generated and reinforced through the detailing visits for individual component drugs. Note also that the detailing stock is not deterministic (as in, e.g., Narayanan et al. 2005) but is stochastic (as in, e.g., Dubé et al. 2005).

In our empirical setting, t indexes the month. Goodwill stocks are updated each month based on the detailing activities in the previous month. During a month, there may be multiple patients visiting the physician. So a physician could make multiple prescribing decisions in a month, one for each patient, but all decisions in a month are based on the same goodwill stocks for the month. Given that we observe detailing activities at a monthly level, our approach is

an approximation to a more continuous accumulation of goodwill.

We do not include a price term in the latent utility function for the following reasons. First, HIV treatment is typically paid through insurance or patient assistance programs. Second, HIV drug prices remained stable in our study period. Thus the physician- and regimen-specific intercepts provide a reasonable control for price levels and allow us to focus on detailing decisions. Song et al. (2012) use a model of linear pricing to analyze the welfare effects of combination therapy using data from the colorectal cancer drug category. They incorporate firms' pricing decisions because most oncology drugs are infused into a patient intravenously in a physician's office. Unlike drugs that are distributed through pharmacies, physicians purchase oncology drugs and then bill the patients or their insurance companies after administering the drugs as needed. So in their case, prices are important in physicians' purchase decisions. By contrast, in the HIV category, drugs are typically distributed through pharmacies and covered by insurance or patient assistance programs. Therefore, we take the prices as exogenous and study the issues involved in firms' detailing decisions.[6]

Our demand specification focuses on the impact of detailing on physicians' prescription decisions because direct-to-consumer advertising is limited in this category. We have also explored an alternative specification that incorporates time- and regimen-specific fixed effects. These fixed effects may capture the impact of other unobserved demand shocks including other promotional expenditures and clinical studies. Our estimate for detailing responsiveness (β), carry-over effect (λ), and the mean of detailing contribution effects (γ) do not change significantly (0.246 versus 0.238; 0.829 versus 0.834; 0.912 versus 0.895, respectively). None of the γ_{bj} changes significantly as well. In addition, we find no significant impacts of those fixed effects in the detailing policy functions that we subsequently include. This reassures us about our demand specification and the estimated detailing effects.

Let y_{ijt} indicate the choice of regimen j by physician i at time t. As the error term follows a type-I extreme-value distribution, the choice probability for regimen j can be written as

$$P_{ijt} = P(y_{ijt}=1) = \frac{\exp(V_{ijt})}{\sum_l \exp(V_{ilt})} = \frac{\exp(\alpha_{ij} + \beta_i \log(1+G_{ijt}))}{\sum_l \exp(\alpha_{il} + \beta_i \log(1+G_{ilt}))}. \quad (3)$$

A drug's detailing enhances the goodwill of all of the regimens that include that drug. Therefore, it may increase the choice probabilities for these regimens but reduce the choice probabilities for any other regimens in the choice set. Next we formally examine how the choice probability for a regimen j is affected by the detailing for drug b. To simplify notation, we drop the physician and time subscripts. Let R_b denote the set of regimens that contain drug b. For any regimen $j \in R_b$, we have

$$\frac{\partial P_j}{\partial D_b} = \frac{\partial P_j}{\partial V_j}\frac{\partial V_j}{\partial D_b} + \sum_{\substack{l\in R_b \\ l\neq j}} \frac{\partial P_j}{\partial V_l}\frac{\partial V_l}{\partial D_b} = \beta P_j\left(\frac{\gamma_{bj}(1-P_j)}{1+G_j} - \sum_{\substack{l\in R_b \\ l\neq j}} \frac{\gamma_{bl}P_l}{1+G_l}\right). \quad (4)$$

The two terms in the parentheses indicate two different effects. The first term is a direct effect: Detailing for brand b increases the choice probability for regimen j. The second term is an indirect effect: Detailing for brand b also helps its other regimens and hence may reduce the choice probability for regimen j. Note that the positive direct effect is present only if regimen j contains brand b, i.e., for any regimen $j \ni nR_b$, we have the negative indirect effect only

$$\frac{\partial P_j}{\partial D_b} = \sum_{l\in R_b} \frac{\partial P_j}{\partial V_l}\frac{\partial V_l}{\partial D_b} = -\beta P_j \sum_{l\in R_b} \frac{\gamma_{bl}P_l}{1+G_l}. \quad (5)$$

Based on the marginal effects presented in Equations (4) and (5), we now discuss the detailing elasticity of demand. In our model, computing detailing elasticity is complicated by the fact that a drug's sales are the sum of sales of all regimens that contain the focal drug. Let M be the number of new patients to a physician in a certain month. The demand for drug b at an individual physician is given by

$$Q_b = M \sum_{j\in R_b} P_j. \quad (6)$$

The own detailing elasticity of demand for drug b can be derived as

$$\eta_{bb} = \frac{\partial Q_b}{\partial D_b}\frac{D_b}{Q_b} = \frac{\beta D_b}{\sum_{j\in R_b} P_j}\left(1 - \sum_{j\in R_b} P_j\right)\sum_{j\in R_b}\frac{\gamma_{bj}P_j}{1+G_j}. \quad (7)$$

If each regimen contains only one drug, then our model reduces to the standard model, and the own detailing elasticity in Equation (7) becomes

$$\eta_{bb} = \beta\gamma_b D_b \frac{1-P_b}{1+G_b}.$$

The cross elasticity of demand for drug a with respect to detailing for drug b is given as

$$\eta_{ab} = \frac{\partial Q_a}{\partial D_b}\frac{D_b}{Q_a} = \beta D_b\left(-\sum_{\substack{j\in R_b \\ j\notin R_a}} \frac{\gamma_{bj}P_j}{1+G_j} + \sum_{\substack{j\in R_b \\ j\in R_a}} \frac{\gamma_{bj}P_j}{1+G_j}\sum_{j\notin R_a} P_j \Big/ \sum_{j\in R_a} P_j\right). \quad (8)$$

The main effect of detailing for drug b is to increase the sales of the regimens that contain drug b, thus having a negative *competition* effect on the sales of drug a. This competition effect is reflected by the first term in the parentheses. Its strength depends on the sales of drug b's own regimens. However, if there are regimens that contain a and b, then detailing for drug b may increase the sales of these regimens, resulting in a positive *spillover* effect on drug a. Such a spillover effect is captured by the second term. The more regimens containing both drugs, and the higher the sales of these regimens, the stronger the spillover effect.

Thus in our model the cross elasticity can be negative or positive depending on whether the competition effect or the spillover effect dominates. In case there is no regimen that contains a and b, there would be zero spillover effect and hence the cross elasticity would be unambiguously negative. Also, for a standard model in which each regimen contains only one drug, the cross elasticity of demand will be reduced to

$$\eta_{ab} = -\beta\gamma_b D_b \frac{P_b}{1+G_b}.$$

Note that the elasticities in Equations (7) and (8) reflect the effects of detailing in the current period only. Because of the carryover effect, detailing in one period will affect the drug demand in subsequent periods, although its impact will decline over time.

4.2. Firms' Optimal Detailing Strategies

Pharmaceutical firms' detailing strategies in the presence of combination therapy are complicated by the following factors. First, each firm owns multiple drugs and each drug may be present in multiple regimens, thus inducing complex spillover and substitution effects between different drugs. Second, given that the effect of detailing will be carried over to future periods, firms need to be forward-looking when deciding on their current-period detailing efforts. Therefore, to guide firms' detailing decisions we incorporate these factors into a dynamic oligopoly detailing game between competing firms, and then solve the dynamic game to determine firms' equilibrium detailing strategies. Following Dong et al. (2009) we focus on firms' detailing decisions at an individual physician level.

The timing of the game is as follows. In the beginning of each period, firms observe the previous goodwill stocks of all regimens and decide their detailing efforts for a physician. Then the goodwill stocks for all of the regimens that include the focal drug are updated by firms' current detailing efforts. The current-period demand and profit are then realized.

Consider a pharmaceutical firm f that markets a set of drugs B_f in the HIV/AIDS category. Each drug $b \epsilon B_f$ can be used in a set of regimens denoted by R_b. The single-period profit for firm f generated from a physician i (suppressed) can be written as

$$\pi_{ft} = \sum_{b\in B_f} [m_b Q_{bt}(G_t) - c_b D_{bt}]. \tag{9}$$

Here m_b is the unit markup and c_b is the cost of detailing for drug brand b. Note that Q_{bt} is the demand for drug b as defined in Equation (6), which depends on G_t, the vector of current goodwill stocks for all regimens in the category.

According to Equation (2), G_t is a function of G_{t-1}, D_t, and τ_t. Because τ_t is not observed by firms when making detailing decisions, firms need to integrate it out and base their decisions on the expected profit function

$$\pi_{ft}(G_{t-1}, D_t) = \int \sum_{b\in B_f} [m_b Q_{bt}(G_{t-1}, D_t, \tau_t) - c_b D_{bt}]\, dF(\tau_t). \tag{10}$$

Note that the current state of the market can be summarized by the state vector G_{t-1}. Denote firm f's detailing strategy by σ_f: $G_{t-1} \to D_{ft}$, where D_{ft} is a vector of detailing decisions for all drugs marketed by firm f. A strategy profile $\sigma = (\sigma_1, \ldots, \sigma_F)$ lists the detailing strategies of all firms. Because of the carryover effect of detailing, firms need to take into account the intertemporal effects of their current detailing decisions, and maximize the expected present discounted values of their profits over a planning horizon. Given a strategy profile σ, firm f's total expected profit is

$$V_f(G \mid \sigma) = E\left[\sum_t \delta^t \pi_{ft}(G, \sigma(G))\right]. \tag{11}$$

A Markov perfect equilibrium (MPE) is a strategy profile σ^* such that

$$V_f(G \mid \sigma^*) \geq \pi_f(G, D_f, \sigma^*_{-f}(G)) + \delta \int V_f(G' \mid \sigma^*)\, dF(G' \mid G, D_f, \sigma^*_{-f}(G)) \tag{12}$$

holds for any state vector G and for any alternative detailing decision D_f. In other words, an MPE requires σ_f to be the best response to σ_{-f} in any subgame starting from an arbitrary state G, and the following Bellman equation is satisfied:

$$V_f(G \mid \sigma) = \sup_{D_f} \left\{ \pi_f(G, D_f, \sigma_{-f}(G)) + \delta \int V_f(G' \mid \sigma)\, dF(G' \mid G, D_f, \sigma_{-f}(G)) \right\}. \tag{13}$$

The solution algorithm involves iterating on the above Bellman equation for all firms, and is built on the modified policy iteration algorithm used by Dubé et al. (2005). In our case, complications arise because a firm

may generate profits from multiple drugs and the demand for a drug may come from multiple regimens. Our profit function in Equation (9) and demand function in Equation (6) incorporate such complications.

Here we follow prior literature and use MPE as the solution concept to characterize detailing investments in the presence of dynamics and competition. The MPE concept is widely used in empirical models of dynamic oligopoly games due to its simplicity and intuitive appeal (Mailath and Samuelson 2006). Although we could use alternative equilibrium concepts, we find MPE to be more appealing than other equilibrium concepts in our empirical context. For example, we could explore a Stackelberg leader-follower game, but it is unclear in what order firms make decisions and why this order exists.

5. Demand Estimation and Spillover Effect

In this section, we first discuss the estimation strategy for our demand parameters, and then present the demand estimates and analyze the spillover effects of firms' detailing.

5.1. Initial Values for Goodwill Stocks

Because the goodwill stock G_{ijt} is not observed, we augment it by treating it as a latent variable and use Metropolis–Hastings to draw it from the posterior distribution of

$$G_{ijt} \mid G_{ij,t-1}, D_{ibt}, G_{ij,t+1}, D_{ib,t+1}, y_{ijt}, \alpha_{ij}, \alpha_{i(-j)}, G_{i(-j)t}, \beta_i, \gamma_{bj}, \sigma_\tau, \lambda; \quad \forall b \in B_j.$$

We also need to set their initial values in our estimation procedure. In total, we have 16 months of data. We use the first 4 months of detailing data to calibrate the initial values of detailing stocks, and the remaining 12 months of data for parameter estimation. To further reduce any potential bias, we set the initial goodwill stocks before the four months. For that purpose, we simulate detailing activities for 12 months before the first 4 months based on the observed detailing data in our sample period. Our estimates are insensitive to our simulation draws due to significant decay after four months.

Our approach is similar to that used by Hendel and Nevo (2006), and follows the spirit of Heckman (1981) in addressing the initial conditions problem. Admittedly it is not a perfect solution because we can only simulate the detailing activities before our sample period. However, due to the fact that the effect of detailing decays sufficiently rapidly over time, we expect the potential impact to be limited in this case.

5.2. Identification

In the demand estimation, we need to fix one of the regimens, e.g., Truvada + Viramune, as the baseline for identification purposes. Conditional on the goodwill stock generation process, the identification of α_{ij} and β_i comes from observations of detailing visits to, and prescription decisions of, individual physicians. For goodwill generation there are 57 drug-regimen specific marginal effects of detailing (γ_{bj}) to be estimated, with each γ_{bj} corresponding to the marginal contribution of drug b's detailing to the goodwill stock of regimen j.[7] Given that some regimens have a very limited number of prescriptions in our study period, it is challenging to separately estimate all these effects. To address this challenge, we specify a Bayesian hierarchical structure by assuming that the drug-regimen specific marginal effects are drawn from a common normal distribution, i.e., $N(\gamma, \sigma_\gamma^2)$. With this specification, the estimation of individual γ_{bj} relies on its related data and the hyper parameter γ.

Note that the identification of λ and γ relies on the functional form specification in our demand model, i.e., the log transformation of the goodwill stock variable. Empirically, we find that the separate Markov Chain Monte Carlo (MCMC) draws of λ and γ tend to be negatively correlated with each other. Such a correlation causes poor mixing of the MCMC chains for λ and γ with high autocorrelation. According to the literature (Roberts and Sahu 1997, Rossi et al. 2012, Royle et al. 2013), block sampling and thinning can be applied in this situation to reduce the high autocorrelation and improve MCMC mixing. We adopt a block sampler to draw λ and γ together and thin it by keeping every 10th draw after extending the number of draws to 1 million. With these two enhancements, we can simultaneously estimate the carry-over parameter and detailing contribution parameter with reasonable reliability. Alternatively, one may fix λ or γ at a predetermined value in the estimation. Our demand estimates and the subsequent counterfactual simulations are qualitatively unchanged when fixing λ at 0.86 based on previous studies (Berndt et al. 1997, Narayanan et al. 2004), or when fixing γ at 1 as in a typical goodwill stock specification Narayanan et al. (2005).

5.3. Endogeneity

Detailing allocation across physicians is often based on each physician's category prescription volume (Manchanda and Chintagunta 2004). This targeting approach may lead to an endogeneity issue in a model that predicts physicians' category prescription volumes. For example, Manchanda et al. (2004) model the total number of prescriptions with a random coefficient Negative Binomial model, where the random intercepts are more likely to drive the number of

details (i.e., firms focus more on physicians who write more prescriptions in the category). By contrast, we model a physician's choice between alternative regimens, which should be less susceptible to this endogeneity concern because regimen choice intercepts are not necessarily correlated with category prescription volume.

However, if firms make cross-physician detailing decisions based on physician-specific regimen intercepts or detailing responsiveness, our estimation may yield biased parameter values. To investigate this potential endogeneity, we adapt the approach used by Manchanda et al. (2004) and jointly estimate drug specific detailing policy functions and the proposed regimen choice model. Specifically, for each drug we regress Z_{ibt}, the logarithm of the monthly number of detailing visits to each physician (plus 1 to avoid taking the logarithm of 0) on X_{ibt}, which includes the following variables: physician-specific detailing responsiveness (β_i); the sum of physician-specific demand intercepts for regimens that contain the focal drug ($\sum_{j\in R_b}\alpha_{ij}$); the sum of lagged goodwill stocks for regimens that contain the focal drug ($\sum_{j\in R_b}G_{ijt-1}$); the sum of lagged goodwill stock for regimens that do not contain the focal drug ($\sum_{j\notin R_b}G_{ijt-1}$); the total detailing visits to the same physician for drugs not in the HIV category; and the average monthly patient visits to a physician for the first four months of our data. Formally, the regression equation for drug b can be written as follows:

$$Z_b = X_b\phi_b + \omega_b, \quad \text{where } \omega \sim \mathrm{N}(0,\sigma_D).$$

Accordingly, the likelihood for the joint model of prescription demand and reduced form detailing policy is given as the following equation:

$$\begin{aligned} L \propto & \left\{\prod_{i=1}^{I}\left[\prod_{j=1}^{J}\prod_{t=1}^{T}(P_{ijt})^{y_{ijt}}\right.\right. \\ & \left.\left. f(G_{ijt}\mid G_{ijt-1},D_{ibt},\gamma_{bj},\sigma_\tau,\lambda;\, b\in B_j)\right] f(\theta_i\mid\theta,\sigma)\right\} \\ & \times\prod_{j=1}^{J}\prod_{b\in B_j} f(\gamma_{bj}\mid\gamma,\sigma_\gamma)\times f(\theta,\sigma)\times f(\gamma,\sigma_\tau,\sigma_\gamma,\lambda) \\ & \times\left\{\prod_{i=1}^{I}\prod_{t=1}^{T}(\sigma_D)^{-1/2}\exp[-\tfrac{1}{2}(Z-X\phi)^T\sigma_D^{-1}(Z-X\phi)]\right\} \\ & \times f(\phi,\sigma_D). \end{aligned}$$

We jointly estimate these regimen-specific regression equations and the demand model with a combination of Gibbs sampling and Metropolis. For those parameters for which full conditional distributions are not from known distribution families, we use a Random Walk Metropolis–Hastings algorithm with a normal candidate density to make these draws. Based on this limited information approach, our demand estimates do not rely on any specific game assumed on the supply side.

5.4. Estimation Results

We use non-informative priors for all homogeneous and hyper parameters. Inferences for demand parameters are based on 1,000,000 iterations thinned by 10 after a burn-in period of 200,000 iterations of the MCMC. The estimates of demand parameters as well as their 95% Bayesian probability intervals are reported in Table 4. The log marginal likelihood is −5,666 for our estimated demand model, while the log marginal likelihood is −5,953 for a demand model without the detailing stock variable (i.e., a model with random brand intercepts only), −5,779 for a demand model with current period detailing, and −5,693 for a demand model with all detailing contribution parameters (γ_{bj}) fixed as 1. The 2log Bayes factor in favor of the proposed model relative to each of the above benchmark models is 574, 226, and 54, respectively. According to Kass and Raftery (1995), a value of 2–6 provides positive evidence, 6–10 provides strong evidence, and >10 provides very strong evidence. Therefore, the 2log Bayes factor indicates that the inclusion of detailing stock greatly improves the model fit and the explanation of physicians' prescribing behavior relative to various benchmark models.

Table 4 shows that Atripla, the fixed-dose combination of Truvada and Sustiva, receives the highest average preference among physicians. It was the only one-pill, once-a-day, HIV treatment option that reduces pill burden and improves compliance. Other top regimens recommended by the HHS, such as Truvada + Norvir + Reyataz, Truvada + Norvir + Prezista, and Truvada + Isentress, also have high preference estimates. The detailing stock effect (β) is estimated to be 0.246 with a logarithmic transformation to account for the diminishing marginal effect of detailing stock. As shown in Table 5, all HIV drugs' detailing visits positively contribute to related regimens' goodwill stock building, and the effectiveness of different drugs' detailing efforts varies from 0.45 to 1.28. The estimates in Table 6 reveal several significant effects of detailing responsiveness, brand preferences, patient volume, detailing in other categories, own lagged goodwill stock, and competitive lagged goodwill stock on firms' detailing decisions. For example, the detailing decisions for Kaletra, Isentress, and Viramune are affected by physicians' detailing responsiveness, while detailing decisions for Prezista and Reyataz are affected by physicians' preferences for their associated regimens. Therefore, it is important to control for such correlations by jointly estimating physicians' prescriptions and firms' detailing decisions.

As shown in Table 7, the own elasticity of detailing ranges from 0.002 to 0.189. The magnitude of these

Table 4. Demand Estimates

Variables	Population mean	95% interval
Regimen intrinsic utility		
Atripla	2.963	(2.555, 3.405)
Atripla + Isentress	−1.984	(−2.855, −1.202)
Epzicom + Isentress	−1.901	(−2.612, −1.257)
Epzicom + Kaletra	−1.095	(−1.605, −0.498)
Epzicom + Norvir + Lexiva	−1.286	(−2.113, −0.508)
Epzicom + Norvir + Prezista	−2.026	(−2.875, −1.188)
Epzicom + Norvir + Reyataz	−0.357	(−0.840, 0.161)
Epzicom + Reyataz	−0.828	(−1.420, −0.317)
Epzicom + Sustiva	−0.921	(−1.475, −0.251)
Epzicom + Viramune	−1.751	(−2.478, −1.052)
Isentress + Truvada + Kaletra	−2.040	(−2.843, −1.335)
Isentress + Norvir + Prezista	−2.145	(−3.282, −1.095)
Isentress + Truvada + Norvir + Prezista	−0.606	(−1.187, 0.025)
Isentress + Truvada	0.641	(0.155, 1.158)
Truvada + Kaletra	0.835	(0.413, 1.297)
Truvada + Norvir + Lexiva	−0.536	(−1.438, −0.007)
Truvada + Norvir + Prezista	0.895	(0.385, 1.440)
Truvada + Norvir + Reyataz	1.739	(1.295, 2.224)
Truvada + Sustiva	−1.258	(−1.939, −0.707)
β detailing stock effect	0.246	(0.142, 0.357)
λ carry-over effect	0.829	(0.805, 0.849)
γ mean of detailing contribution effects	0.912	(0.810, 1.020)
σ_γ S.D. of detailing contribution effects	0.329	(0.257, 0.428)
σ_τ S.D. of detailing stock building	0.721	(0.665, 0.784)
Marginal log-likelihood	−5,666	

effects is consistent with previous findings (e.g., Berndt et al. 1997, Chintagunta and Desiraju 2005, Narayanan et al. 2005). In a standard logit model, drugs compete with each other; increasing a drug's detailing reduces other drugs' choice probabilities. In our framework, a drug's detailing may have competition and spillover effects on other drugs' prescriptions due to the regimen structure. Depending on whether spillover effects dominate competition effects or vice versa, cross-drug elasticity can be negative or positive. To examine the cross-drug effects of one drug's detailing, we follow previous literature on clout and susceptibility (e.g., Kamakura and Russell 1989, Van Everdingen et al. 2009) but calculate them separately for negative and positive cross-drug elasticities.

We define drug a's competitive (spillover) clout as the aggregation of negative (positive) cross elasticities of demand for other drugs (b) with respect to drug a's detailing (η_{ba}). We define drug a's competitive (spillover) susceptibility as the aggregation of negative (positive) cross elasticities of demand for drug a with respect to other drugs' detailing (η_{ab})

$$\textit{Competitive clout}_a = \sqrt{\sum_{b\neq a} 1(\eta_{ba} < 0)\eta_{ba}^2},$$

$$\textit{Competitive susceptibility}_a = \sqrt{\sum_{b\neq a} 1(\eta_{ab} < 0)\eta_{ab}^2},$$

$$\textit{Spillover clout}_a = \sqrt{\sum_{b\neq a} 1(\eta_{ba} > 0)\eta_{ba}^2},$$

$$\textit{Spillover susceptibility}_a = \sqrt{\sum_{b\neq a} 1(\eta_{ab} > 0)\eta_{ab}^2},$$

where $1(\cdot)$ represents an indicator function. From the "Competitive" column in Table 7, we can see that detailing from Atripla, Truvada, and Viramune has the strongest competitive clout on other drugs' prescriptions, while Epzicom, Lexiva, and Viramune are most vulnerable to other drugs' detailing efforts in losing marketing share. As to spillover effects, Epzicom, Prezista, and Reyataz have the strongest spillover clout on other drugs' prescriptions. For example, the detailing visits for Prezista and Reyataz can effectively boost prescriptions for Norvir and Truvada because they are often administered in treatment regimens. On the other hand, Norvir is most susceptible to cross-drug spillover effects, followed by Sustiva and Lexiva. Because Norvir is commonly used to boost the effectiveness of other PI drugs including Lexiva, Prezista, and Reyataz, increased detailing for these drugs would significantly help Norvir.

The clout and susceptibility measures reported in Table 7 are based on cross elasticities. As shown in Equation (8), the cross elasticity is a net effect and can be decomposed into a competition and a spillover effect. To further understand the detailing effects across drugs, we run simulations, each with 20,000 replications, to separate the competition and spillover effects for each cross-drug pair. We first calculate the competition effect of drug a's detailing on drug b's prescriptions by artificially shutting off drug a's detailing effect on any regimens that include drug a but not drug b. The simulation results for all 110 cross-drug combinations of 11 drugs are reported on top of each cell in Table 8. For example, Reyataz can be combined with Epzicom or Truvada. Thus, detailing for Reyataz helps its regimens with Epzicom, and imposes a competition effect on the demand for Truvada. As we can see from Table 8, eliminating the competition effect of Reyataz's detailing would have increased demand for Truvada by 0.47%. Also, detailing for Atripla has strong competition effects on other drugs, leading to the strongest competitive clouts in Table 7. Because Lexiva and Prezista are always prescribed together with Norvir among the regimens under consideration, there is no competition effect of Lexiva or Prezista on Norvir.

We next highlight the spillover effect of drug a's detailing on drug b's prescriptions by artificially shutting off drug a's detailing effect on any regimens that contain drug a and drug b. The simulation results are reported at the bottom of each cell in italics in Table 8. If drug a and drug b can be combined in a regimen, there will be a spillover effect of drug a's

Table 5. Detailing Contribution to Regimen-Level Goodwill Stock from Each Drug

Regimen/Detailing	Atripla	Epzicom	Isentress	Kaletra	Lexiva	Norvir	Prezista	Reyataz	Sustiva	Truvada	Viramune
Atripla	1.09 (0.73, 1.45)								0.58 (0.13, 1.06)	0.51 (0.11, 0.95)	
Atripla + Isentress	1.08 (0.64, 1.47)		1.04 (0.59, 1.53)						0.51 (0.11, 1.18)	0.45 (0.10, 0.82)	
Epzicom + Isentress		0.96 (0.64, 1.33)	1.01 (0.66, 1.37)								
Epzicom + Kaletra		0.98 (0.63, 1.33)		1.05 (0.69, 1.40)		0.63 (0.12, 1.27)					
Epzicom + Norvir + Lexiva		0.84 (0.48, 1.26)			1.05 (0.65, 1.5)	0.91 (0.27, 1.57)					
Epzicom + Norvir + Prezista		0.87 (0.43, 1.23)				0.95 (0.34, 1.63)	1.07 (0.69, 1.65)				
Epzicom + Norvir + Reyataz		0.97 (0.39, 1.40)				0.88 (0.27, 1.49)		1.03 (0.63, 1.48)			
Epzicom + Reyataz		0.81 (0.45, 1.15)						1.05 (0.60, 1.43)			
Epzicom + Sustiva		1.13 (0.86, 1.41)							1.28 (0.76, 1.83)		
Epzicom + Viramune		0.94 (0.59, 1.32)									1.03 (0.68, 1.42)
Isentress + Truvada + Kaletra			0.99 (0.59, 1.35)	0.99 (0.61, 1.31)		0.60 (0.08, 1.22)				0.92 (0.52, 1.43)	
Isentress + Norvir + Prezista			0.97 (0.62, 1.40)			0.93 (0.32, 1.55)	0.95 (0.67, 1.32)				
Isentress + Truvada + Norvir + Prezista			0.95 (0.51, 1.63)			0.91 (0.31, 1.54)	0.91 (0.48, 1.33)			0.94 (0.52, 1.37)	
Isentress + Truvada			1.20 (0.71, 1.67)							1.09 (0.68, 1.47)	
Truvada + Kaletra				0.96 (0.66, 1.24)		0.91 (0.25, 1.57)				0.91 (0.56, 1.33)	
Truvada + Norvir + Lexiva					1.01 (0.64, 1.39)	0.92 (0.32, 1.53)				0.98 (0.63, 1.35)	
Truvada + Norvir + Prezista						0.92 (0.32, 1.55)	1.01 (0.66, 1.40)			1.07 (0.61, 1.47)	
Truvada + Norvir + Reyataz						0.89 (0.21, 1.59)		0.94 (0.70, 1.18)		0.92 (0.5, 1.44)	
Truvada + Sustiva	0.81 (0.49, 1.16)								1.02 (0.45, 1.60)	1.07 (0.63, 1.49)	
Truvada + Viramune										1.07 (0.69, 1.50)	1.07 (0.71, 1.44)

Table 6. Estimates for Detailing Policy Functions

Drug	Intercept	Detailing responsiveness	Sum of intercepts for related regimens	Sum of lagged goodwill stocks for regimens that contain the focal drug	Sum of lagged goodwill stocks from regimens that do not contain the focal drug	Detailing in other categories	Monthly number of patient visits
Atripla	−0.011 (−0.059, 0.035)	0.085 (−0.042, 0.214)	0.001 (−0.006, 0.007)	0.009 (0.005, 0.013)	0.001 (0.000, 0.002)	0.005 (0.003, 0.008)	0.011 (0.002, 0.019)
Epzicom	−0.014 (−0.089, 0.080)	0.049 (−0.066, 0.166)	0.001 (−0.008, 0.011)	0.008 (0.007, 0.009)	−0.001 (−0.002, −0.000)	0.003 (0.001, 0.006)	0.002 (−0.006, 0.010)
Isentress	0.011 (−0.034, 0.056)	0.121 (0.026, 0.219)	0.002 (−0.002, 0.006)	0.010 (0.008, 0.012)	−0.002 (−0.003, −0.001)	0.002 (−0.001, 0.004)	0.009 (0.0004, 0.017)
Kaletra	0.002 (−0.041, 0.043)	0.114 (0.006, 0.224)	0.002 (−0.008, 0.012)	0.023 (0.019, 0.027)	−0.002 (−0.003, −0.001)	0.003 (0.001, 0.005)	0.008 (0.001, 0.016)
Lexiva	0.019 (−0.037, 0.085)	0.007 (−0.089, 0.106)	0.014 (−0.010, 0.041)	0.019 (0.013, 0.025)	0.000 (−0.001, 0.001)	0.005 (0.003, 0.008)	0.005 (0.000, 0.010)
Norvir	−0.002 (−0.029, 0.024)	−0.010 (−0.085, 0.063)	−0.001 (−0.003, 0.001)	0.002 (0.001, 0.003)	−0.002 (−0.004, −0.001)	0.001 (−0.001, 0.002)	−0.001 (−0.006, 0.005)
Prezista	0.031 (−0.016, 0.078)	0.084 (−0.028, 0.203)	0.008 (0.001, 0.015)	0.012 (0.008, 0.015)	0.000 (−0.001, 0.001)	0.002 (−0.000, 0.005)	0.006 (0.001, 0.012)
Reyataz	0.021 (−0.043, 0.079)	0.096 (−0.077, 0.255)	0.009 (0.001, 0.018)	0.017 (0.012, 0.021)	−0.000 (−0.001, 0.0003)	0.001 (−0.002, 0.003)	0.001 (−0.008, 0.009)
Sustiva	0.012 (−0.019, 0.044)	0.003 (−0.085, 0.089)	−0.001 (−0.005, 0.002)	0.005 (0.002, 0.007)	−0.001 (−0.001, −0.000)	−0.000 (−0.002, 0.001)	0.0001 (−0.006, 0.006)
Truvada	−0.007 (−0.048, 0.036)	−0.030 (−0.136, 0.076)	−0.001 (−0.003, 0.002)	0.004 (0.003, 0.005)	−0.001 (−0.002, 0.001)	0.003 (0.000, 0.005)	0.004 (0.000, 0.007)
Viramune	−0.001 (−0.096, 0.113)	0.171 (0.061, 0.283)	0.006 (−0.038, 0.054)	0.021 (0.014, 0.028)	−0.000 (−0.001, 0.000)	0.005 (0.003, 0.008)	0.001 (−0.007, 0.009)

Table 7. Own Elasticities and Cross-Drug Competitive (Spillover) Clouts (Susceptibilities)

		Competitive		Spillover	
	Own elasticity	Clout (hurt others)	Susceptibility (being hurt)	Clout (help others)	Susceptibility (being helped)
Atripla	0.074	0.172	0.029		0.007
Epzicom	0.137	0.024	0.103	0.055	0.024
Isentress	0.122	0.045	0.065	0.013	0.003
Kaletra	0.139	0.040	0.071	0.010	0.002
Lexiva	0.176	0.030	0.089	0.016	0.026
Norvir	0.002	0.004	0.047	0.006	0.044
Prezista	0.100	0.041	0.046	0.032	0.002
Reyataz	0.072	0.047	0.049	0.036	0.019
Sustiva	0.004	0.016	0.022	0.007	0.043
Truvada	0.018	0.083	0.053	0.004	0.022
Viramune	0.189	0.048	0.096	0.006	0.009

detailing on drug b's prescriptions and vice versa. For example, because Reyataz can be combined with Truvada, detailing for Reyataz has spillover effects on the prescription of Truvada. As we can see from Table 8, eliminating the spillover effect of Reyataz's detailing would have reduced demand for Truvada by 1.35%. This spillover effect is stronger than the corresponding competition effect of 0.47%, leading to an overall spillover effect, reported in Table A1 in Online Appendix A. Also, the regimen Atripla + Isentress induces a spillover effect of Atripla's detailing on Isentress. However, this spillover effect is dominated by the competition effect from Atripla's detailing on Isentress. As shown in Table A1 in Online Appendix A, prescriptions for Isentress would have *increased* after eliminating all detailing for Atripla. Similarly, Norvir receives spillover effects from detailing for Lexiva, Prezista, and Reyataz, and such spillover effects dominate the competition effects from these drugs, making Norvir the most susceptible in spillover effects. Our results therefore show that it is critical to account for the complicated nature of interactions among drugs and regimens while trying to understand the effects of detailing in such categories.

Table 8. Impacts of Removing Detailing Competition Effects and Spillover Effects of a Drug

% change in Rx\Detailing	Atripla	Epzicom	Isentress	Kaletra	Lexiva	Norvir	Prezista	Reyataz	Sustiva	Truvada	Viramune
Atripla		1.24 (0.79, 1.72)	1.69 (1.01, 2.45) *−0.10* *(−0.28, 0.07)*	1.20 (0.71, 1.74)	0.52 (0.31, 0.77)	0.12 (−0.01, 0.23)	1.43 (0.42, 2.39)	1.63 (0.59, 2.66)	−0.01 (−0.49, 0.37) *−0.68* *(−1.26, −0.26)*	3.68 (2.07, 5.43) *−3.39* *(−5.36, −1.84)*	0.83 (0.54, 1.16)
Epzicom	7.67 (4.59, 11.13)		2.15 (1.36, 3.15) *−0.95* *(−1.61, −0.52)*	1.57 (0.97, 2.33) *−1.18* *(−2.19, −0.44)*	1.45 (0.73, 2.45) *−2.04* *(−3.23, −1.13)*	0.18 (0.08, 0.30) *−0.24* *(−0.41, −0.09)*	2.22 (1.04, 3.46) *−1.07* *(−1.88, −0.35)*	1.49 (0.73, 2.40) *−3.89* *(−6.24, −1.52)*	0.54 (0.17, 1.00) *0.02* *(−0.83, 1.04)*	9.90 (6.35, 14.09)	2.24 (1.38, 3.37) *−2.33* *(−3.62, −1.31)*
Isentress	8.12 (4.81, 12.01) *−0.35* *(−0.98, 0.27)*	1.98 (1.26, 2.8) *−0.99* *(−1.71, -0.49)*		1.62 (0.96, 2.43) *−0.70* *(−1.57, −0.01)*	0.83 (0.48, 1.32)	0.17 (0.07, 0.30) *−0.06* *(−0.14, −0.01)*	2.92 (0.99, 4.95) *−2.18* *(−3.5, −0.73)*	2.12 (1.00, 3.35)	0.55 (0.20, 0.99) *−0.03* *(−0.13, 0.07)*	7.94 (4.49, 11.77) *−6.98* *(−10.20, −3.63)*	1.37 (0.80, 2.08)
Kaletra	7.66 (4.27, 11.39)	1.96 (1.23, 2.85) *−1.42* *(−2.46, −0.56)*	2.08 (1.24, 3.09) *−0.74* *(−1.41, −0.17)*		0.96 (0.52, 1.54)	0.14 (0.05, 0.26) *−0.31* *(−0.65, −0.04)*	2.47 (0.92, 4.02)	2.88 (1.08, 4.82)	0.61 (0.23, 1.09)	8.25 (4.93, 12.22) *−6.92* *(−10.59, −3.46)*	1.57 (0.84, 2.53)
Lexiva	8.30 (5.13, 12.14)	5.29 (3.23, 7.75) *−7.53* *(−11.32, −4.32)*	2.64 (1.63, 3.97)	2.28 (1.33, 3.58)		0.19 (0.09, 0.32) *−0.70* *(−1.21, −0.30)*	1.91 (1.03, 2.94)	2.50 (1.45, 3.8)	0.65 (0.25, 1.16)	9.94 (6.25, 14.71) *−7.74* *(−11.55, −4.11)*	4.51 (2.64, 6.82)
Norvir	5.42 (2.88, 8.20)	1.06 (0.63, 1.5) *−1.55* *(−2.12, −0.99)*	1.74 (0.93, 2.64) *−0.45* *(−0.73, −0.20)*	1.49 (0.78, 2.20)	*−1.64* *(−2.33, −1.02)*		*−3.58* *(−5.70, −1.45)*	0.18 (0.06, 0.33) *−3.26* *(−5.24, −1.37)*	0.42 (0.14, 0.77)	4.43 (2.55, 6.55) *−4.23* *(−6.43, −2.21)*	1.13 (0.72, 1.61)
Prezista	4.89 (2.02, 7.9)	1.38 (0.61, 2.14) *−0.55* *(−1.00, −0.17)*	2.26 (0.9, 3.73) *−1.44* *(−2.31, −0.64)*	1.38 (0.58, 2.2)	0.41 (0.21, 0.66)	0.09 (0.01, 0.17) *−0.22* *(−0.44, −0.03)*		1.76 (0.44, 3.06)	0.36 (0.1, 0.70)	6.04 (2.33, 9.61) *−5.57* *(−9.30, −1.73)*	0.79 (0.41, 1.29)
Reyataz	5.40 (2.53, 8.5)	0.91 (0.50, 1.35) *−2.86* *(−4.2, −1.67)*	1.40 (0.71, 2.16)	1.39 (0.67, 2.14)	0.68 (0.37, 1.08)	0.08 (0.02, 0.15) *−0.24* *(−0.48, 0.02)*	1.83 (0.38, 3.24)		0.43 (0.07, 0.85)	5.22 (2.72, 8.02) *−3.97* *(−6.97, −1.34)*	0.78 (0.47, 1.18)
Sustiva	5.43 (−7.89, 17.54) *−3.19* *(−9.74, 5.13)*	0.98 (0.41, 1.75) *−5.58* *(−9.02, −2.29)*	0.75 (0.09, 1.55)	0.52 (−0.17, 1.09)	0.61 (0.18, 1.44)	0.06 (−0.07, 0.18)	0.60 (0.03, 1.17)	0.69 (−2.48, 2.38)		3.79 (−1.3, 8.61) *−2.16* *(−6.78, 1.83)*	0.50 (0.22, 0.98)
Truvada	6.30 (3.58, 9.38) *−0.04* *(−0.46, 0.43)*	2.06 (1.36, 2.78)	0.24 (0.07, 0.43) *−1.73* *(−2.48, −1.07)*	0.15 (0.06, 0.28) *−1.24* *(−1.77, −0.76)*	0.27 (0.14, 0.45) *−0.59* *(−0.91, −0.32)*	0.03 (0.01, 0.06) *−0.11* *(−0.22, −0.01)*	0.21 (0.02, 0.38) *−1.53* *(−2.49, −0.51)*	0.47 (0.21, 0.75) *−1.35* *(−2.26, −0.48)*	0.47 (0.10, 0.93) *0.01* *(−0.25, 0.23)*		0.31 (0.17, 0.49) *−0.97* *(−1.38, −0.64)*
Viramune	9.82 (5.96, 14.34)	4.85 (2.96, 7.06) *−5.39* *(−8.65, −2.96)*	2.85 (1.79, 4.18)	2.51 (1.46, 3.81)	2.85 (1.53, 4.69)	0.35 (0.18, 0.56)	2.40 (1.31, 3.74)	2.35 (1.39, 3.57)	0.83 (0.39, 1.44)	11.91 (7.78, 17.30) *−10.72* *(−16.00, −6.54)*	

Notes. Roman numbers are for competition effects and italicized numbers are for spillover effects.

6. Optimal Detailing in Combination Therapy

We numerically solve the dynamic detailing game between competing firms to examine the optimal detailing strategies for firms. In particular, we examine specific cases in which spillover effects of detailing give rise to incentives for free riding, and show how such incentives change according to the market environment and regulations. Through policy simulations, we investigate the managerial and policy implications of such spillover effects and free riding behavior. For example, managers may be interested in strategies that can internalize the spillover effects and reduce the incentive for free riding. For regulators, we show that policies that are effective elsewhere may have unintended consequences under combination therapies and spillover effects of detailing.

6.1. The Case of Norvir

Norvir is a PI drug manufactured by Abbott Laboratories. It is typically used to boost the efficacy of several other PI drugs including Lexiva from GSK, Prezista from Tibotec, and Reyataz from BMS. As shown in Table 7, Lexiva, Prezista, and Reyataz exert strong clout while Norvir exhibits strong susceptibility in terms of spillover effects. Therefore, Abbott may curtail detailing for Norvir and rely on GSK, Tibotec, and BMS to promote the Norvir-boosted regimens. In addition to Norvir, Abbott also produces Kaletra, a combination drug with Norvir as an active ingredient. Thus Kaletra competes against Norvir + Lexiva, Norvir + Prezista, and Norvir + Reyataz to form regimens with NRTI drugs such as Truvada and Epzicom. This strengthens the incentive for Abbott to focus its detailing efforts on Kaletra and free ride on others' detailing efforts to increase Norvir prescriptions.

To formally investigate free riding in this case, we focus on the detailing competition involving the aforementioned drugs, i.e., Kaletra, Norvir, Lexiva, Prezista, and Reyataz. By restricting attention to these drugs, we effectively assume that physicians choose from the following "composite regimens": Kaletra, Norvir + Lexiva, Norvir + Prezista, Norvir + Reyataz, Reyataz, and others.[8] We then set up and solve the dynamic detailing game for these drugs between Abbott, GSK, Tibotec, and BMS at a representative physician.[9] To alleviate the computational burden when solving the game numerically, we artificially set a ceiling of at most two detailing visits for each drug per month, because a ceiling puts a limit on the range of our state variable, the goodwill stock. This assumption may reflect supply-side constraints such as difficulties in scheduling more frequent detailing visits with a physician. It may also account for demand-side features that are currently missing from our demand specification, e.g., extremely frequent visits may not be more informative or persuasive but may actually alienate physicians. However, this assumption is nonessential as we have verified that increasing the ceiling from two to three or four does not change our findings.

Table 9. A Detailing Game Involving Kaletra, Norvir, Lexiva, Prezista, and Reyataz

	Max 2/Month	Max 1/Month	25% price hike for Norvir	50% price hike for Norvir
Detailing for				
Kaletra *by Abbott*	1.162	1.000	1.162	1.147
Norvir *by Abbott*	0.001	0.133	0.039	0.073
Lexiva *by GSK*	0.532	0.410	0.500	0.472
Prezista *by Tibotec*	1.050	0.991	1.025	1.001
Reyataz *by BMS*	1.782	1.000	1.778	1.776
Market share				
Kaletra	0.082	0.082	0.082	0.082
Norvir + Lexiva	0.024	0.024	0.024	0.024
Norvir + Prezista	0.099	0.101	0.099	0.099
Norvir + Reyataz	0.206	0.195	0.206	0.207
Reyataz	0.014	0.013	0.014	0.014
Others	0.576	0.586	0.575	0.575

After solving for firms' equilibrium detailing strategies, we simulate their monthly detailing decisions and market evolution path over 24 months. The results are summarized in the first column of Table 9. Abbott focuses its detailing resources on Kaletra rather than Norvir, while Lexiva, Prezista, and Reyataz engage in intense detailing competition. Lexiva expends fewer resources probably due to its smaller market share than Prezista and Reyataz. Our results highlight the incentive to free ride in the case of Norvir: The diligent detailing efforts for Lexiva, Prezista, and Reyataz will spill over to help prescriptions of Norvir.

Now we explore the factors that affect this free-riding incentive. First, the pharmaceutical industry is highly regulated and regulations often have a significant impact. The heavy detailing expenditure by the industry has drawn the attention of the public and policy makers. Because of increasing ethical and healthcare cost concerns, some European countries have imposed limits on firms' detailing activities (e.g., Stremersch and Lemmens 2009, Llopart et al. 2012). In the United States, many physicians have imposed restrictions on detailing visits and it is more difficult for pharmaceutical sales representatives to access physicians (Chressanthis et al. 2012, 2014). In this context, we simulate the impact of a potential regulation that prohibits more than one detailing visit per month for the same drug. Results presented in the second column of Table 9 indicate that, constrained by the access limit, Reyataz would significantly reduce detailing activities. As a result, Abbott would engage in more detailing for Norvir to compensate for the lower detailing levels of its complementary drug.

Second, the pricing of Norvir has been a contentious issue. Abbott raised its price by 400% in December 2003 (before our data period), from \$1.75 to \$8.57 a day, which caused public protests, government investigations, and lawsuits. Even after the price hike, Norvir remained the cheapest component in a typical three-drug regimen such as Truvada + Norvir + Reyataz, according to a monthly cost of \$321 for Norvir but \$1,100 for Truvada and \$927 for Reyataz in 2009. The lower Norvir markup may also contribute to its free-riding incentive. We want to examine how such incentives would change when its price and markup could be raised further, e.g., when a new tablet formulation was launched (Evans 2009).

In the third and fourth columns of Table 9, we report the simulation results for a 25% and a 50% markup increase for Norvir. The higher markup for Norvir would lead to more detailing for Norvir. Note that Lexiva, Prezista, and Reyataz would benefit from the increased detailing for Norvir and start to cut down on their own detailing. We recognize, however, that our model does not include strategic pricing; so our results should be interpreted with caution.

In summary, our results demonstrate that Abbott has incentive to rely on other high-clout brands' detailing activities to help Norvir, a high-susceptibility brand. Regulations that limit sales representative access to physicians and a higher price for Norvir would reduce this free-riding incentive and increase detailing for Norvir.

6.2. The Case of Generics

As discussed earlier, there has been a trend to restrict the detailing activities of pharmaceutical firms. An important policy goal of such detailing restrictions is to increase the use of generic drugs in place of branded drugs. Generics typically do not engage in any detailing activities. As a result, detailing restrictions on branded drugs are expected to increase the market share of generic drugs (Larkin et al. 2014) and reduce healthcare costs.

Things can be different in combination therapies, where a generic drug may be prescribed together with certain branded drugs and hence may benefit from the detailing activities for these branded drugs. In such cases generics can be regarded as an extreme instance of a high-susceptibility brand, and always free-ride on detailing for complementary branded drugs. If detailing is restricted, it is unclear whether the demand for generic drugs would increase or decrease. For example, faced with detailing restrictions, a combination of two branded drugs may have some flexibility in reallocating their detailing efforts, while a combination of a generic drug and a branded drug does not have such flexibility.

Table 10. A Detailing Game Involving Atripla, Truvada, and Generic Epzicom

	Max 2/Month	Max 1/Month
Detailing for		
Atripla		
by Gilead	1.669	1.000
by BMS	0.000	0.000
Truvada *by Gilead*	0.207	0.841
Reyataz *by BMS*	1.435	1.000
Market share		
Atripla	0.637	0.634
Truvada + Reyataz	0.186	0.197
Epzicom + Reyataz	0.177	0.169

Therefore, under combination therapies we expect detailing restrictions to potentially hurt generics. Although all major drugs in the HIV category were under patent protection in our study period, we explore the counterfactual scenario in which a generic version is available for Epzicom, whose patent expires in 2016. We consider the competition between a generic Epzicom + Reyataz, Truvada + Reyataz, and Atripla.[10] Based on our empirical estimates, the preference for Epzicom + Reyataz is lower than that for Truvada + Reyataz, but we do not know the preference for a generic Epzicom + Reyataz. To account for generic versions being cheaper and hence more appealing, we assume that the preference for generic Epzicom + Reyataz would be on par with that for Truvada + Reyataz. However, our results hold for various levels of parameter values and are largely insensitive to this assumption.

By solving the dynamic detailing game involving these composite regimens, we can see from Table 10 that a more restrictive "ceiling" policy on detailing frequency would reduce the demand for the generic version of Epzicom. Specifically, the market share for a generic Epzicom + Reyataz would decrease from 17.7% to 16.9%. For policy makers, detailing restrictions are often proposed to increase social welfare by reducing wasteful expenditures and encouraging generic use. Our counterfactual simulations reveal unintended consequences of curtailing detailing in the context of combination therapies in the presence of spillover effects of detailing.

6.3. The Case of Atripla

Atripla is a fixed-dose combination of Truvada (from Gilead) and Sustiva (from BMS). Because Truvada and Sustiva can be combined with other drugs to form regimens that compete against Atripla, Gilead and BMS are faced with the decision of how much resources to allocate to Atripla versus Truvada or Sustiva. To analyze firms' detailing strategies in this and similar situations, we study a dynamic detailing game involving Atripla, Truvada, and Sustiva, in which physicians are

Table 11. A Detailing Game Involving Atripla, Truvada, and Sustiva

	Which firms detail Atripla?		
	Gilead & BMS	Independent firm	Merged firm
Detailing for			
Atripla		2.000	2.000
by Gilead	0.000		
by BMS	0.889		
Truvada *by Gilead*	0.952	2.000	0.017
Sustiva *by BMS*	0.446	0.032	0.056
Market share			
Atripla	0.558	0.562	0.615
Truvada + Sustiva	0.009	0.008	0.008
Truvada	0.387	0.388	0.329
Sustiva	0.010	0.008	0.009
Others	0.037	0.033	0.039

assumed to choose from the following composite regimens related to the three drugs: Atripla, Truvada + Sustiva, Truvada, Sustiva, and others. Here the composite regimen "Truvada" represents all regimens that include the drug Truvada except Truvada + Sustiva (which we listed as a separate regimen). The same applies to the composite regimen "Sustiva." Again the preference for each composite regimen is assumed to be the inclusive value of the preferences for all of the original regimens it includes.

We numerically solve this dynamic detailing game and report the 24-month simulation results in the first column of Table 11. Our results suggest that, even though Gilead receives about 64% of the revenue from Atripla, BMS would intensively detail Atripla while Gilead would free-ride on BMS' efforts. The stronger incentive from BMS to detail Atripla might come from the fact that its Sustiva is a much weaker brand than Gilead's Truvada and hence the profit from Atripla is far more important to BMS than to Gilead. Our results highlight Gilead's free-riding incentive on Atripla in an unconstrained detailing game.

In the presence of combination therapies, it is important for firms to adopt strategies that address the issue of free riding. In reality Gilead and BMS decided to market Atripla through a joint venture. Although we do not have information on the specific terms of the joint venture and how they allocate their detailing resources, we study an extreme case in which the joint venture on Atripla is treated as a separate firm, making independent detailing decisions to maximize its own profit from Atripla. As we show in the second column of Table 11, this hypothetical market structure would induce more intensive detailing for Atripla and Truvada because they now compete against each other. Although this increases the overall sales of Atripla, Truvada, and Sustiva, the total profit from these drugs would actually decline because of higher detailing expenditures.

Alternatively, firms may consider merging their assets in the HIV category to internalize the complementarities and substitution effects under combination therapy. Notably in November 2009 GSK and Pfizer transferred all their HIV assets into a joint venture, ViiV Healthcare, marketing 10 drugs in the category. Our model can be adapted to study what would happen if a joint venture is created to market all three drugs, i.e., Atripla, Truvada, and Sustiva. In the third column of Table 11, we show that in this setup the merged firm would reduce detailing for Truvada and focus on Atripla alone. Although this strategy leads to lower sales for the three drugs combined, their total profit would increase by 2.5% due to savings on detailing costs.

Therefore, the ownership structure has a significant impact on firms' detailing decisions for combination drugs. Firms may adopt strategies to internalize the spillover effects of detailing and alleviate the concern of free riding.

In the case of Atripla, we observe that Gilead and BMS formed an alliance to market the drug. Although we do not have specific information about the possible detailing coordination between the two firms, we conduct counterfactual simulations to incorporate the spirit of this market feature and show that our model can be used to analyze how the two firms would act if they jointly maximize their total profits. Not only may firms coordinate in terms of detailing frequency but also their sales content may be aligned. For example, some firms may push a certain regimen more than another. With detailing content information available, future research can explicitly take the coordination into consideration in demand modeling and incorporate that into a dynamic detailing game on detailing frequencies and information content.

Given the possible coordination between firms' detailing efforts for combination therapies, there might be a concern as to how to handle (unobserved) coordination that might be part of the data generation process, i.e., the data we use in model estimation. However, our detailing equation reflects possible coordination effects in a reduced-form manner. (i) The detailing allocated to a particular drug will depend not just on the preferences for that drug but also preferences for other drugs in the regimen. Our model explicitly accounts for such effects by including the physician's regimen-specific preferences in the detailing equation for a given drug. (ii) Our detailing equation includes the sum of lagged goodwill stocks for regimens that contain the focal drug. As these stocks include the spending levels of all of the other drugs in the regimen, the detailing equation captures how the focal brand's detailing adjusts to changes in detailing in the previous period by another brand from the same regimen as the focal brand. (iii) To control for the coordination

of detailing decisions across brands due to unobservables, we allow the error terms of the detailing equations to be correlated across all brands.

7. Conclusions

Combination therapies lead to complementarities and substitution effects between the drugs involved, which in turn complicate the marketing efforts for these drugs. The marketing effort for one drug may spill over to its complementary drugs. This paper examines the extent of such spillover effects of firms' detailing activities. We show that detailing for one drug not only increases its own demand but also helps those drugs that can be used together with it.

Based on our estimates for the effectiveness and spillover of detailing, we investigate firms' optimal detailing strategies under combination therapies. We focus on situations in which the spillover effects of detailing induce firms to free ride on others' detailing efforts. Through policy simulations, we show that the spillover effect and the issue of free riding have rich managerial and policy implications.

The framework developed in this study is not confined to combination therapy in the pharmaceutical industry. Products from different companies are often consumed together in a bundle. Our model can be applied to study firms' promotion decisions in such cases. For example, Intel and Dell engage in cooperative advertising campaigns in which Intel would reimburse Dell a sizable portion of Dell's advertising expenditures involving Dell computers with an Intel CPU. This setup can help alleviate the concern of free riding from either party. As we have shown in Section 6, an agreement between firms may internalize the spillovers and have a significant impact on firms' optimal advertising decisions. Thus, our model can be used to provide guidance for firms to set up their advertising arrangements.

Several limitations of this paper may present avenues for future research. First, we focus on the role of detailing and abstract away from price and other marketing activities such as direct-to-consumer advertising. As we have shown in this research, the price of a drug does affect a firm's incentive to detail. With appropriate data it may be fruitful to investigate how firms can use a combination of these marketing mix instruments to improve profits in a category characterized by combination therapies.

Because of the computational burden, we are unable to solve the full detailing game including all regimens. Instead, we focus on a few limited setups while controlling for outside factors. As detailing by other drugs may have spillover effects on the focal drugs, our imperfect control for such effects could influence our findings derived from the solutions to the partial detailing games on which we focus. We acknowledge this as a limitation of our paper, although we are confident that our results hold in a wide range of market environments.

For simplicity, our model assumes a uniform detailing cost of \$150 for each visit. We recognize that detailing multiple drugs on the same trip would result in cost savings. Although it is possible to allow for such cost savings in our model, we do not have information about the magnitude of such cost savings. Furthermore, given that we solve for firms' detailing decisions at a monthly level, we would need to make additional assumptions on the number of trips to adjust for the cost savings. For these reasons, we solve for firms' equilibrium detailing decisions using a uniform detailing cost per visit.

In summary, we have taken the first steps toward understanding the prescription behavior of physicians and the detailing behavior of firms in an increasingly important domain of the pharmaceutical industry. We hope that future research will answer the many questions that remain to be addressed in this domain.

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Endnotes

[1] In a typical discrete choice framework the alternative products are assumed to be substitutes, in which case previous studies have examined competitive clout and susceptibility (e.g., Kamakura and Russell 1989). In our context clout and susceptibility can be on competitive or spillover effect. We provide a more detailed discussion in Section 5.

[2] See Manchanda and Honka (2005) and Stremersch and Van Dyck (2009) for more integrative reviews of the pharmaceutical literature.

[3] This number might appear small. Note however that: (i) We focus on HIV specialists; and (ii) other studies with data from this provider use data from primary care physicians (Dong et al. 2009, Chintagunta et al. 2012) or data from primary care physicians and specialists (Venkataraman and Stremersch 2007).

[4] We focus on prescriptions for new patients only and our data set does not include any patient identifiers.

[5] We examine the first and last prescription decisions observed in our data for each physician. The regimen switching pattern summarized in Table 3 indicates significant substitution between regimens.

[6] As shown by Ching (2010), pricing can be important in another situation, i.e., when generic firms enter the market after a patent expires. We do not observe such an event in our study period.

[7] We also included additional γ_{bj} terms in the model to allow for detailing spillover across chemically-equivalent combinations. With these additional terms, for example, the detailing for Truvada or

Sustiva could contribute to the goodwill stock of Atripla, and the detailing for Atripla could help sales of Truvada + Sustiva.

[8] More details are available in Online Appendix B. Although we try to ensure that these composite regimens provide reasonable approximations to reality, it should be noted that the goal of our supply-side analysis is not to precisely match the observed detailing levels and market shares. Instead, we intend to identify situations in which spillover effects generate incentives for firms to free ride on others' detailing efforts, and further examine how such incentives vary according to the market environment.

[9] All demand parameters at this physician are set to be the population means. We use a monthly discount factor of 0.99, corresponding to an annual interest rate of 11%. Because there is no guarantee that a unique solution to our dynamic oligopoly game exists, we verify uniqueness by using different starting values and ensuring that they converge to the same solution.

[10] They represent the top regimen containing Epzicom, top regimen containing Truvada, and top overall regimen. Note that Atripla is jointly marketed by Gilead and BMS, as we discuss in further detail in Section 6.3.

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